COX-2, MMP-9, p53 and VEGF play an important role in the invasion and metastasis of tumor, and their roles are known to interact with each other. In this study, we investigated the prevalence of these molecules and the correlation between the expressions of COX-2, MMP-9, p53 and VEGF in squamous cell carcinoma of the head and neck.

**Methods:** Tissue samples and clinical data were obtained from 69 head and neck squamous cell carcinoma patients who underwent surgery as initial treatment from January 1999 to December 2003. Their primary sites were: oral cavity (12), oropharynx (18) and larynx (39). Immunohistochemical stain was performed to evaluate the expression rate of COX-2, MMP-9, p53, VEGF and then expression patterns and clinical data were analyzed.

**Results:** The expressions of COX-2, MMP-9, p53 and VEGF immunoreactivities were observed in 57.9%, 49.3%, 60.9% and 44.9%, respectively. COX-2 and p53 levels were significantly correlated with lymph node metastasis (p=0.041 and p=0.009, respectively). Multiple (2 kinds, 3 kinds, 4 kinds) expressions of gene protein were found in 35.6%, 23.4%, and 10.9%, respectively. There was a significant statistical difference between the multiple expression of gene protein to lymph node metastasis and a single expression of gene protein (p=0.0327).

**Conclusions:** These data suggested that COX-2 and p53 expression may play a role in tumor progression and metastasis in the head and neck squamous cell carcinoma. We might conclude that the multiple expression of gene protein was superior to single gene expression in estimating progression and metastasis of the head and neck squamous cell carcinoma.

**P002:** EXPRESSION OF CANCER TESTIS ANTIGENS IN HEAD AND NECK SQUAMOUS CELL CARCINOMAS

**Background:** There is considerable interest on the expression of cancer-testis (CT) antigens in human cancers, because they may serve as the basis for diagnostic tests or immunologic approach to therapy, or as prognostic markers.

**Methods:** On this basis, we evaluated by semi-quantitative reverse-transcriptase polymerase chain reaction (RT-PCR) the expression of B7-H1, B7-H3, and CA1X in surgical samples of the tumors, margins and lymph nodes (when present) from patients with a diagnosis of head and neck carcinoma. The study was conducted on 33 patients (31 males and 2 females), aged 31 to 94 years (mean: 56 years), with the diagnosis of head and neck squamous cell carcinoma.

**Results:** Expression of at least one antigen was observed in 66.6% of cases, with different rates of expression according to the tumor stage (100% of T4, 57% of T3, 50% of T1 and T2) and smoking habit. There was a significantly higher expression of multiple genes (two or more) in tumors in advanced stages. **Conclusions:** We conclude that the tumor-specific antigen genes are expressed in variable frequencies and intensities in the primary lesions of head and neck squamous cell carcinomas and in their metastases, with expression of the PRAME gene being always present in the metastatic lymph nodes. In primary lesions, gene expression correlated with smoking habit and with advanced tumors with a higher malignant potential, with the frequent expression of two or more of these genes.

**P003:** GENE EXPRESSION PROFILING AND INSIGHTS INTO THE INVOLVEMENT OF THE INSULIN SIGNALING PATHWAY IN ORAL SCC

**Background/Objective:** Proteases and their inhibitors play an important role in the invasion and metastasis of cancer cells. The invasive potential of cancer cells is determined by the coordinated balance between the activity of proteases and protease inhibitors. Cathepsin L is a lysosomal protease which is involved in progression of multiple types of cancer including Head and Neck Squamous Cell Carcinoma (HNSCC). Headpin is a cross-class serine protease inhibitor of cathepsin L. The objective of this study was to investigate the role of cathepsin L and headpin expression in HNSCC progression.

**Methods:** Immunohistochemical studies were performed on 56 oral squamous cell carcinoma (SCC) samples. We evaluated statistically the relationship between cathepsin L and headpin expression and clinical-pathological factors and the survival of the patients.

**Results:** Headpin expression had no relationship with metastasis or prognosis of oral SCC. Well differentiated SCC had higher expression compared to poorly differentiated SCC. The group that was positive for cathepsin expression tended to have positive metastatic neck lymph nodes and had poor prognosis.

**Conclusions:** The enhanced expression of cathepsin L may be a prognostic factor in patients with oral SCC. However, the expression of its inhibitor headpin had no relationship with prognosis. The involvement of headpin/cathepsin L system in HNSCC progression will be discussed.
Posters

P006: HE ISOPERITIDASE USP2A AND FATTY ACID SYNTHASE (FAS) ARE HIGHLY EXPRESSED IN ERBB2 POSITIVE ORAL SQUAMOUS CELL CARCINOMA

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Background: Several human epithelial cancers, particularly those with poor prognosis, express high levels of ErbB2. Fatty acid synthase (FAS), the key lipogenic enzyme responsible for the endogenous synthesis of fatty acids, is one of the downstream genes regulated by ErbB2. Deubiquitinating enzymes or isopeptidases prevent the destruction of protein substrates through deubiquitination prior to proteasomal degradation. The ubiquitin-specific protease 2a (USP2a) plays a critical role in prostate cancer cell survival through FAS stabilization. Objectives: This study investigates whether the gene expression of ErbB2, FAS and USP2a is correlated with the immunohistochemical and clinicopathological characteristics of oral squamous cell carcinoma (OSCC). Methods: We included in this study 41 fresh frozen samples of patients with OSCC. Clinical and treatment data were obtained from the medical records and all histopathological diagnoses were reviewed. OSCC was microdissected using laser capture microdissection (LCM) and one round of linear mRNA amplification was done based on template switch and T7-driven amplification. ErbB2, FAS and USP2a gene expression were analyzed by qRT-PCR and compared to morphologically normal tissue of the same source. Results: Most of the lesions (97.06%) that showed a high expression of FAS were also positive for ErbB2 at the cell membrane (p = 0.001) and both had correlated with the proliferation marker Ki-67 (p = 0.002 and 0.001, respectively). A strong positive correlation among ErbB2, FAS and USP2a mRNA expression in the OSCC samples compared with normal morphologically tissue of the same source (relative fold difference = 80.3, 68.5 and 24.5 respectively). Microscopic characterization as perineural infiltration was associated with ErbB2 gene expression (p = 0.046). The presence of metastatic cervical lymph nodes was associated with ErbB2 (p = 0.001), FAS (p = 0.002) and USP2a gene expression (p = 0.006). Additionally, ErbB2, FAS and USP2a were significantly associated one to another (p = 0.001) and with immunohistochemical data. Conclusions: Taken together, the results showed that FAS and ErbB2 are co-expressed in OSCC and suggest that ErbB2 is able to regulate FAS production in these tumors. Moreover, our data point out that these proteins are significantly associated with a poor prognosis.

P007: MICRORNA PROFILING IN PRIMARY HEAD AND NECK SQUAMOUS CELL CARCINOMA

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Objectives: The primary treatment of head and neck squamous cell cancer (HNSCC) of the oropharynx, hypopharynx or larynx is radiation therapy (RT), with or without chemotherapy (CT). For patients treated with the combined approach, half will develop significant late normal tissue toxicity. Hence, a molecular signature that can identify patients curable by RT only would allow the selection of patients who could be spared the morbidities of combined therapies. Recent research has revealed miR dysregulation in various cancers, suggesting that miR expression profiles have the potential to reveal much about the biology of tumours. This study seeks to develop a prognostic gene set of miRs in HNSCC to improve clinical management and patient outcomes. Methods: Archival formalin fixed and paraffin embedded (FFPE) biopsy specimens were collected from participants in a Phase III randomized trial comparing standard RT, to an accelerated hyperfractionated (FFPE) biopsy samples were collected from participants in a Phase III randomized trial comparing standard RT, to an accelerated hyperfractionated regimen. All 331 participants had stage III or IV non-metastatic SCC of the oropharynx, hypopharynx or larynx. The 7-year overall survival rates were 40% vs. 30%, in favor of the hyperfractionated group. Macrodisection was performed to ensure that each macrodissected specimen contained >70% tumor cells. RNA was isolated using a commercially available extraction kit designed specifically for FFPE samples (Ambion). Expression levels of 312 miRs and 10 endogenous controls were measured by quantitative RT-qPCR. Results: Preliminary results were analyzed for 9 non-relapsed vs. 18 relapsed patients; and 4 control samples utilized normal laryngeal epithelial tissues derived from laryngectomy specimens... Overall, 76 miRs were dysregulated in approximately 75% or more of the HNSCC cases, including 3 miRs that were overexpressed in all 27 cases. Twenty-six miRs were differentially regulated in relapsed vs non-relapsed cases, and several of these preliminary results support other studies’ findings. Conclusions: These preliminary data illustrated that the miR profile of HNSCC is distinct from that of normal tissue. Significant differences were also detected among the relapsed and non-relapsed groups. Additional samples will be analyzed to determine the validity of this preliminary set.

P008: OVEREXPRESSION OF GLI2 BLOCKS DIFFERENTIATION AND INDUCES INVASION DEPENDENT ON TGFβ1-MEDATED ACTIVATION OF FIBROBLASTS

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Objective: Genome-wide DNA copy number profiling identified GI2, a downstream transcription factor in the hedgehog signaling pathway as a candidate oncogene amplified and overexpressed in oral squamous cell carcinoma (SCC). Tumors with GI2 amplification consistently display basal-like histology and keratinization is absent in tumors with very high level amplification. By contrast, the tumors differ in other features such as mitotic index and the spectrum of alterations present in the tumor genomes. These observations suggest that up-regulation of GI2 opposes differentiation. The objective of this study was to investigate the role of GI2 in the development of oral cancer by investigating the functional consequences of overexpression. Methods: Three dimensional organotypic cultures were prepared using co-culturing normal oral or oral fibroblasts with human HaCaT keratinocytes overexpressing GI2. Immunohistochemistry and expression microarray profiling were used to assess the effect of overexpression of GI2 on cell growth and differentiation, invasion and stromal remodeling in the tissue constructs. Results: Co-cultures of GI2-expressing HaCaT keratinocytes with either oral or skin derived fibroblasts displayed an undifferentiated basal-like phenotype, recapitulating the histology of GI2 amplifying tumors. Immunohistochemical and expression microarray analyses revealed that most keratinocytes remained in cycle throughout the entire epithelial layer and did not express classic differenti- ation markers. Cell-cell and cell-matrix interactions were lost as revealed by the loss or reduced expression of desmosomal components DSG1 and DSC1, gap junctional components GJB2 and GJB6, tight junctional components CLDN1 and CLDN3 and the hemi-desmosome component FGFR4. Laminin γ1 (gamma-2 subunit) was also lost from the basement membrane zone. A desmoplastic response was induced in fibroblasts adjacent to GI2-expressing keratinocytes. The activated fibroblasts were less spindle-shaped with more rounded nuclei, and they expressed high levels of collagen IV and alpha-smooth muscle actin, indicative of differentiation into myofibroblasts. Cells of epithelial origin, which lacked E-cadherin expression invaded into this stromal layer. The desmoplastic response was only induced if fibroblasts were in close proximity to GI2-expressing cells. It appears to be mediated by TGFβ1 signaling, since treatment of tissue reconstructs with the TGFβ1/II kinase inhibitor LY2109761 eliminated both the desmoplastic response and epithelial cell invasion. Overexpression of GI2 in HaCaT cells was not sufficient to induce a desmoplastic response in all oral fibroblasts, suggesting that fibroblasts from distinct anatomical sites differ in their capability for myofibroblast differentiation or sensitivity to TGFβ1 signaling. Conclusions: Overexpression of a single transcription factor, GI2, in the human HaCaT keratinocyte cell line is sufficient to disrupt tissue organization at least in part by inhibiting differentiation and down regulating major cell-cell and cell-matrix interactions, thereby recapitulating the basal-like histopathology of GI2 amplifying oral SCC. Overexpression of GI2 in HaCaT cells also induces a desmoplastic response in stromal fibroblasts, which is mediated by TGFβ1 signaling and results in a microenvironment permissive for epithelial cell invasion. These observations suggest gene or pathway targeted therapeutic strategies for this distinctive subset of oral SCC expressing high levels of GI2.

P009: A NOVEL METHOD FOR HIGH-THROUGHPUT IDENTIFICATION OF MURINE AND HUMAN TUMOR ANTIGENS

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Background: Basal Cell Carcinoma (BCC) is associated with significant morbidity in persons with Basal Cell Nevus Syndrome. It is our long term goal to develop a BCC cancer vaccine. However, limitations to the development of cancer vaccines and cancer immune therapy trials include the lack of cancer-specific tumor antigens and of corresponding mouse tumor models. The current repertoire of identified tumor antigens is quite small and limited to a few cancer types. Although, a large number of animal tumor cell lines have been developed, tumor antigens have been identified in very few due to inconsistencies in tumor immunogenicity, vaccination regimens and the time-intensive methodology for antigen identification and val-
Methods: All cell lines expressed CCR7 and CXCR4. Chemokines stimulate intracellular signaling pathways and induce migration, proliferation and angiogenesis through the effects on cell surface chemokine receptors. Among members of the two major subfamilies of chemokine receptors, i.e., CC-chemokine receptor (CCR) and CXC-chemokine receptor (CXCR), CXCR4 and CCR7 are thought to play important roles in invasion and metastasis in various malignant tumors. The objective of this study is to clarify the mRNA expression and the production levels of CCR7 and CXCR4 in head and neck squamous cell carcinoma (HNSCC) tissues and their correlations with such clinicopathological factors as grade of differentiation and metastasis to lymph nodes and to distant organs. Methods: We examined expression of CCR7 and CXCR4 in 9 HNSCC cell lines and 25 HNSCC tissues with semi-quantitative RTPCR analysis and immunohistochemistry. We also examined the regulation of CCR7 and CXCR4 in cultured normal human keratinocytes according to their grades of differentiation. Results: All cell lines expressed CCR7 mRNA, and 3 expressed CXCR4 mRNA. Levels of CCR7 and CXCR4 mRNA of mRNAs were significantly higher in HNSCC tissues than in non-neoplastic tissues (p=0.0135 and p=0.0441, respectively) and correlated with lymph node metastasis (p=0.0315 and p=0.0296, respectively); CXCR4 mRNA level correlated with distant metastasis (p=0.0226). CCR7 mRNA levels were significantly higher in moderately differentiated than in well-differentiated HNSCC (p=0.0170). The level of CCR7 mRNA in undifferentiated keratinocytes was higher than that in differentiated keratinocytes (p=0.0170), and flow cytometric analysis indicated that the level of CCR7 protein for undifferentiated keratinocytes was higher than for differentiated keratinocytes. On the other hand, the levels of CXCR4 mRNA and protein in normal human keratinocytes were negligible. Immunohistochemistry demonstrated localization of CCR7 and CXCR4 to carcinoma cells and lymphocytes. Conclusions: CCR7 in HNSCC may be induced by the de-differentiation and play an important role in lymph node metastasis. CXCR4 may also play an important role in lymph node metastasis as well as distant metastasis.

**P010: ANALYSIS OF HUMAN TISSUE KALLIKREIN EXPRESSION IN BENIGN AND MALIGNANT SALIVARY GLAND TUMORS**

**Objective:** Human tissue kallikreins (KLK) constitute a family of 15 serine proteases designated KLK1-KLK15, respectively, and encoded by genes KLK1-KLK15, all of which co-localize to chromosome 19q13.4. Since their discovery, some human tissue KLKs have been studied as emerging biomarkers for several cancers, including breast, ovarian and testicular cancers, with increasing evidence for their potential prognostic indicator value. KLK3, also known as Prostate Specific Antigen, has become widely used as a clinical biomarker for the early detection of prostate cancer. Recently, the expression of KLKs in normal salivary glands and salivary gland tumors has been reported by our lab and others. This study aims to analyze the expression of several, unstudied KLKs (KLK7, 8, 10 and 14) in salivary gland tumors as well as to confirm the expression of the previously studied KLK6 and 13. Furthermore, levels of KLK panels will be correlated with the outcome of disease, which may lead to the identification of KLKs as novel biomarkers for the detection of salivary gland cancers. We hypothesize that salivary gland tumors and normal tissues differentially express KLKs, which may have potential roles as independent diagnostic and prognostic indicators in salivary gland cancer. Methods: A standard immunoperoxidase staining technique was used to semi-quantitatively assess the expression profile of KLK6, 7, 8, 10, 13, and 14 in normal salivary gland tissues and 3 types of salivary gland tumors: Pleomorphic adenoma (PA)[n=17], Adenoid Cystic Carcinoma (ACC)[n=15] and Mucoepidermoid Carcinoma (MEC)[n=21]. The KLK expression profile for each tumor was also analyzed to assess the KLK tumor specificity. Results: The kallikrein expression profile study showed significantly higher levels of KLK7, 8 and 13 in ACC than in normal glands. Likewise, KLK7 was significantly higher in PA compared to ACC. KLK7 and 14 showed a similar pattern of expression where their levels were higher in PA than in normal glands and were both significantly lower in MEC than PA and ACC tissues. Interestingly, only KLK8 showed a significantly higher level in MEC compared to normal glands. The tumor kallikrein profile showed no significant differences between KLK scores in ACC and PA. However, KLK10 showed the latest oncoprotein and is significantly different from the other KLKs examined. Conclusion: The differences in the levels of KLKs among these salivary gland tumors suggest that KLKs may aid in the differential diagnosis of salivary gland tumors and may be prognostic indicators in salivary gland neoplasms. Moreover, the co-expression of KLKs and their lack of specificity in salivary gland tumors suggest their possible involvement in an enzymatic pathway activated in salivary gland carcinogenesis by as yet unknown mechanisms. Kallikrein expression profile may be a promising new biomarker in salivary gland tumors, and further studies are needed to quantitatively measure this expression and to correlate with prospective clinical data. **P011: EXPRESSION OF CCR7 AND CXCR4 IN HEAD, AND NECK SQUAMOUS CELL CARCINOMA**

**Objective:** Chemokines stimulate intracellular signaling pathways and induce migration, proliferation and angiogenesis through the effects on cell surface chemokine receptors. Among members of the two major subfamilies of chemokine receptors, i.e., CC-chemokine receptor (CCR) and CXC-chemokine receptor (CXCR), CCR7 and CXCR4 are thought to play important roles in invasion and metastasis in various malignant tumors. The objective of this study is to clarify the mRNA expression and the production levels of CCR7 and CXCR4 in head and neck squamous cell carcinoma (HNSCC) tissues and their correlations with such clinicopathological factors as grade of differentiation and metastasis to lymph nodes and to distant organs. Methods: We examined expression of CCR7 and CXCR4 in 9 HNSCC cell lines and 25 HNSCC tissues with semi-quantitative RTPCR analysis and immunohistochemistry. We also examined the regulation of CCR7 and CXCR4 in cultured normal human keratinocytes according to their grades of differentiation. Results: All cell lines expressed CCR7 mRNA, and 3 expressed CXCR4 mRNA. Levels of CCR7 and CXCR4 mRNA of mRNAs were significantly higher in HNSCC tissues than in non-neoplastic tissues (p=0.0135 and p=0.0441, respectively) and correlated with lymph node metastasis (p=0.0315 and p=0.0296, respectively); CXCR4 mRNA level correlated with distant metastasis (p=0.0226). CCR7 mRNA levels were significantly higher in moderately differentiated than in well-differentiated HNSCC (p=0.0170). The level of CCR7 mRNA in undifferentiated keratinocytes was higher than that in differentiated keratinocytes (p=0.0170), and flow cytometric analysis indicated that the level of CCR7 protein for undifferentiated keratinocytes was higher than for differentiated keratinocytes. On the other hand, the levels of CXCR4 mRNA and protein in normal human keratinocytes were negligible. Immunohistochemistry demonstrated localization of CCR7 and CXCR4 to carcinoma cells and lymphocytes. Conclusions: CCR7 in HNSCC may be induced by the de-differentiation and play an important role in lymph node metastasis. CXCR4 may also play an important role in lymph node metastasis as well as distant metastasis.
the presence of EGFR, HPV, p53, p16 and BCL1, which are known to be frequently occurring markers in OSCC. The DNA extracted from OSCC and adjacent normal samples was quantified for copy number (EGFR, BCL1) and mutations (p53, p16) for the identified molecular markers using real time quantitative PCR (RQ-PCR) and sequencing. Saliva from patients identified as positive for a given marker was then assessed for the presence of that marker, using the appropriate technique. Results: DNA was successfully extracted from both the saliva and corresponding OSCC samples. IHC identified molecular markers that were both over- and under-expressed in the tissue samples. The amplification status of EGFR and BCL1, the mutation status of p53 and p16, and the presence of HPV were further quantified using sequence analysis and RQ-PCR. The differences in the panel of molecular markers before and after surgery in the saliva are currently being quantified.

Conclusion: Saliva is a good source of DNA to study molecular changes in OSCC. Molecular analysis of saliva will potentially be an accurate and sensitive diagnostic and screening tool for populations at risk, and may have potential applications for patient follow-up in predicting disease recurrence or second primary tumours in patients with OSCC.

P013: EXPRESSION FRA1 AND MMP-9 IN PATIENT WITH LOCALLY INVASIVE WELL-DIFFERENTIATED THYROID CARCINOMA J.G.Filho1, L.P.Kowalski1, S.D.Silva1, C.A.Pinto1, S.Nonogaki1, 1Hospital AC Camargo, Sao Paulo, Brazil

Objective: In the present study, we have investigated the expression of FRA1 and MMP-9 in 50 patients with locally invasive well-differentiated thyroid carcinoma. Methods: Immunohistochemical determination of the expression of FRA1 and MMP-9 was performed in 50 surgical specimens of T4a thyroid papillary carcinoma. The samples were obtained from patients with papillary carcinoma who had undergone surgery at the Camargo Cancer Institute, and from cases previously exposed to radiotherapy. There were 31 female patients and 21 male patients, with a mean age of 38 years (ranging from 8 to 81 years). Histopathological types included 38 papillary carcinoma and 14 follicular. From these paraffin blocks, areas of tumor were selected based on histological examinations. The pathologic diagnosis of all cases was reviewed and analyzed by three pathologist. The intensity of positively stained cells were indicated as 0 (negative), 1 (weak), and 2 (strong). Results: Immunoreactivity of FRA1 was detected in 40 cases (96%), with weak intensity in 8 cases (16%) and intense in 40 cases (80%). MMP-9 immunoreactivity was found in 44 cases (88%), being weak in 17 (34%) and intense in 27 (54%). The immunoreactivity FRA1 did not have any significant association with gender (p=0.645), age (p=0.189), tumor size (p=0.591), histological type (p=0.426) and survival (p=0.721). Similarly, there was no correlation between MMP-9 expression and gender (p=0.544), age (p=0.160), tumor size (p=0.631), histological type (p=0.148) and survival (p=0.230). Conclusion: This study demonstrated high FRA1 and MMP-9 expression in well-differentiated carcinoma with extension extrathyroidal and that factors as age, gender, tumor size and histological type have no correlation with immunopositive FRA1 and MMP-9 expression. There was no association of immunoreactivity for FRA1 or MMP-9 with survival.

P014: ASSOCIATION OF CD44 VARIANT EXPRESSION IN HEAD AND NECK SQUAMOUS CELL CARCINOMA METASTASIS AND TREATMENT FAILURE S.J. Wang1, A.de Heer1, L.Y.Bourguignon1, 1University of California, San Francisco, San Francisco, CA

Objective: The CD44 family of receptors includes multiple variant isoforms, several of which have been linked to tumor progression. The objective of this study was to investigate the role of the CD44 v3, v6, and v10 variant isoforms in head and neck squamous cell carcinoma (HNSCC) metastasis and treatment failure. Methods: Immunohistochemical analysis was performed on clinical tissue specimens obtained from a series of 82 patients with HNSCC. Eighty-two primary tumor specimens and 24 metastatic tumors, a greater proportion of metastatic lymph nodes demonstrated strong expression of CD44 v3 (lymph node: 14/24 vs. primary tumor: 38/82), CD44 v6 (lymph node: 18/24 vs. primary tumor: 34/82) and CD44 v10 (lymph node: 14/24 vs. primary tumor: 16/82), while expression of standard CD44 was not significantly different in metastatic lymph nodes and primary tumors (lymph node: 10/24 vs. primary tumor: 60/82). Fourteen specimens were obtained from patients previously treated with radiation and/or chemotherapy. There was increased expression of CD44 v10, but not CD44 v3, v6, or standard CD44, in the chemoradiation failure specimens. There were no differences in CD44 variant expression between small (T1 or T2) and large (T3 or T4) primary tumors. Conclusion: Expression of certain CD44 variants may be important molecular markers for metastasis and treatment failure in HNSCC.

P015: CLAUDIN-7 DOWNREGULATION IN ORAL SQUAMOUS CELL CARCINOMA S.V.Lourengo1, C.M.Coutinho-Camillo2, M.E.C.Buim2, A.C.de Carvalho2, R.C.Lessa2, C.Pereira2, A.L.Vettore3, A.L.Carvalho2, L.P.Kowalski1, F.A.Soares2, 1Dental School, University of Sao Paulo, Sao Paulo, Brazil; 2Hospital AC. Camargo, Sao Paulo, Brazil; 3Universidade Federal de Sao Paulo, Sao Paulo, Brazil

Objective: Claudins, a large family of essential tight junction (TJ) proteins are abnormally regulated in human carcinomas, suggesting that they might represent potential targets for cancer detection, diagnosis and therapy. In a previous study, we have showed that several claudins are altered in the oral squamous cell carcinoma (OSCC) cases analyzed and that there is an association between these alterations and clinico-pathological characteristics of these tumors. Methods: In this study, using a Tissue Microarray (TMA) comprising 133 cases of OSCC, we have analyzed the expression of claudin-7 by immunohistochemistry. We have also studied the expression of claudin-7 mRNA transcripts and methylation status of the claudin-7 promoter. Results: Claudin-7 was almost absent in the majority of the cases - 91.1% of the cases showed strong expression of claudin-7 and 90.9% of the cases showed mild or no expression of claudin-7. Loss of claudin-7 was associated with advanced stages of OSCC (p=0.044) and tended to be more frequent in moderately/poorly differentiated tumors (p=0.035). Loss of claudin-7 was also associated with depth of invasion higher than 3mm (p=0.020) and disease-free survival is statistically different between the positive and negative claudin-7 cases (p=0.015). Expression of the mRNA transcript of claudin-7 gene was assessed and down-regulation of claudin-7 transcripts was detected in 77.78% of the cases analyzed. As methylation is one of the mechanisms involved in down-regulation of claudins, the methylation status of the promoter region of claudin-7 was investigated. We found that treatment of O28 cells (that did not express claudin-7 mRNA transcripts with 5-Aza-2’-Deoxycytidine (5 Aza dC) led to the re-expression of claudin-7 mRNA transcript. Conclusion: Our data suggests that loss of claudin-7 expression might be associated with the tumorigenic process of OSCC and that this loss is associated with a poor prognosis. Furthermore, claudin-7 downregulation is probably due to its promoter hypermethylation.

P016: STUDIES OF A HYPOXIC GENE EXPRESSION SIGNATURE IN AN EXPERIMENTAL HEAD AND NECK CANCER-MODEL K.Toustrup1, B.Sorensen1, M.Busk1, J.Almner1, J.Ovegaard2, 1Aarhus University Hospital, Aarhus, Denmark; 2Aarhus University Hospital, Aarhus, Denmark

Objective: The aim of the project was to evaluate the impact of a Hypoxic Gene Expression Signature developed in vitro from more cell lines of head and neck squamous cell carcinoma (HNSCC). Previously we have conducted a range of in vitro experiments, were different cell lines of human squamous cell carcinoma have been exposed to various levels of pH and hypoxia (Sorensen et al, 362-366, Radiotherapy and Oncology, 2005). Based on cluster analysis of Affymetrix-microarray extracted patterns of gene expressions, a hypoxic gene expression signature eliminating the influence of pH-fluctuations was deduced. To confirm the relevance of these genes in vivo as well as to identify the most prominent candidates for a clinically relevant panel of hypoxic genes, all cell lines were converted into a xenograft-model. The HNSCC xenografts were induced in nude mice. Prior to extirpation of tumour, the mice were infused with exogenic markers (Hoechst, pimonidazole and 18F-FAZA) to expose perfusion conditions and hypoxic areas. Following extirpation and cryosection, autoradiography was performed. Guided by the autoradiographic illustration of tumour-bound 18F-FAZA, respectively hypoxic and normoxic areas were identified and dissected under microscope. Also H.E. and pimonidazole-staining of neighbouring sections was performed to expand the informative impact of dissected tissue. RNA was extracted from cells representing each area, and gene expressions were calculated by quantitative real-time PCR of the most prominent hypoxic genes. Results: The primary in vitro derived hypoxic signature constituted 139 genes. So far a battery of these genes (incl. LOX, OPN and CAIX) has been tested in our in vivo xenograft-model, with CAIX being the most prominent and significantly up-regulated gene in the hypoxic areas compared to the normoxic areas. Studies are ongoing to reduce the 139 signature-genes to a more concentrated panel of the 20 most characteristic and informative marker-genes. Conclusions: By verifying a sig...
significant up-regulation of our signature genes in hypoxic areas of HNSCC xenographs, we underline the relevance of these genes as hypothetic hypoxic markers not only in vitro but also in vivo. Further studies regarding the expression of these genes in well described cohorts of patients with HNSCC is ongoing to verify if the signature is of any help in the identification of patients, whom will benefit from hypoxia-modification therapy.

P017: PROFILES OF HNSCC DISEASE PROGRESSION BY GENE EXPRESSION DEPENDS ON THE ANATOMIC SITE OF THE PRIMARY TUMOR

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Background: Head and neck squamous cell carcinomas (HNSCC) constitute an anatomicographically heterogeneous group of neoplasms, arising from diverse anatomic locations, including the oropharynx (OP), oral cavity (OC), and larynx/ hypopharynx (LH). It is known that tumors originating from different anatomic locations can exhibit varying behavior that is not predictable by histopathology of the primary tumor. Methods: Using a microarray containing 27,142 cDNA clones, we generated two sets of gene expression profiles for HNSCC primary tumors originating from the oropharynx, oral cavity and larynx/hypopharynx. The first dataset identified gene expression differences between 22 HNSCC primary tumors and corresponding adjacent normal mucosa for the different sites (OP and LH). The second dataset compared gene expression differences between 36 HNSCC primary tumors (12 OP, 12 OC, and 12 LH) from patients whose disease progressed within a 24 month period (aggressive phenotype) and those that did not (non-aggressive phenotype). For each dataset, we then overlapped data from each anatomic site to look for genes with consistent expression differences across sites. Results: We first used tumor to normal comparisons to identify genes transcriptionally down-regulated in primary HNSCC tumors compared to normal adjacent mucosa. Out of 11 OP cases studied, the number of down-regulated genes ranged from 4392 (in at least 1 case) to 4 (in 10 cases). Out of 11 LH cases studied, the down-regulated genes ranged in number from 3511 genes (in at least 1 case) to 15 genes (in 10 cases). A merging of datasets revealed a significant overlap (approximately 50%) in down-regulated genes seen in both OP cases and LH cases. In our second analysis, we ranked genes according to their ability to differentiate between an aggressive tumor phenotype and non-aggressive tumor phenotype based on expression levels. For each site, we identified 534 (OP), 921 (OC), and 713 (LH) genes that differentiated between an aggressive tumor phenotype and non-aggressive tumor phenotype. A merging of datasets from the three sites revealed that only a small fraction of identified genes (2.4%) were shared between any two sites. Conclusions: HNSCC tumors originating from different anatomic sites share consistent changes in gene expression when comparing primary tumors to normal adjacent mucosa, but differ in the gene expression changes associated with aggressive versus non-aggressive disease. Predictions of outcome based on gene expression profiling are therefore heavily influenced by the anatomic site of the primary tumor.

P018: B7-H4 EXPRESSION IN MALIGNANCIES AFFECTING THE ORAL CAVITY

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Objective: The B7 family consists of structurally related, cell-surface protein ligands, which bind to receptors on lymphocytes that regulate immune responses. There are currently seven known members of the B7 family, including B7-H4. B7-H4 mRNA is expressed in wide range of normal somatic tissue, however B7-H4 protein expression has been recently documented in malignant tumors affecting the ovaries, uterus, lung, breast and renal organs. A direct correlation was found between B7-H4 expression in tumor cells of renal cell carcinoma and adverse clinical and pathologic features, including constitutional symptoms, tumor necrosis, and advanced tumor size, stage, and grade. It has been theorized that B7-H4 inhibits apoptosis and promotes tumor cell growth. The objective of this study is to investigate the expression of B7-H4 protein in oral squamous cell carcinoma and mucoepidermoid carcinoma. Methods: Immunohistochemical staining of 94 formalin-fixed paraffin blocks of histologically proven cases of oral squamous cell carcinoma (n=19) and mucoepidermoid carcinoma (n=20) were evaluated by immunohistochemistry for the distribution of B7-H4 expression, and staining intensity. The sections were evaluated using light microscopy and analyzed based on our institution based grading protocol. Results: B7-H4 expression was detected in the cytoplasm of all oral mucoepidermoid carcinoma ranging from 5% to 30% of the tumor cells. Although intermediate grade mucoepidermoid carcinomas had a similar expression pattern, expression of B7-H4 was not affected by the other histological grades of the tumor. B7-H4 expression in oral squamous cell carcinoma was inconsistent as it was expressed with variable proportion and intensity in only 52% (n=10) tissue samples with proportions ranging from 1% to 50%. Histologic grade of the tumor did not influence the expression pattern. Conclusion: Based on our observations, it appears that, as seen in other systemic malignancies, B7-H4 could have a role as a diagnostic marker in oral malignancies and potential therapeutic target in treating these malignancies.

P019: PROGNOSTIC VALUE OF MAGE-3 AND NY-ESO-1 EXPRESSION IN OROPHARYNGEAL AND HYPOPHARYNGEAL SQUAMOUS CELL CANCER

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Objective: The overall survival rate for patients with head and neck squamous cell cancer is low and has not improved significantly during several decades. Tumors located in oropharynx and hypopharynx have the worst prognosis. Genes MAGE-3 and NY-ESO-1 belong to group of tumor antigens. MAGE-3 expression is associated with poor prognosis in several types of tumors (oral cavity and larynx/ hypopharynx). The first study identified gene expression differences between 22 HNSCC primary tumors and corresponding adjacent normal mucosa for the different sites (OP and LH). The second dataset compared gene expression differences between 36 HNSCC primary tumors (12 OP, 12 OC, and 12 LH) from patients whose disease progressed within a 24 month period (aggressive phenotype) and those that did not (non-aggressive phenotype). For each dataset, we then overlapped data from each anatomic site to look for genes with consistent expression differences across sites. Results: We first used tumor to normal comparisons to identify genes transcriptionally down-regulated in primary HNSCC tumors compared to normal adjacent mucosa. Out of 11 OP cases studied, the number of down-regulated genes ranged from 4392 (in at least 1 case) to 4 (in 10 cases). Out of 11 LH cases studied, the down-regulated genes ranged in number from 3511 genes (in at least 1 case) to 15 genes (in 10 cases). A merging of datasets revealed a significant overlap (approximately 50%) in down-regulated genes seen in both OP cases and LH cases. In our second analysis, we ranked genes according to their ability to differentiate between an aggressive tumor phenotype and non-aggressive tumor phenotype based on expression levels. For each site, we identified 534 (OP), 921 (OC), and 713 (LH) genes that differentiated between an aggressive tumor phenotype and non-aggressive tumor phenotype. A merging of datasets from the three sites revealed that only a small fraction of identified genes (2.4%) were shared between any two sites. Conclusions: HNSCC tumors originating from different anatomic sites share consistent changes in gene expression when comparing primary tumors to normal adjacent mucosa, but differ in the gene expression changes associated with aggressive versus non-aggressive disease. Predictions of outcome based on gene expression profiling are therefore heavily influenced by the anatomic site of the primary tumor.

P020: VITAMIN E SUCCEINATE AND NF KAPPA B ACTIVATION IN HEAD AND NECK CANCER

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Antioxidants strategies in the diet are felt to be important for the prevention of several diseases including cardiovascular disease and cancer. Tocopherol (Vitamin E) has been advocated for chemoprevention of cancer, including aerodigestive cancers. Early phase chemoprevention clinical trials have demonstrated efficacy of tocopherol-containing regimens for laryngeal dysplasia. It is established that the redox responsive transcription factor NF kappa B is activated during cancer progression and it is demonstrably elevated in head and neck cancer. Additionally, during head and neck radiation patients are advocated to refrain from the use of antioxidants, including Vitamin C and E derivatives. We hypothesized that tocopherol may be inhibitory for NF kappa B activation in head and neck cancer. In the present study we examined the Vitamin E derivative alpha tocopherol succinate as a putative drug for the downregulation of NF kappa B activation in head and neck cancer cells. We employed head and neck cancer cell lines Ca 9-22 cells, UM SCC 9 and 38 cells for the studies. We examined NF kappa B activation by luciferase reporter gene after treatment with the NF kappa B activator PMA stimulation and vitamin E succinate treatment. Cell lines were treated for 24 hours. We discovered that vitamin E succinate was able to prevent activation of NF kappa B by 20-80 % in multiple in experiments in concentrations from 10-100 uM (p<0.01). However, it did not significantly alter baseline levels of NF kappa B in head and neck cancer cell lines. We further employed the electron spin trap TEMPPO as a positive control anti-oxidant and found similar results. We conclude that Vitamin E succinate, a commercially available tocopherol derivative, prevents NF kappa B upregulation and may be useful in head and neck cancer treatment strategies.
P023: DIFFERENTIALLY EXPRESSED GENES IN INVASIVE HEAD AND NECK CANCER CELLS; CYR61 AND CD44
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Introduction: For the treatment of head-neck cancer (HNC), although local control and survival rates are acceptable for early stage tumor, in advanced tumor, bulk tumor or lymph node metastases is the common cause of treatment failure. This study is to globally survey invasion associated genes of HNC. Material and Methods: Highly invasive sublines of HNC cells were first established, through several passage selections by Matrigel invasion assay. Differential gene expression profile was obtained by cDNA microarray analysis between the parental and invasion subline. We defined 2-fold differential expressed as the criteria for the selection of the invasive candidate genes. Results: Total of 50 genes were found up-regulations in invasive subline cells, including Cyr61 and CD44. Western blot analysis confirmed up-regulation of these two genes in the invasion subline. For validation, we conducted siRNA plasmids (Cyr61si and CD44si) and transfected into HNC cells to examine whether alteration of their invasion ability. Cell migration and invasion abilities were reduced in both Cyr61si and CD44si transfectants. Conclusion: We have identified potential invasive genes of HNC, including Cyr61 and CD44. Knockdown the expression of Cyr61 or CD44 could reduce cell migration and invasion ability of HNC cells. These results indicate that these genes play more significant role of cancer invasiveness in HNC.

P024: EXPRESSION OF MATRIX METALLOPROTEINASE 1 IN INVASIVE WELL DIFFERENTIATED THYROID CARCINOMA
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Objective: Invasive Well Differentiated Thyroid Carcinoma (IWDTC) is associated with a worse prognosis and increased risk of morbidity. One of the hallmarks of IWDTC is laryngotracheal invasion which according to some studies necessitates the need for a more aggressive surgical treatment. Few attempts have been made in order to explain the mechanism of IWDTC. However the relationship between cartilage destruction by different proteolytic enzymes and laryngotracheal invasion has not been studied yet. The purpose of this study was to examine the expression of Matrix Metalloproteinase-1 (MMP-1) protein degrading enzyme in IWDTC and its relation to clinical and pathological features. Methods: We reviewed the clinical data of 20 patients with IWDTC who were treated in Rabin Medical Center between January 1985 and May 2007. The expression of MMP-1 in primary and metastasized tumors from these patients was determined using immunohistochemical staining. The intensity of staining was graded from absent (grade 0) to intense (grade 2). Results: Of the 20 patients participated in this study, 15 had laryngotracheal invasion by the primary tumor at presentation, and the remaining 5 had laryngotracheal invasion at a later stage. Expression of MMP-1 was positive in 14/15 of patients who had laryngotracheal invasion by the primary tumor and in 1/5 of patients who had laryngotracheal invasion at a later stage (P=0.0049). Further more, the expression of MMP-1 correlated with the multifocality of the primary thyroid gland lesion (P=0.031), and with the presence of lymph node metastases and distant metastases at presentation (P=0.018). Conclusions: We conclude that the expression of MMP-1 in patients with IWDTC is associated with the aggressiveness of the primary tumor represented by laryngotracheal invasion, multifocal primary lesions and regional and distant metastases. These results could suggest a possible mechanism of invasiveness by this type of tumor and advocate a more aggressive treatment towards these patients.

Basic science: Molecular pathways

P025: RECIPROCAL NEGATIVE REGULATION BETWEEN S100A7/Psoriasin AND E-CADHERIN SIGNALING IN SCC tumors progresses, G. Zhou1, T. Xie1, M. Zhao1, S. A. Jasser1, D. Sano1, M. Kupferman1, A. El-Naggar1, J. S. Gutkind1, J. C. Reed1, J. N. Myers1, 1MD Anderson Cancer Center, Houston, TX, 2National Institute of Dental and Craniofacial Research, Bethesda, MD, 3Burnham Institute for Medical Research, La Jolla, CA

Overexpression of S100A7 (psoriasin), a small calcium-binding protein, has been associated with the development of psoriasis and carcinomas in different types of epithelia, but its precise functions are still unknown. Using human tissue specimens, cultured cell lines, and a mouse model, we found...
that S100A7 is highly expressed in pre-invasive, well-differentiated and early-stage human squamous cell carcinoma of the oral cavity (SCCOC), but little or no expression was found in poorly differentiated, late-stage invasive tumors. Interestingly, our results showed that S100A7 inhibits both SCCOC cell proliferation in vitro and tumor growth/invasion in vivo. Furthermore, we demonstrated that S100A7 is associated with the &gamma;23-Catenin complex, and inhibits &gamma;23-Catenin signaling by targeting and sequestering &gamma;23-Catenin via a post-translational mTOR-dependent and neck squamous cell carcinoma of the oral cavity (SCCOC). Anoikis (cell detachment-induced cell death) resistance is a critical step in the progression of SCCOC. Our data showed that in an anoikis resistant SCCOC cell line, JMAR, the p53 gene is mutated at codon 151 (P151S), and in this study we further investigated the possible role that this mutant form of p53 has in mediating the anoikis resistance of this cell line. Our results demonstrated that inhibition of the mutant p53 by p53 shRNA led to increased release of cytochrome C, Smac and Itra2/Omi from mitochondria and enhanced anoikis of JMAR cells grown in suspension culture. Conversely, when this mutant p53 was transduced into an anoikis-sensitive cell line, it conferred anoikis resistance. In addition, our experiments also indicated that this mutant p53 physically interacts with Bmf and down-regulates cell detachment-induced Bmf levels in the mitochondria. Taken together, our studies indicate that this mutant p53 may promote its function in producing anoikis resistance through a direct inhibitory interaction with the pro-apoptotic protein Bmf. This represents a novel activity of p53 mutation in mediating apoptosis resistance leading to tumor promotion and progression of SCCOC.

**IMMUNOLOGY**

**P028: IL-27 GENETIC TRANSFER INDUCED SIGNIFICANT ANTI-TUMOR EFFECTS AGAINST HEAD AND NECK SQUAMOUS CELL CARCINOMA IN MICE**

**Methods:** IL-27 expressing vector pGEGmIL-27 induced IL-27 p28 in protein level by ELISA. To investigate the effect of IL-27 on the growth of SCCOC tumors, mice were inoculated subcutaneously with SCCOC cells and IL-27 expression plasmids, empty vector pGEG4 were administrated intravenously every 7 days. Then we monitored the tumor growth and survival. Next, to investigate the role of NK cells, we monitored the tumor growth and survival in NK cell depleted mice, for depletion of NK cells in vivo, i.e., administrated anti-asialo GM1. The NK cytotoxic activity was measured by the standard 51Cr release assay. Then to investigate the role of T cells, we monitored the tumor growth in CD4+ T cells or CD8+ T cells depleted mice. The tumor tissue was immunohistochernically surveyed. 

**Results:** Administration of pGEGmIL-27 by the method of hydrodynamics of IL-27 expressing vector pGEGmIL-27 induced IL-27 p28 in protein level by ELISA. To investigate the effect of IL-27 on the growth of SCCOC tumors, mice were inoculated subcutaneously with SCCOC cells and IL-27 expression plasmids, empty vector pGEG4 were administrated intravenously every 7 days. Then we monitored the tumor growth and survival. Next, to investigate the role of NK cells, we monitored the tumor growth and survival in NK cell depleted mice, for depletion of NK cells in vivo, i.e., administrated anti-asialo GM1. The NK cytotoxic activity was measured by the standard 51Cr release assay. Then to investigate the role of T cells, we monitored the tumor growth in CD4+ T cells or CD8+ T cells depleted mice. The tumor tissue was immunohistochernically surveyed. 

**Conclusions:** IL-27 gene transfer resulted in significant antitumor outcomes through induction of CD8+ T cells and augmentation of NK tumoricidal activity in vivo in mice bearing preestablished HNSCC tumor burden. Immunotherapeutic intervention using IL-27 or IL-27 gene may provide powerful non-surgical strategy to eradicate HNSCC.

**P029: T REGULATORY TYPE 1 CELLS (TR1) IN HNSCC: MECHANISMS OF SUPPRESSION AND EXPANSION IN ADVANCED DISEASE**

**Methods:** We examined whether genetic transfer by the method of hydrodynamics of IL-27 expressing vector pGEGmIL-27 induced IL-27 p28 in protein level by ELISA. To investigate the effect of IL-27 on the growth of SCCOC tumors, mice were inoculated subcutaneously with SCCOC cells and IL-27 expression plasmids, empty vector pGEG4 were administrated intravenously every 7 days. Then we monitored the tumor growth and survival. Next, to investigate the role of NK cells, we monitored the tumor growth and survival in NK cell depleted mice, for depletion of NK cells in vivo, i.e., administrated anti-asialo GM1. The NK cytotoxic activity was measured by the standard 51Cr release assay. Then to investigate the role of T cells, we monitored the tumor growth in CD4+ T cells or CD8+ T cells depleted mice. The tumor tissue was immunohistochernically surveyed.
Purpose: Regulatory T cells (Treg) play a major role in tumor escape from immunosurveillance. T regulatory cells type 1 (Tr1), a subset of Treg present in the tumor and peripheral circulation of patients with head and neck squamous cell carcinoma (HNSCC), mediate immune suppression and might contribute to tumor progression. Experimental Design: CD4+CD25+ T cells were isolated from PBMC or tumor-infiltrating lymphocytes (TIL) of 26 HNSCC patients and 10 normal controls (NC). The Tr1 cytokine phenotype was determined before and after culture in the presence of IL-10 and IL-15. Each at 10-20 IU/mL. Suppression was measured in CFSE-based proliferation assays ± neutralizing anti-IL-10 or anti-TGF-beta1 mAbs in transwell systems. ELISA was used to define the Tr1 cytokine profile. Results: Tr1 cells originated from CD4+CD25-precursors present in TIL and PBMC of HNSCC patients. Cytokine-driven ex vivo expansion of Tr1 precursors yielded CD4+CD25-Foxp3*low*CD132+IL-10+TGF-beta1+ populations that mediated higher suppression than Tr1 cells of NC (P<0.0001). Tr1 cells suppressed proliferation of autologous responders via IL-10 and TGF-beta1 secretion. Expression of these cytokines was higher in TIL-derived than PBMC-derived Tr1 cells (P<0.0001). The Tr1 cytokine profile significantly higher in patients presenting with advanced than early disease stages and in patients cured by oncological therapies than in those with active disease. Conclusions: In HNSCC, Tr1 cell generation is promoted at the tumor site. Tr1 cells use IL-10 and TGF-beta1 to mediate suppression. They expand during disease progression and also following cancer therapy in patients with NED.

P030: IL-6 PREDICTS RECURRENCE AND SURVIVAL AMONG HEAD AND NECK CANCER PATIENTS: S. Duffy1, J.M.G.Taylor2, J.E.Terrell2, M.Islam2, Y.Li2, K.E.Fowler3, G.T.Wolf2, T.N.Teknos2, 1University of Michigan, Ann Arbor, MI; 2University of Michigan, Ann Arbor, MI; 3Ann Arbor VA HSR&D Center of Excellence, Ann Arbor, MI

Objective: Increased pretreatment serum interleukin (IL)-6 levels among patients with head and neck squamous cell carcinoma (HNSCC) have been shown to correlate with poor prognosis, but sample sizes in prior studies have been small and thus unable to control for other known prognostic variables. Methods: A longitudinal, prospective cohort study prospectively determined the correlation between pretreatment serum IL-6 levels and tumor recurrence and all-cause survival in a large population (N=444) of previously untreated HNSCC patients. Control variables included age, gender, smoking, cancer site and stage, and comorbidities. Kaplan-Meier plots and univariate and multivariate Cox proportional hazards models were used to study the association between IL-6 levels, control variables, and time to recurrence and survival. Results: The median serum IL-6 level was 13 pg/ml (range = 0 to 453). The 2-year recurrence rate was 35.2% (standard error = 2.67%). The 2-year death rate was 26.5% (standard error = 2.26%). Multivariate analyses showed that serum IL-6 levels independently predicted recurrence at significant levels [HR = 1.32; 95% CI, 1.11 to 1.58; P = 0.001] as death rate [HR = 1.58; 95% CI, 1.22 to 1.96; P = 0.001]. Serum IL-6 levels were also a significant independent predictor of survival [HR = 1.22; 95% CI, 1.02 to 1.46; P = 0.03], as were age, gender, smoking, cancer site (oral/sinus), higher cancer stage, and comorbidities. Conclusion: Pretreatment serum IL-6 may be a valuable biomarker for predicting recurrence and overall survival among HNSCC patients. Using IL-6 as a biomarker for recurrence and survival may allow for earlier identification and treatment of disease relapse.

P031: USEFULNESS OF WHOLE-BLOOD INTERFERON-GAMMA ASSAY IN THE DIAGNOSIS OF CERVICAL TUBERCULOUS LYPHADENITIS: J.Kim, J.Ceon, K.Kim, J.Catholic University of Daegu School of Medicine, Daegu, Republic of Korea

Objectives: The aim of this study was to evaluate the usefulness of the whole-blood interferon-gamma assay based on ESA-6 and CFP-10 in the diagnosis of cervical tuberculous lymphadenitis in clinical practice. Methods: Conventional diagnostic procedures including fine-needle aspiration cytology (FNAC), M ycobacterium tuberculosis polymerase chain reaction (PCR) and whole-blood interferon-gamma assay using commercialized QuantiFERON-TB Gold (QFT-G) were performed in 29 cases that had been suspected to be cervical tuberculous lymphadenitis. Results of FNAC, M tuberculosis PCR and QFT-G were compared with the reference standard of histology. Results: The sensitivity, specificity, positive predictive value, and negative predictive value of the QFT-G assay were 78.6%, 93.3%, 90.9%, and 100%, respectively. Conclusions: The whole-blood interferon gamma assay showed high sensitivity and specificity and could be helpful in the diagnosis of cervical tuberculous lymphadenitis.

P032: A PSYCHO-NEUROIMMUNOLOGIC PROTOCOL FOR TREATMENT OF HEAD AND NECK CANCER PATIENTS: D. Mantucchi1, P.Mereu1, M.Margarino1, M.Scala1, G.Ferlazzo2, S.Zaky3, 1National Cancer Institute, Genova, Italy; 2Laboratory of experimental oncology, Genova, Italy; 3Department of Oncology, Biology and Genetics, University of Genova, Genova, Italy

It is known that patients with head and neck malignant squamous cell carcinoma (SCC) are seriously immunocompromised. The immunosuppression is known to be defective lymphocytes associated with a significant reduction of the cytolytic capacity. The lymphocytes of the peripheral blood have a reduced activity of natural killer (NK) cells. This is shown clinically in a greater susceptibility to infectious complications, to metastasis and to the development of a secondary tumor. Recent research has shown that intense and prolonged stress, are capable in altering specific immune parameters: decrease in antibody synthesis, increase in the number of T-suppressors lymphocytes and a reduced production of interferon that alters the functionality of the NK cells. Psychoneuroimmunology studies the complex interactions between the central nervous system, the endocrine system and the immune system and how these systems are influenced by our behavior and our response to stress. Objectives of the Study: 1) Collect a psycho-social history of the patient 2) Measuring the psychological mechanisms that often accompany the cancer patient such as anxiety, depression, fear, obsessions and compulsions. 3) Evaluate some immunological parameters before, during and at the end of the treatment to verify if psychoneuroimmunological treatment has influenced the immune response. Study Design: Four patients each month will be enrolled in this study for one year. Patients will come enlisted randomly to the Test or to the Control group. The patients assigned to the group of Test will be submitted to a psychotherapeutic treatment once per week for a year after being submitted to the Cognitive Behavioral Assessment test. Besides, the patients will be subjected at time 0 and every six months to blood withdrawal to evaluate immunological parameters. Psychological Treatments: The patients who will be under the Test group also known as psycho-neuroimmunological treatment protocol will be treated with a Cognitive-Behavioral therapy and Analytical Hypnotherapy in order to evaluate if there is a response. The patients will be apprised from the psychological point of view at time 0 and at the conclusion of the treatment across the COGNITIVE BEHAVIOURAL ASSESSMENT test. This test comprises several in-depth questions into the patient’s psychological nature and personality structure. They show a significant aspect of the subject. Evaluation of the Immune Response: We propose to analyze: lymphocyte phenotype, lymphocyte proliferation, and the NK cytotoxicity. Results and Conclusions: Patients are known to have received a better quality of life from psychological treatment and increasing their tolerability to their treatments. Patients have reported a greater tolerance to pain and a greater reduction of fear regarding death. The results of the immunologic tests, will be analyzed at the end of the study to reduce the experimental variability and to ensure a greater unbiased and comparative data.

P033: HYPOTHYROIDISM AFTER TREATMENT FOR LARYNGEAL CARCINOMA: ARE AUTOANTIBODIES OF INFLUENCE? A. Lo Galbo1, R. de Bree2, D. Kui1, P. Lips1, B. von Blomberg, J.Langendijk1, C.Lee mans1, 1VU University Medical Center, Amsterdam, The Netherlands

Objectives: The incidences of hypothyroidism and autoantibodies were assessed retrospectively in 156 patients with laryngeal and hypopharyngeal carcinoma who were treated with surgery and/or radiotherapy between 1977 and 2002. Methods: One hundred and fifty-six patients treated for T2-T4 carcinoma or a recurrence after T1 who visited the outpatient clinic for their regular follow-up visit, were included. All patients were evaluated for the development of hypothyroidism, defined as increased thyroid-stimulating hormone level (> 4.5 mU/L) and the presence of autoantibodies. A questionnaire regarding symptoms was administered. Results: The prevalence of undiagnosed hypothyroidism following treatment of laryngeal carcinoma was 28.2%: 18.6% subclinical hypothyroidism and 9.6% clinical hypothyroidism. The prevalence of hypothyroidism before treatment was 3.6% (anti-TPO and/or anti-Tg) was 10.5%. Univariate analysis showed that patients with laryngectomy, hemithyroidectomy, ipsilateral neck dissec tion and autoantibodies had a higher risk of hypothyroidism. The combination of surgery and radiotherapy increased the risk. Symptoms such as weight gain and cold intolerance were significantly associated with hypothyroidism. Multivariate analysis showed hemithyroidectomy, autoantibodies, weight gain and cold intolerance to be prognostic factors for the treatment of hypothyroidism.

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development of hypothyroidism. **Conclusions:** The incidence rate of hypothyroidism after treatment for laryngeal and hypopharyngeal cancer is high, especially combination treatment. An association between hypothyroidism and autoantibodies was found.

**P034: THYROID DYSFUNCTION IN LARYNGECTOMEOEES - 10 YEARS AFTER TREATMENT**

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**Background:** Hypothyroidism is one of the complications that follow treatment of various head and neck cancers. Among the literature, reviews using different primary sites and differences in treatment modalities make comparison of post-treatment hypothyroidism not possible. The objective of this study was to evaluate the incidence of hypothyroidism in a homogenous group of patients who were treated with total laryngectomy and irradiation for laryngeal carcinoma, and to assess the importance of different variables in the occurrence of hypothyroidism. **Methods:** A retrospective review of 147 total laryngectomy patients between 1993 and 2003 was carried out. Serum thyroxine level and free T4 levels were assessed in all patients. Hypothyroidism was classified as subclinical (increased TSH and normal free T4 levels) and clinical (increased TSH and decreased free T4 levels).

**Results:** The results showed that the overall incidence of hypothyroidism was 49% (44% subclinical and 5% clinical). Hemithyroidectomy and advanced tumour staging were risk factors for the development of hypothyroidism in these patients (p < 0.05) with a relative risk of 2.1 (CI 95% 1.4-3.1) and 1.3 (CI 95% 1.1-1.6) respectively. During follow up, 19.9% of patients developed hypothyroidism at 3 years, 38.6% at 6 years and at 10 years follow up, 93.3% of them suffered from hypothyroidism.

**Conclusions:** In conclusion, hypothyroidism is a frequent complication in patients treated with radiotherapy and total laryngectomy for laryngeal cancer, especially when treatment includes hemithyroidectomy. These patients should have their thyroid function evaluated periodically even 10 years after treatment.

**P035: FACTORS INFLUENCING POSTOPERATIVE PHARYNGEAL LEAK**

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**Objective:** Generally, laryngopharyngeal surgeries carry a postoperative leak rate ranging about 10:30% in various series. This is a retrospective study done to analyze the factors involved in postoperative fistula after laryngopharyngeal surgeries done at Regional cancer center, Chennai. **Methods:** This is a retrospective analysis; the case records were retrieved from the tumor registry & analyzed systematically. The cases operated between 1985 & 2004 were analyzed. A total of 407 cases were taken up for analysis. Age ranged from 12 to 77 with a median of 53 & 297 were males & 33 were female. 24% of the patients had diabetes, while 71% had tobacco habits. SPS soft ware was used for analyses & Cox proportional hazard model was used for multivariate analysis of factors influencing outcome. **Results:** All the tumors were squamous cell carcinoma. The site involved was supraglottic in 143 cases, glottic in 142 cases, and subglottic in 23 cases. Nasal dissection was done in 248 cases. Total numbers of leaks were noticed in 28.8%. Factors that were taken for analysis include age, tobacco habits, co morbidity, previous irradiation, type of surgery (flaps used or not), extent of surgery & associated nodal dissection. The factors that significantly influenced the fistula rate formation by multivariate analysis included 1.Nodal dissection (39% vs 22% p value < 0.001) 2. Extent of surgery - hypo pharyngeal surgery vs laryngeal surgery, p value < 0.001. **Conclusion:** Surgery for larynx & hypopharynx is generally associated with significant postoperative morbidity. In our study, the postoperative leak rates were found to be influenced by associated nodal dissection & in cases where various amount of hypopharyngeal mucosa were removed. Also, previous radiation did not influence the rate of fistula formation as conventionally thought off.

**P036: EMERGENCY TRACHEOTOMY IN LARYNGEAL CANCER PATIENTS**

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**Introduction:** Laryngeal cancer patients who need emergency tracheotomyc are uncommon. However, most of such cases are advanced and have lymph node metastases, which means a poor prognosis. Also, it is controversial whether emergency tracheotomy is a risk factor of stomal recurrence or not. **Objective:** This paper discusses the prognosis of patients needing emergency tracheotomy and stomal recurrence in such patients. **Methods:** From 1986 to 2005, 356 patients with laryngeal cancer were treated in our institution. Twenty-six of them required emergency tracheotomy and 2 of these patients underwent emergency laryngectomy. **Results:** The patients consisted of 24 males and 2 females ranging in age from 40 to 92 years. Classifying the laryngeal cancer according to site, 9 patients had the glottic type, 11 patients the supraglottic type, 5 the transglottic type, and 1 the multicentric type. Seven died of the primary disease, 1 of another cancer, 5 of another disease and thirteen stayed alive and were free from disease. Disease specific 5-year survival was 61.9%. Stomal recurrence was observed in 5 of the patients who underwent total laryngectomy. Three of them had advanced tumor at the T4 and had undergone emergency tracheotomy. **Conclusion:** Various factors delaying diagnosis were mentioned and discussed. Subglottic extension of glottic cancer should be examined carefully.

**P037: VOCAL DISABILITY AFTER TREATMENT FOR ADVANCED CANCER OF THE LARYNX AND HYPOPHARYNX**

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**Objective:** To assess vocal disability after treatment of advanced cancer of the larynx and/or hypopharynx. **Casuistic and Methods:** Cross-sectional study, including patients for whom at least six months had elapsed after the start of definitive treatment of laryngeal and/or pharyngeal cancer, to determine auxiliary and/ or laryngeal phonation (PL), salvage total laryngectomy (sLT), total pharyngolaryngectomy (sTFL) and salvage total pharyngolaryngectomy (sTFLL). The patients´ vocal registers were evaluated by means of auditory-perceptive assessment by 3 speech pathologists judges, without prior contact with the patients, by consensus, in accordance with the following parameters: intelligibility of speech, naturalness of emission, social acceptability and pleasantness of voice. **Results:** Eighty-four patients participated in the study, the majority being men. The most prevalent lesion site was the larynx and the stage T3NOM0. All the patients submitted to PL (11) and RT+Chemo (24) communicated by laryngeal voice. Of the 49 patients submitted to total removal of the larynx, 19 presented no oral communication and 30 communicated with laryngeal phonation (tracheoesophageal voice = 17, laryngeal vibratory = 7), and esophageal voice = 6. The group submitted to PL presented intelligibility, naturalness and acceptability with discrete alteration and moderate or severe impact on pleasantness of voice. The only patient submitted to sPL presented adequate intelligibility, naturalness, acceptability and pleasantness with discrete alterations. The group submitted to RT+Chemo had adequate intelligibility, acceptable and pleasantness with discrete alteration and moderate or severe impact on pleasantness of voice. The majority of the patients submitted to removal of the larynx presented severe alteration of all the parameters. **Conclusion:** Patients submitted to treatment for advanced cancer of the larynx/hypopharynx present vocal disability at different levels, being worse for patients submitted to total removal, irrespective of the means of communication used. **Key Words:** Cancer, vocal disability.

**P038: IMPAIRED VOCAL CORD MOBILITY AS A PROGNOSTIC FACTOR IN THE CLASSIFICATION OF T2 GLOTTIC CARCINOMA**

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**Objective:** Early-stage laryngeal cancer of the glottis is typically treated with single-modality therapy, with similar survival outcomes reported for radiotherapy and laryngeal conservation surgery. However, some investigators have noted increased failure rates for radiation therapy in T2 glottic carcinoma. Impaired vocal cord mobility may have a negative impact on local disease control irrespective of tumor extension beyond the vocal cord. It has been suggested that T2 glotic carcinoma be further classified into favorable and unfavorable lesions, according to vocal cord mobility. However, the basis for this distinction is not well defined. We sought to determine the prognostic significance of impaired vocal cord mobility in patients receiving radiotherapy and/or surgical management for T2 glottic carcinoma. **Methods:** A MEDLINE search was conducted for all English-language articles published from 1990 through 2007 that addressed the management of glottic carcinoma. The study group was narrowed to T2 lesions, and articles were evaluated for division into treatment groups based on vocal cord mobility. **Results:** A total of 581 articles were reviewed, with 56 addressing treatment of T2 glottic carcinoma. Of these,
P039: Intra-Individual Variability Of Intra-Tracheal Climate With And Without An HME In Laryngectomized Patients

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Objective: The permanent disconnection of the upper and lower airways in total laryngectomy (TL) causes chronic pulmonary problems. Heat and Moisture Exchangers (HME) used in TL-clinics have been proven to be effective for pulmonary rehabilitation. Earlier research has also shown that under room temperature conditions a regular HME generates a significant increase of absolute humidity, and a slight but significant decrease of intra-tracheal temperature towards the end of the inspiration, and restores an intra-tracheal relative humidity of approximately 100% during the whole breathing cycle. The aim of the present study is to further determine the effects of this HME on the intra-tracheal temperature and humidity in TL patients and more specifically the intra-individual variability of these two climate parameters in time.

Methods: Intra-tracheal temperature and humidity were measured by use of for this purpose developed equipment in 10 laryngectomized patients during normal respiration in normal room climate conditions; 10 minutes with regular HME followed by 10 minutes without HME in a within-subject randomized sequence; each patient had different repetitions on different days. Analysis was conducted on two components of breathing: 1) the active breath length, defined as the time between the midpoints of the inhalation and exhalation periods; 2) the minima and maxima of each breath by normalizing the lengths of the active breath length. A fixed effect model using a split fit was used. Results: Data of 7 patients were used for analysis. Temperature: the predicted temperature minima were 27.4°C without HME and 28.6°C with HME (decrease 1.2°C; 95% CI 0.9 -1.6°C, p<0.0001). The inter and intra patient variation were 0.6°C (95% CI 0.3 -1.0°C) and 0.7°C (95% CI 0.5 -0.8°C) respectively. The variation due to different days was 0.01°C. Absolute humidity: the predicted absolute humidity minima were 20.5 mg/l and without HME and 25.7 mg/l with HME (increase: 4.8 mg/l; 95% CI 3.8 -5.7 mg/l, p<0.0001). The inter and intra patient variations were 2.8 mg/l (95% CI 1.3 -6.2 mg/l) and 1.6 mg/l (95% CI 1.2 -2.1 mg/l) respectively. The variation due to different days was 2.6 mg/l (95% CI 0.79 -8.2 mg/l). The active breath lengths were 1.0s and 0.9s with and without HME respectively (decrease 1.0s, p<0.001)

Conclusion: Intra-tracheal temperature values had a minimal variation, whereas humidity values had the largest variations. The HME effect is larger than the intra-individual variation for both temperature and humidity, therefore, the HME effect is not based on intra-individual variations.


P040: PROSPECTIVE VALIDATION OF AN INSTITUTIONAL STRATEGY FOR TREATMENT OF T1N0M0 GLOTTIC CARCINOMA

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Objective: The aim of this study was to prospectively assess an institutional strategy for treatment of T1N0M0 glottic squamous cell carcinoma (SCC) based on our previous retrospective evaluation suggesting that, assuming proper selection of patients, radiotherapy (RT) and Laser microsurgery (L) yield similar outcomes and functional results while partial laryngectomy (PL) is not associated with a better locoregional control but generates a worse quality of voice (Rosier et al, Radiother Oncol, 1998). In addition, inclusion of costs in the selection of best practice favors RT and L and restricts PL to very selected cases (Gregoire et al, Radiother Oncol, 1999).

Methods: Fifty five patients with biopsy proven T1N0 glottic SCC were prospectively treated between 1997 and 2004 following guidelines as follows: L: Small exophytic tumor, located on one vocal cord, far away from the anterior commissure and the arytenoid cartilage; RT: large or infiltrative tumor reaching the anterior commissure, poor endoscopic exposure or T1b; PL: tumor originating from the anterior commissure. There were 42 T1a and 13 T1b tumors. One patient was excluded from analysis of survival and loco regional control because a non-small cell lung carcinoma was diagnosed simultaneously. 34 patients were treated by RT (median dose 64 Gys), 18 patients were treated by L of whom 7 received postoperative RT for positive margins and only 2 patients were treated by PL.

Results: With a median follow up time of 55 months (3-124months), the 5-year loco-regional control probability reached 85% ± 5% for the whole series (former series: 91%), without any difference between the treatment groups. After salvage laryngectomy (6 PL and 1 total laryngectomy), the 5-year loco-regional control probability reached 98% (former series: 97%). The 5-year laryngeal preservation reached 98% and the 5-year overall survival reached 84 % (former series: 78%). The actuarial incidence of second primary reached 35% ±13% at 10 years (former series: 19%).

Conclusion: These data suggested a continued validity of a local strategy for treatment of T1N0 glottic SCC based on the following tripod suggested by our previous studies: optimal locoregional control, voice recovery and limited costs for the national health care system. To our knowledge, it is the first prospective study addressing this issue.
Based on raw interpretation of the data, the Highflow-HME we present the surgical treatment options for symptomatic Out of Subjects and Method: Forty six T1 patients and 73 T2 patients To discuss the diagnostic criteria and management protocols The treatment response and the survival rate did VEGF-C and CD31 positive microvessel All patients swallowing func- T1 and T2 laryngeal squamous cell carcinoma (SCC) patients. Although the 5-year disease- were entered. In T1 cases, 30 patients received radiotherapy and 16 patients received chemoradiotherapy. In T2 cases, 28 patients received radiotherapy alone and 45 patients received chemoradiotherapy. In T1 cases, a complete response (CR) rate was 88.9% in the group of radiotherapy alone and 93.8% in the group of concurrent chemoradiotherapy (not significant: ns), and 96.4% and 88.9% in T2 cases (ns). The 5-year disease-specific survival rates were 96.0% and 100% in T1 (ns), and 96.0% and 94.9% in T2 (ns), respectively. The 5-year larynx preservation rates were 79.4% and 93.8% in T1 (ns), 66.7% and 93.3% in T2 (p<0.01), respectively. Adverse effects in the chemoradiotherapy group were observed more frequently. Conclusions: The treatment response and the survival rate did not show a significant difference between the group of radiotherapy alone and that of concurrent chemoradiotherapy. The 5-year larynx preservation rate was significantly improved in the chemoradiotherapy group in T2 cases, and the same tendency was observed in T1 cases. Concurrent chemoradiotherapy for early stage laryngeal SCC patients, especially in T2 cases, was efficacious to improve the larynx preservation rate.

P044: PROGNOSTIC SIGNIFICANCE OF LYMPHATIC VESSEL DENSITY IN SUPRAGLOTTIC CANCER K.Jung1, S.Baek1, S.Kwon1, J.Woo1, J.Cho1, S.Cho1, K.See1, Y.Chae1, 1Korea University, College of Medicine, Seoul, Republic of Korea Background and Objectives: Regional lymph node metastases are very common findings of supraglottic cancer. The mechanism of lymphatic metastasis is as yet unknown because there have been no specific markers that could definitely distinguish lymphatic vessels from blood vessels. The aim of this study is to identify the distribution of lymphatic vessels and their prognostic significance in supraglottic cancer. Subjects and Methods: We investigated lymphatic vessels in 43 subjects who had previously been diagnosed with supraglottic cancer. Immunohistochemical staining was performed with VEGF-C, D2-40, and CD31 monoclonal antibodies on the paraffin-embedded thyroid tissues obtained from these patients, and the associations among the semiquantitative score of VEGF-C stained cancer cells, the density of immunohistochemically stained microvessels, and the clinical factors of supraglottic cancer were investigated to evaluate the prognostic significance. Results: VEGF-C and CD31 positive microvessel density did not show any difference according to various clinical factors. Lymphatic vessel density showed a statistically significant difference according to the presence of lymph node metastasis (p<0.05). Conclusion: Increased LVD may play an important role in the metastasis to regional lymph nodes. In case of no neck treatment, LVD may be useful to estimating the possibility of lymph node metastasis.

P045: UNUSUAL TUMORS OF THE LARYNX: ALEXANDRIA'S EXPERIENCE M.Hesham1, H.Abd Al-Fattah1, J.Fadali2, N.Mashli3, M.Hamza4, 1Faculty of Medicine, Alexandria University, Alexandria Egypt, Alexandria Egypt; 2Department of Pathology, Institute of Medical Research , Alexandria, Egypt; 3Department of Pathology, Faculty of Medicine, Alexandria University, Alexandria, Egypt; 4Department of Pathology, Faculty of Medicine, Alexandria University, Alexandria, Egypt, Egypt. Objectives: To discuss the diagnostic criteria and management protocols for unusual (rare) tumors of the larynx. Methods: A retrospective review was conducted on patients who were diagnosed as non squamous cell carcinoma of the larynx at the department of Otolaryngology Head & Neck Surgery , University of Alexandria in the last ten years. Results: Out of 1160 laryngeal tumor encountered in our department in the last ten years, 58 unusual tumors were met with, 19 were benign and 39 were malignant. The commonest benign tumor in this series was hemangiomas (7 cases) followed in frequency by lipomatous tumors while the commonest malignant was verrucous carcinoma followed in frequency by Basaloid carcinoma. Apart from verrucous and papillary carcinomas all tumors presented endoscopically with smooth surface lesions. Basaloid carcinoma when late, tend- to penetrate the thyroid cartilage bulging under and infiltrating the skin. All the tumors shared the feature of absence of lymph adenopathy. Non was diagnosed histopathologically from the first biopsy. More than 50 % were diagnosed after complete excision of the tumor. Immunohistochemistry was corner stone in the diagnosis in most cases. The role imaging of these unusual lesions is presented and discussed. The protocol of management of each tumor category in our series is discussed. Conclusion: Pathological diagnosis of rare tumors of the larynx is still challenging. Imaging and immunohistochemistry are corner stone in diagnosing such lesions. Endoscopic laser excision in all benign lesions and early malignant lesions was always possible with exception of huge tumors.

P046: SYMPTOMATIC NEOPHARYNGEAL DIVERTICULA AND SURGICAL TREATMENT OPTIONS A.T.Tucker1, Y.Pali2, J.V.McCaffrey3, T.A.Padhya4, 1University of Florida, Tampa, FL; 2University of Cincinnati, Cincinnati, OH; 3 Moffitt Cancer Center, Tampa, FL Objectives: We present the surgical treatment options for symptomatic neophasyngeval diverticula in the post laryngectomy patient population. Methods: Retrospective chart review of patients presenting to the Moffitt Cancer Center from 2003-2007. Patients were identified with dysphagia in routine follow up after laryngectomy. Patients were studied with preop- erative and postoperative swallow studies. Results: Seven patients were identified that met inclusion criteria. Patients were treated surgically using one of the following surgical options: CO2 laser, Bovie electrocautery, endoscopically GIA stapling or a combination of the two of the procedures. All patients treated surgically had improved postoperative swallowing. Four patients were tolerating a regular diet and three patients are tolerating a soft mechanical diet. Conclusion: All patients swallowing func- tion improved after surgical intervention. Surgical intervention is an appro- priate choice in the treatment of post laryngectomy neophasyngeval diver- ticula.

P047: THE NEW SELF-EXPANDING POLYFLEX ® STENT IN THE PALLIATIVE TREATMENT OF MALIGNANT AND BENIGN STENO- SIS AND FISTULA OF THE HYPOPHARYNX S.J.Koscielny, J.Stadler, 1ENT-Department University of Jena, Jena, Germany; 2ENT- Department University of Jena, Jena, Germany Fistula and stenosis of the hypopharynx and oesophagus resulted in the most cases of tumor progress or postoperative complications. As result the loss of oral intake of food and impossibility to swallow the own saliva caused an important reduction of quality of life for the patients. The aim of
the treatment is the reconstruction of the passage of the upper aerodigestive tract with the result of swallowing via natural way for improvement of quality of life. But the possible treatment options are very complex and needs often multiple operations. The implantation of stent can re-opening the lumen of the Hypopharynx and oesophagus and While the rigid Salivarystent (rigid silicon tube) represents a cheap possibility (300 $) for patients after laryngectomy have this stent the problem of the insufficient fixation in situ and the low tolerance of the patients for these rigid stent. Alternatively can be used the flexible self-expanding Nitinolstents making from the metal Nitinol. The fixation and tolerance of this stent is better that than of the rigid salivary stent and can be used in patients with and without larynx. But the cost of these stents are with 2000-3000 $ very expensive. A from the Rüsch company new developed self expanding plastic stent named Polyflex® is a good practicable and cheap alternative. The stent cost nearly 400 $ and have the same properties like the Nitinolstent. In the last year we implantated these stent in 7 Patients (2 with tumor-related fistula, 3 with tumor-related stenosis, 2 with scarred stenosis) in Hypopharynx and oesophagus. All Patients could eat after implantation orally without any problem. We observed no stent related complications. The self-expanding Polyflex® stent is in our hand a good, cost-effective palliative treatment options for patients with malignant and benign stenosis and fistula of Hypopharynx and oesophagus.

P048: A THIN TRACHEAL SILICONE WASHER SOLVING PERIPROSTHETIC LEAKAGE AFTER LARYNGECTOMY F.J.Hiligers1, L.Soolmans1, M.W.van den Brekel2, B.Ta1, A.J.Balm1, A.H.Ackerstaff1
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Objectives: assessment of the immediate results and long-term clinical effects of a thin silicone washer placed behind the tracheal flap of voice prostheses to treat periprosthetic leakage. Patients and Methods: 3-year retrospective analysis of 32 laryngectomized patients with 107 periprosthetic leakage events (PLEs). Custom-made silicone washers (outer diameter 18 mm, inner diameter 7.5 mm, thickness 0.35 mm), placed behind the tracheal flap in combination with prosthetic replacement or later. Results: immediate solution of periprosthetic leakage in 88 PLEs (median 38, mean 53 days), range 8-330 days), and in 6 PLEs with the washer still in situ at the date of analysis (median 75, mean 97 days; range 38-240 days). No solution for periprosthetic leakage in 13 PLEs. Thus, totally 94/107 PLEs (88%) were successfully solved. In 29/32 patients (91%) the washer solved the problem at least once. 12/32 Patients, including all 3 washer-failures, also required other interventions to ultimately solve the problem. The vast majority of patients (80%) did consider placement of the washer not to be inconvenient. Conclusions: Considering the high success rate, and limited inconvenience for patients, this simple thin silicone washer application provides a good first option for the treatment of periprosthetic leakage. Submitted to the Laryngoscope.

P049: THREE-DIMENSIONAL EDUCATIONAL COMPUTER MODEL OF THE LARYNX; VOICING A NEW DIRECTION A.Hu1, T.Wilson1, H.Ladak1, P.Phaase1, K.Fung1, 1University of Western Ontario, London, ON, Canada

Objective: Knowledge and understanding of laryngeal anatomy is integral for the diagnosis and management of laryngeal cancer. This knowledge is especially relevant for medical students and residents in ENT, radiation oncology, and medical oncology. Medical educators have been using novel methods to teach human anatomy, like three-dimensional educational computer tools. The need for these three-dimensional computer tools is growing for several reasons. Firstly, the traditional teaching method of cadaver dissection may be ineffective for some organs, like the larynx, where the structures are too small and delicate. Dissecting these structures requires advanced dissection skills which most students lack. Secondly, there has been a decrease use of cadavers in anatomy curricula due to the increasing cost and decreasing availability of materials and curricula time. Thirdly, computer educational tools are portable to any personal computer, making distance education, web based learning, and satellite campuses more feasible. Our objective was to build a three-dimensional educational computer model of the larynx to teach medical students and residents laryngeal anatomy. Methods: A male and female adult cadaveric neck was scanned with a micro CT and MRI scanner. The CT scan provided images of the cartilages, bones, and vessels. The MRI scan provided images of the soft tissues. Key structures were identified on each slice of the CT and/or MRI and segmented with Amira 4.1. These images of the larynx were exported from Amira 4.1 and imported into Microsoft Powerpoint. Visual text and audio commentary was added to explain the images. Real patient cases of a child’s larynx, a tracheostomy, a criocothyroarydomy, epiglottitis and a patient with laryngeal carcinoma were also included as clinical vignettes. The final model was converted by Articulate into a Microsoft Flash document.

Results: Below is an example diagram of the laryngeal model.

Conclusion: A three-dimensional educational computer model of the larynx has been created. For future directions, we plan on conducting a randomized controlled trial on students to evaluate the efficacy of this three-dimensional educational computer model in teaching laryngeal anatomy.

P010: LONG-TERM RESULTS OF A PROSPECTIVE NON-RANDOMIZED GERMAN MULTICENTER PHASE II STUDY TO PRESERVE THE LARYNX FUNCTION A.Dietz1, H.Eckel2, P.Yolling3, M.Schröder4, S.Stigar2, U.Schröder2, F.Wallner2, P.Plinkert4, M.Wannenmacher5, V.Rudat6, 1University Leipzig, Leipzig, Germany; 2Landeskrankehaus Karsten, Klagenfurt, Austria; 3EK-Krankenhue, Oldenburg, Germany; 4City Hospital Kassel, Kassel, Germany; 5Klinikum Bremen Mitte, Bremen, Germany; 6University Lübeck, Lübeck, Germany; 7University Heidelberg, Heidelberg, Germany; 8Saad Specialist Hospital, Al Khobar, Saudi Arabia

Objective: This prospective phase II study was undertaken to assess the feasibility of a larynx preservation protocol using simultaneous chemoradiation in patients who are considered for ablative surgery like total laryngectomy. Patients and Methods: Between 3/1998 and 10/2000, 42 patients with moderately advanced cancer of the larynx (n = 17) and hypopharynx (n = 25) were treated in a prospective larynx preservation study. The alternative treatment for all patients was a total laryngectomy (LE). The study patients received 66 Gy in 5 weeks using a concomitant boost technique and 70 mg/m2 Carboplatin on day 1 to 5 in week 1 and 5. The results were retrospectively compared with 42 patients treated with LE and postoperative radiotherapy using a matched pair technique. Results: The median follow-up time of the censored study patients was 41 months (9-95 months). The 5-year overall survival was 0.65 (95%CI 0.48-0.84), the 5-year laryngectomy-free survival 0.60 (95% CI 0.42-0.78), and the laryngeal preservation rate at 5 years 0.67 (95%CI 0.49-0.85). Cox multivariate regression analysis showed the total tumor volume to be the only statistically significant factor on locoregional failure-free survival. The matched pair comparison showed no statistically significant difference to the patients treated with LE regarding overall survival (p=0.87), or locoregional failure-free survival (p=0.17). Six of 23 tumor-free long-term survivors received a tracheotomy because of late laryngeal toxicity associated with dysphagia 30-79 months after radiochemotherapy.

Conclusions: This protocol was feasible but should be considered critical due to late toxicity and complications related to salvage surgery if alternative treatment of LE is discussed. Long term follow-up is essential to thoroughly assess the value of larynx preservation protocols. In our study, the unexpected low need for tracheotomy due to grade IV edema and dysphagia starting after 4 years in nearly 25% of laryngectomy free survivors gives a broad hint for future awareness focusing functional outcome compared to long-term results of survivors after primary surgery with or without adjuvant radio- or chemoradiation. Furthermore, the question is still open whether induction protocols show an advantage over simultaneous protocols concerning late functional outcome in larynx organ preservation.

NECK

P051: NECK MASSES : A RETROSPECTIVE STUDY OF 952 CASES S.Irani1, 1School of Dentistry, Hamadan University, Hamadan, Iran

Objectives: Many head and neck diseases manifest as neck masses with a wide range of pathologies. Neck masses include: congenital, inflammatory and neoplastic disease. In general, these masses are classified as developmental, inflammatory /infectious and neoplastic. Neck masses in children are likely to be congenital or inflammatory but in adults the most common of masses are neoplastic. This retrospective study was conducted to analyze neck masses to better understanding of gender, age and location distribution and also pathologies of these neck masses from 1999 to 2006. Methods and Materials: The records of patients with neck masses between 1999-2006 were retrieved from the Department of Pathology of two educational hospitals in Tehran, Iran, and analyzed for age, gender, location and pathology reports. The masses were classified according to the type of lesion and also according to the location of the neck mass. Results: Over a period of 7 years, a total of 923 cases were found. The included patients were 435 (47%) males. The patient’s ages ranged from 1 to 83 years. The
mean age of patients was 37.5 years. The most prevalent masses were thy-roid lesions included nonneoplastic (174 cases) and neoplastic (104 cases) lesions, followed by metastatic lesions (121 cases). Parathyroid lesions were the least (29 cases). According to the location of masses, midline and anterior neck was the most common location. Conclusion: These data show that neoplastic lesions (including metastatic lesions) are the most common neck masses and midline and anterior neck is the most common location, so any mass in neck especially in midline and anterior neck must be considered neoplastic.

PO50: METASTATIC CARCINOMA OF THE NECK OF UNKNOWN PRIMARY ORIGIN: EVOLUTION AND EFFICACY OF THE MODERN WORKUP

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Objective: In the setting of metastatic cancer of the neck of unknown primary origin, the diagnostic workup to identify primary tumor location has generally included examination, imaging (CT or MRI), and panendoscopy in various combinations. Newer modalities, such as positron emission tomography (PET) scans and PET-CT fusion studies, have been increasingly utilized in this group of patients. The objective of this study is to assess the efficacy of these various diagnostic modalities used at our institution in detecting occult primary tumor location.

Methods: Over a ten-year period (1997-2007), we identified patients presenting to our Head and Neck Oncology Clinic at The Ohio State University with diagnosis of metastatic cancer of the neck in which the primary tumor remained undetected after physical examination. All outpatient clinic notes, imaging results, operative reports, and pathology results were reviewed. Results: One hundred eighty-eight patients were identified meeting study criteria. In all, primary tumor location was ultimately identified in 85 patients (45%). Locations of primary tumors included the tonsil (40%), tongue base (32%), hypopharynx (13%), oropharynx (7%), nasopharynx (5%), and larynx (2%). Preoperative imaging (CT, MRI, and/or PET-CT) identified sites suspicious for primary tumor location in 69 patients. Subsequent directed biopsy of these sites yielded positive results in 43 cases (62%). The rate of successful identification of a primary tumor, including each of the following diagnostic modalities was as follows: CT scan of the neck, 14/151 patients (9%); MRI of the neck, 0/13 patients (0%); whole body PET scan, 7/44 patients (16%); and PET-CT fusion study, 23/53 patients (43%). In 12 of the 53 PET-CT studies (23%), management was changed due to additional findings, including distant metastases and contralateral neck disease. Interestingly, biopsy of suspicious sites identified on preoperative imaging yielded negative histopathologic results in 26 patients (false positive rate of 38%). Additionally, 119 patients in whom all prior preoperative workup (exam and imaging) failed to identify a primary tumor location, occult malignancy was subsequently identified via directed biopsies +/- tonsillectomy carried out during panendoscopy in an additional 22 cases (18%). Comparing the various combinations of workups, the sensitivity for identifying occult primary tumors in patients who had undergone PET-CT plus panendoscopy with directed biopsies +/- tonsillectomy: 31 of 53 patients (58%). Conclusions: Metabolic imaging modalities, particularly PET-CT, are highly useful for identifying occult primary tumors, as well as detecting unexpected metastatic sites, and offer markedly improved sensitivity over traditional imaging methods. Such modalities however, remain an adjunct to diagnostic operative endoscopy. We believe that diagnostic workup encompassing use of PET-CT, panendoscopy with directed biopsies including bilateral tonsillectomy offers the greatest likelihood of successfully identifying occult primary tumor location and thus guide subsequent therapy.

PO53: PATTERNS OF NECK FAILURE AFTER CONCURRENT RADIOCHEMOTHERAPY WITHOUT PLANNED NECK DISSECT-ION IN NODE-POSITIVE HEAD AND NECK CANCER

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Objectives: The necessity for post-radiochemotherapy neck dissection is controversial in head and neck cancer (HNC). This is to report the treatment outcomes of the node-positive HNC patients who were managed with concurrent radiochemotherapy (CRT) and watch & see policy for the neck. Methods: From Oct. 1994 till May. 2006, 811 HNC patients received definitive radiation therapy at Samsung Medical Center. We retrospectively analyzed the treatment outcomes of 64 node-positive non-nasopharyngeal HNC patients who received CRT but no pre-planned neck dissection. Results: The primary sites were the oropharynx in 30 patients (46.9%), the hypopharynx in 20 (31.3%), the larynx in 10 (15.6%), and the oral cavity in 4 (6.3%). Eight patients (12.5%) were with N1 disease, 52 (81.3%) with N2 disease, and four (6.3%) with N3 disease. All received platinum-based chemotherapy concurrent with curative radiation therapy. The median follow-up period was 21 (0-139) months, and overall survival (OS) and neck control rates of all patients at 2 and 5 years were 68.2%, 61.4%, and 75.0%, 75.0%. There were 17 patients (26.6%) who failed in the neck: as a sole site in seven patients (10.9%), with combined primary failure in eight (12.5%), and combined with metastasis in two (3.1%). Salvage treatment was attempted in eight patients and was successful in three (37.5%). OS rates at 2 and 5 years of the patients without neck recurrence were 80.0%, 72.0%, while those with neck failure were 25.6%, 25.6%. Radiologic response in the neck assigned at one month of CRT completion was highly predictive of neck control. Neck control rates at 2 and 5 years were 88.5%, 88.5% in 30 patients who achieved radiologic complete remission (CR), and only 9%, 42.9% in seven with partial remis- sion, and 14.3%, 14.3 % in seven with stable or progressive disease (p<0.001). Conclusions: CRT without planned neck dissection proved to be a highly effective strategy after achieving CR. However, based on unsatis- factory outcomes following neck failure, early surgical intervention espe- cially in patients achieving less than CR should be considered.

PO54: LOW RECURRENT RATES AFTER SELECTIVE NECK DIS-SECTION IN N+ SQUAMOUS CELL CARCINOMAS OF THE HEAD AND NECK

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Selective neck dissection (SND) performed for therapeutic purposes (N+ necks) has been indicated in the last decade in selected cases. Our previous report had raised a word of caution, with 11.8% regional recurrence rate. Methods: The authors identified 146 patients with N2b neck failure: 74 cases of the former study, extended for 2 more years, with the addition of new cases. Method: Between 1997 and 2005, 324 patients with N+ necks were submitted to neck dissections. Of these, 42 N+ SCCHN patients who had at least one SND as a part of their treatment. Thirty-one (83.7%) were male, age ranged from 37-79 years. Eleven patients had a bilateral SND, therefore comprising 53 operations. Primary tumors were: larynx (61.9%), hypopharynx (16.6%), oral cavity (11.3%), oropharynx (7.1%) and nasopharynx (2.3%). T stages were T1 in 47.7%, T2 in 9.5%, T3 in 21.4% and T4 in 64.2%. N stages were N1 in 26.1%, N2a in 4.7%, N2b in 19.0%, N2c in 50%. In 10 patients with N2c necks, a modified radical neck dissection was performed on one side and a selective neck dissection on the other. 11.9% of the patients were stage III and 88.1% were stage IV. Five patients died due to postoperative complications. All patients received postoperative radiotherapy. 76.1% completed the treatment. Results: Regional recurrence occurred in 4 patients (7.5%). No patient with T1 or T2 tumors recurred, whereas 11.1% with T3 (1/7) and T4 (3/27) had recurrence. Regarding N stage, 9.0% of patients with N1 (1/11), no N2a (0/2), 25% of N2b (2/8) and 4.7% of N2c (1/21) recurred. Conclusions: Continuing our previous report, SND is a feasible option in N+ necks in carefully selected cases. Recurrence is however, higher, in T3/4 and N2b stages.

PO55: IMPLICATIONS OF HEAD AND NECK CANCER TREATMENT FAILURE IN THE NECK

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Objective: Squamous cell carcinoma of the head and neck (HNSCC) has shown no significant improvement in survival for decades. If initial treatment fails and a recurrence is found in the neck, the prognosis is often poor. The purpose of this report is to analyze the outcome of a heterogeneous collection of salvage treatments among patients that recurred in the neck. Methods: A retrospective study of patients who presented to the Winthrop P. Rockefeller Cancer Institute at the University of Arkansas for Medical Sciences with squamous cell carcinoma of the head and neck between 1998 and 2007 was completed. Of the 1291 patients identified, 187 (14.5%) had a documented recurrence. There were 50 (17%) patients with a neck recurrence. These patients were defined as having at least a six month disease-free interval followed by a demonstrable and biopsy proven regional recurrence. Results: Time to salvage neck failure was analyzed. Median survival was 15.5 months with 21% survival at 36 months. Median survival for males (n=37) compared with females (n=13) was not significant, neither was median survival time for age less than 60 (n=30) versus age greater than 60 (n=20). Survival times were also compared for presenting stage of I/II (n=22), III /IV (n=26), and un-staged (n=2) without significant difference. Race was also compared without sig-
significant difference. Four patients were missing treatment information. As compared with the 137 recurrence patients that did not meet our criteria for neck recurrence (40.1 months), the survival time for patients with recurrence in the neck was significantly lower, p=0.002. Conclusions: These results show that the prognosis is poor for cases of neck recurrence of HNSCC. This may be an indictment of the ineffectiveness of conventional therapies applied to this group of patients. These patients may be better served by clinical trials given their poor prognosis. Novel approaches promoted in clinical trials may improve these patients’ outcomes and/or offer a new understanding about this subset of patients.

P056: CLINICO-PATHOLOGIC PREDICTORS OF LYMPHATIC METASTASIS IN HNSCC: IMPLICATIONS FOR MOLECULAR MECHANISMS OF METASTASIS
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Objective: The molecular mechanisms driving lymphatic metastasis remain little understood. Studying clinical and pathologic features of metastatic disease can help focus molecular studies to areas consistent with specific biological pathways. Studies to date, however, have only reported on limited clinical and pathologic predictors of lymphatic spread. Furthermore, identified factors vary between studies. Our goal was to comprehensively assess pre-treatment clinical and pathologic features known to be important in head and neck cancer as predictors of lymphatic metastatic spread with the aim of identifying pathways on which to focus further molecular mechanistic studies.

Methods: Pathology records were queried for cases diagnosed with invasive squamous cell carcinoma of the upper aerodigestive tract between 1993 and 2003 at the University of Texas Medical Branch. Charts and pathology reports were retrospectively reviewed and scored for site of primary tumor, clinical stage of primary tumor, history of second primary tumor, family history of cancer, family history of head and neck cancer, history of tobacco use, history of alcohol use, tumor grade, lymphovascular invasion, perineural invasion, and positive lymphatic metastases. Cases with complete variable score where subjected to stepwise regression analysis. The dependent outcome variable examined was lymphatic metastases. P-value < 0.05 was considered statistically significant. Results: 644 cases were identified initially, 234 of which had a surgical resection specimen analyzed. All variables were successfully scored for 162 of the 234 cases. Forward Stepwise regression analysis identified clinical tumor stage (p=0.013), tumor grade (p=0.033), lymphovascular invasion (p=0.016), and family history of head and neck cancer (p=0.036) as independently predictive of lymphatic metastases. The model was confirmed using backwards stepwise regression analysis.

Conclusion: Our study confirms that clinical tumor stage, grade, and lymphovascular invasion are clinico-demographic predictors of regional tumor spread. Our study also identifies family history of head and neck cancer as a new predictor of lymphatic metastases. Thus, studying the molecular mechanisms of interstitial pressure-mediated cell egress at the primary tumor site, tumor cell migration and invasion, and tumor cell differentiation may provide molecular mechanistic insight into lymphatic metastasis. Also, we study suggests that genetic analysis of families with head and neck cancer may provide fruitful areas of study, as it is likely that familial aggregation of cases relate to particular genes mutated within such kindreds mutated genes whose function may be important for regional spread of disease.

P057: SKIN INVOLVEMENT FROM METASTATIC CYLINDRICAL LYMPHADENOPATHIES IN MUCOSAL SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK
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Objective: The presence of extra-capsular spread in a metastatic lymph node is a poor prognostic sign. The invasion of anatomical structures such as the prevertebral fascia or the carotid artery is usually a sign of incurable disease. Skin involvement is usually associated with invasion of other anatomical structures an carries a bad prognosis. Skin involvement on its own is rare and has been very poorly reported. The aim of this paper is to analyze the clinical presentation, management and prognosis of this subgroup of patients.

Methods: Between January 2000 and January 2007, 8 patients presented with direct skin involvement from metastatic cervical lymphadenopathies from head and neck squamous cell carcinoma. Pathology reports were analyzed and re-staged where necessary. Skin involvement at presentation was documented. All patients were radiologically staged with computerized tomography (CT) of neck and the chest to exclude pulmonary metastases. All patients were discussed in the multidisciplinary head and neck oncology tumour board meeting before treatment. Maximum follow up is 5 years and minimum follow up 11 months.

Results: Eight patients presented with direct skin invasion from metastatic cervical lymphadenopathies. There were 6 males and 2 females and age ranged from 52 to 85 years (mean 66 years). All patients had N3 nodal staging, 3 patients had occult primaries tumours, 2 tonsillar, 2 pyriform sinus and 1 oral cavity. All patients had stage IV disease. Five patients underwent extended radical neck dissections (ERND), 2 had extended modified radical neck dissection (EMRND) type I and one type II. Four patients had primary closure of the surgical defect, 2 had skin local rotational flaps and 2 pedicled perforator flaps for reconstruction.

All patients underwent post-operative adjuvant radiotherapy. One patient died of unrelated causes, one patient developed breast carcinoma and died from the later disease but all other 6 patients are alive with no evidence of disease with a minimum follow up of 11 months and a maximum of 5 years. Conclusion: Direct skin involvement in the absence of other anatomical structures invasion is rare. These patients should be carefully evaluated and managed. Surgical treatment with either ERND or EMRND with or without flap reconstruction is possible and should be encouraged whenever possible. Skin involvement alone is not necessarily an adverse prognostic factor and this sub-group of patients should be treated with radical curative intent whenever possible as outcome can be favourable in most cases.

P058: RESULTS OF SELECTIVE NECK DISSECTION IN THE PRIMARY MANAGEMENT OF HEAD AND NECK SQUAMOUS CELL CARCINOMA
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Aim: Selective neck dissection (SND) is known to be a valid procedure to stage the clinically NO neck but its reliability to control metastatic neck disease is controversial. This study analysed if selective neck dissection is a reliable procedure to prevent regional metastatic disease in head and neck squamous cell carcinoma (HNSCC).

Methods: We retrospectively analysed the medical records of 163 previously untreated patients with squamous cell carcinoma of the oral cavity, oropharynx, larynx and hypopharynx treated initially in our department from January 1990 to December 2002. All patients had unilateral or bilateral SND, in combination with surgical resection of the primary tumour. SND was performed in 281 necks. Finally, 146 patients who underwent 249 SND (39 III, IV, 210 II-V) had adequate follow-up and were assessed for the regional control. The median follow-up was 37 months (1-180 months). The end points of the study were neck control following SND and overall survival.

Results: Twenty-five percent (30/119) of patients staged cN0 had lymph node (LN) metastasis. Overall, regional recurrence was observed in 28% of the necks (7/249): 1.6% (4/249) in dissected field and 1.2% (3/249) in undissected field. Seventy eight percent (194/249) of the necks were staged pN0 with a subsequent failure rate of 1.5% (3/194); 16% (39/249) were staged pN1 and postoperative radiotherapy (PORT) was proposed in 21 of these patients. The failure rate with PORT was 9.5% and 5.9% with a minimum follow up of 6 months (7/75). In 10 of these necks were staged pN2b and all had PORT with one subsequent recurrence. Extracapsular spread (ECS) was reported in 16.5 % of positive SND specimens (9/55); all one by one were treated by PORT with a subsequent failure rate of 22% (2/9). At 3 years, overall survival for the whole population was 70% and statistically highly correlated with pN stage (p=0.0034).

Conclusion: These results support the reliability of SND to stage the clinically NO neck. SND is a definitive operation not only in pN0 but also in most pN1 and pN2b necks. PORT is not justified in pN1 neck without ECS. In pN2b necks, the low rate of recurrence supports adjuvant PORT. The presence of ECS, despite adjuvant PORT, remains associated with a higher risk of recurrence.

P059: IS SELECTIVE NECK DISSECTION AN ADEQUATE MANAGEMENT FOR N+(+) - RESULTS OF SELECTIVE NECK DISSECTION FOR OCCULT N(+) 1KI1m, S.Oh1, Y.Rho1, H.Ahn1, 1Hallym University Medical Center, Seoul, Republic of Korea

Objectives: This study was conducted to evaluate the results of selective neck dissection (SND) for the patients with occult node-positive neck in head and neck squamous cell carcinoma and to predict the oncologic efficacy of SND in patients with node-positive neck.

Methods: A retrospective review was undertaken on 153 previously untreated patient with T1-4 SCC of oral cavity (13 cases, 22%), oropharynx (9 cases, 23%), larynx (10 cases, 25%), hypopharynx (8 cases, 20%) neck with clinically negative side neck underwent 243 SND and followed for a minimum of 2 years or until patient death at a single institute.

Results: On pathologic examination, occult positive neck node was detected in 40 (16.4%) of 243 necks in 40 patients. The primary tumor was staged as T1 (3 cases, 8%), T2 (13 cases, 32%), T3 (13 cases, 32%) and T4 (11 cases, 28%). And out of 40 patients with
occult positive neck, 15 patients (38%) underwent unilateral SND and 25 patients (62%) underwent bilateral neck dissection, ipsilateral comprehensive neck dissection and contralateral SND. Postoperative radiation therapy to the neck was administered to 31 patients (77%). Extracapsular extension of tumor was present in 5 patients (12.5%), and Overall 3 patients (8%) experienced disease recurrence in the neck. Two of these recurrences were in the side of the neck that had undergone SND, for a regional control rate of 95%. Conclusions: These results support the use of selective neck dissection for staging and treating the clinically negative neck and the possibility of applying in carefully selected patients with node-positive head and neck squamous cell carcinoma.

P060: EFFECTIVENESS OF SELECTIVE AND RADICAL NECK DISSECTION FOR REGIONAL PATHOLOGICAL LYMPHADENOPATHY AFTER CHEMORADIATION

**Authors:** Van der Putten L, G.B.van den Broek², R.de Bree¹, M.W.M.van den Brakel², A.J.M.Blom², F.J.P.Hoepbers³, P.Doormaat³, C.René Leemans³, C.R.Y.Rasch³, K.L.Palazzi-Churas¹, H.M.Geye¹, D.Khuntia¹, P.M.Harari¹

**Affiliation:** ¹University Medical Center, Amsterdam, The Netherlands; ²The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands; ³The Netherlands Cancer Institute - Hyde Park, NY

**Purpose:** The use of H&N IMRT is relatively new regarding nodal control and healing following ND. Our early experience with the technique is promising. However, long-term follow-up is crucial for establishing the role of post-IMRT selective ND. The purpose of this study is to report the perioperative outcomes of patients treated with H&N IMRT and systematic neck dissection (ND).

**Methods:** A retrospective cohort study was conducted at our institution between January 2007 and May 2019. Patients with head and neck squamous cell carcinoma who underwent IMRT and ND were included. Data was collected on demographics, tumor characteristics, treatment details, and outcomes. The primary outcome was the incidence of complications, and secondary outcomes included disease control and overall survival.

**Results:** A total of 150 patients were included in the study. The median age was 62 years (range: 21-86), and 68% of patients were male. The most common primary site was the oropharynx (42%), followed by the larynx (28%) and hypopharynx (13%). All patients received concomitant chemoradiation, with the majority of patients receiving concurrent chemotherapy. The median dose of radiation was 70 Gy to the primary site using delayed concomitant boost irradiation, with 31 patients (21%) receiving a concomitant boost to 70 Gy. The median time interval from completion of IMRT to ND was 5 months (range: 2-12 months).

**Conclusion:** The results of this study suggest that post-IMRT selective ND is a feasible and safe approach for managing regional nodal disease in patients with H&N squamous cell carcinoma. Further long-term follow-up is necessary to confirm the efficacy of this approach.

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**P060: EFFECTIVENESS OF SELECTIVE AND RADICAL NECK DISSECTION FOR REGIONAL PATHOLOGICAL LYMPHADENOPATHY AFTER CHEMORADIATION**

**Authors:** Van der Putten L, G.B.van den Broek², R.de Bree¹, M.W.M.van den Brakel², A.J.M.Blom², F.J.P.Hoepbers³, P.Doormaat³, C.René Leemans³, C.R.Y.Rasch³, K.L.Palazzi-Churas¹, H.M.Geye¹, D.Khuntia¹, P.M.Harari¹

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**Conclusion:** The results of this study suggest that post-IMRT selective ND is a feasible and safe approach for managing regional nodal disease in patients with H&N squamous cell carcinoma. Further long-term follow-up is necessary to confirm the efficacy of this approach.
We included 37 patients undergoing unilateral neck dissection. A retrospective study (median follow-up: 6.2 years) of 50 consecutive patients, who underwent a selective or (modified) radical surgical neck dissection (only) for suspected regional residual or recurrent disease after cisplatin containing concurrent chemoradiation (70 Gy). Cisplatin was administered intra-arterially 4x150mg/m² (n=21) or 3x100mg/m² i.v. (n=15) and 6mg/m² i.v. (n=14). Results: Postoperative complications occurred in 25 patients and were mostly wound related (38%) i.e. infection in 28% or delayed wound healing in 10%. Swallowing deteriorated after salvage neck dissection in 12% of the cases. In patients with complications, surgery was been more extensive (in duration and number of dissected levels) and peroperative blood loss was more pronounced (p<0.01) than in patients without complications. Wound complications appeared not to be associated with pre-operative HB value (p=0.24). Neither were pre-operative Body Mass Index (p=0.81) or serum Albumin concentration (p=0.28), which were assessed as parameters of nutritional status. No relation was observed between cisplatin dose and complication rate. Five years overall survival was 51% and was not influenced by postoperative complications. Conclusion: Complications after salvage neck dissection occur in about half of the patients and predominantly wound infections are observed. Complications are rather related to extensiveness of surgical procedure than to different chemotherapeutic regimens. Shorter and (super) selective dissections and the affected levels could reduce complication rate. In our series nutritional status and analysis of blood parameters are not decisive in identifying the patient at risk for complications after surgical surgery of the neck.

P064: DRAINAGE TIME IN RADICAL NECK DISSECTION: INFLUENCE OF TRANSOPERATIVE FLUID PERFUSION G. Duran1, F. Gallegos1, M. E. Rendón1, D. M. Hernández1, 1Hospital de Oncología, CMN SXXI. IMSS, Mexico DF, Mexico

Objective: We undertook this study to determine the impact of transoperative intravenous fluid management in patients subjected to radical neck dissection on the number of days of cervical drainage. Methods: We conducted a retrospective analysis of patients subjected to some type of radical neck dissection due to neoplasia originating in the area of the head and neck during a 2-year period. Variables analyzed were volume of blood loss, type of neck dissection, surgical time, anesthesia time, and volume of fluids administered transoperatively. Variables were correlated with the number of days that the patient remained with cervical drainage. Results: A total of 120 patients with a diagnosis of head and neck cancer were analyzed. Average age was 58.3 ± 17.3 years and 50% of the cases were males. There was no significant difference with regards to age by gender. The most frequent indications for neck dissection were thyroid cancer (36.6%), cancer of the larynx (15.8%) and cancer of the tongue (7.5%). The most frequent types of dissection were modified radical in 47 cases (39.2%), lateral in 22 cases (18.3%) and supraomohyoid in 16 cases (13.3%). Median duration of the different surgical approaches was 3 h 55 min and was related in a direct proportional manner with the type of neck dissection performed. Median anesthesia time was 4 h 30 min. Median blood loss was 278 mL (average 200 mL). In 75% of the patients, blood loss was <343 mL. Volume of blood loss was related to the volume of fluids administered (median 2.7 liters, average 1.9 liters). Classical radical dissection was performed in 13 patients in whom the median permanence of the drains was greater than in the other types of dissection, although this was not statistically significant (p = 0.08). There was no difference in the time of drain removal among the different types of neck dissection. An apparent association was found between the volume of fluids administered and the number of days that drains were in place; the greater the quantity of fluids, the greater the number of days (p = 0.001). Patients who had drain removed during the first 7 days had an average of 1500 mL infused. Patients who had an average of 3000 mL of fluid had drainage of 10 days. When the perfusion was >3000 mL or more, the majority of patients had drainage >10 days. Conclusions: The number of days of cervical drainage is associated with hospital stay and probably to postoperative complications. In the present series a statistically significant relationship was found between the quantity of fluids infused and the number of drainage days. Although there were more drainage days in those who were subjected to radical neck dissection, the difference was not significant. We did not find any correlation between number of drainage days and type of dissection. A meticulous surgical technique and an anestheisa procedure that carefully assesses fluid balance could decrease the number of drainage days.

P065: INTERNAL JUGULAR VEIN PRESERVATION IN NECK DISSECTION FOR N2A-N2B ORAL AND OROPHARYNGEAL CANCER PATIENTS E. P. Martins1, J. G. Filho1, L. G. Araújo1, J. Magrin1, P. Kowalski1, 1Hospital AC Camargo, Sao Paulo, Brazil

Objective: Lymph node metastasis is common in patients with oral and oropharyngeal squamous cell carcinoma and the radical neck dissection remains the gold standard surgical treatment. However, the morbidity of the operation is significant. The aim of this study was to evaluate the incidence and risk factors of regional recurrence in patients with N2a and N2b neck metastasis, submitted to a classic or a modified radical neck dissection with preservation of internal jugular vein. Methods: We retrospectively reviewed the medical records of 95 pN+ consecutive patients with oral and oropharyngeal squamous cell carcinoma submitted to surgical treatment from 1993 to 2002. The site of the primary tumor was the oral cavity in 46 and oropharynx in 49 cases. The clinical stage of the neck was N2a in 27 and N2b in 68 cases. There were 43 radical neck dissections and 52 modified radical neck dissections. The internal jugular vein was preserved in 29 of these. All cases were pN+. Adjuvant radiotherapy was used in 82.1% of the patients. Results: During the study period, 55.8% of the patients did show recurrence. Rates of the first regional recurrence occurred in 12 patients (12.6%). In the 95 ipsilateral neck dissections, regional recurrence occurred in 6.3% of the cases. In the 66 cases where the internal jugular vein was not preserved, regional failure occurred in 11%, and in the 29 cases where the internal jugular vein was preserved, regional failure occurred in 17 (p=0.299). Conclusion: By analyzing the results, we may consider that modified radical neck dissection with internal jugular vein preservation may be safely performed in selected patients with neck node metastasis of oral and oropharyngeal carcinoma.

P066: SHOULDER FUNCTION EVALUATION AFTER NECK DISSECTION C. B. Massini1, T. R. Rodrigues1, D. C. Giannella1, G. B. Carvalho2, L. G. Silva2, S. C. Derrani1, L. P. Kowalski2, A. L. Carvalho3, 1Universidade de São Paulo, São Paulo, Brazil, 2Hospital ACCamargo, São Paulo, Brazil; 3Hospital de Cancer de Barretos, Barretos, Brazil

During neck dissection, the shoulder is at risk to disability even when the accessory nerve is preserved. Objective: The aim of this study is to evaluate the pain and shoulder function in a prospective fashion. Methods: This is a prospective study, design to evaluated the pain, shoulder function, range of motion and middle and lower trapezius muscle strength. Patients were evaluated preoperative and postoperative (30 days) after unilateral neck dissection through the visual analogue scale for pain, Constant's Shoulder Scale, universal goniometer and muscle strength scale proposed by Kendall. Results: We included 37 patients undergoing unilateral neck dissection. The majority of the patients were males (67.6%), with ages ranging from 26 to 80 years (median, 60 years). The type of neck dissection was: selective in 76.3% of patients, modified radical in 21.6% and radical in 2.1%. The accessory nerve was preserved in 86.5% of cases. We observed a worsening of the patients in the postoperative period in all the variables measured, with 73.0% of patients presenting worsening in the pain scale, 94.6% of patients had a reduction in the Constant's score, 94.6% in the flexion of shoulder, 45.9% in extension, 94.6% in the abduction, 43.2% in external rotation, 21.6% in internal rotation, 78.4% impaired middle trapezius muscle strength and 91.6% of worsening in lower trapezius muscle strength. Conclusions: Despite the preservation of the accessory nerve during the procedure in the majority of the cases, the neck dissection caused some degree of pain and dysfunction in range of motion of the shoulder and the trapezius muscle strength in the postoperative period in almost all patients. Long-term prospective evaluations of those patients are ongoing to verify the possible return of the function after physiological rehabilitation and adaptation.

P067: SELECTIVE SURGICAL TREATMENT OF CLINICALLY AND RADIOLOGICALLY NEGATIVE NECKS WITH SENTINEL NODE BIOPSY IN HEAD AND NECK CANCER: RESULT OF A 10-YEAR EXPERIENCE H. F. Kohler1, F. M. Gripp1, E. Etchebehere1, E. Camargo2, A. Altemani1, A. N. Crespo1, 1State University of Campinas, Campinas, Brazil; 2State University of Campinas, Campinas, British Indian Ocean Territory

Background: The elective neck treatment in patients with squamous cell carcinoma (SCC) of head and neck is suitable when neck is clinically negative and probability of lymphatic metastasis is greater than 20%. However, with this criterion, up to 80% of surgical specimens will be histopathologically negative. The absence of a method that can determine
Prospective clinical study was accomplished with 17 consecutive patients with SCC of head and neck, staged as T1 (greater 3 millimeters of thickness) to T3 of oral cavity, oropharynx (T1 to well defined T3) and larynx (T1 and T2 supraglottic and T3 glottic), from May, 2005 to December, 2007. All of them were CN0, without previous treatment and radiologically negative at neck with CT scan. Injection of radiocolloid was done in four sites around the tumor. Resection of primary tumor was done first with evaluation of margins with frozen section. The neck was was exposed and controlled with GF after CT, usually two hours after the injection. All neck levels were studied during surgery with GF. Usually 2.5 lymph nodes per patient were detected with gamma probe intraoperatively. Ressected SLN was directed for conventional histopathological analysis with hematoxilin-eosin staining, step serial section, and immunohistochemistry evaluation. In the presence of adverse prognostic factors, primary tumor, or multiple metastatic lymph nodes or extracapsular spread (ECS), SLNs were submitted to rapid frozen section (RT) with or without chemotherapy. Subjects were followed after surgery monthly with clinical exam and half-yearly with neck CT scan in the first two years. Only patients with at least one year of follow-up were included.

Results: Neck recurrence rate was 5.9% (1/17). Five out of 17 patients (29%) were sentinel node positive, four of whom were classified as N1 and one as M2B. The average follow up time was 18 months, with a range from 12 to 30 months. Ten patients were submitted to adjuvant RT because multiple metastases or ECS in SLN or presence of perineural or vascular invasion. Four of them were also submitted to chemotherapy because the presence of ECS. The only patient that recurred was SLN negative without adverse factors in primary tumor. Conclusion: Neck recurrence after selective treatment of neck with SNB was of 5.9%.

P068: THE USE OF AUTOLOGOUS PLATELET AND PLASMA PRODUCTS FOLLOWING SALVAGE NECK DISSECTIONS

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Background: Patients undergoing primary chemoradiotherapy or radiotherapy for advanced head and neck mucosal cancers often require salvage neck dissections. Early wound complications and late neck fibrosis are concerns following surgery in these patients. As well, prolonged wound drainage and lack of tissue adhesion may delay wound healing. Autologous fibrin and thrombin can provide the adhesive qualities for healing the SAN.

Methods: Patients undergoing neck dissection for cervical metastases without primary site resections were selected for this study. Patients considered to be at higher risk of wound problems were treated with APA. The APA was derived and processed at the time of surgery from 60cc of the patient’s own blood and applied to the neck dissection wound immediately prior to skin closure. Post-operative wound drainage, complications, and length of hospital stay were compared with neck dissection patients who underwent standard wound closures without use of APA. The long-term post-operative cervical skin fibrosis was quantified in the neck dissection patients using the Cutometer MPA 580 by a blinded examiner. Validated parameters labeled “R2” and “F0” were compared between the two cohorts. Results: Twenty-six patients undergoing 31 neck dissections were included in this study. The mean follow-up time was 12 months. Sixteen patients used in 12 neck dissections were compared to 14 patients who did not receive APA. A statistically significant difference (p = 0.03) was seen in the postoperative drainage (APA: 253cc vs. no APA: 345). Furthermore, the average length of stay for the APA group was 3.13 days vs. 3.86 for the control group (p = 0.004). The Cytomter detected a significant difference in skin visco-elasticity between the study group (R2 = 0.86, F0 = 13.13) and the control group (R2 = 0.77, F0 = 15.98) (p = 0.05, p = 0.05). Conclusion: The application of APA in neck dissections resulted in decreased post-operative drainage, length of stay in hospital and neck skin fibrosis. The potential benefits of these products warrants further investigation.

P069: WITHDRAWN

P070: SURGICAL ANATOMY OF THE SPINAL ACCESSORY NERVE (SAN) IN THE UPPER NECK: DEFINITION OF LEVEL IIb

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Objective: This study was conducted to identify the anatomical variations of spinal accessory nerve (SAN) in the upper neck, the landmark of anterior and inferior border of level neck IIb (Submuscular recess) and evaluate its effect upon the border and the number of lymph nodes (LN) in level IIb.

Methods: Between January 2006 and June 2007, 76 previously untreated consecutive patients with head and neck cancer, who underwent neck dissection (ND) were prospectively enrolled into this study. There were 57 males and 19 females (mean, 61.1 years). In 76 patients, 110 NDs were performed (42 unilateral and 34 bilateral). The relationship between the SAN and the adjacent structure (Internal jugular vein (IJV), Sternocleidomastoid muscle (SCM), Clavicular head of LNs) in level IIb were investigated. Results: SAN crossed the UV ventrally in 36 (32.7%), and dorsally in 68 (61.8%) and passed through the UV in 6 (5.5%). SAN ran along the inner surface of SCM and made branch to the SCM without penetration of the muscle in 44 (49.5%) while 61 (55%) gave branch to the SCM by penetration. Cervical roots contribution to SAN was seen from C2 in 58 (92.2%) and C2 & C3 in 43 (69.1%), but the other 9 (8.2%) did not have any contribution from C2. Relationship between SAN with UV, SCM, and cervical roots were bilaterally symmetric in 85.3%, 82.4%, and 73.5%, respectively. The mean number of LNs of level IIa and level IIb was 6.7 and 8.5 in cases where SAN crossed UV ventrally, and 6.9 and 5.5 in dorsally crossing cases. Portion of LN number consisting level IIb out of total LN number in level II was 56.7% in ventrally crossing cases and 44.2% in dorsally crossing cases. Conclusions: In this study, diverse anatomical variations of SAN in the upper neck region were observed, and different from the previous studies, SAN crossing the UV dorsally (61.8%) was more found than crossing ventrally. Since anterior and inferior border of level IIb depends on the course of SAN, one should consider that level IIb would be defined as more broad group, if the nerve courses leaning towards to ventral side, SAN ran along the inner surface of SCM without penetration (44.5%), and there were variety of cervical roots contributions along its course, thus one must be aware of these anatomical variations and should perform meticulous dissection to minimize the risk of injuring the SAN.
could then be analyzed and classified with Sunderland’s nerve injury classification with possible determination of potential nerve recovery. Results: The Dissector Plasmaknife required minimal training to establish operative use, very similar to monopolar electrosurgery. The set up process was similar to electrosurgery instrumentation. All nerve specimens were successfully dissected and removed safely. No thermal damage or neural damage was noted from the forty sciatic nerve specimen submitted to pathology. No major pathological differences were noted in the two dissecting techniques. Conclusions: Use of the Gyrus Dissector Plasmaknife in nerve dissection appears to be a safe and effective alternative to conventional methods. This technique also centers on some advantages over conventional methods with the ability to simultaneously cut and coagulate tissue with minimal thermal spread and minimal damage to adjacent innocent tissues.

P072: EARLY IDENTIFICATION AND MANAGEMENT OF CAROTID BLOWOUT IN ADVANCED HEAD AND NECK CANCER PATIENTS

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Objective: Carotid blowout (CB) is a devastating complication of recurrent head and neck cancer and its aggressive treatment. Little data exist predicting patients at risk for CB, evaluating preventive management strategies, or treating CB within 6 months of reirradiation. In this investigation we sought to determine the rates of CB in a prospective cohort undergoing concurrent chemotherapy and reirradiation. Furthermore, we sought to define predictive factors and management strategies for CB. Methods: 1) Retrospective review of patients experiencing CB in a prospective phase II protocol of induction chemotherapy with pemetrexed and gemcitabine followed by possible resection followed by concurrent carboplatin/pemetrexed and daily radiotherapy for previously radiated patients with recurrent or second primary head and neck cancer (“Pem/Gem”); and 2) retrospective review of hospital records to identify additional head and neck cancer patients who suffered CB. Results: Nine of 35 Pem/Gem patients (25%) suffered rupture of the carotid artery or one of its named branches within one year following chemotherapy and reirradiation. Timing of CB was during treatment (1), within 6 months (4), and 6-12 months (4). Five of the 9 patients with CB survived. Eighteen of the 35 patients treated on Pem/Gem survived > 6 months following reirradiation, with 6 (33%) of these experiencing and surviving CB. Neither post-induction tumor resection nor post-reirradiation surgical intervention correlated with CB or time to CB. Pre-reirradiation involvement of the carotid or major branches on CT scan did not correlate with CB. However, 4 of 5 patients with CB within 6 months of reirradiation had contiguous involvement of the thyroid cartilage and carotid artery on pre-reirradiation CT compared with none of the late CB and only 1 of 12 patients who survived > 6 months without CB. Hospital records identified an additional 7 patients with CB, 5 of whom survived. Examining all 16 patients with CB, 12 (75%), had been reirradiated and 9 (56%) had localized infection. Furthermore, mechanical trauma to the carotid from the devitalized thyroid cartilage was confirmed at surgery in 2 patients (13%) and suspected in an additional 4 (26%). Management of CB included four treated with surgical ligation of the artery (2 [50%] survived), 8 treated with embolization (all survived), and 4 received no treatment (all died). Of the 10 patients who survived, 3 (33%) suffered labile blood pressure with suspected baroreflex failure and 1 (10%) suffered stroke. Conclusions: Patients undergoing reirradiation are at risk for CB. Contiguous involvement of the carotid and thyroid cartilage on pre-treatment CT scan may predict for early CB. Mechanical trauma to the carotid by the thyroid cartilage in the setting of local infection/necrosis or tumor may play a role in the pathogenesis of CB. Patients who underwent surgical intervention did worse compared to endovascular management. Despite its devastating nature, CB is not necessarily a terminal event. Based on these results we advocate careful attention to the carotid in recurrent head and neck cancer patients, including early test balloon occlusion and intervention in patients at high risk for rupture.

P073: THE CLINICAL EFFICACY OF ENDOVASCULAR MANAGEMENT OF CAROTID BLOWOUT SYNDROME IN HEAD AND NECK CANCER PATIENTS

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Objective: Carotid blowout syndrome (CBS) is one of the most devastating complications associated with therapy for head and neck cancers (HNC). Endovascular treatment have been used in the patients with CBS because surgical management of CBS is usually difficult on the previously irradiated or infected fields. The purpose of this study was to evaluate the efficacy of endovascular treatments of CBS in 16 patients with HNC in a clinician’s perspective. Methods: This retrospective study reviewed 16 HNC patients with CBS on their clinical, treatment, and outcome data. All patients underwent permanent embolization or revascularization with covered stent graft of the affected carotid artery, and the efficacy was evaluated. Results: All patients received multimodality treatments including radiation therapy with a mean total dose of 78.5 Gy. CBS was caused by direct carotid invasion of persistent or recurrent tumors in 8 patients and pharyngocutaneous fistula in 7 patients and laryngeal chondroradionecrosis in 1. External and common carotid arteries were most common rupture sites of CBS, which were occluded by embolization in 11 patients and revascularized by covered stent placement in 5 patients. Immediate hemostasis was achieved in all patients; however 7 patients had recurrent CBS, all of whom were retreated effectively by endovascular management. Three patients had a stroke and four had extrusion of intervention materials from infected wounds. Most patients died of tumor progression with a mean survival time of 5 months from initial CBS and only two patients survived. Conclusion: The endovascular therapy of both permanent occlusion and stent graft in the HNC patients with CBS may be effective in arresting carotid hemorrhage. However, re-bleeding and complication rates were significant because of poor infected wounds and tumor progression. The long-term efficacy may not be high in these HNC patients with poor survival outcomes, particularly those with infected wounds.

P074: EXTRUSION OF EMBOLIZATION COILS THROUGH THE CAROTID ARTERY IN A HEAVILY RADIATED NECK

H.T.Nguyen1, H.W Lin1, J.D Richmon1, D.G.Deschler1, Massachusetts Eye and Ear Infirmary, Boston, MA

Objective: To present a rare complication of embolization coil extrusion through the carotid artery and into pharyngeal soft tissue in the setting of severe soft tissue radionecrosis. Methods: Case review and a review of the literature. Results: We describe a case of a 55 year old man with massive bleeding from the oral cavity as a result of right external carotid artery erosion following two rounds of radiation for a tongue base squamous cell carcinoma and a subsequent transglottic primary requiring total laryngectomy. Intraoperative frozen section of the tongue base revealed only necrotic inflammation, and no bleeding source was identified. With continued intermittent and acute oral bleeding, the patient underwent an uncomplicated coil embolization of the right internal, external and common carotid arteries. Subsequently, however, the patient developed spiking fevers, and imaging demonstrated edematous changes surrounding the coil sites. An exploration of the neck revealed significant extrusion of embolization coils out of the internal carotid artery and into the soft tissues of the neck and pharynx, and consequently an en bloc resection of the internal and external carotid arteries, the internal jugular vein, and the vagus nerve was performed. In addition, a formalized pharyngocutaneous fistula was created for salivary diversion. An ensuing episode of acute hemorrhage from the proximal carotid stump, however, required emergent endovascular stenting of the innominate artery and pectoralis major soft tissue coverage to control the bleeding. A review of the literature on arterial embolization reveals coil extrusion to be a rare and potentially life-threatening complication. Conclusions: We report an unusual case of embolization coil extrusion through the carotid artery in the context of widespread radionecrosis. Although the incidence of coil extrusion is remarkably low with few cases reported in the literature, a high index of suspicion should be maintained in the setting of significant soft tissue necrosis and spiking temperatures. Appropriate management requires early recognition and proper removal of foreign material with wound stabilization.

ORAL CAVITY I

P075: QUALITY ASSURANCE MEASURES IN PATIENTS TREATED FOR EARLY ORAL TONGUE CANCER

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Objective: In head and neck oncology there is a lack of systematic evidence-based data upon which to standardize quality parameters; and it is not clear how these parameters are relevant to outcome measures such as survival. For oral tongue cancer, there is a need to identify parameters that provide a basis for standardization and allowing for the comparison between providers and defining quality indicators that have an overall impact on patient’s outcome. This study aimed to identify
POSTERS

P076: SQUAMOUS CELL CARCINOMA OF THE FLOOR OF MOUTH: OUTCOMES AND PROGNOSTIC INDICATORS

Objective: To review treatment outcomes and prognostic indicators of survival in squamous cell carcinoma of the floor of mouth. Methods: A 10-year retrospective chart review (1994-2004) identified 142 patients with previously untreated squamous cell carcinoma of the floor of mouthtreated with curative intent at the Princess Margaret Hospital. Descriptive statistics, Kaplan-Meier estimates and the log-rank test were used to determine statistical significance. Results: The overall 5-year survival rate was 68%. Five-year cause specific survival was 80%. Death due to floor of mouth disease was 14%. Failure occurred in 24 patients (17%). Regional failure was most common at 12%, followed by local (9%) and distant failure (2%). Second primary cancers occurred in 18%. On univariable analysis male gender, advanced pathologic TN stage, extracapsular spread, and tumour thickness >5 mm were statistically significant prognostic indicators of reduced 5-year survival. Conclusions: Over the last decade there has been a trend toward more aggressive management of the neck and improved local, regional and distant failure rates.

P077: DOES THE NUMBER OF LYMPH NODES HARVESTED DURING NECK DISSECTION AFFECT SURVIVAL IN ORAL TONGUE CARCINOMA?

Objective: To evaluate the relationship between the number of lymph nodes harvested during neck dissection and survival. Methods: Forty-seven patients with a primary diagnosis of oral tongue squamous cell carcinoma treated consecutively from 2004-2007 were included in the study. Pathology reports were retrospectively analyzed to assess the number of lymph nodes harvested during neck dissection, which was related to patient outcomes. Cox proportional hazards models and Kaplan-Meier was used to evaluate survival. Results: Overall 3-year survival rate was 81.2%. TNM stage distribution was stage I, 19.1%, II, 14.9%, III, 17.0%, and stage IV, 48.9%. All deaths were due to oral can- cer and occurred in the stage IV group (7/47, 14.9%). The results of a Cox proportional hazards model revealed no significant association between the total number of lymph nodes harvested and patient survival (p=0.94, 95% CI 0.97-1.03). Among patients with at least 10, 20 or 30 nodes harvested, the 3-yr survival was 78.4%, 81.1% and 77.3%. Corresponding rates among patients with fewer than 10, 20, or 30 nodes harvested was 100%, 81.8% and 84.2% respectively. Five patients had <10 lymph nodes harvested, with no patients dying from disease as compared to seven of forty-two patients (16.7%) dying of disease with >10 lymph nodes harvested. Neck dissections with less than 20 lymph nodes harvested were noted in 12 patients with two patients dying from oral cancer over a 3-year period. Neck dissections with greater than 20 lymph nodes harvested were observed in 35 patients with 5 deaths occurring in this group. Less than 30 lymph nodes harvested was seen in 22 patients, which was associated with 3 deaths and greater than 30 lymph nodes harvested were observed in 25 patients with 4 deaths reported. There was no statistically significant difference in survival between all three groups with p-values of 0.29, 0.79, and 0.67. In contrast, the number of positive lymph nodes was significantly associated with worse survival (p-value<0.001, 95% CI, 1.33-2.80). This model suggests a doubling of the risk of death for each additional positive node. Furthermore, the presence of any positive lymph nodes trended toward significance, with 21 patients having N0 pathologic necks with only 1 death at 3 years (94.7% 3-yr survival) as compared to 26 patients with N+ disease accounting for 6 deaths with a 3-yr survival of 69.2% (p-value=0.07). Tumor stage and grade were also statistically significant factors in affecting overall survival. Patients with stage I and II disease had 100% 3-yr survival compared to 70.1% for stage III and IV disease (p=0.03). Histologic grade was noted to be significant with a 100% survival in patients with grade 1, 2 disease as compared to 71.3% for grade 3, 4 histology (p=0.04). Conclusions: Total number of lymph nodes harvested during standard oncologic neck dissection does not appear to affect overall patient survival with oral tongue carcinoma.

P078: ELECTIVE NECK DISSECTION (END) VERSUS SAME-DAY SENTINEL LYMPH NODE BIOPSY (SLNB) IN MANAGEMENT OF NO STAGE LIP CANCER

Introduction: The most reliable method in detecting cervical lymph node (CLN) micrometastases in NO-stage lip cancer is (EBND). Since the risk of the micrometastases is around 20%, EBND is an over-treatment in majority of patients. This study examines the role of SLNB in accurate staging as a same-day procedure. Material and Methods: Twenty-eight patients with T1-T2 lip cancer were studied (19 men and 9 women, median age: 57 years, range: 34-65 years). All patients underwent Vexcision of primary lesion with primary closure. Patients with stage I and II disease had 100% 3-yr survival compared to 70.1% for stage III and IV disease (p=0.03). Histologic grade was noted to be significant with a 100% survival in patients with grade 1, 2 disease as compared to 71.3% for grade 3, 4 histology (p=0.04). Conclusions: Total number of lymph nodes harvested during standard oncologic neck dissection does not appear to affect overall patient survival with oral tongue carcinoma.
Background: One of the controversies in sentinel lymph node (SLN) biopsy is the definition of micrometastases (MMs) and isolated tumour cells (ITCs) and their clinical importance in terms of the need for further neck dissection. We have previously designated all viable metastases in the neck dissection specimen, regardless of size. However, this poses significant interpretive problems for the pathologist. The UICC/TNM classification sets a minimum size for MMs as 0.2mm, below which the deposit is labelled as ITC. Aim: We have compared the UICC/TNM definition of MMs and ITCs with our previously published sentinel node protocol to assess how the adoption of the UICC/TNM criteria would affect the staging of micrometastatic disease in the neck.

Material and Methods: Ninety nine SLNs from 46 patients were examined in a stepwise manner as outlined in previous publications. The histological findings were reassessed by using the UICC/TNM definitions for MMs and ITCs. Results: The initial node excision at 2.5 mm intervals revealed a metastasis in 57 SLNs from 24 patients. Using the TNM definitions, seven of these patients (8 SLNs), had micrometastases (0.2 - 2.0 mm), only one of which had additional metastases in the neck dissection specimen. Additional work-up at 150 um intervals and cytokeratin staining was carried out for 21 patients (42 SLNs). Using the TNM definitions, the examination revealed micrometastases in 17 patients (17 SLNs). Five of the six patients with micrometastases had a neck dissection, all showing other metastases in the rest of the neck dissection. Five patients had ITCs only, and one had metastases in a non-SLN of the subsequent neck dissection specimens. Conclusion: The UICC/TNM classification provides an objective, uniform method of detecting micrometastases and ITCs. Metastases in other non-SLNs were common when a micrometastasis was detected in a SLN, indicating need for further treatment of the neck. When only ITCs were found in a SLN, the likelihood for other metastases was low. A larger study is required to establish the use of these definitions and delineate an acceptable level of wrongly down-staged ITC patients who have other metastatic neck disease.

P080: WITHDRAWN

P081: DISTRIBUTION OF INTRA-ORAL SQUAMOUS CELL CARCINOMA: A REVIEW OF 100 CASES FROM THE REGIONAL UNIT OF NORTHERN IRELAND S.Dustagheer1, M.H.Basheer1, C.Semple1, A.Songra1, D.Gordon1, 1Plastic and Maxillofacial Service, Belfast, United Kingdom

Objective: We reviewed a cross sectional sample of 100 cases of intra-oral SCC that were managed in our regional referral centre. The patients who had disease that was amenable to surgical resection. The purpose was to use the standard mouth map as a visual representation to demonstrate topographical distribution and supplement available data on this subject. Methods: Retrospective data review was carried out from the medical notes. Information on demographics and histological diagnosis was retrieved. The staging and locations of these intra-oral lesions had been recorded on mouth charts at the time of examination under anesthesia by our senior author in all patients within this study. These were compiled electronically to generate a pictorial summary. Results: The wet tumor mass at the lips to 8.5 mm anterior inferior pillars, including hard and soft palate, and anterior two thirds of the tongue. From the data collected, a color coded distribution and frequency mouth map was created. Squamous cell carcinoma was the most common histological type of carcinoma observed in all the sites with the tongue being the commonest site. We further discuss data available. Conclusions: The basic patterns emerging in the paper are consistent with expectations from published data. Comparative studies and their findings are discussed. Our study confirms that the mouth map is a useful tool to illustrate patterns the disease.

P082: TREATING ADVANCED ORAL CAVITY VERRUCOUS CARCINOMA WITH CHEMORADIOTHERAPY: SHOULD NON-TRADITIONAL TREATMENTS BE REVISITED? S.H.Patel1, K.Putyinia1, 1University of Illinois at Chicago, Chicago, IL

Objectives: We present a case of a patient with locally advanced oral cavity verrucous carcinoma. Due to the advanced nature of the presenting disease we were motivated to explore non-surgical treatment options. Thus we reviewed these options and employed a chemoradiotherapy regimen for our patient and assessed the subsequent response. We also review the literature regarding treatment of head and neck verrucous squamous cell carcinoma in the context of non-surgical treatments. Methods: Description of the clinical course of a 51-year-old African American male with oral cavity (hard palate) T4 NO MO verrucous carcinoma treated with induction chemotherapy and subsequent concurrent chemoradiation is presented, along with a review of the literature concerning the treatment of head and neck verrucous squamous cell carcinoma. Results: Chemoradiotherapy was decided to be this patient’s best treatment option as his surgical resection would have included bilateral total maxillectomies. After diagnosis and negative metastatic workup, our patient underwent treatment with induction intravenous chemotherapy using 2 cycles, 21 days apart, consisting of 5-fluorouracil and cisplatin. Of importance to this significant, our patient had dramatic, near complete resolution of his tumor mass after the induction chemotherapy alone. He then underwent concurrent chemoradiation with radiation therapy. Approximately 2 months after completion of treatment he underwent palate biopsies of his primary site along with a unilateral selective neck dissection for questionable pre-treatment nodal disease. Both specimens were negative for malignancy. To this date, 4 months from completion of treatment, the patient is free of recurrence. We also review and discuss the findings present in the current literature on the treatment of verrucous carcinoma of the head and neck. Included in this discussion are the clinical presentation, histopathological findings, and the ongoing controversy regarding the optimum treatment of verrucous carcinoma. We also review the limited literature on the use of chemoradiotherapy in treatment regimens for verrucous carcinoma.

Conclusions: We present a case of successful complete response of advanced oral cavity verrucous carcinoma using induction chemotherapy followed by concurrent chemoradiotherapy and radiation therapy. Our patient had a near complete response after induction chemotherapy alone and after completion of his treatment has excellent functional results and is free of recurrence. The treatment regimen outlined for this patient is contrary to the majority of the literature, which advocates surgical resection in treating oral cavity verrucous carcinoma. We propose that this regimen be strongly considered in patients whose surgical morbidity and functional deficits would be extensive, in “unresectable” patients, in patients who refuse surgery or in patients who are poor surgical candidates. An expanded study with higher power would be recommended to confirm the results of this case report.

P083: PATTERN OF INVASION - AN INDEPENDENT ROBUST PROGNOSTIC INDICATOR IN ORAL SQUAMOUS CELL CARCINOMAS R.Jain1, P.Trivedi1, 1The Gujarat Cancer & Research Institute, Ahmedabad, India

Objective: The Pattern of tumor invasion is reported to be an important predictor of recurrence and survival in surgically treated head & neck squamous cell carcinoma. In this study we have retrospectively assessed the significance of this prognostic indicator in a relatively homogeneous population of squamous cell carcinomas. Methods: The retrospective study was confined to 128 previously untreated patients who had surgery for squamous cell carcinoma of the oral tongue between 2002 and 2004. There were 89 men and 39 women who ranged in age from 20 to 78 years (median 46.5 years). All the patients underwent radical surgical resection of the primary tumor i.e. Hemiglossectomy (120 cases) with curative intent or partial Glossectomy (8 cases) with immediate reconstruction using skin graft, myocutaneous flaps, or free flaps. Classical (38 cases) or modified (85 cases) radical neck dissection was performed in all patients with clinically positive neck nodes and no node dissection was done in 5 cases. Histology slides of tumor were reviewed in all the cases and pattern of invasion was evaluated and graded from 1 to 4, varying from consistently well defined pushing border (Grade 1) to diffuse infiltration and cellular dissociation (Grade 4). Results: With higher grades of infiltration (Grade 3 or 4; 109 patients), the tumors tended to be larger (p=0.031). The nodal involvement was significantly greater in those with grade 3 or 4 patterns (p=0.05). There was a significant increase in the incidence of local, nodal and distal recurrence in patients with high grade invasive patterns (p=0.025). The Pattern of Invasion strongly related with group stage, with increase in stage with invasive grade (p=0.035). It also related well with the Broder’s / WHO grading (p=0.028), Broder’s / WHO grade increasing with increasing grade. Cumulative Disease Free Survival was significantly reduced when the Pattern of Invasion was of higher grade on Univariate and multivariate analysis (p=0.014) & (p=0.002) respectively. Conclusion: Pattern of Invasion correlates well to the variables with previously reported high prognostic values and when used alone is a robust prognostic indicator in oral squamous cell carcinomas.

P084: THE TREATMENT RESULT OF POSTOPERATIVE RADIO- THERAPY ON INTERMEDIATE RISK ORAL SQUAMOUS CELL CARCINOMA T.Fang1, K.Fan1, S.Huang1, H.Wang2, E.Y.Chen1, 1Guzhang Cancer Research Institute, China

Objective: The Pattern of tumor invasion is reported to be an important predictor of recurrence and survival in surgically treated head & neck squamous cell carcinoma. In this study we have retrospectively assessed the significance of this prognostic indicator in a relatively homogeneous population of squamous cell carcinomas. Methods: The retrospective study was confined to 128 previously untreated patients who had surgery for squamous cell carcinoma of the oral tongue between 2002 and 2004. There were 89 men and 39 women who ranged in age from 20 to 78 years (median 46.5 years). All the patients underwent radical surgical resection of the primary tumor i.e. Hemiglossectomy (120 cases) with curative intent or partial Glossectomy (8 cases) with immediate reconstruction using skin graft, myocutaneous flaps, or free flaps. Classical (38 cases) or modified (85 cases) radical neck dissection was performed in all patients with clinically positive neck nodes and no node dissection was done in 5 cases. Histology slides of tumor were reviewed in all the cases and pattern of invasion was evaluated and graded from 1 to 4, varying from consistently well defined pushing border (Grade 1) to diffuse infiltration and cellular dissociation (Grade 4). Results: With higher grades of infiltration (Grade 3 or 4; 109 patients), the tumors tended to be larger (p=0.031). The nodal involvement was significantly greater in those with grade 3 or 4 patterns (p=0.05). There was a significant increase in the incidence of local, nodal and distal recurrence in patients with high grade invasive patterns (p=0.025). The Pattern of Invasion strongly related with group stage, with increase in stage with invasive grade (p=0.035). It also related well with the Broder’s / WHO grading (p=0.028), Broder’s / WHO grade increasing with increasing grade. Cumulative Disease Free Survival was significantly reduced when the Pattern of Invasion was of higher grade on Univariate and multivariate analysis (p=0.014) & (p=0.002) respectively. Conclusion: Pattern of Invasion correlates well to the variables with previously reported high prognostic values and when used alone is a robust prognostic indicator in oral squamous cell carcinomas.
To investigate the treatment result and dose response on post-
Recently new concepts for the treatment of oral squamous
2005, 302 patients of OSCC who was treated by radical surgery and PORT. Patients were classified as intermediate risk group when the risk fac-
tor(s) listed below was found in pathologic samples: 2002 AJCC stage III or IV, presence of perineural spread or vascular invasion, or negative sur-
gical margin with a distance < 3 mm. Patients with multiple nodal meta-
tases, positive surgical margin, or extracapsular spreading were excluded.
According to our treatment guideline, these patients were indicated to receive PORT. The prescribed dose of PORT ranged from 59.4 to 66.6 Gy (median: 63 Gy). The median follow-up period was 39.2 months (range: 2-
83 months). Results: The 3-year overall and recurrence-free survival rates for all patients were 73% and 70%, respectively. Univariate analysis revealed that differentiation and perineural spread, lymphovascular inva-
sion, bone invasion, vascular invasion (lip, hand palms, and cricoarytenoid trage), invasion depth 267 10mm, and margin distance 266 4mm were the signif-
ificant prognostic factors (p < 0.05). Radiation dose 267 63 Gy possessed borderline significance (p = 0.07) with an inferior recurrence-free survival. Besides, we also found that presence of multiple significant factors of un-
ivariate analysis correlated with disease recurrence (p < 0.001). Recurrence rate increased with the number of risk factors. The 3-year recurrence-free survival rates were 82%, 76%, and 45% for patients with no, 1 or 2 risk factors and 3 or more risk factors, respectively. After multivariate analysis, number of risk factors and lymphovascular invasion were found to be sig-
nificant prognostic factors (p < 0.001). Conclusion: Our analysis indicat-
ed that PORT is an effective treatment for intermediate risk OSCC patients who required radical surgery. Presence of multiple risk factors and lymphovascular invasion correlated with poor prognosis. Dose modification could not decrease the disease recurrence rate. Concurrent chemotherapy should be consi-
ered if there were 3 or more risk factors of recurrence.

**P085: RESULTS OF THE TREATMENT OF 136 PATIENTS UNDER-
WENT MAJOR GLOSETOMY**

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Objectives: Advanced cancers of the oral cavity continue to be a thera-
papeutic challenge. Despite significant improvements in radiation therapy
techniques and adjuvant chemotherapy, patients usually die after a short
period. Recent progress in reconstructive techniques has made major glos-
sectomy (subtotal, near total, total or extended total) a reasonable palliative
and potentially curative approach. This report presents the experience of a
single institution in the treatment of patients with advanced squamous cell
carcinoma of the oral cavity submitted to major glossectomy. Methods: A
total of 136 patients with advanced squamous cell carcinoma of the oral
cavity who underwent primary major glossectomy from 1985 to 2005 were
analysed. Ages ranged from 18 to 76 years (median, 54 years). There
were 119 men (86%) and 17 women (14%). Primary tumor sites were oral
tongue (66 cases), base of the tongue (31 cases), floor of the mouth (34
cases) and other parts of the mouth (5 cases). Tumor stages were: 38 T2,
98 T4, 44 N0, 32 N1, 50 N2a-c, and 10 N3. The types of glossectomy were as follows: 24 subtotal, 41 near total and 71 total. A neck dissection
was performed in all patients. One hundred and fourteen patients were
reconstructed with pectoralis major myocutaneous flap, 12 with microvas-
cular free flaps and 8 with other flaps. Results: The mean duration of hos-
pital stay was 10 days (ranging from 1 to 162 days). Postoperative complica-
tions occurred in 65%(8). The most common complications were wound
infection (31 patients) and fistula (18 patients). At the study closing
date, 11 patients were alive without disease, 89 died of cancer, 24 died of
causes not related to cancer or treatment and 5 were lost to follow-up.
The disease specific survival rates at 2 and 5 years were 39% and 32%,
respectively. No significant difference was observed related gender, age, stages T and N, and presence previous treatment.

Conclusions: Major glossectomy can be performed safely in a select
group of patients with advanced tongue and floor of the mouth cancer with
acceptable morbidity and survival rates, being the most important postop-
erative complications the presence of wound infection and fistula.

**P086: LONG-TERM SURVIVAL IN PATIENT WITH ORAL SCC:
RESULTS OF A PROSPECTIVE STUDY OF ADJUVANT AND NEOADJUVANT THERAPIES**

P.A. Kessler1, A. Bloch-Birnholz2

G.G. Grabenbauer2, F.W. Neujam2, R. Sauer2, 1University of Maastricht, Maastricht, The Netherlands; 2University of Erlangen, Erlangen, Germany

Introduction: Recently new concepts for the treatment of oral squamous
cell carcinomas (SCC) have been developed, which include preoperative
simultaneous neoadjuvant radiochemotherapy (RCT) and one stage opera-
tion with excision of the tumour and reconstruction. When we consider long-
term survival, we find substantial evidence that combined treatment based
on neoadjuvant RCT is superior to adjuvant treatment including operation
and postoperative radiation. Patients and Methods: We studied two
groups consisting of 74 patients given neoadjuvant treatment and 54 treat-
ed surgically. Ninety-nine patients suffered from stage III and IV diseases
according to the UICC criteria. Long-term survival was estimated by the
Kaplan-Meier method. Results: Neoadjuvant treatment increased the
prospect of a long term survival free of tumour. Kaplan-Meier curves esti-
mated a 5-year tumour-free survival in oral SCC category T1 as 83% in the
neoadjuvant group and 70% in the adjuvant group; the corresponding fig-
ures for T2 were 79% and 57%, for T3 68% and 33% and for T4 51% and
30% respectively. The difference for T1, T2 and T4 tumours was signifi-
cant. The preoperative radio- and chemotherapy were shown to be effec-
tive by the fact that pathohistologically resection specimens were free of
tumour in 28 patients in the neoadjuvant group. Four patients died during
the preoperative combination treatment. Of the patients in the adjuvant
group 65% and in the neoadjuvant group 72% survived the observation
period. Conclusion: The neoadjuvant treatment results in better 5-years-sur-

vival rate. However, adjuvant treatment. Moreover, patients must be selected care-
fully. A randomisation seems not to be possible.

**P087: COMBINED SURGERY AND POST OPERATIVE RADIATION
IN HIGH RISK EARLY T STAGE ORAL TONGUE CANCER**

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Objectives: Factors associated with adverse prognosis in early T stage
squamous cell carcinoma oral tongue (SCCOT) include; large tumour size,
high grade, tumour thickness > 5 mm, perineural infiltration, lymphovas-
cular invasion, positive surgical margins and neck node metastasis. While surg-
ery is the mainstay of treatment the role of post operative radiotherapy
(PORT) continues to evolve. In this study we examine the prognostic factors and
determine survival following combined surgery and PORT in high risk
early T stage SCCOT. Patients and Methods: Between November 2004 and Febru-
ary 2007, 37 patients with T1 or T2 oral tongue squamous cell carcinoma were
treated with combined surgery and PORT at Shaukat Khanum Memorial Hospital and Research Centre. There were 19 (51%) males and 18 (49%) female patients. The median age of the group was 49 years (range 16–65 years). Pathological tumor stages were T1N0 16%,
T1Np+ 22%, T2N0 30% and T2Np+ 32%. Tumors were staged according to the AJCC 6th edition (American Joint Commission on Cancer). Partial glossectomy was done with marginal clearance of 1 cm all around the
tumour. Selective neck dissection was done in patients with N0 disease.
Tumour close to or involving the midline required bilateral neck dissec-
tion. Radiation dose was 2.0 Gy per fraction, once a day, 5 days a week to a
total dose of 60 - 66 Gy in 30 – 33 fractions. Results: Kaplan Meier esti-
mates for 3 year disease free survival (DFS) is 67%. Positive neck nodule dis-
aease had a negative influence on survival, 3 year DFS for patients with N0
versus > N+ disease was 93% and 44% respectively (p=0.005). At the time
of last follow up 10 patients (26%) have failed treatment; local 5%, regional
16% and distant metastasis in 3% patients. All patients with recurrence
have died of their disease. On univariate analysis surgical margins (< 2 mm
vs > 2 mm) p=0.03, tumour thickness (< 5mm vs > 5 mm) p=0.04, grade
well vs moderate vs poor vs) p=0.0001 and N stage (N0 vs N+ p=0.001)
were significant prognostic factors influencing survival. Lymphovascular
invasion p=0.64, perineural infiltration p=0.12, and T stage (T1 vs T2
p=0.93 were not significantly associated with survival. On multivariate
analysis the only significant prognostic factor was tumour grade. The risk of
failure in patients with poorly differentiated tumours was significantly high-
er (hazard ratio [HR], 8.7; 95% confidence interval [CI] 2.0 to 37.8;
p=0.003). Conclusion: Survival of patients with high grade tumours and
neck nodal metastasis in SCCOT following surgery and PORT is poor.
Concurrent chemoradiation should be routinely considered for these patients.

**P088: WHEN DOES SKIN EXCISION ACHIEVE AN ADEQUATE**

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LOCAL CONTROL RATE OF SQUAMOUS CELL CARCINOMA IN INVOLVING THE BUCCAL MUCOSA? C. Liao1, T. Yen1, S. Huang2, 1Chen2, J.T. Chang2, H. Wang2, S. Na2, C. Tsuei2, L. Lee1, C. Huang2, 1Chang Gung Memorial Hospital, Taoyuan, Taiwan Republic of China; 2Chang Gung Memorial Hospital, Taoyuan, Taiwan Republic of China

Objective of the Study: We hypothesized that, in patients with buccal mucosa squamous cell carcinoma (BSCC), skin excision would improve the 5-year local control rate when the distance between the invasive front of the tumor and the skin is 03C 13 mm as determined by imaging. We undertook this study to test this hypothesis. Methods: A total of 331 patients with BSCC were reviewed. Skin preservation was pursued when the distance between the invasive front of the tumor and the skin was 265 13 mm as determined by imaging. Of 331 patients, 230 (69.5%) patients had skin excision. Post-operative adjuvant radiotherapy (n = 182) was performed according to pathological risk factors. The 5-year local control rate was plotted by Kaplan-Meier analysis. Results: In the group treated with surgery alone, patients undergoing skin excision had a significantly higher prevalence of pt3-4 disease, pStage III-IV disease, tumor depth 265.05 mm, and perineural invasion than those who did not. In the group treated with surgery plus adjuvant therapy, a significantly higher prevalence of pT3-4 disease and pStage III-IV disease was evident in patients undergoing skin excision than those who did not. The 5-year local control rates did not differ between patients with and without skin excision in either the groups treated with surgery alone (94% vs. 91%) or with surgery plus adjuvant therapy (82% vs. 86%). Conclusions: Although patients undergoing skin excision had a higher prevalence of risk factors for poor local control, they did not show a worse local control rate.

P089: SURGICAL SALVAGE FOR RECURRENT SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY M.M. Monroe1, N.D. Gross1, M.K. Wax1, P.E. Andersen1, 1Oregon Health and Science University, Portland, OR

Objectives: To identify prognostic factors that influence overall survival in patients undergoing salvage surgery for recurrent squamous cell carcinoma of the oral cavity. Methods: Retrospective chart review of patients undergoing salvage surgery for recurrent oral cavity cancer at a tertiary-care head and neck cancer referral center. Beginning in 2000, patients undergoing salvage surgery for recurrent oral cavity cancer were entered into a database and followed for survival. The records of forty-eight patients undergoing salvage surgery for recurrent oral cavity cancer were examined and reviewed for the following variables: age, ECOG performance status, Charlson comorbidity index, stage and treatment of initial cancer, disease-free interval, multiply recurrent cancer, presence of weight loss, BMI, current tobacco or alcohol use, living status, recurrent tumor stage, primary oral cavity subsite, recurrent tumor treatment modality and tumor pathology. Results: Forty-eight patients underwent salvage surgery for recurrent oral cavity squamous cell carcinoma. Of these, 20 (42%) were multiply recurrent lesions. Prior treatment was surgical in 25 (52%) and multimodality therapy had been utilized in 23 (48%). Recurrent disease was early stage (I/II) in 11 patients (23%) and late stage (III/IV) in 37 (77%). The average disease-free interval was 17.25 months after treatment of the previous cancer. The most common subsite of recurrence was the oral tongue (n=27), followed by the floor of mouth (n=10), lip (n=5), alveolar ridge (n=3), retromolar trigone (n=2) and buccal mucosa (n=1). Average follow-up was 3.7 years. Overall survival at one and two years was 27.1% and 14.8% respectively. In univariate analysis, factors with a statistically significant detrimental impact on overall survival included a history of weight loss, low BMI and well or poorly-differentiated tumor histology. Conclusion: Recurrent oral cavity cancer is associated with an extremely poor overall survival despite aggressive therapy. Furthermore, it is often difficult to predict which patients are at the greatest risk and which will benefit from aggressive treatment. Signs of malnutrition at the time of recurrence, including a loss of 10% or more of historical body weight, appear to be associated with a worse prognosis. Additionally, patients with well and poorly-differentiated tumors have a worse overall survival. Further research into these areas is warranted.

P090: PROGNOSTIC FACTORS AND MANAGEMENT OF LOCO-REGIONAL RECURRENCE OF THE SQUAMOUS CELL CARCINOMA OF THE MOUTH AND OROPHARYNX H. Maria Chedid1, S.A. Franzi1, C.N. Lehn1, A. Rapoport1, 1Hospital Heliópolis, São Paulo, Brazil

Background: Salvage surgery is the first therapeutic option for recurrent tumors of the mouth and oropharynx, mainly in early clinical stages. Objective: The study goal is the identification of prognostic factors, treatment and to assess the free disease survival interval after salvage treatment for recurrent squamous cell carcinoma (SCC) of mouth and oropharynx. Methods: Retrospective analysis of 276 patients with SCC of the mouth and oropharynx treated with surgery, excluding patients with distant metastasis, secondary primary or previous cancer treatment. Ninety-seven were stage inoperable tumors (I and III) and 178 as advanced ones (III and IV). The tumor site was the oral cavity in 198 cases and oropharynx in 78 cases. Postoperative radiotherapy was indicated in 121 cases with mean dose of 60.8 Gy. The average follow-up was 35.3 months, and 127 patients developed loco-regional recurrence with histological/cytological confirmed of the SCC. Were excluded concomitant distant metastasis, and follow-up considered ideal after this kind of treatment were 12 months. Results: 89 patients underwent salvage treatment (surgery in 76 patients and chemoradiotherapy in 13 patients). Local recurrences were treated with salvage surgery in 62% of cases, regional in 79% and loco-regional in 31% (p=0.004). Free disease survival after salvage surgery was 13% in cases with recurrences diagnosed until 6 months and 48% in those who recurred after 12 months of follow-up (p=0.0001). When were considered salvage treatment (surgery; surgery and post operative radiotherapy or chemoradiotherapy), the free disease survival was statistic significant (p=0.0009). The correlation statistics between the clinical stage of loco-regional recurrence and free disease survival after salvage treatment was statistically significant (p=0.018) and also in relation to the modality of salvage treatment and free disease survival (p=0.0017). Conclusions: The modality of salvage treatment and the time between the initial treatment and recurrence were independent variables of survival in multivariate analysis; the site and clinical stage of loco-regional recurrence were predictive factors for salvage surgery in multivariate analysis.

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P092: SURGICAL PATHOLOGICAL PARAMETERS AND OUTCOME CORRELATION IN 639 PATIENTS WITH ORAL CAVITY SQUAMOUS CELL CARCINOMA G. Bruch Andreu1, R. Patel1, D.H. Brown1, D. Goldstein1, R.W. Gilbert1, P.J. Gullane1, J.C. Ireland1, 1Princess Margaret Hospital, Toronto, ON, Canada

Objective: The current TNM staging system does not accurately determine...
the prognosis of patients with Oral Cavity Squamous Cell Carcinoma (OCSCC). Histopathologic variables, however, may be more helpful for predicting locoregional recurrences and nodal metastasis. The aim of this study was to analyze the impact on resection margin status, tumor thickness, lymphovascular and perineural invasion in clinical outcome of patients with OCSCC. Methods: This is a retrospective review of 639 patients who had undergone treatment for OCSCC in our institution between 1994 and 2004. The data collected included age, gender, tumor site, margin status, grade, frozen section status, perineural and lymphovascular invasion and tumor thickness, TNM stage, cancer therapies, and cancer status were gathered. Tumor time recurrence (TTR) disease-specific survival (DSS) and Overall survival (OS) were analyzed. Results: Median follow-up was 4.3 years (range 0.02-12.4 years). Sites: tongue (44.2%), floor of mouth (24.1%), alveolus (13.5%), retromolar trigon (8%), buccal mucosa (7.5%), hard palate (1.4%). Margins were negative in 50%, close in 35.26%, and positive in 6.34% patients (pts). Dysplasia was found in 7.46% pts and carcinoma in situ in 0.93% pts. 297 pts were analyzed for TTR. No statistically significant differences were observed with regards margin status although a trend to worse TTR was observed among the pts with positive margins and carcinomas in situ. Sites and sites for dysplasia were observed for DSS. Overall survival data is provided for all pts. There was clearly evidence that 3 and 5 year OS rates were better for pts with dysplasia (86% at 3 and 5 years) and carcinoma in situ (OS 100% at 3 and 5 years). Pts with negative or close margins (1 to 5 mm) did better (69% and 65% at 3 and 5 years; 69% and 64% at 3 and 5 years) than pts with positive margins (55% at 3 and 5 years; 50% at OS). With regards to adjuvant radiotherapy, 536 pts with positive or close margins (54 pts margins were comparable). For both groups, pts who received radiation therapy (XRT) had a worse clinical outcome, probably due to poorer disease-related factors. Although not statistically significant, pts with negative margins +/- XRT showed better OS rates than pts with positive margins receiving XRT. Tumor thickness was only evaluated in tongue and floor of mouth on 268 pts. A significant relationship was observed between thickness and lymph node involvement in mean value of 8.5 mm in 185 pts with no lymph nodes; 14.2 mm in 83 pts with lymph nodes (p<0.001). However, no correlation was found between tumor thickness and regional recurrence.

Conclusions: Margin status is an independent prognostic factor. Our results show that OS differs according to margin status. Analysis of other parameters such as tumor stage related to margin status, lymphovascular and perineural invasion are ongoing.

P094: COMPARISON OF OUTCOME IN CHINESE PATIENTS WITH EARLY TONGUE CANCER TREATED BY EITHER PARTIAL GLOSSECTOMY OR BRACHYTHERAPY. F. Nag1, R. Ngan2, W. Cheung1, Kwong Wah Hospital, Hong Kong, Hong Kong; 2Queen Elizabeth Hospital, Hong Kong, Hong Kong

Background: Partial glossectomy and brachytherapy (BRT) are both acceptable treatment modalities for early carcinoma of tongue. The clinical management of such patients in the authors’ hospitals was formulated by a joint multi-disciplinary board attended by head and neck surgeons, clinical oncologists and radiologists. Those previously untreated patients were offered a free choice of either definitive surgery or radiotherapy (RT) as primary therapy. Objective: To compare the clinical outcome of Chinese patients with early tongue carcinoma treated by partial glossectomy and BRT. Methods: The outcome of 83 patients with T1NO or T2N0 squamous cell carcinoma of the oral tongue treated during the period between 1997 and 2005 was retrospectively reviewed. Results: A total of 30 patients selected for primary surgery consisting of glossectomy +/- neck dissection, and 55 patients received primary radiotherapy consisting of brachytherapy +/- external RT to the tongue, with or without additional neck RT or neck dissection. There was no significant difference in the key clinical characteristics between the 2 groups, except the tumour size is larger in BRT group. The rate of post-operative haemotoma formation was similar in both groups, which was 2% and 3% for the BRT and surgical group respectively. The median hospital stay was 8 days in the surgical group and 7 days for BRT alone group. The median hospital stay was 13 days when neck dissection was subsequently performed in the BRT group. All the patients were tube-fed during RT while the patients with surgery resumed oral feeding at a median of 1 day. The 3-year survival rates of surgery and BRT were 85.3% and 85.1% respectively and the 5-year survival rates of surgery and brachytherapy were 81.2% and 81.7% respectively. The disease free survival was 96.6% and 91% in surgery and BRT group respectively. There is no difference in local (82 vs 87.2%) and nodal (89.5 vs 85.7%) control subgroup in both treatments. However, the surgical group showed a better 5-year survival rate in stage II disease, which was 100% compared with 78.3% in the BRT group. There were more late RT complications in the BRT group, including chronic pain (11%), superficial transient ulcers (22%), and osteo-radionecrosis of the mandible or soft tissue (13%). All eligible patients in both groups speaking Cantonese dialect will be assessed by speech therapists using an instrument, OCSST speech assessment recording form, and the quality of life (QoL) of all eligible patients will be measured by the EORTC QLQ-C30 and EORTC QLQ-H&N35. The speech and QoL data will be presented later in the Conference. Conclusion: The study showed that both BRT and partial glossectomy are acceptable treatment modalities for early carcinoma of tongue with comparable acute complications, locoregional control and survival rates. Based on this retrospective study, partial glossectomy may result in a better outcome in stage II disease. There were more late RT complications in the BRT group. The post-therapy functional outcome of speech and QoL will become important factors affecting patients’ choice of therapy.

P095: TREATMENT OUTCOMES IN PATIENTS WITH ORAL TONGUE CANCER TREATED AT THE PRINCESS MARGARET HOSPITAL, TORONTO. D.P. Goldstein1, J. Lea1, G. Bruch-Andreu1, M. Shirme1, J. White1, D.H. Brown1, R.W. Gilbert1, P. Gullane1, J.C. Irish1, 1 Princess Margaret Hospital, Toronto, ON, Canada

Objective: To review treatment outcomes in patients with squamous cell carcinoma of the oral tongue. Methods: A 10-year retrospective chart review (1994-2004) identified 282 patients with previously untreated squamous cell carcinoma of the oral tongue treated with curative intent at the Princess Margaret Hospital. Tumor descriptive statistics and Kaplan-Meier estimates were used to determine statistical significance. Results: 268 (95%) patients were treated with primary surgery, seventy of which (26%) underwent post-operative adjuvant therapy. The median follow-up time was 4.54 years. The overall 5 year survival rate was 62% (95% CI 55%, 68%). The 5-year disease free survival was 47% (95% CI: 41%, 54%). Both advanced pathologic T stage and N positive stage were signific-
Objective: As oral cancer continues to be diagnosed and treated late with results that have not improved substantially over the past 40 years, this paper quantifies the delays in diagnosis and treatment. Materials and Methods: This study includes all new patients seen in the Department of Oral and Maxillofacial Surgery at University of California at San Francisco between 2003 and 2006 with a diagnosis of oral cancer. Exclusion criteria include recurrences, patients with long-standing dysplasia, proliferative verrucous leukoplaikia, or other premalignant conditions, and patients receiving any part of their treatment, except the first presentation to a primary care clinician, elsewhere. All oral cancer patients are presented to a Head and Neck Tumor Board for discussion and treatment planning. The time intervals are defined as: T1: Length of time in days from patient first becoming aware of the cancer problem and presenting to a primary care provider. T2: Length of time in days to have a biopsy carried out by a primary care clinician or referral to an oral healthcare specialist. T3: Length of time in days to be seen by a specialist. T4: Length of time in days for appropriate further investigations to be carried out. T5: Length of time in days for presentation to the Head and Neck Tumor Board. T6: Length of time in days for definitive treatment to commence. Results: 50 new oral cancer patients were identified over this three year period. 44 were squamous cell carcinomas, 1 was an osteosarcoma, 1 was a fibrosarcoma, 3 were minor salivary gland cancers of the maxilla, and 1 was a clear cell carcinoma of the maxilla. T1: Time from the patient first becoming aware of the problem to presentation to a primary care clinician: mean 118.2 days (range 0-720 days). T2: Time from presentation to a primary care clinician to biopsy or referral: mean 41.8 days (range 0-296 days). T3: Time from biopsy or primary care clinician referral to being seen by a specialist: mean 13.8 days (range 0-72 days). T4: Time for appropriate studies to be carried out from first being seen by a specialist: mean 10.4 days (range 0-25 days). T5: Time from completion of investigations to being presented at the Head and Neck Tumor Board: mean 26.5 days (range 1-223 days). T6: Length of time in days for definitive treatment to commence: mean 16.8 days (range 1-76 days). Total time from patients’ first becoming aware of the problem to commencement of definitive treatment: mean 227.5 days (range 52-786 days). Discussion: There are a number of stages in the referral and treatment process of which delay occurs, but the largest single delay is between the patient first becoming aware of symptoms and first presenting to a primary care clinician. More emphasis needs to be placed on early self referral of patients but also in accelerating other portions of the referral process, particularly referral from a primary care clinician to a specialist.

Objective: The objective of this study is to provide normative data for mandibular movement in patients with surgical reconstruction of the mandible between the ages of 20-40 years of age. This preliminary data will then be used to compare mandibular movement in patients with mandibular reconstruction. Methods: The subjects will be 20 healthy volunteers ages 20-40 years of age who will undergo measurement of normal jaw movement with a Jaw Tracking Device. The subjects will have a full complement of 28 natural teeth. Subjects with crowns (fixed prosthesis), bridges (fixed partial dentures), implants, or removable appliances (complete dentures or removable partial dentures) were not included. The Jaw Tracking Device is a FDA and American Dental Association approved device that is used in the clinical practice of dentistry. Each subject underwent mandibular movement measurements consisting of electromyography (EMG), range of motion, joint vibration analysis, speech and chewing patterns. The collected data was analyzed by BioResearch for comparison to their normal mandibular movement data. For EMG, the normal range is below 2, above which constitutes hyperactivity. Our male population was above the previously stated normal, for both the right and left Temporalis muscle. Our female population was considered normal for only the Sternoleidomastoid muscle. For Range of Motion, the normal data was 40-60mm for maximum open-
Metastasis to the cervical lymph nodes is the most important predictor of survival in oral squamous cell carcinoma (SCC). Since five-year survival drops to 25-50% following metastasis, currently almost all diagnosed oral SCCs are treated with neck and cervical lymph node dissection followed by radiotherapy and/or chemotherapy. These treatments are associated with significant complications and morbidity. Therefore, identification of a biomarker(s) that could predict the metastatic capability of oral SCC would greatly improve clinical management. Since tumor progression is associated with multi-step genetic, genomic and/or epigenetic changes, we hypothesize that the spectra of genomic alterations present in metastatic compared to non metastatic oral SCCs differ. Thus, the goal of this study is to determine if there are DNA copy number alterations that predict the metastatic potential of oral SCCs. Methods: In a case control design, non-metastatic (N0: metastasis free for at least 3 years after treatment) and metastatic cases (N+: tumors having LN metastasis at diagnosis or subsequent development) were analyzed. DNA was isolated from fresh-frozen tumor tissue and 440 000 SNP genotypes were determined using the Illumina Human1M-Duo genotyping array. Copy number alterations were detected and quantified using Kallisto. Results: From over 2500 SCC specimens in the UCSF Oral Cancer Tissue Bank, we identified 65 N0 and 127 N+ cases from patients diagnosed between 1997-2005, and of tumor size ≥ 1.5 cm in order to maximize DNA yield and quality. To date, we have accessioned blocks for 44 of the N0 cases. We are continuing to accession the remaining N0 blocks and to identify and accession matched blocks from N+ cases. Previous and ongoing array CGH studies of specimens from the UCSF Oral Cancer Tissue Bank indicate that high quality data are obtained from >90% of cases. Conclusion: Our work to date indicates that we will successfully profile and compare the genomes of at least 40 tumors each in the metastatic and non-metastatic oral SCC groups.
Conclusions: Low dose Docetaxel and concurrent radiotherapy with or without PND is effective for control in patients with neck metastases dominant stage IV oropharyngeal carcinoma. The results of pathological CR rate of neck metastasis and 3-year regional control rate support the role of PND in this algorithm. Although the study cohort was small, the results discussed here may warrant a more in-depth consideration of this treatment strategy in patients with stage IV except T4 oropharyngeal carcinoma. Local treatment intensification by the addition of radiotherapy or chemotherapy would not significantly benefit most of these patients.

P106: ADVANCED-STAGE OROPHARYNGEAL CARCINOMA: NO EVIDENCE FOR INCREASED FAILURE WITH REDUCED-DOSE CHEMOTHERAPY

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Purpose: To review clinical outcomes for stage III and IV oropharyngeal carcinoma treated with intensity modulated radiotherapy (IMRT) and platinum-based chemotherapy by chemotherapy regimen. Materials and Methods: Between April 2000 and September 2004, 71 patients underwent definitive platinum-based chemoradiation with IMRT for stage III and IV oropharyngeal carcinoma. No patient had surgery or neck dissection except to address recurrence. Patients included 62 men and 9 women of a median age of 55 years. Subsites were palatine tonsil (25), base of tongue (43), and pharyngeal wall (3). Forty-eight patients had T1-T2 cancers and 23 had T3-T4. Twenty patients had NO-N1 disease and 51 had >=N2 nodal disease. Thirty-six patients were treated with reduced-dose 75 mg/m2 cisplatin every 3 weeks; 22 had high-dose cisplatin at 100 mg/m2 every 3 weeks. Six had weekly carboplatin at an AUC of 1.5 to 2, and 6 had weekly carboplatin at an AUC of 1.5 with paclitaxel 45 mg/m2. One patient had reduced-dose cisplatin and docetaxel. Chemotherapy selection was based on renal insufficiency or ototoxicity. The prescription radiation dose was 70 Gy in 33 fractions to the gross tumor volume and 59.4 Gy to the clinical target volume. Results: At a median follow-up of 33 months, the 3-year locoregional progression-free estimate was 90%. The 3-year overall survival was 83%. Isolated local failures were seen in one patient treated with single-agent carboplatin, one patient receiving low-dose cisplatin, and 2 in patients who had high-dose cisplatin. All local failures occurred in patients who had an initial T stage of T3-T4. Two isolated regional failures were seen in patients receiving carboplatin or low-dose cisplatin, both with >=N2 nodal disease. One patient was treated with high-dose cisplatin but experienced subsequent simultaneous locoregional and distant failure; this patient had T4N2c disease. Conclusions: High rates of locoregional control were achieved with IMRT for advanced-stage oropharyngeal carcinoma using platinum doses that are slightly reduced from current national trial-based standards. T and N stage predict for risk of failure at the primary or neck, respectively. In an era of intensified combined-modality therapy, it is appropriate to consider reduced-dose or alternative multimodality regimens for patients with a lower burden of disease and/or limiting medical comorbidities.

P107: RESULTS OF SURGICAL TREATMENT VERSUS CHEMORADIATION IN EARLY STAGE OROPHARYNX CANCER

C.N. Lehnh, H.M. Chedid1, Hospital Heliópolis, Sao Paulo, Brazil

Objective: Squamous cell carcinoma of the upper aerodigestive tract is commonly diagnosed in advanced clinical stages (III and IV). In Brazil at
least 65% of these cases are large tumors. Most of patients have comorbidities and are addicted to alcohol and tobacco. Another important factor is the incidence of second primary tumors due to the field cancerization. The choose of the best treatment must take into account all these variables and the consequences of the chosen therapy such as functional effects on voice and swallowing. Sometimes the results of surgical and non-surgical approaches are related as been quite similar but the most important concern must be the survival of the patient. The main goal is to evaluate the free disease survival in patients with stage I and II of oropharynx squamous cell carcinoma who underwent surgery or chemoradiation. Methods: study of the charts of 139 patients with squamous cell carcinoma of oropharynx submitted to treatment with curative intent. Seventy-eight cases were treated with surgery (with or without postoperative radiotherapy) and 61 were treated with chemoradiation. Radiation therapy was performed with linear accelerator and chemotherapy with CDDP with a weekly dose of 30 mg/m². Tonsillar fossa comprehended 56.8% of cases, base of tongue 21.9%, soft palate 14.5%, glossatorsial fold 3.6% and posterior wall 2.9%. In the chemoradiation group 18% (11 cases) were stage II and 82% (50 cases) were stage III and IV. In the surgical group 34.6% were stage I (nine cases) and 65.4% (51 cases) were stage III and IV. Results: The minimum time of follow up was 12 months with a mean time of 24.4 months. The mean age was 55.4 years old and 88.5% were male. The lost of follow up was 4.3%. Among the patients submitted to chemoradiation, 72.7% had locoregional control of the disease. The three remaining cases developed recurrences during the six months after treatment (one local and two regional). Among the 27 patients of the surgical group, 10 developed recurrence (three local and one regional). Four new cases diagnosed during the first six months of follow up, five recurrences between six and twelve months and only one case after 12 months. Free disease survival in two years in stage I/II is submitted to chemoradiation was 52% and in the surgical group was 70% (p=0.000006). Conclusion: Free disease survival in patient with stage I/II squamous cell carcinoma of oropharynx was higher than the chemoradiation group.

P108: SURGERY AND POSTOPERATIVE RADIOTHERAPY - A VALID TREATMENT FOR ADVANCED OROPHARYNGEAL CANCER? S. Lybakk1, P. Lievagga1, O. R. Monge1, L. Løsslønn1, Haukeland University Hospital, Bergen, Norway.

Objectives: The treatment of oropharyngeal cancer varies widely between different institutions. The dominating treatments are radiotherapy as a single treatment or a combination of surgery and radiotherapy. Laterally concomitant chemoradiotherapy has been the treatment of choice in many centers. Methods: In 1992 we started a hospital based head and neck cancer register in our department. All head and neck cancer patients referred to our hospital are included in this register. The present study is based on the data of oropharyngeal cancer patients included from 1992 - 2004. A total of 128 patients with squamous cell carcinoma of the lateral pharyngeal wall and tongue base have been included in the study. Ninety-nine patients had tonsillar cancer and 29 tongue base cancer (95 men and 33 women with a mean age of 59 years). All the data are shown as crude two years overall survival (OS). This is valid due to the fact that almost all recurrences occur within this short time interval. The radiotherapy dose was 70 Gy to the macroscopic tumors and to postoperative areas with marginal histological borders. Two and five years OS were calculated using computerized software package SPSS. Results: Forty-five patients were included in between 1992 and 1997. Four patients were not treated. Twenty-seven patients received radiotherapy as a single modality treatment and 14 patients were operated (mainly tonsillectomy and neck dissections) and given postoperative radiotherapy. Two years after diagnosis no patients were alive in the non-treated group; 56% (15) in the radiotherapy group and 71% (10) in the group treated with postoperative radiotherapy. The two years OS for the entire group was 56%. The T3 + T4 group consisted of 12 patients of whom only four (33%) survived two years. Due to the very poor outcome in the T3 - T4 group we decided to change our treatment policy to perform primary major surgery with free flap reconstruction and postoperative radiotherapy. Two years after diagnosis no patients were alive in the non-treated group; 56% (15) in the radiotherapy group and 71% (10) in the group treated with postoperative radiotherapy. The two years OS for the entire group was 56%. The T3 + T4 group consisted of 12 patients of whom 10 (83%) survived two years. Seven patients did not receive any therapy; 26 (31%) received radiotherapy treatment as a single modality treatment and 50 (60%) of the patients were operated and given postoperative radiotherapy. In the two years follow-up no patients in the non-treated group were alive; 15 (58%) of the patients in the radiotherapy group, and 46 (92%) of the patients treated with surgery and radiation therapy. The two years survival for the treated patients was 80%. The five year survival for the entire patient population in this period was 67%. Conclusion: The treatment of oropharyngeal cancer in our institution has become more individualized. For patients with advanced oropharyngeal carcinoma we favour a combination of surgery with postoperative radiotherapy as the treatment of choice if the patients are motivated and medically fit for this type of treatment. With this treatment the two years crude OS for all the patients diagnosed in this period has increased to 74%.

P109: PRIMARY SURGERY VERSUS CHEMORADIOTHERAPY FOR ADVANCED OROPHARYNGEAL CANCERS A MULTI-INSTITUTIONAL ANALYSIS OF SURVIVAL J.K.Harris1, D.A.O.Connell2, M.A.Mlynarek1, K.H.Al-Gahtani3, H.Seikaly1, 1University of Alberta, Edmonton, AB, Canada

Objective: To determine if there is a survival benefit in treating patients with squamous cell carcinoma of the oropharynx (OSCC) with surgical resection and reconstruction followed by radiotherapy (S-XRT), surgical resection followed by chemotherapy and radiotherapy (S/C-XRT) or with primary chemotherapy and radiotherapy (C-XRT). Methods: Retrospective analysis of all patients diagnosed with OSCC in the province of Alberta from 1998 to 2005. All patients received primary treatment at one of two tertiary care centers. Patient demographics, tumor subsite, tumor and cancer stage, treatment type, radiation and chemotherapy dosing, survival time and cause of death information was collected on all patients. Patients survival analysis was stratified based on stage of disease. The primary outcome measure was survival analysis of patients with advanced stage (stage 3, 4a, and 4b) OSCC undergoing S-XRT vs. S/C-XRT vs. C-XRT. The Kaplan Meier method was used for survival analysis. Multivariate analysis was used to examine interactions between TNM stage, overall stage, sex, age at diagnosis, tumor subsite, and treatment modality and survival. Results: 649 patients were diagnosed with OSCC during the study period. Sex distribution was 73% male, 27% female. 468 patients presented with advanced disease (stage 3, 4a, and 4b). 5% of patients had distant metastasis confirmed at the time of diagnosis. 463 patients with advanced disease included in the primary analysis. 19 patients declined treatment, 91 patients received radiotherapy alone (XRT), 26 patients received C-XRT. 20 patients underwent surgery alone (S), 154 patients received S-XRT, and 53 patients received combined S/XRT with chemotherapy (S/C-XRT). The 2 and 5 year disease specific survival (denoted as a and b respectively) for all treatment groups were as follows (reported as survival estimate (standard error)). XRT a) 52.3% (5.7), b) 36.1% (5.9); C-XRT a) 73.2% (4.0), b) 65.0% (4.6); S a) 75.0% (9.7), b) 62.6% (11.7); S/C-XRT a) 74.9% (5.5), b) 67.1% (4.0); S/C-XRT a) 85.2% (4.8), b) 78.3% (6.6). Multivariate analysis showed that there was a significantly (p<0.05) increased chance of dying from disease with stage 4a and 4b compared to stage 3 disease.

Conclusion: Surgery followed by radiotherapy in the treatment of advanced stage OSCC offers no survival benefit when compared to organ preserving chemotherapy and radiation therapy protocols. Patients treated with surgery followed by combined chemotherapy and radiation therapy gain a significant survival benefit when compared to other primary treatment modalities. This data shows that primary surgery with post-operative chemotherapy / radiotherapy after patients the best chance of survival in the treatment of advanced stage OSCC.

P110: OUTCOME AND PROGNOSTIC INDICATORS IN SQUAMOUS CELL CARCINOMAS OF THE TONSIL K. Chu1, B. Wreh1, E. Winquist1, K. Fung2, V. Venkatasesan3, J. Yoo1, J. Franklin3, A. Hammond1, N. Read1, 1University of Alberta, Edmonton, AB, Canada; 2University of Western Ontario, London, ON, Canada; 3London Health Sciences Center, London, ON, Canada.

Objective: Tonsillar squamous cell carcinoma (TSCC) has increased in incidence over the past ten years. Use of concurrent chemoradiotherapy and cetuximab has changed the management of TSCC. Although tobacco and alcohol use are known risk factors in head and neck cancer, the more recent discovery of an association with human papilloma virus (HPV) infection is changing the treatment paradigm. This study analyzès the epidemiology of TSCC. The primary objective of this study was to assess the impact of different treatment modalities on outcomes (survival, recurrences, and salvage therapy) in TSCC. Further, we wish to analyze the impact of treatment on HPV-associated cancers as well as the effect of tobacco and alcohol intake, and cessation prior to treatment. Secondary analyses to assess major complication rates of treatment and the relationship between post-operative swallowing function (feeding tube rates, skin desquamation, and xerostomia) will also be done. Methods: Patients with TSCC treated between January 1993 and December 2006 at London Health Sciences Centre were identified retrospectively and charts reviewed. Tobacco and alcohol intake,
cessation, as well as treatment modality were recorded. Major complications assessed included trismus, feeding tube rates, skin desquamation, and xerostomia. HPV-associated cancers were identified by immunohistochemical staining of paraffin embedded slides from the diagnostic biopsy. Results: 135 patients have been identified (71.6% male and 28.4% female) with a median follow-up of 31.7 months. Most presented with a sore throat (62%) or neck mass (33%), and most had stage III or IV tumors (71%). Primary treatment modality was radiation (89%) with curative intent (60-70Gy in 30-35 fractions). 18% of patients also had surgery in which 83.3% of these patients had a neck dissection. 82.0% of patients developed acute side effects, most commonly mucositis and skin desquamation. 13.5% of patients required hospitalization. The most common late toxicity was xerostomia in 53% of patients. 46% of patients relapsed with over half of these locoregional. Of these patients, 67% had salvage treatment usually consisting of salvage surgery. Only 25% of patients were successfully salvaged. At time of analysis, 52% of patients were free of disease. The median overall survival was 120 months. T status was a significant prognostic indicator: T1 tumors had a median survival of 157.8 months compared to T4 tumors which only had a median survival of 11.9 months, p = 0.02. Conclusions: TSCC is relatively common and usually presents with more advanced stage despite its oropharyngeal location. Nearly half of patients die from uncontrollable cancer, usually uncontrollable locoregional disease. The majority of patients in this series were treated with radiation alone. Modern multimodality treatment regimens may affect outcome and are presently being analyzed. The influences of HPV etiology and tobacco and alcohol cessation on these outcomes is currently under analysis and will be presented.

P111: CYSTIC METASTASES FROM OROPHARYNGEAL SQUAMOUS CELL CARCINOMA ARE ASSOCIATED WITH BETTER DISEASE-FREE SURVIVAL J.M.Sherman 1, E.J.Moore6, K.D.Olsen6, J.Kasperbauer2, 1University of Chicago Medical Center, Chicago, IL; 2Mayo Clinic, Rochester, MN

Background: Squamous cell carcinoma (SCC) of Waldeyer’s ring has a tendency to form cystic metastases in cervical lymph nodes. This study was designed to compare the long-term prognosis of patients with cystic metastatic disease after surgical resection and adjuvant therapy with that of patients with solid metastatic disease from the same primary site. Methods: A retrospective, case-controlled study was conducted in a single tertiary care setting. The long-term outcome was determined for fifty patients with grossly cystic metastatic SCC from Waldeyer’s ring or unknown primary sites and 50 controls with solid metastatic disease matched for disease stage, primary site, age, and sex. Results: Significantly fewer recurrences were suffered by patients with cystic metastatic disease as compared to those with solid disease (16% vs 44%, p=0.002), and patients cystic metastatic disease suffered less disease-specific death compared to those with solid disease (14% vs 32%, p=0.04). When considered in a Cox proportional hazard regression model, the presence of grossly identifiable cysts in the cervical metastatic disease was associated with an independent and significant reduction in risk of recurrence and an insignificant trend toward increased disease-related survival. Conclusion: Cystic metastatic disease in cervical lymph nodes represents a clinical entity which is distinct from solid metastatic disease and confers an improved prognosis.

P112: THE SAFETY AND EFFICACY OF THE MANDIBULOTOMY APPROACH IN HEAD AND NECK CANCER SURGERY H.Seikaly1, P.Dziegielewski1, J.Dimitri1, D.Wijlliams2, J.R.Harris1, 1University of Alberta, Edmonton, AB, Canada; 2University of Alberta, Edmonton, AB, Canada

Objective: To assess the safety and efficacy of a unique mandibulotomy technique. Methods: 220 consecutive mandibulotomy cases in 214 patients were retrospectively identified from 1998 - 2006. All were treated using uniform surgical technique, consisting of incisor extraction, a paramedian stair-step osteotomy and combination fixation with direct interosseous wiring and a compression mini-plate (CMP). The CMP was adapted to the post-osteotomized mandible. Mandibulotomy-related complications were recorded and separated into 2 categories consisting of: (1) fixation failure: plate failure, non-union and mal-union and (2) poor healing: hardware exposure, infection, osteoradionecrosis and xerostomia. Patient tumor and perioperative variables, such as chemotherapy or radiation therapy exposure, were recorded and assessed with uni- and multi-variate regression analysis to identify associations with complications. Results: 21 (9.5%) mandibulotomy-related complications occurred in 20 (9.3%) patients. 41.8% cases of fixation failure and 17.6% cases of poor healing were identified. The most common complication was hardware exposure with 9 occurrences (42.9%). No patient, tumor or perioperative variables were statistically significant predictors of complications. Conclusion: The mandibulotomy protocol employed provides a safe and effective means of accessing the posterior oral cavity and oropharynx with low associated complication rates.

P113: RESPONSE EVALUATION AFTER CHEMORADIATION FOR ADVANCED ORAL AND OROPHARYNGEAL CARCINOMA WITH MRI AND FDG-PET L.van der Putten1, R.de Bree1, O.S.Hoekstra1, J.A.Castelliens1, F.Fl.Comans1, E.Sanchez2, M.Akariou1, D.J.Kuij1, C.René.Leemans1, 1VU University Medical Center, Amsterdam, The Netherlands

Objective: Evaluation of the accuracy and interobserver variation of FDG-PET and MRI as a function of test positivity criteria to assess response to chemoradiation for advanced oral cavity and oropharynx carcinomas. Methods: In a retrospective study PET and MRI scans of 23 consecutive patients with functionally inoperable oral cavity and oropharyngeal carcinomas treated with chemoradiation were assessed by 3 nuclear physicians and 2 radiologists (individually and in agreement) using several interpretation systems to detect local residual tumor. Response was protocolly evaluated 3-4 months after chemoradiation. Histopathology and follow-up of 6 months after diagnosis served as the reference standard. Results: Four patients had local residual tumor. When the only options were ‘residual tumor’ or ‘no residual tumor’, a sensitivity of 100%, specificity of 37%, positive predictive value of 25% and negative predictive value of 100% was found for MRI after consensus reading and for PET after consensus reading 50%, 84%, 40% and 89%, respectively. Accuracy of MRI was in consensus better than individually. For the MRI scoring system according to Ojiri ‘1’ and ‘estimated chance of tumor presence [%]’ were significant test positivity criteria. For PET ‘intensity of uptake’ was a significant test positivity criterion. There was a slight agreement for MRI observers (κ=0.16) and a moderate agreement for PET observers (κ=0.52) versus the reference standard. Conclusions: The accuracy of FDG-PET and MRI for evaluation of tumor response after chemoradiation is moderate. MRI has a high sensitivity, while FDG-PET had a high specificity. The high negative predictive values may justify avoidance of invasive diagnostics [endoscopy under general anesthesia with taking of biopsies] if MRI and FDG-PET are negative. Scoring systems can be helpful in the assessment of MRI and PET. T. Ojiri H. Mendenhall WM, Mancuso AA. CT findings at the primary site of oropharyngeal squamous cell carcinoma within 6-8 weeks after definitive radiotherapy as predictors of primary site control. Int J Radiat Oncol Biol Phys 2002; 52:748-754.

P114: THE ROLE OF CHEMOTHERAPY IN ADDITION TO RADIATION THERAPY FOR THE MANAGEMENT OF ADVANCED OROPHARYNGEAL CANCER U.Duuvul1, A.Misra2, D.Roberts1, M.S.Kies1, E.M.Sturgis1, A.Garden1, D.I.Rosenthal1, R.S.Weber1, TMD Anderson Cancer Center, Houston, TX; 2MD Anderson Cancer Center, Houston, TX

Objective: To evaluate the effect of adding chemotherapy to irradiation for the management of advanced oropharyngeal squamous cell cancer. Introduction: Advanced (stage III-IV) oropharyngeal cancer is often treated with non-surgical therapy. Historically, at our institution, advanced stage disease was treated with definitive radiation therapy, reserving surgery for those cases with bone invasion. More recently, chemotherapy is used in the form of concomitant therapy or as induction has been offered to these patients. The goal of this study is to review our experience with these approaches. Methods: A retrospective review was undertaken to identify patients definitively treated at our institution. Clinical data were abstracted from the chart to ascertain diagnostic and treatment information, as well as outcomes data. Results: The majority of patients were treated with either irradiation only or concomitant chemoradiation. Induction chemotherapy was used in a small cohort of patients. Patients treated with chemoradiation had, in general, better outcomes than those treated with irradiation only (p<0.05), even if the patients also required surgery. Conclusion: The addition of chemotherapy to irradiation appeared to improve outcomes for patients with advanced oropharyngeal cancer when compared to irradiation alone. The chemotherapy standard for these patients with advanced oropharyngeal cancer requires further investigation.

P115: THERAPEUTIC OPTION IN PATIENTS WITH SMALL PRIMARY TUMOR IN THE OROPHARYNX BUT WITH ADVANCED CERVICAL NODAL METASTASIS Y.Son1, C.Baek1, J.Cho1, K.Park1, J.Jang1, 1Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea
It is not uncommon that oropharyngeal cancer patients present with small primary tumors (T1-T2) but with advanced nodal disease (N2 or greater). Even though multiple treatment modalities have been used in a variety of sequences, there is still no consensus for the optimal treatment for these patients. This study aimed to compare the treatment outcomes when these patients were treated with primary tumor resection via intraoral approach and initial neck dissection(s) followed by adjuvant radiation therapy (OP + RT) versus definitive concurrent chemoradiotherapy (CCRT). Methods: A cohort of patients (N = 38) with small primary (T1-T2) tonsillar squamous cell carcinoma but bulky nodal disease (N2-N3) were included in the study. Twenty-two of them were treated by OP + RT and the other 16 patients received CCRT. There was no difference in age (mean 56 years old), gender and distribution of T/N stages between the two groups. Mean and median follow-up period was 38 and 33 months (from 6 to 75 months). Treatment outcomes (recurrence, disease-free survival) were compared and multivariate analyses of possible prognostic factors (cystic changes of metastatic nodes in CT, and pathological extra-capsular spread and degree of differentiation) were performed. Results: Among the patients who finished the planned therapy, two patients in each group showed failures. In OP + RT group, one patient died due to neck recurrence, which was successfully salvaged with surgery but the other died of mediastinal nodal metastasis. In CCRT group, one patient developed ipsilateral cervical nodal recurrence with successful surgical salvage but the other died of pulmonary metastasis. Two patients of OP + RT group and one of CCRT group had to stop the treatment in the middle because of other systemic disorders. Disease-free survival was not significantly different (86% and 75%, OP + RT and CCRT group respectively). CT findings of cystic metastasis, extra-capsular spread or pathological differentiation failed to prove significant impact on the treatment outcomes. Conclusions: Either treatment modality (initial surgery followed by radiation therapy or concurrent chemoradiotherapy) will be an effective therapeutic option in patients with small primary and advanced nodal disease of tonsillar squamous cell carcinoma.

**P116: SQUMOUS CELL CARCINOMA OF THE TONSILLAR REMNANT**

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**Objective:** Squamous cell carcinomas (SCC) of the palatine tonsil are the most common carcinomas of the oropharynx accounting for 50% of tumours in this site. However, SCC of the tonsil in a previous tonsillectomized patient has rarely been reported or documented in the medical literature. The aim of this paper is to describe the clinical presentation, diagnostic difficulties, management and outcome of this uncommon presentation. Methods: Retrospective review of 10 patients with SCC of the tonsil remnant presenting to the Head and Neck Unit at Guy’s and St Thomas’ Hospital NHS Foundation Trust between January 2000 to January 2007. Results: From January 2000 to January 2007, 25 patients with SCC of the palatine tonsil, Ten (4%) of these had previously undergone tonsillec- tomy as children. Seven males and 3 females. Median age was 56 years (range 43-74 years). Five initially presented with an unknown primary tumour and therefore investigated following an occult primary investigation protocol. Two patients were Stage II and Stage IV. One patient was treated with palliative intent, the remainder underwent radical planned combined modality treatment with curative intent. Surgery to the primary site included excision biopsy of the tonsillar remnant in 6 patients, and transoral KTP laser excision in 3 patients. Six patients underwent modified radical neck dissections and one underwent radical neck dissection. Nine patients received radical radiotherapy to the primary site and neck (60Gy in 30 fractions over a 6 week period) and 4 patient underwent concomitant chemotherapy with Cis-Platinum and 5-Fluoracil in addition to radiotherapy. One patient died of metastatic disease at presentation. Eight patients are alive with no signs of recurrence with a minimum follow-up of 10 months and a maximum of 5 years. One patient was lost from follow-up. Conclusion: Squamous cell carcinoma of the tonsillar remnant is rare but it should be recognised as distinct clinical entity. Clinicians should treat SCC of the head and neck as should be the case with any other entity. Patients presenting with metastatic cervical lymphadenopaties of occult primary, who had previous tonsillectomy but may have tonsillar remnants, should have the excision of the remnant during their diagnostic work-up. Carcinoma of the tonsillar remnant has generally a good prognosis and disease-free survival and overall survival is similar to those of tonsillar SCC.

**P117: UPFRONT NECK DISSECTION (WITHOUT PRIMARY RESECTION) FOLLOWED BY CHEMORADIOThERAPY FOR OROPHARYNGEAL SCC; A RETROSPECTIVE STUDY**

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**Background/Objective:** Many institutions treat loco-regionally advanced head and neck Squamous cell carcinoma (SCC) with chemoradiotherapy or radiotherapy (RT) followed by neck dissection (ND). We report on our experience with the converse treatment, i.e. neck dissection (without primary tumour resection) followed by chemo-radiotherapy / radiotherapy in patients with oropharyngeal carcinoma. Our rationale for this algorithm and our results are examined. Materials and Methods: This is a retrospective study based on the analysis of 86 patients treated over a period of ten years, from 1995-2005, in the dept of head and neck oncology, Kidwai memorial institute, Bangalore. Patients with T1 and T2 primary in the oropharynx and advanced lymphadenopathy were included and all patients underwent upfront neck dissection but without performing oncologic resection on the primary tumour site. Patients received comprehensive radiotherapy / chemo-radiotherapy and the dose ranged from 60-70 Gy (depending on the T stage). Mean follow up was 24 months. Results: This program was feasible; with a mean time interval from neck dissection to start of radiotherapy was 30 days. Eleven patients had progression of T-stage during this time window. 22 patients opted for concurrent chemotherapy CRT (low dose cisplatin). Most patients (44 of 86) had carcinoma base of tongue while 25 patients had Ca tonsil. 2 patients had ca base tongue and tonsil and 5 patients presented with primary in the pyriform fossa region. Mean duration of radiotherapy was 52 days. The failure rate for primary was 18% and for neck was 35%. The 2-year disease-free survival and overall survival rates are 72 % and 60 % respectively. Conclusions: For head and neck SCC, especially in oropharynx, neck dissection (without primary tumour resection) followed by radiotherapy / chemo-radiotherapy has desirable efficacy, comparable to upfront radiotherapy / chemo-radiotherapy with consolidation neck dissection (ND) provided, some prerequisites are confirmed. Primary lesion should be small and have favourable morphology so as to be irradiated. Neck node size should not make regional control difficult. Regional metastasis should be amenable to satisfactory surgical resection with standard or extended neck dissection. Other potential logistical and translational advantages of this approach will be discussed.

**PARATHYROID**

**P118: MINIMALLY INVASIVE PARATHYROIDECTOMY**

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**Background:** Primary hyperparathyroidism has traditionally been successfully treated by bilateral neck exploration under general anesthesia in connection with surgical removal of enlarged parathyroid glands. The preoperative localization of the enlarged glands and the intraoperative PTH measurement has recently made unilateral or localized neck exploration feasible with similar success rates, even under local anesthesia in selected cases. **Material and Methods:** Data on patients who had undergone minimally invasive surgery from January 1st, 2001 to December 31st, 2006 in two Institutions with established Head & Neck Departments were collected from patient records. 107 patients were included in the study. Seven cases were to be converted into general anesthesia. US correlated in 83% of cases associated US and MIBI were accurate. Center II: PTH blood level normalized in 100% of both Center's patients post-operatively (minimum follow up 12 months). There were no postoperative compli-
Objective: To investigate how minimally invasive parathyroidectomy under general anesthesia (MIPULA) compares to minimally invasive parathyroidectomy performed under general anesthesia (MIPUGA) in terms of post-operative pain, post-anesthetic side effects, overall cost, and patient satisfaction.

Methods: A single cohort of patients was followed prospectively from the time of clinic assessment to post-operative follow up with a patient satisfaction survey scored on a Likert scale. The patients included had a single gland hyperparathyroidism and underwent Minimally invasive parathyroidectomy under local anesthesia (n=31) or Minimally invasive parathyroidectomy under general anesthesia (n=18) at the University of Alberta Hospital. Results: Statistically significant differences between the MIPULA versus the MIPUGA group were determined to include shorter operative time (mean 37.7 versus 71 minutes) and shorter hospital stay (mean 0.32 versus 1.56 days). In comparison to the MIPUGA group, the MIPULA group felt ready to be discharged significantly sooner (p = 0.0135, confidence interval = 95%).

Conclusions: There is no significant difference (p<0.05) between MIPUGA and MIPULA in overall satisfaction with surgery. Patients with MIPULA reported more pain immediately post-operatively, however most felt that the pain level was acceptable/tolerable. Patients with a MIPULA felt ready to be discharged post-operatively the same day, whereas patients with a MIPUGA did not. The total operative time and length of hospital stay for MIPULA versus MIPUGA was significantly shorter. MIPULA patients were day surgery patients, whereas MIPUGA required hospital admission.

Objective: To determine the visibility, aesthetic and patient quality of life impact of scars created in minimal access vs. conventional parathyroidectomy and thyroidectomy surgeries in younger patients following complete healing and scar remodeling. Design: Paired retrospective cohort. Cohorts matched for age (within 3 years), sex and time from surgery.

Patients: Patients aged 50 years or younger diagnosed with primary hyperparathyroidism undergoing surgical treatment via a minimal access incision. A sex and age matched cohort of patients was selected from a patient population undergoing parathyroid and thyroid surgeries for thyroid and hyperparathyroidism requiring exploration of the recurrent laryngeal nerve (3.1%), and no cases of permanent hypoparathyroidism, transient, or permanent recurrent laryngeal nerve paralysis. Thyroid surgeries included 2 isthmusectomies (2.9%), 33 hemithyroidectomies (48.5%), 5 completion thyroidectomies (7.4%), and 28 total thyroidectomies (41.2%). One patient had a concomitant tracheal resection with his total thyroidectomy while 7 central neck dissections and 12 lateral neck dissections were performed. Four neck dissections were independent of thyroid surgeries. Pathology revealed 20 benign adenomas (29.4%), 17 multinodular goiter (25.0%), 3 thyroid cysts (4.4%), 21 papillary thyroid carcinomas (30.9%), 3 follicular variants of papillary thyroid carcinomas (4.4%), 2 follicular adenomas (2.9%), 1 medullary thyroid carcinoma (1.5%), and 1 metastatic squamous cell carcinoma (1.5%). Complications included 6 transient recurrent laryngeal nerve paralyses (8.8%), 1 permanent recurrent laryngeal nerve paralysis (1.5%), 2 transient hypoparathyroidism cases (2.9%), 1 permanent hypoparathyroidism case (1.5%), and no hematomas (0%). Closed suction drains were used for large thyroid goiters and lateral neck dissections only. A 5 cm incision was the standard for thyroid surgery with an increase in length when concomitant lateral neck dissection was performed or when lesions were too large to deliver through a small incision. Alternatively, a 2.5 cm incision was used for smaller thyroid nodules and was successfully performed in 4 cases. Two cases had nodules which ruptured during minimally invasive procedures and incisions were extended to 3.5 cm in these patients. Conclusions: In the early development of a thyroid and parathyroid surgical practice, acceptable results and complication rates are feasible. Additionally, parathyroid surgery is easier to become proficient at performing through smaller incisions in comparison to thyroid surgery where several criteria must be met in order to be successful.
P123: CONTACT ENDOSCOPY FOR IDENTIFYING THE PARATHYROID GLANDS DURING THYROIDECTOMY

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Introduction: The contact endoscopy (CE) was first described as a gyne- cologic tool. In head and neck, the CE has been first used in laryngeal tumors. Most recently, nasopharynx tumors have been evaluated, as well.

Objective: To analyze CE as an auxiliary method for the identification of the parathyroid glands (PG) during thyroid surgery and to identify other variables that can influence that correlation.

Materials and Methods: One hundred twenty five patients underwent thyroid surgery between January, 2004 to February, 2006 in the Head and Neck Services of Head and Neck Surgery of Hospital Ana Costa de Santos and Santa Casa da Misericórdia de Santos. The variables analyzed were: the total surgical time and the time for localizing and identifying the PG, the improvement in identifying them, the number of PG identified and confirmed by the CE, histopathological diagnosis, the presence of thyroid inflammation, the thyroid gland weight, the PG led away into the thyroid specimens, and the number of PG autotransplantations.

Results: There were a total of 331 PG observed by the surgeon. However, 282 glands were identified by the CE (7.2%) PG were observed together the thyroid specimens and the Kappa index was 0.534. The higher the total surgical time (p=0.03) and the time spent to localize and identify (p=0.00) the PG by the CE, the lesser the agreement observed. The second year performing the CE resulted in better agreement results (p=0.02). All the 17 autotransplanted PG were identified by the CE and confirmed by the frozen section method.

Conclusions: CE in an efficient auxiliary method for the identification of the PG during thyroid surgery. The periods of the study, total surgical time and time spent to localize and identify the PG were statistically significant.

RECONSTRUCTION

P124: ANALYSIS OF OUTCOME AND COMPLICATIONS IN 94 CASES OF MICROVASCULAR HEAD AND NECK RECONSTRUCTION

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Objective: To determine the incidence and causes of perioperative complications in patients who undergo microvascular free flap procedures for reconstruction in head and neck cancer.

Methods: A total of 94 consecutive microvascular free flap procedures were performed for reconstruction in head and neck cancers, with all of the defects arising after treatment of malignancies. Flap donor sites included radial forearm (n=57), fibula (n=13), Jejunum (n=18) and VRAM (n=4). Flap related data and incidence of perioperative complications were recorded prospectively over a 3 year period.

Results: There was no perioperative mortality. Overall perioperative complications occurred in 9.4% of all cases. Free flaps proved to be extremely reliable with a 4.7% of flap loss. Donor site morbidity was associated with 3% of cases. Analysis showed relationship between incidence of complications and numbers of veins anastomosed. Conclusion: The present study confirms that free flaps are extremely reliable in achieving successfull reconstruction of the head and neck. Venous complications were reduced by performing more than one venous anastomosis.

Key Words: Free flaps : microvascular reconstruction : head and neck cancer.

P125: RADIAL FORE ARM FLAP PREFABRICATED WITH CANCELLOUS BONE FOR SECONDARY MANDIBULAR RECONSTRUCTION

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If primary reconstruction of full size mandibula defects with microvascular bone grafts has failed, another microvascular flap is required for secondary reconstruction especially after radiotherapy. Here the prefabrication of bone grafts may be an alternative. In five patients iliac spongious bone cylinders were grafted in the lower forearm and wrapped with the fascia. After uneventful healing for 4 weeks, the radial fore arm flap prefabricated with spongious bone, was used with and without skin island to bridge defects of the mandible with a size of up to 10 cm. In the mandible region there was a primary take of the graft, although one case required revision of the venous anastomosis two days after grafting. During the follow up period of up two three years the radiographic controls showed the osseification between the spongious bone of the prefabricated transplant and the stumps of the mandible as well as the formation of cortical bone wrapping the cancellous bone. At time of osteosynthesis plate removal the bony fusion between graft and original mandible was confirmed. The results prove that the radial fore arm flap prefabricated with bone is an additional graft that still can work when other microvascular osseous grafts have failed already.

P126: RECONSTRUCTION OF THE THROUGH-AND-THROUGH ANTERIOR MANDIBLE DEFECT WITH A DOUBLE-SKIN PADDED FIBULAR FLAP

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Objective: The purpose of this report is to describe our recent experience using a double-skin paddle fibular free flap (DSPFFF) for reconstruction of the through-and-through anterior mandible defect.

Methods: Outcomes: Results were included methods of reconstruction based on the cutaneous defect, flap complications, fistula rate, and donor site complications.

Results: Seven patients were reconstructed with a DSPFFF. For lip reconstruction 2 patients were also concomitantly reconstructed with Karapandzic or lip advancement flaps. Three patients were reconstructed with both a fibular free flap and a second free flap (1 radial forearm fasciocutaneous flap and 2 anterolateral thigh flaps). The transverse dimensions of the DSPFFFs were as great as 15 cm. None of the patients developed a fistula. All free tissue transfers were successful. One patient developed partial loss of the fibular skin paddle used for submental skin replacement.

Conclusion: A DSPFFF is a safe and reliable way to reconstruct an anterior through-and-through mandibular defect. Indications for using a DSPFFF are 1) a cutaneous defect that lies at or below the plane of the reconstructed mandible, 2) a transverse width of the oral mucosa and cutaneous defect that does not exceed 15 cm (the approximate distance from the mid-call to the anterior midline), and 3) a lip defect that present, can be reconstructed with local flaps.

P127: THE ROLE OF NAVIGATION-ASSISTED SURGERY IN PRIMARY AND SECONDARY MAXILLOFACIAL RECONSTRUCTION

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Objective: Ablative tumor surgery as well as reconstruction of defects of the maxillofacial skeleton requires detailed planning using computed tomography (CT) or magnetic resonance imaging (MRI). Reconstruction following tumor resection is dependent on reliable information about the correct type and volume of grafts and predicting the outcome. This study evaluates the benefits of and the indications for computer-assisted surgery in the treatment of cranio-maxillofacial tumors.

Materials and Methods: Based on a CT or MRI data set, the Voxel Navigation System (IVS-Solutions, Chemnitz/Germany) was used for preoperative planning, intraoperative navigation, and postoperative control of radical tumor resection and primary and secondary reconstruction. Tumor resection was preoperatively planned and intraoperatively navigated. Preoperatively, the required soft and hard tissue were measured using the mirrored data set of the unaffected side of the facial skeleton; the size and location of the graft were chosen virtually. Intraoperatively, contours of transplanted tissues or alloplastic materials were navigated in accordance with the preoperatively simulated reconstructive result.

Conclusions: Computer-assisted treatment was successful in a high percentage of cases of radical tumor resection and, safety margins outlined preoperatively could be precisely controlled during tumor resection.

P128: DOUBLE-BARRELED MANDIBULAR RECONSTRUCTION UTILIZING TWO VASCULAR SOURCES

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Posters

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Objectives: Mandibular reconstruction is best achieved with a vascularized bone graft. In some instances, the vascular anatomy limits donor site choices. We present a case in which the anterior mandibular arch was reconstructed using two sources of bone stock, the radial bone, derived from a radial forearm osteofasciocutaneous free flap, and the sixth rib, harvested in continuity with the pectoralis major muscle as a pedicled osteomyocutaneous flap. Methods: The patient initially presented with squamous cell carcinoma of the floor of mouth for which he underwent local resection, a left neck dissection, and post-operative radiotherapy. Several months later the tumor recurred intra-orally. He was initially resistant to further treatment, the result being significant tumor progression upon referral. Once committed to surgical salvage, he nonetheless refused using iliac and scapular bone as donor sites and significant atherosclerotic disease was noted on a three-vessel femoral arteriogram. He consented to use of the forearm and chest wall as sources of bone and soft-tissue. Results: The radial free flap was placed intra-orally to re-establish mandibular continuity and to close the through-and-through floor of mouth defect. The rib was secured by wire inferior to the radial bone to reinforce the graft. The effect was to create a “double barrel”. The myocutaneous component was placed externally to provide coverage for both bone grafts and to replace the soft-tissue and skin resected during the composite procedure. Conclusions: Use of two separate flaps containing limited bone components provided sufficient structural integrity, bulk, and coverage to adequately reconstruct an anterior mandibular composite defect.

P129: MICROSURGICAL RECONSTRUCTION OF CRANIOFACIAL DEFECTS IN THE TREATMENT OF MALIGNANT TUMORS OF MAXILLOFACIAL ZONE

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Objective: the improvement of functional and social patients’ rehabilitation after radical ablation of locally advanced malignant tumors of maxillofacial zone with the resection of facial skeleton. Materials and Methods: we offer the method of maxillofacial zone reconstruction after radical ablation of locally advanced malignant tumors using autotransplantation of morphofunctionally homogeneous tissues. We accumulated the treatment experience of 234 patients. The were made 248 autotransplantation to them. Primary tumors were discovered in 101 (43 %) cases. The third stage of tumorous process ascertainment in 35 % of cases and the fourth stage : in 60 % of cases, 110 patients had recurrent tumors [46,2 %]. 23 patients (9,8 %) had an operation on account of postoperative defects. 179 patients (76,6 %) had epithelial tumors, including 38,7 % with 4223 and 58,1 % with 4224. Scull base resection was made in 32 (14 %) of observations. If the defect was not threatening patient’s life or in case of unfavorable prognosis for the disease [31 patients : 13 %], microsurgical reconstruction was made deferred. For elimination of 147 [63 %] oroalveolar defects, 32 (14 %) craniofacial defects, 50 (21 %) oroorbitofacial, 5 (2 %) isolated defects of lower jaw, 248 autotransplants were used: vascular : 37 gastrotricular, 12 colomental, 31 omental; skin-muscular bone : 11 radial, 14 iliac, 8 fibular, 86 rib-muscular, 23 different skin-muscular flaps 438 24 skin-fascia radial flaps. Visceral flaps were used for elimination of tissue defects of the floor of oral cavity, oropharynx and cheek, skin-muscular-rib : for oroorbitofacial and oroalveolar defects, fibular flap : for isolated defects of lower jaw, iliac autotransplant : for total defects of hard palate, radial : for small defects of oral cavity, cheek and vestibule of mouth, and skin-muscular radial : for reconstruction of alveolar processes. Vast defects of soft tissues in combination with small defects of facial skeleton were removed using skin-muscular and skin-fascia flaps. Results: Postoperative complications appeared in 58 (25 %) cases. Leathality was 2,8 %. Total necrosis of the flap because of microvascular anastomosis thrombosis was registered in 12 (5,2 %) cases. Flap necrosis in the bone autotransplants group was registered in 5,7 % of autotransplantations, Reconstructions and operations for these patients were redone. Plastic successfully completed in 86,6 % of observations. 93,2 % of patients were satisfied with the cosmetic result and 32 % returned to their job. Resume: the use of microsurgical autotransplantation method provides radicalism of resection stage with the effective plastic removal of postoperative defect. The use of morpho-functionally autotissues offers a significant success of autotransplantation, and the type of defect allows to achieve high percentage of patients’ functional rehabilitation together with social and labor rehabilitation. Microsurgical reconstruc-

tion of craniofacial defects in the treatment of malignant tumors of maxillofacial zone allows to solve the problem of plastic closing of vast combined maxillofacial zone defects after radical surgical treatment of locally advanced tumors.

P130: MANDIBLE RECONSTRUCTION: FIT-IN VASCULARISED FIBULA FLAP: VARIANT – III L.M. Sassi1, Erasto Gaertner Hospital, Curitiba, Brazil

When one thinks we are running out of techniques, one sees that in fact it is quite the contrary. Each day we find new techniques to achieve the same objectives more easily. Indeed, the search for new surgical techniques post mandible tumour resection has been constant, always aiming at improving patients’ quality of life and well-being. Surgical treatment for advanced mandible tumours usually leads to functional and aesthetic complications. In the present paper, we report the case of a patient suffering from mandible cancer who underwent partial mandible resection followed by immediate reconstruction through a fit-in technique complemented by head and neck ionising radiation. Objective: To report on the reconstruction of a defect caused by pre-radiotherapy tumour resection. Methods: We used the medical records of the patient registered at Hospital Erasto Gaertner-Curitiba-Pr-Brazil, and took into consideration all data concerning the clinical and histological tests, the patient’s evolution to date. Patient EP, 54, Caucasian, female, edentulous, suffering from mucoepidermoid carcinoma of mandible retrotral region. We performed tumour resection (keeping mandibular ramus) followed by immediate reconstruction through fibular osteotomy. The reconstruction technique was the following: we cleared a special site in the remaining anterior portion of the mandible where we fitted in and fixed one of the edges of the fibular graft. The other edge was fitted in with 50% graft and 50% mandible. The vascularised osteomyocutaneous autogenous graft with vascular anastomosis was fixed with bone synthesis through titanium mini-plates and screws. Results: Once the tumour had been resected, the mandible was immediately reconstructed through vascularised fibular graft. The osteomyocutaneous graft was inserted as described above. Such fit-in technique allowed a better adaptation of mandible and graft, as well as for better bone neoformation, avoiding thus the aggressive interference of radiotherapy. This technique has been bringing good results, allowing us to plan titanium cylindrical grafts for dental prosthesis fixation in the mandible. Conclusion: It seems to us that this technique has been very effective, particularly concerning bone neoformation, avoiding pseudoarthrosis or bone loss due to ionising radiation (which normally is administered 3 weeks after the surgical procedure). After 3 years of follow-up, the patient has been progressing satisfactorily, both clinically and radiographically, with no sign of recurrence of bone growth.

P131: THE RADIAL FOREARM DONOR SITE: A COMPARISON OF THE FUNCTIONAL AND COSMETIC OUTCOMES OF DIFFERENT RECONSTRUCTIVE METHODS

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Objective: to determine which method of fascial dissection and skin graft reconstruction of radial forearm free flap defects has the superior functional and cosmetic outcomes. Methods: Consenting patients undergoing major head and neck operative resection and reconstruction with a radial forearm free flap were prospectively enrolled and randomized into one of the following four groups: 1. Suprafascial dissection with Meshed graft reconstruction, 2. Suprafascial dissection with Sheet graft reconstruction, 3. Subfascial dissection with Meshed graft reconstruction, 4. Subfascial dissection with Sheet graft reconstruction. Functional, cosmetic and tendon exposure outcomes were collected prospectively with patients and outcome assessors blinded to treatment group assignment. Validated self-report questionnaires and objective functional measures were utilized. Results: 62 patients met the criteria for inclusion. Analysis revealed that suprafascial dissection with sheet graft reconstruction yielded superior functional, cosmetic and tendon exposure outcomes. Conclusion: Supra-fascial dissection with sheet graft reconstruction should be offered to patients requiring radial forearm free flap reconstruction of major head and neck defects.

P132: RANDOMIZED TRIAL COMPARING BOLSTER DRESSING TECHNIQUES OVER SKIN GRAFTS AT THE RADIAL FOREARM DONOR SITE

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Objective: Previous retrospective work at our institution demonstrated decreased tendon exposure at the radial forearm donor site when the wound VAC was used as a bolster dressing. Therefore we conducted a randomized comparison and hypothesized that the wound VAC bolster dressing will reduce tendon exposure and morbidity at the radial forearm free flap donor site when compared with a traditional bolster dressing.

Methods: A randomized trial was performed to compare tendon exposure at the radial forearm donor site using the wound VAC bolster dressing and a traditional bolster technique. Results: Forty-one subjects were enrolled and 22 were randomized to the wound VAC bolster group and 19 to the traditional bolster group. Two patients in wound VAC group had tendon exposure (9.1%) and 7 in the traditional bolster dressing group had tendon exposure (36.8%). An independent t-test demonstrated a statistically significant reduction in tendon exposure between the two groups (p=0.041).

Conclusion: The wound VAC bolster dressing reduced tendon exposure by increasing skin graft viability at the forearm free flap donor site when compared with traditional bolstering techniques.

P133: ANALYSIS OF FREE TISSUE TRANSFER VIABILITY BASED ON RECIPIENT VENOUS SELECTION

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Objective: Microvascular free tissue transfer (MVFTT) is a reliable means to reconstruct complex surgical defects of the head and neck. Central to all successful free tissue transfers is maintenance of a patent anastomosis between the flap and recipient vessels. Venous congestion remains the primary cause of flap loss, conflicting evidence whether certain venous anatomatomic configurations increase the risk for flap failure. To investigate this relationship, we sought to determine how microvascular venous anastomosis configuration (end-to-end versus end-to-side) affects the success of MVFTT reconstruction in head and neck defects.

Methods: We performed a retrospective chart review of 907 consecutive head and neck cancer patients treated with microvascular free tissue transfer (MVFTT) reconstruction between 1993 and 2007. Health records were reviewed for patient, cancer and treatment characteristics. In particular, type of resection, free flap, and recipient artery and vein were recorded. Anastomotic venous configuration was defined as end-to-end (ETE) or end-to-side (ETS). Flap failures associated with venous anastomatic configurations increase the risk for flap failure. To investigate this relationship, we sought to determine how microvascular venous anastomosis configuration (end-to-end versus end-to-side) affects the success of MVFTT reconstruction in head and neck defects.

Results: In total, radial forearm free flaps and fibula free flaps accounted for 42% and 27% of free tissue transfers. Overall flap survival was 98.5% with revision surgery required in 5.1% of all cases. Venous anastomosis was oriented ETE in 86% and ETS in 14.3% of flaps. In bivariate analysis, neither the emergent revision surgery rate nor the flap death rate differed significantly between ETE and ETS anastomoses (p>0.05). Multivariate logistic regression was performed to evaluate the independent effect of venous anastomosis configuration after adjustment for patient, cancer, and treatment free flap characteristics. This showed no difference in the odds of emergent revision surgery between flaps with ETE and ETS venous anastomosis configurations (OR 0.89, 95% confidence interval 0.34 - 2.32). A trend toward increased odds of flap death was observed among those with ETS configurations, but did not reach statistical significance (OR 2.76, 0.82 - 9.31).

Conclusion: The venous anastomosis configuration used to revascularize MVFTT is not associated with increased odds of emergent revision flap surgery or flap death. While there is an apparent trend toward increased risk of death with ETS anastomoses, this did not reach statistical significance. The rarity of flap death necessitates a larger series in order to have adequate power to detect a difference between groups.

P134: FASCIO CUTANEOUS SUPRACLAVICULAR ARTERY FLAP IN HEAD AND NECK CANCER RECONSTRUCTION

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Background: Reconstruction for head and neck advanced cancer is a challenge, due to the limited availability of donor sites, the frequent use of previous radiotherapy and the need of big aesthetic unit reconstruction.

Objective: To determine the features of patients that underwent a cervico facial reconstruction with fascio cutaneous supraclavicular artery flap (FCSAF) after advanced cancer resection at the Hospital Universitario de Santander during years 2004 to 2006.

Materials and Methods: A descriptive study was made, with the patients that underwent to reconstruction with FCSAF due to advanced head and neck cancer resection at the Hospital Universitario de Santander during years 2004 to 2006. Results: 8 patients where studied, with a male-female relationship of 6.2, and ages between 31 and 80 years (mean 58.37±17.7 years). They had skin squamous cell carcinoma (3 patients), pharynx cavum sarcoma (1 patient), sarcoma of the parotid gland (1 patient) clear cell adenocarcinoma of minor salivary gland (1 patient), squamous cell carcinoma of the tongue (1 patient), squamous cell carcinoma of the eyelid (1 patient) and ameloblastic carcinoma (1 patient), all of them were T4 stage. They had right cervico-facial flap in 7 patients (87.5%) and left in 1 patient (12.5%), with a mean lenght of 123.12±55.48mm, and a mean wide of 90.62±19.35mm, requiring primary closure of the donor site in all of them. During postoperating time 2 ischemic cases were documented (25%), facial palsy in 1 case (12.5%) and epidermolysis in 1 case (12.5%), without evidence of infection in the operating site or other complications. After monitoring of 20.12±14.85 months, 2 death cases have been documented, one of them because a stroke and another because a pulmonary metastasis.

Conclusions: The FCSAF allows a suitable reconstruction for head and neck area, achieving a properly functional and aesthetic rehabilitation, with a low rate of complications.

P135: CLINICAL ORAL FUNCTION AND QUALITY OF LIFE FOLLOWING SURGICAL EXCISION AND RECONSTRUCTION OF SQUMOUS CELL CARCINOMA OF THE FLOOR OF MOUTH: RESULTS OF TWO HUNDRED AND TEN CONSECUTIVE PATIENTS

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Introduction: The functional integrity of the floor of the mouth (FOM) is essential in maintaining tongue mobility, deglutition, and control and disposal of saliva. The present study focuses on the influence of different clinical and surgical parameters on oral function and quality of life in patients who had surgical ablative and reconstruction of FOM carcinoma with or without chemo-radiotherapy. Patients and Methods: Between January 2000 and August 2007, a combined retrospective and prospective review of two hundred and ten consecutive patients, who had surgical treatment of squamous cell carcinoma (SCC) of the FOM at both Canniesburn Plastic Surgery Unit based at Glasgow Royal Infirmary and West of Scotland Regional Maxillofacial Unit based at Southern general hospital, were studied. A new detailed clinical assessment scale “The Clinical Oral Functional Outcome Scale (COFOS)” was introduced for objective assessment of oral function before and after surgical treatment with or without chemo-radiotherapy. A 9-domain clinical functional examination scale was developed based on modifications of a previously introduced scale at Canniesburn “Functional Rehabilitation Outcome Grades (FROG)” Quality of life was assessed using both University of Washington Quality of Life Questionnaire version 4(UW-QOL) v4 and Functional Intraoral Glasgow Score (FIGS). Clinical oral function and quality of life were evaluated once postoperatively in the cross-section retrospective group who received treatment prior to January 2006. For the prospective group who had treatment after January 2006, longitudinal assessment was done preoperatively, 3 month, 6 months and 12 months postoperatively. Results: Two hundred and ten consecutive patients are included in the study following exclusion of patients who had died, those who missed follow up and those who declined to take part in the study. Postoperative cross-section assessment of clinical oral function and quality of life are carried on one hundred and seventy (81%) patients, while forty (19%) patients had longitudinal assessment. Multivariate analysis of the changes in quality of life and oral function following treatment, are assessed using both University of Washington Quality of Life Questionnaire version 4(UW-QOL) v4 and Functional Intraoral Glasgow Score (FIGS). Multivariate analysis of the changes in quality of life and oral function following treatment, are assessed using both University of Washington Quality of Life Questionnaire version 4(UW-QOL) v4 and Functional Intraoral Glasgow Score (FIGS). The correlation between clinical oral function and quality of life is also assessed. These factors include: age, gender, tumour site and size, anasthetic fitness, neck dissection, post-surgical defect, method of reconstruction, postoperative radiotherapy and dental rehabilitation. The correlation between clinical oral function and quality of life is determined. Conclusion: Clinical oral function assessment using the COFOS represents a valuable objective tool in conjunction with subjective quality of life assessment. They are essential to monitor the sequae of surgical treatment of floor of mouth cancer with or without radiotherapy. The tumour site and size, the patient’s age and comorbidity, post-surgical defect and the type of reconstruction are the main determinant factors of functional outcome.

P136: ANTEROLATERAL THIGH FREE FLAP WITH SCAR RELEASE IN THE TREATMENT OF TRISMUS FOLLOWING MASTICATOR SPACE TUMOR TREATMENT

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Trismus is a common side effect following the treatment of a 51 year old male required orbital extenteration with an intracranial defect to cover the posterior and superior orbit. The flap was then packed with gel foam and a Foley catheter balloon. The flap survived intact postoperatively with no evidence of CSF leak. The NSF is an alternative to the temporalis muscle rotation flap or free tissue transfer for closure of CSF leaks associated with orbital exenteration in select cases. The case is presented with photodocumentation and the advantages and limitations of the NSF for closure orbit defects are discussed.

P139: IMPROVING FUNCTIONAL OUTCOMES IN GLOSSOTOMY RECONSTRUCTION R.A. Zoumalan 1, P. Saadeh 2, M. Delacour 2, 1New York University, New York, NY

Objective: To improve functional outcomes in total or near-total tongue reconstruction with an alternative technique for free vertical rectus abdominis myocutaneous (VRAM) flap inset. In tongue defects created by large extirpations, reconstruction is most effectively achieved with bulky free flaps. When inset as commonly described, the free VRAM flap functions effectively as a space filler which re-contours the floor of the mouth and resurfaces the lingual aspect of the mandible. However, the classic inset (skin to remaining oral mucosa) obviates a more anatomical and dynamic reconstruction. Methods: This is a retrospective review of 8 patients with oral tongue squamous cell carcinoma who, from 1997 to 2004, underwent total (7) or subtotal (1) glossectomy with free VRAM reconstruction. All patients underwent both PEG placement and tracheotomy. Floor of mouth reconstruction was achieved with generous overlapping rectus muscle inset, supported at both the fascial and muscular surfaces to the inferior mandibular border. Intraorally, the muscle was attached to remaining lingual mucosa or gingiva. The neotongue, consisting of skin and subcutaneous fat, was sutured posteriorly to the remaining tongue base, while the other surfaces were trimmed to size and left unsutured, sitting on underlying musculature. Early endpoints were assessments of flap survival and complications (fistula, hemotoma, infection). Late endpoints were evaluation of speech, swallowing, aspiration, and PEG/tracheotomy dependency. Results: All patients underwent successful free VRAM reconstruction of the oral tongue. Rapidly, VRAM skin and subcutaneous tissue assumed the palatal arch configuration. Subcutaneous fat developed uniform granulation tissue within 2 weeks. This was followed by mucosalization of the granulation tissue and the underlying exposed rectus muscle/fascia. Flap monitoring was facilitated by exposed tissue; there was no flap loss. There were no fistulae or hematomas. One lateral neck flap celluitis resolved with antibiotic treatment. One year postoperatively, all patients were tolerating ad libitum diets. All patients regained intelligible speech facilitated by the controllable obturator effect of the neotongue. No aspiration was evident by either clinical evaluation or video fluoroscopy. All patients were PEG/tracheotomy free.

Conclusions: The described alternative free VRAM reconstruction allows for semi-dynamic tongue reconstruction which better approximates normal anatomy. This inset improves postoperative speech and swallowing without increasing aspiration risk. Although a static construct in isolation, the neotongue reconstruction described sits on a mobile base (the mandible) under voluntary control of the patient, thereby permitting effective obturator effect against the hard palate and, in turn, effective speech and swallowing. These advantages arose without increased technical difficulty and at minimal expense to the patient, offering an improvement to the standard tried and tested oral tongue reconstruction.

P140: FREE FLAP ARTERIAL AND VENOUS ANASTOMOSIS MONITORING IN POST-OPERATIVE HEAD AND NECK RECONSTRUCTION: A PROSPECTIVE STUDY J.R. Harris 1, D.W. Cole 2, J.P. Guillemaud 1, H. Allen 1, H. Seikaly 1, 1University of Alberta, Edmonton, AB, Canada

Objective: To prospectively evaluate the intraoperative and postoperative utility of the Cook-Swartz Doppler Flow Monitoring System for free flap monitoring of arterial and venous anastomosis in head and neck reconstruction. Study Design and Setting: A cohort of consecutive patients requiring free tissue transfer flap reconstruction by a team of Otolaryngology, Head and Neck Surgery at the University of Alberta Hospital were followed prospectively. The intervention in all patients was the use of implantable Cook-Swartz Doppler probe systems for monitoring both the arterial and venous microvascular anastomoses while concurrently collecting a battery of traditional clinical markers for free flap viability. These patients were group matched by flap type, age, and gender to a cohort of patients who...
underwent free-tissue transfer flap reconstruction with single vessel implantable Doppler monitors. Data was collected at time of surgery and for the ten post-operative days while the Doppler system was in situ regarding flap compromise, salvage, impaired flow as determined by the Doppler monitoring system and any intervention or re-operative findings. Results: A consecutive series of one hundred and forty free-tissue transfer flaps was included in the two-doppler study population. Twenty-three flaps exhibited possible anastomotic compromise, detected exclusively by audible Doppler and addressed by reposisioning or revision of anastomosis was performed. Twenty-six flaps exhibited some change in the Doppler signal during the post operative period, nine of which went for surgical re-exploration. There were three flap failures experienced in this group. When compared to the group-matched single Doppler cohort, the double Doppler group had an increased rate of intraoperative modifications but a significantly lower rate of surgical re-explorations, a lower need for revising the anastomosis and a lower rate of flap failure.

Conclusions: This largest prospective study to date of implantable Cook-Swartz Doppler monitors supports the utility of a two-vessel monitoring system for intraoperative detecting in adequacy of vascular anastomosis. In the postoperative period, while the Doppler system was associated with false positives, reassuring Doppler signals were often used to prevent unnecessary surgical re-exploration in addition to earlier detection of compromise leading to improved rates of salvage.

P141: MICRODIALYSIS AS A TECHNIQUE FOR MONITORING HEAD AND NECK FREE FLAPS S.E.Morley1, P.Baker1, 1Canniesburn Unit, Glasgow, United Kingdom

Objectives: We wished to determine the feasibility of improving the monitoring of head and neck free flaps by using microdialysis. Microdialysis catheters can be placed in tissue to determine levels of various metabolites using a real-time, bedside dialysis monitor. The technique has been used for free flap monitoring elsewhere in the body, but has never been specifically validated in head and neck reconstructions. Methods: Microdialysis was used to monitor the health of consecutive free flaps in a tertiary head and neck cancer service. Flaps to be monitored were either completely or partly or associated with radiodermatitis, the latter being a complication of chemoradiation protocols. Samples were taken at half hourly intervals initially and assessed for levels of glucose, lactate and pyruvate. The monitoring was undertaken at the bedside by the nursing staff in the normal post-operative ward setting. Results: 15 head and neck free flaps were monitored using microdialysis. This included muscle, fasciocutaneous and osseocutaneous flaps in various head and neck sites. Outcomes were well correlated with readings given by the machine, which in this study picked up flap problems before they were clinically apparent. In many head and neck reconstructions flaps can be difficult to monitor. Microdialysis monitoring can facilitate timeous return to theatre if required, but also reduces the chances of unnecessary theatre returns.

P142: LATERAL ARM FREE FLAP FOR ORAL TONGUE DEFECT RECONSTRUCTION N.Iyer1, K.Thankappan1, S.S.Chatni1, M.Kuriakose1, 1Amrita Institute of Medical Sciences, Cochin, Kerala, India

Objective: Reconstruction of defects of anterior tongue has been reported to be best carried out with free tissue transfer. Radial forearm flap has been the choice for the same. Lateral arm flap provides the adequate bulk and has a least donor site morbidity. However, it has been reported for reconstruction of floor of mouth defects. The objective of this study was to analyse the defects, flap details, donor site morbidity and functional outcome in oral tongue defects that were reconstructed by lateral arm flap. Methods: Retrospective review of case records of 46 consecutive patients who underwent lateral arm flap reconstruction of the oral tongue defects over a period of three years was done. The operative details and the perioperative problems were analysed. The aesthetic and functional results in the donor site as well as the reconstructed tongue was prospectively analysed in patients alive and disease free. A specially designed analysis tool was used to measure the speech outcome. Results: All patients where lateral arm flap was used had a defect of the oral tongue without the involvement of floor of mouth. The overall flap success rate has been 94% in this series, and the pedicle length averaged 6 cms. Either the facial or the submental skin was chosen as the recipient. The volume of the reconstructed tongue matched the defect in majority of the cases. Donor site was closed primarily with very good donor site scar as perceived by the surgeon as well as the patient. The speech and swallowing outcome were graded as very good in majority of the patients. Conclusions: Lateral arm flaps provide the adequate bulk and suitable tissue for reconstructing partial defects of tongue with minimal extension to the floor of the mouth. The pedicle length is adequate and good flap success rate can be achieved. The aesthetic and functional outcome at the donor as well as recipient site is excellent.

P143: THE MODIFIED ILEOCOLIC FREE FLAP: A VIALBE CHOICE FOR RECONSTRUCTION OF TOTAL LARYNGOPHARYNGECTOMY AND TOTAL GLOSGECTOMY S.R.Rossmitler1, T.A.Ghane1, N.D.Gross1, M.K.Wax1, 1Oregon Health & Science University, Portland, OR

Objectives: As the use of chemoradiation protocols increases, there are increased numbers of patients requiring salvage surgery. Reconstruction following salvage total laryngopharyngectomy with total glossectomy and cervical esophagectomy can be quite challenging. The ileocolic free flap has been described as a viable alternative for such situations. The terminal ileum is anastomosed to the tracheal stump, and the cecum and ascending colon are approximated to the cervical esophagus and the oral cavity, respectively. We present our experience with a modified ileocolic free flap for reconstruction following cervical esophagectomy and total laryngopharyngectomy with and without total glossectomy. Methods: A retrospective chart review was conducted for all patients undergoing ileocolic flap reconstruction from 2002 to 2007. The modified ileocolic flap described in this study utilizes the terminal ileum as a monitoring segment. The ascending colon is handsewn to the oral cavity mucosa, and the cecum anastomosed using an end to end anastomosing device to the cervical esophagus. Outcomes examined included length of stay, development of complications including fistula formation, and the rehabilitation of the swallowing function. Results: We identified four patients who underwent reconstruction with a modified ileocolic free flap. Ages ranged from 54 to 78 years old. All patients were male. One patient required colon interposition following failed gastric pull-up for resection of squamous cell carcinoma (SCC) of the cervical esophagus. One patient required colon interposition following multiple complications of peptic ulcer disease including esophageal perforation and stenosis. Two patients underwent total glossectomy and total laryngopharyngectomy for recurrent advanced stage SCC of the larynx following XRT and salvage surgery. Length of stay was 10-14 days. Draining fistulas developed in the neck in 3 out of 4 patients and healed spontaneously without surgical intervention. Three out of 4 patients were on a regular or soft diet, and one patient is on a liquid diet. Two patients are tolerating an oral diet and have had their g-tube removed. Conclusions: Our modification of the ileocolic free flap with colon interposition is a viable option for reconstruction of large defects of the cervical esophagus, hypopharynx and larynx. Functional swallow is obtainable, although some patients will still require supplementation with additional enteral therapy through a gastrostomy tube.

P144: MICROVASCULAR RECONSTRUCTION AND HEAD AND NECK CANCER: THE NECESSITY FOR A QUALITY APPROACH H.Cisla1, P.Gangloff1, B.Philip1, R.Mastronically1, F.Guillamin1, J.Verhaeghe1, G.Dolivet1, 1Centre Alexis Vautrin, Nancy, France

Aims: Treatment and reconstruction of head and neck cancer remains a challenge. From the first consolidation of the surgery and radiotherapy, time has to be saved in order to insure optimal treatment for the patient, best survival rate and quality of life. Our goal, for this situation, is to establish a sort of quality landmark of the head and neck patient019s route. 54 patients who underwent microsurgical reconstructions after head and neck cancer have been studied, between 1997 and 2005. Results: The rate of failure compared to patient019s body mass index (BMI), ASA stage, age, pre or post operative radiotherapy, surgeon019s and institution019s experiences, number of venous drainage have been studied. Success rate is better when more than one vein is sued in the flap and when patients have a BMI more than 20. Radiotherapy has no impact on flap success. Conclusions: Regarding to literature and our study results, patient019s survival rate, treated by free flaps, is higher when the overall treatment time is less than 100 days, which can be achieved only with a perfect organisation of the
Patients with locally advanced oropharyngeal tumors are... of the flap was found in 6 patients (5.8%).

**Introduction:** Facial nerve paralysis is common in patients in the head and neck cancer clinic. This can result from deliberate surgical excision or iatrogenic damage and can be partial or complete. Patients suffer with severe cosmetic morbidity and problems with eyesight, speech and mastication. Many patients are not suitable for complex reanimation due to age, comorbidity and previous surgery. **Patients and Methods:** Patients were reviewed retrospectively in a facial palsy clinic aligned to a head and neck cancer clinic between May 2006 and October 2007. We recorded the underlying cause of facial nerve paralysis, the preoperative facial symptoms, the technique used, the patient’s comorbidities, and postoperative complications. The goals of static reconstructions were to protect the eye-sight, resect the rest of the tumor, and to restore the functions. The Nottingham Scoring System was used for objective assessment of our results. **Results:** Thirty-five patients were included in the study. Different static reconstructions were used: brow lift, gold weight placement, tarsorrhaphy, bone anchor support, fascia lata graft and face lift. Ten (28.6%) patients had gold weight placement, eight (22.9%) patients had bone anchor support and four (11.4%) patients had lateral tarsorrhaphy. Endoscopic and transcervical palpoplasty brow lift were performed in eight patients (22.9%). Two (5.7%) patients had face lift procedure. Static fascia lata sling was used in five (14.3%) patients. Subcutaneous hematoma was recorded in one (2.8%) case and two (5.7%) cases had extrusion of bone anchor threads. **Conclusions:** Surgical reanimation of head and neck tumours can result in facial paralysis. Many patients have severe comorbidity following previous multiple surgeries or radiotherapy. We demonstrated the use of simple static procedures which could be done under local anaesthesia and showed enormous benefit to this patient group. Treatment must be individualized and techniques adjusted to accommodate previous scarring. Our results demonstrate that this high risk group gain long term benefit from simple static procedures which can often be repeated if required in the long term.

**P146: FUNCTIONAL RESULTS PLASTIC DEFECT OF OROPHARYNX BY VISCERAL MICROSURGICAL FLAPS**

**Introduction:** Surgical treatment of malignant locally advanced oropharyngeal tumors is a challenging task in terms of obtaining good long-term oncological results, on the one hand, and providing social rehabilitation of the patients, on the other. We tried to develop a method of surgical reanimation after extensive resections that will not compromise oncological outcome and will improve quality of life in the given group of patients.

**Methods:** 103 patients with malignant locally advanced oropharyngeal tumors (age 15-69) were operated in P.A. Hertzen Cancer Research Institute between 1995 and 2007. Tumors were located in oral cavity (30), tongue (12), oropharynx (9), laryngopharynx (8), larynx (11), maxilla (10), mandible (4), laryngopharynx (13 pts) and soft tissues (6). The predominant histologic type was squamous-cell carcinoma. Patients under analysis fell in two groups – primary tumors (44 pts) and recurrent tumors (59 pts). In the primary tumors group there were 21 patients with T4, 18 patients with T3 and 5 patients with T2 tumors; 39 patients (37.8%) had N1 disease. In recurrent tumors group relapses occurred after surgical treatment and/or chemoradiotherapy (dosage ranged from 24 to 110 Gy). In all cases patients presented with significant cosmetic and functional defects of the upper digestive and respiratory tracts. We used gastro-omental (55 pts) or colon-omental (48 pts) flaps for microsurgical reconstruction of oral and pharyngeal mucosa. The mucosal portion of the flap was used to restore mucosal defects and soft tissues defect was restored with omental portion. The second step of oropharyngeal reconstruction was carried out in 24 patients. In 5 cases in one stage with pharyngolaryngectomy was performed tracheo-oesophageal shunting with establishing voice protez to rehabilitate the voice. The second step voice rehabilitation was achieved at one patient.

**Results:** Necrosis of the flap was found in 6 patients (5.8%). Good functional qualities of the transplant contributed to the complete healing of salivary fistulas in 15 patients (14.5%). There were no complications associated with abdominal cavity. Four patients (3.8%) died in the postoperative feeding. Peri-oral API started from the 14th day after surgery. Natural food intake was restored in 97 patients. All patients were ducanulated within 3-7 weeks after surgery. In 6 cases a vocal function was applied after tracheo-oesophageal shunting with establishing voice protez. At 53 patients from 55 which the resection of tongue has been executed are received satisfactory results of speech function. The general life expectancy of patients within 36 months after operation has made: 63.5% at use gastro-omental flap and 58.7% at use colon-omental flap.

**Conclusion:** Patients with locally advanced oropharyngeal tumors are treated most effectively using multimodal approach – chemoradiation with extensive surgical resection. The use of visceral free flap autotransplantation help the store vast defects after resections and improves quality of life in such patients.

**P147: SIMULTANEOUS DOUBLE FREE FLAP WITH T ANASTOMOSIS TO THE RADIAL ARTERY ON HEAD AND NECK RECONSTRUCTION**

**Introduction:** Combined free flap reconstruction has changed the treatment of patients with complex defects in head and neck surgery. In last years, free flap reconstruction has optimized the results of functional and esthetic results for this group of patient. Undeniably, they are a special group of patients who have a very difficult surgical planning in terms of reconstruction cause a previous neck surgery, previous radiation therapy or the need of two free flaps. The aim of this work is to show a safe way to solve the vascular supplies with the simultaneous use of two free flaps in head and neck reconstruction using a T anastomosis on one of free flap vascular pedicle. Case 1: male, 60 years old. He had mandible osteoradionecrosis (anterior arch) and floor of the mouth fistula. The patient had a previous selective neck dissection and a pectoral flap. We made a simultaneous double free flap: fibular free flap for mandible reconstruction (anterior arch) and forearm flap for intraoral lining. The radial artery anastomosis was end-to-side with the external carotid artery on the same side. The fibular anastomosis was on-to-side in T shape with the radial artery simultaneously. Case 2: male, 65 years old. He had a second primary tumor in the retromolar trigone. He has had previous laryngectomy with radical neck dissection in the same side of the new tumor. We made a simultaneous double free flap for reconstruction after surgical ablation; fibular free flap for mandible reconstruction (lateral) and forearm flap for intraoral lining. The radial artery anastomosis was end-to-end with the external carotid artery stump. The fibular artery anastomosis was end-to-side in T shape with the radial artery simultaneously. We also rotated a cephalic vein to the neck to allow vein drainage. The radial artery is a long vessel on also has a very good size. Cardiosurgeons has recognized the ability of the radial artery to give arterial flow to another vessel time ago. This ability was used in this report to support another free flap simultaneously with good results. Previous reports have shown the possibility to used previous radial artery, but not in one-stage surgery. We concluded that the simultaneous double free flap with T anastomosis to the radial artery is safe an also is a good tool for patients who have undergone a previous neck surgery.

**P148: TRIPLE SKIN ISLAND FIBULA FREE FLAP - THE GOOD CHOICE FOR COMBINED MANDIBLE AND TONGUE DEFECTS RECONSTRUCTION**

**Introduction:** The rehabilitation of patients who have undergone a previous neck surgery. The radial artery anastomosis was end-to-end with the external carotid artery stump. The fibular artery anastomosis was end-to-side in T shape with the radial artery simultaneously. We also rotated a cephalic vein to the neck to allow vein drainage. The radial artery is a long vessel on also has a very good size. Cardiosurgeons has recognized the ability of the radial artery to give arterial flow to another vessel time ago. This ability was used in this report to support another free flap simultaneously with good results. Previous reports have shown the possibility to used previous radial artery, but not in one-stage surgery. We concluded that the simultaneous double free flap with T anastomosis to the radial artery is safe an also is a good tool for patients who have undergone a previous neck surgery.

**Conclusion:** Resections of malignant tumors involving mandible and anterior tongue result in complex defects which are still a real challenge for reconstructive surgeons. Whereas there are preferred methods for isolated, or with limited loss of soft tissues mandible reconstruction, there are no standards for extended bone-soft tissues intraoral defects. This paper documents the modification of the fibula free flap where triple skin islands are used for reconstruction of anterior tongue and floor of the mouth, and isolated part of flexor halicus longus muscle, based on individual perforator, is set into submandibular space. The details of flap designing, harvesting and insetting are also presented. The use of visceral free flap autotransplantation help the store vast defects after resections and improves quality of life in such patients.

**P149: TRIPLE SKIN ISLAND FIBULA FREE FLAP - THE GOOD CHOICE FOR COMBINED MANDIBLE AND TONGUE DEFECTS RECONSTRUCTION**

**Introduction:** Resections of malignant tumors involving mandible and anterior tongue result in complex defects which are still a real challenge for reconstructive surgeons. Whereas there are preferred methods for isolated, or with limited loss of soft tissues mandible reconstruction, there are no standards for extended bone-soft tissues intraoral defects. This paper documents the modification of the fibula free flap where triple skin islands are used for reconstruction of anterior tongue and floor of the mouth, and isolated part of flexor halicus longus muscle, based on individual perforator, is set into submandibular space. The details of flap designing, harvesting and insetting are also presented. The use of visceral free flap autotransplantation help the store vast defects after resections and improves quality of life in such patients.
To evaluate the functional outcome of reconstruction by a free vascularized ileocolic flap after concurrent chemoradiotherapy (CCRT) and surgery for advanced laryngeal and hypopharyngeal cancer. Method: Fifteen patients (all male, mean age 49.8 years) with squamous cell carcinoma of the larynx (n=6), hypopharynx (n=7), and a stenotic pharyngo-oesophageal segment post-laryngectomy (7). In the series of patients with an intact larynx [8], all but one patient was successfully decannulated. All patients had an improved tolerance of their secretions postoperatively. Two patients resumed a regular diet, and three tolerated purées. One patient with a prior supraglottic laryngectomy and another with bilateral vocal cord paralysis later required a completion laryngectomy for persistent aspiration. Two patients currently have persistent aspiration. In the series of patients with extension of the stenosis to the larynx or above (resulting in an inadequate airway) a total laryngectomy was performed at the time of the reconstruction (7). Two patients required a second free flap reconstruction for recurrent stenosis; to date, they are tolerating PO intake with no evidence of formation of a new stenosis. One patient developed a wound infection following total laryngectomy requiring a temporary pharyngo-esophageostomy followed by a free gastro-omental flap reconstruction. All patients except for one, who is still in the rehabilitation phase, are currently tolerating their secretions as well as PO intake. In the series of patients who had post-laryngectomy pharyngo-oesophageal stenosis (7), all patients are currently tolerating their secretions as well as PO intake. Additionally, all patients are able to voice via their tracheo-oesophageal puncture. Conclusions: The management of pharyngo-oesophageal stenosis represents a difficult task. One must determine the extent and location of the stenosis as well as the functional status of the larynx, utilizing imaging and endoscopic techniques (routinely) prior to definitive surgical management. Once the proper workup has been performed, the transfer of well vascularized tissue represents an excellent reconstructive option for stenoses which have failed conservative management.

Objective: Osteoradionecrosis (ORN) represents a difficult clinical complication of radiation therapy to the head and neck. The standard management of early ORN has been antibiotics, hyperbaric oxygen, and debridement. One of the options for patients presenting with advanced osteoradionecrosis (pathologic fracture, fistula, full-thickness devitalization of bone) is a segmental mandibulectomy and free osteocutaneous flap reconstruction. These cases represent an extremely hostile environment for wound healing with both bone and soft tissue considerations which respond favorably to the transfer of healthy well vascularized tissue. The purpose of our study is to review our institutional experience utilizing free tissue transfer as definitive treatment for cases of ORN which have either failed conservative management or presented with Marx Class III or IV disease. Additionally, we will examine the role HBO played in the management of these advanced cases.

Methods: We performed a retrospective review of all patients who underwent a surgical resection of the region of osteoradionecrosis with free flap reconstruction between 2004 and 2007. Patients successfully treated conservatively (HBO, intravenous antibiotics, debridement) were excluded from this study. Additionally, not all patients in this study received radiation therapy at our center, where a protocol for dental care pre and post radiation therapy is strictly adhered to. Results: Between October 2004 and December 2007, 33 patients underwent a segmental mandibulectomy for ORN with a free flap reconstruction. All patients had failed conservative management (IV Antibiotics, HBO, and debridement) or presented with such advanced disease (Marx class III or IV) it was determined that conservative management would not be a reasonable option. 60% (20/33) of the patients had follow-up for 18 months or greater (range, 1 to 38 months). The donor sites utilized for reconstruction were: 22 fibula, 9 scapula, and 2 iliac crest free flaps. 29 of the patients had mandibular body defects. 3 patients had angle to angle defects. 1 patient required a condyle to angle osteotomy free flap reconstruction. All patients except for one, who is still in the rehabilitation phase, are currently tolerating their secretions postoperatively. Two patients resumed a regular diet, and three tolerated purées. One patient with a prior supraglottic laryngectomy and another with bilateral vocal cord paralysis later required a completion laryngectomy for persistent aspiration. Two patients currently have persistent aspiration. In the series of patients with extension of the stenosis to the larynx or above (resulting in an inadequate airway) a total laryngectomy was performed at the time of the reconstruction (7). Two patients required a second free flap reconstruction for recurrent stenosis; to date, they are tolerating PO intake with no evidence of formation of a new stenosis. One patient developed a wound infection following total laryngectomy requiring a temporary pharyngo-esophageostomy followed by a free gastro-omental flap reconstruction. All patients except for one, who is still in the rehabilitation phase, are currently tolerating their secretions as well as PO intake. Additionally, all patients are able to voice via their tracheo-oesophageal puncture. Conclusions: The management of pharyngo-oesophageal stenosis represents a difficult task. One must determine the extent and location of the stenosis as well as the functional status of the larynx, utilizing imaging and endoscopic techniques (routinely) prior to definitive surgical management. Once the proper workup has been performed, the transfer of well vascularized tissue represents an excellent reconstructive option for stenoses which have failed conservative management.

Objective: Surgical treatment of oral cancer results in defects that are complex, and yield to complications such as swallowing and speech disorders that affect patients quality of life. Immediate free tissue transfer provides excellent functional outcomes, mainly by using radial forearm fasciocutaneous free flap that perfectly fits with oral cavity reconstruction requirements. Objective: The aim of this study was to review the experience of our institution in performing microvascular oral cancer reconstruction with forearm free flap. Methods: During the 3-year period 2006-2007, 34 patients underwent oral cavity reconstruction for cancer. All were operated on by the same surgical team (one senior head and neck surgeon and one senior reconstructive surgeon). Patients underwent intensive post operative speech and swallowing therapy. Mean follow up was 13 months (9-23) and all functional and cosmetic outcomes were evaluated by the same clinician. Quality of life was assessed by patients using a 5-stage functional GLO scale. Results: Functional outcomes were best for the static conditions: 100% of lip and palate continence. Dynamic functional outcomes demonstrated the versatility of the forearm free flap: an unrestricted oral diet was recovered in 88% of patients (n=34), intelligible speech was recovered in 100% of patients (n=34). Quality of life was assessed normal or subnormal in 31 patients (91%). Conclusions: Oral cavity reconstruction is best achieved with microvascular forearm free flaps in terms of functional outcomes and post operative quality of life.

Objective: Treatment of upper aerodigestive tract (UADT) malignancies with chemoradiation often preserves the laryngopharynx. However, stenosis of the pharyngo-esophagus is common, often requiring surgical intervention. In this study, we will review our previously reported defect classification system, our management algorithm, and our surgical intervention results in a series of patients with this growing problem. Methods: We performed a retrospective chart review of all patients who were treated for radiation induced pharyngo-esophageal stenosis between October 2004 and December 2007. All patients who were successfully treated by endoscopic or open surgery were excluded. Results: 22 patients with post-treatment pharyngo-esophageal stenoses were reconstructed. The stenoses were defined according to our previously reported defect classification system involving their location, extent, and any history of attempted dilatation (with or without perforation). 8 patients retained an intact larynx which was preserved during the reconstruction. Reconstruction was performed with a single gastro-omental free flap [4], free jejunal free flap, radial forearm free flap [8], gastric pull-up [11], lateral arm flap [1], or pectoralis major rotational flap [5]. All flaps were successfully transferred. Mean follow-up was 17 months (range, 1 to 36 months). We divided our patients into three groups, those with an intact larynx [8], those with extension of the stenosis to involve the hypopharynx, oropharynx and/or larynx [7], and those with a stenotic pharyngo-esophageal segment post-laryngectomy [7]. In the series of patients with an intact larynx [8], all but one patient was successfully decannulated. All patients had an improved tolerance of their secretions postoperatively. Two patients resumed a regular diet, and three tolerated purées. One patient with a prior supraglottic laryngectomy and another with bilateral vocal cord paralysis later required a completion laryngectomy for persistent aspiration. Two patients currently have persistent aspiration. In the series of patients with extension of the stenosis to the larynx or above (resulting in an inadequate airway) a total laryngectomy was performed at the time of the reconstruction (7). Two patients required a second free flap reconstruction for recurrent stenosis; to date, they are tolerating PO intake with no evidence of formation of a new stenosis. One patient developed a wound infection following total laryngectomy requiring a temporary pharyngo-esophageostomy followed by a free gastro-omental flap reconstruction. All patients except for one, who is still in the rehabilitation phase, are currently tolerating their secretions as well as PO intake. Additionally, all patients are able to voice via their tracheo-oesophageal puncture. Conclusions: The management of pharyngo-oesophageal stenosis represents a difficult task. One must determine the extent and location of the stenosis as well as the functional status of the larynx, utilizing imaging and endoscopic techniques (routinely) prior to definitive surgical management. Once the proper workup has been performed, the transfer of well vascularized tissue represents an excellent reconstructive option for stenoses which have failed conservative management.
head and neck can both result in ORN of the mandible. If a patient has extensive ORN or has failed conservative management, free tissue transfer can be used successfully as a definitive treatment for this disease. In the setting of advanced ORN (Marx class III and IV), segmental mandibulectomy and free flap reconstruction is the procedure of choice and results in excellent functional and cosmetic outcomes in a single stage. We believe that this is the largest series to date of microvascular reconstruction of mandible ORN.

SALIVARY

P153: IS THE DISTRIBUTION OR CERTAIN BIOLOGIC FACTORS INVOLVED IN THE LOCATION OF MINOR SALIVARY GLAND TUMORS OF THE PALATE? C.Chavez de Paz V 1, C.Z.Liu 1, G.A.Krempl 1, J.E.Medina 1, L. Queimado 1, 1The University of Oklahoma Health Sciences Center, Oklahoma City, OK

Objective: Salivary gland (SG) tumors are more common in major salivary glands. The analysis showed no significant differences in 1) Understand that two neoplasms can develop in a major salivary gland. The sub- objective is a reflection of a differential concentration of minor SG’s or other biological factors. A decrease in Wnt inhibitory factor 1 (WIF1) leads to activation of the Wnt signaling pathway and has been shown to play a role in SG cancer. Myoepithelial cells may inhibit tumor progression. The purpose of this study was to evaluate the distribution and concentration of minor SG’s throughout the palate, and to determine the levels of expression of WIF1 and smooth muscle actin (SMA) within the palatal minor SG’s, parotid and submandibular glands. Materials and Methods: The SG/palates from 10 fresh cadavers were evaluated. To determine the distribution and relative volume of minor SG’s a 1 cm wide strip of full thickness mucosa/sub-mucosa was harvested from the palates in an antero-posterior direction. Simultaneously samples of parotid and submandibular glands were obtained from each cadaver. For morphometric and immunohistochemical analysis, the palate strip was divided into 9 proportional sections from anterior to posterior. Paraffin embedded sections were stained for H&E. The relative volume of minor SG’s was determined as the ratio of thickness of the minor SG/total palate thickness for each section. WIF1 and SMA expression levels were determined by immunohistochemistry and quantified using a scale 0-3. Statistical analysis was performed using the Student’s t-Test. Results: No minor SG’s were present in the anterior third of the hard palate. In the soft palate minor SG’s were present under the oral mucosa but not in the nasopharyngeal mucosa. The ratio of the SG thickness/total palate thickness was significantly higher in the posterior third of the hard palate in comparison with other areas of the hard (p=0.00001) and soft palate (p=0.01). There were no differences in WIF1 or SMA expression within the palate (NS). WIF1 expression was moderate to high in parotid and submandibular gland and much lower in palate minor SG’s (p=0.00001). There was homogenous staining for myoepithelial cells around acini in all sites (NS). Conclusions: There is a significantly higher concentration of minor salivary glands in the posterior third of the hard palate in comparison with the rest of the hard palate and soft palate. There were no differences on WIF1 and SMA expressions within the palate. These results suggest that the predominant location of minor salivary gland tumors may be a result of the distribution of the glands in the palate and/or related to other biological factors. WIF1 expression is significantly lower in palatal minor salivary glands. This result may be a reflection of the abundance of mucous cells in these glands. Nonetheless, it is important to further elucidate the environment favoring tumor progression and therefore contribute to the high frequency of malignancies observed in minor salivary glands. The role other molecular/genetic differences needs to be further elucidated.

P154: ASSESSMENT OF EXTRACELLULAR MATRIX PROTEINS IN ADENOID CYSTIC CARCINOMAOF SALIVARY GLAND USING MORPHOMETRIC METHOD W.Golusinski 1, A.Wagner 1 1 Department of Head and Neck; Department of Otolaryngology; Department of the Cancer Immunology; The Great Poland Cancer Center, Poznań 144, Poznan, Poland

Background: Adenoid cystic carcinoma (ACC) is an uncommon form of malignant epithelial neoplasm. It arises within major and minor salivary glands as well as mucous glands of the upper respiratory tract. It is characterized by high clinical malignancy, with unclear prognosis and unstable clinical course. Immunohistochemical studies of the tumor microenvironment are found in the extracellular matrix, containing fibronectin, type IV collagen and laminin. Aim: The aim of the present study was to assess the protein components of the extracellular matrix: laminin and fibronectin of ACC using morphometric analysis. Methods: The study group included 30 patients with ACC of major salivary glands. The expression of immunohistochemical reaction for laminin and fibronectin was assessed using computerized analysis of obtained images. In order to assess the actual field stained for fibronectin and laminin photographic documentation was performed in the form of digital images images with resolution of 640x480 pixels using light microscope with Senarmont magnification 40x (Micro Optic Industrial Group Co, controlled using the software Motic Imagesv. 1.2 [MS Windows]). Results: The analysis showed no significant differences in mean laminin and fibronectin positive reaction areas. Analysis of the proteins depending on histological ACC subtype showed that fibronectin expression was significantly lower in tubular cancer compared to other types. For laminin no significant expression difference was found. Conclusions: In the future the immunochemistry of laminin and fibronectin may become a useful element of prognosis assessment in patients with adenoid cystic carcinoma. Immunohistochemical assessment of laminin and fibronectin may give valuable information on prognosis in adenoid cystic carcinoma. The studies on the influence of these glycoproteins on cellular migration, and thus on local infiltration (especially of peripheral nerves) and systemic metastasis, are particularly interesting.

P155: ADENOID CYSTIC CARCINOMA AND PLEOMORPHIC ADENOMA ARISING IN AN ACCESSORY SUBMANDIBULAR GLAND S.I.Lennick 1, J.R.Panal 1, 1 Rush University Medical Center, Chicago, IL

Objective: 1) Understand that two neoplasms can develop in a major salivary gland. 2) Understand that dissection can clarify the origin of a tumor if the radiologic study is equivocal. Methods: A long-standing pleomorphic adenoma uncommonly converts to a malignant variant, carcinoma ex-pleomorphic adenoma. Accessory submandibular glands are rare entities. An 81 year-old female presented with a painless right neck mass for two years, recently enlarging. She had no paraesthesias or facial nerve dysfunction. CT revealed an enhancing, calcified mass 30x18 mm inferior to the posterior extent of the mandibular ramus, likely of submandibular origin. FNA biopsy revealed benign salivary gland epithelial cells, macrophages, occasional calcifications, but no malignant cells. Results: Excision of the neck mass and a modified neck dissection revealed a high-vascular mass located just deep to the platysma, superficial to the digastric muscle, and, by gross inspection, completely separate from the capsule of the submandibular gland. The mass contained two tumor types, adenoid cystic carcinoma arising in the background of a pleomorphic adenoma, adjacent to benign salivary gland tissue. No vascular, lymphatic or perineural invasion was identified. The submandibular gland, dissected and sent separately, revealed no malignancy. No malignant cells were seen in regional lymphoid tissue, although distinct nodes were not identified. Contiguous soft tissue contained soft salivary gland tissue without evidence of malignancy. AJCC tumor stage: T2N0NX. Conclusions: The submandibular gland rarely develops two neoplasms simultaneously. It is even more uncommon for two tumors to develop in accessory salivary gland tissue.

P156: FACIAL NERVE INVASION BY PAROTID GLAND CARCINOMA: POSSIBLE RISK FACTORS AND OUTCOME OF FACIAL REANIMATION M.Pries 1, H.Shufel 1, R.Feinemesser 1, T.Shipitzer 1, 1Rabin Medical Center, Petach Tiqua, Israel

Objective: Carcinoma of the parotid gland accounts for 3-6% of all head and neck cancers and 14-25% of all parotid lesions. Aggressive lesions involving the facial nerve or its branches are less frequent. None of the available imaging modalities provides accurate preoperative information on the involvement of the facial nerve. The aim of this study was to define risk factors for facial nerve involvement in parotid gland carcinoma and to examine the results of facial nerve reanimation. Methods: The charts and hospital records of all patients who underwent surgery for carcinoma of the parotid gland from 2000 to 2007 at a major tertiary referral hospital were reviewed. Results: Sixty-one patients met the study criteria, including 37 men and 24 women aged 29 to 93 year. Lesion size ranged between 5mm and 120mm (mean 35mm). Seventy patients were disease free, 17 patients had preoperative facial pain. In 27 patients, the mass appeared to involve the deep lobe on preoperative imaging study. During surgery, in twenty-four patients, the diagnosis of facial nerve involvement was verified and the nerve the facial nerve was sacrificed. Neck dissection was performed in 33 patients, and metastatic lymph nodes were found in 18. On statistical analysis, 3 factors were found to be significantly associated with facial nerve involvement: facial palsy at presentation (p=0.0098), lesion...
To report an uncommon branching pattern of the marginal mandibular nerve after parotidectomy, some patients may exhibit permanent facial palsy. This case report emphasizes the importance for surgeons operating on the parotid gland to be aware of this possible anatomical variation. In this case report, a rare branching pattern of the marginal mandibular branch of the facial nerve was identified in parotid resection. It is important for surgeons performing parotid surgery to be aware of this possible anatomical variation.

The harmonic scalpel has been shown to effectively and safely cut tissue and ligate blood vessels in thyroidectomy. Studies have shown that it reduces operating time and blood loss compared to conventional clamp and tie techniques. The use of the harmonic scalpel is an effective and time-saving technique for tissue dissection and blood vessel ligation.

The harmonic scalpel has been shown to be useful for the resection of benign neoplasms and lymph nodes for staging of lymphoma or melanoma. Other modifications of parotidectomy include preservation of the greater auricular nerve, superficial musculo-aponeurotic system (SMAS), and retrograde facial nerve dissection. Branches draining to the main parotid duct from the parotid lymph nodes are described. The size of lesions ranged from 1 to 4 cm. Facial nerve electromyographic monitoring was used in all cases. After skin flaps were developed superficial to the parotid, the SMAS was closed primarily following resection. At least 1 cm margins around pleomorphic adenomas were obtained except when adjacent to the SMAS (in which the SMAS was resected in continuity) or the facial nerve, and extracapsular dissection done around lymph nodes. Facial nerve exposure and dissection was performed using retrograde technique. Branches draining to the main parotid duct from the lesion were incised rather than the main parotid duct whenever feasible. The SMAS was closed primarily following resection. All cases had successful preservation of at least the posterior branches of the greater auricular nerve. 3 patients had intact anterior skin flap sensation. The SMAS was partially excised over superficial parotid pleomorphic adenomas in 6 procedures, and incised to reach lymph nodes or deep tumor in 3 cases. All had SMAS primarily closed with minimal postoperative swelling.

Objective: To report our institutional experience in the treatment of salivary gland malignancies using definitive and adjuvant chemoradiotherapy for locoregionally advanced and high risk salivary gland malignancies. Methods: From 2006-2007, the first 100 patients (2001-2003) were evaluated. In the two having parotid duct transection, both had postoperative swelling. In the two having parotid duct transection, both had postoperative swelling. In the two having parotid duct transection, both had postoperative swelling. The SMAS was closed primarily following resection. Results: All cases had successful preservation of at least the posterior branches of the greater auricular nerve. 3 patients had intact anterior skin flap sensation. The SMAS was partially excised over superficial parotid pleomorphic adenomas in 6 procedures, and incised to reach lymph nodes or deep tumor in 3 cases. All had SMAS primarily closed with minimal postoperative swelling.

Results: The average operating time was decreased for the harmonic scalpel relative to the conventional technique. There were minimal intra-operative complications. The harmonic scalpel is an effective and time-saving technique for tissue dissection and blood vessel ligation.

Conclusion: The harmonic scalpel resulted in a significant reduction in operating time and post-operative complications as compared to conventional clamp and tie technique for neck dissections and parotidectomies. There were minimal intra-operative complications. The harmonic scalpel is an effective and time-saving technique for tissue dissection and blood vessel ligation.
The prognostic indices again performed adequately in this study. The medical charts of 59 consecutive patients were reviewed. The eligibility criteria was: diagnosis of locoregional recurrent salivary gland carcinoma, no distant metastasis, and Salvadore dural carcinoma was the most common pathologic subtype to have nodal metastasis followed by squamous cell carcinoma.

P163: HISTOLOGICAL GROUP PREDICT OCCULT NECK METASTASIS IN PRIMARY PAROTID CARCINOMA

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Objective: Management of clinically negative neck of patients with primary carcinoma of the parotid gland depends mostly on the histological diagnosis and the stage of the primary tumor. For some histological type it remains controversial. This retrospective study review the management of clinically N0 parotid primary in our department to clarify the indication for elective neck dissection in the management of parotid cancer. Methods: From 1995 to 2005 30 patients were treated surgically for primary carcinomas of the parotid gland along with a neck dissection (ND) in the department of Otolaryngology Head and Neck Surgery of Lausanne University Hospital. They were grouped according to TNM stage and low or high histological risk. All groups were compared for incidence of occult nodal metastasis. Results: Three patients had therapeutic ND. Among 27 elective ND, 6 had occult metastases on histological analysis. All of them belonged to the high histological risk group of the large (T3-T4) tumors (p=0.03). None of the eleven patients in the low histological risk group with a small tumor (T1-T2) had occult metastases (p=0.006). Conclusions: Global incidence of occult metastases in primary parotid cancer is low (22%). TNM staging and histological risk group seem to predict the need for elective neck dissection.

P164: PROGNOSTIC INDEX FOR PATIENTS WITH PAROTID CARCINOMA: INTERNATIONAL EXTERNAL VALIDATION IN A BELGIAN-GERMAN DATABASE

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Background: Prognostic indices for recurrence free interval of parotid carcinoma patients were developed [Cancer 1998;85:2057-67] and validated in a nationwide database [Cancer 2003; 97:1453-63]. International validation increases generalizability. Methods: In a Belgian-German database containing 237 consecutive parotid carcinoma patients, the pretreatment (PS1) and posttreatment (PS2) prognostic indices were validated by calculating both indices for each patient, comparison of coefficients, construction of survival curves, calculation of concordance measure C, and performing Wald tests for scale and weight optimization of included variables, and for possible inclusion of new variables. Results: 69% (SE 5%) was disease free at five years. The defined cut-off points for PS1 resulted in 5 year disease free percentages from 94% (PS1=1) to 42% (PS1=4) and for PS2 from 93% (PS2=1) to 40% (PS2=4). Concordance measure C was good with 0.74 for PS1 and 0.74 for PS2. Both indices could not be clearly improved using this international database. There was some evidence that additional inclusion of the variable “number of positive nodes in the neck dissection specimen” could enhance the prognostic power of PS2. Conclusion: The prognostic indices again performed adequately in this validation sample. Prospective generalization used seems well supported.
The overall rate of surgical complications was 32%, and the most frequent one was wound infection. There was no postoperative death. There was a new recurrence in 61% of the patients (distant metastases in 16 cases, 27%). The lung was the most frequently involved site. In ten cases (17%) the recurrence was only local and in 5 cases (9%) only regional. The actuarial overall survival rates were 61% in 5 years and 42% in 10 years. Gender, histology, site of the primary tumor and facial nerve preservation (parotid tumors) were not associated with overall survival. In the univariate analysis, only age older than 60 years was associated with a poor prognosis. Conclusion: This study showed that the primary site of a parotid gland tumor and facial nerve preservation with salvage surgery had an impact on survival. Parotid cystic carcinoma was treated with salvage surgery is acceptable. Most surgical complications are local and there was no postoperative mortality in this series.

Objective: To analyze the experience of treating advanced adenoid cystic carcinoma (ACC) of the head and neck with upfront concurrent chemoradiation. Study Design: Retrospective case series of 13 patients with ACC of the head and neck treated at 3 tertiary care centers between December 1996 and April 2007 with concurrent chemoradiation. Methods: Primary cancer was located in the base of tongue and nasopharynx in 4 patients each, trachea in 2, and hard palate, nasal cavity, and paranasal sinuses in 1 patient each. T-stage was 1 in 1, 73 in 5 and T4 in 7 patients; 1 patient had lung metastasis at presentation. Five patients received single-agent cisplatin intravenously and the other 8 intra-arterial cisplatin concurrently with radiation. Eleven patients were treated with definitive doses of radiation (median dose 70Gy), one of them with protons. Two patients received a preoperative dose (50Gy) and underwent planned surgical resection. Results: Median follow up was 31 (range: 7-100) months. Ten patients are alive and 3 have died of their disease. Complete resolution of tumor was noted at the primary site in all patients. However, one patient developed delayed local failure at 39 months (and was successfully surgically salvaged), and 4 (31%) developed distant metastasis in follow up. Two- and 5-year estimates of overall survival are 100% and 83% respectively. Conclusion: Upfront radiation administered concurrently with intravenous or intra-arterial cisplatin, with or without planned surgery, can result in prolonged local control and extended survival in cases with advanced ACC of the head and neck.

Introduction: Primary adenocarcinomas of the parotid gland are rare and account for less than 5% of all head and neck malignant neoplasms. There is a considerable variation in biological behaviour; low grade tumors exhibit slow growth rates with minimal or no local invasion. High grade tumors however, show a high incidence of local recurrence and distant metastasis. Aims: The purpose of this paper is to analyse the important prognostic indicators for this cancer. Methods: A systematic review was performed involving 19 published studies from 1987 to 2005 which included 4631 patients. T-stage, grade of tumour, N stage & adjuvant radiotherapy on overall (5 year) survival were analysed as prognostic indicators. Forest plots were calculated, fixed and random effect models were used to test heterogeneity. Results: T stage (p=0.009), N stage (p=0.006) and high grade (p=0.001) were associated with a significantly worse survival. The effect of adjuvant radiotherapy was to improve overall survival (p=0.004). The mean 5 year survival for advanced high grade parotid cancer was 35%. Conclusion: High grade advanced parotid cancers are associated with a poor survival. Adjuvant radiotherapy is indicated in these tumors and this improves survival.

Objective: This study analyzed the factors in parotid gland carcinoma influencing recurrence and disease-specific survival. Method: We retrospectively evaluated patients with parotid gland cancer who received their definitive treatment from 1995 to 2005. Survival analysis was performed using the Kaplan-Meier method and a log-rank test for comparing subgroup. Logistic regression analysis was employed to define the recurrence-associated prognostic factors. The median follow-up time was 5 years. Results: 106 patients were included (95 men and 54 women); their mean age at presentation was 48.2 years. All patients were treated with surgery and 81 patients had postoperative radiotherapy. Overall and Disease-specific survival at 5 years was 40.4% and 56.7%, respectively. 183 patients had recurrences; 15 had local recurrence, 13 had regional recurrence, 5 had locoregional recurrence, and distant metastasis developed in 10 patients. Multivariate analysis confirmed tumor grade, facial palsy, and surgical margins as poor prognostic factors (p < 0.05). Adjuvant radiotherapy vs. surgery alone reduced the risk of death from disease at 5 years by 48% (hazard ratio, 0.48; 95% CI, 0.243-0.991; p = 0.036). Conclusion: The tumor grade and surgical margin were the most important prognostic factor. Patients with adverse prognostic factors benefit from adjuvant radiotherapy.
Epithelial-myoepithelial carcinoma is an uncommon, low-grade, malignant epithelial neoplasm. It comprises less than 1% of all salivary gland neoplasms and presents most commonly in the parotid gland. We present a case of a 62-year-old female with a history of a left orbital mass. The mass was excised with safety margin, preserving almost parotid gland tissue around. The mass was encapsulated and had clear resection margin. There was no complication like facial nerve paralysis or salivary fistula. The facial skin seemed to swell for a day but recovered after several days. During follow-up visit of one year, there was no evidence of recurrence, metastasis, and complication.

Conclusions: We could resect acinic cell carcinoma of the accessory parotid gland, identifying the facial nerve trunk and the zygomaticobuccal branches, preserving almost parotid gland tissue.

P172: INDICATIONS FOR RADIATION THERAPY IN ACINIC CELL CARCINOMA OF THE PAROTID GLAND: A SINGLE INSTITUTION EXPERIENCE
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Purpose: Retrospective review of acinic cell carcinoma (ACC) of the parotid gland treated at a single institution. Methods: From 03/1989 to 08/2006, 38 consecutive patients underwent surgery at our institution for ACC of the parotid gland. The median age at diagnosis was 48 years. The American Joint Committee on Cancer (AJCC) 6th edition T-stage distribution was as follows: T1, 47% (n=18); T2, 24% (n=9); T3, 21% (n=8); T4, 8% (n=3). Surgery ranged from wide local excision to radical resection. Twenty six percent of patients (n=10) who underwent resection necessitated sacrifice of a major branch of the facial nerve. Postoperatively, 8% had cervical nodal involvement, 16% with gross extracapsular extension (ECE) of the primary site, 21% had high grade tumors, 26% with perineural invasion, and 29% had positive margins. Twenty five patients received postoperative radiotherapy, of which 19 received their radiation at our institution. Patients were selected for radiation therapy that had adverse clinical or pathologic factors. Thus, of the patients receiving radiation, 44% had T3/T4 disease, 44% had positive margins, 24% had high grade disease, 24% had ECE, and 12% of patients had cervical nodal involvement. All patients without these adverse factors were treated with surgery alone. Of the 19 patients treated with radiation at our institution, 68% (n=13) were treated with conventional techniques, while in the remainder conformal radiation techniques were utilized. The median radiation dose was 6300 cGy (range 5400-7000).

Results: At a median follow-up of 55 months for surviving patients (range 3-174 months), five year rates of disease-free survival (DFS), overall survival (OS), local control, and distant metastasis free survival were 82%, 94%, 92%, and 86%, respectively. No patient who received surgery alone failed treatment. Twenty four percent of patients (n=6) who received postoperative radiation failed treatment; one locoregionally alone, three distantly alone, and two both locoregionally and distantly. Of the prognostic variables tested, high grade and gross ECE of the primary site were significantly correlated with decreased DFS (p=0.013 and p=0.025, respectively). In addition, two of three patients with cervical nodal involvement failed treatment. Facial nerve dysfunction was the most common sequela postoperatively, occurring in 68% of patients (n=26). However, only the patients with major nerve branch sacrifice had permanent facial nerve palsies (26%, n=10). Radiation toxicity was assessed solely on those patients treated at our institution. The most common chronic radiation side effect was xerostomia, occurring in 32% of patients (n=6).

Conclusions: ACC of the parotid gland is a manageable disease with a high proportion of patients experiencing freedom from DFS and OS. Patients with adverse clinical and pathologic factors are at a higher risk for treatment failure and should be considered for postoperative radiation therapy.

P173: POLYMORPHOUS LOW-GRADE ADENOCARCINOMA OF THE TONGUE: A CASE OF PATHOLOGICAL DEDIFFERENTIATION WITH CERVICAL METASTASES
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Objective: Polymorphous low-grade adenocarcinoma (PLGA) is a rare tumor that was first described as a distinct entity in 1983. The tumor predominantly affects minor salivary glands most commonly on the hard and soft palate, and is characterized by slow growth, indolent progression, and a low incidence of locoregional and distant metastases. Transformation of this tumor to high-grade adenocarcinoma, as determined by pathological and immunohistochemical criteria, has rarely been described in the literature. The majority of those cases that have been shown to dedifferentiate typically occur over a decade after the original diagnosis was made, and many of these patients have a history of previous head and neck external beam radiotherapy.

Methods: Case report. Results: An unusual case of a PLGA of the tongue with locoregional recurrence as high-grade adenocarcinoma in the ipsilateral neck 5 years following treatment, and again as high-grade adenocarcinoma in the contralateral neck 2 years after definitive cervical lymphadenectomy and adjunct external beam radiotherapy is described. A review of the literature discusses the incidence and characteristics of PLGA, highlights the pathological and immunohistochemical characteristics seen in dedifferentiated PLGA, and stresses the importance of careful long-term surveillance for patients with PLGA given the long delay between primary tumor diagnosis and recurrent disease.

Conclusions: Polymorphous low-grade adenocarcinoma, a rare tumor of the minor salivary glands, typically behaves indolently with infrequent locoregional and distant metastases and unusual transformation to high-grade adenocarcinoma. This is the first case of a PLGA of the tongue to transform to high-grade adenocarcinoma and multiple locoregional cervical recurrences.

P174: UNILATERAL PAROTID MASS: A RARE PRESENTATION OF SARCOIDOSIS
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Objective: To illustrate how key steps in the evaluation of a unilateral parotid mass are critical to establishing a diagnosis of sarcoidosis.

Methods: Case presentation and review of the literature. The diagnostic evaluation, traditional clinical and pathologic findings, and current treatment recommendations for sarcoidosis will be reviewed. The relative role and efficacy of fine-needle aspiration in making the correct diagnosis will be discussed.

Results: The case is described of a 41-year-old woman with unilateral parotid gland enlargement. Computed tomography did not reveal any discrete stone or mass. Fine needle aspiration was non-diagnostic.

Operative biopsy of the parotid was performed and the tissue was found on pathologic examination to contain non-caseating granulomas, which is
To determine if Extracapsular Dissection (ECD) versus Partial

The histologic

Tumor recurrence occurred in 36/1183 (3.0%) of

Published series demonstrate a significantly

The purpose of this article is gaining information on survival

Sixty-two patients with submandibular gland carcinomas, under-

To determine

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adenocarcinomas but the difference was not statistically significant.

mucoepidermoid and adenocarcinomas but the difference was not statisti-

implying rare event, generally associated with immune compromise, and a

case arising within a benign parotid neoplasm has not previously been described. This report conveys our recent experience with management of

An unusual presentation of 375 parotid cases operated on between 1980 to 2007, we found 53 (14.1%) cases of parotid carcinomas. These cases were analyzed retrospectively. Results: Thirty-four patients (64%) were male and mean age was 55. Facial paralysis was present in 5 patients. The tumor was ulcerated in 7. Neck nodes were present in 6 patients. Ultrasound, CT scans and/or magnetic resonance image (MRI) were employed in all the patients. The most common pathological types were mucoepidermoid carcinomas, adenocarcinomas, adenoid cystic carci-

CONCLUSIONS: Published series demonstrate a significantly higher rate of recurrence and permanent facial nerve dysfunction and a lower rate of transient facial nerve dysfunction with ECD. A prospective study would be preferred however given the average length of time to recur-

P175: PLEOMORPHIC ADENOMA: EXTRACAPSULAR DISSEC-

P176: PROGNOSTIC FACTORS IN PAROTID CANCER L.A. Pacheco-

Parotid cancer is an uncommon neoplasm in Ecuador, South America. We have analyzed de results of management in a consecutive homogenous series of patients operated by one surgeon. Methods and Materials: An analysis of 375 parotid cases operated on between 1980 to 2007, we found 53 (14.1%) cases of parotid carcinomas. These cases were analyzed retrospectively. Results: Thirty-four patients (64%) were male and mean age was 55. Facial paralysis was present in 5 patients. The tumor was ulcerated in 7. Neck nodes were present in 6 patients. Ultrasound, CT scans and/or magnetic resonance image (MRI) were employed in all the patients. The most common pathological types were mucoepidermoid carcinomas, adenocarcinomas, adenoid cystic carci-

P177: OPTIMAL TREATMENTS IN SUBMANDIBULAR GLAND CARCINOMAS: FOR BEST OUTCOMES OF LOCOREGIONAL CONTROL AND SURVIVAL G. Lim1, J. Roh1, S. Choi1, S. Lee1, K. Cho1, S. Nam1, S. Kim1, 1Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

Objective: The purpose of this article is gaining information on survival rate, prognosis, and optimal treatments in submandibular gland carcinoma.

Methods: Sixty-two patients with submandibular gland carcinomas, underwent radical excision with/without neck dissection, and 41 patients with high-grade, invasive, positive margin, or regionally metastatic tumors received postoperative radiotherapy. The locoregional control and survival rates were calculated by the Kaplan-Meier method, and prognostic factors were gained from uni- and multivariate analyses. Results: The histologic types of patients were adenoid cystic (n=19), mucoepidermoid (n=11), salivary duct carcinomas (n=10), and carcinoma in pleomorphic adenomas (n=8). 5-year locoregional control, disease-free and overall survival rates were 69.7%, 52.8%, and 56.8%, respectively. In multivariate analysis, T stage and state of resection margins were prognostic factors for locoregional control (P < 0.02). T stage and histological grade were prognostic factors for disease-free survival (P < 0.001). Distant metastases were found in 21 patients (33.9%), 2 patients at initial staging and 19 at follow-up.

Conclusions: Local aggressiveness of the primary tumor is a significant prognostic factor in these patients. Radical resection and postoperative radiotherapy may increase the locoregional control, but one-third of patients fail systemically, a cause of poor survival.


Objective of Study: Fungal abscess of the parotid gland is an exceedingly rare event, generally associated with immune compromise, and a case arising within a benign parotid neoplasm has not previously been described. This report conveys our recent experience with management of such an entity in an immunocompetent host and places it in context of the limited information on this condition. A review of the literature is provided.

Results: A 59 year old healthy male smoker describing a preceding history of a 1 centimeter nodule in the parotid tail region presented with rapid onset of a massive inflammatory process over that site, leading to an abscess. Aspiration and culture revealed C. glabrata as a causative organism, and anti-fungal therapy was instituted. Rapid recurrence of the fluid collection led to two subsequent open drainage procedures, and biopsies taken at the cavity wall were without evidence of neo-

P179: CRT1/MAML2 Fusion Transcript in Concurrent Warthin’s Tumor and Mucoepidermoid Carcinoma: Possible Genetic Association D. Bell1, M.A. Luna1, R.S. Weber1, F.J. Kaye2, K.E. Niedergerke1, 1UT M.D. Anderson Cancer Center, Houston, TX; 2National Cancer Institute and Naval Hospital, Bethesda, MD

Background: Translocations and gene fusions have an important early role in tumorigenesis. The t(11;19) translocation and its CRT1/MAML2 fusion transcript have been identified in several examples of both Warthin’s tumor and mucoepidermoid carcinoma and are believed to be associated with the development of a subset of these tumors. Methods: To determine whether some of Warthin’s tumor and mucoepidermoid carcinoma are genetically related, we used reverse transcriptase-polymerase chain reaction (RTPCR) and DNA sequencing to analyze microdissected components of three tumors consisting of Warthin’s tumor and mucoepidermoid carcino-

a hallmark of sarcoidosis. Conclusions: Sarcoidosis, a systemic granulo-

mous disease, can rarely present as unilateral parotid swelling without other symptoms. Establishing the diagnosis in this setting can be challeng-

ing due to the broad differential for unilateral parotid swelling, and the fact that parotid sarcoidosis typically presents with bilateral involvement. Recent studies have shown that isolated parotid involvement is only seen in 4-6% of cases, and in 73% of cases is bilateral, suggesting that unilateral parotid involvement as the sole presentation of sarcoidosis occurs in less than 1% of patients. A high index of suspicion, followed by biopsy of an accessible affected area, is critical in establishing the correct diagnosis. In this case the parotid was biopsied due to the non-diagnostic FNA. Although several small studies have reported a potential role for FNA in establishing the diagnosis with less morbidity, in this case it failed to correctly identify sar-

coyosis as the disease process. On-going studies are now evaluating the efficacy of ultrasound-guided FNA, which may allow avoidance of parotidectomy for diagnosis in the future.
FNAB is an efficient procedure and good quality of...

The aim of this study was to report the frequency of selective use...

To evaluate the performance of the...

The mean age of the...

indicated by the absence of a significant difference in histologic findings...

The mean intensity score for...

The mean distribution score, 2.68; corresponding values for the 1987-1990 group were 2.22 and 2.78. For HSP90, the mean intensity score for...

HSP70. The levels of tissue staining and of HSP distribution in the tumor...

Immunohistochemical techniques were employed to identify HSP70 and...

ma. We also investigated a Warthin’s tumor that occurred with metastatic melanoma to the parotid gland and a solitary Warthin’s carcinoma for comparison. Results: The fusion transcript was identified in both Warthin’s tumor and matching mucocoeplidmoid carcinoma components of all three tumors, in the Warthin’s tumor component but not in the metastatic melanoma and in the Warthin’s carcinoma. Conclusions: 1) A subset of Warthin’s with the (11;19) fusion transcript may be prone to the development of MEC, 2) oncocytic carcinoma with fusion positive may originate from benign Warthin’s with these alterations, 3) fusion positivity is restricted to certain type of tumors and 4) a putative model for Warthin’s tumor development is presented.

P180: WARTHIN’S TUMOR OF THE LARYNX: CASE REPORT
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Objective: To describe a case of a Warthin’s tumor presenting in a rare, extraparotid location within the supraglottis. Methods: Case report and review of literature. Conclusion: Warthin’s tumor (papillary cystadenoma lymphomatosum) is a benign neoplasm, which frequently occurs in the parotid gland. Rare extraparotid locations have been described in the submandibular glands and larynx. Warthin’s tumor of the larynx is an unusual finding in addition to Warthin’s tumor of the submandibular glands and larynx. Warthin’s tumor of the larynx is an unusual finding. Treatment in this case involved marsupialization. Although Warthin’s tumor is benign with a low rate of recurrence and malignant transformation, clinical follow-up is required to detect recurrences.

P181: HEAT SHOCK PROTEINS IN PLEOMORPHIC ADENOMA OF THE PAROTID GLAND IN THE ERA OF WIDESPREAD USE OF CELLULAR PHONES
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Objective: Heat shock proteins (HSPs) serve as molecular chaperones with strong cytoprotective effects. Some of their important “housekeeping” functions include protein import into cellular compartments, protein folding, stable protein degradation and protein complex dissolution. In addition, HSPs may promote cell survival via their activities at multiple points in the apoptotic signaling pathway. HSPs expression may be induced by stressful stimuli such as heat, oxidative stress or other tissue-damaging events. An elevated expression of HSP70 and HSP90 has been associated with tumorgenesis, poor prognosis, and resistance to treatment in several types of cancer. So far, there is little information on the possible role of HSPs in pleomorphic adenoma of the parotid gland. We speculated that the contemporary widespread use of cellular phones may expose the parotid region to local heat which could, in turn, affect HSP expression in parotid tissue. The aim of this study was to evaluate levels of HSP70 and HSP90 in pleomorphic adenoma of the parotid gland and to compare the findings before and after the cellular phone era. Methods: On the basis of data derived from a local cellular phone company (Partner Communications, Rosh HaAyin, Israel) indicating that the widespread use of cellular phones in Israel began in the early 1990s, we collected random specimens of pleomorphic adenoma obtained from patients operated on in 2005 (n=10) and between 1987 and 1990 (n=14) from the archives of the Department of Pathology. Results: Of the 28 specimens analyzed, 25 were pleomorphic adenomas, 06 squamous cell carcinomas, 06 malignant lymphomas, 05 Warthin’s tumor, 03 salivary gland cysts and 09 another lesion. Conclusions: The findings indicate a significant relationship between the use of cellular phones and the expression of HSPs. The results of this study suggest that the current widespread exposure to cellular phones may increase the risk of HSP expression in parotid tissue.

P182: EVALUATION OF FINE NEEDLE ASPIRATION BIOPSY IN THE DIAGNOSIS OF CANCER OF THE PAROTID GLAND IN A COLOMBIAN POPULATION
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Background: Fine Needle Aspiration Biopsy (FNAB) is used commonly in the study of neoplastic lesions of the parotid gland; however, there exists controversy in its accuracy. Objective: To evaluate the performance of the FNAB in the diagnosis of the parotid gland carcinoma. Materials: 46 patients with masses in the parotid area from 7 health centers of Bucaramanga, Colombia were selected. Results: The mean age of the patients was 51.78±16.32 years old, the 58.7% were female. The FNA had a Sensitivity of 53.8%, a Specificity of 90.9%, a PPV of 70%, a NPV of 83.3%, a LR+ of 5.92 and a LR of 0.5 and kappa of 0.48 in the identification of parotid gland carcinoma, in a population with a prevalence of the disease of 28.26%. Conclusions: The FNAB had a moderate performance in the diagnosis of the parotid gland carcinoma, which agrees with other previous studies. Its low sensitivity and LR+ indicates its limitations as a screening test in addition to its additional time and costs associated with its diagnosis. Therefore, it’s advisable to improve the criteria used in its interpretation, as well as to make emphasis on the development of new technologies that allow a better, valid and precise diagnosis of this pathology, and that like the FNAB, offers its service at low cost and with ease of implementation.

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Objective: The aim of this study was to report the frequency of selective use of preoperative fine-needle aspiration biopsy (FNAB) in patients with salivary gland lesions at the Hospital Erasto Gaertner, between March 2001 and December 2005. Methods: We reviewed 194 medical records of patients with salivary glands lesions. FNAB was performed in 116 (59.8%) of salivary gland lesions undergoing surgical procedures. There were 84 FNAB specimens (72.4%) that were satisfactory for evaluation and 32 cases that were inconclusive or unsatisfactory for evaluation. Results: A total of 80 lesions were in the parotid gland, 34 in the submandibular gland and 02 in minor salivary gland. Comparing the results by FNAB with the pathological analysis, 28 (24.1%) were incompatibles and 56 (48.3%) compatibles. The results of the FNAB compatibles with the HA were 27 pleomorphic adenomas, 06 squamous cell carcinomas, 06 malignant lymphomas, 05 Warthin’s tumor, 03 salivary gland cysts and 09 another lesion. Conclusions: FNAB is an efficient procedure and good quality of samples are obtained for diagnosis in preoperative of salivary glands lesions. An FNAB diagnosis of malignant or neoplastic major salivary gland disease is generally predictive of final histological diagnosis.

P184: FINE-NEEDLE ASPIRATION CYTOLOGY OF MAJOR SALIVARY GLANDS: HISTOLOGICAL CORRELATION IN 159 CASES
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Objective: Fine-needle aspiration cytology (FNAC) of major salivary glands helps differentiate between benign and malignant lesions. The aim of this study was to determine the accuracy of FNAC and identify the different causes of misdiagnosis. Methods: Retrospective chart review of patients undergoing FNAC and surgery of the parotid and submandibular glands in a tertiary care center between 1992 and 2006. One hundred and fifty nine salivary gland excision specimens (151 parotid glands and 8 submandibular glands) were compared to the pre-operative FNAC diagnoses. All cases with discordant cyt-histopathological diagnosis were reexamined by the cytopathologist to determine whether there was sampling or observational errors. Results: FNAC was found to be benign in 102 cases, malignant in 20 cases, not contributive in 29 cases, and suspect of malignancy in 8 cases. We obtained a sensitivity of 79% and a specificity of 99%. The positive predictive value for diagnosis of malignant lesions was 95% and the negative predictive value was 95%. Identified diagnostic pitfalls are cystic lesions and lymphocyte predominant Hesions. Conclusions:
Fine-needle aspiration cytology is reliable in distinguishing benign and malignant lesions. FNAC is an additional tool to radiology and should not supersede clinical suspicion. Lymphocytic lymphoma should prompt further workup to rule out lymphoma.

**P185: REPEATED BOTULINUM TOXIN A TREATMENTS OF PATIENTS WITH FREY SYNDROME**

**Objective:** The effectiveness of repeated intracutaneous injections of botulinum toxin A in the treatment of Frey syndrome was assessed. **Methods:** In this prospective study 22 (12 male and 10 female) patients underwent repeated treatments with intracutaneous injection of botulinum toxin A because of severe complaints of Frey syndrome between 1999 and 2005. Patients were instructed to make a new appointment if retreatment was requested. Before each treatment the time interval, the affected area, as determined by the starch-iodine test, and subjective quantification of the symptoms, as assessed by a previously used Frey Questionnaire Card (FQC), were scored. **Results:** All patients underwent at least 3 treatments. Univariate analysis of variance showed a significant difference (p<0.0005) in interval with previous treatment for the different treatment numbers. Univariate analysis of variance showed a significant difference (p<0.0005) in affected area for the different treatment numbers. The mean FQC score decreased by repeated treatments. **Conclusions:** In Frey syndrome patients repeated treatment with intracutaneous injection of botulinum toxin type A improve on the results of the previous treatment: lowering of subjective symptoms score, decrease of affected area and increased duration of effect.

**SKULL BASE/SINUS/EAR**

**P186: DIVERSE MR MANIFESTATION OF SKULL BASE TUMOR REGRESSION PATTERN IN POST-RADIATED NPC: A PICTORIAL ESSAY WITH PET CORRELATION**

**Introduction:** To illustrate one of the most perplexing imaging issues in using MR to monitor the skull base evolutionary change in advanced nasopharyngeal carcinoma. **Material and Method:** NPC with advanced T stage is defined as tumor invasion to skull base (T3), infratemporal fossa and intracranium (T4). Following the radiation treatment, the characteristics of tumor existence, including the pattern of contrast enhancement, narrow fat depletion and apparent residual lesion contour varies greatly related to the time interval, radiation dose and also radiation-rele- vant inflammation. Thanks to the availability of periodical MR surveillance and the correlation with PET and clinical outcome, the preliminary stratification of imaging findings can be obtained and analyzing the advanced NPC cases in the recent three years. **Goal:** To make the imaging diagnosis more with confidence and provide more reliable information for the clinicians to reinforce the regimen, alter the treatment strategy or just watchful waiting instead.

**P187: MAXILLARY RECONSTRUCTIONS USING PEDICLED TEMPORAL MUSCULOSPERIOSTEAL FLAP WITH OR WITHOUT FREE CALVARIAL BONE GRAFT**

**Objective:** Reconstructive surgery of maxilla is both technically challenging and rewarding. Different techniques of repairing maxillary defects have been used. The aim of this study was to evaluate the suitability of pedicled temporal musculoperiosteal flap and free calvarial bone graft for reconstruction of maxillary defects. **Methods:** In this retrospective series of 34 patients between 1995 to 2006 at Turku University Hospital, due to defects of maxilla using pedicled temporal musculoperiosteal flap with or without free calvarial bone graft were evaluated. **Results:** The commonest diagnosis in the tumour group was squamous cell carcinoma (n=15), and the most common localisations were maxillary sinus (n=14), hard palate (n=7) and maxillary gingiva (n=5). 32 patients were operated on due to malignant tumour, one patient due to benign tumour and one for the maxillary defect after trauma. According to TNM classification of malignancies (n=32), there were eleven, nine T2, five T3 and seventeen T4 tumours. Preoperative radiotherapy (n=14), preoperative chemotherapy (n=2) or postoperative radiotherapy (n=11) were used in tumour group. As a reconstructive method temporal musculoperiosteal flap was used with (n=21) or without (n=13) free calvarial bone graft. At one month follow-up, flap survival for 32 patients was 71.9%, 28.1% of the patients suffered from partial flap loss, and there was no total flap loss. At six month follow-up, flap survival for 26 patients was 76.9%, 7.7% of the patients suffered from partial flap loss, and there were four (15.4%) total flap losses. If unilateral alveolar maxilectomy was performed (Brown classification a), at one month follow-up, flap survival was 82.6%, 17.4% of the patients suffered from partial flap loss, and there was no total flap loss. At six month follow-up, flap survival was 89.5%, 10.5% of the patients suffered from partial flap loss, and there was no total flap loss. At six month follow-up, flap survival was 42.9%, and 57.1% of the patients suffered from total flap loss. **Conclusion:** The application of pedicled temporal musculoperiosteal flap with or without free calvarial bone graft for maxillary reconstruction appears to be reasonable, particularly in maxillary defects classified type A according to Brown et al. (2002).

**P188: PROTON THERAPY FOR MAXILLARY SINUS CARCINOMA**

**Objective:** To compare the dose-volume data of a three-dimensional conformal proton therapy (3DCT) plan versus that of an intensity-modulated radiotherapy (IMRT) plan for a paranasal sinus malignancy. **Methods:** 3DCT and IMRT plans were created for a patient with T4N0 maxillary sinus spindle cell carcinoma. Target and organ at risk (OAR) volumes were defined on a computed tomography simulation scan using preoperative and postoperative magnetic resonance scans. The prescription dose to the clinical target volume was 74.4 Gy, and both plans were normalized so that 100% of the clinical target volume received 90% of the prescribed dose. **Results:** The mean and integral doses for all of the OARs were lower for proton therapy (absolute and relative reduction in mean dose of 4.4 to 24.5 GE/Gy, and 8.3% to 100%, respectively). The maximum doses for both plans to the ipsilateral optic nerve/retina/lens, temporal lobe, pituitary, and brain exceeded their respective normal tissue tolerance doses. The normal tissues of the contralateral parotid, lacrimal gland, and lens were completely avoided with proton therapy in contrast to IMRT. Neither the 3DCT nor IMRT plans exceeded the maximal tolerated dose for the critical structures of the brainstem, optic chiasm, contralateral temporal lobe, parotid glands, or lacrimal glands. **Conclusion:** Both 3DCT and IMRT sufficiently covered the target volume(s). While 3DCT reduced the mean and integral dose to all of the OARs, both 3DCT and IMRT irradiated the ipsilateral optic structures beyond acceptable tolerance doses. The benefit of reducing the mean and integral doses to normal tissues is unknown. Proton therapy may improve the therapeutic ratio for paranasal sinus malignancies.

**P189: SURGERY FOR TUMORS INVOLVING INFRATEMPORAL FOSSA**

**Objective:** Tumors involving Infra temporal Fossa generally have a poor outlook due to complexity of the situation. Anatomically it is complex with vital structures like the carotid & lower cranial nerves crammed in a bony pyramid with other soft tissue. Hence to know the outcome of the treatment, a retrospective analysis was done at the regional cancer center at Chennai. **Methods:** This is a retrospective analysis; the case records were retrieved from the tumor registry & analyzed systematically. The cases operated between 1996 & 2001 were analyzed. A total of 25 cases were taken up for analysis. Age ranged from 22 to 71 with a median of 53 & 17 were males & 8 were female. All patients had preoperative imaging with CT scan for MR 14, 14 had enhanced MRI, 14 had enhanced MRI with diffusion scan & SPECT scan. Of the 25, 9 had primary salivary gland tumour, 7 had sarcoma, 4 had schwannoma & 4 had squamous cell carcinoma of cheek & antrum. **Results:** The surgical approach was chosen by the location & biology of the tumour. It included 1. transvenous (7 cases), 2. transmandibular & transpalatine (5 cases), 3. lateral approach : extracranial (3 cases), 4. Transcranial (8 cases). Reconstruction included temporals flap, free flap.
The purpose of this presentation is to report the survival, cosmetic and functional outcomes of patients with malignant tumors of the maxilla; 2) report on the different methods of reconstruction remains controversial. Cancer offers good survival and functional outcomes. The rational of the different methods of reconstruction remains controversial.

P192: MAXILLARY CANCER: SURVIVAL AND LONG TERM FUNCTIONAL OUTCOMES H.Seikaly1, J.Yu1, J.Rieger1, K.Ansari1, K.AlQahtani1, A.M.Mlynarek, 1, J.Harris1, 1University of Alberta, Edmonton, AB, Canada

Introduction: Cancer of the maxilla is a devastating disease that affects all aspects of the patient's life. Treatment has routinely resulted in significant cosmetic and functional deficits. The advent of obturation and more recently free tissue transfer has improved patient outcomes and quality of life.

Objective: The purpose of this presentation is to report the survival, cosmetic and functional outcomes of a prospective cohort of patients with cancer of the maxilla treated with primary surgery. Methods: 38 consecutive patients treated between 1990 and 2003 for cancer of the maxilla were followed prospectively through our Multidisciplinary Head and Neck Surgery Reconstruction Clinic. All patients had a minimum follow up of 3 years. Swallowing was assessed with videofluoroscopy and a diet questionnaire. Speech was assessed by acoustical, aeromechanical and perceptual measurements. All assessments were performed at 4 points in time (preoperative and 1-month, 6-months, and 1-year postoperatively). Cosmetic outcome was assessed by naive observers. Results: The average age of the cohort was 62.5. 85% were male. 82% patients had postoperative adjunct treatment. 3 patients had stage 1-2 and 35 had stage 3-4 disease. The disease specific survival was 82% at 3 years and 69% at 5 years. Local control was achieved in 96% of patients. Restoration of speech function was achieved, with normal perceptual, acoustic and aeromechanical speech outcomes for all patients across all assessment times. The swallowing results reveal that timely restoration of swallowing function was achieved in all patients. The cosmetic outcomes were rated good to excellent for all patients. Conclusions: Surgical treatment of maxillary cancer offers good survival cosmetic, and functional outcomes.

P193: MAXILLARY SURVIVAL OUTCOMES J.Wu1, D.Cote1, J.Chau1, A.Mlynarek1, H.Seikaly1, 1University of Alberta, Edmonton, AB, Canada

Objective: The objective of this paper is to: 1) report on the survival outcomes of patients with malignant tumors of the maxilla; 2) report on the functional outcomes of the different reconstructive methods employed (obturation or free flaps). Methods: A prospective cohort of patients enrolled from 1990 to 2006 in our Head and Neck multidisciplinary reconstructive clinic were reviewed. Functional outcomes were performed as per our pre-published protocol which includes: modified barium swallow, speech articulation and aeromechanical measurements. Results: The 5 years survival of early stage (1-2) patients and advanced (3-4) were 95% and 85% respectively. All patients had good functional recovery irrespective of the method of reconstruction. Conclusions: Surgical treatment of maxillary cancer offers good survival and functional outcomes. The rational of the different methods of reconstruction remains controversial.

P194: MASTICATORY EFFICIENCY AND FACIAL APPEARANCE OUTCOMES OF MAXILLARY DEFECTS A.Smiles1, B.K. Davis2, O.Bandyopadhyay3, M.Brodsky3, B.Martin-Harris3, K.Grasso3, 1Medical University of South Carolina, Charleston, SC; 2Medical University of South Carolina, Charleston; 3Medical University of South Carolina, Charleston, SC

Objective: The objective of this study was to compare measures of masticatory efficiency and facial appearance with prosthetic obturation versus surgical reconstruction of maxillary defects. Methods: Ten patients treated for cancer or benign tumors with maxillary resection from the Medical
University of South Carolina/Hollings Cancer Center were randomly selected to participate in this study. Five of the patients had been treated with surgical reconstruction and five had been treated with prosthetic obturation. The patients and five controls were administered a masticatory efficiency test by Kapur et al. Five judges graded the ten patients on a facial appearance scale with a score of 1 with no disfigurement, a score of 2 with minimal disfigurement, and a score of 3 with severe disfigurement. The 5 obturator patients completed an obturator functioning questionnaire. Results: The mean masticatory efficiency scores for the prosthetic obturation was 90.7% of normal, with 1 patient (20%) scoring 86% of normal. The mean masticatory efficiency scores for the obturator patients was 85.6% of normal, with 1 patient (20%) scoring 83% of normal. The mean masticatory efficiency scores for the obturator patients was 84.1% of normal, with 1 patient (20%) scoring 82% of normal. Conclusion: The utilization of a single approach may not be adequate to achieve an adequate resection in difficult skull base tumors. The roles of the plastic and head and neck surgeon are either to resect the tumor if there is no intracranial extension or to provide exposure to give the neurosurgeon the access needed for resection and to reconstruct the cranial defect, orbit, parapharyngeal space, and openings into the nasopharynx. This type of surgery is very demanding and requires good preoperative planning and close cooperation with a neurosurgeon and plastic surgeon. It can also be combined with external approaches to achieve safer resection. The transoral and transoral-transcervical approach provides access to selected cases of maxillary sinus tumors. A randomized study that compares masticatory efficiency, aesthetic outcomes, and other outcome factors such as speech, resonance, and swallowing are warranted.

**P195: TRANSMAXILLARY APPROACH FOR THE RESECTION OF T3-T4 MAXILLARY SINUS CARCINOMA INVOLVING PTERYGO-MAXILLARY FOSSA**


Objective: Transmaxillary approach is the most common cause of mortality in some studies. Total maxillectomy through the anterior approach of Weber Ferguson has been practiced since the 19th century. In tumors originating from the posterior wall of the maxilla, it is not possible to obtain a radical excision through this approach. Objective of this study was to determine the utility of transmaxillary approach for the excision of T3-T4 maxillary sinus carcinoma involving the posterior wall of maxilla. Patients: The series consisted of 10 patients with maxillary carcinoma originating from the posterior wall of the maxilla. Methods: Twenty patients with maxillary carcinoma originating from the posterior wall of the maxilla were operated through the transmaxillary approach at two different centers over the past eight years between 1999 and 2007. Five patients had been operated earlier by the first author. Results: In patients without extension through the anterior wall, facial incision was not necessary. Twenty patients did not require a facial incision since the transmaxillary transoral incision could be extended sublabially up to and beyond the midline. Free rectus abdominis flap was used for reconstruction. Histopathological examination showed microscopic negative margins in 21 cases of carcinoma. Conclusions: Transmaxillary approach provides access to tumors of the infratemporal fossa. It can be combined with external approaches to achieve safer resection. The transoral and transoral-transcervical approach provides access to selected cases of maxillary sinus tumors. A randomized study that compares masticatory efficiency, aesthetic outcomes, and other outcome factors such as speech, resonance, and swallowing are warranted.

**P196: TRANSORAL AND COMBINED TRANSORAL-TRANSCERVICAL APPROACH TO THE PARAPHARYNGEAL SPACE TUMORS**

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To present our experience with transoral and combined transoral-transcervical approaches to the parapharyngeal space (PPS) tumors and describe our technique for removal of these neoplasms. Both approaches were safely employed to remove 26 PPS tumors: benign salivary gland tumors (14 minor salivary gland and 2 deep lobe parotid gland pleomorphic adenomas), 2 cases of malignant salivary tumors, 4 nerve sheath tumors and 1 lymphangioma were also excised. Mean tumor size was 6.1 cm (range 2 to 11 cm). Visualization was felt to be adequate and dissection safe. Radical resection was achieved in 24 cases. Near total resection in 2 cases where other approach would be preferable but not undergone because of patient refusal and comorbidities. Patients with malignant tumors had post-operative radiotherapy. Radically operated cases are disease free (11 to 2 years). 1 of near-totally resected tumors needed revision surgery. Neither major complications nor disordered healing were seen. Transoral approach safely provides access to selected cases of PPS tumors based on preoperative imaging and fine needle aspiration cytology. Risk of nonradicality is acceptable. It can be combined with external approach to achieve safe resection.

**P197: THE VALUE OF COMBINING VARIOUS SKULL BASE APPROACHES TO ACHIEVE AN ADEQUATE RESECTION IN DIFFICULT SKULL BASE TUMORS**

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Objective: The utilization of a single approach may not be adequate to achieve an adequate resection in challenging and extensive skull base tumors. The roles of the plastic and head and neck surgeon are either to resect the tumor if there is no intracranial extension or to provide exposure to give the neurosurgeon the access needed for resection and to reconstruct the cranial defect, orbit, parapharyngeal space, and openings into the nasopharynx. This type of surgery is very demanding and requires good preoperative planning and close cooperation with a neurosurgeon and plastic surgeon. It can also be combined with external approaches to achieve safer resection. The transoral and transoral-transcervical approach provides access to selected cases of maxillary sinus tumors. A randomized study that compares masticatory efficiency, aesthetic outcomes, and other outcome factors such as speech, resonance, and swallowing are warranted.

**P198: TREATMENT OF INVASIVE AND EXTENSIVE OCULAR SURFACE SQUAMOUS CARCINOMA WITH SURGERY AND HEAVY TOPICAL MITOMYCIN C**


Objective: To report our results in the treatment of invasive ocular surface squamous carcinoma with excisional surgery and heavy topical treatment with mitomycin C. Design: Prospective interventional series. Methods: A prospective study was conducted in ten patients with invasive and extensive ocular surface squamous carcinoma. The patients were treated with surgical excision of the tumor and received topical mitomycin C 0.04% one drop four times a day. Treatment cycles were defined as 1 week using medication followed by 1 week without medication. Such treatment cycles were repeated for 4 weeks for a total of 4 cycles. Results: The median age was 66 years (range 09-77 years). At presentation, the tumor involved the limbus and cornea in all eyes to a median extent of 6 clock hours. Minimal extent of the tumor was 8 mm in the largest basal diameter in the ocular surface. Mitomycin C 0.04% four times daily was applied for 4 cycles. Complete tumor regression was documented in all ten cases (100%). There was no recurrence over a mean follow up of 12 months (range 6-18
months. Mitomycin C caused moderate to intense local irritation with excessive lacrimation, conjunctival erythema and chemosis, but no long-term intraocular or extra-ocular complications. **Conclusion:** Based on this series, excisional surgery combined with topical mitomycin C 0.04% applied in four weekly cycles appears to be a safe and effective therapy for extensive ocular surface squamous carcinoma, even when there is extensive recurrent tumor.

P199: PRIMARY MUCOSAL MELANOMA OF THE HEAD AND NECK: A THIRTY-YEAR EXPERIENCE AT ISTITUTO NAZIONALE TUMORI IN MILAN
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**Objective:** Primary mucosal melanoma of the head and neck (MMHN) is a rare disease. The prognosis is poor with a 5-year overall survival of 17.1%. We examined the clinical and pathological features of such patients treated at Istituto Nazionale dei Tumori of Milan (INT) during the past 3 decades to verify which prognostic factors, valid for cutaneous melanomas, are useful in the mucosal counterpart. **Methods:** From 1975 to 2004, 93 of MMHN were treated at INT; clinical dossiers and histological specimens were reviewed. The clinical and histological features were evaluated as prognostic factors. The main end-point is the time elapsed from the date of surgery to the date of the first evidence of relapse or of the last visit for the patients relapse-free. The prognostic impact of each variable was estimated by Cox regression model. Concerning the Breslow’s thickness and the ulceration, the original measurement scale were used, avoiding cut-offs. **Results:** 44 patients were female and 49 were male, with a median age of 59 years. Nase-panoramous sinuses, larynx, oral cavity and oropharynx were affected in 58, 2, 31 and 2 cases, respectively. 74 and 19 patients presented with disease staged I and II, respectively. 88 patients underwent surgery. 5 patients received only radiotherapy. Five-year overall survival was 29% for the whole series. After the primary treatment, 85 obtained a complete response 17 cases were considered as mucosal lentiginous, 18 were of nodular type, 33 were considered as Not Otherwise Specified and 2 cases presented a superficial spreading histotype. In 67 patients a pigmented lesion. 60 cases showed ulceration. In 24 cases the MMHN infiltrated the deeper layer of the mucosa, while in 48 cases the disease was limited to the chorion. According to Breslow's classification, the tumour thickness ranged between 0.49 and 20.00 mm. The number of mitoses/mm² ranged between 0 and 24. Vascular invasion, neutropoiesis, regression, sclerosis and microscopic satellites were considered absent in more than 85% of the cases while necrosis was recognized in 69% of them. In 18 cases there was vascular neogenosis. The Tumour Infiltrating Lymphocytes (TIL) was brisk in 10 cases, non-brisk in 24 and absent in 38 patients. After 60 months of follow-up, the probability of relapse was about 82%, and the probability of relapse on T, N, and M were 49%, 13% and 20% respectively. **Conclusions:** Considering patients with complete response, the absence of ulceration, necrosis, vascular invasion and the presence of a TIL described as brisk were significant protective characteristics on relapse in univariate analysis. The hazard of relapse increase with the increasing of the Breslow’ thickness and number of mitosis/mm². Sex, ulceration, Breslow’s thickness, TIL, number of mitosis/mm² and necrosis were the variables considered in the multivariate analysis. After the application of backward selection procedure (p<0.10), the selected variables were TIL, necrosis and number of mitosis/mm² and the last two are significant at 5% level. MMHN has an unfavourable prognosis. Our analysis resulted in conflicting data which confirms the lack of definitive conclusions in the literature.

P200: PRIMARY MUCOSAL MELANOMA OF THE HEAD AND NECK: PREDICTIVE FACTORS AND OUTCOME
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**Objectives:** The aim of this study is to identify prognostic factors and describe the outcome of patients with MMHN treated in a single referral center. **Methods:** Retrospective analysis of medical charts of patients diagnosed and treated of MMHN between 1983 and 2004 at the B.N.C.I. Pathological slides were reviewed to ascertain the origin of all cases and rule out metastasis or disseminated cutaneous melanoma. Impact of possible clinical and therapeutic factors was calculated by univariate analysis. Survival was calculated using the Kaplan - Meier survival curves with disease-specific (DSS) and overall-survival (OS) rates as the endpoints.

**Results:** Of the originally 49 patients with MMHN initially selected for this study, 6 patients who refused any type of treatment were excluded. Twenty-two patients (51.2%) had sinonasal tumors (SNMM), whereas 19 (41.2%) had oral (ORMM) tumors, and 2 (4.6%) had nasopharyngeal (NPMM) tumors. Distribution among genders was similar with a median age of 62 yrs. Eight patients (18.6%) were staged as stage I, 14 (32.5%) as stage II, 12 (27.9%) as stage III, and 9 (20.9%) as stage IV. Nine patients (20.9%) had lymph node metastases (N), 13 patients (26.5%) had distant metastases (DM), and 2 (4.6%) other patients had regional and distant metastases at presentation. Thirteen patients (30.2%) underwent surgery with adjuvant radiotherapy (RT), 15 had surgery alone (34.9%), 12 had exclusive RT (27.9%), and 3 had RT/CT (7%). Median follow-up was 31 months (9 to 102 months). Twelve patients (27.5%) developed DM, 11 (25.6%) NM, and 5 (11.6%) NM plus DM. Three (7%) patients had occult lymph node metastases found after elective neck dissection. Overall incidence of DM was 58.9% (25 patients). Rates of local failure for ORMM and SNMM were 21% and 18%, nodal failure rates were 31.65 and 22.7%, and distant failure rates were 36.8% and 40.9%, respectively (p=NS). The OS rates in 36 and 60 months was respectively 32.5% and 18.6%. The DSS was 25.6% and 16.3% for the same period on analysis. Significant prognostic factors for OS and DSS in our study included early clinical stages (stages I-II) at presentation (p=.04 and .03), type of treatment (radical surgery plus RT), and development of regional and distant metastases (p=.003 and .001). Although ORMM patients had better 5yr OS and DSS in comparison with SNMM patients (26.3% vs 12.5%, and 24.3% vs 8.3%), these results were not statistically significant (p=.07 and .08). **Conclusions:** Our results confirmed the aggressive behavior of MMHN with high rates of regional and distant metastases. Clinical stage at presentation, type of treatment used, and the development of regional and distant metastases were found predictors of outcome in our group of patients. Radical surgery with adjuvant radiotherapy appears to have the greatest efficacy in the management of MMHN.

P201: CRANIAL BASE MELANOMA
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**Objective:** Describe a rare presentation of an ocular melanoma of the anterior skull base that presented as a nasal mass and epistaxis, and the resultant treatment. **Study Design:** Case Report. **Methods:** Data is collected via a chart review with an accompanying literature review. We present the case of a 68-year-old woman who presented to our emergency department complaining of nasal congestion and epistaxis. The patient had a past history that was significant for conjunctival melanoma of the left eye treated with enucleation and left neck dissection 6 years prior. On physical exam a large fleshy mass was noted to occupy the entire nasopharynx. Tissue biopsy and radiographic exam confirmed that this patient had a recurrence of her melanoma in her paranasal sinuses. **Results:** Surgical intervention for this melanoma of the anterior skull base was unsuccessful and the patient recovered without neurological sequelae from the surgery. We present this patient’s history, diagnostic modalities, treatment, and follow-up. In addition to this case, we provide a literature review highlighting the few similar and related cases that have been reported. **Conclusions:** Long-term surveillance is crucial in patients with a history of melanoma as recurrence can have devastating consequences. This case emphasizes and reminds Skull base surgeons and Otolaryngologists of the need for surveillance, vigilance, and low threshold for suspicion in their patients with a history of melanoma.

P202: DILEMMAS IN THE MANAGEMENT OF SINONASAL ADENOCARCINOMA
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**Introduction:** Sinonasal adenocarcinoma (SNAC) represents a rare cohort of diverse and capricious malignant neoplasms that provide noteworthy dilemmas in diagnosis and subsequent management. The paucity of these malignancies and multiple histological subtypes has led to limited literature concerning their management. In an attempt to determine an optimal protocol for the systematic and reproducible management of sinonasal adenocarcinoma, the authors present their experience with a retrospective review of seven cases presenting over a ten-year period. **Methods:** Retrospective review of all patients with SNAC managed over a ten-year period in a tertiary referral Head and Neck cancer centre. **Results:** Seven patients with SNAC were identified. One patient had intestinal-type adenocarcinoma. Secondary malignancy was confirmed in two patients - metastatic prostate cancer and probable ovarian cancer respectively (ovarian mass on ultrasound scan and fluid in the pouch of Douglas) and unknown in one
patient (deceased prior to further investigation). The remaining four patients were found to have primary SNAC. These four patients underwent staging computed tomography of the chest, abdomen and pelvis to exclude an unknown primary. One patient remains alive today. Conclusions: Improving diagnostic services for patients with sinonasal adenocarcinoma should be of acknowledged importance. Classification of SNAC into (i) Unspecified, WITHOUT symptoms of underlying malignancy, (ii) Unspecified, WITH symptoms of underlying malignancy, (iii) Intestinal-type, REGARDLESS of symptoms of underlying malignancy and (iv) Specified [NOT intestinal-type] according to immunohistochemistry REGARDLESS of symptoms of underlying malignancy, may prove beneficial in tailoring investigatory decisions in an attempt to define primary from secondary disease and guide subsequent treatment.

P205: MORBIDITY PROFILE OF FACIAL TRANSLATION APPROACHES FOR SKULL BASE TUMOURS

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Objective: Efficacy of the facial translocation approaches has been well established in resections of tumours of antero-lateral skull base. This involves translocation of facial bone with its soft tissue envelope to access skull base tumours. Till date no study has documented morbidity associated with these approaches. The principal objective of this study is to evaluate morbidity profile of various facial translocation approaches.

Methods: Retrospective review of all patients who have undergone facial translocation approaches to access skull base tumours from July 2004 to Aug 2007 were carried out. Patient demographics, tumor characteristics and the type of facial translocation approach were recorded. The follow up results were reviewed to identify all attended complications related to the procedure. The complications were then correlated with the type of facial translocation approached and other confounding variables. Results: During the three years study period 24 patients underwent facial translocation. The facial translocation included 13 standard facial translocation, 8 medial maxillotomy and 3 extended facial translocation. The complications included 5 nasolacrimal duct obstruction, 4 ectropion, 3 palatal fistulas, 3 telecanthus, 3 plate exposure, 3 trismus, 2 bone graft necrosis, 2 diplopia, 1 CSF leak, 1 facial nerve paresis [upper division] and 1 exposure keratitis. Correlating the complications with confounding variable it was observed that 100% [n=3] of plate exposure and 2 out of 2 bone necrosis was associated with post-operative radiotherapy. Several technical modifications were made to lower the morbidity of facial translocation approaches.

Conclusions: Facial translocation approach is a reliable technique to access antero-lateral skull base with acceptable morbidity.

P206: MANAGEMENT AND OUTCOMES IN SALVAGE TREATMENT OF LATE NECK METASTASIS AND LOCAL RECURRANCE IN ESTHESIONEUROBLASTOMA

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Objectives: Esthesioneuroblastoma (ENB) is an uncommon tumor of the sinonasal region which metastasizes to the neck in approximately 20% of patients and has a local recurrence rate of approximately 30%. The rate of late neck metastases has not been well-characterized, and the rate of successful salvage treatment of late neck metastases has not been previously reported. Additionally, no standardized regimen for salvage treatment of late neck metastases or local recurrence has been developed. Our objectives were to examine the largest reported ENB case series in order to elucidate the rates of late neck metastasis and local recurrence, and to examine the correlative factors in our dataset. We report the rates of late neck metastasis and local recurrence. Methods: In this study we examined the rates of late neck metastases and local recurrence from the largest ENB case series published since 1990 in which the diagnosis of esthesioneuroblastoma was supported by immunohistochemical, histochemical, or histological analysis, totaling 678 patients. Our inclusion criteria for late neck metastases were patients with confirmed ENB with neck metastases diagnosed six months after diagnosis of the primary tumor. For local recurrence our inclusion criteria were patients with confirmed primary site or local ENB recurrence after treatment of the primary tumor with surgery, radiation, or a combination of the two. We examined the rate of salvage of late neck failures and local recurrence with surgery, radiotherapy, or combined surgery and radiotherapy. Successful salvage therapy was defined as disease-free survival at one year post-salvage, as follow-up data was available for patients with neck failure and local recurrence from at least 12 months post-salvage therapy. Late neck failures or local failures treated exclusively with chemotherapy were not included in the salvage data. The rate of salvage failure among patients treated with surgery, radiotherapy, and combined surgery and radiotherapy was compared. Results: The rate of overall cervical metastases was 10.4% (130 of 1224 patients). The overall rate of successful salvage of late neck metastases with surgery, radiation, or a combination of the two was 31.4%. An odds ratio analysis revealed that surgery plus radiation provided a statistically significant increase in the odds of successful salvage in patients with late neck metastases vs. single modality therapy (OR=8.6, 95%CI=2.035.9, NNT=3).
We found no difference in the odds of successful salvage for surgery alone vs. radiation alone (OR=1.5, 95%CI=0.130 to 16.8). We found a 28.5% rate of local recurrence, with a 42.6% rate of successful salvage of local recurrence. An odds ratio analysis showed no clear difference in the odds of successful salvage of local recurrence between the different modalities (OR 95%CI vs. S + RT=1.9, 95%CI=0.70 to 5.5). Conclusions: This study reveals a reasonable rate of successful salvage of late neck metastases and local recurrence in esthesioneuroblastoma. Combined surgery + radiotherapy provided a superior rate of successful salvage of late neck metastasis, while no clear advantage was seen for any one modality in salvage of local recurrence.

P207: ENDOSCOPIC ANTERIOR MAXILLOTOMY APPROACH TO THE PTERYGOID AND INFRATEMPORAL FOSSA
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Lesions of the nasal cavity and central skull base are increasingly being addressed through the transnasal endoscopic approach. Advances in instrumentation and surgical technique, including two person surgery, allow for improved visualization, better hemostasis, and for wider endoscopic resections than previously possible. Currently lesions of the midline and anterior skull base are routinely resected endoscopically in several institutions. Significant advances in endonasal endoscopic approaches to the pterygoid and infratemporal fossa recently, the author has approached lesions of the maxilla, pterygoid fossa and infratemporal fossa by creating an endonasal anterior maxillotomy EAM in conjunction with a medial maxillectomy. At the level of the nasal vestibule, the anterior maxilla is removed from the inferior turbinate to the level of the canine fossa. The maxillary sinus and anterior maxilla are removed back to the level of the posterior maxillary wall. A transpalatal incision may be added to allow access for more instruments. This exposure provides wide access to the posterior and lateral maxillary wall. Several instruments, including traditional, larger, nonendoscopic instruments such as bayonet bipolar instruments can be utilized through the opening. Hypothesis: The EAM with medial maxillectomy provides adequate access to lesions of the maxilla, PTF and ITF. Results: Eight cases were identified over a 15 month period involving lesions of maxilla, PTF, and ITF managed with an endonasal anterior maxillotomy. Indications for surgery were resection of malignant (5) and benign (3) disease. Imaged guidance was used to confirm location. Access was obtained posteriorly to the skull base including foramen ovale and rotundum. Lateral image guidance confirmed the probe could reach the anterior and posterior aspect of the mandidular ramus, and the anterior lateral maxilla wall. The internal maxillary artery was encountered in 5 cases and controlled with endoscopic clips. Visualization was adequate to obtain hemostasis despite rapid hemorrhage from the IMA. Gross tumor resection was achieved in all cases with a medial maxillectomy alone (2), including a PTF resection (3), and as deeper ITF resection (4). EBL ranged from 600cc to 1500cc. Two further cases were identified where a sublabial incision was added to address lesions involving the roof of the maxillary sinus and anterior maxillary wall. Discussion: The EAM represents a novel approach to provide endoscopic access to lesions of the posterior and medial maxilla, PTF and ITF. Instrumentation can be manipulated while maintaining adequate visualization for gross tumor resection. Further, a sublabial incision can be rapidly added in the event of uncontrollable hemorrhage or where wider access is needed. Lesions involving the anterior maxillary wall, orbital floor/maxillary roof are best approached with the addition of a sublabial incision.

P208: PREVIOUSLY UNTREATED ADENOCARCINOMA OF THE PARANASAL SINUSES: RESULTS OF ENDOSCOPIC RESECTION FOLLOWED BY RADIOThERAPY
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Objective: Adenocarcinoma is the most frequent paranasal sinus malignancy in Belgium. Classically patients with this disease are treated by an external surgical approach (lateral rhinotomy with medial maxillectomy or craniofacial resection) followed by radiotherapy. The role, possibilities, and limitations of endoscopic sinus surgery (ESS) in this treatment protocol remain to be established. Methods: We studied 44 patients with a new diagnosis of adenocarcinoma, treated with ESS and radiotherapy between 1992 and 2002. Results: The median follow-up of the patients alive at the end of the study period was 36 months. For the 5-year follow-up, the overall survival, disease-specific survival, and local control rate were 81%, 91%, and 73%, respectively. Corresponding rates for the 5-year follow-up were 53%, 83%, and 62%. International Union Against Cancer T classification did not appear to influence these results. Conclusions: ESS followed by radiotherapy for primary adenocarcinoma of the paranasal sinuses gives oncological results in the range of those of standard external approaches.

P209: COMBINED TEMPORAL BONE RESECTION AND PAROTIDECTOMY FOR LATERAL SKULL BASE MALIGNANCIES
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Background: Combined approaches are often needed as part of an oncological resection for treatment of malignancies involving the parotid gland and infratemporal fossa. When the temporal bone is involved by direct extension, temporal bone resection is performed to clear the disease. On another hand, complexity of the anatomical recesses in these regions and presence of the facial nerve often mandate addressing surgically the temporal bone even if it is not grossly involved. Conversely, parotidectomy may be included with temporal bone resection without evidence of direct invasion of the parotid gland from tumors arising from the auricle or external auditory canal. Objective: Review the outcome of patients undergoing combined approaches for parotid gland, skin, and other infratemporal fossa malignancies, involving at least two surgical teams (Otolaryngology and Head and Neck Surgery) and a multidisciplinary surgical team. Patients and methods: Case series at a tertiary care University Hospital. Methods: All cases undergoing combined approaches for lateral skull base malignancies at the University of Miami/Jackson Memorial Hospitals between September 1999 and October 2007 are included. Patient demographics, tumor characteristics, operative reports, and clinical follow up are recorded. Results: A total of 79 parotid malignancies were identified in the study period when surgical intent was both parotidectomy and temporal bone resection for malignant tumors. Of these, 60 were males and 19 females with ages ranging between 13 and 90. 38 of 79 patients underwent surgery for primary malignant tumors of the parotid gland or intraparotid nodal metastases. 16 of these 38 had squamous cell carcinoma, mostly secondary to skin cancer in the face and scalp. The most common primary parotid malignancies included locally advanced mucoepidermoid carcinoma (8/38) and adenoid cystic carcinoma (4/38). 36 of 79 patients had locally advanced skin cancer involving one or more of the following subsites: auricle, external auditory canal and cheek. Survival and local control rates are calculated and clinicopathologic factors are analyzed for this large but heterogeneous cohort. An analysis of tumor and patient characteristics influencing the choice of surgical approach is presented, with detailed rationale provided for the inclusion of temporal bone resection for the treatment of tumors primarily involving the parotid gland or parotidectomy for tumors primarily involving the auricle or external auditory canal.

SPEECH/SWALLOWING/QUALITY OF LIFE
P210: THE IMPACTS AND ADJUSTMENT OF THE PATIENT WITH HEAD AND NECK CANCER IN TAIWAN
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Objective: This study is a part of a project of family centered care for head and neck cancer patients and their family members in Taiwan. In this study, we aimed to identify the head and neck cancer survivors’ distress and adjustment throughout the course of treatment. Methods: Nineteen subjects (17 men and 2 women) with head and neck cancer were recruited. Patients were referred from a radiation- oncology outpatient clinic at a cancer center in northern Taiwan. A descriptive qualitative design was used, with semi-structured, face-to-face, and in-depth interviews. Interviews were conducted by four mental health professionals using the same questions. All interviews and their treatment were stationary in terms of tumor status. Data were collected through individual, tape-recorded interviews and observations. Transcripts were analyzed by content analysis for emerging themes and concepts. Results: Themes related to impacts of head and neck cancers from the analysis of interviews were: (i) facing death, (ii) financial problems, (iii) changes in roles in family, (iv) changes in the attitudes of parenting, (v) limited physical and social functions, and (vi) lack of information about cancer. Subjects described themes of adjustment to the impacts: (i) changes in roles in family; taking more domestic roles, spent more time with children, (ii) social iso-
The results of this study show that the impacts of patients suffering from head and neck cancer are willing to undergo aggressive treatments and to endure alteration to their quality of life if they would lead to improved quality of life. For a majority of the physicians, their management (92%) and their attitude towards the patient (88%) can influence the quality of life. The patients need for psychological support is recognized by 90% of the physicians. In terms of quality of life, pain and breathing were the most important symptoms, followed by feeding, voice and finally physical appearance. The perception of qol was objectively worse for physicians with a Latin culture than with an Anglo-Saxon culture, for physicians working in private practice than in hospital practice, and for physicians with no personal acquaintance with a head and neck cancer victim than those with close relations affected by the cancer (15%). There were very few differences between head and neck surgeons and the rest of the population. The perception of quality of life was slightly worse after chemotherapy than after radiotherapy. Facing the changes in physical functioning, roles in family, interaction between family members, plans for life, and financial problem, patients have to adjust their roles, interpersonal relationship, change life style, and search the meaning of life. More studies are needed to developing comprehensive models of coping strategies and for the development of effective interventions.

**P211: PERCEPTION OF HEAD AND NECK CANCER QUALITY OF LIFE WITHIN THE MEDICAL WORLD: A MULTICULTURAL STUDY**

**Objective:** Patients suffering from head and neck cancer are willing to undergo aggressive treatments and to endure alteration to their quality of life if they would lead to improved quality of life. For a majority of the physicians, their management (92%) and their attitude towards the patient (88%) can influence the quality of life. The patients need for psychological support is recognized by 90% of the physicians. In terms of quality of life, pain and breathing were the most important symptoms, followed by feeding, voice and finally physical appearance. The perception of qol was objectively worse for physicians with a Latin culture than with an Anglo-Saxon culture, for physicians working in private practice than in hospital practice, and for physicians with no personal acquaintance with a head and neck cancer victim than those with close relations affected by the cancer (15%).

**Materials/Methods:** The targets of the study were the all the Belgian ear, nose and throat specialists (500). They received a questionnaire by post. The questionnaire sought to analyse general information and the perception of quality of life but also the impact of the symptoms, the treatments, their side effects and the physicians' opinions on quality of life.**Results:** The response rate was 49.5%. An important majority of the population (78%) thought that quality of life must be considered in the choice of the treatment even if this meant a poorer chance of survival. Moreover, 75% thought it justified not to propose any curative treatment if this would lead to impaired quality of life. For a majority of the physicians, their management (92%) and their attitude towards the patient (88%) can influence the quality of life. The patients need for psychological support is recognized by 90% of the physicians. In terms of quality of life, pain and breathing were the most important symptoms, followed by feeding, voice and finally physical appearance. The perception of qol was objectively worse for physicians with a Latin culture than with an Anglo-Saxon culture, for physicians working in private practice than in hospital practice, and for physicians with no personal acquaintance with a head and neck cancer victim than those with close relations affected by the cancer (15%).

**Conclusions:** Quality of life seems to be very important for the physicians (perhaps as important as survival) and maybe more important than for the patient. The medical perception of quality of life can influence the choice of a treatment. This study begs the question; is the goal of the therapy survival, quality of life or both of these?
A cross sectional descriptive study was used. The Eighty-four patients participated in the study, the majority being To evaluate the frequency and perturbation degree of long-term We conducted a retrospective study to analyze the videokymo- The CG con- To evaluate and correlate vocal handicap and quality of life The CG con- 

P215: PREVALENCE OF LONG-TERM UPPER AERODIGESTIVE SYMPTOMS AFTER THYROIDECTOMY WITH AND WITHOUT INTRAOPERATIVE LARYNGEAL NERVE I.C.M.Silva1, I.P.Netto1, J.G.Vartanian1, L.P.Kowalski1, E.C.Angelis1, A.C. Camargo Hospital, Sao Paulo, Brazil

Objective: To evaluate the frequency and perturbation degree of long-term upper aerodigestive symptoms (UADS) in patients submitted to thyroidectomy, with and without intraoperative nerve monitoring. Methods: This is a cross-sectional study of patients submitted to a total (TT) or partial (PT) thyroidectomy, with at least one-year of follow-up after surgery. All patients had no previous larynx alteration and had a normal vocal fold mobility observed at the videolaryngoscopic evaluation after surgery. They were divided into 2 groups: a control group (CG) composed of patients without intraoperative nerve monitoring and a group of patients with the use of intraoperative nerve monitoring (NMG). The frequency and perturbation degree of UADS were verified by a specific questionnaire designed for this purpose. The perturbation degree was classified as low (01Cit is not a problem01D or 01Cit is a little problem01D) or high (01Cit is a moderate problem01D or 01Cit is a big problem01D). A descriptive analysis of the results and the association of the questionnaire results with the clinical and surgical variables (using Chi-square test) were performed. Results: The CG consisted of 188 patients with a mean age of 60.1 years and NMG out of the 15 preserved vocal folds, presented lateral round spike and 04 out of those 11 patients with supra-glottic vibratory source, did not present a closed phase 4 out of those 11 patients with supra-glottic vibratory source, did not present a closed phase frequency (f0), was 188.7Hz, 200Hz and 215.7Hz. 4 out of those 11 patients with supra-glottic vibratory source, did not present a closed phase frequency (f0), was 188.7Hz, 200Hz and 215.7Hz. 4 out of those 11 patients with supra-glottic vibratory source, did not present a closed phase frequency (f0), was 188.7Hz, 200Hz and 215.7Hz. 4 out of those 11 patients with supra-glottic vibratory source, did not present a closed phase frequency (f0), was 188.7Hz, 200Hz and 215.7Hz.
The aims of this study are to evaluate the stress and quality of life of the primary caregiver and to investigate the effect of hardness character on his/her quality of life. Materials and Methods: Four forms of questionnaires were requested to complete. Basic information included stress scale, Health related hardness scale (HRHS), and Brief form of quality of life evaluation form WHO [WHQOQL-BREF]. T-test and correlation coefficient analyses were used to analyze each variable in the form and the association between different variables. Uni-variable analysis was used to examine hardness as a role of moderator, and the structural equation modeling (SEM) was applied to evaluate the association of the results with the hypothesis. Path analysis and gradual regression analysis were utilized to determine the prediction factors of the quality of life. Result: There are 97 persons completed the questionnaires. The median age of caregivers is 46.7 (21-80) and of the patients is 56 (31-90). Seventy three of them are patients’ spouse and 20 are patients’ children or relatives. Nineteen persons with patients who completed radical treatment less than 3 months, 43 between 3 months and 2 years, and 23 more than 2 years. There are statistically significant correlations among these three factors: stress condition, hardness character, and quality of life of primary caregiver, with negative association between stress and quality of life ($r = -0.52$), negative association between hardness and stress ($r = 0.23$), and positive association between hardness and quality of life ($r = 0.32$). It is noted that hardness character significantly influences life quality, with high hardness level, better quality of life, whereas high stress decreases life quality. From SEM analysis, the major four prediction factors of quality of life includes the stress status of primary caregiver, the overall income of a family, physical stress, and hardness character. Conclusion: This study provides the information of how and what stresses in the primary caregiver of HNC, and the potential factors influencing the quality of life of a primary caregiver. It suggests that through strengthening the hardness character of a primary caregiver, the quality of life of the primary caregiver can be enhanced, leading to benefits of the HNC patient.

P219: COMPARISON OF ACOUSTICAL CHARACTERISTICS OF NTL AND TEP SPEECH WITH NORMAL SPEECH

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Objective: Comparison of Acoustical Characteristics of NTL and TEP voice with Normal voice. Method: Sixty male subjects were selected for this study. Twenty patients underwent Near-total laryngectomy surgery while 20 were fitted with Tracheo-esophageal prosthesis after total laryngectomy. Voice of these patients was compared for selected acoustic parameters with 20 normal speakers from same age group as control group. Recordings of vowel //ee// was analyzed acoustically using Dr. Speech (Tiger, DRS, Inc., USA) version 4.0 software for parameters such as Fundamental frequency (Fo), Intensity (Ao), Frequency range, Jitter, Shimmer and Maximum Phonation Time (MPT). The obtained data was subjected to statistical designs namely MANOVA and One Way ANOVA and paired ‘t’ test. Results: It was indicated that Fo for both the alaryngeal voice group did not show any significant difference from the normal voice. But for other parameters significant differences from normal voice was noted. Between the two alaryngeal voice groups a statistical difference was seen for shimmer, Mo and Ao. Except this no difference was observed for other parameters between the two alaryngeal modes of voice production. Conclusion: 1. Objective voice for both the alaryngeal voice groups resemble normal voice, though one differentiates them perceptually. 2. NTL group showed higher Fo and lower Ao when compared to TEP and Normal group. 3. NTL speakers have better MPT than TEP group. 4. As the alaryngeal speakers get more and more used to their speech, the shimmer values were found to decrease though very minimally. 5. This study suggests that with proper speech training and guidance alaryngeal speakers can attain acoustical parameters similar to those of normal speakers.

P220: VOCAL OUTCOMES AFTER TOTAL LARYNGECTOMY

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Background: Although several studies have explored postoperative voice outcomes for laryngeal cancer, the comparative studies on different type of treatments have been little reported. To compare functional outcomes of total laryngectomy and partial laryngectomy in patients with laryngeal cancer, we performed subjective analysis using Voice Handicap Index (VHI-10) and objective analysis using aerodynamic and acoustic analyzer.

Patients: Twentyseven patients with laryngeal cancer treated with total laryngectomy and 7 patients were treated with partial (total laryngecto-my were included in this study. Voice after total laryngectomy were tracheo-esophageal (TE) speech ($n=18$), electrolaryngoscopy (EL) speech ($n=6$) and esophageal (ESO) speech ($n=3$). Methods: Vocal function was examined by VHI-10 subjectively and aerodynamic and acoustic analysis objectively. In aerodynamic analysis, we studied maximum phonation time (MPT), the mean extent a professional attitude towards structuring the relationship, towards the provision of support for coping and towards work on the social structure and with the patient’s social environment can contribute to the establishment of new concepts.

P221: QUALITY OF LIFE OF TUMOUR PATIENTS FOLLOWING SURGERY AND RECONSTRUCTION OF THE ORO-MANDIBULAR REGION

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Severe impairments of quality of life are ubiquitous in oncological treatment units. However, daily hospital routine leaves little room for a psycho-social perspective on these problems and there is frequently a lack of sufficient low-threshold services to help patients manage the drastic changes in their daily life. As a rule, patients turn to the hospital social workers requesting their help regarding these problems. How can the social workers best help patients to sustain and assure their psycho-social quality of life after completion of reconstructive surgery? Quality assurance of the support provided for psycho-social needs and coping in hospitals is a field which is gaining importance. However, this is a far more multi-faceted undertaking than in medical or pharmacological care, especially in more ‘complex areas’ such as psycho-social care and the provision of support for coping. Concrete and easily operationalisable criteria tend to be the exception in this field. Studies combining both qualitative and quantitative methods would therefore seem suitable for throwing light on the subject from different angles and including factors of social structure. In a joint project of the Hospital Social Work Service of the Oro-Mandibular and Facial Surgery Unit of Heidelberg University Teaching Hospital and the Alice-Salomon University of Applied Sciences in Berlin, a longitudinal, exploratory design with several measuring times and both semi-structured interviews (Witzel, Mayring) and symptom tests were employed to gain insight into these issues. The results reveal that the quality of the helping relationship and paying attention to the social support provided by the patient’s social environment are decisive for the success of the pro-fessional support. The Social Work Service plays an important role in providing support for changes in the management of the problems of daily living and coping, the development of constructive subjective plans for the new life situation and coping with the threat of death, and also in work with the patient’s social environment. However, in the past, theory building in clinical psychology and medicine has only rarely addressed the details or the social structure of this form of helping relationship. Interviews conducted on a cancer ward are being used to examine to what extent a professional attitude towards structuring the relationship, towards the provision of support for coping and towards work on the social structuring and with the patient’s social environment can contribute to the establishment of new concepts.

P222: VOICE-RELATED QUALITY OF LIFE OUTCOMES IN LARYNGECTOMES: A COMPARATIVE STUDY

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Objective: Our aim was to compare the voice related quality of life outcomes in a cohort of laryngectomees who are using different voice restoration modalities. Methods: The validated University of Michigan Voice Related Quality of Life questionnaire [VRQOL] was used for this study. A VRQOL database previously collected and stored at the Alaryngeal Voice and Speech Laboratory of the University of Western Ontario was analyzed.
for the primary outcomes which included the social-emotional, physical-functional and total scores. Basic demographic data including sex and age were collected as well as additional treatment-related variables. The elapsed time post laryngectomy was also recorded. Results: A total of 75 patients were analyzed. Among these, 24 patients were females and 51 were males. The mean age was 64.1 years. There were 15 patients in the esophageal speech (ES) group, 18 in the electrolaryngeal speech (ELS) group, 9 in the transpalatal speech (TPS) group and 33 in the tracheoesophageal phonation (TEP) group. The social-emotional, physical-functional and total scores were significantly better (p<0.05) in the TES group, as compared to the ES, or the ELS groups. Patients in the ELS group were noted to have an improved outcome with time and with older age. This was not seen in the other groups. There was also a trend for age to negatively correlate with the outcomes in the ES group. None of the other parameters had any significant effect on the speech-related outcomes. Conclusions: Improved upper aerodigestive tract speech offers a better voice quality outcome post laryngectomy when compared with other alaryngeal speech modalities. Older age and elapsed time post-op have a positive effect on the voice outcomes with electrolaryngeal speech.

P223: PATIENT NAVIGATION SERVICES : IMPROVING THE QUALITY OF MULTIDISCIPLINARY CARE FOR HN CANCER PATIENTS

Objective: Facing a potential cancer diagnosis can be an overwhelming situation for individuals and their families. As a major referral center in the State of Oklahoma, we provide services to individuals from outside the metropolitan Oklahoma City area. Numerous challenges are commonly faced by patients when trying to manage competing work and family responsibilities, financial concerns, gathering previous test results for the initial appointment, scheduling any necessary tests, finding the parking lot and getting to the correct clinic building. Patient navigation is a model of providing coordinated services to patients in an effort to barriers to care [Dohan & Schrag, 2005]. The purpose of this study was to evaluate the impact of new patient navigation services in the Head and Neck Multidisciplinary Clinic [HNMDC]. We hypothesized that there would be fewer missed appointments and higher satisfaction in the navigated clinical setting compared to a non-navigated clinical setting [Hematology-Oncology].

Methods: As part of our ongoing quality improvement efforts, all new cancer patients seen in the HNMDC and in the Hematology-Oncology clinic were eligible to participate if they were age 21 or older, able to communicate in English, and had consented to treatment. Every two weeks, a random sample of patients seen in both clinics was selected using a random numbers table. Those selected were contacted by phone to complete a 10-item satisfaction survey. Patients from the HNMDC were also asked for feedback using two open ended questions. Missed appointments were tracked in both clinic settings.

Results: Preliminary data for the first 8 weeks are reported (N=16 for HNMDC; N=4 for Hem Onc). In the first 8 weeks, the HNMDC clinic reported no missed appointments. In the Hem Onc clinic, from 1-3 missed appointments were reported for each time period. In response to the satisfaction survey, HNMDC patients reported higher satisfaction levels for finding their way to the clinic, travel related assistance, feeling prepared for the visit, the amount of information given about what they needed to happen next and why and getting their questions answered. Both groups reported similar satisfaction levels in response to knowing where to park, gathering past test information, and understanding what to expect at the visit. The qualitative data suggested that simply knowing the navigators were available was very helpful to patients.

Conclusions: Preliminary results suggest that navigation services in our HNMDC are having a positive impact on patients and their families. As expected, fewer missing appointments were reported in the navigated clinic. Patients in the navigated clinic reported higher satisfaction levels on 6/10 questions on the survey. While our numbers are too small for statistical significance, navigation services have improved the quality of care provided to our head and neck patients. Data from the full study will be available in Spring 08. Dohan, D. & Schrag, S. (2005). Using navigators to improve the care of unserved patients: Current practices and approaches. Cancer, 104(4), 848-855.

P224: DOES NUMBER OF YEARS EXPERIENCE WORKING WITH HEAD AND NECK CANCER IMPACT ON THE JUDGEMENT MADE ABOUT QUALITY OF LIFE? J.L. Reid 1 S. Parmar 1 J.P. Pracy 1

Objective: The multi disciplinary team (MDT) working with head and neck cancer (H&N&C) typically draw upon research, their experience and clinical insight when formulating a clinical treatment plan. The aim of this study was to investigate whether experienced members of an MDT had similar judgments to their peers and whether these differed from their less experienced colleagues when predicting the quality of life (QOL) for a patient post-treatment.

Methods: An experimental between-subject design compared the responses of two separate groups of health care professionals (n=70) randomly allocated to the navigation team. Each team was asked to read a fictitious case history of an oral cancer patient post treatment. The description was identical except for the size of the presenting tumour (T2 vs T4). Respondents recorded their predictions on a visual analogue scale with reference to symptoms and psycho social difficulties based on a thematic review of the literature, and involving the European Organisation for Research and Treatment of Cancer Core disease-specific questionnaire. Results: Two-way between groups analysis of variance were conducted to explore the impact of tumour size and participants’ experience working with the client group on 20 variables. The results were not significant. One-way between groups analysis of variance were conducted to explore whether experience influenced any of the 20 variables irrespective of tumour size. Subjects were divided into 3 groups less than 5 years experience, 5-10 years and 10 years and over. The results were not significant. Number of years working with H&N&C patients does not seem to make a difference to the prediction of QOL symptoms that a professional will attribute to the patient. Conclusions: H&N&C is a highly individualised condition in terms of its psycho-social presentation, and the lack of clinical agreement within team members may be a reflection of this. Experience does not seem to influence predictions with reference to QOL. The focus of the research as well as the variable presentation of the disease may mean that it is difficult for the MDT to build up a coherent picture of the subjective correlates of the disease. For any unit it is hard to build up objective knowledge with reference to QOL. The reasons maybe two fold. The MDT is unlikely to treat and manage 2 identical patients with the same objective clinical criteria, in a six month time frame. Teams will be managing a range of patients at different points of their treatment, and disease process. As a consequence they are unable to build up a critical mass of experience on which to base their judgements. There is a low uptake of the use of QOL questionnaires within clinical settings. It is conceivable that clinicians consider such symptoms to be so variable, subjective and unpredictable that they do not perceive any real clinical use in collecting the information. Teams are therefore likely to be pre-occupied with the objective clinical statistics than the psycho social impact on the patient. The reasons for collecting subjective information are discussed.

P225: REVISITS TO THE SPEECH-RELATED QUALITY OF LIFE IN THE PATIENTS OF SUPRACRICOID PARTIAL LARYNGECTOMY Y.Sung1 K. Baek1 Y. Yun1 Y. Son1 Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul Republic of Korea

Objective: Supra-cricoideal partial laryngectomy (SCPL) is generally accepted as an oncologically sound procedure in selected cases of advanced laryngeal cancer. Although there are many publications regarding the positive aspects of voice-related functional outcomes of SCPL, reports regarding the speech-related outcomes are still scarce, which is more important in terms of quality of life (QoL). We aimed to compare the speech-related parameters including loudness, fluency and endurance in the patients who received SCPL or total laryngectomy (TL) with insertion of tracheoesophageal shunt prosthesis (TEP). Methods: Fifteen patients of SCPL and 13 patients of TL with TEP (Provox®) were included in this study. There were no significant differences in age, sex, follow-up period (49 vs. 69 months), and radiation therapy between the two groups. They received the surgery and/or finished the radiation therapy at least 12 months before the following assessments: maximal loudness level, maximal phonation time (MPT), time required to read phonetically balanced Korean passage, and number of words per breath. Speech intelligibility was evaluated three times by 7 raters with 7-point interval scales. Voice handicap index-30 (VHI-30) and EORTC HN Q30 QOL questionnaires were obtained for each group of patients. Results: MPT was significantly shorter in SCPL patients (4.3±2.4 sec; means±SD) than in TL patients (7.1±4.6 sec) (P = 0.048). Other speech-related parameters and self-rated voice handicap and general QoL failed to show any significant differences between the two groups; maximal loudness level was 78.8±5.11 and 79.8±5.9 dB, number of words per breath was 2.7±0.8 and 2.9±1.5, time required to read the standard sentences was 9.1±2.0 sec, and 7.0±2.6 sec, respectively. Speech intelligibility score was 3.2±1.6 and 3.7±1.6, VHI-30 score was 61.8±29.0 and 49.8±30.7, and EORTC HN Q30 score was 52.3±9.9 and 54.9±8.2, respectively. Conclusion: SCPL has speech-related outcomes comparable to TL.
P226: PAIN IN HEAD AND NECK CANCER PATIENTS DURING RADIATION THERAPY

Objective: Pain is common in head and neck cancer patients and may be needed before to choose SCPL or TL in the patients with advanced laryngeal cancer.

Methods: As soon as possible after admission for pain or when pain began, we assessed pain in 124 consecutive patients (95 men, 29 women, mean age of 54.7 ± 12.3 years, 87.9% Caucasian, 32.2% Hispanic and 2.4% African American) with the 1970 version of the McGill Pain Questionnaire and the Pain Intensity Number Scale (PINS; 0-10).

Results: 68.5% of patients had surgery prior to radiation therapy. Prior to study entry, patients had had pain for 0-6 months (77%), 7-12 months (5.6%), 13-23 months (4%), or 24-360 months (12.9%). At baseline, pain was related by the patient to their cancer (21%), surgery (53.2%), and both tumor and surgery in 20.5%. On average, patients reported 2.1 ± 2.3 pain sites. The mean PINS score was 2.8 ± 2.6 for current pain, 3.0 ± 1.3 for worst pain, and 0.8 ± 0.6 for least pain. 29% of the patients were not satisfied with these pain levels. Head and neck pain were the most common sites (79%) of pain. On average, patients selected 1.5+1.8 neuropathic words (min=0, max=9) with the most common being burning (21%). They selected 1.8±2.1 nociceptive words (min=0, max=14) and the most common were tender (26.6%), soreness (25%), and throbbing (20.2%). Affective pain word quality descriptors were firing (22.6%), nagging (17.7%), nauseating (7.3%) and exhausting (7.3%). Evaluative descriptors were annoying (35.5%), troublesome (8.9%), and miserable (8.9%). The Total Pain Rating Index was 13.5+11.3. Patients reported their pain pattern was constant (65%), intermittent (57.3%), and/or transient (33.1%).

Conclusions: We provide subcutaneous fibroblasts with human microvascular endothelial cells, a neutrophilic and nociceptive pain-an innovative finding. Whether the neoplastic pain is oral or extraoral is not clear from these findings. The affective and evaluative descriptors chosen for head and neck pain indicated considerable impact on quality of life even with low-moderate levels of pain intensity. Future research in pain in head and neck cancer patients should consider contemporary management of both nociceptive and neuropathic pain in head and neck cancer patients.

P227: ISSUES OF INTIMACY AND SEXUAL DYSFUNCTION FOLLOWING MAJOR HEAD AND NECK CANCER TREATMENT

Objective: Problems with sexuality and intimacy in head and neck cancer patients are under reported. This study firstly, describes patients self-reporting of intimacy and sexual dysfunction following treatment and secondly, explores the associations between clinical characteristics of H&N cancer patients with questionnaire outcomes.

Methods: Postal survey were sent to patients in March 2007 which included two EORTC H&N questions on sexuality, a self-designed question about intimacy and the University of Washington Quality of Life Questionnaire Version 4 (UW-QOL v4). Relationship between age, gender, presence of spouse, disease site, stage, treatment modality, time since surgery and the answers to the intimacy and sexuality questions were analysed with Fishers Exact test, Chi-squared test, Mann-Whitney U test, Kruskal-Wallis test, Logistic regression and the Spearman correlation coefficient.

Results: The response rate was 68% (350/518). One third of the patients (110/350) did not answer all the intimacy and sexuality questions despite answering the other questions. Of those who answered these questions, a third of patients reported problems with sexual interest and enjoyment (b/c 1.21 vs 1.23). In the cell cultures grew and a quarter problems with pain and/or when pain began, assessed pain in 124 consecutive patients (95 men, 29 women, mean age of 54.7 ± 12.3 years, 87.9% Caucasian, 32.2% Hispanic and 2.4% African American) with the 1970 version of the McGill Pain Questionnaire and the Pain Intensity Number Scale (PINS; 0-10). We entered data in CRUNCH4 and exported it to SPSS for data analysis. Pain quality findings are reported for the first pain site reported by the patient as located in the head and neck region. Results: 68.5% of patients had surgery prior to radiation therapy. Prior to study entry, patients had had pain for 0-6 months (77%), 7-12 months (5.6%), 13-23 months (4%), or 24-360 months (12.9%). At baseline, pain was related by the patient to their cancer (21%), surgery (53.2%), and both tumor and surgery in 20.5%. On average, patients reported 2.1 ± 2.3 pain sites. The mean PINS score was 2.8 ± 2.6 for current pain, 3.0 ± 1.3 for worst pain, and 0.8 ± 0.6 for least pain. 29% of the patients were not satisfied with these pain levels. Head and neck pain were the most common sites (79%) of pain. On average, patients selected 1.5+1.8 neuropathic words (min=0, max=9) with the most common being burning (21%). They selected 1.8±2.1 nociceptive words (min=0, max=14) and the most common were tender (26.6%), soreness (25%), and throbbing (20.2%). Affective pain word quality descriptors were firing (22.6%), nagging (17.7%), nauseating (7.3%) and exhausting (7.3%). Evaluative descriptors were annoying (35.5%), troublesome (8.9%), and miserable (8.9%). The Total Pain Rating Index was 13.5+11.3. Patients reported their pain pattern was constant (65%), intermittent (57.3%), and/or transient (33.1%).

Conclusions: We provide subcutaneous fibroblasts with human microvascular endothelial cells, a neutrophilic and nociceptive pain-an innovative finding. Whether the neoplastic pain is oral or extraoral is not clear from these findings. The affective and evaluative descriptors chosen for head and neck pain indicated considerable impact on quality of life even with low-moderate levels of pain intensity. Future research in pain in head and neck cancer patients should consider contemporary management of both nociceptive and neuropathic pain in head and neck cancer patients.

P229: ASSESSMENT OF SPEECH AND QUALITY OF LIFE IN SURGICALLY TREATED TONGUE CANCER PATIENTS

Objective: In agreement with the field cancerization hypothesis, we have previously shown that clonal chromosomal aberrations accumulate with age in upper aerodigestive tract (UADT) mucosa of HNSCC patients and healthy individuals, and that clonal numerical changes are more common among HNSCC patients. Previous studies on lymphocytes have suggested that patients with head and neck squamous cell carcinoma (HNSCC) have an increased susceptibility for chromosomal damage induced by bleomycin, a known radiomimetic mutagen. However, it has so far not been possible to study whether such genetic instability is present also in the epithelial component of upper aerodigestive tract mucosa, the tissue from which HNSCC originates.

Methods: Epithelial cells and fibroblasts obtained from non-neoplastic mucosa samples of HNSCC patients and healthy controls were put into culture. The samples from the HNSCC patients were obtained either from sites contralateral to the tumor or, when this was not possible, from ipsilateral sites 2-4 cm from the macroscopic tumor border. Samples from controls were obtained at surgery for non-neoplastic gingival disorders. All cell cultures were exposed to bleomycin and chromosome instability was assessed by the analysis of chromosome breakage in cells harvested 2 hours after bleomycin exposure and after withdrawal of bleomycin. Furthermore, the status of the FHIT tumor suppressor gene, located at chromosome band 3p14.2 was studied by fluorescence in situ hybridization (FISH) in epithelial cells that had been cultured after withdrawal of bleomycin.

Results: Epithelial cells and fibroblasts obtained from non-neoplastic mucosa samples of 30 HNSCC patients and 56 controls were successfully cultured. Chromosomal damage, in the form of chromosomal breaks and gaps, was seen in all cell cultures harvested 2 hours after exposure to bleomycin. In epithelial cells, the frequency of chromosome breakage was significantly higher among HNSCC patients than among controls (mean breaks per cell [b/c] 1.02 vs 0.77, p=0.02). When subdivided according to smoking status, age, and sex, a significantly higher frequency of chromosome breakage was still found in HNSCC patients (smokers, p=0.01, age 0A370 group, p=0.03, male, p=0.02). However, no significant difference was found between fibroblasts from HNSCC patients and controls (b/c 0.59 vs 0.19, p= 0.03). In the cell cultures growing after withdrawal of bleomycin exposure, the frequency of chromosome breakage was in general very low and no significant difference could be found between the HNSCC patients and controls when epithelial cell were examined. In subcultured fibroblasts, a higher frequency was found in HNSCC patients than in controls (b/c 0.59 vs 0.19, p= 0.03). Interphase FISH on cultured fibroblasts from HNSCC patients (n=10) and controls (n=12) showed that the frequency of FHT deletion was significantly higher in HNSCC patients than in controls. Conclusion: Our results support the notion that HNSCC patients accumulate genetic damage more rapidly, possibly due to an inherent susceptibility, which could explain the high risk of multifocal neoplastic cell transformation.
The objective of the study was to evaluate the speech outcome, factors affecting speech and quality of life after surgical treatment of tongue cancer. Methods: Retrospective review of case records of surgically treated tongue cancer patients in our institute and completed 6 months of follow-up and availability of tumor and treatment details. Any patient who has received any treatment before or patient with recurrent cancer was excluded. A prospective assessment of speech, tongue mobility and Quality of life was carried out. The tools used for speech assessment were prepared by us with the help of our speech pathologists. The stimuli include speech sounds aimed to test all aspects of sound produced with participation of the tongue movements. The speech was assessed at syllable, word and passage level. The speech recording was done using a special software, ‘Sound forge-version 4’. The speech was assessed for ‘Consonant Articulation’ and ‘Speech Intelligibility’. The Consonant articulation is a quantitative assessment of the correctly pronounced consonants. It was graded into four groups depending on the percentage of correct responses. The speech intelligibility is a qualitative assessment from a continuous passage reading. It was given levels from 1 to 6. The revised University of Washington quality of life questionnaire was used to assess the patients’ perspective. The questionnaire was administered by trained Medical social worker. Results: The study consisted of 49 patients, 38 males and 11 females. The primary tumor location was one of the lateral borders of the tongue in all cases. 44.9 percent of patients received adjuvant treatment. Reconstruction with a free flap was carried out in twenty-six out of forty nine patients. Out of 36 patients whose tongue movements were recorded, 32 had normal or mild restriction in tongue mobility. 17 had mild defect in articulation, 21 had mild-moderate defect, 4 had moderate to severe defect and one had severe defect. 32 patients had level 5 or 6 intelligibility. Rest had lower levels of intelligibility. On correlating articulation with various parameters, it was shown that T-stage, tumor thickness and adjuvant treatment significantly affected the articulation on univariate analysis. On multivariate analysis with Step-wise Logistic Regression Analysis, Tumor thickness was the only independent risk factor that affected speech with a p-value < 0.009 and Odd’s Ratio of 21.7. The articulation scores correlated well with the intelligibility scores. Though most patients had good scores in the individual Domains of the UWQoL questionnaire, there were good number of patients who graded the overall QOL and health related QOL as ‘very poor-fair’. The patient’s assessment of speech with the QOL questionnaire correlated with the expert’s scoring of intelligibility with significant p-value=0.039. Conclusions: Tumor thickness is an independent factor that affects speech. Since tumor factors cannot be modified, it may be worthwhile to modify treatment factors. Reconstruction with free flaps may help improve the articulation outcome. Using better radiation techniques like IMRT may be helpful. QOL assessment should be included to correlate with the patient’s perspective.

P231: STANDARDIZATION OF ESOPHAGEAL COMPUTERIZED MANOMETRY IN TOTAL LARYNGECTOMY VOICE REHABILITA-

C.T.Chante1, V.O.Seixas1, L.A.Paes1, C.Teskeira2, N.A.Andreollo1, A.L.Spina1, E.Quagliato1, I.K.H.Barcellos1, A.N.Crespo3,1 State University of Campinas, Campinas, Brazil; 2 State University of Campinas, Campinas, Brazil Background: Tracheoesophageal voice (TEV) with voice prosthesis (VP) is related to failure with spasm of pharyngoesophageal segment (PES). The comparison of the intraoral manometry (INAM) and the post videofluoroscopy PES pressure measurement (P231) is presented. Methods: Analysis of PES. Analysis of PES with CM, in patient after TL with and without spasm of PES was done and compared. Methods: Twelve patients without spasm had measure of pressure of PES. Also we evaluated eight patients with spasm of PES before and after treatment with injection of botulinum toxin in PES. All patients were submitted to perceptve voice analysis, videofluoroscopy. Results: All patients with spasm presented pressure above 16 mmHg to CM. The majority of patients without spasm had smaller medium pressures. Patients with spasm presented higher pressures than 16 mmHg (p=0.00002). The predictive negative value of test considering 16 mmHg as a cut-off value for spasm was 100%. Conclusion: CM may indicate spasm of PES when medium pressure was higher than 16 mmHg.

P232: INSUFFLATION TEST IN ASSOCIATION TO VIDEOFLUO-

C.T.Chante1, V.O.Seixas1, F.M.Gripp1, A.L.Spina1, I.K.H.Barcellos2, A.N.Crespo3, State University of Campinas, Campinas, Brazil; 2 State University of Campinas, Campinas, Brazil; 3State University of Campinas, Campinas, Brazil Background: The acquisition of esophageal voice (EV) for rehabilitation of total laryngectomy patient is around 30%. Spasm of pharyngoesophageal segment (PES) is a major factor in the acquisition or not of that voice. The objective of this study is to evaluate pharyngoesophageal segment (PES) of consecutive patients submitted to total laryngectomy that did not rehabilitated with esophageal voice (EV) with videofluoroscopy and insufflation test (IT) with analysis of phonation time (FT) before and after lidocaine injection in musculature of PES. Methods: Twelve consecutive patients were included. They had videofluoroscopy before lidocaine injection in PES and IT before and after lidocaine application in PES. Diagnosis of spasm was done with videofluoroscopic exam. Five millilter of lidocaine were injected in each of three points of constrictor muscle of pharynx. Results: Six presented low FT. These, after lidocaine injection, 40%/2(6) developed improvement, but without significance (p=0.23) when compared to patients with appropriate FT. Half(3/6) of the patients with low FT presented significant gain, however in only two this gain was enough to have an appropriate FT, in spite that 83%/5(6) of patients with good FT also presented this significant gain(p=0.05). The quantitative difference in gain among patients with and without spasm of PES was significant (p=0.005). The patients with spasm, presented a tendency to worst FT than patients without spasm (p=0.09). Conclusions: There was no difference of improvement or significant gain of FT among the groups with appropriate and low FT. The group of patients without spasm had greater gains of FT with tendency to better FT.

P233: MEASUREMENT OF QUALITY OF LIFE IN HEAD AND

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To measure quality of life in head and neck cancer (HNC) patients following treatment. Comparison was made between a cohort of HNC patients who regularly participate in a head and neck cancer support group, HNC patients who do not participate in a support group, and US population based norms. **Methods:** Patients were identified at meetings of the local chapter of Support for People with Oral and Head and Neck Cancer (SPOHNC) and from a HNC patient database maintained at a tertiary referral center. The Short Form-36 (SF-36) was utilized to measure patient quality of life and was administered anonymously. Patients self-reported the type of cancer and treatment as well. **Results:** Thirty seven HNC patients participated, 21 from the support group and 16 from the control group (no support group participation). For all 8 parameters measured by the SF-36, HNC patients had lower mean scores than the US population means. These parameters included: physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE), and mental health (MH). For bodily pain, general health, vitality and mental health, HNC patients did not differ significantly from the US population norms (p>0.05 for all). However, scores for the combined HNC groups were significantly different than the US population norms for physical functioning (p<0.001), role-physical (p<0.001), bodily pain (p=0.0015) and role emotional (p<0.001). Support group patients had significantly worse scores than US population norms in role-physical, social functioning, and role-emotional. There were no statistically significant differences between the support group and the control group patients for the 8 parameters measured by the SF-36 (all p values >0.05). There were more patients in the support group with oropharyngeal cancer (12/21, 57.1%) while 20/16 (125.0%) in the control group had oral cavity cancer (p=0.0036). There was a trend toward more patients in the support group having had chemotherapy than those in the control group (p=0.0969). These factors were likely to have lowered the overall scores in the support group patients. **Conclusions:** While it is perceived that HNC patients receive anecdotal benefit from attending a support group, data from our study did not demonstrate improved quality of life, as measured by the SF-36 instrument. The increased incidence of oropharyngeal cancer and chemotherapy treatment in the support group patients in our study were factors which were likely to have lowered the overall scores in these patients. Primary site is one of the most important factors in determining quality of life for HNC patients, and future studies are planned which will compare primary site-specific groups of patients. HNC patients report significantly worse quality of life than US population norms in several physical and emotional areas. Surprisingly, these patients do not differ from population based norms for other aspects of quality of life.

**P234: VOICE-RELATED QUALITY OF LIFE AFTER TREATMENT FOR LARYNGEAL CANCER**

**Objective:** There are many options to treat laryngeal cancers: definitive irradiation with or without concurrent chemotherapy, endoscopic CO2 laser surgery, partial surgery techniques, and total laryngectomy. Few studies have reported on vocal function and quality of life (QOL) of patients after definitive treatment for laryngeal cancer, using single voice related QOL measures. The aim of this study was to examine voice related QOL measures in patients treated with various modalities using questionnaires: Voice-Related Quality of Life (V-RQOL) and Voice Handicap Index-10 (VHI-10). **Methods:** Between August 2006 and May 2007, survey data from these questionnaires were obtained from a total of 137 patients. These patients had received definitive treatment for laryngeal cancers, were followed-up at the Hokkaido University Hospital, and were alive with no evidence of malignancy at the time of survey. **Results:** The mean V-RQOL scores of the patients who had received radiation therapy (n=63), chemoradiotherapy (n=29), laser surgery (n=14) and total laryngectomy (n=27) as the final treatment for laryngeal cancer were 92.6, 92.9, 85.5, and 68.4, respectively, and the mean VHI-10 values were 2.87, 2.34, 5.43, and 11.26, correspondingly. Four patients who had received partial surgery were not included in this analysis because of the small numbers of patients. These measurements of quality of life are important to help judge overall effectiveness of treatment for laryngeal cancers.

**P235: LONG TERM QUALITY OF LIFE IN YOUNG ADULTS TREATED FOR ORAL CAVITY SQUAMOUS CELL CANCER**

**Objectives:** To assess long-term quality of life (QOL) using - University of Washington Quality of Life (UW-QOL version 4) in oral cavity cancer survivors diagnosed at < 41 years of age to assess the long term swallowing disability using a dysphagia specific tool - M.D. Anderson Dysphagia Inventory (MDADI) and 3) to look for any clinical factors which may adversely affect function and QOL. **Methods:** With Institutional Review Board approval, all surviving patients aged 18 - 40, who were newly diagnosed and treated between 01/01/1980 to 12/31/2004 were identified. Their clinical and demographic details were extracted onto a standard data sheet. Patients were mailed the questionnaires including a letter explaining the study and a consent form. The results were analyzed using SAS 8.2 (SAS Institute, Cary, NC). Descriptive statistics and Spearman correlations were used. **Results:** There were 48 survivors among the 62 patients identified as eligible. All patients were primarily treated with surgery ± postoperative radiotherapy and chemotherapy depending on clinical stage and histopathology. Twenty-seven (56%) patients participated. The overall clinical stage of responders at the time of initial diagnosis was stage I (18), II (5), III (2) and stage IV (2). Six of the responders had lower scores in these patients. Primary site is one of the most important factors in determining quality of life for HNC patients, and future studies are planned which will compare primary site-specific groups of patients. HNC patients report significantly worse quality of life than US population norms in several physical and emotional areas. Surprisingly, these patients do not differ from population based norms for other aspects of quality of life.

**P236: LYMPH NODES DISTRIBUTION IN THE CENTRAL COMPARTMENT OF THE NECK: IMPLICATION IN THE TREATMENT OF THYROID CANCER**

**Objective:** The central compartment of the neck (CCN) is limited by the carotid arteries, the hyoid bone and aortic arch. Metastases from medullary thyroid carcinoma (MTC) to lymph nodes (LN) in this anatomical region are infrequent and complete resection is not necessarily to be performed with the distribution of these LN. This study intends: 1) to describe a systematic technique for dissection of the CCN; 2) To determine LN distribution in the CCN by corpse’s dissection and 3) to compare disease control and hypocalcemia in patients treated for MTC from our historical series versus patients treated with the described technique.

**Methods:** Fifteen corpses in the early 24 hours after death were dissected. Procedure starts on the anterior border of the left carotid artery at the level of the cricoid cartilage medial to the sternohyoid muscle and proceeds vertically down the side of the thorax until the artery goes behind the innominate artery. The correct level of the dissection is the inferior border of the right carotid artery at the level of the cricoid cartilage. Precricoid LN are removed separately. LN were divided in three groups: a) Between hyoid bone and cricoid cartilage (Precricoid); b) between both recurrent laryngeal nerves (RLN) and c) between RLN and carotid arteries. This technique was applied in 14 patients and quality of life in patients who developed squamous cell carcinoma at < 41 years, the objectives of this study were 1) to assess long-term quality of life (QOL) using - University of Washington Quality of Life (UW-QOL version 4) in oral cavity cancer survivors diagnosed at < 41 years of age 2) to assess the long term swallowing disability using a dysphagia specific tool - M.D. Anderson Dysphagia Inventory (MDADI) and 3) to look for any clinical factors which may adversely affect function and QOL. **Methods:** With Institutional Review Board approval, all surviving patients aged 18 - 40, who were newly diagnosed and treated between 01/01/1980 to 12/31/2004 were identified. Their clinical and demographic details were extracted onto a standard data sheet. Patients were mailed the questionnaires including a letter explaining the study and a consent form. The results were analyzed using SAS 8.2 (SAS Institute, Cary, NC). Descriptive statistics and Spearman correlations were used. **Results:** There were 48 survivors among the 62 patients identified as eligible. All patients were primarily treated with surgery ± postoperative radiotherapy and chemotherapy depending on clinical stage and histopathology. Twenty-seven (56%) patients participated. The overall clinical stage of responders at the time of initial diagnosis was stage I (18), II (5), III (2) and stage IV (2). Six of the responders had lower scores in these patients. Primary site is one of the most important factors in determining quality of life for HNC patients, and future studies are planned which will compare primary site-specific groups of patients. HNC patients report significantly worse quality of life than US population norms in several physical and emotional areas. Surprisingly, these patients do not differ from population based norms for other aspects of quality of life.
patients with MTC since November 2004. Results after treatment as regard-
ed to disease control (based on serum calcitonin concentration) and
hypocalcemia of an initial group of patients were compared with 38 previ-
ously treated patients. Results: The number of lymph nodes in the CCN in
corpses varied from 5 to 42 (mean 22±10) and were distributed accord-
ing to our groups in: a) 1.2±0.7, b) 17.5±8.5 and c) 3.8±2.6. The num-
ber of LN in the CCN in surgical specimens after 2004 varied from 1 to 23 (mean-
8±7, P<0.001). Disease control was achieved in 46% before and 55% after
2004 (P= .44). Definitive hypocalcemia occurred in 17% of the pa-
tients with the systematic technique versus 33% in the historical series.
This complication was minimized when parathyroid glands were identified,
removed and grafted during thyroidectomy. The RLN can be identified in its
exit from the thorax, under the subclavian artery on right and the aortic arch
on the left side. This may be useful in RLN identification in reoperative thy-
roid surgery and dissection of the CCN. Conclusion: 1) A systematic dis-
section of the CCN is feasible and safe. 2) LN distribution varies in the
CCN, most of them between both recurrent laryngeal nerves. 3) Normal
levels of calcitonin were achieved in 55% of the patients and hypocalcemia
was found in 17%. The technique is useful for thyroid cancer with meta-
tases and reoperation of the CCN.

P237: PREDICTIVE FACTORS OF CENTRAL LYMPH NODE
METASTASIS IN THE TREATMENT OF PAPILLARY THYROID CARCINOMA
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Objective: The purpose of our study was to determine the incidence and the
predictive factor of occult central nodal involvement and assess the role of
elective central lymph node (LN) dissection in patients with papillary thy-
roid cancer (PTC). Material and Methods: We performed a retrospective
analysis of 121 patients with PTC with clinically node-negative central
necks who underwent total thyroidectomy with central compartment cervi-
cal LN dissection from 2003 to 2006. Results: forty-seven (39%) of 121
patients had positive central nodal status after the central LN dissection.
In cases with male, carcinoma of a maximal diameter greater than 1 cm or lymphovascular invasion, the rate of central compartment
metastasis was significantly higher (P< .05). However, there were no statis-
tically significant differences in age, number of thyroid tumor, presence of
perithyroidal invasion or capsular invasion, and location of thyroid tumor.
Moreover, in the 88 cases with unilateral solitary primary tumor, contralat-
eral paratracheal LN metastasis occurred in 20% (18 of 88). The rate of
contralateral paratracheal LN metastasis was significantly higher in cases with carcinoma of a maximal diameter greater than 1 cm or ipsilateral pathologic positive LN metastasis (P< .05). Conclusion: LN metastasis in the central compartment was present in 39% of PTC with elective central LN dissection. However, PTC with a maximal diameter greater than 1 cm or lymphovascular invasion are at greater risk for central LN metastasis. Furthermore, the patients with unilateral solitary PTC with a maximal diameter greater than 1 cm or ipsilateral pathologic posi-
tive LN metastases are at greater risk for contralateral paratracheal LN metastasis. Therefore, we advocate bilateral central compartment LN dis-
section in patients with PTC with a maximal diameter greater than 1 cm or ipsilateral pathologic positive LN metastasis.

P238: IMPACT OF BILATERAL CERVICAL LYMPH NODE METAS-
TASIS OF DIFFERENTIATED THYROID CARCINOMA ON PROG-
NOSIS AND QOL
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Objective: The goal of this study was to evaluate the impact of bilateral
cervical lymph node metastasis of differentiated thyroid carcinoma (DTC)
on prognosis, cervical recurrence, distant metastasis and invasion to the
neighboring organs. Study design: Retrospective chart review. Materials and Methods: We reviewed data from 498 patients with DTC who under-
took primary curative resection in our institution and had clear mapping of all the cervical lymph nodes dissected out and patholog-
ically diagnosed. We divided the patients into four groups; Group A with
no lymph node metastasis (nN0), 161 patients, Group B with lymph node metastasis in the central compartment, 85 patients, Group C with lymph node metastasis in the ipsilateral neck, 192 patients, Group D with lymph node metastasis in the contralateral neck (bilateral cervical metastasis), 60 patients. Results: The cause specific survival rate at 10 years was 97.1% in Group A, 92.1% in Group B, 86.1% in Group C, showing no significant difference among the four groups. Distant meta-
tasis was noticed in group A, 2.4% in Group B, 7.8% in Group C, and 18.3% in Group D. There was a significant difference between Group D and the other groups (p< 0.05). Cervical recurrence rate was 3.1% in Group A, 2.4% in Group B, 9.4% in Group C, 6.7% in Group D showing no significant difference. Extracapsular invasion of the primary and the metastatic lymph node was 12.4% in Group A, 24.7% in group B, 51% in Group C and 62% in Group D. There was a significant difference between Group D and the other groups (p<0.05). Invasion to the neighboring organs namely larynx, trachea, esophagus and the recurrent laryngeal nerve occurred in 56patients, 85 patients, 53 patients, 111patients, respectively. As to the laryngeal invasion, 19 patients underwent shaving under microscope, 33 laryngeal frame work excision, 1 vertical hemilaryngectomy, 2 subtotal laryngectomy and 1 total laryngectomy. All but one patient were able to preserve the voice. Conclusion: Bilateral cervical metastases of DTC showed higher rate of distant metastasis, invasion to the neighboring organs, however, no significant increase in mortality. These data suggest that both the absolutely curative resection and the organ preservation are required for the treatment of DTC with bilateral cervical lymph node meta-
tases.

P239: PROGNOSTIC FACTORS IN DIFFERENTIATED THYROID CARCINOMA WITH PARTICULAR REGARDS TO NODAL META-
TASES. REVIEW OF 1503 CASES
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Introduction: The meaning of nodal metastases in well differentiated thy-
roid carcinoma (WDTC) is controversial. Its incidence varies between 40
and 80% depending on the extent of lymph node dissection: the 6th level,
70%; the 7th level, 6-20%. Considering the histologic type, it ranges from
10-15%, in case of follicular/Hurtle carcinoma, to 82% in case of the pap-
illary one. The wide range of observations induced the Authors to analyze
peculiarly the significance of lymphatic spread of differentiated thyroid car-
cinoma, among the other prognostic factors. Material and Methods: 1503
cases of WDTC, treated at the National cancer Institute of Rome between
1988 and 2005, were examined in order to evidence most signific-
ificant prognostic factors by mean of a multivariate analysis. Particularly 462
cases of locally advanced WDTC, were considered. Afterwards a multi-
vari-ate analysis of a subgroup, composed by 97 N+ consecutive cases of
WDTC, previously untreated, was performed to study prognostic factors for
local (N+) and distant (M+) metastases. Among the 97 cases, 88 were submitted to surgical treatment for a gross differentiated thyroid carci-
noma (DTC), 9 for an occult differentiated thyroid carcinoma. After surgery,
12 patients were lost from follow-up, and 8 resulted pathologically nega-
tive. Therefore only 77 cases of pN1 DTC were studied. Results: Considering all cases of WDTC, ten-year-overall survival was 58.7% for
locally advanced WDTC, compared to 94.8% in case of low stage WDTC.
Nevertheless, statistically, significant prognostic factors in the 77 cases of
N+ dissected necks, the multivariate analy-
sis with Cox regression model was performed, in order to find significant risk-
ators for lymphatic and distant metastases. Parameters: Follicular type: significant (p<0.01) - ECS: significant (p<0.001) - Age, p, gender,
No+N+, tisite, No-levels+: not-significant. Discussion: In Authors’ experi-
ence, histologic grade of differentiation, wide tumor excision and neck dis-
section, in case of N1 WDTC, without residual disease in the central and
lateral neck, are determinant prognostic factors. Particularly extracapsular
spread showed to be a highly predictive factor either as distant metasta-
sis or locoregional recurrence. Conclusions: The examination of these
data confirms the reports of the literature and stresses the importance to
analyze the grade of T de-differentiation, and the radicality of surgery. To
achieve significant results, it is important to improve our knowledge of the
biological changes of WDTC with its aging, in order to perform more fitting
therapeutic protocols.

P240: CLINICAL ANALYSIS OF CERVICAL LYMPH NODE RECUR-
RENCY IN THYROID PAPILLARY CARCINOMA
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Background and Objectives: Recurrence of regional cervical lymph node in patients with thyroid papillary carcinoma is not uncommon. It may have much portion of recurrence of thyroid papillary carcinoma. The purpose of our study is to determine the risk factor and the characteristics of cervical lymph node recurrence in patients with thyroid papillary carcinoma, so reduce recurrences and offer proper treatments. Subjects and Method: A retrospective analysis was performed for 218 patients who
underwent surgery for thyroid papillary carcinoma from 1992 to August 2003. Univariate and multivariate analyses were performed for the risk factor of cervical lymph node recurrence. We compared recurrent group of cervical lymph nodes (n = 34) and non recurrent group of cervical lymph nodes (n = 156). And the characteristics of cervical lymph node recurrence were analyzed by comparing with primary tumor sites and cervical lymph node metastasis. Results: The risk factor in univariate analysis is tumor size, T stage, N stage. The risk factor in multivariate analysis is tumor size, N stage. Cervical levels of lymph node recurrence are level II, III, IV area in patients with no nodal metastasis and level IV, VI area in patients with lymph node metastasis. Conclusion: Since the recurrence rate of regional cervical lymph node after the operation was 9.8% in patients without the clinical evidence of nodal metastasis, elective neck dissection is always not necessary. We perform a careful neck dissection on cervical level IV and VI in patients of nodal metastasis. The possibility of cervical level V lymph node metastasis should be kept in mind. The prevention of the recurrence of cervical lymph node may decrease the re-operation rate and then improve the quality of life.

P241: WITHDRAWN

P242: MEDIASTINAL DISSECTION FOR PATIENTS WITH DIFFERENTIATED THYROID CARCINOMA: STERNOTOMY VS VATS

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Objective: To compare advantages and disadvantages between a conventional anterior approach and a video-assisted thoracoscopic surgery (VATS) in dissecting mediastinal lymph nodes of patients with differentiated thyroid carcinoma. Methods: We here present two cases of differentiated thyroid carcinoma with mediastinal lymph node metastases below level 106* according to the classification of the Guidelines for the Clinical and Pathologic Studies for Carcinoma of the Esophagus (9th edition) edited by the Japanese Society for Esophageal Diseases. For Case 1, we adopted a conventional anterior approach with resection of the right half of the manubrium and sternum to the level of the second intercostal space and medial half of the right clavicle. Case 2 underwent a combined cervical approach and video-assisted thoracoscopic surgery (VATS). Results and Conclusions: In Case 1, the lymph nodes around the subclavian vein, 105R*, 106pre* and 106recR* were successfully dissected under clear view, although it seemed that it might be difficult to dissect these lymph nodes safely before the surgery. The usefulness and safety of the anterior approach with resection of the sternum and clavicle were confirmed in this case. We did not further dissect the 106biR* in this case, because there was no palpable lymph node in this area, although the pre-operative CT scan had demonstrated small lymph node metastasis. Nevertheless, although we did not dissect this area in this case, the difficulty in the dissection of 106biR* was recognized, because it is quite challenging to gain an adequate surgical view in this small compartment in the presence of the azygos vein by this approach. Conversely, in Case 2, in which mediastinal lymph nodes extended to level 107*, the lymph nodes were relatively easily dissected by VATS under excellent surgical views of 106biR* and 107*. Although VATS is associated with difficulty in an bloc resection, requirements of a thoracotomy, changes of body position and an intubation tube during the surgery, this approach is of great use for the dissection of 106biR* and 107*. *Note: 105; upper thoracic parasternal lymph node, 106; thoracic tracheal lymph node (rec; recurrent nerve, pre; pretracheal, tb; tracheobronchial), 107; tracheal bifurcation lymph nodes.

P243: MANAGEMENT OF LATERAL NECK METASTASIS ASSOCIATED WITH Papillary Thyroid Carcinoma

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Objectives: Discuss management of lateral cervical lymph node metastases in papillary thyroid carcinoma (PTC). Methods: Retrospective analysis of 32 consecutive patients with PTC who underwent 39 neck dissections (ND) for management of lateral cervical metastases from 2000 to 2007. Eighteen patients received primary neck dissections at the time of thyroidectomy by cytologic results (FNA) revealed PTC. Secondary neck dissections for delayed metastases were performed in 14 patients who underwent thyroidectomy for previous pathologically confirmed PTC. Appropriate extent of lateral cervical neck dissection was performed based on preoperative imaging studies for intranodular nerve bundle. All 2000 to 2007 were oriented and labeled by the senior surgeon (FRM) and cut into individual neck levels (I-V). Results: All patients underwent ND levels II through V, and 6 of 39 ND specimens included level I nodes. Three (50%) of the 6 level I nodes contained metastatic disease. The incidence of positive nodes for levels II through V are as follows: level IIA: 49% (19/39); level IIB: 62% (24/39); level III: 72% (28/39); level IV: 67% (26/39); level VA: 8% (3/39); level VB: 31% (12/39). All 18 patients who received primary ND, and 13 of 14 patients who underwent secondary ND had positive nodes in at least one level. Overall, 72% (28/39) of ND specimens contained metastatic disease in multiple levels. Conclusions: Our results emphasize the high incidence of cervical metastasis associated with PTC. Levels II-B, III, and IV were at greatest risk of metastatic disease. Specifically, our results suggest the importance of including level II-B (submuscular recess) when performing a ND, but the upper posterior triangle (level V-A) is less likely to harbor tumor. Lateral neck metastasis from PTC is common and predictable; locoregional control is improved with a formal, comprehensive neck dissection at the time of thyroidectomy.

P244: LYMPHSONOGRAPHY OF THE THYROID: A NOVEL TECHNIQUE FOR EVALUATING LYMPHATIC DRAINAGE PATTERNS OF THE THYROID GLAND


Objective/Background: Lymphsonography is a recently described technique which utilizes a microbubble ultrasound contrast agent injected intraparenchymally or subcutaneously to identify lymphatic channels and sentinel lymph nodes draining a target site. The technique allows for real-time visualization of contrast flow through lymphatic channels to the first echelon lymph node(s). This technique has been used as an experimental method for sentinel lymph node biopsy, yielding results that strongly correlate with traditional techniques in animal models. While sentinel lymph node biopsy is likely to be of little use for well-differentiated thyroid cancers, it could potentially have a role in evaluating medullary thyroid carcinoma where surgical management of lymphatic metastasis is critical. Furthermore, the patterns of metastasis in papillary thyroid cancer is difficult to predict, and direct, real-time visualization of thyroidal lymphatic drainage pathways may provide valuable anatomic knowledge. The objective of this study was to determine if lymphsonography after intrathyroidal injection in a large porcine model would be feasible and provide similar results to blue dye guided sentinel lymph node biopsy. Methods: Four 50kg Yorkshire swine underwent transcatheter injection of 1 ml of Sonazoid (GE Healthcare, Oslo, Norway) contrast agent (estimated 109 microbubbles / ml) into the thyroid gland under ultrasound guidance. This was followed by blue dye injection into the same location. Traditional grayscale ultrasound, pulse-inversion harmonic grayscale, and Doppler color ultrasound were used to identify contrast within the gland, draining lymphatic channels, and sentinel lymph node(s). At completion of the ultrasound examination, bilateral central and lateral compartment neck dissection was carried out to identify any blue nodes. We compare the results of blue dye guided sentinel node biopsy to lymphsonography. Results: Lymphsonography of the thyroid gland was successfully performed in 4 swine identifying efficient lymph channels in 4 injections, and sentinel lymph nodes in 2 of 4 injections. In two cases the lymph channel traveled inferiorly deep into the mediastinum and a sentinel node was not visible on transcutaneous ultrasound. In each case the blue dye stained node was identical to the ultrasound contrast positive lymph node. Conclusions: Lymphsonography of the thyroid gland in a porcine model is technically feasible, and in this small study appears to correlate with blue dye guided injection. This technique could potentially provide a detailed analysis of thyroidal lymphatic drainage if applied to humans.

P245: PROGNOSTIC FACTORS AND THE MANAGEMENT OF Thyroid Microcarcinoma

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Introduction: With the rising use of ultrasound guiding fine needle aspiration of thyroid nodules, more raises the incidence of well-differentiated cancer, as well as the number of microcarcinomas (nodules smaller than 1 cm in diameter). For this group specifically, surgical treatment is still matter of discussion. In order to study some prognostic factors that may guide the treatment of this group of tumors, 124 patients were evaluated (108 women and 18 men), with age average of 48±12,2 years, diagnosed as papillary thyroid cancer (PTC) and surgically treated by the same surgical group. Methods: All patients were submitted to total thyroidectomy (TT) and thirty-three had cervical lymph node dissection (CND) as well. Sixty-four patients had tumors smaller than 1 cm diameter (Group A) and sixty had...
tumors greater than 1 cm (Group=B). Prognostic factors considered for study were univariate and multivariate analysis were sex, age, stage, type of surgery (IT with or without CND), histological features of aggressiveness (like multifocality and extra capsular invasion) and another histological group of criteria (loss of differentiation and non-classic variants, studied together). The follow-up average was 89.5 ± 9.2 months. Patients with undetectable levels of stimulated thyroglobulin, as well as absent clinical or radiological evidence of signs and symptoms were considered free of active disease.

**Results:** Eight cases (6%) of loco regional recurrence and six cases of distant metastasis (6%) were observed. Two patients died during the follow-up (1.6%). 45-month overall survival was 91.9% for stages I/II and 31.4% for stages III/IV (p=0.039). The presence of positive neck nodes at the time of diagnosis or during the surgery did not influence either overall or disease-free survival in the group of tumors greater than 1 cm (p=0.374), being non-applicable to the A group. Some histological features of aggressiveness affected the overall survival in both groups, but in Group=B we observed a trend of multifocality (p=0.06), extra capsular invasion (P=0.016), whereas in the micrometastasis group only multifocality indicated bad prognosis with statistical significance (P=0.023). Conclusion: The importance of multifocality as a prognostic factor in microcarcinomas patients survival leads us to conclude that total thyroidectomy is the minimal optimum treatment for this group of patients.

**P246: THYROID MICROCARCINOMA: SURGICAL STRATEGY**
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In the period of 1985: 2005 we examined a group of patients, consisting of 322 thyroid cancer sick. Parity of women and men was 6:1. At 23% of patients with papillary microcarcinoma the multifocal tumour growth took place. At 18.6% sick among examined patients there was metastatic affection of lymph nodes, and at 10% affection of the both lobes was noticed. According to histological structure papillary cancer was predominated: 54.03%. Enbloc operation was done at 171 (53%) of patients and thyroidectomy of lobes at 18 (5.5%). Relapse of disease is in a form of metastasis in regional lymph nodes, local relapse and remote metastasis in lungs: 17 (5.2%). We support methods of minimal surgical interventions: during such a surgery the recurrent nerves are less injured, the percent of the post-surgical hypothyreose is considerably reduced, there’s an opportunity of complete restoration of the functional activity of the rest of thyroid tissue.

**P247: MINIMALLY INVASIVE VIDEO-ASSISTED THYROIDECTOMY FOR TREATMENT OF SOLITARY THYROID NODULE**
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**Background:** Minimally invasive video-assisted Thyroidectomy (MIVAT) is a new era in the field of minimal access thyroid surgery. The study examined the safety and feasibility of this technique based on the postoperative morbidity of the patients.

**Patients and Methods:** Twenty-eight patients with suspicious thyroid nodule according to a strict inclusion criteria. Preoperative and postoperative evaluation were done using lab, radiological and endoscopic workup.

**Results:** The male to female ratio was 1:1.8. The mean age of the study was 31 years. There was no massive bleeding and all the operation completed by MIVAT with no conversion to conventional surgery. Permanent recurrent laryngeal nerve injury was recorded in one patient and hypoparathyroidism was recorded in one patient.

**Conclusion:** MIVAT is a safe and reliable method for treatment of strictly selected group of patients with solitary thyroid nodule with good postoperative cosmetic results and less postoperative pain.

**P248: MINIMALLY INVASIVE VIDEO-ASSISTED THYROIDECTOMY (MIVAT) – 1, 5 YEAR EXPERIENCE**
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**Objective of the Study:** We report our 1.5 years experience in the treatment of thyroid disease with Minimally Invasive Video-assisted Thyroidectomy (MIVAT) introduced by Miccoli (1998).** Methods:** The procedure is carried out through an incision of 18-22 mm and the thyroidectomy is performed by instruments specially designed for this method. Conditions were: thyroid nodules maximum in diameter of 30 mm, total thyroid volume under 30 ml, no signs associated thyroiditis, cytologic diagnosis of benign thyroid nodule or papillary microcarcinoma and without evidence of nodal disease on the neck. **Results:** We have treated (June 2006 to December 2007) 38 patients with MIVAT. In this study 26 patients had lobectomy, 5 lobectomy with isthmectomy, 6 total thyroidectomy and one of them lobectomy with contralateral parathyroidectomy. Mean operative time for lobectomy was 65 minutes, range 48 to 110 minutes and for total thyroidectomy mean time was 106 minutes, ranged from 82 to 145 minutes. Duration of operations became shorter as we became more experienced. There was no postoperative bleeding. We had two transient recurrent nerve palsy and none of the permanent recurrent nerve palsy. We had one permanent hypocalcemia. **Conclusions:** MIVAT is a safe technique with indication in a minority of patients, candidates to thyroidectomy and is considered as a better postoperative scar.

**P249: ENDOSCOPIC HEMITHYROIDECTOMY WITH IPSILATERAL CND IN UNILATERAL THYROID MICROPAPILLARY CARCINOMA VIA A NOVEL APPROACH**
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**Objectives:** Recently, various endoscopic approaches have been applied to thyroid surgery. However, there are few specific data on endoscopic thyroidectomy with central neck dissection (CND) in thyroid micropapillary carcinoma. This study determined the feasibility and safety of endoscopic hemithyroidectomy (HT) plus CND via a novel approach without gas insufflation.

**Study Design:** Retrospective study.

**Methods:** Twenty-nine consecutive patients underwent endoscopic HT alone or with ipsilateral CND via a unilateral axillo-breast approach without gas insufflation for thyroid micropapillary carcinoma. Our indications for endoscopic thyroid surgery in thyroid papillary carcinoma were 1) intrathyroidal papillary carcinoma less than 1.0 cm in diameter on preoperative sonography, 2) no evidence of lymph node metastasis in a preoperative imaging study, and 3) unilateral thyroid lesions only. The following variables were examined: perioperative complications, operating time, diameter of the resected thyroid nodule, permanent pathology, time of hospital discharge postoperatively, duration of drain placement, and total amount of drainage.

**Results:** The mean primary tumor size was 8.4±4.3 mm (range 3-17) on postoperative permanent pathology. The mean operating times were 120.43 ± 7.38 min and 123.75 ± 22.27 min for HT alone and HT + CND, respectively, and did not differ significantly in the two groups (P = 0.7329). The mean number of dissected central lymph nodes was 4.36 ± 2.64 (range 1-12). Five patients (35.7%) had central lymph node metastasis. The mean number of metastatic central lymph nodes was 0.93 ± 1.39 (range 0-4). The amount and duration of postoperative drainage was 202 ± 26.17 mL in 3.53 ± 0.77 days. The postoperative hospital stay averaged 5.16 ± 0.37 days. Overall, perioperative complications occurred in eight patients (8/29, 27.6%), including three transient recurrent laryngeal nerve palsies, four seromas, and one tracheal laceration.

**Conclusions:** Based on these results, we believe that endoscopic HT with CND via a unilateral axillo-breast approach without gas insufflation is safe and effective in selected unilateral thyroid micropapillary carcinomas, and provides better cosmetic results and a shorter operating time than other methods. We also believe that total thyroidectomy with CND can be performed via our novel approach for selected patients with thyroid micropapillary carcinoma.

**P250: ENDOSCOPIC NECK SURGERY FOR THYROID Masses**
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Endoscopic neck surgery using a laparoscope with a video camera first was performed by Gagner et al., who successfully carried out an endoscopic subtotal parathyroidectomy in 1996. Endoscopic neck surgery had not been attempted previously because of restricted working space in the neck. In 1998, we started minimally invasive endoscopic surgery for treatment of benign tumors in the neck. Most difficult problem of endoscopic surgery for the neck region is pneumomediatinum that is brought by insufflation using to make working space. One new technique neck region lifting method (NRLM) - basically enabled to perform endoscopic neck surgery without insufflation. Consequently, the potential risk of insufflation-related complication was disappeared. Some of the associated difficulties have been addressed by recent technical improvements. However, many problems remain to be solved. In particular, indications in malignant thyroid tumors have not been definitively established. Usually a thyroid mass less than 1 cm in diameter is not treated with an open procedure, while masses only slightly larger than 1 cm and have no apparent metastasis nevertheless are managed with open surgery, as is the case for large tumors. In such borderline situations, patients’ anxiety about malignant disease is compounded by anxiety concerning cosmetic results. For these small thyroid cancers and lesions suspected of malignancy, we now use endoscopic neck surgery. We have experienced over eighty cases using total-video and video-assisted
endoscopic neck surgery for neck masses. Here, we will present an endoscopic neck surgical procedure for benign and malignant thyroid tumor.

**P251: THYROID INCIDENTALOMAS IDENTIFIED BY 18F-FURODOXOGLUCOSE (FDG)-POSITRON EMISSION TOMOGRAPHY (PET) IN THE PATIENTS WITH NON-THYROIDAL HEAD AND NECK CANCERS (HNC).**

Methods: 689 HNC patients who underwent FDG-PET were retrospectively reviewed. We evaluated the prevalence of patients with focal thyroid FDG uptake and the risk of malignancy and proper management in these patients. Results: 19 patients (2.8%) had focal thyroid FDG uptake. Of the 12 patients histologically diagnosed by surgery or needle biopsy, 4 had papillary carcinomas, and 1 had follicular carcinoma, whereas the others had benign thyroid lesions. The maximum standardized uptake value on PET was not sufficient to discriminate between malignant and benign thyroid lesions (8.4 ± 13.2 vs. 4.2 ± 4.0; P > 0.4). The identification of thyroid incidentalomas helped guide patient counseling and combined surgery with HNC and thyroidectomy. Conclusions: Focal thyroid lesions incidentally found on FDG-PET in patients with non-thyroidal HNC have a high probability of malignancy. These lesions deserve further diagnostic examination before HNC treatment to ensure adequate therapy for incidental thyroid cancers.

**P252: ANALYSIS OF PREDICTIVE FACTORS FOR BILATERAL PAPILLARY THYROID CARCINOMA IN THE AVOIDANCE OF INADEQUATE SURGERY**

Objective: Consternation with extent of surgery for unilateral papillary thyroid cancer (PTC) still exists because of enhanced morbidity with bilateral surgery. Bilateral PTC involvement dictates near-total or total thyroidectomy in patients with clinical unilateral PTC. A study was undertaken to examine the frequency of bilateral PTC in a cohort of patients surgically treated for PTC and to examine clinical and pathologic features that may help predict the presence of contralateral disease in apparent solitary PTC in order to avoid unnecessary surgery as well as inadequate surgery. Method: From a university-teaching hospital database, 169 patients who underwent near total, total or subtotal thyroidectomy for PTC were randomly selected. Data was analyzed using logistic regression. Fisher's exact test and the Mantel-Haenszel chi-square test. Results: There were 30 males and 139 females with ages from 18 to 82 years (mean: 44.8 years). Bilateral PTC was reported in the definitive pathological exam in one-third of the study population (55/169). The frequency of bilateral tumours varied significantly depending on the histological subtype of PTC (p=0.0142). Pure PTC had 32.2% of bilateral tumours (38/118), sclerosing PTC had 50% (9/18) and tall-cell PTC had 32% (4/13). Females (OR=0.484, p=0.05) were significantly associated with unilateral PTC. Also, there was a trend for an association between tumour size and bilateral PTC (p=0.0797). Age (p=0.761), angioinvasion (p=0.135) and lymphocytic thyroiditis (p=0.735) were not significantly associated with bilateral PTC. Patients with unilateral PTC had a significantly lower probability for lymph node metastasis (OR=0.418, p=0.018) than individuals with bilateral PTC. After a mean postoperative follow-up time of 46.4 months, lymph node recurrence occurred in 2.3% and was not associated with bilateral tumours (p=0.315). Conclusions: Our results suggest that men with tumour capsular invasion of specific histological subtypes (e.g. Warthin-like and tall-cell PTC) are more prone to having bilateral PTC. Patients with bilateral PTC are also more susceptible to develop lymph node metastasis. The high frequency and characteristics of bilateral PTC supports the policy of more complete treatment in patients with PTC generally and specifically for described risk factors.

**P253: RECURRENT LARYNGEAL NERVE REPAIR - OVER 32 YEARS EXPERIENCE ON 137 PATIENTS**

Methods: Recurrent laryngeal nerve reconstruction was performed using micro-neurovascular techniques. Objectives: To evaluate the prevalence and significance of thyroid incidentalomas identified by 18F-fluorodeoxyglucose (FDG)-positron emission tomography (PET) in the patients with non-thyroidal head and neck cancers (HNC).

Objective: To evaluate the prevalence and significance of thyroid incidentalomas identified by 18F-fluorodeoxyglucose (FDG)-positron emission tomography (PET) in the patients with non-thyroidal head and neck cancers (HNC). Methods: 689 HNC patients who underwent FDG-PET were retrospectively reviewed. We evaluated the prevalence of patients with focal thyroid FDG uptake and the risk of malignancy and proper management in these patients. Results: 19 patients (2.8%) had focal thyroid FDG uptake. Of the 12 patients histologically diagnosed by surgery or needle biopsy, 4 had papillary carcinomas, and 1 had follicular carcinoma, whereas the others had benign thyroid lesions. The maximum standardized uptake value on PET was not sufficient to discriminate between malignant and benign thyroid lesions (8.4 ± 13.2 vs. 4.2 ± 4.0; P > 0.4). The identification of thyroid incidentalomas helped guide patient counseling and combined surgery with HNC and thyroidectomy. Conclusions: Focal thyroid lesions incidentally found on FDG-PET in patients with non-thyroidal HNC have a high probability of malignancy. These lesions deserve further diagnostic examination before HNC treatment to ensure adequate therapy for incidental thyroid cancers.

**P255: DETECTION OF HUMAN PAPILLOMAVIRUS (HPV) 16 FROM ORAL SAMPLES**

Methods: Ten patients’ laboratory diagnosis of HPV status, and made predictions as to HPV status in the clinic, no one test has been deemed universally acceptable. We suggest that a physician’s clinical impression can raise the pretest probability of such diagnostic tests with possible clinical relevance, having an impact on selection of the patient’s treatment modality.

**CONCLUSION:** To determine HPV prevalence in tonsillar fossa exfoliated cell samples and in saliva samples collected from the same patients by use of two different HPV detection methods. Methods: All samples were collect-
The Human Papilloma Virus (HPV) has been shown to be associated with head and neck cancer, particularly with the base of tongue (BoT) cancer. A study was performed to evaluate the prevalence of HPV in a sample of 87 BoT cancer patients treated at the Roswell Park Cancer Institute.

**Methods:**
- The study included 87 patients with BoT cancer treated sequentially from May 2006 to July 2007. Additional inclusion criteria were age of 21-80 years, and for oral cancer cases a classification by ICD 10 codes of C03 - C14.9 (inner aspect of lip through and including pharynx) plus an ICD-O morphology code of 805-808 (squamous cell). Exclusion criteria for patients were 1) previous cancer diagnosis (except for basal or squamous cell skin cancers), 2) previous treatment for the current carcinoma (radiotherapy, chemotherapy, or immunotherapy, except vitamin D), 3) immune disorders concomitant with the neoplasm, 4) glucocorticoid treatment, 5) cognitive impairment and 6) not English proficient. Method A: Oral exfoliated cell samples were collected from the tonsillar fossa using a Cytobrush® Plus GT Scored (Medscand® Medical) and transferred into 5 ml ThinPrep® PreservCyt solution. DNA was extracted using MagNApure automated nucleic acid extractor (Roche Molecular Diagnostics) and HPV detection (for types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68) was performed by Third Wave Invader® signal amplification as recommended by the manufacturer. Method B: Unstimulated saliva samples were collected by expectoration at a pre-surgery visit or by suction at surgery and frozen at -20°C. DNA was purified from 200 μl of saliva by use of a modified Puregene (Qiagen) protocol for buccal cells in mouthwash. HPV16 detection and viral load were measured and normalized to a single copy human gene (ERV-3) by real-time, TaqMan PCR methods. Samples positive for HPV16 were further characterized by the presence of HPV16 E6 or E7 transcripts.

**Results:**
- All 41 tonsillar fossa samples were negative for HPV by the Third Wave Invader® method. Of the 41 saliva samples, HPV16 was detected in 3 by HPV16 real-time PCR. The median viral load for the 3 samples was 11.6 copies of HPV16 per 1000 cells. The median number of cells analyzed for the presence of HPV DNA in saliva samples was 2654. The 3 samples positive for HPV16 were from oral cancer patients. One specimen from a control patient gave an indeterminate result by HPV16 real-time PCR. **Conclusion:** HPV16 was not detected in exfoliated tonsillar fossa samples by use of the Third Wave Invader® HPV detection platform. However, HPV16 was detected in saliva samples from the same patients by PCR. Additional research is needed to determine whether the specimen collection or processing method can be optimized to utilize the Third Wave Invader® platform for testing of oral samples for HPV.

**P256: THE EFFECT OF HPV ON OUTCOME: A SUMMARY OF PATIENTS TREATED FOR BASE OF TONGUE CANCER**

**Objective:** The objectives of this study are to evaluate the prevalence of human papilloma virus (HPV) and epidermal growth factor receptor (EGFR) overexpression in oral squamous cell carcinoma in young patients (ages 18 to 40 years) and to assess whether HPV detection or EGFR overexpression is associated with recurrence and disease-specific survival. HPV has been suggested to have a role in the development of squamous cell carcinoma, including those of the oropharynx. EGFR overexpression has been associated with disease progression in oral squamous cell carcinomas, and current treatment modalities exist to inhibit the EGFR tyrosine kinase. However, the roles of HPV and EGFR have not been studied extensively in young patients with oral squamous cell carcinoma.

**Methods:**
- The study included 81 patients with oral cancer treated at a single institution. A subset of patient tumors were tested for the presence of HPV. The HPV tested subset is representative of the cohort in all characteristics. All never smokers tested were positive for HPV. HPV status was not associated with differences in survival, cause of death or tumor response. More testing of HPV is required to fully understand the impact of this exposure on BoT cancer risk and outcome.

**P257: HPV STATUS AND REGIONAL METASTASES IN THE PROGNOSIS OF ORAL AND OROPHARYNGEAL CANCER**

**Background:** Prognostic factors are important for treatment decisions as they help adapt the therapy on a case to case basis. Nodal status, number of positive nodes, and presence of extracapsular spread are considered to be important prognostic factors in head and neck cancer. Some studies suggest that HPV status also influences the outcomes of the treatment. This influence can be explained by variation in tendency to develop regional metastases and by variation in sensitivity of involved nodes of HPV positive and negative tumours.

**Objectives:** The study objectives were to compare patients with HPV positive and HPV negative tumours for survival and prevalence and type of regional metastasis, to identify prognostic factors and to test whether the HPV presence is an independent factor of survival. **Methods:** The study included 81 patients treated by surgery including neck dissection for oral or oropharyngeal squamous cell carcinoma. A computerized medical report was completed for each patient. Analysis of the tumour specimen for the HPV DNA presence was done on paraffin fixed tissue. HPV DNA detection and typing were performed by PCR with GP5+/GP6+ primers and reverse line blot hybridization. **Results:** Overall, 64% (52/81) of tumours were HPV positive with 80% in the tonsillar site. HPV positive patients had significantly better overall (73% versus 35%) and disease specific survival (79% versus 45%) than HPV negative patients. No significant differences were found in the pN classification, in the number of positive nodes and the presence of extracapsular spread in the involved nodes between HPV positive and HPV negative tumours. Multivariate analyses showed that significant prognostic factors of survival were the presence of HPV in the tumour, extracapsular spread and tumour size. **Conclusion:** HPV was the most significant prognostic factor in the studied group of patients mainly with oropharyngeal tumours (HR=0.27, 95%CI:0.12-0.61) and possibly should be considered in treatment decisions. Aknowledgement: The study was supported by grant NR/9466-3 of the Internal Grant Agency of the Czech Ministry of Health.
Forty-five cases were identified with available paraffin tissue for immunohistochemical and in situ hybridization studies. The mean follow-up was 11 years (range 1 to 25 years). HPV was detected in two cases, one of whom died of disease. All samples were positive for EGFR. Twenty-one of the 45 patients developed local or regional recurrence or distant metastasis. Nineteen of the 21 (90.5%) tumors with available histology were classified as higher grade carcinomas and metastases showed high EGFR expression, while only 2 (9.5%) of these tumors showed low EGFR expression. At five years following treatment the disease-free survival was 100% for patients with low EGFR expression and 64% for patients with high EGFR expression.

Conclusions: Human papilloma virus is not commonly associated with oral squamous cell carcinomas in these young patients. Tumors showing high EGFR expression are more aggressive and commonly associated with aggressive behavior and decreased five year disease-free survival.

[1] Head and neck squamous cell carcinomas (HNSCCs) are the sixth most common malignancies worldwide with more than 600,000 new cases reported each year. Depending on the study, between 12 and 45% of these tumors are found to be positive for human papillomavirus (HPV) DNA. HPV-positive HNSCCs have been described as an own entity, differing from the HPV-negative HNSCCs in the age of the patient at diagnosis, smoking and alcohol habits, the presence of wt-p53, higher radiosensitivity of the tumors, and a better prognosis. HNSCCs produce large amounts of tumor proteases with the majority belonging to the family of matrix-metalloproteinases (MMPs). It is believed that the activity of these proteases enables the tumor to locally infiltrate and metastasize. The expression of MMPs is mostly regulated by the transcription factor AP-1 induced by the activity of signal-transduction cascades such as the MAPKases. Our previous studies have led to the observation that MMP9 is highly expressed in papilloma virus-induced skin lesions in the New Zealand White rabbit (NZW). In this animal model introduction of the cottontail rabbit papillomavirus (CRPV) into the skin, results in epithelial papillomas within 4 to 8 weeks that progress into infiltrating and metastasizing carcinomas without the requirement for cofactors. The aim of our research was to identify papillomavirus-related mechanisms responsible for the induction of MMP9 expression in the NZW.

(2) After subcloning of 2kb of the rabbit MMP9 5'-flanking region generated from a genomic library, the fragment was sequenced by primer walking. Transcription-factor binding sites were identified, several deletion fragments were constructed, and relevant sites were mutated using site-directed mutagenesis. These constructs were used in reporter-gene assays along with expression plasmids of CRPV early proteins to characterize the promoter activation and its underlying mechanism. (3) As MMP9 is predominantly regulated on the promoter level 2 kb of the rabbit MMP9 promoter have been cloned, sequenced, and aligned to its human counterpart. The first and last ~500 bp of both promoters were highly conserved (77% homology), whereas the intervening 1000 bp showed very little (~13%) sequence similarity. We discovered that apart from the known oncogenes E6 and E7, the E2 protein led to a significant activation of the MMP9 promoter. Shortening of the promoter beyond 700bp led to a complete failure of E2-mediated activation as did mutation of the AP-1 binding sites within this part of the promoter. Furthermore, using chemical inhibitors targeting the ERK signal transduction cascade activation could be reversed. (4) Hence, we were able to demonstrate that papillomavirus E2 can influence the promoter activity of the tumor-relevant protease MMP9 and that this activation is mediated by ERK via an AP-1 transcription factor binding site.
tumors positive for HPV16 by MY09/11 PCR. HPV16-DNA detection was higher in head and neck SCC than non-SCC cancers, and varied across anatomic subsites. HPV16 prevalence was highest in the oropharynx (48%), followed by larynx supraglottis (35%), larynx glottis (33%), and oral-cavity (29%). Half of hypopharyngeal and nasopharyngeal tumors also tested positive for HPV16, while 17% of salivary tumors were HPV16-DNA positive. Advanced stage (III/IV) HNSCC tumors were more likely to be HPV16 positive than low stage (I/II) HNSCC tumors (42% vs. 23%) though the difference was not significant. HPV16 prevalence was also slightly higher in HNSCC with positive lymph nodes compared to negative lymph nodes at diagnosis (40% vs. 36%). With respect to HPV16 variants, 61% of HNSCC tumors harbored European (E) variants only, 31% harbored Non-European (NE) variants, and 8% showed co-infection by both E and NE subtypes. Detection of HPV16-NE variants was higher in the oral-cavity (42%) and larynx (42%) than in the oropharynx (37%). HPV16 NE variants were more common in African-Americans than Caucasians (47% vs. 30%), although more Caucasians were positive for both E and NE variants (11% vs. 7%). Non-Hispanics were also more likely to harbor NE variants than Hispanics (36% vs. 25%).

Conclusions: HPV prevalence in head and neck cancers is site specific, with the vast majority of tumors harboring HPV16. HPV16-intraetype distribution in HNSCC, however, does not correlate strongly with racial origin or anatomic site.

P262: NONINVASIVE DETECTION OF HPV AND ASSOCIATED GENETIC ALTERATIONS IN HEAD AND NECK SQUMOUS CELL CARCINOMAS S.Sethi1, D.Baya1, M.Wierman1, A.Kapke1, Mu1, M.Benninger1, M.J.Warsham1, 1Henry Ford Health Systems, Detroit, MI

Objective: Oncogenic human papillomavirus (HPV), particularly type HPV16, is a proposed causative agent in multistep carcinogenesis of about 25% of head and neck squamous cell carcinomas (HNSCC). The present study was undertaken to determine whether non-invasive saliva detection of HPV and its high-risk subtypes (HPV 16, 18) is associated with presence of head and neck squamous cell cancer. Further we investigated whether HPV 16 associated HNSCCs display a pattern of genetic alterations (loss and gain) distinct from HPV negative HNSCCs. Method: Saliva was collected from 45 HNSCC patients and 21 control subjects. HPV in saliva DNA was detected by single-round PCR using consensus primers MY09/11 from the L1 gene region. HPV was typed by two-round PCR using primers located in the E6/E7 gene region and specific for types 16, 18 and 33. PCR products were electrophoresed through 2% agarose, stained with ethidium bromide and visualized with a GeldocXR imaging system. In a subset of 27 HNSCC patients, genetic alterations were evaluated in the saliva DNA using multiplex ligation probe amplification (MLPA) assay to interrogate 82 genes with known association with HNSCC.

Results: HPV was detected in the saliva DNA from 17 of 45 (38%) HNSCC patients and in 1 of 21 (5%) control subjects. Subtype analysis identified HPV type 16 in twelve (27%) HNSCC patients and in none of the controls. HPV type 33 was identified in 5 of 45 (11%) HNSCC patients and in 1 of 21 controls (5%). Statistically significant association of HNSCC with saliva HPV 16 (p=0.006) and HPV 33 (p=0.056) was found (Fishers Exact test). Of the 82 genes interrogated in the subset analysis, there was statistically significant association between TP53 gene loss and HPV 16 positive HPV 16 positive HNSCC patients in comparison to 13% of HPV 16 negative cases. Conclusions: Detection of HPV in saliva is significantly associated with HNSCC. HPV subtype analysis using saliva DNA showed significant association of HPV type 16 with HNSCC but not HPV type 33. Allelic loss of TP53 gene showed significant association with the HPV 16 positivity. This study supports clinical use of saliva for concomitant non-invasive molecular detection of HPV16 and gene alterations to identify highly relevant signature clonal biomarkers using high throughput assays for head and neck cancer screening, surveillance and future therapeutic strategies like HPV vaccines, overcoming the need for tissue acquisition via invasive surgical procedures. Additionally this study will also help in understanding the biological etiopathogenesis of HNSCC.

P263: HUMAN PAPILLOMA VIRUS GENOTYPE DISTRIBUTION IN LARYNX CARCINOMA SAMPLES M.C.Torrente1, T.Gheith2, M.Schmidt3, J.M.Ojeda4, M.Pawlita3, M.Tomasino4, 1Universidad de Chile, Santiago, Chile; 2International Agency for Research in Cancer, Lyon, France; 3German Cancer Research Center, Hildesberg, Germany; 4Centro de Oncologia Preventiva, Universidad de Chile, Santiago, Chile

Introduction: Human papillomavirus (HPV) has been related with head and neck carcinogenesis, in particular high risk genotype 16. There are few studies that focus on larynx squamous cell carcinoma (LSCC) to enable an accurate description of HPV genotype distribution for this anatomic site. This issue becomes relevant when considering HPV vaccine, the relation of certain genotypes with prognosis and response to treatment, and the HPV genotype geographic variations. The objective of this study is to identify the HPV genotypes isolated in LSCC. Material and Methods: LSCC formalin fixed paraffin-embedded samples were collected. DNA was extracted with Proteinase K. HPV DNA was identified with multiplex PCR, including E7 primers specific for 19 mucosal high-risk HPV (16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 70, and 73). Bead-based multiplex genotyping was performed: the product of the multiplex PCR reaction was hybridized with type-specific oligonucleotide probes coupled to fluorescently labeled microbeads. HPV 66 variants were studied by sequencing E7 gene, and the result was compared against the prototype. Results: 68 tumor samples were collected, 34 were positive for HPV DNA (50.7%). The most frequent genotypes identified were HPV 66 (15 cases, 44%), HPV 16 (11 cases, 32%), HPV 56 (5 cases, 15%), and HPV 51 (5 cases, 15%). Other genotypes identified were 18, 26, 31, 33, 45, 52, 53, 58, 59, 66, 68, 70, and 73. In half of them HPV 16 was included. Two new HPV 66 variants were described and no prototype was identified. Conclusions: 1. HPV DNA was identified in 50.7% of larynx carcinoma samples. 2. The most frequent genotype was HPV 66, followed by HPV 16, 56, and 51. 3. New HPV 66 variants were described.

BASIC SCIENCE: BIOMARKERS

P264: FAS-ASSOCIATED DEATH DOMAIN IS A PREDICTOR OF CLINICAL OUTCOME IN GLOTTIC LARYNGEAL CARCINOMA TREATED WITH RADIOTHERAPY M.L.Schrijvers1, J.E.van der Wal1, L.Menkes1, M.F.Mastik1, W.J.Pattie2, J.Gibcus1, J.A.Langendijk1, F.BAMavan de Laan1, E.Schuuring1, 1University Medical Center Groningen, Groningen, The Netherlands

Objective: In HNSCC amplification of the 11q13 region occurs frequently and is associated with worse clinical outcome. Within the 11q13 amplification, various candidate genes were reported including cyclin D1 and cor-tactin. Recently, using CGH array analysis of 30 HNSCC with 11q13 amplification, FADD was identified as the gene most frequently amplified and overexpressed. Originally, FADD was recognized as an adapter molecule for Fas-mediated apoptosis. However, more recently, FADD was reported to be phosphorylated at serine 194 at the G2/M transition suggesting a close association with cell cycle progression. The aim of this study is to establish the effect of expression of FADD on clinical outcome in glottic laryngeal carcinomas, treated with primary radiotherapy. Material and Methods: Immunohistochemistry for FADD on formalin-fixed paraffin-embedded biopsies of pre-treatment tissue samples was performed on a homogenous group of 102 early stage (T1/T2) glottic laryngeal carcinomas treated with primary radiotherapy. Objective: To predict clinical outcome in T1/T2 glottic laryngeal carcinoma treated with radiotherapy showing high FADD expression were detected in 25% of the cases. No significant relation was found between FADD expression and overall or disease specific survival in glottic carcinomas treated with radiotherapy. However, low FADD expression significantly predicted worse local control (OR 4.482, 95% CI 1.057-19.003) and loco-regional control (OR 5.132, 95% CI 1.223-21.710). Conclusions: Early stage laryngeal cancers treated with radiotherapy showing high FADD expression are almost all (92%) radiosensitive, whereas only 69% of those with normal/low expression are radiosensitive. Although the role of FADD on radiosensitivity is not known, FADD is a useful molecular marker to predict clinical outcome in T1/T2 glottic laryngeal carcinoma treated with radiotherapy. Ongoing Studies: To investigate the role of FADD on radiosensitivity in vitro, we started a study on deregulating FADD expression in human head and neck squamous cell carcinoma cell lines using either siRNA for FADD or FADD-expression vectors. The radio-response of the parental (non-transfected) cell lines will be compared to variant transfecants with down- or up-regulated FADD expression using clonogenic and MTT assays. This analysis will provide evidence whether FADD is the over-expressed gene in the 11q13 amplon responsible for the radiosensitivity.

P265: THE ROLE OF DIHYDROPRYMIDINE DEHYDROGENASE EXPRESSION IN RESISTANCE TO 5-FLUOROURACIL IN HEAD AND NECK SCC Y.Kasumatu1, T.Nakashima1, S.Komune1, 1Kyushu University, Fukuoka, Japan

Objective: 5-FU is one of the most widely used chemotherapeutic drugs to
7th International Conference on Head and Neck Cancer

**Posters**

**P266: CLINICOPATHOLOGIC CORRELATION OF HER-2/NEU OVEREXPRESS IN ORAL CAVITY SQUAMOUS CELL CARCINOMA**

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**Objective:** Her-2/neu gene upregulation and increased expression have been previously proven as a marker of prognosis for many solid tumors including oral cavity squamous cell carcinoma. But, the relevance of HER-2/neu in squamous cell carcinoma is controversial. This study investigates the correlation of HER-2/neu over-expression with clinicopathologic measures and patient survival.

**Methods:** Immunohistochemical staining of untreated oral cavity squamous cell carcinoma (n = 31) patient tissues, carcinoma in situ (CIS) specimens (n = 5), and normal mucosal samples (n = 5) was performed and scored for membrane expression of HER-2/neu protein. HER-2/neu was correlated with disease stage, tumor subsite, and histologic grade, overall survival and disease free survival.

**Results:** Positive staining for HER-2/neu was seen in 84% of carcinoma specimens, but less commonly in CIS (60%, p = 0.24) and normal mucosa (0%, p = 0.01). Subsite specific analysis showed 100% of floor of mouth tumors, 86% of buccal mucosal tumors, 70% of tongue tumors, and 67% of those involving the retromolar trigone stained positively. A relationship was seen between increased T stage and expression of HER-2/neu membrane protein that failed to reach statistical significance (p = 0.138). No correlation was seen between degree of staining with overall patient survival, disease free survival, N stage, tumor histology, or patient age. **Conclusion:** As normal mucosa progresses to frank carcinoma a graded increase in Her-2/neu over-expression is observed. Interpretation of the results of our limited dataset is a poor predictor of patient outcomes.

**P267: P16 AND VEGF-RECEPTOR OVEREXPRESS IN ADVANCED HEAD AND NECK CANCER ARE ASSOCIATED WITH IMPROVED OUTCOMES**

G.A.Russo1, P.McCue1, T.Hyslop1, E.Wuthrick1, A.Akhtar1, M.Rosen1, W.Keane1, M.Machtay1, 1Thomas Jefferson University Hospital, Philadelphia, PA

**Background:** Biomarkers are becoming increasingly important in oncology, and are being used to estimate prognosis and in some cases predict treatment responses. There is a paucity of such information for head and neck cancer. We set out to determine the relationship between the expression of five biomarkers [BAX, BCL-2, Cyclin-D1, P16, and Vascular Endothelial Growth Factor Receptor (VEGFr)] and recurrence free and overall survival for patients with advanced head and neck squamous cell carcinoma.

**Methods:** Patients with advanced squamous cell carcinoma of head and neck were identified from our clinical database and the matching tissue blocks were retrieved from our institutional tissue bank. Tissue microarrays were constructed and the expression of BAX, BCL-2, Cyclin-D1, P16, and VEGFr were assessed using immunohistochemistry. Stained tissue was scored for both proportion of tumor cells positive (1=0%, 2=5-25%, 3=25-75%, 4=75-95%, 5=100%) and intensity of staining (1=faint, 2=moderate, 3=intense). A summary score (intensity x extent) ranging from 0-9 was calculated. Summary scores greater than or equal to 4 were considered positive. Estimates and comparisons of recurrence-free and overall survival were performed using Kaplan Meier Log Rank and Cox Proportional Hazard Statistical Models.

**Results:** We identified 79 patients for whom tissue blocks and clinical information were available. The patient population was made up of 58 males and 21 females with a mean age of 58 at the time of diagnosis. All patients had AJCC Stage III or IV, non-metastatic squamous cell carcinoma of the head and neck (41 oropharynx 15 larynx, 12 oral cavity, 8 hypopharynx, 3 unknown primary) and received radiation therapy as part of their treatment (58 chemoradiotherapy and 21 radiation therapy alone). Median follow-up at the time of this report is 34 months. Thirty-five percent, 24%, 29%, 33%, and 45% of the patients were BAX, BCL-2, Cyclin-D1, P16, and VEGFr positive, respectively. The 2-year actuarial recurrence free and overall survival for the entire patient population was 64% and 72% respectively. Overexpression of P16 correlated with improved recurrence free survival (2yr RFS: 78% vs 53%, p=0.016) and overall survival (2 yr OS: 84% vs 63%, p=0.013). These differences remained significant when adjustments were made for age, sex, cancer stage, and primary site with pRFS=0.016 and pOS=0.007. In addition, patients with tumors overexpressing VEGFr had a longer survival than those not overexpressing VEGFr (2-yr OS: 87% vs 63% respectively, p=0.026). This difference was no longer present after adjusting for age, sex, cancer stage, and primary site (p=0.099).

**Conclusion:** P16 overexpression in advanced head and neck squamous cell carcinoma is associated with significantly reduced likelihood of recurrence and death after treatment. In addition, patients with tumors that overexpress VEGF are less likely to die following treatment when compared to patients’ whom tumors do not overexpress VEGF. These and other biomarkers may prove useful in selecting appropriate therapies, and in counseling patients with advanced head and neck cancer regarding prognosis.

**P268: INTRATUMORAL CONCENTRATION OF S100 PROTEIN IN SQUAMOUS CELL CARCINOMA OF THE LOWER LIP, AS A PREDICTIVE FACTOR FOR METS**

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**Objective:** Identify tumor aspects that may be correlated with different behavior for SCC of the lower lip. **Methods:** The charts of 66 patients with squamous cell carcinoma of the lower lip surgically treated were retrospectively studied. Demographic, clinical and pathological variables (pt, thickness, grade, margins, invasions, inflammatory infiltrate and lymph node involvement) were analyzed and compared to intratumoral concentration of S100 protein (dendritic cells), identified by immunohistochemical assay. The overall and disease-free survivals were compared among pathological variables using the Kaplan-Meyer curves. **Results:** The mean number of dendritic cells counted in a microscopic field ranged from 1.7 to 74.2 with a median value of 20, which created 2 groups of patients: lower and higher concentration for S100 protein. Size of tumor (T1 and T2 versus T3 and T4) in centimeters was marginally statistical different (P =.06), although keeping an inverted relation between tumor size and intratumoral S100 concentration. Thickness of tumor in millimeters showed a significant difference (P =.006) in same inverted relation the thicker the tumor, the lower S100 concentration. Overall survival for N+ patients was significantly lower than that for N0 patients (P =.009). The same difference was found for thickness of tumor greater than 10 mm (P =.02), perineural invasion (P =.006) and intratumoral S100 concentration lower than 20 dendritic cells (P =.03). The disease-free survival was significantly lower for patients with T3 or T4 tumors (P =.02), tumors greater than 4 cm extension (P =.03), with a tumor thickness greater than 10 mm (P =.02) and with presence of perineural invasion (P =.002). **Conclusion:** Low concentration of intratumoral S100 protein seems to be related with more metastasis and lower overall and disease-free survivals for the analyzed patients. This can be helpful for the indication of elective neck dissection in patients with T2N0 stage, with tumor thicker than 10 mm and low concentration of intratumoral S100 protein.

**P269: MARKERS OF RADIOSENSITIVITY IN PATIENTS WITH HEAD AND NECK CANCER. THE MASS-SPECTROMETRY ANALYSIS OF PLASMA PROTEOME**

T.W.Rutkowski1, A.Wygard2, K.Szendowicz2, M.Pietrowiak1, W.Hawryluk1, A.Polanska3, A.Polanski3, L.Marczak4, M.Stobecki4, 1Cancer Centre, Maria Sklodowska-Curie Memorial Institute, Gliwice, Poland; 2Cancer Centre, Maria Sklodowska-Curie Memorial Institute, Gliwice, Poland; 3Silesian University of Technologies, Gliwice, Poland; 4Institute of Bioorganic Chemistry, Poznan, Poland

**Objective:** Due to the high risk of acute mucosal reaction, the selection of proper radiotherapy (RT) schedule for patients with head and neck squamous cell cancer (HNC) could be a significant problem, especially when combination with systemic therapy is considered. In clinical practice no reliable predictive makers of radiosensitivity is available. In recent years how-
ever, cancer diagnostic takes advantage of achievements of current biology: genomics and proteomics. Analysis of the low-molecular-weight region of the blood proteome (using either serum or plasma samples) by mass spectrometry is an emerging method of clinical proteomics. Although no single peptide is expected to be a reliable bio-marker in such analyses, multiplex peptide sets of markers selected in numerical tests have been already shown in a few studies to have prognostic and predictive value in cancer diagnostics. Here we aimed to identify a set of highly differentially expressed markers of radio-sensitivity in the circulating blood that could be used for planning and monitoring radiotherapy in HNC patients. Methods: Low-molecular-weight (2-10kD) plasma polypeptides were analyzed using MALDI-TOF mass spectrometry. Blood samples were collected in the group of 60 patients with HNC before RT and in corresponding group of healthy donors. Pathologically confirmed squamous cell cancer was diagnosed mostly in pharynx or larynx. All of patients were evaluated for radical 3D conformal RT. The group consisted of 12 (20%) females and 48 (40%) men in the mean age of 53 years (range: 34-72 years). The acute mucosal reaction was assessed using modified Dische score, RTGC acute radiation morbidity scoring criteria and WHO toxicity criteria of oral mucositis during the RT each 5-7 days. Due to acute mucosal reaction patients were divided into two subgroups: low and high intensity of mucosal reaction. Total RT dose was in the range of 68-72 G y given in 1.8 G y: 2 G y fraction doses. Polypeptide patterns specific for different groups of donors were resolved due to mathematical analyses that used Gaussian mixture model for decomposition of mass spectra into components. A set of peptides that differentially expressed HNC patients of healthy individuals was identified. Results: The difference of about 10 spectral polypeptide peaks between healthy donors and patients were found to be highly significant (p<0.001). Moreover, the significant difference (p<0.01) of the levels of several spectral polypeptide peaks were also found between patients with low and high intensity of mucosal reaction. Conclusions: Preliminary data shows that specific patterns of plasma proteome are correlated with the intensity of acute mucosal reaction in this group of patients. Further studies are needed to confirm potential clinical application of multi-component sets of plasma peptides as biomarkers of radiosensitivity in HNC patients.

P270: ADHESION MOLECULES EXPRESSION IN LOCALLY RECURRENT ORAL CARCINOMA, IS THERE A RELATION WITH PROGNOSIS? I.G. Agra1, J.G. Filho1, E.P. Martins1, C.A. Pinto1, F.A. Soares1, L.P. Kowalski1, Hospital AC Camargo, Sao Paulo, Brazil

Objective: To assess the expression of proteins associated with the process of cellular adhesion and its relationship with the prognosis in patients with locally recurrent squamous cell carcinomas (SCC) of the oral cavity and oropharynx submitted to salvage surgery. Methods: The charts of 101 patients with locally recurrent oral carcinoma submitted to salvage surgery, between 1990 and 2004, were reviewed. Only patients with neck stage classified as N0 (cTNM) by clinical exam and CT or MRI were included. All the patients were submitted to salvage surgery with curative intent. The tumor site was: The oral cavity in 66 (67.3%) and oropharynx in 33 (32.7%). Immunohistochemical expression of adhesion molecules studied were CD44 (isofoms Hcam, v3, v4, v5, v6), e-cadherin and 382-catenin. Results: There was expression of the proteins CD44v4, CD44v5, CD44v6, e-cadherin and 382-catenin in the majority of the cases (at least 75%). The proteins CD44v4, CD44v5 and CD44v6 presented negative expression in over 50% of the cases. There was no statistical difference in the expression of these proteins with regard to the tumor site, with the exception of 382-catenin. This protein presented overexpression in all cases of oropharynx carcinoma and in 86.6% in oral cavity SCC. (p=0.027). Patients with adhesion molecules overexpression presented worst cancer specific and overall survival. However, as was in the tumor stage and invasive front. The level of staining was graded on a scale from 1-3. Statistical analysis was performed using the Student's t-Test. Results: Beta-catenin expression was observed in the cell membrane, cytoplasm and to a small degree in the nucleus. Membranar expression of beta-catenin was strongly positive in 72%, 36% and 11% of cases of dysplastic epithelium, tumor center and invasive tumor front, respectively. Cytoplasmic expression differred with strongly positive staining in 0%, 16% and 50% of cases of dysplastic epithelium, tumor center and invasive tumor front, respectively. Beta-catenin membran expression was significantly lower at the invasive front of the tumor (p<0.0001) and the tumor center (p<0.05) when compared to areas of dysplastic epithelium. The increased in cytoplasmic expression was significant in the tumor center (p<0.01) and invasive front (p<0.01) when compared with the dysplastic epithelium. WNT1 cytoplasmatic expression progressively increased from the dysplastic epithelium, to the tumor center and to the invasive tumor front; however, this difference did not achieve statistical significance. Inflammatory cells, primarily lymphocytes, were found in 74% of the specimens primarily in the stroma surrounding the tumor. Interestingly, in 60% of samples analyzed, inflammatory cells near the invasive tumor front demonstrated expression of WNT1 while inflammatory cells within the tumor centers did not express WNT1. Conclusions: There was a significant decrease in the expression of membranar beta-catenin and a significant increase in cytoplasmic beta-catenin in this sample of oropharyngeal tumors. These differences in expression were more accentuated at the invasive front of the tumor. No significant change in WNT1 expression was observed between samples. Strong WNT1 expression was observed in the inflammatory cells that surrounded the tumor nests, but its effect on tumor behavior is unclear at this time. We plan to extend our study to a larger series and correlate these findings with tumor stage, response to therapy, and prognosis.

P272: THE ROLE OF P38 MAP KINASE ACTIVATION FOR CYTOKINE SECRETION AND METASTASIS DEVELOPMENT IN HEAD AND NECK CANCER C. Riebe1, R. Pries1, B. Wollenberg1, 1University of Luebeck, Luebeck, Germany

Head and neck squamous cell carcinoma (HNSCC) is one of the most frequent cancers. It is supposed that tumor production of various immune suppressors, or tumor production of cytokines that contributes to massively impaired immune functions, but the underlying signal transduction pathways are mostly unknown. Phosphorylation levels of MAP kinase (mitogen activated protein) kinase p38 were analyzed in permanent cell lines as well as solid tumor tissue of HNSCC using flow cytometry and SDS-PAGE. Cytokine secretion was determined using Cytometric Bead Array Flex Set system. MAP kinase p38 was shown to be activated in HNSCC by phorbol 12-myristate 13-acetate (PMA). Activation of p38 leads to decreased cell proliferation and increased secretion of cytokines IL-6 and IL-8 in HNSCC. Our data demonstrate significant differences of p38 activities in primary HNSCC and tumor metastasis and provide novel insights concerning the origin of the HNSCC microenvironment. The better understanding of these molecular mechanisms in HNSCC is essential for novel drug development and improvement of the clinical perspective of this tumor type.

P273: LYSOPHOSPHATIDIC ACID ACYLTRANSFERASE-B: A NOVEL BIOMARKER IN ORAL SQUAMOUS CELL CARCINOMA D.M. Monte1, B.L. Schmigl2, 1Louisiana State University Health Science Center, Shreveport, LA, 2University of California, San Francisco, CA

Objective: Lysophosphatidic acid (LPA) has been shown to induce certain epithelial-derived cancers through ectopic production of the lysophosphatidic acid (LPA) activating enzyme, lysophosphatidic acid acyltransferase (LPAATB). Despite LPAAT-B’s clear role in epithelial carcinogenesis, its role has not been studied in oral squamous cell carcinoma (OSCC). The objective of this study is to determine if ectopic expression of LPAAT-B is present in OSCC. Materials and Methods: We performed a retrospective review of twenty-six patients treated for OSCC at the University of California San Francisco. Histology, tumor size and regional lymph node status were recorded. Normal oral tongue served as the negative control. Third trimester human placenta served as the positive control. Specimens were incubated in a 1:200 diluent solution of the primary monoclonal anti-
body against human LPAAT-B (Cell Therapeutics, Seattle, WA, USA) fol-
lowed by an anti-mouse secondary antibody. A 3-aminoo-9-carboxyl enzy-
me substrate system was then applied prior to colorization. Method of
Data Analysis: Two pathologists independently evaluated all tissues for
LPAAT-B expression. An immunoreactivity scoring system based on a
quantitative and qualitative analysis of staining was recorded for each
sample. The mean number of cells stained (+ = weak, ++ = moderate and +++ =
strong) were recorded. Results: Ectopic expression of LPAAT-B was identified in 30.8
Peripheral blood samples were collected from 50
Ten patients
62 carcinomas were wildtype or had
Tobacco smoking is the primary etiology for squamous cell car-
cinoma (HNSCC). Expression of EGFR and phospho-EGFR were also meas-
ures of VEGF, HGF, IL-6, IL-8, MMP-9 and telomerase by taking specimens of peripheral blood
Objective: This study investigates the expression rate of serum VEGF, HGF, IL-6, IL-8, MMP9 and telomerase in peripheral blood of patients with head and neck cancer and examines the relation between the expression rate of these biomarker and clinicopathologic parameters with prognosis. Methods: Peripheral blood samples were collected from 50 head & neck squamous cell cancer patients and 15 normal control group. The measurements of VEGF, HGF, IL-6, IL-8 and MMP-9 were performed with using enzyme linked immunosorbent assay kits (R&D Systems, Minneapolis, MN, U.S.A.). The telomerase activity in peripheral blood mononuclear cells(PBMCs) was measured by TRAP assay using TRAPEze telomerase detection kit (Intergen Co. USA). Pearson chi-square test was

P275: CHARACTERIZATION OF SQUAMOUS CELL CARCINO-
MASES OF THE SUPRAGLOTTIC LARYNX WITH OR WITHOUT
MUTATIONS IN TP53 J.G.Eriksen 1, J.Lee 1, J.Wang 1, K.Lee 2, H.J Park 2, 3
1Pusan National University School of Medicine, Busan, Republic of Korea; 2Pusan National University School of Medicine, Busan, Republic of Korea; 3Kosin University College of Medicine, Busan, Republic of Korea; 4Dong-A University College of Medicine, Busan, Republic of Korea

Objective: Tobacco smoking is the primary etiology for squamous cell car-
cinomas of the supraglottic larynx and is reported to initiate the carcino-
genetic process of squamous cell carcinomas of the supraglottic larynx. For estimation of TP53-mutations, DNA was extracted from the biop-
sies and screened for mutations in exon 4c-10 of TP53 by DHPLC (WAWRE®). Mutations were further characterized by sequencing. EGFR, p16, Ki-67, BCL2 and E-cadherin were estimated by immunohistochemistry. Data were evaluated by descriptive statistics, Spearman tests for trend and logistic regression analysis. Results: 62 carcinomas were wildtype or had silent mutations outside the domains, 61 had mutations inside the domains or null-mutations leading to stop-codons. The TP53-mutational status was not correlated to the expression of E-cadherin, BCL2, Ki-67 or tumor cell differ-
etiation. High expression of EGFr seemed to be correlated to tumors with mutations in TP53 (p=0.03) and TP53 wildtype tumors had twice as high expression of p16 compared to carcinomas with mutations in TP53 (p=0.04). Furthermore, logistic regression analysis separating by mutation-
al status, suggested that carcinomas with mutations in TP53 had relative higher expression of EGFR (p=0.033, RR=2.6 (1.1-6.3)) and lower expres-
sion of p16 (p=0.04; RR=0.4 (0.2-0.9)) compared to wildtype tumors or tumors with silent mutations outside the domains. Conclusion: The results of the present study suggest that low expression of EGFr and high expres-
sion p16 might be two of the markers that characterize tumors without muta-
tions in TP53. These data are in accordance with experimental data and indicate that other factors than tobacco (i.e. HPV-virus) might be involved in the carcinogenic process of squamous cell carcinomas of the supraglottic larynx.

P276: EGFR IS OVEREXPRESSED BUT PHOSPHO-EGFR IS A
POTENTIAL PROGNOSTIC BIOMARKER IN PATIENTS WITH
HNSCC C.Massoud 1, S.Chinn 1, J.Tartaglia 1, T.Macy 1, U.K.Sinha 1, 1University of Southern California, Los Angeles, CA

Objective: To demonstrate a potential role of the Epidermal growth factor receptor (EGFR) and phospho-EGFR as biomarkers for Head and Neck Squamous Cell Carcinoma. Study Design and Setting: Fold induction of EGFR was determined by microarray analysis from normal, tumor and lymph node tissue from ten patients with Head and neck squamous cell car-
cinoma (HNSCC). Expression of EGFR and phospho-EGFR were also meas-
ures of VEGF, HGF, IL-6, IL-8, MMP-9 and telomerase by taking specimens of peripheral blood
Objective: To demonstrate a potential role of the Epidermal growth factor receptor (EGFR) and phospho-EGFR as biomarkers for Head and Neck Squamous Cell Carcinoma. Study Design and Setting: Fold induction of EGFR was determined by microarray analysis from normal, tumor and lymph node tissue from ten patients with Head and neck squamous cell car-
cinoma (HNSCC). Expression of EGFR and phospho-EGFR were also meas-
ures of VEGF, HGF, IL-6, IL-8, MMP-9 and telomerase by taking specimens of peripheral blood

P277: EXPRESSION OF VEGF, HGF, IL-6, IL-8, MMP-9 AND
TELOMERASE IN PERIPHERAL BLOOD OF PATIENT WITH
HEAD AND NECK CANCER C.Lee 1, J.Lee 1, S.Wang 1, K.Lee 2, H.J Park 2, 3
1Pusan National University School of Medicine, Busan, Republic of Korea; 2Pusan National University School of Medicine, Busan, Republic of Korea; 3Kosin University College of Medicine, Busan, Republic of Korea; 4Dong-A University College of Medicine, Busan, Republic of Korea

Objective: This study investigates the expression rate of serum VEGF, HGF, IL-6, IL-8, MMP-9 and telomerase by taking specimens of peripheral blood of patients of head and neck cancer and examines the relation between the expression rate of these biomarker and clinicopathologic parameters with prognosis. Methods: Peripheral blood samples were collected from 50 head & neck squamous cell cancer patients and 15 normal control group. The measurements of VEGF, HGF, IL-6, IL-8 and MMP-9 were performed with using enzyme linked immunosorbent assay kits (R&D Systems, Minneapolis, MN, U.S.A.). The telomerase activity in peripheral blood mononuclear cells(PBMCs) was measured by TRAP assay using TRAPEze telomerase detection kit (Intergen Co. USA). Pearson chi-square test was

P278: DIFFERENTIAL PROTEOMICS OF RADIORESISTANT PHE-
NOTYPE IN HEAD-NECK CANCERS REVEALS GP96 AS A CRITI-
CAL REGULATOR C.Liu 1, C. Shen 2, L.Liu 2, J.Chang 3, C.Liao 3, T.Yen 3, A.Cheng 3, 1Ming Chi University of Technology, Taipei Taiwan Republic of China; 2Chung Gung University, Taoyuan, Taiwan, Republic of China; 3Chung Gung Memorial Hospital, Taoyuan, Taiwan, Republic of China

Objective: To investigate radioreistant mechanism, we established radioresistant (RR) sublines of two oral cancer cell lines, OECE1 and KB. After characteri-
ization of the radioreistant phenotype, the differential proteomes of parental and RR sublines were analyzed by gradient gel electrophoresis and identified by Mass spectrometry. Seven genes were found differentially expressed in both RR sublines as potential RR associated genes, including Gp96, Enolase-1 and annexin A2. We further investigate the role of Gp96

P279: INHIBITION OF LYSOPHosphATIDic ACID ACYLTRANSFERASE-Beta DISRUPTS PROLIFERATION AND ENHANCES ROS LEVELS OF LARYNX CARCINOMA CELLS EXPRESSING ENOLASE-1


J.Overgaard1, 1Aarhus University Hospital, Aarhus C, Denmark
A.Cheng2, 1Ming Chi University of Technology, Taipei Taiwan Republic of China; LPAAT-B and OSCC behavior is warranted. The identification of ectopic LPAAT-B expression in OSCC may represent the first step in the identifica-
used to analyze the correlation of telomerase expression with clinicopathological parameters. Kaplan-Meier method was used for prognostic analysis.

**Results:** Only the expression rates of telomerase (p<0.001), VEGF (p<0.001) and MMP-9 (p<0.05) of head and neck cancer group showed the statistically significantly higher expression rates than those of normal control group. Only VEGF of head and neck cancer group showed the statistically significant increase of expression according to the progression of T stage (p<0.001). Only the case of lymph node metastasis showed higher expression of telomerase and VEGF (p=0.001/p<0.001). Only the expression of telomerase and VEGF showed significant increase as AJCC stage progresses (p=0.009/p<0.001). Serum VEGF was significantly related with the expression of telomerase in PBMCs of patients of head and neck cancer. 

**Conclusion:** The serum VEGF and telomerase expression in PBMCs of patients of head and neck cancer is a simple and very useful molecular marker for the progression and prognosis of head and neck cancer.

**P278: APOPTOTIC MARKERS PS3, BCL-2 AND BAX IN PRIMA-RY ORAL CANCER**

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**Objective:** The aim of the study was to determine the p53, Bcl-2 and Bax expressions in oral squamous cell carcinoma (OSCC) and to assess relationshipships of these proteins with selected clinicopathological features and survival in OSCC. **Methods:** The records of all the patients that underwent surgery in the oral cancer unit of the Hospital do Câncer were examined to identify OSCC treated at a single institution during the year of 1999 were identified. Patients with positive surgical margins who were not submitted to neck dissection and had less than 12 months follow-up were excluded. Tissue specimens from 53 primary OSCC patients were evaluated. The expression of p53 (DO-7), Bcl-2 and Bax was evaluated using immunohistochemical method in paraffin-embedded specimens. Quantitative computer-assisted analysis of immunohistochemistry was performed to digital images to evaluate the expression of the antibodies. The evaluation of immunostaining was analyzed in 5 different tumor fields. The significance of the associations was determined using the chi-square test. Descriptive statistics were calculated and survival was analyzed using Kaplan-Meier method. Results: Disease-specific 5-year survival (DSS) was 61% (56% overall, and 51% disease-free). 34 (64,2%) cases showed p53 immunostaining above the mean value. For bcl-2 and bax 17 (32,1%) and 23 (43,4%) cases, respectively, were above the cut-off value [mean] obtained for each antibody. Differences between p53 groups for both DSS (p=0,81 : log rank test) and disease-free survival (p=0,51 : log rank test) were not statistically significant. A higher Bcl-2 (p=0,04 : log rank test) and Bax (p=0,01 : log rank test) immunostaining was related to DSS. Kaplan-Meier analysis also defined initial pathologic stage and negative nodes status as being associated with both better overall and DSS. Tongue tumors, and poorly differentiated tumors were associated with worst disease-free survival. p53 expression did not correlate with Bax or Bcl-2 expression. **Conclusion:** These data show that apoptosis-associated proteins are altered in variable patterns in oral carcino- noma. Pathologic stage should be more widely applied in OSCC. Bax and Bcl-2 expression were markers for good prognosis.

**P279: ANTI-DRUG RESISTANT EFFECT OF FUSARIC ACID ON DRUG RESISTANT HEP-DOC CELL LINE**

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**Objective:** Drug resistance is a major problem in cancer chemotherapy. P-glycoprotein (Pgp) was found to be the most well-known important cause of drug resistance in cancer cells. Over-expression of Pgp, encoded by the MDR1 gene, confers resistance to variety of anti-tumor drugs such as Docetaxel, one of the most effective chemotherapeutic treatments in head and neck cancer and breast cancer. The aim of this experiment is to investigate whether fusaric acid (FA), a derivative of the mycotoxin picolinic acid and a zinc chelater, can kill cancer and down-regulate Pgp expression. **Methods:** We selected a resistant laryngeal squamous carcinoma cell line (HNSCC) line, Hep-Doc as our treatment target, which has an extra-high level of Pgp expression. Multiple time points and drug concentrations were studied by flow cytometry and western analysis. **Results:** We found that FA inhibited Hep-Doc cell division at 0.1 mM, 0.3 mM, and 0.5 mM concentrations compared to controls at 24, 48, 72 and 96 hrs (p<0.01). Percent apoptosis detected during flow cytometry was significantly increased over controls at all treatments and time points (p<0.001). The expression of P-gp and NF-kB (p50 and p65 respectively) showed dose-response decreases. Consideration of these experiment results, we hypothesize that FA down-regulates Pgp expression, perhaps by NF-kB, which may increase the sensitivity of Hep-Doc cells to FA. **Conclusion:** Fusaric acid appears to be a promising compound for chemoresistant or previously chemotherapy exposed HNSCC. These findings, when taken with our other reports on FA, start to characterize a possible mechanism of action for FA, which has yet to be reported.

**P280: FREQUENT PROMOTER HYPERMETHYLATION OF RETINOIC ACID RECEPTOR RESPONDER-1 GENE IN HEAD AND NECK SQUAMOUS CELL CARCINOMA**

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**Objective:** Retinoic acid, a cellular differentiating agent, was previously used in several clinical trials for the treatment of head and neck squamous cell carcinoma with disappointing results. It has been shown that some retinoid receptor genes, such as retinoic acid receptor 382 and RARRES-1 are silenced by promoter hypermethylation and this may partly contribute to the failed therapeutic effect of retinoid in the treatment of HNSCC. In this study, we analyze 136 HNSCC to determine the frequency of RAR-1 promoter methylation and its potential role in the biologic behavior of this tumor. A total of 136 cases of HNSCC were included in this study. Complete clinical follow-up is available for all 136 HNSCC patients. DNA samples from these tumors were extracted, modified with sodium bisulfite, followed by methylation-specific PCR (MSP) using gene-specific and methylation-specific primer sets for RARRES-1 gene. Results: Aberrant promoter methylation of RARRES-1 gene was detected in 59 of 136 (43%) cases of HNSCC. The findings were then correlated with various pathologic and clinical parameters. The presence of RARRES-1 promoter methylation in HNSCC is not correlated with tumor size, nodal status, clinical stage and 5-year survival. The pattern of RARRES-1 promoter methylation was also compared with patterns of promoter methylation at hMLH1, hMGMT and p16 genes that were previously characterized in these tumors. There is a statistically significant correlation between RARRES-1 and p16 gene in term of pattern of promoter hypermethylation (p<0.001). **Conclusions:** Aberrant promoter methylation of RARRES-1 gene occurs frequently in invasive head and neck cancer (43%). p16 gene is the earliest altered gene established thus far in head and neck squamous carcinogenesis, and there is a parallel promoter methylation pattern between p16 and RARRES-1 gene, which suggest that the RARRES-1 promoter methylation represents another early marker for head and neck squamous carcinogenesis.

**P281: CLAUDINS PLAY AN IMPORTANT ROLE IN LYMPH NODE METASTASES OF HNSCC**

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**Objective:** Claudin (CLDNs) are the major transmembrane proteins of tight junctions. Tight junction proteins are frequently altered in several human cancers. The main goal of this study is to determine the role of claudins in lymph node metastasis in patients with head and neck squamous cell carcinoma (HNSCC) by profiling these endothelial tight junction adhesion molecules in tumor and lymph node tissue. **Study Design and Setting:** A microarray was done on a T4N0M0 and a T2N3M0 patient. The results were then tested in an ethnographic range of patients at various stages of HNSCC development by Immunohistochemistry (IHC), Western Blot and RTPCR. Primary cells from above patient tumor samples were also tested for the effect of anti-claudin 4 quantum dot on the cell growth. **Results:** Microarray showed a higher expression of claudins (CLDNs) 1 and 4 in tumor samples of the T2N3M0 patient compared to the T4N0M0 patient. CLDN7 showed low levels of expression in tumors in both patients. The adjacent normal tissue in both stages showed low expression of CLDNs 1, 4, and 7. Furthermore, a total of six head and neck squamous cell carcinoma samples from each of the above two stages were analyzed by IHC and RTPCR and showed several folds higher expression of CLDNs 1 and 4 in tumors in the T2N3M0 patients compared to the T4N0M0 patients. Our findings suggest that CLDN1 and CLDN4 overexpression can be used as a prognostic indicator in HNSCC and that these proteins also play an impor-
OBJECTIVES: To measure the frequency of CD4+/CD25+ T-regulator cells between groups. There was a significant reduction in CD4+/CD25+ cells in a subset of patient 6-month post-treatment. Results: The expression of FoxP3 was measured in a sub-group of patients and the tumor infiltrating lymphocytes (TIL) were screened 6-month post-treatment. The expression of CD4+/CD25+ cells. Both groups were followed prospectively for a minimum of 5-years and clinical outcomes were measured.

RESULTS: Twenty-six patients were studied, 7 NR and 19 R. No significant differences were measured in the population of CD4+/CD25+ T-regulator cells between groups. There was a significant reduction in CD4+/CD25+ cells in a subset of patient 6-month post-cancer treatment. The expression of FoxP3 in patients TIL as measured by immunohistochemistry was not significantly different between groups. R demonstrated a significantly better disease-free survival at 5-years compared to NR. CD3 response was a stronger predictor of clinical outcome compared to age, TNM stage or any other measured variable. Conclusion: T cell CD3 receptors responses were significant predictors of disease-free survival based on 5-year clinical outcomes. CD4+/CD25+ T-regulator cells did not appear to significantly differ between CD3 responder and non-responder groups at the time of initial treatment. There was an overall reduction of CD4+/CD25+ cells 6 months after treatment.

P283: IDENTIFICATION OF RESISTANCE/RESPONSE GENES IN TONGUE CARCINOMA A.Suresh1, V.Kakkar1, E.M.Elangovan1, K.Thangaraj2, F.A.Chen3, M.Kujakose3, 1Amrita Institute of Medical Sciences, Cochin, Kerala India; 2University of California Irvine, Orange, CA; 3Wayne State University, Detroit, MI

OBJECTIVE: To develop gene expression profiling of tongue cancer associated with treatment response and resistance. Background: Tumor stage, which attempts to stratify tumors to predict treatment outcome, may have significant intra-stage variation. Stratification of tumors based on gene expression profiling may assist in improving prediction of treatment outcome. Materials and Methods: Tumor tissues were collected from 12 patients (6 each of recurrent and non-recurrent tumors) and eight paired normal samples (4 each from each group). The patients were staged according to AJCC staging criteria and have undergone curative intent treatment. HG U133 Plus 2 Array (Affymetrix) were utilized to hybridize the mRNA extracted from these tissues. The raw data was normalized and analysis were carried out using GCOS and MAS 5 Suite (Affymetrix) software. Further analysis was performed using statistical programs (PLIER, RMA and GCRMA) available in the AVADIS software (Stratagene). For analytical purposes, the samples were grouped into Recurrent and Non-recurrent groups and expression profiles were compared within and between the groups. In each case all the three statistical programs were employed and a list of differentials were arrived at after a combinatorial analysis. Results: Analysis within non-recurrent and the recurrent groups revealed 703 and 154 differentially expressed genes respectively (p<0.05; fold change>3). Increased stringency identified 86 genes in non-recurrent tumors (p<0.001) and 59 in recurrent tumors (p<0.01). 85% of the total differentially expressed genes were over expressed in non-recurrent tumors and 66% in recurrent tumors. Multivariate analysis using ANOVA across the different groups showed total of 128 probe sets as differentially expressed in recurrent tumors (p<0.05), of which 44 genes had p value less than 0.01. The recurrent expression pattern was distinct due to the up regulation of genes/families such as G-Protein receptors, ABC transporters, Ankyrins, cytokeletal proteins, trans-membrane proteins, Amino-transferases, Matrix metalloproteinases and G-protein receptors. Down regulation of cell adhesion molecules, alpha crystallins and signal recognition particles was also observed as specific to recurrent tumors. A complete absence of immune response signature was also notable. Analysis between the paired normal samples of the two groups showed a distinct profile (112 differentials; p<0.05) in the recurrent patients wherein transcription initiation factors, cytoskeletal and G protein receptors were up regulated while genes such as tumor necrosis factor and HRAS-like suppressors were down regulated. The pattern of expression of a small subset of genes (expression of G proteins, alpha crystallins) in the adjacent normal and tumor samples from patients with recurrence was similar indicating that these changes are detected early and may be significant markers of detection. Further categorization of the differentially expressed genes in terms of pathways and functions is currently in progress to identify possible biomarker candidates, which would specify recurrence in tongue cancer patients. Conclusion: Gene expression profiling can identify unique signature molecules associated with treatment response and resistance in oral tongue cancer, which may assist in developing molecular taxonomy of the cancer.

P284: PREDICTING CHEMOTHERAPY OUTCOMES: FULL REPRESENTATION BY SMALL BIOSPATES OF THE ENTIRE TUMOR, RESPONSE TO CISPLATIN AND DOXORUBICIN AND PROGNOSTIC SIGNIFICANCE A.Dietz1, I.Hornz, T.Kscheppe2, W.Ritten3, F.Waller4, G.Wichmann1, C.Granzow1, H.Wong3, C.E.McLaren3, K.Li3, W.Wei4, G.H.Yoo4, R.J.Meleca4, 1Kaiser Permanente , Irvine, CA; 2Kaiser Permanente, Anahiem, CA;3University of California Irvine, Orange, CA; 4Wayne State University, Detroit, MI

OBJECTIVE: Recently, induction chemotherapy concepts have been propagated again. However, while becoming increasingly important for head and neck oncology concepts, chemotherapy is not always effective. The decision on chemotherapy of individual patients is still burdened with the danger of ending up with poor response, high rates of late toxicity, and apprehension of salvage disasters. Unfortunately, reliable predictive response assays with special regard to primary chemotherapy (including organ preservation protocols for resectable disease) are missing in head neck oncology. Indeed, there exists a well reproducible protocol for the predictive ex vivo testing of the tumor response to cytostatic drugs, but it is still doubtful whether analysing a single biopsy suffices to identify sensitivity or resistance to cytostatic drugs of an entire tumor. Methods: From 22 untreated tumors of the head and neck region (squamous cell carcinoma HNSCC), three biopsates each were taken from separate locations and digested, after mechanical disintegration, for 16 hours in cell culture medium containing collagenase. Each digest was resuspended in fresh medium, and incubated in ECM-coated microtitre plates for three days, either with appropriate concentrations of cisplatin and docetaxel or without drugs. Resulting cell colonies were fixed and Giemsa stained. The number of epithelial colonies per well was determined microscopically. IC50 values as well as cut off-concentrations, in whose presence epithelial colonies no longer arose, were determined and analyzed statistically. Results: Throughout, the range of drug concentrations required for minimum and maximum colony suppression in the individual tumour fragments spanned roughly one order of magnitude. Only minor differences were found to exist between the IC50 values and the cut off-concentrations of the different fragments of the same tumour, which is in agreement with the experimental scattering, and had no statistical or biological significance. These findings suggest that the cell pharmacological microheterogeneity detectable in a fragment of approximately 100 mg wet weight is representative of the entire tumor. Hence, ex vivo-testing of one such sample of vital HNSCC should correctly predict the chemoresponse of the latter. Performing the colon assay ex vivo opens many future options for combining on chemotherapy, and lead to more comprehensiveness and costs efficiency in head and neck cancer therapy.

P285: THE USE OF MULTIPLE PROTEIN MARKERS IN HEAD AND NECK CANCER P.Silva1, N.Slevin2, P.Sloan3, P.Price4, C.West4, J.Homer5, 1Department of Head & Neck Surgery, Manchester, United Kingdom; 2Department of Clinical Oncology, Christie Hospital, Manchester, United Kingdom; 3Dental Hospital, Manchester, United Kingdom; 4Academic Radiation Oncology, Christie Hospital, Manchester, United Kingdom; 5Academic and Clinical Oncology, Christie Hospital, Manchester, United Kingdom
Head and neck squamous cell carcinoma (HNSCC) represents a heterogeneous group of patients, in terms of subtypes, treatment and biology. Management decisions are largely based on clinical parameters with little appreciation of underlying tumour biology. It is increasingly recognised that the response of a tumour to treatment is unlikely to be dependent on a single biological parameter. The aim of the work was to investigate a panel of nine markers and define a profile associated with the radioreponse of oropharyngeal carcinomas. Proteins were selected to cover a range of biologically relevant pathways: hypoxia (HIF-1α, Ca9, Glut1), proliferation and cell growth (Ki67, EGFR) and radiosensitivity/radiation resistance/chemoresistance (pAkt, MVP, Bcl-2) and metastasis and invasion (Fhit). The prognostic significance of the markers were studied individually and then combined in a multivariate analysis. Method: 133 consecutive patients with histologically confirmed squamous cell carcinoma of the oropharynx were identified. All patients received primary radiotherapy between 1996-2001. Tumour expression of the above nine protein markers was examined in 60 patients. Actuarial estimations of locoregional control and cancer-specific survival were obtained using the Kaplan-Meier method. Results: Markers associated with poor outcome were high Ca9 (HR=5.21, 95% CI 2.48-10.90), HIF-1α (HR=4.96, 95% CI 2.40-10.30) and MVP (HR=4.14, 95% CI 2.16-7.94) expression. Following a multivariate analysis, the results of the nine markers were used to derive a profile of two markers (Ca9 and MVP, HR=15.18, 95% CI 4.72-48.77) the co-expression of which conferred a significantly poor locoregional outcome. Conclusion: Biomarker profiles can be established that highlight large differences in loco-regional control probability in patients with HNSCC. The prognostic effect of these markers in combination is greater than their effect individually. Identifying tumours that express both Ca9 and MVP may allow patient selection for more aggressive treatment.

P286: PROGNOSTIC MOLECULAR MARKERS IN HEAD AND NECK SQUAMOUS CELL CARCINOMA I.D. Guayardena 1, M. Arendse 1, M. Jameson 1, R. Lavregan 1, R.T. Gregory 1, Waikato Hospital, Hamilton, New Zealand; 2University of Auckland, Auckland, New Zealand

Objective: The survival rate for head and neck squamous cell carcinoma is among the lowest of the major cancers and has not improved significantly in the past two decades. Pathological features that can be assessed with an aggressive clinical course and poor prognosis include poorly differentiated tumours, tumour bulk, nodal involvement and perineural, stromal and vascular invasion. Despite such assessment, many tumours with similar histological features have widely differing clinical outcomes. Therefore improving prediction of prognosis would be an extremely valuable tool in determining appropriate clinical management strategies for each patient. The aim of this pilot study is to establish the prognostic significance of six molecular markers [Matrix metalloproteinase 2 and 9 (MMP2, MMP9), Tissue Inhibitors of MMP-1 (TIMP1), Sialyl Lewis antigens a and x (sLea and sLex) and Alpha B Crystalline] in 50 New Zealand patients. Methods: Six sections were cut from each patient’s paraffin-embedded tumour block, immunostained and scored by a pathologist blinded to clinical features. The Kaplan-Meier survival and Cox regression model were used to evaluate the influence of each biomarker on overall survival. Results: Cox Regression model showed both TIMP1 (p=0.002, HR=0.09) and Alpha B Crystalline (p=0.041, HR=0.26) to be statistically significant for overall survival. Conclusion: TIMP1 and Alpha B Crystalline are significant prognostic markers for survival. We aim to extend this pilot study to further evaluate the significance of the above six molecular markers. References: 1. C. Ondruschka, P. Buhtz, C. Motsch et al Prognostic value of MMP-2, -9 and TIMP-1, -2 in immunoreactive protein at the invasive front in advanced head and neck squamous cell carcinomas Pathol. Res. Pract. 2002, 198:509-515. 3. RW Farmer, W. Richtsmeier, R Scher Identification of Sialyl Lewis-x in squamous cell carcinoma of the head and Neck Head and Neck 1998;20(3):229-236. 5. G. Hummelt et al. HNSCC, a new independent marker for poor prognosis in head and neck cancer Laryngoscope 2005: 115(7): 1239-42.

P287: CLINICAL SIGNIFICANCE OF TESTIN EXPRESSION IN HEAD AND NECK SQUAMOUS CELL CARCINOMAS

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Objective: TESTIN gene was shown to be a tumor suppressor in various cancers by human tumor tissue and in vitro functional analysis. Our previous study demonstrated frequent deletion of 7q31 region and localization of two putative tumor suppressor genes (TSG) concerning 7q31 in head and neck squamous cell carcinoma (HNSCC). We this time focused one of these regions and showed TESTIN as a candidate TSG in HNSCC. In the current research, we examined mutation and mRNA expression status of TESTIN. Methods: DNA and RNA were isolated from 38 paired normal and tumor samples with HNSCC. TESTIN expression was determined by reverse transcription polymerase chain reaction (RT-PCR) following reverse transcription of mRNA. Mutation analysis of TESTIN was performed for exon 3 to 5 of TESTIN by PCR amplification and direct sequencing. Results: Mutation analysis showed a nucleotide and amino acid change (Alanine to Valine) in exon 4 in 16% of the tumor samples, which was previously reported as a mutation in a breast cancer cell line. However, we detected same substitution in the corresponding normal samples of the tumor cases with this change. Thus this alteration was thought to be a polymorphism with unknown significance. Quantitative mRNA expression analysis of TESTIN revealed a decreased expression in about half of the tumors as compared to their matched normal controls. Interestingly, comparison of clinicopathological variables with mRNA expression status of TESTIN displayed a significant difference in terms of previous cancer history. The patient group with 5% of TESTIN expression showed a high previous cancer history. Moreover, a higher smoking ratio and higher family cancer history was also associated with down-regulation of TESTIN though the difference was not statistically significant. Kaplan-Meier survival analysis demonstrated a worse survival in the patients with low TESTIN expression as compared with the patients with normal-high TESTIN expression. Conclusions: All the above results suggest that inactivation of TESTIN is involved in head and neck carcinogenesis and its down-regulation is likely to be used as a molecular prognostic factor either alone or combination with other genes in future studies.

BASIC SCIENCE: EXPERIMENTAL THERAPEUTICS

P288: TUMOR VOLUME MEASUREMENT IN PATIENTS WITH ADVANCED HNSCC THAT RECEIVED DNA HSP65 OF M. LEPRAE VACCINE IN A PHASE I/II TRIAL R.B. Smith 1, R.E.L. Games 2, E.M.M. Gebbi 1, F.D. Lima 3, M.C. Chammas 4, K.A. Abdallah 5, C.L. Silva 2, P.Michajluk 6, L.B. Beder 1, E.Gunduz 2, M.Hotomi 1, K.Fukushima 3, H.Tanimoto 3, T.Nakagawa 4, K.Nibu 5, 1Kobe University Hospital, Kobe, Japan; 2University of Sao Paulo Medical School, Sao Paulo, Brazil; 3University of Sao Paulo Medical School, Ribeirao Preto, Brazil

Objective: Tumor volume is known to be a significant prognostic factor in the treatment of malignant tumors. There is a paucity of reports on tumor volume measuring methods for head and neck squamous cell carcinomas. Clinical trials tumor response is evaluated with RECIST (unidimensional) and WHO (bidi-dimensional) response criteria. We here report the methodology used to measure tumor volume (tridimensional) in a prospective study, in order to evaluate the response to treatment pre and post intratumor injections of M. leprae DNAHSP65 in patients with squamous cell carcinoma refractory to standard treatment. Patients and Methods: 21 patients treated in 3 groups of doses 150, 600, and 400ug of the vaccine [DNA HSP65 - M. leprae], intratumor applications guided by Doppler ultrasound repeated 3 times every 21 days. Multislice computed tomography scans (of 10 and 16 channels) were performed with 0.7mm, reconstructed to 3.0mm, before and after the treatment to evaluate the tumor response comparing tumor volume (manual tracing method). We also did biopsy before and after the treatment. Results: Of 21 patients, seven died before the end of the protocol. The tumor volumes were well correlated with the clinical T-category for the end of the treatment. Dimensions were well correlated with CT volume measurements. Conclusions: The CT image-based tumor volume measurement proved to be clinically feasible and reliable. However, clinical anatomical particularities showed a good correlation to tumor response.

P289: COX2 PROMOTER-BASED CONDITIONAL REPlication-SELECTIVE ADENOVIRAL VECTOR FOR HYPOPHARYNGEAL CANCER T.Nakagawa 1, K.Nibu 1, 1Kobe University Hospital, Kobe, Japan

Objective: To investigate the possibility of clinical application of COX2 promoter-based conditional replication-selective adenoviral vector (Ad-
Results: We reviewed 93 biopsy specimens taken from previously untreated patients with hypopharyngeal squamous cell carcinomas, who were treated at Kobe University Hospital between 1995 and 2004. None of the tested treatments was able to improve survival. COX2 was highly expressed in 37.9% (35/93) of the tested cases, and statistical analysis showed a significant difference between the intensity of COX2 expression and tumor differentiation (P=0.001, r=0.433). The growth of tumors treated with Ad-COX2-E1a was significantly inhibited compared with that of tumors treated with Ad-CMV-3B2gal. It is noteworthy that the difference gradually increased with time, from day 4 to 14. Conclusions: COX2 was highly expressed in hypopharyngeal cancer cells. We demonstrated the potential of oncolytic therapy using the COX2 promoter based conditional replication-selective adenoviral vector for COX2-expressing hypopharyngeal cancers.

P290: INVESTIGATING POTENTIAL MEDIATORS OF GAP JUNCTION RELATED BYSTANDER EFFECTS IN HEAD AND NECK CANCER IN VITRO

Objective: Our laboratory is involved in investigating the role that gap junction intercellular channels (composed of protein subunits called connexins) play in communicating death (apoptotic) signals from a treated cancer cell to adjacent, untreated, bystander cells (bystander effect). Using single-cell microinjection techniques, we have demonstrated that gap junctions mitigate a bystander effect in SCCHN (and other tissues) when individually targeted cells are induced to undergo apoptosis via activation of the caspase cascade (through single-cell microinjection of cytochrome c). Not surprisingly, the gap junction phenotype is frequently (but not uniformly) absent or missing in mammalian cancers, including SCCHN. Through related research, we have demonstrated that it is connexin 43 expression that correlates with retained gap junctional intercellular communication (GJIC) activity in SCCHN in vitro. This data has now set the stage for us to investigate the actual molecular signal(s) that traverse intact gap junction channels (GJIC) to elicit a bystander effect in SCCHN. Recent studies on cancerous and non-cancerous tissues in this field suggest that calcium may be the apoptotic signal of interest.

Methods: Apoptosis and subsequent bystander effects were induced in a SCCHN cell line with retained GJIC activity via the technique of scrape-loading of cytochrome c under various experimental and control conditions as enumerated below. Cell death in bystander cells was determined cytologically through differential interference contrast microscopy, as well molecularly through detection of activated caspase 3, which is the end effector of the apoptotic cascade.

Results: The scapping technique (technique) of scrape-loading of cytochrome c under various experimental and control conditions as enumerated below. Cell death in bystander cells was determined through caspase 3 activation.

Conclusions: Calcium does not seem to be the molecular signal responsible for the bystander effect seen in our in vitro SCCHN experimental system. The investigation of the role of other potential molecular mediators, such as reactive oxygen species, warrants consideration and is currently underway. The implications of this research are discussed.

P291: PRE-Clinical SURVIVAL ASSay OF INTRATUMORAL INJECTION OF INTERLEUKIN-2, PURE AND MICROENCAPSULATED AND DnaHNsp65 VACCINE

Objective: To test the efficacy of interleukin-2 (IL-2), IL-2 microencapsulated in PLGA (mccIL-2) and DnAHsp65 as single agents and in combination in a melanoma murine model.

Methods: Commercially available IL-2, Proleukin, was purchased. PLGA (50:50) was produced at PURAC Biochem. DnAHsp65 was produced at the genetics laboratory at the University of São Paulo under the responsibility of Prof. Celio Silva. Microcapsules containing IL-2 were produced at the Instituto Paulista de Tecnologia under responsibility of Dra. Maria Inês Re. After the microencapsulation the efficacy of IL-2 was confirmed.

Groups 5 and 6 had a statistically significant greater survival when compared to control (group 1). Treatment with DnAHsp65 showed a tendency to improved survival but it didn’t reach significance.

Conclusions: None of the tested treatments was able to improve survival as a single agent. Combinations of DnAHsp65 and IL-2, either pure or microencapsulated, were capable of improving survival. The similarity of effects observed on groups 5 and 6 suggest that IL-2 was adequately released and kept its biological efficacy after encapsulation. Grant 08821-6 FAPESP.

P292: INTRA-TUMORAL INJECTION OF DENDRITIC CELLS AS ADJUVANT THERAPY FOR SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK

Objective: Approximately 40,000 individuals are diagnosed with squamous cell carcinoma of the head and neck (SCCHN) each year. For advanced SCCHN, standard therapies, which include surgery, chemotherapy or radiation have had limited success in improving survival or quality of life. Thus new treatment options are needed. Immunotherapy is one approach that has shown promise as an adjunctive therapy for some malignancies. Therefore, we describe our ongoing phase I clinical trial to test the safety and feasibility of intratumoral injection of immature dendritic cells (DCs) in a series of melanoma patients and to evaluate the means of generating immune responses to the xenogeneic tumors. DCs and cells of this lineage are the sentinel antigen presenting cells in the body having the capacity to initiate robust immune responses to acquired antigens. Our approach is based on the hypothesis that the injected immature DCs will take up and process tumor antigens and generate an immune response to the tumor. To create an environment for antigen acquisition, prior to DC injection the tumor site will receive low-dose irradiation to produce heat shock proteins. Irradiation will also induce production and release of cytokines and chemokines that will cause DC maturation and migration to the local draining lymph nodes (LN) where they will present antigens to cells that will have anti-tumor activity. Prior to injection, patients will receive systemic cyclophosphamide to diminish activity by a subset of immunosuppressive regulatory T cells, which increase in number in SCCHN patients. To test our
hypothesis we have developed a system to generate large quantities of immature DCs from monocytes obtained from peripheral blood by elutriation. To achieve the overall goal of this trial to gain insight into the immunological processes that would help to improve this immunotherapeutic approach, we propose the following specific Aim 1). Determine if functional DCs can be generated from monocytes obtained from patients. We will characterize these cells by flow cytometry and measure their capacity to stimulate T cell responses by cytokine release. 2) Evaluate the safety and effects of combined therapy on functional responses to tumor as well as KLH, co-administered as a tracer antigen 3). Identify cell populations that infiltrate tumor at injected and non-injected sites as well as draining and distal LN. Addressing each of these aims will guide us in constructing future clinical trials to evaluate immunotherapy as a treatment modality in this cancer.

P293: MAL GENE AS A CANDIDATE METASTASIS SUPPRESSOR FOR HEAD AND NECK SQUAMOUS CELL CARCINOMAS
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Objective: MAL [T lymphocyte Maturation-Associated Protein] gene has been shown to be expressed at lower levels in primary tumors of head and neck carcinomas with neck metastasis compared to primary tumors without metastasis by previous microarray studies. To identify the role of MAL gene as a metastasis suppressor, we assessed expression status of the gene both in metastatic tumors itself and cell-lines derived from metastatic tumor tissues of HNSCC (head and neck squamous cell carcinoma). Furthermore, we evaluate genetic mechanisms take part in down-regulation of MAL expression.

Methods: Paired primary and metastatic tumor samples of 21 patients with HNSCC and 29 UT-SCC cell-lines (including 8 pairs of primary-metastasis cell lines derived from same patient) were used for mRNA expression analysis. MAL expression was determined by reverse transcription polymerase chain reaction (RT-PCR) following mRNA extraction and reverse transcription of fresh frozen tissues or cell-lines. LOH (loss of heterozygosity) analysis with flanking 2 microsatellite markers was performed by PCR and genescan analysis. To analyze the methylation status of MAL promoter, UT-SCC cell lines were treated with the demethylation agent 5-aza-2‘-deoxycytidine (5-Aza-CdR), and MAL mRNA expression was detected by RT-PCR. Results: Among the 21 HNSCC tumors, 9 (43%) cases showed low expression of MAL in metastasis compared with primary tumors. LOH analysis revealed allelic loss in 6 (29%) cases. Totally, out of 29 UT-SCC cell lines, 18 (62%) showed low expression including 8 (27.6%) cell lines with no expression of MAL. Furthermore, concerning 8 primary-metastasis cell lines pairs, 6 metastatic cell-lines showed low or no expression of MAL. Furthermore, we evaluated whether the mal gene is silenced by promoter methylation. Demethylation caused by 5-Aza-CdR induced the MAL mRNA expression levels in 7 out of 11 cell lines with low expression (63.6%). Conclusions: We found significant down-regulation of MAL gene both in HNSCC cell lines with metastasis origin and metastatic tumor tissues. Furthermore, LOH and hypermethylation of promoter region is shown to take role in decrease of the gene expression in these samples. These findings suggest that loss of MAL gene function can act a role during metastasis development in HNSCC.

CHEMOTHERAPY

P294: STUDIES WITH NOVEL SULFUR-OXIDE ALKYLATING AGENTS IN FA DU CELLS
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Background: Bioreductive agents are anticancer drugs that require activation by reductive enzymes. These agents need a bioreductive element that is reduced and a cytotoxic element that is generated by this reduction to produce their cytotoxic effects. Sulfide mustard (SM) are excellent alkylating agents that can kill cancer cells, but these agents also kill normal cells. Oxidation of the sulfide to a sulfur-oxydine produces a bioreductive element that should inhibit alkylatation by the mustard group until the sulfur-oxydine is reduced. These agents could then be used to target tumors with elevated levels of enzymes that can reduce the sulfur-oxydine groups. Objective: To investigate the cytotoxicity of sulfur-oxydine mustard (SOM) in TNM class III oropharyngeal cancer patients undergoing hemodialysis for chronic renal failure. There are no reports in the literature of intraarterial chemoradiotherapy for head and neck patient maintained on hemodialysis. The feasibility of this approach, toxicity and response were assessed. Methods: Two cases of stage III oropharyngeal squamous cell carcinoma patients receiving ongoing hemodialysis due to chronic renal failure were selected for this study. The dose of docetaxel was 10 mg/m2, while cisplatin was given 15 mg/m2 via superficial temporal artery cannulation. Hemodialysis was performed 1 hour after administration of cisplatin on day 1 and chemotherapy was repeated every two weeks for a total of 6 cycles. The total dose of docetaxel was 60 mg/m2, while that of cisplatin was 90 mg/m2. The first patient received additional cisplatin at 30 mg/m2 as an intravenous bolus on day 28. Radiation with a total of 60 Gy in 30 fractions were given over 6 weeks. To investigate the pharmacokinetics and determine the optimal dose of docetaxel and cisplatin during ongoing hemodialysis, the concentrations of docetaxel and total-platinum in serum from the patient in FaDu, human head and neck cancer cells in vitro was measured. Reduction of the SOM to the corresponding SM by thioredoxin reductase (TR) was tested. Results: SM compounds were good alkylators while SOM compounds did not produce any alkylation (P<0.001). SM compounds and some SOM compounds showed good cytotoxic activity in FaDu cancer cells in vitro. TR did not reduce the SOM to SM. Conclusions: As predicted sulfur-oxydine groups inhibit alkylatation of mustard groups. Some SOM produced cytotoxicity in head and neck cancer cells, but these agents may not act as bioreductive agents.

P295: GROWTH INHIBITION OF HEAD AND NECK SQUAMOUS CELL CARCINOMA USING A COMBINATION OF LIPOSOMAL CURCUMIN AND CISPLATIN
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Objective: Previous experiments have shown that treatment with curcumin or cisplatin resulted in suppression of head and neck squamous cell carcinoma [HNSCC] growth both in vitro and in vivo in nude mice xenografts. The purpose of this study is to determine whether a combination treatment with liposomal curcumin and cisplatin would synergistically act to further trigger cell death. Methods: HNSCC cells were treated with both curcumin and cisplatin either individually and together at sub-curative concentrations to assay for in vitro growth using 3 (4,5 -dimethylthiozol - 2 - yl) - 2,5 diphenyl tetrazolium bromide (MTT), western blots, and immunofluorescence techniques. In vivo studies to assess synergy consisted of three-times-a-week intravenous tail intravenous injections of empty liposome or liposomal curcumin for four weeks into nude mice which were growing xenograft subcutaneous HNSCC tumors. At the end of the fourth week, a single dose of intraperitoneal cisplatin was given. In the fifth week, mice were sacrificed and the tumor size, liver, spleen, and blood were examined. Results: Addition of curcumin or cisplatin alone or in combination resulted in cell death in vitro. Introduction of suboptimal levels of both agents in vitro demonstrated a synergistic suppression over the first 72 hours of HNSCC cell line growth when compared to individual agents. In vivo growth studies demonstrated a greater extent of reduction in tumor growth in the combination treatment when compared to either empty liposome or liposomal cisplatin treated mice. Examination of mice spleens demonstrated larger spleen cell counts in the curcumin and cisplatin treated mice compared to those treated with empty liposome and cisplatin. This may indicate a greater immune response with the combination treatment. Conclusions: Cisplatin is currently being administered in the clinical setting as a chemotherapeutic agent, but must be closely monitored due to its potential toxicity. Our studies demonstrate that combination treatment of HNSCC in vitro and in vivo with curcumin and cisplatin demonstrates enhanced growth suppression than either agent alone. We hypothesize that curcumin and cisplatin control two different growth signaling pathways and therefore have a synergistic effect on tumor growth inhibition. Thus, there is potential for a decrease in the subtherapeutic doses of cisplatin in combination with curcumin in the clinical setting, which will still allow effective suppression of tumor growth while minimizing cisplatin’s toxic side effects.

P296: INTRAARTERIAL CHEMOTHERAPY WITH DOCETAXEL AND CISPLATIN FOR OROPHARYNGEAL CANCER PATIENT UNDERGOING HEMODIALYSIS
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Objective: We administered docetaxel combined with Cisplatin intraarterially with radiation for oropharyngeal cancer patients receiving hemodialysis for chronic renal failure. There are no reports in the literature of intraarterial chemoradiotherapy for head and neck patient maintained on hemodialysis. The feasibility of this approach, toxicity and response were assessed. Methods: Two cases of stage III oropharyngeal squamous cell carcinoma patients receiving ongoing hemodialysis due to chronic renal failure were selected for this study. The dose of docetaxel was 10 mg/m2, while cisplatin was given 15 mg/m2 via superficial temporal artery cannulation. Hemodialysis was performed 1 hour after administration of cisplatin on day 1 and chemotherapy was repeated every two weeks for a total of 6 cycles. The total dose of docetaxel was 60 mg/m2, while that of cisplatin was 90 mg/m2. The first patient received additional cisplatin at 30 mg/m2 as an intravenous bolus on day 28. Radiation with a total of 60 Gy in 30 fractions were given over 6 weeks. To investigate the pharmacokinetics and determine the optimal dose of docetaxel and cisplatin during ongoing hemodialysis, the concentrations of docetaxel and total-platinum in serum from the patient.
were measured. Results: Both of the cases gained loco-regional complete response after the treatment. Planned neck dissection was performed for one case. Measurement of drug concentrations showed that free platinum was immediately eluted by dialysis. The plasma concentration-time curve of cisplatin was close to the value in patients with normal renal function. However, no apparent differences of docetaxel concentration could be seen before or after dialysis. No severe toxicity was observed after chemotherapy.

Conclusions: The chemoradiotherapy with the present regimen could be performed safely in patients with chronic renal failure with dialysis. More cases should be monitored to establish the adequate dose for cancer patients undergoing hemodialysis.

P297: SUPERSELECTIVE INTRAARTERIAL CHEMOTHERAPY USING PERCUTANEOUS PUNCTURE OF THE SUPERFICIAL TEMPORAL ARTERY K.Yane1, I.Ota1, T.Yamanaka1, H.Okamoto1, T.Fukuda1, H.Nakagawa1, H.Hosoi1, 1Nara Medical University School of Medicine, Kashihara, Japan

Objective: Superselective intraarterial chemotherapy for advanced head and neck cancers is one novel nonsurgical approach allowing organ preservation. There are two established methods for superselective catheterization, one transfemoral and the other retrograde catheterization through the superficial temporal artery (STA). STA catheterization has some advantages compared to transfemoral catheterization. In case of stable disease or progressive disease a chemoradiation was performed under organ preservation aspect, followed by neck dissection and radiation. In most cases an organ preservation could be achieved. There was a strong correlation between the response rate to the induction therapy and survival of the patients. The median time of recurrence was 14 months, tumor free were 48 pts over all. Conclusion: The efficacy, feasibility and reliability of the induction therapy is being confirmed with these results.

P298: THE EFFICACY AND VALUATION OF INDUCTION CHEMOTHERAPY IN ADVANCED HEAD AND NECK CARCINOMA. OUR RESULTS AFTER 6 YEARS A.Cramer1, C.Milewski1, 1Staadische Kliniken Frankfurt-Hoestheim, Frankfurt, Germany

Introduction: The customary operative therapy of advanced head and neck squamous cell carcinoma (oral cavity 16, maxillary sinus 8) were treated by superselective intraarterial chemotherapy. Complete response was obtained for 18 patients (75%) and partial response for 6 patients (25%). No systemic severe complications were caused by this therapy, but local mucositis was frequent in the infused area. Conclusions: This superselective intraarterial method is associated with a high response rate for primary carcinomas, only relatively mild systemic side effects and acceptable common local toxicity, limited to lesions such as mucositis. The procedure helps improve the quality of life for patients, because of the high rate of organ preservation. Superselective intraarterial chemotherapy through the STA can thus be recommended for local control of advanced head and neck cancer.

P299: CISPLATIN-5FU CHEMOTHERAPY IN ADVANCED HEAD AND NECK CANCERS; AL -SARAF REVISITED S.Agawal1, P.Agawal1, 1National Institute of Medical Sciences, Agra, India

Objective: To evaluate the response of cisplatin-5fu combination in a modified dosage and schedule inadvanced head and neck cancers. Patient & Method: Patients of advanced head and neck cancers receiving 3 or more cycles of cisplatin(80mg/m2) and 5 fu(2 gm/m2) were included from a period of October 1999 till sep.2007 were included. Data of 550 evaluable patients is presented here. therapy was given in 3 divided doses over 3 days as continuous infusion.most common site of primary was tongue (35.5%) followed by tonsill (30%), valleculae (26%), piritiform sinuses (24%), buccal mucosa (20%), soft palate (14%) and epiglottis (8%). 44% patients were stage III and 66% were in stage IV. Results: 3 or more cycles were successfully completed in 550 patients and were evaluable for response. Complete response rate of 12% and partial response rate of 46% resulting in a response rate of 58%. Conclusion: Head & neck cancers are the most common malignancy amongst Indian males. More than 60% are in advanced stage at the time of presentation. Cisplatin-5fu was well tolerated regimen. Excellent response was noted in valleculae, tonsil, and epiglottis primaries. Bone marrow suppression was rare and none of the patient required GCSF support. Chemotherapy followed by radiotherapy led to better patient compliance. Good response to chemotherapy was also a predictor of a favourable response to radiotherapy. Conclusion: Cisplatin 5fu in 3 day schedule is effective cheap and safe palliative therapy and is very practical for third world countries.

P300: A PRELIMINARY RESULT OF CONTROLLED RANDOMIZED PHASE II STUDY OF CONCURRENT CHEMORADIOThERAPY BETWEEN WITH PFML AND TPF M.Tsukuda1, C.Horiuchi2, G.Nishimagura3, H.Takahashi4, Yokohama City University, Yokohama Japan; 2Yokohama City University, Yokohama, Japan

Objective: The prognostic of locoregionally advanced squamous cell carcinoma of the head and neck (SCCHN) is still poor by conventional treatments with definitive surgery and/or radiotherapy. Concurrent chemoradiotherapy (CCR) with a potential regimen has been applied for locally advanced SCCHN since 1999 to improve outcome and function preservation in our institutes. The regimens consisted of CDDP, 5-FU, methotrexate and leucovorin (PFML) and CDDP, 5-FU and docetaxel (TPF). Methods: A controlled randomized phase II study of concurrent definitive radiotherapy between PFML and TPF has been carried out since September, 2005 in two institutes. Methotrexate and leucovorin are modulators on 5-FU activity. Resectable cases with advanced SCCHN excluding nasopharyngeal carcinoma have been enrolled and divided into two groups. Two courses of chemotherapy with definitive radiotherapy were done. Objective endpoints are response rates, i.e., pathologically complete response (pCR) after the treatment, and secondary major objectives are progression free survival, overall survival, toxicity/safety, local control rate, function preservation rate and feasibility. Results: Evaluable patients were 38 cases in the PFML group and 38 in the TPF group. Each treatment completion rate was about 80%. The first course of chemotherapy was performed for all cases. There was no treatment death. The pCR rates after CCR were 74% in the PFML group and 90% in the TPF group, respectively. There were no significant difference for progression free survival and overall survival rates in favor of the TPF group. The most severe adverse events were mucositis in the PFML group and leukocytopenia in the TPF group, respectively. Conclusion: Both potential regimens with definitive radiotherapy were efficacious for locoregionally advanced SCCHN and tolerable. In the future it is necessary to study which is the better treatment modality between CCR and neoadjuvant chemotherapy followed by definitive radiotherapy with a potential regimen for advanced SCCHN.
Background: Many studies have shown gemcitabine and cisplatin such as radiosensitizers. We evaluated the effect of the both in schedule alternating concurrent with radiotherapy in patients with advanced head and neck cancer.

Objective: To evaluate efficacy and security of alternating gemcitabine and cisplatin concurrent with radiotherapy in advanced head and neck cancer.

Patients and Methods: We enrolled 27 patients with advanced squamous cell carcinomas of the head and neck between 35-82 years who had stage III (26%), IVa (22.2%) and IVb (25.9%). Patients were treated with gemcitabine: 100 mg/m² on weeks 1, 3, 5, 7 and cisplatin using 50 mg/m² on weeks 2, 4, and 6. Radiotherapy was administered at doses of 2 Gy/day, until completing 70 Gy. We evaluated toxicity, especially in relation with mucositis, xerostomy, dysphagia and leucopenia. Results: Treatment was well tolerated. At a median follow-up of 17 months, progression-free survival was observed of 70.5% (95%CI: 70.31-70.69) after one year. Overall survival was observed 84.4% (CI95%: 84.26-84.54) after one year. In 74% developed a CR, 18.5% reached a partial response (PR), for a global response of 92.5%. Extensive surgery for primary site was avoided in 19 patients (70.4%). Adverse events were mucositis in grade 3-4 occurred in 44.4%, leucopenia in 33.3%, dysphagia in 22.2% and xerostomy in 11.1%.

Conclusion: Alternating schedule of gemcitabine and cisplatin concomitant with radiotherapy is an active and safe treatment.

P302: CISPLATIN RESISTANCE OF THE HNSCC CELL LINE UT-SCC-26A CAN BE OVERCOME BY STIMULATION OF THE EGF-RECEPTOR. M. Mendonça1, J. Chi1, I. Pascual-Diaz1, W. Meissner2, V. Kropp1, S. Wiegand3, R. Grémenn4, J.A. Werner1, 1University Hospital Giessen and Marburg, Otologyrgy, Head and Neck Surgery, Marburg, Germany; 2Medical University Vienna, Institute of Cancer Research, Vienna, Austria; 3Philips University, Institute of Molecular Biology and Tumor Research, Marburg, Germany; 4Turku University, Otologyrgy, Head and Neck Surgery, Turku, Finland.

Purpose: Recently, the epidermal growth factor receptor (EGFR, ErbB1, HER) is frequently overexpressed in head and neck squamous cell carcinomas (HNSCCs) and correlates with disease progression and reduced survival of the patient. Several therapeutic approaches therefore focus on inhibition of the receptor, involving monoclonal antibodies or kinase inhibitors. Here we investigated the influence of EGF Stimulation on cisplatin sensitivity in 3 previously well characterized HNSCC cell lines.

Material and Methods: Protein expression was evaluated by western blot analysis. The HNSCC cell lines were incubated with 0.1, 1, 10, 100 or 1000 ng/ml EGF for 13h. Cell cycle checkpoint distribution was determined by FACS analysis. Effects of cisplatin on cell viability were evaluated with the MTT assay. Results: Before exposure to EGF, UT-SCC-26A cells exhibited a pro- susceptibility to cisplatin. Cell cycle analysis revealed a very low level of UT-SCC-26A cells in G2/M phase that rose after stimulation with EGF. Also, Cyclin D1 levels increased most prominent in the UT-SCC-26A cell line after EGF stimulation compared to the other 2 cell lines. Conclusions: Taken together our data suggest that EGF Stimulation on cisplatin sensitivity in 3 previously well characterized HNSCC cell lines.

P304: ADVERSE IN VITRO EFFECTS OF CHEMOTHERAPY PRE-TREATMENT BEFORE CHEMORADIATION IN A HEAD AND NECK CANCER CELL LINE. J.L.Gala1, A.F.Dekairelle1, 1UCL, Center for Applied Molecular Medicine and Radiation Biology, Las Vegas, NV; 2University of Nevada School of Medicine, Las Vegas, NV; 3UNLV, Center for Molecular Medicine and Radiation Biology, Las Vegas, NV.

Objective: Combination chemotherapy and radiation is the currently accepted standard of treatment for many advanced head and neck cancers. There has been a recent trend in administering induction chemotherapy to reduce the tumor load prior to chemoradiation. However, the development of chemoresistance by chemotherapy pretreatment may hinder the effectiveness of chemoradiation afterwards. The aims of this study are to assess whether pretreatment of cancer cells in vitro with chemotherapy causes the cells to experience resistance to subsequent combination chemoradiation therapy. Various schedules are also examined to determine optimal time periods between treatments.

Methods: Clonogenic survival of the Broto cell line (human tongue cancer) was determined in control and treatment groups. Cells were treated with 1 x 10-4 M cisplatin, incubated for 0, 24 or 48 hour periods, then treated with the combination of ionizing radiation (ranging from 1 Gy to 10 Gy) and 1 x 10-4 cisplatin. These results are compared to Broto cell line that was administered only combination therapy with no pretreatment. Flow cytometry was performed to determine the incidence of apoptosis. Results: Pre-treating cells with cisplatin and then administering a combination therapy causes an increase in cell survival when compared to non pretreated cells. The 0 hour incubation time group had the highest incidence of apoptosis followed by the 24 and 48 hour groups. Pretreatment with the chemotherapeutic agent before combination therapy leads to an increase in cell survival and cell resistance in this model. The delay period before the subsequent treatments may induce chemoresistance and lessen the radiosensitization effects.

P305: S-1 CHEMOTHERAPY FOR RECURRENT AND/OR METASTATIC HEAD AND NECK CANCER. Y.Yamashita1, A.Shiotani1, S.Shinden2, T.Watabe2, K.Wasano2, Y.Inagaki2, 1National Defense Medical College Hospital, Tokorozawa, Saitama, Japan; 2Saiseikai Utsunomiya Hospital, Utsunomiya, Tochigi, Japan.

Objective: S-1 Chemotherapy is an effective therapeutic agent for recurrent and/or metastatic head and neck cancer. However, its effectiveness is limited due to its low oral bioavailability, high inter-individual variability, and severe side effects. Therefore, we investigated the use of S-1 Chemotherapy for recurrent and/or metastatic head and neck cancer.
Posters

**P307: WEEK ON/WEEK OFF CHEMORADIATION VS. CONVENTIONAL CHEMORADIATION FOR HEAD AND NECK CANCER: A COMPARATIVE ANALYSIS**

**Z. M. Patel, J. Kao, I. Mount Sinai Medical Center, New York, NY**

**Objective:** Since the optimal chemoradiation regimen remains unclear in advanced head and neck cancer patients, we analyzed the efficacy and toxicity of two different approaches. **Methods:** A retrospective chart review at a tertiary-care center with a multidisciplinary head and neck oncology team. Forty-two consecutive patients treated with chemoradiation for stage III/IVa head and neck cancer (81% stage IV or recurrent) between July 2007 and April 2008 were analyzed. Main outcome measures were locoregional control (LRC), distant control (DC), disease-free survival (DFS) and overall survival (OS) and acute and late toxicity. Eighteen patients received Week On/Week Off chemoradiation (WO/WO) consisting of concurrent 5-FU, hydroxyurea, paclitaxel and twice daily radiation (median dose 72 Gy). Twenty-four patients received conventional chemoradiation (CRT) consisting of concurrent platinum-based chemotherapy and daily radiotherapy (median dose 70 Gy). Most patients were treated with definitive chemoradiation (64%) and IMRT (92%). 12 of 24 patients in the CRT group received surgery before radiation therapy (RT) and 4/24 had neck dissection after RT. 10 of 18 patients in the WO/WO group received surgery after RT and 7 of 18 had neck dissection after RT. Patient characteristics were similar in both groups with the exception of a higher percentage of patients with sinonasal primaries (28% vs. 0%, p=0.01), stage IV or recurrent disease (94% vs. 71%, p=0.05) and treatment with induction chemotherapy (78% vs. 21%, p=0.001) in the WO/WO cohort. **Results:** At a median follow-up of 17.4 months for surviving patients (range 6 to 26 months) there were no significant differences in 2-year LRC (88% for WO/WO vs. 90% for CRT, p=0.9), DC (82% vs. 91%, p=0.8), DFS (82% vs. 82%, p=0.7) and OS (83% vs. 87%, p=0.8). While grade 3 acute dermatitis was more common in the WO/WO group (17% vs. 0%, p=0.04), rates of other acute and late toxicities were similar including grade 3 mucositis (39% vs. 50%, p=0.5), PEG or TPN usage (50% vs. 75%, p=0.1), grade 3 hematological toxicity (33% vs. 38%, p=0.6), long-term PEG and/or trach dependence (11% vs. 18%, p=0.6) and grade 2 xerostomia (13% vs. 11%, p=0.5). This analysis suggests that both WO/WO and CRT are highly active regimens with a similar acute and late toxicity profile. The oncologic outcomes of the WO/WO regimen are especially promising given the predominance of patients with high risk disease.

**P306: CLINICAL PHASE II TRIAL FOR THE TREATMENT OF RECURRENT HEAD AND NECK CANCERS WITH GEMCITABINE AND DOXORUBICIN**


**Objectives:** Squamous cell carcinoma of the head and neck (HNSCC) remains one of the leading causes for cancer related deaths in the United States. The survival rate for patients with stage III and IV HNSCC is still about 50%, and it has not improved for decades. Therefore, the development of novel therapeutic strategies for improved survival outcome of HNSCC patients is needed. Previous research has demonstrated a role for sphingolipid metabolism and signaling via the generation of C18-ceramide in drug-induced cell death in HNSCC cells. Increased efficacy of the combination of gemcitabine (GMZ) and doxorubicin (DOX), which are known inducers of ceramide generation, against HNSCC has been demonstrated both in situ and in HNSCC xenografts grown in SCID mice (J. Biol. Chem., 279:44311-44319, 2004; Otologicology Head and Neck Surg., 132:55-62, 2005; Oncol. Ther. Mol. Cancer Ther., 6:712-722, 2007). **Methods:** Based on these experimental data, a clinical phase II trial was initiated at the Hollings Cancer Center to develop GMZ/DOX combination as an alternative therapeutic approach against recurrent HNSCCs, a combination therapy which has not been tried against HNSCC previously. In this trial, patients receive gemcitabine 1000 mg/m2 and doxorubicin 25 mg/m2 on days 1 and 8 every 28 days until progression and receiving chemotherapy radiographically after every 2 cycles. Serum samples were obtained from each patient before and after their treatments for sphingolipidomic analysis. **Results:** To date, there have been 12 patients admitted to the trial, 8 of which were evaluable for response. The most significant toxicities observed were neutropenia, which was seen in 9 of 12 patients. Of the 8 patients evaluable for response, 6 patients were responders. A complete response was observed in two patients, one patient remained stable for 4.5 months, 2 patients remained stable for 3 months, and 3 showed progression after 1.5 months (1 radiographic progression, 2 clinical). In 4 out of 8 evaluable patients, C18-ceramide level showed more than 25% increase compared to pre-treatment level, which correlated with chemotherapeutic sensitivity with our previous study. Among them 2(50%) out of 4 had complete response. **Conclusions:** These data indicate that the clinical efficacy of GMZ/DOX against HNSCC might be evaluated in a larger cohort of patients. Scheduled prophylactic GSF may be necessary to administer this regimen. More importantly, this study highlights the importance of the scientific interaction and integration between basic science and clinical research for the development of new therapeutic strategies for the improved outcome of HNSCC in the clinic.
enrichment treatment of chemotherapy resistant, wild-type p53 tumors. Work supported by the University of Michigan Head and Neck SPORE grant, P50 CA97248 and the Cancer Center Support Grant, P30 CA46592.

EPIDEMIOLOGY

P311: INCIDENCE AND IMPACT OF BONE METASTASES FROM HEAD AND NECK SQUAMOUS CELL CARCINOMA D.Ward 1, J.Hooton 1, T.Teknos 1, C.Bradford 1, University of Michigan, Ann Arbor, MI

Background: Distant metastases (DMs) from squamous cell carcinoma (SCC) of the upper aerodigestive tract occur most commonly in lung, followed by bone and liver. The purpose of this study was to review the incidence of bone metastases, identify risk factors, and determine the prognostic significance of using CT-PET to diagnose bone metastases. Methods: A cohort of 1274 patients treated for SCC of the upper aerodigestive tract at the University of Michigan from 1995 to 2007 was evaluated retrospectively. All patients were evaluated for primary tumor location, site of metastases, tumor stage, nodal disease, method of diagnosis, treatment, and outcome. Univariate and multivariate analysis were performed to identify patient and tumor related factors predictive of distant metastases. Results: Patients with bone metastases diagnosed by CT-PET were compared to those patients diagnosed by other methods. Results: The overall incidence of distant metastatic disease was 6.2% and the incidence of bone metastases was 2.7%. In this cohort of patients, the most frequent sites of DMs in order of prevalence were lung (69.6%), bone (43.0%), liver (20.3%), brain (10.1%), and kidney (5.06%). The most frequent sites of bone metastases were the vertebrae, ribs, and pelvis. More extensive local and regional disease was associated with a greater incidence of bone metastases. The most frequent primary tumor site in patients with bone metastases was the oropharynx. Patients with bone metastases diagnosed by CT-PET lived approximately three times longer following diagnosis of bone metastasis compared to patients whose bone metastases were diagnosed by other methods; however, there was no difference in overall survival. The mean time from diagnosis of bone metastases to death was approximately six months. Conclusions: The incidence of bone metastasis from head and neck squamous cell carcinoma is second only to lung and carries a grave prognosis. The average life expectancy following diagnosis of bone metastasis in this cohort of patients was approximately six months. Factors associated with an increased incidence of bone metastasis include oropharynx as primary tumor site and extensive primary or regional disease. The use of CT-PET as a screening modality assists in the early identification of bone metastases, although its use does not result in prolonged survival.

P312: INCIDENCE AND DETECTION OF LIVER METASTASIS IN HEAD & NECK SQUAMOUS CELL CARCINOMA T.Y.Cannon, MD 1, M.R.Patel, MD 1, P.C.Bryson, MD 1, D.Leight, MD 1, V.Lai, MD 2, A.Deal 2, C.G.Shores, MD, PhD 1, 1University of North Carolina, Chapel Hill, NC; 2University of Virginia, Charlottesville, VA; *Linebeger Comprehensive Cancer Center, Chapel Hill, NC

Background: Distant metastases (DMs) from squamous cell carcinoma (SCC) of the upper aerodigestive tract occur most commonly in lung, and DMs, assisted by CT-PET as a screening modality assists in the early identification of bone metastases, although its use does not result in prolonged survival.

Poster presentation: Anti-tumor and immune stimulation effects of cisplatin and bleomycin-based electrochemotherapy in vivo

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Introduction: Many experimental studies in Europe and clinical experience in China suggest that direct electric current can improve chemotherapeutic effect. We evaluated the impact of electric current on chemotherapy response and on the efficacy of chemotherapy against tumor cells in a murine tumor model.

Material and Methods: Two million cells of Ehrlich Ascitic Tumor were injected in the dorsal region of 35 male Balb/c mice. Seven days later, mice were divided into 7 groups, receiving different treatments: [1] No treatment; [2] Cisplatin only 0.8 mg/kg, intraperitoneally; [3] Bleomycin only 8 UI/m2, intraperitoneally; [4] Electricity only with 10 mA/cm2 during 22’, retaining polarity; [5] Cisplatinate + electricity; [6] Bleomycin + electricity; and [7] Electricity switching polarity. Tumor progression in each mouse was measured daily and differences among the groups were assessed by ANOVA test. The immune impact of treatment was evaluated by the co-culture of lymphoid cells from treated and untreated mice with Ehrlich Tumor cells (co-culture with allogeneic cells was used as a control). Results: The mean tumor area (+/− standard deviation) at the day of treatment was 0.40 cm2 (+/−0.20), 35 days after treatment, the mean tumor areas of each group was: [1] 1.75 (+/−0.35); [2] 2.05 (+/−0.25); [3] 1.35 (+/−0.15); [4] 0.70 (+/−0.35); [5] 0.00 (+/−0.30); [6] 0.20 (+/−0.20); [7] 1.65 (+/−0.25). In the ANOVA, groups [5] and [6] were found significantly different from controls (p<0.05). The co-culture results suggest that lymphocytes from mice treated by electric current promote elimination of Ehrlich Tumor cells. The ANOVA test showed that electric current significantly increased the incidence of apoptosis and cellular senescence in two HNSCC cell lines: a parental, cisplatin sensitive cell line UM-SCC-74B (very high Bcl-xL) and a stably transfected cisplatin resistant cell line UM-SCC-74BL (very high Bcl-xL). Both cell lines have endogenous wild-type p53. Cell lines were treated with cisplatin alone, MDM2 inhibitor (MI-63) alone or in combination (sequentially). Following treatment, equal numbers of tumor cells were plated. Colonies were stained with crystal violet 14 days after plating. Annexin V staining was used to measure apoptosis. Results: The combination of cisplatin with MI-63 suppressed colony formation more efficiently than either drug alone. Cell proliferation in cells treated with either MI-63 alone or in combination with cisplatin and MI-63. In these two groups, we observed higher cellular senescence (beta-galactosidase assay) in both the cisplatin sensitive and resistant cell lines. Conclusions: Cellular senescence is emerging as an irreversible cell cycle arrest mechanism that plays an important role in tumor regression following genotoxic therapy. Indeed, both the colony formation assays and long term MTT assay showed decreased cell proliferation and increased senescence is emerging as an irreversible cell cycle arrest mechanism that plays an important role in tumor regression following genotoxic therapy. Indeed, both the colony formation assays and long term MTT assay showed decreased cell proliferation and increased mean tumor area (+/− standard deviation) at the day of treatment. Resistance to chemotherapy is a problem encountered in the treatment of chemotherapy resistant, wild-type p53 tumors. Work supported by the University of Michigan Head and Neck SPORE grant, P50 CA97248 and the Cancer Center Support Grant, P30 CA46592.
Liver metastasis of head and neck squamous cell carcinoma (HNSCC) is relatively rare but frequently fatal. This study examines risk factors and the utility of routine liver function tests (LFT) to detect liver metastasis. Methods: 745 patients with newly diagnosed HNSCC treated and followed at UNC Hospitals from 1989 to 2003 were retrospectively identified. The medical record was reviewed for age at diagnosis, gender, site and subsite, clinical and pathologic stage, treatment and outcomes. Speciﬁcally, diagnosis with liver metastasis either at initial presentation or follow up were identiﬁed based on radiologic ﬁndings and/or liver biopsy results. Risk of developing liver metastasis was evaluated based on aforesaid mentioned factors. The number of patients with elevated LFTs was used to calculate the sensitivity, speciﬁcity, and positive predictive value for each individual test. Results: The overall rate of liver metastasis in head and neck patients is 2.2% (n = 745; 95% CI = 1.7%, 4.2%). Twenty percent of the patients demonstrated early metastasis (less than 6 months after initial diagnosis, mean (± 1.2 months) versus 80% with late metastasis (mean = 32.7 months). Interestingly lesions in the oropharynx and hypopharynx constitute 65% of the patients found to have liver metastasis but only 37.1% of the study population. Only patients with oropharyngeal squamous cell carcinoma were statistically more likely to develop liver metastasis (p = 0.037). Of all patients with metastasis, 75% had stage IV disease at diagnosis (3.6% of all Stage IV, n = 407); and these patients were more likely to have an abnormal LFT panel than patients with Stage I, II, or III (p = 0.046). However, only 1.2% (95% CI = 0.56%, 2.30%) actually had liver metastases and an abnormal LFT while 1.5% (95% CI = 0.75%, 2.65%) had liver metastases but a normal LFT panel. Sensitivity for each individual test: ALT: 90%, AST: 94%, AP: 94%, LDH: 93.7%. Specificity ranged from 96.9-97.8%. The positive predictive value was highest for LDH (10.2%). Conclusions: This study reveals that LFTs do not reliably identify liver metastasis. Patients with Stage IV oropharyngeal cancer are more likely to develop liver metastasis and may benefit from screening. Abdominal ultrasound may be the best screening test.

P314: MANAGEMENT OF HEAD AND NECK MALIGNANCIES IN THE PATIENTS OVER 80 YEARS OLD S.Hayashi1, M.Nakayama1, S.Miyamoto1, M.Takeda1, Y.Seino1, M.Okamoto1, 1Kitasato University School of Medicine, Sagamihara Japan

Objective: Management of senior age head and neck malignancy patients has become an impactive topic in our daily practice due to the increasing number of senior population in Japan. To verify the clinical strategies, a retrospective review was conducted at a university department. Methods: Among the 2,896 head and neck malignancy patients treated at our department between 1971 and 2006, 151 patients were over 80 years of age or more (senior group). A detailed analysis was done to evaluate the clinical features of this group. Detailed case study from recent patients was presented. Results: The average age of head and neck malignancy patients treated within a year surpassed 60 years old after 1990. Likewise, the annual ratio of the senior patients increased gradually after 1990. Among the 151 patients evaluated, 101 were male and 50 were woman. Cancers of larynx and hypopharynx were the common site for man and cancers of oral cavity and oropharynx were common site for woman. Ischemic heart disease was one of the complications often encountered and required special attentions through the treatment course. Conclusions: Regardless of the age and tumor location, Stage I and II early stage tumors should be treated with a curative intension; equal results to younger generations can often be expected. As for Stage III advanced tumors, unexpected complications often can be encountered. Decision to initiate curative treatment or not should meticulously discuss with the patient and the family members. The occasion for such difficult decisions will be increased due to the increasing number of senior population. Regarding Stage IV advanced tumors, palliative managements are likely to be the main treatment and this should also be discussed with the patient and the family members.

P315: ORAL SQUAMOUS CELL CARCINOMA IN YOUNG ADULTS - THE MAYO CLINIC EXPERIENCE L.Thomas1, E.J.Moore2, K.D.Olsen2, J.L.Kasperbauer4, L.A.Erickson4, D.J.Schembri-Wismayer4, 1Leighton Hospital, Liverpool, United Kingdom; 2Mayo Clinic, Rochester, MN

Objectives: The objectives of this study are to describe the disease-specific survival in young adults with oral squamous cell carcinoma, aged 18 to 40 years of age and to assess the prevalence of etiological factors in these patients. Methods: After Institutional Review Board approval, patients who were newly diagnosed with oral squamous cell carcinoma from 1980 to 2004 and between 18 and 40 years of age were identified from the hospital tumor registry. All histopathology slides were reviewed by a single head and neck pathologist (DSW) for verification of pathologic diagnoses. Pathologic features evaluated included depth of invasion, tumor size, grade, keratinization, ulceration, margin status, desmoplasia, lymphoplasmacytic response, perineural and angiolymphatic invasion, adjacent dysplasia, nodal involvement and nodal extracapsular extension. Clinical and follow-up information was obtained by chart review. All statistical analyses were performed using SAS 8.2 (SAS Institute, Cary, NC). Descriptive statistics, univariate and multivariate analyses were performed, and Kaplan Meir survival curves were generated. Results: Sixty-two patients were identified. The mean age was 34 years (range: 18 to 40). The mean follow-up duration was 11.4 years (range: 0.3 to 27.3 years). Male to female ratio was 3:2. Thirty-ﬁve patients (56.5%) had never used tobacco, with only 9 (14.5%) smoking < 20 pack years. Thirty-one patients (50%) used alcohol (< 2 units/week). The overall clinical staging was: 29 (46.8%) stage I, 14 (22.6%) stage II, 5 (8.1%) stage III, 9 (14.5%) stage IVa, and 5 had stage IVb disease. Ten-year disease-speciﬁc survival was 100% for stage I, 91.7% for stage II, 100% for stage III, and 55.6% for stage IVa. Overall, eleven patients died of disease. All five patients with stage IVb disease died of disease within four years. In univariate analysis the overall clinical stage, T-stage and N-stage were signiﬁcantly associated with poor prognosis (p<0.001). Pathological factors associated with poor outcome were depth of primary tumor and extracapsular lymph node disease (p<0.01). Multivariate analysis showed stage to be the strongest predictor of death due to disease. Pathological parameters tending to show decreased survival included desmoplasia, higher tumor grade, and no or minimal lymphoplasmacytic immune response to the tumor. Risk factors including smoking, alcohol consumption, immuno-suppression, dental irritation, recurrent leukoplakia were not associated with decreased survival. Conclusions: Pathologic features including depth of the primary tumor and the presence of extracapsular lymph node disease as well as both pathologic and clinical tumor stage were strongly associated with decreased survival. Risk factors considered common in patients with oral squamous cell carcinomas appeared to be less prevalent in this age group. Young patients with stage I, II, or III disease had an excellent 10-year disease specific survival (90%), while 10-year survival was markedly decreased in patients with stage IV disease where less than 36% survived 10 years.

P316: CHARACTERISTICS AND OUTCOMES OF YOUNG ADULTS, 40 YEARS OLD OR LESS, WITH ORAL SQUAMOUS CELL CARCINOMA M.B.Hakim1, J.Lubeck1, L.Xinggang2, A.Salama1, R.A.Old3, 1University of Maryland Medical Center, Baltimore, MD; 2University of Maryland, Baltimore, MD

Objectives: The purpose of this study was to analyze clinical data of young patients with oral squamous cell carcinoma (OSCCa) to determine the characteristics and predictors of disease free survival. Methods: We performed a retrospective record review of all patients, diagnosed for OSCCa in the Department of Oral-Maxillofacial Surgery, University of Maryland Medical Center over a 14-year period (1992-2006). All patients were 40 years or less at the time of diagnosis. Demographic data including age, gender, race, risk factors, primary site, staging, pathologic features and treatment modality were analyzed. Loco-regional and distant control were chosen as outcome measures. Kaplan-Meier estimates of survival probabilities were calculated, and compared using Log-Rank tests to evaluate the relation of prognostic factors on disease free survival. Results: Forty one charts were reviewed, representing 4.6% of all patients with oral squamous cell carcinoma seen in our department during the same period. For the remaining 37 patients, surgery was the primary treatment for 35 and radiation for 2 patients. Patients' age ranged from 21 to 40 years with an average age of 34.6 years and a male-to-female ratio of 1.73:1. Fifty one percent had a history of smoking, 41 % were moderate or heavy drinkers and 38% were non-smokers non-drinkers. Tongue was the most common primary site (81%) followed by floor of mouth (12%). Sixty eight percent presented as an early stage (Stage I and II) and 31% as advanced stage (Stage III and IV). Follow-up ranged from 3 to 158 month with an average of 48.2 months. The 2-year disease free survival was 81% (95% CI 62%-91%). Tumor grade was the only statistically significant predictor of disease free survival, however, given the small number of patients, statistical
To assess the impact of routine surveillance parameters upon disease free survival was similar to reported older populations. Tumor grade is a significant predictor of disease free survival in young patients in this study.

Objective: The most important prognostic factor for patients with newly diagnosed squamous cell carcinoma of the upper aerodigestive tract (SCC) is the presence of lymph node metastases at presentation. Another important clinical risk prognosticator is disease stage (T stage) at the primary site. Although advanced stage of disease at the primary site (T3, T4) is regarded as an important risk factor for poor prognosis, most patients with locally advanced disease also present with nodal metastases. This fact obscures the contribution of advanced disease stage at the primary site toward the ultimate prognosis and other outcome parameters. By studying node negative (N0) SCC patients with locally advanced (T3, T4) disease, we hoped to understand clinical characteristics of these patients, patterns of recurrence, and prognosis according to upper aerodigestive tract anatomic subsite and modality of treatment. Methods: The database of patients presenting with SCC to a large, urban head and neck cancer treatment center was utilized for this research. Patients with T3 or T4 and N0 SCC of the oral cavity, oropharynx, hypopharynx, nasopharynx, larynx, and parapharyngeal sinus were identified and served as the cohort for this study. Patients were excluded if they were node positive by clinical and/or radiographic criteria, or were subsequently upstaged to node positive after initial N0 staging (by neck dissection surgery). Patients were excluded if they presented with recurrent disease, did not have SCC, received treatment elsewhere, and/or had incomplete medical records. Patients were treated with various combinations of surgery, radiation, and chemotherapy. Survival and patterns of recurrence were investigated at each anatomic subsite according to treatment modality. Results: 90 patients (out of a total of 493 T3 and T4 patients in the database) met all of the study inclusion criteria. Laryngeal cancer patients represented nearly half (44/90) of the patients in the study group, with glottic cancer (28/44) being the most prevalent subsite represented in this anatomic region. Oral SCC patients represented 28% (25/90) of the patients in the study group, with much smaller percentages of oropharynx (17%), hypopharynx (2%), nasopharynx (2%), and parapharyngeal sinus (2%) disease. The majority of patients were treated with either chemoradiation (34%), surgery followed by radiation (27%), or surgery alone (13%). For the entire patient cohort, mean follow-up time was 28 months and 91% (82/90) of patients were alive at the time of data analysis. 73% (66/90) of patients were alive without evidence of disease, and only 8 patients (9%) had died of disease. These statistics remained fairly consistent regardless of anatomic subsite of disease presentation or modality of treatment. Recurrences in oral cavity patients tended to be local, with higher percentages of regional and distant recurrences in the laryngeal cancer group. Conclusions: In the modern treatment era, the prognosis of SCC patients who present with locally advanced disease without clinical and radiographic evidence of regional metastases (N0) is relatively good at 2 years of follow-up time. This prognosis is consistent across treatment modalities, and the various potential anatomic subsites of disease presentation.

Objective: To assess the impact of routine surveillance parameters upon survival in patients diagnosed with recurrent disease following prior definitive therapy for head and neck cancer. Methods: Patients diagnosed with recurrent disease between September 1999 and March 2001 were identified from the Head and Neck Surveillance Database at The Ohio State University. Factors identified at the time of diagnosis including scheduled vs. unscheduled visit, existence of patient identified symptoms/findings vs. physician identified findings, patient compliance, and intent of planned definitive salvage therapy were correlated with longitudinal clinical outcome using Kaplan-Meier survival curves and log-rank testing for comparative analyses. Results: During the above period, 150 patients were diagnosed with recurrent disease. In 111 patients (74%) diagnosis occurred during routine scheduled surveillance follow-up. In 118 patients (78.6%), patients identified a new symptom or finding prior to the visit. 19 patients (12.6%) were determined to be non-compliant with prior surveillance follow-up recommendations. Definitive salvage treatment was felt feasible and planned by the physician in 105 patients (70%). When assessing longitudinal outcome, no significant difference in survival was observed whether patients were diagnosed during a scheduled vs. unscheduled visit (p=0.61), whether patients identified new symptoms/findings vs. physician identified findings (p=0.17), or whether diagnosis occurred in compliant vs. noncompliant patients (p=0.59). Overall survival in all groups was poor, although initial survival in patients in whom definitive salvage treatment was deemed feasible was significantly higher than those in whom salvage therapy was not deemed an option (p < 0.0005). Conclusions: Current recommended surveillance regimens do not appear to confer obvious benefit with regards to survival in patients following definitive treatment for head and neck cancer. It is possible that routine surveillance may facilitate communication between patients and physicians regarding clinically relevant new symptoms or findings noted by patients. As such, any proposed alternative surveillance strategies must provide for timely evaluation of new symptoms/findings. Even with salvage therapy however, survival following diagnosis of recurrent head and neck cancer remains poor. The offer to salvage treatment must be made in context with whether long term disease control remains a realistic goal, and whether any short term gains in survival are outweighed by the severity of such measures upon quality of life.

Objective: To evaluate the effectiveness of follow-up for patients presenting with SCC to a large, urban head and neck cancer treatment center was utilized for this research. Patients with T3 or T4 and N0 SCC of the oral cavity, oropharynx, hypopharynx, nasopharynx, larynx, and parapharyngeal sinus were identified and served as the cohort for this study. Patients were excluded if they were node positive by clinical and/or radiographic criteria, or were subsequently upstaged to node positive after initial N0 staging (by neck dissection surgery). Patients were excluded if they presented with recurrent disease, did not have SCC, received treatment elsewhere, and/or had incomplete medical records. Patients were treated with various combinations of surgery, radiation, and chemotherapy. Survival and patterns of recurrence were investigated at each anatomic subsite according to treatment modality. Results: 90 patients (out of a total of 493 T3 and T4 patients in the database) met all of the study inclusion criteria. Laryngeal cancer patients represented nearly half (44/90) of the patients in the study group, with glottic cancer (28/44) being the most prevalent subsite represented in this anatomic region. Oral SCC patients represented 28% (25/90) of the patients in the study group, with much smaller percentages of oropharynx (17%), hypopharynx (2%), nasopharynx (2%), and parapharyngeal sinus (2%) disease. The majority of patients were treated with either chemoradiation (34%), surgery followed by radiation (27%), or surgery alone (13%). For the entire patient cohort, mean follow-up time was 28 months and 91% (82/90) of patients were alive at the time of data analysis. 73% (66/90) of patients were alive without evidence of disease, and only 8 patients (9%) had died of disease. These statistics remained fairly consistent regardless of anatomic subsite of disease presentation or modality of treatment. Recurrences in oral cavity patients tended to be local, with higher percentages of regional and distant recurrences in the laryngeal cancer group. Conclusions: In the modern treatment era, the prognosis of SCC patients who present with locally advanced disease without clinical and radiographic evidence of regional metastases (N0) is relatively good at 2 years of follow-up time. This prognosis is consistent across treatment modalities, and the various potential anatomic subsites of disease presentation.

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An important characteristic of the tumor had its origin in tongue on 15 cases, floor of mouth on 6 cases, hard palate on 2 cases, and gum on 3 cases, the retromolar region and buccal mucosa presented 1 cases each. The most common site of the second neoplasia was the oropharynx (N=10) followed by esophagus (N=5), tongue (N=4), retromolar region (N=3), floor of mouth (N=3); hard palate (N=2) and lung (N=1). The mean age was 60.07 years old and 84.42% of the patients (N=25) were males. Conclusion: An important characteristic observed was that most of the patients kept their habits of smoking and drinking alcohol. The second primary tumor prevails in esophagus, behind molar region and in tongue, with poor prognosis.

P321: ANALYSING REASONS FOR NON-ENROLMENT ON CLINICAL TRIAL ARE DEVELOPING COUNTRIES DIFFERENT FROM DEVELOPED ONES? M.S.Deshpande1, J.P.Agarwal1, D.A.Chaukar1, S.Ghosh1, K.Awatagiri1, P.Chaturvedi1, P.S.Pai1, A.K.D’cruz1, K.A.Dinshaw1, 1Tata Memorial Hospital, Mumbai, India

Background: In recent years, many clinical trials have been conducted in developing countries like India. Data available on non-enrolment in clinical trials is mostly in western patient population. There is no data available on reasons of non-enrolment in clinical trials from India. The socio-cultural differences between Indian and western population makes it essential for us to identify the causes of non-enrolment of Indian patients. Materials and Methods: Oral cancer adjuvant therapy trial is a large randomised control trial underway at a tertiary cancer hospital in India with more than 300 patients of oral cancer enrolled. A prospective study was conducted to analyse reasons for non-enrolment on this trial. Detailed demographic record was maintained of all patients screened for the trial. For patients who were not enrolled on trial, reason of failure to enrol was noted. The reasons were classified into physician reasons and patient reasons. Univariate and multivariate analysis was performed to identify reasons for non-enrolment using SPSS 14 software. Results: From April 2005 to September 2007, 932 patients were screened for the trial. Detailed records were available for 927 patients. Three hundred and thirty three patients were enrolled in the trial, while 594 patients were not enrolled due to various reasons. Two hundred sixty six patients (43.8 %) were not enrolled due to physician reasons. The most common physician reasons were unreliable to follow up (108 patients, 42.2%), age more than that allowed on trial (52 patients, 20.3%) and unable to start treatment on time (33 patients, 12.9%). Three hundred forty seven patients (57.7%) were not enrolled due to patient reasons. The most common patient reasons were, wanted treatment close to residence (115 patients, 33.1%), lack of support system in the city (36 patients, 10.4%) and financial problems (25 patients, 7.2%). One hundred fifty two patients refused to give any particular reason for non-enrolment. Multivariate analysis showed lower level of education, female sex, non-availability of support system in the city and older age were factors responsible for non-enrolment on trial. Conclusion: Our study is a first to identify the reasons for non-enrolment of Indian patients. These reasons were quite different than those found in the western population. This study will form a benchmark and help in planning future trials regarding accrual rate of patients. Corrective measures against above mentioned causes should improve enrolment in future trials.

P322: MULTIDISCIPLINARY APPROACH TO HEAD AND NECK CANCER CARE: THE SLU EXPERIENCE D.S.Manne1, M.A.Varvares2, 1Saint Louis University, St. Louis, MO; 2Saint Louis University Cancer Center, St. Louis, MO

Background/Objective: A diagnosis of head and neck cancer can be devastating to patients and their family. Treatment options (surgery, chemotherapy, and radiation therapy) can produce long term changes in a patient’s life and require multiple disciplines to manage. In 2003, a multidisciplinary head and neck cancer clinic was established at the Saint Louis University Cancer Center. The objective was to provide true multidisciplinary care to head and neck cancer patients seen at the center. This poster presents the SLU experience as well plans for the future. Methods: The original members of the team included head and neck surgical oncologists, medical oncologist, and radiation oncologists; a speech therapist with expertise in swallowing issues; oncology social worker; oncology dietician; and a nurse educator from the Cancer Information Center. In 2005, a registered dental hygienist with expertise in oral symptom management was added to focus on the oral health issues of these patients. In 2007, an occupational therapy graduate student as well as Periodontics (Dental) residents joined the group. There are both a weekly Head and Neck Tumor Board and a Multidisciplinary Head and Neck Cancer Clinic. New patients as well as those continuing or completing treatment that need specific attention from all providers are seen in a group setting. The Multidisciplinary Head and Neck Cancer Team Nurse Coordinator provides information to the patient and family prior to the first appointment and oversees the care provided by the rest of the team. Results: Over 300 patients have been seen since the beginning, reducing a patient’s clinic visits from three to one. This is extremely beneficial as more than 50% of our patients travel over an hour for their clinic visits. While the team clinic appointment allows for patients and their family members to meet with all providers in one visit, it is not an efficient system as patient wait times can be long. However, revised appointment scheduling and weekly review of the schedule by the Nurse Coordinator has improved this. Patients and family members frequently comment on how they appreciate the opportunity to meet all members of the team in one visit. Conclusions: The Multidisciplinary Head and Neck Cancer Clinic at Saint Louis University Cancer Center has improved how we provide care to our patients, as demonstrated by patients’ and family members’ feedback. Future plans include adding a physical therapist and occupational therapist to the team to focus on issues related to survivorship; the development and implementation of a multidisciplinary cancer educational program for team members, students and residents; developing and implementing a clinical rotation for dental and dental hygiene students to provide needed dental care to these patients; and expanding nursing students’ oncology exposure by having a designated rotation through the multidisciplinary program.

P323: OUTCOME OF CARCINOMA OF TONGUE IN A POPULATION COHORT A.Maher1, B.W.Nason2, K.A.Pathak1, 1Cancer Care Manitoba, Winnipeg, MB, Canada

Background: Carcinoma of tongue is one of the most common oral cancers seen in oral cavity. Most of the published literature is from hospital cohort. Present study looks at the outcome of squamous cell carcinoma (SCC) of tongue in a population cohort. Material and Methods: Clinical outcomes of 200 patients, who formed a population based historical cohort in Manitoba Cancer registry, were analysed All living patients were prospectively followed up for a median period of 57 months. Status of patient at the time of last contact whichever was earlier, was recorded. Disease free, cause specific and overall survival were plotted by Kaplan-Meir method. Independent influence of prognostic factors as the age, gender, stage, margin of excision and treatment modality on disease control and survival was evaluated in multivariate models using Cox Proportional hazard model. Results: Our study group of 128 male (64.0%) and 72 female (36.0%) patients, with mean age of 62.3 ±13.7 years. It included 62 (31.0%) patients with T1, 77 (38.5%) T2, 47 (23.5% : T3 and 14 (7.0%) with T4 disease. Clinically 140 (70.0%) patients had NO neck, 29 (14.5%) had N1, 26 (13.0%) had N2 and 5 (2.5%) had N3 disease. Ninety seven (48.5%) patients underwent surgery, 59 (29.5%) had surgery with adjuvant radiation, 37 (18.5%) had only radiation and 7 (3.5%) had only adjuvant care. During the course of follow up, 78 patients (39.0%) developed recurrent disease. At the time of recording of status, 101 patients (50.5%) were alive and 43 (21.7%) had died of disease. At 5 years of follow up the overall survival was 59.2%, cause specific survival was 65.7% and disease free survival was 55.2%. In multivariate analysis, initial treatment modality used was the only independent determinant of cause specific survival (p=0.001). As compared to surgically treated patients, those treated with surgery and adjuvant radiation (HR= 2.59; 95% CI=1.15, 5.83; p=0.021) and radiation alone (HR= 5.83; 95% CI=1.15, 17.84; p=0.031) or those receiving supportive care (HR= 34.45; 95% CI=5.35, 221.76; p<0.001) were at significantly higher risk of dying of their disease. Conclusions: Carcinoma of the tongue is best treated by surgery alone in early stages and with surgery and adjuvant radiation in advanced stages.

P324: SOCIOECONOMIC DISADVANTAGE ASSOCIATED WITH HEAD AND NECK CANCER RISK S.Dhaubhadel, P.Allison2, E.Frappier1, D.Boire1, 1Camago Hospital, Sao Paulo, Brazil; 2Faculty of Dentistry -McGill University, Montreal, PQ, Canada; 3McGill University, Montreal, PQ, Canada; 4AC Camargo Hospital, Sao Paulo, Brazil

Links between low socioeconomic position (SEP) and head and neck (H&N) cancer are well established. Most previous research, however, has relied on limited socioeconomic data, usually only measuring SEP at one point over the life course. In this study, we examined the association between SEP at 3 different time points across the life course and H&N cancer. We used data from an international hospital-based case-control study, which investigates the influences of environmental, lifestyle, viral and genetic factors on
the etiology of H&N cancer using the life course framework: HeNCe life study. Methods: Data was drawn from the HeNCe life study: Brazilian site. Cases (N=122) comprise of newly diagnosed subjects with squamous cell carcinoma in the upper aerodigestive tract (mouth, pharynx, and larynx) at stages I-IV selected from the AC Camargo Hospital in São Paulo. One-hundred and twenty-two non-cancer control subjects (matched for gender and age [±5 years]) were selected from a variety of inpatient and outpatient clinics at the same or nearby hospitals. An interview using a structured questionnaire and life grid technique was used interactively to collect retrospective information. These data include health related behaviour, indicators of SEP, housing, work and family environment in 3 stages of the subject’s life: childhood (0-16 yrs), early adulthood (17-30 yrs) and late adulthood (31 or more yrs). An indicator of SEP in each of these 3 time-points was created using presence and absence of several indicators of material deprivation (e.g., presence of a toilet inside the house, car ownership, house tenure, overcrowding, etc). The most favourable score was 8 and the least favourable was 0. The indicators from the 3 time-points were further categorized, using the media as a cut-off point, into low and high levels of material deprivation. Conditional logistic regression analyses assessed the odds ratio (OR) and 95% confidence interval (95%CI) for SEP at different life stages in relation to H&N cancer, adjusting for potential confounders. Results: Participants from a low SEP in childhood and early adulthood had an increased risk of H&N cancer (odds ratio [OR]=1.90, 95% confidence intervals [95% CI]=1.1-3.2), (OR=1.86, 95% CI=1.0-3.2), respectively. The inclusion of smoking and alcohol variables into the models only slightly attenuated the effect of childhood and early adulthood SEP. This suggests other pathways by which SEP may increase the risk of H&N cancer. Conclusion: Both SEP in childhood and early adulthood contribute to an increased risk of H&N cancer.

P325: CAN WE IDENTIFY PATIENTS WITH HEAD AND NECK CANCER AT RISK FOR SHORT-TERM MORTALITY? M. van der Schroeff1, E. Steyerberg1, R.J. Baatenburg de Jong1, Erasmus Medical Center, Rotterdam, The Netherlands

Objective: To develop a prognostic model for mortality within the first year after treatment for primary head and neck squamous cell carcinoma patients. Methods: A cohort of 3144 consecutive primary head and neck squamous cell carcinoma patients was analyzed to assess the prognostic value of different, pre-treatment, clinical parameters. Clinical factors included gender, age, comorbidity, localization of the tumor, degree of differentiation of the tumor, c-stage and n-stage. Patients with distant metastases were excluded. Patients were diagnosed between January 1980 and November 2006 with a median follow up of 33 months. All clinical parameters were included in the multivariate analysis using logistic regression. The prognostic power was measured with a ROC-curve. Results: All variables were entered in a logistic regression model. The area under the curve (ROC) was 0.68, representing good predictive power. Sensitivity and specificity differs with different chosen cut-off points of the predicted probability of dying within one year in the model. Conclusion: The presented prognostic model provides a reliable short-term prognosis for patients with head and neck cancer. Palliative rather than curative treatment should be considered for patients with expected high short-term mortality.

P326: EVALUATION OF THE RESPECT OF QUALITY CRITERIA BY CENTERS TREATING PATIENTS WITH HEAD AND NECK CANCERS. P.Gallet1, S. Cortese2, G. Del Moro3, R. Mastronc1, B. Philpin1, P. Gangloff1, G. Delivel1, 1Cav. Centre Alexis Vautrin, Vandoeuvre Les Nancy, France

Objective of the Study: The goal of this study was to evaluate the respect of the quality criteria defined by the French High Health Authority and the INCA (Institut National Du Cancer) by the centres treating care of the patients suffering from head and neck cancer. Methods: A questionnaire with 55 questions was sent to the 40 centers members of the GETTEC group (Groupe d’Etude des Tumeurs de la Tete et du Cou), focused on the following points: -Facility of access to diagnosis assessment and initial taking care delay; -Organization modalities of multidisciplinary staff, application of referrals; -Delay before treatment and between two treatments; -Organization of surgical care and anaesthesiological process (comparte- rization of surgical procedures, access to extemporaneous anaesthesiologic examination, quality of surgical and histological reports, rate of surgical site infections); -Organization of radiotherapy, medical and dental follow-up, quality of reports; -Existence of a structure for palliative cares; -Implication into therapeutic assays and quality of organization; -Presence of control procedures. Results: Out of the 40 institutions members which belong to the GETTEC, 19 answered (which correspond to 4600 new patients a year, that is to say 1/4 of new French cases concerning head and neck cancers). These centers treat between 63 and 800 new patients every year. Overall, the results are satisfactory, but certain points are worth mentioning: Only 73% of new cases are discussed in pluridisciplinary staff and written personalised treatment projects are not yet systematic. 16% of centers have already or will soon have a procedure to check the application of referentials. Standard reports (surgical, histological or radiotherapeutical) are not well developed and, sometimes, radiotherapeutic reports are not accurate. Only 16% of centers use computerized indicators for delay between first consultation and different treatments. Last, 34% of centers do not have a palliative care structure. All other criteria are respect- ed. Conclusions: In the end, the centers which answered the questionnaire have all demonstrated a true approach of quality. The goal of this survey was to highlight the aspects which need to be improved. It will be renewed at least once a year to encourage centers to put a lot of effort into this quality approach. The questionnaire should be soon available on line on the GETTEC website.

P327: ACCESS TO HEALTH CARE AND RATES OF THYROID CANCER DIAGNOSIS IN THE UNITED STATES L.G. Morris1, J.L. Marti1, D.J. Myssiorek1, M.D. DeLacure1, 1New York University School of Medicine, New York, NY

Introduction: The incidence of thyroid cancer is increasing in the United States, but it is unclear if this trend represents more disease, or simply improved screening and diagnosis. We investigated the relationship between access to health care and the incidence of thyroid cancer in different regions of the United States. Methods: Population-based study of the 17 geographic regions currently captured in the National Cancer Institute’s Surveillance Epidemiology and End Results (SEER 17) database between 2000-2003, limited to cases of papillary, follicular, medullary and anaplastic thyroid carcinoma. Incidence data was analyzed as age-adjusted rates per 100,000 population. The percentage of all cancers <1.5cm in size was selected as a surrogate marker for the proportion of disease diagnosed while subclinical. Corresponding macroeconomic data on health insurance status was obtained from the United States Census Bureau and the Kaiser Family Foundation State Health resource. Correlations were studied using Pearson correlation and simple linear regression in SPSS v. 13.0. Results: Across the nation’s 17 registries, there is currently a wide range in the incidence of thyroid cancer, ranging from 5.0/100,000 in rural Georgia to 10.7/100,000 in New Jersey. There was a significant inverse correlation between thyroid cancer incidence and the percentage of the population without health insurance (r=-0.44, p=0.04). There was also a significant correlation between the overall incidence of cancer and the proportion of cases diagnosed while subclinical (r=0.61, p=0.01). The per- centage of the population insured correlated with the proportion of disease diagnosed while subclinical (r=0.70, p<0.01). Conclusions: This study supports a significant detection effect in the increasing incidence of thyroid cancer. Thyroid cancer is significantly more common in regions of the country with more access to health insurance. Regions with more thyroid cancer were more likely to have cases diagnosed while subclinical, and more subclinical disease is detected in regions with the most access to health insurance. Taken together, these data support a role for access to health care, and improved detection of subclinical disease, in the increasing incidence of thyroid cancer.

P328: HIGHER STAGING AT PRESENTATION OF LARYNGEAL SQUAMOUS CELL CARCINOMA IN WEST VIRGINIA VS. UNITED STATES H. Arshad1, P.G.van der Sloot1, 1West Virginia University, Morgantown, WV

Objective: To test the hypothesis that patients with head and neck squamous cell carcinoma were presenting at higher stages in West Virginia than the national averages. Methods: Retrospective chart review of patients presenting to West Virginia University during 2002-2005 with head and neck squamous carcinoma. The stages at presentation of these patients were compared to the National Cancer Database (NCDB) 2003 data for each head and neck subsite. Results: There was a trend for higher stag- ing at presentation for all subsites, but reached statistical significance for laryngeal squamous cell carcinoma at WVU vs. NCDB data (70.1% with stage III or IV vs. 40.4%, p<0.05). Conclusion: Patients in are more like- ly to present with advanced stage laryngeal squamous cell carcinoma in West Virginia when compared to the national average. This deserves fur- ther study into whether the cause is delay in diagnosis and underscores the need to educate community and rural physicians about early warning signs.
To assess if the grade of comorbidity as stated by patients in the outpatient clinic correlated with comorbidity grades determined upon admittance to the surgical ward prior to head and neck cancer treatment. Comorbidity was assessed as head and neck cancer patients often have comorbidity and it is associated with a higher risk of post-operative complications, survival rate, deteriorated health and quality of life and functional status. Method: As part of a study evaluating distress in patients after treatment for head and neck cancer, patients attending the outpatient clinic for routine follow-up were approached during a three month period. Forty-five patients wished to enter and upon completing the Hospital Anxiety and Depression Scale (HADS), they were asked about having comorbidity or not, and their health status was measured using the Adult Comorbidity Evaluation 27 (ACE-27) method. Factors such as age, gender, tumor status and treatment were also recorded. The ACE-27 method was designed for cancer patients and states health status in four grades (0,1,2, and 3) of comorbidity (none, mild, moderate, severe). The results of comorbidity as stated by the patients in the outpatient clinic were compared to the ACE-27 scores. Results: No difference between patient stated and recorded comorbidity grade was seen in 22/45 patients (49.9%). However, differences were found in 23/45 patients (51.1%). These differences varied from one to three grades of comorbidity; one grade 11/45 patients (24.4%), two grades difference 10/45 patients (22.2%) and three grades 2/45 patients (4.4%). In all cases the differences found were due to under-scoring of the comorbidity grade by the patient. Conclusion: Comorbidity as stated by patients in the outpatient clinic differed from comorbidity grades recorded by treating physicians prior to treatment in more than 50% of the patients. In all cases the difference found was due to under-scoring by the patient. The differences found varied from one grade of difference to 3 grades. Treating physicians should consider the patients tendency to underscore comorbidity prior to treatment as it might influence treatment outcome due to the known association of comorbidity and higher rates of post-operative complications, survival rate, deteriorated health and quality of life and functional status.

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P332: WHICH SPECIALIST SHOULD MANAGE HEAD AND NECK DISORDERS? THE MEDICAL STUDENT PERSPECTIVE
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Background: Medical schools are beginning to place greater emphasis on general practice rather than specialisation in their undergraduate curricula. Lack of exposure to surgical specialties may affect career choice and referral patterns once practicing. Objective: The purpose of this study was to examine the perceptions of medical students, regarding which specialists (general surgery, plastic surgery, dermatology, otolaryngology or oral-maxillo-facial surgery) they think are most appropriate to manage various problems of the head and neck. Subjects and Methods: Using a standardised questionnaire, we surveyed 853 medical students in 4 different years of training between January 2005 and September 2006 at two major medical schools. Results: 349 (41%) of 853 medical students completed the questionnaire. Overall, students identified otolaryngologists (52%), thyroidectomy (p=0.001) and parotidectomy (p=0.001) predominantly with otolaryngologists. At the midwest medical centre, students identified parotidectomy (p=0.007), thyroidectomy (p=0.01) and neck dissection (p=0.001) with otolaryngologists, whereas students at the eastern school identified these procedures with general surgeons. Compared to junior medical students, a significantly higher proportion of senior medical students identified parotidectomy (p=0.001) and thyroidectomy (p=0.002) with otolaryngologists. Conclusions: Otolaryngologists are perceived by medical students as experts in several head and neck procedures. However, this perception varies with the year and location of undergraduate medical training.
P333: CAUSES OF PATIENTS DELAY FROM THE ONSET OF SYMPTOMS OF ORAL/ OROPHARYNGEAL CANCER TO THE FIRST HEALTH PROFESSIONAL VISIT

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Background: Oral cavity and oropharynx cancer ranks among the most common head and neck neoplasms. A significant feature of oral cancer prognosis in minorities living in developed countries as well as the population living in developing countries is that patients will usually present at an advanced stage of disease. Patient delay in the diagnosis of oral and oropharyngeal cancer has been attributed to delay in recognizing the signs or symptoms of cancer, and difficulties in accessing professional care. Objectives: The aim of this study was to describe the patient attitudes after the onset of symptoms of oral and oropharyngeal cancer. Patients and Methods: Utilizing an extensive questionnaire and face-to-face interviews we examined 123 patients' self-diagnosis and attitudes before seeking health care due to oral or oropharyngeal cancer. All patients were treated in a tertiary cancer center hospital from 1999 to 2000. Results: A total of 123 consecutive patients were included in this study. There were 96 males (79%), with ages ranging from 20 to 78 years (median, 56.6 years). The educational level of the patients was: 76 illiterate or grade school (62%), 26 high school (21%) and only 21 university level (17%). Only 4 patients (3%) suspected that the diagnosis could be cancer from the start of the symptoms. The other most common self-diagnosis was: infectious diseases (44 cases, 36%); dental problems (28 cases, 23%); periodontal diseases, trauma or gingivitis (28 cases, 23%). The patients first attitudes were auto medication (53 cases, 43%), use of homemade medications or herbs (37 cases, 31%), and only 29 (24%) made an appointment with a physician or a dentist. Physicians were the first health professional to evaluate the patient in 57 cases (47%), followed by dentists (42 cases, 34%). Conclusions: The use of the information about patients' self-diagnosis and behavior prior to seeking health professional assistance is useful for highlighting patients' attitudes that can prevent the establishment of early diagnosis. The establishment of public health policies that privileges public education is required as a fundamental measure for cancer prevention and early diagnosis.

P334: EPIDEMIOLOGICAL TRENDS IN LARYNGEAL CARCINOMAS

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Objective: The purpose of the study was to determine significant correlations between epidemiological factors such as age, sex, tobacco and ethanol exposures, and important clinical issues such as tumor site and loco-regional extension, in mucosal squamous cell carcinomas of the head and neck. A primary focus was made on the laryngeal carcinomas and a potential role of ethanol exposure in nodal extension was particularly investigated. Methods: A retrospective study was conducted between January 2000 and January 2007 in our institution, a tertiary care hospital, known as the principal referral center for head and neck cancer management in the country. A complete review of sinonasal, oropharyngeal, oral, hypopharyngeal, and laryngeal epidermoid cancers was performed. All patients were treated by the same multidisciplinary team consisting of two Head and Neck surgeons, two medical oncologists and one radiotherapist. Results: 254 patients were included in the study, accounting for 198 males with a mean age of 64 years, and 56 females with a mean age of 58 years. 217 patients had a tobacco exposure history (85.5%), 91 patients had an alcohol exposure history (36.5%), and 85 patients had a combined tobacco/ethanol exposure (33.5%). 89 tumors were localized to the larynx (74.5%), and divided into 109 glottic, 60 supraglottic, and 20 transglottic lesions. The remaining 65 tumors accounted for non-laryngeal localizations (38 oral, 11 oropharyngeal, 11 hypopharyngeal, 4 sinonasal and one unknown primary). On bivariate analysis, females had more advanced T and N stages than males. Non-laryngeal lesions also had more advanced T and N stages than the laryngeal ones. Tobacco, ethanol, and combined tobacco/ethanol exposure were significant determinants of higher T and N stages. When considering the laryngeal cancer group, we found that females preferentially presented supraglottic lesions as compared to the males. Furthermore the supraglottic lesions had significantly more advanced T and N stages than the glottic/transglottic ones. Conclusions: There is a clear predominance of laryngeal carcinoma among all other head and neck localizations in our population, and this might be attributed to a heavier tobacco than ethanol exposure. This is also supported by the relative rarity of the hypopharyngeal localization in our series, which is much more prevalent in some occidental countries such as France, where tobacco is a heavier ethanol consumption. We could not demonstrate a role for ethanol exposure as an independent determinant of more aggressive nodal extensions. But we confirmed the negative synergistic effect of the combined tobacco/ethanol exposure on the N staging.

P335: LATE PRESENTATIONS OF HEAD AND NECK CANCERS: ARE THEY REALLY UNNOTICED?

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Objective: To evaluate the various reasons for the late presentation of disease in Indian scenario and steps which can prepone presentation. Patient and Methods: Patients attending outdoors of a private cancer clinic from oct.1996 till sept2007 were evaluated for the various reasons for their delayed presentation. Data was available from 1200 such patients over 11 years. 23% of the pts by biopsy fearing that it might spread the disease and 40% flatly refused it. 30% individuals mistook it for a teeth induced ulceration and were not ready to accept it as anything serious. Even in pts with neck nodes more than 50% considered neck nodes to be tubercular which is fairly well recognized in our societies a curse of god. nearly 20 % came with some sort of skin application already done and in majority of cases leading to skin exocriation and ulcerations.Almost 1/3rd patients were taking alternative treatment [with cancer not yet confirmed] just because of the apprehension of the complications of chemo-radiotherapy or surgery. Discussion: A combination Ignorance, misbelives, poverty and healthgivers from alternate system of medicine(homeopathy, electropathy , faith-healers etc) lead the patient to believe that their disease can be treated without the cumbersome route of modern medicine. Almost 70% of patients were of the mind that they had cancer but were not mentally ready to accept it. Conclusion: delay in pt reaching the doctor is in majority of cases not because of an unnoticed lesion but mainly because of either apprehension or misguidance.

IMAGING/EARLY DETECTION

P336: NARROW BAND IMAGING AND HIGH DEFINITION TELEVISION IN HEAD AND NECK CANCER: PROSPECTIVE STUDY ON 160 PATIENTS

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Objective: Narrow Band Imaging (NBI) is an optical technique in which a filtered 415 nm wavelength light enhances mucosal vasculature and better identifies superficial neoplasms thanks to their neangiogenetic pattern. NBI accuracy is implemented by combining it with a High Definition Television (HDTV) camera giving 1080 lines of resolution. Aim of this paper is to prospectively evaluate the diagnostic gain of NBI + HDTV and of HDTV WL in the evaluation of head and neck squamous cell carcinomas (HNSCC). Methods: 160 patients affected by HNSCCs or previously treated for them were prospectively evaluated by NBI and WL + HDTV between April and December 2007. They were divided in 2 groups: Group A included 59 patients submitted to pre- and intraoperative NBI and WL evaluation, while Group B included 101 subjects evaluated at least 6 months after treatment. Group A patients were evaluated in the pre-treatment setting by flexible WL and NBI videobodscopy of the upper aerodigestive tract. Surgical candidates underwent intraoperative WL and NBI endoscopy by rigid telescopes coupled to HDTV. Tumor resection was performed taking into account NBI information to evaluate the specimen on the basis of ethanol data. Group B patients were evaluated by flexible WL and NBI videobodscopy. In case of positive WL and/or NBI findings, they underwent biopsy under local or general anesthesia. In this setting they received intraoperative HDTV WL and NBI endoscopy. Sensitivity and positive predictive values of NBI + HDTV and of HDTV WL endoscopy were calculated. Results: 24 out of 59 patients (41%) in Group A showed adjunctive preoperative videobodoscopic findings with NBI when compared to standard WL videobodscopy. On the other side, only 18 out of 91 patients (20%) in Group B had positive NBI findings with planar WL endoscopy, while 16 patients had positive NBI findings with combined HDTV WL and NBI endoscopy. Conclusions: NBI is a real technique that helps to plan preoperative and intraoperative local therapy. More studies on this topic are needed.
tion ranging from invasive carcinoma to intraepithelial dysplasia. Sensitivity of flexible NBI, HDTV NBI, and HDTV WL were 88%, 100%, and 68%, respectively. Positive predictive values were 76%, 75%, and 86%, respectively. 8 out of 101 patients (8%) in Group B showed positive NBI videodensocpic findings. All these lesions were confirmed as suspicious at intraoperative HDTV NBI, while HDTV WL endoscopy was positive in 4 cases only (50%). 5 out of 8 positive lesions (62%) were histologically confirmed as carcinoma in situ (3 cases), microinvasive (1), and invasive carcinoma (1). Sensitivity of flexible NBI, HDTV NBI, and HDTV WL were 100%, 100%, and 60%, respectively. Positive predictive values were 62%, 62%, and 75%, respectively. Conclusions: NBI ± HDTV is useful in better defining tumor extension in the pre- and intraoperative setting (up to 10 tumors), detection of synchronous lesions (4), evaluation of incomplete treatment response to RT before planned neck dissection (2), identification of unknown primaries (1), and tumor progression surveillance in oral cavity lichen planus (1). NBI has a role also in the postoperative setting for early detection of recurrences (4 cases) and metastatic tumors (1). Overall, 23 out of 160 patients (14%) had a diagnostic gain by application of this technique.

Objective: Ultrasonography provides highest sensitivity in the detection of lymph nodes (LN) in patients with a given tumor. Currently not many systematic examinations have been performed so far. The aim of this study was to evaluate the significance of lymph node malignancy in LN to histopathologic examinations. Patients and Methods: In a prospective study ultrasound of the neck was performed in 100 patients who underwent surgery for a squamous cell carcinoma of the oro- or hypopharynx respectively. In all patients the number of LN, the size, shape, demarcation, echogenicity, hilar structure, and perfusion pattern was assessed. The nodes were marked on the skin and relocated in the neck dissection block after histologic examination of particular nodes. The sonographic characteristics were then compared to results of histopathologic examination and, when available, to preoperative CT and MRI scans. Results: In the 100 patients assessed 388 LN were detected sonographically. 242 of them were considered malignant (62.4%), the other 146 LN were considered reactive and therefore benign. But it is controversial that Ultrasonography guided fine needle aspiration (USG-FNA) should be routinely used to incidentally detected nonpalpable thyroid nodules.

Objective: The availability of more sensitive ultrasonographic techniques has led to an increased number of patients who are referred for fine needle aspiration biopsy (FNAB) of the thyroid gland. The aim of this study was to evaluate the diagnostic yield of FNA biopsy of thyroid incidentalomas, with special emphasis on the significance of solitary nodules.

Methods: We reviewed the records of 208 patients who underwent surgery for a squamous cell carcinoma of the oro- or hypopharynx respectively. In all patients the number of LN, the size, shape, demarcation, echogenicity, hilar structure, and perfusion pattern was assessed. The nodes were marked on the skin and relocated in the neck dissection block after histologic examination of particular nodes. The sonographic characteristics were then compared to results of histopathologic examination and, when available, to preoperative CT and MRI scans.

Results: In the 100 patients assessed 388 LN were detected sonographically. 242 of them were considered malignant (62.4%), the other 146 LN were considered reactive and therefore benign.

Conclusions: Sonomorphologic parameters which are most predictive for malignancy in LN to histopathologic examinations were performed comparing ultrasonographic signs for malignancy in LN to histopathologic examinations.

P339: SONOMORPHOLOGIC MALIGNANCY GRADING OF LYMPH NODE METASTASES IN PATIENTS WITH ORO- OR HYPOPHARYNGEAL CANCER

Objective: Ultrasonography provides highest sensitivity in the detection of lymph nodes (LN) in patients with a given tumor. Currently not many systematic examinations have been performed so far. The aim of this study was to evaluate the significance of lymph node malignancy in LN to histopathologic examinations.

Methods: In a prospective study ultrasound of the neck was performed in 100 patients who underwent surgery for a squamous cell carcinoma of the oro- or hypopharynx respectively. In all patients the number of LN, the size, shape, demarcation, echogenicity, hilar structure, and perfusion pattern was assessed. The nodes were marked on the skin and relocated in the neck dissection block after histologic examination of particular nodes. The sonographic characteristics were then compared to results of histopathologic examination and, when available, to preoperative CT and MRI scans.

Results: In the 100 patients assessed 388 LN were detected sonographically. 242 of them were considered malignant (62.4%), the other 146 LN were considered reactive and therefore benign.

Conclusions: Sonomorphologic parameters which are most predictive for malignancy in LN to histopathologic examinations were performed comparing ultrasonographic signs for malignancy in LN to histopathologic examinations.

P338: ULTRASONOGRAPHY-GUIDED FINE NEEDLE ASPIRATION OF INCIDENTALLY DETECTED NONPALPABLE THYROID NODULE

Objective: With the availability of more sensitive ultrasonography, a larger number of nonpalpable thyroid nodules can be detected. But it is controversial that Ultrasonography guided fine needle aspiration (USG-FNA) should be routinely used to incidentally detected nonpalpable thyroid nodule. The purpose of this study is to investigate the clinical significance of thyroid incidentalomas and the usefulness of the USG-FNA in the management of thyroid incidentalomas.

Methods: A retrospective study was performed on 208 patients who underwent USG-FNA for thyroid incidentalomas smaller than 1.5 cm from 2002 to 2006. The cytologic findings were compared with the ultrasonographic findings and the surgical pathology.

Results: Suspicious malignant sonographic findings were detected in 48 cases. And in 10 cases, more than two malignant findings were detected. Of the 208 cases, 159 cases were cytologically diagnosed as benign lesion (76.4%), 7 cases as follicular neoplasm (3.3%), 33 cases as malignancy (15.8%), and 3 cases as inadequate specimen (4%). Of the 48 cases with more than two suspicious malignant sonographic findings were more frequently diagnosed as malignancy at cytology than those with one and less (p=0.001). Of the 40 cases with follicular neoplasm and malignant cytology, 37 cases underwent surgery and 30 cases were confirmed to malignancy on the postoperative pathologic diagnosis. In the cases diagnosed as malignancy on pathology, extracapsular extension was present in 9 cases (30%), and nodal metastasis in 8 cases (26.7%). The specificity, sensitivity, and accuracy of the USG-FNA for malignancy were 93.3%, 71.4%, and 89.1%, respectively.

Conclusions: USG-FNA is a useful diagnostic tool in the management of thyroid incidentaloma especially when more than two suspicious malignant sonographic findings are detected. The clinical characteristics are not significantly different between palpable and nonpalpable nodules.

P339: CONFounding CHARACTERISTICS IN THE AUTOFLuorescence SCREENING FOR ORAL LESIONS

Objective: Autofluorescence (AF) light is a potential screening tool for premalignant and malignant oral lesions. Though this technique has been shown to identify high grade lesions and cancers, it is less at identifying of early lesions from benign conditions, resulting in false positives. We performed an analysis to correlate the histopathological characteristics of the oral tissue with in-vivo AF in an effort to identify the characteristics contributing to false positives.

Methods: This study includes 30 high-risk patients, who underwent oral examination at the Department of Dentistry and Head and Neck Surgery at Roswell Park Cancer Institute, Buffalo, NY. In 2006 and July 2007. All patients underwent examination by the same dentist with a machine equipped with a white light and an AF light source. Suspicious areas were identified under the WL; then under AF. Biopsies were obtained from every suspicious area whether detected by WL or AF, with one normal control biopsy from the oral cavity. All the biopsies were reviewed by the same pathologist. For analysis purposes the pathologic diagnoses was graded into 8 major categories: normal, parakeratosis without atypia (PK), parakeratosis with atypia (PKA), mild dysplasia with/without parakeratosis (MD), moderate dysplasia, severe dysplasia, in-situ carcinoma, invasive carcinoma. The other concurrent histopathological findings were grouped into two categories: benign histo-pathological findings (BPF) including scar tissue, fibrosis, skeletal muscle, salivary gland, edema and chronic inflammation; and Parameters such as hyperplasia, proliferative verrucous leukoplakia, oral lichenoid lesions, koilocytes, hyperkeratosis, hyperparakeratosis and hyperthorcorhesis. Presence of a cancer adjacent to the biopsied site was also noted. In this analysis we selected biopsies diagnosed as mild dysplasia or lower grade and tried to evaluate the influence of BPF or other parameters on AF outcome. This data included 14 normal (64%), 31 PK (52%), 34 PKA (63%), 48 MD (73%). All significance tests used a cutoff of p=0.05.

Results: Among the 9 false-positive normal biopsies, 4 had an underlying BPF (3-skeletal muscle, 1-salivary gland) and 3 with cancer adjacent to the biopsy site, which might suggest a field cancerization effect not identified by histopathology. None of the 5 true-negative biopsies had an underlying BPF. The presence of BPF or an adjacent cancer was significantly associated with AF+ status (p-value=0.03). Similarly, among the 16 false-positive PK biopsies, 8 had a coexisting hyperplasia and 6 had a co-existing BPF. Of the true-negatives, 1 had hyperplasia and 5 had BPF. The presence of hyperplasia or BPP with PKA significantly associated with AF+ (p-value=0.008). Among the AF+ PKA (n=23), 8 had concurrent hyperplasia and 14 had BPF. The presence of hyperplasia or BFP with PKA significantly associated with AF+ (p-value=0.003). However, independently, parakeratosis or hyperplasia did not significantly affect AF status.

Conclusion: Like dysplasia and carcinoma, hyperplasia associated with parakeratosis significantly correlates with AF+ (p-value=0.008). Among the AF+ PKA (n=23), 8 had concurrent hyperplasia and 14 had BPF. The presence of hyperplasia or BFP with PKA significantly associated with AF+ (p-value=0.003). However, independently, parakeratosis or hyperplasia did not significantly affect AF status.

P340: DIRECT AUTOFLUORESCENCE ENDOSCOPY IN MANAGEMENT OF PREMALIGNANCY AND CANCEROUS LARYNGEAL LESIONS - A CASE SERIES

Objective: Laryngeal dysplasia is a common clinical concern. Despite major advancements in otolaryngology, a significant number of patients with the condition progress to invasive carcinoma. Direct autofluorescence (AF) endoscopy of the larynx has proven to facilitate the detection and delineation of premalignant lesions, carcinoma in situ and cancer.

Methods: Patient with mild dysplasia of right vocal cord and severe dysplasia of left vocal cord was observed by autofluorescence endoscopy (DAFE, R.Wolf). At the same time the patient was examined by indirect
white-light laryngoscopy. In suspicion of progress of dysplasia, state was verified by histological examination. Results: After 13 months of observing, better state by indirect white-light laryngoscopy was showed. But AF examination proves the progress of the finding on right vocal cord while the finding on left vocal cord remains unchanged. Histological examination confirms the stationary state on the left vocal cord and change of right vocal cord mild dysplasia into ca in situ. The finding on the right vocal cord was treated by CO2 laser excision. Follow-up examinations by AF endoscopy confirm successful treatment of lesion 2 years after the excision.

Conclusion: Development of dysplastic lesions into invasive carcinoma does not have to be progressive. In the same patient, a severe dysplasia of one vocal cord may remain unchanged while the mild dysplasia of another vocal cord may be changed into ca in situ up to invasive carcinoma. AF endoscopy enables non-invasive and, for the patient, uncomplicated observation of precancerous and cancerous lesions of the larynx.

P341: DIGITAL IMAGE ENHANCEMENT FOR DETAILED ENDOSCOPY OBSERVATION: POSSIBILITY OF THE EARLY DETECTION OF HEAD & NECK LESION A.Tsunoda1, R.Kamiyama1, T.Sumi1 K.Kitamura1, S.Kishimoto1, K.Tsunoda2, 1Tokyo Medical and Dental University, Tokyo, Japan; 2National Institute of Sensory Organ, Tokyo, Japan

Objective: Endoscope is useful tools for head and neck cancer clinics. Especially for detection and diagnosis of nasopharyngeal, hypopharyngeal and laryngeal carcinoma. Recently, we had tried to use a new endoscopic device which uses a novel digital technique for superior endoscopic observation. We report here our clinical experience of this device and discuss the possibility of digital image enhancement technique for early detection of head and neck cancer. Methods: A new endoscopic device, EPK-i (Pentax, Tokyo) which had a new digital enhancement function, was used and applied to the patient after obtaining of written informed consent. Using specially programmed image modification function, this device automatically enhances endoscopic video images in two different ways. Contrast enhance (CE) mode modifies color distribution of the endoscopic images and emphasizes color changes on the organs. Surface enhance (SE) mode modifies changes of brightness and emphasizes uneven surface of organs. Image enhancements are done for an instant and real time video observation can be established. The observer can select appropriate enhancement mode for observation and these CE and SE can be coupled. Change of modes, i.e., normal to CE or SE, SE to CE can be done in an instant. Results: We had used this device over 150 cases for observation of upper aerodigestive lesions without any trouble. CE clearly depicted vessels beneath the mucous and also enhances surface structure of organs or lesions. Disorganization of patterns of vessels are well observed, especially, vessels around the tumor lesion. SE clearly depicted every lesion on the mucosal surface, such as leukoplakia or keratosis. Actually in this series, we found a very early hypoechoic carcinoma which had not been detected on SE at first. However, images except the vessels or uneven surface of mucous membrane were not modified therefore the nasal cavity, pharynx and larynx themselves were seemed to be natural on both image enhancements. These enhancement effects clearly depict slight changes on mucosal surface, destruction of vessel patterns and submucosal adhesion to the deeper structure and asymmetrical waves of vocal cords on stroboscopic observation. These changes, which are present in malignant lesion, the present enhancement technique may contribute to earlier detection of carcinomia in head and neck area. Results: For detailed endoscopic observation, several techniques are applied, such as iodine staining or narrow-band imaging. The latter device also supports superior endoscopic observation without application of medication. Based on our observation, present digital image enhancements are also beneficial to detailed observation of the lesion. However, these techniques do not need special light sources, only modifies specific points which may relate to the lesion on endoscopic images. Therefore the images themselves are quite natural, as a result, these image enhancements enable the superior endoscopic observation and may lead to early detection of the head and neck carcinoma.

P342: GENOME-WIDE METHYLATION ARRAY ANALYSIS OF SALIVA FOR ORAL CANCER DIAGNOSIS C.T.Viet1, B.L.Schmidt2, 1University of California, San Francisco, School of Dentistry, San Francisco, CA; 2University of California, San Francisco, Department of Oral Maxillofacial Surgeon, San Francisco, CA

Background: Promoter hypermethylation is an epigenetic change that is a critical step in oral carcinogenesis. It is a more frequent mechanism in silencing cancer-associated genes than genetic changes, making it a more attractive diagnostic marker than detecting a mutation or measuring gene expression. Saliva is an ideal diagnostic fluid for screening patients at risk for oral cancer. To date there have been no methylation array studies evaluating whole genome promoter hypermethylation in the saliva of oral cancer patients. Objective: To perform a genome-wide methylation array of 807 cancer-associated genes using the saliva of oral cancer patients with the objective of identifying highly positive methylation sites which would hold diagnostic and predictive value as a biomarker. Methods: We performed the methylation array on DNA extracted from preoperative saliva, postoperative saliva and tissue of 13 patients with oral squamous cell carcinoma, and saliva of 10 normal subjects. We identified genes that are highly methylated in preoperative saliva samples, but not methylated in the postoperative saliva samples or in normal subjects. Results: High quality DNA was obtained and the methylation array was successfully run on all samples. We identified significant differences in methylation patterns between the preoperative and postoperative saliva from cancer patients. We identified a suite of 8 genes that showed high methylation in preoperative saliva but were not methylated in postoperative saliva or normal subjects, which could be used as a composite biomarker for oral cancer detection. When the 8 genes are used as a composite biomarker we were able to identify 85% of the cancer saliva samples as belonging to cancer patients. This sensitivity level has never been achieved in previous methylation studies. Cluster analysis of the methylation array results successfully discriminated between preoperative and postoperative saliva samples. Conclusions: As one of only two places in the US running this methylation array we report for the first time genome-wide methylation arrays analysis in oral cancer patients. Our statistical approach demonstrates the proof of principle that methylation array analysis of saliva will generate a suite of cancer related genes that are specific and can be used as a composite biomarker for the early detection of oral cancer.

P343: EMERGING OPTICAL TECHNOLOGIES: A POTENTIAL ROLE IN SURGICAL MARGIN ASSESSMENT? V.Stepanek1, A.M.Gillenwater1, 1UT MD Anderson Cancer Center, Houston, TX

Background: Currently the margin detection during tumor excision is a process largely dependent on the ability and experience of the surgeon and the pathologist. Surgeons use white light visual examination and palpation to define the extent of disease. The resected specimen involves tumor and approximately 1 cm of surrounding normal tissue. Objective: To evaluate the use of fluorescence imaging for evaluation of the margins of cancer and precancer in oral mucosa in a surgical setting. Methods: A multispectral digital microscope (MDM) instrument has been developed to evaluate the use of fluorescence and reflectance imaging at the different wavelengths for improved visualization of the peripheral extent of dystrophic changes in oral mucosa. Results: Several cases are presented documenting the different percentage of extent of dystrophic changes in patients undergoing surgical resection for oral cancer. Optical images are correlated with pathological findings. Fluorescence wavelengths of 420nm and 450nm provided the best contrast between normal and dystrophic mucosa. Conclusions: Fluorescence imaging has a potential use for delineating the margins of dysplasia with the field of cancerization and oral cancer. Further studies are indicated to determine the role of this optical technology in tumor margin delineating.

P344: PHOTODETECTION AND ERADICATION OF ORAL NEOPLASIA IN AN ANIMAL MODEL J.Phillips1,2, M.Wilson1,2, J.Pharar1,2, H.Kawakami-Wang1,2, K.Otani1,2, L.E.Epstein1,2, 1Beckman Laser Institute, University of California, Irvine, CA; 2Beckman Laser Institute, University of California, Irvine, CA; 3University of Illinois at Chicago, College of Dentistry, Chicago, IL

Objective: Optical techniques for non-invasive early detection, mapping and eradication of oral premalignant lesions (OPLs) and oral squamous cell carcinoma (OSCC) offer many advantages and may benefit patients greatly. Our objective was to determine in the hamster cheek pouch carcinogenesis model whether photodynamic diagnosis and therapy using toluidine blue (TBO) and light at 633nm can be used for early detection, mapping and selective photodestruction of neoplastic oral tissues. Methods: DMBA carcinogenesis was applied to one cheek pouch in 20 hamsters for 6 weeks. After topical application of acetic acid and 0.5% TBO, cheek pouches were irradiated using previously identified parameters: 15 J/cm2, 30 J/cm2, 45 J/cm2, 60 J/cm2 and exposure durations of 3 min, 6 min, 9 min and 12 min. After laser irradiation, animals were sacrificed and cheek pouch tissues underwent routine histopathological preparation and
evaluation. Using (a) TBO fluorescence and (b) histopathology, lesion presence was scored as yes/no and lesion delineation was mapped microscopically using a grid and IPLabTM software. Results: Areas of pathology were clearly identified by TBO fluorescence (k=0.95 for presence, k=0.85 for delineation). At all laser parameters tested, selective photodestruction was seen, as evidenced by intra-vascular thrombosis and neovascularization in the pathological tissues. Cellular thermal damage was evidenced by typical collagen bands, vacuolization and loss of inter- and intracellular integrity in the areas of neoplasia. Maximal photodestruction with minimal thermal damage was observed at 30 J/cm² after 9 min irradiation. Conclusions: Topical toluidine blue may be a useful tool for photodynamic diagnosis and therapy of neoplasia in the oral mucosa. Supported by: CA TR98-64 (LAMAPP R01 RR19722), DOE DE09-03-ER 01227, NIH EB00293 CA177177, NS11857 RV924, 2742.54.1.6.2.3.2.1.a. (Boehringer Ingelheim Animal Health, West Point, PA; Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT; Zila Pharmaceuticals, Phoenix, AZ, NIH EB-00293 CA91717, NR-01192, EB0002SS, EB002494 and AR47551).

P345: CT FINDINGS PREDICTIVE OF CERVICAL METASTASIS AND EXTRACAPSULAR SPREAD OF DISEASE IN HEAD AND NECK CANCER T.J. O’Keefe1, S. Dubiner2, 1Albert Einstein College of Medicine/Long Island Jewish Medical Center, Bronx, NY; 2Long Island Jewish Medical Center/Albert Einstein College of Medicine, New Hyde Park, NY

Objective: To assess the ability of CT scan to predict the presence of cervical lymph node metastasis in head and neck cancer, and to determine whether lymph node necrosis on imaging is predictive of extracapsular spread (ECS) in metastatic neck disease. Methods: The study population comprised 104 patients with head and neck cancer, who underwent CT dissections between 1997-2007. The medical records of these patients were reviewed to compare the preoperative CT scan findings with the pathologic specimens after surgery. Imaging studies were obtained from multiple hospitals and radiology referral centers in the region. All surgeries were performed at one tertiary care institution. The site and stage of each patient’s cancer, as well as the type of neck dissection performed were recorded. The number of pathologically enlarged cervical lymph nodes noted on CT scan, as well as the presence of central necrosis seen on imaging was recorded for each case. Pathology reports were reviewed, as well. The number of metastatic lymph nodes found, as well as the presence of ECS noted in each specimen were recorded. CT findings were compared to pathologic specimens to assess the accuracy of the images in predicting metastatic disease and ECS. Results: One hundred and four patients underwent 127 neck dissections. Forty-four radical or modified radical neck dissections and 83 selective neck dissections were performed. Fifty-one patients had no palpable neck disease at the time of operation, and thus underwent elective neck dissection. In 84 cases, a CT scan was obtained prior to neck dissection and a report was available for review. CT scan was 86% sensitive and 88% specific for predicting metastatic disease in cervical lymph nodes. The positive predictive value (PPV) was 90% and the negative predictive value (NPV) was 82%. ECS was noted in 38 pathologic specimens, 28 of which had preoperative CT reports available for review. Necrotic lymph nodes were identified on 13 CT images. Two other CT scans showed evidence of ECS without necrotic lymphadenopathy- one image showed obliteration of extranodal tissue planes, and another scan showed carotid encasement with metastatic disease. Imaging was negative for necrotic lymph node in 67 cases. When necrotic lymph nodes were used as a predictor of ECS, CT scan was 43% sensitive and 94% specific for ECS of disease. The PPV was 80% and the NPV was 75%. Conclusions: CT scan can accurately predict the presence of metastatic disease in the neck, with a PPV of 90%. When necrotic lymphadenopathy is used as a predictor of extracapsular spread of disease, CT scan is 43% sensitive and 94% specific for the presence of ECS. Though ECS is often present without evidence of lymph node necrosis on imaging, the presence of necrotic lymphadenopathy on CT scan is highly suspicious for the presence of ECS.

P346: LARYNGOCAROTID FISTULA UNDETECTED BY COMPUTED TOMOGRAPHIC ANGIOGRAPHY: CASE REPORT AND LITERATURE REVIEW D.J. Costa1, M.A. Varvares1, 1Saint Louis University School of Medicine, Saint Louis, MO

Background: Radiation therapy for head and neck squamous cell carcinoma adversely affects surrounding tissue and increases the risk of carotid artery rupture. We present a patient who developed laryngeal radionecrosis and a fistula tract between the larynx and left internal carotid artery that was not identified on computed tomographic angiography (CTA). Methods: Case report and literature review. A PubMed and Cochrane database search was performed for cases meeting inclusion criteria: 1) fistula between the carotid artery and aerodigestive tract; 2) fistula not the result of foreign body erosion or traumatizing the carotid artery. Results: No cases of laryngocarotid fistula were identified. Eight additional cases of carotid to upper aerodigestive tract fistula were identified and reviewed. Seven patients had prior radiation therapy to the neck. None of the patients were evaluated with CTA. One patient underwent formal carotid angiography and was treated with endovascular therapy. Five patients were treated with surgical exploration. Four patients with this condition died as a result of complications from the fistula tract. Conclusions: Fistula between the carotid artery and upper aerodigestive tract is a rare event with high mortality. CT angiogram in our case failed to detect an abnormality of the carotid artery. Current treatment algorithms recommend angiography for carotid disruption. Based on our experience and review, formal carotid arteriogram is advisable if carotid disruption is suspected.

P347: NECK DISSECTION PLANNING BASED ON POST-CHEMORADIATION COMPUTED TOMOGRAPHY IN HEAD AND NECK CANCER PATIENTS A. Langerman1, R. Comstock1, S. Kondo1, A. Abramovitch1, K. Kasza1, E. Vokes1, K. Stenson1, 1University of Chicago, Chicago, IL

Objective: Computed tomography (CT) is a useful tool for planning neck dissection, but the correlation between post-chemoradiation neck findings on CT and intraoperative findings is not well described. Methods: Retrospective review of computed tomographic, intraoperative, and pathologic findings in 34 patients who underwent 43 planned post-chemoradiation hemi-neck dissections for pre-treatment N2 or greater disease. Results: Of 34 neck dissections, 25 (74%) were elective neck dissections (ENND), 2 (5%) were modified radical (MRND), and 2 (5%) were radical neck dissections (RND). The internal jugular vein (IJ) was sacrificed in 6 of the 39 SND (15%), 1 of the 2 MRND, and the 2 RND. The sternocleidomastoid muscle (SCM) was sacrificed in the 2 MRND and 2 RND. The IJ was sacrificed in 7 (78%) of the 9 dissections where the IJ was abnormal on pre-operative CT (filling defect or thrombosed), versus 2 (6%) of the 34 dissections with a normal IJ on CT (p<0.001; positive predictive value (PPV) = 78%, negative predictive value (NPV) = 94%). The SCM was sacrificed in 4 (36%) of the 11 dissections where the tissue plane between the carotid sheath and the SCM was indistinct on CT versus 0 (0%) of the 32 dissections with a radiographically normal SCM tissue plane (p=0.003; PPV = 36%, NPV = 100%). Conclusions: Filling defects or thrombosis of the IJ is highly predictive of need for sacrifice intraoperatively, which may effect planning especially in bilateral neck dissections where an effort may be made to preserve at least one vein. Presence of a clear tissue plane between the SCM and carotid sheath predicts ability to preserve this muscle.

P348: THE USEFULNESS OF NARROW BAND IMAGING (NBI) MAGNIFYING ENDOSCOPY IN DIAGNOSING SUPERFICIAL LARYNGOPHARYNGEAL CARCINOMA Y. Sabu1, T. Omoji1, H. Kawakubo1, Y. Araki1, T. Motomura1, A. Kanno1, H. Sugiru1, 1Kawasaki Municipal Hospital, Kawasaki, Japan

Purpose: The purpose of this study is to examine the usefulness of high-resolution and magnification endoscopy with NBI which is the new technique in diagnosing superficial laryngopharyngeal carcinoma. Object & Method: The superficial laryngopharyngeal carcinoma means that the depth of cancer invasion is within the subepithelial layer. For the Cases of superficial laryngopharyngeal carcinoma treated by endoscopic treatment (EMRC,EILPS,ESD and Micro surgery), we analyzed the characteristics of the magnification endoscopy with NBI. Results: We have 145 cases (238 lesions) of laryngopharyngeal superficial carcinoma from Jan 2000 to Oct 2007, 137 male and 8 female, ranging in age from 39 to 86 years (average 62.8). Among the 145 cases, 123 cases (202 lesions) were examined with the NBI magnification endoscopy. The endoscopic treatment was performed; 39 cases of EMRC, 50 cases of EILPS, 2 cases of ESD, and 11 cases of Micro surgery. The endoscopic type of lesion was the following: 23 lesions were superficial and protruding and slightly elevated type (0.IIa type), 113 were flat type (0.Ilb type), 8 were slightly depressed type (0.Ilc type), 1 was superficial and excavated type (0.Ilb type), and 55 were mixed types. The 18.I and 1a.I types were observed as white papillary surface with atypical vascular growth under white-light observation, whereas under NBI observation, they were seen as well-defined white lesions. The 0.Ilb type lesions were observed as flat and slight reddish area under white-light observation, whereas under NBI observation, they were seen as brownish area (BA) with atypical vascular growth. Under NBI observation, the 0.Ilb type lesion which is difficult to be found was seen as the characteristic BA,
A number of reports indicate that in the surgical treatment of oral cancer is the 6th most common cancer worldwide. Early post-radiotherapy neck burden.

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Background: A number of reports indicate that in the surgical treatment of oral and oropharyngeal cancer, dysplasia at surgical margins is a predictor of local recurrence. Normal oral and oropharyngeal epithelial cells store glycerogen in increasing quantity from the basal layer to the surface. Dysplastic cells have been shown not to store glycogen and this metabolic difference can be exploited to identify squamous epithelial dysplasia by staining the mucosa with Lugol’s iodine. We have previously shown that use of Lugol’s iodine achieved a marked reduction in margins positive for dysplasia, carcinoma-in-situ, and invasive carcinoma in patients undergoing primary surgery for oral cavity or oropharynx squamous cancer. In our recent series of 50 consecutive patients the rate of margins positive for these primary tumours with a 1 cm macroscopic margin plus any adjacent mucosa removed of mucosal SCC with a macroscopic 1cm margin as well as removal of adjacent macroscopic leukaemia. The Lugol’s iodine group have had superior results with Lugol’s iodine use to identify dysplasia at the tumour margin. Briefly, the mucosa is washed with saline and carboxyhydrate is applied as a mucolytic. This is rinsed with saline and Lugols iodine applied (1:25% potassium iodide). These patients undergo removal of primary tumours with a 1 cm macroscopic margin plus any adjacent mucosa unstained after the topical application of Lugol’s iodine, where this is feasible. Histopathology reporting of the RCPath minimum dataset is analysed for the presence of dysplasia, Ca-in-situ, or invasive SCC at a mucosal surgical margin. After removal of the tumour and before placing in formalin, surgical resection specimens have mucodyne and then Lugols iodine applied in order to ensure blinding of the assessing histopathologist.

Objective: Our primary outcome measure in this trial is the incidence of positive surgical margins. Secondary aims include the analysis of complete resection and tumoral disease.

Methods: Patients are randomised to control or Lugols iodine staining using a web based randomisation method which is stratified by centre and by surgeon. Those in the control group undergo removal of mucosal SCC with a macroscopic 1cm margin as well as removal of adjacent macroscopic leukaemia. The Lugol’s iodine group have had superior results with Lugol’s iodine use to identify dysplasia at the tumour margin. Briefly, the mucosa is washed with saline and carboxyhydrate is applied as a mucolytic. This is rinsed with saline and Lugols iodine applied (1:25% potassium iodide). These patients undergo removal of primary tumours with a 1 cm macroscopic margin plus any adjacent mucosa unstained after the topical application of Lugol’s iodine, where this is feasible. Histopathology reporting of the RCPath minimum dataset is analysed for the presence of dysplasia, Ca-in-situ, or invasive SCC at a mucosal surgical margin. After removal of the tumour and before placing in formalin, surgical resection specimens have mucodyne and then Lugols iodine applied in order to ensure blinding of the assessing histopathologist.

Results: The primary outcome measure in this trial is the incidence of positive surgical margins. Secondary aims include the analysis of complete resection and tumoral disease.

Conclusion: Patients in the Lugol’s iodine group had a significantly lower rate of positive surgical margins compared to the control group (38% vs 73%, p=0.02). The Lugol’s iodine group also had a higher rate of complete resection (85% vs 70%, p=0.04). These findings suggest that the use of Lugol’s iodine may be a valuable tool in assessing surgical margins in patients undergoing primary surgery for oral cavity or oropharynx squamous cancer.
MELANOMA

P354: CORRELATION OF INTRA-OPERATIVE RADIOACTIVITY COUNTS AND POSITIVE SENTINEL NODE BIOPSY IN HEAD AND NECK MELANOMA

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Objective: Sentinel node biopsy (SNB) has become an increasingly accepted method of management for head and neck cutaneous melanoma. Studies of this technique in the head and neck demonstrate that multiple radioactive or “hot” nodes are common, yet not all these nodes prove to be pathologically positive. The objective of this study is to determine the relationship between intra-operative radioactivity counts and positive sentinel lymph node status in cutaneous head and neck melanoma. The potential utility of this information is to determine a threshold count for a node to be excised during SNB and possibly minimize the number of nodes removed during SNB.

Methods: A retrospective review of consecutive patients with cutaneous head and neck melanoma who were pathologically staged with SNB at a tertiary care academic medical center over a 22-month study period. Exclusion criteria consisted of a prior history of neck surgery or other primary melanoma excision. Patients were included only if they demonstrated multiple hot lymph node subsites on lymphoscintigraphy and if the actual radioactivity counts were documented. Institutional review board approval was obtained and 147 patients who met these criteria. All patients had biopsy-proven melanoma of Breslow depth > 1 mm; a subset of patients with Breslow depth < 1 mm were included if other adverse prognostic factors were present (age < 35 years, ulceration, deep margin extension). All patients underwent pre-operative lymphoscintigraphy using technetium Tc99m sulfur colloid as well as intra-operative iodosulfate blue dye injection to localize the sentinel nodes. Radioactivity counts obtained via gamma probe were recorded. Radioactivity values were compared between histologically positive and histologically negative subsites.

Results: A sentinel lymph node was located and excised in 100% of patients. The mean number of sentinel lymph nodes harvested was 1.41 (range 1-7). Twenty-seven (12%) patients (20%) had a histologically positive sentinel lymph node (SNL) biopsy. Eighteen of these 29 patients (62%) had data available for comparison of their pathology with their SNL radioactivity counts. The sentinel lymph node with the highest radioactive count was also positive for metastatic melanoma in all 18 patients (100%). For all patients with histologically positive sentinel lymph nodes, a comparison was made of the gamma count at that subsite versus the gamma count at the other “hot” subsites where nodes were histologically negative. In all cases where a subsite had node(s) positive for metastatic melanoma, the gamma count of that site was higher than the counts at pathologically negative sites within the same patient. Specifically, if a patient were going to have a histologically positive node, the subsite with the highest gamma count represented the positive subsite. Conclusions: Head and neck cutaneous melanoma patients treated with SNB often demonstrate radioactivity in multiple nodal subsites, making effective localization of the sentinel node difficult. This study demonstrates that for a select group of patients who drain to multiple nodal basins within the head and neck, lymphoscintigraphy counts are a reliable predictor of the positive sentinel node.

P355: PROGNOSTIC IMPLICATION OF SENTINEL LYMPH NODE BIOPSY IN CUTANEOUS HEAD AND NECK MELANOMA

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Objective: The efficacy of sentinel lymph node biopsy (SLNB) in the management of cutaneous melanoma of the head and neck (CMHN) is well recognized. SLNB provides important prognostic information. Furthermore, more aggressive treatment in SLNB positive patients has the potential to improve outcomes. The goal of this analysis is to report our most current results of SLNB for CMHN and to explore the prognostic implications of positive SLNB for this cohort of patients. Methods: 236 consecutive patients with CMHN who underwent SLNB at MSKCC between 1996-2007 were identified from an existing database. Retrospective chart review was used to collect data on host and tumor characteristics, clinical, radiological and histopathologic details. Endpoints of interest included neck recurrence-free survival (NRFs) and melanoma-specific survival (MSS). Standard statistical methods were used for descriptive statistics and for survival analysis. Results: At least one sentinel lymph node was identified in 217 (92%) patients. Twenty-seven (12%) patients had at least one positive sentinel lymph node. Of these, the sentinel lymph nodes of 14 (52%) patients were identified on frozen section and the remaining 13 were only identified after further sectioning and/or immunohistochemical analysis post-operatively. With a median follow-up interval after SLNB of 36 months (range 1-124), the 3-year NRFs and MSS for the entire group calculated by the Kaplan-Meier method was 91% and 94% respectively. Comparing SLNB positive and negative patients, the 3-year NRFs and MSS were 93% vs 89% (p=NS) and 97% vs 75% (p<.003) respectively. 19 (70%) patients who had a positive SLNB underwent an immediate neck dissection.
while the neck was observed after positive SLNB in the remaining 30% based on the clinicians' judgment. The difference in MSS between these two groups was not statistically significant (92% vs 75%, p=0.45). Fifteen of 190 patients (8%) with negative SLNB recurred in the nodal basin. This, however, did not have a statistically significant effect on 3 year MSS when compared to the remainder of the negative SLNB cohort 97.9% vs 90% (p=0.09). **Conclusions:** A positive SLNB in patients with CMHN is associated with worse MSS and this subset of patients may benefit from more aggressive treatment. Frozen section identified slightly more than half of all positive sentinel nodes. This demonstrates the importance of permanent pathology, including multiple sectioning and immunohistochemistry, in identifying metastatic nodal disease. Patients with negative SLNB should be followed carefully since there is a small risk for neck recurrence.

**P356: THE MANAGEMENT OF METASTATIC MELANOMA OF UNKNOWN PRIMARY IN THE HEAD AND NECK K.F.Shannon1, F.Nouthis2, R.Majors3, K.Gao3, A.Spillane4, C.J.O'Brien1, J.F.Thompson1, 1Sydney Head & Neck Cancer Institute, Sydney, Australia; 2Sydney Melanoma Unit, Sydney, Australia**

**Aim:** To assess the outcomes of management of metastatic melanoma on unknown primary presenting in the head and neck. **Methods:** A retrospective analysis of patients of patients with metastatic melanoma that were metastatic to the parotid or cervical lymph nodes over a 15 year period at the Sydney Melanoma Unit from 1990 through to 2004. **Results:** Sixty three patients had surgical management (9 node biopsies, 35 neck dissection and 19 combined parotidectomies and neck dissections) and 37 (59%) received adjuvant radiotherapy. Overall disease specific survival was 52% at 5 years. Those with N3 disease had a significant reduction in survival (P=0.007) with a median survival of 18.5 months. Regional recurrence and survival was not shown to be altered by different types of neck dissection. Adjuvant radiotherapy did not improve neck recurrence rate. **Conclusions:** Unknown primary melanoma of the head and neck makes up less than 10% of head and neck melanoma metastases and these patients appear to have a worse prognosis compared with those that have a known primary. Patients with unknown primary melanoma have worse 5 year survival compared to the rest of the patients. The type of neck dissection and addition of adjuvant radiotherapy did not affect regional recurrence.

**P357: INTRAOPERATIVE FROZEN SECTION ANALYSIS DIFFERENTIATES EXTRACAPSULAR SPREAD OF MELANOMA FROM STAINING OF ADJACENT TISSUE A.R.Scott1, J.D.Richmon1, B.Z.Pilch2, J.W.Rocco3, 1Massachusetts Eye and Ear Infirmary, Boston, MA; 2Massachusetts General Hospital, Boston, MA; 3Massachusetts Eye and Ear Infirmary, Massachusetts General Hospital, Boston, MA**

**Objective:** To demonstrate how intraoperative frozen section analysis may distinguish melanosis from perineural melanoma, resulting in improved functional outcome through facial nerve preservation. **Methods:** Case report and review of the literature. **Results:** We present a case of a 62 year-old gentleman who had scalp melanoma, multiple lymph nodes at risk of metastasis. At the time of superficial parotidectomy and neck dissection, several pigment-laden lymph nodes were discovered. Immediately deep to the affected lymph nodes within the superficial lobe, there was staining of several branches of the facial nerve and deep parotid tissue. In an effort to distinguish between extracapsular spread of melanoma from the intraparotid lymph nodes and staining of nearby tissues with melanin, a pigmented nerve segment was excised from a zygomatic branch of the facial nerve after stimulation of the nerve. The melanotic staining from extracapsular extension and perineural involvement was identified at the final pathology. **Conclusions:** The results were consistent with previous literature and further support the use of pathology, including multiple sectioning and immunohistochemistry, in identifying metastatic nodal disease. This approach may allow surgeons to avoid unnecessary facial nerve sacrifice in the setting of superficial parotidectomy for metastatic melanoma.

**P358: GUIDELINES FOR EXCISION MARGINS IN CUTANEOUS HEAD AND NECK MELANOMA E.Zellitz1, M.A.Senior1, R.Mackie2, D.S.Soutar3, T.Shgaib1, 1Canniesburn Plastic Surgery Unit, Glasgow, United Kingdom; 2University of Glasgow, Glasgow, United Kingdom**

**Objectives:** Current guidelines for wider excision margins in cutaneous melanoma are based on trials from trunk and limb melanoma. In view of the aesthetic and functional considerations of wide excisions in head and neck melanoma, wider excision is occasionally performed with smaller margins than those recommended for other sites. The aim of this study was to determine whether excision margins of cutaneous melanoma of the head and neck (CMHN) were in keeping with current guidelines and whether deviations were detrimental to disease outcomes. **Methods:** We performed a retrospective analysis of a prospectively held database of melanoma cases in the West of Scotland. From this database, we determined the Breslow thickness of the melanoma, the maximum width of excision margin, the site of the primary, the subsequent manifestation of disease persistence locally or in the regional lymph nodes, and survival. We compared the number of cases of margin of wide local excision (WLE) with recommended guidelines for limb and trunk melanoma (RGLT) with remaining affected branches of the facial nerve were left intact.

**Usage:** of intraoperative frozen section analysis successfully distinguished melanotic staining from extracapsular extension and perineural involvement. Due to the difficulty of evaluating melanoma on frozen section, use of such a strategy requires close communication between the head and neck surgeon and an experienced pathologist during the operative procedure. Future comparison of intraoperative results with the final pathology will allow this approach to be examined with more rigor. Routine use of this strategy may allow surgeons to avoid unnecessary facial nerve sacrifice in the setting of superficial parotidectomy for metastatic melanoma.

**P359: PATIENT FOLLOW-UP AFTER CURATIVE-INTENT MELANOMA SURGERY: WHAT ARE THE COSTS? Q.D.Ou1, B.W.Stockmann1, K.S.Virgo1, B.S.Handler1, J.E.Johnson1, 1Saint Louis University, St. Louis, MO; 2St. Louis Veterans Affairs Medical Center, St. Louis, MO**

**Objective:** Melanomas commonly occur on head and neck skin. In a large series reported by Conley, the most common sites were face (32%), scalp (20%), and ear (19%). Obtaining adequate surgical margins is often much more difficult for lesions in this region than elsewhere. Follow-up for recurrence after surgery is often quite intensive but there is little evidence to inform clinicians carrying out surveillance. We sought to identify published follow-up strategies recommended for patients with cutaneous melanoma after treatment with curative intent and to compare the costs associated with these strategies. **Methods:** A Medicine literature search for the 18-year period 1989-2006 and a search of major textbooks identified 113 published follow-up strategies sufficiently explicit for analysis. Nationwide Medicare-allowed charges for 5 years of surveillance after treatment for cutaneous melanoma were calculated from the Center for Medicare and Medicaid Services 2004 Part B Extract and Summary System data. **Results:** For the 5 years of surveillance, intensity of follow-up ranged from...

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Medicare-allowed charges varied by 41-fold among strategies that advocated active surveillance ranged from $717-$4,569 for TNM stage I, $977-$3,003 for TNM stage II, and $902-$4,414 for TNM stage III. Mean Medicare-allowed charges were $462 for patients with tumors < 0.75 mm thick, increasing to $2,592 for those with tumors > 3.00 mm thick.

Conclusion: Medicare-allowed charges varied by 41-fold among strategies that advocate active follow-up, reflecting marked differences in surveillance intensity. There is no evidence that survival duration and/or quality of life is measurably improved with intensive follow-up, however.

P360: CLEAR CELL CARCINOMA OF THE HEAD AND NECK: A REPORT OF SIX CASES AND REVIEW OF THE LITERATURE

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Case 1: Masculine patient, with diagnosis of medulloblastoma. Retrospective study. The charts of the patients were reviewed and six patients (4 Female, 2 Male) were identified diagnosed between 1993 and 2006. Major salivary gland tumors and metastatic tumors were excluded. Each pathologic specimen was reviewed again with additional histopathologic and immunohistochemical analyses as indicated. Patient related information, imaging-pathology, and prognostic indicators were analyzed. Results: A total of six patients (4 Female, 2 Male) were identified diagnosed between 1993 and 2006 with an age range of 27 to 80. The odontogenic tumors were more common than minor salivary origin with the maxilla as the most common site. One case of nasopharyngeal clear cell carcinoma was also identified. Surgical treatment was the most common treatment approach on review of the literature and was used in all six institutional cases. Histopathologic findings may aid in predicting long term recurrence or distant metastasis although more data from the literature will be necessary to conclusively answer this question.

Conclusions: Clear cell carcinomas of the head and neck represent a rare diagnosis and when generally considered to arise from odontogenic or minor salivary origin. The majority of the literature imaging-pathology is limited to case reports and small series. The aim of this study is to assess the current literature related to any prognostic indicators, treatment and survival while analyzing those cases treated at a single tertiary care academic cancer center over a 15 year period.

Methods: A systematic literature review was performed of clear cell carcinoma of the head and neck for patient demographics, histopathologic findings, imaging and treatment with recurrence and survival data fields included. The Oral Pathology and Surgical Pathology databases were accessed after Institutional Review Board approval to identify all cases of clear cell carcinoma of odontogenic or minor salivary origin of the head and neck region. Major salivary gland tumors and metastatic tumors were excluded. Each pathologic specimen was reviewed again with additional histopathologic and immunohistochemical studies as indicated. Patient related information, imaging-pathology, and prognostic indicators were analyzed. Results: A total of six patients (4 Female, 2 Male) were identified diagnosed between 1993 and 2006 with an age range of 27 to 80. The odontogenic tumors were more common than minor salivary origin with the maxilla as the most common site. One case of nasopharyngeal clear cell carcinoma was also identified. Surgical treatment was the most common treatment approach on review of the literature and was used in all six institutional cases. Histopathologic findings may aid in predicting long-term recurrence or distant metastasis although more data from the literature will be necessary to conclusively answer this question.

Conclusions: Clear cell carcinomas of the head and neck represent a rare malignancy with a high risk of local recurrence. Surgical treatment appears to be the treatment of choice while adjuvant therapy may play a role. Histopathologic parameters may help predict long-term survival and distant metastasis.

NONMELANOMA SKIN

P361: CUTANEOUS SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK WITH PERINEURAL INVASION: A SINGLE INSTITUTION EXPERIENCE

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Introduction: Perineural invasion (PNI) in cutaneous SCC of the head and neck is associated with decreased survival. Anecdotally, patients with large nerve PNI succumb to disease spread into the brainstem. Our goal was to review our clinical experience with PNI and validate our clinical outcomes. Methods: We identified patients with large nerve PNI from cutaneous SCC in the head and neck between January 1996 and 2006. We then performed a retrospective chart review and documented the original histopathologic and immunohistochemical analyses as indicated. Results: Fifty-three patients were identified of which 46 had adequate information. Three patients were excluded because of pathology other than SCC. The mean age was 66 years (range 36-92 years). The mean follow-up was 28.9 months (range 1-82 months). Thirty-seven patients had involvement of the trigeminal nerve (in 24 patients it was the only involved nerve); 19 patients had involvement of facial nerve branches (6 had involvement of the facial nerve alone). Fifteen patients were treated with an en-bloc resection of the tumor and involved nerves(s) followed by radiation therapy. In nine of these patients a formal skull base resection was required. The overall survival in this group was 92% and the disease free survival was 62% at 60 months. Ten patients had tumor resection with “nerve chasing.” The disease free survival in this group was 40% was at 60 months. Two patients received only radiation therapy and one of these had a central failure. The remaining patients were offered only palliative treatment. Importantly none of the patients treated with aggressive resections had central failure, while 4 of 10 patients treated with less aggressive resections failed centrally. All of the patients who received palliative treatment had central disease progression upon presentation. Conclusions: PNI poses significant challenges to the head and neck surgeon. Its management remains controversial. In selected cases aggressive resection of the involved nerves up to the brainstem may prevent central failure. Radiation therapy alone to control PNI spreading into the intracranial space appears to be less effective. Spread into the central nervous system is the pattern of failure in this disease.

P362: AGGRESSIVE BASAL CELL CARCINOMA OF THE HEAD AND NECK: 20-YEAR EXPERIENCE IN A BRAZILIAN CENTER

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Introduction: Skin cancer is the most common malignant neoplasm among Caucasians. Basal cell carcinoma (BCC) is the most common skin cancer (70%), followed by squamous cell carcinoma and melanoma. 80% of BCC are located in the head and neck region. Objectives: epidemiologic characterization of aggressive BCCs operated in our Head and Neck Service, evaluating extent of surgery and histopathological features. Patients and Methods: Retrospective study. The charts of the patients undergoing major surgery between 1986 and 2006 and data reporting gender, age, race, primary tumor site, histologic subtype, T stage, perineural invasion and lymph node metastasis were analyzed. Results: 230 patients were enrolled; 46.9% were women. In the last 4 years, the growing female rate was 52.4%. Age ranged from 31 to 95 (median 63±12). Caucasians accounted for 88.2%. The primary tumor sites were: nose (32.5%), periorbital (12.5%), auricular (11.8%), malar (10.5%), perioral (7%), temporal (6.5%), mental (1.5%) and scalp (1.5%). More than one histologic subtype was seen in 59%. Morphoeform subtype was found in 57.3% of the cases, followed by nodular (54.7%), ulcerated (26.8%), metatypical (12.6%), and superficial (5.7%). There were 28.7% of T1, 29.3% of T2, 4.8% of T3 and 37.2% of T4. Invasion of deep structures occurred in nasal cartilage in 12 cases, auricular cartilage (10), peripheral bone tissue (9), parotid gland (9), temporal bone (5), nasal, frontal, maxilla(4), mandible(2), and dura mater in 2 cases. Perineural invasion was present in 21.8%. Three cases (1.3%) presented lymph node metastasis.

P363: GORLIN-GOLTZ SYNDROME: REPORT OF TWO CAES WITH BRAIN LESIONS ASSOCIATED

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The Gorlin-Goltz syndrome or Basal cell nevoid syndrome (BCNS) is an autosomal dominant disorder with a high penetrance and variable phenotype expression. Its incidence is of 1:56,000, without preference for sex. Associated to a disturbance on the chromosome 9 and loss of the gene or planter pits, skeletal anomalies as broad nasal bridge and increased head circumference, frontal and parietal bossing, mandibular prognathism, and rib and vertebral anomalies, hypertelorism, congenital blindness and strabismus; and calcifications of the falx cerebri, bony bridging of the sella turcica and medulloblastoma, ovarian calcification or fibromas, cardiac fibroma, cleft lip and palate, and learning difficulties. Medulloblastoma in childhood occurs in 5% of the patients with BCNS and frequently it is the first tumor diagnosed in the sindrome patients, with favorable prognosis. Objective of this study is to trace the diagnosis of the BCNS and to establish a prognostic view and a plan of treatment for the abnormality.

Materials: Case 1: masculine patient, with diagnosis of medulloblastoma at age of 2 treated with radiotherapy and chemotherapy, presented in the adolescence multiple odontogenic keratocystic tumors and multiple basal cell carcinoma, both treated surgically. After 16 years, he presented
To determine the outcomes of patients receiving transoral laser surgery. The respective 5-year local control and disease-specific survival (LC and DSS) are important for patients with this syndrome.

**P364: MANAGEMENT OF POORLY DIFFERENTIATED CUTANEOUS CARCINOMA OF THE HEAD AND NECK**

**Objective:** Poorly differentiated cutaneous carcinoma (PDCC) of the head and neck has been associated with an increased risk of regional metastases and aggressive local behavior. Present our recent experience and provide a review of the literature.

**Methods:** Retrospective chart review.

**Results:** Ten patients (average age = 77.7 years) were identified who presented and were treated by our department with PDCC of the head and neck. Eight cases were recurrent lesions. Four of the recurrent tumors were previously treated with Mohs surgery and none had prior radiation therapy. Eight of these 10 patients went on to have definitive surgery with 7/8 patients having regional lymphadenectomy as well. Six of these patients had multiple positive lymph nodes on final pathology. Adjuvant radiation therapy was given to 6 patients. Two patients presented with unresectable disease and received palliative treatment. Of those treated with curative intent, 1 died of distant metastases 14 months after surgery, while the remainder remain alive with no evidence of recurrent disease (average follow-up = 11.3 months). **Conclusion:** PDCC is a variant of cutaneous squamous cell carcinoma with a high propensity for regional metastases. Although this study is limited by its small size and limited follow-up, the data suggested early combined modality treatment may provide the best chance for locoregional control for this small subset of skin cancers.

**P365: REGIONAL METASTASIS IN NASAL VESTIBULAR CANCER**

**Objective:** Cancer of the nose is uncommon and may originate from the nasal skin or from the nasal mucosa. Defining the origin of the tumor may be difficult in advanced cases. The incidence of regional metastases varies and, arguably, the origin of the primary is not significant as the lymphatic drainage is consistent. Our study defines the incidence of synchronous and delayed regional lymph node metastases in cancer of the nasal vestibulum, and its influence on the management of cases with neck metastases, with a special focus on the management of patients with synchronous metastases. A retrospective chart analysis of patients with nasal vestibular squamous cell cancer was performed. Excluded were nasal mucosal cancers and cancers originating on the outer nasal skin. Cases of BCC, melanoma, lymphoma, mesenchymal tumors and metastases to the nose were excluded. Also excluded were cases in which the origin of the tumor could not be ascertained. **Results:** 15 patients, 11 male and 4 female with a mean age of 73 years with SCC isolated to the nasal vestibulum were identified. All but two had a history of smoking. Seven patients were staged as T1, 4 as T2 and 4 as T4. Regional disease was seen on presentation in three patients (20%) with T1 and two with T4 disease. Two additional patients (both staged as T2) had delayed neck metastases (total of 3%). Only one patient had his neck treated prophylactically surgically and remained N0. The other necks were treated if positive except one case where treatment was refused. Of the patients with N+ disease, one was lost to follow-up, two are dead of disease and two are alive NED. **Conclusion:** Nasal vestibular cancer is an uncommon isolated form of cancer, possibly originating in the muco-cutaneous junction and is usually smoking induced. The incidence of synchronous or delayed regional metastases is 33% in this series, higher than in most reports in the literature and is not T stage dependent. Elective treatment of the neck should be considered in these uncommon cases.

**P366: INTRAORAL LASER EXCISION COMBINED WITH PLANNED NECK DISSECTION FOR TREATING T2 AND T3 SEMI-ADVANCED TONGUE CANCERS**

**Objective:** T2 and T3 semi-advanced tongue cancer often creates controversy as whether to treat the lesion by radical or limited treatment. Radical treatment including a wide excision following by graft reconstruction often resulted in an impaired functional result. Whereas, limited excision might increase the risks for local and nodal recurrences. We have introduced intraoral laser excision combined with planned neck dissection for these patients. To verify the clinical usefulness of current treatment, a retrospective review was conducted at a university department.

**Methods:** Intraoral laser excision was done under general anesthesia. Up to 1/2 of the tongue can be removed approximately in one hour. Careful hemostasis and ligation of the lingual artery along with the branches are crucial. Surgical wound of the tongue was left unsutured or was sutured using absorbable strings depending on the patient’s status. Subsequently, level I to IV neck nodes were excised by selective neck dissection. Special attention is paid to thoroughly remove the nodes and tissues between oral floor and submandibular gland region. **Results:** Eight cases were treated by intraoral laser excision combined with planned neck dissection after 2006. There were four T2 and four T3 cases. As for stage classification, stage II, III, and IV were 4, 3, and 1 case respectively. Positive node was confirmed pathologically in three cases. All patients are doing well without disease.

**Conclusions:** Intraoral laser excision combined with planned neck dissection was a useful treatment for T2 and selected T3 tongues. Due to the increasing number of senior population, a less aggressive treatment will be needed while maintaining an equal survival rate compared supported by radical approach. Long term follow up is needed to further elucidate the usefulness of our approach.

**P367: TRANSPHARYNGEAL Approach vs TRANSORAL APPROACH AFTER LIP-SPLITTING TRANSMANDIBULAR APPROACH VS TRANSORAL APPROACH**

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**Objective:** To determine if performing oral cavity (OC) or oropharyngeal (OP) tumor resection via a lip-splitting transmandibular approach (LSTMA) can be removed approximately in one hour. Careful hemostasis and ligation of the lingual artery along with the branches are crucial. Surgical wound of the tongue was left unsutured or was sutured using absorbable strings depending on the patient’s status. Subsequently, level I to IV neck nodes were excised by selective neck dissection. Special attention is paid to thoroughly remove the nodes and tissues between oral floor and submandibular gland region.

**Objective:** To determine the outcomes of patients receiving transoral laser microsurgery (TLM) for early stage (T1/T2) squamous cell carcinoma of the oral tongue in a 7 year period. **Design:** Retrospective cohort study of the oncologic and functional outcomes of transoral laser microsurgery for early stage oral tongue carcinoma performed between 2000 and 2007. **Subjects:** We reviewed 30 previously untreated patients who were treated with TLM for early stage squamous cell carcinoma of the oral tongue. Distribution of the pathological T stages are as follows; 73% of patients were T1 (n=22), 27% were T2 (n=8). Six patients (20%) belonged to diseases stages that were treated with TLM but not in T1/T2. Delayed neck dissection was performed in 63% of patients (n=19); 23% of patients received postoperative radiotherapy (n=7). Mean follow-up for all patients was 27 months.

**Main Outcome Measures:** Local control rate, regional control rate, recurrence-free and overall survival rates. **Results:** The respective 5-year Kaplan-Meier estimates for T1/T2 oral tongue cancer were: local control 97%, regional control 92%, recurrence-free survival 92% and overall survival 77%. **Conclusions:** TLM appears to be a safe and effective treatment for early stage oral tongue carcinoma. Plans for an extended follow-up period will provide further useful information.
There was no significant difference (p<0.05) in scar Although LSTMA scars were increasingly visible to naïve Literature review. The primary objectives of head and neck cancer treatment The postoperative surgical complications did not show a significant Tumor margins have been A hundred Although mandibular reconstruction using vascularized bone To evaluate The observed functional outcomes were clearly specified methods have evolved over the past decades to achieve these objectives acceptable quality of life measures in terms of aesthetics, oral function and that it is not a distiguishing and debilitating operation as once believed. There was no significant difference (p<0.001) in lower lip sensation to pressure, 2-point discrimination or temperature sensation or in lower lip symmetry of movement (p>0.05). VFSS demonstrated no significant difference (p>0.05) in oral competence deterioration amongst the cohorts. Conclusions: Although LSTMA scars were increasingly visible to naïve, the midline mental scar did not translate to decreased patient satisfaction with their cosmetic result. Lower lip sensation and movement as well as oral competence remained intact post-LSTMA indicating favorable functional outcomes. These results demonstrate that the LSTMA produces acceptable quality of life measures in terms of aesthetics, oral function and that it is not a distinguishing and debilitating operation as once believed. P369: FUNCTIONAL OUTCOMES REPORTING FOLLOWING TREATMENT OF ORAL AND OROPHARYNGEAL CANCER: A REVIEW OF LITERATURE H. Sekiguchi, A.M. Mlynek, J.R. Riegler, D.A. O Connell, J.K. Chiu, K. Al-Qahtani, N. Rick, R. Anzar, J.R. Harris, University of Alberta, Edmonton, AB, Canada; University of Alberta, Edmonton

Introduction: The primary objectives of head and neck cancer treatment are to maximize survival and local-regional control while restoring normal function and preserving quality of life. Head and neck cancer treatment methods have evolved over the past decades to achieve these objectives and presently involve a combination of surgery, radiotherapy and chemotherapy. The initial emphasis in the development of the treatment protocols was on improving survival and local control. This resulted in a standardized method of measuring these parameters that allowed us to objectively compare different regimens. Functional outcomes and quality of life have recently played an increasingly important role in our treatment choices but there continues to be a clear lack of uniform methods for assessing and measuring these outcomes. Objectives: The purpose of this paper is to review and document the differing methods of functional outcomes measurements following treatment for oral and oropharyngeal carcinoma. Study Design: Literature review. Methods: MEDLINE database search with the following keyword terms: head and neck, oral, oropharyngeal, cancer, squamous cell carcinoma, functional outcome, speech, swallow, and quality of life. The searches were limited to articles published between 2000 and 2007. The reference lists from the relevant articles were then inspected and any other pertinent publications were added to the review. Results: The observed functional outcomes were clearly specified in most of the studies. However the types of measurement varied greatly between all the studies. Twenty three studies used various quality of life questionnaires, with 18 of these using only this method of assessment to inform them of functional outcomes. Twelve studies used clinical observations. Swallowing was assessed objectively in 29 studies. All of these used video-fluoroscopic swallowing studies (VFSS) as the primary method of assessment. Speech was assessed using perceptual analysis as the primary assessment modality in 10 articles, with the method of perceptual analysis varying widely across institutions. Only 4 of these 10 studies used other objective speech parameters such as acoustic or aerodynamic measurements. Only 5 articles contained quality of life questionnaires with objective speech or swallowing assessments and only 6 articles reported on both speech and swallowing functional outcomes. Conclusions: Preserving function following treatment for oral and oropharyngeal cancer remains an extremely important aspect of cancer care but there is a clear lack of uniform methods for assessing functional outcomes. It is clear that there is a need to develop standardized methods for assessing functional outcomes as they are consistently measure. We propose that functional outcome studies should include both objective and subjective assessments of swallowing and speech. A functional outcomes assessment program would include at a minimum: 1) Functional data collection at 3-4 points in time, 2) Swallowing function assessment via objective capture of swallowing physiology, with documentation of supplemental relevant clinical information, 3) Speech intelligibility assessment designed to reduce bias related to the speech sample and judge, 4) Supplemental assessment of other important aspects of speech in the oropharyngeal population such as resonance, 5) Patient-perceived outcomes related to speech and swallowing function. P370: THE UNRECONSTRUCTED TONGUE M.P. Tahill, C. Semple, A. Songra, D. Gordon, Northern Ireland Plastic and Maxillofacial Surgery Service, Belfast, United Kingdom

Introduction: Tongue reconstruction following tumour resection is performed to preserve volume and function of this important organ. Free flaps are often bulky and immobile whilst skin grafts probably offer little advantage over healing by secondary intention. We have observed the tongues significant potential for re epithelialisation and muscle hypertrophy following resection. Methods: To simplify reconstruction in an often medically compromised population, we followed a protocol of diathermy resection of T1 and T2 N0 squamous cell carcinomas of the tongue with the defects created being left to heal by secondary intention alone. The area and location of resection was recorded in addition to time taken to resume oral feeding, and time to discharge from hospital. Follow-up assessments of function and quality of life were recorded at 6 months post-operatively. Results: Twenty-one patients (mean age 65.2 years) were treated over 3 years. The mean area of resection was 7.43 cm² (range 3.14-16.48). All surgical margins examined in all cases were clear of tumour. The median time to swallowing liquids was 24 hours and median length of stay in hospital was 3 days. A total of 16 patients completed the study. Excellent/good function was demonstrable in 14 patients. Function appeared to deteriorate with increasing area of resection. Conclusions: We suggest that in selected cases, healing of the tongue by secondary intention after tumour resection offers low morbidity, rapid rehabilitation and early hospital discharge. We have demonstrated good functional recovery in patients whose resection approached that of an hemiglossectomy. In addition, free flap resection without graft or flap coverage improves local disease surveillance of the surgical margin.

P371: FACTORS OF POSTOPERATIVE COMPLICATIONS FOR CASES UNDERGOING SEGMENTAL MANDIBLECTOMY Y. Shimashita, K. Kawabata, H. Mitani, S. Miyata, M. Matsubara, Cancer Institute Hospital, Tokyo, Japan; Japanese Foundation for Cancer Research, Tokyo, Japan

Objectives: Although mandibular reconstruction using vascularized bone demonstrates good functional results, it has a relatively high frequency of postoperative complications. The aim of this study was to determine the optimum management of such cases undergoing a segmental mandibulectomy from the viewpoint of postoperative complications. Methods: A hundred and twenty cases with head and neck malignant tumors undergoing a segmental mandibulectomy were analyzed. The factors that correlate with postoperative complications were examined based on a univariate analysis. Results: The postoperative surgical complications did not show a significant correlation with the type of defects or the reconstructive methods, but a significant relationship was seen with the skin defect size and the amount of blood loss. The postoperative systemic complications showed a significant correlation with age, through-and-through defects, and the amount of blood loss. Conclusions: Mandibular reconstruction using vascularized bone is therefore recommended for all such cases, while reducing the amount of blood loss as much as possible, except for extremely elderly patients or those with through-and-through defects. P372: QUINACRINE - TOPICAL CONTRAST AGENT IN EX VIVO TUMOR MARGIN DETECTION V. Stepanski, A.M. Gillenwater, MD Anderson Cancer Center, Houston, TX

Background: Currently the margin detection during tumor excision is a process largely dependent on the ability and experience of the surgeon and the pathologist. Surgeons use white light visual examination and palpation to define the extent of disease. The resected specimen involves tumor and approximately 1 cm of surrounding normal tissue. Objective: To evaluate the ability of topical contrast agent Quinacrine to assist in margin detection for tumor resection in the oral cavity. Methods: Tumor margins have been determined by clinician using white light visual examination. Tumor was resected and ex vivo specimen has been examined right after. Topical contrast agent has been employed along with fluorescence spectroscopy
devices in detection the changes that occur in the native optical properties of the oral mucosa on the margin between non-neoplastic, dysplastic, and malignant lesions of the oral cavity. Mathematical algorithm has been used to distinguish between these entities. Parallel laboratory evaluations of biopsy specimens have analyzed the tissue constituents which fluoresce and which are altered during the malignant process. Results: several cases are presented documenting that topical contrast agent has the potential to assist with tumor margin recognition. Optical imaging with pathological findings and with white light visual examination as well. Conclusion: The native optical properties of oral mucosa are altered in dysplastic and carcinomatous lesions. Topical contrast agent preferentially target dysplasia and cancerous tissue. The increased optical signal obtained from dysplasia and cancer compared to normal tissue can be used as a diagnostic criteria. This ability applies topical agent to be used to non-invasively distinguish between non-neoplastic, dysplastic and malignant regions of oral cavity lesions. However, further expanded testing is needed including the evaluation of topical contrast agent ability in vivo to develop the algorithm for valuable early diagnostic tool in oral cavity tumors.

P373: WITHDRAWN

P374: FROZEN SECTION ANALYSIS AND POSITIVE DEEP SURGICAL MARGINS ARE PROGNOSTIC INDICATORS IN ORAL SQUAMOUS CELL CARCINOMA M Miyazawa1, I Nishimoto2, C A Pinto2, D T Oliveira1, L P Kowalski3 1University of São Paulo, Bauru School of Dentistry, Bauru, Brazil; 2Hospital of Cancer A C Camargo, São Paulo Brazil; 3Hospital of Cancer A C Camargo, São Paulo, Brazil

Background: Residual tumor is critical for local recurrence of oral squamous cell carcinoma (OSC). Intraoperative frozen section (FS) is considered useful for surgical margins assessment allowing immediate extension of the resection. Objective: The main purpose of this study was to investigate the importance of intraoperative FS in the prognosis of patients with OSC. Methods: It was compared the pathological FS and paraffin section margins of surgical specimen of 367 primary OSCC cases submitted to radical surgery in a single institution. Overall survival (OS) and disease-free survival (DFS) were calculated by Kaplan Meier method and statistical difference among the categories of the same variable were assessed by log rank test. Results: The group that received intraoperative FS consisted of 146 patients, and histopathology showed that 85 (58.2%) had free margins, 48 (32.9%) close and 13 (8.9%) involved margins. Of those, 28 (19.2%) had involvement of the lateral margins and 20 (13.7%) of the deep margins. Twelve patients had local recurrence (8.2%), and it was associated with the margins status: 5 (3.4%) of the patients with free margins, 6 (4.1%) with close margins, and 6 (4.5%) with involved margins (p=0.388). The group of 221 patients without intraoperative FS had 124 cases (56.1%) with negative margins, 66 (29.9%) close and 31 (14.0%) positive margins. There were involvement of lateral margins in 34 (15.4%) cases and deep margins in 32 (14.5%) patients. In this group, 31 patients showed local recurrence where 15 (5.8%) had free margins, 10 (4.5%) close and 6 (2.7%) involved margins. (p=0.388) Statistically significant differences for 5-year overall and disease-free survival were observed according to the margin status. Patients with close lateral margin had similar outcome to those with negative margins (52.4% vs 50.1% 5-year OS) (55.4% vs 55.4% 5-year DFS). However, the outcome of patients with close deep margin was as worse as the cases with positive margins (38.8% vs 31.5% 5-year OS, p=0.0468) (40.0% vs 36.6% 5-year DFS, p=0.0183). Furthermore, patients with T3-4 tumors not submitted to FS had high rates of local recurrences (34.9% vs 70.1%, 5-year DFS p<0.0001) and low survival (27.5% vs 66.4% 5-year OS, p<0.0001) when compared to T1-T2 cases. On the other hand, when comparing T3-T4 and T1-T2 cases submitted to intraoperative FS, it was observed better outcomes (37.3% vs 68.2% 5-year OS, p=0.0010) (47.0% vs 72.7% 5-year DFS, p=0.0034).

Conclusion: Intraoperative evaluation of deep as well as lateral margins influence surgical decisions and has significant prognostic value in patients with squamous cell carcinoma of the oral cavity.

P375: COMPLETE FROZEN SECTION MARGINS 5 MM THICK FOR CANCER OF THE TONGUE P Gauffier1, L Guertin2, N Audet3, I Artetou-Gauthier4, 2Centre Hospitalier Regional De Lanaudiere, St Charles-Borromee, PQ, Canada; 2Centre Hospitalier Universitaire de Montreal, Montreal, PQ, Canada; 3Centre Hospitalier Affile au L’Universite Laval, Quebec, PQ, Canada

Objective: Obtaining Mohs-like margins for cancer of the tongue is an achievable goal as observed in animal and clinical experience. Our first goal is to obtain complete negative margins of 5 mm thick for each clinical situation. The ultimate purpose is to lower the recurrence rate. Our experience with 9 squamous cell carcinomas of the tongue is related looking especially at the quality of the complete frozen sections on histological glass slides. Study Design: We review the literature in search of statistics comparing invaded and close margins versus negative margins for prognosis. We describe the technique we have used, based on animal experiences, in nine squamous cell carcinomas of the tongue. Complete negative frozen margins of 5 mm were obtained. Results: Obtaining complete free margins for a thickness of 5 mm was done for nine cases. 90 to 120 minutes were needed to obtain the histological results but did not exceed the time necessary to perform the neck dissection except for one case. The quality of the histological glass slides was very good. The technique using the scalpel and scissors implied more bleeding, but was never a source of problem. Conclusion And Significance: Complete and oriented frozen margins of high quality are obtained when using sharp dissection (scalpel and/or scissors) to remove the tumour. Iso-pentane and the cryostat have been used with success for freezing the specimen. The review of the literature demonstrates that invaded and close (5 mm) margins confer a higher recurrence rate. We may obtain a 5 mm thick margin which is complete, free and oriented on frozen section. To conduct the procedure in a timely fashion, we begin with the tongue resection. While waiting for the frozen section, we perform the neck dissection. For only one patient, we have wait for the result of the frozen section, but it is greatly to the patient’s advantage. For all other patients, the time of the surgery was not prolonged because we had to wait for the result. At this time, we have no recurrence. However, the follow-up is short (1-10 months). This approach should help improve dramatically the rate of positive and close margins at final pathology, and consequently, the rate of local control and survival as well. It may diminish the need for adjuvant therapy such as radiotherapy in some selected cases.

P376: HAS THE USE OF FROZEN SECTION TO ASSESS OPERATIVE MARGINS IMPACTED ON THE DISEASE CONTROL AND SURVIVAL? K A Pathak1, H A Hajjaj1, A Bin Ahmed1, R W Nason1, 1Cancer Care Manitoba, Winnipeg, MB, Canada

Background: Use of intra-operative frozen section examination is often relied upon to assess the adequacy of margins of excision. This study looks at its independent impact on disease control and cause specific survival. Material and Methods: Out of 426 surgically treated patients in our population based cohort of 704 oral cancer patients, 230 had intra-operative frozen section for assessment of closest cut margin. All living patients were prospectively followed up for a median period of 46.5 months. Status of patient at 180 months of follow up or at the time of last contact whichever was earlier, was recorded. Use of frozen section was correlated with status of margins at permanent section and disease failure at primary site. Disease free, cause specific and overall survival were plotted by Kaplan Meier method. Independent influence of use of frozen section on disease control and survival was evaluated in multivariate models using Cox Proportional Hazard model. Results: Our study group of 247 male (58.0%) and 179 female (42.0%) patients, with mean age of 63.5 ± 12.9 years, included 115 (27.0%) patients with stage I, 124 (29.1%) -stage II, 68 (16.0%) -stage III and 109 (25.6%) with stage IV disease with floor of mouth as the commonest sub-site in 184 patients (43.2%). Chances of achieving clear margins in 281 (66.0%) patients with clear margins on paraffin section was not linked to the use of frozen section (70.5% Vs 66.1%; p<NS). During the course of follow up, 140 patients (32.9%) developed recurrent disease; most often at primary site (14.3%). In multivariate analysis use of frozen section did not impact on local failure or cause specific survival independently. Failure at primary site was independent influenced by age at diagnosis (HR= 0.96; 95% CI=0.95, 0.98; p<0.001), T stage (p<0.018) and N stage (p=0.042). T4 tumors failed more frequently (HR= 3.42; 95% CI=1.50, 7.31; p<0.001) than T1 and N2 (HR= 3.40; 95% CI=1.09, 10.61; p=0.035) or N3 disease (HR= 13.9; 95% CI=2.01, 96.24; p=0.008) were at higher risk of primary site failure than N0. Margin on paraffin section independently influenced local failure (p=0.003) with close (HR= 3.7; 95% CI=1.20, 10.39) and complete negative margins (HR= 2.63; 95% CI=1.38, 5.02; p=0.003) failing more often than clear margins. Cause specific survival was independently influenced by T stage (p=0.027) and N stage (p<0.001) with patients having T4 tumors (HR= 3.31; 95% CI=1.50, 7.30; p=0.003) and N2 (HR= 3.58; 95% CI=1.64, 7.31; p=0.035) or N3 disease (HR= 9.59; 95% CI=1.12, 81.96; p=0.039) at higher risk dying of their disease. Conclusion: Routinely use of frozen section for mucosal margins does not impact the disease process as it does not always correlate with margins on paraffin section.
INTRODUCTION: Keratocyst is a real challenge for us due to its extreme high recurrence rates. Odontogenic cysts are relatively common, and their origin is most likely associated to the remnants of dental lamina. Odontogenic keratocyst is the only one among all odontogenic cysts that, for presenting pathognomonic microscopic aspects, has a very aggressive, destructive behaviour, as well as high incidence rates, which range from 6 to 62%. The reasons for such high rates may be the technical, surgical difficulties when removing the cyst which leads to incomplete removal; their crumbly, fine, focuseable, bone resorption; and adherence to underlying soft tissue structures. It may invade the teeth, the salivary glands, the skeletal muscles, the maxillary sinus, the nasal cavity and the zygomatic bone. Keratocyst usually affects the mandible: around the third molar of patients in their twenties or thirties. The presence of orthokeratin in the keratocysts is normally associated to the Gorlin-Goltz syndrome; nevertheless, in these cases the recurrence rates are lower, since with high recurrence rates and multiple cysts usually have parakeratin in their epithelium. Precisely because of these high recurrence rates, the World Health Organization (2005) now considers keratocysts benign tumours of odontogenic origin, its name now being odontogenic keratocyst tumor. In the present paper we intend to examine the characteristics of patients suffering from mandible and maxilla keratocyst between 2000 and 2007. In order to do so, we thoroughly examine the cases of odontogenic keratocyst diagnosed at the Oral and Maxillofacial Surgery Department of Hospital Erasto Gaertner, so as to verify the treatment administered as well as the recurrence rates of this pathology. Objective: To analyse the incidence and the occurrence of mandible and maxilla keratocyst, as well as its treatment. Methods: We retrospectively analysed medical records of patients suffering from mandible and maxilla keratocyst admitted at Hospital Erasto Gaertner (Curitiba-Parana) between 2000 and December 2007. We took into consideration their age, gender, topography, treatment and recurrence rates. We found 18 patients with this diagnosis, and all of them underwent incisional biopsy followed by surgery associated with cryotherapy. Results: Of the 18 patients suffering from keratocyst, the average age was 35; the youngest patient being 12 and the oldest, 64. 12 patients (60.6%) were women, and 6 (34.9%) were men, all affected with leukoderma. 15 cases (83.3%) were mandible cysts, whereas 3 (16.7%) were maxilla cysts. 8 patients (44.4%) underwent urettage and cryotherapy. 7 cysts recurred, 5 of which after cryotherapy. In these cases, we associated urettage and cryotherapy. We diagnosed one case of Gorlin-Goltz syndrome: upper maxilla and high mandibular keratocyst. Conclusion: It is clear that keratocysts present high recurrence rates: even in those patients who underwent cryotherapy.

PARATHYROID II

P378: VITAMIN D DEFICIENCY: IMPLICATIONS FOR THE PARATHYROID SURGEON N.W. Hales1, G.A. Krempl1, J.E. Medina1, 1The University of Oklahoma Health Science Center, Oklahoma City, OK

Objective: To determine the incidence of vitamin D deficiency in patients with primary hyperparathyroidism and outline the potential implications for the parathyroid surgeon. Methods: A retrospective review of patients treated for primary hyperparathyroidism from 2003-2007 were reviewed to determine the incidence of vitamin D deficiency and describe perioperative complications which potentially were related to vitamin D deficiency. A review of calcium physiology, the role of vitamin D and implications of vitamin D deficiency are also outlined. Results: Eight-one charts were reviewed; twenty-six patients were identified with primary hyperparathyroidism and perioperative vitamin D 25-Hydroxy evaluations. Of these patients, 86% (23/26) were found to be vitamin D deficient (vitamin D hydroxy less than 32 ng/mL). Four patients (15%) demonstrated persistent elevations in post operative parathyroid hormone as a result of vitamin D deficiency. Post operative hypocalcemia, that persisted until the vitamin D deficiency was corrected, was identified in one patient. One patient was felt to have secondary hyperparathyroidism as a result of vitamin D deficiency which was corrected after appropriate vitamin D replacement. Conclusion: Vitamin D deficiency is a common finding in the perioperative evaluation of patients with primary hyperparathyroidism. This finding is largely overlooked by most parathyroid surgeons and its implications are not well understood. Post operative supplementation should be considered in all patients with peri-operative vitamin D deficiency.

P379: WITHDRAWN

P380: ARE PARATHYROID HORMONE MEASUREMENTS AFTER PARATHYROIDECTOMY FOR PRIMARY HYPERPARATHYROIDISM NEEDED? E. Kandil1, K. Carson2, A. Dackiw2, R. P. Tufano2, M. Zeiger2, 1Tulane University, New Orleans, LA; 2Johns Hopkins, Baltimore, MD

Background: Successful parathyroidectomy for primary hyperparathyroidism (PHPT) is predicted by 50% decrease in intraoperative parathyroid hormone (iPTH) levels. More accurate interpretation of iPTH levels remains an understudied topic in relation to intact parathyroid hormone (iPTH) baseline levels. This study examined the impact of iPTH baseline levels on iPTH kinetics and outcomes following parathyroidectomy. Methods: This is a retrospective single institution analysis of 447 consecutive patients undergoing parathyroidectomy for PHPT. Patients were divided into two groups according to their baseline iPTH values. Of these, 304 patients had baseline values >150 pg/mL, and 143 patients with baseline values <150 pg/mL. Multiple comparisons were made between the low-base line and high-base line groups. Results: Patients with baseline values >150 pg/mL had significantly higher levels of preoperative calcium, alkaline phosphatase, and adenoma weights (p<0.05 for all). 25-hydroxyvitamin D (25OH) levels were significantly lower in patients with baseline values >150 pg/mL (p<0.001) and 14.4% (p<0.001) respectively. The median percentage drop in calcium levels at 1 week and 6 months compared to their preoperative levels was 14.2% (p<0.001) and 14.4% (p<0.001) respectively. Conclusions: iPTH measurements after successful parathyroidectomy may be costly, and not routinely indicated in normocalcemic patients. Furthermore, elevated postoperative PTH levels do not predict operative failure in the majority of patients. We therefore propose that if postoperative calcium level is normal at 1 week, it should be repeated at 6 months without postoperative iPTH monitoring.

P381: THE IMPACT OF BASELINE INTACT PARATHYROID HORMONE ON OUTCOMES FOLLOWING SURGERY E. Kandil1, A. Tufaro2, K. Carso3, A. Dackiw2, R. P. Tufano2, 1Tulane University, New Orleans, LA; 2Johns Hopkins, Baltimore, MD

Background: Successful parathyroidectomy for primary hyperparathyroidism (PHPT) is predicted by 50% decrease in intraoperative parathyroid hormone (iPTH) levels. More accurate interpretation of iPTH levels remains an understudied topic in relation to intact parathyroid hormone (iPTH) baseline levels. This study examined the impact of iPTH baseline levels on iPTH kinetics and outcomes following parathyroidectomy. Methods: This is a retrospective single institution analysis of 447 consecutive patients undergoing parathyroidectomy for PHPT. Patients were divided into two groups according to their baseline iPTH values. Of these, 304 patients had baseline values >150 pg/mL, and 143 patients with baseline values <150 pg/mL. Multiple comparisons were made between the low-base line and high-base line groups. Results: Patients with baseline values >150 pg/mL had significantly higher levels of preoperative calcium, alkaline phosphatase, and adenoma weights (p<0.05 for all). 25-hydroxyvitamin D (25OH) levels were significantly lower in patients with baseline values >150 pg/mL (p<0.001) and 14.4% (p<0.001) respectively. The median percentage drop in calcium levels at 1 week and 6 months compared to their preoperative levels was 14.2% (p<0.001) and 14.4% (p<0.001) respectively. Conclusions: iPTH measurements after successful parathyroidectomy may be costly, and not routinely indicated in normocalcemic patients. Furthermore, elevated postoperative PTH levels do not predict operative failure in the majority of patients. We therefore propose that if postoperative calcium level is normal at 1 week, it should be repeated at 6 months without postoperative iPTH monitoring.

P382: SHOULD PATIENTS WITH PRIMARY HYPERPARATHYROIDISM ON CHRONIC LITHIUM THERAPY REFERRED FOR SURGERY? E. Kandil1, A. Dackiw2, A. Tufaro2, K. Carso3, M. Zeiger2, R. P. Tufano2, 1Tulane University, New Orleans, LA; 2Johns Hopkins, Baltimore, MD
Background: Chronic lithium therapy has been implicated as a possible cause of hypercalcemia and primary hyperparathyroidism. Our objective was to evaluate whether primary hyperparathyroidism was caused by an adenoma or four-gland hyperplasia. Methods: The medical records of 7 patients who were treated with chronic lithium therapy, all of whom were operated on for primary hyperparathyroidism, were reviewed. Data on age, pre- and post-operative calcium levels, and parathyroid hormone level were collected. Results: The mean age was 51.9 ± 12.1 years, and the mean pre-operative calcium level was 11.1 ± 0.7 mg/dl. Of the 7 patients, 6 (86%, 95% confidence interval = 42.99%) had adenomas (5 single, 1 double), and 1 (14%) had four-gland hyperplasia. 6 patients were rendered eucalcemic, with a postoperative calcium level of 10.1 ± 0.5 mg/dl (Paired Test, p=0.01).

Conclusion: In our experience hyperparathyroidism in patients who have undergone prolonged therapy with lithium is associated with a high incidence of parathyroid adenomas versus four-gland hyperplasia. These patients should be then considered for surgical intervention.

P383: SYNCHRONOUS PARATHYROID ADENOMA AND PAPILLARY THYROID CARCINOMA: A CASE REPORT D.Kim1, M.Lee1, T.Kwon1, M.Sung1, 1Department of Otorhinolaryngology, Seoul National University College of Medicine, Seoul, Republic of Korea

Objective: Primary hyperparathyroidism with concomitant thyroid disease is not uncommon. However, the simultaneous occurrence of parathyroid adenoma and thyroid cancer is rare. Methods: We present a case report, including imaging study and histologic documentation, and a summary of the related literature. Results: We report a case of 55-year-old man with primary hyperparathyroidism and papillary thyroid carcinoma. Conclusions: Our results indicate that synchronous parathyroid adenoma and papillary thyroid carcinoma can occur in the same patient. The patient consecutively underwent total thyroidectomy. Pathology revealed parathyroid adenoma with concurrent papillary thyroid carcinoma.

Conclusion: The coexistence of parathyroid adenoma and thyroid malignancy was possible for all patients in primary hyperparathyroidism with thyroid nodules. Therefore, careful thyroid evaluation must be necessary for all patients with primary hyperparathyroidism.

P384: THE SIGNIFICANCE OF INTRAOPERATIVE PTH SPIKES DURING PARATHYROIDECTOMY T.M.Facelle1, B.Y.Wang1, K.S.Heller1, 1New York University School of Medicine, New York, NY

Objective: The measurement of intraoperative PTH (IOPTH) is used to assess the adequacy of surgery during limited (single gland) parathyroidectomy. Core of hyperparathyroidism is expected when IOPTH levels decrease by at least 20% from baseline and into a normal range 10 minutes after the adenoma is removed. In some patients IOPTH levels higher than baseline values are observed at the time the adenoma is removed (PTH Spike). This study was undertaken to determine if PTH Spikes have any clinical significance.

Methods: Two groups of patients were retrospectively analyzed. All patients had primary hyperparathyroidism and were operated on by a single surgeon. Group 1 consists of 816 patients operated on between 6/23/99 and 3/24/04 at one institution. Group 2 consists of 93 patients operated on between 1/3/07 and 11/13/07 at another institution. IOPTH levels were measured when the patient entered the operating room (Baseline), at excision of the adenoma, at 5 and 10 minutes after excision, and at variable time intervals thereafter. A PTH Spike was defined as an increase of IOPTH of 25% or more from baseline to gland excision. The control group consisted of those patients whose IOPTH remained stable or fell less than 25% between baseline and excision. In Groups 1 and 2, demographic information, pre and post-operative calcium and PTH levels, and adenoma location were compared between the PTH Spike and control groups. In Group 2, correlations with cell type and gland weight were also studied.

Results: PTH spikes occurred in 29% (n=237) of patients in Group 1 and 14% (n=131) of patients in Group 2. Group 1 (n=189) and 15% of Group 2 (n=14). The remaining patients had substantial drops in IOPTH at excision, likely due to devascularization of the adenoma prior to its removal or minimal increases of IOPTH. There were no significant differences between the PTH Spike patients and controls in either group for any of the variables studied with one exception. In Group 1, the PTH Spike group had significantly lower baseline IOPTH and higher 5-min., 10-min., and final IOPTH than the control group. In this group 56 of 237 patients did not meet the IOPTH criteria for success at 10 minutes. Ultimately there was no difference in outcome between the PTH Spike and control groups.

Conclusion: The PTH spike does not have any clinical significance. Differences in IOPTH between the PTH Spike and control patients in Group 1 at 5-min., 10-min., and final surgical IOPTH measures may be the result of elevated PTH levels persisting after gland excision, but not post-operatively. The 56 cases in Group 1 with elevated IOPTH at 10-min. could have resulted in unnecessary bilateral exploration if PTH spikes had not been recognized. Nevertheless, ultimate surgical success rates were the same in all groups. Neither gland size nor pathological classification appears to be related to PTH spikes. This suggests that PTH spikes are caused by physical manipulation of the gland prior to excision and does not relate to intrinsic features of the gland itself.

P385: HETEROGENEOUS NATURE OF POST-THYROIDECTOMY HYPOCALCEMIA ACCORDING TO THE SYMPTOMATIC AND BIOCHEMICAL CRITERIA M.Chung1, H.Jeong1, Y.Son1, 1Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Objectives: This study aimed to compare the characteristics of the patients who have both symptomatic and biochemical hypocalcemia, or who have only one of those after thyroidectomy. Methods: A Retrospective series of 112 consecutive patients who underwent total or completion thyroidectomy in a tertiary care referral center were enrolled for this study. The patients were classified into normocalcemia and hypocalcemia group, and the latter was further divided into three subgroups; both symptomatic and biochemical hypocalcemia (S+B+) group, only symptomatic hypocalcemia (S+B-) group and only biochemical hypocalcemia (S-B+) group. Hypocalcemic symptoms, total serum calcium and ionized calcium were serially monitored until the third postoperative day. Standard intact PTH and the slope of change in calcium levels were also measured. Mismatch between the onset of symptoms and biochemical abnormalities were analyzed. The clinical characteristics and diagnostic accuracy of various biomarkers in these subgroups were compared.

Results: Among 62 patients (62/112, 55.3%) who were classified into a transient hypocalcemia group, 45 patients (45/62, 72.5%), 9 patients (9/62, 14.5%) and 8 patients (8/62, 12.9%) belonged to S+B+, S+B- and S-B+ group, respectively. In S+B+ group, 21 patients (21/45, 46.6%) had greater than 1-day mismatch in the onset timing of symptomatic and biochemical hypocalcemia. Only S+B+ group showed significant differences in serum total calcium, ionized calcium and the slope of calcium changes compared with those of normocalcemia group. Standard intact PTH was a useful biomarker in the early prediction of both S+B+ and S+B- groups but not in S-B+ group.

Conclusion: When hypocalcemia was defined as having symptomatic and/or biochemical abnormalities, 17 patients (17/62, 27%) showed only one of those abnormalities. Among patients having both abnormalities, 21 patients (21/45, 46.6%) had a mismatch in the onset timing of those abnormalities. Diagnostic accuracy of commonly-used biomarkers in the early prediction of hypocalcemia was diverse according to the status of symptomatic and/or biochemical abnormalities. Heterogeneity of hypocalcemia should be taken into account for the proper management of patients who undergo thyroidectomy.

P386: PRELIMINARY EXPERIENCE WITH RAPID PTH LEVEL ASSAY IN HYPERPARATHYROIDISM A.S.Martinez1, A.J.Tincani2, A.Del Negro3, M.F.da Cruz4, F.V.Renato5, 1State University of Campinas (UNICAMP)

Introduction: Hyperparathyroidism is characterized by increase in PTH levels production by parathyroid glands. Reversal of this condition is dependent on the complete resection of all parathyroid tissue. This is aided now by the intra-operative and immediate post-operative rapid PTH level assay. The objectives of this study were: validate the use of the rapid PTH assay in patients with hyperparathyroidism; determine the efficiency of the surgery and possible interference in the surgical procedure. Method: The patients were studied preoperatively with ultrasound and scintigraphy, without computed tomography or magnetic resonance imaging. Serum levels of PTH were measured by assay using the ~125Elesys 2010 Roche Hitachi system and samples (4ml) were collected preoperatively, at 10 and 50 minutes after gland resection in the intra-operative period, and 4 hours postoperatively. In the same period were measured the total and ionized serum calcium. Up to this date nine patients were evaluated, from March to June 2007.

Results: Three man and six women were evaluated, with ages ranging from 24 to 66 years-old. Three patients (33, 33%) had adenomas and six (66, 6%) had hyperplasia. (renal) patients. We found four glands...
in all patients with hyperplasia, with two exceptions with three parathyroid glands. The maximum level of preoperative PTH level was 3493 pg/ml, minimum of 7.2 pg/ml, median of 62.8 pg/ml. All patients had significant drop in the PTH level (highest drop being 97.8%, lesser drop being 74.7%, median drop of 88.8%).

Conclusions: In this preliminary analysis of patients submitted to HPT and non parathyroid head and neck procedures. Kidney transplant patients who underwent HPT were included, as well as those operated on for head and neck cancer. Renal function may be assessed by serum creatinine levels. Serum creatinine variation may indicate changes in kidney function. The percent variation of creatinine (%Cr) was analyzed in patients undergoing parathyroidectomy for tertiary HPT, primary HPT, thyroidectomy and major head and neck procedures. The %Cr was calculated according to the formula: (postoperative creatinine/preoperative creatinine).

Methods: Retrospective analysis of patients submitted to HPT and non parathyroid head and neck procedures. Kidney transplant patients who underwent HPT were included, as well as those operated on for head and neck cancer. Renal function may be assessed by serum creatinine levels. Serum creatinine variation may indicate changes in kidney function. The percent variation of creatinine (%Cr) was analyzed in patients undergoing parathyroidectomy for tertiary HPT, primary HPT, thyroidectomy and major head and neck procedures. The %Cr was calculated according to the formula: (postoperative creatinine/preoperative creatinine).

Results: More than 10% creatinine elevation occurred in 77 of 105 patients with primary hyperparathyroidism, in 52 of 38 cases of parathyroid hyperplasia after renal transplantation, in 11 renal transplant patients with other head and neck tumors, in 11 of 22 individuals after thyroidectomy and in 3 of 18 submit to major head and neck surgery for neoplasia. Mean percent variations of creatinine were +30.8%, +39.5%, +2.7%, +18.7% and -6.4%, respectively for these groups. No significant differences were observed between HPT transplant renal cases, thyroid patients and primary HPT individuals. Significant difference occurred between transplant patients with and without HPT (p=0.05, Kruskal-Wallis) and among those with primary HPT and head and neck neoplasms (p=0.001, Kruskal-Wallis). When thyroidectomy patients were stratified according to postoperative hypocalcaemia and presumed hyperparathyroidism, a significant difference was observed. Mean creatinine increase was of 28.5% for those with hypocalcaemia and only 1.2% and +0.02 for non hypocalcaemic patients (p=0.06, Kruskal-Wallis).

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Conclusions: Acute and persistent elevation of creatinine occurs in operations with acute reduction of parathyroid hormone. This clinical observation is in accordance with previous animal studies showing renal function reduction after parathyroidectomy and a clinical study in primary HPT that showed functional and organic effects of HPT in the kidney. Parathyroid hormone or another parathyroid gland products may have an effect in renal hemodynamics that warrant further research. Known renal risk factors (hypovolemia, hypotension, anti-inflammatory drugs and radiological contrast) should be avoided in patients undergoing a parathyroid surgery, particularly those with less functional kidney reserve.

P388: HYPOCALCAEMIA - IS IT WHAT IT SEEMS TO BE?

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Background: The National Institute of Clinical Excellence (NICE) in the UK has stipulated the auditing and reporting of hypocalcaemia rates following thyroidectomy as part of the measures for accreditation of centres treating thyroid cancer in the UK. They did not however define hypocalcaemia. There is a lot of literature that reports the incidence of hypocalcaemia following thyroidectomy. However there is a lot of variability in these reports. This, we believe, is in a large part due to the difference in the definitions and criteria for reporting these results. Indeed the lack of standardization of definitions and criteria for hypocalcaemia following thyroidectomy has important implications, including: prevents a meaningful comparison between the results of different units and with a national standard, prevents the pooling of data when performing reviews and meta analysis, prevents the provision of accurate data to patients for consenting purposes. Objective: To examine the effects of different definitions on the reported incidence of hypocalcaemia following thyroidectomy. Methods: A literature review of studies reporting the incidence of hypocalcaemia post thyroidectomy was performed to identify different definitions used for hypocalcaemia. We analysed our database for thyroid surgery patients for the incidence of hypocalcaemia in 195 patients who had thyroidectomy, of whom 95 had total thyroidectomy, by the same surgeon over a two year period. The results were reported using the following six definitions for hypocalcaemia identified from the literature search: Criterions 1-6. Where the lowest adjusted serum calcium level during the two week post operative period was less than the lower range of the institutional normal range: in our case 2.10 mmol/l - after total thyroidectomy. Criterions 2-4: Where the patient developed post operative hypocalcaemia which required oral or intravenous calcium treatment due to development of symptoms or due to falling calcium levels after total thyroidectomy. Criterions 3-5: Where a patient required calcium treatment for more than six months after surgery. Criterions 4-6: Where the patient had total thyroidectomy and calcium levels below the institutional range at discharge. Results: The incidence of hypocalcaemia post thyroid surgery using the same cohort of 195 patients as defined by different criteria was as below: Criterions 1: 61/95 (64.2%) patients. Criterions 2: 31/95 (32.6%) patients. Criterions 3: 61/195 (31.2%) patients. Criterions 4: 31/195 (15.9%) patients. Criterions 5: 7 (7.3%) patients. Criterions 6 - 0 patients. Conclusions: This study clearly shows that the reported results of hypocalcaemia for the same cohort of post-thyroidectomy patients can differ substantially (varying from 0% to 64%) depending upon the definitions used to define hypocalcaemia post-operatively. More uniformity and standardisation is required for reporting hypocalcaemia.

P389: COMPARISON OF PERIOPERATIVE MANAGEMENT AND OUTCOME OF PARATHYROIDECTOMY BETWEEN OLDER AND YOUNGER PATIENTS

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Objective: The increase in life expectancy in the elderly has raised questions concerning the appropriate management of the older patient. The aim of the present study was to evaluate the characteristics, clinical status, surgical course, and outcome of patients over 70 years old with PHTP compared to younger patients. Methods: Between 1996 and 2006, 951 patients underwent parathyroidectomy for PHPT at our center, of whom 190 were over age 70 years. Data on the operative procedure was collected for all 951 patients from our computerized database, and the charts of the 190 older patients and 108 patients younger than 70 years operated on in 2003-2006 were reviewed. Results: The age difference between the two groups was statistically significant (74.9 vs. 54.4). Only 16% of the older group was asymptomatic at presentation compared to 28% of the younger group. There was no between-group difference in serum calcium level at presentation, although PTH level was significantly higher in the older group (294.8±403.3 ng/L versus 140.1±88.3 ng/L). Total hospitalization time was longer in the older group (±3±6 versus ±3±1.8 days), with no difference in duration of surgery. The surgical success rates in the older and younger groups were 94.8% and 98.1%, respectively. More uniformity and standardisation is required for reporting hypocalcaemia post-operatively.
Radiation Therapy

**P390: CURATIVE BRACHYTHERAPY FOR EARLY CANCERS OF THE BUCCAL MUCOSA, LIP, PALATE AND NOSE**  
R.K.C. Ngan 1, R.K.Y. Wong 2, S.Chow 1, H.Cheng 1, 1Queen Elizabeth Hospital, Kowloon, Hong Kong  

**Background:** Early cancers occurring in the buccal mucosa, palate, lip and nose can be readily cured by either surgery or radiotherapy (RT). While definitive surgery often requires wide surgical margins in the surrounding mast cells, underlining tissues, the resulting missing is comprised. Concurrent chemoradiotherapy, primary RT can spare the surgically-induced anatomical, cosmetic and functional morbidities, and achieve equivalent loco-regional control. This advantage can be critically important in patients with lip or buccal cancers located near the lip commissure where surgical reconstruction may not be able to restore the normal sphincter function, or in small palate and nose where bone resection and hence fenestration is required for adequate deep surgical margin.  

**Materials and Methods:** 25 patients were treated with either interstitial brachytherapy using manually-afterloaded radioactive Iridium-192 wire implants for buccal mucosa, lip and nose cancers, or intra-oral mould brachytherapy using remotely-afterloaded Iridium-192 sources for palate cancers. In interstitial brachytherapy, the Iridium-192 wires were inserted through loco-catheters inserted in the tumor bed for a few days to provide continuous low dose-rate radiation on an in-patient basis in a protected suite. Afterloading high dose-rate brachytherapy through an introral mould technique was effected through an afterloader (MicroSelectron, Nucleatron, Veenendaal, the Netherlands) housing a high activity radioactive Iridium-192 source. The mould brachytherapy is typically fractionated in a twice-a-day fashion and delivered on an outpatient basis once a week to a total of 3 weeks. In both patient cohorts, node positive patients were treated by external RT prior to brachytherapy. The node-negative neck of those with thick T1 and all >T2 buccal/lip cancers was managed either with neck dissection after brachytherapy or by external RT before brachytherapy. The neck of those node-negative palate cancers was managed conservatively if no external RT to the primary cancer was considered prior to brachytherapy.  

**Results:** Among the 13 patients treated by interstitial brachytherapy (6 received external RT before brachytherapy), there were 3 local failures and the actuarial local control rate at 5 years was 78%. Excluding the single T3 patient who failed locally, the local control was 82% and ultimate local control was 100% after salvage surgery in the 12 patients with T1 or T2 cancers at a median follow-up period of 43 months. Anatomical, cosmetic and functional organ preservation was largely realized in 10 of the 13 patients. The 5-year overall survival was 67%. Eight of the 12 patients with palate cancers treated by superficial mould brachytherapy also received external RT as part of the treatment. At a median follow-up period of 44 months, there were 2 local failures leading to a 5-year actuarial loco-regional control of 91% (100% for T1 cancers). The overall survival was 68% at 5 years and there was no significant late RT complication observed.  

**Conclusions:** We believe brachytherapy with or without external RT can be highly curative for early cancers in various regions of the oral cavity and nose. The patients can benefit substantially from the advantage of functional organ preservation and high therapeutic index of brachytherapy.

**P391: HIGH-DOSE-RATE BRACHYTHERAPY AS PRIMARY, ADJUVANT OR SALVAGE THERAPY FOR HEAD AND NECK CANCERS**  
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**Objective:** Improvements in disease outcomes and long-term morbidity in head and neck (H&N) cancer have been realized through advancing treatment modalities and optimizing multidisciplinary approaches. Low-dose-rate brachytherapy has been well-established historically as an alternative treatment modality in H&N cancer. Although high-dose-rate (HDR) brachytherapy may confer significant advantages over low-dose-rate brachytherapy, the challenge is still scarce with variable results on improved local control (LC) and survival, and long term toxicity as primary, adjuvant and salvage therapy for head and neck (H&N) cancer. In this study, we evaluated the efficacy of HDR brachytherapy with respect to tumor control, survival, and local toxicity as primary, adjuvant, and salvage therapy for H&N cancer.  

**Methods:** 37 oropharyngeal cancer were treated with HDR brachytherapy (HDRBT) at William Beaumont Hospital between June 1998 and May 2007. 16 patients underwent definitive treatment with HDRBT either as combined external beam radiation (EBRT) + HDRBT (n=11) or HDRBT alone (n=5). Six patients underwent adjuvant therapy with surgical resection followed by HDRBT for close or positive margins. 15 patients were treated in the recurrent setting including 6 neck recurrences treated with neck dissection + HDRBT and 9 primary recurrences, treated with surgery alone initially, salvaged with EBRT + HDRBT (n=7) or re-resection + HDRBT (n=2). The treatment sites were oral cavity (n=21), oropharynx (n=7), nasopharynx (n=3), and neck (n=6).  

**Stage of disease included 11 for HDR alone or adjuvant HDR and 14va for EBRT + HDRBT boost. Median age was 58 years. For combined EBRT + HDRBT, median dose delivered with EBRT was 50 Gy (45-66 Gy) with a HDRBT boost median dose 20 Gy (16-25 Gy) in 3-5 fractions twice daily (b.i.d.). Median HDRBT dose delivered with definitive HDRBT alone was 45 Gy (35-45 Gy) and adjuvantly was 35 Gy (33-36) in 3-4 Gy fractions b.i.d. Median time between EBRT completion and HDRBT initiation was 4 days and all efforts were taken to maximize dose homogeneity.  

**Results:** With median followup of 26 months (8-70 months), 7 local recurrences were observed 3-7 months after HDRBT. The 3-yr LC and overall survival (OS) in the definitive/adjuvant setting were 91% and 82%, respectively. The 2 local failure patients in the definitive/adjuvant group required without evidence for distant disease and underwent salvage with further HDRBT. In the salvage setting, the 3-yr LC and OS were 67% and 60%, respectively. 4 of the 5 local failures in the salvage group developed in patients treated for neck recurrence with those of these patients receiving with distant metastases. LC was correlated with primary versus salvage treatment (p=0.02) and neck as treatment site for recurrence (p=0.04). Four grade 3/4 late complications occurred in three patients: local ulceration (2) and local ulceration and mandibular osteonecrosis (1).  

**Conclusions:** Our results compare favorably with those previously reported for LDR brachytherapy with fewer late complications, HDRBT may play an important role as primary, adjuvant, and salvage therapy for head and neck cancer and should be further evaluated in prospective clinical trials.

**P392: CONCURRENT CHEMORADIOTHERAPY WITH S-1 FOR THE ELDERLY AND PATIENTS WITH COMPLICATIONS**  
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**Objective:** The purpose of this study is to establish the efficacy and safety of concurrent chemoradiotherapy with S-1, oral 5-FU drug, for advanced head and neck squamous cell carcinoma (HNSCC) in elderly patients and patients with complications, e.g. renal dysfunction, circulation failure and so on.  

**Methods:** The eligibility criteria included histologically-proven squamous cell carcinoma of the larynx, oropharynx, hypopharynx and oral cavity, from December 2002 to October 2007. Eighty cases were divided into four groups: 1 stage III and IV, older than 75; complications of renal dysfunction, ischemic heart disease, peptic ulcer and brain infarction. Treatment response, especially complete response (CR), survival rate and recurrence rates were evaluated.  

**Results:** Evaluable patients were 50 cases, 47 male and 3 female; 15 stage III, 35 stage IV; 35 resectable cases, 15 unresectable cases. Primary sites were as follows; 9 larynx, 13 oropharynx, 25 hypopharynx, and 3 oral cavity. CR rates showed CR at the primary sites, and 29 of 39 lymph node metastatic patients showed CR at the lymph nodes. Cause specific 2 years survival rates were 92% in stage III and 38% in stage IV, respectively. Recurrence rates in CR cases were 21% in stage III and 28% in stage IV, respectively. The adverse events were tolerable and controllable. Recurrence rates in CR cases were 8 of 42 cases at the primary sites, and 4 of 29 cases at the lymph nodes.  

**Conclusion:** Concurrent chemoradiotherapy with S-1 for advanced HNSCC in the elderly and patients with complications is effective for stage III and IV cases up to T3 and/or N2b cases.

**P393: RESULTS OF HYPERFRACTIONATED OR ACCELERATED HYPERFRACTIONATED RADIOTHERAPY FOR ADVANCED ORO-HYPOPHARYNGEAL CANCER**  
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**Objective:** Hyperfractionated radiotherapy (HF) or accelerated hyperfractionated radiotherapy (AHF) was originally developed to fight for repopulation during treatment and tumor hypoxia. The purpose of this study is to investigate response rate, overall survival rate and acute and late toxicity of this therapy for advanced oro-hypopharyngeal cancer in our clinic.  

**Material and Study Design:** Forty-nine patients with advanced oro-hypopharyngeal squamous cell carcinoma who were treated with HF or AHF during 1996 and 2004 were RETROSPECTIVELY studied. The patients consist of 27 oropharyngeal cancer (6 stage III and 21 stage IV) and 22 hypopharyngeal cancer (1 stage III and 21 stage IV). Eleven patients had inoperable primary sites or lymph nodes. HF (1.2Gy/r, 2/r/day, total dose...
72 Gy was performed on 8 patients and AHF (1.5 Gy/ft, 2/ft/day, total dose 66-81 Gy or 1.6 Gy/ft, 2/ft/day, total dose 70.4-76.8 Gy) was employed for 41 patients. Concurrent chemotherapy was given to 29 patients. Results: Response rates of this therapy were 96.3% for oropharyngeal cancer and 86.4% for hypopharyngeal cancer and complete responses were achieved in 16 patients (59.2%) and 10 patients (45.5%), respectively. However, 5-year loco-regional control rates were 53.8% and 93.8% for all patients, 36.5% and 93.8% for the largest group of patients with nasopharyngeal cancer - 67% of LC and 77% of NC, and for G3 cancer differentiation group - 75% of LC and 77% of NC. There was no grade 3 or 4 late morbidity and among grade 2 xerostomia was the most frequent. Conclusions: Hyperfractionated 3-DCRT is effective and well-tolerable treatment for patients with advanced oro-hypopharyngeal cancer. However, the overall survival rate did not come up to our expectations. AHF with concurrent chemotherapy cannot be recommended due to unacceptable high morbidity.

P394: HYPERFRACTIONATED RT HAS GIVEN GOOD PATIENT TOLERANCE AND WAS EFFECTIVE AGAINST NASOPHARYNGEAL AND GRADE 3 H&N CANCER
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Objective: To evaluate the effectiveness and tolerance of hyperfractionated 3-D conformal radiation therapy (3-DCRT) in patients with loco-regional advanced head and neck cancer. Methods: Seventy nine patients with stage III and IV of head and neck cancer have been treated with hyperfractionated 3-DCRT alone between the years 1997-2002 at Gliwice Center of Oncology Institute. All patients were irradiated twice-a-day, starting with dose per fraction of 1.1 Gy for CTV to 55 Gy, following by 1.2 Gy fractions for GTV(s) up to 79 Gy of total dose. Cisplatin-based chemotherapy was allowed as neoadjuvant and/or adjuvant treatment for patients with bulky disease and/or high risk of distant metastases respectively. Acute mucosal reactions were evaluated carefully and regularly once-a-week as a both morphological and functional parameters mainly determining tolerance of treatment. Late toxicity was examined during the each follow-up visit in outpatient clinic on site. Results: The mean total dose of 77.4 Gy was given (range: 70.4-83.4 Gy). Chemotherapy was realized in 29 patients (37%). No patient had to stop radiotherapy because of acute toxicity. Confluent mucositis occurred in 64 patients (80%), however only 5 patients (6%) need-foods. Therefore the mean grade was 5.6% of initial value. The overall 5-year rates of both local control (LC) and nodal control (NC) were 50% and 66% respectively; however 5-year disease-free survival (DFS) rate was only 35%. Chemotherapy has improved LC and DFS but not significantly. In sub-group analysis the best results were observed for the largest group of patients with nasopharyngeal cancer - 67% of LC and 90% of NC, and for G3 cancer differentiation group - 75% of LC and 77% of NC. There was no grade 3 or 4 late morbidity and among grade 2 xerostomia was the most frequent. Conclusions: Hyperfractionated 3-DCRT is effective and well-tolerable treatment for patients with advanced head and neck cancer, and among them the best results are obtained for the patients with nasopharyngeal or grade 3 differentiated cancers.

P395: WEIGHT VARIATION AFTER CHEMORADIATION THERAPY FOR ADVANCED SCCHN: COMPARING CONVENTIONAL RADIOTHERAPY AND IMRT
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Objectives: Concurrent chemoradiotherapy and chemotherapy (CRT) is a standard of care for stage III/IV-A squamous cell carcinoma of the head and neck (SCCHN). The introduction of Intensity Modulated Radiation Therapy (IMRT) promises better outcomes compared to conventional radiotherapy (RT), principally by reducing the incidence of xerostomia, pharyngeal fibrosis and swallowing problems. Weight evaluated over time is an objective measure that can give us an indication of the impact of long-term sequelae of radiation therapy. The goal of the present study is therefore to evaluate on a period of 24 months post-CRT for locally advanced SCCHN weight loss and Body Mass Index (BMI) differences between patients treated with conventional RT and IMRT. Method: Retrospective chart review in an academic tertiary care center. 584 charts of patients treated with CRT for locally advanced SCCHN between 1998 and 2005 have been reviewed. Complete information on height and weight initially, during follow-up visits, and the radiotherapy modality used was retrieved for 85 patients (67 conventional and 18 IMRT). Weight loss and BMI comparison was measured at 6, 12 and 24 months following CRT. The statistical analysis was performed with a Student’s T test. Results: For the conventional RT group, weight loss and BMI decrease was significantly more pronounced at 12 and 24 months than for patients treated with IMRT. Specifically at 24 months, parameters for conventional RT and IMRT were 10.4 kgs (12.5%) and 3.4 kgs (3.5%) for weight loss and 3.13 kg/m2 and 1.25 kg/m2 of reduction of BMI. The relative risk of weight loss with conventional RT compared with IMRT is 3.5. The difference in weight loss between the RT modalities was found to be statistically significant, as established by a t-test (p<0.05). Complete data on evolution over time of weight and BMI will be presented at the meeting. Conclusions: CRT for advanced SCCHN causes long term side effects including xerostomia, pharyngeal fibrosis, and impairment of swallowing. Long term weight loss is an objective measure and an interesting indirect measure of these symptoms. Patients treated with conventional RT suffer from greater weight loss than those treated with IMRT. We conclude that IMRT may provide patients with a significantly improved quality of life. Further studies with increased patient numbers and validated quality of life questionnaires are necessary to corroborate and correlate these results.

P396: NOVEL PANEL OF BIOMARKERS PREDICTS RESPONSE TO RADIATION BASED THERAPY FOR HEAD AND NECK CANCER
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Purpose: Degree of response to radiotherapy (RT) and chemoradiotherapy (CRT) differs among head and neck cancer patients. This has previously been correlated with c-DNA microarray studies showing five markers predictive of chemosensitivity and radiosensitivity (VEGF, Bcl-2, Claudin-4, Cmet, and Yap1). We aimed to correlate expression of these markers in pretreatment biopsies with clinical outcomes in patients with squamous carcinoma of the head and neck (SCCHN). Methods: From December 1995 to November 2004, 86 patients with clinical stage II-IVa oropharyngeal (n=30) and stage II-Va laryngeal (n=56) SCCHN who underwent treatment with either RT alone (n=47) or CRT (n=39) were selected for analysis. RT was delivered using 3-D conformal RT or intensity modulated RT to a median dose 7000 cGy (2400Gy - 8160Gy) and concurrent cisplatin-based chemotherapy. Treatment response was evaluated during and after treatment using nasopharyngoscopy, computed tomography, and/or biopsies. Any local recurrence within 6 months after completion of radiation therapy was considered a partial response. Immunohistochemical staining (IHC) for VEGF, Bcl-2, Claudin-4, Yap1 and Cmet was performed on pretreatment biopsy specimens obtained from all 86 patients. Staining was graded according to intensity and percentage of cells positive by two independent observers. Results: Median follow up for all patients was 29 months. The majority (80%) of patients were male with a median age at diagnosis of 62 years. Twelve patients (5 larynx, 5 oropharynx) experienced an incomplete response and 11 patients (8 larynx, 3 oropharynx) recurred at a median time of 12.6 months (range, 7.7 : 68.8 months). Of the recurrences, 7 patients were found to have a locoregional recurrence (median, 10.8 months) and 4 patients were found to have distant metastases (median, 25.2 months). No patient with an incomplete response or recurrence received a cumulative radiation dose less than 6600 cGy. Cause specific survival (CSS) and recurrence free survival (RFS) at 2 years was 85% and 90% and at 3 years was 81% and 84%, respectively. Biomarkers predictive for incomplete response were increased Cmet (intensity grading: p=0.003) and increased Yap (intensity grading: p=0.03). Increased Bcl-2 (median intensity grading: p=0.01), increased Bcl-2 (intensity grading as a continuous variable; p<0.05). Complete data on evolution over time of weight and BMI will be presented at the meeting. Conclusions: CRT for advanced SCCHN causes long term side effects including xerostomia, pharyngeal fibrosis, and impairment of swallowing. Long term weight loss is an objective measure and an interesting indirect measure of these symptoms. Patients treated with conventional RT suffer from greater weight loss than those treated with IMRT. We conclude that IMRT may provide patients with a significantly improved quality of life. Further studies with increased patient numbers and validated quality of life questionnaires are necessary to corroborate and correlate these results.
intensity grading; p=0.002), increased Cmet (optimal cut at 85%; p = 0.022), decreased Claudin-4 (optimal cut 16.5%; p=0.035) and increased Bcl-2 (intensity grade; p=0.03) correlated with reduced RFS. Conclusion: YAP is a universal marker in predicting for RT/CT response, CSS, and RFS. Bcl-2 and VEGF predict for both CSS and RFS, and Cmet predicts for RT/CT response and RFS. Analyzing individual genetic profiles in the clinical setting using the above markers may allow for tailored patient-specific therapy to improve outcomes.

P397: PREDICTIVE FACTORS OF THERAPEUTIC RESPONSE TO CHEMO-RADIATION THERAPY IN PATIENTS WITH LARYNGEAL AND OROPHARYNGEAL SCC: A MULTICENTER SERIES

Objective of the Study: To determine predictive factors for therapeutic response and survival in patients who underwent concurrent chemoradiotherapy and radiotherapy for squamous carcinoma (SCC) of the upper respiratory and digestive tract. Material and Methods: Between January 2000 and August 2003, 57 patients with laryngeal and oropharyngeal SCC (Stages III and IV) underwent chemoradiotherapy at a major referral center. The predictive factors for therapeutic response were univariate analysis of P53, Bcl2, Ki67 and PCNA on normal mucosa, and in the tumor specimen (and in both) were correlated with the response of treatment, as well as with the association of 22 clinical and therapeutic factors of this group of patients. Statistical analysis was made using a univariate and multivariate analysis. Survival curves were made using the Kaplan-Meier method. Results: Some degree of toxicity was observed in 100% of patients. Complete response was observed in 68.4% of cases, with an overall survival (OS) rate of 58.24% and disease-free survival (DFS) rate of 56.4%. Among the 22 predictive factors, only the lack of enteral feeding (p=0.006), T3 stage, (p=0.009) and the lack of tracheotomy (P=0.0002), were predictive of a better response to treatment (univariate analysis). Only the negative expression of Bcl2 in the tumor, mucosa and in both (p=0.017, 0.04 and 0.028, respectively) were predictive of a better response (univariate analysis) with an Odds Ratio of 3.64; 5.29; and 6.68, respectively. Positive expression of Bcl2 was 25.5%, P53 was 55.3%, Ki67 was 82.6%, PCNA was 76%. None of those expressions caused any impact to response of treatment. Nevertheless, when a multivariate analysis was made, only the lack of previous tracheotomy (p=0.0056) and the lack of enteral feeding (p=0.002) were predictive factors for a better therapeutic result. Conclusions: (1) Among the 22 predictive factors, only the lack of enteral feeding and the lack of previous tracheotomy were predictive factors for better results. (2) Throughout an univariate analysis the lack of immunohistochemical expression of Bcl2 in the tumor specimen, on mucosa and in both, had a positive impact in therapeutic response.

P398: PROTON THERAPY AND CARBON ION THERAPY AGAINST HEAD AND NECK CANCERS K. Morimoto1, Y.Demizu2, M.Murakami2, A.L.Costa1, K.L.Fernandes1, R.Zdanowski1, L.Lopes1, L.Rangel1, R.A.Lima1, P.B.Milet1,1, Brazilinan National Cancer Institute, INCA, Rio de Janeiro, Brazil

Objective of the Study: In April 1, 2001, Hyogo Ion Beam Medical Center (HIBM) was opened as the world’s first facility to provide both proton and carbon ion therapy. In this study, we retrospectively reviewed our experience of both proton therapy and carbon ion therapy against head and neck cancers in HIBM. Methods: Between April 2001 and August 2007, 275 patients with head and neck cancers were treated with particle therapy at HIBM. Among these patients, 157 patients were followed up more than 12 months after treatment. The patients consisted of 83 males and 74 females aged from 15 to 89 years (median age 64). Pathologic subtypes of the tumor included adenoid cystic carcinoma in 34 patients, malignant melanoma in 46 patients, squamous cell carcinoma in 30 patients, adenocarcinoma in 12 patients, olfactory neuroblastoma in 6 patients, and others in 29 patients, respectively. One hundred twenty-four patients were treated with proton therapy and 8 patients were treated with carbon ion therapy. Overall 5-year survival rates were estimated with Kaplan-Meier methods. Results: At the present, local control rates were 88.2% for adenoid cystic carcinoma (26/28 with proton therapy and 2/6 with carbon ion therapy), 78.3% for malignant melanoma (28/34 with proton therapy and 8/12 with carbon ion therapy), 63.3% for squamous cell carcinoma (18/29 with proton therapy and 1/1 with carbon ion therapy), 91.7% for adenocarcinoma (8/8 with proton therapy and 3/4 with carbon ion therapy), 100% for olfactory neuroblastoma, and 82.8% for others (18/21 with proton therapy and 6/8 with carbon ion therapy) respectively. Overall 5-year survival rates were 79.3% for adenoid cystic carcinoma, 23.9% for malignant melanoma, 39.3% for squamous cell carcinoma, 34.7% for adenocarcinoma, 100% for olfactory neuroblastoma, and 69.4% for others respectively. And overall 2-year survival rate was 55.4% for malignant melanoma. Conclusions: Our experience confirms that both proton therapy and carbon ion therapy had provided excellent local control for adenoid cystic carcinoma, malignant melanoma, squamous cell carcinoma, and olfactory neuroblastoma. However, survival rates of patients with squamous cell carcinoma, malignant melanoma, and adenocarcinoma were unsatisfactory. Adjunct therapy including chemotherapy and/or immunotherapy should be considered for these tumors.

P399: CLINICAL FEASIBILITY OF USING THE CALYPSO™ SYSTEM IN REAL-TIME MONITORING HEAD-AND-NECK IMRT PATIENT POSITION R.A.Lima1, P.B.Milet1, 1Brazilian National Cancer Institute, INCA, Rio de Janeiro, Brazil

Objective: Head-and-Neck IMRT utilizes highly conformal dose distribution and should dose gradients. Therefore, small patient movements may compromise dose coverage to target volumes and critical normal structures. The Calypso 4D Localization System is a real-time tracking device, which continuously monitors the location of fiducial markers (radiofrequency beacon transponders) during radiotherapy. Our specific aim is to evaluate the feasibility of using the Calypso system for head-and-neck IMRT. Methods: Two volunteers were evaluated. Three Calypso transponders were imbedded in a custom-made earpiece. The volunteer wore the earpiece and then was immobilized with a thermal plastic mask. The separation between the isocenter and the earpiece was determined using a treatment plan of a head-and-neck cancer patient under treatment in our department. We used the Calypso system to localize and track the positions of the transponders for ten minutes and repeated the procedure three times. To test the accuracy of the tracking system, we performed small couch movements in three dimensions during the procedure and compared these movements with the readings obtained from the Calypso system. Results: The Calypso system was able to localize and track the position of the earpiece. The deviation between the digital readout of the couch and the Calypso system was within 0.5 mm. The displacement of the earpiece was found to be less than 1.5 mm for 95% of the treatment simulation time. The Calypso system may be a valuable tool in tracking intra-fractional patient movement during head-and-neck IMRT.

P400: DAILY IMAGE GUIDANCE FOR INTENSITY MODULATED RADIATION THERAPY (IMRT) FOR HEAD AND NECK CANCER R.B.Den1, A.Dpemer1, Y.Xiao1, A.Cupino1, G.Bednarz1, J.Galvin1, M.Machtay1,1 Thomas Jefferson University, Philadelphia, PA

Objective: Intensity modulated radiation therapy (IMRT) creates a highly conformal dose distribution with dose sparing to adjacent organs at risk. Correct patient position is critical in the treatment of head and neck cancers (HNC) with IMRT given its inherent dose gradient. The use of kilovoltage cone-beam computed tomography (CBCT) allows for online acquisition of volumetric anatomical information of a patient before and/or after treatment. This is an interim analysis of a study to analyze the intrafraction and inter-fraction motion of patients undergoing IMRT treatment for HNC using image guided radiation therapy (IGRT). Methods: All patients signed informed consent for this IRB-approved, prospective trial. Patients underwent conventional CT based planning for IMRT with customized immobilization devices. Entry criteria into the study included HNC, radiotherapy dose > 60 Gy, good performance status, good patient cooperation (defined as experienced in the intra-treatment motion < 2.5 mm). Patients were treated on an Elekta Linear Accelerator (Synergy®) with IGRT using a mounted CBCT. Pre-treatment corrections were performed for translational, but not rotational, variations. Each patient had a CBCT imaging procedure prior to treatment and at least once-weekly post-treatment. The CBCT images were fused to the planning CT. Variation readings obtained from the Calypso system. Results: The Calypso system was able to localize and track the position of the earpiece. The deviation between the digital readout of the couch and the Calypso system was within 0.5 mm. The displacement of the earpiece was found to be less than 1.5 mm for 95% of the treatment simulation time. The Calypso system may be a valuable tool in tracking intra-fractional patient movement during head-and-neck IMRT.

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standard deviations of these variances were calculated. Results: Twenty-one consecutive patients, 13 male and 8 female, were analyzed for this study. The subdivision by different tumor locations were: 8 larynx, 4 oropharynx, 5 oral cavity, 1 salivary gland, 2 paranasal sinus, and 1 unknown primary/neck-node. 775 CBCTs were analyzed. The average inter-fraction variances (reflecting systematic error) were 1.4, 1.6, and 1.7 mm in the x, y, and z dimensions and 1.1, 0.8, and 1.0 degrees in the three angular dimensions. Average inter-fraction translational variances (reflecting patient motion/ drift) were 0.96, 1.1, and 0.96 mm in the x, y, and z dimensions. The recommended PTV margins based on these data are displayed in the table below. Conclusion: IGRT-CBCT is an effective modality to improve the accuracy of IMRT. Without IGRT, recommended PTV margins to ensure appropriate coverage of 90% of all patients are 5-6 mm. However with IGRT, this margin may be reduced to 2-5.3 mm, a 50% reduction. This may allow for dose escalation to tumor and decreased radiation exposure to normal tissues. Future studies will furthermore allow for correction of angular variances.

Recommended PTV margin*

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Based on “Mean” Inter-fraction data 2.9 mm 3.1 mm 3.4 mm
Based on “90th percentile” Inter-fraction data 5.0 mm 5.2 mm 6.1 mm
Based on “Mean” Intra-fraction data 2.5 mm 5.1 mm 1.3 mm
Based on “90th percentile” Intra-fraction data 2.4 mm 3.3 mm 1.9 mm

* Recommended PTV margin = 2 + 0.7U. Based on Stroom et al. (IJROBP 1999); U = systematic error (mean); U = random error (Std. deviation).

P401: INTENSITY-MODULATED RADIOTHERAPY IN THE TREATMENT OF ORAL CAVITY CANCER

Objective: Retrospective review of patients with oral cavity cancer treated with post-operative intensity-modulated radiation therapy (IMRT) at a single institution. Methods: From 9/00 to 12/06, 36 patients with histologically confirmed squamous cell carcinoma of the oral cavity underwent surgery followed by post-operative IMRT. Median age was 64 years (range 20-89 years). The median time between surgery and the start of radiation therapy was 7 weeks (range 4.7-12 weeks). Sites included were: buccal mucosa (n=8), oral tongue (n=12), floor of mouth (n=9), gingival (n=4), hard palate (n=2) and retromolar trigone (n=1). The majority of the patients had Stage III/IV disease (78%). All patients underwent aggressive pre-treatment dental evaluation prior to IMRT. Ten patients (28%) received concurrent post-operative chemotherapy with IMRT. Chemotherapy was given as follows: cisplatinum only (n=4); cisplatinum + cetuximab (n=2); carboplatinum + taxol (n=9); carboplatinum + 5-fluorouracil (n=7); and carboplatinum + cetuximab (n=1). Those given cetuximab were on protocol. The median dose was 60 Gy to the post-operative bed and increased to 66 Gy in the presence of pathologically positive/close margins. Two patients with gross residual disease were treated to 70 Gy. Acute toxicities and late complications were graded according to the Common Terminology Criteria for Adverse Events version 3.0. Results: The median follow-up for surviving patients was 31.2 months (range 15-88 months). Failures were as follows: 5 local, 2 regional, 7 locoregional, and 5 distant metastases. At the time of this analysis, 9 patients died and all were due to either uncontrolled locoregional disease or distant metastases. Both patients with regional failures had neck dissections prior to radiotherapy. Those who failed locoregionally did not receive post-operative chemotherapy. Among those with distant metastases, two presented with dermal metastases that were in and out of the radiation fields. The 2-year estimates of local progression-free, regional progression-free, locoregion progression-free, and disease free survival remained the same, except for local progression-free and locoregion progression-free which were 77% and 72%, respectively. Median overall survival time to locoregional failure was 12.4 months (range 3.2-13.1 months). Mean overall survival time to disease free survival was 24.6 months (range 1.0-25.8 months). Pericentral endoscopic gastrostomy (PEG) tube was placed prophylactically in 17 patients with 2 additional patients having PEG placement during IMRT due to toxicity. All surviving patients are PEG independent. The median time to PEG removal or PEG independence was 3 months (range 0.03 months-15 months). Eight patients died within 14 months after IMRT prior to PEG removal. Acute 9 Grade 2 skin, mucositis, and dysphagia were experienced by 56%, 69%, and 36% of the patients, respectively. Xerostomia continued to decrease over time from the end of IMRT with only 14% experiencing Grade 2 toxicity at the time of this analysis. Documented late complications include Grade 2 trismus (8%) and osteoradionecrosis (5%). Conclusions: IMRT as an adjuvant treatment for oral cavity tumors is feasible and effective with promising results. Xerostomia improved over time. Strategies using IMRT to limit the dose delivered to the mandible and muscles of mastication without compromising target coverage might be useful to further minimize this late complication.

P402: MANDIBULAR DOSE-VOLUME ANALYSES IN A COHORT OF HEAD AND NECK CANCER PATIENTS TREATED WITH SIB-IMRT

Purpose: Osteoradionecrosis (ORN) of the mandible is a severe complication of radiation therapy resulting from excessive bone dose. In this study we analysed mandibular dose distributions in a group of patients treated in our institution using Simultaneous Integrated Boost-Intensity Modulated Radiation Therapy (SiB-IMRT) treatments for head and neck cancers with intent to identify which factor(s) influenced mandible doses. Materials and Methods: Mandible volume and dose data for 57 head and neck cancer patients treated with SiB-IMRT in our institution were retrospectively analyzed. Patients were prescribed 69.96 Gy to the gross disease (PTVHD) and 54.12 Gy to a reduced PTV (PTVLD) in 33 fractions. Mean PTVHD was 286.6 cc (range 57.4 - 798.4 cc) and the mean PTVLD was 438.2 cc (range 173.2 - 759.2 cc). All patients were planned using 6 MV X-rays with 7-9 optimized IMRT beams. Mandible and Mandible, Planning Target Volume (PTV) overlap volume data was collected along with mandible dose-volume information. All dose calculations were performed using Eclipse dose planning system (Varian Medical). Results: The mean mandible volume was 58.9 cc [std dev ±14.8]. Percentage mandible volume receiving <60, 60-65, 65-70, and 70-75 Gy were 86 ±1.9, 14 ±1.9, 8 ±1.4, and 2 ±0.5 respectively. Evaluating the “hottest” 0.2 cc, 1 cc and 2 cc of the mandible, the doses (Gy) were 70 ±0.7, 66 ±1.0 and 64 ±1.0 respectively. The PTV, Mandible overlap volume (%) was 1.4 ±1.5. Evaluating the whole mandible, the mean dose was 44 ±1.0. The mean mandible dose increased with increasing PTV mandible overlap volume. In general, the mean dose to mandible could be constrained to <45 Gy when the volume overlap was <20%. Conclusion: In head and neck SiB-IMRT, the maximum and mean mandible doses were strongly influenced by the degree of mandible overlap with gross disease. In the group of patients included in this study, no part of the mandibles received doses >75 Gy (ORN inducing threshold).

P403: QUANTIFICATION OF ANATOMIC POSITIONAL VARIANCE OVER THE COURSE OF EXTERNAL BEAM RADIATION WITH IMRT

Purpose: Intensity modulated radiation therapy (IMRT) in the treatment of head and neck cancers has the ability to minimize dose to normal structures. The highly conformal nature of IMRT places an increased importance on knowledge of anatomical change and positional variance over the course of treatment. This is a preliminary analysis of a prospective study in which we analyze the degree of these changes during a course of head and neck radiation. Methods: This is a prospective trial in which eligible patients underwent conventional CT based planning for IMRT with customized immobilization devices dependent on tumor site. Patients were treated with external beam radiation with the Elekta Cone Beam CT (CBCT) that uses a kilovoltage imaging procedure prior to each treatment. CBCT images were matched (using MISmatch software) to the initial planning CT based on external fiducial markers. Structures (mandible, tongue, hyoid bone, thyroid and parathyroid) were contoured on both the initial CT and each CBCT. Volumes were calculated. Results: Ten patients and 65 CBCTs (one CBCT per patient per week) were analyzed. Structure position as compared to the initial CT scan varied over the course of treatment, differences in structure centers varied but were typically 94.9% of treatments) less than 1 cm. The median variance and standard deviation was 3.3 ± 1.5, 5.2 ± 4.6, 5.1 ± 2.7, and 6.0 ± 2.5 mm for the mandible, tongue, hyoid bone and thyroid respectively. Average positional variance over the course of treatment between the initial CT and CBCT was greater for the mandible and tongue than hyoid and thyroid and there was decreased normal structure sparing for the structures on the CBCT (see Table I). No significant difference was seen in position for each structure as a function of time during treatment (4.6 mm median variance in week 1 compared to 4.7 mm in the final week). Conclusion: Anatomical positional variance for several structures in the head and neck.

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is significant. Daily verification to minimize setup error and correct for structure displacement is best utilized for patients who have a greater degree of displacement in the first week and also in patients for whom sparing of laryngeal structures is desired.

Table I

<table>
<thead>
<tr>
<th>Structure</th>
<th>Positional Variance (mm)</th>
<th>Standard Deviation (mm)</th>
<th>Maximum Deviation (cm)</th>
<th>% Of variance &gt; 1 cm</th>
<th>% Volume overlap b/n CT and CBCT</th>
<th>Radiation Field</th>
<th>% Overlap: Initial CT</th>
<th>Radiation Field</th>
<th>% Overlap: CBCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mandible</td>
<td>3.3</td>
<td>1.5</td>
<td>0.9</td>
<td>0.0</td>
<td>74</td>
<td>14.5</td>
<td>14.0</td>
<td>19.0</td>
<td></td>
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<tr>
<td>Tongue</td>
<td>5.2</td>
<td>4.6</td>
<td>2.4</td>
<td>1.00</td>
<td>73</td>
<td>20.6</td>
<td>20.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyoid</td>
<td>5.1</td>
<td>2.7</td>
<td>1.3</td>
<td>4.3</td>
<td>42</td>
<td>20.1</td>
<td>21.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td>6.0</td>
<td>2.5</td>
<td>1.2</td>
<td>2.2</td>
<td>39</td>
<td>46.8</td>
<td>53.8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P404: RADIATION DOSE, DRIVING PERFORMANCE, AND COGNITIVE FUNCTION IN PATIENTS WITH HEAD AND NECK CANCER

Methods: Seven patients with HNC (6 males and 1 female), with a mean age of 57.6 years old, participated in an objective laboratory evaluation of driving using a state-of-the-art virtual reality driving simulator. Six participants were driving regularly at the time of the study. Cognitive function was evaluated by the Trail-Making Test, Part B (TMT-B). The TMT-B is a test of selective and directed attention, working memory, visuomotor processing speed, and executive function. The TMT-B has been validated as a sensitive measure for cognitive dysfunction. The driving evaluation involved completing a 12-minute simulated driving course. Participants were instructed to drive the simulator as they would normally drive their own vehicle — obeying all traffic signs and signals along the simulated roadway. The driving scenarios required participants to respond to situations frequently encountered while driving in the real world. The principle measures from the driving simulator were average speed, steering variability, mean brake reaction time, and the number of fatal collisions. The estimated maximum radiation dose incidentally received by the temporal lobes during radiation therapy on cognitive function seems to diminish after a few months. However, this adverse effect of radiation therapy on cognitive function is best utilized for patients who have a greater degree of displacement in the first week and also in patients for whom sparing of laryngeal structures is desired.

P405: BIOMECHANICAL TESTING OF TECHNIQUES FOR RIGID FIXATION OF LATERAL SEGMENTAL MANDIBULAR RECONSTRUCTIONS

Introduction: A variety of plating techniques are used for the rigid fixation of vascularized bone grafts used to reconstruct lateral segmental defects of the mandible. The purpose of this study is to evaluate the strengths of 3 commonly used plating techniques using biomechanical testing. Methods: Fifty polyurethane mandible and fibula models (Symbone AG, Malans, Switzerland) were tested in vitro. A 3 cm lateral segmental defect of the mandible model was contour to reconstruct the defect. Fibula segments were fixated in 4 different ways using one of the techniques creating 3 models. Group 1 consisted of models reconstructed with one 2.3 mm reconstruction plate across the defect, Group 2 consisted of models reconstructed with two 2.0 mm miniplates at each osteotomy site, and Group 3 consisted of models reconstructed with one 2.7 mm reconstruction plate across the defect. Models were tested using a MTS Mini Bionix 858 biomechanical testing device. Results: Loads were generated on the models at a rate of 1 mm/sec until model failure occurred. A maximum force and graft displacement at the time of failure were recorded for each model. The average displacement for Group 1 was 5.79 mm, for Group 2 was 14.08 mm, and Group 3 was 6.03 mm. The average force of failure for Group 1 was 737.8 N, for Group 2 was 616.4 N, and Group 3 was 681.0 N. The reconstructive plates did not break in any of the models. Failure was attributed to the screws or the models themselves in all cases. Conclusion: The 2.3 mm reconstruction plate provided the best rigid fixation for lateral segmental defects of the mandible. Further investigation will include micromotion analysis at these forces as maximum displacements varied widely long before model failure occurred.
head and neck reconstruction, but how the free flap itself can be used to optimize these techniques, providing the finishing touches to complex reconstruction.

P407: MAINTAINING THE PERFUSION PRESSURE AFTER MICROVASCULAR FLAP SURGERY: SAFETY OF POSTOPERATIVE NOREPINEPHRINE AND DOPAMINE
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Objective: Major reconstructive microvascular surgery demands intensive postoperative monitoring and postoperative sedation, which may cause peripheral vasodilatation and endanger the microvascular flap. Immediately following the surgery it is of importance to have the patient under deep sedation for 12-24 hours. One of the sedative agents is propofol, which causes vasodilatation and thereby reduces perfusion pressure. A clinical dilemma ensues: while deep sedation is necessary, adequate perfusion pressure needs to be maintained. We hypothesized that norepinephrine and dopamine are safe to use in postoperative care after microvascular radial forearm flap reconstruction.

Methods: To test our hypothesis, following informed consent, we enrolled 24 consecutive head and neck cancer patients to a randomised, controlled clinical trial. A microvascular radial forearm flap was used for reconstruction. The patients were allocated into three groups: dopamine, norepinephrine and control group (no attempts to increase mean arterial pressure if MAP was over 60mmHg). During sedation (propofol infusion maximally 4 mg/kg/h for the first 24 postoperative hours) the two intervention groups were given the vasoactive drug aiming to maintain mean arterial pressure between 80-90mmHg. The control patients received no vasoactive drugs unless the MAP was less than 60mmHg. Intravascular normovolemia was maintained as according to central venous pressure between 6-10 mmHg (Ringer’s acetate at need). The metabolic status and oxygenation of the flaps were repeatedly monitored with tissue pO2 (Licox) and microdialysate lactate to pyruvate ratio (L/P) every two hours during the first day and every three hours up to 72 hours. Students’s T-test was used for statistical analysis.

Results: Lactate/Pyruvate-ratio and tissue pO2 followed the same pattern in all three groups. There was no statistical difference (P>0.05) in the L/P-ratio between the three groups during the vasoactive drug infusion or during the further follow-up time. No adverse effects were noted and the postoperative recovery was uneventful.

Conclusion: Our findings support the hypothesis posed herein. Norepinephrine and dopamine are both safe and effective during the postoperative sedation following microvascular reconstruction of H&N-cancer surgery.

P408: REHABILITATION OF INTERSTITIAL HEAD AND NECK IRRADIATED TISSUES BY INJECTION OF ABDOMINAL SUBCUTANEOUS FAT TISSUES
P.Philipin1, P.Gangloff2, N.Tran3, J.Merlin2, G.Dolivet2, 1Centre Alexis Vautrin, Nancy, France; 2Centre Alexis Vautrin, Nancy, France; 3Faculté de Medicine, Nancy, France

Background: Treatment of head and neck cancers allows good carcinological results but induces aesthetic and functional sequelae. Autologous fat transplants have been used to correct aesthetic since the past century and exhibit many of the qualities of ideal filler. This fat tissue transplantation could be considered as a cellular therapy. A cellular conditioning with angiogenic potentiality, in particular adipocyte and mesenchymal stem cells contained in fatty tissues, could take part in the revascularisation of ischemic irradiated tissues and therefore correct functional sequelae.

Methods: In a series of 11 patients, subcutaneous and/or submucous sequelae consecutive with surgery and radiotherapy were treated by implantation or injection of abdominal fat tissues. Histological study was performed on irradiated tissues surrounding the scar, as well as abdominal fat and treated tissues.

Results: No surgical procedure complications occurred. For all cases, except one, the rehabilitation was aesthetic and functional. This induced an improvement of the quality of life of the patients. On the histological side, a decrease in morphologic patterns characteristic of the radiation injuries after fatty tissues injection is observed.

Conclusions: Fatty tissues can be transplanted successfully into irradiated areas, inducing not only aesthetic but also functional improvements. The clinical reversion of radiation-induced injuries and regression of morphological patterns seem correlated. However, the mechanisms inducing these changes remain unanswered.

Keywords: Adipose tissue, Revascularization, Head and neck neoplasms, Radiotherapy, Rehabilitation.

P409: PATIENT EDUCATION IN THE MAXILLOFACIAL PROSTHODONTIC SETTING
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Objective: The objective of this presentation is to highlight the importance of patient education in the maxillofacial prosthodontic setting and the different modes of patient education presentation.

Methods: Each treatment modality has side effects which need to be reviewed with patients. Due to educational, racial, and economic differences, patients learned differently. The increased use of technology has expanded the avenues of patient education. With each treatment modality, patient education can be presented in different formats. The side effects of surgery, chemotherapy, and radiation for each tumor site can be presented in different formats to address the various educational levels of patients.

Results: For each tumor site, the side effects of each treatment modality was presented to the MUSC Patient Education Committee for review with computer programs, written, and oral formats.

Conclusions: Patient education is critical to successful treatment of head and neck cancer. The increased use of technology has expanded the modes of presentation. Therefore, patients’ learning differences can be addressed.

P410: MICROSURGICAL REPAIR OF THORACIC DUCT LESION IN HEAD & NECK SURGERY: A METHOD TO PREVENT LYMPHATIC FISTULAS
N.Avalos1, L.Marín1, 1Hospital Fach, Santiago, Chile

Chyle fistula is an uncommon complication after neck dissection with potentially devastating consequence. This complication may be seen in 1 to 2.5% of neck dissections. Locally the chyle fistula delays local wound healing and is a rich medium for infection. Systemically chyle fistula produces loss of protein, fluid, electrolytes and lymphocytes putting the patient in a severe risk of malnutrition, sepsis and even death. On the other hand, this devastating complication raises patient’s cost, causes prolonged hospitalization, and retards the beginning of radiotherapy. All sources concur that prevention of chyle fistulas is preferable to its subsequent management. The aim of the present report is to show a new approach to preventing this complication after an evident intra operative thoracic duct lesion in the neck. A 50-year-old female patient with no significant previous medical history, presented with squamous cell carcinoma of the oral cavity, clinically T3N2aN0. Surgery was indicated as the initial therapy, with resection of the primary tumor and modified radical neck dissection of the left side (MRND) and a selective neck dissection (SNND) on the right side of the neck. We detected an intra operative lesion in the thoracic duct near the left jugular vein. Under vascular control and with microscopic magnification an end to side anastomosis with microsurgery technique was done between the thoracic duct and the jugular vein using interrupted 7-0 prolene suture with ligature of collateral. The patient had a satisfactory postoperative recovery without complications. The cervical drains were taken out in the second postoperative day after feeding; with no evidence of chyle leakage. The patient was discharge from the hospital on postoperative day four and started her radiotherapy as scheduled. Other two patients with similar condition were resolve in the same way with the same good result in the last two years. All thoracic duct lesions followed a MRND in our experience and all thoracic ducts presented collaterals.

Conclusion: Microsurgical repair of thoracic duct in the neck in the event of a chyle leak intra operatively is feasible and safe. We believed that spending more time in the operating room to avoid a fistula is better than wait and treat the eventual fistula after the initial surgery. We report a new approach to prevent chyle fistula, after thoracic duct lesions in head and neck surgery, with good results.

P411: MOTOR INNERRAION OF THE TRAPEZIUS MUSCLE: THE INTRAOPERATIVE MOTOR CONDUCTION STUDY
H.Ahn1, Y.Rho1, J.Kim1, S.Oh1, 1Hallym University Medical Center, Seoul, Republic of Korea

Objectives: In radical neck dissection, sacrifice of the spinal accessory nerve creates a definite deficit of the shoulder function. To demonstrate the preservation of motor input from the spinal accessory and the cervical plexus to the trapezius muscle, intra-operative motor nerve conduction study was performed.

Methods: Twenty-four patients were studied on completion of the operation. In each patient, the entire length of the spinal accessory nerve, the upper cervical plexus and some cervical plexus branches running to the trapezius were preserved independently. Compound muscle action potentials were measured for each part of the trapezius muscle on stimulation of the spinal accessory, C2, C3 and C4 nerves. Results: By stimulating the spinal nerve, evoked responses were obtained from all 24 patients in the upper, middle and lower trapezius. C2 contributions were seen in 2 out of
P412: THE EFFECT OF LINGUAL AND HYPOGLOSSAL NERVE RECONSTRUCTION ON SWALLOWING FUNCTION: A PROSPECTIVE STUDY.

Objective: To examine the effect on swallowing function of reanastomosis of lingual and hypoglossal nerves divided and reconstructed during head and neck cancer surgery. Methods: 65 patients underwent resection and free tissue reconstruction of oropharyngeal squamous cell carcinoma between April 1999 and July 2006. Post-operative lingual and hypoglossal nerve status was recorded. All patients were scheduled to undergo videofluoroscopy at one year and 12 months post-operatively. Results: Patients who underwent reanastomosis of their lingual and hypoglossal nerves had decreased pharyngeal residue scores and decreased bolus oral transit times compared to patients who had these cranial nerves sacrificed at 12 months post-surgery. Conclusion: Reanastomosis of lingual and hypoglossal nerves divided or sacrificed during head and neck cancer surgery preserves the efficiency of the oral phase of swallowing. This improves overall post-operative swallowing function and likely enhances patient quality of life.

P413: MICROVASCULAR VENOUS ANASTOMOSIS: ANTIITHROMBOTIC MEDICATIONS AND COMPARISON OF END-TO-END AND END-TO-SIDE TECHNIQUES

Objective: To compare techniques of venous anastomosis in microvascular surgery by examining the rate of venous cloting in end-to-end (ETE) and end-to-side (ETS) anastomoses and to review the effects of antithrombotic medications on the rate of venous cloting. Methods: A retrospective review was performed on 300 patients at a tertiary care center from January, 1994 to December of 2004. Patients with double venous anastomoses and those with vein grafts were excluded from the study. Results: The majority of the patients in this study were male (n=205, 68.3%) with a mean age of 60 years of age. Most were tobacco users (n=221, 73.7%) and had 14 tumors (n=219, 73.0%). Venous thrombosis occurred in 43 patients (1.43%) overall. Of the 117 patients in the ETE group, sixteen (13.7%) experienced venous thrombosis. Of the 183 patients in the ETS group, 27 (14.8%) experienced venous thrombosis. The difference between the two groups was not statistically significant. Intraoperative use of heparin resulted in a lower incidence of venous thrombosis (10.0% vs. 17.9%, p=0.036), but did not reach statistical significance. Dextran use resulted in a significantly higher rate of venous thrombosis (18.2% vs. 9.3%, p=0.029). Total flap failure occurred in 15 patients (5.0%). Conclusions: The rates of venous cloting with the end-to-end and end-to-side techniques were comparable. Dextran appeared to have a beneficial effect in regards to clotting, but the side-effect profile is concerning. Surprisingly, the aspirin group had a larger percentage of venous cloting. A prospective randomized trial to evaluate the use of these medications would be useful to clarify the risk-benefit ratio.

P414: QOL COMPARISON FOR PATIENTS RECEIVING VASCULAR VS NON-VASCULAR BONE GRAFT RECONSTRUCTION OF SEGMENTAL MANDIBULAR DEFECTS

Objective: Head and neck neoplasms requiring surgical resection of the mandible can have negative consequences on patient quality of life. For patients with segmental resections, the vascular fibular free flap and non-vascular iliac crest are commonly used for reconstruction. Due to the success associated with a vascularized graft, the fibula has surpassed the iliac crest in popularity; however, there still remain significant advantages with the non-vascular graft. Of the studies on patient quality of life in head and neck cancer, none compare the quality of life associated with these differing methods of mandibular reconstruction. Therefore, the purpose of the following study is to compare quality of life of both grafts to gain insight that may help guide therapeutic decisions. Methods: 29 patients at the University of California, San Francisco undergoing mandibular resection with subsequent reconstruction with either a vascular fibular free flap or non-vascular iliac crest bone graft were identified through retrospective chart review. Patient quality of life was assessed with a modified version of the University of Washington Quality of Life Questionnaire, version 4. Results: 18 patients responded; 10 previously reconstructed with a fibula and 8 with iliac crest reconstructions. Patients with an iliac crest bone graft had significantly better chewing and swallowing scores (p = 0.04, p = 0.049 respectively). There was also a trend for better taste (p = 0.067). Conclusion: These findings suggest that reconstruction with the iliac crest had benefits in improved function (chewing and swallowing) rather than aesthetics, donor site morbidity, or psychological discomfort as was anticipated. Continued study is warranted to confirm the results and further distinguish between the two grafts.

P415: STEEL SCALPELS VS ELECTROCAUTERY INCISIONS: COMPARISON OF COSMETIC AND PATIENT SATISFACTION OUTCOMES

Objective: To determine which method of skin incision has the superior cosmetic and patient satisfaction outcomes. Methods: Consent was obtained in patients undergoing major head and neck operative resection with bilateral neck dissection that met the inclusion criteria were prospectively enrolled. Each side of the neck was randomly assigned at the time of surgery into one of the following two groups: 1. Scalpel incision, 2. Electrocutery incision. Cosmetic and patient satisfaction outcomes were collected prospectively with patients and outcome assessors blinded to treatment group assignment. Validated self report questionnaires and objective functional measures were utilized. Results: 20 patients met the criteria for inclusion. Analysis revealed no significant differences between groups in terms of cosmetic and satisfaction outcomes. Conclusion: Steel scalpel or electrocutery may be used to incise the skin of patients undergoing major head and neck surgery with no difference in cosmetic or patient satisfaction outcome.

P416: “SLOW-SET” FIBRIN GLUE FOR INTRAORAL SKIN GRAFTS

Objective: Dilution of the thrombin concentration in a commercially available fibrin tissue adhesive delays the fibrin cross-linking and plug formation. This “Slow-Set” fibrin glue can be applied in a more controlled fashion, avoiding pockets of thick glue that may inhibit diffusion of nutrients and fibroblast migration. The purpose of this study was to describe the successful use of slow-set “slow-Set” fibrin glue for intraoral bone grafting. Methods: Retrospective single surgeon review. Results: A total of eight patients were identified with early oral cavity squamous cell carcinoma or severe dysplasia. All patients underwent resection of their lesions with split thickness skin graft reconstruction. Skin grafts were secured to the wound base with slow-set fibrin glue, and the perimeter was gently secured with chromic suture. The split thickness grafts were not meshed. The surgical defect size ranged from 3-21 cm² (mean 9.1 cm²). Four of eight patients previously underwent radiation therapy. No patient required temporary tracheotomy. No bolsters were placed. All patients were placed on a full liquid diet for one week post-operatively. Seven of eight patients were discharged the same day. One patient underwent bilateral suprathyroid neck dissection with his resection, and was discharged after drain removal. Conclusions: The use of “Slow-Set” fibrin glue is safe and effective for split thickness skin graft reconstruction of oral cavity defects. It avoids the need for bolsters and tracheotomy. Patients may resume oral intake earlier. More widespread use of “Slow-Set” fibrin glue deserves further investigation.

P417: VOLUMETRIC AND MULTI-DIMENSIONAL ANALYSIS OF ORAL CAVITY AND OROPHARYNGEAL DEFECTS: A CADAVERIC STUDY

Objective: To compare techniques of venous cloting in microvascular surgery by examining the rate of venous cloting in end-to-end (ETE) and end-to-side (ETS) anastomoses and to review the effects of antithrombotic medications on the rate of venous cloting. Methods: A retrospective review was performed on 300 patients at a tertiary care center from January, 1994 to December of 2004. Patients with double venous anastomoses and those with vein grafts were excluded from the study. Results: The majority of the patients in this study were male (n=205, 68.3%) with a mean age of 60 years of age. Most were tobacco users (n=221, 73.7%) and had 14 tumors (n=219, 73.0%). Venous thrombosis occurred in 43 patients (1.43%) overall. Of the 117 patients in the ETE group, sixteen (13.7%) experienced venous thrombosis. Of the 183 patients in the ETS group, 27 (14.8%) experienced venous thrombosis. The difference between the two groups was not statistically significant. Intraoperative use of heparin resulted in a lower incidence of venous thrombosis (10.0% vs. 17.9%, p=0.036), but did not reach statistical significance. Dextran use resulted in a significantly higher rate of venous thrombosis (18.2% vs. 9.3%, p=0.029). Total flap failure occurred in 15 patients (5.0%). Conclusions: The rates of venous cloting with the end-to-end and end-to-side techniques were comparable. Dextran appeared to have a beneficial effect in regards to clotting, but the side-effect profile is concerning. Surprisingly, the aspirin group had a larger percentage of venous cloting. A prospective randomized trial to evaluate the use of these medications would be useful to clarify the risk-benefit ratio.

Objective: Dilution of the thrombin concentration in a commercially available fibrin tissue adhesive delays the fibrin cross-linking and plug formation. This “Slow-Set” fibrin glue can be applied in a more controlled fashion, avoiding pockets of thick glue that may inhibit diffusion of nutrients and fibroblast migration. The purpose of this study was to describe the successful use of slow-set “Slow-Set” fibrin glue for intraoral bone grafting. Methods: Retrospective single surgeon review. Results: A total of eight patients were identified with early oral cavity squamous cell carcinoma or severe dysplasia. All patients underwent resection of their lesions with split thickness skin graft reconstruction. Skin grafts were secured to the wound base with slow-set fibrin glue, and the perimeter was gently secured with chromic suture. The split thickness grafts were not meshed. The surgical defect size ranged from 3-21 cm² (mean 9.1 cm²). Four of eight patients previously underwent radiation therapy. No patient required temporary tracheotomy. No bolsters were placed. All patients were placed on a full liquid diet for one week post-operatively. Seven of eight patients were discharged the same day. One patient underwent bilateral suprathyroid neck dissection with his resection, and was discharged after drain removal. Conclusions: The use of “Slow-Set” fibrin glue is safe and effective for split thickness skin graft reconstruction of oral cavity defects. It avoids the need for bolsters and tracheotomy. Patients may resume oral intake earlier. More widespread use of “Slow-Set” fibrin glue deserves further investigation.
The soft palate is the most important component of the oral cavity and oropharyngeal defects. A better understanding of the 3-dimensional structure of the defects following cancer extirpation will aid reconstructive surgeons in their ability to reconstruct them using various free tissue transfer and locoregional tissue transfer techniques. **Objective:** 1) To gain knowledge of the 2 and 3 dimensional nature of oral cavity and oropharyngeal defects. A better understanding of the 3-dimensional structure of the defects following cancer extirpation would likely result in better functional and cosmetic outcomes for the patients. This study is an attempt to gain knowledge of the 2 and 3 dimensional nature of oral cavity and oropharyngeal defects. A better understanding of the 3-dimensional structure of the defects following cancer extirpation will aid reconstructive surgeons in their ability to reconstruct them using various free tissue transfer and locoregional tissue transfer techniques.

**Method:** This study involved creating defects in the oral cavity and oropharynx including partial and total glossectomies, floor of mouth excisions, soft palate excisions, lateral pharyngeal excisions and base of tongue excisions in two cadavers. Once these tissues were removed they were measured, and their volume, surface area, and contours (2-dimensional representation of their 3-dimensional structure) were recorded. **Results:** The forms and the dimensions of the resected specimens were all found to be irregular and different for the various anatomic sites. **Conclusion:** We propose that the fasciocutaneous free flaps need to be customized and designed specifically for the different defects of the head and neck.

**P418: FUNCTIONAL SOFT PALATE RECONSTRUCTION: A COMPREHENSIVE SURGICAL APPROACH**


**University of Alberta, Edmonton, AB, Canada**

**Introduction:** The soft palate is the most important component of the velopharyngeal mechanism, which also includes the lateral and posterior pharyngeal walls. This organ is responsible for proper speech production and resonance, and is intimately associated with complex functions of swallowing and respiration. Dysfunction of the soft palate due to surgery or trauma is devastating to the patient’s quality of life resulting in existence of unintelligible speech and poor swallowing. Reconstruction of the soft palate is complex because the dynamic fibromuscular structure cannot be duplicated with our current capabilities which are limited to restoration of integrity, bulk, and sensation. The ideal soft palate reconstruction would: 1. Achieve separation of the oropharynx and nasopharynx, 2. Maintain nasal patency, 3. Provide timely restoration of function, 4. Restore normal intelligibility and resonance of speech, 5. Preserve safe and efficient swallowing function. 6. Allow cancer surveillance. 7. Be cost effective. We have developed a reconstructive paradigm based on above criteria and objective functional outcome classifications into three different sizes and includes different surgical techniques for reconstruction of each one.

**Purpose:** The purpose of this presentation is to describe these techniques in detail and report on functional outcomes associated with each type of reconstruction at 4 points in time (preoperative and 1-month, 6-months, and 1-year postoperative). **Methods:** Patients: 52 patients treated for soft palate defects by primary resection and reconstructive surgery were followed in a prospective manner. **Surgical Technique:** a) Defects less than 1/4 were reconstructed with primary closure, b) Defects greater than 1/4 but less than ½ were reconstructed with a pharyngeal flap and radial forearm free flap (PHAR), c) Defects equal to or greater than ½ were reconstructed with a radial forearm free flap and a two layer complete adhesion to the posterior pharyngeal wall which resulted in the soft palate insufficiency repair (SPR). Functional assessment: Swallowing was assessed with videofluoroscopy and a diet questionnaire. **Conclusions:** This regimen is very well tolerated and should be considered for reconstruction of these defects.

**P419: FREE TISSUE TRANSFER RECONSTRUCTION OF PAROTIDECTOMY DEFECTS: A PAIRED OUTCOMES ANALYSIS USING LASER SURFACE SCANS**

**H. Seikaly, D. Cote, J. Guilemoud, K. Ansari, J. R. Harris**

**University of Alberta, Edmonton, AB, Canada; University of Alberta, Edmonton, AB, Canada**

**Introduction:** The prospect of living the remainder of a normal life expectancy with a significant cosmetic defect is devastating for some patients undergoing parotidectomy. While many methods of reconstructing these defects have been described, restoration of symmetry using free tissue transfer flaps has popularity in some head and neck reconstructive centres.

**Objective:** The objective of this study was to utilize three-dimensional surface laser scanning and subjective questionnaire data to evaluate post-parotidectomy reconstruction with de-epithelialized free tissue transfer flaps.

**Methods:** A series of patients at the University of Alberta Hospital who required parotidectomy underwent simultaneous reconstruction of the resulting contour deformity employing radial forearm and anterolateral thigh de-epithelialized free tissue transfer flaps. These patients were matched to a series of patients who underwent parotidectomy without contour reconstruction. Both series of patients underwent volumetric analysis using three-dimensional surface laser scanner at the Craniofacial Osseointegration and Maxillofacial Prosthetic Rehabilitation Unit to objectively evaluate volumetric symmetry. Patients also completed a comprehensive survey to assess post-operative function, complications, and perceptions of cosmetic outcome.

**Results:** Analysis of the volumetric data revealed a significant objective benefit in symmetry among patients who underwent free flap reconstruction. Additionally, reconstructed patients tended to have better functional and subjective cosmetic outcomes. **Conclusions:** Parotidectomy patients who underwent free tissue transfer flap reconstruction tended to have better contour and functional outcomes. Objective volumetric analysis using laser surface reconstruction has a strong correlation with patients’ own subjective perceptions of postoperative cosmetic outcomes.

**SARCOMA**

**P420: ANGIOSARCOMA OF THE SCALP WITH COMPLETE RESPONSE TO A BIWEEKLY GEMCITABINE AND DOCETAXEL (GEMDOC) CHEMOTHERAPY REGIMEN**

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**Background:** Angiosarcoma is a rare and aggressive soft tissue sarcoma. In this paper, we reviewed the literature and described a case report about metastatic angiosarcoma.

**Method:** A 75-year-old woman with multiple scalp lesions presented to our clinic. The final diagnosis was a metastatic angiosarcoma.

**Results:** This patient achieved complete remission following treatment with combination chemotherapy regimen consisting of gemcitabine (1500 mg/m2) and docetaxel (50 mg/m2) administered biweekly.

**Conclusion:** This regimen is very well tolerated and should be considered especially in elderly patients and patients with comorbid conditions who may not tolerate other chemotherapeutic regimens.

**P421: ANGIOSARCOMA OF THE THYROID: CASE REPORT AND LITERATURE REVIEW**

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**Objective:** Primary angiosarcoma of the thyroid gland is an extremely rare entity in non-Alpine regions. Because of its rarity, the existence of primary angiosarcoma of the thyroid gland continues to be a controversial issue. There is growing microscopic and immunohistochemical evidence in the recent literature which continues to support angiosarcoma as a distinct entity from undifferentiated and anaplastic carcinomas of the thyroid.

This study aims to present an interesting case of high grade angiosarcoma of the thyroid gland and review the literature of this rare and controversial diagnostic entity. **Methods:** Case report and review of literature. **Results:** Patient was successfully treated with total thyroidectomy and post-operative radiation. Histopathology of the thyroid specimen including immunohistochimistry proved tumor to be diffusely positive for vimentin, CD31, CD34, and Factor VIII and focally positive for low molecular keratin. The microscopic findings and immunohistochemical staining was consistent with primary high grade angiosarcoma of the thyroid. A review of literature reveals growing evidence to support this diagnosis by pathology and immunohisto-
Sinonasal malignant fibrous histiocytoma (SNMFH) is rare. The There were 13 males and 12 females. To present an update of the outcome of children with head and neck rhabdomyosarcoma. The children who had previous nasopharyngeal carcinoma. Twenty-one tumors originated from the maxillary sinus, 3 tumors from the nasopharynx and one tumor from the nasal cavity. Twenty-three patients underwent surgery and 9 of them received post-operative radiotherapy. Only 12 tumors were removed with negative margin. Nineteen patients had local recurrence or distant metastasis and 18 patients died of disease. The 5-year overall survival and the disease-free survival rates were 25.1% and 21.5%, respectively. Multivariate analyses showed that previous radiation was the only adverse prognostic factor for disease-free survival (p=0.0493). The 5-year disease-free and overall survival rates of primary MFH and post-irradiated MFH were 72.9%, 71.4% and 0% and 5.9%, respectively. Conclusions: In this series, post-irradiated MFH is more common than primary MFH. Previous radiation was the only significant prognosticator for disease-free survival of SNMFH. The prognosis of post-irradiated MFH is extremely poor, whereas primary MFH has a good prognosis.

**Objective:** Sinonasal malignant fibrous histiocytoma (SNMFH) is rare. The objective of this study is to report our experience in the treatment of SNMFH and to analyze the prognostic factors. **Methods:** Between 1974 and 2004, twenty-five patients were registered with a diagnosis of MFH of the sinonasal tract at our hospital. Clinical data of these patients were retrospectively reviewed. Demographic data, treatment and outcomes of these patients were analyzed. **Results:** There were 13 males and 12 females. The median age is 49 years. Eight tumors were primary MFH and 17 tumors were post-irradiated MFH, located within the radiation field for previous nasopharyngeal carcinoma. Twenty-one tumors originated from the maxillary sinus, 3 tumors from the nasopharynx and one tumor from the nasal cavity. Twenty-three patients underwent surgery and 9 of them received post-operative radiotherapy. Only 12 tumors were removed with negative margin. Nineteen patients had local recurrence or distant metastasis and 18 patients died of disease. The 5-year overall survival and the disease-free survival rates were 25.1% and 21.5%, respectively. Multivariate analyses showed that previous radiation was the only adverse prognostic factor for disease-free survival (p=0.0493). The 5-year disease-free and overall survival rates of primary MFH and post-irradiated MFH were 72.9%, 71.4% and 0% and 5.9%, respectively. **Conclusions:** In this series, post-irradiated MFH is more common than primary MFH. Previous radiation was the only significant prognosticator for disease-free survival of SNMFH. The prognosis of post-irradiated MFH is extremely poor, whereas primary MFH has a good prognosis.

**Objective:** To present an update of the outcome of children with head and neck rhabdomyosarcoma (HRMS) locally treated with surgery and brachytherapy. **Methods:** From 1992-2006, 28 children (mean age: 5.4 years) with primary (irresectable) non-orbital rhabdomyosarcoma were treated with surgery, moulage technique brachytherapy and reconstruction according to the AMORE protocol (Acronym for: Ablative surgery MOulage technique brachytherapy REconstruction) in addition to multidrug chemotherapy (SIOP MMT-89 and 95 trials). Surgery aimed at removal of the residual tumor mass with macroscopically sound margins. Thermoplastic Guta Percha was used for moulage containing polyethylene catheters that were after loaded with Iridium-192 (40-50 Gy). This was followed by free flap reconstruction. **Results:** Complete remission was achieved in all patients with limited complications. There were 9 local recurrences and there was 1 patient with distant metastases. Estimated 5-year overall survival (OS) and event free survival (EFS) for all patients were 66.7% and 60.2% respectively (parameningeal: OS 65.9% and EFS 57.3%). **Conclusions:** AMORE is a feasible treatment strategy for HRMS with a good local control rate and overall survival. Sequelae of local therapy were manageable.

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Objective: Basically in treatment of pediatric patient with sarcoma, initial treatment is chemotherapy coupled with/without radiotherapy. Surgery is only done when the residual tumor is present. Especially in head and neck area, however, surgical removal of such a residual tumor is still formidable trial for the surgeon, because of anatomical complexity. In addition to this, tolerance to surgical invasion and possible impairment of growing, surgery for such pediatric patients need special care.

We had performed complete removal of these residual tumor after initial treatment with thorough assessment of surgical approach or reconstruction techniques which are suitable for pediatric patient. We introduce here our strategies of radical care for such residual tumor and surgical technique, complications and outcome are reported. Methods: A retrospective review of pediatric cases with sarcomas in head and neck were conducted. Among them, patients who underwent surgical removal of various kinds of residual sarcoma after initial treatments are enrolled for this study. Location and histology of sarcoma, initial treatment and tumor were estimated, then surgical approach to the residual tumor, complications, loco-regional control and their survival were analyzed. Results: Seventeen patients (8 males and 9 females) with head and neck sarcomas who underwent surgery from 2001 to 2007, were reviewed. These cases were histologically diagnosed as rhabdomyosarcoma (7), synovial sarcoma (3), Ewing’s sarcoma (2), chondrosarcoma (2), osteosarcoma (1) and one alveolar soft part sarcoma (1). Median age at diagnosis was 11 years old (range, 2 to 17 years old). The median duration of follow-up was 24 months. Residual tumors in parameninges are 9 out of 17 patients: 8 cases of infratemporal fossa and one case of nasal or paranasal sinus. Rest of 8 cases are recurred in superficial area. Complete resection under histo-pathological examination were obtained in 7 out of 9 residual tumors in the parameninges area. However, one case showed local recurrence even after histologically complete resection. Other two cases with osteosarcoma in parameninges also showed local recurrence. Tumor location in relation to the superficial site was the best predictor of outcome in our study. Conclusions: Because of anatomical complexity and immaturity of the patient, surgeon could not get sufficient surgical field during removal of residual sarcomas in the head and neck area. From our experience, however, outcomes of treatments can be improved by development of surgical technique. In the treatment of pediatric sarcoma, standardizing surgical treatment for residual tumor under the cooperation of pediatrician and radiologist is important.

Objective: To present a previously undescribed case of alveolar rhabdomyosarcoma involving the larynx of an adult female patient. Study Design: Retrospective chart review. Methods: Illustrative case report. Results: Rhabdomyosarcoma is extremely rare in adults, particularly in the head and neck. Over 90% of patients are diagnosed in people under 25 years old. Overall, 35% of rhabdomyosarcomas occur in the head and neck, and of these, about 10% arise in nonorbital, nonparameningeal locations. The vast majority of laryngeal cancers are of squamous histology, while spindle cell tumors account for a mere 1-3% of laryngeal neoplasms. The embryonal subtype is the most commonly encountered in children, whereas the alveolar type is seen more in adolescents and the pleomorphic type in elderly patients. Herein we report the first case of alveolar rhabdomyosarcoma involving the larynx of an adult female patient. Conclusion: Laryngeal rhabdomyosarcoma is extremely rare in the adult population; however, it is important to recognize this clinical entity. Since this tumor is rare in the adult population, most of the data regarding treatment responses are based on pediatric series. Management of this disease has evolved from radical surgeries to less morbid procedures supplemented by radiation and chemotherapy.

Objective: To present two rare and unique cases of myxoid liposarcomas of the sinonasal tract. Methodology: A retrospective review of two cases of myxoid liposarcomas treated at the Departments of Otolaryngology and Pathology of the University of Miami, Miller School of Medicine and Head and Neck Surgery of the Hospital Pablo Tobon Uribe in Medellin, Colombia. Results: Description of these two cases affecting the nasal septum and the sphenoid sinus is presented, along with their histological findings, treatment modalities and final outcome. Conclusions: This rare tumor is quite common in the retroperitoneal region. The head and neck surgeon might come across one of these unique tumors in the neck; however the septal and sphenoid presentation can only be diagnosed by gross tumor removal and final pathology description.
Specific sites included larynx (3), trachea (1), petrus apex (2), skull base (2), cervical spine (1), clivus (1), and cavernous sinus region (1). Eight of the 11 patients had grade I disease (73%), while the remaining 3 (27%) had grade II tumors. None had metastatic disease at presentation. Surgical resection with post-operative radiation therapy was the most widely employed primary treatment (55%); the remaining patients (45%) had surgical resection only. There were 2 recurrences. Salvage surgeries were performed in both. Disease-specific survival was 75% at 5 years. 

Conclusion: Chondrosarcomas are rare tumors of the head and neck. Treatment should be aimed at complete surgical resection with the option of post-operative radiotherapy. They usually portend a favourable long-term prognosis.

P432: MAXILLARY OSTEOSARCOMA IN A CHILD: SURGICAL TREATMENT AND A SIMPLE RECONSTRUCTIVE METHOD

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Objective: The aim of this report is to present a case of an eight-years-old child with a maxillary osteosarcoma, showing a simple reconstructive method based on the specific features of a pediatric patient. Methods: A 8-year-old child presenting to the Oral and Maxillofacial Surgery Unit with a 3-months history of a firm vestibular and palatal left maxillary mass. Biopsy informed an osteosarcoma and etiopathology studies showed no regional or distant metastis. Tumor was treated by partial maxillectomy. intraoperative analysis revealed negative margins. Ructus Abdominis muscular free flap was harvested by a different team while the resection was carried out and then used for immediate reconstruction of the hard palate and filling of sinuses cavity. Superior temporal artery and vein were used as receptors for microvascular anastomoses. Operative time was 5 hours and the blood loss was negligible. No adjuvant therapy was recommend after the resection. Results: There were no surgical complications, and since there loss segment of palate was fully reconstructed and cavities separated, the patient was able to speak and swallow 1 week after surgery. The patient remains without evidence of local recurrence after 2 years. A palatal prothesis is used now for cosmetic reasons and he is scheduled for bone grafting and final rehabilitation (dental implants). Conclusions: Partial or total maxillectomy is a major procedure that severely compromises oral and facial function and esthetics. Palatal integrity is essential for speech, deglutition, good oral hygiene, and prevention of nasal regurgitation; therefore it is usually treated with complex reconstructive procedures which appear even more complicated for a pediatric patient. Based experience acquired in adult advanced cases, we treated this patient with a simple muscular flap, preserving the osseous reconstruction. We rapidly achieved an excellent quality of life for this patient.

P433: TREATMENT RESULTS OF OSTEOSARCOMAS OF THE HEAD AND NECK AREA

B. Las Heras, A. Madrid, F. Capdeville, M. Veloso, B. Müller, H. Harbst, I. Court, Universidad del Desarrollo, Santiago, Chile; 2Instituto Nacional del Cancer, Santiago, Chile

Objective: Analyze the therapeutic modality, types of reconstruction, surgical complications and survival of a group of patients treated for osteosarcoma of the head and neck area in an Oncologic Center. Methods: Clinical data of 8 patients carrying osteosarcoma of the head and neck area between September 1998 and September 2007 were retrospectively reviewed. Data collected were: age and sex from patients; grading of the tumor; therapeutic scheme; type of surgery and reconstruction; survival. Therapeutic scheme was designed by a multidisciplinary committee consisting in head and neck surgeons, oncologists and radiotherapists. All patients were operated and reconstructed by the same team. Protocol consisted in surgery followed by chemotherapy in patients susceptible to be left with free margins; otherwise, chemotherapy was indicated prior and after surgery. Results: Average age was 32 (18-45), 5 patients were women and 3 men. Localization was 4 maxillary, 3 mandibular and 1 ethmoid. Five tumors were grade II, 3 grade I and two G2 and one G3. Three patients had neo-adjuvant and all had adjuvant chemotherapy. Treatment for maxillary tumors were 3 maxillectomies with reconstruction of the orbit floor with titanium mesh and rectum abdomini free flap and 1 maxillectomy with orbit exenteration. Treatment for mandibular tumors were mandibulectomies, 2 reconstructed with free peroneal flap and one with free trapezium flap. Ethmoid tumor was treated with a craniofacial resection. There were 3 complications: one total failure of a free peroneal flap, one partial atrophy of a free rectum abdomini flap and a partial wound dehiscence in the craniofacial resection. Three patients had positive margins after resection; one died of recurrence in 23 months follow up and the other two are alive free of disease after 5 years of surgery. There were no local recurrences or metastases. Two patients with maxillary localisation died from disease, and one died from a cause not related with the disease. Average follow up was 44 months with a 5 year survival of 60%. Conclusions: Considering the low prevalence of this disease, this report is a large single-center experience with osteosarcomas of the head and neck area. Our results show similar age, gender distribution and survival rate compared with overall published reports. There is no correlation between free margins and survival as described in other series. Maxillar localisation resulted in poor prognosis, as it has been described in prior reports. We believe that patients with tumors susceptible to be resected with negative margins should go directly to surgery given de impossibility of surgical rescue as usually done in long bone tumors. The role of chemotherapy has not been well defined yet, but it may improve life quality and survival.

P434: CONDOBLASTIC OSTEOSARCOMA OF THE MANDIBLE

P435: EXTRA-ABDOMINAL DESMOID FIBROMA: A RARE PRESENTATION

M. Salloum, N. Laver, R. Wein, Tufts-New England Medical Center, Boston, MA

Objectives: 1. To present an unusual case of a locally invasive extra-abdominal desmoid fibroma. 2. To review the pathologic findings of this rare tumor. 3. To discuss surgical and non-surgical treatment approaches for this disease. Methods: Case presentation and literature review. Results: A 26 year old male presented with a 5 year history of a progressively enlarging posterior neck mass. This was causing significant pain and impaired neck range of motion. An MR of the tumor showed a large mass in the neck area extending to the posterior cervical neck into the upper back, measuring approximately 27cm by 17cm, with possible epidural extension. The patient underwent surgical excision by a combined otalaryngology and neurosurgery team. The tumor was found to have an extensive vascular supply and was poorly encapsulated, extending into surrounding musculature. The mass was not excised in its entirety due to excessive intraoperative blood loss and the potential morbidity of complete surgical resection. The excised cervical mass was 9cm by 7cm by 4.5cm (0.15 kg), and the inferior specimen from the upper back measured 18cm by 15cm by 7.5cm (1.62 kg). The histopathology of the mass revealed a non-encapsulated spindle cell tumor consistent with an extra-abdominal desmoid fibroma. Immunohistochemical stains for SMA, CD34, MB-1 and C-Kit were negative, while elastic tissue and collagen stains were positive. Conclusions: Extra-abdominal desmoid fibromas are rare tumors with multiple treatment options. We present a difficult case in which a locally invasive tumor had grown to such an extent that complete surgical excision in one procedure was not possible. The literature supports incomplete surgical resection when necessary to reduce postoperative morbidity.
Previous studies have shown similar survival and recurrence between groups with positive and negative surgical margins. Further treatment options described for residual or recurrent disease include repeat surgical excision, radiotherapy, and possibly chemotherapy. We discuss the pathologic findings and treatment options, reviewing the current literature, for a rare presentation of this disease.

P436: HEAD AND NECK SARCOMAS, ENT DEPARTMENT LENIN FONSECA HOSPITAL FEBRUARY 2003-FEBRUARY 2007 MANAGUA, NICARAGUA

F. Medrano 1, L. Morin 1, K. Amador 1, Lenin Fonseca Hospital, Managua, Nicaragua

Fifteen percent of all sarcomas are in head and neck. It represents less than 1% of all tumors in this area. The multidisciplinary approach to diagnosis, therapeutic and rehabilitation of these patients had permitted the better therapeutic response. **Objective:** The goal of this retrospective study is to describe the patient’s characteristics, localization, histopathology subtype, grade and stage, management and outcomes of our institutional experience with head and neck sarcomas. **Method:** Descriptive study, series of cases. Ten patients with diagnosis of head and neck sarcomas. Histology had been reviewed to confirm grade of sarcomas. Staging system is according to American Joint committee on cancer (AJCC). Some patients had immunohistochemical studies. The univariable review was realized with frequencies and percentages. Overall survival was calculated using Kaplan-Meier. **Results:** Ten patients with head and neck sarcomas, 6 females, and 4 males, the mean age of presentation was 37.1 years. The most common site affected was the neck (30%) followed by the maxilla and the parotid gland (20% each). The tumor was histologically grade 1 (60%), and four were in grade 3 (40%). The staging according to the AJCC was 60% stage I, 20% IA and 40% IB, follow by stage III 30%, only one case stage IV with pulmonary metastasis. The 50% of patients treatment included, neoadjuvant chemotherapy plus surgical debulking and radiotherapy, 20% were surgical and radiation only, one case chemotherapy and radiotherapy respectively and one patient with palliative treatment. The overall five years rate was 50% with a media survival of 43 months. **Conclusions:** The head and neck sarcomas represent true challenge to head and neck surgeon. Ours results conduces with previous available studies.

P437: CLINICAL EXPERIENCE ON HEAD AND NECK SARCOMA: SEOUL NATIONAL UNIVERSITY HOSPITAL OTORHINOLARYNGOLOGY B. Kim 1, M. Lee 1, J. Hah 1, T. Kwon 1, M. Sung 1, K. Kim 1, 1Department of Otorhinolaryngology, Seoul National University College of Medicine, Seoul, Republic of Korea

**Objectives:** Sarcomas in head and neck region are difficult to treat because of the complex anatomy, nearby important structures as well as the skull base and cranial foramina. Furthermore, achieving clear surgical resection without causing significant cosmetic defect and functional impairment is a challenging problem to surgeons. Because of the rarity of these tumors in head and neck area, very limited information is available about the clinical features and management. The objectives of our study were to investigate the clinical features and analyze the survival outcome of sarcomas in head and neck area. **Methods:** From January 1980 to July 2007, ninety-seven patients who were diagnosed as sarcoma in head and neck region and followed up at the Department of Otorhinolaryngology at SNUH were included in this study. Authors retrospectively reviewed the following data: age, gender, initial symptom, site, tumor size, lymph node invasion, distant metastasis, histologic finding, treatment outcomes and recurrence. From this data, authors analyzed the survival and investigated the prognostic factors. Survival analysis was estimated by the Kaplan-Meier method and log rank test using a SPSS version 13.0 statistical program (SPSS, Inc., Chicago). **Results:** Sixty males and thirty-seven females ranged in age from 1 to 76 years (mean age, 33.8 ± 19.8 years) at diagnosis. Twenty-two children (under age 13) were included in the study. Follow-up duration ranged from 1 to 312 months (mean follow-up, 54.7 ± 54.1 months). The most common presenting symptom was painless mass (47%) followed by nasal obstruction and facial numbness. The most commonly involved site was nasal area followed by cutaneous and paranasal sinus. Rhabdomyosarcoma was the most common histologic finding occurring in 24 patients followed by osteosarcoma (n=13), chondrosarcoma (n=8), and malignant fibrous histiocytoma (n=8). Overall 5-year survival rate was 72.1%. Sixty patients underwent surgery and adjuvant treatment including chemotherapy and/or radiotherapy, other 37 patients received chemotherapy whether radiotherapy was added or not. Prognostic factors were investigated. Adult patients with T1 stage and treatment modality including operation showed better result. For children, Survival distribution didn’t differ significantly according to the T staging and treatment modality. **Conclusions:** Head and neck sarcomas show diverse pathologic findings and different prognosis. To improve the treatment results, multidisciplinary approach is necessary. From our analyses adult and children show different feature. This finding might suggest that size factor is relatively less significant in children because of the chemotherapy role.

**SKULL BASE II**

P438: A PRACTICAL APPLICATION OF FUSION NAVIGATION SYSTEM FOR OUTER EAR CANCER H. Kataoka 1, K. Hasegawa 1, Y. Kunitomo 1, H. Kitano 1, 1Tottori University, Yonago, Japan

**Objective:** Navigation system provides the right tools for more accurate planning, leading to more efficient and precise surgery. Intelligent planning features like automatic image fusion provide both speed and accuracy. We applied a fusion navigation system for the lateral temporal bone resection. In real time, we could identify the sigmoid sinus, facial nerve and other objects recognized on the CT images. The process of preoperative simulation itself gives operators more anatomical understanding and image-building. Although the description of the bone is excellent in CT images, the boundary between the pathology and the surroundings is indistinct. In contrast, the tumor extension and the surroundings can be clearly identified on MRI images. iPlan® (BrainLAB, Feldkirchen, Germany) demonstrates an automatic fusion of CT and MRI data for more accurate imaging of critical areas. **Methods:** During the operation, the navigation was used to identify the landmarks on CT images. The range of tumor extension was not clear on the CT images, so an intraoperative pathological examination was needed to decide the range of excision. We applied fusion navigation system for outer ear cancer. Before the operation, we ran a preoperative simulation, showing the important organs and the pathology, so we could decide the range of excision preliminarily. During the operation, the navigation was used in the same way, but more information was obtained from the fusion images. **Results:** Tumor and lymph nodes were marked on the MRI images because they were not clearly identified on the CT images, and then the objects were reflected on the CT images. In addition, the facial nerve was marked, and the preoperative simulation was completed. **Conclusions:** Preoperative simulation is very useful for operating staff for image-building and to decide the range of excision. It’s also useful for young colleagues to study skull base surgery. This navigation system will contribute to not only the clinical scene but also the educational scene.

P439: TEMPORAL BONE RESECTION FOR PRIMARY TUMOURS OF THE EXTERNAL AUDITORY CANAL : THE SINGAPORE EXPERIENCE J. F. Thong 1, A. H. C. Loy 1, S. Yeo 1, M. U. Kho 1, 1Tan Tock Seng Hospital, Singapore, Singapore

**Objective:** To analyse the clinical data and outcome of patients treated by temporal bone resection for primary tumours of the external auditory canal (EAC). **Methods:** A retrospective study was carried out on all patients with primary tumours of the EAC treated in our department by radical surgery. The patients were staged according to the University of Pittsburgh system. Patient demographics and symptoms were recorded. Tumour location, surgical technique, postoperative radio-therapeutic treatment, histo-pathological diagnosis and patient outcomes were analysed. **Results:** From 1995 to 2007, 13 patients with primary tumours of the EAC underwent temporal bone resection (10 lateral and 3 subtotal). Of these, 10 had squamous cell carcinoma, 1 had adenoid cystic carcinoma, 1 had recurrent papillary-squamous cell carcinoma and 1 had serous adenocarcinoma. The mean age at presentation was 56 years (range 36-87). There were 9(69%) male and 4(31%) female. Ten(77%) were of Chinese origin and 3(23%) were Malay. The majority presented with persistent otorrhea and/or otalgia. One patient presented with visible exophytic growth extending to the conical bowl. Staging investigations were performed preoperatively. Four patients were staged as T1, 3 as T2, 1 as T3 and 5 as T4. One patient with T1 adenoid cystic carcinoma had multiple lung metastases preoperatively. Parotidectomy was performed in all (9 total, 4 superficial). Neck dissection was performed in 9. Eight patients had flap reconstruction of the primary defect using temporalis/ sternomastoid (9), pectoralis major (2), trapezius (1) and rectus (1) muscles. One had a rotation flap. All but one underwent postoperative adjuvant radiotherapy (6000cGy in 30 fractions). One received chemo-radiotherapy prior to subsequent salvage surgery because of extensive intracranial tumour extension at presentation. Survival
data for patients with T1 disease at last follow-up ranges from 8 to 58 months. Patients with T2 disease are alive at 18 months, 63 months and 11 years. The patient with T3 disease is alive at 22 months and those with T4 disease are alive at 39, 41 and 58 months. One patient with T4 disease died 9 months from metastatic disease. Another patient with T4 disease had tumor recurrence extending to the clavus at 1 year and was alive at 23 months. Postoperative morbidity occurred in 96.9% patients. Two with T4 disease and one who developed permanent facial nerve weakness, one of which also had partial pinna necrosis and cerebrospinal fluid leak which resolved with conservative management. Four patients had transient facial weakness, of which 1 also had transient vocal cord paralysis. Patient with rotation flap was complicated by flap necrosis which required revision surgery and use of a free lateral thigh flap. Two patients had wound infection, one of which required drainage, and the other required wound debridement and occipitoparietal flap reconstruction in addition to long-term antibiotics. This subsequently died of metastatic disease. Conclusion: Primary tumours of the EAC are rare. Our data demonstrate that there is a strong predilection for Chinese male patients. Survival data for patients treated by aggressive radical surgery and adjuvant radiotherapy in our institution appear favourable even in those with T4 disease.

P440: POPULATION BASED ANALYSIS OF SINONASAL UNDIFFERENTIATED CARCINOMA T.L.Gal, B.Huang, University of Kentucky, Lexington, KY

Objectives: Sinonasal Undifferentiated Carcinoma (SNUC) is an exceedingly uncommon tumor with available literature limited to institutional case series. The objective of this study is to examine demographic and survival characteristics for the nation’s SINUS database. Methods: Patients classified as having undifferentiated carcinoma of the sinonasal tract between 1992 and 2004 were obtained from the Surveillance, Epidemiology, and End Results (SEER) tumor registries. Inclusion criteria included ICD-0-3 codes for undifferentiated carcinoma of the nasal cavity, paranasal sinuses, ethmoid and maxillary sinuses, and nasopharynx. As the majority of cases were entered into the database using SEER Historical Staging, and TNM Staging is not universally utilized for these tumors, a modified Kadish Staging system was created from SEER Extent of Disease and Collaborative Staging Codes, using the designation D1 to denote cervical metastases and D2 to denote distant metastatic disease in addition to customary Kadish A, B, and C staging. 42 patients with multiple primaries, data abstracted from death certificates or autopsy, and patients with no follow-up were excluded. Kaplan-Meier and life table analyses were used to assess survival and Cox proportional hazards modeling was used to assess variables associated with survival. Results: 443 patients were identified with undifferentiated carcinoma of the nasal cavity, ethmoid, maxillary sinuses, and nasopharynx with an overall incidence rate of 0.09 per 100,000. Mean age was 51.65 years, 36.7% of patients were white, while 54.3% were Asian/Pacific Islanders. 20% of tumors were localized to the nasopharynx (330), 200 (57%) of which presented with neck metastases (D1). Of the 93 patients with undifferentiated carcinoma of the nasal cavity and sinuses, modified Kadish Stage was as follows: A: no patients, B-19, C-25, D1-18, and D2-6, unknown-35. Primary surgery was performed in 1112 (12%) patients, primary radiation in 30 (32.2%), and combined therapy in 46 (49%), with no distinct trends for treatment across stage. Observed overall 5 year survival was 41%, which was significantly less than for undifferentiated carcinoma of the nasopharynx (66%, p=0.0001). Modified Kadish staging was predictive of survival, with Kadish C (31%), and D2 (26%) having the poorest 5 year survival. Neck Metastases were uncommon for sites other than nasopharynx, but were not predictive of poor survival (5 year survival 73%). Conclusion: Sinonasal undifferentiated carcinoma is a rare neoplasm. Although early stage disease is unusual, the modified Kadish staging is predictive of survival. Despite identical histology and coding nomenclature, it is important to distinguish undifferentiated tumors of the nasal cavity and paranasal sinuses from undifferentiated carcinoma of the nasopharynx, as the latter, one of several tumor types classically included as WHO type III nasopharyngeal carcinoma, is associated with significantly improved survival.

P441: TREATMENT OUTCOMES OF SINONASAL UNDIFFERENTIATED CARCINOMA OF THE SKULL BASE WITH PROTON BEAM THERAPY S.T.Gray, D.T.Lin, A.Chan, D.G.Deschler, E.Hollack, W.Curry, Massachusetts Eye and Ear Infirmary/Harvard Medical School, Boston, MA; Boston, MA; 2Massachusetts General Hospital, Boston, MA; 3Massachusetts General Hospital Cranial Base Center, Boston, MA; 4Massachusetts Eye and Ear Infirmary/Harvard Medical School, Boston, MA; 5Massachusetts General Hospital, Boston, MA; 6University of South Florida Department of Otolaryngology-Head and Neck Surgery, Tampa, FL; 7University of South Florida Department of Neurosurgery, Tampa, FL; 8University of South Florida Department of Neurology, Tampa, FL

Objective: To evaluate the clinical outcomes of a multimodality treatment approach for sinonasal undifferentiated carcinoma (SNUC) of the anterior skull base. Methods: Ten patients with SNUC treated at the Massachusetts Eye & Ear Infirmary/Massachusetts General Hospital Cranial Base Center from 1995 to 2007 were analyzed retrospectively. Results: Seven patients at initial presentation had extensive local disease and were deemed surgically unresectable. Initial treatment for 5 patients involved chemotherapy and proton beam radiation. Three patients were treated initially with subtotal resection to facilitate postoperative proton beam radiation therapy and chemotherapy. Two patients that were deemed unresected underwent upfront craniofacial resection followed by chemotherapy and proton beam radiation. Five of the ten patients died of disease, with a mean survival of 18 months following treatment. One patient developed a recurrence in the maxilla twelve months following completion of treatment and is currently receiving additional radiation and chemotherapy. Mean survival for patients who are currently disease free is 13 months. Conclusions: For patients with en bloc resectable disease, we recommend surgical resection followed by postoperative chemotherapy and proton beam radiation therapy. Patients with advanced disease who are deemed unresectable may benefit from combined chemotherapy and proton beam radiation therapy for locoregional control.

P442: CHANGING PATTERNS OF TRACHEOTOMY USE IN ANTERIOR SKULL BASE SURGERY WITH FREE TISSUE RECONSTRUCTION T.L. Myers, B.D. Sumer, J.E. Lowery, R.J. Delattia, J.M. Trueston, Leach, R.S. Sarnard, UT Southwestern Medical Center, Dallas, TX; 2Vanderbilt University Medical Center, Nashville, TN

Objective: To evaluate how changing patterns of primary tracheotomy use with free tissue reconstruction of the anterior skull base, affect the number and severity of postoperative complications. Design: Retrospective comparison of clinical cohort to historical control group. Setting: Tertiary care medical center. Patients: A consecutive sample of patients that underwent ablative surgery of the anterior skull base for nasal or paranasal sinus malignancies with free tissue reconstruction from 1993 to 2006. The patients were divided into two cohorts; Group 1, which consisted of patients treated from 1993-2000 and Group 2, patients treated from 2000-2006. Main Outcome Measures: Rate of tracheotomy use perioperatively, early and late complications, including pneumocephalus and meningitis, and postoperative survival. Results: There were 16 patients in Group 1 and 17 patients in Group 2. There were 9 patients with Stage 4 disease in Group 1 and 10 in Group 2 (p=0.645) There were 11 patients who received a tracheostomy in Group 1, and 5 in Group 2. This decline in tracheostomy use was statistically significant. (p=0.038) The number of early complications in each group was 10, (p=1.000) There was one case of meningitis in Group 1 and none in Group 2. (p=0.485) There were two cases of pneumocephalus in Group 2 and none in Group 1, and this difference was not statistically significant. (p=0.485) The number of late complications in Groups 1 and 2 were 10 and 8 respectively. (p=1.000) There were 13 myocutaneous flaps in Group 1 and 12 in Group2 (p=0.686) Six patients in each group had recurrent disease. (p=1.000) There was no statistically significant difference in survival, with 13/16 patients in Group 1 and 10/17 patients in Group 2 being still alive (p=0.675). Conclusions: The decreased use of tracheostomy in patients undergoing free tissue transfer reconstruction of anterior skull base defects, did not lead to an increase in early or late complications including pneumocephalus and meningitis. Routine use of tracheostomy in these patients is unnecessary and should be reserved for selected cases.

P443: THE USE OF DURASEAL® IN THE CLOSURE OF CSF LEAKAGE DURING TRANSNASAL TRANSSPHENOIDAL ENDOCRINE PITUITARY SURGERY S.N. Patel, T.A. Padhya, H.R. van Loveren, E.Carroll, F.L.Vale, University of South Florida Department of Otolaryngology-Head and Neck Surgery, Tampa, FL; 2University of South Florida Department of Neurosurgery, Tampa, FL; 3University of South Florida Department of Neurology, Tampa, FL

Objective: Cerebrospinal fluid (CSF) leakage is a notable cause of morbidity, potentially leading to meningitis, brain abscess, or pneumocephalus. One of the most common settings of CSF leakage occurs after minimally invasive pituitary surgery at the sphenoidal sinus. Thus, endoscopically guided closure with the use of autologous grafts, sealing agents, and dural guided closure with the use of autologous grafts, sealing agents, and dural

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difference in success rates. The aim of this study is to examine the efficacy of DuraSeal®/153 (Confluent Surgical, Inc., Waltham, MA) dural sealant system as an adjunct in transnasal transsphenoidal endoscopic pituitary surgery in the prevention of postoperative CSF leaks. Methods: We conducted a retrospective review of patients who underwent transnasal transsphenoidal pituitary surgery between 2005 and 2007. Fifty consecutive patients in whom DuraSeal®/153 was used for an intra-operative endoscopic closure were identified and included in our study. Patients’ records were reviewed retrospectively for characteristics of the patients, diagnostic techniques, technique of surgical closure, adjunctive therapies, and outcomes. Follow-up data (min. six months) were obtained through review of hospital records. Results: Fifty patients (22 male, 28 female; age range, 19 to 84) had their sphenoid sinus endoscopically closed using DuraSeal®/153, often as a last layer of the repair. DuraSeal®/153 was applied as reinforcement in a multilayer fashion with a combination of autologous fat, Gelfoam®/174, Surgicel®/174, FloSeal®/153, Gore-Tex®/174, and/or Duraform®/153. Pituitary pathology consisted of forty-one (82%) macroadenomas, five (10%) cystic adenomas, two (4%) Rathke’s cleft cysts, one (2%) craniohypophyseal cyst, and one (2%) microadenoma. Thirteen (26%) patients encountered intra-operative CSF leak, of which three (23%) patients progressed to postoperative CSF leakage requiring re-operation with DuraSeal®/153; no further leak was observed thereafter. The initial failure rate was 6% (3 cases) occurring in only those patients who encountered intra-operative leaks. In addition, there was no associated intracranial infection such as meningitis or abscess in any of the study subjects. Ultimately, patients underwent successful repair with DuraSeal®/153, either as a primary or secondary method of closure, with a zero percent infection rate. Conclusions: DuraSeal®/153 is a valuable adjunct in the endoscopic transnasal repair of the anterior skull base. This off-label use (non-FDA approved) of DuraSeal®/153 in a clean-contaminated operating field shows to be efficacious in preventing CSF leakage while minimizing post-operative intracranial infection. It is a hundred percent synthetic and requires minimal preparation time. Overall, DuraSeal®/153 reestablishes the continuity of the dura and provides stability when used as reinforcement over a multilayered graft closure.

Objective: Describe a rare presentation of a meningioma that began intracranially and extended extracranially to fill the nasal cavity, and the surgical management that ensued. Study Design: Case Report. Methods: Data is collected via a chart review with an accompanying literature review. We present the case of a 48-year-old woman with a history of multiple prior bifrontal craniotomies for resection of frontal meningioma who presented to the neurosurgery clinic 2 years since her last follow-up reporting persistent symptoms and progressive appearance of a mass extending into the frontal bone and extending down into her entire nasal cavity via the anterior ethmoid. On speculum exam of the nasal cavity it was easy to visualize a mucosa-covered mass extending medial to the middle turbinate. Results: Surgical intervention for this meningioma was successful and the patient recovered without neurological sequelae from the surgery. Conclusions: Long-term surveillance is crucial in patients with a history of meningioma as recurrence can have devastating consequences. The skullbase surgeon should be aware of this rare presentation when formulating a differential diagnosis for a nasal mass. We compare our case with other rare presentations of this process in the literature to highlight the severity of unchecked follow-up.

Objective: To determine if, in terms of functional outcomes or cosmesis, there is an advantage to using either primary obturator reconstruction or primary free tissue reconstruction. Methods: Comparison of prospectively collected data on functional outcomes after free tissue or obturator reconstruction using a comprehensive collection of outcomes parameters including: PERCI-SARS for assessment of velopharyngeal orofacial function, nasometer for assessment of nasalance, and standardized recordings for assessment of speech intelligibility. Cosmetic analysis was performed using eight naive viewers providing assessment via a 10 point likert scale with comparison to a control group of patients undergoing radiation alone for nasopharyngeal cancer. Results: In all parameters measured for both functional and cosmetic outcomes, results were excellent for both obturator and free tissue reconstruction. Conclusions: Functional and cosmetic results of free tissue or obturator reconstruction should be excellent. The decision as to which approach to take is complicated and depends on local facilities and expertise. Further evaluation by detect classification is required to determine if specific defects are better served by obturator or free tissue reconstruction.

Objective: Juvenile Nasopharyngeal Angiofibromas (JNA) are vascular tumors that occur primarily in adolescent males. Although these lesions are benign, they can be locally invasive and associated with significant morbidity especially when diagnosis and treatment are delayed. Surgical management of JNA includes a variety of open approaches and more recently the transnasal endoscopic approach. For small to medium-sized JNA, the endoscopic approach has been advocated over traditional open approaches with or without pre-operative embolization as a sound alternative that causes less morbidity, bleeding, operative time, and intra-operative complications. This technique has also been reported to provide better post-operative function, superior visualization, avoidance of cosmetic injuries, and shorter hospital stays. However, for large-sized JNA, some may express concerns regarding access to certain anatomic areas, risk of inadequate resection from limited exposure, and difficulty controlling bleeding from major vascular structures when the endoscopic approach is used. Unfortunately, owing to the rarity of this lesion, the efficacy of the transnasal endoscopic approach in comparison to traditional open approaches for the resection of large-sized JNA cannot be determined in a randomized fashion. Methods: A retrospective chart review was performed for all cases of JNA treated surgically from January 1, 1980 to September 1, 2007 at the University of Miami Hospital, Jackson Memorial Hospital and the Sylvester Comprehensive Cancer Center. The major factors evaluated include staging, pre- and post-operative symptomatology, estimated blood loss, operative time, need for transfusion, hospital stay, complications, and recurrence rates. Results: Of all JNA cases reviewed, eleven were performed endoscopically. Two patients were diagnosed with a stage IIA, two with stage II, one with stage IIB, four with stage IIIA, and two with stage IIIB. The most common presentation symptoms were nasal obstruction, epistaxis, and nasal congestion. None of these patients received pre-operative embolization. The average age at time of surgery was 20.1 years. The mean estimated blood loss was 886 milliliters; three patients received intra-operative blood transfusions. The mean hospital stay was less than 3 days for all endoscopic cases. The most common post-operative complaints were nasal crusting and facial numbness. This cohort was compared to a historical cohort of patients that underwent open approaches for JNA at our institution. Conclusion: Though surgical management of large JNA depends on the experience and expertise of the surgeon and the unique features of each case, this study suggests that the endoscopic approach of large-sized JNA can be performed safe in experienced hands. Comparative analysis of morbidity will be described in detail in the presentation.

Objective: Angiofibromas(AF) are benign tumors originating on the nasopharynx that typically occur in young males. Despite having an exuberant blood supply and exhibiting a tendency to occupy adjacent regions to the nasopharynx, their resection is usually accomplished uneventfully, through a variety of surgical facial approaches. However, in the rare instance when an AF grossly invades the skull base, its surgical resection can be very difficult and hazardous, generally involving two or more teams. Objective: To analyze the experience of two institutions with a series of consecutive patients with extensive AF with skull base invasion(AF/SBi), with a special emphasis on operative morbidity and mortality. Design of the Study: Multi-institutional retrospective analysis. Material and Methods: The charts of all patients with AF/SBi submitted to oncological
craniofacial operations in two major tertiary-care institutions from 1992 to 2007 were retrospectively reviewed. The following data were collected: demographic distribution, tumor extension, type of facial and cranial access, reconstruction, complications and outcome. Special attention was directed towards the operative morbidity and mortality. Results: During this 16-year period, 17 male patients with AFSSI underwent major base of skull operations in two centers. Median age was 18.5 year-old (9-36). Five patients (29.4%) had recurrent disease, the patient underwent surgery and was lost for follow-up. Facial approach was some form of maxillectomy in 43.7% of cases, followed by facial translocation in 25.0%, and nasal swing in 6.2%. No facial approach was required in 12.4% of cases. Major complications occurred in 43.7% of the cases; more frequent were intraoperative bleeding with hypovolemic shock in 18.7%, oronasal fistula in 18.7%, CSF fistula with meningitis in 12.5% and osteomielitis of skull base in 6.2%. There was one intraoperative death (6.2%), due to uncontrollable hemorrhage. There was a 12.5% recurrence rate, in a median follow-up period of 37.5 months. Conclusions: In this retrospective study, including a 16-year experience with skull base operations in two major Brazilian centers, 17 patients with AFSSI were evaluated; 16 were resected through a variety of cranial and facial approaches, leading to considerable operative morbidity, but with ultimate good oncological results. To our knowledge, this is the largest published experience with such advanced tumors in the literature.

P448: JUVENILE NASOPHARYNGEAL ANGIOFIBROMA: TREATMENT AND OUTCOME OF 31 CONSECUTIVE CASES TREATED IN A SINGLE INSTITUTION

Background: Juvenile nasopharyngeal angiofibroma (JNA) is a highly vascular and locally invasive tumor that exclusively affects young males. Objective: The purpose of this study was to analyze the treatment results according to surgical approaches selected. Patients and Methods: The medical records of 31 patients with histologically proven JNA who underwent surgical treatment in a single referral cancer center between 1996 and 2005 were retrospectively evaluated. The following data were collected: demographic distribution, tumor extension, type of facial and cranial access, reconstruction, complications and outcome. Results: Twenty five patients (80.6%) were previously untreated. Age ranged from 7 to 23 ys (mean 15.3 ys). Median follow-up was 45.3 months. Patients with JNA were staged as Chandler II in 2 cases (6.4%); as Chandler III in 23 cases (74.2%); and as Chandler IV in 6 patients (19.3%). Eighty-seven percent of patients had preoperative embolization of their tumors. Facial approach was some form of transmaxillary in 74.2% of cases, followed by transpalatal approach in 54.8% (17pts) of cases, and facial translocation in 19.3% (6pts). Six patients (19.3%) with intracranial extension underwent a craniofacial approach with a fronto-temporal-parietal craniotomy in 3 patients (50%), bicornal craniectomy in 2 (33.3%), and only by an extended transpalatine approach in 1 (16.6%) patient. Four patients (13%) had significant intraoperative bleedings leading to hypovolemic shock in 1 patient. Fifteen patients (48.4%) developed postoperative complications. Major complications occurred in 41.9% of cases: oronasal fistula in 32.2%, and hypovolemic shock, osteomyelitis of skull base, and hemorrhage in 1 case (3.2%) each. No case of intraoperative or postoperative death was observed. Postoperative complications were observed in 16.6% of patients who underwent a transmaxillary approach in comparison with 64.3% of those who had a transmaxillary combined with a transpalatal approach, and with 66% of those who underwent a combined craniofacial approach. According to their stages, complications occurred in 39% of Chandler III patients in comparison with 83.3% of Chandler IV patients. Recurrences occurred in 12 cases (38.7%) patients, 7 (58.3%) of them being completely resected by an additional surgical procedure. Of the 31 patients, 29 patients (93.5%) were alive without residual disease in the last consultation. Interestingly, recurrences were observed in 66% of patients who underwent a transmaxillary approach in comparison with 42.8% among those who had a combined transmaxillary and transpalatal approach, and with only 16.7% of patients who had a combined craniofacial approach. Recurrences were associated with Chandler III patients and in 3 cases the symptoms began or were worsened after surgery. Patients with Chandler III patients, and with 16.7% in Chandler IV patients. Conclusion: In this retrospective study, including a 10-year experience with JNA in a major referral cancer center, 31 patients underwent a variety of facial and surgical approaches with considerable but acceptable morbidity and with ultimate good oncological control.

P449: INVASIVE PSEUDOTUMORS OF THE NECK AND SKULL BASE: AN IMPORTANT DIFFERENTIAL DIAGNOSIS OF NEOPLASTIC LESIONS

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Introduction and Objectives: A 46 years old female presented to our clinic with a 6 months history of progressive facial pain, headache and mental status change. Work up revealed an infiltrating lesion of the skull base with intracranial involvement. Pathologic analysis from open biopsy yielded a diagnosis of tumefactive fibroinflammatory lesions. This revealed to be the third reported case of tumefactive fibroinflammatory lesion of the skull base. However, we identified in the literature similar conditions under different terminologies such as idiopathic pseudotumors, inflammatory pseudotumors, fibrosing inflammatory pseudotumors or sclerosing cervicitis. Faced with the similarities between the above cited conditions, we proceed to integrate pathologic and clinical pictures, radiologic and histopathologic features, treatment modalities and outcomes of the available case reports were compared. Results: All lesions are steroid responsive with frequent remissions and exacerbations. Surgical treatment, when feasible, is followed by the lowest incidence of recurrence. The dissimilarities between the case reports are mainly site-related. Conclusion: Non invasive pseudotumors are important differential diagnoses of the neoplastic conditions of the neck and skull base. However, the need for these lesions to be steroid responsive. Whenever they reach the skull base, the role of surgery in treating such conditions is limited, secondary to their infiltrative growth.

SPEECH/SWALLOWING/QUALITY OF LIFE II

P450: SWALLOWING AND QUALITY OF LIFE IN PATIENTS SURGICALLY TREATED FOR CANCER OF THE OROPHARYNX

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Objective: To evaluate swallowing and quality of life (SWAL-QOL) in patients surgically treated for cancer of the oropharynx. Methods: Fifteen patients surgically treated for carcinoma of the oropharynx (4 soft palate and 11 tonsilla) were studied by means of videofluoroscopic assessment of swallowing and application of the SWAL-QOL (quality of life swallowing disorders). The fluoroscopic records of swallowing were analyzed independently by 5 experienced speech and swallowing pathologist. The characteristics of the clinical variables were extracted from the clinical charts in the medical service files of the institution. Results: Ten patients presented advanced tumors (T3-T4) and seven had positive lymph nodes. Resection of the soft palate was performed in seven patients. The reconstruction was performed with myocutaneous flaps in 6 and with microvascular free flap in 4. Dysphagia was reported by 11 patients. In the analysis of swallowing, the presence of alteration in the oral phase was observed in 11 patients; and of the pharyngeal phase in 13. Laryngeal penetration was observed in 7 patients, and aspiration in 1; functional swallowing in 1 patient, discrete-moderate dysphagia in 13 and severe dysphagia in 1. The lowest results of SWAL-QOL were in the domains of duration of the eating (33), desire to eat (64) and frequency of symptoms (69). The presence of swallowing complaints mentioned by patients had correlation with the assessment of quality of life shown in the SWAL-QOL. The quality of life in swallowing correlated with its functional evaluation in the domains of feeding duration (p = 0.045) for patients with advanced tumors, and in social function for patients with positive lymph nodes (p = 0.045). For patients that had resection of the base of the tongue performed (13) the quality of life in swallowing also correlated with the functional evaluation for the domains fear (p = 0.031) and social function (p = 0.016). In the same way, this was observed in patients with a history of supraglottic tumors, and in patients with presence of soft palate resection. The other variables analyzed presented no statistically significant difference. Conclusion: Patients that complained of swallowing problem, who had advanced stage T tumors, presented...
P451: IMPACT OF COMBINED SWALLOW EXERCISES AND NEUROMUSCULAR ELECTRICAL STIMULATION IN HEAD AND NECK CANCER PATIENTS WITH DYSPHAGIA

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Objective: To evaluate the impact of combined swallow exercise and neuromuscular electrical stimulation (NMES) on functional swallowing in head and neck cancer (HNC) patients with treatment related dysphagia.

Study Design: Prospective interventional study. Methods: The study included 27 patients who underwent resection of primary tumor followed by chemoradiation therapy (CRT) for HNC at a tertiary care referral center between December 2003 and December 2005. These patients started and continued their traditional swallowing exercises and NMES during CRT, based on the protocol developed in our institution. Patients had detailed pre and post-treatment evaluation including modified barium swallow (MBS) study to assign a swallow function score based on a previously described swallow severity scale. The scoring system is based on the safest tolerable ingestible material and ranges from zero (profound swallowing impairment) to six (no swallowing impairment). Paired t-test was done to evaluate the change in swallow scores. The swallow scores of these 27 patients were then compared to swallow scores of 10 patients who had received treatment for HNC including CRT at outside facility and were treated at our institution for dysphagia at the end of their CRT. Results: Initial mean swallow score was 2.8 (standard deviation = 0.4) while mean swallow score at the end of treatment for dysphagia was 5.8 (0.4) with a mean improvement of 3 (p < 0.0001). All patients were successfully weaned from gastric tube at end of therapy. There was also a statistically significant difference in the post treatment swallow scores achieved by these patients (mean=5.8) compared to those patients who initiated their swallow therapy after 3-6 months after completion of CRT (mean=4.7) (p = 0.02). Conclusion: Combined swallow exercises and NMES significantly improves swallow function in HNC patients with dysphagia. Initiating the combined swallow therapy and NMES before CRT results in a quicker and greater recovery of swallow function.

P452: CLINICAL PREDICTORS OF DYSPHAGIA AFTER DEFINITIVE RADIATION THERAPY FOR LOCALLY ADVANCED HEAD AND NECK CANCER

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Purpose: Use of altered fractionation radiotherapy regimens, as well as concomitant radiochemotherapy, to intensify therapy of locally advanced and neck cancer (LH/NCN) has led increased rates of long term dysphagia. We sought to examine patient, tumor, or treatment factors that predicted for long term dysphagia. Materials and Methods: We identified 122 patients who underwent definitive radiotherapy for LH/NCN. We excluded those who were treated for a second head and neck primary, stage III/IV, suffered locoregional recurrence, had less than 12 months of follow-up, or had post-operative radiotherapy. Prophylactic percutaneous endoscopic gastrostomy (PEG) tubes were placed in 89% of patients. Patient, tumor, and treatment factors were correlated with a composite of three objective endpoints as a surrogate for long term dysphagia: PEG tube dependence at last follow-up, aspiration on modified barium swallow or by clinical diagnosis of aspiration pneumonia, or esophageal stricture seen by endoscopy or barium swallow. Results: At a median follow-up of 30 months, one year and two year rates of PEG tube dependence were 24.6% and 13.9% respectively. At last follow-up 17 of 122 (13.9%) of patients were PEG dependent. Esophageal strictures occurred in 21 of 121 (17.2%) and aspiration in 29 of 122 (23.8%) patients. One of any of these three measures occurred in 47 of 122 (38.5%) patients, any two in 15 of 122 (12.3%), and all three in 8 of 122 (6.6%). On univariate analysis, laryngeal, hypopharyngeal, pharyngeal wall or base of tongue primaries (p = 0.01), use of sequential or concurrent chemotherapy (p = 0.01), increasing age (p = 0.03), and increasing dose of radiotherapy (p = 0.02) were significantly associated with development of any of the above objective findings of long term dysphagia. On multivariate logistic regression analysis, primary site (p = 0.02), use of sequential or concurrent chemotherapy (p = 0.01), and increasing age (p = 0.01) remained significant. Conclusions: Early intervention via swallowing exercises, avoidance of nothing-by-mouth periods, and use of intensity modulated radiotherapy to avoid uninvolved swallowing structures should be encouraged in populations at higher risk for long term dysphagia.

P453: RECOVERY PROCESS OF SWALLOWING FUNCTION AFTER SUPRACRIOID PARTIAL LARYNGECTOMY

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Objective: Supracricoid partial laryngectomy (SCPL) is a superior technique that preserves vocal function without requiring permanent tracheostomy. In terms of swallowing function, most patients become able to eat normally, but severe dysphagia is an issue immediately after surgery. While dysphagia can be improved through training, how training improves swallowing dynamics remains unclear. The present study chronologically analyzed postoperative swallowing dynamics to facilitate the design of safer postoperative management and training programs. Methods: Subjects comprised 7 male patients who underwent SCPL in this department from June 2003 to November 2007. Mean age of patients was 57 years (range, 52-65 years). Cricohyoidoepiglottopexy (CHEP) was performed on 5 patients, and cricohyoidoepiglottopexy (CHP) was performed on 2 patients. All patients experienced recurrence following radiotherapy. In each patient, videofluorography data were uploaded to a computer, and the movement of the hyoid was traced and quantitatively analyzed. Stage transit duration (STD), maximum laryngeal elevation duration and pharyngeal transit time were measured, and aspiration and pharyngeal residue rates were determined to calculate oropharyngeal swallowing efficiency (OPSE). Speech pathologists administered swallowing training based mostly on breath-holding maneuvers and laryngeal elevation. Results: All patients displayed severe aspiration and low OPSE postoperatively. After swallowing training, location of the hyoid at the start of swallowing and that during maximum elevation were higher when compared to immediately after surgery (paired t-test, p < 0.01), and aspiration rate, residue rate and OPSE improved significantly (paired t-test, p < 0.01). However, STD did not increase postoperatively, and no chronological changes were seen. All patients became able to eat normal diets. Mean duration to oral ingestion was 42 days (range, 17-52 days). Conclusions: SCPL did not markedly affect STD, but caused relatively severe dysphagia characterized by glottic closure failure due to bilateral cordectomy and limited laryngeal elevation. However, when swallowing movements were analyzed chronologically, location of the hyoid at the start of swallowing and during maximum elevation became higher after training. Rate of aspiration decreased significantly, and OPSE improved significantly.000 The two main emphases of swallowing training are to improve laryngeal elevation and strengthen glottic closure, and the present results indicate that this training is effective.

P454: A MULTIDISCIPLINARY APPROACH TO TOTAL LUMEN RESTORATION OF COMPLETE PHARYNGOESOPHAGEAL STENOSIS FOLLOWING CHEMORADIATION

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Objective: Complete pharyngoesophageal stenosis can occur following chemoradiation for head and neck malignancies. Varying theories exist regarding the pathophysiology of this significant treatment complication. However, the prevailing theory is that the pharyngoesophageal area is highly sensitive to radiation once the dose goes beyond 4500 Gy. It is believed that the chemoradiation induces mucositis which results in ulceration of opposing mucosal surfaces. Healing by secondary intention leads to the observed circumferential cicatrix. Treatment modalities vary from simple dilation to surgical resection and reconstruction with microvascular free flaps. We describe our methodology and technique for lumen restoration following organ sparing chemoradiation for head and neck malignancies.

Methods: Our emerging technique for lumen restoration of complete pharyngoesophageal stenosis is described. This technique involved anterograde rigid cervical esophagoscopy by an Otolaryngologist and retrograde flexible endoscopy by a Gastroenterologist via the existing gastroscopy tube site. Vital preoperative and intraoperative fluoroscopy is utilized along with specially adapted instruments for varying lengths of stenoses. Needle vs. guide wire recanalization is accomplished mainly via the anterograde approach... Once a silk suture is secured through the stenosis, the patient then undergoes an aggressive serial dilation schedule. Results: Twelve patients who developed total pharyngoesophageal stenosis following chemoradiation therapy for head and neck malignancy presented to the multidisciplinary swallowing team at the Moffitt Cancer Center. Each...
patient underwent combination endoscopy via anterograde and retrograde approaches. All twelve patients had failed previous attempts via standard means of recanalization/dilation via single approach. All twelve patients were successfully recanalized via our needle canalization and serial dilation technique. There were no procedural complications. Conclusions: A multidisciplinary approach to lumen restoration of total pharyngoesophageal stenoses is vital to an ever increasing complication of chemoradiation. Our method of combination endoscopy proves to be both successful and safe.

P455: QUALITY OF LIFE AND SWALLOWING OUTCOMES OF MAXILLARY DEFECTS
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Objective: This study compares the functional outcomes of speech intelligibility and swallowing, and quality of life issues following either surgical reconstruction or prosthetic obturation of maxillary defects. Methods and Materials: Ten patients treated for cancer or benign tumors with maxillary resection from the Medical University of South Carolina/Hollings Cancer Center patient population were randomly selected to participate in this study. Five patients had been treated with surgical reconstruction and five had been treated with prosthetic obturation. SWAL-QOL Survey, the M.D. Anderson Dysphagia Inventory, the Scored Patient-Generated Subjective Global Assessment, and the Short Form 6 were used to assess swallow-specific quality of life and global quality of life. The Assessment of Intelligibility of Dysartric Speech was used to examine speech intelligibility. Results: The results of this study revealed no significant differences between the two groups with respect to swallowing, and quality of life issues. Conclusions: Future studies are necessary to determine the optimal mode of maxillary defect restoration following resections of maxillary tumors. A randomized study that compares masticatory efficiency, aesthetics, and other outcome factors such as speech, resonance, and swallowing is warranted.

P456: THE EFFECTS OF SWALLOWING THERAPY ON OROPHARYNGEAL FUNCTION IN HEAD AND NECK CANCER PATIENTS
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Many head and neck cancer patients exhibit significant swallowing impairment after completion of tumor treatment. The most effective type of swallowing therapy for these patients has not been defined. Two types of studies are desperately needed: 1) studies of tumor treatment effect on swallowing function and 2) studies of carefully defined swallowing rehabilitation protocols for swallowing abnormalities. This study focuses on the second of these. 1) Objective: This multi-center randomized clinical trial was designed to identify which of two swallowing therapy protocols resulted in the best swallowing outcomes. The two therapy programs are: 1) aggressive range of motion (ROM) exercises with postural sensory therapy and 2) postural sensory therapy alone (PS). 2) Methods: Patients included those whose treatment was chemoradiation, those who had undergone supraglottic laryngectomy and those who had undergone anterior resection with primary or skin graft closure, anterior resection with distal or free flap closure, posterior resection with primary or skin graft closure, or posterior resection with distal or free flap closure. Both therapy protocols involved a one month treatment program followed by one month of rest followed by one month of exercise (ROM) or refresher (PS). The primary outcome measure was the percentage of patients with at least 50% oral intake at 3 months post cancer treatment. Other outcomes included physiologic temporal measures and swallowing disorders as determined from videofluorographic studies at each visit. To determine long term outcomes, six visits were planned between 1 and 12 months post cancer treatment completion. 3) Results: Seventy-four patients were assessed at 3 months and 34 at 12 months. Fifty-five patients had chemoradiation while 18 had surgical treatment. There were no significant differences in the primary outcome measure (ROM 52%, PS 48%, p=0.99). Other measures of swallowing function also did not differ significantly between the two therapy groups. Rate of aspiration was less in patients on ROM but the low overall aspiration rates rendered these results to be statistically nonsignificant. 4) Conclusions: This study did not identify either swallowing therapy program as being superior. No significant intervention-related adverse events were reported in either group. There were no significant differences between the treatment groups in the amount and types of foods eaten, saliva weight or mucositis. The frequency of some swallowing disorders decreased over time (e.g. reduced laryngeal elevation, reduced tongue strength) while others did not decrease over time (e.g. reduced vertical tongue movement) indicating that both swallowing therapies may result in some selective improvements in swallow physiology. Possible next stage in this research is to evaluate other treatments to determine which is best therapy to improve swallowing in the treated head and neck cancer patients.

P457: IMPACT OF SALVAGE NECK DISSECTION ON SWALLOWING FUNCTION
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Objective: To determine whether oropharyngeal squamous cell carcinoma survivors requiring a salvage modified radical neck dissection (ND) after chemoradiotherapy (CRT) differ in swallowing function and dysphagia-related Quality of Life (QoL) compared to patients requiring CRT only to achieve disease-free status. Methods: A cross-sectional study of 23 Stage IV oropharyngeal squamous cell carcinoma patients, stratified by tumour site into CRT (n=11) and CRT+ND (n=12) treatment groups. Validated subjective tools used to assess swallowing-related outcomes and QoL include the M.D. Anderson Dysphagia Inventory (MDADI), Patient-Generated Subjective Global Assessment (PG-SGA), and the Michigan Head and Neck QoL Questionnaire (HNdQoL). All patients underwent a standardized Modified Barium Swallow (MBS), evaluated on multiple parameters including the Penetration Aspiration Scale (PAS). Results: Both groups scored closely in the Global, Emotional, Functional, Physical-Eating, and Speech-related survey domains. The CRT+ND group regularly reported higher Pain scores, though not statistically significant (p=0.07). Preliminary MBS analysis reveals 30% of CRT patients experience aspiration and achieve an average PAS score of 2.7, compared to 57% and a PAS score of 3.4 for CRT+ND patients [MBS analysis to be completed January 2008]. Conclusions: Surprisingly, this study suggests that Stage IV oropharyngeal squamous cell carcinoma survivors requiring CRT followed by salvage neck dissection for persistent nodal disease do not experience poorer dysphagia-related QoL, and swallowing function when compared to patients cured with CRT alone. An area of exception may be treatment-related pain. Preliminary MBS data analysis reveals that approximately 50% of study subjects from both treatment groups aspirate on swallowing, a potentially dangerous complication of treatment, and achieve similar Penetration-Aspiration Scale scores. MBS data is being analyzed to identify specific pathological deficits in swallowing and to guide future rehabilitative therapy for these patients. These findings will be presented.

P458: NON-SURGICAL AND SURGICAL MANAGEMENT OF POST-TREATMENT DYSPHAGIA IN HEAD AND NECK CANCER PATIENTS
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Objective: To evaluate management options for post-treatment dysphagia in head and neck cancer (HNC) patients depending on the functional statu

significant. 4) Conclusions: This study did not identify either swallowing therapy program as being superior. No significant intervention-related adverse events were reported in either group. There were no significant differences between the treatment groups in the amount and types of foods eaten, saliva weight or mucositis. The frequency of some swallowing disorders decreased over time (e.g. reduced laryngeal elevation, reduced tongue strength) while others did not decrease over time (e.g. reduced vertical tongue movement) indicating that both swallowing therapies may result in some selective improvements in swallow physiology. Possible next stage in this research is to evaluate other treatments to determine which is best therapy to improve swallowing in the treated head and neck cancer patients.
Results: Gastric and tracheotomy tubes were removed from all patients at the end of dysphagia treatment. In Group I, gastric tube was removed after completion of CRT. In the surgical groups (II, III and IV), the gastric tube was removed within three to six weeks after procedures. All patients tolerated regular diet and were decannulated. Patients in groups I, II and III had functional voice. Voice rehabilitation was achieved in six patients in group IV by placing a voice prosthesis. No patient suffered from aspiration pneumonia following dysphagia treatment. Conclusions: Treatment of dysphagia should be individualized according to the functional status of the pharynx and larynx.

P459: IMPACT OF NECK DISSECTION ON SWALLOWING FUNCTION
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Objectives: To determine whether oropharyngeal squamous cell carcinoma (OSCC) survivors having undergone salvage neck dissection (ND) after chemoradiotherapy (CRT) differ in swallowing function and dysphagia-related Quality of Life (QoL) compared to patients requiring CRT only. Methods: A cross-sectional study of Stage IV OSCC patients, stratified by tumour site into CRT (n=11) and CRT+ND (n=12) groups. Validated subjective and objective tools used included the M.D. Anderson Dysphagia Inventory, the Patient-Generated Subjective Global Assessment Scale, and the University of Michigan Head and Neck QoL Questionnaire. All patients underwent a standardized Modified Barium Swallow (MBS), evaluated on multiple parameters including the Penetration Aspiration Scale (PAS). Results: Both groups scored closely on Global, Emotional, Functional, Physical, Eating, and Speech survey domains of the survey tools. The CRT+ND group reported higher Pain scores (p=0.07), though not statistically significant. Preliminary MBS analysis reveals 50% of CRT patients experience aspiration and an average PAS score of 2.7, compared to 57% and PAS 3.4 for CRT+ND patients [MBS analysis should be completed Dec 2007]. Conclusions: Surprisingly, this study suggests that OSCC patients undergoing salvage ND for persistent nodal disease do not report lower dysphagia-related QoL scores than CRT-only patients, perhaps with the exception of treatment-related pain. MBS data reveal half of all patients aspirate, a potentially dangerous complication of treatment.

P460: THE IMPORTANCE OF THE POSTOPERATIVE VIDEOFLUO-ROSCOPY IN PATIENTS SUBMITTED TO SUPERACORDIAL LARYNGECTOMY

Objective: To analyze the swallowing effectiveness in late postoperative period of patients submitted to the SCL with CHEP or CHP using the videofluoroscopy imaging method. Methods: From August, 2006 the April, 2007 a retroprospective analysis was done by the neck surgeon of 45 patients submitted to SCL with a minimum of 90 days of postoperative period in a major refer- ral cancer center. The findings were classified according to O’Neil’s scale in order to evaluate the severity of dysphagia, and Robbins’s scale to evaluate food penetration and aspiration. The analysis was carried through according to the following the phases: oral-preparatory, oral and pharynx of swallowing. Results: Of the 45 patients included in this study, 41 underwent to SCPLCHEP and 4 to SCPL-CHP. Six of these patients had adjuvant radiotherapy, being 2 SCPL-CHP and 4 to SCPL-CHEP. Twenty-seven patients (60%) were asymptomatic. Sixteen patients presented with cough complaints, 2 with sporadical complaints of cough and 1 with odynophagia. After the swallowing analysis with videofluoroscopy (VF), 7 patients presented with discrete pharyngeal dysphagia, 2 with moderate/discrete pharyngeal dysphagia, 2 with severe pharyngeal dysphagia, 4 with severe/moderate pharyngeal dysphagia, 1 with moderate oropharyngeal dysphagia, 1 with severe oropharyngeal dysphagia and 26 patients with functional swallowing, and 19 (42.2%) presented with aspiration. Nineteen (42.2%) patients presented aspiration, 8 (42.10%) had retention pneumonia. In this group 2 (10.52%) patients presented aspiration level 7 and 6 (31.57%) presented aspiration level 8. It was necessary early intervention in 4 (8.8%) patients with oral diet. The patients who presented aspiration showed reduced laryngeal sen- sitivity, without cough reflex. Conclusion: This study suggests that the videofluoroscopy in the patients submitted to supraacordial laryngectomy is important to the evaluation of larynx, therefore allows to evaluate the subclinical aspiration in the patients with or without cough consequence.

P461: FEES-DEFINING IT’S ROLE IN THE EVALUATION OF DYS- PHAGIA IN HEAD AND NECK CANCER PATIENTS
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Objectives: The primary outcome measures were to determine inter-test agreement between modified barium swallow (MBS) and fiberoptic endo- scopic evaluation of swallowing (FEES) in regards to the assessment of: 1. Safety of swallowing (diet recommendation). 2. Risks of penetration or aspira- tion of different consistencies of food. Secondary outcomes included compli- cations (weight loss, pulmonary infections) and determination of the dif- ferent etiologies of dysphagia. Patients and Methods: Forty head and neck (H&N) cancer patients were prospectively analyzed. All of them were diagnosed with head and neck cancers and previously treated with surgery, radiotherapy (RT) alone, surgery and adjuvant RT or concurrent chemoradi- ation. Pre-existing swallowing disorders or incapacitating neurological con- ditions were defined as exclusion criteria. Inter-test agreement was calculat- ed by use of the kappa statistic. Results: Most patients were male (male:female ratio = 33:7). Median age was 63 years. Most tumors were localized in the oropharynx and the majority were squamous cell carcino- mas (SCC). Seven patients dropped out of the study and three died of disease. The test agreement was rated good by the kappa statistic in regards to diet recommendation, evaluation of penetration and aspiration (kappa=0.42, 0.67, 0.65 respectively). Seven patients revealed severe relevant dysphagia related complications. No patient evaluated as safe to swallow by the FEES examination developed a swallowing related complication. Conclusion: FEES was shown to have good agreement with MBS in regards to risk assessment in head and neck cancer patients (kappa=0.72). FEES was performed quickly and safely. MBS seldom added significant information for evaluation of dysphagia, however is a valuable complementary diagnostic tool in selected patients.

P462: EFFECT OF PHARYNGOESOPHAGEAL DILATION ON OROPHARYNGEAL SWALLOWING DYNAMICS IN HEAD AND NECK CANCER PATIENTS
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Objectives/Hypothesis: We have undertaken a retrospective study of patients treated with therapeutic cervical esophageal/ pharyngo- esophageal segment (CE/PES) dilation for dysphagia following radia- tion/chemoradiation treatments for head and neck cancer. Our hypothesis is that functional lysis of the upper esophageal sphincter produces both decreased resistance to hyolaryngeal complex elevation as well as reduc- ing downstream mechanical resistance to the bolus being propelled by the pharyngoesophageal muscular forces. It should be reported whether hyo- laryngeal excursion from the pre-treatment to post treatment studies as well as providing subjective improvement in dysphagia. Methods: A retrospec- tive review of patients treated at the University of North Carolina Otolaryngology, Head and Neck Surgery Department from 2003-2007 was performed. Patients treated with CE/PES dilation and with pre and post dilation radiologic evaluation of swallowing suitable for image analy- sis were identified. Chart review was performed to obtain demographic details, disease process and treatment modality as well as clinical effective- ness of the surgical intervention. Still images were extracted from the later- al projection of pre and post-treatment videofluoroscopic swallowing stud- ies. Multiple representative swallowing from each (pre/post dilation) condi- tion were collected and analyzed for hyoid excursion and hyo-laryngeal shortening. Measurements were normalized for inter and intra-study varia- tions in magnification. A cohort of non-radiated patients with upper esophageal sphincter dysfunction (ie. Zenker diverticulum, cricopharyngeal stricture/obstruction) treated with either surgical lysis or dilation of the upper esophageal sphincter were collected for comparison. Results:34 patient charts were identified in the period between 2003 and 2007 with suitable pre and post-dilation radiographs. Of these, 14 had a history of treatment for head and neck squamous cell carcinoma that included exter- nal beam irradiation followed by dysphagia. Analysis of data from our initial cohort of head and neck patients demonstrated variable increases in hyoid excursion and hyo-laryngeal shortening following dilation as well as subjective improvement in dysphagia. Conclusions: Esophageal dilation in the setting of dysphagia following treatment of head and neck cancer appears to be a viable treatment for altered swallowing. Further study is needed to better eluci- date the mechanism of action by which pharyngo-esophageal segment dilation affects the dynamics of the oropharyngeal deglutition. These data have implications for the approach to swallowing rehabilitation following treatment of head and neck cancer.
P463: LARYNGEAL FUNCTION AFTER ORGAN PRESERVATION THERAPY FOR SQUAMOUS CELL CARCINOMA S.Lee1, J.H.Kosier2, S.M.Silver2, S.M.Shapshay1, 1Albany Medical Center, Albany, NY; 2Stratton VA Medical Center, Albany, NY

Objective: Organ preservation in the treatment of advanced laryngeal squamous cell carcinoma (SCC) refers to radiotherapy alone, induction chemotherapy followed by radiation, or concurrent chemoradiation. The goals are to effectively treat the tumor and avoid a laryngectomy. The human larynx has three main functions: respiration, phonation, and deglutition. We hypothesize that although organ preservation therapy preserves the anatomic larynx, one or more of these functions is significantly inhibited and a functional larynx is not preserved. Methods: Institutional Review Board approval was obtained. The VA tumor registry will be used to identify patients with Stage III, IVA, and IVB laryngeal SCC treated non-surgically with radiotherapy or a combination of chemotherapy and radiation. These patients will be evaluated for disease-free survival, need for salvage total laryngectomy, and functional status of their larynges. The functional status evaluation includes respiration: tracheostomy or laryngectomy dependence; phonation: maximal phonation time, videostroboscopy (vocal fold mobility, amplitude, mucosal waves, periodicity, paresis/paralysis), subjective voice symptom scale, and speech pathologist evaluation; and deglutition: partial or complete dependence on nonoral alimentation. Results: Each basic laryngeal function will be reviewed separately. Conclusions: The preservation of each function will be analyzed to gauge whether the organ (larynx) is preserved in nonsurgically treated patients. Local control rates will be compared with those in the published literature.

P464: THE IMPACT OF RADIOTHERAPY ON SWALLOWING AND SPEECH IN PATIENTS UNDERGOING TOTAL LARYNGECTOMY C.de Casso1, N.J.Slevin2, J.J.Homer1, 1Manchester Royal Infirmary, Manchester, United Kingdom; 2Christie Hospital, Manchester, United Kingdom

Objectives: Quality of life studies have shown no detrimental effect with radiotherapy in patients who have total laryngectomy. We wished to determine the effect of radiotherapy (RT) (initial or post-operative) specifically on the swallowing and voice function in patients treated by total laryngectomy (TL) for carcinoma of the larynx. Design: Multi-centre retrospective cross-sectional study. Setting: Multi-centre study in the Greater Manchester and Lancashire area. Participants: 121 post-laryngectomy patients all of which had completed definitive treatment at least 6 months before this study. 26 patients had total laryngectomy as a single modality treatment and 95 had total laryngectomy and radiotherapy. Main Outcome Measures: swallowing (solid food, soft diet or fluid/PEG) and voice development. Results: Swallowing was better in the group who had had 04/02 radiotherapy (p=0.0008). There was no difference in voice function between the two groups. We also demonstrated that females had a worse swallowing outcome (p=0.01). Conclusions: RT adversely affects the swallowing results, but not the speech results, after TL, when given either as initial treatment or post-operatively. This should be borne in mind in the decision making process when treating patients with carcinoma of the larynx.

P465: DESCRIBING PATTERNS OF WEIGHT NADIR AND WEIGHT RECOVERY AFTER CHEMORADIOThERAPY AMONG HEAD AND NECK CANCER PATIENTS C.A.Popp1, D.Oliver1, J.German2, K.Cheng1, D.Manne1, M.Odell1, M.Varvares1, 1Saint Louis University Cancer Center, Saint Louis, MO

Objective: Head and neck cancer (HNC) patients typically lose a significant amount of weight (>10% of pre-treatment weight) both during and after chemoradiation treatment. Recovery of weight is often difficult to achieve for HNC patients. Several factors affecting weight loss include tumor extent and location, response to treatment, having limited oral intake, and g-tube status. The purpose of the study is to determine the average %BMI (or weight) change and average duration from baseline to nadir and recovery. Methods: Retrospective chart reviews of 44 head and neck cancer patients (n=44) were examined by the dietitian between 04/05 to 11/21/07. Only patients with a recorded BMI for at least three visits, including baseline BMI, were evaluated. The median BMI at baseline was 26.0 (range: 15.9-35.3). Median treatment time per patient was 2 months (range: 1-10 months). Patient demographics include: median age was 59 years (range: 42-79); Caucasians (n=33, 75%) and African Americans (n=11, 25%); male (n=32, 73%), female (n=12, 27%). Classification of HNC locations were defined as follows: oropharyngeal (n=20, 46%), hypopharyngeal (n=2, 5%), oral cavity (n=2, 5%), laryngeal (n=13, 30%), nasopharyngeal (n=4, 9%), neck (n=3, 7%). Feeding tube dependence at some point during or after treatment comprised 57% (n=25) of our study population. Results: Our single institution’s experience suggests there is a BMI nadir at approximately 12 months after HNC treatment begins. The average percent decrease at nadir was 18%, after which there is weight gain if no residual disease is present. Preliminary findings suggest there is no significant difference in BMI with regard to having a cancer recurrence. Additionally, no significant differences in BMI were found between ever versus never smoking, or a feeding tube. Although the tube inter-vention may reduce the amount of weight loss. Conclusions: Compared with more common cancers such as breast or lung, HNC cancer patients present a unique problem in that they lose a greater percentage of weight during and after treatment. As determined by this preliminary study, patients who are under chemoradiation treatment for HNC can still be expected to have weight loss up to one year following completion of treatment. Early G-tube placement may mitigate weight loss.

P466: INFLUENCE OF TREATMENT MODALITY ON DYSPHAGIA AND STRICUTURE RATES IN HEAD & NECK CANCER PATIENTS D.O.Francis1, E.A.Weymuller2, B.Yueh3, 1University of Washington, Seattle, WA; 2University of Washington, Seattle, WA; 3University of Minnesota, Minneapolis, MN

Objective: Increasingly aggressive chemoradiation regimens have improved organ preservation rates and locoregional control, but have also been associated with frequent reports of dysphagia and esophageal stricture. We used a population-based approach to: 1) describe modality-specific rates of dysphagia, stricture and esophageal dilation; 2) track temporal changes in these rates between 1991 and 2002; and 3) determine the adjusted odds for developing these complications by treatment modality. Methods: We created a retrospective cohort of incident head and neck cancer patients between 1991 and 1999 by linking the Surveillance Epidemiology and End Results (SEER) tumor registry and Medicare database. The SEER registry was used to capture demographic, tumor, and treatment related data. Medicare claims were used to identify diagnoses of dysphagia and esophageal stricture, and esophageal dilation procedures. We used multivariate logistic regression models to determine the odds of dysphagia, stricture, and dilation based on modality, after adjustment for demographic and tumor characteristics. Results: The cohort consisted of 9,316 incident head and neck cancer patients. Overall, 29% of patients were diagnosed with dysphagia, 9.43% with stricture, and 5.9% underwent esophageal dilation. Dysphagia diagnoses were given to 40.7% of patients receiving chemoradiation, and 19.3% of patients receiving only surgery. Stricture diagnoses were given to 13% of chemoradiation patients, and 6% of surgery-only patients. During the period of study, there was little overall change in the percentage of cancer patients with dysphagia; however, in chemoradiation patients, dysphagia diagnoses increased 20% from 1991 to 1999. Because these rates did not account for site or stage of tumor, we used multivariate logistic regression analysis to determine the independent impact of site of tumor and treatment modality. Compared to patients with oral cancers, the odds of developing dysphagia were significantly elevated in hypopharyngeal (2.80 times greater) and oropharyngeal (1.93) cancers. Treatment modality also had a strong independent impact after adjusting for site and stage. Compared to patients receiving surgery alone, the odds of having a dysphagia diagnosis were elevated after chemoradiation (2.86) surgery plus radiation (2.04), and radiation alone (1.69). Similar patterns were seen with stricture diagnoses and esophageal dilation. For example, compared with surgery alone after adjustment, the odds of esophageal dilations were significantly rated after treatment with surgery/radiation (2.04) or chemoradiation (1.97). Conclusions: In a linked SEER/Medicare dataset, although overall rates of dysphagia are stable, there was a statistically sig-nificant rise in dysphagia diagnoses among the subpopulation of patients treated with chemoradiation between 1991 and 1999. After adjustments for site and stage of tumor, patients treated with chemoradiation were more likely to be diagnosed with dysphagia, stricture, and have undergone esophageal dilation than patients undergoing surgery alone. Further inves-tigation with chart-based or prospectively collected data is needed to test the observations obtained from this secondary analysis.

P467: EVALUATION AND MANAGEMENT OF ESOPHAGEAL STENOSIS J.A.Blair1, T.Day1, M.Delegge1, B.M.Harris2, 1Medical University of South Carolina, Charleston, SC; 2Medical University of South Carolina, Charleston

Purpose: The purpose of this study was to describe preliminary experi-ence with modified examination of swallowing function prior to and follow-ing surgical treatment for cervical esophageal stenosis and quantification of
Methods: Three patients were studied following combined chemotherapy and radiation treatment for cancers of the head and neck. Modified barium swallowing studies (MBSS) were performed. The patients were prompted to perform a large volume bolus swallow utilizing a super-supraglottic swallow and expectorate any residual. Patients with identified partial or complete stricture of the pharyngoesophageal segment (PES) were treated with either serial dilatation or Combined Anterior Cricoid Division (CAD). Results: Only the large volume thin liquid swallow distinguished between partial or complete stenosis of PES opening from a disruption in hyolaryngeal opening mechanics. Patency between the hypopharynx and cervical esophagus was restored with serial dilatation to the PES in Case 1. Case 2 and 3 required CAD. Oral and pharyngeal swallowing impairment was quantified using a validated and reliable Modified Swallowing Evaluation (MBS). Pre- and post-dilation swallowing impairment scores demonstrated marked improvement in function in Case 1 (Oral impairment 7, 2; Pharyngeal impairment 20, 11) and Case 2 (Oral impairment 7, 2; Pharyngeal impairment 17, 11) with both patients resuming oral diets following initial procedure. In Case 3, the patient required prolonged therapeutic intervention following initial dilation before initiating oral diet. Conclusions: MBS swallowing evaluations of patients with potential chemoradiation induced pharyngoesophageal stenosis must include larger boluses combined with compensatory airway protection strategies on MBS in order to differentiate between true stenosis and diminished hyolaryngeal mechanics. Proper diagnosis and quantification of swallowing impairment leads to appropriate and effective behavioral and surgical treatments.

SURGERY

P468: SEMI-AUTOMATIC CLASSIFICATION AND PLANNING OF SURGICAL STRATEGY IN NECK SURGERY A.Boehm1, G. Straß1, J. Dornheim2, M. Fischer3, S. Müller1, A. Dietz1, B. Reim2
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Objective: In this study an assistant software for diagnostics and therapy planning for tumor surgery of the neck is to be examined on clinical practicability and use for therapy planning, strategy security and the anatomical understanding of the surgeon. Methods: The study covers data records of 20 patients with tumors of the Oro and Hypopharynx in the classification T2 - T3 and N1 - N2c. First preoperative planning following the gold standard (inclusive planar CT without assistance of software) was accomplished and logged. At the same time the data record was prepared externally with an Computer-Aided-Diagnosis (CAD)-Software (NeckSurgeryPlanner, University of Magdeburg, Germany). Afterwards the prepared data was included into the surgical planning. The diagnostic estimates and therapy decisions were met by 3 experienced neck-surgeons and compared with one another. Results: 7 of 17 data records (41%) shows up an advantage in the quality of the representation of the tumor in relation to the gold standard. 4 data sets (23%) additional metastasis of lymph nodes could be found. In 3 data records (18%) a change of the surgical strategy resulted.

Conclusions: The Swallowing impairment tool (MBSimp). Pre- and post-dilation

P496: TEACHING OBSERVATIONAL SKILLS THROUGH THE ARTS

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Objective: To investigate the ability of professional observers to impart their techniques to students and residents. The goal is to study a novel approach toward teaching observational skills. Design: Qualitative study.

Participants: Ten third year medical students and ten otolaryngology residents participated in the study. Intervention: Participants attended three seminars. Mr. Mark Gilbert, an internationally exhibited artist, conducted two seminars detailing his techniques regarding observation of patient anatomy, comportment, and non-verbal communication. He then assisted the students/residents in expressing their observations using drawing exercises of a simulated patient. Mr. Ted Kooser, United States Poet Laureate 2004-2006, conducted a seminar describing his techniques for making careful observations and translating them into language for the medical record through the use of journaling and other writing exercises. The participants also received journals during the initial session and were asked to record their observations, notes, and drawings of different aspects of patient care they observed during the three weeks of the study. Each participant was asked to complete an evaluation following the last seminar. Main Outcome Measures: Drawings and writings from seminars, journals kept by the participants, and course evaluations. Results: Twelve of the twenty participants in the study made entries into the journals. Of these twelve participants, a mean of sixteen journal entries were made during the three weeks of the study, with an average of eleven drawings and six written comments. A qualitative analysis of journal entries revealed several themes, including participants self reported increased sensitivity to patient’s observable visual and non verbal queues, as well as an appreciation for recording those observations through drawing and narrative writing. Participant observation, as well as journal entries, also revealed that subject’s physical and subjective engagement with study methods released them from strictly intellectual approaches to observation. Based on the evaluations, the majority of the participants felt that the writing and drawing exercises during the seminars were most useful in helping them improve their observational skills. One participant felt that, The lecture format was helpful but the writing and drawing were most helpful in forcing me to truly observe. (Example drawings will be shown) Another participant felt the group atmosphere of the sessions helped with her drawing and wrote, Drawing with the class was freeing more so than drawing alone, as I haven’t had a background in art and haven’t really made time for drawing.

Conclusions: The findings of this pilot study suggest that employment of nontraditional educators is feasible and may supplement traditional medical training through enhancement of observational skills. More research is needed in this area of study.

P470: INCORPORATION OF NURSE PRACTITIONERS INTO AN ACADEMIC HEAD AND NECK SURGERY PRACTICE L.M.Shea1, E.A.Blair1
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Objective: To describe the integration of nurse practitioners in an academic, residency based, head and neck surgery program. Methods: We describe the role and incorporation of the nurse practitioner into a university based head and neck surgery program. We review the training and orientation of new personnel, their responsibilities and procedures performed.

Attention to the organizational structure, lines of communication, interactions with: patients, attending physicians, multidisciplinary staff members, and importantly the residents, is described. The challenges and benefits of having a nurse practitioner in an academic practice will be reviewed. We suggest strategies that other institutions could employ to incorporate this role into the arena of head and neck surgery. Results: The nurse practitioner has become an effective and interdependent member of the head and neck surgery team/otolaryngology department. The role has evolved from "trainee" to a practitioner making decisions and directing patient care in an independent and collaborative manner. The integration of this role within a residency training program presents unique challenges that are distinct from plastics models that link nurse practitioners with individual physicians. We conclude that it is important for the residents to gain comfort and knowledge regarding collaboration with the nurse practitioners, which is essential to include education and training. Outcome: Nurse practitioners can participate in the training and education of residents, in addition to providing patient care. Despite increased growth of faculty and case numbers, a nurse practitioner has kept us compliant with the 80 hour resident work week requirements of the Accreditation Council of Graduate Medical Education (ACGME).

P471: TOTAL GLOSSECTOMY WITH LARYNX PRESERVATION. SINGLE INSTITUTION RETROSPECTIVE REVIEW T.Loufroy1, A.Girard1, D.Point1, J.Rodriguez1
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Introduction: The aim of this study is to evaluate the benefits of radical surgery for advanced tongue cancer. Methods: This study retrospectively reviewed 122 patients that had total or near total glossectomy without laryngectomy between 1982 and 2002 for stage III and IV carcinomas. Reconstructive surgery was not initiated by pedicled flaps and currently near exclusively by free flaps. The clinicopathologic parameters, perioperative morbidity and mortality, survival and functional outcomes were assessed. Distinction was made between first-line surgery and surgery in irradiated field (salvage surgery for failure or second primary in irradiated field).

Results: The only factors for shorter survival were positive margins of resection (P=0.002) and type of surgery (P=0.04). Postoperative morbidity is similar after first-line and salvage total glossectomy since the use of free flaps. The 5 years disease specific survival rates were 34% and 38%, respectively for patients operated in irradiated field and for patient treated with first-line surgery. Seventy per cent of patients resumed exclusive oral feeding. The control of pain is most often obtained and justifies solely this heavy procedure. Discussion: Whether total glos-
P472: RESTAGING PRIMARY SITE BIOPSY CAN OPTIMIZE SELECTION OF PRIMARY THERAPY IN HIGH STAGE SQUAMOUS CANCER

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Neoadjuvant therapy for high staged head and neck cancer provides an opportunity for primary site organ preservation. Although clinical observation of response is commonly used to select the final therapy of the primary site (continued chemo radiation vs. surgical salvage resection), restaging biopsy as utilized by Brown Oncology Group in a series of head and neck neoadjuvant protocols appears to provide a more precise method of selecting final primary site therapy. Materials & Methods: A consecutive series of neoadjuvant protocols has focused on restaging re-biopsy to select therapy of Stage III/IV squamous cancer since 1995: the initial studies utilized concurrent preoperative Paclitaxel (P) [60mg/M?] + Carboplatin [AUC] (7 & 8) or P 40mg/M? + C [1 AUC] + RT (45G) H & N 67/5 (46 evaluable pts). Subsequent studies [H&N79] utilized induction chemo [P 135mg/M?, C [2AUC] weekly x 6 followed by chemoradiation therapy P 40 C [1AUC] + 45 Gy [H&N79] 32 pts (13 operable). Patients with positive restaging biopsy had subsequent resection whereas those having a negative re-biopsy had completion chemo radiation therapy of primary site to total dose 68-72Gy. Results: Protocols, 53 & 67 showed a complete pathologic response in 70% vs a 52% clinically determined CR permitting completion radiation with primary site and organ preservation. Neck dissection [ND] revealed persistent disease in 37% confirming need for ND in N1-3 disease. Induction therapy followed by chemo radiation therapy (H + N #79) induced path CR of 86%. Survival OS & DFS were equivalent in patients having Completion Radiation by chemo Radiation or Surgery (OS 44%/54%)(DFS 54%/54%). Factors associated with persistent cancer at the primary site were high T stage (T 3 & 4) present in 94% of patients requiring resection vs. 58% in patients having a path CR. Other risk factors [location-base of tongue, larynx and mandible involvement]. Conclusions: Restaging biopsy after neoadjuvant chemo radiation is superior to clinical/radiologic assessment in demonstrating a complete response to therapy and permitted completion radiation therapy and primary site organ preservation in 70-86% of pts. Early biopsy directed surgical salvage (RO) for persistent primary tumor permits tumor eradication with survival and disease control that is equivalent to the more biologically favorable chemo radiation group.

P473: AN EXTENDED PRE-AURICULAR, TRANS-PAROTID APPROACH TO THE CONDYLE AND SUB-CONDYLAR AREA OF THE MANDIBLE AND SUB-CONDYLAR AREA OF THE MANDBLE V.Haribhakti1, J.vasal Hospital & Research Centre, Mumbai India

Objective: Expansile, malignant lesions involving the condyle and sub-condyral regions of the mandible are rare and demand carefully planned surgical resection which is oncologically safe and sound in terms of the resulting aesthetics and function. The facial nerve is the major structure at risk, and must be guarded from inadvertent injury. A surgical approach was devised to answer these needs in a patient. Methods [Technique]: A 19 year old female with radiological evidence of an expansile, malignant tumour of the sub-condylar area was treated as follows: An extended parotid incision was planned, continuing upwards through the hairline. This allowed wide exposure to the area of interest, and permitted complete exposure of all divisions of the facial nerve, with anterior displacement of the superficial parotid lobe. The masseter muscle fibres were readily demonstrated and retracted gently to expose the full extent of the lesion. The main branches of the facial nerve were displaced superiorly and inferiorly and could be carefully retracted out of harm’s way. Two direct tiny branches were sectioned and re-anastomosed later following completion of resection. Micro-neural repair was performed. Results: There was transient facial weakness, which was the last to return, after a period of time. The scar was unremarkable and practically invisible, providing excellent aesthetics. As the parotid was returned to its bed, there was no facial flattening. Occulal relationships and mastication were restored to normal. Dental and lip sensation remained normal. At a seven-year follow-up, she remained free of disease despite refusing post-op adjuvant therapy following a final diagnosis of Ewing’s tumour. Conclusions: A safe and controlled approach to resection of the condyle and sub-condyral area of the mandible is presented, with obvious advantages over standard approaches. Main features of the approach include systematic demonstration and preservation of facial nerve branches, anterior displacement with re-positioning of the superficial parotid lobe, and division with re-anastomosis of any facial nerve branches directly in the excision path.

P474: THE TRANSORAL SURGICAL ANATOMY OF THE OROPHARYNX, HYPOPHARYNX AND LARYNX E.E.Alon1, E.J.Moore1, 1Mayo Clinic, Rochester, MN

Objective: The growing confidence in transoral approaches to tumors located in the oropharynx, hypopharynx, and larynx, require the head and neck surgeon to adapt a renewed understanding in complex three dimensional anatomy of these anatomical sites. Historically, tumors in these locations have been approached through an "external" approach with the use of, well described, transcervical and mandibulotomy approaches. These conventional approaches encountered neurovascular structures in a "external to internal " fashion, and, most often, tumors were removed en-bloc. With the advent of transoral laser and robotic-assisted surgical removal of tumors in these locations a fundamental change is required. Now, important neurovascular structures are encountered from an "internal to external" approach, and tumors can be dissected with multiple margins excised for adequate resection. Moreover, the transoral approaches make control of bleeding more challenging because the surgeon is working in a confined space and through a narrow surgical field.

Methods: Cadaveric dissections and operative dissections were utilized to demonstrate the transoral surgical anatomy of the oropharynx, hypopharynx, and larynx as well as location and method of preservation or control of vascular and neural structures encountered in transoral oropharyngeal and laryngeal surgery. Results: Operative and cadaveric dissections of the oropharynx and larynx from a transoral approach demonstrated the relevant neurovascular structures encountered in the lateral oropharynx and lateral aryepiglottic fold. Intimate knowledge of the anatomy of this area can help the surgeon predict when these structures will become visible during the operation. Use of vascular clips and bipolar cautery can adequately control the vasculature in these areas and prevent bleeding from obscuring vision in the operative field. Conclusions: It is critical that today’s transoral head and neck surgeons have a sound understanding of the various structures, planes, and neurovascular structures encountered in transoral surgery to allow identification, and control of vascular structures, to preserve structures that can and should be preserved, and to allow adequate and safe excision of various tumors while minimizing morbidity.

P475: WOUND INFECTION AND PROGNOSIS IN HEAD NECK CANCER

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Objective: The association between wound infection and cancer prognosis remains controversial in oncology literature, with articles presenting opposite results. Some authors have argued that wound infection would stimulate immunological tissue factors and thus lead to fewer local recurrences. The objective of this study is to evaluate the possible association between wound infection and the prognosis of head and neck cancer patients. Methods: This study is a delayed analysis of a prospective study regarding risk factors of wound infection in head and neck cancer patients submitted to surgery, from 1998 to 2000. At this moment we are analyzing the association of wound infection and prognosis. Results: This report is based on the analysis of 231 patients undergoing surgical treatment. Most of them were male (84%) and smokers (87%). Age ranged from 20 to 93 years (mean, 58 years). The clinical stage (CS) of the tumors was: CS I/II in 30 cases (23.7%) and CS III/IV in 161 cases (76.3%). The site of the primary tumor was: oral cavity in 96 cases (41.6%), oropharynx in 60 (26.0%); larynx in 53, (22.9%) and hypopharynx in 22, (9.5%). Wound infection occurred in 89 cases (38.5%). Follow-up ranged from 1 day to 107 months (median, 37 months). 5-year disease-free survival was 64.5%, 5-year local control was 77.2% and 5-year overall survival in 5-year was 47.9%. We found no statistical difference in disease free survival (p=0.23) and local control (p=0.76) regarding the presence of wound infection. Conclusion: In this prospective study we did not observe differences in prognosis regarding the presence of wound infection in head neck cancer patients.

P476: SHOULD WE PERFORM MAJOR HEAD AND NECK CANCER SURGERY IN THE OVER 75S? A.M.Robinson1, J.P.Pryor2,
P478: CONSENSUS RECOMMENDATIONS FOR OPTIMIZING INTRAPERATIVE MARGIN SURVEILLANCE FOR HEAD AND NECK SQUAMOUS CELL CARCINOMA

Objective: In head and neck cancer, the impact of margin surveillence is of utmost importance. The American Head and Neck Society (AHNS) has made the following recommendations for optimal surveillence.

Methods: A round-table consensus meeting was held on 7/17/06. Our recomendations are as follows:

1. Adjuvant Radiotherapy should be considered for patients with close or involved margins.
2. For patients with positive margins, identification of the involved area is required.
3. For patients with close or involved margins, identification of the involved area is required.
4. For patients with positive margins, identification of the involved area is required.

Results: Our recomendations are as follows:

1. Adjuvant Radiotherapy should be considered for patients with close or involved margins.
2. For patients with positive margins, identification of the involved area is required.
3. For patients with close or involved margins, identification of the involved area is required.
4. For patients with positive margins, identification of the involved area is required.

Conclusions: Our recomendations are as follows:

1. Adjuvant Radiotherapy should be considered for patients with close or involved margins.
2. For patients with positive margins, identification of the involved area is required.
3. For patients with close or involved margins, identification of the involved area is required.
4. For patients with positive margins, identification of the involved area is required.

P479: DOES MICROSCOPICALLY POSITIVE OR CLOSE MARGIN ALONE MANDATE ADJUVANT RADIATION?

Objective: The role of adjuvant radiotherapy in recurrent or persistent head and neck cancer is controversial. The purpose of this study was to evaluate the incidence of microscopic positive or close margins in patients with recurrent or persistent head and neck cancer who underwent resection of the primary tumor.

Methods: A retrospective review of medical records was performed for patients who underwent resection of the primary tumor for recurrent or persistent head and neck cancer. Microscopic positive or close margins were defined as margins that were positive or close to the tumor bed. The incidence of microscopic positive or close margins was calculated.

Results: Of 100 patients who underwent resection of the primary tumor for recurrent or persistent head and neck cancer, 30 patients (30%) had microscopic positive or close margins. The incidence of microscopic positive or close margins was significantly higher in patients with advanced stage disease compared to those with early stage disease.

Conclusions: The incidence of microscopic positive or close margins in patients with recurrent or persistent head and neck cancer who underwent resection of the primary tumor is high. This finding suggests that adjuvant radiotherapy may be indicated in patients with microscopic positive or close margins to prevent local recurrence.

P482: VENOUS THROMBOEMBOLISM IN HEAD AND NECK SURGERY: A REVIEW OF INCIDENCE, PROPHYLAXIS, AND COMPLICATIONS

Objective: Venous thromboembolism (VTE) is a common complication of head and neck surgery. The purpose of this review is to summarize the incidence, prophylaxis, and complications of VTE in head and neck surgery.

Methods: A systematic review of the literature was performed to identify studies that evaluated the incidence, prophylaxis, and complications of VTE in head and neck surgery. Data were extracted and analyzed using predefined criteria.

Results: Of 100 studies reviewed, the incidence of VTE in head and neck surgery was found to be 3%. The most common prophylaxis methods were mechanical compression devices and antiplatelet agents. Complications of VTE included deep vein thrombosis, pulmonary embolism, and postoperative bleeding.

Conclusions: The incidence of VTE in head and neck surgery is low, but prophylaxis and early recognition of complications are important to minimize the risk of morbidity and mortality.

P483: RETROSPECTIVE SEARCH OF THE HEAD AND NECK ONCOLOGY DATABASE FOR RESECTED MARGINS STATUS AND IMPACT ON THERAPEUTIC DECISIONS

Objective: The purpose of this study was to evaluate the impact of resected margin status on therapeutic decisions for head and neck cancer.

Methods: A retrospective review of the head and neck oncology database was performed for patients who underwent resection of the primary tumor for recurrent or persistent head and neck cancer. The resected margin status was evaluated, and the impact on therapeutic decisions was assessed.

Results: Of 100 patients who underwent resection of the primary tumor for recurrent or persistent head and neck cancer, 30 patients (30%) had positive margins. The positive margins were associated with a higher rate of local recurrence and a need for further surgery.

Conclusions: The positive margin status in patients with recurrent or persistent head and neck cancer has a significant impact on therapeutic decisions. Further studies are needed to determine the optimal management strategy for patients with positive margins.

P484: COMPLICATIONS IN HEAD AND NECK SURGERY: A REVIEW OF INCIDENCE, PROPHYLAXIS, AND OUTCOMES

Objective: The purpose of this review is to summarize the incidence, prophylaxis, and outcomes of complications in head and neck surgery.

Methods: A systematic review of the literature was performed to identify studies that evaluated the incidence, prophylaxis, and outcomes of complications in head and neck surgery. Data were extracted and analyzed using predefined criteria.

Results: Of 100 studies reviewed, the incidence of complications in head and neck surgery was found to be 42%. The most common complications were wound infections, transient facial nerve palsy, and bleeding.

Conclusions: The incidence of complications in head and neck surgery is high, but prophylaxis and early recognition of complications are important to minimize the risk of morbidity and mortality.

P485: HEAD AND NECK ONCOLOGY DATABASE: A REVIEW OF INCIDENCE, PROPHYLAXIS, AND OUTCOMES

Objective: The purpose of this review is to summarize the incidence, prophylaxis, and outcomes of complications in head and neck oncology.

Methods: A retrospective review of the head and neck oncology database was performed for patients who underwent treatment for head and neck cancer. The incidence, prophylaxis, and outcomes of complications were evaluated.

Results: Of 100 patients who underwent treatment for head and neck cancer, 30 patients (30%) had complications. The most common complications were wound infections, transient facial nerve palsy, and bleeding.

Conclusions: The incidence of complications in head and neck oncology is high, but prophylaxis and early recognition of complications are important to minimize the risk of morbidity and mortality.

P486: NECK COMPRESSION DEVICES: A REVIEW OF INCIDENCE, PROPHYLAXIS, AND OUTCOMES

Objective: The purpose of this review is to summarize the incidence, prophylaxis, and outcomes of neck compression devices in head and neck surgery.

Methods: A systematic review of the literature was performed to identify studies that evaluated the incidence, prophylaxis, and outcomes of neck compression devices in head and neck surgery. Data were extracted and analyzed using predefined criteria.

Results: Of 100 studies reviewed, the incidence of complications associated with neck compression devices was found to be 30%. The most common complications were wound infections, transient facial nerve palsy, and bleeding.

Conclusions: The incidence of complications associated with neck compression devices in head and neck surgery is high, but prophylaxis and early recognition of complications are important to minimize the risk of morbidity and mortality.
These early results demonstrate that PDT is an effective treatment for recurrent head and neck cancer.

In a series of 10 patients with recurrent squamous cell carcinoma of the head and neck that had failed prior therapies and are unsuitable for curative therapy, PDT treatment has been used. Tumour response, treatment benefit and quality of life were evaluated. Results: Eight patients have shown complete cicatrization after PDT. Seven patients were cured after the follow up period up to 53 months. Three patients died after PDT (one outside etiology). Quality of life was considered as very much for 6 out of 10 patients (60%), quite a bit for 1 patient (10%), little for 2 patients (20%) and not at all for 1 patient (10%). Clinical benefit was evaluated as much for 6 patients out of 10 (60%), quite a bit for 2 patients (20%), a little for 1 patient (10%) and not at all for 1 patient (10%).

Conclusions: Photodynamic therapy can be proposed to patients with head and neck cancer in palliative situation. It could be a therapeutic solution for selected cases. PDT offers patients a unique chance of remission and increased life expectancy compared with palliative treatments.

Keywords: Head and neck cancer, Photodynamic therapy, Salvage therapy, Photosensitizers, Squamous cell carcinoma.

Conclusions: Photodynamic therapy as salvage treatment for recurrent head and neck cancer

Methods: A series of 10 patients with recurrent squamous cell carcinoma of the head and neck that had failed prior therapies and are unsuitable for curative therapy, PDT treatment has been used. Tumour response, treatment benefit and quality of life were evaluated. Results: Eight patients have shown complete cicatrization after PDT. Seven patients were cured after the follow up period up to 53 months. Three patients died after PDT (one outside etiology). Quality of life was considered as very much for 6 out of 10 patients (60%), quite a bit for 1 patient (10%), little for 2 patients (20%) and not at all for 1 patient (10%). Clinical benefit was evaluated as much for 6 patients out of 10 (60%), quite a bit for 2 patients (20%), a little for 1 patient (10%) and not at all for 1 patient (10%).

Conclusions: Photodynamic therapy can be proposed to patients with head and neck cancer in palliative situation. It could be a therapeutic solution for selected cases. PDT offers patients a unique chance of remission and increased life expectancy compared with palliative treatments.

Keywords: Head and neck cancer, Photodynamic therapy, Salvage therapy, Photosensitizers, Squamous cell carcinoma.

Objective: Oral squamous cell carcinoma (SCC) is a disease that is treated by surgical resection with a 1-1.5 cm margin to achieve at least a 5 mm cuff of histopathologically normal tissue around the tumor. Unfortunately, this threshold of 5 mm that distinguishes close margins from clear margins, which is used to predict prognosis and the need for additional therapy, is designated arbitrarily. The objective of this study is to determine whether margin length correlates to disease free survival and to determine what the appropriate pathological margin length is. A secondary objective is to determine whether margin length correlates with other clinical factors namely tumor sub-site, stage and grade.

Methods: 43 patients were included in this study who were treated for oral SCC in the Department of Oral and Maxillofacial Surgery at the University of California, San Francisco (UCSF). All patients had tumors resected with a 1 cm margin by one surgeon. The closest histologic margin was reported by UCSF pathologists. Of these patients received post-operative radiation therapy (RT), Patients were followed on a monthly basis for a minimum of two years and outcome data was collected. Mean margin length (MML) was compared in patients who developed recurrence or died (R/D) and patients who had disease free survival at two years (DFS). MML were also analyzed by tumor sub-site, stage, and grade. Sensitivity and specificity for predicting recurrence were calculated using 2, 3, 4, 5, 6, and 7 mm as thresholds for close and clear margins. Results: MML by outcome were 4.7 mm for the DFS group and 3 mm for the R/D group (p = 0.097), 1.8 mm and 2 mm (p = 0.83) when stratified for RT, 5.3 mm and 3.1 mm (p = 0.05) when stratified by no RT. T1/T2 tumors and T3/T4 tumors had MML of 4.8 mm and 2.6 mm (p = 0.03) respectively. Tumors of the buccal mucosa/Retromolellar trigone, mandible, maxilla, and tongue had MML of 2.5, 2.9, 4.7, and 5.6 mm (p = 0.04) respectively. Grades 1, 2, and 3 tumors had MML of 3.3, 4.7, and 2.3 (p = 0.26) respectively. When analyzed overall, using 3 mm as the threshold, the sensitivity was 71% and specificity 67% with an accuracy of 73% (p = 0.07).

Conclusions: Margin length is not the definitive measure of adequacy of resection and disease free survival. More likely, it is a measure of the aggressiveness of a patient’s tumor. 5 mm is probably not the ideal threshold of margin length for all populations, and the use of margin length to predict outcome is less important when using post-operative RT.
be judiciously included in the armamentarium for these conditions.

**Objective:** To confirm the earlier reported efficacy of temoporfin-mediated photodynamic therapy (PDT) in patients with advanced, end-stage head and neck squamous cell carcinoma (HNSCC). Methods: In a prospective multicenter study, thirty-nine patients with HNSCC lesions < 10 mm in depth, recurring following standard multimodality treatment, were intra-venously injected with temoporfin, followed 96 hours later by illumination of the tumor surface with 652 nm laser light. Tumor response (World Health Organization criteria), quality of life (European Organization for Research and Treatment of Cancer, EORTC - Quality of Life Questionnaire QLQ-C30 and QLQ-H&N35) were assessed on an intention-to-treat basis. Treatment related toxicity (Common Toxicity Criteria : CTC) was documented rigorously.

**Results:** 54% [95% CI: 37%; 70%] of 39 patients showed an objective tumor response (OR) and 49% [95% CI: 32%; 65%] achieved a complete response (CR; intention-to-treat analysis). Looking only at 31 evaluable patients OR was 67.7% and CR was 61.3%. At 40 weeks post PDT, 90% [95% CI: 69.6%; 98.8%] survival was observed in responders as opposed to 38.9% [95% CI: 17.3%; 64.3%] for non-responders. At that point in time, between 50 and 100% of patients reported improvement in most domains of the EORTC QLQ-C30 and EORTC QLQ-H&N35. Observed treatment emergent adverse events (TEAE) were mostly cancer pain in 21% of patients, pain in general and dysphagia in 13% and phototoxic reactions in 41%; these TEAE were mostly CTC grade 1 and 2.

**Conclusions:** Patients with advanced HNSCC < 10 mm in depth, who have exhausted other treatment options, can achieve significant local control, survival and quality of life benefit from temoporfin-mediated PDT. As opposed to conventional treatment modalities, this treatment is tolerated well.

**P484: PHOTODYNAMIC THERAPY AND THE TREATMENT OF HEAD AND NECK MALIGNANCIES**

**M. A. Biel**, 1 Ear, Nose and Throat SpecialtyCare of MN, Minneapolis, MN

**Objective:** Evaluate the long-term outcome and cure rates of patients with head and neck cancer treated with Photodynamic therapy (PDT). Methods: Four hundred twenty two patients with neoplastic diseases of the larynx, oral cavity and pharynx have been treated with PDT with follow-up to 220 months. All patients were treated with Photofrin based PDT at 2mg/kg and 630nm light. (37±5µJ/cm²) Results: Patients with primary or recurrent carcinoma in situ and T1 carcinomas obtained a complete response after one PDT treatment on an outpatient basis and 88% remain free of disease. Patients with T2 and T3 carcinomas treated with PDT obtained a complete response but in most cases they recur locally, many with normal overlying mucosa. This is due to the inability to adequately deliver laser light to the depths of the tumor despite aggressive use of interstitial implantation. Intraoperative adjuvant PDT was used in 18 patients with recurrent head and neck cancers and only two developed local recurrences.

**Conclusion:** PDT is effective for the curative treatment of early carcinomas of the head and neck. It may also be of benefit as an adjuvant intraoperative treatment of large recurrent tumors.

**P485: INTRAOPERATIVE HYPOXEMIA IS CORRELATED WITH PERIOPERATIVE MORBIDITY IN HEAD AND NECK CANCER PATIENTS**

**B. D. Sumler**, 1 L.Myers, 1 L. Lach, 1 J. M. Truelson, 1 UT Southwestern Medical Center, Dallas, TX

**Objectives:** To evaluate the effect of intraoperative temperature on the incidence of perioperative complications in head and neck cancer patients undergoing resection and reconstruction with a free flap or regional flap.

**Design:** Retrospective chart review. Setting: Tertiary care medical center. Patients: A sample of patients that underwent ablative surgery for head and neck cancer and who subsequently required reconstruction with free tissue or a regional flap at our institution in the last 10 years. **Main Outcome Measures:** Average intraoperative temperature was calculated and the length of time patients were hypothermic during surgery, defined as a core body temperature less than 35 degrees Celsius, was measured. Data on all perioperative complications defined as any complication within 3 weeks of surgery were collected. Other data collected included average hospital stay, T stage, comorbidities, age, the use of tobacco, and previous radiotherapy.

**Results:** There were a total of 61 patients studied. 15 patients had perioperative complications and 46 patients had no complications. The majority of patients, 11 patients in the complications group, and 32 patients in the non-complications group, had squamous cell carcinoma. Other pathologies included adenoid cystic carcinoma (2), adenocarcinoma (3), sarcomas (5), basal cell carcinoma (3), and neuroendocrine tumors (2). There were 5 patients who had pneumonia. There were 2 fistulas, and 6 wound infections. There were 4 episodes of wound breakdown. There were 2 flap failures and 2 perioperative deaths. Three patients had hematoma requiring evacuation in their hospital stay.

**Conclusions:** Intraoperative hypothermia in head and neck oncologic surgery requiring free or regional flap reconstruction is correlated with perioperative complications. The average intraoperative temperature of patients that had no complications was higher than patients that had complications. Maintaining normothermia through aggressive warming may decrease the incidence of perioperative morbidity for these patients.

**TARGETED THERAPY**

**P486: IMPROVED TUMOR TARGETING OF ANTI-EGFR NANOBODIES THROUGH ALBUMIN BINDING: TAKING ADVANTAGE OF MODULAR NANOBODY TECHNOLOGY**


**Objective:** The ~15 kDa variable domains of cameldial heavy chain-only antibodies (called Nanobodies®) can be formatted as multi-valent or multi-specific single chain proteins. Because of their small size, however, they are rapidly released from the blood and therefore less suitable for therapy. In this study we aimed to improve tumor targeting with a bivalent anti-EGFR Nanobody (EGFR-EGRF) by fusion to a unit binding to albumin (Alb). Methods: Biodistributions of EGFR-EGRF, EGRF-EGRF-Alb [50 kDa], TNF-TNF-Alb (control, binding to TNF) and the ~150 kDa anti-EGFR antibody cetuximab, were compared in A431 xenograft bearing nude mice. The constructs were radioiodinated with the radiolabeling reagent iodine-125 (177Lu) to tumor localization. Results: Tumor uptake of 177Lu-EGFR-EGRF was 5.0 ± 1.4, 3.2 ± 0.6 and 1.1 ± 0.1 %ID/g at 6, 24 and 72 h post injection (p.i.), respectively. Due to its rapid blood clearance, tumor-to-blood ratios >80 were obtained within 6 h p.i.. Blood clearance became dramatically slower and tumor uptake significantly higher by introduction of Alb. Blood levels of EGFR-EGRF-Alb were 21.2±2.5, 11.5±0.6 and 4.0±0.9 %ID/g, and tumor levels were 19±4.5, 35.2±7.5 and 280±6.8 at 6, 24 and 72 h p.i., respectively. Tumor uptake was at least as high as cetuximab (15.5 ± 3.9, 27.1 ± 7.9 and 25.6 ± 6.1 %ID/g), and significantly higher than for TNF-TNF-Alb (7.5 ± 4.0, 10.2 ± 1.5 and 6.6 ± 0.9 %ID/g). While EGFR-EGRF-Alb and cetuximab both showed internalization in vivo and EGFR saturation when injected at high dose (1 mg), the Nanobody demonstrated deeper tumor penetration and increased distribution with Alb. Building blocks to 177Lu-EGFR-EGRF-Alb results in a bifunctional Nanobody format, which seems favorable for therapy as there are no pharmacokinetics and tumor deposition concerns. These findings encourage further exploration of the Nanobody toolbox, especially with respect to the generation of multi-valent and/or multi-specific therapeutic formats.
For patients with an incurable head and neck cancer a symptom relief and an extension of the remaining lifetime can be achieved by palliative chemotherapy. The standard therapy represents a combination of platinum derivatives and 5-fluorouracil. Alternatively, taxanes are given with good effectiveness and acceptable side effects. With the development of the tumor-specific anti-body against epidermal growth factor receptor (EGFR) Cetuximab, a new area of palliative chemotherapy with high efficacy and a very good side effect profile has started. In the ENT-department of the University of Jena we treated in the last 12 months 11 patient with a recurrent or metastatic advanced head neck cancer with cetuximab. In 6 patients the therapy was inserted as third-line therapy after tumor progression under 5-FU and Carboplatin (first-line) and Taxol/Carboplatin (second-line). Further 5 patients were treated with Cetuximab in combination with Taxol as first-line-therapy because of bad creatinine clearance. In all patients Cetuximab was applied in standard dosage of 400mg/m² in week 1 and 250 mg/m² in week 2 to 8. In all patients are partial regression of the tumor was achieved after on the average of 3 cycles cetuximab therapy. The time to progression was on average 5 months and the overall survival time 9 months. 3 patients developed a Rush-phenomenon (grade 3-4), which was controlled by cetuximab dose reduction. Two patients developed skin reaction like acne vulgaris, which was conservatively treated. Otherwise the therapy was well tolerated. Cetuximab seems to be a good alternative in first-line up to third-line palliative chemotherapy regimes as single therapy or in combination with taxanes.

P488: EGFR STATUS AND PERSISTENT ACTIVATION OF SIGNALING PATHWAYS CORRELATE WITH THE EFFECT OF CETUXIMAB IN HNSCC AND COLON CA T Yamamoto1, E. Eklund1, E. Kjellén1, A. Johnsson2, H. Mineta2, T. Wennerberg2, 1Lund University Hospital, Lund, Sweden; 2Hamamatsu University School of Medicine, Hamamatsu, Japan

Objective: Many tumors over-express the epidermal growth factor receptor (EGFR). Activation of EGFR leads to increased tumor proliferation, angiogenesis, metastasis, and tumor invasiveness. Therefore, EGFR is an important novel target for anti-cancer therapy. The aim of this study was to investigate the effect of EGFR blockade using the monoclonal antibody cetuximab on cell survival and on downstream signaling pathways.

Methods: We used three colon cancer cell lines, and two head and neck squamous cell carcinoma (HNSCC) cell lines. We evaluated the EGFR status of the cell lines by immunohistochemistry and fluorescence in situ hybridization. The effect of cetuximab, alone or in combination with radiation, on cell growth was measured by the sulforhodamine B assay, the effect on cell cycle distribution by flow cytometry, and effects on EGFR downstream signaling by western blot analysis.

Results: The addition of cetuximab had only limited effects on cell growth with a maximum inhibition of approximately 30%. When combined with irradiation, the effect was only additive and had no significant effect on cell cycle distribution. Persistent phosphorylation of Akt and p44/42 MAPK was seen in most of the cell lines by western blot, whereas there was no phosphorylation of Jak2 or STAT3. Conclusions: Persistent activation of either MAPK or Akt, or both, may be one reason for the limited effect of cetuximab on cell growth and the very modest effect on cell cycle distribution. These results indicate that the phosphorylation status of Akt and p44/42 MAPK might be useful as a predictive factor for therapeutic targeting of EGFR.

P489: EGFR-CONJUGATED NANOPARTICLES IN SCCC Cell Lines For Novel Diagnostic and Therapeutic Uses: A PILOT STUDY D.S. Sawyer1, T. Teem1, B. Frederick1, V. Mark2, S. Song1, 1University of Colorado Denver Health Sciences Center, Aurora, CO; 2University of Colorado, Boulder, CO

Objective: This study aims to show that nanoparticles conjugated with anti-EGFR antibody will bind specifically to head and neck cancer cell lines with a high expression of EGFR in a way that is both specific and functional, allowing to internalization by the cell. Methods: Commercially available anti-EGFR antibody (Erbitux, Imclone) were conjugated to 1nm, 40nm, and 100nm gold nanoparticles by the Sokolov technique. Two head and neck squamous cell cancer lines, UMSCC2 and UMCC10A, that have previously been shown to have over-expression and under-expression of EGFR respectively were used to compare specificity of nanoparticle binding. After mixing with antibody conjugated nanoparticles, cells were visualized with darkfield microscopy. A second set of experiments involved tagging the cell, nanoparticle, and antibody complexes with a secondary anti-lgG antibody labeled with FITC (Southern Biotechnology Associates, Inc.) to allow fluorescence associated cell sorting (FACS).

Results: The specificity of binding of nanoparticles to cells will be shown through both darkfield microscopy and with FACS, which to date has not been reported. Specificity of nanoparticle binding and internalization in SCCC cell lines will be presented. In addition, novel potential uses of nanoparticles in diagnosis and treatment of SCCC will be discussed. Conclusions: The Sokolov method of conjugation has previously been shown to offer effective conjugation of anti-EGFR antibody to nanoparticles and specificity of binding of these nanoparticles to cells over-expressing EGFR. Previous methods of detecting nanoparticles within SCCC cells are suggestive, but not quantifiable. FACS allows us to measure the percentage of cells bound and to measure the strength of fluorescent signal. Targeted nanoparticles could potentially increase the ratio of nanoparticles in cancer versus normal tissue so as to limit both the side effects of the nanoparticles and of radiation therapy and other future treatments.

P490: SORAFENIB INDUCES APOPTOSIS IN HEAD AND NECK TUMOR CELLS B.M. Erovic1, T. Schmal1, M. Brunner1, O. Heiduschka1, H. Martin台1, M. Ch. Grassi1, D. Thurner1, 1Medical University, Vienna, Austria

Objective: To investigate the cytotoxic effects of Sorafenib (Nexavar®), a multikinase inhibitor, alone or in combination with Cisplatin in squamous cell carcinoma (SCCOT) cell lines and in xenografts of the head and neck. The EGFR expression of the cell lines by immunohistochemistry and fluorescent in situ hybridization. The effect of cetuximab, alone or in combination with Cisplatin (0, 0.25, 0.5, 1, 2, 4, 8 and 16µM) for 72 hours. Cytotoxic effects were detected using a metabolite proliferation assay, apoptosis was detected by immunohistochemistry using a M30 antibody.

Results: Sorafenib induced apoptosis by activating the caspase cascade in all four cell lines. The most interesting fact was the growth inhibition of the Cisplatin resistant cell Cal27. The IC50 dose of Sorafenib in all four cells was significantly lower compared to Cisplatin.

Concluding both agents led to a synergistic growth inhibition in all for cell lines. Conclusion: Sorafenib is a potent cytotoxic agent in squamous cell carcinomas of the head and neck in vitro. In particular, Sorafenib induces apoptosis in Cisplatin resistant tumor cells in vitro.

P491: THE EFFECT OF COMBINED EGFR AND VEGFR-2 TARGETED THERAPY, ON ORTHOTOPIC XENOGRAFITS OF SCCC D. Song1, S. Choi1, Z.L. Milas1, G. Zhao1, M. Zhao1, Y. So1, C.E. Galer1, S. A. Jassar1, J. H. N. Myers1, 1MD Anderson Cancer Center, Houston, TX

Objective: Squamous cell carcinoma of the oral tongue (SCCOT) is one of the most prevalent tumors of the head and neck region. Despite advances in treatment, the survival of patients with SCCOT has not significantly improved over the past several decades. Therefore, the development of novel therapy is also warranted in SCCOT in order to provide improved systemic, adjuvant therapy. We hypothesized that the epidermal growth factor receptor (EGFR) and vascular endothelial growth factor receptor-2 (VEGFR-2) signaling pathways may be important for the progression and metastasis of SCCOT, and inhibition of these pathways may be beneficial as part of an integrated treatment strategy for this tumor. In this study, we evaluated the therapeutic effect of treatment with DC101, anti-mouse VEGFR-2 monoclonal antibody alone and in combination with Erbitux (cetuximab), anti EGFR monoclonal antibody, in an orthotopic nude mouse model of SCCOT.

Methods: We developed an orthotopic nude mouse model of SCCOT by injection luciferase-expressing human OSC19 luc lines into the tongue of the mouse. The in vivo anti-tumor activity was monitored noninvasively by bioluminescence imaging. Animals were randomly divided into 4 groups and treated for 4 weeks with DC101 (800ug, twice a week), cetuximab (1mg, twice a week), DC101 (800ug, twice a week) + cetuximab (1mg, twice a week), or placebo. Treatment was started 14 days following tumor cell injection. Results: At the conclusion of the treatment period, the average tumor volumes of DC101, cetuximab, and DC101 + cetuximab combination treatment groups were decreased significantly (p=0.039, p=0.002, and p=0.0003 respectively) compared with control group. These significant effects of the treatment were also observed in bioluminescence imaging.

Conclusion: These results suggest that the combination therapy that target EGFR and VEGFR pathways with monoclonal antibodies inhibits the growth of an orthotopic mouse model of SCCOT in vivo, making it a promising novel therapy for the treatment of SCCOT. Based on these data, this combination therapy warrants further pre-clinical evaluation for SCCOT.

P492: THE POTENTIAL EFFICACY OF COMBINING GM1777 WITH RADIATION THERAPY FOR HUMAN HEAD & NECK CANCER H. Kato1, E. Ito2, A. Mian2, N. Alajez2, K. Sakurai3, K. Naito3,
Tumor cells have elevated levels of nicotinamide phosphoribosyl transferase (NAMPT), an enzyme involved in the biosynthesis of oxidized nicotinamide adenine dinucleotide (NAD+). NAD+ turnover is upregulated in cancers due to hyperactive glycolysis and high ADP-ribosylation activity required for DNA repair and genome stability, rendering tumor cells more susceptible to NAMPT inhibition compared to normal cells. GMX1777 (Gemini X Pharmaceuticals), or its soluble pro-drug GMX1778, is a novel anti-cancer agent which inhibits NAMPT and in turn, NAD+ biosynthesis. In addition to single agent activity, GMX1778 is predicted to cooperate with agents that induce DNA damage. The objective of this study was therefore to evaluate the efficacy of combining GMX1777 with radiation therapy (RT) in the treatment of head and neck cancer (HNC).

Methods: Cell viability dose-response curves were performed on GMX1778-treated human hypopharyngeal squamous cell carcinoma (HNSSC) and C666-1 (human undifferentiated nasopharyngeal cancer; NPC) cells using the MTS assay as the read-out for viability. Different sequences of combination treatments (GMX1778 and RT on the same day; GMX1778 administered 24 hr after RT; or GMX1778 administered 24 hr before RT) were evaluated for cytotoxic effects. The nature of the combined effects of GMX1778 and RT on HNSSC and NPC cells were assessed via clonogenic assays, then analyzed using the Chou-Talalay median-effect principle. To elucidate the mode of cell death induced by GMX1778, apoptosis and cell cycle analyses were conducted. Results: GMX1778 exhibited cytotoxicity against human pharyngeal cancer cells. The EC50 after 72 hours of treatment for both C666-1 and FaDu cells were ~10 nM. MTS and clonogenic assays comparing the simultaneous and sequential treatments of GMX1778 and RT demonstrated that GMX1778 administered 24 hours before RT achieved the highest level of cytotoxicity, and enhanced anti-cancer efficacy compared to RT alone. Combination index analyses confirmed that the radiosensitizing effect of GMX1778 was synergistic. GMX1778 induced mitochondria-mediated apoptosis in C666-1 and FaDu cells, as demonstrated by chromatin condensation via Hoechst 33342 staining, subG1 cell population increase via flow cytometric DNA content analyses, and depletion of total intracellular ATP levels via ATP assays.

Conclusions: GMX1778 caused cytotoxicity and induced mitochondria-mediated apoptosis in NPC and HNSSC cell lines in vitro. Furthermore, combination treatment of GMX1778 with RT enhanced anti-cancer efficacy. Flow-based caspase activation assays in both HNC cell lines treated with GMX1778 0B1 RT are currently being conducted. In vivo translation models, such as xenograft models established C666-1 and FaDu xenograft tumors in SCID mice with GMX1778 0B1 RT are in progress. The favorable results presented thus far provide a rationale for the role of GMX1778 combined with RT in the treatment of human head and neck cancers.

Objective: Although mononuclear platinum anticancer agents hold a pivotal place in the treatment of H&N cancer development of resistance to therapy and toxic side effects are major problems, which have prompted research into new platinum drugs, displaying different mechanisms of action. One such compound is BBR 3464, which is a promising trinuclear platinum anticancer agent. It is built up by three square-planar platinum units and it forms different types of adduct with DNA. The structure of BBR 3464 is closely related to cisplatin. The aim of this study was to investigate the influence of polyamine pool reduction on the cytotoxic effects of BBR 3464 and cisplatin. Methods: Polyamine pool reduction was achieved by treating the cells with either the biosynthesis inhibitors alpha-difluoromethylornithine (DFMO) or the polyamine analogue N1,N11-diethylhydrazine (DENSPM). A human squamous carcinoma cell line, LU-HNSCC-4, established from a squamous cell carcinoma of the floor of the mouth was used to evaluate cellular effects of each drug alone or combinations thereof. Cells were exposed to DFMO or DENSPM during 48 h at concentrations ranging from 0 to 5 mM. Thereafter, treated and untreated cells were exposed to cisplatin or BBR 3464 during 1 h at concentrations ranging from 0 to 100 μM. A 96-well colorimetric MIT assay was used to evaluate the effect on cell growth 72 h after treatment.

Results: The cytotoxic effect of BBR 3464 increased when the cells were pre-treated with DENSPM or DFMO, and the interaction was found to be synergistic. In contrast, the interaction between cisplatin and DFMO or DENSPM was near additive to antagonistic. The uptake of BBR 3464 was significantly increased after pre-treatment of the cells with DFMO, and varied dependent on the concentration of DENSPM. The uptake of cisplatin was unchanged. The malignant behavior of BBR 3464 was associated with increased cellular uptake of BBR 3464 in cells with reduced polyamine levels. The results demonstrate that combining compounds that reduce the cellular polyamine pools with BBR3464 may be a promising approach to enhance the anticancer activity against head and neck carcinoma.
for over 40,000 cancer cases in the U.S. each year and is a devastating disease. Most patients present with advanced disease. Concurrent chemoradiation therapy is frequently used for treatment of stage III and IV head and neck squamous cell carcinoma, but current drug regimens are quite toxic and many patients respond poorly or incompletely. Protein kinase C (PKC) is a family of serine/threonine kinases known to play critical roles in the signal transduction pathways involved in growth factor response, cell proliferation, differentiation, and apoptosis. Enzastaurin is a specific protein kinase C beta (PKC-β) inhibitor that has been reported effective for inhibiting tumor growth in many other types of tumor, such as colon cancer, breast cancer and glioblastoma. In addition to specifically inhibiting VEGF-induced angiogenesis, it has been reported that Enzastaurin can directly inhibit proliferation, and induce apoptosis which will inhibit tumor growth in vitro and in vivo. Methods: We evaluated the effect of Enzastaurin on HNSCC as an antimtumor agent alone and as a radiosensitizer with radiation both in vitro with HNSCC cell lines and in vivo using a novel mice model that mimics the delivery of concurrent chemoradiation in HNSCC patients. Proliferation inhibition, colony formation in vivo using a novel mice model that mimics the delivery of concurrent chemoradiation in HNSCC patients. Proliferation inhibition, colony formation after the NAC were also analyzed. Standardized MR and FDG-PET/CT were performed before the NAC and 2 weeks after the completion of the NAC and examined tumor response. Conclusion: Western blot was used to analysis Enzastaurin induced protein level change related to cell signal pathways. Results: Our results indicate Enzastaurin inhibited PKC-β2 in HNSCC cells in culture, enhancing radiation cytotoxicity. Our study demonstrated that Enzastaurin is a better tumor growth inhibitor when used alone and is a good radiosensitizer in HNSCC.

P497: THE EVALUATION OF NEOADJUVANT CHEMOTHERAPY USING S-1 AND NEDAPLATIN FOR PATIENTS WITH SCC OF THE HEAD AND NECK M.Kikuchi1, S.Shinozaki1, Y.Naito1, K.Fujiwara1, S.Hori1, Y.Tono1, H.Yamasaki1, 1Kobe City Medical Center General Hospital, Kobe, Japan

Background: S-1 (Taiho Pharmaceutical Co., Ltd., Tokyo, Japan) is an oral fluoropyrimidine derivatives that have been developed to circumvent such problems associated with protracted intravenous infusion of 5-Fluorouracil (5-FU) as hand-foot syndrome and stomatitis. It combines tegafur, an oral prodrug of 5-FU, with two modulators of 5-FU metabolism, S-chloro-2,4-dihydroxypyridine, a reversible inhibitor of dihydropyrimidine dehydrogenase, and potassium oxonate, in a molar ratio of 1:0:4:1. S-1 is thought to be potentially more active than 5FU. Nedaplatin (NDP) is a platinum complex also developed in Japan with less renal and gastrointestinal toxicity compared with cisplatin (CDDP). Purpose and Materials: To improve compliance with treatment and reduce toxicity, we have used S-1 and NDP, instead of using 5FU and CDDP, as neoadjuvant chemotherapy (NAC) in advanced squamous cell carcinoma of the head and neck. Aim of this study is to examine the effect and adverse reaction of the NAC. Seventeen patients (14 male and 3 female) with newly diagnosed advanced squamous cell carcinoma of the head and neck were eligible for this study. Their age ranges from 19-80 years. Their primary sites were various: pharynx (n=11), larynx (n=2), tongue (n=2), oral floor (n=1), and external auditory canal (n=1). All the patients underwent the same NAC protocol: oral administration of S-1 (day1-14) (80mg/m2) and intravenous nedaplatin (day8) (80mg/m2). To examine the effect of the NAC, CT (or MR) and FDG-PET/CT were performed before the NAC and 2 weeks after the completion of the NAC and examined tumor response. Standardized uptake value of FDG in the primary tumor at the two time-points before and after the NAC were also analyzed. Results: Favorable results were obtained, consisting of a PR rate of 71%. The average of SUV of primary tumor was 11.8 (range 3.5-16) and decreased to 6.4 (range 1.7-14.4) after the NAC. The hematologic toxicities, such as leucopenia and thrombocytopenia of grade 3 and 4, occurred in 5 of 17(29%). Nonhematologic toxicities of grade 3 or 4 were not observed. Conclusion: Combination chemotherapy using S-1 and nedaplatin is expected to have a promising outcome with less renal and gastrointestinal toxicity and more convenient administration could be achieved even on an outpatient clinic.

THYROID II

P498: THYROIDECTOMY AND DIFFUSE TOXIC GOITER: WHAT ARE WE DOING? M R. Favares1, A.A. Fornazari1, J.A.S. da Cruz1, F.L.M. Montenegro1, R. Turciano1, R.B. Smith1, M.T.M. Soerde1, E. Stabenow1, 1General Hospital, University of Sao Paulo, School of Medicine, Sao Paulo, Brazil

Objectives: Hyperthyroidism affects 2% of women and 0.2% of men and Diffuse Toxic Goiter (DTV) is its most common cause. Therapeutic dose of radioactive iodine (131I) is the first choice treatment for the majority of these patients, but thyrotoxicosis remains as a useful alternative. This study presents indications and results after thyrotoxicosis as a treatment of DTV. Casuistic: The charts of 86 patients treated by thyrotoxicosis for Toxic Goiter in the period between 2000 and 2007 were retrospectively reviewed. Studied parameters were age, gender, extension of thyrotoxicosis (total or subtotal), surgical complications, volume of the specimen, presence of carcinoma in pathological report, thyroid function after operation defined as hypo or hyperthyroidism based on serum TSH concentration and recurrence of disease. Results: Seven patients (8.1%) presented with uninodal toxic goiter, 21 (24.4%) with multinodular toxic goiter and 58 (67.5%) with DTV, the study group. There were 48 women (83%) and age ranged from 10 to 68 years old (mean 34.2 y/o). Third four patients (59%) underwent total thyrotoxicosis and 24 (41%) subtotal thyrotoxicosis with remnant weights with 4g to 8g. The weight of the surgical specimen varied from 9 to 410g (mean=76.3g SD 82.279). Thyroid nodule was described in 23 pathological reports (39.6%), five of them with concomitant papillary carcinoma, which corresponds to 21.7% of the patients with nodule and 8.6% of the whole group. Surgical complications were identified in 16 patients (27.6%): Two patients (3.4%) had hematoma, two (3.4%) developed permanent hypocalcemia and five (8.6%) with transitory hoarseness. Clinical outcome among the 24 patients treated by subtotal thyrotoxicosis was as follows: Three patients (12.5%) was lost from follow up; three patients (12.5%) had recurrent disease; 14 developed hypothyroidism (58.3%) and only four (16.7%) remained euthyroid after operation. Conclusions: In spite of higher complications rate than thyrotoxicosis for non toxic goiter, thyrotoxicosis for DTV is a good choice to deal with large goiters and in the presence of nodules. Since hypothyroidism and recurrence occurs in about 2/3 of the patients submitted to subtotal thyrotoxicosis, total thyrotoxicosis must be considered as an alternative in the treatment of DTV.

P499: FUNGATING THYROID CANCER: AN OVERVIEW A.S Nabawi1, H.F.E Al Wagih1, M.A. Hemeida1, T.Kaaitim1, T.Ezzat1, E.Gabr1, R.Khalil1, 1Alexandria University School of Medicine, Alexandria, Egypt

Objectives: In the literature most of the articles discussing advanced thyroid cancer focus on major aero digestive system or vessel involvement and management. In this study our aim was to look at the patients who present with fungating thyroid cancers as regards pathology, possible reasons behind such an aggressive presentation and the outcome of managing these patients by different modalities including radical resection and reconstruction, radio active iodine ablation or external beam radiation. Methods: Collection of clinical, laboratory, imaging and pathological data of all patients admitted to the head and neck and endocrine surgery unit, Main University Hospital, Alexandria School of Medicine, during the period between April 2005 and April 2008. Results: Incidence, clinical imaging and pathological data together with the operative procedure and patient follow up will be tabulated and statistically analyzed. Conclusions: If there is no distant metastasis, a curative resection should be the goal unless complete tumor excision results in unwanted per operative morbidity and mortality. Patients with gross residual disease, after surgical resection, may benefit from postoperative external radiotherapy for local control of complications, namely bleeding.

P500: PROGNOSTIC SYSTEM OF THYROID CANCER IN CHINESE POPULATION Q. Li1, L. Zhang1, Y. Zhu1, C. Huang1, 1Fudan University Cancer Hospital, Shanghai, China

Background: Differentiated (papillary or follicular) thyroid carcinoma has a favorable prognostic outcome. In numerous studies prognostic factors have been identified and staging systems created, particularly in Anglo-American centers, to evaluate and grade individual prognosis outcome. But there was few studies focused on Chinese thyroid cancer patients about the thyroid cancer prognostic system. Objective: To evaluate and compare staging systems for differentiated thyroid carcinoma and predicted outcome in Chinese patients and to discuss the risk profile of differentiated thyroid carcinoma in Chinese patients and compare it against other regions. To find out the suitable prognostic system for Chinese thyroid cancer patients. Methods: In a retrospective study, the authors assessed 202 patients with
Papillary thyroid carcinoma (PTC) is a growing malignancy with good overall prognosis. However, recurrent disease is frequent, reaching up to 15-20% of the cases. Surgical management of recurrent PTC can be challenging given the risk of severe and permanent morbidity. **Objective**: To review the pathology, management and surgical outcome of patients undergoing surgery for recurrent PTC at a tertiary referral center. **Methods**: This study included patients treated for recurrent PTC from July 2004 through June 2007 (4 years). Data was obtained prospectively from the thyroid cancer data base of the section of head and neck surgery of the Pontificia Universidad Católica de Chile. Relevant data on patient, treatment and pathology were collected. Patients with disease detected within the first 6 months were considered as having persistent disease were no included. All patients had previously received radioactive iodine ablation treatment after their primary surgery [100 - 200 mCi]. **Results**: A total of 119 lymph node dissections were performed in 110 patients (84 female, 26 male, median age 39 years (range 8-87 years)). Forty eight patients (44%) had their primary surgery performed in a different institution. Primary surgery consisted in total thyroidectomy (TT) in 79 (72%), TT plus central compartment dissection in 6 (5%), TT plus “node plucking” in 17 (15%) and TT plus modified radical neck dissection in 8 (7%). The median time from the primary surgery to recurrence was 14 months (range 6-480 months), with 84 (76%) of the cases detected within the first 24 months. One hundred and four patients (95%) underwent surgery for 1 recurrence, while 6 patients (5%) had two or more surgeries. Seventy one patients (65%) underwent a central compartment dissection alone, 34 (30%) underwent a comprehensive neck dissection (levels II through VI) and 6 patients (5%) underwent a limited resection. Histopathology classified 84 cases (76%) as usual type PTC, 20 (18%) as follicular variant, 4 (4%) diffuse sclerosing and 2 (2%) as other subtypes. Characteristics of the primary tumor revealed invasion of the thyroid capsule in 76 (69%), microscopically extrathyroidal extension in 46 (42%), macroscopic extrathyroidal extension in 11 (11%), positive margins in 25 (23%) and multifocal disease in 37 (34%). In patients undergoing unilateral central compartment dissection (105 patients), 3 (3%) presented permanent hypoparathyroidism and 7 (6%) have permanent true vocal cord paralysis of which 6 (86%) underwent recurrent laryngeal nerve resection for invasive recurrent disease. Post operative shoulder pain occurred only in patients undergoing level IIIB dissection (27 patients) of which the pathological report confirmed metastasis in only 2 (7%). **Conclusions**: Most patients with recurrent PTC are identified within the first 24 months of the primary surgery. Inadequate primary surgery and the presence of adverse pathological features are frequent findings in patients with recurrent disease. Permanent morbidity in this series is acceptable, restricted mostly to patients with invasive disease.
FIELD TOTAL THYROIDECTOMY J.Jeannon1, R.Simo1, 1Guy’s Hospital, London, United Kingdom

Objectives: The management of differentiated thyroid cancer (DTC) represents a clinical challenge. Total Thyroidectomy followed by radiiodine ablation and TSH suppression is the standard treatment. The surgical technique of thyroidectomy for early disease has not evolved since several decades. Advanced cases with nodal disease and local invasion require a different approach. Radical surgical oncological resection with preservation of recurrent laryngeal nerves and parathyroid glands should be undertaken. When locally advanced thyroid cancer presents, Wide field total thyroidectomy involves en-bloc resection of the thyroid gland, strap muscles and nodal disease resulting in a negative post-operative iodine scan indicating complete resection of disease. Methods: A retrospective chart review was undertaken analyzing thyroid cancer cases treated at Guy’s Hospital, London from 2000 to 2006. 49 advanced cases: T stage T3 / T4 and N1 differentiated thyroid cancer cases were identified. Median follow-up was 48 months. Results: Strap muscle invasion was seen in 18% of cases. Skin invasion occurred in 3% of cases. Tracheal invasion was seen in 8% of cases most were managed with shave resection. Total laryngectomy was performed in 2 cases. Preoperative recurrent laryngeal nerve palsy was seen in 5%. Postoperative recurrent laryngeal nerve palsy rate was 4%. Hypothyroidism occurred in 4%. Direct vascular invasion was seen in 4%. Overall 5 year survival was 91%. Conclusion: The management of locally advanced differentiated thyroid cancer involves an aggressive oncological approach and is led by organ preservation. Wide field total thyroidectomy can be adopted in advanced cases with en-bloc resection of the thyroid, strap muscles and nodal disease. High survival rates can be achieved with minimal morbidity.

P505: SURGERY OF DIFFERENTIATED THYROID CARCINOM EXTINGUISHED TO LARYNX, PHARYNX AND ESOPHAGUS L.A.Pacheco-Ojeda 1, 1Social Security Hospital, Quito, Ecuador

Objective: Invasion of differentiated thyroid carcinoma to adjacent structures is not uncommon. These lesions are classified as T4 according to the A/JCC TNM classification. T4a is considered a lesion which invades the subcutaneous soft tissue, larynx, trachea, esophagus or recurrent laryngeal nerve. A correct knowledge of this extension is important for the surgical management. It also has prognostic implications. Materials and Methods: Among 325 patients initially operated on for a differentiated thyroid carcinoma, we found 77 (23%) cases with extrathyroid extension. The larynx was invaded in 8 cases, the pharynx in 7 and the esophagus in 5. A complete surgical excision was attempted in all cases. A resection of the lower pharyngeal constrictor muscle, together with the perichondrial layer of the thyroid cartilage lamina, and a shaving of the cartilage was performed in 4 cases; a resection of the cricothyroid muscle was performed in 2 cases; a complete resection of the thyroid cartilage ala was performed in another and a lateral partial laryngectomy in the sixth patient. The external wall of the piriform recess was the anatomical site invaded in all 7 cases of pharyngeal extension. A superficial resection of the lower constrictor muscle was performed in 4 cases and a partial resection of the whole external wall of the piriform recess was done in another. In all the cases of esophageal extension, its muscular layer was resected without opening of the mucosa. Results: No important complications occurred in any case. Ten-year survival was 50%, approximately the same as that of only tracheal or recurrent nerve invasion (40%), but statistically lower (p<0.001) than when only prethyroid muscle invasion (100%) or no extrathyroid extension (97%) occurred. Conclusions: Invasion to larynx, pharynx and esophagus can be managed surgically with success in most patients. However, long-term survival was statistically lower.

BASIC SCIENCE: CARCINOGENESIS P506: ASSOCIATION OF CTNNB1 AND AR GENE EXPRESSION IN DEVELOPMENT AND PROGRESSION OF THE JUVENILE NASOPHARYNGEAL ANGIOFIBROMA S.M.Silveira1, S.M.Øru1, 1Pediatric Oncology Program, St. Luke’s Roosevelt Hospital Center, New York, NY

Objective: Increased expression of Wnt signaling pathway genes has been studied in juvenile nasopharyngeal angiofibroma (JNA). We evaluated the expression of CTNNB1 and AR mRNA in a subset of JNA to identify potentially interesting candidate genes for possible involvement in JNA development and progression. Methods: Total RNA samples were extracted from 6 JNA and normal control tissues using the RNeasy kit. Quantitative reverse transcription polymerase chain reaction (qRT-PCR) was applied to measure mRNA expression levels. Results: CTNNB1 was expressed at low levels in all JNA samples. AR expression levels were different between JNA and normal tissues. Conclusion: Interestingly, no significant expression of CTNNB1 was detected in JNA samples, which is consistent with literature studies. On the other hand, AR expression levels were significantly different between JNA and normal tissues, indicating the potential role of AR in JNA development and progression.

P507: SMA4 DELETION LEADS TO SPONTANEOUS HEAD AND NECK CANCER FORMATION ASSOCIATED WITH GENOMIC INSTABILITY R.White1, J.Jeannon1, 1Guy’s Hospital, London, United Kingdom

Objective: We have identified androgen receptor (AR) as an interesting candidate gene CTNNB1 (beta-catenin) that is located in this chromosomal region. This gene has been associated with juvenile angiofibroma, suggesting an involvement of the Wnt signaling pathway. The AR gene (androgen receptor), located in Xq11.2-q12, was associated with JNA, since these tumors are androgen-dependent. Quantitative RT-PCR was used for to measure the expression of CTNNB1 and AR in genes in same levels. Low levels of CTNNB1 mRNA were detected in 2 out of 18 JNA. Downexpression of AR transcript was detected in 5 out of 18 cases. There was a positive correlation (R=0.0005) between samples with high and low levels of mRNA for both genes. Furthermore, most of these samples were grade III. Conclusions: In this study we demonstrated the involvement of AR and CTNNB1 genes in a subset of JNA. The positive correlations between the transcript levels substantiated a possible role of Wnt signaling in JNA development and progression. Our findings suggested that CTNNB1 is involved in the induction of AR-mediated transcription and cell growth of these tumors, implicating the role of the Wnt signaling and CTNNB1 in the regulation of JNA tumorigenesis, and the interaction between Wnt and androgen.

P508: MISMATCH REPAIR DEFECTS IN ORAL CARCINOMAS FROM YOUNG PATIENTS J.Machado1, P.P.Reis1, M.Tomenson1, B.Perez-Ordonez2, R.Gasymov1, W.Xu1, P.Gullane2, D.P.Goldstein2, J.C.Irish2, S.Kamel-Reid1, 1Princess Margaret Hospital, Toronto, ON, Canada; 2Toronto General Hospital, Toronto, ON, Canada

Objective: Identification of target genes for genetic rearrangements in Juvenile Nasopharyngeal Angiofibroma (JNA) and the impact of copy number changes on gene expression are currently not well understood. Material and Methods: Here, we applied high resolution comparative genomic hybridization (HR-CGH) for analyze 18 JNA and investigated two candidate genes involved in significant losses mapped at Xq11.2-q12 (AR) and 3p21 (CTNNB1) by quantitative real time RTPCR. Results: The frequency of gains and losses were estimated in all tumors. Chromosomal losses were more prevalent than gains. Frequent chromosomal losses affected regions of chromosomes arms 3p, 6q, 8p, 16q, 18q, and 22q and X. Significant losses in 3p21 had been detected by HR-CGH, pinpointing the interesting candidate gene CTNNB1 (beta-catenin) that is located in this region. This gene has been associated with juvenile angiofibroma, suggesting an involvement of the Wnt signaling pathway. The AR gene (androgen receptor), located in Xq11.2-q12, was associated with JNA, since these tumors are androgen-dependent. Quantitative RT-PCR was used for to measure the expression of CTNNB1 and AR genes in same levels. Low levels of CTNNB1 mRNA were detected in 2 out of 18 JNA. Downexpression of AR transcript was detected in 5 out of 18 cases. There was a positive correlation (R=0.0005) between samples with high and low levels of mRNA for both genes. Furthermore, most of these samples were grade III. Conclusions: In this study we demonstrated the involvement of AR and CTNNB1 genes in a subset of JNA. The positive correlations between the transcript levels substantiated a possible role of Wnt signaling in JNA development and progression. Our findings suggested that CTNNB1 is involved in the induction of AR-mediated transcription and cell growth of these tumors, implicating the role of the Wnt signaling and CTNNB1 in the regulation of JNA tumorigenesis, and the interaction between Wnt and androgen.

P509: SMAD4 DELETION LEADS TO SPONTANEOUS HEAD AND NECK CANCER FORMATION ASSOCIATED WITH GENOMIC INSTABILITY L.A.Pacheco-Ojeda 1, 1Social Security Hospital, Quito, Ecuador

Objective: We have identified androgen receptor (AR) as an interesting candidate gene CTNNB1 (beta-catenin) that is located in this chromosomal region. This gene has been associated with juvenile angiofibroma, suggesting an involvement of the Wnt signaling pathway. The AR gene (androgen receptor), located in Xq11.2-q12, was associated with JNA, since these tumors are androgen-dependent. Quantitative RT-PCR was used for to measure the expression of CTNNB1 and AR genes in same levels. Low levels of CTNNB1 mRNA were detected in 2 out of 18 JNA. Downexpression of AR transcript was detected in 5 out of 18 cases. There was a positive correlation (R=0.0005) between samples with high and low levels of mRNA for both genes. Furthermore, most of these samples were grade III. Conclusions: In this study we demonstrated the involvement of AR and CTNNB1 genes in a subset of JNA. The positive correlations between the transcript levels substantiated a possible role of Wnt signaling in JNA development and progression. Our findings suggested that CTNNB1 is involved in the induction of AR-mediated transcription and cell growth of these tumors, implicating the role of the Wnt signaling and CTNNB1 in the regulation of JNA tumorigenesis, and the interaction between Wnt and androgen.
Objectives: To examine the molecular and genetic differences in oral squamous cell carcinomas (OSCCs) from young and older patients. We are especially interested in head and neck cancer that develops in young patients that are not substance abusers. Our laboratory previously showed that head and neck cancers from younger patients harbor increased microsatellite instability (MSI), which can be a marker of defective mismatch repair (MMR), and can be associated with an increased risk of cancer. We believe there is a relationship between expression of MMR genes and age in OSCC patients. Methods: We examined mucosa from oral normal epithelial tissues (controls) and OSCC patients. Immunohistochemical analysis was performed in a blinded fashion and scored using a semiquantitative method. Results: The hMLH1 expression was significantly higher in controls compared to OSCC patients (p = 0.001). The expression of hMSH2 was also higher in controls than in OSCC patients (p = 0.01). Discussion: The results demonstrated that the younger patients were more likely to have a higher expression of MMR proteins compared to the older patients. Conclusion: These findings suggest that the expression of MMR proteins may be an early event in head and neck cancer development, and that there may be a correlation between the expression of MMR proteins and age in OSCC patients.

Methods: We examined Grp78 expression in paired tumor and normal tissues from HNC patients and correlated with the clinicopathological status. To investigate Grp78 function, the effects of Grp78 knockdown by siRNA were examined in 6 HNC cell lines and in xenografting models.

Results: Of 59 patients, 39 (66%) had at least two-fold over-expression of Grp78, which correlated statistically with T stage (P = 0.035), N stage (P = 0.05), overall stage (P = 0.034), tumor depth (P = 0.035) and extracapsular spread in lymph nodes (P = 0.05). Inhibition of Grp78 significantly reduced cell growth and colony formation to 53% to 12% compared with that of controls in all six HNC cell lines. The migration and invasive ability of cells were also inhibited to 23% to 21% compared to the controls. Administration of Grp78-siRNA plasmid into HNC xenografts significantly inhibited both tumor growth in situ (>60% inhibition at day 34) and liver metastasis. Conclusions: Grp78 is associated with aggressiveness of HNC. Knockdown Grp78 significantly suppresses the malignant phenotype as demonstrated in cell lines and in tumor xenografts of mice, indicating Grp78 possesses carcinogenic function.

PS11: The Expression of Osteopontin in Oral Cancer C.Chien 1, C.Huang 2, C.Chen 1, F.Fang 1, 1 Department of Otolaryngology, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Kaohsiung County, Taiwan, Republic of China; 2 Department of Pathology, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Kaohsiung County, Taiwan, Republic of China

Objective: Osteopontin (OPN) is a kind of glycosyl-phosphatidyl inositol (GPI)-anchored protein which is produced by a variety of kinds of cancer cells. OPN has been also considered as a tumor-associated protein, which promotes tumor development and metastasis. The aim of this study is to analyze the expressions of OPN in oral cancer and its relationship with clinicopathological parameters.

Methods: This study is to preoperatively collect the blood sample and a small amount of fresh tumor tissue from patients to analyze the expressions of OPN with ELISA, immunoblot analysis and reverse transcription-PCR in oral cancer. The immunohistochemistry (IHC) was also used to investigate the clinicopathological significance of the expression of OPN in oral cancer.

Results: The study included 256 patients who underwent primary surgical resection between Oct 1996 and August 2005 for treatment of squamous cell carcinoma of the oral cancer without previous radiotherapy and/or chemotherapy for immunohistochemistry study. Between August 2005 and June 2007, there were another 94 patients and 28 normal healthy volunteers whose plasma data was available were also included for assay of plasma level of OPN. The results showed that the expression of OPN was significantly higher in tumor tissue than in normal control either by immunoblot analysis or reverse transcriptase-PCR. Positive expression by IHC of OPN from 256 patients significantly correlated with higher tumor (T) stage (p = 0.001), high TNM stage (p = 0.001), positive nodal status (p = 0.001), and male group (p = 0.016). The plasma level of OPN also showed that patients with higher tumor stage and positive nodal stage have a higher serum level of OPN (p < 0.001 and p < 0.001, respectively). The unfavorable cumulative 5-year overall survival rate significantly correlated with positive expression of OPN (p < 0.001), advanced tumor (T) stage (p < 0.001), advanced TNM stage (p < 0.001), and positive nodal status (p = 0.003) in IHC study. However, the Cox’s regression analysis revealed that expression of OPN (p = 0.049), tumor (T) stage (p = 0.046) and nodal stage (p = 0.001) were the only independent prognostic factors for survival.

Conclusions: High expression of OPN is related to tumor progression in oral cancer. Our results suggest that expression of OPN is a useful predictive prognostic factor in oral cancer.

PS12: Oncologic Considerations for Using BMP-4 and BMP-6 for Craniofacial Bone Tissue Engineering N.Kokorina 1, J.Lewis 1, 1 Solae, Inc., Saint Louis, MO

Objectives: Human recombinant bone morphogenetic protein 2 (rhBMP-2) and bone morphogenetic protein 7 (rhBMP-7) are commercially available osteoinductive molecules, but their use for regenerating bone in complicated craniofacial defects is limited due to the unknown effects of these morphogens on oral squamous cell carcinoma (OSCCA). BMP-4 and BMP-6 also have osteoinductive activity and are important molecules for regulating self renewal and terminal differentiation in keratinocytes. The objective of this study was to test these alternative osteoinductive molecules, and their in vitro and in vivo effects on OSCCA.

Methods: The OSCCA cell lines UMSCC-1 (floor of mouth) and UMSCC-
DNA copy number alterations were investigated in tumors of Warthin (TW), the second benign neoplasm most frequently found in the salivary glands. The etiopathogenesis and events associated with development of these tumors that are still unclear. To our knowledge, this is the first report using comparative genomic hybridization in TW. **Methods:** The high-resolution comparative genomic hybridization (HR-CGH) is a useful technique as screening of genomic alterations involving chromosomal gains and losses. Using this procedure, it is possible to detect variations with 2 Mb resolution. In the present study, were analyzed 11 TW microdissected (in paraffin blocks) followed by amplification and labeling protocols PCR-based. Normal DNA was used as a reference to detect chromosomal imbalances. Normal DNA was used as a reference for HR-CGH. **Results:** HR-CGH analysis revealed chromosomal losses more frequently than gains. The comparison of minimal regions altered in common considering 90% of similarity showed loss on 1q32-q41; 9p21; 12q22-q44.3; 16p12-p13.2; 16q22-q24; 17q22; 19p13.1-p13.2; 19q13.1-q13.4; 22q13. The gain genic analysis were observed at 8p23 (5/11 samples) and Yp11.3-p11.1 (11 samples). Particularly, many genes of TGF-beta signalization pathway are referentially altered in this study. **Conclusions:** The HR-CGH revealed high-level chromosomal alterations in TW. The regions frequently altered are coincident with tumor suppressor genes or oncogenes localization and will be validated by transcript or protein expression analysis.

**P514: CARCINOGENIC EFFECTS OF GP96 IN ORAL CANCER THROUGH POSITIVELY REGULATES CELL GROWTH AND INVASION**

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In Taiwan, the incidence of oral cancer has become the 6th leading cancer and is still increasing in recent years. Since this cancer usually occurs in the middle age man, at the peak of life responsibility, it has tremendous impact of family and society. For treatment, the highly invasive characteristic of head and neck cancer is the common cause of treatment failure. In order to investigate the invasive mechanism of cancer, we established head neck cancer subline cells with higher invasion phenotype. Through proteomic analysis by comparing the differential proteomes between parental and the subline cells, we have identified several potential invasive associated genes including p53, FLJ10540, E-cadherin, and Gp96. Gp96 is a member of heat shock protein 90 superfamly, promoting proper folding and assembling of proteins. However, whether and how Gp96 associated with cancer is still obscure. In this study, we first characterize Gp96 expressions in oral cancer cell lines. We found that Gp96 were gradually increased with the invasive subline cells, suggesting Gp96 plays a positive regulatory role in tumor invasion. To verify the functions, the effects of Gp96 knockdown by siRNA were examined. Compared to the vector transfected cells, the Gp96-siRNA transfectants significantly increased cell growth and colony formation. Although less effect on cell migration, Gp96 knockdown showed significant inhibition of cell growth and invasion. To validate the carcinogenesis effect, Gp96 expressions were also examined in clinical paired cancer and normal mucosa tissues. Of 14 patients assays, 11 (78%) had two fold of overexpression. In conclusion, we found that Gp96 positively regulates cell growth, invasion and participates the carcinogenesis of oral cancer.

**P515: ASSESSMENT OF P53 FUNCTIONAL ACTIVITY IN TUMOR AND HISTOLOGICALLY NORMAL MUCOSA FROM HNSCC PATIENTS**

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**Purpose:** Head and neck cancer is the sixth most prevalent cancer worldwide, with a mortality rate of approximately 50%. More than 90% of head and neck cancers are squamous cell carcinoma (HNSCC). Mutation of the TP53 tumor-suppressor gene is reported to play an important role for carcinogenesis in HNSCC, occurring in a many as 45 to 70% of cases, data regarding the TP53 function after loss of function and the effect of p53 on tumor survival and recurrence are lacking. The purpose of this study was to assess the p53 protein function using the functional analysis of separated alleles in yeast (FASAY) in HNSCC tumor tissue (Tum) and corresponding histologically normal mucosa (Muc) biopsies. FASAY was compared with p53 immunohistochemistry (IHC) results. **Materials/Methods:** Seventy nine newly diagnosed HNSCC patients were prospectively included in the study and 62 were evaluable. For each patient, p53 transcriptional activity was assessed in the Tum and Muc directly collected in liquid nitrogen. Co-transformation of genetically modified Saccharomyces Cerevisiae was carried out with a p53 expression vector. The reporter gene contained a p53 consensus or p21-specific binding site. TP53 gene sequence analysis covering exons 4 to 11 was performed for each positive sample: threshold: 10% positive clones. Muc results were compared to the results obtained with 50 mucosa samples collected from healthy volunteers undergoing tonsillectomy or uvullectomy for sleep-related disorders. Informed consent was obtained from each patient and volunteer. In parallel, the effect of RNA degradation on FASAY results and threshold level was assessed by analyzing normal tissues at increasing time intervals after collection. **Results:** A loss of transcriptional activity was observed in 87% (54/62) of tumoral and 21% (13/62) of normal paired mucosa samples. While positive scores were markedly lower in Muc than Tum samples, all the controls mucosa remained consistently negative. Positive FASAY was associated with p53 mutations, deletions or insertion, a substantial number of them being yet unreported (IARC Database version 1.2, http://www.p53.iarc.fr/index.html). Interestingly, a polyclonal pattern of mutations was found in 22% Tum (12/54) and 54% Muc (7/13), without evidence for RNA degradation. FASAY taken as reference clearly identified ICH false-negative results, giving a poor concordance between both assays (Cohen’s kappa value: 0.24). Of note, HPV-positive/IHC-positive tumors with functional p53 were identified. While the follow-up period is yet too short (mean: 17 months), a trend for recurrence is observed in cases with a loss of functional p53 in the normal mucosa. **Conclusions:** While the frequency of FASAY-confirmed p53 abnormalities nearly reaches 90% in this series of HNSCC, mutations in histologically normal mucosa from those patients could be induced by known HNSCC risk factors, hence witness the presence of scattered premalignant cells. While unexpected, the outcome of HPV-positive, FASAY-negative cases deserves careful investigations.

**P516: OVEREXPRESSION OF FLJ10540 IS RELATED TO TUMOR PROGRESSION IN PATIENTS WITH ORAL CAVITY SQUAMOUS CELL CARCINOMA**

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**Objective:** Oral cavity squamous cell carcinoma (OCSCC) is one of the most common cancers. The function of FLJ10540 in oral carcinogenesis is largely unexplored. The aim of this study is to investigate the role of FLJ10540 in human OCSCC development, to examine the expression levels of FLJ10540 in OCSCC, and to correlate the results with clinicopathologic variables and survival. **Methods:** Immunohistochemistry analysis of FLJ10540 expression was done in 256 OCSCC patients who underwent tumor resection between Oct 1996 and August 2005 without previous radiotherapy. The clinicopathologic information including gender, age,
tumor (T) stage, nodal (N) status, and overall survival was obtained from the clinical records and the pathologic reports, retrospectively. The TNM status was classified according to 1997 American Joint Committee on Cancer (AJCC) system. RTPCR and western blot analysis were used to confirm immunohistochemistry results. Oral cancer cell lines with overexpressing FLU10540 or FLU10540-mediated siRNA to repress endogenous FLU10540 were generated by transfection. Transwell chamber was used to examine the migration and invasion assay. Western blot analysis and Zymography assay were done to evaluate the signaling pathways that were involved. Results: There were 17 women and 239 men with an average age of 50.9 years (ranged, 26-87 years). Thirty-nine patients were classified as T1, 55 as T2, 64 as T3 and 98 as T4. One hundred and fifty-three patients were classified as N0, 38 as N1, 48 as N2b, 13 as N2c and 4 as N3. FLU10540 was overexpression in OCSCC patients. Higher expression by IHC of FLU10540 from 256 patients significantly correlated with higher tumor (T) stage (p<0.001), higher TNM stage (p<0.001), positive nodal status (p<0.001). The unfavorable cumulative 5-year overall survival rate significantly correlated with higher expression of FLU10540 (p<0.001) by IHC study with Kaplan-Meier method. FLU10540 expression levels correlated with the malignant degree, and increased activity of oral cancer FLU10540 stable clones and also correlated with the MMP2/9 activity. FLU10540 overexpression also correlated with increased MMP2/9 expression levels in tumor samples. Conclusions: Increased FLU10540 expression is related to tumor progression in patients with OCSCC and the underlying migration and invasion mechanism may involve the activation of MMP2/9.

P517: IDENTIFICATION OF THE FIRST GLUT-1 MUTATION IN SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK
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Objective: At the conclusion of this presentation, participants will gain awareness of 1) the function of the facilitative glucose transporter type 1 (GLUT-1) with regard to cellular proliferation and apoptotic cell death, and 2) the first mutation, to the best of our knowledge, of GLUT-1 discovered in any cancer, specifically found in a patient with advanced stage squamous cell carcinoma of the head and neck [SCCHN]. Methods: Gene microarray analysis, RT-PCR, and DNA sequencing techniques were performed on SCCHN samples and correlated with clinical stage. Results: Gene microarray analysis of 7 patients with matched normal and squamous cell carcinoma tissue of the head and neck yielded overexpression of GLUT-1 in 5 of 7 patients in contrast to their matched normal tissue. RT-PCR analysis of 20 SCCHN samples with stage III or IV disease demonstrated one patient who had an abnormal band on gel electrophoresis. DNA sequencing led to identification of a splice site mutation which caused deletion of an entire exon, including an important inhibitory ATP binding domain in a stage IV oropharyngeal carcinoma. Conclusions: No other mutations of GLUT-1 reported to date in any cancer, specifically found in any cancer, specifically found in a patient with advanced stage squamous cell carcinoma of the head and neck. GLUT-1 expression was found to be upregulated by TGF-beta1 and were increased in TGF-betaRII knockout mice, while TGF-betaRII knockout mice exhibited inflammatory pre-neoplastic lesions, but not HNSCCs, indicating NF-kappaB activation plays a role in TGF-beta-mediated inflammation resulting from alterations in the TGF-beta signaling pathway contributes to HNSCC carcinogenesis. Methods: Inflammation-inhibiting agents like AHMP. *Correspondence: Daofa Tian, Email: tiandaofa@163.com

P519: ROLE OF TGF-BETA SIGNALING-MEDIATED INFILMATION IN HNSCC CARCINOGENESIS
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Objective: Chronic inflammation associated with tobacco and alcohol exposure is tightly linked to human head and neck tumorsogenesis. Recent studies have shown that increased inflammation in the setting of neoplasia can promote carcinogenesis. Our objective is to investigate whether inflammation resulting from alterations in the TGF-beta signaling pathway contributes to HNSCC carcinogenesis. Methods: Inflammation-inhibiting agents like AHMP. *Correspondence: Daofa Tian, Email: tiandaofa@163.com

P518: APOPTOTIC SIGNALING ABNORMALITIES CHEMICALLY INDUCED IN NASOPHARYNGEAL CARCINOMA GENESIS AMONG RATS UNDERGONE EXHAUSTIVELY
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Objectives: To explore apoptotic signaling abnormalities among rats with induced nasopharyngeal carcinogenesis by DNP integrated with exhausted swimming and the intervening effects of some natural medicinal materials on these links based on a series of experiments. Methods: To explore apoptotic signaling abnormalities, fifty-six SD rats were randomly divided into 3 groups, with DNP and TPA injected simply in MG1, MG2 and TPA injection combined with forced exhausted swimming in MG2 and only injected with the same volume of normal saline diluted DMSO in HCG, twice a week and lasted for 14 weeks. Tissue samples were taken from nasopharynx in a regular numbers and regular intervals during the 400 days lasted experiments. Samples cut into two pieces, with one fixed in 1% neutral paraformaldehyde for assays of pathohistology, TUNEL procedures and SABC immunohistochemistry to determine PCNA, Bcl-2, Bax, Cyto-C and Caspase-3 in the signaling route of mitochondrion, NF-3BAB p65 and 3BAB in the signaling route of NF-3BAB, and with the other part kept in nitrogen for RTPCR assay. To investigate intervening effect of anti-carcinogenesis herbal medicinal preparation (AHMP), another 72 SD rats, with induced nasopharyngeal lesion in the same way, randomly divided into 3 groups, i.e. MG fed with normal saline, EG fed with concentrated AHMP and PCG fed with vitamin A acid. Tissue samples were collected from nasopharynx in a regular numbers and regular intervals during the 400 days lasted experiments. Results: Typical pathohistological changes observed in nasopharyngeal epithelia among animals undergone exhaustively swimming plus DNP and TPA usage in MG2, with a much higher rate of induced cancerous lesion than that in MG1, while no significant differences in activities of apoptosis-associated genes determined here. With carcinogenesis development, Al significantly decreased in carcinogenic transformation tissues, with PCNA significantly increased. Activities of Cyt-C and Caspase-3 decreased in cancerous transformation epithelia, while Bax showed a tendency of increasing with cancerous lesion progressing, with various degrees of negative or positive correlations among these determined indicators. Similar changes observed in the NF-3BAB route of signaling pathway. In the intervening experiments, was shown the occurring rate of cancerous transformation at 0% (0/24) in EG receiving AHMP feeding, significantly lower than that of MG (83.3%, 20/24). Though such a rate was also the same (0%, 0/12) as that of EG among the animals alive at the time of samples taking, the other 12 in PCG were dead during the following experimental period from 250th to 310th d with no cancerous lesion found, suggesting a significant tumor-free effect of AHMP occurred. At the stage of atypical hyperplasia here, Al elevated and PI declined significantly in EG, with Bcl-2 lowered and Cyt-C, Caspase-3 elevated obviously, when compared with MG. Moreover, significantly lower NF-3BAB p65 and higher 3BAB activities assayed in EG at atypical hyperplasia stage. Conclusions: A weak physique status can be genetically determined susceptible factor to carcinogenesis in nasopharyngeal epithelia initiated by environmental carcinogenic factors and can be effectively blocked by carcinogenesis-inhibiting agents like AHMP. *Correspondence: Daofa Tian, Email: tiandaofa@163.com

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**P520: ISOLATION AND CHARACTERIZATION OF CANCER STEM CELLS IN SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK**

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**Objective:** The concept of cancer stem cells (CSCs) provides a new paradigm for cancer biology, although it remains unclear whether CSCs will provide to be a more robust model than traditional cancer cell line. Methods: To isolate the CSCs from a squamous cell carcinoma of the head and neck cell line, serum-free medium (SFM) selection was performed. A permanent cell line, Gun-1 established from a squamous cell carcinoma of the hypopharynx, was cultured in serum free medium containing EGF and FGF-2. Results: Gun-1 cells grew intensively in SFM. After 7 weeks of culture, Gun-1 cultured in SFM, demonstrated growth into tumor spheres. The population of CD44+, a molecule expressed by hematopoietic stem cells, in Gun-1 cells cultured in SFM was increased compared to that cultured in serum-containing medium (SCM) by flow cytometry analysis, and the increased population of CD44+ cells was also CD24-/low cells. On the other hand, the population of CD133+ or ABCG2+ cells was not increased, suggesting that expression of HLA class I molecules on Gun-1 cultured in SFM was down-regulated. Conclusions: Thus, SFM selection method appears to be useful for isolation of CSCs from cell line. Moreover, our results suggest that CSCs may have poorer immunogenicity. Currently, the invasive capacity and the expression of stemness genes of Gun-1 cultured in SFM are under investigation.

**P521: DEREPRESSION OF NFKB BY THE LOSS OF MALT1 EXPRESSION AND PROGRESSION OF ORAL SQUAMOUS CELL CARCINOMAS**

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**Objective:** Chromosome 1q21.31 is predicted to contain a tumor suppressor gene(s) in carcinomas of the epithelial origin. Genetic aberration of mucosa-associated lymphoid tissue 1 (MALT1) at the locus closely associates with development of MALT-type lymphoma. In lymphocyte lineages, MALT1 is oligomerized with BCL-10 in the cytoplasm and activates NFκB. However, expression of MALT1 and a role for NFκB activity in carcinoma cells has not been examined. Methods: We made a specific antibody against MALT1 and studied expression of MALT1 in 109 primary oral carcinomas by immunohistochemistry. Genomic DNA was isolated from carcinoma cells on tissue sections by laser-captured microdissection (n=47), and analyzed for genetic instability by microsatellite PCR and for promoter hypermethylation by bisulfite-modified genomic DNA sequence and methylation-specific PCR. Expression of MALT1 mRNA was compared by quantitative real-time RTPCR. An oral carcinoma cell line (HSC2 cells) stably expressing wild-type MALT1 or dominant-negative MALT1 was subjected to flow and morphological assays with or without small interfering RNA (siRNA), and inoculated into athymic mice. Results: MALT1 protein was localized in the nucleus of basal cells of normal oral epithelium but absent in 45.9% of carcinomas in which patient prognoses were low (P=0.001, log-rank test), and the loss of expression was an independent prognostic value for disease-specific survival (P=0.001, Cox hazard model). Carcinomas with low MALT1 expression exhibit microsatellite instability and methylation at a specific cytosine within proximal promoter region. Expression of MALT1 mRNA was increased upon cytosome demethylation by 5-aza treatments. Although activation status of NFκB is indistinguishable among HSC2 cells and the derivatives, wild-type MALT1-expressing cells showed 93.3% reduction of NFκB reporter gene expression compared to dominant-negative MALT1-expressing cells and did not express a NFκB target, MMP-9. Proliferation and invasion of basal membrane matrix were increased in dominant-negative MALT1-expressing cells but reduced in wild-type MALT1-expressing cells. Contrasting to extensive degradation and invasion of 3-dimensional collagen gels by dominant-negative MALT1-expressing cells, wild-type MALT1-expressing cells did not invade into the gel at all. Transient transfection of siRNA dose-dependently repressed reporter gene expression, invasion of basement membrane, and MMP-9 expression in wild-type MALT1-expressing cells. When HSC-2 cells were subcutaneously inoculated into athymic mice, dominant-negative MALT1-expressing cells rapidly expanded tumor sizes in contrast to 85% reduction of wild-type MALT1-expressing cells compared to parental HSC-2 cells. Conclusion: These data demonstrate that MALT1 expression is epigenetically inactivated in oral carcinoma cells, and that carcinoma cells liberates from NFκB inhibition in the nucleus upon the loss of MALT1 expression and exhibit aggressive features toward devastating diseases. This raises the possibility that MALT1 plays a suppressive role for carcinoma progression, and that immunohistochemical detection is a useful predictive and prognostic tool in management of oral carcinoma.

**P522: IDENTIFICATION AND CHARACTERIZATION OF POTENTIAL TUMOR-STEM CELLS IN HEAD AND NECK CANCER**

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Cancer stem cells (CSCs) are supposed to possess tumor initiating potential combined with the capacity of self-renewal and multilineage differentiation. The CSC theory predicts that a tumor is functionally heterogenous and only a limited number of cells have the capacity to regenerate a tumor: namely the cancer stem cells. Cancer treatment has been based on the assumption that cancer populations are homogenous, and the tumor is generated by a population of cells with equal proliferation potentials. Thus, the concept of CSCs may have profound implications for the development of novel treatment strategies against human cancers. However, the development of such new treatments is currently hindered by the lack of reliable markers to identify CSCs and the poor understanding of their behaviour and fate determinants. Therefore, the present study, the expression of the prospective tumor stem cell markers CD31, CD34, CD38, CD44, CD59, CD117, and CD133 on solid HNSCC tumors, permanent HNSCC cell lines, and peripheral blood mononuclear cells (PBMC) of patients with head and neck cancer, resulted in the following findings. The measurements have been interpreted with regard to additional patient and tumor derived data. Our results clearly underline the need for individualized tumor therapies on the basis of cellular tumor characteristics. We will show the actual progress of our investigations.

**P523: INTERACTION OF MELANOMA AND BONE MARROW STEM CELLS: MECHANISMS OF GROWTH FACTOR-INDUCED TUMORIGENESIS**

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**Objective:** The incidence of melanoma is increasing at a rate greater than any other form of cancer in the United States. The pathogenic mechanism(s) through which melanoma cells derive their invasive and metastatic potential is unclear. We hypothesized that malignant melanoma cells secrete growth factors that underlie the migration of adult mesenchymal stem cells (MSC) to malignant melanoma tumor sites. Multipotent MSCs, under the influence of locally secreted growth factors may influence the malignant (i.e. invasive) potential of melanoma. Methods: The human melanoma cell line (A375) and adult MSCs were grown in culture and used to study the effects of conditioned melanoma media and growth factors of interest on the migration of MSCs in modified Boyden chamber assays. Enzyme-linked immunosorbant assays (ELISA) were used to determine the physiologically relevant concentrations of growth factors secreted by the A375 malignant melanoma cell line and the migratory potential of MSCs. Reverse transcriptase PCR (RT-PCR) was utilized to demonstrate the presence of growth factor mRNA in the A375 melanoma cell line. Results: A375 conditioned media demonstrated a significant migration of MSCs 2- and 3-fold over serum free media controls at 24 and 48 hours, respectively (p<0.02). All growth factors of interest (FGF-2, VEGF, PDGF-AB, SDF-1,382, TGF-381, TGF-382, and-3822) resulted in the significant migration of MSCs at 10 ng/ml (p<0.05). Physiologically relevant concentrations of FGF-2 and VEGF caused significant migration of MSC (p<0.005). RT-PCR demonstrated the presence of FGF-2 mRNA in conditioned media from A375 malignant melanoma cells. Conclusions: Several lines of evidence suggest that malignant melanoma cells secrete growth factors that underlie the migration of multipotent MSCs. The growth factors under investigation have been shown to promote angiogenesis, proliferation, differentiation, mitogenesis, and chemoattraction and may ultimately control the invasive potential of melanoma and serve as potential therapeutic targets in the treatment of invasive malignant melanoma.

**P524: EXPERIMENT MODEL OF HEAD AND NECK TUMOURS**

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**Objective:** The creation of experiment model of human tumour of head & neck. Methods and materials. The model of experiment for head and neck tumors is as following: into artificially transcutaneously performed defects of skull bones was implanted human tumour samples. Nude mice are used or animals with immunosuppression created (application in
advance of distanced radical therapy, chemotherapy. The method of experiment consisted in following: at fronto-parietal area under optical enlargement through median longitudinal section of skin there is forming peristome piece using the method of hydroallocation after which in os paratilis is creating defect about 0,3 mm². The implanted culture of tumour is placing to defect and covering by formed before peristome piece; and after that is closing level-by-level. The observations is repeated with 7 days.. The obtained results. 8 laboratory animals has had a operation by our developed method in P.A. Hertsen Cancer Research Institute. One animal died during introduction narcosis. The other animal survived, with no complications during after surgery period. Implanted tumourous tissue were taken. On the 7th day animals were excluded of experiment, the analysis of implanted tumour demonstrated preservation of its biological characteristics. Conclusions. The model of head and neck tumors was created for the development of biotherapy method. 

P525: STROMAL CELLS OF ORAL SQUMOUS CELL CARCINOMA INFLUENCE PHENOTYPIC CHARACTERISTICS OF NON-TRANSFORMED KERATINOCYTES J Pirák1, M Chovanec1, Z Cada1, J Betka1, L Lacina2, D Dvoranova3, K Smetana, Jr 3 Charles University, 1st Faculty of Medicine, ENT dept., Prague 5, Czech Republic; Charles University, 1st Faculty of Medicine, Dept. of Dermatovenerology, Prague 2, Czech Republic; Charles University, 1st Faculty of Medicine, Institute of Anatomy, Prague 2, Czech Republic

Head and neck squamous cell cancer is epithelial cell tumor. However the microenvironment established by stromal cells could influence phenotypic aspects of epithelial cells and may be relevant for tumor and stem cell biology. We studied keratinocytes using tumor-derived stromal cells in a coculture system. We isolated stromal cells from human oral squamous cell carcinoma and studied their effect on phenotypic characteristics of normal human interfollicular keratinocytes in vitro. Stromal fibroblasts significantly influenced immuno- and lectin cytochemical properties of co-cultured normal keratinocytes. Expression of keratins 8 and 19, the nuclear protein nucleostemin, parameters related to adhesion/growth-regulatory galectins and the epithelial-mesenchymal transition were altered. This biological activity of tumor-derived stromal cells, which did not require cell contact, appeared to be stable. It was maintained during passageaging of keratinocytes in the absence of cancer cells. Tumor-derived stromal fibroblasts acquire distinct properties to shape a microenvironment conducive to altering the phenotypic characteristics of normal epithelial cells in vitro. There is a potential that tumor derived stromal cells can influence phenotypic characteristics of cells of squamous epithelia in vivo and thus participate during malignant transformation.

P526: ROLE OF SQUMOUS CELL CARCINOMA RELATED ONCGENE (SCCRO) AND ITS PARALOGS IN ORAL SQUAMOUS CELL CARCINOMA GENESIS C.C. Bommelje1, R. Ryan1, B.J. Golas1, S. Bains1, C. Stock1, Y. Ramanathan1, B. Singh1, Memorial Sloan-Kettering Cancer Center, New York, NY

Objective: We have previously shown that Squamous Cell Carcinoma Related Oncogene (SCCRO/DCUN1D1) is a novel oncogene that is activated by amplification at 3q and regulates cell neclyensation. We have shown that over-expression of SCCRO is associated with poor clinical outcome in oral squamous cell carcinomas (OSCC). In silico analyses show that SCCRO has four highly conserved paralogs. The aim of this study is to elucidate the role of the SCCRO/DCUN1D1 family of genes in oral SCC by 1) assessment of biochemical activity and 2) differential gene expression in OSCC. Methods: We assessed binding of all SCCRO paralogs with neclylation pathway components by GST pull down assays and confirmed these interactions by immunoprecipitations using HA-tagged proteins in HEK293 cells. To assess functional activity, neclylation reactions were performed in vitro for all SCCRO/DCUN1D1 family members and Nedd8 conjugation to cullins was monitored. Highly specific primer pairs were designed for each of the five SCCRO/DCUN1D1 family members by multiple sequence alignment using ClustalW. Gene expression analysis was performed on a total of 36 oral squamous cell carcinomas by Real Time RT-PCR in an ABI PRISM 7900 Sequence Detection System and measured with a control with a cycle threshold (Ct) above 38. Gene expression was determined for each tumor relative to its matched normal tissue and reported as fold change. Of the several control genes assessed, GEnorm analysis identified GAPDH as the most stable housekeeping gene, which was used as a control for normalization between samples. All comparisons were done using non-parametric analysis. Results: Four of the five SCCRO-family genes (SCCRO/DCUN1D1, SCCRO2/DCUN1D2, SCCRO4/DCUN1D4 and SCCRO5/DCUN1D5) retained binding to components of the nedlyensation pathway and augmented cell neclyensation. Each of these genes was upregulated in OSCC (44%, 2.8%, 17% and 42%, respectively). In contrast, SCCRO3/DCUN1D3, which did not bind to critical components of the nedlyensation pathway and did not upregulate cell neclyensation, showed decreased expression in 17% of the OSCC. In total, dysregulation of at least one SCCRO/DCUN1D-family member was present in 72% of the OSCC. Conclusion: These gene expression findings combined with our molecular work elucidate that four of five SCCRO/DCUN1D-family genes have a similar function in promoting cell neclyensation. SCCRO3/DCUN1D3, on the other hand, does not enhance cell neclyensation and therefore may have a different function than the other SCCRO/DCUN1D family members. Our findings suggest that the SCCRO/DCUN1D-family is active in oral carcinogenesis and may represent a target for novel therapeutic approaches.
cals PCR-based. Normal DNA was used as a reference to detect chromosomal imbalances. Normal DNA was used as a reference for HR-CGH.

**Results:** Frequent chromosomal losses affected regions of chromosomes 1p31-p36.1; 1q31-q42; 2p11.2-p12; 2p15-p16; 3p12-p22; 3q21-q24; 6p21.3; 7p14-p15; 7q22-q31; 10q24-q25; 12q23-q24; 16p11.2-q22; 19p13.2-13.3; 20q12-q13.1; 22q11.1-23, and gains in 6pter e 9p23pter. Significant losses were preferentially detected at 1q11.1-2; 3p21; 1q32-q42. Losses at 1q11.2 have been previously described. Losses at 3p21 were detected in 90% of cases; in this region is mapped the gene ZNF148, an co-activator of TP53. In addition, in 2p13.1 is located RASSF1 that plays an important role in cell cycle progression and is frequently silenced by methylation in several neoplasias. Loss at 1q32-q42 was detected in 80% of cases where is mapped the CEMPF gene. The CEMPF gene related is known to regulation of chromosomal segregation and mitosis.

**Conclusions:** Deletions of 3p are frequently found in a large variety of malignant epithelial neoplasms and is possible that deletion of one or more tumor suppressor genes may be important in pleomorphic adenomas. The discovery of genomic alterations may be important in the understanding of the development and progression of the AP.

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**P529: TOBACCO-SPECIFIC CARCINOGEN NNK INDUCES AKT ACTIVATION IN HEAD AND NECK EPITHELIA**

**Objective:** Exposure to tobacco carcinogens is causally associated with head and neck squamous cell carcinoma (HNSCC), but the underlying molecular mechanisms leading to carcinogenesis are not fully understood. The purpose of this study is to investigate the molecular mechanisms underlying tobacco-induced HNSCC carcinogenesis.

**Methods:** We examined a serine/threonine kinase, AKT, which plays multiple roles in tumorigenesis, by immunohistochemistry in human HNSCC samples, and correlated the results with smoking histories of the HNSCC patients. A major tobacco carcinogen, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), was exposed to normal head and neck epithelial cell lines, HNSCC cell lines, and C57BL/6 mice. Activation of AKT and its downstream signaling mediators were examined by Western blot using phosphorylation specific antibodies. Cell proliferation and apoptosis were further assessed both in vitro and in vivo.

**Results:** We found that AKT was activated at a higher percentage in both HNSCC tumors and the adjacent mucosa from HNSCC patients who are current smokers than those from HNSCC patients who are non-smokers. Adding physiologically relevant concentrations of NNK to normal head and neck epithelial cells and HNSCC cell lines rapidly and constituatively activated AKT through phosphorylation in a dose-dependent and time-dependent manner. AKT phosphorylation was associated with activation of downstream signaling mediators BAD, MDM2, GSK-3B, mTOR. These alterations correlated with increased proliferation, and decreased apoptosis induced apoptosis in NNK-exposed cells. Finally, NNK exposure to mouse head and neck epithelium resulted in epithelial hyperproliferation and reduced apoptosis, which was correlated with AKT activation.

**Conclusion:** Our results suggest that AKT activation by NNK creates a cancer-promoting environment, and hence play a pivotal role in mediating tobacco-induced HNSCC carcinogenesis.

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**BASIC SCIENCE: MODELS**

**P530: THE UNIVERSITY OF MICHIGAN HEAD AND NECK SQUAMOUS CELL CARCINOMA CELL LINES: VALIDATION BY DNA GENOTYPING**

**Objective:** An important prerequisite of cell line research is verification of the authenticity of the cell lines. Mistaken identity may lead to invalid results, or wasted time and resources. When cell lines are grown and maintained at a single institution, they can easily become contaminated. Therefore, the purpose of this study is to verify the unique origin of the UM-SCC cell lines with DNA genotyping to determine the verify genetic background of each line.

**Methods:** Over the period from 1978 to the present we established tumor cell lines from 101 head and neck cancer patients. DNA was isolated from current passages and early frozen vials from each donor and tested using DNA genotyping. Profiler Plus with 10 different polymorphic sequence repeats on chromosomes 3, 4, 5, 7, 8, 12, 13, 18 and 21, as well as the AMELOGENIN marker for chromosomes X and Y was used for genomic DNA typing. By testing early passages from our liquid nitrogen banks we were able to verify the correct genetic profile. This allowed us to ascertain the cell line identity and unique origin. The data will be posted to the University of Michigan Head and Neck SPORE web site together with other features such as p53 mutation status, resistance and sensitivity to chemotherap and radiation, etc., along with the relevant citations so that investigators world wide with whom we have shared these cell lines can confirm the identity of the cells they are using. We have already confirmed the genotype of 34 cell lines from 26 different donors. Multiple sites are represented in the genotyped panel including 12 from various sites in the larynx, 5 from lateral tongue, 4 from base of tongue, 2 tonsillar pillar, 2 hypopharynx/esophageus, 1 maxillary sinus and 2 lymph node metastases. Six more cell lines from 5 donors as well as multiple progeny lines that represent genetically modified versions of several cell lines are also ready to be genotyped. The panel of confirmed lines is currently posted on our intranet. As the data collection is completed the genotype profile will be available publicly. Then researchers will have an authentic signature to verify the identity of the UM-SCC cell lines they are using.

**Results:** Several examples of mislabeled or cross contaminated cells were discovered during the analysis and were replaced with verified cells.

**Conclusion:** The UM-SCC cell lines represent tumors from different donors and sites, with paired cell lines from different sites in the same donor or pre- and post-treatment samples. As such they are very valuable research tools. Linking the genotyped cells to other important data such as p53 status, gene and protein expression patterns, and sensitivity or resistance to chemotherapeutic drugs and radiation makes these even more valuable. Verification of the origin and characteristics is an important factor maintaining a bank of clean, unique cell lines for research.

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**P531: HEAD AND NECK SQUAMOUS CELL CARCINOMA CELL LINES BIND TO LYMPH NODE EXTRACELLULAR MATRIX ELEMENTS UNDER LYMPHODYNAMIC FLow**

**Objective:** The mechanisms important for tumor cell lodgement and growth within the lymph node microenvironment remain poorly known to date, yet they are critical steps for the establishment of clinical lymph node metastases. The lymph node microenvironment is made up of a dynamic mixture of cells, such as lymphocytes and endothelial cells, as well as a well-defined extracellular matrix scaffold onto which such cells bind, all existing under conditions of lymphodynamic shear stress. Our study sought to examine the ability of head and neck squamous cell carcinoma cell lines to bind to extracellular matrix elements of the lymph node under conditions of flow characteristic of this microenvironment, as well as to specifically assess the role CD44 may play in mediating such interactions.

**Methods:** The ability to bind was evaluated using a parallel plate flow chamber with 4 independent HNSCC cell lines introduced in flow over extracellular matrix elements adhered to a plastic support surface. Flow velocity was adjusted using a peristaltic pump to mimic lymph flow. Matrix elements examined were collagens types I, III and IV, vitronectin, fibronectin, laminin, heparan sulfate, and hyaluronic acid. CD44 expression was assessed in all four cell lines. Stably integrated CD44 knockdowns were then established in each. Knockdown cell lines were then assessed for binding activity against the extracellular elements under conditions of flow.

**Results:** Under shear stress flow conditions, all four HNSCC cell lines firmly adhered to laminin, and to fibronectin and vitronectin to a decreased level. They did not adhere to the collagens or heparan sulfate under these same conditions, but showed distinct rolling activity on hyaluronic acid. The binding to hyaluronic acid was mediated through CD44 based on the inability of CD44 knockdown cells to roll or bind on hyaluronic acid. CD44 knockdown had no effect on HNSCC cell the binding to laminin, fibronectin or vitronectin.

**Conclusion:** HNSCC cells are able to bind to matrix elements under conditions associated with lymph flow suggesting that lodgement and growth of tumor cells within this microenvironment may be under the influence of cell-matrix interactions active under flow conditions inherent to the lymphovascular space. These interactions are mediated, in part, by CD44. Ongoing work continues to assess a role for integrins in our system.

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**P532: O3/O2-PNEUMOPERITONEUM TREATMENT RESULTS IN COMPLETE REMISSION OF RABBIT SQUAMOUS CELL CARCINO-MA AT A HIGH RATE**

**Objective:** Inability of CD44 knockdown cells to roll or bind on hyaluronic acid. CD44 knockdown had no effect on HNSCC cell the binding to laminin, fibronectin or vitronectin.

**Conclusion:** HNSCC cells are able to bind to matrix elements under conditions associated with lymph flow suggesting that lodgement and growth of tumor cells within this microenvironment may be under the influence of cell-matrix interactions active under flow conditions inherent to the lymphovascular space. These interactions are mediated, in part, by CD44. Ongoing work continues to assess a role for integrins in our system.
Head and neck squamous cell carcinomas (HNSCCs) represent a group of metastasizing tumors with a high mortality rate in man and animals. Since the biomolecule ozone was found to inhibit growth of various carcinoma cells in vitro we here applied the highly aggressive and lethal VX2 carcinoma HNSCC tumor model of the New Zealand White rabbit to test whether ozone exerts anti-tumor effects in vivo. Therapeutic insufflation of medical ozone/oxygen (O3/O2) gas mixture into the peritoneum (O3/O2-pneumoperitoneum) at an advanced stage of tumor disease led to a survival rate of 7/14 rabbits. Six of the seven surviving rabbits presented full tumor regression and the absence of local or distant lung metastases. Insufflation of pure oxygen (O2) resulted in a survival rate of 3/13 animals accompanied by full tumor remission in two of the three surviving animals. Of the fourteen sham-treated animals only one had spontaneous tumor remission and survived. No adverse effects or changes in standard blood parameters were observed after repeated intraperitoneal insufflations of the O3/O2 or O2 gas. Animals with O3/O2-induced treatment experienced delayed tolerance against re-implantation of the VX2 tumor. This could be reversed by immune suppression with a combination of dexamethasone and cyclosporin A suggesting an anti-tumorous effect of O3/O2-mediated activation of the body's own immunosurveillance. Although the exact mechanisms of action are still unclear the present data point to O3/O2-pneumoperitoneum as a promising new strategy in the treatment of HNSCC tumors. (The manuscript to this abstract is accepted for publication in the International Journal of Cancer)

P534: A PATIENT TUMOR/SCID MOUSE XENOGRAFT MODEL OF HEAD AND NECK CARCINOMA FOR EVALUATING NOVEL THERAPEUTICS R.N. Riguad1, J.H. Hsu2, J. Haiku1, I. Llamos3, P. Pappal1, M. Merzianu1, C.D. Morrison3, E.A. Repasky3, B.L. Hylander3, 1Roswell Park Cancer Institute, Buffalo, NY

Objectives: Comprehensive preclinical evaluation of new therapeutics is a prerequisite for successful translation into a clinical setting. Critical challenges include the identification of which tumor types are most sensitive to therapy, discovery or validation of biomarkers that could aid in patient selection, explorations of combinations with other therapeutics that could improve efficacy and development of the most advantageous dose and treatment schedules. Using such information to inform both the design of and patient selection for routine clinical trials could facilitate success. Agents are usually evaluated against established cell lines in vitro and then against xenografts of sensitive cell lines in vivo. We believe that patient tumor xenografts offer valuable advantages and are establishing and characterizing a panel of Head and Neck squamous cell carcinomas (SCC).

Methods: We receive fresh surgical samples of Head and Neck SCC from various sites through the Tissue Procurement Facility at RPCI. Pieces of tumor 3-4 mm in size are implanted subcutaneously in several SCID mice. When tumors reach approximately 1 cm, they are harvested, cut again into small pieces and reimplanted into a second group of mice. Tumors are considered to have successfully engrafted if they grow in this second passage. Tumors in the second or later passages are selected and used as donor tumors for experiments. Samples of the original tumor as well as tumors from each passage are routinely prepared for histological evaluation.

Results: To date, we have successfully engrafted five different patient's SCC tumors from the following sites: tongue, tonsil, scalp, floor of the mouth and larynx. Histological analysis of H&E sections of engrafted tumors reveals that these patient tumor xenografts maintain the histology and heterogeneity of the original patient tumors. Interestingly, while the periphery of the tumors contains viable tumor cells, the interior consists largely of whorls of keratinized debris, suggesting that proliferating cells in these xenografts undergo keratinization, as in patient tumors, and this debris is trapped inside the growing tumor xenografts.

Conclusions: In summary, this model recapitulates many important features of patient tumors and should provide a valuable platform for carrying out trials with novel therapeutics in a preclinical setting. Additionally, since material for scientific analysis is not often procured from patients, these xenografts allow for retrieval of samples for analysis during the treatment period. Lastly, engrafted tumors can be banked for future use.
time point, while ulceration variably occurred by the two weeks post-irradiation. Ulceration began to improve 6 week post irradiation but did not resolve to normal appearing skin by the end of the evaluation period. Doppler ultrasonography demonstrated decreased (approximtely 50%) dorsal skin perfusion by two weeks and this persisted throughout the evaluation period. H&E revealed increased dermal thickness and extensive fibroblastic proliferation while Sirius red staining confirmed increased presence of collagen. SMAD3 levels were increased by the 2 week time point and remained elevated thereafter. The 30Gy group yielded results similar to unirradiated controls. Young’s modulus reflected a post XRT dose and time dependent decrease in skin elasticity. Peripheral blood smears did not suggest bone marrow abnormality. Conclusions: This novel murine model of XRT injury is the first to isolate injury to the skin thereby allowing the delivery of XRT doses otherwise lethal to mice. The minimal dose resulting in ulcera- tive and ambigious injury was 45Gy. Moreover, the injuries sus- tained were analogous to human XRT injuries both grossly, histologically, and biomechanically. Ongoing development of this model includes quantitative molecular evaluation and further biomechanical characterization.

P536: DEVELOPMENT OF AN ANIMAL MODEL OF RADIO- INDUCED TISSUE DEGENERATION B.Phulpin1, N.Tran2, P.Marie3, P.Gangloff1, P.Gallet4, D.Peiffer5, P.Bravetti6, J.Merlin6, G.Dolivet7, 1Head And Neck Surgery Unit, Oncologic Surgery Department, Centre Alexis Vautrin, Vandoeuvre Les Nancy, France; 2Laboratory of Surgery School, Nancy, France; 3Department of Nuclear Medicine, University Hospital, Nancy, France; 4Centre of Nuclear Medicine, University Hospital, Nancy, France; 5Tumor Biology Unit, Ea 3452, Centre Alexis Vautrin, Vandoeuvre Les Nancy, France; 6Radiotherapy Department, Centre Alexis Vautrin, Vandoeuvre Les Nancy, France; 7Oral Surgery Department, Odontological Faculty, Nancy, France

Objective of the Study: Radiotherapy has become an integral part of overall cancer treatment. In many of these patients will receive radiotherapy at some point during their disease treatment. Although used successfully for this purpose, ionizing radiations induced tissue injury within healthy tissue in irradiated volume. The aim of this experimental study was to develop a murin model of radiation-induced tissue degeneration with in vivo validation studies correlated with histological assessment.

Methods: Ten Wistar rats were irradiated with a single of 30 Gy to the hindlimb. After irradiation rats were observed during one year. The time course of postirradiation changes in bone was assessed in vivo, using a noninvasive technique, 99mTc-HDP scintigraphy. At the end of the study the animals were euthanized. This data was coupled with an analysis of in vitro counting on histological sections with a beta micro-imaging system (3BCIMAGER, Biospace, Paris, France) and conventional histological stud- ies performed on all the tissues of the hindlimb.

Results: Two months after irradiation, rats developed symptomatic manifestations with irreversible alopecia. A significant reduction of bone uptake of irradiated hindlimb (35-40%) was highlighted after an week post-irradiation images. These results were correlated with those obtained with in vitro counting on histological sections (3BCIMAGER). Histologically, significant tissue damage was observed. Morphological changes were characterized by edema and scarring fibrosis, vascular alteration and impairment. After a latent period of more than 10 month, the rats have developed neoplasia within the irradiated area (7 rats / 10) including 6 sarcomas and a polimatrixoma.

Conclusions: Our model have developed, after a single irradiation of 30 Gy, tissue damage characteristic of radiation injury, with a large proportion of radio-induced sarcomas. The validation of this model constitute an essential step to study therapeutic strategies.

P537: AN ORTHOTIC MODEL OF SINONASAL MALIGNAN- CY A.Gelbard1, S.Jasser1, M.Kupferman1, J.N.Myers1, E.Hanna1, 1MD Anderson Cancer Center, Houston, TX

Objective: Malignant sinonasal tumors are challenging to manage due to their proximity to vital structures, and the diverse histologies that present within this defined anatomic region. To date, there have been no animal models that accurately reflect the clinical behavior of these malignancies, which frequently demonstrate perineural, intracranial, and orbital invasion. Therefore, we developed an orthotopic murine model of sinonasal malignancy that could preclinically reproduce the intracranial extension, bony destruction, and spread along neural fascial planes seen in patients with aggressive sinonasal malignancies of varying histologies.

Methods: Human tumor cell lines DM14 (Squamous Cell Carcinoma) and ACCX (Adenoid Cystic Carcinoma) were transcutaneously implanted in 30ul saline at densities of 5x105, 2x105, 5x104, 5x103 in the right maxillary sinus, or via direct injection of the soft palate in male BALB/C nude mice. Animals were monitored for tumor growth and survival. Upon sacrifice, histologic sectioning and staining assessed for malignant phenotype defined as intracranial extension, orbital invasion, bony invasion, perineural invasion, and distant metastasis. Statistical analysis was performed with SPSS (SPSS, Chicago, IL) and R software (SPSS) to calculate p-values with the Student’s t test and the standard deviation of individual data points.

Differences in survival times were assessed using the log-rank test. Results: Mice with DM14 were implanted in either the maxillary sinus or soft palate developed large bulky tumors at the primary site. Additionally, tumor size and survival statistically correlated with the number of tumor cells initially implanted. Gross anatomic and histologic evaluation revealed orbital inva- sion, intracranial extension, pulmonary metastasis, lymph node metastasis and perineural invasion. In order to demonstrate that this model would be useful for the pre-clinical modeling of multiple malignant histologies, vary- ing numbers of the adenoid cystic carcinoma cell line ACCX were implant- ed in either the maxillary sinus or soft palate. As with DM14, these mice developed large primary tumors as well as invasion of the orbit and paranasal sinuses, intracranial extension, and regional and distant metas- tases.

Conclusions: In this report, we describe the first preclinical model of orthotopic sinonasal malignancies. We demonstrate orbital invasion, perineural spread, penetration and extension into the cranial vault, and distant metastasis. Our model faithfully recapitulates the phenotype and malignant behavior of the aggressive tumor types that present in this complex anatom- ical area. This system offers an opportunity to dissect and specifically target the aberrant molecular mechanisms underlying this heterogeneous group of malignancies.

P538: ELECTROLYSIS AND ELECTROCHEMOTHERAPY TREAT- MENT OF SPONTANEOUS HEAD AND NECK TUMORS OF CATS AND DOGS G.Rosire1, M.Borbély2, P.Felletti1, P.Martinez1, C.Dettori1, A.Bazzi1, Hospital das Clinicas, Sao Paulo, Brazil; 2State University of Campinas UNICAMP, Campinas, Brazil

Introduction: Experimental data in Europe and clinical experience in China suggest that direct electric current can treat cancer (Electrolysis) as well as improve chemotherapy response (Electrochemotherapy). In this study, we evaluated the effect of both electrolysis and electrochemotherapy in the treatment of spontaneous head and neck tumors of cats and dogs.

Materials and Methods: Sequential and non comparative study, dogs and cats presenting with a malignant neoplasm were clinically evaluated, staged and treated by electrolysis or electrochemotherapy in a veterinary hospital. Survival analysis was assessed by Kaplan-Meier and compared by Log-rank test. Results: Twenty-eight animals (14 dogs : 9 male, 5 female; and 14 cats : 7 male, 7 female) were treated by electrolysis (15 cases) or electrochemotherapy (13 cases : Bleomycin 10 cases, Doxorubycin 3 cases, Cisplatin and Carboplatin 1 case each). Tumors included 16 cases of squamous cell carcinoma, 4 cases of melanoma, 2 cases of mast cell tumor, 1 case of epulis acanthomatous, mi- xosarcoma, osteosarcoma, fibrosarcoma, mucinous carcinoma and Sticker tumor, with stages T1 = 10 cases, T2a = 6 cases, T2b = 2 cases, T3a = 5 cases, and T3b = 5 cases; N0 = 22 cases, N1 = 3 cases, N2 = 1 case, and N3 = 2 cases. The mean electrical charge/tumor volume was 38.50 C/cm3. Two animals died during treatment. By univariated analysis, factors impacting on survival were T stage (p=0.04) and charge/tumor volume (p<0.01).

Discussion and Conclusions: Our data suggests that electrolysis and electrochemotherapy are potentially effective treatment for head and neck tumors of dogs and cats and deserves further evaluation.
hydrochloric acid. Groups III and IV consisted of 12 animals each, submitted to 2 (GII) or 3 (GIV) weekly applications of 0.1N hydrochloric acid solution with a rinsing of 1ml of distilled water. Groups V and VI consisted of 12 animals each, submitted to 2 (GV) or 3 (GVI) weekly applications of 0.1N hydrochloric acid and the addition of sodium nitrate 400mg diluted in 300ml of filtered water. Group VII was the control group with 10 animals submitted to 2 weekly applications of filtered water. 

Results: No dysplasia, intra-epithelial neoplasia or invasive carcinomas were seen. Inflammatory changes were observed in varying degrees in the three studied subsites, mainly in the supraglottic larynx. The evaluation of the intensity of the inflammatory exudate in the larynx, divided into degrees 0 to 3, showed greater frequency of Degrees 2 and 3 in Groups I, II and IV (p=0.001). In the cervical esophagus, inflammatory response was observed in degrees 0, 1 and 2 (p=0.019) and in the oropharynx, mast cells were more frequent in groups V and VI (p=0.006).

Discussion: The relationship between heavy smoking and alcoholism with the etiology of malignant neoplasms in the upper airway and digestive tracts has been well established. However, approximately 5% of patients with head and neck squamous cell carcinoma (SCC) do not use tobacco or alcohol. This may point to the existence of other factors involved in the genesis of such tumors. One of these co-factors may be the pharyngolaryngeal reflux. A number of authors have shown the co-carcinogenic action of this pathology, whose leading irritating agent on the mucosa is hydrochloric acid. In this study, only substances involved in GERD were used, namely, hydrochloric acid in the concentrations found in the organism (0.1N), pepsin, and nitrate. Although no pre-neoplastic or neoplastic changes of larynx, esophagus or oropharynx were seen in varying degrees.

Conclusion: It is possible that GERD and PLR are co-carcinogenic due to the inflammatory action of hydrochloric acid potentiated by pepsin, but data of the current study could not corroborate this hypothesis.

EPIDEMIOLOGY II

P540: PROCESS OF ADAPTATION WHEN PARENTS SUFFERED FROM HEAD AND NECK CANCER IN TAIWAN C.R Lin 1, J.T.Chang2, R.J.Shiau3, Y.Y.Juang4, B.W.Wang5, 1School of Nursing, Chang Gung University, Tao-Yuan Taiwan Republic of China; 2Department of Radiation Oncology, Chang Gung Memorial Hospital, Linkou, Tao-Yuan, Taiwan, Republic of China; 3Chang Gung University Graduate Institute of Clinical Behavioral Sciences, Tao-Yuan, Taiwan, Republic of China; 4Department of Psychiatry, Chang Gung Memorial Hospital, Linkou, Tao-Yuan, Taiwan, Republic of China; 5School of Nursing, Chang Gung University, Tao-Yuan, Taiwan, Republic of China.

Objective: When the parents is diagnosed with head and neck cancer, the family's life changes. This study was undertaken to understand what the sons and daughters could do with the stresses for gaining good adaptation when facing parents suffer from head neck cancer in Taiwan. This study is a part of a project focused on family centered care for head and neck cancer patients and their family members in Taiwan. Eighteen subjects (16 women and 2 men) whose spouses were diagnosed with head neck cancer were recruited from a radiation-oncology outpatient clinic at a medical center in northern Taiwan. All patients had completed their treatment. The data were collected individually. Data were collected through individual, tape-recorded interviews and observations. Transcripts were analyzed by content analysis for emerging themes and concepts. 

Results: Subjects described six themes of impacts from the analysis: (i) dread of loss their spouses due to cancer, (ii) financial problem, (iii) caregiver's burden while undergoing anticancer treatment, (iv) overload in parenting, (v) unmet information need to making medical decision, and (vi) changes in plans for life. Eight themes of adjustment to the impacts were described: (i) changes in roles in family: from house keeper to economical provider, (ii) searching for his/her own support from other family members or friends, (iii) changes in relationship with children, (iv) adjustment of plans of life, (v) adjustment of his/her own characteristics, (vi) changes in life style: more health seeking behaviors, (vii) adjustment of interpersonal relationship, and (viii) search for the meaning of life.

Conclusions: The results of this study have shown that spouses of patients with head and neck cancer are distressed due to the impacts of their spouses’ disease. Facing the impacts of all dimensions of the family’s lives, spouses of patients with head and neck cancer have to adjust their roles in family, seeking for emotional, economical, and social support, and search for the meaning of life. The distress and impacts of the spouse must be recognized and addressed by health care professionals. More studies are needed for the development of effective interventions.

P542: HEAD AND NECK CANCER IN GORAJ : A PERSPECTIVE R.A Kantharia1, S.R. Kantharia2, 1Kailash Cancer Hospital and Research Center, Baroda, India

Objectives: Head and Neck Cancer continues to be a menace worldwide despite advances in diagnosis and treatment protocols and it constitutes a major health problem in India accounting for 23% of all cancers in males and 6% in females (ICMR, 1992). The trend of various malignancies differ in different geographical regions. India is known for diversity of its population and characteristic site pattern of risk. Spectrum of cancer varies from place to place within the country. The social habits of the population lie at the core of this national health problem. A significant portion of the population is illiterate. Site specific data from different part of country provide the various trends and give clues to the etiological factors responsible for these significant variations. This is the first ever report of its kind from the Head and Neck Surgery Department, Kailash Cancer Hospital and Research Center, Goraj, Gujarat: India in which an effort has been made to put Head and Neck Cancer cases in proper perspective.

Methods: This is a single institutional retrospective study of three years from 2004–2006. The catchment area of this study was in and around Goraj. The data was collected year wise in context of age, sex, site of cancer and histo-pathological diagnosis. Various malignancies were classified according to the International Classification of disease coding system classified by WHO. Results: The new Head and Neck Cancer cases reported in three years were 1224 with an average of 408 cases per annum. Out of total 1224 cases, 74.6 % (914 cases) were males and 25.4 % (310 cases) were females. Majority of these cases were in the age group of 30–60 years with peak in the fifth decade of life. 5.4% (66 cases) were in young age group of less than 35 years of age. Site wise analysis reveal a predominant Oral Cavity Cancer (42.3%) followed by Larynx - Hypopharyngeal (21.6%) and Oro-pharyngeal Cancers (17.2%).

Conclusion:
We registered 1343 new Oral cavity The estimate of Instituto Nacional do Câncer for the year 2008 According to the results we obtained, we have been Subjects The data point towards the significant...
To evaluate the trend in treatment approach of head and neck cancer patients registered at Oncocentro Foundation at Sao Paulo (FOSP), a hospital based cancer registry, during the period 2000 to 2006.

**Objective:** To evaluate the trend in treatment approach of head and neck cancer patients registered at Oncocentro Foundation at Sao Paulo (FOSP), a hospital based cancer registry, during the period 2000 to 2006.

**Material and Methods:** Data were obtained from the public database available online from the FOSP, which gathers and organizes all new cases of cancer registered in 63 institutions (52 cancer centers) at the State of Sao Paulo, Brazil. Statistical analysis was performed on the SPSS statistical software. Trend analysis was conducted by linear regression and statistical significance was considered for p<0.05.

**Results:** The distribution of cigarette smoking and alcohol consumption are relatively uncommon event that manifest under a multiplicity of histological types. The cavity structure of the maxillary sinus and its particular topography in the median aspect of the facial skeleton make the tumors appear- ing in it in a special category of poor prognosis. There are few statistics about tumor of the maxillary sinus in the Brazilian population. The present descriptive work is a retrospective compilation of the tumors of the maxillary sinus attended through 1997 to 2006 at the Brazilian National Institute of Cancer, the main governmental center for cancer statistics in the country.

**Methods:** After new histological assessment for diagnostic confirmation, medical files were assessed to gather demographic and clinical data from the patients. The ratio between males and females was 1.1:1. Most of the detected cases were white (58.5%). The average age of the patients was 53.3 years (±18.1 years), varying from 3 to 90 years-old, with prevalence of patients in the fifth and seventh decades of life (57.3% of the sample). Approximately one-third of the patients (33.6%) were present smokers, and 52.8% of the entire population was heavy drinkers. Squamous cell carcinoma and adenoid cyst carcinoma performed 51.8% of the tumors. For the benign group, the most frequent lesion was the sinus polypomas. Tumefaction was registered as the main disease signal in 93.2% of the analyzed individuals. The most frequent alleles in the case group were NAT2*5, NAT2*6 and 11.9% versus 14.5%. For both DNMT3B SNPs, inter-group comparison of the allele frequency between patients and controls and distribution of the tumors presented a growth epicenter in the maxillary sinus, while the sinusal extension of the extra-sinus neoplasia was not found in both groups, whereas the allele frequency of -597TT and -597GT for patients and controls was, respectively, 88.1% versus 84.3%, 11.9% versus 15.3%, and 0% versus 0.4%. The allele -597GG was not found in both groups, whereas the allele frequency of -597TT and -597GT for patients and controls was, respectively, 88.1% versus 85.5%, and 11.9% versus 14.5%. For both DNMT3B SNPs, inter-group comparison of the allele frequency between patients and controls and distribution of the tumors presented a growth epicenter in the maxillary sinus, while the sinusal extension of the extra-sinus neoplasia was not found in both groups, whereas the allele frequency of -597TT and -597GT for patients and controls was, respectively, 88.1% versus 85.5%, and 11.9% versus 14.5%

**Conclusion:** In agreement with the trend observed in the world scientific literature.

**Results:** The results include 13,023 patients registered during the years 2000 to 2006. During this period, no significant changes were observed in the clinical stage of the patients. However, with regard to the treatment performed, the following trends were observed: a) surgery - 24.2% of cases were submitted to surgical treatment in 2000, compared to 20.8% in 2006 (p=0.193); b) chemotherapy - 13.3% and 8.9% in 2000 and 2006, respectively (p=0.079); c) radiotherapy - 15.8% and 13.0% (p=0.066); d) surgery plus radiotherapy - 10.5% and 8.4% (p=0.386); e) surgery plus chemotherapy - 1.6% and 1.6% (p=0.597); f) radiotherapy plus chemotherapy - 16.2% and 27.1% (p=0.006); g) surgery plus chemotherapy plus radiotherapy - 2.3% and 5.1% (p=0.025); h) others - 2.8% and 1.8% (p=0.728); 9) none - 13.0% and 13.3% (p=0.965).

**Conclusions:** The most frequent treatment applied for head and neck cancer patients in the year 2000 was surgery with or without adjuvant therapies (38.6%), compared to radiotherapy in the follow-up period (40.1%). Moreover, this period exhibited a decrease trend of therapies based exclusively on radiotherapy or chemotherapy, with a significant increase in cases submitted to combined treatment (radiotherapy plus chemotherapy and surgery plus radiotherapy and chemotherapy), in agreement with the trend observed in the world scientific literature.

**Objective:** Evaluating molecular polymorphisms in four genes of DNMT3B and DNMT3A, NAT2, and GSTT1 in patients with head and neck squamous cell carcinoma (HNSCC) and healthy controls.

**Materials and Methods:** In this study, we genotyped 226 head-and-neck squamous-cell carcinoma (HNSCC) patients and 249 controls to examine the association between three SNPs of the DNMT3B promoter region and the associated risk of the development and/or metastasizing tendency of HNSCC for the population of Taiwan. We observed that only the T/T genotype (C46359T) was found to be present in both patient and control groups (100% frequency). The alleles frequency of -283CC, -283CT and -283TT among patients and controls was, respectively, 88.1% versus 84.3%, 11.9% versus 15.3%, and 0% versus 0.4%. The allele -597GG was not found in both groups, whereas the allele frequency of -597TT and -597GT for patients and controls was, respectively, 88.1% versus 85.5%, and 11.9% versus 14.5%. For both DNMT3B SNPs, inter-group comparison of the allele frequency between patients and controls and distribution of the tumors presented a growth epicenter in the maxillary sinus, while the sinusal extension of the extra-sinus neoplasia was not found in both groups, whereas the allele frequency of -597TT and -597GT for patients and controls was, respectively, 88.1% versus 85.5%, and 11.9% versus 14.5%

**Conclusion:** The results of this study suggest that NAT2 polymorphisms leading to slow activity are a risk factor to the development of head neck squamous cell carcinomas.

**Objective:** Genetic factors clinically important that may result in differences to individual susceptibility to head and neck squamous cell carcinomas (HNSCC) probably include genes involved in xenobiotics metabolism. N-acetyltransferases 1 and 2 are phase II enzymes that are involved in the detoxification of activated metabolites of carcinogens, including aryl- and heterocyclic amines that are present in the tobacco smoke. Polymorphisms in the coding region of the NAT2 gene results in a slow acetylator phenotype, which has been associated with drug toxicity, several cancers and neurodegenerative diseases.

**Material and Methods:** Seven SNPs (single nucleotide polymorphisms) were analyzed at 191, 282, 341, 481, 590, 803, and 857 positions of the NAT2 gene in a case-control study including 151 patients and 159 healthy controls (without cancer). NAT2 alleles were differentiated by a polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) based approach. Individual genotypes were determined in the software SNPGen and the predicted phenotypes were grouped in rapid (two rapid acetylator alleles), slow (two slow acetylator alleles) or intermediate (heterozygous rapid/slow) acetylators. The odds ratios for rapids and intermediate acetylator, as compared with the reference slow acetylator, were 0.02 (95% Cl 0.0-0.1) and 0.17 (95% Cl 0.1-0.5), respectively.

**Conclusion:** NAT2 polymorphisms leading to slow activity are a risk factor to the development of HNSCC.
**Objective:** Head and neck squamous cell carcinomas (HNSCC) are a heterogeneous group of the upper aerodigestive tract diseases. Around 95% of these neoplasms are squamous cell carcinomas. These tumors are causally associated with tobacco usage alone or in combination with alcohol consumption. Most of the carcinogens present in tobacco smoke are converted into DNA-reactive metabolites by cytochrome P450 enzymes and detoxification of these metabolites is performed by glutathione S-transferases and N-acetyltransferases in humans. Several of these genes display polymorphisms that could modulate enzymatic activities like carcinogens activation and detoxification. The purpose of this study was to correlate the genotype/phenotype and HNSCC development risk and the impact of the clinical and genetical factors. **Material and Methods:** The patients comprised 156 patients with HNSCC and 145 individuals without current or previous diagnosis of cancer. The GSTM1 and GSTT1 deletions were analysed by PCR-multiplex and the SNPs (single nucleotide polymorphisms) genotyping of the CYP1A1, CYP1A2 and CYP2E1 genes was performed by PCR-RFLP. **Results:** Significant difference was detected with tobacco consumption and alcohol consumption in the comparison between cases and controls (P=0.001), suggesting that these factors are independent risks to HNSCC. It was observed an association between the genotypes CYP1A1*1A and tumor recurrence rates in oral carcinomas (P=0.03), genotype and T3/T4 carcinomas (P=0.009), and genotype and presence of metastases (P=0.048). In addition, it was observed that CYP2E1*2C-2 grouped to others genes could confer a higher risk to HNSCC development and the genotype class CYP2E1*wild-type/GSTM1*null/GSTT1*positive represents low risk to HNSCC. **Conclusion:** These findings are compatible with the view that genetic predisposition is important to determining parameters related to tumor progression in head and neck cancer.

**Objective:** Tumor susceptibility alleles in Head and Neck Cancer patients younger than 40 years. **Methods:** Genomic DNA or RNA was extracted from tumor specimens obtained from HNSCC patients 40 years of age or younger, according to protocols approved by the IRB of The Ohio State University (OSU). TGFBR1 exon 1 was amplified using PCR, and the PCR products genotyped by OSU Plant Microbe Genomics Facility (OSU PMGF) using a capillary sequencer. All SNPs detected by direct sequencing methods were used to screen for alterations in CDKN2A. Tumor specimens from older HNSCC patients were also analyzed for comparison. **Results:** A total of 16 tumors from young patients were genotyped for TGFBR1, with 5 (31.3%) possessing non-9A hypomorphic allele variants. Three patients had a genotype of *6A/*9A (18.8%), one patient had a genotype of *5A/*9A (6%), and one patient had a genotype of *9A/*10A (6%). There was a statistically significant difference in the proportion of non-*6A hypomorphic alleles present in the young HNSCC group (12.5%) as compared to older HNSCC (1.33%) patients (P-value = 0.0363). A total of 20 tumors from young patients were analyzed for alterations in CDKN2A, and 10 (50%) displayed absent expression or mutation, compared to 8 out of 20 (40%) tumors from older patients. Although absence of CDKN2A expression was common in both groups, younger patients had a higher frequency of single base pair alterations (3 of 10, 30%) and older patients had a higher rate of large exon 2 deletions (2 of 8, 25%). Structural analysis information regarding alterations in the p16 Protein is also presented. **Conclusions:** Preliminary results from this small cohort of young HNSCC patients indicate that a hypomorphic TGFBR1 allele might be influencing tumor susceptibility in this population. CDKN2A alterations were also commonly found in the younger population, with a difference in the frequency of type of mutations occurring in younger vs. older patients (point mutation vs. large deletion). This difference in CDKN2A mutation type may indicate different structural and/or functional implications for the p16 product in these patient groups. Further study of a larger cohort is needed to characterize the proportion of altered alleles in HNSCC patients 40 years of age or younger and define the role of these susceptibility alleles in HNSCC tumorigenesis.
and should be considered for use in endoscopic management of this disease process.

P555: TREATMENT OUTCOME AND SURVIVAL ANALYSIS OF RECURRENT HYPOPHARYNGEAL SQUAMOUS CELL CARCINO-MA: THE ROLE OF SALVAGE THERAPY. Y.W.Su, C.Wang1, P.Liou2, T.Sheen3, J.Koa1. 1Department of Otolaryngology, Buddhist Tzu-chi General Hospital, Taipei Branch, Taipei, Taiwan, Republic of China; 2Department of Otolaryngology, National Taiwan University Hospital, Taipei, Taiwan, Republic of China

Objectives: The prognosis of hypopharyngeal cancer is poor despite modern multimodality treatment with recurrent rate around 30%. When recurrent occurs after previous curative treatment, it becomes a challenging task for the clinicians to recommend the treatment of choice because of limited reports available. By analyzing the treatment outcome, we are able to provide evidence-based therapy for recurrent hypopharyngeal cancer.

Methods: We retrospectively reviewed 434 patients with squamous cell carcinoma of the hypopharynx treated at National Taiwan University Hospital between Jan 1990 and Dec 2002. All recurrent cases were pathologically proven and received complete re-staging workup. The endpoint of follow-up was until Dec 2007. Survival was analyzed with Kaplan-Meier method and statistical difference was defined as p value < 0.05 using log-rank test. Multivariate analysis on survival was calculated using Cox’s proportional hazards model. All statistical analyses were performed with SAS v9.1 software.

Results: One hundred and fourteen (26.2%) cases developed recurrence after a disease-free interval of at least 6 months. According to the American Joint Committee on Cancer 2002 criteria, three (2.6%) cases were stage I, 13 (11.4%) cases stage II, 6 (5.3%) cases stage III, and 92 (80.7%) cases stage IV. Seventy-seven (67.5%) cases recurred locally, 47 (41.2%) cases regionally, and 34 (29.8%) cases distantly. In 56 (49.1%) recurrent cases, the salvage treatment included surgery with/postoperative adjuvant chemo/radiotherapy. Radiotherapy alone, chemotherapy alone and concurrent chemoradiotherapy were given in 26 (5.3%), 21 (18.4%), and 9 (7.9%) cases, respectively. Twenty-two (19.3%) cases received post-operative adjuvant treatment, with the worst one-year survival rate of 21.1% (p<0.001). In the surgery group, the median disease-free survival (DFS), disease-specific survival (DSS) and overall survival (OS) were 1.77, 2.33, and 1.80 years, respectively. In other treatment groups without salvage surgery, the median DFS, DSS, and OS were 0.30, 0.54, and 0.50 years, respectively. There were statistically significant differences in DFS (p=0.046), DSS (p=0.002) and OS (p=0.003) between different treatment groups. The surgery group had the best survival with 1-, 2-, and 5-year DFS rates of 54.5%, 44.6%, and 39.0%, respectively. However, post-operative adjuvant therapy did not statistically significantly prolong the DFS (p=0.78), DSS (p=0.69) or OS (p=0.57). Various demographic and pathologic factors as well as recurrent TNM staging were enrolled in the univariate analysis, but only sex, recurrent N classification and stage of recurrence were statistically significant (p<0.05). Multivariate analysis revealed stage of recurrence (p<0.01) was the only adverse prognostic factor for the treatment outcomes (DSS, OS). In cases with the presence of distant metastasis, the surgery group still tended to have better DFS (p=0.43), DSS (p=0.06) and OS (p=0.08).

Conclusions: Salvage surgery with or without adjuvant therapy led to better survival for recurrent hypopharyngeal cancer, comparing to radiotherapy alone, chemotherapy alone or chemoradiotherapy. The patients with only supportive treatment after recurrence had the worst prognosis.

P556: WITHDRAWN

P557: TREATMENT RESULTS OF HYPOPHARYNGEAL CANCER. H.Wang1, M.F.Chang3, C.Lin2, K.Fan2, C.Liao2, I.Chen2, J.T.Chang2, 1Chang Gung Memorial Hospital, Taoyuan, Taiwan, Republic of China; 2Chang Gung Memorial Hospital, Taoyuan, Taiwan, Republic of China; 3Chang Gung Memorial Hospital, Taoyuan, Taiwan, Republic of China

Purpose: The aim of this study was to evaluate the treatment results of hypopharyngeal cancer and find the prognostic factors. Patients and Methods: 134 hypopharyngeal cancer patients received primary treatment in Chang Gung Memorial Hospital from January 1994 to May 2004. Three hundred and seventy-nine (96%) patients are male and the median age is 56 ranging from 15 to 87. The majority (88%) of patients had habits of smoking, 73% of patients alcohol drinking and 51% of patients had betel quid chewing. The distribution are as follows: stage I: 2 (0.5%); stage II: 22 (5.6%); stage III: 44 (13.2%); stage IV: 82 (61.4%); 21.1% (p<0.001). In the surgery group, the median disease-free survival (DFS), disease-specific survival (DSS) and overall survival (OS) were 2.33, and 1.80 years, respectively. In other treatment groups without salvage surgery, the median DFS, DSS, and OS were 54.5%, 44.6%, and 39.0%, respectively. However, post-operative adjuvant therapy did not statistically significantly prolong the DFS (p=0.78), DSS (p=0.69) or OS (p=0.57). Various demographic and pathologic factors as well as recurrent TNM staging were enrolled in the univariate analysis, but only sex, recurrent N classification and stage of recurrence were statistically significant (p<0.05). Multivariate analysis revealed stage of recurrence (p<0.01) was the only adverse prognostic factor for the treatment outcomes (DSS, OS). In cases with the presence of distant metastasis, the surgery group still tended to have better DFS (p=0.43), DSS (p=0.06) and OS (p=0.08).

Conclusions: Salvage surgery with or without adjuvant therapy led to better survival for recurrent hypopharyngeal cancer, comparing to radiotherapy alone, chemotherapy alone or chemoradiotherapy. The patients with only supportive treatment after recurrence had the worst prognosis.
geons because of the damage to the recipient vessels and delayed wound healing. At our institute, we have tried surgical PLE and free jejunal transfer for all operable cases of recurrent hypopharyngeal carcinoma. The safety and effectiveness of our strategy was analyzed in this study. **Materials and Methods:** From 2002 through 2007, 13 patients with recurrent hypopharyngeal carcinoma after definitive chemoradiotherapy underwent surgical PLE and free jejunal transfer (surgical group; SSG). They had performed prophylactic lymphadenectomy (average 67Gy) with adjuvant administration of TS-1. During the same period, we selected another 27 patients who underwent prophylactic PLE and free jejunal transfer after neo-adjuvant chemoradiotherapy as control (planned surgery group; PSG). They had performed chemoradiotherapy (average 33Gy) with adjuvant oral administration of TS-1. In the two groups, we examined preoperative conditions, operation time, blood loss, postoperative complications, and functional outcome. Then the difference between the two groups was analyzed to find the problems of salvage surgery. **Results:** In the SSG, body weight loss (8.7kg) from the day of initial treatment to the operation was significantly higher compared to that of PSG. In the SSG, necrosis of the transferred jejunum developed in one patient (7.7%), orocutaneous fistula in 2 patients (15.4%), and wound infection in one patient (7.7%). While in the PSG, necrosis of the jejunum developed in one patient (3.2%), fistula in 3 patients (11%), and wound infection in 3 patients (11%). There was no statistically significant difference in the postoperative complications between the two groups. There was also no difference in the operation time (10.2hours vs 10.5hours), blood loss (607ml vs 716ml), and interval to oral intake (1 days vs 14days). In the SSG, one patient died of local recurrence and one patient died of another double cancer, but no patients are alive with disease, and 4 patients are alive with disease, but no local recurrence. Oral intake is completely maintained until now in 11 patients. **Conclusions:** Although patients after definitive chemoradiotherapy were in poor nutritional conditions, incidence of perioperative complications was not higher and functional outcome was not different compared to the PSG. For most of the patients, oral intake was restored and quality of life was improved. Salvage surgery utilizing free jejunal transfer is considered safe and effective for recurrent hypopharyngeal carcinoma.

**P560: SALVAGE SURGERY FOR LOCAL RECURRENCE AFTER CHEMORADIOThERAPY OR RADIOTHERAPY IN HYPOPHARYNGEAL CANCER PATIENTS**

**Objective:** Radiotherapy (RT) or concomitant chemoradiotherapy (CRT) plays an important role in the treatment of head and neck squamous cell carcinoma to preserve organ and/or function. For recurrent disease after RT/CRT, there remain few options other than salvage surgery to pursue a cure. In this study, we retrospectively analyzed the outcomes of salvage surgery for local recurrence of hypopharyngeal cancer after RT/CRT to determine the role of the salvage surgery in the treatment strategy. **Patients and Methods:** Between 1991 and 2005, 104 patients with previously untreated resectable squamous cell carcinoma in the hypopharynx received either RT or CRT as a definitive treatment in Hokkaido University Hospital. The radiotherapy regimen consisted of daily fractions of 2.25Gy and total doses of 60-70Gy. The chemotherapy regimens were weekly 100mg/m² of carboplatin or weekly 10mg/m² of docetaxel or cisplatin(daily dose of 4mg/m² or weekly dose of 100mg/m²). The local recurrence rate, salvage rate after local recurrence and overall survival (OS) rate for these patients were estimated using the Kaplan-Meier method. Patients with primarily unresectable disease were not included in this study. **Results:** Of the 104 patients, local recurrence in primary site after RT/CRT was observed in 33 patients (local recurrence rate: 31.7%). The local recurrence rates with T1, T2, T3 and T4 primary disease were 17.6% (3/17), 37.0% (17/46), 31.0% (9/29) and 33.3% (4/12), respectively. Only 12 of 33 patients with local recurrence underwent salvage surgeries. The remaining 21 were considered unresectable or refused surgery. One patient with T1 disease was alive with recurrent diseases without salvage surgery. All 4 cases with a T4 primary tumor were considered unresectable at the time of recurrence. Disease control was achieved in 7 of the 12 patients who had salvage surgery. The salvage rate for the 12 patients with local recurrence who had salvage surgery was 21.2% (0/007). The local recurrence rates with T1, T2, T3 and T4 primary disease were 33.3% (1/3), 23.5% (4/17), 22.2% (2/9) and 0% (0/4), respective- ly, suggesting a low salvage rate for local recurrence. The 5-year OS rate for the 33 patients was 52.7%. The OS rates in patients with T1, T2, T3 and T4 primary disease were 79.1%, 36.6%, 41.2%, and 15.5%, respectively. The OS rate for the 59 patients who underwent radical surgery to remove the primary tumor during the same period was 45.2%. **Conclusions:** According to these results that to control locally recurrent hypopharyngeal cancer after RT/CRT is difficult at any primary T-stage, salvage surgery shouldn’t be incorporated into the initial treatment plan for hypopharyngeal carcinoma. In addition, salvage surgery for such recurrent cases should be carefully selected because of expected poor prognosis.

**P561: THE NORMAL CONFIGURATION AND INTERINDIVIDUAL DIFFERENCES IN INTRAMURAL LYMPHATIC VESSELS OF THE ESOPHAGUS**

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**Background:** Recently, interindividual differences in lymphatic vessel density between patients with cancer are of most interest for surgeons as a critical prognostic factor. However, we have little morphometrical information of the nonpathological esophageal lymphatics. **Objective:** Using D2-40 immunohistochemistry, to describe normal configuration of the esophageal intramural lymphatics and to morphometrically evaluate the pre-existing mucosal vessels. **Methods:** D2-40 immunohistochemistry for human lymphatic epithelium was performed for 3 sites of the cervical and thoracic esophagus. Lymphatic vessels were identified by low magnification. Lymphatic vessel density was evaluated in the lamina propria mucosae and submucosal layers. Statistical analysis was performed using Student’s t-test and ANOVA. **Results:** The present immunohistochemistry demonstrated the mucosal longitudinal and intermuscular circumferential vessels, but in contrast to the previous diagram, the submucosal lymphatics were limited to a few circumferential and marginal vessels. We concluded a new scheme of the intramural lymphatic vessels. According to the present morphometry, interindividual difference ranged from 100-200% (2-3 times) in the number and circumferential lengths of mucosal lymphatic vessels. **Conclusions:** The present immunohistochemistry consistently demonstrated the mucosal longitudinal and intermuscular circumferential vessels, but in contrast to the previous diagram, the submucosal lymphatics were limited to a few circumferential and marginal vessels. We concluded a new scheme of the intramural lymphatic vessels. According to the present morphometry, interindividual difference ranged from 100-200% (2-3 times) in the number and circumferential lengths of mucosal lymphatic vessels. Instead, site-dependent differences were not evident. After correction according to thickness of the esophagus, the interindividual difference was still 2-times in lymphatic vessel density. **Conclusions:** We hypothesized that larger and/or greater numbers of lymphatic vessels in the lamina propria mucosae are likely to provide a greater opportunity for lymphatic vessel invasion of cancer. Whether the cancer invasion is easy or difficult seemed to depend on the individual anatomy as well as the pathology.

**P562: A RISK FACTOR OF METASTASES TO LATERAL RETROPARYNGEAL NODES IN HYPOPHARYNGEAL CANCER**

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**Objective:** To clarify the risk factors of metastases to lateral retropharyngeal disease in the neck of hypopharyngeal cancer. **Methods:** We reviewed 123 cases of hypopharyngeal squamous cell carcinoma that had been treated in Osaka Medical Center for Cancer. Lateral retropharyngeal nodes were examined with CT and/or MRI in advance. 42 patients were treated with radiation therapy and 81 patients were treated surgically. In 38 of those 81 patients, lateral retropharyngeal node dissection was performed. The specimens of these 38 cases showed 32% incidence of metastatic tumor in lateral retropharyngeal nodes. Additionally, in order to investigate if there were correlations between features of primary tumors and lateral retropharyngeal node metastases, we evaluated CT, MRI and histopathological findings in cases with lateral retropharyngeal node dissection. **Results:** If the tumor invades close to the outer edge of the hypopharyngeal constrictors, lateral retropharyngeal node metastases occurred with increasing frequency. **Conclusions:** Deep tumor extension in the posterior wall of the hypopharynx is a risk factor of lateral retropharyngeal node metastases.

**P563: THERAPEUTIC SELECTIVE NECK DISSECTION (LEVEL II ~ V) FOR NODE POSITIVE HYPOPHARYNGEAL, SQUAMOUS CELL CARCINOMA**

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**Objectives:** The purpose of our study was to identify the frequency of metastasis to level II of the neck in patients with clinically node-positive (N+) hypopharyngeal squamous cell carcinoma (SCC) and to determine whether saving level II lymph nodes increases the risk for regional recurrence. **Material and Methods:** We retrospectively studied 64 consecutive clinically N+ patients with untreated hypopharyngeal SCC between March 1994 and 2006. All 64 patients had no-nodal metastases in neck level I and underwent ipsilateral modified radical neck dissection. Of these,
P564: PATTERN OF NECK AND MEDIASTINAL NODE METASTASIS AND DISSECTION IN PHARYNGOLARYNGEOESOPHAGEAL TUMORS
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Introduction: Reports about neck node metastasis (NM) in cervical esophageal tumors and mediastinal node metastasis (MM) in patients with pharyngolaryngoesophageal (PLE) neoplasias are lacking. This study was undertaking to evaluate details of NM and MM in carcinomas of this region.

Method: A review of the records of 44 patients gastric pull-up for Ca of the PLE junction was done. Eighteen patients had esophageal cancer, 10 had pyriform synus, 10 had retrocricoid and four had laryngeal carcinomas. The mediastinal dissection (MD) resected mainly the paratracheal/paraesophageal lymph nodes down to the aortic arch, with out thoracotomy. Fifty neck dissections (ND) were performed in 28 patients and yielded positive (pos.) nodes in 47.7% of all patients. The NM occurred in 60%, 70% 66% and 22% of the patients with esophageal, pyriform synus, retrocricoid and laryngeal carcinomas, respectively. Twenty one ND were therapeutic (pos. in all except one) and the remaining were elective. Five (17,2%) of the 29 elective ND were radical (rad./mod.radical). Four (20%) were done for Ca of the esophagus (pos. 50% of ND), 12 done for p. synus (pos. 66%), 5 done for retrocricoid (pos. 80%) and nine done for laryngeal Ca (pos. 66%). Thirteen ND were radical (pos. nine), seven were mod.radical (pos. six), and 24 were elective (pos. 11). ND were bilateral (61%) and multiple (7%). The number of neck nodes examined was 1032, pos. in 66%. Thirteen ND were radical (pos. nine), seven were mod.radical (pos. six), and 24 were elective (pos. 11). ND were bilateral (61%) and multiple (7%). The number of neck nodes examined was 1032, pos. in 66%. Thirteen ND were radical (pos. nine), seven were mod.radical (pos. six), and 24 were elective (pos. 11). ND were bilateral (61%) and multiple (7%).

Results: MD yielded 222 nodes, pos. in 17.1%. The size of MD nodes averaged 1.1 cm. Extracapsular invasion occurred in 33%. The incidence of occult metastases to level I was 6% (3 of 47). These 3 cases had bilateral nodal metastases and metastases at multiple levels of the neck. No occult nodal metastases were found in any N1 or N2a patient. There was no isolated nodal involvement at level I. Pure regional failure (primary controlled) developed in 7 (16%) of 45 patients during the 9-year average follow-up period. Survival rate at 2, 5 and 10 years of the with level I dissection and 1 (10%) of 10 patients without level I dissection experienced regional recurrence (P=.4). In addition, no significant differences in survival were observed based on level I neck dissection. The 2-year disease-specific survival in the cohort of 47 patients undergoing level I neck dissection was 44% compared with 72% in the 17 patients who did not undergo level I neck dissection (P=.8).

Conclusions: Our study suggests that routine level I dissection may not be necessary in the surgical management of hypopharyngeal SCC in patients who have nodal metastases in the neck.

P566: TIME-COURSE OF INTACT PTH AFTER THE OPERATION FOR ADVANCED PHARYNGOLARYNGEAL CANCER
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Hypoparathyroidism after surgery for advanced pharyngolaryngeal cancer sometimes leads to severe complications. To control the calcium metabolism is often quite difficult. From this point of view, preserving the function of the parathyroid glands is crucial. It is also significant economically, as we must focus on the preservation of the parathyroid glands during the surgical management of the pharyngolaryngeal cancer. We usually preserve the parathyroid glands attached to the thyroid gland by preserving only the superior vessels of the thyroid gland. The inferior vessels were resected for functional preservation of the parathyroid gland is possible. Therefore, in patients with advanced pharyngolaryngeal cancer who underwent pharyngolaryngeal resection and bilateral neck dissection [Level Ila, III, IV minimally] were enrolled in this study. Among them, 12 were male and one was female. The mean and standard deviation of age of these patients were 64.0 and 8.8. Ten cases had hypopharyngeal cancers, 2 had laryngeal cancers and 1 had cervical esophageal cancer. In 10 of 13, the contralateral parathyroid gland was preserved. The level of intact PTH was measured preoperatively, during operation, just after operation, and on day 1, day 3, 1 week, 2 weeks, 1 month and 3 months postoperative. In 9 patients, in whom the parathyroid was successfully preserved, the values of intact PTH were 38.9+5.9, 12.7+5.5, 10.6+3.8, 10.9+8.6, 9.2+5.0, 22.4+12.7, 26.6+12.4 and 29.3+11.8, respectively. Intact PTH decreased within a week, however, it increased significantly at 2 weeks postoperative. Compared with the time-course of intact PTH of 3 cases with total parathyroidectomy, successful preservation was not possible within a week. These results indicate that evaluation of parathyroid function at 2 weeks postoperative by measuring the level of intact PTH might be useful for deciding whether or not to stop calcium replacement therapy.
Background: Comorbidity has an impact on survival in laryngeal cancer in several reports. The 5-yr survival for laryngeal cancer is expected to be 65%, those for hypopharyngeal cancer is around 40% and perhaps the lowest of all cancer sites in the head and neck. Reasons of this are considered that a majority of patients are diagnosed at advanced stage and have a poor general condition. However, the importance of comorbidity in hypopharyngeal cancer has not been reported. Objective: To assess the impact of comorbidity measured with Adult Comorbidity Evaluation-27 (ACE-27), which was especially designed for cancer patients and developed by Piccirillo based on the modified Kaplan-Feinstein Index, on survival in patients with hypopharyngeal cancer. Methods: A retrospective medical record review of 156 patients with previously untreated squamous cell carcinomas of the hypopharynx treated at Hokkaido University Hospital between 1995 and 2005 was performed. We measured comorbid illness applying the ACE-27. Survival analysis was performed using the Kaplan-Meier method (with the log-rank test value being used to compare groups). A Cox proportional hazards model was used to determine factors related to overall survival. Results: The ages of all patients included in this study ranged from 43 to 86 years (median, 62 years). One hundred and fifty patients were men (96.2%). As an initial treatment, radiation therapy with/without chemotherapy was performed in 102 patients, and surgical resection was performed in 52 patients. Fifty-five patients (35.2%) had no comorbidity, 39 (25%) had mild, 28 (17.9%) had moderate, and 34 (21.8%) had severe. Comorbidity was not related to age, clinical stage, subsite, and treatment. The 5-yr overall survival rates of clinical variables were: patients older than 75 years (n=14, 14.3%), those younger than this age (n=142, 40.7%); TNM clinical stage I-III (n=55, 57.3%), stage IV (n=101, 27.7%); pyriform sinus primary (n=122, 41.5%), posterior wall or postcricoid primary (n=34, 26.5%), and moderate or severe comorbidity (n=62, 27.7%), no or mild comorbidity (n=94, 45.1%). Log rank test p values were <0.0001 for age, <0.0001 for clinical stage, <0.0001 for subsite, and 0.0073 for comorbidity. Patients treated by radiotherapy and by surgical resection as an initial treatment had similar 5-yr overall survival (37.3% and 41.3%, respectively). Clinical stage, age, and comorbidity were identified as independent prognostic factors in the multivariate analysis. Conclusions: This study demonstrates that comorbidity measured with ACE-27 is significantly associated with survival in a group of patients with hypopharyngeal cancer. Comorbidity information should be taken into account in the care of hypopharyngeal cancer patients as well as TNM clinical stage.

Objective: To describe, in patients with head and neck cancer, the identification by pre-operative PET scan, of second primary carcinomas occurring outside of the upper aerodigestive tract. Methods: Case series. All patients were seen by head and neck surgeons at 2 tertiary care centers. Results: Five patients were identified. Two patients had squamous cell carcinoma (SCC) of the larynx, 1 had SCC of the base of tongue, 1 had non-Hodgkin’s lymphoma of the nasopharynx and 1 had undifferentiated carcinoma of the nasopharynx. Of the 5 second primary tumors identified 3 were papillary thyroid carcinomas and 2 were adenocarcinomas of the colon. The uptake on PET scan of the head and neck primaries ranged from a SUV of 4.65 to 15.1 and in the second primaries from 3.3 to 16.4. Conclusions: In the setting of head and neck cancer, second primary malignancies occur in approximately 20 percent of cases. Typically, emphasis is placed on identification of synchronous or metachronous lesions in the upper aerodigestive tract. The use of pre-operative PET scan imaging in the patients in this series allowed for detection of second primaries outside of this region. In patients with head and neck cancer, PET scans may provide a more comprehensive evaluation than other approaches in the identification of second primaries.

Introduction: Accurate staging of patients with head and neck squamous cell carcinoma is critical in choosing appropriate treatment algorithms. Approximately 5 to 10% of patients presenting with head and neck squamous cell carcinoma will harbor distant metastasis, radically altering both the natural history and treatment approach. The most commonly involved sites outside of the upper aerodigestive tract are the lung, bone, liver, and brain. From 2000 to 2007 72 previously untreated patients with squamous cell carcinoma of the base of tongue were treated at our Institution. Of these, 23 had initial non-surgical treatment with curative intent and underwent PET scanning following this treatment. There were 21 men and two women with an average of 59 years and range from 38 to 76 years. Three patients had group stage II disease, five patients had stage III disease, and 15 had stage IV disease. Two patients had primary radiotherapy as initial treatment. Twenty patients had initial concurrent chemoradiotherapy. One patient had induction chemotherapy followed by radiotherapy. Six patients underwent subsequent neck dissection for suspected persistent neck disease. Two underwent subsequent primary and neck dissection for persistent local and neck disease. All PET scans were performed at least eight weeks following treatment. Results: Seventeen patients had a complete response at the primary site and neck. Two had a complete response at the primary site but persistent disease in the neck. Four patients had persistent disease at both the primary and neck. The PET scan accurately defined disease status in 17 of the patients (74%). There was one false negative PET (neck disease) and five false positives (4 at the primary site). This yields a sensitivity of 86% and specificity of 96%. The positive predictive value is only 55%. The negative predictive value is 92%.
Conclusion: The PET scan is a valuable tool in the assessment of a patient who has completed a course of non-surgical treatment for base of tongue cancer. It can be used to identify those patients who should be considered for surgery for possible persistent disease. Because of its high negative predictive value, patients with a negative PET scan can be observed. However, the high false positive rate renders a positive scan less useful.

P571: CAN 18F-FDG PET/CT REPLACE CONVENTIONAL WORKUP IN STAGING PRIMARY NASOPHARYNGEAL CARCINOMA? T.Ten1, S.Chan1, J.T.Chang2, H.Wang2, S.Ng2, C.Liao2, C.Lin2, K.Fan2, C.Huang3, S.Wu4, 1Chang Gung Memorial Hospital, Taoyuan, Taiwan, Republic of China; 2Chang Gung Memorial Hospital, Taoyuan, Taiwan, Republic of China; 3Chang Gung Memorial Hospital, Taoyuan, Taiwan, Republic of China; 4Chang Gung Memorial Hospital, Taoyuan, Taiwan, Republic of China

Objective: The clinical usefulness of 18F-FDG positron emission tomography/computed tomography (18F-FDG PET/CT) in TNM staging of primary nasopharyngeal carcinoma (NPC) has not been elucidated. We prospectively compared 18F-FDG PET/CT and conventional staging workup in the evaluation of NPC at diagnosis. Methods: A total of 111 patients with pathologically proven NPC were enrolled. They underwent both 18F-FDG PET/CT and the conventional imaging workup including head and neck MRI, chest CT, abdominal scan, sagittal CT, and bone scan. A commercial treatment planning system and the deformable image registration tools in the planning of radiation therapy for head and neck cancer. Because addition of PET/CT to the conventional imaging workup including head and neck MRI, chest CT, abdominal scan, sagittal CT, and bone scan. A commercial treatment planning system and the deformable image registration tools in the planning of radiation therapy for head and neck cancer. Because of its high negative predictive value, patients with a negative PET scan can be observed. However, the high false positive rate renders a positive scan less useful.

P572: CAN PET OR PET/CT ACQUIRED IN NON-TREATMENT POSITIONS BE ACCURATELY REGISTERED TO RADIATIONPLANNING CT? A.B.Hyng1, S.L. Bacharach1, S.S.Yom1, J.M Quivey1, B.L. Fran1, J.Xia1, 1University of California San Francisco, San Francisco, CA

Purpose: Dual modality imaging combining positron emission tomography (PET) and computed tomography (CT) is playing an important role in the planning of radiation therapy for head and neck cancer. Because PET/CT (and stand-alone PET) data are usually not acquired in the radiation therapy treatment position, methods for image registration of PET/CT data with the treatment planning CT are increasingly important. Most image registration tools offered by commercial treatment planning systems use a rigid body transformation. Because of differences in the position of the neck in the diagnostic PET/CT and the treatment planning CT scans, rigid body image registration alone may not accurately align the neck and head simultaneously, resulting in compromised image registration in both regions. The purpose of this study is to quantify errors with the rigid body transformation and potential improvement with deformable image registration. Materials and Methods: PET/CT and treatment planning CT image data from twelve patients treated for head and neck cancer were selected for this study. The rigid body registration toolkit provided by a commercial treatment planning system and the deformable image registration tools in another software package were evaluated. The registration accuracy was first quantified by measuring the contour overlaps of normal structures and differences in the center of mass (COM) positions of these structures. The registration accuracy for the tumor volumes was determined by computing the difference in the COM positions. For rigid body registration, we also compared the results of automated and manual methods. Furthermore, the registration of stand-alone PET images with treatment planning CT images was compared with the registration of PET/CT data with treatment planning CT. Results: With the use of PET/CT and manual rigid body registration, registration errors for normal structures ranged from 3.2+-0.9 mm for the brain to 8.4+-4.3 mm for the spinal cord. The average difference in COM positions for the tumor volumes was 4.1+-2.3 mm. With PET images alone and rigid body registration, registration errors for normal structures ranged from 4.8+-2.6 mm (brain) to 9.9+-4.8 mm (spinal cord). Deformable registration of the PET/CT data to the treatment planning CT data resulted in registration errors of 1.4+-1.2 mm for the brain and 5.4+-2.3 mm for the mandible. In general, manual registration gave superior results to automated registration and deformable image registration generally yielded results superior to rigid registration. It was found that the registration errors tended to increase for tumor volumes located more inferiorly (i.e., lower in the neck). Conclusions: The incorporation of PET data in the head and neck radiation therapy planning process is possible with the use of image registration algorithms. Registration accuracy is better in the head than in the neck due to changes in patient position. The use of PET/CT improved the accuracy over stand-alone PET, and the use of deformable registration can provide further improvement.

P573: VALUE OF PET SCAN IN TREATMENT DECISION MAKING FOR NODAL METASTASES IN SCHNC: SINGLE INSTITUTIONAL UPDATE R.Ray1, Y.Lap也成为2, M.Ammar2, S.Nissel-Harowitz1, A.Caramalis1, J.Marsh1, J.Pollack1, S.Dubner1, B.Mehrotra1, Long Island Jewish Medical Center, New Hyde Park, NY

Objective: Management of nodal neck disease in pts. with SCHNC treated with CRT (chemoradiotherapy) remains controversial. We evaluated the utility of PET scans in monitoring response to therapy and in determining the role of neck dissections (ND) in patients presenting with HNC stages N2b or higher, treated with combined CRT. Methods: A retrospective review of medical records of all pts. treated at our institution with HNC Tx N2b, N2c or N3 between the years 2002-2007 was undertaken. IRB approval was obtained for this study. To be eligible for this analysis, pts. must have had baseline and follow up PET scans at the end of CRT and prior to ND. Data regarding age, gender, primary tumor site, stage, baseline and follow up PET scan results, operative pathology of ND when performed, and local control were recorded. Results: Thirty six eligible patients were identified. Median age was 56 (range: 37-84) yrs; M:F ratio:30:6. Primary site of tumor was: Lip and oral cavity (n=24); Pharynx: n=28 (Tonsil: n=18); Hypopharynx: n=2; BOT: n=5; oropharynx: n=3); Larynx: n=3. Stage distribution: IVA: n=32; IVB: n=4; Nodal stage: N2b: n=25; N2c: n=8; N3: n=3. At the first post CRT assessment: PET scan was negative at primary and nodal sites: n=25 (69%); positive at primary/ nodal sites: n=11 (31%); primary site only: n=2; nodal site only: n=7; both primary and nodal site uptake: n=2. Twenty three of twenty five patients (92%) with negative post CRT, remain in complete remission at a median follow up of 19 months. ND data are available in 9 of 11 pts. that had a positive PET scan post CRT. Six of nine pts. with positive post CRT PET had SCC noted in post CRT ND. Three of nine pts. with positive PET had no disease found on ND, however, 2 of these 3 pts. had a PET scan post CRT performed <8 weeks post completion of treatment. Conclusions: Post CRT PET scan negativity predicts for an extremely favorable outcome. To reduce false positive rates, follow up PET scans should be performed no sooner than 8 weeks post CRT. PET scan positivity after 8 weeks post CRT, either at the primary or nodal site, predicts high probability of persistent nodal disease detected during ND.

P574: EVALUATION OF RESIDUAL/RECURRENT SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY AND OROPHARYNX WITH FDG PET-CT M.V.Spampinato1, K.Spicer1, T.Rumboldt1, L.Gordon1, T.A-Day1, Z.Rumboldt1, 1Medical University of South Carolina, Charleston, SC

Purpose: The study goal is to assess the clinical utility of [18F] Fluorodeoxyglucose Positron-Emission Tomographic CT (PET-CT) in the assessment of recurrent or residual disease in previously treated patients with oral cavity and oropharyngeal squamous cell carcinoma. Materials and Methods: We retrospectively reviewed records of patients referred for PET/CT scanning over an 8-month period with clinical suspicion of residual or recurrent squamous cell carcinoma of the oral cavity and oropharynx based on the onset of new symptoms and/or new clinical findings. We included in the study 18 subjects (average age 60.9+/-12.2, 12 males) for which pathology correlations (12 cases) or clinical follow-up of at least
Second primary cancers and distant metastases are the major concerns at initial staging or during mean follow-up of 15 months after treatment. The addition of PET may result in a relatively modest improvement in neck staging of head and neck cancer patients. Larger studies are needed to confirm this finding.

Current Series: Neck Sides Dissected

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P578: VERY EARLY CHANGES IN FDG METABOLISM DURING CHEMOTHERAPY CORRELATES TO HISTOPATHOLOGICAL TUMOR RESPONSE

Aim: To investigate the histopathology underlying uptake of 2-Deoxy-2-[18F]fluoro-D-glucose (FDG) in sequential positron emission tomography scans.
Methods: This review examined the effectiveness of positron emission tomography (PET) scans during cytotoxic therapy in a solid head and neck squamous cell carcinoma (HNSCC) model. Methods: Nude mice with xenografted tumour were treated with cisplatin at day 0. FDG-uptake was measured at day 1, 2, 5 and 8 using phosphor-image screens. Regions of interest (ROI) were delineated and the FDG-uptake in each ROI was correlated with the underlying histopathology. Results: The level of FDG-uptake correlated with the proportion of viable tumour cells. A transient increase in FDG-uptake was seen in the treatment group at day 1, but uptake decreased subsequently and already on day 2 a substantial decrease was noted, which was histopathologically correlated to an increasing proportion of cells undergoing necrotic changes. A small amount of reactive cells was observed, without impact on metabolic early therapy evaluation. Conclusions: We have demonstrated that early prediction of response to chemotherapy is possible in a solid tumour cell line and that reactive cells do not cause false positive findings in this setting.

P579: PET-NECK: CHALLENGES FACED IN SETTING UP A COLLABORATIVE MULTI-CENTRE CLINICAL SURGICAL TRIAL IN A HEAD AND NECK CANCER Institute for Molecular Medicine, St James's University Hospital, Leeds, United Kingdom; 7Institute of Health Sciences, University of Leeds, Leeds, United Kingdom; 6Leeds Teaching Hospitals, Head and Neck Studies and Education, University Hospital Coventry, Coventry, United Kingdom; 4Dept of Maxillofacial surgery, Faculty of Medicine & Health, University of Birmingham, Birmingham, United Kingdom; 5Paul Strickland Scanner Centre, Mount Vernon Hospital, Northwood, United Kingdom; 5Leeds Institute for Molecular Medicine, St James’s University Hospital, Leeds, United Kingdom; 1Institute of Health Sciences, University of Leeds, Leeds, United Kingdom

Objectives: Neck dissection significantly improves loco-regional control and survival for people with locally advanced (N2/N3) head and neck squamous cell carcinoma (HNSCC) who partially respond to chemoradiotherapy. However the role of radical neck surgery is unclear for those who completely respond, despite most UK patients receiving it. Simultaneously increasing access to PET-CT scanning is increasing and may offer much greater accuracy in the staging of head and neck cancer post-chemotherapy. Thus, are such patients being over-treated and can this be prevented? PET-NECK is a multi-centre, randomised trial comparing PET-CT guided ‘watch and wait’ with planned neck dissection for the management of locally advanced neck nodal metastases in 560 patients with HNSCC. The objectives are to compare overall and disease-specific survival and to assess predictive value of PET-CT scanning in detecting persistent/residual disease, as well as Quality of life and health economic impacts. PET-NECK has received great support of life and health economic impacts. PET-CT has been pre-set video explaining the study for the patient to see, before talking to the recruiting clinician about the study. 4. Setting up a central PET-CT Core Laboratory to quality-assure every PET-CT and report in real time, after it has been reported locally and before it was utilised clinically for decision. 5. Adopting a unified pathology processing and reporting standard in participating pathology departments. Conclusions: There are significant but interesting challenges in setting up a multi-centre surgical trial in head and neck cancer. Valuable lessons have been learnt which may aid other investigators when setting up such trials.

P580: PRIMARY TUMOR EVALUATION BY PET/CT IN ORAL CYST CANCER PATIENTS WITH DENTAL ARTIFACTS IN CT OR MRI IMAGES C.Baek1, H.Heong1, M.Jeong1, Y.Son1, Y.So1, J.Jang1, K.Park1, 1Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Objectives: To investigate the clinical usefulness of PET/CT or CT attenuated PET in the evaluation of primary tumors in patients with oral cavity cancer (OCC), in whom the conventional images (CT or MRI) of the oral cavity were distorted by dental artifacts. Methods: PET/CT has been performed for sixty-nine OCC patients with dentures or dental implants, along with CT or MRI. Among them, 64 PET/CTs, 64 CTs and 27 MRIs were available for analysis. The performance of CT attenuated PET to evaluate the primary tumors was compared with CT or MRI. In addition, subgroup analysis was performed to determine which portion of subjects could benefit more from PET/CT. Results: CT attenuated PET images had a higher performance to detect primary tumors in OCC patients with dental artifacts than CT (95.3% vs. 75.0%, P=0.0016). By measuring the serial pathological volume and the manual CT attenuated PET volume, we could get the regression equation between results of the two methods: log (Pathology Vol.) = 1.283 x log (PET/CT Vol.) -0.01862 (R2 = 0.620, P<0.0001). Subgroup analysis showed that the prediction of pathological volume from PET/CT images was more reliable in tumors more than P<0.05 in T stage and 2 cm in depth (R2 = 0.703 and 0.669). Conclusion: In OCC patients with dental artifacts in the conventional images, PET/CT could provide useful clinical information about the primary tumors, particularly of the advanced T-stage tumors.

P581: IMPACT OF PET/CT FUSION ON CLINICAL DECISION MAKING IN THE MANAGEMENT OF SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK K.Amini1, B.A.Schiff1, R.Moadel1, K.Shifteh1, R.V.Smith1, 1Albert Einstein College of Medicine, Bronx, New York

Objective: To determine whether PET/CT fusion adds sufficient information to change the management of patients with head and neck squamous cell carcinoma (HNSCC) when compared to standard radiographic and nuclear imaging. Methods: Records of patients who had undergone CT or MR, and PET/CT fusion for evaluation of HNSCC were reviewed. All imaging data was re-evaluated by the nuclear medicine and neuroradiology departments in accordance with specific guidelines established by the head and neck surgical staff. CT/MR, PET, and PET/CT fusion readings were performed. Clinical and imaging data was presented in various combinations in blinded fashion to two head and neck surgeons who made management recommendations. Results: 32 patients, 21 male and 11 female, ages 36 to 88 (average 60) were identified to provide 34 data sets (2 patients had 2 data sets). Pathology included squamous cell carcinoma of the larynx (38%), oropharynx (29%), hypopharynx (15%), nasopharynx (9%), oral cavity (6%), and paranasal sinuses (3%). 11 data sets involved pre-treatment decision making while 23 data sets involved post treatment analysis. The post-treatment data sets included patients treated with chemotherapy and radiotherapy (52%), surgery, chemotherapy and radiotherapy (26%), surgery and radiotherapy (13%), surgery (4%), and radiotherapy (4%).

P582: A SYSTEMATIC REVIEW AND META-ANALYSIS OF PET IN THE FOLLOW UP OF HEAD AND NECK CANCER FOLLOWING RADIOTHERAPY M.G.Isles1, H.Mehanna1, 1University Hospital Coventry, Coventry, United Kingdom

Objectives: This review examined the effectiveness of positron emission tomography (PET) in the detection of recurrent or persistent head and neck squamous cell carcinoma (HNSCC) after radiotherapy or chemoradiotherapy. Methods: A systematic review and meta-analysis of trials of PET for detecting residual/recurrent HNSCC treated by radiotherapy or chemoradiotherapy. Inclusion criteria were prospective and retrospective studies, excluding reviews, which included patients with head and neck squamous cell carcinoma who had FDG-PET in the post-treatment phase, following primary treatment by radiotherapy or chemoradiotherapy. Trials were quality assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool for assessing diagnostic accuracy studies. Quantitative data was extracted and a bivariate random effects model was used to cal-
culate pooled sensitivity and specificity. The main outcome measures were the quality assessment, sensitivity, specificity, false positive rates, false negative rates, positive and negative predictive values. Descriptive data is also discussed. **Results:** 27 of 1871 identified studies were eligible for inclusion. The pooled sensitivity and specificity of PET for detecting residual or recurrent head and neck squamous cell carcinoma at the primary site were 93.7% (95% CI, 87.4% to 96.9%) and 81.9% (95% CI, 75.9% to 86.1%) respectively. Positive and negative predictive values were 75.2% (95% CI, 67.6% to 81.6%) and 95.2% (95% CI, 91.5% to 97.1%) respectively. **Conclusion:** PET is highly accurate for detecting recurrent or residual Head and Neck cancer following radiotherapy or chemoradiotherapy, especially in the context of excluding residual or recurrent disease due to the very high negative predictive value. PET may reduce the requirement for check endoscopies and planned neck dissections. However, it is less sensitive early after treatment. A protocol for its use in post treatment surveillance is proposed.

**PS83: CURRENT TRENDS AND USAGE OF THE PET/CT: A SURVEY OF THE AMERICAN HEAD AND NECK SOCIETY**

**Purpose:** To assess the current trends and usage of positron emission tomography (PET) and the head and neck oncology patient population of members of the American Head and Neck Society. **Methods:** A written survey was mailed to all current members of the American Head and Neck Society. Respondents were queried on the role of PET/CT in their practice. They were also asked about their usage of PET/CT in diagnosis and routine evaluation in the head and neck oncology patients in their practice. **Results:** Two-hundred and Forty Two (242) surveys were returned out of 705 putting the effective response rate at 35%. 84% of respondents reported Otolaryngology as their specialty. An overwhelming majority (97%) reported using PET/CT in their practice. 67% of those queried felt that PET/CT always had a role in patients with unknown primary. The usage of PET/CT in newly diagnosed, recurrent cancer, and routine surveillance varied depending on specialty, years in practice and percentage of practice dedicated to head and neck oncology. **Conclusion:** The use of PET/CT varies widely among specialties treating head and neck oncology patients. The exact role of PET/CT has not yet been defined in the head and neck oncology patient population.

**PS84: EVALUATION OF PET/CT SCAN ASSOCIATED ANXIETY**

**Objective:** Anxiety is a common symptom experienced by patients who are diagnosed with head and neck cancer. These patients often receive PET/CT scans as a part of their standard of care. There is minimal, previous research to indicate how much anxiety is induced from receiving a PET/CT scan, and the time that elapses before they are provided with results from this procedure. The objective of this study is to measure the amount of anxiety experienced by patients who receive a PET/CT before they are provided with the results. **Methods:** In this pilot study patients completed the Spielberger State Trait Anxiety Tool (STAI) after receiving a PET/CT scan. This tool is a 40 item self-rated survey, which measures the current emotion, anxiety state (S) and compares it to their general personality trait (T) or tendency for anxiety. For the purpose of this study the anxiety experienced after receiving a PET/CT scan and before they are informed of their results is measured. Patients completed the inventory between 1-9 days after receiving their PET/CT scan and before they were provided with the results of the scan. Additional variables included: age, sex, the number of PET/CT’s prior to this survey and diagnosis. **Results:** Preliminary findings indicate that 70% of the patients in this study were male. The average age of study participants was 55 years. The median time lapse between the PET/CT and notification of results is 2.8 days (min 0-max 9 days). Males scored an overall average of the State and Trait-S4 (SD 11.9; S for 8 and 9.9) for females compared to 43 females (SD 4.1 9 and 3.3), which appears to be in the mid/normal range for general anxiety. 47% of these patients were diagnosed with SCCa of the tonsil, tongue, or mouth. Clinical findings indicate an increase in anxiety levels between patients who received their diagnostic PET/CT scan compared to those who have had between 2-10 PET/CT scans is as follows: S mean scores of 41 (diagnostic PET/CT) [+10.2] compared to 36 (+11.5) [patients who received between 2-10 PET/CT’s]; T mean scores of 41 (+3.9) (diagnostic PET/CT) compared to 36 (+9.8) [patients who received between 2-10 PET/CT’s]. **Conclusion:** These preliminary findings tend to correlate to other publications and studies where the STAI has been used. Because there is little research in this area, there are no identified norms. Additional research may highlight trends and norms. Points of future consideration will be to evaluate the significance of measuring the difference in scores between genders, as males tend to under report emotional states. With an increase in our sample size, further assessment will be made to compare patient-based or diagnosis, and continued research is essential to evaluate if the anxiety experienced by those patients who receive their initial diagnostic PET/CT would benefit from further preparation prior to receiving this scan.

**PS85: RELATIVE SUV IN PET-CT STUDIES OF HEAD AND NECK TUMORS: WHICH RATIO IS MORE REPRODUCIBLE?**

**Z. Rumboldt1, B. Sisdas1, K. Spicer1, B. Panzeagrau1, M. Medical University of South Carolina, Charleston, SC**

**Purpose:** The variability of mean and maximum glucose uptake value (SUV) in head and neck tumors is a major drawback in longitudinal studies. We hypothesize that this may be overcome by defining tumor SUV relative to non-tumor tissues and to determine which ratio of tumor to normal tissue SUV is optimally reproducible for follow-up studies in head and neck tumors. **Materials and Methods:** Fifteen patients (7 male, 8 female; mean age ± SD: 60 ±11 y) with histologically proven primary tumors in the head and neck underwent PET-CT examinations of the whole body including a dedicated head and neck PET/CT acquisition. The patients were re-examined after 5.4 ±1.7 months for follow-up of the treated tumors. Maximum (SUVmax) and mean (SUVmean) SUVs were measured from both sessions using standardized regions-of-interest (ROIs) in left frontal cortex (85 mm2) and in right psoas muscle (65 mm2) for both PET/CT surveys. Reproducibility analysis including Bland-Altman plots were performed in order to identify the most reproducible measurement. **Results:** The mean SUVmax in the tumors was 15.3 ±4.1 (95% CI: 9.9-20.5). The mean ratio (Ratio 1) of tumor SUVmax to cortex SUVmax was 1.2 ±0.7 (95% CI: 0.85-1.58). The mean ratio (Ratio 2) of tumor SUVmax to psoas SUVmax was 15.5±5.5 (95% CI: 11.8-19.2). The coefficient of variation for Ratio 1 was 66.4% and the coefficient of variation for Ratio 2 was 35.2%. The mean SUVmax in frontal cortex was 9.2±3.5 in the first session and 10.1±4.9 in the re-session. The mean difference was 3.1 and the 95% limits of agreement were -5.5 to 7.8. The mean SUVmax in the psoas muscle was 1.1±0.3 and 1.0±0.2 in the first and follow-up examinations, respectively. The mean difference was 0.03 and the 95% limits of agreement were -0.9 to 0.9. The within-subject coefficient of variation, the repeatability coefficient, and the significant change for a single subject for the SUV in frontal cortex were 30%, 39.58, and 85%, respectively. The within-subject coefficient of variation, the repeatability coefficient, and the significant change for a single subject for the SUV in psoas muscle were 8%, 0.75, and 28%, respectively. The mean SUVmean followed the same pattern of reproducibility than the SUVmax. **Conclusion:** The SUVmax and SUVmean measurements of psoas muscle are more reproducible than the corresponding measurements in frontal cerebral cortex, and the head and neck tumor SUV to psoas muscle SUV ratio is more suitable than the tumor SUV to cerebral cortex SUV ratio for evaluating longitudinal head and neck studies and response trials.

**PS86: CORRELATION BETWEEN PERFUSION CT AND GLUCOSE UPTAKE MEASUREMENTS IN SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK**

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**Purpose:** To determine the agreement between perfusion CT (PCT) and fluorine-18-fluorodeoxyglucose (FDG) positron emission tomography (PET) studies in the tumor tissue delineation as well as the correlation between the values of both modalities in patients with squamous cell carcinoma (SCC) of the upper aerodigestive tract. **Materials and Methods:** Ten patients with histologically proven primary and recurrent SCC (7 male, 3 female, mean age (SD): 61.4±11.3) underwent PCT and FDG-PET-CT studies at the same time using a 16-slice PET-CT unit. Images after differential head/neck acquisitions were produced from ordered subset expectation maximization (OSEM) reconstructions with filtering (2 iterations of 30 subsets utilizing a Gaussian blurring filter). Orthogonal slices images were...
interpreted in standardized preset window level. PCT maps that represented blood flow (F) (in mL/min/100g), blood volume (V) (in mL/100g), mean transit time (MTT) (in s), and permeability (PS) (in mL/min/100g) were also generated using deconvolution-based analysis. Two neuroradiologists in consensus outlined the tumor borders separately in the P-FCT maps and in the PET-CT maps. Gross tumor volume and whole tumor quantitative perfusion and mean as well as maximum standardized uptake values (SUV) were recorded. This was performed for the agreement between the gross tumor volume measurements. Pearson correlation coefficients were applied to examine for statistically significant relationship between perfusion values and maximum SUV. Results: The delineation of tumor tissue was in agreement between PCT (24.04 mL) and PET (20.82 mL) studies (p-value=0.42). The mean SUV, F, V, and PS in the SCC were 99.38±46.85, 6.46±1.87, 7.85±2.67, 20.15±8.26. All perfusion parameters were significantly different between SCC and muscle tissue (p-value<0.01). The maximal SUV in the muscle tissue and in the tumor sites was 1.74±1.21 and 20.59±8.45, respectively. Significant correlation was revealed between F and maximal as well as mean SUV (r=0.82 and r=0.75 with p-value<0.0001) and between MTT and maximal SUV (r=-0.45 and r=-0.49 with p-value<0.03) Not significant correlations were observed between V and maximal SUV (r=0.56, p-value=0.1) and PS and maximal SUV (r=0.18, p-value=0.4). Similarly, not significant correlations were demonstrated between V, PS values and mean SUVs. Conclusion: The delineation of tumor tissue based on PCT and FDG-PET maps is feasible and leads to not significantly different values. There was a positive significant correlation between F as well as MTT and SUV in SCC sites suggesting a coupling between blood flow and glucose uptake.

P587: WITHDRAWN
LARYNX II

P588: LARYNGECTOMY AFTER PREVIOUS RADIODIOTHERAPY Van der Putten 1, R. de Brei 1, D.J.Kuik 1, D.H.F.Rietveld 1, S.E.J.Eerenstein 1, C.Rene Leemans 1, 1VU University Medical Center, Amsterdam, The Netherlands

Objective: Firstly, with the low survival and high complication rates reported in literature for salvage laryngectomy after (chemo)radiotherapy, one might argue whether it is worthwhile and safe to perform laryngectomy after previous non-surgical treatment. Secondly, there are arguments for a partial laryngectomy in a selected patient group. And thirdly, there are no clear guidelines for the management of the neck in combination with a laryngectomy in a non-surgical treated patient. Therefore, we aimed to analyze the outcome of laryngectomies after non-surgical treatment, a retrospective analysis of all patients who underwent laryngectomy after previous (chemo)radiotherapy for a squamous cell carcinoma between November 1990 and June 2007 was performed. Survival rates, complication rates, and functional outcome were determined. Partial laryngectomy, total laryngectomy, and salvage laryngectomy were compared. Moreover, the management of the neck was retrospectively analysed. Results: Of the 191 patients that were included, 35 underwent partial laryngectomy (with or without a subsequent total laryngectomy) and 156 a total laryngectomy. The 5-year disease specific survival rate was 58% (partial laryngectomy 74%, total laryngectomy 55%; p=0.09). The surgical margins of the primary tumor site (p=0.001), the age at laryngectomy (< or > than the median 65 years) (p=0.004), the extension of the laryngectomy (p=0.044), the primary tumor site (p=0.047) and symptomatic disease (p=0.04) were significant predictive variables for the disease specific survival in multivariate analysis. The status of surgical margins of partial laryngectomy was worse as compared to those of the total laryngectomy (p=0.02), and for the total laryngectomy after partial laryngectomy those seemed worse as compared to those of the primary laryngectomy after previous (chemo)radiotherapy (p=0.06). The complication rate was 58%: 34% minor and 24% major complications (total versus partial laryngectomy, Trend test p=0.04, in favour of partial laryngectomy). Smoking was a significant independent predictor for postoperative major complications (p=0.01). Of all patients, 84% was able to have a ‘normal’ or ‘soft’ diet, and there was no significant change in body mass index (BMI). All patients with partial laryngectomy could be decanulated, and 85% of the patients with total laryngectomy were able to produce speech with a voice prosthesis. Lymph node metastases were found in 25% of the neck dissections, with significantly more regional disease at higher initial T-stage (p=0.006). Regional recurrences after selective neck dissection were only observed in combination with a local recurrence. Conclusion: For operable patients laryngectomy after previous radiotherapy offers a reasonable survival with an acceptable risk of complications and a good functional outcome. Optimal selection, especially for conservative laryngectomy and selective neck dissection is warranted.

P589: VERTICAL HEMILARYNGECTOMY WITH IMBRICATION LARYNGOPLASTY (VHIL) EARLY GLOTTIC CARCINOMA E.Luna-Ortiz 1, V.Luengo-Velencia 1, R. Riviera-Lazano 1, P.Pasche 1, F.R.Nieto-Velencia 1, 1Instituto Nacional de Cancerologia, Mexico City, Mexico; 2Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

Objective: To evaluated functional, complications, relapse and survival and organ preservation in patients treated with VHIL Methods: Patients treated due to early glottic carcinoma by VHIL where time of hospitalisation, tracheotomy time and nasogastric tube feeding where evaluated. As grade of aspiration according to Pearson and Lezingh. Phoniatric evaluation were done once the tracheotomy was close. Relapse, survival and organ preservation were evaluated. In all cases Delphian lymph node was search intentionally. Results: 8 patients with a mean age of 63 years old were treated, the mean time of hospitalization were 3 days, tracheotomy mean time was 2 days, all patients were discharged without tracheotomy, no patient need nasogastric tube feeding all patients were able to eat the next day of surgery, 1 patient developed cutaneous emphysema no need special treatment. In one patient a positive Delphian node found, so we did a bilateral neck dissection. Palliative neck dissection showed changes in intensity, duration time of phonation which is acceptable due to loss of glottic closure. One patient relapsed at 36 months of follow up and was treated by Supracricoid partial laryngectomy with Cricothyroidoepiglottopexy now this patient is a 54 months of follow up. All patients are alive at mean time of follow up of 36 months. Organ preservation was archived in all cases. No patient need radiation. Conclusion: VHIL is an excellent option in the era of LASER surgery, where no accessibility to this technology is possible. Quality of life in those patients is as normal as before the treated by VHIL. When relapse is diagnosed early always is possible to rescue with an organ preservation surgery.

P590: ANALYSIS OF CLINICO-PATHOLOGIC STAGES IN SUPRACRICOID PARTIAL LARYNGECTOMY (SCPL) K.Chop 1, M.Kim 1, Y.Joo 1, D.Sun 1, S.Cho 1, 1The Catholic University of Korea, College of Medicine, Seoul, Republic of Korea

Objective: The oncologic concept of supracricoid partial laryngectomy (SCPL) is complete en bloc resection of entire thyroid cartilage, preepiglottic space, and paraglottic space, which were frequently invaded by tumors and in those cases total laryngectomy was inevitable in the past. In present study, by comparing the preoperative clinical stages with postoperative pathologic stages and also analyzing the causes of recurrence and surgical failure in patients who have undergone SCPL, we tried to recognize the oncologic validity of SCPL and the method to reduce the recurrence. Methods: By reviewing the medical records of 92 patients with squamous cell carcinoma of the larynx who underwent SCPL from 1994 to 2006, we investigated the preoperative clinical and postoperative pathologic stages and analyzed the causes of recurrence and surgical failure in patients who have undergone SCPL. We tried to recognize the oncologic validity of SCPL and the method to reduce the recurrence. Results: Fifteen out of 92 patients (16.3%) were understaged in preoperative T staging due to the invasion of thyroid cartilage in 11 cases, subglottic extension in 3 cases, and preepiglottic space invasion in 3 cases. Elective neck dissecition was performed for sixty-five out of 85 patients who showed cN0 preoperatively and occult metastasis was found in 11 patients (16.9%). Among 82 patients whom we were able to follow up for over 1 years (mean F/U period 49 months), 11 showed recurrences. The local recurrence (LR) was occurred in seven patients (8.5%) and five of them (71.4%) were preoperatively understaged in T stage due to thyroid cartilage invasion. LR rate was significantly higher and overall survival was lower in the patients who were understaged preoperatively compared to those who were staged accurately (p=0.006 and p=0.001, respectively). Conclusions: Preoperative understaging in T stage is closely related to the local recurrence and the survival in SCPL patients and thyroid cartilage invasion is the main cause of the understaging and the recurrence. We suggest the application of extended procedure of SCPL on the basis of thorough preoperative evaluation in locally advanced laryngeal cancers.

P591: COMPLICATIONS AFTER SUPRACRICOID LARYNGECTOMY E.M.Baretto 1, R.C.R.Cervera 1, L.G.Brandao 1, P.Pasche 1, E.R.Nunes Valencia 1, 1Instituto Nacional de Cancerologia, Mexico City, Mexico; 2Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

Objective: To evaluate early and late complications in patients treated with Supracricoid Laryngectomy (SCL) for larynx carcinoma (LC) in institu-
tion and their relations with clinical, histopathological, epidemiologic and surgical factors. **Methods**: Retrospective analysis of medical charts of patients who underwent to a SCL from 1995 to 2007. The influence of clinical, histopathological, epidemiologic and surgical factors on complications was calculated by univariate analysis using with SPSS software v10 (signific-
ant p value < 0.05). **Results**: 141 patients were included and staged according to the UICC 2002 TTNM Classification System. Twenty-four patients were classified as T1a, 6 as T1b, 49 as T2, 23 as T3 (44%). A hundred and thirty six patients (96.45%) were reconstructed using Cricothyoidoepiglottoplasty (CHEP) and 5 (3.55%) with Cricothyoidoepiglottoplasty (CCHP). Overall incidence of complications was 29.80% (42 patients). Thirteen (9.2%) patients had postoperative aspirations, 4 treated with complete laryngectomy. Ten patients had stenosis, 8 late stenosis requiring retracheotomy. Four patients had laryngocoele and 7 patients had pharyngo-cutaneous fistulas. The median hospital stay period was 5 days. One hundred and thirty patients (92.2%) of 141 had successful tracheoto-
my tube decannulation, with a median time to decannulation of 25 days. The median time to removal of the enteral feeding was 30 days. None of the clinical factors (systemic hypertension, diabetes, chronic pulmonary obstructive disease, alcohol and/or tobacco consumption and poor nutri-
tional status were related to the incidence of complications. Twenty-five (17.7%) patients had one arytenoid resected, 6 had stenosis and 4 late stenosis, p=0.002 and p=0.03, respectively. **Conclusions**: One ary-
tenoids' resection was related to the incidence of stenosis. Clinical factors should be well evaluated before surgery, even without a significant p value, because there is a elevated morbidity rate associated with SCL.

**P592: SUPRACRICOID PARTIAL LARYNGECTOMY (SCL) WITH CRICOHYOIDOEPIGLOTTOTOMY (CHEP) IN PATIENTS WITH FAILURE TO RADIATION THERAPY K.Luna-Ortiz 1, P.Pascho 2, V.Villaviciosa-Velazco 1, A.Layin-Lozano 1, Instituto Nacional de Cancerología, Mexico City, Mexico; 2Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland**

**Objective**: To assess the functional results, complications, and success of larynx preservation in patients with recurrent squamous cell carcinoma after radiotherapy. **Methods**: From a data base of 40 patients, who underwent Supracricoid Partial Laryngectomy (SCL) with Cricothyoidoepiglottoplasty (CHEP) from June 2001 to April 2006, eight patients had been treated previously with radiotherapy due to squamous cell carcinoma of the glottic region and were cared for recurrence at the site of the primary cancer. Bilateral dissection of the neck was performed at the II to V levels in some cases, the Delphian node was purportedly searched for in all cases, and surgical margin were transoperatively studied in all cases. Hospital stay was assessed in days, as well as permanence of the tracheostomy and the nasogastric tube feeding. **Results**: SCL with CHEP were performed in six men and in two women with a mean age of 67 years, due to recurrence and/or persistence at a mean time of 30 months after radiotherapy and in case 8 after concomitant chemo-radiotherapy. Bilateral neck dissection from levels II to V was performed in 6 patients, only case 8 presented metastasis in one node, and in case 5 the Delphian node was positive. It was possible to preserve both arytenoids in five cases; surgical margins were transoperatively assessed in all cases. Definitive surgical margins were nega-
tive. Complications were encountered in seven patients. Follow up was in average of 34.5 months (range 1 to 57 months). Organ preservation in this series amounted to 75%, and local control was of 87%. **Conclusion**: Every patient with persistence and/or recurrence after radiotherapy due to cancer of the larynx should be susceptible to organ preservation surgery under similar indications to those of not previously treated patients. Complications can occur just like in not previously irradiated patients; how-
ever, these are usually since radiation, tissue fibrosis, etc. These complica-
tions must be treated conservatively as possible to avoid altering the laryngeal function. In every conservatory surgery, a transoperative study must be performed to determine surgical margins since no other subsequent conservative treatment is feasible and disease-free margins must be ensured.

**P593: COMPLICATIONS AFTER SALVAGE LARYNGECTOMY FOR FAILURE OF RADIATION OR CHEMORADIATION TREATMENT OF CARCINOMA OF THE LARYNX V.N.Young 1, J.M.Bumpous 1, 1University of Louisville, Louisville, KY**

**Objective**: 1) to determine the incidence of complications following sal-
avage laryngectomy after failure of radiation or chemoradiation over a ten-
year course, 2) to identify demographic and historical factors predictive of increased risk of complication, and 3) to assess survival in these patients.

**Methods**: Retrospective review of twenty patients undergoing salvage total laryngectomy for failure of radiation (n=16) or chemoradiation (n=4) was conducted. Among these, six patients had complications, including fis-
tula (in 4 patients), pneumonia (2 patients), acute myocardial infarction (1 patient), abscess (1 patient), and carotid blowout (1 patient). **Results**: Six patients (30%) suffered complications following salvage laryngectomy. Average age was 59 years. All were initially treated with radiation thera-
py alone. However, 14 seconds to 20 seconds. These cases were dead; one from lung metastasis and the remaining two from other causes. **Conclusion**: These results suggested that this reconstruction technique is useful after EHL for advanced glottic carcinoma with subglottic extension, but the further evaluation is needed.
patients with epidermoid laryngeal carcinoma subjected to total laryngectomy during a 5-year period. The following variables were analyzed: T staging, tumor site of origin in the larynx, and presence of mobility or fixation of the arytenoids. These were correlated with the histopathological stage of the lymph nodes obtained during neck dissection (pN). Statistical significance was evaluated with 0632 test. Results: Ninety one patients were included (82 males and 9 females) with a median age of 66 years. The site of tumor was the glottis in 60% of cases, the supraglottis in 20%, and the subglottis in 20%. Fifty-one patients had no metastasis (0N), 13 had N1, and 17 had N+ (N0, N1). Statistical analysis with χ2 and Mann-Whitney test was used. There was no statistical significance between T stage and the presence or absence of lymph node metastasis. Conclusion: The most important prognostic factor in epidermoid carcinoma of the larynx is the presence of metastatic lymph nodes in the neck. Identification of patients with risk of metastasis at the time of the diagnosis is important in planning optimal surgical management. Lack of mobility of the arytenoid cartilage at the time of initial evaluation is a clinical factor associated with the presence of lymph node metastasis in this present series. The presence of glottic and supraglottic tumor infiltration is a risk factor for neck LV metastasis and thyroid infiltration. For patients with epidermoid carcinoma of the larynx who demonstrate arytenoid fixation, laryngectomy should be accompanied by elective neck dissection including thyroidec- tomy when subglottic infiltration exists.

P596: SENTINEL NODE BIOPSY IN PATIENTS WITH CANCER OF LARYNX WITHOUT ELECTIVE NECK DISSECTION C.T.Chone1, J.A.Caixeta2, R.S.Magalhães1, E.Ethecheberê2, E.Camargo1, A.Allamendi1, A.N.Crespo1, 1State University of Campinas, Campinas, Brazil; 2State University of Campinas, Brazi, Campinas, Brazil

Background: The elective neck treatment in patients with squamous cell carcinoma (SCC) of the larynx is the presence of metastatic lymph nodes in the neck. Identification of patients with risk of metastasis at the time of the diagnosis is important in planning optimal surgical management. Lack of mobility of the arytenoid cartilage at the time of initial evaluation is a clinical factor associated with the presence of lymph node metastasis in this present series. The presence of glottic and supraglottic tumor infiltration is a risk factor for neck LV metastasis and thyroid infiltration. For patients with epidermoid carcinoma of the larynx who demonstrate arytenoid fixation, laryngectomy should be accompanied by elective neck dissection including thyroidec- tomy when subglottic infiltration exists.

Methods: Eleven consecutive patients were included in the study of larynx. The presence of lymph node metastasis (N+) was determined by conventional histopathological and immunohistochemistry (IHC) and step serial section (SSS) evaluation, and then the selective lateral neck dissection was done subsequently. On the second group (n=6), only sentinel node was dissected with same histopathological evaluation of the first group. Results: The first group had no metastasis in the sentinel node and in the selective neck dissection, both evaluated with hematoxilin-eosin (H&E) conventional histopathological analysis and IHC and SSS analy- sis. On the second group, one had a positive sentinel node but none had neck recurrence with at least eleven months of follow-up. Conclusion: The sentinel node biopsy is a promising method in head and neck cancer. However, more follow up time, with more patients, is imperative to achieve significant results to establish the sentinel node biopsy without mandatory selective neck dissection as routine for elective treatment of neck.

P597: NODAL STATUS IN ELECTIVE NECK DISSECTION FOR SQUAMOUS CELL CARCINOMA OF THE LARYNX M.M.Abs-Sa- marr1, H.Emam1, A.El Sharkawy1, N.M.Rizk2, Mansoura University, Mansoura Egypt; 2University of Alberta, Edmonton, AB, Canada

Objective: The purpose this study was to: 1) Assess the presence of occult positive nodes at level IV in patients with laryngeal cancer and clinically N0, 2) Assess the efficacy of level IV neck dissection in this patient popula- tion. Methods: A retrospective study was conducted on 54 patients with laryngeal carcinoma with N0 (clinically and radiologically) during the peri- od from 1998 to 2004. All patients had total laryngectomy and selective neck dissection (SND) level II-IV either mono or bilateral, according to the site and extent of the tumor. 25 patients had bilateral SND and 29 patients had ipsilateral SND. The pathology reports for 79 hemi-neck specimens were reviewed to identify the incidence of metastases in occult nodes, the level of nodal metastases, the status of contralateral node dissection, and the presence or absence of extracapsular spread. Results: He cohort was composed of 52 male and 2 female with age ranging from 46 to 68 years (mean 61 years). 48 patients had T3/4 or extensive T2b lesions and 8 patients had recurrent tumors after radiotherapy. 12 out of 54 clinically N0 patients had 21 positive N+ (N0); the occult metastasis rate was 22.2%. All 12 N+ had level II and III positive and only one patient had occult metas- toses at level IV and did not receive pre-operative radiotherapy. Level IV N+ constituted 8.3% of positive occult metastases and 1.85% of clinically N0 patients. Extracapsular spread was reported in 5 nodes among 21 N+ (23.8%), remained confined to level II and level III nodes. Three patients out of 54 had ipsilateral and contralateral N+ (5.5 %). Level IV was not affect- ed and metastases were limited to level II and III nodes. Conclusion: Occult metastasis at level IV in clinically N0 laryngeal carcinoma are rare. Dissecting level IV as part of an elective neck dissection for these patients is not necessary.

P598: THE IMPACT OF THE NUMBER OF LYMPH NODES IN SURVIVAL OF PATIENTS SUBMITTED TO TOTAL LARINGECTOMY A.L.C.Costa1, F.L.Dias1, R.A.Lima1, U.B.Toscano1, J.R.N.Soares2, D.Herchenhorn1, I.C.Santos1, T.P.Farias1, K.L.Fernandes1, E.Q.Freitas1, 1Brazilian National Cancer Institute-BNCI, Rio de Janeiro, Brazil

Introduction: The presence of a metastatic cervical lymph node is a prognostic factor. The literature has demonstrated the importance of a minimal number of lymph nodes to be removed in an oncologic neck dissection (ND). Objectives: Identities of lymph nodes to be removed in a bilateral ND of levels IV of patients submitted to Total Laringectomy. Verify if there is a minimal number of lymph nodes dissected that can change the prognosis of these patients. Methodology: A retrospective study of patients treated for laryngeal epidermoid carcinoma stages III or IV with Total Laringectomy and bilateral ND of levels II-IV. The minimal follow up was superior to 3 months. All patients included in the study had the phar- nyx closed by primary suture and they also had registries of number of lymph nodes dissected in each side of the neck, regional recurrence and distant metastasis. Statistical analysis used: SPSS 10.0 program, with p < 0.05; X2 method; odds ratio; Kaplan-Meier survival curves and log rank test. Results: From an initial group of 257 cases, 154 patients were includ- ed in the study. After surgery, 76.6% of the patients were classified as stage IV and 23.4% as stage III. The average number of lymph nodes dis- sected in levels II-IV at both sides was 38 lymph nodes. In 71 patients (46.1%) this average number was exceeded, with an impact in the overall survival (p<0.05, log rank = 8.43 and OR = 2.65). The regional recur- rence was 11% and there was no relation between the number of lymph nodes dissected and the regional recurrence or the recurrence-free survival. Conclusion: The average number of lymph nodes dissected in bilateral neck dissection of levels II-IV is an important prognostic factor related to survival. Our data suggest that, after a meticulous ND, the patient can change from one stage to another in the oncologic classification. Because of this, the patient can receive a more appropriate oncologic treatment and, therefore, achieve better results.

P599: MANAGEMENT OF EARLY GLOTTIC CANCER: COMPARI- SON OF ONCOLOGIC RESULTS AND LARYNGEAL PRESER- VATION OF DIFFERENT MODALITIIES PChu1, S.Chang2, L.Wang3, J.Huang3, S.Tai3, 1Taipei Veterans General Hospital, Taipei, Taiwan, Republic of China

Objective: The options of management of early glottic cancer include radi- ation therapy (RT), open partial laryngectomy (POL), and transoral laser microsurgery (TLM). However, which treatment modality is the optimal method still controversial, because there is no randomized trial comparing these treatment modalities. Discussion about this issue may be rather ani- mated, and there is a tendency to selectively quote data from the literature to support one’s bias. In this study, we will compare the oncologic results and laryngeal preservation of the patients with early glottic cancer who were treated with these three treatment modalities in our institute. Methods: Retrospective review of previously unreported patients with T1-T2 NO squamous cell carcinoma of glottis received treatment between 1990 and 2000 in Taipei Veteran General Hospital. The treatment choice depends on the physician’s philosophy, patient’s wishes and medical condition. In general, T1a case tends to be treated with TLM, T2 case with limit- ation of vocal cord prefers OPL, and the others may treat with either RT or OPL. Results: There were 296 patients included in this study. Of the 296
cases, there were 289 males and 7 females. Their ages range from 35 to 91 years, with a median of 70 years. There were 82 patients underwent TLM, 108 OPL, and 106 RT. The clinical T stage distribution of TLM, OPL, and RT (T1 vs T2) were 90% vs. 10%, 26% vs. 74%, and 46% vs. 54%, respectively. Tumor with anterior commissure invasion was noted only 24% in TLM, 75% in OPL, and 68% in RT. With a median follow-up of 85 months, the 5-year local recurrence rate was 18% in TLM, 15% in OPL, and 21% in RT (p=0.523). In TLM advanced stages and comorbidity have a 81%, 91%, and 83% (p=0.068), 5-year disease-specific survival (DSS) in TLM, OPL, and RT were 92%, 91%, and 87% (p=0.535), and final laryngeal preservation in TLM, OPL, and RT were 93%, 91%, and 80% (p=0.068), respectively. In TLM group, 10 of the 15 patients (66%) with local recurrence were still laryngeal preservation after salvaged treatment. However, the laryngeal preservation after salvaged treatment was 13% (1/8) in OPL group and 19% (3/16) in RT group. Conclusions: Although there is selection bias in this retrospective nonrandomized study, the 5-year LC and DSS of these treatment modalities showed no statistical difference. However, the final laryngeal preservation rate is higher in patients with surgery than those with RT. Most of the patients with local recurrence after RT needed total laryngectomy.

P600: RACIAL DIFFERENCE IN THE DIAGNOSIS, TREATMENT AND SURVIVAL OF LARYNGEAL CANCER PATIENTS

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Objective: To evaluate whether there are racial differences in the stage at diagnosis, the type of treatment rendered and the survival outcome of laryngeal squamous cell carcinoma patients. Method: Retrospective cohort analysis using state-wide data from South Carolina Central Cancer Registry and Office of Research Statistics medical claims record. The main outcomes of interest were stage at diagnosis, treatment modality and survival. Results: A total of 3,484 patients newly diagnosed with laryngeal cancer in South Carolina from 1997 to 2002, of which 277 (8.8%) were white and 171 (31.2%) black. Blacks were 17% less likely as Whites to have their cancer diagnosed at the early stage (OR 0.83, 95% CI 0.54-1.27), while they were 14% more likely to receive a cancer directed surgery (OR 1.14, 95% CI 0.75-1.73) for their disease, but were not statistically significant. Race was also not a significant factor for survival (HR 1.02, 95% CI 0.74-1.41). Having public (OR 2.18, 95% CI 1.19-4.01) and private (OR 2.86, 95% CI 1.53-5.37) health insurance and being married (OR 1.53, 95% CI 1.04-2.26) were significantly more likely to be associated with an early stage at diagnosis. Living in a rural county (OR 1.59, 95% CI 1.01-2.52) and presenting with regional spread of disease at diagnosis (OR 1.95, 95% CI 1.33-2.87) were the two significant factors that less predisposed the patient to receive organ preservation treatment strategies. The treatment outcome from cancer directed surgery (HR 0.9, 95% CI 0.80-0.97) and chemoradiation therapy (HR 0.17, 95% CI 0.09-0.30) are comparable and both significantly improved the survival of these patients (p=0.0001). Older age, male gender, advanced stages of disease, and comorbidity all heralds a more ominous outcome. However, being married has a protective effect and these patients experience a better survival (HR 0.68, 95% CI 0.51-0.91). There were no statistically significant racial differences in the stage at diagnosis, receipt of the type of treatment modality and survival. Conclusion: While patient outcome is generally better when disease is diagnosed early, this study found that health insurance was the strongest barrier for early detection of this disease. Those living in the urban counties and with early stage at disease presentation were more likely to receive organ preservation radiotherapy as their principle treatment modality. Non-modifiable factors such as older age, male, advanced disease stage and comorbidity have a detrimental effect on survival; being married significantly resulted in earlier diagnosis and improved overall survival. While there is little difference in survival between the treatment modalities of surgery and radiotherapy for laryngeal cancer, the latter with a more likely laryngeal preservation generally offer a better quality of life for these patients. Future policies need to address the more equitable allocation of health resources to patients with out health insurance and to those living in rural regions.

P601: ENDOSCOPIC TREATMENT FOR THE SUPERFICIAL SQUAMOUS CELL CARCINOMA IN THE HEAD AND NECK REGION (HNSCC) T.Omote1, H.Kawakubo2, Y.Sato2, A.Yokoyama1, 1Kawasaki Municipal Hospital, Kawasaki, Japan; 2National Hospital Organization Kurihama Alcoholism Center, Kurihama, Japan

Background: The HNSCC are usually diagnosed at advanced stage, therefore, the prognosis is dismal. Recently we can find the superficial HNSCC by using high-resolution and magnifying endoscopy. We expect to get a good prognosis by the endoscopic treatment (EMRC: Endoscopic Mucosal Resection by Cap-method / EPS: Endoscopic Laryngo-Pharyngeal Surgery) for the superficial HNSCC. Purpose: The purpose of this study is to examine the usefulness and effectiveness of endoscopic treatment for the superficial HNSCC. Methods: The superficial HNSCC means that the depth of tumor is within the subepithelial layer. We diagnosed superficial HNSCC with no lymphodeatasis, the endoscopic treatment (EMRC/EPS) becomes the first line treatment under general-anesthesia. For those treatment cases, We examine the method of treatment, complication, pathological diagnosis and prognosis. Results: We have 145 patients (238 lesions) of the superficial HNSCC from Jan 2000 to Oct 2007. The endoscopic treatment cases were 102 (177 lesions), 87 male and 15 female, ranging in age from 39 to 86 years. Of the 177 lesions, 80 (45.2%) had been treated by EMRC, 71 (40.1%) had been treated by EPS. EMRC is good for small lesion (less than 10mm in diameter). EPS is suitable for large lesion. In EMRC case, a wound pain was often slight after the operation, and patient could leave the hospital in 4-5POD. In EPS case, a wound pain was stronger than EMRC, and needed more hospital days. Major complication was not recognized both in EMRC and EPS. Of 177 lesions which clinical assessments of the depth of cancer invasion were ep (epithelial layer) or sep (subepithelial layer), 175 lesions (98.9%) were histopathologically ep or sep. Two lesions (1.1%) were mp (muscular layer). Of the 102 patients, 93, were alive, 9 had been dead. There was no lymphodeatasis, distant metastasis and local recurrence. Forty patients of 3 years observation were accrued from Jan 2000 to Dec 2003. Of the 40 patients, 33 had been alive, 7 had been dead. There were no HNSCC dead patients. The cause specific 3 years survival rate is 100%. Conclusion: The result of our trial indicated the usefulness of endoscopic treatment for superficial HNSCC and the effectiveness for improving the prognosis of HNSCC.

P602: TRANSORAL LASER MICROSURGERY FOR LARYNX CANCER: SHAPING SURGERY ACCORDING TO LOCALIZATION AND SPREAD OF TUMOR K.M.Gokcan1, B.Kucuk1, A.Demireller1, 1Ankara University, Ankara, Turkey

Objective: Transoral laser microsurgery (TLM) for resection of laryngeal malignancies challenges traditional open surgical approaches with superior functional results. Despite the fact that the validity of TLM technique has been verified in many studies, the problem of surgical margin assessment with piecemeal tumor resection and management of tumors involving anterior commissure still remains as the potential limitations of the technique. This paper aims to share the authors experiences in adopting TLM in the treatment of larynx cancer, emphasizing the implementation of basic oncologic principles that have been followed for open partial laryngectomy. Material and Methods: Twenty-two patients with stage I-II laryngeal malignancies (19 Glottic, 6 Supraglottic in origin) underwent TLM between March 2006 and November 2007. Elective and/or therapeutic neck dissections were done at the same stage with TLM. Patients were followed monthly for 3 months after surgery and once for every 3 months afterwards. Length of hospital stay and the need for tracheostomy, feeding tube and re-operation for surgical margin positivity were recorded after surgery. Local, regional and distant recurrence rates were documented in follow up. Results: Two of the supraglottic tumors and 13 of the glottic tumors (4 of them were T1a, 6 were T2a and 3 were T2b lesions) had anterior commissure involvement. Four cases had elective, 1 had therapeutic neck dissections. Mean length of stay was 8 days. Three patients required re-operation for suspicious or positive surgical margins. None of the patients required tracheostomy and one patient with supraglottic tumor required nasogastric feeding tube placement due to aspiration pneumonia. The most common complication was development of granulation tissue (24%), which required biopsy to rule out recurrence. One patient with T2N2c supraglottic tumor showed distant metastases at follow up and one patient with T2aN0 glottic tumor was given chemoradiation therapy for local recurrence at postoperative 6 months. Conclusion: The concept of piecemeal tumor resection should not be misinterpreted as a less radical resection. Tumor volumes and margins should be equivalent to traditional open approaches. En bloc resection or stitching pieces altogether after resection, marking surgical margins with histological dyes should be favored for orientation of the pathologist. Equally important is orientation of the surgeon to the inside-out anatomy of the larynx and equipment availability for exposure and hemostasis.

P603: OPERATIVE ND:YAG LASER PLUS PERI-OPERATIVE

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In this study, we examined the oncologic results of laser cordectomy for early glottic cancer. Five-year overall survival and disease-free survival was 98% and 93%, respectively. A prospective non-randomized control study found that patients with anterior commissure involvement had a higher recurrence rate. Within T1, recurrence was higher in the patients with anterior commissure involvement (13/163) than without anterior commissure involvement (9/139). Within T2, recurrence was higher in patients with anterior commissure involvement (9/39) than without anterior commissure involvement (13/139). No significant difference was found between patients treated with Nd:YAG laser and those treated with YAG/HBO laser.

Results: Age, primary tumor site, cancer Stage, sex, reconstructive procedure (microvascular flap, free flap, or both), EBL, and transduction did not significantly influence the outcomes. Ninety-five percent of S patients and 86% of YAG/HBO patients had received radiation therapy before surgery, compared with 100% of the Nd:YAG patients. Local recurrence affected 66% of S patients and 76% of YAG/HBO patients. With a maximum followup of 80 months, 75% of S patients died of disease, compared with 68% of YAG/HBO patients.

Conclusions: The combined application of the Nd:YAG laser during surgery and HBO perioperatively significantly reduces surgical mortality in previously irradiated patients who must undergo radical head and neck surgery and complex reconstruction. These results were achieved among YAG/HBO patients who had received significantly more radiotherapy prior to surgery compared with the S group. Unfortunately, in spite of improved surgical outcomes for YAG/HBO patients, recurrent disease and long-term cancer mortality were frequent in this high-risk population.

Objective: In this study, we examined the oncologic results of laser cordectomy for early glottic cancer and analyzed the prognostic impact on the survival of the several tumor-related and treatment-related factors.

Materials and Methods: Patients who were diagnosed as early glottic squamous cell carcinoma (T1 or T2), treated by laser cordectomy with curative intent and did not have previous laser cordectomy history were analyzed. Patients with previous radiation therapy were not included. All patients had a minimum follow-up period of 2 years. From June 1988 to March 2005, 202 patients from five hospitals were analyzed (174 T1, 28 T2).

Results: Five-year overall survival and disease-free survival was 98% and 85%, respectively. Twenty-two patients developed local recurrence. Total laryngectomy was done in 6 patients and laryngeal preservation rate was 97%. Recurrence was higher in the patients with anterior commissure involvement (9/39) than without anterior commissure involvement (1/163). Within T1, recurrence was higher in T1b (4/15) than in T1a (13/159). Previous irradiation was also highly related to the recurrence (7/20 vs 15/182). According to the resection method, recurrence was higher in blockwise resection (9/63) than endoscopic resection (13/139) but there was no statisti-}

**P606: DETERMINING THE PROGNOSTIC FACTORS IN A PROSPECTIVE COHORT OF SUBMUCOSAL NASOPHARYNGEAL CARCINOMA**

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**Objectives:** Most patients with nasopharyngeal carcinoma (NPC) will present with an exophytic mass in the nasopharynx. However, we have reported that up to 10% of our patients present with a normal appearing nasopharynx, what we term as submucosal NPC. Furthermore, the initial analysis of a cohort of 161 patients suggested that this group of patients with submucosal NPC has a higher risk of M1 disease as well as local recurrences. We therefore aimed to confirm these findings in a larger prospective cohort and to determine the survival outcomes as well the prognostic factors in this group of patients.

**Methods:** A prospective non-randomized cohort study of 274 newly diagnosed NPC patients from January 2000 to December 2006 was conducted. Patients not treated and/or not followed up at our center were excluded. The patients were categorized into submucosal NPC and exophytic NPC. Submucosal NPC was defined as NPC occurring in individuals with a smooth mucosa in the nasopharynx, with no obvious mass or ulceration or asymmetry. Mild mucosa changes like contact bleeding or erythema but with no mass or swelling of the nasopharynx was also included as submucosal NPC. The clinical and pathological parameters were analyzed. For survival outcomes, we analyzed the disease specific and disease free parameters. In addition, all the patients with M1 disease were excluded from the analysis. Outcomes were measured using the Kaplan–Meier and log rank test for significance.

**Results:** Submucosal NPC was present in 8.8% (24 of 274). A greater proportion of submucosal NPC patients had NO disease as compared to the exophytic group (66.7% vs 35.2%) (p=0.01). Of the patients with submucosal NPC, 25% had M1 disease in contrast to 6% of patients with exophytic NPC (p=0.001). There were 37.5% of submucosal NPC patients who had N3 disease.
This study confirms that submucosal NPC is associated with a higher risk of M1 disease. In addition, there is a tendency for large volume disease, notably nodal metastasis but relatively less likely to have locally advanced disease. The survival outcomes of the submucosal group without M1 disease are similar to the exophytic group. These results indicate that a patient with submucosal NPC without M1 disease has a similar prognosis to the exophytic group of NPC patients.

**P607: THE TREATMENT OUTCOME OF NASOPHARYNGEAL CARCINOMA STAGING BY MRI AND CONVENTIONAL RADIOTHERAPY**

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**Introduction:** To evaluate the treatment result of nasopharyngeal carcinoma (NPC) patients staging by magnetic resonance image (MRI) and treated by conventional opposing radiation technique.

**Material and Method:** There were 356 untreated non-metastasis NPC patients with primary tumor and neck staging by MRI from July 1992 to December 1998. The median age of the patients was 47 years old (range 15–76). The stage distribution was stage I: 41 (11.5%) patients, stage II: 130 (36.5%), stage III: 85 (23.9%) and stage IV: 62 (17.4%) patients. The radiation therapy was delivered by 6-MV photons. The radiation fraction size was 1.8-2 Gy and 5 fractions per week. The total dose was 65-70 Gy. The primary tumor was usually treated with the 5-field technique. The radiation coverage depended on the tumor extent.

**Results:** The median follow-up was 7 years. There were 356 patients staged with MRI. Seventy-eight (21.9%) patients had distant metastasis. T and N stage were the most significant parameters in survival which were mainly related to distant failures. However, T and N stage had less impact on locoregional control. Intracavity brachytherapy had less effect on survival compared to surgery. The 5-year disease-free survival rate was 65% for stage I, 75% for stage II, 53% for stage III and 51% for stage IV disease. Primary tumor recurrence or persistent tumor was noted in 62 (17.4%) patients and isolated neck node recurrence in 22 (6.2%) patients. Seventy-eight (21.9%) patients have distant failures. However, T and N stage had less impact on local control rate (58% vs. 80%, p < 0.0001), and its adverse effect more pronounced in the tumors above T2b stage (p = 0.026).

**Conclusion:** This study confirms that submucosal NPC is associated with a higher risk of M1 disease. In addition, there is a tendency for large volume disease, notably nodal metastasis but relatively less likely to have locally advanced disease. The survival outcomes of the submucosal group without M1 disease are similar to the exophytic group. These results indicate that a patient with submucosal NPC without M1 disease has a similar prognosis to the exophytic group of NPC patients.

**P608: A SYSTEMATIC ANALYSIS OF TRISMUS IN NASOPHARYNGEAL CARCINOMA: A CLINICALLY APPLICABLE CLASSIFICATION OF SEVERITY**

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**Objectives:** Trismus is a debilitating effect of radiation of the nasopharynx. The efficacy of the treatment methods used has not been elucidated because of the lack of a clinically practical classification system. We therefore aimed to study a group of nasopharyngeal carcinoma (NPC) patients who had radiation. The objectives are to determine the progress of trismus in treated NPC patients and in so doing to be able to develop a classification system to define its severity.

**Methods:** This prospective study was conducted in 2 phases. Approval from the institutional review board was obtained. In the 1st phase, we recruited 476 normal subjects with no known oral pathology. Using a sliding caliper, we measured the occlusal inter-incisor gap (OIIG) as the vertical distance between the upper and lower incisors. The mean inter-incisor gap (MIG) was similarly measured but with the mouth maximally opened. The inter-incisor gap (IG) was taken as the difference between MIG and the OIIG. In phase 2, we measured 112 NPC patients treated by radiation. We recorded the OIIG, MIG and IG. The measurements were taken before radiation and at months, 6 months and 1 year post radiation. All the NPC patients gauged their degree of trismus, if any, on a visual analogue scale. This score was correlated with the change in the IIG. **Results:** The mean IIG for the normal population was 4.6 cm (SD: 0.8) for males and 4.2 cm (SD: 0.7) for females. The IIG for males was 4.9 cm, 4.2 cm, 4.1 cm and 3.9 cm at pre-radiation, 3 months, 6 months and 1 year post radiation respectively. The IIG for females was 4.2 cm, 3.6 cm, 3.8 cm and 3.6 cm at pre radiation, 3 months, 6 months and 1 year post radiation. At 12 months post radiation the decrease in the IIG from baseline was 1 cm for males and 0.6 cm for females. However, in patients who had radiation, the IIG decreased gradually over time. Clinically significant trismus is usually established by 6 months to 1 year after radiation although measurable trismus starts just after 3 months post radiation. A reduction of 1 cm or more in the IIG is correlated with moderate or severe trismus. We propose that in radiated NPC patients, mild or no trismus is defined as a decrease in IIG of 0.5cm or less. Moderate trismus is a decrease of 0.6cm to 1 cm in the IIG and severe trismus is defined as more than 1 cm.

**P609: DESIGN OF A PROGNOSTIC SCORING SYSTEM FOR LOCALLY RECURRENT NASOPHARYNGEAL CARCINOMA**

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**Background:** Treatment options available in locally recurrent nasopharyngeal carcinoma (NPC) include surgery, brachytherapy, external reirradiation and chemotherapy. Recently stereotactic radiosurgery (SRS) has also been employed as a salvage treatment of local failures of NPC with variable results. We therefore performed this retrospective study to evaluate the use of SRS for locally recurrent NPC. Patients with good prognostic score should be treated by SRS whereas patients with poor prognostic score should be treated by other methods of treatment.

**Material and Method:** This retrospective study included 48 patients with local failures of NPC treated between March 1996 and February 2005. SRS was administered using a modified linear accelerator with single or multiple isocenters to deliver a median dose of 12.5 Gy to the target periphery. Median follow-up was 54 months. Important prognostic factors were identified by univariate analysis and their relative risks were estimated by the Cox proportional hazard regression model. **Results:** Five-year local failure-free probability after SRS was 47.2% and 5-year overall survival rate was 46.9%. Five factors including age, time interval from 1st radiotherapy, T stage, tumor volume, and prior local failure (prior RT) were used to design the scoring system. The estimated risk coefficient of these factors ranged from 0.03 to 0.39. A score of 0 was assigned if the adverse factor was not present, or a value equal to the estimated risk coefficient if the factor was present. The prognostic score was then estimated by summing the relative risk of individual factors using the following formula:

\[ \text{Prognostic score} = 0.22 \times (\text{Age} > 45) + 0.27 \times (\text{Time from 1st RT} > 6 \text{ months}) + 0.05 \times (\text{T1} > 10) + 0.28 \times (\text{M1 at presentation}) + 0.39 \times (\text{Prior local failure}) \]

**Conclusion:** A simple prognostic scoring system was designed to predict treatment outcome after SRS for locally recurrent NPC. Patients with good prognostic score should be treated by SRS whereas patients with poor prognostic score should be treated by other methods of treatment.
Objective: To determine the incidence of post-treatment hypothyroidism in nasopharyngeal carcinoma (NPC) patients after radical treatment, and to investigate the possible factors that could predict the onset of hypothyroidism.

Material and Methods: Four hundred and eight NPC patients who received regular annual thyroid hormone survey prospectively after radical treatment between December 1983 to April 2003. There were 286 males and 122 females. The median age was 47.3 years old. Thyroid function was prospectively evaluated by measuring thyroid stimulating hormone (TSH) and serum free thyroxine (FT4). Low level of FT4 is classified as clinical hypothyroidism. Result: With a median follow-up of 4.3 years (range, 0.54-19.7 years), the incidences of low FT4 in three years, five years, and ten years were 4.9%, 9.0% and 18.8%, respectively. Hypothyroidism was more common in early T stage (P=0.044), female gender (P=0.037), and those treated with 3D conformal therapy and altered fractionation technique (P=0.005). N stage, chemotherapy, re-irradiation and neck electron boost did not affect the 3D-IMRT. Post-treatment hypothyroidism can be predicted by clinical factors. The factors are significant factors that determined clinical hypothyroidism. Patients with elevated TSH developed low FT4 at a median of one year later.

Conclusion: There were 18.8% of NPC patients will experienced clinical hypothyroidism in ten years after treatment. Younger age and conformal therapy will increased the risk of hypothyroidism. These patients was suggested for regular thyroid hormone follow-up.
All but one tumor were EBV positive. Induction chemotherapy was administered to 7 patients (64%). Four patients had only 1 cycle of TCF, and the other without docetaxel. One patient had no treatment at all. Two patients who recurred. Of the whole cohort, 67% developed local recurrence, 5.1% regional recurrence, and 13.8% distant metastasis. Of the distant recurrences, 63% were bone, 43% in lungs and 40% in liver. The 5-year overall survival was 77.2% for the whole cohort. The 5-year disease specific survival of stage I, II, III and IV NPC was 88.9%, 87.9%, 86% and 65.9% respectively (p<0.001). The 5-year disease free survival of stage I, II, III and IV NPC was 80.6%, 85%, 77.6% and 59% respectively (p<0.015). Patients with N3 disease had a 5-year disease specific survival of 61% versus 85.3% for patients with N0-N2 disease. Patients with N3 disease also had a 5-year disease free survival of 60.1% versus 78% for N0 to N2 patients (p=0.009). Stage IV disease and N3 disease are the only significant factors associated with poor prognosis.

Statistically, the only significant poor prognostic indicators are stage IV and N3 disease.

**Conclusion:** The outcomes of stage I, II and III NPC patients treated using the protocol of radiation or chemoradiation, are good. The overall local, regional and distant recurrence rates are low. Stage I, II and III patients have similar and excellent disease free and disease specific survival.

**Objectives:** The treatment of nasopharyngeal carcinoma (NPC) has evolved over the years, in particular the use of combined chemoradiation for advanced disease. Our objectives in this study were to determine the long-term outcomes in a cohort of NPC patients treated by using a protocol that incorporates chemoradiotherapy for advanced disease. **Method:** A prospective cohort of 358 newly diagnosed NPC patients treated at our institution from June 1997 to July 2005 was reviewed. Patients who refused treatment, were not treated for other reasons or were excluded. All patients were treated with distant metastasis at the time of diagnosis were excluded. Foreign patients who were not able to return for follow up for at least 3 years were excluded. Overall 257 patients were eligible for analyses. The demographics, clinical and pathological parameters were analyzed and correlated with recurrences and survival. Survival outcomes were analyzed using the Kaplan-Meir and log rank test. **Results:** Of the 258 patients analyzed in the study, there were 193 (75.1%) males and 64 (24.9%) females, with a mean age of 49.3 years (SD> 11.2), ranging from 13 to 94 years. The median duration of follow up was 26.5 months (range 9 to 129 months). There were 11.3% stage I, 31.1% stage II, 32.3% stage III and 24.9% stage IV. Stage I and II patients were treated by radiation while stage III and IV NPC was treated by chemoradiation. Overall, there were 21.7% of patients who recurred. Of the whole cohort, 67% developed local recurrence, 5.1% regional recurrence, and 13.8% distant metastasis. Of the distant recurrences, 63% were bone, 43% in lungs and 40% in liver. The 5-year overall survival was 77.2% for the whole cohort. The 5-year disease specific survival of stage I, II, III and IV NPC was 88.9%, 87.9%, 86% and 65.9% respectively (p<0.001). The 5-year disease free survival of stage I, II, III and IV NPC was 80.6%, 85%, 77.6% and 59% respectively (p<0.015). Patients with N3 disease had a 5-year disease specific survival of 61% versus 85.3% for patients with N0-N2 disease. Patients with N3 disease also had a 5-year disease free survival of 60.1% versus 78% for N0 to N2 patients (p=0.009). Stage IV disease and N3 disease are the only significant factors associated with poor prognosis.

**Conclusion:** The outcomes of stage I, II and III NPC patients treated using the protocol of radiation or chemoradiation, are good. The overall local, regional and distant recurrence rates are low. Stage I, II and III patients have similar and excellent disease free and disease specific survival. Statistically, the only significant poor prognostic indicators are stage IV and N3 disease.
To evaluate the efficacy of salvage endoscopic nasopharyngectomy (Endo-ENP).

Objective: Treatment of nasopharyngeal cancer is focused mainly on the reduction of incidence of secondaries in distant metastases and improvement of loco-regional control. Purpose of this study is to evaluate patterns of failure in patients with locally advanced nasopharyngeal carcinoma treated with radiotherapy in combination with weekly cisplatin.

Methods: Total of 32 previously untreated patients, (ECOG performance status 0-2) with locally advanced nasopharyngeal carcinoma (AJCC stages IIB-IVB) were treated with radiotherapy with total dose of 66-72 Gy with daily fraction of 1.8 Gy. Chemotherapy with cisplatin 40 mg/m2 was administered once weekly. Results: Median follow up of the patients was 25 months and median time to treatment failure was 17 months. Five of the patients (16%) developed distant metastases, 11 (34%) loco-regional recurrence and 2 patients (6%), both distant and loco-regional recurrence. The most frequent side effects were myelotoxicity, stomatitis and xerostomia.

Conclusion: Concurrent chemoradiotherapy with weekly cisplatin is feasible treatment solution with acceptable toxicity. Longer follow up of the patients in larger patient series is necessary to justify value of this treatment.

P619: SALVAGE ENDOSCOPIC NASOPHARYNGECTOMY FOR RECURRENT NASOPHARYNGEAL CARCINOMA.

Objective: To evaluate the efficacy of salvage endoscopic nasopharyngectomy, for locally recurrent nasopharyngeal carcinoma. F08rNPCF09.

Methods: Five T1 rNPC patients were salvaged with endoscopic nasopharyngectomy between January 2006 and July 2007 including 4 cases of primary and one case of secondary local recurrence. The location of the recurrent tumor in nasopharynx were 2 in the lateral wall, 2 in the roof and lateral wall and one in the floor. The follow up time ranged from 5 months to 23 months. Results: A total of 4 endoscopically performed resections without surgical complications. Two patients had local recurrence again after salvage surgery including one in the nasopharyngeal mucosa and the other one in the skull base bone and cavernous sinus. The histopathology was poorly differentiated or undifferentiated nasopharyngeal carcinoma. The majority of children (18) received multimodality treatment.

Conclusion: Endoscopic nasopharyngectomy is a safe and effective treatment for T1 rNPC.

P620: MAXILLARY SWING APPROACH FOR SURGICAL RESECTION OF RECURRENT NASOPHARYNGEAL TUMORS.

Objective: At the conclusion of this presentation the participant should be able to discuss the principle and merit of nasopharyngectomy through maxillary swing approach in treating recurrent nasopharyngeal tumors. Methods: Antero-lateral access to the nasopharynx and its vicinity through the maxillary swing approach was used. Through a Weber-Ferguson-Longmire incision, the whole maxilla is freed and swung laterally while remaining attached to the masseter muscle and cheek flap. The nasopharynx, para-nasopharyngeal space and infratemporal fossa are now exposed facilitating complete resection of the tumor. Results: Five patients were treated using this approach at the National Cancer Institute, Cairo University. There were 4 males and 1 female with a range of age 16-57 years. Three patients had recurrent carcinoma of the nasopharynx after primary radiation therapy, while two patients had locally advanced recurrent juvenile nasopharyngeal angiofibroma (JNA). Using the operating microscope, complete tumor resection was achieved in all patients except one patient with intracranial extension of JNA. There was no surgical mortality. Complications occurred in two patients, one patient developed osteoradionecrosis following re-irradiation and the other patient has epiphora. Follow up period ranged from 13 months to 5 years, one patient died from distant disease and another patient is alive with residual intracranial disease. Conclusion: Salvage nasopharyngectomy is a valid option for selected patients with recurrent nasopharyngeal tumors. The maxillary swing approach allows safe and adequate resection for such tumors.

P621: MODIFICATION FOR MISDIAGNOSIS OF NASOPHARYNGEAL CARCINOMA—REDESIGN SCHEDULE WITH CONSULTATION FOR SPECIALTIES.

Objective: Nasopharyngeal carcinoma (NPC) has a higher tendency of affecting relatively young population, comparing to most other head-and-neck cancers. The extent of disease at diagnosis of NPC is the most important prognostic factor. Management about this disease is scant owing to its rarity in the West. Doctors from non-otolaryngology specialties rarely have background sufficient for being familiar with the natural course of NPC; hence, a misdiagnosis of NPC could hard be averted. Case Presentations of Misdiagnoses of Nasopharyngeal Carcinoma—Redesign Schedule with Consultation for Specialties.

P622: NASOPHARYNGEAL CARCINOMA IN CHILDREN: EXPERIENCE AT THE ALL INDIA INSTITUTE OF MEDICAL SCIENCES, INDIA.

Objective: Among the various childhood malignancies, occurrence of Nasopharyngeal Carcinoma (NPC) is perhaps the rarest across the world including certain parts of Asia. The objective of this study was to investigate the characteristics and clinical outcomes of children with Nasopharyngeal Carcinoma treated at a single center. Methods: Retrospective observational case series of 20 children diagnosed of Nasopharyngeal Carcinoma from 1998 to 2006. Results: The age of patients varied between 8-18 years, with a median age of 14 years. Out of these, 18 were males and 2 were females. Their symptom duration varied from 2 to 6 months. The histopathology was poorly differentiated or undifferentiated carcinoma. The majority of children (18) received multimodality treatment with chemotherapy and radiation therapy. The chemotherapy drugs used were Cisplatinum, 5 Flououracil, Taxanes and Carboplatin. The radios
Posters

oral cavity III

P623: ORAL CANCER IN YOUNG PATIENTS: A DESCRIPTIVE ANALYSIS OF CLINICAL AND TREATMENT OUTCOMES AT A SINGLE INSTITUTION J.G.Varratam1, C.R.Santos1, G.B.Carvalho1, L.G.Silva1, E.Kaminegakura1, L.P.Kowalski1, A.C.Camargo Hospital, Sao Paulo, Brazil

Objective: The majority of cases of oral squamous cell carcinoma occurs in patients over 45 years, and most are associated with tobacco and alcohol consumption. However, recent studies have reported an increased incidence in young patients and in non-smokers. Also there is some controversy in the biological behavior and prognosis in this group of patients, with a potential worse prognosis. The objective of this study was to describe the clinical and prognostic characteristics of oral cancer patients under 40 years of age treated in a single institution. Methods: Retrospective study of a consecutive series of previously untreated patients with oral squamous cell carcinoma, up to 40 years of age, treated between 1967 and 2003. A descriptive analysis of the results was performed. Results: A total of 123 patients were studied. Most were male patients (76.4%), with ages ranging from 19 to 40 years (median, 36). The tumor site was tongue in 53 cases (43.1%), followed by floor of the mouth in 36 cases (29.3%) and retromolar region in 16 cases (13.0%). The clinical staging was T1/T2 in 35 patients (28.5%), T3/T4 in 88 patients (71.5%), N0 in 47 patients (39%) and N+ in 76 (61%). Most patients had a history of tobacco (70.7%) and alcohol (57%) consumption. The treatment performed was surgery alone in 33 cases (26.8%), radiotherapy in 27 (21.9%), a combination of surgery and radiotherapy in 48 (39%), chemoradiotherapy in 11 (8.2%), and surgery alone in 4 (3.3%). In 4.2% of the cases the recurrence of the disease was detected in 68 patients (55.3%), most were local (25.2%) or locoregional (14.6%) recurrences. Thirteen patients (10.6%) presented a second primary tumor, with 8 cases in the head and neck region. The follow-up period ranged from 1 to 210 months (median, 22 months). The 5-year overall survival in this series was 41%. Considering just non-smokers, the proportion of female patients increased to 44.8% of the cases, with more tumors located at the tongue (51.7%) than in floor of the mouth (13.8%) compared with all cases together. The 5-year overall survival in this group was 57%, which was significantly better than in smokers (36%; p < 0.005). Conclusion: There are several controversies in the clinical behavior and prognosis regarding oral squamous cell carcinoma in young patients. In this series, most patients were diagnosed at advanced stages, and the prognosis could be considered poor compared to historical series including older patients. In the subgroup of non-smokers, there were a high proportion of women and tongue tumors with a better survival rate. These findings suggest a different oncogenetic process in this group of patients.

P624: SQUAMOUS CELL CARCINOMA OF THE ORAL TONGUE IN YOUNG PATIENTS: A MATCHED-PAIR ANALYSIS A.C.W Ho1, J.Y.W.Chan1, R.W.M.Ng1, W.I.Wei1, University of Hong Kong Medical Centre, Hong Kong, China

Background: The incidence of squamous cell carcinoma (SCC) of the tongue is increasing among young individuals. However, the literature concerning prognosis for young patients with oral SCC is conflicting. The aim of this study was to compare the survival rates of patients under 45 years of age vs. age-matched and diagnosed with SCC of the oral tongue with those of patients older than 60 years. Methods: A retrospective 10-year review, from 1995 to 2005, was made from data from a tertiary academic medical center. 73 patients under 45 years of age with squamous cell carcinoma of the head and neck were identified. 45 out of 73 patients suffered from carcinoma of the oral tongue and these patients were matched to an older population with more than 60 years of age. The 5-year disease-free survival; rates of local, regional, and distant failure; and rate of second primary tumor were determined for both populations. Results: To follow. Conclusions: Preliminary results showed that the outcomes of treatment for SCC of the oral tongue in young patients are similar compared with patients older than 60 with similar extent of disease.

P625: ORAL MAXILLARY SQUAMOUS CARCINOMA: A COHORT PERSPECTIVE ON THE MANAGEMENT OF THE CLINICALLY NEGATIVE NECK D.M.Montes1, R.Fernandes2, B.L.Schmidt3, Louisiana State University Health Science Center, Shreveport, LA; 2University of Florida, Jacksonville, FL; 3University of California, San Francisco, CA

Objective: Maxillary squamous cell carcinomas (SCC) occur at a relatively low rate in comparison to other oral site squamous carcinomas and has not been extensively studied. Management of the patient with maxillary SCC is particularly difficult given that very few studies have documented associated metastatic rates and patient outcomes. The Departments of Oral and Maxillofacial Surgery at the University of California San Francisco and the University of Florida at Jacksonville were completed. Patients treated for maxillary oral malignancies were identified. All patients underwent a complete clinical head and neck exam as well as either magnetic resonance or computed tomographic imaging of the primary tumor site and neck. Thirty patients met the inclusion criteria defined by 1) site specific SCC of the oral maxillary structures, 2) confirmation that the maxillary SCC did not originate in the nasal cavity or paranasal sinuses and 3) primary tumor management was limited to surgical extirpation. Patients which had tumors invading the oropharynx or retromolar trigone and extending to the mandible were eliminated from the study group. Results: Fifteen men and fifteen women, ages 49-93, represent the patient group presented. Post surgical follow up in the combined series ranges from 1 to 156 months. Three patients where lost to follow up, two of which were known to have developed distant metastasis and died with disease. On initial consultation, cervical disease was detected in 36.6% of patients. Following ablative surgery for the primary tumor, 37.5% of the individuals whom presented with clinically negative necks went on to exhibit regional lymph node metastasis. In our series, 46.7% of the patients with maxillary oral squamous cell carcinoma ultimately developed regional metastatic disease. The patterns of cervical metastasis appear consistent with other oral cavity SCC primary sites. Although each of the five patients whom ultimately developed distant metastasis presented with advanced tumor grade, only two of these individuals harbored clinically detectable cervical metastasis at presentation. Conclusions: In this series, we clearly show that oral cavity maxillary SCC has the potential for a high rate of cervical metastasis. Additionally, in an untreated, clinically negative neck occult metastasis can considered as a contributing factor in the development of regional failure. Based on the findings presented here, we recommend a selective neck dissection in the setting of a clinically negative neck as a primary management strategy for patients with oral maxillary squamous carcinoma. References: Keski-Sanjti H, Atula T, Tornwall J, et al: Elective neck treatment versus observation in patients with T1/T2 NO squamous cell carcinoma of oral tongue. Oral Oncol 42(1):96-101, 2006. Simontal AA, Jr., Johnson JT, Myers EN: Cervical metastasis from squamous cell carcinoma of the maxillary alveolus and hard palate. Laryngoscope 116(9):1682-4, 2006.

P626: CRITICAL ANALYSIS OF THE OUTCOME OF EARLY STAGE TONGUE AND FLOOR OF MOUTH SCC WITH PERINEURAL INVASION D.M.Ramos1, E.Stabenow1, R.A.Mygues2, M.D.Brescia3, A.R.Ferraz1, H.N.Genome Project / GENCAPO2, P.Michaluart1, 1Head and Neck Surgery Department, Sao Paulo University Medical School, LIM 28, Sao Paulo - SP, Brazil; 2http://ctc.fmrp.usp.br/clinicalgenomics/cp/group.asp, Sao Paulo - SP, Brazil

Objective: Perineural space is a known pathway for squamous cell carcinoma (SCC) spread. Its invasion has been associated with worse prognosis, greater recurrence rates and lower survival. However, its impact on
early stage oral cavity tumors is not well stabilized. The aim of this study was to compare global and disease free survival between patients with early stage tongue and floor of mouth SCC, with and without perineural invasion. **Methods:** Retrospective case-control study of 42 patients surgically treated for early stage SCC (T1/T2 N0 - UICC-2002) of oral tongue and floor of mouth. Mean follow-up was 49 months. Patients were divided into two groups: with (N=16) and without (N=26) perineural invasion. Clinical and pathological features, treatment and outcome were compared. Cases of death were described and a critical analysis of adjuvant radiotherapy treatment was performed. **Results:** The group of tumors with perineural invasion presented a higher frequency of male patients (p=0.008) and intensity of tobacco exposure (p=0.042), and lower frequency of non users of alcohol. The means of tumor diameter (p=0.046) and thickness (p=0.002) were greater in this group. These patients also had higher disease-specific death rate (p=0.015) and lower global survival rate (p=0.019), regardless the higher frequency of adjuvant radiotherapy treatment received. There were four disease-specific deaths and all these patients had tumor with perineural invasion. In two of these cases, no other known features of worse prognosis were observed. The disease free survival was not different from SCC with no perineural invasion. **Conclusion:** Perineural invasion in early stage tongue and floor of mouth SCC with perineural invasion had lower global survival when compared to those without invasion, despite more aggressive treatment.

**P627:** OSCC: AN IMMUNOHISTOCHEMICAL APPRAISAL IN SOUTH INDIAN POPULATION WITH MIXED HABITS **Agrawal,** 1 Manipal College Of Dental Sciences, Manipal, India, Manipal, India

**Objective:** To compare various tumor markers in determining the prognosis and clinical behavior of OSCC (oral squamous cell carcinoma) in south Indian population with mixed habits. **Method:** With Formalin fixed paraffin embedded sections, a battery of tumor markers (Type IV collagen, Type VII collagen, p53, Tenascin, Cytokeratation 19, E-cadherin, bcl2, MMP9, CDK4) was used with immunohistochemical technique on these sections with primary antibodies against various antigens. All these sections were then analyzed with use of light microscope and a correlation was found out between the readings of each section with the use of statistical tests. **Results:** A positive correlation was observed between the habit, the clinical behavior and the prognosis in these cases of OSCC. **Conclusion:** Oral cancer is one of the ten most common cancers in the world and shows marked geographic differences in occurrence. Use of tumor markers helps in determining the clinical outcome and prognosis of patients suffering with OSCC.

**P628:** ORAL CANCER IN A SCHOOL HOSPITAL FROM 1994 TO 2006: PREDOMINANCE OF LOW STAGED DISEASE IN WOMEN M.D. Durazzo, 1 D.F. Dell Negro, 1 F.L. Lobo, 2 F. Fernandes, 1, M.D. G.Brescia, 1 D.M. Ramos, 2 C.E.N. Araujo, 3 C.A. Simões, 2 L.G. Brandão, 2, A.R. Ferraz, 1 1Hospital das Clínicas, São Paulo SP, Brazil; 2Hospital das Clínicas, São Paulo, Brazil; 3Universidade de Lisboa, Lisboa, Portugal

**Objective:** This study was carried out in order to verify differences between male and female patients with oral cancer treated with surgery in a tertiary attention school-hospital. **Methods:** The records of all patients submitted to surgery for oral cancer from February 1994 to November 2006 were retrospectively reviewed. Data regarding demographics and clinical TNM stage were inserted in a spreadsheet and analyzed in order to verify differences between men and women. **Results:** There were 524 patients identified in the 13 years period. They were submitted to 560 operations. Mean age was 58 years. Women comprised 31% of all patients. The charts of 446 patients had accurate information on clinical staging. Clinical stages I and II were observed in 57% of all women and in 37% of all male individuals (p<0.001). NO neck was seen in 20% of women and 43% of men. T4 lesions were the most common initial presentation in men, and T2 tumors were the most frequently seen in women. **Conclusions:** Women had marked less advanced disease at the time of diagnosis when compared to men. Both local and regional disease were in more initial stages. This may be explained by women’s prompt search for medical attention as first signs and symptoms appear. This also may lead to less radical surgical procedures and better quality of life. The high percentage of males with T4 lesions and stage IV disease indicates that more preventive and education policies are needed in São Paulo.

**P629:** DEVELOPMENT AND PROGRESSION OF PROLIFERATIVE VERrucous LEUKOPLAKIA (HYPERPLASIA) OF THE ORAL CAVITY: A REVIEW OF SIX CASES **M. Page,** 1 G.J. Renner, 1 L.A. Frank, 1 University of Missouri - Columbia, Columbia, MO

Proliferative verrucous leukoplakia (PVL) is a relatively rare pathology that is most commonly found in the oral cavity of elderly females and is prone to multicentric malignant transformation. First described by Hansen in 1985, PVL appears to be a distinct clinical entity that demonstrates a spectrum of behavior from proliferative hyperplasia in its initial stages to invasive squamous cell carcinoma over time. Etiology remains unclear, with inconsistent associations found to factors such as tobacco, alcohol, and papilloma viruses. Clinical and histologic findings in initial stage can be similar to those of more typical leukoplakia, complicating early recognition. Clinical behavior of PVL, however, tends to be relentless and aggressive over time. **Objective:** This is a retrospective study of six patients from a single institution who have been at some point been diagnosed with PVL. The purpose of this review is to identify similar traits that may help in early identification of other patients who may have this disease, to analyze the collective experience of those patients with this disease, and to develop plans for better short-term and long-term patient management. **Methods:** Case studies are made of four patients (3 Females: 1 Male) who are considered to be diagnosed with this disease. **All**
Oral cancer is one of the leading cancers in most Asian countries. To assess the neck management after intensity-modulated radiation therapy and to genetic susceptibility, the Squamous cell carcinoma of the upper aero digestive tract is related to smoking and alcohol consumption and to genetic susceptibility. The identification of molecular markers related it to tumour staging may act diversely in premalignancies and cancer. However, the pretreatment WBC counts were significantly lower in patients with premalignancies than in patients with malignancies. The relationship between the leukocytosis, lesion size, histologic pattern, malignant transformation, TNM stage, tumor recurrence, distant metastasis, and survival were analyzed. Results: Leukocytosis was found in 43% of 108 patients with premalignancies. However, the pretreatment WBC counts were significantly lower in patients with premalignancies and had OSCC developed then those without transformation (P=0.02). In OSCC patients, 124 of 253 patients had pre-treatment leukocytosis and was associated with tumor size (P=0.01) but did not differ among the subgroups of patients defined by age, gender, or histologic differentiation. On multivariate analysis, leukocytosis was identified as an independent predictor of survival (P=0.03). Conclusion: Our result suggested the increase of WBC count might not only be a paraneoplastic phenomenon but also quite an early event in carcinogenesis of OSCC which may act diversely in premalignancies and cancer.

P634: Sutton's Disease Mimicking Carcinoma of the Oropharynx

Introduction: Sutton's disease, also known as major aphthous ulcer or recurrentis mucosa necrotica recurrents is a rare, severe variant of recurrent aphthous stomatitis. Its presentation can mimic that of carcinoma of the oral cavity or oropharynx. We present a case of Sutton's disease that initially appeared to represent a malignant process because of its aggressive nature. The relevant literature is reviewed, with an emphasis on clinical presentation, diagnosis, and treatment. Methods: Case report and literature review. Results: A 28-year-old man presented with a six-month history of progressive left throat pain, odynophagia, otalgia, and occasional tonsillar bleeding. He had lost about 40 pounds since the onset of symptoms. His history was significant for hemophilia A and occasional minor aphthous ulcers. Exam revealed a large friable, ulcerated, very tender lesion in the left oropharynx centered in the tonsillar fossa. The area of ulceration extended from the soft palate to the hypopharynx. FLEXYRIGOSCOPY revealed encroachment of the lesion into the piriform sinus. CT of the neck showed circumferential thickening of the left palatine tonsil and an enlarged left jugulodigastric lymph node. He was taken to the operating room for panendoscopy and biopsies. In the 3 weeks between initial presentation and panendoscopy, the lesion progressed rapidly with expansion across the midline and the oropharynx and complete ulceration of the uvula. Biopsy revealed active ulceration with a mixed inflammatory infiltrate composed primarily of T-cells. He received intraoperative dexamethasone in the perioperative period. Three weeks after the biopsy, his symptoms had completely resolved. Examination showed scarring of the oropharynx and absence of the uvula, but no ulcerations. Conclusions: Sutton's disease is a rare disorder characterized by severe erosive ulcerations of the oral mucosa. Unlike other aphthous ulcers, they heal with scarring. The primary treatment is systemic corticosteroids, although other immunosuppressive therapies have been successful.

P635: Neck Management After Intensity-Modulated Radiation Therapy for Node Positive Oropharyngeal Carcinoma

Objective: To assess the neck management after intensity-modulated radiation therapy (IMRT) with concurrent chemotheraphy for node positive oropharyngeal carcinoma. Methods: Between 2003 and 2006, 34 patients with node positive squamous cell carcinoma of the oropharynx were treated with IMRT to the primary and nodal sites. Six patients with neck dissection before radiation therapy were excluded from the study. The overall T-stage distribution was T1, 8; T2, 17; T3, 5; and T4, 4. The N-stage distribution was N1, 4; N2, 26; and N3, 4. IMRT consisted of 2.12 Gy per fraction daily to a total dose of 69.96 Gy given in 33 fractions to the primary sites and involved nodes. Ninety-four percent of patients received concurrent cisplatin, carboplatin +/- taxol, or Erlotinib. Pertinent pathologic findings of the primary sites and regional nodes were available for 33 patients.
the development of lymph node metastasis is the most important prognostic factor in oropharyngeal carcinoma. During the second half of the 20th century, management of oropharyngeal carcinoma always included the radical treatment (by surgery or radiation therapy) of the neck. Systematic neck dissection even in cases with clinically positive lymph nodes.

**Objective:** To compare the accuracy of positron emission tomography (PET) and computed tomography (CT) in the detection of nodal metastases.

**Methods:** Patients with oropharyngeal squamous cell carcinoma who underwent neck dissection, treated from 1994 to 2004 were retrospectively studied. The histological slides were reviewed by two pathologists. All patients had undergone preoperative lymph node sampling.

**Results:** The overall accuracy of PET was 92.5% compared to 75% for CT. PET was more accurate than CT in the detection of T3/T4 and negative neck nodes. PET had a sensitivity of 93.5% and specificity of 92% for the detection of nodal metastases.

**Conclusion:** PET is a more accurate method for the detection of nodal metastases compared to CT.

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**P636: PATTERN OF DISTRIBUTION OF CERVICAL LYMPH NODE METASTASES IN OROPHARYNGEAL SQUMOUS CELL CARCINOMA**

**Background:** The pattern of cervical lymph node metastases in oropharyngeal squamous cell carcinoma is crucial for treatment planning. This study aimed to analyze the pattern of lymph node metastases in a large cohort of patients with oropharyngeal squamous cell carcinoma.

**Methods:** A retrospective analysis of 100 consecutive patients with oropharyngeal squamous cell carcinoma who underwent neck dissection was performed. The primary sites included tonsillar fossa, base of tongue, and vallecula.

**Results:** The most common primary sites were tonsillar fossa (70%), base of tongue (16%), and vallecula (6%). The posterior triangle was involved in 56% of cases, and the submandibular region in 44%.

**Conclusion:** The pattern of cervical lymph node metastases in oropharyngeal squamous cell carcinoma is predominantly retropharyngeal and submandibular, with a high proportion of posterior triangle involvement.

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**P637: DISTANT METASTASIS AND 2ND PRIMARY TUMOR IN ORO- AND HYOPHARYNGEAL CARCINOMA: CLINICAL IMPACT OF FDG PET AND MDCT**

**Objective:** To evaluate the clinical impact of 18F-fluorodeoxyglucose positron emission tomography (FDG PET) and multidetector row computed tomography (MDCT) in the detection of distant metastases and second primary tumors in oropharyngeal and hypopharyngeal cancer.

**Methods:** A retrospective analysis of 181 patients with oropharyngeal squamous cell carcinoma was performed. PET and MDCT were analyzed for the presence of distant metastases and second primary tumors.

**Results:** PET detected distant metastases in 20% of patients, while MDCT detected 14%. PET detected second primary tumors in 10% of patients, compared to 6% with MDCT.

**Conclusion:** PET is more effective than MDCT in the detection of distant metastases and second primary tumors in oropharyngeal and hypopharyngeal cancer.
Eighty-two percent of the patients
We performed a retrospective analysis of 110 consecutive
Methods: 119 patients with previously untreated, resectable nonmetastatic stage III/IV head and neck squamous cell carcinoma were recruited between August 1996 and February 2002. They were randomized to either of two treatment protocols - radical surgery with adjuvant radiotherapy or concurrent chemoradiotherapy. We analysed the subset of 81 patients with tumors at non-laryngeal sites (oral cavity, oropharynx, hypopharynx and maxillary sinus). Results were analysed by intention-to-treat. Results: The median follow up for patients in the chemotherapy arm was 6.5 years (95% CI 5.6, 7.2) while that of the surgery arm 5.9 years (95% CI 5.2, 7.1). There was a statistically significant difference in the 3-year disease free survival (DFS) rates for the two groups - surgery with adjuvant radiotherapy 50.9% versus concurrent chemoradiotherapy 21.9% (p=0.019, log-rank test). No difference in the 5-year overall survival was found between the 2 treatment arms - 42.5% for surgery with adjuvant radiotherapy and 25.3% for those who had combination chemotherapy with concurrent irradiation (p=0.299, log-rank test). Patterns of recurrence did not differ between the two treatment groups. Locoregional recurrence alone, metastatic disease alone or both were similar regardless of treatment assigned. Conclusion: Contrary to our expectations, subset analysis of a randomized controlled trial suggests that concurrent chemoradiation for resectable stage III/IV non-laryngeal head and neck squamous cell carcinoma has similar overall survival and pattern of recurrence over 6.5 years as conventionally treated patients.

Objective: To review the long-term survival and pattern of recurrence of resectable, non-laryngeal head and neck squamous cell carcinoma treated with concurrent chemoradiation. Methods: 119 patients with previously untreated, resectable nonmetastatic stage III/IV head and neck squamous cell carcinoma were recruited between August 1996 and February 2002. They were randomized to either of two treatment protocols - radical surgery with adjuvant radiotherapy or concurrent chemoradiotherapy. We analysed the subset of 81 patients with tumors at non-laryngeal sites (oral cavity, oropharynx, hypopharynx and maxillary sinus). Results were analysed by intention-to-treat. Results: The median follow up for patients in the chemotherapy arm was 6.5 years (95% CI 5.6, 7.2) while that of the surgery arm 5.9 years (95% CI 5.2, 7.1). There was a statistically significant difference in the 3-year disease free survival (DFS) rates for the two groups - surgery with adjuvant radiotherapy 50.9% versus concurrent chemoradiotherapy 21.9% (p=0.019, log-rank test). No difference in the 5-year overall survival was found between the 2 treatment arms - 42.5% for surgery with adjuvant radiotherapy and 25.3% for those who had combination chemotherapy with concurrent irradiation (p=0.299, log-rank test). Patterns of recurrence did not differ between the two treatment groups. Locoregional recurrence alone, metastatic disease alone or both were similar regardless of treatment assigned. Conclusion: Contrary to our expectations, subset analysis of a randomized controlled trial suggests that concurrent chemoradiation for resectable stage III/IV non-laryngeal head and neck squamous cell carcinoma has similar overall survival and pattern of recurrence over 6.5 years as conventionally treated patients.

Objective: The treatment of oropharyngeal squamous cell carcinoma (OSCC) remains controversial. The purpose of this study is to review our experience in the treatment of OSCC and to evaluate the oncologic outcome and factors affecting locoregional recurrence. Materials and Methods: We performed a retrospective analysis of 110 consecutive OSCC patients treated primarily by surgery and/or postoperative radiotherapy at Yonsei University Severance Hospital in Korea between May 1992 and December 2004. Results: Eighty-two percent of the patients had advanced disease (stage III or IV). The 5-year overall survival and disease specific survival rate (DSSR) were 58% and 65%, respectively. According to sub-sites, that of soft palate or posterior pharyngeal wall, tonsillar area, and base of tongue was 80%, 62%, and 51%, respectively (P<0.05). The 5-year DSSR according to the American Joint Committee on Cancer stages was 94% for early stage and 56% for advanced stage (P<0.05). The overall recurrence rate was 38% (42 patients). The most frequent site of recurrence was the neck (46%). Only 14% of the patients with recurrences were successfully treated. Positive resection margins and presence of pathologic lymph node influenced the recurrence at primary lesion and in neck, respectively, in a statistically significant manner. Conclusions: Surgery and postoperative radiotherapy continue to provide a superior outcome in patients with advanced OSCC. However, further study with randomized study design will be necessary to assess the oncologic and functional superiority of surgery or chemoradiation.

Objective: Cyclooxygenase (COX)-2 has been shown to be overexpressed in oral carcinogenesis. This study evaluated the microscopic changes associated with celecoxib, a COX-2 inhibitor, in a hamster buccal carcinogenesis model using in vivo multiphoton autofluorescence microscopy and second harmonic generation microscopy. Methods: Oral lesions were induced in the buccal pouches of 10 hamsters by a 6-week painting of 9,10-dimethyl-1,2-benzanthracene (DMBA). The hamsters were then randomly divided into 2 groups based on the DMBA treated group continued on a basal diet, while the other 5 (celecoxib group) received a diet containing 1000 ppm of celecoxib for 10 weeks. Buccal cheek lesions were imaged weekly by multiphoton autofluorescence and second harmonic generation microscopy. Multiphoton autofluorescence provided contrast for the multi-layered mucosa, revealing a highly fluorescent surface keratinizing layer, epithelial cells, and lamina propria. Second harmonic generation microscopy provided contrast specific to collagen in the lamina propria. Cross-sectional micrographs (x-z) provided a clear indication of the basement membrane. Morphometric parameters such as epithelial thickness and nuclear size were analyzed. Lesions were biopsied at the end of the study and processed for histology. Results: Both the superficial keratin layers and the deep epithelial layers showed progressive increase in thickness throughout DMBA-induced carcinogenesis. Before the introduction of celecoxib diet, there were no significant differences in both epithelial thickness and nuclear sizes between the control and celecoxib groups. Average thickness of the epithelial layers was significantly greater in the control group in the post-celecoxib study period. Higher degrees of nuclear polymorphism were observed in the control group compared to the celecoxib group. Upon cessation of the study, the treatment of biopsy-confirmed squamous cell carcinoma and high-grade dysplastic lesions were also significantly higher in the control group. Conclusions: Noninvasive imaging by multiphoton autofluorescence microscopy and second harmonic generation microscopy successfully monitored microscopic changes throughout carcinogenesis, revealing differences between the control and celecoxib-treated groups. This study provides supporting evidence that celecoxib delays malignant transformation during oral carcinogenesis.

Objective: Zinc and copper are the essential trace metals. Higher level or deficiency may lead to unwanted effects. The role of copper and zinc was assessed in Oral Sub Mucosis Fibrosis (OSMF) subjects, chewers of areca nut and tobacco and non-chewers for comparison. Methods: A total of 93 chewers, 21 OSMF subjects and 23 non-chewers were included in the study. The concentration of Copper and Zinc was measured in biological media i.e. serum, saliva etc by Atomic absorption Spectrophotometer. Results: Analysis of serum, saliva and urine revealed that serum copper level was highest in subjects with OSMF followed by chewers and non-chewers in descending fashion. The saliva copper level was also highest in subjects with OSMF. Urinary copper level was also similar in both chewers and non-chewers, whereas it was lower in subjects with OSMF. However, all these changes were statistically non-significant. The reason for lower levels of urinary copper among OSMF subjects is not understood. Serum zinc level was found to be in descending fashion in non-chewers, chewers and subjects with OSMF respectively, the difference in each group being statistically significant. The saliva zinc level also showed a similar pattern of changes. Conclusion: An inverse relationship was observed between serum copper and zinc levels in subjects with OSMF, chewers and non-chewers. The study found level of zinc in descending order from non-chewers, chewers and OSMF patients. The study signifies the role of zinc deficiency in OSMF and suggests the need to explore the possibility supplementation of zinc for the control of OSMF.

Objective: To identify the targeting organ of precancerous lesion among LMP1-mt53 transgenic mice by microinjection procedures in our laboratory, study carried out in generation F3 of positively
expressing transgenic mice at 12 months age, with the negatively expressing ones as controls. All these mice were randomly divided into four pairs of groups, group with induced precancerous lesion naturally developing (GLND), strengthened carcinogenesis-inducing group with carcinogen DNP (SCIGD) without TPA, group of mice as in SCIGD with anti-carcinogenesis herbal medicine (ACHM) treatment (CIATG) and simply treating group with ACHM (STGA). In addition, one single group of wild mice as blank controls (WMBG) was set up in each group. By the end of experiment lasted 4 months, tissue samples were taken from main organs fixed in 4% formaldehyde. HE staining used for histopathological evaluation, immunohistochemistry to detect expression of LMP1-mp53 to certify their successful transferring and activities of targeting genes in AP-1 signaling pathway, and Western blotting utilized to further confirm the data from immunohistochemistry. Results: Wild animals in WMBG determined no atypical hyperplasia in main organs, while 70.3% of those positive SCIGD determined precancerous lesion in nasopharyngeal and/or nasal mucosa (22/30), a few even developed into carcinoma in situ, with LMP1 and mp53 expressing highest here and no such lesion determined in other organs. In contrast, precancerous lesion was not detected in negatively expressing GLND. 90.0% among positive SCIGD mice, while only four detected with atypical hyperplasia here (13.3%, 4/30) among positive STGA, and those positive in CIATG showed only 16.7% (5/30) with the lesion. In the nasopharyngeal and/or nasal mucosa with atypical hyperplasia and positively expressing LMP1-mp53 in GLND, shown were significant differences in expression of TRAF2, c-Jun and p16, compared with other groups like GLND among negatively expressing transgenic and wild mice. Typically showed were up-regulated TRAF2 and c-Jun and down-regulated p16, suggesting abnormalities in regulating signal transduction in AP-1 signaling pathway. Compared with CIATG and STGA among negative mice and wild mice, expression of TRAF2 and c-Jun were significantly down-regulated and that of p16 was recovered to normal level in these epithelia following treatment of ACHM for those positive animals, either treated with or without DNP (CIATG and STGA among positive mice), with the atypical hyperplasia significantly improved to a relatively normal status. This meant that pathological signaling transduction network was blocked and self-balancing mechanisms recovering in signaling pathway. Conclusions: Targeting genes have successfully transferred and function mainly in nasopharyngeal mucosa as targeting organ developing induced precancerous lesion. TRAF2 and c-Jun Expression is up-regulated while p16 is down-regulated with lesion developing. Some agents can inhibit transferred LMP1-mp53 genes expressing to prevent induced lesion from development, with underlying mechanisms by down-regulating TRAF2 and c-Jun and up-regulating p16 in AP-1 signaling pathway.

P645: COMBINATION PPAR-GAMMA & RXR-ALPHA AGONISM IN HEAD AND NECK CANCER B.R. Ross 1, F.G. Ondrey 1, B.R. Wuerzt 1, F.G. Ondrey 1, 1University of Minnesota Medical School, Minneapolis, MN

Molecularly directed therapies for head and neck cancer represent a new development in the treatment of this disease. In addition to cytotoxic chemotherapy, novel treatments directed at the EGF receptor have been recently FDA approved for combination with radiation therapy. One benefit of these treatments might be improved tumor cell kill with less toxicity to the host than is encountered with conventional chemotherapy. PPAR-gamma is a nuclear receptor that has been recently targeted by our group for clinical chemoprevention. In the present study, we examined the potential utility of combining and FDA approved retinoid, 9-cis-retinoic acid, with a prototypical preclinical PPAR-gamma-agonist, ciglitazone, as a treatment for head and neck cancer in a cell line model. We first employed PPAR-gamma luciferase reporter experiments with oral cancer cell lines CA-9-22 and NA. We discovered that the addition of 1-10 38CM 9-cis-retinoic acid to a given concentration ciglitazone significantly increased PPAR-gamma reporter gene activation over each agent individually, unless high concentrations of either agent were individually cytotoxic. Next we were able to demonstrate a significant dose-dependent decrease in cell proliferation in both cell lines after treatment with either agent alone, or in combination, as judged by MTT assay. Finally, combination therapy with both drugs significantly increased apoptosis, as judged by caspase 3 activation, than either drug individually. We conclude that combination treatment with PPAR-gamma/RXR-alpha agonists ciglitazone and 9-cis-retinoic acid represents an effective combination therapy for preclinical head and neck cancer.

P646: FROM LICHEN TO SQUAMOUS CELL CARCINOMA: 4 CASE REPORTS L. F. Choksi 1, B. D. Udr 2, A. Kacker 2, J. Bocker 1, J. Boyle 1, 1Memorial Sloan-Kettering Cancer Center, New York, NY; 2Weill Medical College of Cornell University, New York, NY

Objectives: In order to investigate potential targets for tobacco related cancer prevention the objective of this research was to utilize oral buccal mucosa biopsies from smokers and non-smokers to identify Tobacco Smoke (TS) induced changes in the transcriptome. The investigators sought also to further define the signal transduction pathway by which tobacco smoke (TS) induces CYP1A1, CYP1B1 in a human premalignant oral epithelial cell line. Potential targeted therapies like CK2 inhibitors were evaluated for their ability to disrupt this pathway in vitro. Methods: 18 patients, 9 never smokers and 9 active smokers (at least a 15 pack year history) were recruited and biopsies were obtained from the buccal mucosa. This tissue was utilized to perform RTPCR and results were compared to data from a previous in vitro study. In vitro experiments were performed with drugs such as CK-2 (casein kinase-2) inhibitors to determine their effects on TS mediated Aryl Hydrocarbon Receptor (AhR) signaling. MSK-Leuk1 cells were incubated with TS extract with and without co treatment with CK2 inhibitors. Lysates were analyzed for protein expression by western immunoblotting and for gene expression by RTPCR. Results: There were significant differences in gene expression analyzed by RTPCR between smokers and non-smokers. Several of these genes such as CYP1A1 and CYP1B1 are known to be activated by AhR signaling as demonstrated in a previous in vitro study. In the
in vitro model CK2 inhibitors block TS mediated activation of these same genes. **Conclusions:** TS mediated AhR gene expression is significantly altered in the oral mucosa of current smokers. Some of the same changes are abrogated by disrupting AhR signaling using CK-2 inhibitors. There may be potential targets in the AhR signaling pathway with potential utility in tobacco related cancer prevention.

**P648: INDIGO NATURALIS, INDIGO AND INDIRUBIN SUPPRESS CELL GROWTH AND INDUCE APOPTOSIS IN ORAL SQUAMOUS CANCER CELL**

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**Objective:** Oral cancer is one of the most common cancers in Taiwan, especially in male population. Oral squamous cell carcinoma (OSCC) accounts for more than 95% of all malignant neoplasms in the oral cavity. The malignant transformation of OSCC involves a multi-step process of aberrant genetic events following the action of various carcinogens, which may come from chronic use of factors such as tobacco, alcohol, and betel quid (BQ) in Taiwanese population. In the carcinogenesis process, the normal epithelial cells will transform into pre-cancerous lesions (PML), and then some of these lesions may get worse to OSCC. Indigo naturalis is dried powder and prepared from the leaves and stems of Chinese herb, Baphicacanthus cu-sia (Nees) Bremek(Acanthaceae), Polygonum tinctorium Ait.(Polygonaceae) and Isatis indigotica Fort. ( Cruciferae). They are used to clear away heat and toxic material, cool the blood and disperse heat in the liver. It is applied permanently and professionally for febrile disease.

**Methods:** We collected Indigo naturalis from different localities, Taipan, Guangzhou, Hong Kong and Macao. All Indigo naturalis were carried out the MTS, direct caspase-3 and TUNEL assay to measure the effects on cell growth and apoptosis in HSC-3 and CAL-27 cell lines of OSCC. Moreover, we quantized the major components, Indigo and Indirubin in all Indigo naturalis by HPLC analysis, respectively. Repeated the above in induced cell. Results: In our initial data, the Indigo naturalis derived from Taiwan, not from Guangzhou, Hong Kong and Macao were shown the inhibition in cell proliferation in human oral cancer cell line HSC-3 and CAL-27. The inhibition was shown a time- and dose- dependent manner. Our results also demonstrated that Indigo naturalis, Indigo and Indirubin have differential capabilities of apoptosis inducing in HSC-3 and CAL-27. Indirubin have the greatest effect.

**Conclusions:** Compared with MTS, direct caspase-3 and TUNEL assay, we demonstrated that the Chinese herbal Indigo naturalis isn’t only a member of dyes, but also a potential tumor drug in OSCC.

**P649: HELP AND HEALTH CARE SEEKING BEHAVIOR IN A RURAL HEAD AND NECK CANCER POPULATION**

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**Objective:** Incidence and mortality rates of HNSCC exhibit diverse patterns and trends across geographic regions and populations across the United States. Previous research has consistently shown that certain populations, such as poor, rural populations like those found in rural Appalachian Kentucky, while having generally lower rates of these types of cancers, are extremely likely to suffer disproportionate mortality, negative side effects, and encounter challenges while seeking and obtaining cancer therapies. Little is actually known as to the true patterns of disease in this population and the reasons for delays in diagnosis. It is our hypothesis that in addition to difficulties with access to care, there are differences in health care seeking behavior in these populations which may impact not only timely diagnosis but completion of and compliance with therapy. Our specific aim is to identify and examine determinants of decision making among HNSCC patients in a rural, Appalachian population.

**Methods:** Previous quantitative studies have not been able to capture the experience as thoroughly explain why some head and neck cancer patients delay help seeking and treatment. Use of qualitative methods, grounded theory in particular, will enable a more complete exploration of underlying beliefs and meanings that go beyond what quantitative studies can investigate. Data for this study will come from semi structured, convergent interviews with newly diagnosed HNSCC patients. Transcription, analysis, and theoretical sampling will occur simultaneously. Transcribed data will be imported into NVivo 7, a qualitative data analysis software package (QSR International). After coding, categories, themes, and core concepts will be identified and then sorted within the analysis package, including direct participant quotations. Visual modeling of the analyses and the research findings will provide a mechanism to demonstrate relationships within the data and is consistent with the Grounded theory approach.

**Results:** The results of this study will enable a more complete examination of determinants of cancer help seeking behavior by focusing on the individual, the health care provider, the medical system, and the environmental or community context. We anticipate that the results of this study will support our hypothesis that health behavior, particularly delay in help seeking, is strongly impacted by multiple, competing characteristics, such as demographic variables, social structure, access to care, and perceived and evaluated health.

**Conclusions:** Clinical advances in treatment modalities will be more successful if patients can be moved to treatment earlier. This study offers more advanced understanding of patient related determinants that influence help seeking, and in particular, the reasons for delay in obtaining treatment.

**P650: ONE-DAY CAMPAIGN FOR ORAL CANCER PREVENTION AND DIAGNOSIS IN PARANÁ STATE - BRAZIL**

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**Objective:** Oral cancer prevention and diagnosis at early stages.

**Methods:** Professionals all across the State of Paraná (Brazil) received training for attending to patients on a single day of 2002. Patients over 30 years old answered a 105-item questionnaire and had a clinical exam. The assumption was that in addition to difficulties with access to care, there are differences in help seeking behavior, particularly delay in help seeking, is strongly impacted by multiple, competing characteristics, such as demographic variables, social structure, access to care, and perceived and evaluated health.

**Results:** The results of this campaign were: 7638 clinical exams in 58 cities, 66.7% of the patients had never undergone preventive exams; 17.4% had never heard of it; 62.5% were under-paid women (<US$150.00); 58.0% completed elementary school, and 58.0% even less; 26.2% were illiterate; 52.5% never see the dentist; 57.2% wore full dentures. The exams revealed 1522 lesions (22.6%), 16.1% of the patients presented suspicious lesions drank alcohol and 21.0% smoked. Most lesions were traumatic 761 (50%) and inflammatory I (reddish) 87 (5.7%), cases. Cancer suspicious lesions were found in 42 (2.8%). The patients who needed a biopsy were sent to the closest health centre.

**Conclusion:** Most patients were underpaid, illiterate and poorly-educated. Preventive campaigns of this sort have a great potential of increasing the chance of cure of malignant cancer through early detection, prevention through education and treatment of early lesions. Our main aim is to improve the quality of life of the population through orientation and treatment of benign lesions.

**P651: ORAL CANCER PREVENTION AND EARLY DIAGNOSIS ON A CAMPAIGN TARGETED TO ELDERLY PATIENTS IN PARANA/BRAZIL**

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**Objective:** The number of oral lesions afflicting elderly patients in rising significantly, which calls our attention to the necessity of preventive campaigns.

**Methods:** For 19 years we developed a number of campaigns aiming at oral cancer prevention and early detection. Such campaigns were promoted by Liga Paranense de Combate ao Cancer (Cancer League of Paraná) and Unidos dos Gaknas in Curitiba. They took place on public squares of many cities, where health stands were put up. Each of the cities was visited once or twice every year, and each visit lasted from 1 to 3 days, with an average of 60-70 visitors a day. We obtained the anamnesis of all patients through a database of 105 items, and all information we gathered was registered in medical records. In addition to clinical support, all patients were instructed about cancer prevention through pictures of cancer and brochures both with health carts and hapahopatic measures. When we diagnosed lesions, we sent the patients to the nearest health centres, such as Hospital Erasto Gaertner (Curitiba).

**Results:** We performed 8,688 clinical exams in 19 cities of Paraná between the years 1898 and 2007. 1801 (20.77%) of these patients were elderly, i.e. above 60 years of age. 51.1% of the patients was male (921 patients), underpaid (< than 2 minimum wages, poorly-educated 962 (elementary
Most patients who took part in the campaign were male, such programmes need to be strengthened in real sense. Minimizing morbidity and mortality due to cancer through prevention is of increasing the chance of cure of malignant cancer through early detection, prevention through education and treatment of early lesions. Our main aim is to improve the quality of life of the population through orientation and treatment of benign lesions. We also strongly recommend developing campaigns oriented towards male patients, in order to attract their attention as well.

Methods:
Participants were screened for oral and laryngeal cancers during three NASCAR race events. Screening were completed by 45 Otolaryngologists or Oral Maxillo Facial Surgeons. Results were analyzed using descriptive statistics for demographic variables. Multiple logistic regression with abnormal findings as the outcome variable and demographic variables were used to determine the likelihood of abnormal findings. Predictive statistics were used to develop a model for predicting the probability of abnormal findings in head and neck cancer screenings. Discussion: The demographics of NASCAR fans indicate that they are at high risk for the development of a variety of head and neck cancers with the high incidence of smoking/smokeless tobacco. There is a need for widely adopted and greatly intensified preventive initiatives with which are tobacco related can be prevented which justifies the prioritized approach of increasing the chance of cure of malign cancer through early detection, prevention through education and treatment of early lesions. The themes suggested by this elicitation study suggest the latter and now require validation in a larger patient sample. As specific barriers to earlier detection are identified and validated, opportunities to intervene and eliminate the disparity will become apparent.

Results: 23 of 24 participants presented with advanced stage HNSCCA. Overall, 10% experienced barriers to obtaining early medical care, though 30% were hesitant to seek care due to perceived barriers (transportation and cost). Definitive treatment began for 81% of participants within three months of initially seeking care. Conclusion: The timelines described by the majority of participants did not support the original hypothesis. Once the participants chose to seek care, definitive treatment followed within a reasonable timeframe. To explain the advanced stage at presentation, either the tumor growth rate was more rapid than is typical for whites, or, the participants began to seek care when the tumor was already at a more advanced stage. The themes suggested by this elicitation study suggest the latter and now require validation in a larger patient sample. As specific barriers to earlier detection are identified and validated, opportunities to intervene and eliminate the disparity will become apparent.

Objective: Minimizing morbidity and mortality due to cancer through prevention and early detection. Global Thrust and Country Scenario: As per World Health organization there is a great need for giving major emphasis to the primary prevention and early detection of preventable mortality and morbidity rather then face the burden of costly treatment. Through appropriate preventive and early detection efforts 40% of all cancers in India can be cured.WHO estimates that 91% of oral cancers in India are directly attributable to the use of tobacco, fortunately they can be prevented. Also, Due to prevailing socio economic factors like illiteracy, ignorance and poverty with added factors like poor personal hygiene, marriage of girls at an early age, multiple repeated pregnancies, cancer of cervix is frequently encountered with the occurrence of 19.8% per 100,000 women around delhi. India one third of woman above 15 yrs use some form of tobacco and most women belong to the poor, uneducated and rural background. Of all deaths 4% female deaths are tobacco related. Worlds highest incidence for oral cancer is among woman in Bangalore and Chennai in India. In India cancer is the fourth most common cause of death which is around 5 lac deaths per year with 8 lacs new cancer cases every year. Unfortunately 70% cancers are detected when it is too late. At least one third of cancers can be cured if detected early, another one third cancers which are tobacco related can be prevented which justifies the prioritized need for widely adopted and greatly intensified preventive initiatives with equal emphasis in early detection. Methodology: Attracted by the magnitude of cancer epidemic broad based and well planned cancer prevention and awareness, educational campaigns, training and early detection efforts were started nearly 10 years ago purely on voluntary basis. To sum up the various activities undertaken by the charity are organizing lectures, talks, exhibition etc in communities, workplaces, schools, public mass meetings, listings of government offices, in service clubs, training for self examination of oral cavity, breast in early sign n symptoms of cancers. Organizing early detection camps in rural areas along with display of exhibits, organizing seminars, meetings of government offices, in service clubs, training for self examination of oral cavity, breast in early signs of cancers are considered as the importance of awareness and early detection of cancer and avoiding use of risk factors, also changing the life style and quitting tobacco use in any form. Conclusion: Such programmes need to be strengthened in real sense. Though early detection, prevention and control of common cancers is on one of the important component of national cancer control programme yet there is need for a strong public health effort for implementing the above efforts in true sense especially at the horizontal level and also the involvement of NGO’s should be encouraged and strengthened with province. There is striking racial disparity in the incidence and survival of head and neck squamous cell carcinoma (HNSCCA). One apparent cause is an advanced stage of presentation in African Americans compared to whites. The purpose of this study was to elicit barriers to early treatment of HNSCCA among African American men. We hypothesized that limited access to medical care (e.g. no physician in community or inability to pay) would be the primary barrier to early treatment. Methods: Structured interviews were completed with twenty four African American men who had survived treatment for HNSCCA. Trained interviewers elicited the participants’ experiences from the time of symptom recognition to the time of receiving definitive care. Transcripts were analyzed contextually by three investigators.

Results: 23 of 24 participants presented with advanced stage HNSCCA. Only one participant was refused care initially for financial reasons. Overall, 10% experienced barriers to obtaining early medical care, though 30% were hesitant to seek care due to perceived barriers (transportation and cost). Definitive treatment began for 81% of participants within three months of initially seeking care. Conclusion: The timelines described by the majority of participants did not support the original hypothesis. Once the participants chose to seek care, definitive treatment followed within a reasonable timeframe. To explain the advanced stage at presentation, either the tumor growth rate was more rapid than is typical for whites, or, the participants began to seek care when the tumor was already at a more advanced stage. The themes suggested by this elicitation study suggest the latter and now require validation in a larger patient sample. As specific barriers to earlier detection are identified and validated, opportunities to intervene and eliminate the disparity will become apparent.
improved infrastructure and national government should not only offer technical support but liberal financial support frequently. Since prevention and early detection of cancer is the only tool for putting a check on poverty in developing and under developed world.

P655: ORAL CANCER PREVENTION AND EARLY DIAGNOSIS: A ONE DAY CAMPAIGN TARGETED TO ELDERLY PATIENTS IN PARANA/BRAZIL

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Abstract: The number of oral lesions afflicting elderly patients in rising significantly, which calls our attention to the necessity of preventive campaigns. Objectives: To develop a campaign aiming at oral cancer prevention and early detection. Such campaigns were promoted by Liga Paranense de Combate ao Cancer (Cancer League of Parana) and Uniao dos Gakusseus de Curitiba. They took place on public squares of many cities, where health stands were put up. Each of the cities was visited once or twice every year, and each visit included from 3 to 5 days, with an average of 60.7% of visits a day. We obtained the anamnesis of all patients through a database of 105 items, and all information we gathered was registered in medical records. In addition to clinical support, all patients were instructed about cancer prevention through pictures of lesions and brochures both on self-exam and prophylactic measures. When we diagnosed lesions, we sent the patients to the nearest health centres, such as Hospital Erasto Gaertner (Curitiba). Results: We performed 8,668 clinical exams in 20 cities of Paraná between the years 1898 and 2007. 1,801 (20.77%) of these patients were elderly, i.e. above 60 years of age. 51.1% of the patients was male (921 patients), underpaid (< 2 minimum wages, poorly-educated 962 (elementary school or below, 59.6%), aged between 61 and 70 (62.4%). More than half (60.7%) did not see the dentist regularly, and very poor oral hygiene was found in 54.2% of the cases, 73.0% of which wore full or partial dentures. 31.7% (570) of the patients was edentulous and wore no denture. We found 412 lesions (22.9%) among which 356 (86.4%) was oral and the others, of skin. Most oral lesions were traumatic 171 (48.0%) and inflammatory 76 (21.3%). Reddish lesions were present in 32 (9.0%) of the patients, and leukoplakia in 25 (7.0%) (others: 7.8%). We found cancer suggestive lesions in 24 cases (6.7%), out of which 20 were biopsied (5.6%), and 2 actually had the cancer diagnosis confirmed. The other patients who needed a biopsy were sent to the closest health centre. Conclusion: Most patients who took part in the campaign were male, underpaid, illiterate and poorly-educated. Patients aged 60 or more generally had extremely poor oral hygiene, wore dentures, e presented high incidence of oral lesions. Preventive campaigns of this sort have a great potential of increasing the prevalence of tobacco consumption in Colombia runs near the 19.8% of the general population. Our study showed that compared to the rest of the population, only twelve percent of well trained and educated professors of medicine still smoke. Considering the fact that they are working in one of the leading medical schools in the country, that they are in charge of teaching future generations of doctors, and that above all they are responsible for the health of thousands of fellow Colombians, this percentage is still too high. With no doubt smoking is not only a bad habit to break, but also a disease difficult to fight.

P656: EVALUATION OF A CLINIC BASED INTERVENTION TO ASSIST CANCER PATIENTS TO STOP SMOKING

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Objective: In patients diagnosed with cancer, smoking cessation improves health outcomes. Despite this fact, provider-delivered cessation interventions are not routinely incorporated into clinical visits with patients. This study evaluates an effort to alter smoking cessation practice patterns in a dental/surgical clinic for cancer patients. Methods: A quasi-experimental study design was used to compare practice patterns and smoking cessation outcomes associated with an enhanced smoking cessation treatment program (EC) compared to usual care (UC). Adult smokers were accrued via a self-administered survey from May to July for the UC group and from July to Sept 2007 for the EC group. All providers attended a training program on smoking cessation as part of enhanced care that included systematic delivery of advice to quit, assistance (smoking cessation medication, education materials) and telephone support at 1 week. Results are reported from a follow-up telephone interview conducted with patients one month after their clinic visit for the UC group (n=66) and EC group (n=55). Results: At one month, smokers who were exposed to the EC intervention were more likely to report being asked about their smoking status (92.7% vs. 71.2%, p<0.003), to be informed of the benefits of quitting (52.7% vs. 51.2%, p<0.031), to be advised to quit (78.2% vs. 51.5%, p=0.002), to be prescribed stop smoking medication (29.1% vs. 4.5%, p<0.001) and to have received a support call (52.7% vs. 10.7%, p<0.001) by someone in the clinic compared to those exposed to the UC condition. Self reported quit attempts (UC 50.9% vs. EC 52.1%, p=0.905) and quit rates (UC 17.5% vs. EC 13.2%, p = 0.529) were similar for both groups. Conclusion: Our intervention was successful in increasing the delivery of a standardized evidence based smoking cessation intervention, but this did not translate into higher rates of quitting at one month post-clinic visit. It is possible that this relatively brief stop smoking intervention was simply not intense enough to alter the smoking habits of this patient population. The clinical effectiveness of the intervention may only be revealed after repeated efforts to persuade and assist these patients to alter their smoking behavior.

P657: SMOKING HABITS OF PROFESSORS OF CLINICAL MEDICINE IN A MEDICAL SCHOOL IN MEDI LLIN COLOMBIA

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Objective: A research study was designed to determine the frequency and demographics of smoking habits among professors of clinical medicine of the University of Antioquia Medical School. We wanted also to establish patterns of education from those smoking doctors to their patients in relation with or without their medical problem. Methodology: A prospective study was conducted filling out a pre-established form that was distributed among the different departments of Clinical and Surgical specialties of the University of Antioquia Medical School in Medellin, Colombia between June and September 2006. Results: Out of the 243 professors that ended up filling out the form, almost 121 (49.8%) of them described a past history of tobacco consumption and 29 (11.9%) of them were active smokers while the study was conducted. There were no statistical significant differences among the habit of tobacco consumption among the different specialties. A significant number of doctors (190- 78.2%) asked their patients about tobacco use regardless of their medical problem that prompted to seek medical attention. Almost 56.4 % of them (N= 137) advised the patient to quit smoking. Conclusions: According to government studies, the prevalence of tobacco consumption in Colombia runs near the 19.8% of the general population. Our study showed that compared to the rest of the population, only twelve percent of well trained and educated professors of medicine still smoke. Considering the fact that they are working in one of the leading medical schools in the country, that they are in charge of teaching future generations of doctors, and that above all they are responsible for the health of thousands of fellow Colombians, this percentage is still too high. With no doubt smoking is not only a bad habit to break, but also a disease difficult to fight.

P658: INTEGRATION OF A HYPERBARIC OXYGEN THERAPY MEDICAL UNIT INTO AN ACADEMIC HEAD AND NECK SURGERY DIVISION

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Objective: To understand pertinent factors to successfully integrating a hyperbaric oxygen therapy medical unit into an academic head and neck surgery division in an academic medical center. Methods: A qualitative study was designed to compare practice patterns and smoking cessation outcomes associated with an enhanced smoking cessation treatment program (EC) compared to usual care (UC). Adult smokers were accrued via a self-administered survey from May to July for the UC group and from July to Sept 2007 for the EC group. All providers attended a training program on smoking cessation as part of enhanced care that included systematic delivery of advice to quit, assistance (smoking cessation medication, education materials) and telephone support at 1 week. Results are reported...
experience of a fully operational/full service hyperbaric oxygen therapy unit, staffed primarily by head and neck surgeons and under the management of the director of the head and neck surgery division, is reviewed. Specific attention is placed on administrative, staffing and patient characteristics which allow the operation to continue in a self-sustaining and clinically successful manner. Results: During the four year period from 10/03 : 9/07, annual averages of 2,165 HBO treatments were administered in 2,384 patients with 31 different cancer sites. The majority of the HBO treatments were for chronic wounds related to tissue radiation necrosis (Bone/Soft Tissue), vascular insufficiency and diabetes mellitus. The most common emergency indication was carbon monoxide poisoning. The primary associated complication with treatment was seizure (1 per 1000 treatments). Staffing increased from 6 certified HBO physicians to 10 during that period. Currently, there are 4 fellowship-trained HBO physicians. Conclusion: The DBHMOHB can be successfully integrated into and maintained within an academic head and neck surgery division. Factors essential for success include: committed division members motivated for the success of each effort, a critical number of physicians to limit the call burden, placement within a medical center, with ready physician access for consultation and complication management. Benefits for the head and neck surgery division include: access to an important medical specialty for the management of wound complications related to XRT, referrals for subsequent reconstruction in patients outside of the division, potentially positive financial advantage in the advancement of associated projects. Future directions include research in basic science related to HBO, use of HBO as a treatment adjunct to XRT and outcomes assessments.

P659: THE ROLE OF BLOOD TRANSFUSION PRIOR TO RADIO-THERAPY IN PATIENTS WITH HNSCC - EVALUATION OF DAHANCA 5&7 RANDOMIZED TRIALS

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Objective: There is evidence that the level of hemoglobin (Hb) is an important prognostic factor for response to radiotherapy (RT) in patients with head and neck cancer. Patients with low pre-irradiation Hb levels have worse loco-regional control and survival. This can be caused by a number of mechanisms, but has been connected with hypoxia in the tumor. It has been shown that modification of hypoxia can cause a better loco-regional control and disease specific survival. Hb level can be raised either by transfusions or by treatment with erythropoiesis stimulating agents. Experiments have shown that a rise in Hb level by transfusion can cause higher tumor oxygenation, that modification of hypoxia can cause a better loco-regional control and survival. This can be caused by a number of mechanisms.

Methods: Patients were randomized to treatment arms were well balanced regarding tumor characteristics and treatment modalities. Transfusions were able to raise Hb levels above level for transfusion. The treatment effect was evaluated using the intention to treat principle using 5-year actuarial values for loco-regional recurrence, disease-specific survival and overall survival. Results: A total of 472 patients with low Hb levels were included. Tumors were located in the supraglottic larynx, pharynx and oral cavity. Among these, 236 were randomized to receive transfusions. In the majority of the cases transfusions were able to raise Hb levels above level for transfusion. The treatment arm was 16/38(42%) of whom had PEG tubes placement, compared to those who were treated with RT alone.

Results: More patients who received CR, and or oral cavity/oropharyngeal cancer had PEG tubes placement, compared to those who were treated with RT alone, 0.55), disease specific survival (40% vs. 48%; p-value 0.15) or overall survival (24% vs. 31%; p-value 0.17). There was no difference in the number of distant metastases. In multivariate analyses there was no effect of transfusion on endpoints. Conclusion: Transfusion prior to radiotherapy was unable to improve the effect of radiotherapy in a large patient material with low Hb values.

P660: HYPOFRACTIONATED PALLIATIVE RADIOTHERAPY IN NON-NASOPHARYNGEAL INCURABLE HEAD NECK SQUA-MOUS CELL CARCINOMA

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Background and Purpose: A proportion of advanced stage head and neck cancer patients are incurable and have a limited life expectancy. The study aimed to offer a course of hypofractionated palliative radiotherapy and evaluate the effect on pain response rate, local control (LC) and progression free survival (PFS).

Patients and Methods: Between 2000 and 2005, 110 patients of incurable squamous cell carcinoma of head and neck treated with palliative radiotherapy (40 Gy in 16 fractions). Distressing symptoms were assessed before starting of treatment. Patients having good objective regression at tumor and nodal sites with acceptable toxicity received further escalation of dose till 50 Gy. In our analysis three strata were made in order to compare symptomatic improvement viz percentage relief <50%, percentage relief in between 50 to 75% and >75% symptomatic relief. Most common distressing complaint was pain in 109 (99%) patients, dysphagia in 97 (88%) patients, neck nodal swelling in 95 (86%) and hoarseness in 30(27%) patients prior to starting of radiotherapy. The severity wise distribution of for most frequent symptoms index, pain and dysphagia was 22(20%), 72(65%), 13(13.6%) and 44(40%), 52(47.3%), 10(9.9%), mild, moderate and severe, respectively. 11 patients (10%) had complete response(CR) and 80 (72.7%) patients had complete and partial response (PR). At completion of radiotherapy 26%, 57% and 17% of patients had <50%, 50-75% and >75% symptomatic relief. At last follow up with median of six months the percentages relief were 22%, 14% and 64%. The over all progression free survival (PFS) and local control (LC) at 12 months was 65.1% and 67% respectively. On multivariate analysis weight >50 Kg (p=0.049) and radiotherapy dose of more than 40 Gy (0.012) is found to be important prognostic factor for PFS and LC. None of the patient died due to toxicity and acute and late morbidity of skin / mucosal reactions were acceptable.

Conclusion: Hypofractionated radiotherapy is an effective treatment modality for sustainable symptoms relief with good overall response rate and acceptable毒性.
P662: POOR COMPLIANCE WITH CHEMORADIOTHERAPY PREDICTS PERSISTENT REGIONAL DISEASE IN ADVANCED HEAD AND NECK CANCER M.O. Patadia 1, N. Holloway 2, F. Rosen 2, U.A. Patel 1, 1Northwestern University, Chicago, IL; 2Stroger Hospital of Cook County, Chicago, IL

Objective: Combined chemoradiotherapy is frequently used as primary therapy for advanced-stage squamous cell carcinoma of the head and neck. Neck dissection following treatment is planned for patients initially staged with N2a or greater nodal disease. It remains unclear which patients will have persistent neck disease after treatment and benefit most from neck dissection. At Cook County Hospital, we perceive that patients have a high incidence of persistent neck disease at the time of dissection. Previous studies here have demonstrated poor compliance to chemoradiation with unacceptable treatment interruptions. The objective of the current study is to determine if poor compliance to chemoradiation results in increased rate of persistent neck disease following treatment. Methods: Patients undergoing primary chemoradiotherapy followed by planned neck dissection for advanced squamous cell carcinoma of the head and neck from 2003 to 2007 were identified from tumor conference records at Cook County Hospital. Medical charts were reviewed to extract data including age, gender, race, primary site, TNM stage, radiographic staging prior to and following treatment and pathological findings of neck dissection. Radiotherapy charts were reviewed to extract total dose received, duration of treatment, and missed treatment days. Poor compliance was defined as total treatment interruption > 14 days while patients were considered compliant with < 14 days interruption. Univariate and multivariate analysis was performed to assess impact of poor compliance upon pathological response identified in neck dissection specimens. CT scan findings were used to assess correlation between imaging results after chemoradiotherapy and pathological response rates. Results: There were 44 neck dissections performed on 40 patients included in the study. All patients completed concomitant chemoradiotherapy with total dose > 70 Gy. Of 40 patients, 18 (45%) were found to have positive pathology for carcinoma in neck dissection specimens while 22 (55%) demonstrated a complete response in the neck. There were 13 (35%) with poor compliance to radiotherapy (> 14 days treatment interruption) and the remaining 26 (65%) had less than 14 missed days. For the 14 patients with poor compliance, only 3 (21%) had a pathologically negative neck dissection while 11 (79%) had persistent disease. For the compliant group, 19 (73%) had a negative neck dissection while only 7 (27%) showed persistent disease. This difference was statistically significant (p = 0.003) with a hazard ratio of 9.9 for poorly compliant patients having a positive neck dissection. Multivariate logistic regression showed ethnicity, primary site location, and T or N stage were not significant in predicting positive pathology and that compliance remained the only significant associated variable. Restaging with CT scan after chemoradiation also failed to demonstrate significant association for positive versus negative pathology. Conclusions: This study demonstrates a high rate of persistent disease on pathology of neck specimens following chemoradiotherapy in our patient population. Poorly compliant patients are at significantly higher risk and may require neck dissection following treatment. This variable was more predictive than pre-treatment variables as well as the post-treatment CT scan. Further studies investigating patterns of failure after chemoradiotherapy in the poorly compliant patient population are warranted.

P664: RELATIONSHIPS BETWEEN PAIN AND COPING STRATEGIES IN PATIENTS UNDERGOING RADIATION THERAPY FOR HEAD AND NECK CANCER D.J. Fischer 1, D.J. Wilkie 2, Y.O. Kim 2, 1University of Illinois at Chicago College of Dentistry, Chicago, IL; 2University of Illinois at Chicago College of Nursing, Chicago, IL

Objective: Most literature on coping mechanisms in head and neck cancer (HNC) patients has addressed coping as it relates to the disease; however, the effect of coping upon cancer-related pain has not been assessed. Over 90% of HNC patients report pain associated with the tumor, whereas in 20% the pain is secondary to therapy. The aim of this study is to explore the relationship between sensory pain characteristics and coping strategies in a population of patients undergoing treatment for head and neck cancer. Methods: This was a cross-sectional study of 124 consecutive patients (77% male, mean age 54.7 ± 12.3 years) undergoing radiation treatment for head and neck cancer. Coping strategies were measured with the 8 subscales of the Coping Strategies Questionnaire (CSQ). Baseline data were collected on sensory pain characteristics (McGill Pain Questionnaire, MPQ) and pain intensity (Pain Intensity Number Scale). Descriptive statistics and Pearson correlation coefficients (r) were performed with SPSS (Chicago, Illinois). Results: The number of pain sites, which averaged 2.1 ± 2.2 different sites, was related to diverting attention (r = 0.3, p < 0.01), interpreting pain sensations (r = 0.3, p < 0.05), and increasing pain behavior (r = 0.3, p < 0.05), whereas higher levels of least pain were associated with catastrophizing coping (r = 0.5, p < 0.01). Conclusions: This study demonstrates pain intensity and its components are related to different coping strategies.

P663: CONCURRENT WEEKLY PLATINUM AND RADIATION FOR UNRESECTABLE SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK S. Limaye 1, S.N. Horowitz 1, A. Carmali 1, B. Mehrotra 1, 1Long Island Medical Center, New Hyde Park, NY

Objective: Concomitant chemoradiotherapy with platinum, given every three weeks, has been a standard treatment option in the management of unresectable squamous cell carcinoma of head and neck (SCCHN). Many patients are unable to tolerate the toxicity of platinum used at a higher dose, every week. The objective of the present study was to evaluate the efficacy and feasibility of concurrent weekly platinum with radiation in such patients who have poor performance status and multiple comorbidities. Methods: Data was reviewed retrospectively on patients treated between 2003-2007 at our institution with weekly platinum and radiation for unresectable SCCHN. Patients were treated with weekly Carboplatinum AUC = 2(n=9) or Cisplatinum at 35mg/m2 (n=16) or both (n=2) given concurrently with radiation. Median duration of treatment was 6 weeks. Treatment response was elicited by clinical exam, PET and CT scans. Results: Twenty seven patient charts were identified. Twenty three patients had primary unresectable disease and four had recurrent disease. Stage III (n = 2), Stage IV A (n = 21) and Stage IV B (n = 4) cancers of oral cavity (n=5), oropharynx (n=17), hypopharynx (n=2) and occult primary with neck adenopathy (n=2), were treated. Twenty two patients had chemotherapy only and one had addition of external beam radiation. Nineteen patients (70%) had complete remission, two (7%) had partial remission and 6 (22%) had progression of disease at the first follow-up imaging. Median duration of follow up was 13+ months (range 5-36months) for patients that are alive and 11 months for the dead (range 5-17 months). Sixteen patients (59%) needed PEG placement even though the treatment was well tolerated. The disease free and overall survival rates were 7 months and 16 months for the patients treated for primary disease and 3 months and 20 months for those treated for recurrent disease. The overall survival rate at the end of first year was 83% for primary disease and 75% for recurrent disease. Conclusion: Concomitant weekly platinum and radiation therapy for unresectable squamous cell carcinoma of head and neck results in a complete response rate and comparative survival in patients with poor performance status and comorbidities. Prospective trials should be designed based on performance status scales to further validate the feasibility of this regimen.
Background: Treatment options for patients with recurrent or new primary squamous cell carcinoma of the head and neck (SCHN), occurring in a previously irradiated area, are limited. If salvage surgery is not possible or if poor prognostic features are identified after salvage surgery, re-irradiation with or without concurrent chemotherapy may be considered.

Objectives: To determine the safety, efficacy, and prognostic factors associated with re-irradiation of head and neck squamous cell carcinoma.

Methods: Data from prospective and retrospective reports on re-irradiation with or without chemotherapy either primarily or after salvage surgery at a tertiary care cancer center between 1998 and 2007 were reviewed. Included were patients in whom the re-irradiation field significantly overlapped with the previous treatment fields. Analyses were based on intention to treat, including patients who did not complete planned radiation. Results: There were 69 patients, including 44 patients with unrelenting disease before re-irradiation. Median age was 62 (35-81) years. Disease sites were oropharynx (48%), oral cavity (28%), larynx (16%), and other (8%). The median sum of tumor and nodal diameter was 3 (0.5-10) cm. The median duration between previous radiation and re-irradiation was 33 (2-284) months. Median re-irradiation dosage was 60 Gy, resulting in a cumulative lifetime dose of 120 (1-144) Gy. The most common adverse event was dysphagia requiring feeding tube. No carotid rupture was documented. Of the 7 patients who received concurrent cetuximab and re-irradiation, 1 patient developed grade 3 skin toxicity. Conclusion: Salvage re-irradiation with or without chemotherapy, though associated with significant toxicities, can produce long-term survival. Predictors of better survival include receiving higher re-irradiation dosage and a lower tumor bulk.

P667: FAILURES IN MICROVASCULAR RECONSTRUCTION

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Objective: To review our experience with microvascular reconstruction for head and neck defects after ablative resection focusing on patients with complete flap loss. We assess the choice in secondary reconstruction and the outcomes in this subset of patients.

Methods: A retrospective review of 119 consecutive patients who underwent 127 free tissue transfers from 1999-2007. Results: We identified 11 patients with failed primary free tissue transfers (patient-specific success rate = 91%). In comparison with our series as a whole this subgroup was similar in terms of demographics except for a higher proportion of women (73% vs. 39%). Disease characteristics (pathologic diagnosis, location, and prior treatment status) and types of free tissue transfer were relatively similar. There was a predominance of previously treated recurrent oral cavity squamous cell carcinoma defects reconstructed with a technically sound operation. Failures were divided evenly into intraoperative failures likely due to technical issues such as arterial anastomosis or pedicle geometry and postoperative failures associated with wound problems such as hematoma or infection. The secondary reconstructive plan included regional tissue transfer (n=4), secondary free tissue transfer (n=4), and conservative management (n=3). In patients undergoing a second transfer, another failure occurred in 3 cases (75%). Follow-up of at least one year demonstrates a recurrence and mortality rate in this subgroup of 44%. Conclusions: Microvascular free tissue transfer has been proven as a reliable and effective means of restoring form and function in head and neck reconstruction. However, very few studies have addressed the outcomes of patients with a failed free flap. Although our study group is limited in size, we have observed that in patients with intraoperative failures defects are reconstructed with a technically sound operation. Secondary free flap has a higher likelihood of failure. Consideration should be given for other forms of reconstruction.

P668: THE SAFETY AND EFFICACY OF THE HOMEOPATHIC MEDICATION TRAUMEEL S FOR THE TREATMENT OF RADIATION-INDUCED MUCOSITIS

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Objective: The objective of this study was to determine the safety of TRAUMEEL S for prevention of oral cavity mucositis in head and neck cancer patients undergoing post-operative radiation therapy. Methods: This was a prospective phase I trial with a control arm (normal saline), with dose escalation in cohorts of 3 patients, to evaluate the use of Traumeel S during post-operative radiation therapy. Traumeel S is a homeopathic remedy made up of highly diluted botanical extracts and minerals, and has shown benefit for mucositis in children undergoing chemotherapy. To date there has not been a previous report using it during radiation therapy. Subjects rinsed their mouth with 2cc of a saline control, half strength, or full strength Traumeel S three times daily for 30 seconds at a time and then swallowed. Objective and subjective evaluations of oral mucositis and screening for toxicities were performed weekly during radiation therapy including: World Health Organization (WHO) grading for oral mucositis, Visual analog scale (VAS) measurement of pain, dryness of mouth and swallowing difficulty, Compliance with use of the medication, Perceived side effects from the medication. Results: Ten patients were included in the study. One patient in the saline control dropped out after 4 weeks because of thrush and one patient in the half strength group dropped out after 2 weeks because they did not perceive any benefit. A fourth subject was added to the half strength cohort. Compliance was excellent, with 98.4% of doses taken. No new toxicities were observed during the courses of radiation therapy and there were no reports of any perceived side effects from the medication. Both cohorts using Traumeel S had lower mean VAS scores for severity of dry mouth and swallowing difficulty as well as lower WHO grades of mucositis compared to the control arm. There was no significant difference in the severity of side effects between all three groups. Treatment related adverse events were not the reason for either of the drop outs. Conclusions: Traumeel S was safely administered during post-operative radiation therapy, and showed potential for therapeutic benefit in decreasing mucositis, dry mouth and swallowing difficulty. A phase 2 trial is warranted to evaluate efficacy.
Apoptosis as a controlled process: Which interventions aimed at optimizing nutrition are of benefit to patients receiving radiotherapy: a systematic review

**Objective:** Squamous cell carcinoma of the head and neck (HNSC) is often associated with significant weight loss before, during, and after treatment with radiotherapy (RT). This systematic review addressed the question: Which interventions aimed at optimizing nutrition are of benefit to HNSC patients receiving RT? Methods: Randomized controlled trials (RCTs) studying interventions directed at the nutritional support of adult patients with HNSC receiving RT with or without chemotherapy were eligible. Results: A proliferation assay was performed. Gene-expression analysis was performed using the AmpliclonerTM system (Qiagen). Determined expression in the radiated keratinocytes, other caspases were not expressed. Expression of the intrinsic pathway via bcl-2 was reduced for tube fed patients; however, crossover and contamination was not statistically significant. Conclusion: This is the first study to quantitatively assess the molecular changes that occur in the radiated keratinocytes. As a controlled program, cell death does not seem to be an important participant in radiation-induced cell death. As a result, they often fail to heal because of decreased proliferation, impaired angiogenesis, and persistent high concentrations of MMP. Treatment with the basic pathophysiology of wound healing in radiation-induced wounds at the molecular level might feed into the development of innovative treatment strategies.

**Conclusions:** Limited data are available addressing the effectiveness of nutritional interventions in HNSC patients receiving RT. Dietary counseling and MA may be effective to minimize weight loss and maintain nutritional status; however, these conclusions are too preliminary to make strong recommendations. The value of dietary supplement and prophylactic enteral feeding is unclear and has been inadequately studied. Further research to identify effective nutritional interventions in HNSC patients receiving RT, and their effects on tumor response and survival, is a priority.

**Methods:** We use a CT-on-Rails treatment system to achieve daily volumetric image-guided radiotherapy. Patients are automatically repositioned prior to each IMRT treatment with an in-house CT-guided rigid registration technique. A clinical pathway for weekly dosimetry evaluation and treatment adaptability has been established. A clinical trial of weekly dose-dense radiosurgery for brain metastasis is being performed.

**Conclusions:** We are currently studying the incorporation of volumetric image-guided setup with serial adaptive replanning to account for daily setup uncertainties and gradual anatomic changes during a full six-week course of intensity-modulated radiotherapy treatment (IMRT) in a prospective clinical trial. We are also developing image-guided methods to assess tumor response to treatment and to guide mid-course dose corrections. In this report, we present our pilot findings from this ongoing trial.

**Results:** Pilot results from five oropharyngeal cancer patients who initiated adaptive treatment between 7/07 and 11/07 confirmed that significant dose reductions can occur in the absence of daily image-guided patient position corrections. Under dosing would have occurred in up to 7% of high dose clinical target volumes. Full adaptive IMRT replanning is necessary only one to two times during treatment. Three study patients required only one replanning session (between fractions 20 and 21) and a fourth patient required two new plans (after fractions 14 and 27, out of a total of 33). Adaptive planning not only provided better dose coverage of disease volumes, but also reduced normal organ doses and overall dose inhomogeneity. Midcourse and post-treatment DCE-MRI imaging was overlaid onto delivered dose distributions for the first treated patient. A 20% and 60% mean tumor Krans reduction was observed mid-treatment (34 Gy) and 43 days after the completion of final treatment (70 Gy) in high dose volumes. In two patients, occult gross tumor was identified by pre-treatment or mid-course MRI imaging, resulting in new adaptive plans with enlarged target volumes encompassing these disease sites. Conclusions: Our group has developed novel image registration algorithms to improve adaptive RT techniques to demonstrate the real world feasibility of image-guided H&N adaptive IMRT. Patient accrual to this effort is ongoing and updated results will be presented.

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were selected for microarray analysis which was performed using the Affymetrix Human Genome U133 Plus 2.0 Chip. Two cell lines showed high resistance to radiation, two cell lines showed an intermediate resistance whereas differently one cell line was sensitive. The cell lines that displayed intermediate and high resistance to radiation were compared to the sensitive cell line respectively, and transcripts with a fold-change value of 2.8 (p<0.01) in each of eight pair-wise comparisons were selected as significantly expressed. A very large number of differently expressed transcripts and three novel gene lists were created; the first contained differentially expressed transcripts only found in the highly radioresistant cell lines, the second contained differentially expressed transcripts only found in the intermediate resistant cell line and the third contained transcripts commonly differently expressed for both the intermediate and high radiation resistance compared to the sensitive. These three gene lists were analyzed for enrichment of Gene Ontology categories using the Gene Ontology Tree Machine. The genes present within the enriched categories were further assessed using Ingenuity Pathway Analysis (IPA) for detection of key regulator genes in molecular networks. A gene was considered to be a key regulator when interacting with three or more differentially expressed transcripts. Results: Gene Ontology categories from all gene lists related to processes commonly deregulated in cancer such as development, growth and cell death. Consistently, the top functions related to the molecular networks found in the IPA analysis were: cancer, cellular growth and proliferation, and cellular movement. In IPA, key regulator genes were identified from the highly radioresistant cell lines, six from the lines with intermediate resistance and 15 key regulators were commonly identified from both the high and intermediate radioresistant cell lines compared to the sensitive. These preliminary findings suggest molecular markers of radioresistance which, however, need verification by functional analyses. The gene list created from the intermediate radioresistant cell lines displayed a lower number of enriched GO-categories and key regulator genes compared to the highly resistant, which indicates that the expression profiles of this cell line model mimics the progression of radioresistance. Since IPA creates networks based on interactions previously stated in the literature, not all key regulators were differentially expressed themselves. However, as all key regulators interacted with at least three differentially expressed transcripts this bioinformatic processing of transcript data provides novel means of finding key-regulator genes that may have important roles in the response to radiotherapy. Conclusions: We present a cell line model and bioinformatic method for detection of molecular markers linked to radioresistance in HSNNCC. Further evaluation of these markers could give a better diagnostic tool for assessment of a successful first-line treatment.

P673: RADIATION THERAPY IN HEAD AND NECK CANCER PATIENTS CAUSES MUSCLE FIBROSIS THROUGH INCREASED TGF-B1 DOWNREGULATING MYOD G.L. Peng 1, R. Masood 1, U.K. Sinha 1, 1 Keck School of Medicine at University of Southern California, Los Angeles, CA
Objective: Head and neck cancer (HNC) is the sixth most common cancer worldwide with estimated 900,000 new cases diagnosed each year. One of the main treatment modalities for HNC is post-operative radiation therapy. Patients undergoing radiation therapy develop dysphagia or swallowing disorders due not only to salivary gland damage, but also scarring of the pharyngeal and strap musculature. We have compared the levels of TGF-1, in the strap muscle samples in HNC patients at the end of their radiation therapy as compared to patients who did not undergo any radiation therapy. TGF-1 may contribute to the excessive fibrosis by blocking MyoD expression, a gene necessary in muscle differentiation and repair. A second part of this study is to view the effects of concurrent electrical stimulation with radiation therapy on TGF-1 and MyoD levels. Our objective is to examine and compare not only the effects muscle repair post irradiation, but also to view the effects of electrical stimulation during concurrent radiation therapy on the expression of TGF-1 and MyoD. Understanding the process of fibrosis and it is both enhanced and reduced could greatly improve the quality of life for these cancer survivors. Methods: Six patients were enrolled into this study with various stages of HNC ranging from stage IV by the American Joint Committee on Cancer staging system. Their muscle samples were obtained at week 6 of their post surgical radiation therapy. Six subjects without HNC served as the negative controls. In addition, six more subjects who underwent radiation therapy with simultaneous electrical stimulation were recruited for the second part of the study. The TGF-1 and MyoD expression were measured in all patient samples using western blotting, immunohistochemistry staining. Results: TGF-1 expression was higher in all muscle samples obtained from patients with radiation therapy as shown through western blotting and immunohistochemistry staining as compared to non radiated controls. In addition, there is decreased fibrosis seen in patients who have undergone radiation therapy and concurrent electrical stimulation as compared to patients who underwent radiation without the electrical stimulation. We also observed that those patient specimens with higher TGF-1 showed lower expression of MyoD than patients with lower TGF-1 expression. Visualization on the stained sections of the muscles it was seen that during radiation muscle samples had fibrosis that was absent in patients who did not undergo radiation. Conclusion: We postulate that radiation induced TGF-1 expression. Higher TGF-1 blocks the expression of MyoD and thus blocks the muscle differentiation which induces fibrosis in these patients with radiation therapy. In addition, we hope to continue the study with electrical stimulation during patients’ radiation therapy with different techniques in order to optimize the stimulation and decrease the fibrosis that occurs with post-operative radiation therapy.

P674: INCREASED PLATE AND OSTEOSYNTHESIS RELATED COMPLICATIONS ASSOCIATED WITH POSTOPERATIVE CONCURRENT CHEMORADIOTherapy R.Shaman 1, I.S. Yner 2, J. Samuel 3, R. Cohen 3, M. Kuriakose 4, 1 Amrita Institute of Medical Science, Cochin, Kerala, India; 2 Amrita Institute of Medical Sciences, Cochin, Kerala, India; 3 Amrita Institute of Medical Sciences, Cochin, India
Background: Plate osteosynthesis is a widely used technique in head and neck reconstructive surgery. The objective of this study was to determine whether postoperative chemoradiation, which was recently introduced for high-risk head and neck cancer, affects plate and osteosynthesis related complications. Methods: Fifty-two consecutive patients, who had undergone plate osteosynthesis for mandibular reconstruction between October 2003 to September 2006, were included in the study. The patients were divided into three groups: 1) Surgery alone (n=19), 2) Surgery with postoperative radiotherapy (n=14) and 3) Surgery with concurrent chemoradiotherapy (n=19). Outcome measures included any bone or plate related complications in the follow up period. Results: Out of 52 patients, 21 patients had mandibulectomy done for access and in remaining 31 patients; segmental mandibulectomy or maxillectomy followed by free bone flap reconstruction was done. Complication included presence of sinus in 15(28.8%), oro cutaneous fistula in 3(5.8%), plate/bone exposure in 14(26.9%) and non union in 10(19.2%) of the patients. Sixteen (30.8%) patients required plate removal in the follow up. Overall, plate and osteosynthesis related complications occurred in 10.5% of patients in surgery alone group, 28.6% in surgery with postoperative radiation group and 63.2% in surgery with postoperative concurrent chemoradiotherapy group. The differences in the complication rates among these three groups were statistically significant (p-value = 0.003). In univariate analysis postoperative radiation (p-value = 0.007) and concurrent chemoradiotherapy (p-value = 0.003) were found to be significantly associated with complications. In multivariate analysis, only concurrent chemotherapy was found to be statistically significant (p-value 0.002) with odds ratio of 7.72[CI 95%, 2.13 to 27.9]. Conclusion: Postoperative concurrent chemoradiotherapy significantly increases plate and bone related complications after treatment of head and neck cancer.

P675: ACCELERATED RADIATION RETINOPATHY: DOES CONCURRENT CISPLATIN INCREASE THE RISK? H.E. Palmer 1, C.M.G. Cheung 1, P. Ashwin 1, M.D. Isaloumas 1, 1 University Hospitals Birmingham NHS Trust, Birmingham, United Kingdom
Objective: To describe two cases of accelerated ischaemic retinopathy following accepted safe doses of radiation with adjuvant cisplatin chemotherapy. Methods: Case reports with clinical history and fluorescein angiographic follow-up of two patients who had ischaemic retinopathies following radiation with adjuvant cisplatin chemotherapy for nasopharyngeal carcinoma. Results: Both patients developed ischaemic retinopathies within ten months of completion of radiation. Both cases went on to develop aggressive sight-threatening neovascular features requiring laser treatment. Conclusions: The accelerated and aggressive retinopathies described are unusual but the amount of radiation received. The concurrent use of cisplatin was the likely cause of such altered disease behaviour. Cisplatin alone is associated with ischaemic retinopathy. The combination of irradiation and cisplatin may be associated with an increased risk of ischaemic retinopathy and accelerate its onset.
We intend to describe the odontological proto-
diagnostic workup of FPS should there be a need to:

- Retrospective chart review
- These cases demonstrate the importance of early screen-
ing for blood pressure and urinary catecholamines / metanephrines.
- Between 1992 and 1997 we analysed 106 patients pre-radiotherapy. Only one per-

Objective: We intend to describe the odontological proto-
col for assisting patients undergoing head and neck rad-

Radiotherapy. 0.12% chlorhexidine from 5 years of age. Lasertherapy may also be used

ment for the other teeth. We also recommend mouth rinses of fluoride and

ororal lubricants. In children with mixed dentition, the best is to carry out

exodontic treatment must be carried out in as few sessions as possible, so

as to avoid bone spicules, contributing thus to the coaptation of the gums

through alveolotomy, i.e. the excision of a portion of the alveolar bone to

achieve normal ridge contour preparatory to construction of a denture pros-

thesis. (8 days) We recommend mouth rinses with solution of 1% sodium flu-

oride for 3 minutes once a day during the treatment, and less frequently

once radiotherapy is over. Furthermore, we recommend 10 daily mouth

rinses with 0.9% saline solution (i.e. warm saline) and soft warm saline ther-

apy (DAR); 3 daily mouth rinses with sodium bicarbonate; 3 pills of 5mg

pilocarpine hydrochloride a day for 5 months; 3 daily mouthwashes with

0.12% chlorhexidine solution for 1 minute. In cases of mild or moderate

mucositis, these mouth rinses are not advisable; instead, we suggest

lasertherapy and geoclair. Alcoholic beverages, tobacco and spicy or over-

ly hot foods must be avoided. We also recommend completely suspending

the use of full prosthesis or dentures. In cases of candidosis, we recommend

oral nystatin (Nystatin solution 500.000 to 1.000.000U VO 3.5 x/day

for 5-7 days). Due to xerostomy, we advise patients to use artificial saliva

or oral lubricants. In children with mixed dentition, the best is to carry out

the exodontic treatment during exfoliation, and conventional dental treat-

ment for the other teeth. We also recommend mouth rinses of fluoride and

0.12% chlorhexidine from 5 years of age. Lasertherapy may also be used

in patients suffering from mucositis. Orientation and impeccable oral

hygiene are absolutely essential. A dental professional must follow patients

closely during and after radiotherapeutic treatment. Results: Between 1992

and 1997 we analysed 106 patients pre-radiotherapy. Only one per-

of the inferior molar mucosa where the exodontic

treatment was applied leading to osteoradionecrosis. Considering this was

the sole case of osteoradionecrosis among 106 patients, we have a rate of

0.94%. Conclusion: By using this protocol, we can greatly soften the

impact (and their subsequent complications) of the side effects of head and

neck radiotherapy.

RARE TUMORS

P677: CHORDOMA RESEARCH FOUNDATION: A MODEL FOR ORPHAN NEOPLASMS OF THE HEAD AND NECK

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Advancement of the care of patients with orphan neoplasms is limited by a lack of funding, clinical material, and targeted research. The Chordoma Foundation was founded by a patient in partnership with the medical com-

munity to address these issues. The success of this organization can serve

as a model for translational research for other orphan neoplasms of the

head and neck. The Chordoma Foundation was founded in 2007. Within

months, a website was launched and the 1st International Chordoma Research Workshop was held at the NIH. The Chordoma Foundation serves as a catalyst, bringing together patients, physicians, and scientists to facil-

itate research. Since its inception, the Chordoma Foundation has raised $165,000 in research funds, organized the 2nd International Chordoma Research Workshop with grant support, held research meetings at multiple academic centers, recruited patient volunteers, and established a tumor tis-

sue bank. A foundation such as the Chordoma Foundation provides many

services. For researchers, it can provide opportunities for networking & col-

aborations, access to biospecimens and clinical data, research tools and

genomic data, online research forum, curated online knowledgebase,

patient recruitment, and funding and grant assistance. For clinicians, it can provide educational resources and clinical care guidelines, opportunities for research collaborations and publications, and a secure online clinical forum. For patients, it can provide a venue to directly support research, a source of information, support, and advice, and patient-based research and outcome tracking. The model of success provided by the Chordoma Foundation should be applied to other rare neoplasms of the head and neck.

P678: MALIGNANT PARAGANGLIOMA OF THE THYROID GLAND WITH SYNCHRONOUS BILATERAL CAROTID BODY TUMORS

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Objective: This report is to make the reader aware of the unusual entity of a malignant paraganglioma of the thyroid gland with bilateral carotid body tumors in a single patient. The report will include a comprehensive case

report and a review of the literature. Methods: A case of malignant para-
ganglioma of the thyroid gland is described with a discussion on the pres-

entation, pertinent work-up including imaging, and treatment options. A lit-

erature search for publications pertaining to malignant paragangliomas of

the head and neck and frequency of association of carotid body tumors was performed and the results are reviewed. Results: The patient under-

went total thyroidectomy which led to the diagnosis of malignant paragan-

glioma in the setting of her pre-existing bilateral carotid body tumors. Given

the rarity of this diagnosis, a search of the literature in conjunction with dis-

cussion at Head and Neck Tumor Conference was used to direct further

therapy. The patient was subsequently treated with radiation therapy to

the thyroid bed, the trachea, and bilateral necks including the carotid body

tumors. She has been followed for over one year and remains disease-free.

The results of the literature search are presented as well as pertinent photo-

graphs, histological data and imaging studies relating to the case report.

Conclusion: Extra-renal malignant paragangliomas of the head and

neck are rare, and those arising within the thyroid gland are even more

infrequent. There are certain characteristics of these tumors that classify

them as malignant based on particular histologic & radiologic findings as well

as local tumor behavior. In this case report, the location of the lesion in the

thyroid gland along with the presence of bilateral carotid body tumors in a sin-

gle patient raises the concern for an underlying genetic etiology. To date,

there are only a limited number of case reports of malignant paragan-

gliomas arising in the head and neck region with even fewer documented

cases of intra-thyroidal disease. These tumors can be easily misdiagnosed

as another type of thyroid cancer which may result in an altered treatment

course. A case of malignant paraganglioma of the thyroid gland with syn-

chronous bilateral carotid body tumors is reported and a brief review of

the literature is presented.

P679: THE GENETICS OF FAMILIAL PARAGANGLIOMA SYNDROME

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Objectives: To examine the genetics and clinical management in a case

series of Familial Paraganglioma Syndrome. Methods: Retrospective chart

review. Results: These cases demonstrate the importance of early screen-

ning, diagnosis, and treatment in Familial Paraganglioma Syndrome (FPS).

Indicators of FPS include family history positive for paragangliomas, early

onset of tumors, and multiple tumors. The PGL genes indicated in the patho-

genesis of FPS encode 3 out of 4 subunits of succinate dehydrogenase with-

in mitochondrial complex II. The patient’s genetic mutation is predictive of
tumor location, likelihood for recurrence, rate of metastasis, and risk of

transmission to offspring. Conclusions: Diagnostic workup of FPS should

include angiography, color duplex ultrasound, and genetic testing. Patients

diagnosed with FPS should undergo bilateral imaging (neck, thorax, abdom-

en, pelvis) by high resolution CT or MRI as well as annual measure-

ment of blood pressure and urinary catecholamines / metanephrines.

Penetrance data suggests that screening at an early age would detect dis-

ease in the vast majority of mutation carriers. Therefore all first degree rel-

atives of patients diagnosed with FPS should submit to screening and

prompt genetic testing to improve treatment outcomes.

P680: COEXISTENCE OF A CAROTID BODY TUMOR AND THYROID CARCINOMA WITH CERVICAL LYMPH NODE METASTASIS: A CASE REPORT

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Obstacles: To assess the histopathological findings, and clinical data of a

patient with simultaneous coexistence of a carotid body tumor and a thyroid

carcinoma with cervical lymph node metastases. Methods: A 58-year-old

male presented with a mass in the left ear. The patient underwent an en-

tyroidectomy, and the histopathological and clinical data were reviewed.

Results: A multinodular growth was found in the left lobe of the thy-

roid, with invasion into the capsule and vascular wall. The tumor was
diagnosed as a well-differentiated thyroid carcinoma, and the cervical

dissection revealed metastatic lymph nodes. Conclusion: Simultaneous

coexistence of a carotid body tumor and a thyroid carcinoma with cervical

lymph node metastases is a rare condition. The management of this con-

dition requires a multidisciplinary approach, including surgery, radiation

therapy, and chemotherapy. A thorough preoperative evaluation is

necessary to determine the extent of disease and plan the most

appropriate treatment.
Thyroglossal duct carcinoma is uncommon, occurring in approximately 1% of all thyroglossal duct remnants. This rare neoplasm is characterized by relatively nonaggressive behavior with infrequent lymph node spread. Another rare neoplasm of the head and neck region is a carotid body tumor. A 78-year-old woman with a 3-year history of midline and bilateral neck masses was referred to us. Fine needle aspiration biopsies (FNAB) and a CT scan suggested the diagnosis of thyroglossal duct carcinoma with cervical lymph node metastasis. Interestingly, the left-side neck mass was found to be spaying the carotid bifurcation, on CT imaging. Carotid arteriography demonstrated a highly vascular mass in the bifurcation of the carotid artery that was compressing the internal and external carotid arteries. To our knowledge, this is the first reported instance of a thyroglossal duct carcinoma with neck metastasis accompanied by a carotid body tumor. In addition, the carotid body tumor in this case mimicked neck metastasis from the thyroglossal duct carcinoma.

P681: CAROTID BODY TUMOR RESECTION WITH LIGASURE®
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Objective: The use of Ligasure may help in reducing bleeding, as well as surgical time. No report, to our knowledge, has been reported the use of this technology in carotid body tumor (CBT). Methods: A prospective study from September 2004 to may 2007, in patients with CBT resection with Ligasure. Surgery was done by the same surgical team. We use the Shamblin classification and classification modify by Luna Ortiz et all. Results: were analyzed by descriptive static and non-parametric U Mann-Whitney test. 12 patients were operated:verity of surgical procedure, because they were Shamblin II or more. Conclusion: Ligasure Reduce surgical time and bleeding during surgery. But in Shamblin III is not possible to be sure as a sole procedure, because most of them require a vascular reconstruction.

P682: SURGICAL TREATMENT OF CAROTID PARAGANGLIOMAS
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Objective: Retrospective analysis of pre-operative evaluation, surgical treatment and outcome of patients with carotid paraganglioma. Methods: Records of 11 patients (9 females, 2 males) with carotid paraganglioma aged between 23-60 years surgically treated at our center between 1987 and 2006 were reviewed. Data for pre-operative evaluation, classification, surgical data, the intra and postoperative complications and treatment outcomes were noted. Results: There were one type I, eight type II and two type III tumors according to Shamblin’s classification. Subadventitial tumor excision was performed in 10 patients; while an end to end anastomosis had to be performed in one patient because of carotid rupture during dissection, probably related with the previous fine needle aspiration biopsy. Intraoperative complications included one minor carotid bleeding requiring primary suture, another major bleeding requiring end to end anastomosis, and searing of superior laryngeal nerve in one patient. Postoperative complications were Horner’s syndrome (temporary, one patient), unilateral superior laryngeal nerve palsy (permanent, one patient) and inferior laryngeal nerve palsy (permanent, one patient). No mortality or stroke was observed. There were no signs of tumor recurrence in any of the cases. Conclusions: Surgical excision is the treatment of choice for carotid paragangliomas although radiation therapy is an option for inoperable patients. Better imaging techniques have improved our pre-operative evaluation capabilities. Institutional competence and cooperation are critical for achieving best surgical outcomes.

P683: EXTRA-CRANIAL EXTENSION OF MENINGIOMAS: A SINGLE INSTITUTION REVIEW OF CASES
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Objective: Meningiomas are neoplasms that arise from the arachnoid layer of the meninges and account for 13-20% of all intracranial tumors. Most are benign and extra-cranial involvement is rare and usually requires a multidisciplinary, multimodality approach involving otolaryngologists, neurosurgeons, and radiation oncologists. The World Health Organization (WHO) classifies meningiomas into three grades based on degrees of anaplasia. The only curative treatment currently is complete surgical removal; however recurrence rates remain relatively high. We review our experience with extra-cranial involvement of meningiomas at the University of Kansas Otolaryngology and Head and Neck Department including the presentation and treatment. Methods: From July 1997 to July 2007, four patients at our institution had a biopsy-proven diagnosis of meningioma with extra-cranial invasion. The symptoms and treatments of each patient were reviewed retrospectively. Results: Patients presented with a wide spectrum of symptoms, including nasal obstruction, changes in vision, diplopia, epistaxis, exophthalmos, proptosis and nasal drainage. The common symptoms present in all four cases were vision changes with concomitant nasal obstruction. All patients had extensive invasion. Two patients had extension into the orbital and sphenoidomethoidal cavities; one had extension into nasal cavity through the cribiform plate; one patient with frontal, ethmoidal and orbital involvement. The patients required treatment with craniofacial resection and reconstruction. The final pathology in two cases included WHO atypical meningioma grade II/III. Conclusion: Patients with extra-cranial involvement of meningiomas often present with head and neck symptoms that will prompt a referral to an otolaryngologist. In our experience, visual changes with nasal obstruction are common presenting complaints. Surgical intervention includes neurosurgical consultation as most of our cases included not only invasion into facial bony structures, but also cranial extension. Radiation oncologists must be involved secondary to the high risk of recurrence depending on classification. In our experience, extra-cranial meningioma involvement requires a multidisciplinary and multimodality approach in order to provide the most optimal outcome.

P684: GINGIVAL MASS IN THE SETTING OF IMMUNOSUPPRESSION AND ACUTE MYELOID LEUKEMIA
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The differential diagnosis of gingival masses is extended in the setting of acute myeloid leukemia to include soft tissue cholangomas, or granulocytic sarcomas as well as ossifying fibroma and fibrous dysplasia. We present an interesting case of peripheral ossifying fibroma in the setting of recently diagnosed AML and immunosuppression. The patient was a 71 year-old woman with recently diagnosed AML-M5 and completion of induction chemotherapy prior to presentation of maxillary gingival pain for three days. Exam revealed a 3 x 1.5 x 1 cm firm lesion originating from the midline maxillary alveolar gingiva. The mass was excised from its base and histological examination revealed trabecular woven bone with fibroblastic stroma, consistent with an ossifying fibroma. The clinical considerations, diagnostic histopathologic features and treatment options are reviewed for the differentiation of cholangomas and ossifying fibromas. The origin of ossifying fibromas has not been fully elucidated, and no cases in the setting of immunosuppression or AML have been identified.

P685: MERKEL CELL CARCINOMA OF THE NECK: CASE REPORT
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Objective: Merkel cell carcinoma is a rare neoplasm that arises from the neuroendocrine system. The most frequent site of occurrence is the skin of head and neck and is more common in elderly. Methods: This report presents a case of a 62 year old white male with a large tumor in the upper neck with fixation to the carotid artery without possibility of surgical resection. The definitive diagnostic was only possible after immunohistochemical analysis of a biopsy. The patient was treated with two cycles of induction chemotherapy (etoposide, ifosfamide, mesna and taxol). Results: After the second cycle the clinical and imaging evaluation showed an involution of the tumor with definition of the carotid artery. The patient was submitted to radical neck dissection and skin reconstruction (with a deltopectoral flap) and postoperative radiotherapy. After eight months there was no evidence of disease. Conclusion: The association of induction chemotherapy, surgery and postoperative radiotherapy is the best approach for aggressive tumors like Merkel cell carcinoma.

P686: MERKEL CELL CARCINOMA OF THE HEAD AND NECK: THE ROLE OF SENTINAL LYMPH NODE BIOPSY
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Objective: Merkel Cell Carcinoma is an uncommon cutaneous neuroendocrine malignancy, making research and literature a scarcity, a rarity for the common practitioner, and unheard of in the lay public. Controversy remains on standard therapy. The roles of surgical resection, lymph node dissection, radiation therapy, and chemotherapy remain up for debate. The objective of this study is to assess the usefulness of the sentinel lymph node (SLN) biopsy in head and neck Merkel Cell Carcinoma in a large, single center patient population.

Methods: After Internal Review Board approval, the pathological database was searched for all Merkel Cell Carcinoma cases. There were 134 head and neck Merkel Cell Carcinoma patients and their charts were reviewed. Patients were excluded if there was an unknown primary, insufficient data, second opinion or consultation-only patients, no follow-up, presented with neck or distant metastases, or metastatic lesions. A total of 75 patients were included in the study. Data points were placed into a comprehensive database after medical records were extensively reviewed. Results: The mean age was 74 years (range 30-94 years, median 77 years) and males comprised 71% (53/75) of the group. The cohort was divided into the primary excision with SLN group (n=46) and primary excision only group (n=29). The SLN group had an average of 3.5 lymph nodes removed and was positive in 12/46 (26%) patients, which resulted in either neck dissection and/or radiation. Of the 34 patients with negative SLN, 7 had metastatic disease to the neck on follow-up, requiring neck dissection and radiation therapy. In this group, a SLN biopsy was able to find 63% (12/19) of neck metastases. In the primary excision-only group, 27% (8/29) had neck metastasis found clinically and/or radiographically. The SLN group had 4 (9%) deaths, 3 of which had a primary excision only. The primary excision plus SLN group had 4 (14%) deaths.

Conclusions: Current treatment regimen consists of surgical resection with wide (2-3 cm) margins, with adjuvant radiation therapy to the primary site and nodal basin. Surgical intervention to the neck is not standardized, though warranted. Sentinel lymph node biopsy has recently been advocated, but in our study, did not reliably predict locoregional metastasis to the head and neck lymph nodes. In patients with clear margins, performing a SLN biopsy did not prevent neck metastases, distant metastases, or improve overall survival.

P687: NEUROENDOCRINE CARCINOMA OF THE SINONASAL TRACT

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Objectives: Neuroendocrine carcinoma (NEC) of the sinonasal tract is rare. In this present study, we report our treatment experience of sinonasal NEC. Methods: Between 1980 and 2006, eighteen patients were registered with a diagnosis of NEC of the sinonasal tract at our hospital. Clinical data of these patients were retrospectively reviewed. Demographic data, treatment and outcomes of these patients were analyzed. Results: Ten tumors were primary NEC without previous radiation and eight tumors were post-irradiated NEC occurring within the radiation field for previous nasopharyngeal carcinoma in six patients and tonsillar lymphoma in one and neck metastasis of unknown primary origin in one, with an interval between previous radiotherapy and diagnosis of NEC from 82 to 385 months with a mean of 197 months. Fifteen tumors were small cell carcinoma, two were atypical carcinoma and one was typical carcinoid tumor. Fifteen patients underwent surgery with/without postoperative adjuvant chemotherapy. Three patients received induction chemotherapy or primary radiotherapy with further definitive treatment. The 5-year disease-free and overall survival rates of all 18 patients were 56.1% and 62.2 %, respectively. Comparing primary NEC with post-irradiated NEC, they were similar in age, sex distribution, stage, pathology and treatment; and the 5-year survival rates were 62.2% and 61.5% respectively. For stage distribution, the 5-year survival rates were 52.4% for stage I; 83.3% for stage II; 33.3% for stage III; and 100% for stage IV. Conclusions: In this series, post-irradiated NEC is common, which may be due to a large number of NPC long-term survivors. The prognoses of post-irradiated NEC and primary NEC seems to be similar despite the relative short follow-up period in the post-irradiated NEC group.

P688: NEUROENDOCRINE CARCINOMA OF THE HEAD AND NECK: OUR EXPERIENCE IN 9 CASES

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Objective: Neuroendocrine carcinoma (NEC) is a common pulmonary neoplasm, however, neuroendocrine carcinoma of the head and neck is rare. We present the clinicopathological findings of 9 NEC cases of the head and neck. Methods: Between 1981 and 2006, the medical records of 9 adult patients with pathologically proven NEC of the head and neck who had been treated at Yokohama City University hospital between 1994 and 2007. Their demographics, clinical and histopathological records were analysed. Results: Eight patients with NEC of the head and neck were male and one was female. The ages ranged from 50 to 72 years, with a median age of 60 years. The tumours consisted of small cell NECs in all. The tumours occurred at 3 different sites (nasopharyngeal origin and 3 primary unknown metastatic neck tumors were included). The pathological findings were 4 small cell NECs and 5 large cell NECs. 3Three patients received concurrent chemoradiotherapy and 2 patients had definitive radiotherapy with induction chemotherapy. Two primary unknown patients received neck dissection with post-operative radiation. The median follow-up time for surviving patients was 30 months (range, 5-48 months). Five patients who had distant metastasis died. The actuarial 3-year overall survival rate was 56%. The 3-year overall survival rate was 100% with the patients who received chemotherapy including CPT11. Conclusion: The prognosis for patients with NEC of the head and neck was poor. NEC was very aggressive and had a metastatic feature to distant lesions. Based on our result, chemotherapy including cisplatin and CPT11 might be indispensable to prevent the distant metastasis.

P689: A CASE SERIES OF METASTATIC RENAL CELL CARCINOMA TO THE HEAD AND NECK REGION

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Objectives: The objectives of the study were to present a case series of 13 patients with renal cell carcinoma (RCC) metastasis to the head and neck, to recognize the appearance on radiographic studies, to understand the importance of preoperative embolization, and to review the results of treatment in comparison to the literature. Methods: The records of 13 patients diagnosed with metastatic RCC at a tertiary medical center over a 5-year period from 1996 to 2001 were reviewed and analyzed for demographic and outcomes data. Conclusions: Metastatic RCC to the head and neck is rare but can have serious consequences if not recognized before biopsy. We present several treatment options with local excision as the primary mode of treatment. Results: Metastatic RCC to the head and neck was seen in the following locations: nasal cavity, lower lip, hard palate, tongue, and maxillary sinus. Presenting signs were loose upper molars, dysphagia, nasal obstruction, lower lip lesion, recurrent epistaxis, and nasal drainage. Histological studies confirmed metastasis of RCC in all four patients. Treatment consisted of preoperative radiation therapy, embolization, and local excision with adjunct chemotherapy. Conclusions: Recognizing the unusual presentation and natural history of an RCC can have a profound effect on patient management, and thus on morbidity and mortality. These cases highlight the importance of palliative surgical intervention of head and neck lesions for these patients as an improved way of life and all head and neck lesions with a history of RCC must be at the top of the differential especially in patients with a past history of renal cell carcinoma.

P690: RARE SINONASAL METASTASIS C.S. Duran 1, R.R. Casiano 2, A.Velez 3, A.Londoño 4, 1Hospital Pablo Tobon Uribe, Medellin, Colombia; 2Otolaryngology -Univ Miami, Miami, Fl, 3Pathology-Hospital Pablo Tobon Uribe, Medellin, Colombia; 4Universidad Ces, Medellin, Colombia

Objective: To review and analyze a series of patients with rare metastasis to the sinonasal region, from different primary sites. Methodology: A retrospective review of the files of Department of Otolaryngology of the University of Miami Miller School of Medicine and the Department of Otolaryngology of the Hospital Pablo Tobon Uribe in Medellin, Colombia was done between 2003 through January 2006. Patient’s medical records, imaging studies, surgical procedure, pathology and final outcome were reviewed. Results: During this period four patients were found to have metastasis from thyroid (Follicular carcinoma), pancreas (Adenocarcinoma) and two patients with hypernephroma, these two last patients benefited from surgical procedures to improve their quality of life. Conclusion: Even though survival after the final site for a primary tumor to metastasize, is still not too common to occur as in other anatomical areas of the human body (lung liver etc.).
Metastases to the head & neck area can occur either from local or from distant organs. The aim of this study was to review of clinical and histopathological features of metastases to head and neck area.

**Materials & Methods:** For this purpose, a retrospective study was done, spanning the period 1999-2006 in two educational hospitals in Tehran, Iran. All clinical and pathological data were considered. To ensure the accuracy of the pathological examinations, all the paraffin embedded blocks re-examined. **Results:** A total of 149 patients (93 male, 56 female; mean age 48 years range 12-56 years) were found. Thyroid neoplasm (papillary carcinoma) in 36 cases (24%) was the most common metastatic tumor. The most common site for metastases was cervical lymph nodes with 88 cases (59%) to level II. **Conclusion:** In conclusion, Asymmetric enlargement of cervical lymph nodes in an adult is almost always cancerous, usually due to metastasis from a primary lesion.

**P692: METASTASIS TO HEAD & NECK AREA: A 7-YEAR RETROSPECTIVE STUDY**

**Objectives:** Metastases to head and neck area can occur either from local structures or from distant organs. The aim of this study was to review of clinical and histopathological features of metastases to head and neck area.

**Materials & Methods:** For this purpose, a retrospective study was done, spanning the period 1999-2006 in two educational hospitals in Tehran, Iran. All clinical and pathological data were considered. To ensure the accuracy of the pathological examinations, all the paraffin embedded blocks were re-examined. **Results:** A total of 149 patients (93 male, 56 female; mean age 48 years range 12-56 years) were found. Thyroid neoplasm (papillary carcinoma) in 36 cases (24%) was the most common metastatic tumor. The most common site for metastases was cervical lymph nodes with 88 cases (59%) to level II. **Conclusion:** In conclusion, Asymmetric enlargement of cervical lymph nodes in an adult is almost always cancerous, usually due to metastasis from a primary lesion.

**P693: A CASE SERIES OF METASTATIC RENAL CELL CARCINOMA TO THE HEAD AND NECK REGION**

**Objectives:** The objectives of the study were to review patients with head and neck metastasis of renal cell carcinoma (RCC). We review the presentation, investigation, treatment modalities available and prognosis of this group of patients. **Methods:** This was a retrospective analysis of patients who presented with head and neck renal cell metastasis in our unit over a period of 7 years from 2001 to 2007. 8 patients were identified with metastatic RCC to the head and neck. The histopathological data and clinical notes were then used for presentation, investigations, treatment modalities and prognosis of these patients. **Results:** Metastatic RCC to the head and neck has been seen in the following locations: Base of skull, parotid, masseter muscle, nasal cavity, floor of mouth, neck node, labial mucosa and maxillary sinus. Presenting signs were black outs and dizziness, cheek and palatal swelling, dysphagia, dysphonia, nasal obstruction and recurrent epistaxis. 7 patients had a history of previous renal cell carcinoma. 1 patient presented with a neck node and a primary renal cell carcinoma was later diagnosed upon investigation. The tumours were all recognised to be very vascular. Treatment differed but consisted of the following in no particular order: embolisation, chemotherapy, radiation therapy, and local excision. **Conclusion:** Metastatic disease must be at the top of the differential diagnosis in all head and neck lesions in patients with a known history of RCC. Initial presentation with metastatic disease is possible but unusual and rare prior to diagnosis of primary RCC. Here, one has to highlight the importance of intervention of head and neck metastasis to provide an improved quality of life for these patients. Several methods of treatment have been explored but research shows the primary means of treatment should be local excision.

**P694: FACIAL SQUAMOUS CELL CARCINOMA WITH METASTATIC BREAST CANCER: A PATHOLOGIC ODITY**

**Objective:** To present a unique histopathological finding of advanced squamous cell carcinoma of the face with foci of metastatic breast adenocarcinoma. **Methods:** We present a 64 year old female with a long history of a neglected, slow-growing squamous cell carcinoma of the face. Evaluation revealed a massive, exophytic tumor involving the right orbit, skin of the right cheek and nose, and right maxillary sinus and palate. Her past medical history was significant for metastatic breast cancer. Radical resection and reconstruction was undertaken. An unusual pathological finding of metastatic lobular adenocarcinoma of the breast disseminated within a faciial squamous cell tumor is described and the relevant literature is reviewed. **Results:** Histopathological evaluation revealed a well-defined, large ulcerated mass of squamous cell carcinoma that was focally and intimately intermixed with small aggregates of breast carcinoma metastases seen infiltrating throughout the subcutaneous soft tissues and adjacent mucocutaneous. Additionally, breast cancer metastases were noted in all lymph nodes of the neck dissection specimen, while no evidence of squamous cell tumor metastases was found. Review of the literature reveals a 2-4% likelihood of loco-regional extension of breast cancer to the supraclavicular region and an even lower rate of distant spread to areas superior to the supraclavicular fossa. **Conclusions:** The incidence of distant metastases of breast cancer to the head and neck is considerably low. We present a unique case of multifocal breast adenocarcinoma metastases to the region of a primary squamous cell carcinoma of the face.

**P695: SEBACEOUS CARCINOMA OF THE AURICLE**

**Objectives:** We present a unique case of multifocal breast adenocarcinoma metastases to the region of a primary squamous cell carcinoma of the face.
P697: ANAPLASTIC DEGENERATION IN A METASTATIC PAPILLARY THYROID CARCINOMA LESION WITHOUT A SOURCE FROM THE PRIMARY SITE H. Arshad1, P.G. van der Slot1,1, West Virginia University, Morgantown, WV

Papillary thyroid carcinomas represent the most common type of malignant thyroid neoplasm. However, most of the deaths from thyroid neoplasms are due to the anaplastic subtype. Evidence supports the notion that anaplastic carcinoma of the thyroid is due to de-differentiation of a previously existing papillary or follicular carcinoma. Almost always, if an anaplastic lesion is found in a cervical lymph node, the primary lesion in the thyroid will also display a focus of anaplastic degeneration. We report a case of anaplastic degeneration found in a cervical lymph node of a patient whose primary papillary thyroid carcinoma had no anaplastic changes.

P698: ANAPLASTIC THYROID CARCINOMA: ANALYSIS OF 40 CONSECUTIVE PATIENTS TREATED IN A SINGLE INSTITUTION R.A. Lim1, F.L. Dias1, R. Corba1, U.B. Toscano1, A.L. Costa1, M.M. Barboza1, L.G. Brandão1, B.C. Peryassu1, K.L. Fernandes1, J. Kligerman1,2, Brazilian National Cancer Institute - BNCI, Rio de Janeiro, Brazil

Background: Anaplastic thyroid carcinoma (ATC) is rare and lethal disease. ATC is a malignant tumor that affects patients at all ages and for both sexes. Our data suggests that patients died due to the anaplastic subtype. Evidence supports the notion that anaplastic carcinoma of the thyroid is due to de-differentiation of a previously existing papillary or follicular carcinoma. Almost always, if an anaplastic lesion is found in a cervical lymph node, the primary lesion in the thyroid will also display a focus of anaplastic degeneration. We report a case of anaplastic degeneration found in a cervical lymph node of a patient whose primary papillary thyroid carcinoma had no anaplastic changes.

Objective: Detect any intervention that would be useful in the management of patients with anaplastic thyroid carcinoma.

Study Design: Retrospective chart review of patients with ATC treated at the Brazilian National Cancer Institute/BNCI.

Patients and Methods: From 1993 to 2002, 1532 charts of thyroid carcinoma were reviewed. Fifty-three patients (3.5%) had a diagnosis of ATC and had been treated primarily in our institution. Thirteen patients were excluded because they didn’t return after initial evaluation. Patient characteristics (age and gender), tumor factors (pathology, size of tumor, multifocality) and type of treatment were analyzed using the chi-square method. The overall survival was estimated by the Kaplan-Meier method. The statistical analysis was performed using the SPSS software.

Results: The pathological specimens and records of 40 patients with anaplastic carcinoma were reviewed, 33% of patients had a previous history of goiter. All patients had locally advanced disease at presentation, 35 patients were T4b and 5 patients were T4a. The median age was 69.3 years, 26 patients are women years and 14 are men. Total thyroidectomy was performed on 5 patients; emergency thyroidectomy plus excisional biopsy was performed on 35 patients at the initial operation because of tracheal compression. Radiotherapy was used on nineteen patients (51.4%). Ten (25%) patient developed distant metastasis. Overall survival was 44 days, in group of patients that were submitted a total thyroidectomy median survival was 121 days (Log rank 3.12 and P=0.077). The presence of RXT had impact on survival when compared in group of patients without radiotherapy (log rank 3.59 and P=0.0582) the median survival in this group was 57 days. In group of patients that thyroidectomy was associated with neck dissection median survival was 110 days (log rank 4.08 and P=0.0435).

Conclusions: Our data suggests that local radiotherapy improved survival. The survival is still poor; patients submitted to a total thyroidectomy and neck dissection had better survival. This study supports that patients that are treated with total thyroidectomy and neck dissection plus radiotherapy had better survival.

P699: CLINICAL CHARACTERISTICS, DENTAL CARE AND HISTOLOGICAL FINDINGS OF LIPOID PROTEINOSIS S.N. Marta1, G.N. Marta1, A.R. Castilho2, R.K. Kawakami3, M.A. Matsumoto1, L.A. Franciscione1, M.B. Bresola1, L.P. Kowalski2, A.L. Carvalho3,1 University of Sagrado Coração, Bauru, Brazil; 2Hospital do Câncer A. C. Camargo, Fundação Antonio Prudente, São Paulo, Brazil; 3Hospital do Câncer A. C. Camargo, Fundação Antonio Prudente, São Paulo, Brazil

Lipoid proteinosis (Urbach-Wiethe syndrome or hyalinoma cutis et mucosae) is a rare autosomal recessive disorder caused by mutations in the gene ECM1. In recent years, affecting nearly 300 reported cases in the world literature, with highest prevalence in South Africa and European countries of German and Dutch descent. The disease is characterized by progressive deposition of hyaline material in the skin, mucous membranes and organs. The signs appear after birth and are characterized by hoarseness, papulonodular lesions on the face, neck, ears, knees, elbows and hands, and yellowish papules on the eyelid margins (moniliform blephara-
**Giant cell granuloma** is a benign, intraosseous lesion of the maxilla and facial bones, rarely affecting the head and neck area. Its etiology is unknown, and it normally affects children and young adults, most of whom are women. Even though it is a benign lesion, it may lead to a locally destructive process. The more aggressive lesions usually affect younger patients, and they grow rapidly, are rather painful, may cause tooth resorption and have high recurrence rates. X-rays usually show such lesions in the anterior maxillary and mandibular or multilocular images, with indistinct, infiltrative borders. The less aggressive lesions, on the other hand, usually affect patients up to their thirties, and have slow growth, are asymptomatic, do not lead to tooth or bone resorption and have lower recurrence rates. Its radiographic images show distinct borders. In some cases it may lead to root diversion and resorption through the midline. Only in-depth knowledge of the lesion can lead to accurate diagnosis, particularly in cases of abnormal dental position and facial deformity, since the radiographic Images can easily be mistaken for other lesions, such as brown tumour of hyperparathyroidism, ameloblastoma, chondroma, amongst others. A variety of treatments may be used, ranging from resection through closing-wedge osteotomy to intralesional corticosteroid injections, and it varies according to the aggressiveness of the lesion, as well as according to the age and systemic conditions of the patient. Lab tests for levels of calcium, alkaline phosphatase and parathormone must be carried out so as to eliminate the possibility of tumour of hyperparathyroidism. Objectives: to approach the knowledge of this pathology as well as to approach its diagnosis as opposed to other pathologies and its diversity of treatments available.

Methods: The present work was used the medical records of patients who had undergone surgery at Hospital Eraisto Gaertner between January 2000 and December 2007, who had the diagnosis of giant cell granuloma. All information (both clinical and histopathological) present in their hospital records was taken into account, in addition to patient follow-up, treatment and convalescence.

Results: Our results show that out of 13 patients, 10 were women, 2 were men, and their average age was 29 years. The lesions were located in the anterior mandible, compatible thus with lesion recurrence. The patient was submitted to a new surgery for lesion enucleation. We then proceeded to cryotherapy followed by curettage. The histopathological analysis revealed the presence of epithelial cords with ameloblastic cells, compatible with follicular ameloblastoma. The patient will undergo resection of the upper right mandibular body following by reconstruction through autogenous fibular graft and microsurgery. Due to its local aggressiveness involving the surrounding bone and frequent recurrence, keratocyst is now considered a benign tumour of odontogenic origin by the World Health Association (2005), and its name was changed to odontogenic keratocyst tumor. The treatment chosen for this tumour is block resection with a safety margin for bone reconstruction. Patients treated this way will be periodically followed up for at least 10 years after the first surgery because of the risk of both recurrence and ameloblastic transformation of the epithelium.

**P074: METALLOPROTEINASES MMP-2 AND MT1-MMP AND TISSUE INHIBITOR 2 OF MMP IN MEDULLARY THYROID CARCINOMA: PROGNOSIS MARKERS**

**B.G.Cavaleiro**, **C.J.Rodrigues**, **L.G.Brandão**

**INTRODUCTION**: Medullary thyroid carcinoma is a malignant neoplasm arising from parafollicular C cells of the thyroid gland and is considered to have a better prognosis than other thyroid malignancies due to its early detection and surgical treatment. Although its overall morbidity and mortality are low, the disease is considered serious when the disease presents a genetic predisposition. The identification of molecular markers that can be used for disease monitoring, risk stratification and early detection is essential for the individualization of treatment and the optimization of patient outcomes.

**MATERIALS AND METHODS**: Patients with medullary thyroid carcinoma who underwent thyroidectomy from January 2000 to December 2015 were included in the study. The medical records of these patients were reviewed, and patients who had undergone thyroidectomy were subjected to clinical and mediastinal staging. The patients were stratified into three groups: patients with high-risk features (≥3 criteria), patients with intermediate-risk features (1–2 criteria), and patients with low-risk features (<1 criterion). The expression levels of metalloproteinases (MMP-2, MMP-9) and tissue inhibitors of metalloproteinases (TIMP-1, TIMP-2) were assessed using immunohistochemistry in primary neoplasms and its correlations with clinical and pathological features were evaluated. The expression of the proteins was assessed by immunohistochemistry using specific antibodies for each protein. The intensity and percentage of immunostaining were evaluated according to the criteria described by the American Society for Clinical Pathology. The statistical analysis was performed using the SPSS software, and the significance of the differences between groups was assessed using the chi-square test and the Kaplan-Meier method. A p-value of <0.05 was considered statistically significant.

**RESULTS**: A total of 100 patients with medullary thyroid carcinoma were included in the study, of which 60 had high-risk features, 30 had intermediate-risk features, and 10 had low-risk features. The expression levels of MMP-2 and TIMP-2 were significantly higher in patients with high-risk features compared to those with low-risk features (p = 0.045 and p = 0.023, respectively). The expression levels of MMP-9 and TIMP-1 were not significantly different among the three groups. The Kaplan-Meier survival analysis showed a significant difference in survival between the high-risk and low-risk groups (p = 0.037), with a median survival of 7 years for patients with high-risk features and 12 years for patients with low-risk features. The expression levels of MMP-2 and TIMP-2 were significantly higher in patients with high-risk features compared to those with low-risk features (p = 0.045 and p = 0.023, respectively). The expression levels of MMP-9 and TIMP-1 were not significantly different among the three groups. The Kaplan-Meier survival analysis showed a significant difference in survival between the high-risk and low-risk groups (p = 0.037), with a median survival of 7 years for patients with high-risk features and 12 years for patients with low-risk features. The expression levels of MMP-2 and TIMP-2 were significantly higher in patients with high-risk features compared to those with low-risk features (p = 0.045 and p = 0.023, respectively). The expression levels of MMP-9 and TIMP-1 were not significantly different among the three groups. The Kaplan-Meier survival analysis showed a significant difference in survival between the high-risk and low-risk groups (p = 0.037), with a median survival of 7 years for patients with high-risk features and 12 years for patients with low-risk features.

**CONCLUSION**: The expression of metalloproteinases and their tissue inhibitors is an important factor in the development and progression of medullary thyroid carcinoma. The identification of these biomarkers can be used for the early detection and monitoring of medullary thyroid carcinoma, and the development of targeted therapies for patients with high-risk features may improve outcomes. Further studies are needed to validate these findings and to develop targeted therapeutic strategies for medullary thyroid carcinoma.
A retrospective chart review was conducted to describe clinical and imaging characteristics of the advanced intraocular tumors and metastatic disease at the Brazilian National Cancer Institute (INCA), Rio de Janeiro, Brazil from 1987 to 2006, with newly diagnosed retinoblastoma. The patients were classified using the International Classification of Retinoblastoma in intraocular cases and Chantada international classification of retinoblastoma staging system for extracocular disease. Results: Unilateral disease was present in 143 (60%) of cases. Mean age of unilateral intra-ocular disease at diagnosis was 32 months and of bilateral intra-ocular disease 18 months. For extra-ocular disease, mean ages at diagnosis were 39 months for unilateral cases and 21 months for bilateral cases. The median times from presenting signs to diagnosis for patients with intra-ocular disease were 6 months (range: 0.25-45 months). Extracocular disease was present in 38.2% of the patients and the mean time from presenting signs to diagnosis was 11 months (range: 0.5-34 months). Longer delays in diagnosis were associated with the most severe cases and lowest survival rate in patients with bilateral retinoblastoma and extra-ocular disease U=2,36 (p=0.018). Higgest mortality was also associated with longer delays for diagnosis in extra-ocular disease (51.2%) compared to intra-ocular disease (27.8%) (p<0.001). Conclusion: Advanced cases with delayed diagnosis are related to higher mortality in this series of patients. Given the great number of patients in advanced intra-ocular stages, established extra-okcular disease and high mortality, it is evident and mandatory to work in a cooperative group to develop a national early detection program.

Background: Advanced intraocular tumors and metastatic disease at diagnosis are not rare in developing countries. Objective: We aimed to report the presentation status, clinical characteristics and outcomes of late diagnosis from presenting signs to diagnosis of retinoblastoma in a government health institution. Methods: A retrospective chart review was conducted of 210 patients who presented to the National Institute of Cancer (INCA), Rio de Janeiro, Brazil from 1987 to 2006, with newly diagnosed retinoblastoma. The patients were classified using the International Classification of Retinoblastoma in intraocular cases and Chantada international classification of retinoblastoma staging system for extracocular disease. Results: Unilateral disease was present in 143 (60%) of cases. Mean age of unilateral intra-ocular disease at diagnosis was 32 months and of bilateral intra-ocular disease 18 months. For extra-ocular disease, mean ages at diagnosis were 39 months for unilateral cases and 21 months for bilateral cases. The median times from presenting signs to diagnosis for patients with intra-ocular disease were 6 months (range: 0.25-45 months). Extracocular disease was present in 38.2% of the patients and the mean time from presenting signs to diagnosis was 11 months (range: 0.5-34 months). Longer delays in diagnosis were associated with the most severe cases and lowest survival rate in patients with bilateral retinoblastoma and extra-ocular disease U=2,36 (p=0.018). Higgest mortality was also associated with longer delays for diagnosis in extra-ocular disease (51.2%) compared to intra-ocular disease (27.8%) (p<0.001). Conclusion: Advanced cases with delayed diagnosis are related to higher mortality in this series of patients. Given the great number of patients in advanced intra-ocular stages, established extra-okcular disease and high mortality, it is evident and mandatory to work in a cooperative group to develop a national early detection program.
Background: An unusual case of malignant carcinosarcoma involving the maxillary sinus, with combination of poorly differentiated squamous carcinoma, undifferentiated spindle small round blue cells and immature atypical cartilaginous tissue with no neuroepithelial elements is reported. We propose the descriptive term of carcinosarcoma, to avoid confusion with sinonasal teratocarcinosarcoma, which contains immature elements of all 3 embryologic layers. The patient underwent surgery with post-operative cisplatin-based chemoradiation and developed recurrent disease 3 months later. Design: Case report with review of literature. Setting: Tertiary care medical center.

Clinical History: A 59 year old man presented with 6 month history of a progressively enlarging left nasal and maxillary mass with complete left nasal obstruction, anosmia, epistaxis, proptosis, epiphora, diplopia, and exophthalmos. Initially, he was treated with antibiotics and allergy medications with no relief of symptoms. Physical examination and image studies (CT and MRI) revealed a large submucosal mass (6.8cm) filling the entire left nasal cavity with extension to the anterior wall of maxillary sinus and inferiorly into the gingivobuccal sulcus, eroding through the alveolar ridge and superiorly into the orbit, the ethmoid and maxillary sinuses. A transoral biopsy was taken, and pathology was consistent with invading papilloma. Subsequently, a combined endonasal and transoral, Caldwell Luc resection of this left maxillary tumor was performed. Results: Pathology revealed that tumor consisted of at least 2 lineages of cellularity with an inverted pattern and transitional-type morphology including invasive non-keratinizing squamous carcinoma with undifferentiated spindle cell component, and atypical immature cartilage. Immunostains showed tumor cells were positive for cytokeratin AE1/AE3, Cam 5.2, EMA, CD99, Vimentin, but negative for GFAP and synaptophysin. MIB1 staining for S100 protein, consistent with a T4aN0 invasive sinonasal carcinosarcoma. The patient was given postoperative radiation and cisplatin-based chemotherapy. A repeat MRI reported no evidence of disease. However, on follow up 3 months later, the patient noted recurrent epistaxis and new left cervical level II lymphadenopathy. Biopsy of the left maxillary mass was suggestive of undifferentiated tumor. The patient underwent expanded cisplatin-based chemotherapy and radiation therapy. Currently, he is still undergoing treatment.

P713: WEGENER’S GRANULOMATOSIS OF THE SKULL BASE R.D.Hart1, M.Grandy1, S.Mark Taylor1, M.Bullock1, J.Nasser1, J.R.B.Trites1,1 Dalhousie University, Halifax, NS Canada

Wegener’s granulomatosis is an uncommon multisystemic disorder of unknown etiology. It is characterized histologically by necrotizing granulomatous vasculitis. It commonly involves the upper and lower respiratory tract and kidneys, but other organ systems can also be affected including the orbits, central nervous system and skull base. Localized disease that does not involve the kidneys or lung is rare. A review of the English literature demonstrates that Wegener’s granulomatosis limited to the skull base is very unusual. In this report, a 36 year old female presented with multiple, right sided cranial neuropathies and imaging findings (CT and MRI) suggestive of a malignant tumor of the nasopharynx and skull base. After an extensive workup including multiple biopsies and serology a diagnosis on Wegener’s granulomatosis was made. There were no renal or pulmonary findings associated with the diagnosis. The patient was started on cyclophosphamide and prednisone with complete resolution of the cranial neuropathies and involution of the skull base mass as seen on repeat CT and MRI. This case represents an extremely rarely encountered subtype of “localized” Wegener’s granulomatosis.

P714: LANGERHANS’ CELL HISTIOCYTOSIS OF THE HEAD AND NECK REGION M.K.Ikeda1, J.G.Filho1, A.Carneiro1, L.P.Kowalski1,1 Hospital AC Camargo, Sao Paulo, Brazil

Objectives: Langerhans’ Cell Histiocytosis (LCH) is a rare entity that includes a group of histological similar disorders characterized by the proliferation of Langerhans’ cell with non classical presentation and neck involvement. The objective this study is to evaluate the clinical characteristics and treatment results of patients with LCH treated in a single institution. Methods: We reviewed the medical records of 45 consecutive patients with LCH treated from 1980 to 2001. Only patients with pathologic diagnosis were included in the study. Chi-square test was used to determine significant associations between the variables studied (age, gender, symptoms, lesion site, extent of involvement, and recurrence). Survival analyses was performed by Kaplan-Meier method. Results: There were 12 female and 33 male patients, with a mean age of 3 years (ranging from 1 to 63 years). Seventy-six percent of the patients had less than 8 years of age at presentation. The most common presenting complaint was tumor in 42 (93%) patients and pain in 27 (60%) patients. Thirty-three patients had lesions involved cranio-facial bones (15 skull, 9 mandible, and 9 maxilla) and neck lymph node involvement in 12 patients. No significant differences were observed between the clinical variables (age, gender, lesion site). The follow-up period ranged from 1 to 302 months (median of 100 months). During the study period, 23 patients remained with no evidence of recurrent disease, 4 patients were alive with recurrent disease, 10 patients died of disease, 1 patient died for other cause, and 2 were lost to follow-up. The overall survival rates at 5 and 10 years were of 78% and 76%. No correlations were observed between survival rates and clinical variables studied (age, gender, lesion local e number of lesion). Conclusion: LCH is a systemic disease that occur more frequently in pediatric patients. In our study, no correlation was observed between the clinical variables and survival.

P715: LANGERHANS CELL HISTIOCYTOSIS PRESENTING AS A NECK MASS IN AN ADULT T.H. Alexander1, K.T. Brumund1,1 University of California-San Diego, San Diego, CA

Introduction: Langerhans cell histiocytosis (LCH) is a rare dendritic cell proliferative disorder with unknown etiology and a widely variable clinical course. Although primarily a disease of children, LCH can occur in any age group. We present a case of predominantly pulmonary LCH presenting as a cervical mass in an adult. The diagnosis was made based on a reevaluation of a case. Review of the literature is presented with a focus on clinical presentation, radiographic and pathologic diagnosis, and treatment in adults. Methods: Case report and literature review. Results: A 52-year old smoker presented with a 5-month history of enlarging right level 2 neck mass and fatigue. Complete head and neck exam was remarkable only for the neck mass. Fine needle aspiration (FNA) of the neck mass was non-diagnostic, but suggested a differential including Hodgkin’s lymphoma, sarcoma, and poorly differentiated carcinoma. High resolution CT of the neck and chest revealed a 2 cm jugular bulge node, a 1.5 cm pre- carinal node, and multiple bilateral pulmonary nodules. An open excisional biopsy of the neck mass was performed. Histology and immunohistochemistry revealed a lymph node with atypical histiocytic proliferation. The cells were CD1a and S100 positive, consistent with a diagnosis of LCH. Serial CT scans over the next 6 months showed slow resolution of the pulmonary nodules without treatment. Conclusion: Adult LCH often presents with involvement of the head and neck and can mimic other disorders such as malignancy. The head and neck surgeon plays an important role in the diagnosis and treatment of LCH and should be familiar with its presentations.

P716: LANGERHANS CELLS: ORAL MANIFESTATIONS J.M. Sossi1, L.P. Pombal1, G.P. Camargo1, J. L. Dissenha1, J.L. Schussel1, P.A.G. Pedruzzo1, N.G. Skare1, B.V. Oliveira1,1 Erasto Gaertner Hospital, Curitiba, Brazil

Langerhans cell histiocytosis (LCH) is the result of clonal proliferation of Langerhans cells, which in turn may be associated to other inflammatory cells such as eosinophilic cells, macrophages, lymphocytes and neutrophils. The wide clinical spectrum of the condition may range from a sole, asymptomatic osteolytic lesion to the involvement of one or more organs. However, one the maxilla is afflicted by LCH, the main symptoms are localised pain, facial growth, tooth mobility, gum bleeding, toothache and cephalgia, in addition to sensory disturbances. Prognostic is associated with lesion topography and the extension of the pathology. The involvement of other organs (liver, spleen, lungs and hematopoietic system) and the lack of response to the initial treatment are commonly associated to weak prognostic. LCH treatment includes surgical resection, local radiotherapy, corticotherapy and chemotherapy. The present study consists of the retrospective analysis of the medical records of patients with a confirmed diagnosis of oral Langerhans cells histiocytosis. Objective: To carry out a retrospective analysis of medical records of patients with a confirmed diagnosis of oral Langerhans cells histiocytosis admitted at the Oral and Maxillofacial Surgery Department of Hospital Erasto Gaertner (Curitiba-Paraná). Methods: After the approval of the Ethics and Research Committee of the Hospital, we started our retrospective study of oral manifestations of Langerhans cells histiocytosis admitted at the Oral and Maxillofacial Surgery Department of Hospital Erasto Gaertner (Curitiba-Paraná).
Endemic Burkitt Lymphoma, an Epstein-Barr virus (EBV) positive malignancy, is an important model for understanding EBV oncogenesis and treatment. In laboratory and animal tumor models, latent EBV present within tumor cells responds to various types of cytotoxic therapies by inducing lytic specific viral genes (e.g. BMRF1 and BZLF1) that phosphorylate the nucleoside analog drug, ganciclovir, converting it into a toxic form. This activated drug not only prevents replication but also kills the host tumor cell. If this occurs in EBV associated human cancers, the addition of ganciclovir to initial chemotherapy treatment will increase cancer specific cytotoxicity. Our objectives were to determine whether a single round of chemotherapy induces EBV lytic switches from the latent to lytic phase in an EBV associated cancer. Methods: 3-15 year olds with expanding, solid maxillary or mandibular masses consistent with Burkitt Lymphoma presenting to Kamuzu Central Hospital were enrolled. Fine needle aspiration was performed prior to initiation of chemotherapy and 3-5 days after chemotherapy on 10 out of a planned 25 patient cohort in this interim analysis. Aspirated material was fixed into Paraffin-Cyt and paraffin embedded blocks were prepared for histochimical analysis of EBV lytic proteins (BMRF1 and BZLF1 immuno-histochemistry), latent EBV encoded RNA (EBER in situ hybridization), and H & E to facilitate interpretation of EBV stains. Results: In situ hybridization revealed 80% of the samples collected prior to treatment with cyclophosphamide are positive for EBER (latent EBV encoded RNA) while 60% of samples collected 3-5 days after treatment are EBER negative. Immunohistochemical analysis of the lytic specific proteins BMRF1 and BZLF1 in paired samples demonstrated no significant expression before or after chemotherapy. There have been no adverse events. Conclusions: The interim analysis of this proof of principle study reveals that after 3-5 days of cyclophosphamide treatment in children with pathology proven Burkitt Lymphoma, the lytic cycle of EBV is not induced. To achieve statistical significance, the study will be completed.

P718: CONCURRENT RADIOTHERAPY AND HAART FOR LOCALIZED PLASMA BLASTIC LYMPHOMA IN AIDS: CASE REPORT AND LITERATURE REVIEW
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Background: Plasmablastic lymphoma (PBL) is an unusual lymphoma most commonly found in the head and neck area especially in the oral cavity causing bone destruction in early stages, most seen in HIV-positive patients as an AIDS-related entity. The current advocated treatment for PBL is highly active anti-retroviral therapy (HAART) in association with standard or dose-adjusted chemotherapy regimen for lymphoma. The utility of radiation therapy for PBL has remained unclear when used as adjunctive to chemotherapy and/or HAART. Methods: We report a case of PBL in a previously undiagnosed HIV-positive patient, presenting with a solitary, tender, and localized lesion in the upper lip extended to pre-maxilla and maxillary alveolar ridge. The patient was prescribed HAART and concomitant local radiation therapy at 23.4 Gy. before chemotherapy. Results: Complete local clinical response was observed in 4 weeks of treatment and has been sustained it after 32 months follow-up in this patient. Conclusions: Immunosuppressed AIDS related PBL patients who developed tender localized lesion limited in the head and neck area without signs of systemic manifestation. The combination of localized low dosage of radiation therapy and HAART seem to induce local remission of the initial lesion and improve immune status before starting the systemic chemotherapeutic treatment. We review the literature on the diagnosis and treatment of localized PBL in the head and neck area.

P719: THE EFFICACY OF THP-CVP FOR LOCALIZED NON-HODGKIN'S LYMPHOMA OF THE HEAD AND NECK
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Objective: THP-CVP is the one of CHOP-like regimen reported in 1993, included pirarubicin, cyclophosphamide, vindesine and prednisolone. That is exchanged doxorubicin and vincristine in CHOP to pirarubicin and vindesine on purpose to reduce the side effect of those cardiotoxicity and neutroxticity. We had treated localized early-stage non-Hodgkin’s lymphoma of the head and neck with combination therapy of THP-CVP and radiation till rituximab was introduced and investigated the efficacy of the regimen retrospectively. Methods: Subjects were the patients with clinical stage 1 and 2, non-cavitary of the head and neck who received combina- tion therapy of THP-CVP and radiation between October 1994 and June 2006. Those included bulky 14 cases with 6 centimeters of mass or over. The total number of patients was 76 consisting of 42 males and 34 females. A range of age was from 19 to 84 years old and median age was 61. The classification of pathological type was conformed to the WHO classification and an unclassifiable case according to that was excluded. The dose of THP-CVP was 40mg/m2 (day 1) of pirarubicin, 750mg/m2 (day 1) of cyclophosphamide, 0.06mg/kg (day 1, max 3mg/body) of vindesine and 100mg/body (day 1-5) of prednisoline. The number of administration times was 5 courses every 3-4 weeks as a rule because relapse cases had been prominent with 3 courses formerly. Nevertheless they were adjusted to 4 complications, stage and effectiveness. Radiation therapy was performed 30-40Gy by involved field concurrently with initial two courses of THP-CVP, and especially 45-50Gy in nasal NK/Tcell lymphoma or bulky case. Results: The 5-year overall survival rate of the total cases was 60.9%, and the cases with THP-CVP of 3 or 4 courses (23 cases) was 55.1% and 5 or 6 courses (30 cases) was 70.3%. Prognostic factors were also analyzed retrospectively. The 5-year overall survival of stage 1 (46 cases) was 59.9% and stage 2 (30 cases) was 62.3%. That of 60 years old and under (37 cases) was 71.0% and 61 years old and over (39 cases) was 51.1%. That of B cell lymphoma (67 cases) was 68.2% and T/NK cell lymphoma (9 cases) was 33.3%. Classified according to International Prognostic Index (IPI), that of low risk (59 cases) was 72.5% and low-intermediate risk (16 cases) was 20.2%. It showed statistically significant differ- ence in age, pathological type, and IPI. There were no serious side effects related to the regimens. Conclusions: This result suggested that THP-CVP combined with radiation therapy was safe and effective for the patients with lymphoma of younger, B cell type and low risk in IPI. On the other hand, it is necessary for the patients of T/NK cell lymphoma to treat with more inten- sive chemotherapy. With regard to age and IPI, there was some possibility that the reduction of dose and the extension of interval were excessive.

P720: SURGICAL TREATMENT OF MANTLE CELL LYMPHOMA THAT FAILED TO RESPOND TO CHEMOTHERAPY: A REPORT OF ONE CASE
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Case: A 65-y-old male admitted complaining of left parotid area mass. He was diagnosed with mantle cell lymphoma after excisional biopsy and went under cyclus of chemotherapy. We report a case of observation of bilateral neck mass during follow up and thus bilateral neck dissection was carried out to totally remove the neck mass. Introduction: Lymphoma is a type of cancer that begins in a lymphocyte, usually in a lymph node or occasionally in another organ. It is divided into two major categories: Hodgkin lymphoma and non-Hodgkin lymphoma. Mantle cell lymphoma (MCL) is one of several subtype of B-cell lymphoma. MCL usually begins with lymph node enlargement; it can spread to other tissues such as the marrow, liver and gastrointestinal tracts. Sometimes it can begin in a lymphocyte outside a lymph node, such as in the gastrointestinal tract. MCL is treated like other aggressive B-cell lymphomas with multidrug therapy, often five agents combined. New agents, such as bortezomib (Velcade) can be used in patients who have progression in their disease. Clinical trials are expected to introduce improvements in current treatment approaches. Results: There has been notable progress in the treatment of MCL over the last three decades with a near doubling of overall survival, even though relapse are still common. Most patients respond well to initial chemotherapy. However, the most patients relapse and the chance of a second or return. Treatment resistance may develop, which means that patients become less responsive to chemotherapy. In case of our patient, the mass was limited within the neck and removed by bilateral neck dissection and no further recurrence is observed so far. Conclusions: Most mantle cell lymphoma patients receive treatment combination chemotherapy. But, it has tendency to tumor after chemotherapy. We like our case, planning of chemotherapy after total surgical resection of the neck mass that could be a new way of treatment.
To review a series of patients with Sinonasal Lymphomas in order to determine the role of the otolaryngologist and the approach and treatment of this particular group of patients. An effective and immediate way to relieve their symptomatology (nasal obstruction, proptosis, cranial nerve palsy, etc.), without affecting or compromising the definitive treatment given by the oncologist.

**Methodology:** A retrospective review of the Department of Otolaryngology of the University of Miami School of Medicine plus one of the author’s personal files were reviewed during the period March 2001 through March 2005. Patients’ medical records, imaging studies, surgical procedure, pathology, and final outcome were reviewed especially in regards to relieve them from their symptoms.

**Results:** Nine patients were collected from this search. Patients came with an array of multiple symptoms such as proptosis due to orbit invasion with frank decrease in their visual fields that certainly improved once an endoscopic orbit decompression was performed. In the same way their nasal obstruction was relieved giving the patient a better quality of life while they were waiting for the final evaluation, work up, and treatment by the oncologist.

**Conclusions:** Even though our data reflect a limited number of patients, the findings provided, suggest that for the specific patients affected with advanced Sinonasal Lymphomas such as the ones described, the Endoscopic approach might benefit the patient by not only allowing the surgeon to obtain a confirmatory tissue sample of lymphoma with out undergoing extensive open procedures. In addition, that would offer the patient an immediate treatment modality that may alleviate his symptomatology faster, while all of his definitive treatment is given. Measures such as nerve and orbit decompression, tumor debulking for airway opening, etc. are not intended to replace, at any time, the final treatment given by the hematologist and or the radiation therapy doctor.

**P722: THE EFFICACY OF CHEMOTHERAPY FOR EARLY NK/T CELL LYMPHOMA OF HEAD AND NECK**

**Objective:** We undertook the present study to analyse the efficacy and characterize the therapeutic outcome of chemotherapy and combined modality treatment in patients with extranodal NTCL of head and neck.

**Materials and Methods:** Between September 1993 and March 2007, 83 patients with head and neck tumours were included. The histologic diagnosis was NK/T-cell lymphoma, nasal type arising in head and neck were treated in Seoul National university hospital, Seoul, Korea. Patients diagnosed were treated curative by using radiotherapy (RT), chemotherapy (CT) and combined modality treatment (CMT). Chemotherapy consisted of doxorubicin based regimen (CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) and COPBLAM (cyclophosphamide, vincristine, procarbazine, bleomycin, doxorubicin, prednisolone) and IMPEX (lasmide, methotrexate, etoposide and prednisolone) regimen. Result: Excellent rate of tumor response above CR or PR was achieved in groups of CT alone and CMT. For 29 patients receiving CT alone, 25 (86.2%) of 29 patients achieved CR or PR. For 29 patients receiving CMT, 26 (89.7%) of 29 patients achieved CR or PR. The 5-year OS in CMT group were higher than those in RT alone group but there was no significance (P = 0.927), The 5-year OS and DFS in CMT group receiving IMPEX regimen chemotherapy were significantly higher than those in RT alone group (P = 0.047). Conclusion: Chemotherapy addition to radiotherapy, especially IMPEX regimen appears to confer survival benefit in NK/T-cell lymphoma of head and neck.

**P723: NON HODGKIN LYMPHOMA OF THE THYROID GLAND: CASE REPORT**

**Objective:** Non Hodgkin lymphoma type B is the most common lymphoproliferative disease arising in thyroid gland. This case report presents a 64 year old woman with a type B, large cells non Hodgkin lymphoma with a high IPI (International prognostic index).

**Methods:** The patient was submitted to undergo the tumoral and endoscopic biopsy of the specimen. Computed tomographies of neck, thoracic and abdominal cavitie and bone marrow biopsy were used for staging.

**Results:** The patient was staged as an IVE according to the Ann Arbor System. There were respiratory and digestive compression symptoms. The treatment consisted of eight cycles of cyclophosphamide, doxorubicin, vincristin and prednisone.

After the first stage of treatment the patients had complete remission of the compression symptoms and after the fourth one there was a complete (clinical and radiological) response. **Conclusion:** this case illustrated the importance of the chemotherapeutic approach even for cases with advanced stage of non-Hodgkin thyroid lymphoma.

**P724: HEAD AND NECK NON HODGKIN LYMPHOMA, ENT DEPARTAMENT, LENIN FONSECA HOSPITAL, FEBRUARY 2003-2007**

**Objective:** The aim of the present is to describe the patient’s characteristics, histopathology subtype, staging and prognosis factor of head and neck NHL.

**Methods:** Descriptive study, series of cases, 25 patients with diagnosis NHL confirmed, some patients with immunohistoquimic study. Ann Arbor staging system was used for these patients. The international NHL prognostic factor were used in each cases. The unfavorable variable was realized with frequency and percentage: 25 patients were males (32%) and 16 (68%) males, the most affected age group was 60-69 years old 25%, follow of 50-59 years old 20% The age group 20-29 old and 30-39 were 12% each group and less than 20 years old 8%, similar to age group 70-79 years old and older than 80 years old 20%. The mean age was 50.4 years and the age range was 10-89 years old. The most frequent localization was the oropharynx 52% follow by nasosinusal area 28%, neck and orbit 8% each one and nasopharynx 4%. The staging according Ann Arbor was IIA 52%, IA 20%, IIb 15%, IIIa 8%, and only 4% to IVB. The histologic subtype was non specific NHL 52%, Natural Killer NHL 20%, follicular variant and small lymphocytic 8% each one, lymphoplasmoisic, mixed cell, nodular sclerosis 4% each one. The good prognostic factor of the patients were 60% in all patients less than 60 years old, 52% of these patients had stage Ann Arbor II, 80% without symptoms and 80% with only one extra nodal site. The treatment used in all patients was chemotherapy and radiotherapy.

**Conclusion:** Head and neck NHL affected more males patients, it showed a bimodal behavior related to age groups, the most affected localization was Oropharynx follow by nasosinusal area, The diagnosis was done in early stages, most of the patients were asymptomatic and the majority with only one extra nodal area affected.

**P725: SERIAL DYNAMIC SONOGRAPHIC CONTRAST ENHANCEMENT CHANGES IN CERVICAL LYMPH NODES: BEFORE AND AFTER TREATMENT FOR LYMPHOMA**

**Objective:** Over a quarter of non Hodgkin Lymphomas (NHL) has an extra nodal presentation. The head and neck is the second most common area after gastrointestinal tract affected by NHL. This illness comprise heterogeneous groups of tumors with different histological types, but generally have a good prognosis compared with squamous carcinomas. The aim of the present is to describe the patient’s characteristics, histopathology subtype, staging and prognosis factor of head and neck NHL.

**Methods:** Descriptive study, series of cases, 25 patients with diagnosis NHL confirmed, some patients with immunohistoquimic study. Ann Arbor staging system was used for these patients. The international NHL prognostic factor were used in each cases. The unfavorable variable was realized with frequency and percentage: 25 patients were males (32%) and 16 (68%) males, the most affected age group was 60-69 years old 25%, follow of 50-59 years old 20% The age group 20-29 old and 30-39 were 12% each group and less than 20 years old 8%, similar to age group 70-79 years old and older than 80 years old 20%. The mean age was 50.4 years and the age range was 10-89 years old. The most frequent localization was the oropharynx 52% follow by nasosinusal area 28%, neck and orbit 8% each one and nasopharynx 4%. The staging according Ann Arbor was IIA 52%, IA 20%, IIb 15%, IIIa 8%, and only 4% to IVB. The histologic subtype was non specific NHL 52%, Natural Killer NHL 20%, follicular variant and small lymphocytic 8% each one, lymphoplasmoisic, mixed cell, nodular sclerosis 4% each one. The good prognostic factor of the patients were 60% in all patients less than 60 years old, 52% of these patients had stage Ann Arbor II, 80% without symptoms and 80% with only one extra nodal site. The treatment used in all patients was chemotherapy and radiotherapy.

**Conclusion:** Head and neck NHL affected more males patients, it showed a bimodal behavior related to age groups, the most affected localization was Oropharynx follow by nasosinusal area, The diagnosis was done in early stages, most of the patients were asymptomatic and the majority with only one extra nodal area affected.

**Aim:** To evaluate the sonographic contrast enhancement pattern of lymphomatous cervical nodes, before and after treatment. **Methodology:** Lymphoma patients with proven cervical nodal involvement were recruited. Subjects underwent routine ultrasound to identify involved cervical lymph nodes. A representative lymphomatous cervical lymph node was chosen for continuous sonographic monitoring after administering intravenous sonographic contrast. This dynamic enhancement sonographic data was then analyzed for the rate and amount of enhancement. Time-enhancement curves were drawn for comparison. The same lymph node was identified for identical assessment one-month after completing chemotherapy.

**Results:** A total of eleven patients were recruited with eight having completed the imaging and clinical follow-up (mean age 58.4 years, range 25-77; four males and four females). There was a decrease in size for all lymph nodes after treatment. For contrast enhancement, all patients had significant delay in time to peak enhancement after treatment (mean of 2983ms, range 1297 to 15545ms, p = 0.019). The change in the peak amount of contrast enhancement was variable (three with lower peak and three higher after treatment; mean -3.3%, range -17.4 to 10.8%, p =
0.398. **Conclusion:** The significant delay in contrast enhancement after treatment suggests an increase in vascular resistance (shrinkage of vessels) or reduced vascular leakage within lymph nodes. This may be a more appropriate parameter for monitoring lymphoma treatment response than a single time-point measurement of contrast enhancement.

**RECONSTRUCTION III**

**P726: MULTIPLANAR RECONSTRUCTION FOLLOWING MAXILLECTOMY**

**Introduction:** Total maxillectomy after the ablative tumor resection often creates a complex threedimensional facial defect. Traditionally, the reconstruction is achieved commonly using the rectus myocutaneous free flap transfer and the focus had been mainly to separate the oral cavity from the nasal cavity. However nasal obstruction is a frequent postoperative complaint because of blockage of the nasal cavity by the muscle component of the flap. Recently our division adopts the technique of multi-planar repair following maxillectomy in which all the missing functional surfaces were rebuilt using one flap as a single stage operation. This approach allows the patency of the nasal channel to be restored in addition to cover the mucosa of the oral cavity. **Objective:** A clinical review was conducted to summarize our experience on the multi-planar reconstruction following maxillectomy using the free myocutaneous flap. We also compared the efficacy of anterolateral thigh myocutaneous (ALT) flap and the vertical rectus myocutaneous (VRAM) flap with regards to this kind of reconstruction. **Methods:** Nine patients were included between January of 2005 and November of 2007. Details were collected on the patient's age, gender, pathology of the neoplasm, preoperative chemotherapy or radiotherapy, and co-morbidities. The extent of tumor resection, types of defect, flap harvesting technique, results of flap transfer, flap-related complications, and donor site morbidity were retrospectively reviewed. **Results:** There were 8 men and 1 woman and their ages ranged from 45 to 75 years (mean, 58.7 years). Six patients had subtotal maxillectomy and three patients had total maxillectomy performed. ALT flap reconstruction was used in 6 cases with the flap width ranged from 6 to 12 cm (mean, 8.2 cm) and flap length ranged from 12 to 30 cm (mean, 18.2 cm). Primary closure of the rhin donor sites was possible in all cases. VRAM flap were used in 3 patients to resurface the lateral nasal wall and the palate. The width of flaps ranged from 5 to 8 cm (mean, 6.3 cm) and the length of flaps ranged from 13 to 19 cm (mean, 15.3 cm). All abdominal wall donor sites were closed directly. One patient developed abdominal wall incisional hernia requiring repair. The flap survival was 100 percent. All patients had good-to-excellent oral competence, and they were able to breath through the restored nasal passage. **Conclusion:** ALT flap provides a larger skin paddle and its use is associated with minimal donor site morbidities.

**P727: TORACODORSAL ARTERY PERFORATOR FLAP FOR THE TREATMENT OF A VOLUMETRIC DEFECT IN A PATIENT WITH ROMBERG SYNDROME**

**Background:** The main characteristic of the Parry-Romberg Syndrome is progressive hemi facial atrophy. This defect has been treated for years with a variety of free flaps, the most common being the omentum, the parascapular flap, and head and neck free flap reconstruction. Due to the endoscopic examination of free flap perfusion in this study. Each participant was examined three times (intraoperatively, 24 hours and 72 hours postoperatively) each examination involved an i.v. application of ICG followed by an endoscopic examination. The obtained video sequences were evaluated concerning timing of onset and maximum of fluorescence following application of ICG for the transplanted and the surrounding areas. The results of injury occurrence and the obtained ICG fluorescence were collected over a period of four weeks after surgery for each patient, and were compared to those gained from fluorescence angiography. **Results:** Following fluorophore application, all patients showed near-infrared ICG fluorescence in both transplanted tissue as well as in autogenous surrounding areas. The time of onset as well as of maximum fluorescence values was delayed in the transplanted tissue when compared to the surrounding tissue, whereas the maximum fluorescence intensity reached similar levels in both tissue types. One free flap which failed after an unusually long period of 3 weeks had shown exceptionally low fluorescence intensities in the transplanted tissue. The results of fluorescence angiography and the obtained video sequences were evaluated concerning timing of onset and maximum of fluorescence following application of ICG for the transplanted and the surrounding areas. The results of injury occurrence and the obtained ICG fluorescence were collected over a period of four weeks after surgery for each patient, and were compared to those gained from fluorescence angiography. **Objective:** To describe the use of vacuum assisted closure (VAC) dressings in the management of cutaneous defects following complex revision head and neck free flap reconstruction. **Methods:** Two cases are reported in which patients required a revision free flap reconstruction of the head and neck. At the completion of the flap inset, a cutaneous defect remained due to the added bulk of the free flap and retracted, fibrotic skin flaps from prior irradiation treatment. The exposed free flap muscle was covered with a VAC dressing in order to both close the wound and stimulate a healthy bed of granulation tissue over the irregular muscle bed. At completion of treatment the granulation tissue was either skin grafted or allowed to re-epithelialize. Additionally, a literature review of the use of VAC dressing in revision free flap reconstruction in the head and neck. **Conclusions:** Negative pressure dressings can be safely placed directly over myocutaneous free flaps to assist in the closure of associated cutaneous defects after revision head and neck reconstruction. The VAC dressing seals off the cutaneous defect and allows for rapid, uniform granulation tissue formation over an irregular muscular bed.

**P729: ENDOSCOPICAL EXAMINATIONS OF FREE FLAP PERFUSION IN THE HEAD AND NECK REGION USING RED-EXCITED INDOCYANINE GREEN**

**Background:** The aim of the current investigation was to prove the feasibility and to explore the clinical benefit of endoscopically guided free flap perfusion measurements in the head and neck region using red-excited Indocyanine Green (ICG). **Methods:** So far, 10 patients who underwent reconstructive surgery including free tissue transfer to the head and neck region took part in this study. Each patient was examined three times (intraoperatively, 24 hours and 72 hours postoperatively) each examination involved an i.v. application of ICG followed by an endoscopic examination. The ICG fluorescence was delayed in the transplanted tissue when compared to the surrounding tissue, whereas the maximum fluorescence intensity reached similar levels in both tissue types. One free flap which failed after an unusually long period of 3 weeks had shown exceptionally low fluorescence intensities in the transplanted tissue. The results of injury occurrence and the obtained ICG fluorescence were collected over a period of four weeks after surgery for each patient, and were compared to those gained from fluorescence angiography. **Results:** Following fluorophore application, all patients showed near-infrared ICG fluorescence in both transplanted tissue as well as in autogenous surrounding areas. The time of onset as well as of maximum fluorescence values was delayed in the transplanted tissue when compared to the surrounding tissue, whereas the maximum fluorescence intensity reached similar levels in both tissue types. One free flap which failed after an unusually long period of 3 weeks had shown exceptionally low fluorescence intensities in the transplanted tissue. The results of injury occurrence and the obtained ICG fluorescence were collected over a period of four weeks after surgery for each patient, and were compared to those gained from fluorescence angiography. **Objective:** To describe the use of vacuum assisted closure (VAC) dressings in the management of cutaneous defects following complex revision head and neck free flap reconstruction. **Methods:** Two cases are reported in which patients required a revision free flap reconstruction of the head and neck. At the completion of the flap inset, a cutaneous defect remained due to the added bulk of the free flap and retracted, fibrotic skin flaps from prior irradiation treatment. The exposed free flap muscle was covered with a VAC dressing in order to both close the wound and stimulate a healthy bed of granulation tissue over the irregular muscle bed. At completion of treatment the granulation tissue was either skin grafted or allowed to re-epithelialize. Additionally, a literature review of the use of VAC dressing in revision free flap reconstruction in the head and neck. **Conclusions:** Negative pressure dressings can be safely placed directly over myocutaneous free flaps to assist in the closure of associated cutaneous defects after revision head and neck reconstruction. The VAC dressing seals off the cutaneous defect and allows for rapid, uniform granulation tissue formation over an irregular muscular bed.
with artificial connective tissue supports (typically fibroblast containing collagen gels) to generate a tissue-engineered epithelium. More recently, Ponce et al. (Angiogenesis 2004; 7:295-305) incorporated endothelial cells into the connective tissue support such that branched tubular endothelial structures can be developed. To provide an oral tissue with a vascular network that can support the incorporation of myocytes, the next step is to stabilise the primitive vascular network with pericytes and vascular smooth muscle cells. Methods: In preliminary studies different numbers of keratinocytes, fibroblasts and endothelial cells were seeded onto inert membranes. Subsequently these cells were incorporated into an artificial connective tissue matrix. The tissue morphology was assessed by examination of haematoxylin and eosin stained sections and vascular networks by immunohistochemistry with anti CD31. Results: The ratio of endothelial cells to fibroblasts that gave the best vascular networks with inserts was used to develop similar networks using the artificial connective tissue matrix. The distribution of the vascular network was detected with anti CD31.

Conclusion: Combining different cell types has the potential to generate tissue-engineered epithelium with vascular elements. Keywords: tissue engineering, blood vessels, reconstruction, head and neck carcinoma.

P731: WORLDWIDE MORBIDITY AND MORTALITY IN GASTRIC PULL-UP FOR HEAD AND NECK CANCER A.S. Martin1, A.J. Tincani2, A.Del Negro1, M.F.da Cruz3, F.V.Renato4, 1State University of Campinas [UNICAMP], Campinas, São Paulo, Brazil; 2State University of Campinas [UNICAMP], Campinas, São Paulo, Brazil; 3State University of Campinas [UNICAMP], Campinas, São Paulo, Brazil; 4State University of Campinas [UNICAMP], Campinas, São Paulo, Brazil

Introduction and Objective: Resection of the hypopharynx and cervical esophagus with immediate reconstruction is a major concern of surgeons around the world, as is the morbidity and mortality in gastric pull-up. The objective of this report is to compare our data with the literature to date. Patients: Forty patients underwent gastric pull-up from 1985-2000, with main index tumors located in esophagus (17 cases), hypopharynx (17) and larynx (6). Results: Locoregional (LR) and systemic complications occurred in 82.5% and 55% of the patients, respectively. However, serious complications occurred in 60% of the cases. The most important LR complications were surgical wound infection (WI) (27.5%), gastrectomy perforation (GP) (5%), and tracheal wall necrosis (TWN) (7.5%), chylous fistula (CF) (5%) and carotid rupture (CR) (2.5%). The most important systemic complications included pneumonia (55%), sepse (12.5%) and pulmonary embolus (PE). Hospital mortality was 20% (eight cases), the direct causes being arterial rupture (three cases), pneumonia and sepsis (three), cardiac arrhythmia and PE (one case each), but infection was a contributing factor in all cases. Literature: We found about 47 publications from 1960-1997, revealing approximately 1700 cases. The literature median complication rate was 62% among all authors, varying from 22% to 90%. The median rate for WI, fistula, IAR, TWN, CA and CF was 19.4%, 14.5%, 8%, 8.9%, 4.5% and 3.1%, respectively. Mortality rate varied from 0% to 33%, with a median rate of 12% (55.3% with mortality up to 10%, 36% between 11 and 20% and 8.5% with mortality of more than 20%). The direct causes of the mortality in the literature were basically the same as ours, with some differences. Conclusions: Morbidity and mortality in gastric pull-up for pharyngo-esophageal cancer continues to be a major concern in our series and in the literature. Better selection of patients, improvement in pre-operative nutrition and better control of infection may reduce these high rates.

P732: THE USE OF POLYVINYLIDENE FLUORIDE AS A MORPHOGENIC BIOMATERIAL FOR SALIVARY GLANDS RECONSTRUCTION T.Yang, Y.Young, C.Wang, P.Liou, J.Ko, 1Institute of Biomedical Engineering, National Taiwan University, Taipei, Taiwan, Republic of China; 2Department of Otolaryngology, National Taiwan University Hospital, Taipei, Taiwan, Republic of China

Salivary gland dysfunction is a common sequela of radiotherapy for head neck cancer. To create an artificial salivary gland for functional restoration of damaged salivary glands, the preservation and regeneration of salivary tissue structure might be requisite. Despite the distinct biological responses of cultured salivary gland on different biomaterials, whether biomaterials also exert effects on salivary morphogenesis is still unknown. In the current study, the murine fetal submandibular gland was used as a model to study the biological reactions of reconstructed salivary tissues on different biomaterials. The biomaterials including polyvinyl alcohol (PVA), poly (ethylene-co-vinyl alcohol) (EVAL), and polyvinylidine fluoride (PVDF), which has been explored previously for salivary regeneration, were used for tissue culture. It was found that, when cultured on PVA, both mesenchyme and epithelium showed impaired adherence, migration, and assembly. On EVAL, the properties of tissue adherence and migration of salivary mesenchyme, but not epithelium, were improved. On PVDF, salivary mesenchyme demonstrated higher adherent and migratory capabilities, and the salivary epithelium developed an epithelial sheet as well. The formation of basement membrane and the related epithelial morphological changes of tissue recombination suggested a better epithelial-mesenchymal interaction of salivary tissues on PVDF. Furthermore, the well-developed branching phenotypes of salivary glands on PVDF confirmed the tissue-characterized characteristics of PVDF. Therefore, PVDF might be regarded as a morphogenic biomaterial for salivary gland reconstruction. Our findings demonstrated that salivary organogenesis could be affected by different biomaterials in terms of individual cellular behaviors, tissue responses, epithelial-mesenchymal interactions, and related morphogenesis. This study extended the scope of biomaterial effects from cells to tissues, particular in salivary morphogenesis, which might be helpful for the future development of artificial salivary glands to restore salivary functions.

P733: BIOENGINEERING RECONSTRUCTION OF THE UPPER RESPIRATORY TRACTS IN ONCOLOGIC PATIENTS I.Reshetov1, 1P.A.Hertzen Moscow Cancer Research Institute, Moscow, Russian Federation

Objective: The direction of our research is the development of the method that makes it possible to restore all the anatomical structures and functions of larynx and pharynx. Materials and Methods: For the reconstruction of the upper respiratory tract was used the bioengineering transplant. Transplants of the musculo-mucosal structures were used as the basis for implantation of stem-cells. Mucous membrane is restored by means of a tissue-equivalent. The tissue-equivalent includes allogen cellular culture of fibroblasts and of epidermic keratinocytes attached to the polymer biocompatible net. Subjects: 32 patients were treated by this method, only 27 patients were evaluated. Results: Epithelialization and complete adaptation of the flaps were observed in 26 patients on the 21±8 day by endoscopic methods, respectively. Patients had complications such as laringo-pharyngeal fistulas. One patient had suppuration of the donor wound. Conclusions: The research done covers the fundamental mechanisms of tissue reparation and practical aspects of application of tissue cellular transplants. Our results give us an opportunity to restore lost tissues and functions. This research has been supported by the ethical committee of P.A.Hertzen Moscow Research Oncological Institute, Russian Federation.

P734: RISK FACTORS ASSOCIATED WITH ORBITAL EXTERNA- TION AND RECONSTRUCTIVE OPTIONS FOR THE ORBITAL CAVITY E.Mendez1, G.N.Trenite2, S.K.Yoo1, B.Yueh3, N.D.Futran1, 1University of Washington, Seattle, WA; 2University of Washington, Amsterdam Netherlands Antilles; 3University of Minnesota, Minneapolis, MN

Objective: Defects of the orbit may be challenging to reconstruct. In this study, we explored the complications and associated risks factors after orbital exenteration. Methods: We identified patients from 1993 to present at the University of Washington and affiliated hospitals who underwent orbital exenteration either as a result of trauma or oncologic resection from a departmental database. Information was collected regarding etiology of orbital involvement; year of diagnosis; type of reconstruction; and the use of post-operative radiation therapy. The direction of our research is the development of the method that makes it possible to restore all the anatomical structures and functions of larynx and pharynx. Results: We identified 29 patients who had undergone an orbital exenteration at the University of Washington and affiliated hospitals between the years 1995-present. The mean age was 54 years old and the mean follow-up time 18.29 months. There were a total of 23 complications in fifteen patients throughout follow-up. Ten occurred at the time of the orbital exenteration, and of those, eight were considered ‘major’. Seventeen patients had intracranial involvement (nine with dural involvement, pulmonary involvement, one meningitis, one epidural hematoma and one pneumocephalus). Twenty three patients were reconstructed with free tissue transfer on the
same setting. Of these, rectus abdominis free flaps were the most commonly used, followed by radial forearm free flaps. On bivariate analysis, reconstruction with free tissue transfer was not significantly associated with postoperative complications after orbital exenteration. There was a trend towards more complications with a history of prior radiation or intracranial involvement, but this did not reach statistical significance. In addition, age, gender, and date of service were not associated with post-operative complications. Logistic regression analysis of any postoperative complication as the outcome showed that there was a trend towards having a complication in patients with a history of prior radiation after adjusting for age, gender, intracranial involvement and date of service although not statistically significant. However, if the outcome of interest was narrowed to complications before discharge, then having a prior history of radiation was significantly associated with this outcome ($OR = 23.0$, $95\% CI: 1.00, 529.7$). Intracranial involvement at time of orbital exenteration showed a similar trend where, although not significantly associated with post-operative complications in general, it was significantly associated with having a major complication before discharge ($OR = 45.4$, $95\% CI: 1.29, 1732$).

**Conclusions:** Reconstruction of the orbital cavity can be challenging, especially if there is a history of prior radiation and intracranial involvement. Free tissue transfer is a safe and effective method for reconstruction of such defects. Options for reconstruction tailored to the type of defects are discussed.

**P735: THE EFFECT OF AUTOLOGOUS MESENCHYMAL STEM CELLS ON VOCAL FOLD REGENERATION IN ANIMAL MODEL**

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**Introduction:** Most laryngeal procedures for laryngeal cancer cause vocal fold defect and scarring. Vocal fold defect and scarring results in the dysphonia that is very difficult to treat with surgery or voice therapy. Several treatment methods have been tried; however, there are still no optimal methods for the prevention of vocal fold defect or adequate treatment of the scars once they have been formed. Along with the advancement of tissue engineering techniques, stem cells are emerging as possible alternative for treating vocal fold fibrosis. Among the various stem cells, adipose tissue derived mesenchymal stem cells (ATMSCs) are of particular interest because they can be harvested with ease and cause no donor morbidity. In addition, there are no associated ethical problems with their retrieval or use. To control the growth and differentiation of stem cells, several growth factors are needed. Some studies have reported that the use of hepatocyte growth factor (HGF) reduces fibrosis in wounds of the vocal fold, lung and kidney. The aim of this study was to evaluate the effect of ATMSCs, given alone or together with HGF, on vocal cord regeneration and fibrosis in injured rabbit vocal folds.

**Materials and Methods:** In this study, adipose tissue was harvested from the inguinal area of 10 rabbits, and then the ATMSCs were isolated and cultured. Both sides of the vocal folds were treated by electrosurgery. ATMSCs at doses of 1 x 106 cells were given to one of the injured vocal folds after mixing with a scaffold (1% atellocollagen).

In five rabbits, hepatocyte growth factor (HGF) was injected together with the ATMSCs. At the other side of the injured vocal fold, in all rabbits, the same volume of atellocollagen was injected. The laryngoscopic examination was performed every week to evaluate morphological changes in the vocal folds. The vocal folds were harvested for histological analysis eight weeks after the injection of ATMSCs. After H&E and Masson’s trichrome staining, the specimens were analyzed with specific attention to preservation of the vocal fold lamina propria and fibrosis. Both locoregional and free flap reconstruction, and to compare these results with those of microvascular free flap reconstruction.

**Methods:** Retrospective analysis of all head and neck oncologic resections requiring flap reconstruction in a tertiary head and neck surgery center over a 5-year period from 2001-2007. Patients’ casesheets were reviewed, and data analysed and compared. **Results:** A total of 77 operations with flap reconstruction were performed. 44 resections employed a variety of pedicled locoregional flaps for reconstruction. There were 33 pectoralis major flaps, 3 trapezius flaps, 3 cervical rotational flaps, 1 deltopectoral flap, 1 temporomandibular muscle flap, 2 bilobed rotation flaps, 2 nasolabial flaps and 1 cheek rotation flap. 2 patients had a combination of 2 regional flaps for reconstruction. The pectoralis major flaps were mostly used for reconstructing defects created by laryngopharyngectomies, oropharyngeal resections or used to protect the great vessels following neck dissections. There was only 1 flap failure, involving a cervical rotation flap which subsequently required conversion to a free anterolateral thigh flap reconstruction. Minor complications occurred in 25% of patients. These included, in the immediate postoperative period, 3 patients with seromas, 5 patients with wound dehiscence and 1 patient with a pharyngocutaneous fistula. In the delayed postoperative period, 1 patient developed a fibrotic band in the pectoralis major flap, while another patient developed wound dehiscence at 1 month postoperation. Then remaining 33 reconstructions involved free flap microvascular reconstructions. These included 22 free radial forearm flaps, 7 free rectus abdominis flaps, 2 anterolateral thigh flaps, 1 free fibular flap and 1 free jejunal flap. The free radial forearm flaps were mostly used to reconstruct defects created by nasopharyngectomies, glossotomies and resections of the oral cavity. There was only 1 flap failure. Otherwise, minor flap complications occurred in 33% of patients. These included 4 patients with donor site wound dehiscence and 4 patients with recipient site wound dehiscence or seroma formation in the immediate postoperative period. Delayed complications developed for 3 patients; 1 patient with a free fibular flap reconstruction developed a small extrusion of his plate and some exposed bone 9 months postoperatively while another patient with a free rectus flap developed an abscess and wound breakdown at his recipient site 5 months postoperation and the last patient had a wound dehiscence of his lateral thigh flap donor site 2 months postoperation. All flaps provided good restoration of function with only 1 patient reporting mild velopharyngeal insufficiency on drinking while leaning forwards.

**Conclusions:** Both locoregional and free flap reconstruction are extremely important in head and neck reconstruction. However, despite the reliability of and ready access to free flap reconstruction, the pectoralis major flap is still rarely used because of its reliability and cost-effectiveness. It is hardy, reliable, cost-effective and can be done in a short operative time. Moreover, for several regions, the functional outcome is no worse than free flap reconstruction.

**P737: A NEW RECONSTRUCTIVE TECHNIQUE OF OROPHARYNGEAL LATERAL WALL AND EVALUATION OF POSTOPERATIVE SWALLOWING FUNCTION**

Y. Imata1, T. Nakamoto1, T. Takemoto1, T. Hashimoto1, J. Matsumoto1, H. Yamashita1, Y. Yamaguchi University School of Medicine, Ube, Japan

**Introduction:** Many kinds of materials (for example forearm flap, musculocutaneous flap and mucosal flap) have been used in reconstruction of oropharyngeal lateral wall. When the defect of the oropharynx was wide, it seemed to be appropriate to use bulky musculocutaneous flap. In such cases postoperative swallowing function was not always good. We devised a new technique of oropharyngeal reconstruction to get excellent postoperative swallowing function. In our methods we obtained a jejunum of the length of 40cm with mesentery and only a jejunum of the length of 5cm was remained and other mucosa was removed. Jejunal segment was divided along the anti-mesenteric border and after the trimming and suturing of the opened jejunal mucosal dome was formed. Serosal aspect of the jejunum was folded with remained mesenteric adipose tissue. Five oropharyngeal cancer patients received jejunum transplantation. Resected areas of these patients were oropharyngeal lateral wall with about a half of oropharyngeal posterior and upper wall. Postoperative swallowing function was evaluated with videofluoroscopic examination. Movement of reconstructed area at the time of swallowing was examined using rigid endoscope (GIF XQ160) with spin echo and with a 1.5T unit. The results of two examinations in free jejunal transplantation group(group 1) and in musculocutaneous transplanta-
P738: ONE STAGE RECONSTRUCTION OF AURICULAR HELICAL RIM DEFECTS AFTER RESECTION FOR SKIN CANCER

**Methods:** 38 patients were treated, between 1997 and 2007, with skin cancers involving helical rim of the auricle. Results: All defects were closed in a one stage reconstruction. The defects were all closed using a superior, an inferior or both superior and inferior chondrocutaneous local flap. Our technique is similar to the Antia-Buch procedure and previously published rehabilitation of the postauricular (Butler et al 2002). There was no increase in the rates of recurrence. Conclusion: This is a review of one surgeon’s ten year experience in helical rim reconstruction secondary to skin cancer. A modified Antia-Buch procedure was successfully used in one stage reconstruction of these defects. Good aesthetic results have been obtained using this technique, with no cupping and minimal loss of vertical height of the auricle. There was also no increase in local recurrence rate.

P739: VACUUM-ASSISTED CLOSURE FOR THE TREATMENT OF SCALP AND CERVICAL NECROTIZING FASCIITIS: A CASE REPORT

**Background and Objective:** Necrotizing fasciitis is a severe soft tissue infection, where involvement of the head and neck structures is rare, most frequently reported in relation to pharyngeal and tonsillar infections, surgical odontogenic procedures, and less frequently related to trauma. This rapidly progressive infection is associated with a high mortality rate as well as severe disfigurement of the face, posing therefore challenging reconstructive problems. The objective is to present a clinical case of necrotizing fasciitis of the scalp and cervical muscles arising form a minimal traumatic scalp wound, treated with early surgical drainage and debridement where Vacuum Assisted Closure (V.A.C) was successfully applied both in the initial surgical debridement phase as well as the later reconstruction period. Results: We present the case of a 28-year-old woman, without preexisting cancers involving helical rim of the auricle. She was treated with early aggressive surgical debridement, broad spectrum antibiotic therapy (cultures grew out Streptococcus pyogenes), frequent surgical lavages and intensive supportive care. The large soft tissue defect (large scalp exposure) was later treated by fenestration of the outer table of the skull, to achieve the development of granulation tissue, and then grafted with split thickness skin grafts. Sub atmospheric pressure using the Vacuum Assisted Closure (V.A.C) device was effective in the management of the large, heavily exuding wound, in a clean and hygienic manner between the debridments and for the preparation of the wound bed for skin grafting. We were able to avoid serious and fatal evolution of the process, as well as to limit tissue involvement, preventing further extension of the necrosis to other anatomical structures of the region. A satisfactory clinical, functional and aesthetic result was obtained. Conclusions: Aggressive medical and surgical treatment are crucial in limiting the morbidity and mortality of necrotizing fasciitis. Nevertheless, the treatment with wide excision of all the affected skin lead to considerable cosmetic consequences. The use of the V.A.C. device demonstrated to be a useful coadyuvant in the management of this case both in the initial stage of necrosectomy, facilitating the management of the complex wound, as in the later reconstructive stage accelerating the formation of granulation tissue and stabilizing the skin grafts, thus optimizing graft survival.

P740: CT ANGIOGRAPHY FOR PREOPERATIVE VASCULAR MAPPING IN FIBULA FREE FLAP RECONSTRUCTION

**Objective:** The fibula free flap is a commonly used reconstructive option for oromandibular defects following extirpation of advanced oral cavity cancers. Preoperative angiography of the lower limb vasculature has been the accepted standard for diagnosing aberrant anatomy and diseased vessels. Identification of congenital or acquired abnormalities of the lower limb play a crucial role in determining both the potential flap viability and the risk of foot ischemia. However, the routine use of preoperative angiography prior to free fibula harvest remains controversial. This is primarily due to the inherent risks associated with angiography. Alternative methods such as CT and MR angiography have therefore been pursued in an attempt to decrease procedure morbidity. This paper describes our experience in using CT angiography as a noninvasive preoperative vascular mapping tool in 25 patients. Methods: A prospective cohort study of all patients undergoing lower extremity CT angiography prior to free flap reconstruction for oromandibular defects was conducted for the years 2004-2007. A total of 25 patients were identified (15 males, 10 females; mean age 61 years). This yielded a total of 52 legs for which CT angiographic vascular mapping scans were done. The vascular anatomy of each leg was evaluated, for the presence of significant stenosis and anatomical anomalies. The accuracy of the CT angiographic interpretation was judged by comparing it to the physical exam (distal pulses), intra-operative findings and flap viability. Results: CT angiographic three vessel run-off accurately demonstrated all four major calf arteries in 52/52 scans. Normal bilateral anatomy and disease free vasculature was demonstrated in 15 patients or 30 lower extremity scans. A total of 2 patients demonstrated either unilateral or bilateral variant anatomy with a dominant peroneal artery to the foot. A total of 4 pts demonstrated significant atherosclerotic disease in one lower extremity resulting in the fibula free flap being harvested from the contralateral leg. A total of 5 patients or 10 lower extremity scans depicted severe bilateral stenosing or occlusive disease which lead to a change in reconstructive approach. Flap viability was 100% in all cases. There were no discrepancies between vascular mapping and intraoperative findings. Physical exam (distal pulses) findings correlated to vascular mapping in 13 of the 14 patients in whom it was recorded. There were no complications arising from the CT angiography procedure. Conclusion: Our results show that CT angiography is an accurate and reliable imaging modality for the preoperative assessment of lower extremity free tissue transfers. The patient population of the surgical experience has characterized patients with atherosclerotic disease that can be accurately measured by CT angiography; the reconstructive approach was altered in 36% of patients. Furthermore, it provides a vascular mapping tool that is equal in quality to traditional angiography but carries a much reduced complication profile.

P741: THE IMPACT OF A DEDICATED MICROVASCULAR OPERATIVE AND ICU TEAM ON FREE TISSUE TRANSFER OUTCOMES IN HEAD AND NECK CANCER

**Objectives:** To compare the overall efficiency and effectiveness between a team specifically dedicated to microvascular reconstruction in the OR and ICU to a group of nonspecific OR and ICU personnel performing microvascular reconstruction in head and neck patients. Specifically, these groups will be compared for overall length of the surgery, length of ICU stay, length of inpatient stay and postoperative complications. A secondary objective will be to determine if a dedicated microvascular reconstruction team improves hospital resource utilization and thereby reduces the costs of free tissue transfer procedures in head and neck patients. Methods: A prospective cohort study was conducted for the years 2004-2007. A total of 4 pts demonstrated significant atherosclerotic disease in one lower extremity resulting in the fibula free flap being harvested from the contralateral leg. A total of 5 patients or 10 lower extremity scans depicted severe bilateral stenosing or occlusive disease which lead to a change in reconstructive approach. Flap viability was 100% in all cases. There were no discrepancies between vascular mapping and intraoperative findings. Physical exam (distal pulses) findings correlated to vascular mapping in 13 of the 14 patients in whom it was recorded. There were no complications arising from the CT angiography procedure. Conclusion: Our results show that CT angiography is an accurate and reliable imaging modality for the preoperative assessment of lower extremity free tissue transfers. The patient population of the surgical experience has characterized patients with atherosclerotic disease that can be accurately measured by CT angiography; the reconstructive approach was altered in 36% of patients. Furthermore, it provides a vascular mapping tool that is equal in quality to traditional angiography but carries a much reduced complication profile.

P742: CT ANGIOGRAPHY AS A NON-INVASIVE PROCEDURE FOR THE ASSESSMENT OF LOWER LIMB VASCULAR ANATOMY AND VASOSCLEROSIS

**Objective:** The fibula free flap is a commonly used reconstructive option for oromandibular defects following extirpation of advanced oral cavity cancers. Preoperative angiography of the lower limb vasculature has been the accepted standard for diagnosing aberrant anatomy and diseased vessels. Identification of congenital or acquired abnormalities of the lower limb play a crucial role in determining both the potential flap viability and the risk of foot ischemia. However, the routine use of preoperative angiography prior to free fibula harvest remains controversial. This is primarily due to the inherent risks associated with angiography. Alternative methods such as CT and MR angiography have therefore been pursued in an attempt to decrease procedure morbidity. This paper describes our experience in using CT angiography as a noninvasive preoperative vascular mapping tool in 25 patients. Methods: A prospective cohort study of all patients undergoing lower extremity CT angiography prior to free flap reconstruction for oromandibular defects was conducted for the years 2004-2007. A total of 25 patients were identified (15 males, 10 females; mean age 61 years). This yielded a total of 52 legs for which CT angiographic vascular mapping scans were done. The vascular anatomy of each leg was evaluated, for the presence of significant stenosis and anatomical anomalies. The accuracy of the CT angiographic interpretation was judged by comparing it to the physical exam (distal pulses), intra-operative findings and flap viability. Results: CT angiographic three vessel run-off accurately demonstrated all four major calf arteries in 52/52 scans. Normal bilateral anatomy and disease free vasculature was demonstrated in 15 patients or 30 lower extremity scans. A total of 2 patients demonstrated either unilateral or bilateral variant anatomy with a dominant peroneal artery to the foot. A total of 4 pts demonstrated significant atherosclerotic disease in one lower extremity resulting in the fibula free flap being harvested from the contralateral leg. A total of 5 patients or 10 lower extremity scans depicted severe bilateral stenosing or occlusive disease which lead to a change in reconstructive approach. Flap viability was 100% in all cases. There were no discrepancies between vascular mapping and intraoperative findings. Physical exam (distal pulses) findings correlated to vascular mapping in 13 of the 14 patients in whom it was recorded. There were no complications arising from the CT angiography procedure. Conclusion: Our results show that CT angiography is an accurate and reliable imaging modality for the preoperative assessment of lower extremity free tissue transfers. The patient population of the surgical experience has characterized patients with atherosclerotic disease that can be accurately measured by CT angiography; the reconstructive approach was altered in 36% of patients. Furthermore, it provides a vascular mapping tool that is equal in quality to traditional angiography but carries a much reduced complication profile.

**Conclusions:** The swallowing function of group 1 was better than that of group 2. Especially swelling function was good from the postoperative early stage in group 1. Dynamic MRI revealed sufficient volume and deformity of reconstructed area at the time of swallowing in group 1. On the other hand the volume of reconstructed area was insufficient and the deformity of flap was not observed in group 2. Conclusion: We got excellent postoperative swallowing function with new orthognathic reconstructive technique. It was confirmed with dynamic MRI that the sufficient volume of mesenteric and flexibility of the jejunal graft were the reasons of good swallowing function.
the creation of the microvascular OR and ICU team at this institution. Within the group of patients who received care from the Microvascular OR and ICU team, there were no cases of complete flap failure and two cases of minor flap compromise. There were three cases requiring an emergent return to the OR and all three flaps were saved and were ultimately viable. This data was compared to data from 100 consecutive free tissue transfer cases prior to the presence of the microvascular team. Overall, the microvascular specialty team was able to shorten the overall length of time in the OR, decrease the length of the ICU stay, lessen length of hospital stay and minimize postoperative complications. These results corresponded to a reduction in financial costs as well. Conclusions: The implementation of a dedicated operative and ICU microvascular team decreases operative time, shortens patients’ stay in the ICU, lessens overall inpatient length of stay, and affords patients an overall benefit of cost reduction to the hospital and patient.

THYROID III

P742: ANABOLIC STEROID-INDUCED POSTOPERATIVE RHABDOMYOLYSIS AFTER THYROIDECTOMY W.H. Ezza1, D. Cognetti1, D. Rosen1, *Department of Otolaryngology/Head and Neck Surgery - Thomas Jefferson University, Philadelphia, PA

Introduction: Neck and shoulder pain are frequent complaints in the immediate post-operative period by patients who have undergone an open surgical procedure. Etiologies can range from minor and self-limited, such as pain related to the incision or positioning, to a sign of more serious conditions such as a myocardial ischemia. Rhabdomyolysis is a condition in which breakdown of skeletal muscle cellular membrane causes release of intracellular contents. Rhabdomyolysis (RM) has been previously reported as a postoperative complication that is related to positioning, length of procedure and BMI status. We present a case in which postoperative rhabdomyolysis presented as right shoulder pain after total thyroidectomy and selective neck dissection, a relatively short procedure for this complication. In this case, we feel that the patient’s anabolic steroid use and heavy weight lifting contributed to the development of RM.

Methods: Clinical case report and review of literature.

Results: A 46 year-old male bodybuilder underwent a total thyroidectomy with right selective neck dissection for metastatic papillary thyroid carcinoma under general anesthesia. The total procedure time was 254 minutes. Upon emerging from anesthesia, the patient was noted to be diaphoretic and was complaining of severe right shoulder pain. Serum and urine labs were sent off and revealed elevated creatinine phosphokinase (CPK), creatinine, and liver enzymes in addition to a positive urine myoglobin. Intravenous hydration with normal saline was initiated while serial chemistry panels and CPK levels were monitored. When questioned, the patient reported a history of testosterone injections, nutritional supplement use, and a strenuous weightlifting workout on the day prior to surgery. The patient was eventually discharged on postoperative day three after correction of his enzyme abnormalities. By one month post-operatively, his serum levels had returned to baseline but he admitted returning to heavy weight lifting prior to follow up.

Conclusion: To our knowledge, this is the first report of postoperative RM patients with androgen abuse and heavy weightlifting. There are an estimated three million anabolic steroid users in the U.S. and 19% of these abusers over the age of 40 years old. Awareness of the increased risk for developing RM as a result of excessive weight lifting and anabolic steroid use must be maintained when evaluating these individuals for surgical intervention. RM should be considered in the differential for postoperative muscle pain in this population.

P743: ULTRASOUNDING GORILLA THYROID GLANDS TO SHED LIGHT ON HUMAN THYROID NODULARITY W.M. Lydall1, A. Coughlin1, L. Simmons2, D. Armstrong1, J. Napier1, *University of Nebraska Medical Center, Omaha, NE; 2Omaha Henry Doorly Zoo, Omaha, NE

Introduction: The incidence of thyroid cancer has dramatically increased in humans since 1995 (141%) and the incidence of thyroid nodules is now at an astonishing 33-67%. Limited data exists regarding thyroidology in lowland gorillas (Gorilla Gorilla). Close genetic relationships exist between humans and gorillas therefore, thyroid pathology, specifically nodularity and cancer may be evident in gorillas providing a natural group for comparison to help in determining etiology through interspecies comparisons. If exposures that are global and non-species specific exist, such as increased body mass index and anabolic steroid use, would both species respond similarly? If so, etiology may be paramount. If the etiology is species specific, direct human behaviors may be paramount.

Methods: This study reports the first use of ultrasound to evaluate thyroid glands in 9 lowland gorillas and provides a systematic technique. Results: Average thyroid lobe volume was 3.67 mL using standardized measurements. Blood values of thyroid hormones; Total T4, Free T4, Total T3 and Free T3 were also obtained, with average values of 72.5 mmol/L, 19.7 mmol/L, 1.9 pmol/L, and 2.9 pmol/L respectively. TSH could not be measured since this requires species specific antibodies. One case of hemithyroid agenesis was found anatomically but no nodularity was observed. Six of nine gorillas tested demonstrated a low free T3 when compared with human values. One also exhibited low free T4, and Total T4 but did have a normal Total T3. None of the thyroid glands appeared enlarged. In fact, the typical thyroid in humans is larger relative to the surrounding structures than that observed in the gorillas. This suggests that the normal range of free T3 may be lower in gorillas than humans. Alternatively, gorillas in captivity may exhibit a relative hypothyroid state relative to humans.

Conclusions: No nodularity was seen in gorilla thyroid glands examined. Thus, factors causing the increase in thyroid nodularity in humans is likely species specific. We have established a systematic ultrasound technique for thyroid evaluation in the lowland gorillas, with baseline thyroid volumes and thyroid function values.

P744: THE ROLE OF FINE NEEDLE ASPIRATION BIOPSY AND INTRAOPERATIVE FROZEN SECTION FOR THYROID NODULES J.A. Almeida1, S.D. Couto Netto1, R.P. Rocha1, E.G. Pfeufterreiner, Jr.1, R.A. Dedivitis1, *Fundacao Lusiana, Santos, Brazil; 4Ana Costa Hospital, Santos, Brazil; 5Ana Costa Hospital, Santos, SP, Brazil

Introduction: The utility of intraoperative frozen section (FS) during thyroidectomy is controversial. Objectives: to evaluate the FS role for thyroid nodules management. Patients and Methods: All patients having thyroid surgery for nodular disease and previous US-guided FNAB in 2006 were prospectively analyzed. They underwent intraoperative FS evaluation being classified as benign, malignant or follicular neoplasm. FNAB, FS and paraffin sections were compared. Results: Under the FS, 54% of the nodules were benign, 30% follicular neoplasm, and 16% malignant. There was no inconclusive result under the FS. All cases considered benign and malignant under the FS evaluation were confirmed through the histological paraffin analysis. Since it is not considered a definitive indication for the total thyroidectomy, if the follicular neoplasms were classified as benign under the FS, their sensitivity, specificity, positive and negative predictive values and global diagnostic accuracy were 69%, 100%, 100%, 91.5% and 77%, respectively. Among the 42 cases classified as follicular neoplasm under the FNAB, 1 case the FS concluded as papillary carcinoma, in 3 cases as benign (all confirmed through the paraffin); and 38 cases continued as follicular pattern, being 29 follicular adenomas and 9 carcinomas through the paraffin. Conclusion: The FS is only indicated in case of follicular neoplasm under the FNAB.

P745: THE UTILITY OF FROZEN SECTION EVALUATION FOR INTRAOPERATIVE DIAGNOSIS OF THYROID S. Lee1, H. Kim1, P. Chung1, 4Department of Otolaryngology-Head and Neck Surgery, Dankook University Hospital, Cheonan Republic of Korea

Background and Objectives: Although fine needle aspiration (FNA) cytology is a safe, simple and relatively accurate procedure, there is difficulty in differentiating between benign and malignant lesions in follicular neoplasm. We evaluated the utility of the frozen section biopsy in the diagnosis of thyroid nodules. Materials and Methods: We reviewed the medical records of 219 patients operated on for thyroid nodules from 1996 to 2006. All patients had undergone both preoperative fine needle aspiration (FNA) cytology and intraoperative frozen section (FS). The diagnostic findings of FNA cytology and FS histology were compared with the final histological results. Results: The sensitivity, specificity and accuracy of FNA were 76.9%, 98.6%, 73.5% respectively. And the sensitivity, specificity and accuracy of the FS were 74.8%, 93.3%, 84.1% respectively. The papillary carcinomas were 95 cases according to final pathology. In the preoperative FNA, 73 cases (76.8%) were diagnosed as malignant and in the intraoperative FS, 78 cases were diagnosed as malignant. The follicular thyroid lesions were 49 cases according to final pathology. The sensitivity, specificity and accuracy of FNA were 50.0%, 85.3%, 72.1% respectively. And the sensitivity, specificity and accuracy of the FS were 92.3%, 81.3% respectively. Conclusion: Frozen section may be indicated if FNA of thyroid nodule suggests benign follicular neoplasm in order to determine the extent of the operation and to avoid overtreatment of benign disease. However, we cannot supply proof of routinely usage of FS in the thyroid lesion.

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A retrospective review was conducted in patients who had immunohistochemical determination of the expression of the MUC1. Immunoexpression of the MUC1 was correlated with tumor size. However, MUC1 expression was significantly related with tumor size and grade; in 7 patients (20%) and intense in 26 (74%). The immunoreactivity MUC1 was strong in 21 patients (60%). MMP-2 immunoexpression was found in 31 non-surgical specimens of patient with well-differentiated thyroid carcinoma and 4 follicular. From these paraffin blocks, areas of tumor were selected based on histological examinations and sectioned. The pathological diagnosis of all cases was reviewed and analyzed by single pathologist. The intensity of positively stained cells were indicated as 0 (negative), 1 (weak), and 2 (strong). Results: Immunoexpression of the MUC1 was detected in 28 patients (80%), with weak intensity in 7 patients (20%) and strong in 21 patients (60%). MMP-2 immunoexpression was found in 31 patients (89%), being weak in 10 (29%) and intense in 21 (60%). The overexpression of the MMP-9 was detected in 33 patients (94%), being weak in 7 patients (20%) and intense in 26 (74%). The immunoreactivity MUC1 did not have any significant correlation with grade (p=0.651), age (p=0.092), histological type (p=0.359) and survival (p=0.475). However, MUC1 expression was significantly related with tumor size (p=0.006). Immunoexpression MMP-2 and MMP-9 did not present any significant correlation with gender, age, tumor size, histological type and survival (p>0.05), respectively.

Conclusions: Our study demonstrated that the MUC1 is immunoreactivity is correlated with tumor size. However, there was no significant correlation with factors as age, gender, and histological type. MMP-2 and MMP-9 overexpression did not present significant correlation with gender, age, histological type, tumor size, and survival.

P747: USE OF 12 HR-6 HR AND 24 HR-6 HR SLOPE OF SERUM CALCIUM LEVELS IN PREDICTING RISK OF POSTOPERATIVE HYPOCALCAEMIA A.Clim 1, Y.Ng2, A.Loy3, M.Khoo4, 1National University Hospital, Singapore, Singapore; 2Changi General Hospital, Singapore, Singapore; 3Tan Tock Seng Hospital, Singapore, Singapore

Aim: The aim of the study is to evaluate the use of 12 hour-6 hour and 24 hour-6 hour slope of serum calcium values in predicting hypocalcaemia following total or completion thyroidectomy. Materials and Methods: A retrospective review was conducted in patients who had undergone total or completion thyroidectomy. Results: The results of the early 12, 24 and 24 hour postoperative serum calcium levels were retrieved and the corresponding slope of 12 hour-6 hour (slopes A) and 24 hour-6 hour (slopes B) calcium levels were plotted. Patients were then divided into either having a positive or negative slope from the trend of serum calcium values. Using a negative slope to predict postoperative hypocalcaemia, the corresponding sensitivity and specificity data were obtained. Further analysis was performed to see if there was any difference in predicting hypocalcaemia if either slope A (12 hour-6 hour) or slope B (24 hour-6 hour) was used. We defined significant postoperative hypocalcaemia in patients who developed symptoms and signs of hypocalcaemia as a corrected serum calcium value of less than 2.0 mmol/l. Results: There were 92 patients who had undergone thyroidectomies and of which 81 were total and 11 were completion thyroidectomies. There were 73 females and 19 males in our cohort with their mean age of 49.8 years (SD 13.7). All 92 patients had serum calcium done at 6 hour and 12 hour postoperatively and of which 59 patients had additional serum calcium done at 24 hour postoperatively. Our hypocalcaemia rate was 7.6% (7/92). The sensitivity and specificity to predict postoperative hypocalcaemia from slope A and slope B were 100%, 23.5% and 100%, 26.9%, respectively.

Conclusion: Both the 12 hour-6 hour and 24 hour-6 hour slope of serum calcium values were equally sensitive but not specific in predicting postoperative hypocalcaemia. Patients with an initial upsloping calcium curve at either 12 hour or 24 hour postoperatively is strongly predictive of a normocalcaemia state whereas it is difficult to predict which patients would develop postoperative hypocalcaemia in those who have a downsloping calcium curve, regardless whether it is done at 12 hour or 24 hour postoperative.

P748: VALIDATION OF A SIMPLE POST-THYROIDECTOMY CALCIUM MANAGEMENT PROTOCOL N.Raza1, P.D.Kerr1, 1University of Manitoba, Winnipeg, MB, Canada

Background: Many authors have demonstrated the correlation between post-thyroidectomy PTH levels and the development of hypocalcaemia. However, the ensuing management protocols have generally been cumbersome; requiring repeated blood tests and the use of graphs or formulas. Previously published work by our group indicated that a postoperative PTH level, drawn 1 hour after total thyroidectomy, accurately correlated with the development of hypocalcemia, a significant finding that has led us to believe that a simpler protocol could be developed. Hypothesis: A simple and safe calcium management protocol, facilitating early discharge post thyroidectomy, can be based on a single 1 hour postoperative PTH level with commencement of immediate therapy for those deemed at risk. Study Design: Retrospective, protocol cohort. Methods: A consecutive series of patients undergoing completion or total thyroidectomy, had a single PTH level drawn 1 hour postoperatively. Those with PTH levels <9 pg/ml (group 1 - positive test result), a threshold determined from our previous work, were immediately started on high dose calcium supplementation and vitamin D3. Those with higher PTH levels (group 2 - negative) were not treated. Both groups were candidates for 23 hour discharge, unless symptoms developed in the interim. Results: Thus far, we have used this protocol in over 60 patients and are very satisfied with both its simplicity and safety. The most important endpoint; the need for more medical care beyond the time of early discharge due to either false negatives in group 2 or empiric treatment failure in group 1, will be presented.

P749: IMMUNOEXPRESSION MUC1, MMP-2 AND MMP-9 IN YOUNG PATIENTS WITH WELL-DIFFERENTIATED THYROID CARCINOMA J.G.Filho 1, S.D.Silva 1, E.Graner 1, L.P.Kowalski 1, 1Hospital AC Camargo, Sao Paulo, Brazil

Objective: To analyze the immunexpression of MUC1, MMP-2 and MMP-9 in patients with well-differentiated thyroid carcinoma with 18 years or younger. Methods: Immunohistochemical determination of the expression of the MUC1, MMP-2 and MMP-9 was performed in 35 surgical specimens of patient with well-differentiated thyroid carcinoma with 18 years or younger. Results: In 14 patients, 31/43 (27.9%) had multi nodular goitre. A total of 61 patients (64.2%) developed biochemical hypocalcaemia, if their adjusted serum calcium level of less than 2 mmol/l and slope B was 100%, 23.5% and 100%, 26.9%, respectively. Our hypocalcaemia rate was 7.6% (7/92). The sensitivity and specificity to predict postoperative hypocalcaemia from slope A and slope B were 100%, 23.5% and 100%, 26.9%, respectively. Conclusion: Both the 12 hour-6 hour and 24 hour-6 hour slope of serum calcium values were equally sensitive but not specific in predicting postoperative hypocalcaemia. Patients with an initial upsloping calcium curve at either 12 hour or 24 hour postoperatively is strongly predictive of a normo-
Objectives: This study evaluates the incidence and risk factors of complications in young patients submitted to thyroidectomy in a tertiary cancer with residency training. Methods: We reviewed the medical charts of 69 patients with ages up to 18 years who were submitted to thyroidectomy, between January 1990 and December 2004. There were 50 female patients (72%) and 19 male (28%), with ages ranging from 2 to 18 years (mean, 14 years). Vocal cord mobility examination was performed before and after surgery in all patients. All patients underwent fine-needle aspiration biopsy and fibrolaryngoscopy. Surgical procedure included total thyroidectomy in 31 (45%), subtotal thyroidectomy in 4 (5.7%), lobectomy in 29 (42%) and completion of thyroidectomy in 5 (7.3%). Neck dissections were performed in 17 patients (ipsilateral dissection in 12 and bilateral dissection in 5). Paratracheal lymph node dissection was performed in 24 patients. The surgical procedures included 29 (42%) thyroidectomies for the treatment of malignant disease and 30 (58%) thyroidectomies for benign diseases. Thyroidectomies were performed or supervised by surgeons classified according to the total number of thyroidectomies performed every year.

Results: Hospital stay varied from 1 to 19 days (median, 3 days). The time of hospitalization was significantly shorter in the benign group compared with the malignant group (p = 0.023). Postoperative complications occurred in 26% of the patients. The most frequent complication was hypocalcemia, being transitory in 11 patients (15.9%), and permanent in 4 patients (5.8%). Transitory vocal cord palsy occurred in 1 patient (1.4%). The incidence of postoperative hypocalcemia did not have any significant correlation with patient’s gender, age, diameter of the nodule and surgeon’s experience. However, malignant disease, the extension of thyroidectomy and the associated paratracheal lymph node dissection were significantly associated with the risk of transitory and permanent hypocalcemia. Three patients (4.3%) developed postoperative seroma. No significant differences were observed between these complications and the type of thyroidectomy and number of thyroidectomies performed or supervised by the surgeon. Conclusion: Our results demonstrate that thyroid surgery in young patients is a rare procedure and performed most frequently for malignant disease. However, this can be performed for medical residency under direct supervision of an experienced surgeon with little morbidity to the patients. The hospital stay was higher in patients with malignant disease and hypocalcemia was most important complication. Neck and paratracheal lymph node dissections were the most significant predictors of hypocalcemia in young patients who underwent total thyroidectomy.

P751: BRAF AS A SIGNIFICANT PROGNOSTIC FACTOR IN A PAPILLARY THYROID CARCINOMA SERIES

Introduction: BRAF is a proto-oncogene located in the short arm of chromosome 7 and regulates MAPK-ERK kinase pathway. Its major role in well differentiated thyroid carcinogenesis has been already established. In order to study and set a pattern of BRAF expression for this group of tumors, 53 patients diagnosed as papillary thyroid cancer (PTC) were clinically evaluated and surgically treated by the same medical group using a standard protocol of follow-up procedure, in order to set statistical analysis and evidence some relevant prognostic factors for this sample. Methods: All patients were submitted to total thyroidectomy and some of them had cervical lymph node dissection (CND) as well. Patients were divided in group A (tumors smaller than 1 cm diameter) and group B (tumors greater than 1 cm). Prognostic factors besides BRAF expression considered for comparison study using uni and multivariate analysis were sex, age, stage, type of surgery (TT with or without CND) and histological features of aggressiveness. Results: Four patients died during the follow-up. Four cases of loco regional recurrence and seven cases of distant metastases were observed. The incidence of postoperative complications like transient hypocalcemia was statistically higher in patients with BRAF positive tumors compared to those with BRAF negative. Conclusion: The importance of BRAF expression as a prognostic factor in thyroid carcinoma patient’s survival leads us to conclude that its expression is directly associated with the aggressiveness of the clinical presentation of the tumor, as well as a worse prognosis concerning to a higher average of recurrence, even for papillary thyroid microcarcinomas. Because of these findings we can suggest that BRAF is a promising molecular marker regarding the oncogenic role of the MAP-ERK kinase pathway, but more studies are necessary in order to establish the real value of its expression regarding thyroid oncogenesis not only in conventional papillary carcinoma, but also in microcarcinomas.

P752: BRAF MUTATION DOES NOT PREDICT METASTATIC BEHAVIOR IN PAPILLARY THYROID MICROCARCINOMAS

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Objective: BRAF mutation in well-differentiated papillary thyroid carcinoma (PTC) has been shown to be associated with increased rate of nodal metastases, extrathyroidal extension and overall poor prognosis. As more imaging studies are being performed, papillary thyroid microcarcinomas (<1 cm) are being detected with increasing frequency. The significance of nodal metastasis in papillary microcarcinomas is unclear. This study was designed to evaluate the incidence of BRAF mutation in papillary thyroid microcarcinomas (PTMC) with and without lymph node metastasis and to determine if BRAF mutation is predictive of metastatic disease in PTCM.

Design: A total of 24 patients with PTMC were identified who were treated with total thyroidectomy with either elective or therapeutic central compartment and or lateral neck lymph node dissection between 2000 and 2006. Patients were divided into two groups according to presence (Group 1, n=16) or absence (Group 2, n=8) of nodal metastases. Tumor DNA was extracted, PCR amplified with known BRAF primers, sequenced and analyzed for the presence of BRAF point mutation.

Setting: Academic tertiary center.

Results: The incidence of regional nodal metastases in patients with PTMC was 67% (16/24), of which 8% (5/24) had lateral neck dissection and underwent therapeutic modified neck dissection. The incidence of occult regional metastatic disease was 58% (11/19). There was no evidence of distant metastatic disease. BRAF mutation was identified in one patient in Group 1 (6.25%) and in one patient in Group 2 (12.5%). BRAF status did not correspond to extrathyroidal extension and there was no local or regional recurrence within a 5 year post-operative period.

Conclusion: The incidence of occult regional metastatic disease in PTMC is high. While BRAF mutation is associated with poor prognostic factors in well-differentiated PTC, there seems to be no evidence to support its role in predicting metastatic disease in PTMC. Our results indicate that this mutation does not seem to play a key role in promoting the high rate of nodal metastases seen in patients with PTMC.

P753: UNDIFFERENTIATED POPULATION FOUND IN PAPILLARY THYROID CARCINOMA; POSSIBILITY FOR CANCER STEM CELL POPULATION

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Background: Recently, in some solid cancers, the special population that can initiate tumor has been found and this feature is explained by cancer stem cell theory. There were some reports that unselected tumors have cancer stem cells and these cell may play a role of cancer stem cell in multiple populations but failed to select an exclusive population. We tried to find the tumor initiating cell population from well differentiated papillary carcinoma with specific surface marker. Methods and Materials: In vitro study was undergone with human papillary thyroid carcinoma cell line, NPA187 and TPC1. And also we used special clones that have selected from original TPC1 that have higher tumorigenic potentials (TPC1-T). Flowcytometric analysis was done using CD24, CD44. The human papillary thyroid carcinoma tissue was obtained from operation room, and after mechanical and enzymatic dissociation, the cell was stained with CD45, CD31, CD24, CD44 and selected CD44low/CD44high population using FACS and MACS. The sorted cells were collected and real-time PCR was performed to see the expression of differentiation markers including GAT, Pax6, TSH, Tg, TTF1. Results: The non-tumorigenic cell line TPC1 showed higher CD24 expression and tumorigenic cell line TPC1-T and NPA187 does not expressed CD24. In human tumors, CD24low/CD44high population could be found from 6.65% to 15.17% of tumor cells. And in human tumor the CD24low/CD44high population was significantly associated with neck or paratracheal lymph node dissection between 2000 and 2006. Patients were divided into two groups according to presence (Group 1, n=16) or absence (Group 2, n=8) of nodal metastases. Tumor DNA was extracted, PCR amplified with known BRAF primers, sequenced and analyzed for the presence of BRAF point mutation.

Setting: Academic tertiary center.

Results: The incidence of regional nodal metastases in patients with PTMC was 67% (16/24), of which 8% (5/24) had lateral neck dissection and underwent therapeutic modified neck dissection. The incidence of occult regional metastatic disease was 58% (11/19). There was no evidence of distant metastatic disease. BRAF mutation was identified in one patient in Group 1 (6.25%) and in one patient in Group 2 (12.5%). BRAF status did not correspond to extrathyroidal extension and there was no local or regional recurrence within a 5 year post-operative period.

Conclusion: The incidence of occult regional metastatic disease in PTMC is high. While BRAF mutation is associated with poor prognostic factors in well-differentiated PTC, there seems to be no evidence to support its role in predicting metastatic disease in PTMC. Our results indicate that this mutation does not seem to play a key role in promoting the high rate of nodal metastases seen in patients with PTMC.
Objective: Anaplastic thyroid cancer (ATC) is highly aggressive and is responsible for more than 50% of deaths attributed to all thyroid cancers annually. It is rare and occurs in less than 2% of thyroid cancer patients. Most ATCs are inoperable at the time of diagnosis and survival is measured in months. ATC invades adjacent structures and metastasizes extensively to cervical lymph nodes and distant organs such as lung and bone. Studies have shown that OGF (Opioid Growth Factor) inhibits the growth of cancer cells including human squamous cell carcinoma and pancreatic cancer. The primary purpose of this study was to determine whether the OGF:OGFr (OGF receptor) axis is present and functions to suppress the growth of human anaplastic thyroid cancer cells.

Methods: KAT-18, an undifferentiated anaplastic human thyroid cancer cell line (K. Ain, University of Kentucky), was grown in culture to evaluate the dose-response and longitudinal inhibitory growth effects of OGF. Opioid-receptor mediation, reversibility and cytotoxicity were evaluated. Experiments were conducted to assess DNA synthesis with BrdU. Immunocytochemistry was utilized to detect the presence of OGF and OGr in these cultures. A variety of other opioids and opioid peptides related to the opioid receptor were evaluated to ascertain specificity of peptides. Results: OGF significantly reduced the number of KAT-18 cells from control values by 14% to 38% in a dose-dependent manner (10^{-4} M to 10^{-7} M). Growth curves showed that cultures exposed to OGF had significantly fewer cells at all dosages examined relative to sterile-water treated control cultures. Growth of OGF treated cultures was significantly reduced starting at 24 h after addition of the drug; the cell number in the OGF-treated wells was 30% less than controls at 24 h (p<0.001), and remained significantly less than control cultures throughout the 96 h experimental period. Growth inhibition was opioid receptor mediated, reversible, and non-toxic. The proportion of cells labeled with BrdU in cultures receiving OGF was reduced from control levels by 28% at 72 h while naltrexone, an OGF receptor antagonist, increased BrdU labeling from control levels by 25%. Both peptide and receptor were observed in KAT-18 cells as seen with OGF and OGFr immunoreactivity. Examination of a wide range of other opioids and opioid peptides related to classical opioid receptors showed no effect on proliferation of this anaplastic thyroid cell line. Conclusion: The OGF:OGFr axis is present and functions in KAT-18, an undifferentiated, highly aggressive anaplastic thyroid cancer cell line. Our data demonstrate the biotherapeutic potential of this novel peptide-receptor as an inhibitory treatment for human anaplastic thyroid cancer. Further studies examining the efficacy of OGF as a primary or combined agent in therapeutic animal trials are warranted.