Stop by the registration desk and reserve a copy of the Virtual Meeting!

With the Virtual Meeting you will receive streaming content that has been digitally recorded live and published as audio synchronized to the speakers’ PowerPoint presentations. All of the recorded keynote lectures, compelling expert presentations* and meeting information will be accessible to you online 24/7 through the ASTRO website. These recorded sessions provide an excellent informational recap and are a great training tool for continual learning.

When purchased, approximately six weeks after the conclusion of the meeting you will receive an email message with a link allowing you to access the Virtual Meeting. Virtual Meeting rates are as follows:

<table>
<thead>
<tr>
<th>ATTENDEE TYPE</th>
<th>ON-SITE RATES</th>
<th>POST-MEETING RATES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Members</td>
<td>$100</td>
<td>$200</td>
</tr>
<tr>
<td>Residents/Students</td>
<td>$75</td>
<td>$150</td>
</tr>
<tr>
<td>Nonmembers</td>
<td>$200</td>
<td>$400</td>
</tr>
</tbody>
</table>

NOTE:
Upon purchasing the virtual meeting, a link will be emailed to you, giving you 24/7 access to the audio-synchronized presentations*.

*As released for inclusion by the presenters.
Multidisciplinary Head and Neck Cancer Symposium

January 26-28, 2012 | Arizona Biltmore | Phoenix

Table of Contents

Schedule-at-a-Glance.........................................................................................................................2

Abstract Award Recipients ...............................................................................................................4

Abstracts for Plenary and Poster Presentation.................................................................................5

Abstracts for Oral and Poster Presentation .....................................................................................9

Abstracts for Poster Presentation.................................................................................................13

Abstract Author Index.....................................................................................................................69
## Schedule-at-a-Glance

### Wednesday, January 25, 2012

<table>
<thead>
<tr>
<th>Time</th>
<th>Event Description</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>3:00 p.m. - 6:00 p.m.</td>
<td>Registration</td>
<td>Frank Lloyd Wright Ballroom Foyer</td>
</tr>
<tr>
<td>7:00 a.m. - 5:00 p.m.</td>
<td>Registration</td>
<td>Frank Lloyd Wright Ballroom Foyer</td>
</tr>
<tr>
<td>7:00 a.m. - 8:00 a.m.</td>
<td>Continental Breakfast</td>
<td>Frank Lloyd Wright Ballroom F</td>
</tr>
<tr>
<td>7:50 a.m. - 8:00 a.m.</td>
<td>Welcome</td>
<td>Frank Lloyd Wright Ballroom E</td>
</tr>
<tr>
<td>8:00 a.m. - 9:00 a.m.</td>
<td>General Session I – Controversies and New Directions in Chemoradiotherapy</td>
<td>Frank Lloyd Wright Ballroom E</td>
</tr>
<tr>
<td>9:00 a.m. - 9:30 a.m.</td>
<td>General Session II: Keynote I – The Molecular Road to Defining and Targeting High-risk Head and Neck Patients</td>
<td>Frank Lloyd Wright Ballroom E</td>
</tr>
<tr>
<td>9:30 a.m. - 10:00 a.m.</td>
<td>Break in the Exhibit Hall</td>
<td>Frank Lloyd Wright Ballroom F</td>
</tr>
<tr>
<td>10:00 a.m. - 11:30 a.m.</td>
<td>General Session III - Minimally Invasive Surgical Approaches – Who, When, How?</td>
<td>Frank Lloyd Wright Ballroom E</td>
</tr>
<tr>
<td>11:30 a.m. - 12:30 p.m.</td>
<td>Lunch in the Exhibit Hall</td>
<td>Frank Lloyd Wright Ballroom F (Boxed Lunch Provided)</td>
</tr>
<tr>
<td>12:30 p.m. - 2:00 p.m.</td>
<td>Plenary Session</td>
<td>Frank Lloyd Wright Ballroom E</td>
</tr>
<tr>
<td>2:00 p.m. - 3:30 p.m.</td>
<td>General Session IV - Molecular Biology in Head and Neck Cancer for the Clinician – Breakthroughs in 2012</td>
<td>Frank Lloyd Wright Ballroom E</td>
</tr>
<tr>
<td>3:30 p.m. - 4:00 p.m.</td>
<td>Break in the Exhibit Hall</td>
<td>Frank Lloyd Wright Ballroom F</td>
</tr>
<tr>
<td>4:00 p.m. - 5:00 p.m.</td>
<td>Breakout Sessions:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Breakout Session I – PET in Managing the Neck Post Chemoradiation</td>
<td>Frank Lloyd Wright Ballroom E</td>
</tr>
<tr>
<td>5:00 p.m. - 6:00 p.m.</td>
<td>Poster Session and Reception I</td>
<td>Frank Lloyd Wright Ballroom F</td>
</tr>
<tr>
<td>6:15 p.m. - 7:15 p.m.</td>
<td>Case-based Discussions I</td>
<td>Frank Lloyd Wright Ballroom E</td>
</tr>
</tbody>
</table>

### Thursday, January 26, 2012

<table>
<thead>
<tr>
<th>Time</th>
<th>Event Description</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:00 a.m. - 8:00 a.m.</td>
<td>Continental Breakfast</td>
<td>Frank Lloyd Wright Ballroom F</td>
</tr>
</tbody>
</table>

### Friday, January 27, 2012

<table>
<thead>
<tr>
<th>Time</th>
<th>Event Description</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:00 a.m. - 5:30 p.m.</td>
<td>Registration</td>
<td>Frank Lloyd Wright Ballroom Foyer</td>
</tr>
<tr>
<td>7:00 a.m. - 8:00 a.m.</td>
<td>Continental Breakfast</td>
<td>Frank Lloyd Wright Ballroom F</td>
</tr>
<tr>
<td>Time</td>
<td>Event</td>
<td>Venue</td>
</tr>
<tr>
<td>--------------</td>
<td>----------------------------------------------------------------------</td>
<td>--------------------------------------------</td>
</tr>
<tr>
<td>7:55 a.m. - 8:00 a.m.</td>
<td>Welcome</td>
<td>Frank Lloyd Wright Ballroom E</td>
</tr>
<tr>
<td>8:00 a.m. - 9:30 a.m.</td>
<td>General Session V - New Insights into Molecular Biology of SCCHN</td>
<td>Frank Lloyd Wright Ballroom E</td>
</tr>
<tr>
<td>9:30 a.m. - 10:00 a.m.</td>
<td>Break in the Exhibit Hall</td>
<td>Frank Lloyd Wright Ballroom F</td>
</tr>
<tr>
<td>10:00 a.m. - 10:30 a.m.</td>
<td>General Session VI: Keynote II - Customizing Therapy for Patients with Local-Regionally Advanced Head and Neck Carcinoma</td>
<td>Frank Lloyd Wright Ballroom E</td>
</tr>
<tr>
<td>10:30 a.m. - 12:00 p.m.</td>
<td>Oral Abstract Session</td>
<td>Frank Lloyd Wright Ballroom E</td>
</tr>
<tr>
<td>12:00 p.m. - 1:00 p.m.</td>
<td>Lunch in the Exhibit Hall</td>
<td>Frank Lloyd Wright Ballroom F</td>
</tr>
<tr>
<td>1:00 p.m. - 2:30 p.m.</td>
<td>General Session VII – Thyroid Cancer</td>
<td>Frank Lloyd Wright Ballroom E</td>
</tr>
<tr>
<td>2:30 p.m. - 2:45 p.m.</td>
<td>Break</td>
<td>Frank Lloyd Wright Ballroom E</td>
</tr>
<tr>
<td>2:45 p.m. - 3:45 p.m.</td>
<td>Breakout Sessions</td>
<td>Breakout Session IV - Salivary Gland Cancers, Melanoma and Other Less Common Cancers of the Head and Neck Less Common Cancers of the Head and Neck</td>
</tr>
<tr>
<td>3:45 p.m. - 4:15 p.m.</td>
<td>Break in the Exhibit Hall</td>
<td>Frank Lloyd Wright Ballroom F</td>
</tr>
<tr>
<td>4:15 p.m. - 5:15 p.m.</td>
<td>Breakout Sessions</td>
<td>Breakout Session VI - Surgical Management of Residual/Recurrent Disease and Complications of Treatment</td>
</tr>
<tr>
<td>5:15 p.m. - 6:15 p.m.</td>
<td>Case-based Discussions II</td>
<td>Frank Lloyd Wright Ballroom E</td>
</tr>
</tbody>
</table>

**Saturday, January 28, 2012**

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Venue</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:00 a.m. - 12:00 p.m.</td>
<td>Registration</td>
<td>Frank Lloyd Wright Ballroom Foyer</td>
</tr>
<tr>
<td>7:00 a.m. - 8:00 a.m.</td>
<td>Continental Breakfast</td>
<td>Frank Lloyd Wright Ballroom Foyer</td>
</tr>
<tr>
<td>7:55 a.m. - 8:00 a.m.</td>
<td>Welcome</td>
<td>Frank Lloyd Wright Ballroom E</td>
</tr>
<tr>
<td>8:00 a.m. - 9:30 a.m.</td>
<td>General Session VIII – New Issues and Concepts in Radiotherapy for Head and Neck Cancer</td>
<td>Frank Lloyd Wright Ballroom E</td>
</tr>
<tr>
<td>9:30 a.m. - 10:00 a.m.</td>
<td>Break</td>
<td>Frank Lloyd Wright Ballroom Foyer</td>
</tr>
<tr>
<td>10:00 a.m. - 11:30 a.m.</td>
<td>General Session IX – Human Papilloma Virus Issues and Controversies in 2012</td>
<td>Frank Lloyd Wright Ballroom E</td>
</tr>
<tr>
<td></td>
<td>Interactive Session</td>
<td></td>
</tr>
</tbody>
</table>
Congratulations to the 2012 Multidisciplinary Head and Neck Cancer Symposium Travel Grant Winners

Jenny Hoang  
Duke University Medical Center  
Abstracts 112, 115

Nicholas Lukens  
University of Pennsylvania  
Abstract 132

Sujith Mullapally  
All India Institute of Medical Sciences  
Abstracts 129, 168, LBPV6

Madhu Shetti  
University of Washington Affiliated Hospitals  
Abstract 128
Abstracts for Plenary and Poster Presentation

1. Long-Term Follow-Up of the RTOG 9501/Intergroup Phase III Trial: Postoperative Concurrent Radiation Therapy and Chemotherapy in High-Risk Squamous Cell Carcinoma of the Head and Neck


Purpose/Objectives: Previous analysis of this Intergroup trial demonstrated that with a median follow-up among surviving patients of 45.9 months, the concurrent postoperative administration of cisplatin and radiation therapy improved local-regional control and disease-free survival of patients who had high-risk resected head and neck carcinomas. With a minimum of 10 years of follow-up potentially now available for all patients, these results are herein updated to examine long-term outcomes. Material/Methods: 410 analyzable patients who had high-risk resected head and neck cancers were prospectively randomized to receive either radiation therapy (RT: 60 Gy in 6 weeks) or identical RT plus cisplatin, 100 mg/m2 i.v. on days 1, 22, and 43 (RT + CT). Results: At 10 years, the local-regional failure rates were 28.8% vs. 22.3% (p=0.10), disease-free survival was 19.1% vs. 20.1% (p=0.25) and overall survival was 27.0% vs. 29.1% (p=0.31) for patients treated by RT vs. RT + CT respectively. In the unplanned subset analysis limited to patients who had microscopically involved resection margins and/or extracapsular spread of disease, local-regional failure occurred in 33.1% vs. 21.0% (p=0.02), disease-free survival was 12.3% vs. 18.4% (p=0.05) and overall survival was 19.6% vs. 27.1% (p=0.07) respectively. Cause-specific survival trended towards improved outcome with RT + CT for patients whose death was due to the study cancer; however, more deaths not due to the study cancer were observed in patients treated with concurrent cisplatin. Conclusions: At a median follow-up of 9.4 years for surviving patients no significant differences in outcome were observed in the analysis of all randomized, eligible patients. Analysis of the subgroup of patients who had either microscopically involved resection margins and/or extracapsular spread of disease showed improved local-regional control with concurrent administration of chemotherapy. The subgroup of patients who were enrolled only because they had tumor in multiple lymph nodes did not benefit from RT + CT.


M. Gillison1, T. Brououtian2, R. Pickard3, Z. Tong4, W. Xiao5, L. Kahle6, B. I. Graubard7, A. Chaturvedi8, 1Ohio State University, Columbus, PA, 2Ohio State University, Columbus, OH, 3Ohio State University, Columbus, OK, 4Information Management Services, Silver Spring, MD, 5The National Cancer Institute, Rockville, MD

Purpose/Objectives: Human papillomavirus (HPV) infection is the principal cause of a distinct form of oropharyngeal squamous cell carcinoma that is rising in incidence in the United States (U.S.). However, little is known regarding the epidemiology of oral HPV infection. Material/Methods: A cross-sectional study was conducted as part of the National Health and Nutrition Examination Survey (NHANES) 2009-2010, a statistically representative sample of the civilian non-institutionalized U.S. population. Men and women aged 14-69 years examined at mobile examination centers were eligible. Participants provided a 30-second oral rinse and gargle with mouthwash. DNA purified from oral exfoliated cells was evaluated for HPV DNA by PCR and type-specific hybridization. Demographic and behavioral data were obtained by standardized interview. Statistical analysis used NHANES sample weights and accounted for complex survey design to provide unbiased estimates for the total U.S. population. Results: The study population consisted of 5,579 participants. The prevalence of oral HPV infection among men and women aged 14-69 years was 6.9% (95%CI=5.7-8.3). HPV16 prevalence was 0.98% (95%CI=0.70-1.3), corresponding to 2.13 million infected individuals in the U.S. Gender, age, number of sexual partners, and intensity of current cigarette smoking were independently associated with oral HPV infection. Men had a significantly higher prevalence than women for any oral HPV infection (10.1 vs. 3.6%, p<0.001) and for HPV16 infection (1.6 vs. 0.31%, p<0.001). Oral HPV infection had a bimodal distribution with age, with peak prevalence among individuals aged 30-35 (7.3%) and 60-64 years (11.4%). Infection was rare among those without versus those with a history of any kind of sex (0.7% vs. 7.4%, P<0.0001) and increased with number of sexual partners (p-trend<0.001) and cigarettes smoked per day (p-trend<0.001). Conclusions: The higher prevalence of oral HPV infection among men when compared to women is consistent with the higher incidence of HPV-positive oropharyngeal cancer among men.


2. P16 Status Does Not Influence the QOL Effects of Chemoradiation for Locally Advanced Oropharynx Cancer: Results of TROG 02.02

J. G. Ringers, R. Fisher1, L. Peters3, B. O’Sullivan4, A. Trott5, L. Kenny6, R. Young2, D. Rischin4, 1Princess Margaret Hospital, Toronto, ON, Canada, 2Peter MacCallum Cancer Institute, Melbourne, Australia, 3Moffitt Cancer Center, Tampa, FL, 4Royal Brisbane and Women’s Hospital, Brisbane, Australia
Materials/Methods: The 861 patients accrued received definitive radiotherapy (70 Gy/7 weeks) concurrently with 3 cycles of either cisplatin (100mg/m2) or cisplatin (75 mg/m2) plus tirapazamine (290 mg/m2/day) by random assignment, as previously described. QOL was measured with the FACT-H&N at baseline, 2, 5, 12, 23 and 38 months. No significant difference in overall or subscale QOL score change from baseline was observed between arms at any subsequent time point; results for the oropharynx subgroup by p16 status are reported for both treatment arms combined. Results: Of 814 participants who met eligibility criteria and completed baseline QOL, 200 had oropharyngeal primaries and known p16 status; 82 were p16+, 118 were p16-. P16+ patients had better baseline ECOG PS, lower T-category, higher N-category, were younger and were less likely to be current smokers. Baseline mean FACT-H&N score was statistically and clinically significantly better in p16+ patients (120 vs. 107, p<0.001), while at 6 and 12 months post-treatment, no difference in score changes from baseline by p16 status was seen (6 mo, p16+: -1.5, p16 -:8, p=0.061; 12 mo, p16 +: -7, p16 -: -4, p=0.47). Conclusions: P16-associated oropharyngeal cancer has been shown to be a distinct entity with different demographic features. In our study, such patients exhibited better baseline QOL, but did not differ in QOL response to the effects of aggressive concurrent chemoradiation. Given the favorable prognosis of p16-associated oropharyngeal cancer, efforts to reduce the QOL burden of treatment are warranted.


LBPL 2 Correlates of Depression and Anxiety in Patients With Head and Neck Cancer Undergoing Radiation Therapy
J. Ellis*, G. Rodin*, R. Maunder*, J. Jones*, M. Choy*, R. Ehrlich*, C. Malfitano*, J. Ringash*, L. Waldron*, B. O’Sullivan*, . Sunnybrook Health Sciences Centre, Toronto, ON, Canada, Princess Margaret Hospital, Toronto, ON, Canada, Mt. Sinai Hospital, Toronto, ON, Canada, University of Western Ontario, London, ON, Canada

Purpose/Objective(s): The aim of this study was to identify correlates of depression and anxiety in patients with head and neck cancer. Background: High levels of depression and anxiety have been well documented in the literature in patients with head and neck cancer, who have one of the highest suicide rates in cancer. Various demographic and disease related factors have been found in several studies to be associated with depression and anxiety. The unique goals of this study were to explore the relative contribution of individual psychological factors and social difficulty to depression and anxiety in this population and to propose a model in which individual, social, demographic and disease-related factors may lead to or mitigate against the development of depression and anxiety in patients with head and neck cancer.

Materials/Methods: Patients with head and neck cancer were recruited from radiation review clinics at a large cancer hospital. Participants were screened for depression, anxiety, social difficulty and physical distress. Self-report questionnaires were completed on demographics, psychosocial factors and on physical symptoms. Descriptive statistics were calculated for all variables. Bivariate comparisons of variables were made using $\chi^2$, Spearman and Pearson correlation coefficients, Student t tests and ANOVA. Stepwise multivariable regression analyses were undertaken to examine significant correlates of depression and anxiety. Results: Of 482 eligible patients approached, 282 (58%) agreed to participate in this study. Of these, 90 (32%) scored above the cutoff on the social difficulty inventory; 62 (22%) on the PHQ9 for depression; and 34 (12%) on the GAD7 anxiety subscale of the PHQ. Multivariable analyses revealed that a family and personal history of psychiatric illness, greater social difficulty, insecure attachment style, and number of physical symptoms were the strongest correlates of severity of symptoms of depression and anxiety.

Conclusions: In patients with head and neck cancer, the severity of depression and anxiety symptoms are linked to social, individual and relational risk factors such as social difficulty, pre-morbid psychiatric vulnerability and lack of confidence in the availability of support, as well as to physical suffering and demographic factors, as previously found. Further research should concentrate on early identification of markers of individual vulnerability, as well as assessing the impact of early psychosocial and palliative interventions in preventing and relieving depression and anxiety in high-risk populations.

LBPL3  Genomic and Pathway Profiling of Head and Neck Cancer Cell Lines and Correlation with Drug Sensitivity


Purpose/Objective(s): Cell lines retain key genetic aberrations of the originating tumors, which frequently correlate with sensitivity to specific inhibitors. We performed genetic and pathway based profiling of 40 head and neck cancer (HNC) cell lines and correlated them with drug sensitivity in an exploratory fashion as well as genomic data from HNC tumor tissues. Materials/Methods: 40 HNC cell lines were analyzed for mutations and expression using next generation sequencing, copy number using array comparative hybridization (aCGH) and Nanostrix methodologies, and drug sensitivity to 30 clinically relevant targeted therapies using high-throughput viability testing. Integrative genomic analysis was performed resulting in pathway-based profiling of all cell lines. Genetic changes and pathway activity was correlated with drug sensitivity and tumor tissue HNC subtypes. Validation of a selection of results (PI3K, HRAS) was performed. Results: Frequent pathway activation was identified in >10 well established signaling pathways including TP53, PI3K, TP63/SOX2, Cyclin D1, etc, as well as several - for HNC previously unknown - signaling pathways. Cell lines could be associated with expression-based biologic subtypes in HNC tissues suggesting that specific cell lines should be used preferentially for modeling and therapeutic evaluation for HNC subtypes (including HPV(+) cell lines with characteristics of HPV(+)) tumors). RNaseq based expression allowed identification of alternative splicing events and exploratory correlation with drug sensitivity yielded several novel hypotheses that will require additional validation. Possible candidate translocations were identified, but none were recurrent and no clear candidate genes that appear to associate with drug sensitivity were evident. Furthermore we identified and validated the impact of HRAS and PIK3CA mutations on drug sensitivity for commonly used agents specifically resistance to EGFR inhibitors. Expression signatures for several targeted therapies were established and two signatures (PI3K, HRAS) were validated. Conclusions: Genetic changes characteristic of head and neck cancers were identified in virtually all HNC cell lines. Pathway based classification of cell lines was achieved and correlated with pathway activity in HNC tumor tissues and in selected cases with drug sensitivity. HRAS and PIK3CA alterations were two examples of many identified correlations that were validated and have potential clinical relevance.


3  Circulating CD4-positive Lymphocyte Levels Predict Response to Induction Chemotherapy (ICT) in Advanced Laryngeal Cancer


Background: Clinical tumor regression after induction chemotherapy (ICT) identifies patients with head and neck laryngeal cancers that are responsive to chemoradation, however, it is an expensive and toxic predictive marker. Patient immune parameters have recently been associated with response to chemotherapy and could potentially identify responding patients. A retrospective analysis of pretreatment peripheral blood T lymphocyte (PBL) subsets in patients enrolled in a Phase II clinical trial was performed to determine if T lymphocyte levels predicted response to ICT in patients with advanced laryngeal cancer. Methods: Pretreatment lymphocyte subpopulations were determined by automated flow cytometry and correlated with response to therapy and overall survival. A total of 163 patients received one cycle of ICT consisting of cisplatin (100 mg/m^2 for 1 day) and fluorouracil (1,000 mg/m^2 for 5 days). Carboplatin (area under the curve = 6) was used in place of cisplatin for patients with renal insufficiency or hearing loss. Patients were examined by direct laryngoscopy before treatment and 3 weeks after ICT to obtain bidimensional measurements of the primary tumor and percent reduction in their product. Lymphocyte data and outcome correlations from the larynx trial (n=97) were compared with similar data analysis from an identical Phase 2 trial involving patients (n=66) with oropharyngeal cancer. Results: Increased CD4 levels predicted response to ICT (p = 0.006) and showed a trend for improved survival (p = 0.15) in patients with laryngeal, but not oropharyngeal cancer. In the combined group of patients, increased CD4 and decreased NK cell levels predicted response to ICT (p = 0.02). For the oropharynx, patients were also grouped by HPV status and comparisons to laryngeal patients were also analyzed. Although the findings suggested that CD8 levels were more closely associated with chemotherapy response in oropharynx cancer, logistic regression interaction modeling showed a much stronger relationship with CD4 cell levels and induction chemotherapy response for patients with laryngeal cancer. Conclusions: These findings suggest the potential importance of the systemic cellular immune system in chemotherapy response in laryngeal cancer and potential usefulness of CD4 lymphocyte levels in predicting clinical outcome.


LBPL4  An International Collaboration to Harmonize the Quantitative Plasma Epstein-Barr Virus (EBV) DNA Assay for Future Biomarker-Guided Trials in Nasopharyngeal Carcinoma (NPC)

Q. Le*, Q. Zhang**, H. Cao**, A. Cheng**, J. T. Chang**, R. Hong**, K. Tsao**, N. Lee**, A. T. Chan**, K. Chan**. 1 Stanford University, Stanford, CA, 2 RTOG Statistical Center, Philadelphia, PA, 3 Chang-Gung University, Taoyuan, Taiwan, 4 Chang Gung University, Taoyuan, Taiwan, National Taiwan University Hospital, Taipei, Taiwan, 5 Chang Gung Memorial Hospital-Linkou, Taoyuan, Taiwan, 6 Memorial Sloan Kettering Cancer Center, New York, NY, 7 The Chinese University of Hong Kong, Hong Kong, Hong Kong

Purpose/Objective(s): Persistently elevated post-treatment plasma EBV DNA has been shown to be the most reliable predictor of relapse in...
NPC patients. However, the lack of a standardized assay has made it difficult to use in a prospective biomarker-driven trial. Here we conducted a study to standardize the assay between four international centers with expertise in EBV DNA.

**Materials/Methods:** Plasma samples of 40 newly diagnosed or treated NPC patients were collected and distributed to four sites. DNA was extracted using the QIAamp DNA Blood Mini Kit and EBV DNA copy number was determined by real-time quantitative PCR using the BamHI-W primer/probe set. All sites used the same protocol but generated their own callibrator (standard) sets. A harmonization study was performed using pooled plasma samples from 23 patients with known EBV copy numbers (approximately 4000 copy/ml) but with the same calibrators and reagent mixture for all sites. Variability between sites, observers and runs were computed using general linear model.

**Results:** For the 40-sample comparison study, the intraclass correlations for each site when compared to the index site (SU) were 0.65 (95%CI: 0.32-0.84), 0.90 (95%CI: 0.81-0.95) and 0.74 (95%CI: 0.53-0.86). The mean ratio of DNA copy number between the highest site and the other 3 sites were 2.7, 3.4 and 15.3. For the harmonization process using the same calibrators and reagent mixture, the largest variability was due to DNA extraction both between and within sites. When pooled DNA (concentration 4000 copies/ml) was provided, the results ranged from 3213 (SD=287) to 4204 (SD=185) copies/ml between sites. However, when plasma samples with the same DNA concentration was provided, the results ranged from 2579 (SD=322) to 13,965 (SD=5512) copies/ml between sites, with one site being an outlier.

**Conclusions:** Quantitative PCR assays, even when performed in experienced clinical labs, can yield large variability in plasma EBV DNA copy numbers. The largest variability is from DNA extraction. A common set of calibrators and reagent mixture can help to reduce variability.

Supported by U10 CA21661 from the NCI

Purpose/Objective(s): We sought to improve the outcomes for loco-regionally advanced nasopharyngeal carcinoma (NPC) by testing the feasibility/safety of adding bevacizumab to chemoradiation. Materials/Methods: Eligible patients with ≥T2b and/or positive node(s) were prescribed 3 cycles of bevacizumab (15 mg/kg) and cisplatin (100 mg/m²) with radiation (70 Gy) followed by 3 cycles of bevacizumab (15 mg/kg), cisplatin (80 mg/m²) and fluorouracil (1000 mg/m²/d). Toxicity during and after treatment were collected along with tumor control endpoints. Results: The 44 analyzable patients were mainly male (65.9%), Asian (52.3%), with a median age of 48.5 years, and had Zubrod 0 (75%) and WHO IIB or III (25%) histology. Tumor stages were IIB 11.4%; III 54.5%; IVA 22.7%; IVB 11.4%. Median radiation dose was 69.96 Gy (65.72-70). Percentages of patients receiving 3 cycles of cisplatin and bevacizumab during radiation were 68.2% and 70.5% while 47.7%, 54.5%, and 52.3% received 3 cycles of adjuvant cisplatin, fluorouracil, and bevacizumab. With a median follow-up of 2.5 years, the estimated 2-year loco-regional progression-free, distant metastasis-free, progression-free and overall survival (OS) rates were 83.7%, 90.8%, 74.7%, and 90%, respectively. No grade 3-4 hemorrhage or grade 5 adverse events were observed. Blood/bone marrow toxicity was the most common Grade 4 adverse event. The incidence of acute grade 3-4 mucositis was 77.3% and late grade 3 xerostomia was 4.5%. Conclusions: It was feasible to add bevacizumab to chemoradiation for NPC treatment. The favorable 2-year OS of 90.9% when compared to prior RTOG NPC trials suggests that bevacizumab might delay progression of subclinical disease.


6 Pre-treatment Neurocognitive Function (NCF) Evaluation in Head and Neck Cancer (HNC) Patients (pts) with Comparison to Healthy Control Participants


Purpose: There is a growing body of evidence on NCF impairment in cancer pts. However, it remains unknown whether this dysfunction is due to anticancer treatment, lifestyle risk factors, and/or to the disease itself. This study reports baseline NCF in newly diagnosed HNC pts prior to any treatment. Materials/Methods: HNC pts were assessed with a battery of NCF tests prior to receiving radiation +/- chemo(bio)therapy.
Domains tested were memory, motor skills, intelligence, language, attention, processing speed and executive function. Test performances were transformed into Z-scores using normative data. Pts also had self-reported subjective assessments of NCF, quality of life (QOL), fatigue, anxiety and depression. Data obtained were compared to a healthy control group who completed the same tests. Results: Eighty HNC and 28 control subjects were assessed. The mean ages were 58 and 52 years, while the male:female ratios were 68:12 and 25:3 (p=0.4) for the HNC and control groups respectively. In the HNC cohort, primary tumor sites included the oropharynx (n=61), larynx (7), hypopharynx (5) and unknown primary (7). There were more HNC pts (45%) compared to controls (3.6%, p=0.001) who had at least a 20-pack year history of smoking. The proportion of subjects who reported heavy alcohol intake (>28 units/week) was not significantly different between the two cohorts (10% vs 0%, for HNC and controls, p=0.11). Objective NCF assessments demonstrated that the HNC cohort performed higher on intelligence testing than the controls (mean Z-score of 0.55 vs 0.10, p=0.02). However, there were no significant differences between HNC and control subjects on tests of memory (-1.00 vs -1.03), motor skills (-0.74 vs -0.39), language (0.02 vs -0.28), attention (0.26 vs 0), processing speed (-0.02 vs -0.13) and executive function (-0.14 vs -0.15). The proportion of individuals with > 3 deficits in different NCF domains was also similar for the HNC (24%) and control (25%) groups. In contrast, HNC pts self-reported more NCF impairment than controls (mean [mn] FACT-COG3 scores 33.7 vs 19.1, p=0.005). HNC pts also described significantly worse QOL (mn FACT H&N scores 33.8 vs 15.5), fatigue (mn FACIT scores 35.1 vs 16.1), anxiety (mn HADS scores 7.0 vs 3.2) and depression (mn HADS scores 3.9 vs 1.3) when compared to controls (p<0.001 for all four parameters).

Conclusions: Although HNC pts were slightly older and had higher smoking exposure, their objective NCF was similar to that of controls. However, HNC pts subjectively reported worse NCF, QOL, fatigue, anxiety and depression, which may reflect their reactions to being newly diagnosed with malignancy and concerns about toxicity from impending treatment. Longitudinal NCF evaluations of both cohorts are warranted.


7 The Relationship Between WHO Grade, EBV and HPV Status in Nasopharyngeal Carcinoma in Non-endemic Population Q. Le*, B. Khong*, H. Cao*, S. Kwok*, R. West*, C. Kong*, , Stanford University, Stanford, CA

Purpose/Objective(s): Although the non-keratinizing or undifferentiated histology of nasopharyngeal carcinoma (NPC) are firmly linked to Epstein-Barr virus (EBV) infection, the connection between EBV and keratinizing or basaloid subtypes is less well established. A small study has suggested a link between keratinizing NPC and oncogenic human papilloma virus (HPV). Here, we evaluate the relationship between tumor histology with EBV, p16 and HPV status. Materials/Methods: We identified 108 NPC patients who were seen at Stanford from 11/1984 to 03/2009 and had available tumor specimens for analysis. Two tissue microarrays (TMAs) were constructed and stained for EBV EBER by in-situ hybridization (ISH) and p16 immunohistochemistry (IHC). EBV negativity was verified by ISH on whole section and PCR. The HPV status in tumors staining positive for p16 (immunohistochemistry) was confirmed by both HPV ISH (Ventana) and quantitative PCR using HPV16/18 E6/E7 specific primer/probe sets. EBV, p16 and HPV status were related to WHO grade. Results: The median age of the patients was 46 and 72% were male. The racial distribution was: 69% Asian, 25% Caucasian, 3% Black and 4% Hispanic. Tumor histology was: 5% keratinizing, 18% non-keratinizing, 72% undifferentiated and 5% basaloid. 105 tumors were assessable for EBV and 99 for p16. Of 13 p16-cases (8) were positive for HPV16/18 by PCR and ISH and 5/6 were in the diffusely positive group. 56% of patients had WHO grade III tumors. Of 13 p16-cases (8) were positive for HPV16/18 by PCR and ISH and 5/6 were in the diffusely positive group. The relationship between WHO histology, EBV and HPV status is as follows: WHO I - 50% EBV(+) and 25% HPV(+), WHO II - 65% EBV(+) and 22% HPV(+), WHO III - 94% EBV(+) and 1% HPV(+), WHO IV - 60% EBV(+) and 0% HPV(+). Conclusions: Although EBV- NPC were more likely to be p16(+) and HPV(+), the majority these tumors did not harbor HPV16/18. Infection with other high risk HPV subtypes cannot be excluded. A more comprehensive evaluation of all oncogenic HPV subtypes is necessary to determine the relationship between HPV and EBV(+) NPC.


8 Significant Reduction in Waiting Time for Diagnosis and Treatment of Head and Neck Cancer in Denmark In 2010 Compared to 2002. First Results of the Danish National Fast Track Program for Cancer C. Grau*, N. Lyhne*, A. Christensen*, M. Alanin*, M. Bruun*, T. Jung*, M. Bruhn*, J. Jespersen*, o. DAHANCA and DSHHO*, , Aarhus University Hospital, Aarhus, Denmark, Copenhagen University Hospital, Copenhagen, Denmark, Odense University Hospital, Odense, Denmark, Copenhagen University Hospital, Herlev, Denmark, Aarhus University Hospital, Aalborg, Denmark

Purpose/Objective(s): Long waiting times for surgery and radiotherapy have been a major problem in most Western countries for several decades. For head and neck cancer, significant tumor progression has been observed during waiting time, and a meta-analysis of clinical observations has shown that the risk of local recurrence and death increases with increasing waiting time for treatment. A Danish study (Primdahl et al. Acta Oncol 2006) showed that compared to 1992, the waiting time before start of radiotherapy was significantly longer in 2002 (median 70 days versus 50 days). In 2008, the Danish national policy of fast track accelerated clinical pathways was introduced. Patients with suspicion of cancer are now given the highest priority in the health care system. Local infrastructure has been improved by eliminating paper charts and clinics twice weekly. Aim: The aim of the current study was to evaluate the potential influence of fast track by comparing waiting times in 2010 to the observations from 2002. Materials/Methods: Charts of all consecutive new patients with squamous cell carcinoma of the oral cavity, pharynx, and larynx at the five Danish head and neck oncology centres from Jan-Apr 2010 were reviewed and compared to similar data from 2002. Number of patients was 253 (2010) vs. 221 (2002). Stage distribution 2010 vs. 2002 was stage I: 22% vs. 20%, stage II: 15% vs. 23%, stage III: 11% vs. 23%, and stage IV: 52% vs. 35%. Primary treatment was radiotherapy (73% vs. 81%), surgery (11% vs. 6%), combined
treatment (4% vs. 1%), or palliative/none (12% vs. 12%). Results: Total time from first health care contact (GP, ENT or hospital) to start of definitive treatment was median 41 calendar days in 2010 compared to 69 days in 2002 (p<0.001). Median time used for diagnosis was 13 days compared to 17 days in 2002 (p<0.001) and median time from diagnosis to treatment start was 24 days in 2010 versus 47 days in 2002 (p<0.001). Significantly more diagnostic imaging was done in 2010 compared to 2002 (CT 59% vs. 21%; MR 43% vs. 16%; US 38% vs. 19%; PET 21% vs. 6%). Conclusions: The study showed a significant reduction in time for diagnosis and treatment of head and neck cancer in Denmark in 2010 compared to 2002. More imaging was used and higher stages seen in 2010. Reducing waiting time by fast track clinical pathways is possible but requires a substantial dedicated concerted effort of the involved health care sectors.


9 Differences in Billing Charges in a Matched Pair Comparison of Intensity Modulated Radiation Therapy (IMRT) vs. 3-D Conformal Radiation Therapy (CRT) for the Treatment of Head and Neck Cancer


Purpose/Objective(s): IMRT is a newer form of radiation therapy that has been rapidly adopted over CRT for treatment of head and neck cancer with the known advantage of IMRT being reduction in xerostomia. To our knowledge, billing differences between these two modalities have never been quantified through chart review. Materials/Methods: We compared patients treated with definitive radiation with or without chemotherapy for squamous cell carcinoma of the larynx, hypopharynx, oropharynx, nasopharynx, oral cavity, or unknown primary between 2000 and 2009. Each patient treated with IMRT was matched to a patient treated with CRT by site, stage and smoking status. Patient demographic and clinical data including Charlson comorbidity Index (CMI) and detailed outcomes were recorded. Itemized billing charges were obtained on each patient. Multivariate linear regression was used to estimate the effect of IMRT versus CRT on long-transformed charges, controlling for clinical and demographic characteristics. Results: From an initial cohort of 380 patients, 188 patients had itemized billing records available and were able to be matched (resulting in 94 matched-pairs). When billing charges were summed from entrance into the UNC system through completion of treatment, patients treated with IMRT had significantly higher charges ($134,144 vs $83,529 for CRT). Average charges from radiation completion through the first year of follow up were also higher for IMRT vs CRT ($34,228 vs $21,955). Controlling for all other clinical and demographic covariates, use of IMRT was significantly associated with increased pre-/on-treatment charges (p=0.002) and total charges (<0.001); however, follow up charges were not significantly different between treatment modalities. Failing treatment resulted in a dramatic increase in follow up charges (96.7% increase, p<0.001; 19.0% total, p=0.001; 11.6% pre-/on-treatment, p=0.086; 46.6% follow up, p=0.018) as did those with CMI>1 compared to patients with CMI=0 (36% increase in total, p=0.039). Age, gender, race, smoking and drinking status did not have significant impact on charges. Outcomes were not significantly different between IMRT and CRT including local control and regional control. Conclusions: Use of IMRT resulted in substantially higher charges for patients with head and neck cancer but follow up care costs were similar. Patients with greater comorbidity appear to require costlier care. As disease control outcomes are similar between IMRT and CRT, emphasis should be on obtaining robust quality of life data to assess the cost effectiveness of IMRT.


10 Do the Quantec Criteria Defined for the Radiation Dose to the Parotid Glands Protect Against Xerostomia?

J. A. Langendijk*1, J. Beet*1, O. Chouvalova*1, C. R. Leemans*1, P. Doornaert*1, B. F. A. M. van der Laan*1, A. Vissink*1, C. Schilstra*1, H. P. Bijl*1, R. J. H. M. Steenbakkers*1, , University Medical Center Groningen, Groningen, Netherlands, VU University Medical Center, Amsterdam, Netherlands

Purpose/Objective(s): Recently, QUANTEC defined dose-volume limits for the dose to the parotid glands. It was stated that severe xerostomia (long-term salivary function <25% of baseline) can usually be avoided if at least one parotid gland has been spared to a mean dose of < 20 Gy or if both glands have been spared to a mean dose of less than < 25 Gy. This prospective study was conducted to evaluate if the QUANTEC criteria protected against physician-rated and patient-rated xerostomia and/or sticky saliva. Materials/Methods: The study population was composed of 353 patients treated with definitive radiotherapy or chemoradiation for head and neck cancer. In all patients, planning CT scan were available including information of the dose to the parotid glands. All patients were subjected to a standard follow-up program in which radiation-induced acute and late toxicity as well as quality of life was prospectively assessed. Toxicity was assessed according to the CTCAE. Patients fulfilling the QUANTEC criteria were classified as LOW RISK and patients not fulfilling these criteria as HIGH RISK. Results: Grade 2-3 acute xerostomia (CTCAE) occurred in 62.4% vs. 33.6% in the HIGH RISK and LOW RISK group, respectively (p<0.001). The prevalence of grade2 late xerostomia (CTCAE) at 6, 12, 18 and 24 months was 43.2%, 47.6%, 42.7% and 41.1% in the HIGH RISK group, respectively. In the LOW RISK group, the prevalence of grade2 late xerostomia (CTCAE) was 18.3%, 16.2%, 9.7% and 8.5%, respectively. In the LOW RISK group, there was a significant gradual reduction of grade2 late xerostomia over time (p<0.01). Among patients with no xerostomia prior to treatment, the mean scores (on a scale of 0-100) for patient-rated xerostomia in the HIGH RISK group were 57, 47, 41 and 45 at 6, 12, 18 and 24 months, respectively. These scores were significantly lower in the LOW RISK group, namely: 33, 26, 20 and 21, at corresponding time points. Among patients with no sticky saliva prior to treatment, the mean scores (on a scale of 0-100) for patient-rated sticky saliva in the HIGH RISK group were 48, 34, 36 and 36 at 6, 12, 18 and 24 months, respectively. These scores were significantly lower in the LOW RISK group, namely: 24, 22, 16 and 16 at corresponding time points. Conclusions: Although significantly lower rates of xerostomia and sticky saliva were found among patients fulfilling the QUANTEC criteria for the dose to the parotid glands, the QUANTEC criteria do not completely protect against the development of clinically relevant patient-rated xerostomia. These data indicate that other factors than the mean parotid dose is important in the development of radiation-induced xerostomia.

11
11 Computed Tomography as a Predictor of Actual Cartilage Invasion in Advanced Laryngeal and Hypopharyngeal Carcinoma

**M. Dominello***, P. Paximadis*+1, J. Abrams*+1, A. Sukari*+1, H. Lin*+1, G. Yoo*+1, H. Kim*+1, , †Wayne State University, Detroit, MI, ‡Karmanos Cancer Institute, Detroit, MI

**Purpose/Objective(s):** Historically, invasion through the thyroid or cricoid cartilage has been cited as an indication for primary laryngectomy over organ-preserving therapy in the management of locally advanced laryngeal cancer. There have been reports of variable sensitivity and specificities associated with computed tomography (CT) as a predictor of cartilage invasion in this clinical setting. The purpose of this study is to report our institutional findings regarding the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for the finding of cartilage invasion on CT in patients with locally advanced laryngeal and hypopharyngeal carcinoma.

**Materials/Methods:** Ninety-two consecutive patients treated from 1999 to 2009 for clinically staged T3-T4 laryngeal (87) or T4 hypopharyngeal (5) squamous cell carcinoma who obtained a preoperative CT of the neck no more than 4 weeks prior to total laryngectomy were reviewed. CT findings were stratified by standardized criteria established to minimize the likelihood of interpretation bias. Findings were classified as having identified invasion through cartilage, minimal or suggested invasion, or no evidence of cartilage invasion. Pathology reports of laryngectomy specimens were then reviewed for evidence of pathologic involvement. The sensitivity, specificity, NPV, and PPV were calculated for the finding of cartilage invasion on CT. Test characteristics were estimated as binomial proportions and Wilson’s method was used to calculate 95% confidence intervals.

**Results:** Of the 92 consecutive patients reviewed, 37 were found to have evidence of cartilage invasion on CT (including reports of invasion through cartilage as well as minimal or suggested invasion). Upon pathologic review, 15 of these (41%) did not have any actual cartilage invasion, yielding a PPV of 59% [95% confidence interval (CI) 43,74]. NPV was 85% [95% CI 74,93]. Sensitivity was 73% [95% CI 56,86] and specificity was 76% [95% CI 64,85]. When considering only the more explicit radiographic finding of invasion through cartilage, we arrived at a PPV of 61% [95% CI 41,78]. NPV was 77% [95% CI 66,85]. Sensitivity was 47% [95% CI 30,64] and specificity was 85% [95% CI 76-92%].

**Conclusions:** CT is an unreliable predictor of actual cartilage invasion in advanced laryngeal and hypopharyngeal carcinoma. Of most clinical concern is the low positive predictive value of this test, even when invasion through cartilage is explicitly reported. In our single-institution review, a large number of patients were treated surgically when organ-preserving therapy could have been offered as a viable therapeutic option. Caution is advised when considering the finding of cartilage invasion on CT during therapeutic decision-making.

**Author Disclosure Block:** None. J. Abrams: None. A. Sukari: None. H. Lin: None. G. Yoo: None. H. Kim: None.

12 Response to Induction Chemotherapy and Dosimetric Analysis of the Use of Post-Induction Chemotherapy Target Volumes in Radiotherapy for Locally Advanced Head and Neck Cancer

**J. J. Caudell***, J. Wilder*, T. Liu*, K. Pitman*, S. Packianathan*, R. Jennelle*, R. D. Hamilton*, S. Vijayakumar*, , University of Mississippi Medical Center, Jackson, MS

**Purpose/Objective(s):** Following induction chemotherapy, current guidelines suggest the use of post-chemotherapy volumes in the planning of radiotherapy. We conducted a phase II trial examining the use of post-chemotherapy volumes. Herein, we report secondary outcomes regarding the response to induction chemotherapy and the comparison of dosimetry to normal tissues using pre- or post-chemotherapy volumes.

**Materials/Methods:** The study was approved by the Institutional Review Board of the University of Mississippi Medical Center (#2009-0189). Patients with Stage IVA-IVB squamous cell carcinomas of the oral cavity, oropharynx, larynx, or hypopharynx were eligible. Per protocol, patients received two cycles of induction docetaxel (75 mg/m2), cisplatin (100 mg/m2) and 5-fluorouracil (750 mg/m2 daily CI over 4 days) every 3 weeks (TPF) followed by cetuximab loading (400 mg/m2) followed by concurrent radiotherapy (66 - 70 Gy) with cetuximab (250 mg/m2). CT simulations were done before and after induction TPF and fused. Gross tumor volume (GTV) was contoured for evaluation of response. Plans were generated for the post-TPF CT using both pre-TPF and post-TPF target volumes and dosimetry to normal tissue was compared via paired t-test. **Results:** Accrual goal was 42 patients, but at 20 patients the trial was closed prematurely following the deaths of 3 patients after 1 cycle of TPF. 17 patients remained for analysis of response to 2 cycles of TPF. Complete response was seen in 1 patient (5.9%), and partial response in 14 (82.4%) patients, with 2 (11.8%) progressing. Median GTV pre-TPF was 65.09 cc (range 20.9 - 187.4) and post-TPF 27.03 cc (range 0 - 210.96 cc). Median percent change in GTV was a 66.3% reduction (range 57.8% growth - 100% reduction). 15 patients had both pre- and post-TPF plans available for analysis. Use of post-TPF target volumes resulted in significantly lower mean doses to the larynx (p = 0.02), ipsilateral parotid (p < 0.001), contralateral parotid (p = 0.02), and trended towards lower mean dose to the inferior pharyngeal constrictor (p = 0.08). There were no significant differences in maximum doses to the cord or brainstem. **Conclusions:** In this population, use of TPF resulted in unacceptable risk of grade 5 toxicity and the trial was closed prematurely. Use of post-TPF target volumes resulted in improved dosimetry to organs at risk. Further work is necessary to determine if this results in improved acute or late toxicity and equivalent locoregional control.

**Author Disclosure Block:** None. J. Wilder: None. T. Liu: None. K. Pitman: None. S. Packianathan: None. R. Jennelle: None. R. D. Hamilton: None. S. Vijayakumar: None.
101 Tumor Infiltrating Lymphocytes (TIL) and Prognosis in Oral Cavity Carcinoma

G. Wolf*, D. B. Chepeha*, E. Light*, A. Nguyen*, E. Chanowski**, D. G. Thomas***, U. M. Head and Neck SPORE Program****, 1University of Michigan, Ann Arbor, MI, 2University of Cincinnati, Cincinnati, OH

Purpose/Objective(s): Immune responses within the tumor microenvironment are increasingly important predictors of tumor biology and outcome. Number, location in the microenvironment and function of TILs appear important and may differ by tumor site and extent. We previously demonstrated that tumor infiltrates of CD4, CD8, FoxP3, and ratios of CD4/CD8 and FoxP3/CD8 were important predictors of survival after chemoradiation in advanced oropharynx cancer. To determine if TILs were of prognostic importance in advanced oral cavity cancer, a tissue microarray was constructed of tumors from patients treated with primary surgery and postoperative radiation, and T cell lymphocyte infiltration was evaluated retrospectively. Materials/Methods: Studied were a cohort of 52 patients treated by one of the authors (DBC) with surgery and radiation for advanced oral cavity cancer. Complete TIL and clinical data were available in 39 patients (Stage 1, 2-11; Stage 3, 4-28). Levels of CD4, CD8, FoxP3 (Treg), CD68 and NK cells were measured by immunohistochemical staining of tumor cores on a tissue microarray. Only cells infiltrating tumor parenchyma were counted. Associations of subset levels and proportions with clinical variables, health behaviors, pathologic staging, and histologic features were assessed using the Spearman correlation coefficient and the non-parametric Kruskal-Wallis test. Associations with time-to-event outcomes determined using univariate and multivariate Cox models. Results: The ratio of CD4/CD8 (p=.01412) and CD8 infiltrates (p=.0523) were associated with tumor recurrence but not overall or disease specific survival (DSS). Lower ratios (and CD4 levels) were also associated with alcohol use (p=.0049) and poor tumor differentiation (p=.02). Interestingly, higher levels of CD68 positive infiltrating macrophages tended to be associated with positive nodes (p=.06) and poorer overall survival (p=.07). The FoxP3/CD8 ratio was lower in patients with higher clinical (p=.0594) and pathologic T stage (p=.0178). For clinical variables, overall survival was significantly shorter for patients with positive nodes (p=.023), ECS (p=.0165), perineural invasion (p=.0282) as well as DSS (p=.0028, p=.0247, p=.0068, respectively). Mean TIL levels for CD4, CD8, FoxP3 were significantly correlated with each other and were higher in surviving patients. Conclusions: Infiltrating immune cell levels in oral cavity cancer appear influenced by health behaviors and tumor characteristics. In contrast to findings in oropharynx cancer patients, infiltrates of potentially immunosuppressive CD68 positive macrophages may be important in metastatic behavior and outcome for patients with oral cavity carcinoma. Immunomodulation to increase CD4 and CD8 infiltrates and decrease CD68 infiltrates may be of clinical benefit.


102 Clonal Evolution of Treatment Refractory Maxillary Sinus Carcinoma

S. Arora1, I. Cherni1, E. Lenkiewicz1, S. Sridhar1, C. Lorenzo1, T. G. Beach1, M. Barrett1, G. J. Weiss1, 1Translational Genomics Research Institute, Phoenix, AZ, 1Sun Health Research Institute at Banner Healthcare, Phoenix, AZ, 1TGen/Virginia G Piper Cancer Center Clinical Trials at Scottsdale Healthcare, Scottsdale, AZ

Purpose/Objective(s): Maxillary sinus carcinoma (MSC) is a rare paranasal sinus cancer. Annually, ~2,000 paranasal sinus tumors are diagnosed in the US and up to 25% develop distant metastasis. In this study, we explored the clonal evolution of the disease in a case of metastatic MSC that became both chemo- and radiotherapy (XRT) resistant. Materials/Methods: The initial MSC surgical resection sample along with several metastatic tumors collected as part of a rapid warm autopsy program in a patient who developed chemo- and XRT refractory disease were examined. We used DNA content-based flow cytometry to isolate distinct populations of aneuploid and diploid tumor nuclei populations. Flow-sorted tumor nuclei populations were profiled using Agilent 1M 60mer oligonucleotide CGH arrays to characterize the different metastatic foci. qPCR analyses were used to confirm the significant aberrations. We also used immunohistochemical (IHC) analyses for c-Kit expression. Results: The patient developed a solitary pulmonary metastasis one year after the initial MSC resection. Subsequently, multifocal treatment-refractory disease developed, including CNS progression within 35 days of brain XRT. We examined the aneuploid population of several metastatic foci (brain, lung, and jejunum) collected at autopsy. We detected several aberrations, including c-Kit amplification. There were additional deleted
regions present in the lung tumor and decrease aneuploid count in the jejunum metastasis. Strong c-Kit IHC staining was present in the primary tumor, and the divergent independent subclonal aberrations arising in metastatic foci were found in the brain, lung, and jejunum. We explored the incidence of two of the most significant aberrations in FFPE tissue of 17 other metastatic foci collected at autopsy, as well as, the patient’s primary resected tumor. The results from these specific aberrations confirmed at least 3 clonal populations. Conclusions Due to the MSC’s resumed growth despite several courses of systemic chemotherapy and XRT, we speculate that acquired secondary genetic changes evolved with the evolution of resistance to these therapies. Utilization of this novel clonal evolution modality to identify a tumor’s Achilles’ heel may provide therapeutic benefit to patients with advanced MSC could accelerate approval of investigational agents in niche populations and advance personalized treatment for rare cancers. [Support from: IBIS Foundation of Arizona and the Scottsdale Healthcare Foundation].


103 Expression of Estrogen Receptor Alpha36 and Alpha66 in Human Thyroid Cancer Cells

Purpose/Objective(s): Thyroid cancer is a female-predominant carcinoma, with a female to male ratio at about 3:1. Experiments have demonstrated that the exposure to a high amount of estrogen can make female animals susceptible to thyroid tumor. The reduction of female hormones by ovariectomy can significantly reduce the incidence of the tumor and application of estrogens to ovariectomized rats increases the incidence. The action of estrogen is usually through its two classical receptors: estrogen receptor alpha (ERα66) and beta (ERβ). ERα36, a variant form of the original ERα66, is recently identified. The overexpression of this ERα36 has been documented in several types of female hormone-related cancers including breast cancer and endometrial cancer, but not yet in thyroid cancer. Materials/Methods: To study the potential role of ERα36 in the proliferation and growth of thyroid cancer, we examined the expression of ERα36 together with ERα66 in six different types of human thyroid cancer cells by Western blot analysis and RT-PCR. Results: The result showed that all six thyroid cancer cell lines expressed a considerable amount of ERα36. However, only three types of thyroid cancer cells had detectable ERα66, indicating that the expression of ERα66 may lose in other thyroid cancer cells. These findings may reflect the situation in human thyroid cancer tissues since around 50% of cases presented without ERα66 expression. Functionally, the variant ERα36 isoform, similar to ERα66, can be activated by estrogen, but ERα36 is a more potent molecule that stimulates the proliferation of tumor cells via activating the extracellular signal-regulated kinases 1/2 (Erk1/2), suggesting that the presence of ERα36 may be a disadvantage feature for thyroid cancer treatment or/and prognosis. Conclusions: The variant form of ERα36 commonly expressed in thyroid cancer cells while the original ERα66 may lose in some cases. ERα36 is a potent pro-proliferative molecule in thyroid cancer.


104 Pilot Study To Evaluate The Effect of Erlotinib Administered Before Surgery in Operable Patients with Squamous Cell Carcinoma of The Head and Neck (SCCHN).

Purpose/Objective(s): Strategies for early detection of cellular response to EGFR inhibitors are critical to personalizing therapy for SCCHN. The glycolytic enzymes responsible for uptake of the positron emission tomography (PET) tracer [18F]-fluoro-2-deoxy-D-glucose (FDG) are regulated by intermediates of the EGFR pathway such as AKT, mTOR and MAPK. It was hypothesized that the inhibition of these EGFR pathway markers could be read by the 18F-FDG uptake by tumor. It is also possible that the EGFR pathway is aberrantly activated in some cancers and that glycolysis and downstream effects are not always linked. Previous in vitro and in vivo studies showed that 18F-FDG uptake changes very early in SCCHN tumor models responsive to EGFR inhibition. We developed a pilot clinical protocol to investigate this further in patients with SCCHN. Materials/Methods: Patients with operable SCCHN with a window of at least 15 days between the time of initial biopsy and established surgery will receive erlotinib 150 mg/day or 300 mg/day if the patient is actively smoking. Smokers metabolize erlotinib rapidly with an MTD that is twice that of non-smokers. Patients must have additional biopsy tissue for laboratory research studies. 18F-FDG PET scan and neck CT with contrast are performed before treatment, 4-6 days through treatment and at the end of erlotinib administration. Results: 11 patients have been treated to date with an average of 18.6 days of treatment. Of the 10 evaluable patients, 7 showed partial response (PR) and 3 patients showed stable disease (SD). 8 patients received erlotinib 300 mg. No grade 3 or 4 toxicities. Early (4-6 days)18F-FDG PET scans showed a decrease in SUV max to 93.25% +/- 18% in patients with SD and to 51% +/- 22% in patients with PR (defined as at least 20% reduction in maximum diameter). This pilot trial will continue to enroll patients to address the primary laboratory research correlative aim. Pre-and post-treatment tumor tissue is available in all patients. Conclusions: Short course treatment with erlotinib in a dose adjusted per smoking status is very active in previously untreated patients with SCCHN. Early changes in the 18F-FDG PET scan uptake can be used as a marker predictive of response to EGFR inhibition.

105  Biomarker Expression in Head and Neck Squamous Cell Carcinoma - Implications for Therapy
R. Feldman1*, A. Kemkes1*, J. Xiù1*, D. Arguëllo1*, G. Basu1*, R. Blevins1*, R. Ashfaq1*, Z. Gatalica1*, D. Loesch1*, R. Bender1*, 1Caris Life Sciences, Phoenix, AZ, 2Caris Life Sciences, Irving, TX

Purpose/Objective(s): Head and neck squamous cell carcinoma (HNSCC) is an aggressive disease with an unpredictable prognosis. Failure of first-line treatment is common, thus additional therapeutic options are in great need. The purpose of this study was to explore biomarker expression profiles of HNSCC for therapeutic strategies that are not commonly pursued. Materials/Methods: In a cohort of 166 patients with HNSCC, biomarkers that are useful in determining sensitivity or resistance to various chemotherapies were analyzed. Expression of ERCC1 (8F1), MGMT(MT23.3), MRp1 (33A6), Pgp (C494), RRM1 (poyclonal), TOP1 (1D6), TOP2A (3F6) and TS (TS106) were assayed by immunohistochemistry (IHC) on a Ventana platform. Slides were then evaluated by a pathologist using intensity grades (0-3) and percentage of tumor cells staining (0-100%). Association of potential benefit and lack thereof was determined based on defined thresholds. Results: The distribution of percentages across all biomarker categories (relative expression) was analyzed by non-parametric Chi Square tests. All differences between relative expression levels attained statistical significance (p<0.001). Our observations demonstrate that the most frequently over expressed biomarkers in HNSCC are MRp1 (90.4%), TOP2A (79.5%), MGMT (76.7%), ERCC1 (51.9%) and RRM1 (44.1%). Conversely, the biomarkers with greatest frequency of negative expression are Pgp (92.2%), TS (58.3%) and TOP1 (57.6%). Based on these data, a large percentage of patients in this cohort may have a little benefit from cisplatin or carboplatin based on ERCC1, irinotecan or topotecan based on TOP1, gemcitabine based on RRM1 and temozolomide based on MGMT. Contrarily, based on the frequency of negative expression values for TS and above threshold values for TOP2A, this cohort may have an increased benefit from 5-fluorouracil or pemetrexed, and doxorubicin or etoposide, respectively. Lastly, the distribution of markers for the classical drug pumps, MRp1 and Pgp were in complete opposition. MRp1 was above threshold in 90% of the cohort, indicating resistance to agents like doxorubicin, etoposide and methotrexate, whereas Pgp was negative in 92% of cases, suggesting a potential increased benefit from paclitaxel or docetaxel. Conclusions: To our knowledge, this is the first comprehensive analysis of biomarkers associated with various chemotherapeutic agents in HNSCC. HNSCC is a challenging disease to treat, with few therapeutic options after failure of first-line regimens. Our data suggest that the fluoropyrimidines, 5-fluorouracil or pemetrexed, and the taxanes, paclitaxel or docetaxel, are potential treatment options for HNSCC as demonstrated by the preponderance of negative expression values of TS and Pgp, respectively, in this cohort.


106  Assessment of Head and Neck Cancer During Radiotherapy with Diffusion Weighted MRI: Comparing the Use of Different b Values
Z. Chang*, F. Yin*, O. Craciunescu*, S. Das*, D. Yoo*, J. Hoang*, D. Brizel*, 1Duke University, Durham, NC

Purpose/Objective(s): Our purpose was to study the utility of diffusion weighted imaging (DWI) in the radiotherapy of head and neck (HN) cancer by assessing the multiple b values and its intrinsic temporal variability. Materials/Methods: In this study, 16 patients with HN cancer were enrolled. The prescription dose received by the patients is 70Gy. Patients were scanned with MRI about 2-week and 1-week prior to radiation treatment (RT) and one week following the start of RT. The first two scans were used to determine intrinsic temporal variability of apparent diffusion coefficient (ADC), and the last was used to calculate changes of ADC after RT. All MRI scans including DWI were acquired on a 1.5T GE scanner. DWI scans were acquired axially using a spin-echo echo-planar imaging sequence. Diffusion-sensitized gradient encoding with 4 different diffusion weighting factors of b = 250, 500, 750, and 1,000 s/mm², and one set of images without diffusion-sensitized gradient encoding (e.g. b = 0 s/mm²) were acquired. ADC maps were calculated for different b values, and a least-square-error (LSE) ADC map was also calculated by combining all the data. Volume of interest (VOI) was defined at primary tumor center to obtain optimal SNR. Descriptive statistics of relative regional ADC denoted as rADC was obtained for VOI. The Wilcoxon signed-rank test was used to assess the differences. Pearson’s product moment correlation analysis was used to test the correlation using r. Statistical significance was considered at p < 0.05. Results: Intrinsic temporal variations of rADC were assessed by different b values: 0.99 ± 0.03 (p = 0.68), 0.97 ± 0.04 (p = 0.96), 1.00 ± 0.03 (p = 0.78), 1.01 ± 0.04 (p = 0.86) and 0.99 ± 0.02 (p = 0.81), respectively for b = 250, 500, 750, 1000 s/mm² and the LSE solution. The effects of radiation in tumor were assessed by changes in rADC. After one week of RT, rADC increased about 17±9% (p = 0.06), 12±10% (p = 0.08), 13±5% (p = 0.05), 18±10% (p = 0.02), and 15±9% (p = 0.02) for b = 250, 500, 750, 1000 s/mm² and LSE solution. The rADC correlation between different b values and the LSE solution was also measured. The corresponding parameter r was 0.52 (p = 0.04), 0.82 (p < 0.01), 0.61 (p = 0.02), and 0.35 (p = 0.18) for b = 250, 500, 750, and 1000 s/mm². After one week of RT, the parameter r was 0.98 (p < 0.01), 0.96 (p < 0.01), 0.95 (p < 0.01), and 0.92 (p < 0.01) for b = 250, 500, 750, and 1000 s/mm². Conclusions: In this study, DWI data indicated non-statistically significant differences between intrinsic temporal variations of rADC and statistically significant changes of rADC after one week of RT. The LSE solution of rADC was statistically superior and all b values correlated well with the LSE solution. When multiple b-values data are unavailable, b = 1000 s/mm² may be recommended due to its better consistency with the LSE solution.


107  Genetic Sequence Variants in Relation to Acute and Late Toxicities in Patients with Head and Neck Cancer Treated with Radiation Therapy
F. Meyer1*, I. Bairati1*, W. Xu1*, A. K. Azad2*, G. Liu3*, 1Laval University, Quebec, QC, Canada, 2Princess Margaret Hospital, Toronto, ON, Canada

Purpose/Objective(s): Genetic variation may partly explain differences in normal tissue toxicities after radiation therapy (RT); yet no clear picture has emerged from RT toxicity studies of common genetic sequence variants (GSV) in candidate genes. In a large cohort of patients with
head and neck cancer (HNC) treated with RT, we assessed whether 8 GSV, systematically selected from published sources, predicted acute or late RT toxicity. TP53 rs1042522; ERCC4 rs1799801; ERCC2 rs1799793; ERCC2 rs13181; XRCC1 rs25487; XRCC3 rs861539; GSTM1 deletion; GSTT1 deletion. **Materials/Methods:** In a secondary analysis of a randomized trial of vitamin E supplementation in 540 stage I-II HNC patients treated with RT, RT toxicities were assessed using RTOG Acute Radiation Morbidity Criteria (during RT, 1 month after RT) and RTOG/EORTC Late Radiation Morbidity Scoring Scheme (at 6, 12 months after RT). The most severe time and tissue-specific RT toxicity, graded 0-4, was taken as an overall measure of acute/late toxicity. All 8 GSV were genotyped from blood leukocyte derived DNA. Ordinal logistic regression estimated odds ratios (OR) and 95% confidence intervals (CI) for toxicity, adjusted for known toxicity predictors in multivariate models. The false discovery rate (FDR) due to multiple testing was taken into account. **Results:** As crude and adjusted ORs associated with GSV were similar, we controlled for FDR by adjusting the p-values associated with the crude ORs. For late toxicity, no statistically significant association was observed with any of the 8 GSV. For acute toxicity, one statistically significant association was observed: The OR of acute toxicity was 1.43 (CI: 1.11-1.85) for the XRCC3 rs861539 (Thr241Met). XRCC3 (X-Ray repair, complementing defective, in Chinese Hamster 3) is part of a BRCA2-FANCDD2-FANCG complex that promotes homologous recombination and interacts with rad51. **Conclusions:** In our study, the rare allele of XRCC3 rs861539 was associated with increased acute RT toxicity, but not late toxicity. Previous studies of this SNP only assessed late toxicity, fibrosis or telangiectasia, with no clear results. Though results are promising, our study also underlines the limitations of the candidate gene approach to identify GSV that could predict RT toxicities.


### 108 Gene Expression Changes in Oral Mucosa in Association with Oral Mucositis in Patients Undergoing Radiation Therapy for Head and Neck Cancer


**Purpose/Objective(s):** Oral mucositis due to head and neck radiation therapy (RT) can significantly diminish quality of life and compromise treatment outcome. Although a complex process, inflammation is likely a major component in its pathogenesis. This pilot study aims to measure gene expression changes in the oral mucosa throughout the course of RT, secondary to mucositis. The goal is to establish potential markers of activity for future studies of potential radioprotectants.

**Materials/Methods:** This was an IRB approved study performed at the University of Pennsylvania. Oral swabs were obtained on five patients undergoing chemoradiation for cancers of the oral cavity or oropharynx. Samples were obtained at baseline prior to starting RT, and weekly throughout the course of RT. Two samples were collected weekly: one from an area receiving high-dose RT, and the other (control) from an area receiving little to no dose. Using real-time reverse transcription polymerase chain reaction (qRT-PCR), the kinetics of gene expression related to anti-inflammatory and inflammatory pathways were determined. Specific genes analyzed included: tumor necrosis factor α (TNF-α), heme oxygenase 1 (HO-1), NADPH dehydrogenase quinone 1 (NQO-1), and the cytokines interleukin 1α (IL-1α), interleukin 1β (IL-1β), and interleukin 6 (IL-6). Data was analyzed using the ΔΔCt method.

**Results:** Gene expression assays revealed marked changes in expression over the duration of the RT course. By the end of the RT course, there was significant (p<0.05) upregulation in IL-1α, TNF-α, and NQO-1 while expression of HO-1 was variable. Expression levels as compared to baseline, pre-treatment controls ranged from several fold in TNF-α, to several hundred fold as in IL-1β and several thousand-fold as in NQO-1. Gene expression from the control site also increased over time to levels comparable to the areas receiving high-dose RT. **Conclusions:** The findings demonstrate the feasibility of this technique in the development of biologic surrogates for radiation-induced mucositis. Study accrual remains ongoing with this methodology used for the evaluation of potential radiation mucosal protectants.

**Author Disclosure Block:** A. Lin: None. E. Andersen: None. R. Pietrofesa: None. J. Sun: None. H. Quon: None. M. Christofidou-Solomidou: None.

### 109 Principle Component Analysis (PCA) of Potential Biomarkers in Patients with Head and Neck Cancer


**Purpose/Objective(s):** The biologic behavior and prognosis associated with head and neck cancer differs by tumor site; underlying reasons for this remain unclear. As more biomarkers are discovered, methods for characterizing combinations of markers are likely to reflect differences in tumor behavior better than single markers or clinical variables alone. Combinations of markers may be useful for risk assessment and personalized treatment planning. PCA can be a useful technique to find combinations of markers. The impact of each biomarker within a principal component (PC) affords interpretability of PCs as constructs and PCs can be tested for prognostic significance. To explore if combinations of markers generated from PCA can reflect differences in prognosis, we studied 163 patients with Stage III/IV laryngeal or oropharyngeal cancer enrolled in two nearly identical Phase II clinical trials of induction chemotherapy (IC) followed by concurrent chemoradiation.

**Materials/Methods:** Pretreatment correlative tumor biomarkers and measures of immune reactivity were assessed. Bcl2, cyclinD1, EGFR, BclxL, PCNA, survivin, and p53 expression were quantified on Tissue Microarrays by immunohistochemistry. Immune reactivity was captured by proportion of cd8, cd4, cd3, and ratio cd4/cd8 cells in the peripheral blood by flow cytometry. Treatment approach and eligibility criteria were similar for both trials; patients differed only by tumor site, oropharynx (N=66) and larynx (n=97). A PCA of all biomarkers followed by multivariable regression identified PCs predictive of response to IC, overall survival (OS), and disease specific survival (DSS). Importance of specific components was confirmed by multivariable Cox modeling and prioritized using a backward selection algorithm. The coefficient weights of markers in important PCs were used as a tool for identifying which biomarkers contribute to prognosis in the multivariable setting.

**Results:** PCA identified 6 independent PCs accounting for over 80% of variability in the biomarkers. Univariate regression resulted in confirmation of the prognostic ability of stage. Multivariable analysis identified several PCs with prognostic value for IC response, OS and DSS after controlling for stage and HPV status. Interestingly, the effect differed significantly across tumor site for two of three prognostic PCs. The coefficients of one PC with differential effect across disease site suggest that it represents immune reactivity. One PC had prognostic value regardless of disease site. **Conclusions:** Principal component regression, and similar methods, may be useful statistical tools to integrate...
Changes in Serologic Levels of Antibodies to HPV 16 Proteins with Therapy Over Time: A Preliminary Assessment

M. Posner*, J. Wong*, G. Dsouza**, R. I. Haddad**, K. S. Anderson*, 1, Mount Sinai School of Medicine, New York, NY, Dana-Farber Cancer Institute, Boston, MA, 2 Johns Hopkins University Medical Center, Baltimore, MD, 3 The Biodesign Institute, Tempe, AZ

Purpose/Objective(s): Human Papillomavirus (HPV) type 16 is associated with the majority of oropharyngeal carcinomas (OPC) identified in the United States today. Specific antibodies (Abs) to four of 6 HPV16 early antigens (EA) - E1, E2 fragments (N and C), E6, and E7 - are readily detected in HPV16OPC patient sera but not in normal controls or partners of HPV16OPC. Changes in Abs levels may be a useful predictive and prognostic marker for response and recurrence in patients with HPV16OPC. Materials/Methods: Serum samples were obtained prior to and at 5 months as well as later time points of treatment from nine untreated patients with OPC in the HOTSPOT cohort study. Abs to all 6 HPV16 EA and 2 capsid proteins were quantified using a novel multiplexed bead assay, with HPV16-specific C-terminal GST fusion proteins captured onto LumineX beads. Antibodies to p21-GST served as a negative control and reference standard for calculation of the specific median fluorescent index (MFI) as described (Anderson et al, BJC, 2011). Individual sera were compared over time by the Paired-Wilcoxon test. Results: Six of the 9 OPC patients with paired samples at 5 months had HPV 16+ tumors. One case each was HPV33 and 35 positive and one case was HPV negative. The ratios of MFI to p21-GST for all 4 HPV16 EA and for L1 and L2 capsid proteins decreased at 5 months after treatment; paired changes in MFI ratio from baseline to the 5 month time point for E1 (48 vs. 22), E2N (36 vs. 13), L1 (3 vs. 1) and L2 (4 vs. 1) for all cases were significant (p = .03 for all comparisons). Paired changes in MFI for control antibodies to C and to N terminal EBNA-1 protein, a viral control, were not significant in the same samples. Conclusions: Patients with HPV16 OPC have detectable Abs to E1, E2 fragments, E6 and E7 proteins which are potential biomarkers for HPV16 OPC. Preliminary data in this small number of patients early in their treatment indicate that Ab activity may decrease significantly as a result of treatment. As additional patients on HOTSPOT are prospectively collected, treatment and long-term outcomes results will be determined providing additional data to understand biology and quantify the prognostic and predictive power of Abs in this disease.


Characterizing Clonal Evolution in Pleomorphic Sarcoma - Case Study

P. Kurywchak*, I. Cherni*, S. Arora*, E. Lenkiewicz*, L. Evers*, T. Holley*, M. Barrett*, G. Weiss*1, 2, TGen, Phoenix, AZ, 2Virginia G Piper Cancer Center Clinical Trials at Scottsdale Healthcare, Scottsdale, AZ

Purpose/Objective(s): Sarcomas are rare, malignant tumors that mostly occur in Caucasians > age 50 and make up <1% of cancers in the United States. Within the two main categories of sarcoma, soft tissue (STS) and bone, 80% of sarcomas begin in soft tissues, with up to 15% originating in head and neck regions. Clinically, sarcomas pose unique challenges due to poorly understood oncopathologies and over 50 described subtypes. This study investigates pleomorphic sarcoma with spindle cell morphology originating in the left maxillary sinus and the changes in the genetic landscape of one patient over the course of his disease. Materials/Methods: Archival tissue from the two successive debulking procedures in the left maxillary sinus and one needle biopsy from the left gluteal mass were obtained from Scottsdale Healthcare hospital. 50 μm formalin-fixed, paraffin-embedded (FFPE) scrolls were sent for flow-sort analysis based on ploidy of the contained cell population. Isolated aneuploid DNA from tumor was then analyzed against isolated diploid DNA from the same sample using comparative array genomic hybridization (aCGH). Semi-quantitative PCR was subsequently used to validate selected targets using primers specific to the amplified/deleted regions across all three collected tumor samples. Results: A 33 year-old male presented with a large pleomorphic sarcoma in left maxillary sinus and underwent a debulking procedure followed by radiation therapy. Three months later, the patient showed signs of local disease progression extending through the left maxillary sinus and underwent second debulking procedure. Fifteen months later, metastatic disease to the left gluteal region was confirmed. Seven targets were identified in the original debulked sarcoma tissue using aCGH: (3 were amplified) and (4 were deleted) based on known relevance to cancer and substantial ploidy differences compared to normal conditions. Interestingly, one major deletion was found in the sample from the second debulking procedure that was not present in the initial debulked tumor. A putative tumor suppressor gene, PAX7, previously linked to childhood alveolar rhabdomyosarcoma, was mapped to this region. From the eight identified targets, three deleted targets were successfully validated using qPCR (CDKN2A, HHAT, TRPC5) with total DNA as the template. Conclusions: Although we cannot exclude the possibility of PAX7 gene being deleted as a result of post-operative radiation treatment, our preliminary results reveal evidence consistent with clonal evolution of tumor cells which could account for rapid disease progression observed in this patient. Identification of potential druggable targets is instrumental to this study and could bare clinical significance in the future. (Support from: IBIS Foundation of Arizona and the Scottsdale Healthcare Foundation).


Criteria for Defining a Significant Intratreatment Metabolic Response to Chemoradiation on FDG-PET for Head and Neck Cancer

J. Hoang*, S. K. Das*, D. S. Yoo*, D. M. Brizel*, Duke University Medical Center, Durham, NC

Purpose/Objective(s): To use FDG-PET to measure the intrinsic variability of glucose metabolism in head and neck cancer (HNC) and to compare it to early treatment changes. Materials/Methods: 17 subjects with AJCC stages III-IVa HNC received 2 baseline PET-CT scans 1 week apart and a 3rd scan after 1-2 weeks of chemoradiation. All 3 studies were performed in the same PET-CT scanner. A radiologist manually traced volumes for the primary tumor and 2 largest nodal metastases to determine SUVmax and SUVmean (manSUV). Automated measurements of SUV (autoSUV) were also obtained from the planning CT based on the gross tumor volumes for the primary tumor and lymph nodes (LN). SUV
repeatability was evaluated with intraclass correlation coefficient (ICC). The percentage changes in metabolic activity on the 2 baseline PETs and changes on the intratreatment PET were compared with the paired t-test. Results: 16 patients had double baseline scans (median interval 10 days, interquartile range 7-13.5) and 15 patients had intratreatment scans (median interval 13 days, interquartile range 12-17). The median radiation dose at the time of the intratreatment scan was 12 Gy (interquartile range 10-14). Mean baseline manSUVmax, manSUVmean, autoSUVmax, autoSUVmean were 14.2, 8.4, 14.5 and 6.1, respectively for the primary tumor; and 10.5, 6.4, 10.8, and 4.6, respectively for LN. All baseline SUV values had excellent repeatability (ICC ≥ 0.90). SUVmean had the smallest absolute baseline variability for both primary tumor and LN: 0.62-0.92 on manSUVmean and 0.35-0.73 autoSUVmean. For the primary tumor, percentage differences in baseline manSUVmax, manSUVmean, autoSUVmax, autoSUVmean were 11, 10, 10 and 13%, respectively, compared to intratreatment percentage differences of 15, 10, 12 and 16%, respectively. Treatment-induced changes were not significantly different from baseline variability (p > 0.4). For LN, percentage differences in baseline manSUVmax, manSUVmean, autoSUVmax, autoSUVmean were 10, 10, 9 and 8%, respectively, compared to intratreatment percentage differences of 19, 17, 12 and 22%, respectively. Treatment-induced changes were significantly greater than baseline variability for manSUVmean, manSUVmax and autoSUVmean (p < 0.05), but not for autoSUVmax (p = 0.4). The 95% confidence normal range for percentage baseline variability in LN manSUVmax and autoSUVmean were 10 ± 16% and 8 ± 15%, respectively. Conclusions: Intrinsic variability in HNC glucose metabolism is less than treatment-induced change for LN but not the primary. SUVmean was the best parameter for evaluating repeatability and treatment induced change. A significant metabolic response early in treatment can be defined as a decrease in SUVmean outside the 95% normal range for baseline variability (>23-26%).

Author Disclosure Block: J. Hoang: B. Research Grant; General Electric. S.K. Das: None. D.S. Yoo: None. D.M. Brizel: None.

113  Hypopharyngeal Cancer in the USA: Population-Based Study of 8.456 Patients Over 3 Decades
H. Zhang*, R. Chen*, O. Hyrien*, M. Milano*, Y. Chen*, University of Rochester Medical Center, Rochester, NY

Purpose/Objective(s): Hypopharyngeal cancer consists of carcinoma of pyriform sinus, postcricoid area, and posterior pharyngeal wall. It is relatively uncommon compared with head and neck cancers of other subsites. Our understanding of hypopharyngeal cancer has been based on published studies with mostly limited patient numbers. We therefore conducted a large population-based study to evaluate the demographics and outcome over more than 3 decades among patients reported to the Surveillance, Epidemiology, and End Results (SEER) program.

Materials/Methods: The SEER database on hypopharyngeal cancer from 1973 to 2008 was analyzed. Patient demographics, cancer stages, estimated 5-year overall survival (OS), and cause-specific survival (CSS) were analyzed. Results: Pyriform sinus carcinoma was the most common hypopharyngeal cancer, consisting of 66.2% of all hypopharyngeal cancer cases. Carcinoma of postcricoid, posterior pharyngeal wall and overlapping area consisted of 2.5%, 7.3% and 3.2% of cases respectively, while carcinoma of unspecified hypopharynx subsites consisted of 20.8% of cases. The ratio of male to female patients was greater (p<0.001) for cancers of pyriform sinus (4.3 : 1) than postcricoid (2.1 : 1), posterior pharyngeal wall (2.7 : 1), or overlapping region (2.8 : 1). More patients with pyriform sinus cancer (68.0%) presented with regional disease vs. localized disease, when compared with cancer of postcricoid (57.6%), posterior pharyngeal wall (52.7%), or overlapping area (64.8%) (p<0.001). The percentage of postcricoid cancers occurring in black patients (21.0%) was greater than with pyriform sinus (15.6%), posterior pharyngeal wall (13.2%) or overlapping area (12.4%) cancers (p<0.001). The estimated 5-year OS and CSS were 38.3% and 54.8% for localized disease vs. 24.5% and 36.6% for regional hypopharyngeal cancer. For localized cancers, postcricoid carcinoma had the worst outcome (OS: 40.1% of pyriform sinus, 12.5% of postcricoid, 38.2% of posterior pharyngeal wall and 58.1% of overlapping area; CSS: 56.4% of pyriform sinus, 36.6% of postcricoid, 54.1% of posterior pharyngeal wall, and 61.1% of overlapping area). Treatment information revealed increasing usage of radiation from 1993 to 2008 in managing regional disease of pyriform sinus carcinoma (p<0.001). Conclusions: The population-based evaluation of hypopharyngeal cancer showed poor survival outcome in general and worse for carcinoma of postcricoid area. Analyses of additional information to evaluate impact of patient demographics, cancer characteristics, and treatment modalities on hypopharyngeal cancer outcome over the 3-decade time may reveal useful information to improve on therapy of hypopharyngeal cancer.

Author Disclosure Block: H. Zhang: None. R. Chen: None. O. Hyrien: None. M. Milano: None. Y. Chen: None.

114  Prognostic Model for Metastatic Nasopharyngeal Carcinoma
A. Bensalem*, A. AMMARI**, A. BENMERZOUK**, K. BOUZID**, CHU DR BENBADIS, Université Mentouri, Algeria, EHS Pierre & Marie Curie, Algiers, Algeria

Purpose/Objective(s): Nasopharyngeal carcinoma (NPC) of the undifferentiated type is known for a more aggressive systemic behavior compared to squamous cell head and neck cancer in general. However, patients(pts) with distant metastases are a heterogeneous group and vary significantly in survival outcome. Materials/Methods: We set out to define the factors of prognostic importance in 120 pts with metastatic NPC. Factors that were considered for inclusion included pt factors (age group, gender, performance status at diagnosis of metastatic disease) and disease factors (number of metastatic sites, specific metastatic sites, disease-free interval, presence of locoregional recurrence). Results: The following factors were found to be independently significant: poor performance status of > ECOG 2 (4), short disease-free interval of < 6 mths (4), presence of liver metastases (2), presence of lung metastases (2) and presence of metastases at initial diagnosis (1).Pts with complete data for the above factors are divided into 3 prognostic groups based on the total score: good prognosis (0 to 6): 55 pts; intermediate prognosis (7 to 10): 21 pts; poor prognosis (>11): 24 pts. The median survival for these groups is 21.5, 12, and 5.8 months respectively. Conclusions: This prognostic model that makes use of easily available information pertaining to patient factors and disease factors may prove useful as a method for risk assessment and stratification of pts with metastatic NPC. This model may be of use in the conduct of clinical trials and the interpretation of treatment studies in metastatic NPC.

Author Disclosure Block: A. Bensalem: None. A. Ammari: None. A. Benmerzouk: None. K. Bouzid: None.
Purpose/Objective(s): To measure the intrinsic pretreatment variability of apparent diffusion coefficient (ADC) in head and neck cancer (HNC) and to compare it to early treatment changes. **Materials/Methods:** 17 subjects with AJCC stages III-IVA HNC received 2 baseline MRI scans 1 week apart and a 3 scan after 1-2 weeks of chemoradiation. MRI scans were acquired on a 1.5T clinical scanner using a 4-channel flexible phase array coil. Diffusion weighted (DWI) scans were acquired in the axial plane using a spin-echo echo-planar imaging sequence and diffusion weighting factor of 1000 mm²/s. On the ADC maps, regions of interest (ROI) were drawn around the primary tumor and up to two lymph nodes in each patient on a patient section containing the largest axial diameter. Lesions with significant artifact from bone, air or metallic hardware were excluded. Baseline ADC repeatability was evaluated with intraclass correlation coefficient (ICC). Changes on the double baseline MRI scans and changes on the intratreatment MRI scan (respectively to the average of 2 baseline MRIs) were compared with the paired t-test.

**Results:** 16 patients had diagnostic quality double baseline scans (median interval 8 days, interquartile range 7-8) and 15 patients had intratreatment scans (median interval 13 days, interquartile range 12-19). The median radiation dose at the time of the intratreatment scan was 12 Gy (interquartile range 6-9). ADC values could be measured in 28 lesions (5 primary lesions, 23 nodes) of which 24 lesions had an intratreatment scan. The mean baseline ADC was 1.152 x 10⁻³ mm²/s (sd 0.242). The two baseline ADC values had excellent repeatability (ICC = 0.86). The mean baseline differences in ADC were 0.088 x 10⁻³ mm²/s (sd 0.097) or 7.3% (sd 6.9). The 95% confidence normal range for baseline variability in ADC was -0.106 to 0.282 x 10⁻³ mm²/s or percentage change by -7 to 21%. The intratreatment differences compared to the average of two baseline studies was 0.335 x 10⁻³ mm²/s (sd 0.261) or 31.1% (sd 25.7). Treatment-induced changes were significantly greater than baseline variability (p<0.0003). **Conclusions:** Intrinsic variability in HNC ADC is less than treatment-induced change. A significant metabolic response early in treatment can be defined as an increase in ADC outside the 95% normal range for baseline variability (> 21%).

**Author Disclosure Block:** J. Hoang: B. Research Grant; General Electric. D.S. Yoo: None. S.K. Das: None. J. Chang: None. O. Craciunescu: None. D.M. Brizel: None.
was performed using the Pubmed database. Lesions arising in a pediatric population in areas where this cultural practice is commonplace. Finally, we aim to describe tumors occurring in children have previously been reported in the literature. However, we have treated a 12 year old girl who presented with a SCC of the tongue tip arising in a lymphangioma. She also chewed betel nut with slaked lime, which is the common practice in Papua New Guinea, therefore relevant to understanding the diverse characteristics exhibited by these tumors. The tumor registry from a tertiary care cancer center was reviewed from 1998-2011. Results: Four cases of axillary node metastasis in patients with head and neck cancer were identified. The patient population includes a patient who developed a second primary and axillary node metastasis 23 years after his initial treatment for head and neck cancer as well as the only reported case of axillary metastases from a head and neck squamous cell carcinoma skin primary. All patients received chemotherapy and radiation in addition to surgery to treat their initial disease. Currently, 2 out of 4 patients are alive, one without evidence of disease following axillary node dissection and one alive with disease. Analysis of the presentations and treatment outcomes is reviewed and a review of the literature is presented in an effort to add to the literature and aid clinicians in identifying patients that may be at high risk of developing axillary metastases. Conclusions: Axillary node metastasis is a rare sequela of head and neck cancer. This can be secondary to tumor blockage at the jugulo-subclavian junction and/or fibrosis of the cervical lymphatics following surgery or radiation therapy resulting in retrograde lymphatic flow. Clinicians should be aware of this potential complication of head and neck cancer.

**Author Disclosure Block:** None. J.D. Deeken: None. K.W. Harter: None. B.J. Davidson: None. K.A. Newkirk: None.

**118** Axillary Node Metastasis In Head And Neck Cancer

R. Comstock*, J. D. Deeken*, K. W. Harter*, B. J. Davidson*, K. A. Newkirk*, , Georgetown University, Washington, DC

**Purpose/Objective(s):** Axillary lymph node metastasis in head and neck cancer is a rare event and few occurrences have been reported in the literature. Alterations in cervical lymphatic flow of the head and neck are believed to play a part in the development of axillary node metastasis.

**Materials/Methods:** The tumor registry from a tertiary care cancer center was reviewed from 1998-2011. Results: Four cases of axillary node metastasis in patients with head and neck cancer were identified. The patient population includes a patient who developed a second primary and axillary node metastasis 23 years after his initial treatment for head and neck cancer as well as the only reported case of axillary metastases from a head and neck squamous cell carcinoma skin primary. All patients received chemotherapy and radiation in addition to surgery to treat their initial disease. Currently, 2 out of 4 patients are alive, one without evidence of disease following axillary node dissection and one alive with disease. Analysis of the presentations and treatment outcomes is reviewed and a review of the literature is presented in an effort to add to the literature and aid clinicians in identifying patients that may be at high risk of developing axillary metastases. Conclusions: Axillary node metastasis is a rare sequela of head and neck cancer. This can be secondary to tumor blockage at the jugulo-subclavian junction and/or fibrosis of the cervical lymphatics following surgery or radiation therapy resulting in retrograde lymphatic flow. Clinicians should be aware of this potential complication of head and neck cancer.

**Author Disclosure Block:** None. J.D. Deeken: None. K.W. Harter: None. B.J. Davidson: None. K.A. Newkirk: None.

**119** Clinico-pathological Study of Salivary Gland Tumors in Ilorin, Nigeria


**Purpose/Objective(s):** Salivary gland tumors comprise less than 3% of all tumors of head and neck with 60 to 80% affecting the parotid glands. This study is a retrospective clinic-pathological review of salivary gland tumors in Ilorin, north central, Nigeria. **Materials/Methods:** This was a retrospective review of all patients seen at ENT and surgical outpatient clinics of the University of Ilorin Teaching Hospital with salivary gland tumor between 2001 and 2010. The patient’s biodata, anatomical locations and histopathological findings of the tumours are presented. The histopathological diagnosis was in accordance with the 1991 WHO classification of salivary gland tumours. All the information retrieved were entered into EPI Info and analyzed descriptively and results presented in tables and figures. **Result:** A total of 56 patients were seen with 24males and 32females (M:F ratio 1:0.8), with the peak age of 21-30years in males and 31-40 among the females The mean age is 38.62yrs (SD = 18.4±2.5). Painless swelling was the commonest presentation and was present in 99% cases. 36 cases were located in the parotid region, 18 were in the submandibular, 12 were in the submandibular and the parotid glands, followed by mucoepidermoid. 24 were benign tumors while 18 were malignant tumors, 14 were infective/ inflammatory. Benign tumors were common in 3rd & 4th decades while as malignant tumors were more common in 5th & 6th decades of life being the commonest and malignant variants in the 5th to 6th decades of life. The data presented here corroborate a number of previous studies and are therefore relevant to understanding the diverse characteristics exhibited by these tumors.

Key: Salivary gland; painless mass; Parotid; Pleomorphic adenoma; Clinico-pathological


**120** Pediatric Squamous Cell Carcinomas of the Tongue: A Rare, but Real and Relevant Problem

S. Yang*, R. Lewandowski*, Mater Children’s Hospital, Brisbane, Australia

**Purpose/Objective(s):** Intra-oral squamous cell carcinomas (SCC) in the pediatric population are an extremely rare entity. Only 6 cases occurring in children have previously been reported in the literature. However, we have treated a 12 year old girl who presented with a SCC of the tongue tip arising in a lymphangioma. She also chewed betel nut with slaked lime, which is the common practice in Papua New Guinea, where she is from. Our aims are to describe this case, which is extremely rare in Westernised societies, and to review the literature regarding pediatric intra-oral SCC. Given the known carcinogenic effect of slaked lime with betel nut chewing, we also investigate the incidence of these lesions arising in a pediatric population in areas where this cultural practice is commonplace. Finally, we aim to describe the association of intra-oral SCCs with lymphangiomas.

**Materials/Methods:** We report our case and describe the histopathology of the lesion. A literature review was performed using the Pubmed database. **Results:** Our patient is only the 7th pediatric case to be reported in the literature. However, to the best of our knowledge, a tongue SCC has never been described as arising in a lymphangioma. Additionally, little has been written about betel
nut chewing in the pediatric population and the subsequent consequences of such a practice. **Conclusions:** Our 12 year old girl presents with a very unusual and interesting entity for a pediatric demographic. The pre-operative assessments lead us to initially believe that her pathology was benign. It is unclear as to whether the major contributing pathogenic factor for the SCC is related to the topical application of known carcinogens such as betel nut and slaked lime, or as a result of the lymphangioma. A marjolin’s ulcer-type phenomenon may be relevant in this circumstance. Additionally, a viral aetiology may be contributory to the SCC. While this is a very rare condition for this demographic, clinicians need to be cognisant of pediatric intra-oral malignancies, as they can easily be misdiagnosed as being clinically benign. This is particularly relevant for those working in areas where betel nut and slaked lime chewing is endemic or for organisations, such as ours, which perform a significant number of aid missions in developing nations where this practice is common.

**Author Disclosure Block:** S. Yang: None. R. Lewandowski: None.

121 **Sinonasal Fibrous Osseous Tumors Presenting with Neurological Sequelae**

K. Newkirk*, W. Jean*, Medstar-Georgetown University Hospital, Washington, DC

**Purpose/Objectives:** Sinonasal fibrous osseous tumors are rare tumors of the head and neck. In most cases of sinonasal fibrous osseous tumors, patients present with symptoms suggestive of sinusitis. Neurological sequelae are rare presentations of these tumors. We presented our experience with sinonasal fibrous tumors presenting with neurological sequelae.

**Materials/Methods:** The tumor registry at a tertiary medical center is reviewed. Two cases of fibrous osseous tumors presenting with meningitis and seizures are presented. **Results:** The first patient was found to have a fronto-ethmoid sinus fibrous osseous tumor after presenting with Streptococcus pneumoniae meningitis. The second patient was found to have a fronto-oral, ethmoid fibrous osseous tumor after presenting with seizures. The clinical presentations and surgical management (including endoscopic and open approaches) are reviewed. A brief review of the clinical presentation, radiographic appearance, diagnosis and management of sinonasal fibro-osseous tumors is provided. **Conclusions:** Sinonasal fibrous osseous tumors are rare tumors of the paranasal sinuses. Surgical approaches, including endoscopic techniques, are appropriate management options for patients presenting neurological sequelae.

**Author Disclosure Block:** K. Newkirk: None. W. Jean: None.

122 **Pilot Study of Functional Infrared Imaging for Early Detection of Mucositis in Locally Advanced Head and Neck Cancer Treated With Chemoradiotherapy**

E. Cohen*, M. Kocherginsky*, G. Shustakova*, J. Salama*, E. Kistner-Griffin*, V. Yefremenko*, V. Novosad*, 1University of Chicago, Chicago, IL, 2Verkin Institute for Low Temperature Physics & Engineering, Kharkiv, Ukraine, 3Duke University Medical Center, Durham, NC, 4Medical University of South Carolina, Charleston, SC, 5Argonne National Laboratory, Argonne, IL

**Purpose/Objectives:** Mucositis, and its clinical sequelae, are consistently reported as the most clinically significant acute toxicity in the treatment of locally advanced squamous cell carcinoma of the head and neck (LA-SCCHN) with chemoradiotherapy. Inter-patient variability in mucositis is accounted for by radiotherapy dosing, fractionation, and volumes but even within the same treatment regimen, there appears differences in normal tissue tolerance. Radiotherapy associated mucositis manifests initially as erythematous areas in the treatment field. These phenotypic changes are accompanied by an intense inflammatory response histologically. We hypothesized that patients destined to display severe mucocutaneous toxicity will demonstrate greater alterations in thermal intensity early in therapy than identically treated counterparts. Detection of these early changes using sensitive thermal imaging technology would allow identification of patients that will require more intensive supportive care.

**Materials/Methods:** Subjects with LA-SCCHN (oral cavity or oropharynx) being treated with the identical chemoradiotherapy regimen underwent baseline and weekly thermal imaging. Changes in temperature of oral mucous membranes compared with a reference area (ΔT) were calculated and correlated to grade of mucositis based on NCI-CTCAE 3.0. In addition, quality of life measured by the Performance Status Scale for Head and Neck Cancer (PSS-HN), weight loss, and need for feeding tube were recorded. **Results:** Thirty-four subjects were enrolled. Grade 3 mucositis and dermatitis was observed in 53% and 21%, respectively. All subjects displayed an increase in temperature within the radiation field. We observed a statistically significant positive association between an early rise in ΔT and mucositis grade (pvalue=0.03). For every 1°C increase in ΔT there was a 0.157 increase in average subsequent mucositis grade. **Conclusions:** Thermal imaging is able to detect small and early changes in temperature of mucosal surfaces that may be associated with development of mucositis in patients being treated with chemoradiotherapy. Larger studies with greater dynamic ranges in mucositis scoring are warranted to evaluate whether this tool can help predict which patients would be in need of early intervention to prevent acute complications.

**Author Disclosure Block:** E. Cohen: None. M. Kocherginsky: None. G. Shustakova: None. J. Salama: None. E. Kistner-Griffin: None. V. Yefremenko: None. V. Novosad: None.

123 **Health-related Quality of Life of Patients Three Years after Radiation Therapy for Early Head and Neck Cancer**

I. Bairati*, F. Meyer*, Laval University, Quebec, QC, Canada

**Purpose/Objectives:** Cancer survivors typically experience progressive improvements in health-related quality of life (HRQOL) following initial impairments associated with diagnosis and treatments. As previous studies often focused on cancer-free survivors (CFS), little information is available for non-CFS. We compared HRQOL of head and neck cancer (HNC) survivors either living with cancer or cancer-free 3 years after radiation therapy (RT). **Materials/Methods:** A randomized trial was conducted among 540 patients treated with RT for stage I or II HNC to test whether vitamin E supplementation improved outcomes. HRQOL was assessed prospectively prior treatment and 3 years after RT with two validated instruments, the EORTC QLQ-C30 and the Head and Neck Radiotherapy Questionnaire (HNRQ). The EORTC functional scales and global health status are scored 0 to 100 (100 for perfect functioning); the EORTC symptoms are scored ranged 0 to 100 (0 for no symptom); the HNRQ domains are scored 0 to 7 (7 for no symptom). Three years after RT, 416 patients provided HRQOL data. 85 were non-CFS because they
had been diagnosed with a relapse or a second primary cancer (SPC). T-tests were used to compare HRQOL dimensions at baseline and at 3 years between non-CFS and CFS, as well as their HRQOL changes from baseline to 3 years. Results: At baseline, the HRQOL of future non-CFS and CFS was similar except that future non-CFS experienced more HNRQ throat symptoms (5.7 versus 5.9, p=0.04). At 3 years, the HRQOL of non-CFS and CFS was also similar except that non-CFS had poorer QLQ-C30 global health status than CFS (91 versus 96, p=0.01). Most changes from baseline to 3 years after RT were similar for non-CFS and CFS. There were improvements for emotional and social functioning, sleep and financial difficulties of the QLQ-C30, throat symptoms and psychosocial domain of the HNRQ for both non-CFS and CFS. On the other hand, there were increased HNRQ oral cavity and skin symptoms for both non-CFS and CFS. Few HRQOL changes from baseline to 3 years differed significantly between non-CFS and CFS. Non-CFS experienced a worsening in 4 HRQOL dimensions while CFS showed improvements in these 4 dimensions: global health status (p<0.01), pain (p=0.01) and appetite (p=0.02) of the QLQ-C30 and HNRQ energy (p=0.03). Conclusions: Most changes in HRQOL over the 3 years following RT were similar for CFS and non-CFS. However, patients living with cancer after HNC relapse or SPC experienced increased pain and decreased appetite, global health status and energy while CFS showed improvement in these 4 dimensions.

Author Disclosure Block: None. F. Meyer: None.

124 Survivorship Care Plan Implementation for Head and Neck Cancer: An Alberta CancerBRIDGES Demonstration Project
J. Giese-Davis*1,2, J. McCormick*1,2, L. Shirt*1, L. Zhong*1,2, A. Waller*1,2, H. Lau*1, T.*2, L. Carlson*1,2, Alberta Health Services, Calgary, AB, Canada, University of Calgary, Calgary, AB, Canada

Purpose/Objective(s): The end of active treatment can be confusing for cancer survivors, with many reporting concerns over unanswered questions, and feelings of feelings of abandonment and uncertainty. This time can be especially difficult for head/neck patients who endure a difficult recovery period and lasting effects of treatment. In order to provide a higher level of continuity of care during this time of need, we conducted a study in which we developed and implemented care plans with head and neck cancer patients. We examined their immediate response to receiving this care plan and changes in distress over 6 months.

Materials/Methods: Our multidisciplinary team created this care plan by consensus among oncologists, physicians, psychologists, nurses, social workers, and patients. A nurse specialist created and delivered and individualized care plans for head and neck patients at the end of active treatment [surgery, chemotherapy, and radiation](n=21): 24% p16 positive; treatment = ChemOR (n=11), Surgery+RT (n=4), RT alone (n=1), Surgery alone (n=1); median age at diagnosis=58 years; Male=17. Care plans were also created and delivered to breast cancer patients (N=36) for comparison. The care plan went into the oncology record and we faxed copies to the patients’ family physicians. We assessed patient distress and satisfaction with, usefulness of, emotional impact of, and communication value of the care plans with the nurses, patients, and family physicians. Results: In both tumor groups, patients evaluated their care plans very positively (mean=32 out of 40 for overall satisfaction). We also compared the 6-month trajectory of anxiety and depression with a similar group of patients who had not received the care plan finding that the decrease in anxiety and depression was greater in the care plan group (CP: anxiety mean slope -0.32, SD = 0.46; UC: -0.12, SD = 0.52) (CP: depression mean slope -0.43, SD = 0.82; UC: 0.03, SD = 0.45). However, head/neck survivors rated the usefulness of the care plan significantly lower than the breast group. This is likely because the head/neck group were suffering physically much more at the end of treatment. Topics discussed during nurses and patients in care plan meetings were different between tumor groups. The breast group rated positive affect during the care plan meeting significantly higher than the head and neck group. Conclusions: Head and Neck patients rated the Care Plans as highly satisfactory, of good communication value, and had a positive reaction to receiving it. Over 6 months they decreased on depression and anxiety more than a usual care group. The lower rating of usefulness among head & neck vs. breast cancer patients may reflect the degree of physical symptoms they were experiencing at the point of delivery. Future directions will be discussed.

Author Disclosure Block: None. F. Meyer: None.

125 Interdisciplinary Rehabilitation Programs: Positive Experience from Two University Health Centers
M. Chasen*1, B. Gagnon*1, J. Murphy*1, R. Bhargava*1, N. MacDonald*1, Élisabeth Bruyère Research Institute, Ottawa, ON, Canada, McGill University, Montreal, QC, Canada

Purpose/Objective(s): Patients with head and neck cancer experience multiple physical and psychosocial challenges after initial therapy. The Palliative Rehabilitation programs in Ottawa and the McGill Cancer Nutrition Rehabilitation program in Montreal consist of an interdisciplinary team of professionals whose global objective is to empower individuals who are experiencing loss of function, fatigue, malnutrition, psychological distress, and other symptoms as a result of cancer or its treatment to improve their own quality of life. The aim of this study was to ascertain by subjective and objective measurements if a structured rehabilitation program can influence patients’ wellbeing.

Materials/Methods: Thiry eight patients completed an 8-week interdisciplinary rehabilitation program. Team members including physician, dietitian, physiotherapist, nurse, social worker and occupational therapist examined all patients. Questionnaires were completed prior to and after the intervention. These included: Edmonton Symptom Assessment Scale (ESAS), Distress Thermometer, MD Anderson Symptom Inventory (MDASI), Multidimensional Fatigue Inventory (MFI-20) and a 6 minute walk test. The 8 week program included a bi-weekly exercise program and fortnightly consultation with each team member. Results: There were 32 male and 6 female participants, the mean age was 56.5 years. Patients had squamous cell carcinoma of the following: 12 tongue, 9 tonsil, 4 nasopharynx, 4 larynx, 2 oropharynx, 2 parotid gland, 2 nostril, 1 hypopharynx. One had a chordoma and 1 unknown primary. Stages: I (n=2), II (n=8), III (n=14); IV (n=14). Upon program completion [11, mean]SD; 12 (mean) SD) improvement in the mean Six minute walk distance from [440±101]; 508±108 m (p<0.0001) was noted. Significant improvement was also seen in: distress [4.6 (2.6) ; 3.2 (2.4) (p<0.002)], anorexia [5.1 (3.3) ; 3.5 (2.7) (p<0.01)], shortness of breath [2.9 (2.9) ; 1.4 (1.8) (p<0.001)], depression [3.7 (2.6) ; 2.3 (2.1) (p<0.001), nervousness [3.5 (2.6) ; 2.5 (2.3) (p<0.025)], general activity [5.1 (2.8) ; 3.5 (2.9) .
Factors Associated with Quality of Life Decreases in Head and Neck Radiotherapy Patients

M. Ryan*, J. M. Holland*, C. R. Thomas*, E. K. Fromme*, 1Oregon Health & Science University School of Medicine, Portland, OR, 2Radiation Medicine, Knight Cancer Institute, Oregon Health & Science University, Portland, OR, 3Hematology/Oncology, Knight Cancer Institute, Oregon Health & Science University, Portland, OR

Purpose/Objective(s): Health related quality of life (QOL) is particularly important in the management of head and neck cancer (HNC) patients, where both the disease and the common treatment modalities are often debilitating. This study examined the main factors associated with QOL decreases in HNC radiotherapy (RT) patients. Materials/Methods: Eligible patients were treated with radiotherapy for HNC at OHSU between 2006 and 2008. Participants completed the Functional Assessment of Cancer Therapy - Head and Neck (FACT-H&N) pre- and post-treatment. Pre- and post-treatment scores were compared using the paired sample t-test and the effect of smoking status, surgical history, and chemotherapy on QOL was investigated using the independent sample t-test. Multivariate linear regression was used to evaluate the relationship between total dose, the mean dose to critical structures, and QOL. Results: Of the 160 HNC patients for whom records were available, 83 (59.7%) completed both pre- and post-treatment FACT-H&N surveys. Seventy-nine (95.2%) were male and 4 (4.8%) were female. The average age was 62.0 years. Patients’ QOL declined substantially over the course of treatment (104.7 to 77.3; p<0.001). This was mainly due to decreases in the physical (22.7 to 14.1; p<0.001), functional (16.6 to 11.5; p<0.001), and HNC specific subscales (27.3 to 14.3; p<0.001). The individual items with the greatest change were “I am able to eat as much food as I want” (2.58 to 0.57; p<0.001), “I am able to eat the foods that I like” (2.54 to 0.56; p<0.001), and “I can eat solid foods” (2.78 to 0.98; p<0.001). This decrease in QOL was independent of patients’ surgical history, chemotherapy status, and RT modality. Non-smokers had a higher pre-treatment QOL scores compared to smokers (109.3 vs. 96.0; p=0.01), but suffered a greater decline post-treatment (10.6-point difference; p=0.03). Linear regression analysis found no association between global QOL decrease and total dose, mean parotid dose, mean laryngeal dose, and mean esophageal dose. Mean mandible dose, however, did correlate with global QOL decrease (B=−0.6 QOL points/Gy; p<0.01). Conclusions: The lack of correlation between QOL score, total dose and the dose to critical structures may be because symptom and functional problems occur at doses lower than those typically encountered in the clinic. The correlation between mandible dose and global QOL decrease suggests that this structure may have a higher dose threshold for sequelae. While it is clear that HNC patients suffer significant treatment-related QOL decreases, identifying the main factors is difficult. Identifying the specific elements of QOL affected by RT may lead to better supportive care for HNC patients.

regarding dose to the post-operative bed and elective treatment of lymph nodal regions and neural pathways. We also compared the recommendations of the ROs with the 2010 NCCN guidelines. Materials/Methods: In March 2011, we contacted all radiation oncologists and trainees residing in the USA (n=3788) via their email address listed in the 2009 ASTRO membership directory. Our survey contained clinical vignettes involving M0h micrographically resected CSSC with microscopic PNI (mPNI) or clinical (symptomatic or radiographic) cPNI, including named nerve PNI (nPNI). For each vignette, physicians indicated if ART was appropriate and further specified the dose and volume to treat at standard fractionation. Chemotherapy was not allowed. We defined consensus as 80% concordance. Results: Among respondents (n=352), over 80% recommended ART for cPNI, whereas a mean of 59% recommended ART for mPNI. There was no consensus regarding dose to the operative bed. 30% of respondents would deliver less than 55 Gy at standard fractionation, while the NCCN guidelines recommend 60 Gy in 30 fractions. Only 24% were willing to deliver 66+Gy in cases of radiographically identified gross residual disease while the guidelines recommend treating gross disease to 66-74 Gy. In cases of mPNI, there was a consensus (86%) not to treat elective nodal volumes. Even in the presence of cPNI, only 40% recommend nodal irradiation. For mPNI, there was no consensus for elective neural pathway irradiation; whereas for cPNI a clear consensus (90%) emerged. Stratification based on years post residency (0-10 vs. 10+yrs) and case volume (0-7 vs. 8+ cases per year) did not yield any statistically significant differences. Conclusions: Our data suggests a lack of consensus among ROs regarding dose to the post-operative bed and designation of elective targets (i.e. nodal regions and neural pathways) for resected CSSC with PNI. In contrast to the NCCN guidelines, nearly 30% of ROs underdosed the post-operative bed. The vast majority of ROs omitted elective nodal irradiation even in cases of cPNI. More data is needed in this setting to guide ROs and achieve homogenous practice patterns.


129 3D Conformal Radiotherapy (3DCRT) vs. Image Guided Radiotherapy (IGRT) in Head and Neck Squamous Cell Carcinoma (HNSCC): Early Results of a Phase III Randomized Controlled Study

S. K. Mullapally*, B. K. Mohanty*, S. Bhaskar*, A. Sharma*, S. Thulkar*, A. Thakar*, R. M. Pandey*, G. K. Rath*, 1Department of Radiation Oncology, Institute of Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi, India, 2Department of Medical Oncology, Institute of Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi, India, 3Department of Radiology, Institute of Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi, India, 4Department of ENT, All India Institute of Medical Sciences, New Delhi, India, 5Department of Biostatistics, All India Institute of Medical Sciences, New Delhi, India

Purpose/Objective(s): To compare the early tumour response and acute radiation morbidities between 3Dimensional Conformal Radiotherapy(3DCRT) and Image Guided Radiotherapy(IGRT) in Head and Neck Squamous Cell Carcinoma(HNSCC). Materials/Methods: 41 patients of HNSCC (oropharynx, larynx, hypopharynx) were included in this study and were randomized into 3DCRT and IGRT arms after informed consent and clearance from institutional ethics committee. The treatment plan was radical radiotherapy (RT) or Chemoradiation (CRT) according to the tumor board decision prior to randomization. RT schedule was 70 Gy in 35 fractions over 7 weeks with adaptive replanning after 22 fractions for all patients. In 3DCRT arm, weekly EPID verification was done and in IGRT arm, weekly kV-CBCT was done. The error correction was done if more than 3mm. All the patients were treated on Elekta Synergy. Weekly assessment and recording of toxicities was done using RT OG Acute Morbidity Score and thereafter at 1 month and 3 month post treatment. Response assessment was done by clinical examination at 1 month and 3 month along with response CECT at 1 month. Results: Baseline characteristics including age, stage, site, treatment plan etc were not different between the two arms (p>0.05). During treatment, the Grade I/II skin toxicities in 3DCRT arm was 15% vs. 5% in IGR (p=0.475), Grade I/II mucositis (55% vs. 34%, p=0.3), Grade III/IV mucositis (30% vs. 51%, p=0.3), Grade I/II Salivary reaction (90% vs. 91%, p=0.069), Grade I/II dysphagia (85% vs. 54%, p=0.096) and Grade III/IV (15% vs. 42%, p=0.096) respectively between the 3DCRT and IGRT arms. Post 1 month of treatment, Grade I/II mucositis (80% vs. 73%, p=0.918), Grade I/II Salivary reaction (90% vs. 74%, p=0.268) and Grade I/II dysphagia (75% vs. 69%, p=0.052) between the 3DCRT and IGRT arms respectively. Complete response rates at 1 month was 70% in 3DCRT vs. 57% in IGR (p=0.443) whereas partial response rates were 25% vs. 33% respectively in the 3DCRT and IGRT arms. At 3 months, CR rates were 95% in 3DCRT vs. 71% in IGRT arms respectively (p=0.21). Detailed results will be presented in the conference. Conclusions: Our study compared the clinical benefits of IGRT with 3DCRT in HNSCC in terms of early response and toxicities. We did not find any significant difference between the early response and toxicity severity between the two groups even though limitation of small sample size is present. Larger studies are necessary to prove any clinical benefit of IGR over 3DCRT in HNSCC. Further follow up of this study will reveal any differences in late morbidity and overall survival.


130 Neck Dissection Following Chemoradiation: Significance of Timing and T-Stage


Purpose/Objective(s): Neck dissection (ND) following chemoradiation (CRT) was once a dogmatic recommendation for all patients with N2b or greater neck disease due to the high incidence of post-treatment positive neck specimen pathology. Moreover, performing an “early” ND at 4-12 weeks post-CRT was emphasized in order to maintain relatively normal surgical planes, prior to the onset of radiation-induced obliteratorative endarteritis and fibrosis. Recently, data have strongly supported the use of a 3-month post-CRT PET scan as a tool to predict the necessity of post-CRT ND. The purpose of our study was to compare the incidence of positive pathology of patients undergoing ND at two different post-CRT intervals. Materials/Methods: Databases of patient protocols from the University of Chicago during years 1993-2010 were reviewed. The data from all two-hundred twenty-nine patients who underwent post-treatment ND was examined. One patient was excluded due to incomplete clinical data. Patient demographics and tumor specifics were recorded. Interval between the completion of CRT and ND was calculated. Univariate and multivariate logistic regression analyses were completed comparing the incidence of positive neck specimen pathology with
interval, T-stage, N-stage and primary site. Results: 111 patients underwent ND ≤7 weeks and 116 patients who underwent ND >8 weeks post-CRT completion. There were 82 N1-2 and 29 N3 staged necks in the ≤7 week group; 94 N1-2 and 24 N3 in the >8 week group. The incidence of positive neck pathology was statistically lower in patients who underwent ND at >8 weeks vs the ≤7 week group (p=0.011) by univariate analysis. Those patients with T-stage 1-3 (n=142) were statistically less likely to have positive pathology than those with T4 disease (n=73) (p=0.003). In addition, patients with N3 disease (n=53) were more likely to have positive pathology than those with N1-2c (n=175) at any interval post-treatment. There was no correlation between positive pathology and tumor site. Multivariate analysis revealed the incidence of positive pathology to be higher in the ≤7 week group (p=0.015), in those patients with T4 disease (p=0.01) and in those with N3 disease (p=0.03).

Conclusions: Our data show 1. statistically higher incidence of positive neck pathology in patients with T4 and N3 stage disease and 2. statistically higher incidence of positive neck pathology in patients who underwent ND ≤7 weeks post-CRT. This information supports the concept that viable post-therapeutic cancer cells seen in neck dissection specimens do not necessarily persist. Post-CRT cancer cell death likely reaches equilibrium approximately 3 months after the completion of (chemo)radiation. This phenomenon provides additional elucidation of the reported high negative predictive value of PET scans completed 3 months post-CRT.


131 Do Conventional Computed Tomography Characteristics of Pathological Neck Nodes Apply after Chemoradiation?
M. Alizadeh-Kashani*, W. Guertin*, S. Clavel†, L. Guertin*, D. Soulieres*, E. Fillion*, L. Lambert*, M. Belair*, P. Nguyen-Tan*, †Hopital Notre-Dame, Montreal, QC, Canada

Purpose/Objective(s): Determining nodal response to chemoradiation (CRT) remains a major challenge in head and neck cancer. Computed tomography continues to be at the forefront in evaluating residual disease, however, no definitive CT characteristics have yet produced an effective prognosticator to pathological disease. The purpose of this study was to identify CT characteristics that can properly imply pathologically positive lymph nodes in patients having documented adenopathies treated with CRT. Materials/Methods: This study included 91 patients with node-positive oropharynx, larynx, hypopharynx, oral cavity, or unknown primary squamous cell carcinoma treated with CRT from 1998 to 2010. All patients had a pre CRT CT and a CT 6-8 weeks post CRT followed by a neck dissection. CT characteristics such as extracapsular extension, heterogeneity, greatest axial dimension, nodal volume and nodal regression were documented and correlated to neck dissection outcomes. Results: Post CRT, the average largest dimension for positive nodes was 17mm and 11mm for negative nodes (p ≤ 0.001). The average decrease in volume in positive and negative nodes was 31% and 52%, respectively (p ≤ 0.001). Two-dimensional reduction in size in an axial plane was strongly associated in volume reduction (r = 0.881, p ≤ 0.001). Heterogeneity was associated disease (p = 0.007) after CRT whereas extracapsular spread had no such correlation (p = 0.346). A decrease in nodal size on an axial CT image ≥ 80% had a PPV 26%. A residual lymph size of less than 15mm resulted in an NPV 86% and a PPV of 33%. Conclusions: Standard indicators of malignity in neck nodes such as extracapsular spread, heterogeneity and nodal size are not applicable after CRT. Our study suggests that the only CT characteristics that can safely eliminate residual neoplastic tissue is a reduction of ≥ 80% in diameter on an axial image.


132 Influence of Treatment Duration on Locoregional Control (LRC) Rates in the Management of Locally Advanced Head and Neck Squamous Cell Carcinomas (LA-HNSCC) Treated with Transoral Robotic Surgery (TORS) and Postoperative Radiation (PORT)

Purpose/Objective(s): At the University of Pennsylvania, appropriately selected patients (pts) with LA-HNSCC are managed with initial TORS resection followed by staged neck dissection and PORT +/- chemotherapy as indicated by the pathology of the operative specimens. The total treatment duration (TTD) can exceed 13 weeks. This study investigates the influence of treatment duration on the LRC rate. Materials/Methods: A retrospective review of a prospective single-arm cohort was conducted. Inclusion criteria were: pts with LA-HNSCC treated with TORS resection followed by staged neck dissection (usually 1-3 weeks after TORS), and PORT +/- chemotherapy, with at least one year of follow up. Pts were excluded if they had prior RT to the head and neck, or the interval development of distant metastatic disease prior to initiation of PORT. TTD was defined as the interval from TORS to completion of PORT. Locoregional failure (LRF) was calculated from the date of TORS to recurrence at the primary site or in the neck. Analysis included the use of standard descriptive and comparative parametric statistics (Stata 12). Results: 122 pts were identified, with a median follow up of 2.3 years (range 0.4 - 5.9 years). Pathologic T stage distribution was 32% T1, 41% T2, 17% T3, and 6% T4; pathologic N stage distribution was 2% N0, 12% N1, 10% N2a, 69% N2b, 5% N2c, and 2% N3. 91 pts (75%) had negative (>2mm) surgical margins, 26 (21%) had close (≤2mm) margins, and 4 (3%) had positive margins. 55 pts (45%) had evidence of nodal extracapsular spread (ECS). Median PORT dose was 6600 cGy using a dose-painting IMRT technique in 220 cGy/fraction to areas harboring high-risk pathologic features (positive margins or ECS). 70 pts (57%) received concurrent chemoradiation, most often with Cisplatin. Median time from TORS to initiation of PORT was 9.6 weeks. Median TTD was 15.9 weeks. There were 7 pts with LRF: primary site recurrence in 4 pts, and neck only recurrence in 3 pts, yielding a LRC rate of 94%. The median time to LRF was 10 months. Pts with LRF had a median TTD of 17.1 weeks, compared to 15.9 weeks for pts without LRF (p = 0.24). LRF pts were more likely to have close or positive surgical margins (p = 0.02). For the 57 pts with high risk pathologic features (ECS or positive margins), there was no difference in LRC depending on a TTD greater than or less than the median of 15.6 weeks (p = 0.54). Conclusions: For LA-HNSCC managed with TORS, staged neck dissection, and adjuvant PORT +/- chemotherapy, we report a LRC rate of 94% at a median follow-up of 2.3 years, with a median TTD of 15.9 weeks. These observations support the safety of this treatment approach.

Purpose/Objective(s): Standard platinum-based chemotherapy given concurrently with radiotherapy improves survival in locally advanced head and neck cancer (LAHNC) at the expense of higher toxicity. IMRT and alternative chemotherapy regimens provide a means to help minimize toxicity while maintaining treatment efficacy. Our experience with concurrent IMRT and taxane-based chemotherapy in patients with LAHNC is presented. Materials/Methods: From December 2002 to October 2007, 150 sequential patients with LAHNC were treated with IMRT and concurrent taxane-based chemotherapy for curative intent. Sites included hypopharynx (5), larynx (33), nasopharynx (10), oral cavity (6), oropharynx (90), paranasal sinus (2), and unknown primary (4) with AICC stages III to IVB. A differential IMRT fractionation regimen was utilized and consisted of 2.1 Gy/fraction to 69.3 Gy to gross disease, and 1.7 Gy/fraction to 56.1 Gy to prophylactic nodal sites. Weekly paclitaxel 30 mg/m² and carboplatin AUC 1 were given concurrently with IMRT to all 150 patients. The majority of patients with N2 disease (86%) and all patients with N3 disease also received weekly induction chemotherapy with paclitaxel 60 mg/m² and carboplatin AUC 2. Results: Ninety-six percent of patients were able to complete 5 or more cycles of concurrent chemotherapy and only 8 patients required a treatment break from radiation greater than 5 days. Over 90% of patients received the prescribed radiation dose. Mean percent weight loss was 7% and 53% required PEG placement during treatment. Of these patients, 10 (6.7% of total) required long-term PEG use > 18 months. Grade 4 acute toxicity was minimal with grade 4 mucositis and dermatitis only seen in 2.0% and 4.0% respectively. Sixteen patients developed osteoradionecrosis and 40% developed radiation-induced hypothyroidism. No patients developed nadir sepsis, significant nephropathy, GI toxicity, or late xerostomia grade 3 or higher. Median follow-up was 30 months. Three year disease-free survival and overall survival were 78.8% and 76.5% respectively. Locoregional recurrence occurred in 17% of patients and distant metastasis developed in 9%. These treatment outcomes were comparable to our previously reported results with similar taxane-based chemotherapy and 3D conformal radiation. Only PEG tube requirement > 1 year was found to correlate with overall survival (p=0.0131). Conclusions: Differential-dose IMRT with paclitaxel and carboplatin is well tolerated with excellent dose delivery of both radiation and chemotherapy. Acute and late toxicities are low with impressive tumor control at 3 years, suggesting concurrent taxane-based chemoradiotherapy with IMRT is a reasonable therapeutic option for curative treatment of LAHNC. Author Disclosure Block: G.R. Vlacich: None. R. Diaz: None. S. Thorpe: None. B.A. Murphy: None. W. Kirby: None. R. Sinard: None. P. Murphy: None. J. Netterville: None. W. Yarbrough: None. A.J. Cmelak: None.

134 Clinical-Dosimetric Relationship Between Dry Eye Syndrome and Lacrimal Gland Irradiation after Intensity-Modulated Radiotherapy for Sinonasal Tumors
S. Bath*, R. Sreeraman*, E. Dienes*, L. A. Beckett*, J. Cui*, M. Mathai*, J. A. Purdy*, A. M. Chen*., University of California, Davis School of Medicine, Sacramento, CA

Purpose/Objective(s): Patients receiving radiotherapy (RT) for sinonasal tumors are at increased risk for dry eye syndrome. Previous research has suggested an association between RT dose to the lacrimal gland (LG) and this ocular toxicity. The aim of the present study was to further characterize the relationship between dry eye syndrome and dose to the LG in patients treated by intensity-modulated radiotherapy (IMRT) for sinonasal tumors. Materials/Methods: From January 2005 to August 2011, 40 patients with cancers involving the nasal cavity and paranasal sinuses were treated with IMRT to a median prescribed dose of 6600 cGy (range 3060 to 7000 cGy). The most common histology was squamous cell carcinoma (50%). Nine patients received concurrent chemotherapy with cisplatin. Acute and late toxicity were scored using the RTOG morbidity criteria based on conjunctivitis, corneal ulceration, and keratitis. The paired LGs were retrospectively contoured as separate organs at risk (OAR) on the treatment planning CT scan and the following dosimetric parameters were evaluated: mean dose, maximum dose, V10, V20, and V30. Statistical analysis was performed using the Akaike Information Criterion (AIC) and logistic regression. Results: The maximum and mean dose to the ipsilateral LG was 1924 cGy (range 143 to 7536 cGy) and 1446 cGy (range 111 to 6783 cGy), respectively. The incidence of grade 2 or higher acute and late ocular toxicity was 35% and 25%, respectively. Based on logistic regression, it was determined that the maximum dose to the ipsilateral LG was a better predictor of both acute and late toxicity than mean dose (AICs of 53.89 vs 56.13 and 32.94 vs 33.84, respectively). Logistic regression demonstrated that as the maximum LG dose increases by 100 cGy, the odds of reaching a higher level of acute toxicity increase by 23% (p < 0.001). Similarly, as the maximum LG dose increases by 100 cGy, the odds of a late toxicity grade of 2 or higher increase by 7% on average (p = 0.0204). Age, gender, and concurrent chemotherapy were not significant predictors of acute or late toxicity at the 0.05 significance level. However, Fisher’s exact test did demonstrate an association between acute toxicity and whether patients received concurrent chemotherapy (p = 0.0158). Conclusions: A significant dose-response relationship between maximum dose to the LG and ocular toxicity was established. Our data suggest that minimizing the maximum dose to the ipsilateral LG may significantly decrease the risk of both acute and late ocular toxicity. Further prospective studies with a larger number of patients will be important in validating these findings. Author Disclosure Block: S. Bath: None. R. Sreeraman: None. E. Dienes: None. L.A. Beckett: None. J. Cui: None. M. Mathai: None. J.A. Purdy: None. AM Chen: None.
135  Outcome of HIV Head and Neck Squamous Cell Carcinoma Treated with RT and Chemotherapy
1Department of Radiation Oncology, Beth Israel Medical Center, New York, NY, 2Department of Radiation Oncology, Albert Einstein College of Medicine of Yeshiva University, Bronx, NY, 3Beth Israel Medical Center, New York, NY

Purpose/Objective(s): To report the outcome of radiation therapy (RT) +/- chemotherapy in HIV seropositive patients with Head and Neck Squamous Cell Carcinoma (HNSCC). Methods/ Materials: This is the largest single institution retrospective study to date of 71 HIV patients with HNSCC treated from January 1997-2010. The median age at RT, HIV diagnosis, the duration of HIV seropositive was 51 (32-72), 34 (25-50), and 11 years (6-20) respectively. Seventy patients had SCC and one had submandibular salivary duct carcinoma. AUTC 7th edition stages II, III and IVa/b were: 22%, 27%, 51% respectively. Subsites comprised the LX (37%), OPX (32%), Oral Cavity (13%), HPX (7%), NPX (4%), OP (4%), nasal cavity (3%), and SMD (1%). All patients had ECOG performance scale of (0, 1). Patients were treated definitively with RT +/- chemotherapy (CDDP, carboplatin, or Cetuximab). Fifty patients (70%) were on HAART during treatment, and the median CD4 count was 290 (range, 203-1142). Median dose of 70 Gy (66-70) was delivered to the gross disease, high risk neck 60-63 Gy, low risk neck and lateral retropharyngeal nodes 54 Gy. All fractions were given at the rate of 1.8-2 Gy per fraction. Median duration of treatment was 52 (49- 64) days. Twelve pts (17%) underwent planned neck dissection for N3 disease. The following data were tabulated (CD4, CBC, viral load; before, during and after CCRT), duration of HIV, race, age, gender, HAART type and duration, Stage, LRC, and OS. Results: After a median follow up of 47 months (7-140). The 4-year LRC and OS were 69% and 55% respectively. Seven patients (10%) developed second primary within the first 5 years of completion RT (2 Anal and 5 HNSSC). The LRC for Stages III/IV LX and OPX SCC (which represents >67% of the cohort) was 76, and 70% respectively. A Chi-square test and univariate analysis showed statistically significant relationship between LRC and the duration of RT (P<.001), and positive trends with weight loss <10% and absence of second malignancy. Due to the relatively small sample size with diverse subites, multivariate analysis did not show any statistically significant relationship. Conclusions: HNSCC with coexisting HIV remains a challenging clinical problem. Our data show that definitive RT +/- chemotherapy for HIV seropositive HNSCC appears to be less effective compared to the observed rates of LRC, and OS of other HNSSC without HIV. Due to the advances in the HAART therapy which prolongs the HIV patients’ survival, the likelihood to develop HIV related malignancies increases. It is extremely important to establish better effective regimens to improve outcomes in HIV positive HNSSC pts.


136  The Pharyngeal Wall Structure (PWS) Can Be Used as Surrogate Organ at Risk for Swallowing Dysfunction after Curative (chemo) Radiation in Head and Neck Cancer.
R. Vlasman*, H. P. Bijl*, M. E. M. C. Christianen*, O. Chouvalova*, R. J. H. M. Steenbakkers*, C. Schilstra*, J. A. Langendijk*, , University Medical Center Groningen (UMCG), Groningen, Netherlands,

Purpose: The purpose of this study was to investigate if the Pharyngeal Wall Structure (PWS) could be used as surrogate Swallowing Organ at Risk (SWOAR) for the more detailed delineation of separate SWOARs in terms of its prognostic value with regard to swallowing dysfunction after curative chemoradiation (CH)RT for head and neck cancer (HNC). Contouring of the PWS is less time consuming and is less sensitive to interobserver variability.

Materials/Methods: The PWS was defined as a ring structure with the inner border consisting of the pharyngeal lumen and the outer border defined as the additional 1 cm of the pharyngeal wall. The cranial and caudal borders were defined as the caudal tip of the pterygoid plates and the upper edge of hyoid bone. The study population consisted of 365 consecutive patients with HNC. The primary endpoint was grade ≥ 2 swallowing dysfunction at 6 months after (CH)RT (SWAL-M6). Patient-rated swallowing disorders were assessed using the EORTC QLQ-H&N35 questionnaire. The results were compared with NTCP models based on a more detailed delineation of SWOARs, including separate contouring of the superior, middle and inferior pharyngeal constrictor muscle, the supraglottic area and the cricopharyngeal muscle.

Results: For SWAL-M6 the multivariate analysis revealed an NTCP model based on the mean dose to PWS was most predictive. The NTCP increased significantly with a higher mean dose to PWS (p<0.001) and an odds ratio of 1.083 [95% CI 1.057-1.109] for each Gy increase in dose. Model performance is good with an AUC of 0.79 and comparable with the NTCP model based on separate SWOARs (AUC of 0.80 [95%CI 0.75-0.85]). For patient-rated complaints, including problems with swallowing liquids, soft and/or solid food, the PWS resulted in NTCP models without the PWS as prognostic factors and thus without possibilities to optimize IMRT in contrast with the NTCP models based on delineation of separate SWOARs.

Conclusions: The PWS can be used as a surrogate SWOAR to predict the physician-rated swallowing dysfunction in HNC patients after (CH) RT. For patient-rated swallowing problems in general, the PWS cannot replace a more detailed contouring of separate SWOARs.


137  The Efficacy of Reduced Radiotherapy Dose for Human Papilloma Virus Associated (HPV+) Squamous Cell Carcinoma (SCC) of the Oropharynx Treated with Concurrent Chemoradiation

Purpose/Objective(s): HPV+ oropharyngeal SCC (OPSCC) is chemo- and radiation therapy (RT) sensitive, carrying a better prognosis. We present our updated study on whether lower RT doses could eradicate gross nodal disease as effectively as standard RT doses in HPV+ OPSCC.

Materials/Methods: We retrospectively reviewed T1-4N2-3 HPV+ OPSCC patients treated with definitive chemorT on IRB approved studies with ≥1 year follow-up. In-situ hybridization for high-risk HPV subtypes was positive in all cases. ChemorT consisted of once or twice daily RT with concurrent, standard dose CDDP/5FU wk 1, 4 or CDDP wk 1, 4, 7. All patients previously underwent CT simulation and conventional planning. Conventional fields consisted of a single isocenter, shrinking field technique (opposed laterals, AP supraclav, supplemental electrons).
Because neck dissection was planned, gross nodal disease was not intentionally included in the high-dose, boost fields. The pre-RT, diagnostic FDG PET-CT scan was co-registered to the simulation CT scan to aid in lymph node gross tumor volume (LNGTV) delineation. LNGTV was contoured using MIMVista software and exported to Pinnacle for composite plan dose-volume analysis. Mean dose and D95 for each LNGTV was recorded. Students t-test was used to compare mean dose/D95 anto level II vs levels III-IV-V. retrospective analysis (RP) nodes. Results: Thirty-one patients with 63 LNGTVs were included. Median age was 56; median follow up was 26 months. Never, former, and active smokers comprised 42%, 42% and 16%, respectively. Primary tumor site was base of tongue (15 pts) and tonsil (16 pts). The number of level II, III, IV, V and RP nodes that were involved were 41, 15, 1, 1 and 5, respectively. The mean LNGTV was 7.7cc (range: 0.4-22.3cc) and 3.7cc (range: 0.7-13.5cc) for level II and level III-IV-V-RP nodes, respectively. The mean dose to the level II and level III-IV-V-RP LNGTV was 70.0Gy (range: 56.2-77.3Gy) and 62.7Gy (range: 53.3-72.2Gy), respectively. The mean D95 to the level II and level III-IV-V-RP LNGTV was 66.1Gy (range: 46.8-74.2Gy) and 58.9Gy (range: 45.8-71.3Gy), respectively. The mean dose and D95 for level III-IV-V-RP nodes was significantly lower than level II nodes (p<0.0003). The D95 was ≥60Gy in 21 of 62 (34%) LNGTVs and ≤55Gy in 9 LNGTVs (15%). Follow up PET/CT demonstrated a complete response in 31/31 (100%) patients. One patient later failed in neck and underwent salvage neck dissection 12 months post-chemoRT. All patients are currently NED. Conclusions: HPV+ OPSCC LNs respond to RT doses significantly lower than standard definitive doses when combined with concurrent, high dose CDDP/5FU or CDDP. Further research on de-escalated doses of RT in HPV+ OPSCC should be undertaken.


138 Required Margin Around the GTV in Laryngeal and Hypopharyngeal Cancer: A Histology Study.
C. Terhaard 1,2, J. Caldas-Magalhaes 1,2, N. Kooij 3, N. Kaspers 4, P. Fameijer 4, C. Raaijmakers 4, M. Philippens 4, 1, 2, UMC Utrecht, Utrecht, Netherlands, 3Department of radiotherapy, Utrecht, Netherlands, 4Department of Pathology, Utrecht, Netherlands, 5Department of Radiology, Utrecht, Netherlands

Purpose/Objective(s): Computer tomography (CT) is mostly used for delineation of the gross tumor volume (GTV) for laryngeal and hypopharyngeal tumors. A margin has to be added for unknown microscopic extension to define the clinical target volume (CTV) margin. In general a margin of 1 cm is used. This study aims to determine the minimal CTV margin required, using histology as the golden standard.

Methods/ Materials: Fifteen patients with T1 or T2 laryngeal or hypopharyngeal cancer underwent a computer tomography (CT) scan before total laryngectomy (TLE). The gross tumor volume (GTV) was delineated on CT by two independent observers (GTV1 and GTV2). After TLE, the larynx specimen was fixed with formaldehyde, sliced transversely in 3-mm thick slices, and whole-mount hematoxylin-eosin stained (H&E) sections were obtained. A pathologist delineated all tumor tissue (TT) in the H&E sections. Tumor tissue refers to the main tumor bulk and all the surrounding microscopic disease such as perineural or angioinvasive extensions, if present. A 3D reconstruction of the histological specimen was obtained and subsequently rigidly registered to the preoperative CT scans (registration accuracy=1.5 mm). With this 3D registration method all the delineations could be compared [1]. The corresponding volumes around the GTVs were automatically drawn, and the corresponding tumor tissue coverage was finally determined. Results: The mean (range) volumes of the delineated TT, GTV1, GTV2 were 14.0 cc (3.3 - 67.3), 22.9 cc (7.4 - 81.6), and 21.8 cc (6.3 - 79.0), respectively. CT delineation overestimated the volume of the TT with a mean of 60% (range -17% to +302 %). The mean difference in volume between GTV1 and GTV 2 was 20% (3%-46%). A margin of 5 mm around the GTV covered completely all tumor tissue in 27 out of 30 delineations, and with a margin of 7 mm in 29 out of 30 delineations. This margin was mainly required to cover delineation inaccuracies and perineural extensions. However, the calculation of the margin has some limitations, namely pathology-imaging registration errors and deformations of the pathology data [1]. These limitations might have caused overestimations of the margin up to 2 mm. GTV1+5mm and GTV2+5mm were respectively 57.6 and 53.6 ml. Conclusions: These results indicate that 5 mm is a safe CTV margin to cover 100% of the tumor tissue in 90% of the delineations for patients with s with laryngeal or hypopharyngeal cancer, when the GTV is delineated on CT. The value of using MRI, FDG-PET, or a combination of imaging techniques to improve interobserver variation and GTV delineation is currently under investigation. [1] Caldas-Magalhaes et al., JROBP 2011 (in press)


139 Expanding the Use of Unilateral Radiation Treatment for Stage III-IV Head and Neck Carcinoma
K. Hu 1, M. Kumar 2, B. Culliney 3, M. Urken 4, A. Jacobson 1, T. Tran 4, M. Persky 4, S. Schantz 4, F. Pameijer 4, C. Raaijmakers 4, N. Kasperts 4, J. Caldas-Magalhaes 1, 2, 3, Beth Israel Medical Center, New York, NY, 4New York Eye and Ear Infirmary, New York, NY

Purpose/Objective(s): Unilateral radiotherapy treatment (URT) optimizes the likelihood for preserving baseline salivary and swallowing function by minimizing radiation exposure to the contralateral salivary glands and constrictor muscles. However, there is limited data to determine which patients other than early t- and n-stage oropharynx patients (pts) with lateralized tumors who may be treated with URT. In the present era of functional imaging and highly conformal RT techniques, enhanced pt selection and better normal tissue sparing potentially allow more advanced stage pts to benefit from URT. Materials/Methods: Thirty pts with lateralized lesions 1cm away from midline and pre-treatment PET/CT negative for contralateral neck disease were enrolled for URT and followed prospectively. Pts were as follows: 30M: 5F Age: Median 59yo (36-90) Site: 22 oropharynx 6 oral cavity 2 unknown primary. AJCC Stage IVa: 16 III: 9 II: 2 and I 3. To: 2 To-1: 12 T4: 14 T3: 4 N0-1/14 N2a:14 N2b: 4. 22 pts received platinum-based concurrent chemoradiation. Early stopping rules were implemented to detect any contralateral neck failure. Amifostine was delivered in 16 pts. IMRT was used in 23 pts while 3D in 7 and pts received a median dose of 66Gy (20-70Gy). Results: At a median f/u of 16 months, no pt experienced contralateral nodal failure. 2 yr actuarial oncologic outcomes were: Local control: 100%, ipsilateral regional control 93%, locoregional control 93%: distant metastasis 15%, disease-free survival 79% overall survival 88%. Among 19 pts available for detailed dosimetric analysis, the median mean doses to contralateral structures were: submandibular gland 19.6Gy (10.3-37.4), parotid gland 0.8Gy (0.2-17.6), constrictor muscles 32.8Gy (17.8-41.7), carotid artery 12.4Gy (0.6-28.2) and oral cavity
38.3 Gy (28.0-54.8). Chronic xerostomia was reported as grade 0 in 16 and grade 1 in 14. No patients were PEG-dependent and grade 1 chronic dysphagia was the worse grade reported in 6 pts. **Conclusions:** Unilateral treatment for selected stage III/IV disease is associated with excellent locoregional control and outstanding preservation of salivary and swallowing function with low RT exposure to the contralateral minor/major salivary glands, constrictor muscles and carotid artery. In our experience N2 pts with small tumors 1cm away from midline appear to be the subset of stage IV pts who may be eligible for URRT.


140 The Role of Radiation Therapy in the Management of Benign Lymphoepithelial Cysts of Parotid Glands in HIV Patients

W. F. Mourad1,2, K. S. Hu1, R. A. Shourbaji1, E. Kaplan-Marans1, W. Lin1, J. Dolan1, T. Tran1, M. Urken1, M. Persky1, L. B. Harrison1, 1Department of Radiation Oncology, Beth Israel Medical Center, New York, NY, 2Department of Radiation Oncology, Albert Einstein College of Medicine of Yeshiva University, Bronx, NY

**Purpose/Objective(s):** To report the long term outcomes and tolerance of radiation therapy (RT) of HIV associated benign lymphoepithelial cysts (BLEC) of the parotid glands. Methods/Materials: A total of 30 patients were eligible for our study which makes this the largest single institution retrospective study to date of HIV seropositive patients with parotid BLEC. All patients underwent CT simulation followed by RT. Both parotids were treated with RT dose of 24 Gy via external beam RT (Photons and / or electrons), using daily 1.5-2 Gy per fraction for 12-16 fractions. Six patients (25%) were treated at the rate of 2 Gy per fraction. The median age at RT, HIV diagnosis, the duration of HIV seropositive was 45 years (28-64), 38 years (23-53), and 11 years (6-35) respectively. Results: With a median follow-up of 60 months (8-131 months), the overall response (e.g. satisfactory cosmetic outcomes) was achieved in 93% of the patients [complete response (CR) 80%, and partial response (PR) 13%]. Specifically all pts who received RT at the rate of 2 Gy / fraction had 100% CR. Local failure was 7%; all was treated at the rate of 1.5 Gy per fraction for 16 fractions. All acute toxicities were grade 1 and/or 2, specifically mucositis (48%), xerostomia (45%), skin erythema (41%), and altered taste (14%). None have experienced late complications. A Chi-square test showed statistically significant relationship between satisfactory cosmetic outcomes and the duration of RT (P<.0001), and positive trend between RT outcomes and fraction size of 2 compared to 1.5 Gy (P-Value 0.05). There was no statistically significant relationship between RT outcomes and all other variables (age, race, gender, HAART, CD4 count etc.). Conclusions: Radiation therapy treatment to a dose of 24Gy yields excellent long term control for BLEC of the parotid glands in HIV patients. Larger dose per fraction (2 Gy vs. 1.5Gy) appears to be associated with better local control.


141 Oropharynx Directed Management of Head and Neck Squamous Cell Carcinoma with Occult Primary Site

W. F. Mourad1,2, K. S. Hu1, R. A. Shourbaji1, E. Kaplan-Marans1, W. Lin1, A. Jacobson1, T. Tran1, M. Urken1, M. Persky1, L. B. Harrison1, 1Department of Radiation Oncology, Beth Israel Medical Center, New York, NY, 2Department of Radiation Oncology, Albert Einstein College of Medicine of Yeshiva University, Bronx, NY

**Purpose/Objective(s):** Occult primary (OP) of head and neck squamous cell carcinoma (HNSCC) is commonly treated with comprehensive mucosal (nasopharynx, oropharynx, hypopharynx and larynx) and bilateral neck irradiation. We report our experience with more conservative mucosal sparing technique consisting of irradiating only the oropharynx (OPX) mucosa and bilateral necks. Materials/Methods: This is a single-institution retrospective study of 68 patients with OP of HNSCC treated with definitive RT from 1997-2010. Pts were characterized as follows: median age 58 (range 21-87); 80% Caucasian, 10% Hispanic, 8% African American and 2% Asian; males 75%; N1 9%, N2 75% and N3 16%. Forty percent were treated with IMRT while 60% with 3DCRT with elective radiation therapy directed to the OPX mucosa and bilateral necks. Ninety percent received concurrent chemotherapy (Cisplatin 80%, Carboplatin 4%, or Cetuximab 6%). Gross disease in the neck received 70 Gy, involved neck 60-63 Gy, OPX 60 Gy, uninvolved neck and ipsilateral retropharyngeal nodes 54 Gy. All fractions were given at the rate of 1.8-2 Gy per fraction. Sixteen patients (9 N3 + 7 bulky N2) underwent neck dissection (ND). The median time interval from date of diagnosis to start RT was 60 days (13-70) and the median duration of RT was 50 days (49-63). Results: At a median follow-up of 5.3 years (0.5 - 13.6), the loco-regional control, (LRC) for the entire cohort is 95.6 %. The median time to LRF is 18 months (range 12 - 63). A primary site has emerged in 1 patient (1.5%) who developed subglottic SCCa 2 years after CCRT. Two patients (3%) failed in the neck (originally N3). All the 3 patients were salvaged successfully by surgery. Late CCRT / RT toxicity was; grade (1) xerostomia (67%), dysphagia (35%), altered taste (28%), neck stiffness (15%), skin toxicity (12%), dysphonia (9%), and trismus (6%). One pt with HIV has grade 4 dysphagia. No patients experienced distant metastases. Kaplan-Meier Curve shows the 5-year cause-specific survival, (CSS), to be 100%. Conclusions: Our data show that definitive RT +/- chemotherapy, to the OPX and bilateral neck provides excellent oncologic and functional outcomes. Sparing the mucosal surfaces of the nasopharynx, hypopharynx and larynx seems reasonable and likely reduces toxicity. The only late subglottic larynx cancer is likely to be second primary rather than index cancer.

**142** Prospective Comparison of FDG-PET/CT SUV Measures in HPV-Positive and HPV-Negative Oropharyngeal Squamous Cell Carcinoma (OPSCC)

Hofstra-North Shore LIU School of Medicine, Hempstead, NY

**Purpose/Objective(s):** The relationship between HPV infection status and FDG avidity in OPSCC remains uncharacterized, and may impact staging accuracy and/or treatment response assessment with FDG-PET/CT. Our group is prospectively comparing FDG-PET/CT findings in HPV-positive and HPV-negative OPSCC.

**Materials/Methods:** 36 patients with newly diagnosed OPSCC were enrolled onto this IRB-approved clinical trial between 7/2010 and 6/2011. The cohort consisted of 32 male/5 females with a median age of 62 yrs (range: 43-93). Cases consisted of 19 tonsil/16 base of tongue/1 soft palate tumors, with 3 T1/10 T2/13 T3/10 T4 stage primaries and 1 II/5 III/30 IV overall AJCC stage disease. Twelve tumors overexpressed p16 by immunohistochemistry, 19 tumors were HPV-negative, and 5 are pending confirmatory in situ hybridization for high-risk HPV infection. All FDG-PET/CT imaging was performed according to standardized protocol on the same GE Discovery ST scanner and interpreted by the same radiology team. Maximum standard uptake values (SUVmax) for primary and nodal disease were calculated.

**Results:** All HPV-classified cases were available for analysis. Respectively mean primary SUVmax for HPV- and HPV+ disease was 19.0 +/- 5.6 vs. 15.9 +/- 5.2 (p = 0.15), and 10.1 +/- 5.8 vs. 10.3 +/- 4.2 (p = 0.93) for nodal disease. No significant relationships between SUVmax and primary/nodal size were observed. Nodal disease in either group was equally likely to demonstrate centralized necrosis (33% for both HPV- and HPV+ disease).

**Conclusions:** Baseline primary and nodal FDG avidity was not impacted by HPV infection status. Post-radiotherapy FDG-PET/CT results are maturing and will be presented.

**Author Disclosure Block:** D. Schwartz: B. Research Grant; Resonent Medical. C. Other Research Support; ScIclone Pharmaceuticals. V. Nguyen: None. N. Isaac: None. J. Fantasia: None. S. Parise: None. B. Saltman: None. D. Frank: None. J. Rini: None.

---

**143** Predictive Value of F-18 Fluorodeoxyglucose PET/CT 3 Months after Completion of Radiation Therapy for Head and Neck Squamous Cancer

University of Iowa, Iowa City, IA

**Purpose/Objective(s):** The role of PET/CT in response assessment after radiation therapy (RT) remains undefined. Our previously published data on the accuracy of FDG-PET within 12 months of RT included both FDG-PET and PET/CT data and was based on an SUV cut-off of 3.0. The purpose of this review is to evaluate accuracy in the PET/CT era using clinical context to determine accuracy.

**Materials/Methods:** This is an IRB-approved retrospective review of 192 patients with head and neck squamous carcinoma treated with radiation therapy (median 70 Gy; range: 50-80 Gy) at the University of Iowa after a PET/CT was obtained. Patients received treatment between July 2004 and May 2008 and all patients underwent PET/CT after completion of radiation for response assessment at a median of 14 weeks, range: 3-27 weeks. Scans were considered positive or negative in the head and neck by review of the report in the medical record. Reports in which the wording was equivocal were reviewed by CA and assigned positive or negative based on the ordering clinician’s response to the information. Scans were determined to be true or false based on subsequent pathology reports, imaging, and/or clinical exam findings.

**Results:** Median follow-up for all patients was 2.35 years; median for living patients was 3.12 years. Reports in which the wording was equivocal were reviewed and assigned positive or negative based on the ordering clinician’s response to the information. Scans were determined to be true or false based on subsequent pathology reports, imaging, and/or clinical exam findings.

**Conclusions:** Accuracy of PET/CT assessed within clinical context revealed similar specificity, positive predictive value and negative predictive value to our previously published data based on a cut-off of SUV 3.0. A negative post-RT PET/CT is an excellent predictor of outcome. False positive rates remain problematic.

**Author Disclosure Block:** C. M. Anderson: None. S. Steen: None. Y. Menda: None. M. Graham: F. Consultant/Advisory Board; Siemens. J. Buatti: B. Research Grant; National Cancer Institute.

---

**144** Customized Tongue-Displacing Dental Stents for Oral Mucosal Sparing and Immobilization in Head and Neck Radiotherapy


**Purpose/Objective(s):** Advances in conformal head and neck radiotherapy have allowed greater sparing of normal tissues. However, painful oral mucositis remains a major dose-limiting toxicity. Simple non-customized bite blocks or corks have been used to immobilize oral structures, but are poorly reproducible and provide limited displacement of uninvolved oral mucosa. Customized tongue-displacing dental stents (CTDS) provide rigid and reproducible immobilization and may improve oral mucosal sparing by displacing uninvolved mucosal structures away from high dose radiation volumes. We retrospectively reviewed our clinical experience using CTDS and evaluated dosimetric parameters relating to oral mucosal sparing.

**Materials/Methods:** From August 2008 to May 2011, thirty-seven patients with Stage III-IVB squamous cell carcinoma of the oral cavity (excluding tongue primaries), oropharynx, nasopharynx and paranasal sinuses underwent definitive chemoradiation and CTDS immobilization. A CTDS was designed during pre-radiation dental evaluation in collaboration with the treating radiation oncologist. A light-cured acrylic resin was used to build maxillary/mandibular arches and a tongue paddle incorporated for tongue displacement (depression and/or deviation) away from the primary tumor. CT simulation and daily treatments were performed with CTDS in position. All but one patient was treated with IMRT, and all received 70 Gy to gross disease. We compared diagnostic CT scans without CTDS to the CT simulation scans with CTDS to identify the oral mucosa that was displaced. Using the Pinnacle® treatment planning system, we auto-contoured the region between the stent and the remaining oral cavity, which represented the displaced oral mucosal volume that would have been irradiated without CTDS. This was assigned tissue density and dose-volume histograms generated to determine the volume and dosimetric parameters of the spared oral mucosa.

**Results:** CTDS were well-tolerated with no unexpectedly severe mucosal reactions. Mean volume of oral mucosa spared was 48 cc.
(range 23 - 95 cc). Stage III patients had larger volumes spared compared to Stage IV (mean 66 vs 46 cc). Nasopharyngeal and paranasal sinus patients had the most sparing (mean 59 cc). With CTDs, an estimated mean of 8% of the displaced oral mucosal volume avoided exposure to 70 Gy, 48% avoided 50 Gy, and 76% avoided 35 Gy. Oral mucosa spared by CTDs demonstrated less mucositis in a random sample of patients. No patient had greater than RTOG grade 3 acute mucositis. Mean weight loss during treatment was 8%. There were no unplanned treatment breaks. Conclusions: CTDs achieve superior oral mucosal sparing, provide reproducible immobilization, are well tolerated, and can readily be incorporated into clinical practice.


145 HPV and Survival in Patients with Oropharyngeal Squamous Cell Cancer of the Head and Neck (OPC) Treated with Induction Chemotherapy followed by Chemoradiotherapy (ST) vs. Chemoradiotherapy Alone (CRT): A Retrospective Analysis J. Lorch*, 1, V. Thotakura*, 1, M. Posner*, 1, D. Sher*, 2, V. Nair*, 1, S. Limaye*, 1, R. Tishler*, 1, G. Rabinovitz*, 1, G. Hanna*, 1, R. Haddad*, 1, 1 Dana Farber Cancer Institute, Boston, MA, 2 Mount Sinai Medical Center, New York, NY, 3 Rush Medical Center, Chicago, IL, 4 Beth Israel Deaconess Medical Center, Boston, MA

Purpose/Objective(s): HPV is a major prognostic marker with OPC. The purpose of this study was to compare overall survival (OS) and progression free survival (PFS) in HPV positive and HPV negative cases treated with ST and with CRT. Materials/Methods: A total of 151 patients with OPC and known HPV status were identified retrospectively who were treated at DFIC from 2005-2008. Charts were reviewed and clinical information was recorded. 94 patients were treated with CRT and 57 received ST. Results: For all 151 patients the 3-year overall survival (OS) was 90.2% (92 /106, 95% CI, 84.2 to 96.7) in the HPV-positive and 74.5% (31/45, 95% CI, 62.5 to 88.8) in the HPV-negative group (hazard ratio 0.37, P = 0.006). Among 94 patients treated with CRT, 10/88 (15%) HPV+ died and 6/26 (23%) HPV- died. The 3-year OS was 88.1% (95% CI, 80.0 to 97.0) and 79.9% (95% CI, 65.5 to 97.5), respectively (p = 0.299). PFS was also not statistically different. In patients treated with ST, 4/38 (11%) HPV+ subjects died; 8/19 (42%) HPV- died. The 3-year OS was 94.5% (95% CI, 87.4 to 100) and 66.2% (95% CI, 47.3 to 92.6), respectively. HPV-positive patients treated with ST had better overall survival than HPV-negative patients (HR 0.2, P = 0.004). PFS at 3 years was 89.2% (95% CI, 79.7 to 99.8) in HPV+ and 56.8% (95% CI, 38.1 to 84.9) in HPV- subjects (HR 0.21, P = 0.002). Conclusions: A significant survival benefit for HPV+ patients treated with ST. Given the obvious limitations of a retrospective analysis and a relatively small sample size, these findings should be considered hypothesis generating and should be examined further.


Purpose/Objective(s): In a panel of 27 human head and neck squamous cell carcinoma cell lines, treatment with the EGFR receptor inhibitor, cetuximab exhibits variable growth inhibition when tested in 6 day growth assays. The novel irreversible pan-HER inhibitor, PF-00299804 was tested in this same panel of cell lines to determine effect when compared with cetuximab. Materials/Methods: 27 human head and neck squamous cell carcinoma cell lines from various sources: UMSCC (Univ of Michigan), CAL27, CAL33, FaDu, SCC-4, SCC-9, SCC-15 and SCC-25 (ATCC). HNS (OSI Pharmaceuticals). Cells were seeded in duplicate in 24-well plates at densities of 10,000 to 25,000 cells per well. Cells were treated 24 hours after initial seeding. PF-00299804 was added at 10uM with two fold dilutions over nine dilutions (range 10uM to 0.039uM). At the time of treatment, one set of untreated cells was immediately counted. The remaining wells were counted 6 days after seeding. Growth inhibition was calculated by percent generational inhibition. Assays were repeated for cell lines that did not exhibit 50% growth inhibition at the lowest dose (greater than 50% inhibition at 0.039uM), beginning with a starting dose of 100nM while maintaining the same dilution scheme. EGFR, K-Ras and PI3K Mutation Analysis was performed via use of PCR, sequencing, FISH, Western Blot Analysis, Cell cycle analysis, gene expression. Rosetta Resolver software was used for clustering and statistical analysis profiling. Results: Cell lines sensitive to cetuximab are exquisitely sensitive to PF-00299804. PF-00299804 inhibited the growth of all head and neck cancer cell lines in a concentration-dependent manner. However, there was significant heterogeneity in IC50g values across the panel, with a 4 log-fold difference between the most sensitive and least sensitive cell lines 17/27 cell lines had an IC50g less than 1 uM, 8/27 lines had an IC50g less than 100nM and 4/27 lines had an IC50g less than 10nM. 5/27 cell lines treated with 100ug/ml of cetuximab experienced greater than 60% growth inhibition. all but one of these lines (UMSCC-4) had an IC50g less than 9nM with PF-00299804 treatment. Common oncogene mutations and amplifications are rare in HNSCC. Phosphorylated and total EGFR levels correlate with sensitivity to EGFR-directed therapy. PF-00299804 but not cetuximab inhibits EGFR downstream signaling. Conclusions: That PF-00299804 exhibits potent anti-proliferative activity in cell lines that experienced low response to cetuximab treatment. In the presence of an EGFR ligand, cetuximab does not inhibit pathways involved in cell growth, whereas PF-00299804 significantly inhibits these pathways.

Author Disclosure Block: S. Wong: None. H. Hamidi: None. F. Ather: None. N. Venkatesan: None. R. Finn: None. C. Head: None.
Economic Impact of Unplanned Hospitalizations for Patients with Head and Neck Carcinoma Treated with Induction Chemotherapy and/or Chemoradiation

R. Manon*, T. D. Shellenberger*, T. Johnson*, J. Tseng*, MD Anderson Cancer Center–Orlando, Orlando, FL, University of Texas MD Anderson Cancer Center, Houston, TX

**Purpose/Objective(s):** To evaluate the economic impact of unplanned hospitalizations in a population of head and neck cancer patients treated with chemotherapy and radiation. **Materials/Methods:** A retrospective study of 91 patients with locally advanced head and neck squamous cell carcinoma (SCC) treated at the M.D. Anderson Cancer Center Orlando between 2007–2010 was performed. Records were reviewed and data entry was abstracted based on whether patients received induction/concurrent systemic therapy and were treated with intensity modulated radiation therapy (IMRT). All admission and financial data were abstracted from beginning of treatment (chemotherapy or radiation) until 30 days after the completion of treatment. **Results:** This cohort of patients includes 12 females and 79 males. Median age of patients is 58.8 years. Primary tumor subsites include: 62 patients with SCC oropharynx, 8 patients with SCC unknown primary, 9 patients with SCC larynx, 4 patients with SCC hypopharynx, and 4 patients with nasopharyngeal CA. All patients were treated with IMRT. A total of 35 patients received induction chemotherapy followed by chemoradiation. A total of 56 patients received concomitant chemoradiation. Of the patients who received induction chemotherapy, 8/35 (22%) patients required unplanned readmission during induction therapy. Data regarding hospitalization rates during chemoradiation are as follows: 42/91 (46%) patients were hospitalized during chemoradiation, with a total of 56 admissions. Eight patients required multiple admissions. Range in length of stay for patients requiring unplanned admissions was: 1–65 days. Mean length of stay was 6.98 days. Radiation treatment breaks occurred in 8/91 patients (8.8%). Chemotherapy treatment breaks occurred in 6/49 patients (12%). Mortality rate during treatment was 1% (1/91). The cost per day of hospitalization for this cohort of patients ranged from: $4315–14,662. This equates to an approximate excess cost of $116,700 per patient due to unplanned hospitalizations. **Conclusions:** Unplanned hospitalizations are a source of substantial cost during the course of treatment of head and neck cancer patients. In an era of pressure to provide cost-effective healthcare this may be an area of significant preventable cost. Proposed strategies to decrease re-admission rates include early institution of gastostomy tubes, increased home health services, aggressive intravenous hydration and antiemetic support, use of prophylactic antimicrobials, and early evaluation of patients after each cycle of induction chemotherapy.


Intensity-Modulated Radiotherapy is Associated with Improved Global Quality of Life Among Long-Term Survivors of Head and Neck Cancer

A. M. Chen*, G. Farwell*, Q. Luu*, E. Koulikov*, D. H. Lau*, J. A. Purdy*, University of California, Davis, School of Medicine, Sacramento, CA

**Purpose/Objective(s):** Although intensity-modulated radiotherapy (IMRT) has become widely adopted in the management of head and neck cancer, limited clinical data exists on its potential impact on long-term quality of life. The University of Washington Quality of Life instrument (UW-QOL) is a previously validated, self-administered questionnaire that patients returning for follow-up after completion of radiation therapy for head and neck cancer have routinely completed at our institution. The purpose of this study was to compare long-term quality of life among patients treated with and without IMRT for head and neck cancer. **Materials/Methods:** The UW-QOL scores were retrospectively reviewed for 155 patients with squamous cell carcinomas of the head and neck requiring bilateral neck irradiation for locally advanced disease. Only patients who were clinically without evidence of recurrent disease and with at least 2 years of follow-up were included in this analysis. Eighty-two patients (53%) were treated by definitive radiation therapy, and 73 patients (47%) were treated postoperatively. Eighty-four patients (54%) were treated using IMRT with inclusion of the low neck in an extended field. The remaining 71 patients (46%) were treated with 3-dimensional conformal radiotherapy (3DCRT) using opposed lateral fields matched to a low anterior neck field. Concurrent chemotherapy was administered with radiation therapy for 73 patients (47%). **Results:** The mean global quality of life scores were 67.5 and 80.1 for the IMRT patients at 1- and 2-years, respectively, compared to 55.4 and 57.0 for the 3DCRT patients, respectively (p<0.001). At 1-year after completion of radiation therapy, the proportion of patients who rated their global quality of life as “very good” or “outstanding” was 51% and 41% among patients treated by IMRT and 3DCRT, respectively (p=0.11). However, at 2-years, the corresponding percentage of patients increased to 73% and 49%, respectively (p<0.001). At last follow-up, 80% of patients treated by IMRT reported that their health-related quality of life was “much better” or “somewhat better” compared to the month before developing cancer compared to 61% among patients treated by 3DCRT (p=0.001). On multivariate analysis accounting for gender, age, radiation intent (definitive versus postoperative), radiation dose, T-stage, primary site, use of concurrent chemotherapy, and neck dissection, the use of IMRT was the only variable independently associated with improved quality of life (p=0.01). **Conclusions:** The early quality of life improvements associated with IMRT are not only maintained but apparently become more magnified over time. These data powerful evidence attesting to the long-term benefits of IMRT for head and neck cancer.


The Possible Benefit of a MRI-Accelerator for the Treatment of Head and Neck Cancer


**Purpose/Objective(s):** For the determination of target volumes in laryngeal, hypopharyngeal and oropharyngeal cancer margins for internal motion due to breathing and swallowing have to be adjusted. This increase in target volume may lead to increased toxicity. Due to its superior soft-tissue contrast, MRI has advantage above CT for the visualization of anatomical motion. So, on-line and ultimately real-time MRI guided radiotherapy would be beneficial compared to once-daily CT guided radiotherapy. On-line MRI imaging will also enable to adapt the treatment, using functional data from our hybrid MRI radiotherapy system, the MRI-accelerator. **Materials/Methods:** We have constructed a prototype MRI-
accelerator. This prototype is a modified 6 MV Elekta accelerator combined with a modified 1.5 T Philips Achieva MRI system. The simultaneous and unhampered operation of the MRI and the accelerator is shown by performing diagnostic quality 1.5 T MRI with the radiation beam on [1]. The static prototype allowed gated radiation delivery in a phantom study as well as, real-time on-line reconstruction of the accumulated dose, making treatment adaptation feasible [2]. We calculated the possible gain in reduction of target volumes for supraglottic cancer, reducing our combined margin for internal motion and PTV from 15 mm in cranial direction, and 10 mm in caudal direction, to 3mm using a gating technique. **Results and Discussion:** Due to the smaller margin, the reduction in the primary tumor and boost PTV volumes for supraglottic cancer ranged between 50% and 65%, resulting in a clinically relevant decrease of the dose to the submandibular glands and the swallowing structures. A clinical pilot unit of the MRI accelerator with full gantry rotation and IMRT capabilities is currently under construction and will be installed October 2012. We will investigate, by virtual treatments, the feasibility of MRI-gated treatment of laryngeal, hypo- and oropharyngeal cancer with a 3 mm margin. Secondly, we will investigate the possibility to adapt the dose to (a part of) the GTV based on functional MRI information. **Conclusions:** This proof of concept opens the door towards a clinical prototype to start testing MRI-guided radiation therapy (MRIgRT) in the clinic. Dedicated sequences for MRI-guided radiotherapy treatments will be developed. The use for treatment of H&N cancer of a MRI-accelerator in future may result in a large reduction of target volumes, reducing the risk on complications, and the possibility of adaptation of the treatment based on functional MRI data. [1] Raaymakers BW, Phys Med Biol 2009 [2] Crijns SPM et al, Phys Med Biol 2011

**Author Disclosure Block:** C. Terhaard: None. B.W. Raaymakers: None. L. Vugts: None. C.P.J. Raaijmakers: None. J.J.W. Lagendijk: None.

**150 Dynamic Real-Time Planar MRI to Ascertain Base of Tongue Movement During Simulated Radiation Treatment-The Tongue Also Moves**

J. J. Beitel*1, E. S. Elder*1, T. Fox*, H. Kitajima**, P. Sharma**, K. A. Higgins*, P. A. Hudgins*, D. Martin**, 1Winship Cancer Institute, Atlanta, GA, 2Emory University School of Medicine, Atlanta, GA

**Purpose/Objective(s):** Concurrent chemoradiation is the standard of care for patients with squamous cell cancer of the base of tongue. Morbidity of treatment is dependent on chemotherapy, dose of radiation, the volume irradiated and volume spared. As our imaging and treatment delivery precision improve, we can physically treat tighter margins but the base of tongue has potential movement which should be considered before we choose PTV margins of 3-5 mm. The proximity of the superior constrictors makes the issue critical. Despite the relatively high incidence of base of tongue cancer, very little is known about the movement of either the normal base of tongue or the diseased base of tongue. Most swallowing studies are done with the patient upright, rather than in the supine, immobilized position that is relevant to radiation oncologists. **Materials/Methods:** Four normal volunteers had full head and neck treatment immobilization devices made by our treatment staff. Real-time MRI was performed in the treatment position using our customary immobilization devices. Real-time MRI was performed in the parasagittal plane for 15 minutes. Images were processed and digitally reconstructed into movies with adjustable viewing speeds. **Results:** Cinematography demonstrated that there was continuing movement of the tongue in the anterior/posterior as well as the superior/inferior direction throughout the 15 minute observation. Swallowing frequency was observed to be 2/minute, 0.3/min, 0.5/min and 0.4/min in a 31 y/o, a 46 y/o, a 54 y/o, a 56 y/o. **Conclusion:** The base of tongue is not a static organ and very tight margins would seem inadvisable. According to the literature, the oropharyngeal phase of swallowing varies from 2.2 to 3.78 seconds depending upon whether the subjects have normal salivary flow or xerostomia. At 30 swallows for a 15 minute treatment, one volunteer would have had his tongue "displaced" for a considerable portion of the treatment. **Author Disclosure Block:** J.J. Beitel: None. E.S. Elder: None. T. Fox: None. H. Kitajima: None. P. Sharma: None. K.A. Higgins: None. P.A. Hudgins: None. D. Martin: None.

**151 The Effect of Race on Competing Mortality in Advanced Head and Neck Cancer**

I. MacEwan*1, A. Vazirnia*, E. E. Vokes*4, R. R. Weichselbaum*1, K. L. Mell*1, 1University of California, San Diego, La Jolla, CA, 2University of Chicago, Chicago, IL

**Purpose/Objective(s):** Black patients with head and neck cancer (HNC) have poorer survival and disease control compared to non-black patients, but disparities in death from non-cancer causes (i.e., competing mortality) are less well-defined. The purpose of this study was to estimate racial disparities in competing mortality for advanced HNC patients. **Materials/Methods:** This is a secondary analysis of 537 patients (369 non-black, 168 black) with stage III-IV HNC treated on one of six multi-institutional protocols involving multi-agent chemoradiotherapy with or without surgery. Competing mortality was defined as death due to treatment-related morbidity, intercurrent disease, or unknown cause in the absence of disease recurrence, progression, or second malignancy as competing events. Backward stepwise Cox proportional hazards regression (p<.05) was used to estimate the effect of black race on competing mortality, adjusting for age, sex, smoking, alcohol use, stage, and performance status. The race effect was also evaluated for Charlson comorbidity index and body mass index (BMI) in a subset of 479 patients with these data available. Chi square, Kruskall-Wallis, and t-tests were used to test differences in covariates for black and non-black patients. **Results:** Median follow-up for surviving patients was 53 months. Overall, 110 competing mortality events were observed. Black race was associated with increased rates of comorbidity, smoking and heavy alcohol use, advanced T stage, poorer performance status, decreased BMI, and decreased distance traveled to the treating center (p<.05 for all). Controlling for age, sex, and performance status in the stepwise regression model, black race was associated with increased competing mortality (hazard ratio (HR) 1.83; 95% confidence interval (CI), 1.23-2.70). The effect was similar when controlling for BMI and comorbidity (HR 1.83; 95% CI, 1.12-2.99). When only death due to comorbid disease was included as an event, the effect of race was increased (HR 2.42; 95% CI, 1.33-4.37). **Conclusions:** Black patients with advanced HNC are at increased risk of death from competing non-cancer mortality, particularly death from comorbid disease. Improved strategies to manage comorbid disease would increase the marginal benefit of intensive treatment in black patients.
MRI Analysis of Changes in Tumor Characteristics in Patients with Head and Neck Squamous Cell Carcinoma Treated with Concomitant Chemoradiation


Purpose/Objectives: To assess the utility of different MRI contrasts in target delineation and to quantify the change in primary tumor volume and cellularity using different MRI contrasts in patients with head and neck cancer (HNC) who received concomitant chemoradiotherapy (CRT).

Materials/Methods: This is a prospective pilot study to evaluate advanced MRI images in patients with HNC who received definitive IMRT to 70 Gy in 35 fractions to gross disease combined with concurrent chemotherapy. 9 patients with HNC (1 larynx, 8 oropharynx) were imaged in the treatment position on a 3T Siemens scanner prior to and during week 4 of CRT. Axial images were acquired before and during CRT using STIR, T1 with contrast (T1+C), ΔT1 (T1+C - T1), and apparent diffusion coefficient (ADC) mapped from diffusion-weighted imaging (DWI) (surrogate for cellularity). Pretreatment PET images were also acquired. Primary and nodal gross tumor volumes (GTV) were drawn on each of these image sets. Tumor volume was calculated on all images and cellularity was analyzed on ADC using the mean signal intensity of the contoured volume.

Results: Primary and nodal tumor volumes as defined on each image series were comparable at both the pretreatment and mid-treatment time points. On initial evaluation, the mean primary gross tumor volumes for STIR measured 31.01cm³, for T1+C 29.63cm³, for ΔT1 24.85cm³, for ADC 15.02cm³, and for PET 26.44cm³ (p=0.58). On mid-treatment evaluation (median of fraction 22), the mean primary gross tumor volume for STIR measured 5.38 cm³, for T1+C 5.64 cm³, for ΔT1 4.45 cm³, and for ADC 2.71 cm³ (p=0.77). One patient had a complete response of the primary tumor on imaging by fraction 22. The difference in pre-treatment compared to mid-treatment tumor volume was statistically significant for each of these imaging sequences (p < 0.01). Degree of cellularity within the region of gross disease as measured by ADC was not statistically different between the pre- and mid-treatment volumes (p=0.41). Conclusions: Of all MRI contrasts used in this analysis, contours generated using ΔT1 images were found to be closest to those defined by PET. This suggests that T1+C contours may overestimate target volumes due to confounding flow or contrast agent effects. Volumes defined by ADC were consistently smaller compared to the other MRI contrasts, suggesting the region of high cellularity defined by DWI-derived ADC is a high risk area within the tumor requiring careful attention on initial treatment planning and during adaptive RT.

The Prognostic Significance of Facial Nerve Involvement in Carcinomas of the Parotid Gland

B. E. Terakedis*, B. Bentz*, J. Hunt*, L. Buchmann*, J. Schliesser*, J. Ying*, Y. Hitchcock*, University of Utah Huntsman Cancer Hospital, Salt Lake City, UT

Purpose/Objectives: Involvement of the facial nerve by carcinomas of the parotid gland has several implications. Surgeons are challenged to preserve or reconstruct the facial nerve while still attempting to perform an effective oncologic surgery. Perineural invasion is often an indication for post-operative radiotherapy. Herein we analyze the local control and overall survival rates and the impact of facial nerve involvement for patients treated for carcinoma of the parotid gland. Materials/Methods: Seventy-one patients who were treated with primary surgery, or without radiotherapy, for non-metastatic primary malignancies of the parotid gland from 1988-2006 were included in this analysis. Parotid lymphoma and skin cancer parotid metastases were excluded. Information on patient demographics, tumor characteristics, treatment, recurrence, and survival were collected. A Student’s-t-test and Fisher exact test were used to compare demographics and tumor characteristics. Predictive factors of recurrence were analyzed using the univariate Cox proportional hazards model, with significance defined as p<0.05. Results: Median follow-up was 7.4 years, and median age at diagnosis was 52 years. Mucoepidermoid carcinoma was the most predominant histology (n=23) followed by acinic cell and adenoid cystic carcinoma (n=15 each). Neither grade nor histology were predictors of recurrence or death with the exception of squamous cell carcinoma which was associated with a worse overall survival (Hazard ratio (HR) 6.47, with mucoepidermoid carcinoma as reference, p=0.002). Clinical facial nerve dysfunction (n=16) at initial diagnosis was not a predictor of recurrence (p=0.08) or overall survival (p=0.46). Facial nerve removal due to tumor extension (n=18) and perineural invasion (n=18) were associated with an increased risk of recurrence (HR 2.64 (1.14, 6.12), HR 2.63 (1.13, 6.10) respectively) and death (HR 4.24 (1.67, 10.73), HR 3.98 (1.57, 10.07), respectively). In patients with pathological facial nerve involvement, adjuvant radiation treatment slightly decreased the risk of recurrence however the results were not statistically significant. Conclusions: Facial nerve involvement is a predictor of increased risk of recurrence and death from parotid cancer. Post-operative radiotherapy may provide a benefit in patients with this poor prognostic feature.

Increase in Spinal Cord Dose Due to Weight Loss in Head and Neck Cancer Patients Undergoing Radiation Therapy

F. Siddiqui*, D. Boyle*, M. Weldon*, M. McGee*, K. Kuhn*, P. Werner*, Ohio State University, Columbus, OH

Purpose/Objective(s): Intensity modulated radiation therapy (IMRT) aims at precise dose delivery to the tumor and avoidance of critical structures. It relies on the assumption that tumor size and shape, normal tissue anatomy and patient body contour do not change over the course of RT. This assumption is incorrect and more recently has led to the use of adaptive planning in H&N ca. We wanted to investigate if change in weight (wt) and lateral separation (sep) would lead to increased dose to the spinal cord (SC) and brainstem. Materials/Methods: 10 patients with oropharyngeal cancers treated with chemotherapy+RT to 66-70Gy were selected. All patients had lost wt during RT. Cone beam CT (CBCT) scans were obtained 2-3 times per week for all patients prior to treatment delivery. Mid-week megavoltage CBCT scans were imported into our treatment planning system (Varian Eclipse). These images were co-registered with the planning CT scan while aligning sc and
A statistically significant decrease in RPA recurrence rate was observed in patients who received adjuvant radiotherapy. A larger sample size and longer follow-up for surviving patients was needed to assess the impact of radiotherapy on patient outcomes. Data on the long-term effects in patients treated with RT remain limited.

Author Disclosure Block: none.
follow-up time are required for further analysis of the potential relapse risk factors and better assessment of short and long term complication rates.


157 Chemoselection with Induction Chemotherapy followed by Chemoradiation or Surgery vs. Chemoradiation for Patients (pts) with Locally Advanced Squamous Cell Carcinoma of the Oropharynx (LASCOP)


Purpose/Objective(s): Optimal treatment for HPV- and HPV+ LASCOP is not well defined. Here we retrospectively compare survival and toxicity outcomes from two different organ preservation protocols in pts with LASCOP. Materials/Methods: From 1999-2007, 114 pts with operable stage III/IV LASCOP were enrolled in 1 of 2 chemoradiotherapy (CRT) trials. Pts on trial 9921 were treated with 1 cycle of induction chemotherapy (IC) with 5-FU (1,000mg/m²/d days 1-5) and cisplatin (CP) 100mg/m² or carboplatin (CA) AUC 6 on day 1. This was followed by concurrent CRT: 70 Gy in 2 Gy fractions with CP or CA, dosed as above, on days 1, 2, 22, and 43 in pts with >50% response to IC or surgery in pts with <50% to IC. Pts on trial 0221 were treated with concurrent CRT: 70 Gy in 2 Gy fractions with weekly CA (AUC 1) and paclitaxel (30 mg/m²). These strategies were compared for OS, DSS, toxicities and persistent G-tube dependence at 6 mos using a propensity score matched analysis. The matched dataset consisted of 35 pts from each trial matched on age, stage, smoking and tumor HPV status (p16 IHC), adjusted using multivariate statistics and cluster analysis to account for the correlated nature of the matched pairs. Results: HPV status was balanced across the dataset yielding 27 HPV+ and 8 HPV- tumor specimens from each trial. Of the 70 total pts analyzed, 13 (37%) from 0221 and 5 (14%) from 9921 had ECOG PS 1 (p=0.03). At 6 mos post-treatment, 4 (11%) from 0221 and 9 (26%) from 9921 were G-tube dependent (p=0.12). Grade 3 and 4 toxicities were more frequent in 9921, as were overall toxicities. Of the 70 pts analyzed, 3 from 0221 died w/in 2 yrs (0/3 from disease-specific cause), and 10 pts from 9921 (6/10 from disease-specific cause). There was evidence that OS and DSS was improved in 0221 (p=0.01 for each), with 2 years of follow-up. When stratifying by HPV status, among both HPV+ and HPV- pts, there was a trend for improved DSS in the 0221 cohort. OS did not differ significantly across trials after stratifying by HPV status. Toxicities were less prevalent in 0221 group, including hematologic toxicities, nausea, mucositis, and neuropathy. Persistent G-tube use at 6 months was not significantly different between the two treatment groups. Conclusions: Data from this retrospective review suggests that survival outcomes in pts with HPV+ HPV+ LASCOP are not compromised with weekly chemotherapy and RT (WCRT), and WCRT is generally more tolerable.


158 Tolerance and Toxicity of Concurrent Chemoradiotherapy in HIV Seropositive Patients with Head and Neck Squamous Cell Carcinoma

W. F. Mourad*, K. Hu*, R. A. Shourbaji*, B. Cullinee*, E. Kaplan-Marans*, W. Lin*, A. Jacobson*, M. Urken*, M. Persky*, L. Harrison*. 1Department of Radiation Oncology, Beth Israel Medical Center, New York, NY, 2Department of Radiation Oncology, Albert Einstein College of Medicine Yeshiva University, Bronx, NY, 3Beth Israel Medical Center, New York, NY

Purpose/Objective(s): To report tolerance, acute and late toxicities of radiation therapy (RT) +/- chemotherapy in HIV seropositive patients with Head and Neck Squamous Cell Carcinoma (HNSCC). Materials/Methods: This is the largest single institution retrospective study to date of 71 HIV seropositive patients with HNSCC treated from January 1997-2010. The median age at RT, HIV diagnosis, the duration of HIV seropositivity was 51 (32-72), 34 (25-50), and 11 years (6-20) respectively. Seventy patients had SCC and one had submandibular salivary duct carcinoma. Studies I-II, III and IVA/b were: 22%, 27%, and 51% respectively. All patients had ECOG performance scale of <2. Patients were treated definitively with RT +/- chemotherapy (CDDP, Carboplatin, or Cetuximab). Fifty patients (70%) were on HAART during treatment, and the median CD4 count was 290 (range, 203-1142). Median dose of 70 Gy (66-70) was delivered to the gross disease, ipsilateral neck 60-63 Gy, contralateral neck and lateral retropharyngeal nodes 54 Gy. All fractions were given at the rate of 1.8-2 Gy per fraction. Median duration of treatment was 52 (49-64) days. Results: After a median follow up of 47 months (7-140). The median number of scheduled RT days missed was 3 days (1-7). Chemo/RT related acute toxicity was as follows: median weight loss 20 pounds (6-40) specifically grades 1, 2, 3, and 4 were 11, 13, 11%, and zero respectively. All patients developed (100%) dysgeusia and xerostomia (grades 1-3). Acute mucositis grades 1, 2, and 3 were 41, 42, and 17% respectively. Acute dysphagia and odynophagia grades 1, 2, and 3 were 31, 52, and 17% respectively. Acute skin desquamation (dry and wet) grades 1, 2, and 3 were 66, 20, and 14% respectively. Treatment breaks in excess of 10, 7, and 3 days were 5, 13 and 15% respectively. One required hospitalization for grade 4 (mucositis, dermatitis, dysphagia) and fever. There were no acute RT related fatalities. Chemo/RT related late toxicity was; dysphagia grades (1, 2, 3, and 4 e.g. PEG dependent) were 46, 28, 15, and 11%. Hoarseness of voice grade 1 was 10% with no grades 2-4. Xerostomia grades 1, 2, and 3 were 45, 32, and 23% respectively. Conclusions: HNSCC with coexisting HIV remains a challenging clinical problem. Our data show that definitive RT +/- chemotherapy for HIV seropositive HNSCC appears to be less tolerated compared to the observed rates toxicity of other HNSCC without HIV. It is of paramount importance to establish better tolerated treatment strategies and regimens to improve tolerance and toxicity in HIV positive HNSCC pts.

159 Novel Concepts in Long Term Radiation Induced Dysphagia and Cerebrovasculopathy


*Department of Radiation Oncology, Beth Israel Medical Center, New York, NY, †Department of Radiation Oncology, Albert Einstein College of Medicine Yeshiva University, Bronx, NY, ‡Beth Israel Medical Center, New York, NY

Purpose/Objective(s): Single-institution, retrospective study investigating the impact of definitive radiation therapy (RT) in the management of early glottic cancer on clinical radiation induced long-term dysphagia and Carotid artery vasculopathy and related structures' tolerance.

Materials/Methods: From January 1997-2010, 253 patients who had T1-T2 glottic cancer underwent RT with Co60 or LINAC 6MV photon. RT fields with wedge pair and daily 5 mm bolus were applied in all patients treated with 6 MV photon to avoid under-dose of the anterior laryngeal structures. Bowel larynx (LX), middle and inferior pharyngeal constrictors (PCs), and bilateral carotid arteries (CA) were contoured and dose volume histograms (DVH) were generated to assess the dose delivered. Results: After a median follow up of 6.8 years, a total of 253 patients with median age of 65 were analyzed; Caucasian 80%, males 87%, and T2-23%. The median dose delivered to the LX was 63 Gy (60-72), median fraction size 2.25 Gy. The LX mean dose was 57 Gy to volume of 34 cm3. The LX V50, 60, and 65 were 83, 77, 71 respectively. The PC mean dose was 54 Gy delivered to volume of 15 cm3. The PC V50, 60, 65 were 81, 70, 52 respectively. The CA mean dose was 60 Gy delivered to volume of 4 cm3. The CA V50, 60, 65 were 84, 51 respectively. Patients with acute dysphagia grades 1, 2, and 3, 4 were 81, 19%, and zero respectively. None had clinically RID or RICV. Conclusions: Our study shows that definitive RT, up to 67.5 Gy at 2.25 Gy/fx, to the LX, PCs, and CA is not a predictor of clinically significant RID and RICV. The tolerance of these structures should be revisited in further studies. The separate delineation of these structures as well as others may better identify dose tolerances to maintain function and further prioritize structures' importance in causing RID and RICV.


160 Phase 2 Study of ACE-041, a Novel Inhibitor of ALK1-mediated Angiogenesis, in Patients with Recurrent or Metastatic SCCHN; Study Rationale and Design

A. Jimeno*, J. C. Bendell**, M. S. Gordon***, H. Hurwitz‡, C. Condon**, K. M. Attie#, M. L. Sherman‡, R. B. Cohen‡, S. Sharma‡, †University of Colorado School of Medicine, Denver, CO, ‡Sarah Cannon Research Institute, Nashville, TN, §Pinnacle Oncology Hematology, Scottsdale, AZ, †Duke University Medical Center, Durham, NC, Acceleron, Cambridge, MA, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT

Purpose/Objective(s): Activin receptor-like kinase-1 (ALK1) is a TGFβ superfamily receptor selectively expressed on activated endothelial cells that is required for vascular maturation and the development of capillary beds. ACE-041 is an ALK1 ligand trap, which binds with high affinity to ligands BMP9 and BMP10, and prevents activation of ALK1 receptors. Based on activity in a Phase 1 study in advanced solid tumors, a study of ACE-041 in patients with squamous cell cancer of the head and neck (SCCHN) is planned. A summary of the Phase 1 results and the Phase 2 study design are presented here.

Materials/Methods: A total of 37 patients with advanced, treatment-refractory solid tumors, including 3 SCCHN patients, were enrolled in the Phase 1 first-in-human Phase 1 study. There were 7 dose-escalating cohorts (0.1 to 4.8 mg/kg SC; treatment cycle 3 weeks) and an expansion cohort at 1.6 mg/kg. Results: In the Phase 1 study, one SCCHN patient (base of tongue; refractory to radiation therapy (RT), cisplatin and cetuximab) had a partial response (32.5% decrease in target lesion size), and a 44% decrease in tumor metabolic activity on FDG-PET, and received 10 cycles (30 weeks) at 0.4 mg/kg. A second SCCHN patient (parameningeal; refractory to RT and cetuximab) had a minor response (28.9% decrease), and a 19% decrease on FDG-PET, and received 11 cycles (33 weeks) at 1.6 mg/kg. The third SCCHN patient (vocal cord; refractory to RT, carboplatin, paclitaxel and cetuximab) had progressive disease after 1 cycle at 0.8 mg/kg. ACE-041 was generally well-tolerated. Common AEs included fatigue, peripheral edema, nausea, anemia, headache, anorexia, and dyspnea. Possibly or probably related SAEs included fluid overload and/or congestive heart failure (3), fatigue (1) and left ventricular dysfunction (1). Edema and fluid overload were dose-dependent and responded to diuretic therapy. The planned Phase 2 study is a multi-center, open-label study to evaluate the efficacy, safety and pharmacodynamics (PD) of ACE-041 in recurrent or metastatic SCCHN refractory to platinum therapy. The primary objective is ORR, and a sample size of 29 evaluable patients will provide 80% power to differentiate an ORR of interest (Ha) of 30% from a minimal ORR of 10% (Ho) at a type 1 error of 5%. Secondary objectives include safety, tolerability and pharmacokinetics. Exploratory analyses will examine the association of ALK1 expression and other relevant markers with tumor response and other PD markers. Conclusions: ACE-041 is a first-in-class angiogenesis inhibitor that targets the ALK1 receptor pathway. ACE-041 was generally well-tolerated and demonstrated antitumor activity in a Phase 1 study. A Phase 2 study of ACE-041 in SCCHN is being initiated.


161 Definitive Radiation Therapy for Early Glottic Cancer: Long Term Outcome and Pattern of Failure


*Department of Radiation Oncology, Beth Israel Medical Center, New York, NY, †Department of Radiation Oncology, Albert Einstein College of Medicine Yeshiva University, Bronx, NY, ‡Beth Israel Medical Center, New York, NY

Purpose/Objective(s): To evaluate the impact of different techniques (2 D versus 3 D) on the long term outcomes and pattern of failure for early stage, (T1-T2), glottic cancer and to highlight the important technical considerations for optimal outcomes. Materials/Methods: This is a single-institution, retrospective study investigating the clinical outcomes of single modality radiation therapy (RT) for 253 patients with T1-2 glottic cancer treated from 1997-2010. RT was delivered by 2 D or 3 D RT with Co60r 6MV photons. Fluoroscopy was used to assess the laryngeal motion upon swallowing and bolus was applied with 6 MV photons to avoid under dosage of the anterior commissure. Pts. were...
characterized as follows: median age: 65 and males 87%; T1 77% and T2 (23%). The median dose was 63 Gy, with a median fraction size of 2.25 Gy. Median time interval from date of diagnosis to start RT was 35 days and the median duration of RT was 41 days. Results: At a median follow-up of 83 months (>7 years) the loco-regional control, (LRC) is 98%. LRC for T1 (n=195) is 99.5%, with 1 pt failing at the, anterior commissure. Fifty eight (58) patients with T2 lesions the LRC is 91% with 4 local failures (LF) and 1 regional failure (RF). The median time to LRF was 8 months (range 4 - 63). Clinical RT related grade (1-4) late dysphagia, dysphonia, skin toxicity, carotid artery stenosis and cerebrovascular stroke was zero. Kaplan-Meier Curve shows the 5-year cause-specific survival, (CSS), to be 100%. Conclusions: Single modality RT, 63 Gy at 2.25 Gy/fx, provides an excellent and effective treatment for early stage [T1-T2] glottic cancer with high rates of local control, function preservation and negligible long term toxicity. The overall survival, (OS), in patients presenting with early stage glottic cancer was determined primarily by other comorbidities rather than tumor recurrence.


162 Distant Metastases in Head and Neck Squamous Cell Carcinoma Treated with Intensity-Modulated Radiotherapy


Purpose/Objective(s): To determine the pattern and risk factors for distant metastasis in head and neck squamous cell carcinoma (HNSCC) after curative treatment with intensity modulated radiotherapy (IMRT). Materials/Methods: This is a retrospective study of 284 HNSCC patients treated in a single institution with IMRT. Sites included are oropharynx (125), oral cavity (70), larynx (55), hypopharynx (17), and unknown primary (17). AJCC stage distribution includes I (3), II (19), III (42), and IV (203). There are 224 males and 60 females with a median age of 57. One hundred eighty-six patients were treated with definitive IMRT and 98 post-operative IMRT. One hundred forty-nine patients also received concurrent cisplatin-based chemotherapy. Results: The median follow-up for all patients was 22.8 months (range 0.07 - 77.3 months), 29.5 months (4.23 - 77.3 months) for living patients. The 3-year local recurrence-free survival, regional recurrence-free survival, local-regional recurrence-free survival, distant metastasis-free survival, and overall survival are 94.6%, 96.4%, 92.5%, 84.1%, and 68.95%, respectively. There were 45 patients with distant metastasis. In multivariate analysis, distant metastasis is found to be strongly associated with N stage (p=0.046), T stage (p<0.0001), and pre-treatment SUV of the lymph node (p=0.006), but not associated with age, gender, disease sites, pre-treatment SUV of the primary tumor, or local-regional control. The freedom from distant metastasis at 3 years was 98.1% for no factors, 88.6% for one factor, 68.3% for two factors, and 41.7% for three factors (p < .0001 by log-rank test). Conclusions: With advanced radiation techniques and concurrent chemotherapy, the failure pattern has changed with more patients failing distantly. The majority of patients with distant metastases had no local or regional failures, indicating that these patients might have microscopic distant disease before treatment. The clinical factors identified here should be incorporated in future clinical trials.


163 Concurrent Cisplatin vs. Cetuximab with Definitive Radiation Therapy (RT) for Head and Neck Squamous Cell Carcinoma (HNSCC): A Retrospective Comparison

J. Ley*, P. Mehan*, T. M. Wildes*, D. Adkins*, . Washington University School of Medicine, St. Louis, MO

Purpose/Objective(s): Systemic therapy improves overall survival (OS) if given with RT for locally advanced HNSCC. Cisplatin and cetuximab are commonly used agents but the optimal regimen remains unclear. We performed a retrospective analysis of patients (pts) treated with RT and concurrent cisplatin or cetuximab. Material/Methods: Pts treated with RT with high dose bolus cisplatin or weekly cetuximab between 2005 and 2010 were identified retrospectively from the Washington University IRB approved tumor registry protocol. Pts treated with induction or primary surgery were excluded. Baseline clinical data were identified including age, primary site, HPV status, stage, ECOG performance status (PS), and ACE-27 comorbidity index. Pts were stratified by chemotherapy regimen; survival was estimated using the Kaplan-Meier method and compared between chemotherapy groups using the log-rank test. Results: Of the 63 pts identified, 33 received cisplatin and 30 received cetuximab. T and N categories, stage, and HPV status were balanced in the two treatment groups. The mean age was younger in the cisplatin group compared to the cetuximab group (53 vs. 64yrs, respectively, p= 0.001). The mean ECOG PS was 0.4 (0-2) in the cisplatin group and 1.1 (0-3) in the cetuximab group (p<0.0005). The mean ACE-27 index was 0.9 in the cisplatin group and 1.8 in the cetuximab group (p=0.0018). The mean number of doses of cisplatin or cetuximab received were 2.5 (1-3) and 7 (1-15), respectively. Planned RT dose was delivered in 96.8% of cisplatin pts and 96.7% of cetuximab pts. Mean elapsed days of RT was 49.5 in the cisplatin group and 49.1 in the cetuximab group. At last follow-up, 33 pts are alive without disease, 1 pt is alive with disease, and 29 pts have expired (24 of disease, 1 treatment related mortality, 4 deaths from other causes). Mean follow-up for the 34 surviving pts is 30 months (range 1-58). Disease specific survival (DSS) at mean follow up of 30 months was 79% in the cisplatin group and 27% in the cetuximab group (p<0.0001). OS at mean follow up of 30 months was 72% in the cisplatin group and 25% in the cetuximab group (p<0.0001). Conclusions: In this retrospective study, OS was higher in the pts given cisplatin with RT compared to cetuximab with RT. It is tempting to attribute this OS difference to the larger proportion of pts in the cetuximab group with poor prognostic factors (age, ECOG PS and ACE-27 index). However, DSS also significantly differed between the treatment groups in spite of similar tumor characteristics and treatment delivery suggesting substantial differences in treatment efficacy. In the absence of prospective data comparing cisplatin to cetuximab with RT, these data suggest caution in treating pts who may tolerate cisplatin therapy with cetuximab alone.

Phase I/II Clinical Trial of Re-irradiation with Pemetrexed and Erlotinib followed by Maintenance Erlotinib for Recurrent and Second Primary Squamous Cell Carcinoma of the Head and Neck (SCCHN)


Purpose/Objective(s): Re-irradiation with concurrent chemotherapy has emerged as a treatment option for patients with recurrent or second primary SCCHN who have received prior radiotherapy (RT). Combinations of pemetrexed and EGFR inhibitors have recently demonstrated radiosensitizing effects in vitro and in clinical studies. We propose to incorporate the oral tyrosine kinase inhibitor erlotinib into a re-irradiation strategy, both as a radiosensitizer in combination with pemetrexed and in maintenance post-RT with the goal to improve upon the reported efficacy of combined re-irradiation and chemotherapy, reducing acute and late toxicity.

Materials/Methods: Patients with unresectable loco-regional recurrent or second primary SCCHN will receive re-irradiation with pemetrexed and erlotinib starting the first day of RT. Patients should have received prior head and neck RT to no more than 72 Gy and >75% of the tumor volume should be in areas previously irradiated to >45 Gy. The total cumulative spinal cord dose will be limited to 54Gy. RT total dose will be 60 Gy in 30 daily fractions to gross tumor, with allowed additional 6 Gy to a small area of gross residual disease. During Phase I, erlotinib dose will be escalated from 100 mg to 125 mg and 150 mg daily or until dose-limiting toxicity (DLT) develops in 2/6 patients. A standard 3+3 design will be used. Maintenance erlotinib with dose-adjustment per smoking status will be continued until disease progression, unacceptable toxicity or to a maximum of 2 years. The primary endpoints for the phase II part of the study are progression-free survival at 1 and 2 years with a planned sample of at least 25 patients. Secondary end-points are overall survival, toxicities and QOL evaluations. Correlative studies will use nano LC-MS/mass spectrometry to investigate the level of phosphorylation of tyrosine residues within the cytoplasmic domain of EGFR, bound adaptors and markers of downstream pathways activation in tumor. These results will be corroborated with the response to treatment. Results: Cohorts 1 and 2 of the phase I study have been completed without DLT. Enrollment to cohort 3 began in December 2010. Three patients are alive and free of disease at 8, 18 and 30 months after conclusion of the their re-irradiation. Conclusions: Re-irradiation concurrent with pemetrexed and erlotinib appears efficient and well tolerated at erlotinib doses of 100 and 125 mg. The clinical trial is currently enrolling patients in the final cohort that provides erlotinib at the 150 mg dose level. We expect to complete the Phase I study before the meeting and to present the final results and the dose or erlotinib recommended for the Phase II study at the time of the meeting.


Unilateral Neck Therapy in HPV-Era: Virus-Association Does Not Alter Accepted Regional Spread Patterns


Purpose/Objective: Unilateral neck therapy has been safely practiced for decades for select, lateralized tonsil cancers. Recently, it has been suggested that HPV-associated tonsil cancer, characterized by small primary tumors with advanced regional disease, may be more likely to present with bilateral neck adenopathy, thereby rendering unilateral therapy unsafe. We reviewed the SEER database to determine whether the incidence of bilateral disease is rising.

Materials/Methods: We analyzed the incidence data from the Surveillance, Epidemiology and End Results (SEER) Program of the National Cancer Institute from 1988 - 2008 for oropharynx and tonsil cancer. From 1988-2003, tumor and nodal staging was coded according to the AJCC 3rd Edition Staging Manual. From 2004-2008, tumor and nodal staging was coded according to the AJCC 6th Edition Staging Manual. The staging system change necessitated examination of the two time frames independently. For the purposes of this analysis, we considered localized/limited to one subsite tonsil cancer (1988-2003) and T1-2 tonsil cancer (2004-2008) as small primary tumors that could potentially be treated with unilateral therapy. Percentage change (PC) and annual percentage change (APC) were calculated.

Results: Overall the incidence of both oropharynx cancer and tonsil cancer (APC p < 0.05) is increasing. The incidence of advanced neck disease (N2 or greater) is increasing for both oropharynx cancer and small primary tonsil cancer (APC p < 0.05). The increase in advanced nodal stage for small primary tonsil cancer is largely secondary to a rising incidence in ipsilateral disease (T1-2N2a-b, APC 10.6%, p < 0.05). An increase in bilateral neck disease (T1-2N2c, APC 5.9%, APC = NS) is less pronounced. Conclusions: The incidence of small primary tonsil cancer with advanced regional disease is rising. This increase appears to be dominated by an increase in ipsilateral neck disease. While bilateral neck disease is increasing, it appears to be a consequence of the general trend of increasing rates of tonsil cancer rather than a new behavior of HPV related tonsil cancer. There are no current data to support the implementation of routine bilateral neck therapy for small tonsil cancers.


Chemotherapy Associated Improvement in Survival From Squamous Cell Carcinoma of the Oropharynx is Confined to the HPV Positive p16 Negative Subgroup

E. Junor*, G. Kerr*, A. Oniscu*, S. Campbell*, I. Kouzeli*, C. Gourley*, K. Cuschieri*, Edinburgh Cancer Centre, Edinburgh, United Kingdom, Royal Infirmary of Edinburgh, Edinburgh, United Kingdom, Scottish HPV Reference Laboratory, Edinburgh, United Kingdom, University of Edinburgh Cancer Research UK Centre, Edinburgh, United Kingdom

Purpose/Objective: To determine a) the cause of an improvement in survival from oropharyngeal squamous cell carcinoma (OSCC) in SE Scotland and b) whether this improvement was HPV and p16 subtype dependent.

Materials/Methods: Clinicopathological characteristics and outcome data for patients referred with OSCC from 1999-2001 (cohort 1) and 2003-2005 (cohort 2) were obtained. Molecular HPV detection and immunohistochemistry for p16 were performed from paraffin blocks. Results: Cohort 1 and cohort 2 contained 118 and 136 patients respectively. Kaplan-Meier analysis revealed significantly improved survival in cohort 2 (p<0.0001). Sub-classification according to HPV and p16 status revealed no improvement in survival in Class I (HPV+ve/p16-ve; 47 patients) or Class III (HPV+ve/p16+ve; 77 patients). However in Class II (HPV+ve/p16-ve; 56 patients) an increase in 5-year survival from 36% in cohort 1 to 73% in cohort 2 was detected (p=0.0001). Proportional
hazards analysis of 217 patients treated radically demonstrated that significant variables were p16 (p<0.0001), N stage (p<0.0006) and cohort (p=0.0024). Removing cohort from the variables offered to the model showed that while p16 (p<0.0001) and N stage (p<0.0016) remain significant, chemotherapy (p=0.0163) and T stage (p=0.0139) are now significant. This suggests that much of the cohort effect is due to the higher use of chemotherapy in the second cohort. Conclusions: These data suggest that HPV+ve/p16-ve patients constitute a separate subclass of OSCC who may particularly benefit from chemotherapy. They imply that p16 status cannot be considered a surrogate for HPV status and those trials to de-escalate treatment in HPV+ve OSCC should take p16 status into account.


167  
A Review of Concordance with Established Guidelines in a Cohort of Head and Neck Cancer Patients: Implications on Quality and Process Improvement  
S. K. Mullapally*, B. K. Mohanty*, M. A. Laviraj*, V. Subramani*, S. Bhaskar*, R. M. Pandey*, G. K. Rath*, 1Department Of Radiation Oncology, Institute Rotary Cancer Hospital, All India Institute Of Medical Sciences, New Delhi, India, 2Department Of Biostatistics, All India Institute Of Medical Sciences, New Delhi, India

Purpose/Objective(s): To assess the reproducibility of concordance with established guidelines in head and neck oncology so as to establish the generalizability of a practice-based system of quality assessment. Materials/Methods: A study of concordance was performed by randomly selecting 100 patients from the tumor registry of the M. D. Anderson Cancer Center Orlando treated for squamous cell carcinoma of the oral cavity, oropharynx, larynx, or hypopharynx between June 1, 2008 and September 30, 2009. Of these, 49 cases met criteria for study inclusion. Records were reviewed and data entry was abstracted to analyze concordance for testing, staging, multidisciplinary treatment planning, and evidence-based practice and guidelines of the University of Texas M. D. Anderson Cancer Center. Results: We found 93.9% concordance for testing by appropriate means to determine pretreatment staging. For TNM staging, we found 95.9% concordance agreement in stage category. Among all patients treated, multidisciplinary planning was documented and concordance with best practice was found in 95.7%. Clinically relevant differences were discovered for HPV testing, dental consultation, and alcohol counseling. Other parameters, which fell below benchmark included TNM staging, source documentation, and consistency of staging. Conclusions: The degree to which patients with head and neck cancer are managed by defined measures in pretreatment evaluation, staging, multidisciplinary planning, and execution of care can be objectively assessed. The results of comparisons with benchmarks can be used to critically review clinical practices and identify areas of process improvement, which we expect to translate to improved outcomes and diminished cost in this population of patients.


168  
Setup Uncertainties In Radiotherapy of Head and Neck Cancers: Prospective Evaluation of IGRT vs. 3D CRT In A Randomized Controlled Trial  
S. K. Mullapally*, B. K. Mohanty*, M. A. Laviraj*, V. Subramani*, S. Bhaskar*, R. M. Pandey*, G. K. Rath*, 1Department Of Radiation Oncology, Institute Rotary Cancer Hospital, All India Institute Of Medical Sciences, New Delhi, India, 2Department Of Biostatistics, All India Institute Of Medical Sciences, New Delhi, India

Purpose/Objective(s): To study set up uncertainties during radiotherapy in head and neck cancer with comparative assessment of Image Guided Radiotherapy (IGRT) Versus 3 Dimensional Conformal Radiotherapy (3D CRT) and to derive the population specific CTV to PTV margins. Materials/Methods: 41 patients of head and neck squamous cell carcinoma (oropharynx, hypopharynx, and larynx) were enrolled into this phase III randomized controlled study, after Institutional Ethics Committee. The treatment plan was decided as radical radiotherapy (RT) or concurrent chemoradiotherapy (CRT) as per the disease stage and patients were randomized to IGRT arm (n=21) and 3D CRT arm (n=20).The total dose was 70Gy in 35 Fractions over 7 weeks. In IGRT arm, weekly verification with Cone Beam Computed Tomography (CBCT) was done and in 3D CRT arm, Electronic Portal Imaging Device was used (EPID) weekly. Errors were recorded in mediolateral(X), superoinferior(Y) and anteroposterior (Z) direction and corrected if more than 3mm in any of these. Rotational errors were not compared in this study. Statistical analysis was done using STATA software, version 9.1.CTV to PTV margin was derived using Van Herk’s recipe. Results: The mean of systematic error (µ), standard deviation of systematic error (σ) and standard deviation of random error (o) in X, Y, Z directions for IGRT arm (in mm) were (0.88,0.94,0.64), (0.95,1.63,1.24) and (1.08,1.13,0.01) respectively and for 3D CRT arm were (1.63,0.84,0.53), (1.86,0.91,0.78) and (1.64,0.68,0.68) respectively. On comparison, mean of systematic error in X direction was significantly higher in 3D CRT versus IGRT (1.45 vs. 0.92, p<0.0147) whereas in Y and Z, the difference was not statistically significant (p>0.05). The mean of random error in X direction was similar in both arms (p=0.958) but in Y direction, the random error was significantly higher in IGRT arm (1.68 vs. 0.9, p=0.002) and also in Z direction (1.83 vs. 1.14, p=0.0394).The CTV to PTV margin for the IGRT arm was 2.8mm in X, 4.95mm in Y and 3.54mm in Z and for 3D CRT was 2.5mm, 2.8mm and 2.2mm in X, Y and Z respectively. The CTV to PTV for study population(n=41) was 2.81mm in X, 4.25mm in Y and 3.06mm in Z. Conclusions: The average systematic error and random error during radiotherapy in head and neck cancer with IGRT using CBCT verification or with 3D CRT using EPID is less than 2mm in all directions. Between IGRT and 3D CRT, the systematic error in mediolateral direction was significantly less in IGRT and similar in other directions whereas random errors were more seen with IGRT especially in superoinferior and anteroposterior directions. Differential CTV to PTV margin of 3mm in mediolateral, 4mm in antero-posterior and 5mm in superoinferior direction is proposed when CBCT or EPID is used for verification.

**Purpose/Objective(s):** Panitumumab is a fully human monoclonal antibody targeting the epidermal growth factor receptor (EGFR). PRISM evaluated the safety and efficacy of panitumumab as second-line monotherapy in patients with R/M SCCHN. 

**Materials/Methods:** This is an open-label, single-arm, multicenter trial that enrolled patients with histologically or cytologically confirmed SCCHN. Key eligibility criteria included: at least 18 years old and progressive disease (PD) or intolerance to first-line systemic chemotherapy for R/M SCCHN. Patients received panitumumab 9 mg/kg Q3W until PD or intolerability. Tumor response was evaluated using modified RECIST 1.0 criteria every 6 weeks +/- 1 week. The primary endpoint was objective response rate (ORR); secondary endpoints included disease control (DC) rate, overall survival (OS), progression-free survival (PFS), and safety. Results: 52 patients were enrolled and received at least 1 panitumumab dose; 69% were men; median age was 61 years; ECOG performance score was 0 (38%), 1 (60%), or 2 (2%). The distribution of the primary tumor sites were oral cavity (38%), oropharynx (35%), larynx (25%), and hypopharynx (2%). 79% of patients had metastatic disease and 21% had locoregionally recurrent disease only. 92% of patients received prior radiotherapy, 92% prior platinum-based chemotherapy, 65% prior taxane, 40% prior fluoropyrimidine, and 10% prior EGFR inhibitor therapy. 94% of patients ceased first-line chemotherapy treatment due to PD; 6% due to chemotherapy intolerance. The RECIST confirmed partial response (PR) rate was 4% (2/51 patients) and the DC rate was 39% (20/51 patients). Two patients had an unconfirmed PR and one patient had an unconfirmed complete response; all three were considered to have a best response of stable disease per study criteria. Median PFS was 1.4 months (95% CI, 1.3 - 2.4 months). Median OS was 5.1 months (95% CI, 4.3 - 8.3 months). One patient has prolonged and continued disease stabilization (N = 25 cycles). The most common adverse events (AEs) were rash/dermatitis acneliform (69%), fatigue (33%), dry skin (21%), and hypomagnesemia (21%). 18 patients (35%) had a worst grade 3 AE and 4 patients (8%) had a worst grade 4 AE. Five patients died on study; one was deemed treatment-related (angioedema). Conclusions: Panitumumab monotherapy was generally well tolerated and had activity in previously treated patients with R/M SCCHN in the second-line setting.

**Author Disclosure Block:** D. Rischin: F. Consultant/Advisory Board; Amgen Inc. D. Spigel: None. D. Adkins: G. Other; Eli Lilly, Bristol-Myers Squibb. R. Wein: D. Speakers Bureau/Honoraria; Bristol-Myers Squibb. S. Arnold: None. M.L. Davis: None. N. Singhal: None. A. Xue: A. Employment; Amgen Inc. E. Ownership Interest; Amgen Inc. B. Bach: A. Employment; Amgen Inc. E. Ownership Interest; Amgen Inc.
**Purpose/Objective(s):** Cediranib (AZD2171) is an orally-administered, highly potent pan-VEGFR inhibitor that also targets PDGFRβ and c-kit. A phase II clinical trial was initiated to evaluate the safety profile, clinical response, and biological effects of cediranib in patients (pts) with recurrent and/or metastatic squamous cell carcinoma of the head and neck (RM SCCHN). **Materials/Methods:** Eligible pts had ≤ 2 prior systemic therapies for RM SCCHN, measurable disease per RECIST 1.0, adequate renal, liver and bone marrow function, and no prior antiangiogenic therapy. Response is the primary endpoint. A Simon 2-step design was utilized with accrual continuing to a total of 37 pts if ≥ 1 of the first 12 pts experienced ≥ stable disease (SD). Pts initially received 45 mg of cediranib orally per day in 28 day cycles. The study was amended to decrease the starting dose to 30 mg due to excess toxicity, and to allow for administration by gastrostomy tube. Correlative endpoints include tumor interstitial pressure, pO2, and microvessel density in tumors accessible for biopsy, plasma markers of angiogenesis, circulating endothelial cells, and dynamic contrast enhanced CT to measure tumor blood volume and perfusion. **Results:** To date, 20 pts have enrolled (15 male, 5 female; median age 58.5 years). One pt (5%) had an unconfirmed partial response, but voluntarily withdrew at 2.7 months (mos) due to grade (gr) 3 fatigue. Eight pts (40%) had SD, lasting a median of 3.9 mos. Eleven pts (55%) had progressive disease, with 5 pts (25%) progressing quickly after enrollment. Median progression free survival is 3.1 mos. Mucositis/dysphagia were common, with 5 pts (25%) and 9 pts (45%) experiencing gr 1 and gr 2/3 symptoms, respectively. Six pts (30%) experienced gr 2 fatigue and 8 pts (35%) experienced gr 3/4 fatigue. Gr 2/3 hypertension occurred in 9 pts (45%). Gr 3/4 confusion occurred in 4 pts (20%). Gr 1/2 diarrhea occurred in 11 pts (55%), and nausea or vomiting in 7 pts (35%). Gr 2/3 dehydration occurred in 6 pts (30%). There were also isolated instances of gr 3 cholecystitis and gr 3 hyponatremia. Correlative studies are forthcoming. **Conclusions:** Cediranib has preliminary activity in RM SCCHN. Hypertension, mucositis/dysphagia and fatigue are the most common toxicities, requiring careful monitoring and management. Mucositis/dysphagia may be more common in SCCHN pts as a radiation recall phenomenon. These toxicities appear more tolerable at the 30 mg starting dose. Enrollment in the trial’s 2nd stage is underway.

**Author Disclosure Block:** L. Wirth: Consultant/Advisory Board; Acceleron, Angen, Boehringer Ingelheim, AstraZeneca. J.R. Clark: None. A. Maybury: None. R. Jain: None. J. Rocco: C. Other Research Support; Abbott.

---

**Phase II Clinical Trial of Cediranib Monotherapy in Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck**

L. Wirth*, J. R. Clark*, A. Maybury*, R. Jain*, J. Rocco*; *Massachusetts General Hospital, Boston, MA; *Massachusetts Eye and Ear Infirmary, Boston, MA

---

**Purpose/Objective(s):** Tolerability and Efficacy of Induction Docetaxel, Cisplatin, and 5-Fluorouracil followed by Definitive Therapy for Locally Advanced Squamous Cell Carcinomas of the Head and Neck

J. J. Caudell**, R. D. Hamilton*, R. Jennelle*, S. Vijayakumar*, K. Pitman*, University of Mississippi Medical Center, Jackson, MS

**Materials/Methods:** Between 2003 and 2010 at the University of Mississippi Medical Center, 137 patients with LAHNC began curative intent therapy with induction cisplatin (75 or 100 mg/m2), docetaxel (75 mg/m2), and 5-fluorouracil (750
mg/m² x 5 days or 1000 mg/m² x 4 days; continuous infusion) every three weeks (TPF) for a planned 2 - 3 cycles. Patients lost to follow-up prior to definitive therapy were assumed to have progressed locoregionally but not distantly. Associations were tested via chi-square, and survival estimates were calculated using the Kaplan-Meier method. Results: Median age of patients was 53 years (range 27 - 72). The majority of patients were of low socioeconomic status: 77.4% having Medicaid or no health insurance. Tumor burden was high: 6.6% Stage III, 61.3% Stage IVA, and 32.1% Stage IVB. HPV or p16 status was only available for 18 patients, only 5 (27.8%) were positive. Induction TPF was delivered for a median of 2 cycles (range 1 - 3). Thirteen patients (9.4%) were switched from TPF to another induction regimen following 1 (n=12) or 2 (n=1) cycles. Following TPF, 37 patients (27%) were unable to initiate definitive therapy, secondary to death (n=18), progression of disease (n=9), or noncompliance (n=10). A further 14 (10.2%) patients did not complete or receive planned definitive therapy, secondary to noncompliance (n=7), lack of concurrent chemotherapy (n=3), progression (n=2), or death (n=2). Therefore, 37.2% of patients were unable to receive or complete standard definitive therapy. Patients with a Karnofsky performance status (KPS) <80 were less likely to complete definitive therapy (p = 0.09). Following induction TPF, 9 patients underwent surgery and adjuvant chemoradiotherapy, while 77 patients completed curative intent concurrent chemoradiotherapy. Median follow-up for patients alive at last contact was 20 months. At 2 years the locoregional control was 39.9%, while the distant metastases free rate was 72.3%, and the overall survival rate was 36.7%. Conclusions: In this population of LAHNC patients of low socioeconomic status with a high tumor burden, use of induction TPF precluded 37.2% of patients from initiating or completing planned definitive therapy. Inability to complete all planned therapy was associated with poor KPS.


174 Metformin Improves Outcomes in Head and Neck Squamous Cell Carcinoma

Purpose/Objective(s): Several studies have investigated the role of metformin as a chemopreventative agent for cancer, however its impact on outcome in head and neck squamous cell carcinoma (HNSCC) has not been investigated. In vitro studies of other cell types suggest that metformin may preferentially target cells with a mutation in TP53, which is present in at least 50% of HNSCC. We have previously used a classification of TP53 (wild type, nondisruptive or disruptive mutant) to predict those patients who fail local therapy. In this study, we investigated the impact of metformin on radiation response using this classification in vitro and in vivo. We also examined the effect of metformin use on outcome in patients with HNSCC treated with surgery and post-operative radiation (PORT). Materials/Methods: For in vitro studies, HNSCC cell lines of varying TP53 status were treated with metformin 2h prior to irradiation and clonogenic survival assays were performed. p53 expression was stably inhibited using the use of short hairpin RNA (shRNA). For animal experiments, 100,000 HNSCC cells were injected into the anterior tongue of nude mice. On post-injection day 8, the mouse tongue was irradiated with 5 Gy. Metformin was given for a total of 8 days IP (250mg/kg). Tumors were measured every 6 days until the animals were sacrificed. For clinical studies, the charts of 101 patients treated with surgery and PORT (median dose 60 Gy) for locally advanced HNSCC from 1993-2009 were reviewed. Results: Metformin treatment dramatically radiosensitized HNSCC cells with disruptive mutant TP53 as measured by clonogenic assays, with surviving fraction at 2 Gy (SF2) being decreased by approximately 40%; HNSCC cell lines with wild type were unaffected by metformin treatment. Inhibition of p53 expression rendered wild type HNSCC cells sensitive to radiosensitization by metformin. Metformin treatment potentiated the production of reactive oxygen species and radiation-induced senscence in a p53 dependent fashion. In an orthotopic animal model of HNSCC, metformin treatment had at least an additive effect on tumor volume when combined with 5 Gy of radiation. Finally, the clinical use of metformin by patients being treated with PORT was associated with improved disease free survival and loco-regional control. Conclusions: Metformin acts as a non-toxic radiosensitizer in HNSCC that selectively targets radiosensitive HNSCC both in vitro and in vivo. Furthermore, the concurrent use of this drug during PORT is associated with improved clinical outcome. Prospective trials are necessary to determine the role of this drug in HNSCC.

Author Disclosure Block: H.D. Skinner: None. V. Sandulache: None. T. Ow: None. B. Beadle: None. K. Ang: None. J. Myers: None.

175 Relationship Between Cetuximab-Induced Rash and Survival In Patients with Squamous Cell Carcinoma of the Head and Neck: A Meta-Analysis of Randomized Controlled Trials
N. Tun**, G. M. Villani**, The Brooklyn Hospital Center, Brooklyn, NY

Purpose/Objective(s): Several studies of cetuximab therapy in various cancers including head and neck, colorectal, non-small cell lung and pancreatic cancers, suggested a correlation between overall survival and the presence of cetuximab-induced acne-like rash. Some studies, however, have failed to show an association. We performed a meta-analysis of the relationship between cetuximab-induced rash and overall survival (OS) and progression-free survival (PFS) in patients with squamous cell carcinoma of the head and neck (SCCHN). Materials/Methods: A Medline search for eligible randomized controlled trials was performed. Eligibility criteria included randomized controlled trials of SCCHN involving cetuximab in a treatment arm. The intervention effect estimate and standard error of each study was derived from the hazard ratio (HR) and p value. Generic inverse variance method was applied to compute the overall effect size and HR with 95% confidence interval (CI). As there was no between-study heterogeneity (I² = 0%), fixed effects model was used. Results: Three randomized controlled trials, comprising 493 patients in control group and 490 in cetuximab group, were eligible for analysis: Bonner et al (2010), EXTREME trial (Vermorken et al, 2008) and ECOG study (Burtness et al, 2005). The Bonner study of patients with locally advanced SCCHN compared treatment with radiotherapy versus cetuximab plus radiotherapy. The EXTREME and ECOG studies included patients with metastatic or recurrent SCCHN treated with platinum-based chemotherapy with or without cetuximab. A statistically significant longer OS in patients who developed a cetuximab-induced acne-like rash compared to patients with no rash (HR 0.48, 95% CI 0.33 to 0.68, p = 0.0001) was found on analyzing these three studies. However, there was no significant association between the appearance of the rash and PFS (HR 0.79, 95% CI 0.58 to 1.06, p = 0.12) according to the meta-analysis of data from EXTREME and ECOG studies. Conclusions: The development of skin toxicity may be a surrogate for biologic activity of
may impact radio and both IMRT methods have longer treatment times than 3D institutional, helical tomotherapy.

Purpose/Objective(s): Head and Neck Squamous Cell Carcinoma (HNSCC) is predominantly a disease of the elderly, however their age and co-morbidities may affect their ability to receive standard of care therapy. The purpose of this study was to assess the patterns of care/types of treatments received by elderly HNSCC patients and identify associated variables that may impact receipt of Surgery and primary/adjunct Chemoradiation (CRT). 

Materials/Methods: Using the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database (1992-2007) we identified a retrospective cohort of non-metastatic HNSCC patients and categorized them into different treatment cohorts using Medicare claims. Comparisons were made between Surgery vs. Non-surgery, and CRT vs. non-CRT cohorts. Univariate analysis using Pearson Chi-Square test identified correlations between patient/clinical characteristics and treatment. Multivariate logistic regression estimated which variables (e.g. tumor site, stage, year of diagnosis, age, race, gender, Charlson Co-morbidity Index (CCI), marital status, SEER site, and socioeconomic indicators) were associated with treatment selection. Results: The 13,591 patients meeting eligibility criteria and having complete data available for the analytic variables had a median age of 75 (range 66-104). The majority of patients (64%) received primary Surgery. Comparatively fewer patients (18.7%) received CRT. On multivariate logistic regression comparing Surgery versus non-Surgery, age ≤ 75 (age 65-69 OR = 0.96; 95% CI 0.87 - 1.06; age 70-74 OR = 1.07; 95% CI 0.98 -1.17) and CCI ≥ 1 (OR = 1.00; 95% CI 0.93 - 1.08) were not associated with receipt of definitive surgery. Primary site, year of diagnosis, stage, and gender were all associated with receipt of surgery. Patients with earlier years of diagnosis were more likely to receive surgery. When the same variables were analyzed to examine receipt of CRT, age ≤ 75 (age 65-69 OR = 2.26; 95% CI 2.00 -2.56; age 70-74 OR = 1.93; 95% CI 1.72-2.17) and CCI ≥ 1 (OR = 0.89; 95% CI 0.81-0.99) were independently associated with receipt of CRT. Other covariates associated with CRT included tumor site, stage, year of diagnosis, and gender. Patients with earlier years of diagnosis were less likely to receive CRT. Race and socioeconomic indicators were not significant in either model. We also tested the interaction between age and co-morbidity which was not significant in any model. Conclusions: Age and Co-morbidity may influence the receipt of CRT for elderly HNSCC patients. However, these variables did not influence the receipt of primary surgery. How these variables and treatment decisions impact outcomes and toxicity is not yet understood.


177 A Defect-Based Reconstructive Classification System and Algorithm for TORS Oropharyngeal Defects
J. de Almeida*, C. L. Stucken*, E. M. Genden*, ., Mount Sinai School of Medicine, New York, NY

Purpose/Objective(s): With similar early oncologic outcomes and favorable functional outcomes, transoral robotic surgery (TORS) for oropharyngeal carcinoma is gaining acceptance. A reconstruction algorithm for TORS ablative defects must guide treatment and consider defect site and size, vessel exposure, neck communication, adjuvant treatments, and minimize functional deficits in speech and swallowing.

Materials/Methods: We retrospectively reviewed patients who underwent TORS surgery for oropharyngeal lesions at Mount Sinai School of Medicine from Jan, 2008 - May, 2011 and included those who had surgical defects confined to the oropharynx. Defects were classified from classes I - IV based on defects site, size, vessel exposure, and neck communication. Patient, disease, treatment, reconstruction, and in-hospital functional outcome data were collected. Surgical reconstructions were analyzed based on defect type. Results:Ninety-two patients (75 male, 17 female) with a mean age of 60.8 who underwent TORS surgery for oropharyngeal tumors (88 malignant, 4 benign) were included. Tumors originated from tonsil (62%), tongue base (34%), and palate (4%). Mean tumor size was 2.5 cm and involved an average of 2 subsites of the oropharynx. Six patients had received radiation, and 4 chemotherapy prior to surgery. There were a total of 25 Class I defects, 48 Class II, 5 Class III, and 14 Class IV defects. Class I defects were either allowed to heal secondarily (40%) or with local flaps (60%). Class II defects were allowed to heal secondarily (8%), with local flaps (90%), or with a combination of a local flap and a sternocleidomastoid (SCM) flap (2%). For Class III defects, 2 required closure of neck communication, 1 with a SCM flap, 2 required local flaps, and 1 was allowed to granulate. For Class IV defects, a radial forearm free flap was used in 6 cases, a pectoralis major flap for 1 case, a SCM flap in one case, and a combination of local flaps and secondary healing in 6 cases. Eighteen patients required tracheostomies, all of whom were decannulated before discharge. Four patients required gastrostomy tubes, 2 with class IV defects, 1 with class III, and 1 with class I. Conclusions: We propose a novel reconstructive classification system for transoral robotic surgery ablative defects with an algorithm to guide surgeons in the reconstructive thought process.

Author Disclosure Block: J. de Almeida: A: Employment; Intuitive Surgical, My fellowship salary is paid for in part by intuitive surgical, however, they have no involvement in research during my fellowship term. C.L. Stucken: None. E.M. Genden: None.

178 Acute Hematologic Parameters in Head and Neck Cancer Patients Undergoing Chemoradiotherapy: A Comparison Of 3-D CRT, IMRT, And Helical Tomotherapy

Purpose/Objective(s): Intensity modulated radiation therapy (IMRT) is increasingly used for head and neck cancer (HNC) treatment. At our institution, helical tomotherapy is commonly used to deliver HNC IMRT. Helical tomotherapy treatment times are longer than traditional IMRT, and both IMRT methods have longer treatment times than 3D-conformal radiotherapy (3DCRT). We hypothesized that longer beam-on times may impact radiosensitive, circulating blood cells, with resultant acute hematologic toxicity. 

Materials/Methods: We identified 281 patients
that received HNC chemoradiotherapy from 2001-2010. Our analysis was limited to patients receiving >60 Gy with concurrent weekly cisplatin at 30 mg/m². Using these parameters, 178 patients were available for study. Radiation delivery used 3DCRT in 41 patients (23%), conventional IMRT in 56 patients (31%), and helical tomotherapy in 81 patients (46%). Weekly hematologic parameters including hemoglobin, platelets, and white blood cell (WBC) counts were examined for each patient during their course of chemoradiotherapy. Results: Patients were well balanced with regard to sex, age, and stage. Treatment time, as assessed by delivered monitor units, varied significantly between the 3DCRT (median=502), IMRT (median=1087), and tomotherapy (median=6757) cohorts. Chemoradiotherapy was discontinued or held secondary to hematologic toxicity in 12% of 3D-CRT patients, 5% of IMRT patients and 15% of tomotherapy patients (NS). WBCs were not significantly different at baseline between the three cohorts. WBCs consistently declined through treatment in all three chemoRT cohorts, and these changes from baseline became significant (p<0.05) during the third week of treatment for all groups. No significant differences were detected in WBCs between any of the three cohorts at any timepoint. Hemoglobin and platelet values likewise showed a consistent decline throughout chemoradiotherapy, but no discernible differences were detected between the cohorts. Conclusions: In HNC patients undergoing high dose radiation with concurrent weekly cisplatin chemotherapy, the longer beam-on times associated with modern IMRT delivery techniques do not appear to result in increased acute hematologic toxicity.


179 FDG-PET/CT for Target Volume Delineation in the Intensity Modulated Radiotherapy with Simultaneous Integrated Boost (IMRT-SIB) and Concurrent Chemotherapy (CHT) for Locoregionally Advanced Oropharynx Squamous Cell Carcinoma: Preliminary Results

A. Magli*, E. Moretti*, M. Polsinelli**, M. A. Signor*, T. Ceschia*, O. Geatti*, R. Padovani**, S. Fongione**, **. Departments of Radiation Oncology University Hospital, Udine, Italy, *Departments of Physics University Hospital, Udine, Italy, **Departments of Nuclear Imaging University Hospital, Udine, Italy

Purpose/Objective(s): locoregional control remains a challenge in the management of advanced head-and-neck squamous cell carcinoma. Moderate hypofractionation IMRT-SIB has gained interest as a means of radiotherapy acceleration because of the convenience of single daily fractions and no need to generate separate boost plans [1]. Dose painting with IMRT can escalate radiation dose to target volumes identified by functional imaging such as FDG-PET and has potential to improve the therapeutic ratio. The optimal method of FDG-PET image segmentation remains unclear. To evaluate acute, late toxicity and early outcome of IMRT-SIB in radically locally advanced oropharynx squamous cell carcinoma patients with dose escalation to PET/CT positive tumor sub-volumes. Materials/Methods: between March and June 2009, 5 consecutive patients with advanced HNSCC received IMRT-SIB. The doses were 67.5, 60.0, and 54 Gy in 30 daily fractions to the planning target volumes for GTV disease, high-risk nodes, and low-risk nodes, respectively. Concurrent CHT was given for all patients (CDPP 100 mg/m²; Q28). All the patients underwent diagnostic FDG-PET/CT. The PET/CT and the simulation CT-images were transferred to MIM Software (MIM Software Inc.) On PET scan, GTVs were delineated employing a gradient-based segmentation method. The CT component of the PET/CT scan was registered by using deformable technique to the CT-scan. Subsequently deformation warps were used to transfer PET-GTV from the PET-scan to the planning CT-scan. Results: Of the patients, 100% completed chemoradiotherapy as prescribed. The median treatment duration was 42 days (range, 37-48 days). Grade 3 mucositis and dermatitis occurred in 2 patients and 1 patient, respectively. Grade 2 xerostomia occurred in 1 patient. Median follow-up of 10.3 months (range, 9 -12 months) 100% were feeding tube free after therapy, no soft-tissue fibrosis, esophageal stricture, and trismus occurred. The complete clinical response rate was 100%. Conclusions: these preliminary findings show that IMRT-SIB with dose escalation to 18FDG-PET positive tumor sub-volumes is a feasible technique also when administered concurrently with CHT and might also prove to be biologically more effective.


180 Randomized Phase II Trial of Neoadjuvant Chemotherapy followed by Concurrent Cetuximab-Radiotherapy or Cisplatin-Radiotherapy in Locally Advanced Nasopharyngeal Carcinoma

G. Zhu*, Y. Liu*, X. Guan*, C. Hu*, T. Xu*. Fudan University Shanghai Cancer Center, Shanghai, China

Purpose/Objective(s): To compare the efficacy and toxicity of locally advanced nasopharyngeal cancer (LANPC) patients treated with sequential neoadjuvant chemotherapy followed by concurrent cetuximab-radiotherapy (ERT) or cisplatin-radiotherapy (CRT). Materials/Methods: Patients with histologically confirmed, newly diagnosed (UICC/AJCC stage III to IVB) LANPC were treated with 2 cycles of neoadjuvant chemotherapy every 3 weeks with cisplatin 80 mg/m² D1, docetaxel 75 mg/m² D1, then were randomly assigned to (1) weekly cetuximab (400 mg/m²/initial dose before radiation, then 250 mg/m² weekly), concurrent with radiation. (2) 6 weekly doses of cisplatin (30mg/m²) concurrent chemoradiotherapy. Radiotherapy was delivered using IMRT technique to a total dose of 66-70.4 Gy in 30-32 fractions. Primary endpoints were toxicities, tumor control, survival, and quality of life. Results: From September 2010 to July 2011, 44 patients were randomly assigned to one of the two study arms. Twenty-one patients were randomly assigned to the investigational ERT arm and 23 patients to the control CRT arm. The two treatment arms were well balanced in the baseline characteristics. All patients completed the two cycles of neoadjuvant chemotherapy. Grade 3 neutropenia occurred in 81.8% (36) of patients during neoadjuvant docetaxel-cisplatin chemotherapy, the rate of G4 neutropenia was only 9.1% (10). A 95% clinical response rate (ICR,41PR,25D) was observed after neoadjuvant chemotherapy. Only 1 patient failed to complete the 7- cycle cetuximab. While in the CRT arm, the compliance was 4 patients (17.4%) completed the scheduled 6-cycle concurrent chemoradiotherapy, 12 patients (52.2%) 5 cycles, 5 patients (21.7%) 4 cycles, 2 patients (8.7%) 3 cycles. All patients in both arms completed RT to the prescribed dose on schedule. During the concurrent phase, no significant differences were observed in the rate of neutropenia, but cetuximab did statistically significantly increase the acute toxicities, particularly mucositis, pain and dysphagia. 100% and 85.7% of patients in ERT arm developed G3 and G4 mucositis, while the incidence rate in CRT arm were only 50% and 8.7%, respectively. After a
median follow-up of 5.6 months, we observed 1 distant disease progression in each arm. The 100% survival and local control rate were achieved until now. Conclusions: The preliminary results of our study showed a similar impact on disease control using neoadjuvant docetaxel-cisplatin followed by ERT and CRT. Although better compliance was observed in ERT arm, the increase in acute toxicity limits the implementation of this approach on a larger scale for LANPC patient population.

Author Disclosure Block: G. Zhu: None. Y. Liu: None. X. Guan: None. C. Hu: None. T. Xu: None.

181 Surgical Management of Squamous Cell Carcinoma of the Base of Tongue and Factors Predictive of Outcome

Purpose/Objective(s): Squamous cell carcinoma (SCC) of the base of tongue is the second most common cancer arising from the oropharynx. Existing treatment regimens favor primary radiation therapy. However, there is a shifting paradigm towards primary surgical management for early-stage tumors. The aim of this study was to report our experience in primary surgical management of these patients and identify factors predictive of outcome. Materials/Methods: Review of institutional databases identified 128 patients treated with primary surgery with curative intent between 1985-2005. Seventy-six (59%) patients had T1 or T2 tumors and 43 (34%) had a clinically negative neck. Overall survival (OS), disease-specific survival (DSS) and recurrence-free survival (RFS) rates were calculated using the Kaplan-Meier method. Factors predictive of outcome were analyzed by univariate and multivariate analyses. Results: Five-year OS, DSS and RFS rates were 60%, 70%, and 61% respectively. Fifty (39%) patients developed recurrent disease: 23 local recurrences, 23 nodal and 22 distant metastases. 5-year DSS for T1T2 tumors ranged from 75% for node positive disease to 85% for node negative disease. Multivariate analysis showed pathologic T-classification (pT) and extracapsular-extension (ECE) were significant predictors for DSS; patients with ECE were 1.8 times more likely to die from disease compared to patients with no ECE. For local recurrence, multivariate analysis showed that clinical T and pathological classification were significant predictors; patients with cT4 tumors were 12 times more likely to develop local recurrence. There were no factors predictive for neck or distant recurrence. Conclusions: pT stage and ECE are the main predictors of outcome in base of tongue SCC managed by surgery and PORT. Outcome of patients with early stage base of tongue SCC managed by surgery are excellent with 5 yr DSS of 75-86% These patients may be suitable for transoral robotic or endoscopic surgical procedures.


182 Histological Assessment of Leukocyte infiltration as a Predictor of Response and Demonstration of Pletropic Activity in Neo-adjuvant Head and Neck Cancer Subjects Treated with IRX-2 Immunomodulatory Regimen

Purpose/Objective(s): Patients with head and neck squamous cell carcinoma (HNSCC) have a significant immune dysfunction and treatment with an immunomodulatory regimen that includes IRX-2, cyclophosphamide and indomethacin is an attractive therapeutic option. In preclinical models IRX-2 has been shown to enhance activation of various antigen-presenting cells, activate T cells and protect them from activation induced death, and enhance antigen specific T cell responses in in-vivo models. Materials/Methods: From a previously reported neo-adjuvant Phase 2 trial, there were 25 head and neck cancer subjects where a pretreatment biopsy could be compared to the post treatment surgical specimen with respect to changes in leukocyte subsets, tumor response and survival. The validity of the observed changes in leukocyte subset analysis was increased by averaging the observations of three pathologists (H&E) or two pathologists (IHC), who were given identical blinded specimens for evaluation. To enhance evaluation of consistency among readers, scores were generated using a visual analog scale (VAS) to better quantify the observations between weak (0) and intense (100) lymphocytic infiltration. Results: Both pathologists reported leukocyte infiltration as defined by CD3, CD20 and CD68 was increased in the majority of subjects following treatment with IRX-2. CD3, CD20 and CD68 cell levels in the biopsy samples correlated with each other (i.e. subjects with high CD3 cells had high CD20 and CD68 cells). Following treatment with IRX-2, the increase in CD3 and CD20 cells remained correlated suggesting IRX-2 activity was mediated via the same mechanism. In contrast, the increase in CD68 cells was independent of the CD3 or CD20 cell numbers in the tumor. These observations suggest that IRX-2 acts to increase tumor infiltrating lymphocytes (TIL) and tumor associated macrophages (TAM) in the tumors and the increases may be via separate mechanisms. When subset assessments were correlated with change in tumor size or survival, the most significant independent variable was CD3 cells in the surgical specimen. Conclusions: These studies are consistent with the hypothesis that IRX-2 is a unique immune modulator due to its pleotropic activity on immune mediated anti-tumor mechanisms. We hypothesize that IRX-2 is facilitating the development of anti-tumor immune responses to as yet undefined tumor antigens. These results also confirm the biologic activity of the IRX-2 regimen in head and neck cancer subjects. A randomized clinical trial in head and neck cancer subjects in the neo-adjuvant setting is planned.

Do Patients Undergoing Adaptive Radiation Therapy (ART) Tolerate Radiation Therapy Better? Results of a Prospective QOL Study


**Purpose/Objective:** Anatomical and positional changes during radiation therapy for head neck cancers can result in higher dose to normal structures such as parotid and spinal cord and cause dose inhomogeneity and inadequate coverage of the PTV. ART has been found to be useful in alleviating some uncertainties, but it is not known if this will translate into better outcome both in tumor control and QOL. We present a prospective analysis of QOL in patients undergoing ART and concurrent chemotheraphy for locally advanced head and neck cancers.

**Materials/Methods:** As part of an ongoing prospective IRB approved study, 24 patients undergoing concurrent chemotheraphy and radiation therapy for head and neck cancers at AECOM/MMC complete QOL survey (EORTC QLQ-C30 and QLQ-H&N 35) before, every week during radiation therapy and at 1, 3 and 6 months after completion. The patients were re-simulated for adaptive planning midway through their treatment (based on our data on ART: Int J Radiat Oncol Biol Phys. 2011 Jul 1;80(3):677-85 and Int J Radiat Oncol Biol Phys. 2009 Feb 1;73(2):626-33). Patients were treated to 66-70Gy (2-2.12 Gy/Fraction) to the primary PTV and 54 to 60Gy (1.64-1.8 Gy/Fraction) to the subclinical and high risk PTV. Swallowing structures including base of tongue, constrictor muscles, proximal esophagus and oral cavity were contoured as avoidance structures along with other critical structures. 12% patients required new aquaplast masks, and 20% required new plans during adaptive planning. **Results:** The Global Health Status and Physical Functioning scores fell (mean 58.3 SD 35.4) during the first week of radiation therapy before recovering at the end of second week. There is a second dip in functioning scores (after the 2nd of chemotherapy) at 4th week subsequent to which the scores rise and get stabilized during the latter half of radiation therapy. The Nausea/Vomiting scores correlate with the timing of the end of second week mark before declining gradually. The mean swallowing specific score is worst at 5 weeks (61.1 SD 31.4) and recover gradually thereafter to level better than pre-RT score at 6 months follow up. **Conclusions:** To our knowledge, this is the first study looking at the QOL in patients undergoing ART for head neck cancers. Most studies have reported QOL changes before and after treatment and have not looked at the changes during RT. One would imagine that QOL scores would gradually deteriorate throughout radiation therapy. In our experience however, most of the QOL scores stabilize during the latter half of radiation therapy which might be as a result of ART but can also be due to tumor shrinkage or normal tissue response to radiation therapy. Matched pair analysis is underway to compare similar patients treated without ART.


---

Functional Outcomes and Quality of Life after Chemoradiotherapy for Oropharynx Tumors


**Purpose/Objective(s):** Concomitant chemoradiotherapy provides organ preservation for those patients with oropharynx tumors. We report results of a prospective study examining functional outcomes and quality of life after chemoradiotherapy in patients treated for base of tongue and tonsil tumors. **Materials/Methods:** Seventeen patients with primary head and neck cancer were treated with EBRT and chemotherapy. Pt characteristics were as follows: mean age: 60yr, (41-78 yr); Males: 82%. Sites of treatment were BOT: 41%, tonsil: 59%. All patients were seen baseline (pre-tx) and 3 months post-tx. Functional assessment included the Performance Status Scale (PSS) (List et al., 1996), tongue strength, assessed with the Iowa Oral Performance Instrument (IOPI), jaw opening, and saliva weight (Saxon test, Kohler & Winter, 1985). QOL testing utilized the Eating Assessment Tool (EAT-10), EORTC H&N35. QOL and functioning were compared baseline and 3 months post-tx. Paired t-tests were used to examine difference in mean scores over time, with level of significance set at p<.05. **Results:** PSS scores were significantly lower for 2 of 3 domains at 3 months, including Normalcy of Diet (100 vs 84 p=.001)-16% reduction, Eating in Public (100 vs 90 p=.004)-10% reduction. Understandability of Speech mean scores were 100 (normal) at both time points. Tongue strength was significantly lower (60 vs 50kPa p<.001)-10% reduction. Jaw opening was significantly reduced post-tx (52 vs 47mm) (p<.001)-9.6% reduction. Saliva weight was significantly reduced post-tx (4.9 vs 2.0g p<.001)-59% reduction. QOL scores were significantly worse for the EAT-10 (0.69 vs 10.94 p<.001) and the EORTC H&N35 (42 vs 57 p=.001). Despite statistically significant differences in mean scores from pre to 3 months post-tx, level of functioning was either still within normal limits or only mildly impaired at 3 months for all functional outcomes other than salivary production. **Conclusions:** Concomitant chemoradiotherapy for treatment of oropharyngeal tumors can result in normal to only mildly impaired functional outcomes of diet, and ability to eat in public, as well as tongue strength, jaw opening and QOL 3 months post-tx. Understandability of speech remains unaffected. Salivary flow, however, is moderate-severely impaired 3 months post-tx. Current studies are examining these patients over time to assess change in functioning.


---

Human Papillomavirus (HPV) Related Squamous Cell Carcinoma of the Oropharynx is Associated with Decreased Late Toxicity after Definitive Concurrent Chemoradiotherapy (CRT)


**Purpose/Objective(s):** Late treatment-related toxicity is common after CRT for locally advanced squamous cell cancer of the oropharynx (SCCOP). HPV-related SCCOP is associated with improved disease control and survival and has become increasingly more common. This study explores whether HPV positivity is also associated with a favorable toxicity profile, and whether rates of late toxicity have changed over time. **Materials/Methods:** Patients (pts) with stage III-IVB SCCOP with known in-situ hybridization based HPV status who were treated with CRT were
identified. Treatment consisted of radiation therapy administered once or twice daily to a total dose of 70-74.4 Gy using a conventional 3 field approach, concurrent with either 3 cycles of cisplatin (C) at 100 mg/m² q3 weeks, or with 96 hour infusions of C (20 mg/m²/day) and 5-fluorouracil (1,000mg/m²/day) given during the first and fourth weeks of RT (C/F). Feeding tube dependence (FTD), narcotic use, dietary limitation and trismus were retrospectively assessed for the first two years of follow-up. Univariate (UVA) and multivariate logistic regression analysis (MVA) were performed to identify pt, tumor and treatment related variables associated with late toxicity. We also compared these outcomes with a similarly treated historical cohort of 96 pts with HPV-unknown, stage III-IVB SCCOP using Fisher's exact test. Results: Eighty two pts (88% male; 92% Caucasian) were included in this IRB approved study. Median age was 56 (range: 41-69), and median follow up was 26 months (mth). Primary site was base of tongue (51%), tonsil (46%) and other (3%). 61 pts (75%) were HPV positive (+) and 21 (25%) were HPV negative (-). Current, former and never smokers were 16%, 51% and 33% in HPV + pts and 71%, 19% and 10% in HPV - pts. HPV + pts experienced less late FTD (3mth - 7% vs. 21%; 6mth - 0% vs. 22%; p<0.001), dietary limitation (3mth - 36% vs. 74%; 6mth - 15% vs. 47%; p=0.005), and trismus (3mth - 12% vs. 47%; 6mth 14% vs. 53%; p=0.003) then HPV - pts. Narcotic use was similar between groups. On MVA, HPV positivity was the only variable associated with lower rates of dietary limitation and trismus, while age, tumor stage, smoking status, and type of chemotherapy were not. Compared to our historical cohort, the incidence of FTD (13% vs. 71%; p<0.001), and dietary limitation (44% vs. 86%; p<0.001) at 6 mth post-CRT were lower in all pts in the current cohort, most significantly in HPV + disease. HPV + pts had superior 2yr OS (97% vs. 73%; p=0.01) compared to those with HPV - disease. Conclusions: The incidence of late toxicity after definitive CRT for SCCOP has diminished over time. HPV positivity is strongly associated with decreased late toxicity and its rising incidence may partially account for this change.


---


Purpose/Objective(s): Intensity Modulated Radiation Treatment (IMRT) is becoming a standard of care for head and neck cancer (HNC). We treated HNC using either a moderate hypofractionation (MHF) schedule with 66 Gy at 2.2 Gy per fraction delivered to the gross primary and nodal tumor and standard dose fractionations of 54-60 Gy at 1.8-2.0 Gy per fraction to the elective neck lymphatics. We also treated HNC using a conventional dose and fractionation (CDF) schedule with 70 Gy at 2.0 Gy per fraction delivered to the gross primary and nodal tumor with reduced dose fractionations to the elective neck lymphatics. We analyzed these two cohorts for treatment outcomes. Materials/Methods: Between Nov 2001 and Feb 2009, 89 patients with primary carcinomas of oral cavity, larynx, oropharynx, hypopharynx, and nasopharynx received definitive IMRT with or without concurrent chemotherapy. Twenty patients were treated using the MHF schedule while 69 were treated using the CDF schedule. Patient characteristics and dosimetry plans were reviewed. Patterns of failures including local recurrence, regional recurrence and distant metastasis, disease free survival (DFS) and overall survival (OS), and toxicities, including the rate of feeding tube placement and percent weight loss, were reviewed and analyzed. Results: Median follow-up was 31.2 months. Thirty-five percent in the MHF cohort and 77% in the CDF cohort received chemotherapy. No RR was observed in either cohort. OS, DFS, LR, and DM rates for the entire group at 2 years were 89.3%, 81.4%, 7.1% and 9.4%, respectively. Subgroup analysis showed no significant differences in OS (p=0.595), DFS (p=0.863), LR (p=0.833) or DM (p=0.917) between these two cohorts. Similarly, no significant differences were observed in rates of feeding tube placement and the percent of weight loss. Conclusions: Similar treatment outcomes were observed between MHF and CDF cohorts. A dose of 50 Gy at 1.43 Gy per fraction may be sufficient to electively treat low-risk neck lymphatics.


---


Purpose/Objective(s): Locoregionally advanced squamous cell carcinoma of the upper aerodigestive tract (SCCHN) is frequently managed with chemoradiation. Involved cervical nodes are managed definitively with curative radiation doses in contemporary treatment plans. Controversy has developed with respect to management of involved cervical lymphatics post-treatment. Early treatment protocols called for planned neck dissection in patients regardless of clinical and radiographic disease response in the neck. It was felt that many patients (complete clinical/radiographic responders) were subjected to unnecessary neck operations with this approach. Currently, patients are selected for consolidative neck dissection (CND) after definitive chemoradiation based on defined clinical/radiographic criteria. Our objective was to evaluate our short term experience with CND, with emphasis on criteria for patient selection and clinical outcomes. Materials/Methods: Patients with SCCHN and neck disease ≥N1 treated definitively with chemoradiation at our Center were reviewed. Subset analysis on patients undergoing CND was performed (type of neck dissection performed, pathologic findings in the neck, clinical outcomes). Patients were selected for CND if they had clinically and or radiographically defined involvement of involved cervical lymphatics post-treatment. Early treatment protocols called for planned neck dissection in patients regardless of clinical and radiographic disease response in the neck. It was felt that many patients (complete clinical/radiographic responders) were subjected to unnecessary neck operations with this approach. Currently, patients are selected for consolidative neck dissection (CND) after definitive chemoradiation based on defined clinical/radiographic criteria. Our objective was to evaluate our short term experience with CND, with emphasis on criteria for patient selection and clinical outcomes. Materials/Methods: Patients with SCCHN and neck disease ≥N1 treated definitively with chemoradiation at our Center were reviewed. Subset analysis on patients undergoing CND was performed (type of neck dissection performed, pathologic findings in the neck, clinical outcomes). Patients were selected for CND if they had clinically and or radiographically defined involvement of involved cervical lymphatics post-treatment.

Results: 16 patients had 19 CNDs (3 had bilateral CND). Average patient age was 57 years. 10 patients had oropharynx cancer, 4 had larynx cancer, and 2 had unknown primary disease. 2 patients had stage 3 disease, 14 had stage 4. 13 patients had N2 disease (7 N2C, 5 N2B, 1 N2A), 3 had N1. 15/16 patients had selective neck dissection procedures (lateral dissections), and 3 patients had bilateral selective procedures. One patient had extended radical neck dissection. 8 of the 16 CND patients had no residual carcinoma in their neck dissection specimen. Of these 8 patients, 7 are clinically and radiographically disease free at 1 year mean followup. One of the pathologically N0 patients has developed second primary lung cancer. Of the 8 CND patients who had residual carcinoma in their neck dissection specimen, 4 are clinically and radiographically disease free, 2 have died of locally and regionally recurrent disease, and 2 are alive.


with regional/distant and distant metastatic disease respectively. **Conclusions:** Although followup time is short, our data suggest a trend of poor prognosis and high likelihood of disease recurrence in pathologically positive CND patients. Longer term followup and additional CND cohort patients will verify these results, supporting the need for additional standard and or novel treatment (in the form of clinical trial) in these patients.

**Author Disclosure Block:** D. Frank: None. B. Saltman: None. D. Schwartz: None. B. Mehrotra: None. Y. Lebowicz: None. V. Nguyen: None. A. Johnson: None. J. Rini: None.

**188**  
Comparison of the Application and Changes in Outcomes Between the AJCC 6th vs. 7th Editions to the Staging of Large and Locally Advanced Non-melanoma Skin Cancer  
C. L. Matthiesien*, S. Thompson*, C. Forest*, S. Ahmad*, T. Herman*, C. Bogardus*. , University of Oklahoma Health Sciences Center, Oklahoma City, OK

**Purpose/Objective(s):** Patients with advanced non-melanoma skin cancer (NMSC) lesions may present a unique treatment challenge. We reviewed our experience regarding the use of radiation therapy (RT) for T2-T4 NMSC according to the AJCC 6th edition and analyzed outcomes by lesion T stage. We aimed to investigate and compare the application and outcome analysis of the AJCC 7th edition staging criteria for advanced NMSC. **Materials/Methods:** A retrospective review of 59 patients and 73 large and locally advanced T2-T4 NMSC lesions was performed who received RT from 2004-2010. Fifty-six lesions (76.7%) were previously untreated and 17 (23.3%) were recurrent. Lesion histologies included basal (52.0%) and squamous (48.0%) cell. By the AJCC 6th edition staging criteria, 40 lesions (54.8%) were staged T2, 18 (24.7%) T3, and 15 (20.5%) T4. We then retrospectively restaged each lesion according to the guidelines of the AJCC 7th edition staging manual, repeated our previous analysis, and compared these outcomes. Median patient follow-up at comparative analysis was 18 months (range 2-48) months. **Results:** Following AJCC 6th edition restaging, 66 (90.4%) of lesions were staged T2, two (2.7%) were T3, and five (6.8%) were T4. None of the restaged T stage lesions resulted in lesion upstaging however; 28 lesions (38.4%) were downstaged. No staging changes occurred for T2 lesions, but all 18 (100%) T3 lesions were downstaged to T2, ten (66.7%) T4 lesions were downstaged to either T2 (8) or T3 (2). The most significant factor resulting in the 6th edition T3 lesion downstaging was the changes in size criteria by the 7th edition. The most significant factors for the 6th edition T4 lesion downstaging was the specification of specific anatomic bone invasion for T3 lesions, and the addition of depth criteria and inclusion of primary site ear for T2 lesions. By the AJCC 6th edition staging, disease free survival (DFS) to all therapy (RT/surgery/chemo) vs RT alone was 95.0% and 80.0% for T2 lesions, 77.8% and 66.7% for T3, 60.0% and 53.3% for T4 lesions, respectively. Following AJCC 7th edition re-analysis, DFS to all therapy vs RT alone was 81.8% and 68.2% for T2, 76.7% and 67.6% for T3, and 20.0% for both categories of T4 lesions. **Conclusions:** The AJCC 7th edition staging of NMSC results in a poorer outcome prediction. The elimination of size, and the requirement and specification of bone invasion location as a staging criterion for advanced NMSC has significantly changed the pattern of analysis for these advanced lesions. We propose that in view of such changes in outcomes analysis that the AJCC consider reinstating size as a staging criterion as well as all bone invasions as T4. Such changes would more accurately reflect the clinical findings and restore accuracy to the staging of advanced NMSC.

**Author Disclosure Block:** C. L. Matthiesien: None. S. Thompson: None. C. Forest: None. S. Ahmad: None. T. Herman: None. C. Bogardus: None.

**189**  
Transoral Robotic Surgery for Smokers with Squamous Cell Carcinoma of the Oropharynx  
C. Stucken*, J. R. de Almeida*, C. C. L. Tong*, E. M. Genden*. , Mount Sinai School of Medicine, New York, NY

**Purpose/Objective(s):** Transoral Robotic Surgery (TORS) has been as an effective modality for the treatment of squamous cell carcinoma (SCCa) of the oropharynx (OP). Recent literature suggests that human papillomavirus (HPV) mediated SCCa has a good prognosis; however, a significant history of tobacco use represents a poor prognostic factor, even in patients with HPV-mediated disease. The purpose of our study is to evaluate the functional and oncologic outcomes of a high risk population_smokers_using TORS. **Material/Methods:** At a tertiary medical center, patients with previously untreated OP SCCa underwent treatment with TORS in a prospective trial. Demographic, operative, hospital course, clinicopathologic, adjuvant treatment, and outcomes data were collected. Analyses of outcomes were stratified by smoking status. **Results:** A total of 57 patients (35 smokers and 22 non-smokers) with OP SCCa underwent TORS with or without adjuvant therapy. The mean age was 63.3 for smokers and 52.6 for non-smokers (p=0.02). Other than age, there were no baseline differences between the groups in terms of gender, tumor stage and differentiation, perineural invasion, lymphovascular invasion, margin status, extracapsular extension, adjuvant therapy, and follow-up time. Non-smokers began oral intake sooner than smokers (1.0 vs. 1.8 days, p=0.001). After a mean follow-up time of 16.1 months, preliminary 2-year outcomes data shows local-regional control rates of 97% and 100% (p=0.71), distant metastasis control rate of 100% and 94% (p=0.36), progression free survival of 91% and 91% (p=0.53), and overall survival of 97% and 100% (p=0.43) in the smoking and non-smoking groups, respectively. **Conclusions:** Preliminary results suggest that TORS may provide acceptable oncologic outcomes for both the high-risk smoking population as well as those without a smoking history. This data supports the use of TORS as the primary modality of treatment for high risk population (tobacco users) with OP SCCa. In addition to providing pathologic information to guide a personalized adjuvant therapy plan, TORS induction therapy reduces the tumor burden and appears to demonstrate excellent early oncologic outcomes.

**Author Disclosure Block:** C. Stucken: None. J.R. de Almeida: None. C.C.L. Tong: None. E.M. Genden: None.

**190**  
Results of Salvage Treatment for Locally Recurrent Nasopharyngeal Carcinoma (NPC) - A Single Institution Study  
C. Chen*, W. Fee*, J. Chen*, C. Chan*, B. Khong*, W. Hara*, D. Goffinet*, Q. Le*, . Department of Radiation Oncology, Cancer Hospital of Shantou University Medical College, Shantou, China, Department of Otolaryngology, Stanford University medicine, Stanford, CA, Department of Radiation Oncology, Stanford University, Stanford, CA

**Purpose/Objective(s):** To determine the outcomes of re-treatment in patients with locally recurrent NPC and to compare the local control rate
between different treatment strategies. **Material/Methods:** We retrospectively reviewed the records of patients who received either re-irradiation or surgical resection or both treatments for their local recurrence at Stanford University. Patients were excluded if they had inadequate treatment data or follow up. The end points were local control (LC) and overall survival (OS) after re-treatment. **Results:** Fifty six patients qualified for this study. There were 34 males and 22 females with a median age of 49 years. Thirty three patients had surgery (S-group) as the only retreatment modality (including patients with 2nd or 3rd relapse after radiotherapy), 12 had surgery plus radiotherapy and/or chemotherapy (CMT-group), 22 had radiotherapy or radiotherapy plus chemotherapy (RT-group, including patients with 2nd or 3rd relapse after surgery). There were significantly more rT1-2 tumors in the S-group compared to the CMT- and the RT-group (73% vs. 33% vs. 28%; p =0.005). The median follow up was 60.5 months for 26 living patients. Durable local control was achieved in 28 patients, yielding a 5-year LC of 41.2% and OS of 52.9%. The 5-year LC rate was similar between the 3 treatments: 55.7% for S, 46.7% for CMT and 41.4% for RT, p=0.80. There was a trend for better LC and OS for rT1-2 tumors (LC: 58.3% vs. 28.6%; p=0.345; OS: 65.2% vs. 39.7%, p=0.12). **Conclusions:** Durable local control and respectable survival rate were achieved in retreatment of patients with locally recurrent NPC. Similar local control rates were attained for RT vs. S despite larger recurrent tumors in the RT group.

**Author Disclosure Block:** C. Chen: None. W. Fee: None. J. Chen: None. C. Chan: None. B. Khong: None. W. Harra: None. D. Coffinset: None. Q. Le: B. Research Grant; GSK, Amgen, Varian.

---

**191** Comparison of Feasibility and Efficacy of Induction Chemotherapy followed by Chemoradiotherapy vs. Chemoradiotherapy for Locally Advanced Head and Neck Cancer


**Purpose/Objective(s):** We compared the tolerability and efficacy for patients treated with locally advanced head and neck cancer (LAHNC) treated with induction chemotherapy followed by planned concurrent chemoradiotherapy (SEQ) or concurrent chemoradiotherapy (CRT) at the University of Mississippi Medical Center (UMMC). **Materials/Methods:** The UMMC head and neck cancer database was queried for patients with LAHNC who were treated with definitive intent either with SEQ or CRT recommended. 137 patients treated with SEQ began with induction cisplatin (75 or 100 mg/m2), docetaxel (75 mg/m2), and 5-fluouracil (750 mg/m2 x 5 days or 1000 mg/m2 x 4 days; continuous infusion) every three weeks (TPF) for a planned 2 - 3 cycles. 110 patients in whom CRT was recommended began radiotherapy. Comparisons between treatment groups were tested via Pearson chi-square. To address potential selection bias we used propensity score modeling. Survival estimates were calculated using the Kaplan-Meier method from the date of initiation of therapy stratified by propensity scores and comparisons were tested via log-rank. Cox regression analyses were performed adjusting for propensity scores. **Results:** Patients selected for SEQ in general had poorer prognostic factors: more likely to be black (p = 0.02), Medicaid or no insurance (p = 0.001), male (p = 0.02), higher T-stage (p < 0.001), higher N-stage (p = 0.001), and have hypopharyngeal primary site (p = 0.01). CRT patients were more likely to be older (p = 0.04), and had a trend towards higher pack-year history (p = 0.06). On multivariate logistic regression, higher T-stage (p < 0.001), higher N-stage (p < 0.001) and primary site (p = 0.02) remained significant predictors of selection of SEQ, and were used to create propensity matching groups. Median follow-up for patients alive at last contact was 21 months. Patient receiving SEQ were significantly less likely to complete definitive therapy, 37.2% compared with 12.7% for CRT (p < 0.001). In unadjusted Kaplan-Meier analysis, the 2 year rate of locoregional control (LRC) was 39.9% in the SEQ group and 68.3% in the CRT group (p < 0.001). In multivariate analysis of LRC adjusting for propensity score, CRT remained significant (p = 0.001, HR 0.39, 95% CI 0.22 - 0.69). In unadjusted Kaplan-Meier analysis, the 2 year rate of overall survival (OS) was 36.7% in the SEQ group and 56.8% in the CRT group (p = 0.001). In multivariate analysis of OS adjusting for propensity score, the difference between the groups became non-significant (p = 0.52). **Conclusions:** Patients with LAHNC were less likely to complete definitive therapy when treated with SEQ. This translated into a significant decrement in LRC, but not OS.


---

**192** Primary Proton Radiotherapy for Head and Neck Paragangliomas

**R. S. Grover**, Q. T. Luu, S. C. Teichman, L. N. Loredo, J. D. Slater*, Loma Linda University Medical Center, Loma Linda, CA , 1Stanford Emanuel Radiation Oncology Center, Turlock, CA

**Purpose/Objective(s):** Radiosurgery and fractionated external beam radiotherapy are effective treatments head and neck paragangliomas. Proton beam radiotherapy, by virtue of its unique dosimetric properties, is able to deliver a highly conformal tumor dose while minimizing dose to both midline and contralateral normal tissues. To evaluate its effectiveness, we investigated (1) the local control of paragangliomas receiving primary proton beam radiotherapy, and (2) the acute and late toxicities associated with this treatment. **Material/Methods:** Between 2004 and 2011, 6 patients with 7 paragangliomas of the head and neck were treated with primary proton beam radiotherapy at the James M. Slater, MD Proton Treatment and Research Center in Loma Linda, CA. Treatment and follow-up data for these patients was reviewed. **Results:** At a median follow-up of 48 months (range: 15 - 128 ), local control is 100%, with all tumors noted to be stable as of last follow-up. Acute nausea (grade 2) was noted in two patients. There were no other grade 2, and no grade 3 or higher, acute toxicities. Late toxicity was seen in two patients who noted a minor exacerbation of preexisting symptoms following treatment: one patient with resultant grade 1 hoarseness, and another with grade 1 dysphagia. This second patient also developed late grade 1 dysgeusia. These two patients received 59.4 GyE. All other patients (all receiving 50 GyE) reported stable or improved symptoms after treatment. Maximum dose received to any contralateral parotid gland was 0.5 Gy. One patient received simultaneous treatment (50 GyE) to a pair of large, bilateral, carotid paragangliomas. Total V30 for the right and left parotid glands was 47% and 32%, respectively. This patient has no subjective late xerostomia. **Conclusions:** This series is in agreement with prior published work in its demonstration of radiotherapy as an effective primary treatment for head and neck paragangliomas. Because of its highly conformal nature and lack of exit dose, proton beam radiotherapy can deliver the requisite dose to ipsilateral tumors with essentially no dose to contralateral structures. Acute toxicity was minimal, and late toxicity was essentially zero for doses of 50 GyE. Proton therapy also proved well-tolerated in the primary treatment of a patient with
bilateral carotid body tumors.

**Author Disclosure Block:** R.S. Grover: None. Q.T. Luu: None. S.C. Teichman: None. L.N. Loredo: None. J.D. Slater: None.

**193** The Impact of Treatment Strategy on Prognosis in Head and Neck Cancer Patients with Supraclavicular Nodal Metastases

**F. L. Ampil**, C. Nathan*, G. Caldito*, G. Sangster*, University of Southwestern Louisiana State University Health Sciences Center, Shreveport, LA

**Purpose/Objective(s):** In head and neck cancer (HNC), the lower the level in the cervical lymph node chain, the least it is affected by tumor and the poorer the prognosis. Because of the infrequency of HNC with lower neck nodal metastasis (LNNM), little information is available to guide clinicians undertaking management of this particular complicated neoplastic condition. Our objective was to investigate the prognostic significance of applied modes of therapy in patients with HNC-LNNM in an attempt to determine optimal therapy. **Materials/Methods:** From a total of 2,275 HNC patients, 23 people (1%) were managed with intent to treat for HNC-LNNM between 1989 and 2007. The individuals were classified into three groups: those who underwent definitive surgery and postoperative radiotherapy (eight patients), those who were treated by chemoradiation (nine patients), and those who received single modality therapy (six patients). The median follow-up was 19 months and the study endpoints were locoregional tumor control and survival. **Results:** Locoregional tumor control was achieved in the majority (75%) of the cases and the 2-year survival rate was 48%. The two-year survival rates of people managed by surgery and postoperative radiotherapy, chemoradiation or single modality therapy were 63%, 56% and 17% respectively, (p=0.04). Aggressive therapy resulted in five (22%) long-term (>5 years) survivors. **Conclusions:** Aggressive combined therapy seems appropriate for people with HNC-LNNM because their outcomes were not inferior to those of single-modality treated individuals and should be further investigated in prospective trials.

**Author Disclosure Block:** F.L. Ampil: None. C. Nathan: None. G. Caldito: None. G. Sangster: None.

**194** Chemotherapy, Radiation, and Chemoradiation Compared with Surgery in Patients with Squamous Cell Carcinomas of the Nasal Cavity and Paranasal Sinuses

**K. Thomas**, L. A. Nedzi*, B. D. Sumer*, University of Texas Southwestern Medical Center, Dallas, TX

**Purpose/Objective(s):** The goal of this study was to compare the clinical outcome (overall survival and progression-free survival) of patients with advanced paranasal sinus and nasal cavity squamous cell carcinoma (SCC). This retrospective chart review identified 46 patients with SCC from 1998 to 2010. Patients were stratified into two cohorts: those who underwent surgery with chemotherapy and/or radiation, and those treated non-surgically with chemotherapy and/or radiation therapy. **Materials/Methods:** This study was a retrospective chart review performed in conjunction with tertiary care centers at the University of Texas Southwestern Medical Center at Dallas, TX. Between January 1, 1998 and December 1, 2010, 111 patients were evaluated with the diagnosis of paranasal sinus and nasal cavity cancer. Patients were excluded from the analysis if they did not have a histological subtype of squamous cell carcinoma, if they did not have an advanced stage of III or IV, or if the patient received treatment outside of the UT system with inadequate treatment documentation (total excluded, n = 65). **Results:** There was no statistical difference between the overall survival of the surgical and non-surgical groups, with a median survival of 84.6 months (p = 0.895 by log-rank test). There were no significant differences in time to progression between two treatment groups (p = 0.938 by log-rank test). Median overall survival among patients treated with surgery was 65.9 months. Median overall survival among patients treated with non-surgical treatments did not reach statistical significance. Median progression-free survival for both groups was 24.8 months. Median progression-free survival among patients treated with surgery was 24.8 months. Median progression-free survival in non-surgery group was 49.1 months. Univariate analysis showed no significant association between risk factors and time to progression. In the univariate analysis for the association between risk factors and overall survival, sex was the only variable significantly associated with overall survival. There were no significant risk factors associated with the time to progression in the Multivariate Cox regression. Multivariate Cox regression shows sex is an independent significant risk factor associated with overall survival. **Conclusions:** We found no statistical difference between the overall-survival and disease-free survival for patients with advanced squamous cell carcinomas of the paranasal sinuses and nasal cavity with surgery and adjunctive measures as compared to those treated with only chemotherapy and/or radiation. This pilot indicates that further investigation is warranted regarding the role of surgery in the management of advanced stage SCC of the head and neck.

**Author Disclosure Block:** K. Thomas: None. L.A. Nedzi: None. B.D. Sumer: None.

**195** Biweekly Gemcitabine and Carboplatin in First-Line Metastatic or Recurrent Nasopharyngeal Carcinoma (NPC)—An Early Report


**Purpose/Objective(s):** This phase II study evaluated the activity and safety of carboplatin in combination with gemcitabine (GEM) for the first time in the palliative setting for patients (pts) with undifferentiated/poorly differentiated NPC. **Materials/Methods:** Pts with untreated metastatic (M1) or locoregionally recurrent (LR) NPC were treated with a biweekly carboplatin-gemcitabine regimen (D1: GEM, 1250 mg/m² +Carboplatin, 450 AUC 5 for a max. of 08 cycles. Response was assessed every 4 cycles (RECIST criteria). **Results:** 19 pts accrued before 31st July 2009 were evaluated for toxicity and response; cut-off date for data analysis was 13th Oct 2009. The median age was 47 yrs (range 28-72); 15 were men, all had ECOG status of 0-1. At enrolment, 8 pts (42%) had M1 disease only, 3 (15%) pts had LR only and the rest both M1 & LR. All pts with only LR received radical radiotherapy (RT) at initial diagnosis. A median of 06 cycles (range 4-06) were administered. Best overall response rate was 49%, with 08 partial responses & 10 stable diseases. The median duration of response was 9 months (range 2.8-13). Grade (gr) 3-4 hematological toxicities included neutropenia in 9 pts (47%), thrombocytopenia in 5 pts (26%). Gr 3-4 non-hematological toxicities included gr 3 diarrheas in 4 pts, gr 3 epistaxis in 3 pts. There were no treatment-related deaths and only 1 pt withdrew from study due to drug-related toxicity. **Conclusions:** Gemcitabine-Carboplatin is a promising regimen among pts with metastatic & recurrent NPC. Accrual is ongoing with a planned total sample of 55 pts.
196 Nodal Pathologic Features are Prognostic in Head and Neck Cancer Patients Undergoing Definitive Chemoradiotherapy
M. E. Christensen1,2, P. Paximadis1,2, G. Dyson1,2, D. Kamaras1, A. Sukari1,2, H. Lin1,2, H. Yoo1,2, H. Kim1,2 . 1Wayne State University Affiliated Hospitals, Detroit, MI, 2Barbara Ann Karmanos Cancer Center, Detroit, MI

Purpose/Objective(s): Pathologically defined characteristics of lymph node metastases of squamous cell carcinoma of the head and neck have been demonstrated to affect outcome in multiple surgical series. Their role in the setting of concurrent chemoradiotherapy (CRT), however, is not as well defined. We aim to analyze the prognostic significance of such factors in patients undergoing definitive CRT after upfront neck dissection. 

Methods: Seventy seven patients with biopsy confirmed squamous cell carcinoma of the head and neck and radiographic evidence of bulky or necrotic lymph nodes underwent up-front neck dissection followed by definitive chemoradiation. Final pathology reports were retrospectively reviewed for the presence of extranodal tumor extension (ENE), nodal necrosis, AJCC N-stage, cervical level IV involvement, and total number of nodes positive. These factors were correlated to clinical outcome using multivariate Cox regression.

Results: Median number of nodes sampled per neck specimen was 38 (range: 2 - 78). Median number of nodes positive for SCC per neck specimen was 3 (range: 0 - 48). ENE, nodal necrosis, and cervical level IV positivity were identified in 68%, 56%, and 29% of patients, respectively. Twenty patients were upstaged and 3 patients were downstaged at least one full AJCC N-stage. Analysis confirmed that the presence of nodal necrosis significantly predicted for decreased locoregional control (HR: 5.78) and overall survival (HR: 3.23), while ENE significantly predicted for decreased distant control (HR: infinite), progression free survival (HR: 9.43), and overall survival (HR: 14.66). No other factor significantly predicted for any outcome. Conclusions: We have demonstrated that pathologically confirmed ENE and nodal necrosis significantly decrease survival of patients undergoing concurrent chemoradiotherapy after upfront neck dissection for advanced squamous cell carcinoma of the head and neck. Alternative treatment and follow-up strategies may be warranted in these nodal characteristics, given their prognostic significance and distinct sites of failure.

197 A Phase I Dose Escalation Trial of SRS Boost Treatment of Human Papilloma Virus (HPV)-Unassociated Oropharyngeal Squamous Cell Carcinoma (OPSCC)
D. Schwartz*, S. Parise*, V. Nguyen*, J. Fantasia*, B. Saltman*, D. Frank*. Hofstra-North Shore LI School of Medicine, Hempsted, NY

Purpose/Objective(s): HPV-negative status and/or significant smoking history predict for poor radiation response in patients with OPSCC. To improve disease control outcomes in this population, we are conducting a phase I dose escalation trial of stereotactic radiotherapy boost delivery to primary disease. Materials/Methods: Twelve consecutive patients with newly diagnosed HPV-unassociated OPSCC were enrolled onto this IRB-approved clinical trial between 5/2010 and 6/2011. Eligible patients had HPV-negative disease and/or tobacco exposure history of >10 pack-years. The cohort consisted of 11 males/1 female with a median age of 58.5 yrs (range: 46-64). There were 7 tonsil/2 tongue base/1 soft palate/1 GP sulcus cases, with 5 T2/4 T3/3 T4 primaries and 2 AJCC stage III/10 stage IV disease. Primary disease received 60 Gy, gross nodal disease 66 Gy, and prophylactic nodal target volumes 54-60 Gy with routine IMRT technique in 30 daily fractions. All patients received concurrent chemotheraphy (11 cisplatinum-based, 1 cetuximab). Within one week of IMRT completion, SRS boost treatment was delivered to the primary disease target volume. Initial SRS dose level was set at 8 Gy, and has been delivered to 7 enrolled patients, with 4 patients pending and 1 patient self-removed from protocol. Median follow up for completed patients is 4 (range: 2-8) months. Results: Seven cases are evaluable for initial toxicity and response. On-treatment acute toxicity has been equivalent to standard IMRT. Early post-SRS boost adverse events have been limited mostly to Gr 2 xerostomia, pain, and dysphagia. Solitary Gr 3 dysphagia, facial edema, fatigue, and pain events have occurred and resolved. One patient with bulky T4 disease died of persistent disease. The remaining 6 patients responded completely and are free of disease. Conclusions: 8 Gy SRS boost treatment to primary OPSCC disease is feasible and safe, and step-wise dose escalation is ongoing. Toxicity, safety, and response data continue to be collected and will be reported.

Author Disclosure Block: D. Schwartz: B. Research Grant; Resonant Medical. C. Other Research Support; SciClone Pharmaceuticals. S. Parise: None. V. Nguyen: None. J. Fantasia: None. B. Saltman: None. D. Frank: None.

198 Flare Phenomenon in Trigeminal Schwannomas Treated with Fractionated Stereotactic Radiotherapy

Purpose/Objective(s): Data on radiotherapy treatment of trigeminal schwannomas (TS) and comparison of stereotactic radiosurgery (SRS) versus fractionated stereotactic radiotherapy (FSRT) is limited. Here, we present a retrospective review of our institutional experience treating TS with SRS and FSRT, the largest review within the literature to our knowledge. Materials/Methods: The records of 23 consecutive TS patients treated with SRS and FSRT between 1996 and 2011 were reviewed. At our institution, TS patients are discussed in a multidisciplinary tumor board and treatment decisions for SRS vs. FSRT is based on a thorough discussion evaluating tumor size, symptoms, nerve function, performance status, and patient preference. Results: Ten patients were treated with SRS to a median dose of 13.75 Gy (range 12-14 Gy) and 13 were treated with FSRT to a median dose of 50.4 Gy (range 49.8-50.4 Gy) in 1.8 Gy fractions. Median follow-up time was 32 months (range 0-120 months). Ten patients underwent surgical resection prior to RT. Tumor control was 94.3% with 1 local failure in the SRS group and none in the FSRT group (p = 0.15). Twenty-one patients had adequate follow for analysis of nerve function and symptoms. 42.9% had improved symptoms, 47.6% had no change, and 8.7% had worsening of symptoms (1 in each treatment group). Larger long-term symptomatic improvement occurred in the FSRT vs. SRS group (54% vs. 30%, p = 0.02). Acute toxicity requiring oral steroid intervention was higher in the FSRT vs. SRS group (30.8 vs. 0%, p < 0.01), though lesions treated with SRS were generally larger (mean size 9.5cc vs. 4.8cc, p = 0.12), and lesions in patients with moderate to severe acute toxicity were significantly larger (p < 0.01). A symptomatic “flare phenomenon” was encountered in 2 patients treated with FSRT at days 7 and 48 of treatment. MRI confirmed cystic formation and dramatic increase in size from
6.8cc to 9.5cc and 28.5cc to 34.6cc, respectively, causing brainstem compression and severe symptoms. Both had surgical resection prior to treatment. Only 4 lesions in total had a dimension larger than 3-cm, and 2 of these patients experienced the “flare phenomenon.” The 28.5cc lesion flare resulted in hospitalization due to aphasia and ataxia. Both patients did not require surgical decompression and symptoms resolved.

Both lesions reduced in size and were stable after 32 and 10 month follow-up, respectively. **Conclusions:** Tumor control rates for TS are excellent with both SRS and FSRT with minimal toxicity. This represents the first documented report of a “flare phenomenon” following FSRT for treatment for TS. Flare risk after FSRT in larger lesions that have undergone previous surgical resection should be discussed with patients prior to treatment and prophylactic oral steroid usage may be considered.


---

199 Fractionated Stereotactic Body Radiation Therapy for Re-irradiation of Squamous Cell Head-and-Neck Cancer

**M. Kress**, K. Unger, C. Lominska, I. Deeken, B. Davidson, K. Newkirk, K. Harter, *Georgetown University Hospital, Washington, DC,* University of Virginia, Charlottesville, VA, University of Kansas Hospital, Kansas City, KS

**Purpose/Objective(s):** Stereotactic body radiation therapy (SBRT) has been demonstrated in limited series to be feasible for re-irradiation of squamous cell carcinoma (SCC) of the head and neck. We report on an updated series of patients with SCC of the head and neck who underwent SBRT re-irradiation. **Material/Methods:** From 2002 to 2011, 85 patients with previously irradiated SCC of the head and neck were treated with SBRT to 94 unique lesions. Patients’ median age was 61. Most common initial lesions were oropharynx (19%) and hypopharynx (10%); initial radiation therapy (RT) median dose was 68 Gy (range: 32 - 120Gy). Most common sites of re-irradiation were neck (35%) and oropharynx (17%). Re-irradiated lesions were recurrent (79%), second primary (12%), and/or persistent disease (11%). Intent of therapy was curative in 60% and palliative in the remainder, who either were treated to locoregional disease in the setting of metastases (32%) and/or to selected locoregional disease site(s) (11%). As part of comprehensive re-treatment, some patients underwent surgery (29%); many were treated with chemotherapy (70%). Re-irradiation occurred at a median interval from initial radiotherapy (RT) of 26 months, to a median BED10 of 48 (range: 22 - 74Gy). **Results:** Median follow-up for surviving patients was 17.3 months (0.3-67.8). Median overall survival (OS) for all patients was 7.9 months. Median OS among patients treated with curative intent was 12.2 months; median locoregional control (LRC) was 14.8 months. 2-year Kaplan-Meier estimates of locoregional OS and LRC for patients treated with curative intent were 27% and 30%. Median survival was 6.7 months among patients treated with palliative intent. On univariate analysis, interval from initial RT to re-irradiation of 2 years or more was associated with improved OS in the entire cohort (p=0.03). On multivariate analysis (MVA), this factor persisted as the only significant variable for OS (p = 0.01). For patients treated with curative intent, initial complete response to re-irradiation was associated with improved LRC (p=0.05). On MVA for LRC in patients treated with curative intent, interval from initial RT (p = 0.03) was significant; there was a trend toward significance for use of surgery (p = 0.06). 8 patients had grade 3 or higher acute toxicity (9.4%), including 3 deaths (3.5%); 5 had grade 3 or higher late toxicity (5.9%). **Conclusions:** Fractionated SBRT is feasible for re-irradiation of SCC of the head and neck. With additional follow-up and a larger sample, these patients continue to demonstrate acceptable toxicity with reasonable OS and LRC. More research is needed to determine the optimal SBRT dose and fractionation, to further specify the roles for surgery and chemotherapy, and to predict which patients will derive the greatest benefit from SBRT.

**Author Disclosure Block:** M. Kress: None. K. Unger: None. C. Lominska: None. J. Deeken: None. B. Davidson: None. K. Newkirk: None. J. Hwang: None. K. Harter: None.

---

200 Clinical Factors that Contribute to Daily Setup Error for Head and Neck Cancer Patients Undergoing Radiation Therapy

**S. H. Patel**, J. Varga, M. Lu, N. Wen, I. J. Chetty, B. Movsas, . Henry Ford Hospital, Detroit, MI

**Purpose/Objective(s):** To examine clinical factors that impact upon the magnitude of setup error and variability of head and neck cancer patients undergoing daily kilovoltage/kilovoltage (kV/kV) as image guidance for radiation therapy. **Materials/Methods:** A total of 50 patients were included in this IRB approved retrospective study. They all underwent IMRT for head and neck cancer with daily kV/kV image guidance using the on board imager (OBI) on the Varian Trilogy (Palo Alto, CA) system. Pretreatment orthogonal pair kV/kV images were obtained and patients were shifted based on the match in the AP, LAT, and SI directions. The average overall shift in the AP, LAT, and SI directions (mSHIFT) and overall variation (standard deviation) (mSTD) were calculated. Pretreatment clinical factors consisting of site, stage, chemotherapy, age, definitive/postoperative, PEG tube placement during treatment (PEG), weight loss, mucositis, and dysphagia were gathered for each patient. A nonparametric Wilcoxon test was used to test the association of clinical factors with mSHIFT and mSTD, respectively. **Results:** Overall mSHIFT in AP, LAT, and SI directions was 1.87, 1.92, and 2.02 mm, respectively, and overall mSTD was 1.43, 1.80, and 2.27 mm, respectively. A significant association was found between age (≤ 60 vs. > 60) and mSHIFT (p = 0.031) and mSTD (p = 0.041). Moreover, no significant association was noted between age and direction of shift (AP, LAT, or SI). PEG and mSTD (p = 0.045), and mucositis (grade 1 vs. grade 2/3) and mSTD (p = 0.035) were found to be significantly associated. Amongst patients requiring PEG, 81.25% experienced grade 2 or higher mucositis which was significant by Chi Square test (p = 0.033) Testing for association between percentage weight loss and PEG or mucositis was not significant. **Conclusions:** Daily image guidance plays an important role in managing head and neck radiation therapy. One should pay particular attention to daily localization in elderly patients and those with grade 2 or higher mucositis. Resimulation may benefit this group of patients. Furthermore, the role of cone beam CT needs to be examined in head and neck cancer patients.

**Author Disclosure Block:** S.H. Patel: None. J. Varga: None. M. Lu: None. N. Wen: None. I.J. Chetty: None. B. Movsas: None.

---

201 Gross Tumor Volume (GTV) Reduction after Induction Chemotherapy (IC) for Locally Advanced Head/Neck Cancer (LAHNC)

**V. Gupta**, R. Cotter, S. Blacksburg, K. Misiukiewicz, E. Genden, P. Som, M. Posner, . Mount Sinai Medical Center, New York, NY

**Purpose/Objective(s):** The TAX 324 study reported promising results with TPF-based sequential therapy in which IC is followed by concurrent
chemoradiotherapy (CRT) for patients with LAHNC. As a result, our institution has been utilizing this approach more frequently. We studied radiologic volumetric tumor response to CRT to understand volumetric changes and radiation planning after CRT. **Methods:** We retrospectively reviewed 15 patients with LAHNC who were treated with CRT followed by CCRT from January 2010 to March 2011. Prior to CRT, all patients underwent a diagnostic-quality CT scan of the neck (with contrast) and/or a PET/CT (non-contrast CT) scan. These images were transferred to a radiation treatment planning system and the GTVs (primary tumor and grossly involved lymph nodes) were contoured slice-by-slice. The volumes were recorded. After completing CRT and prior to initiating CCRT, all patients underwent a radiation treatment planning CT simulation (without contrast). The primary tumor and involved lymph nodes were again contoured, and volumes were recorded. CRT consisted of docetaxel, cisplatin, and fluorouracil (TPF) q 3 weeks x 3 cycles (n=7), carboplatin/taxol (n=7), or cisplatin/etoposide (n=1). **Results:** Of the 15 patients studied, the primary site was either oropharynx (n=9), nasopharynx (n=3), hypopharynx (n=2), or larynx (n=1). Mean age was 58 (range, 41-71). 5 patients had stage III disease, 9 patients had stage IVA, and 1 patient had stage IV C. 12 patients were male and 7 patients had a history of smoking. 14 patients completed CRT. One patient developed acute renal failure after 1 cycle of CRT and was started on CCRT after recovering from this event. Prior to CRT, the baseline GTV of the primary and lymph nodes ranged in volume from 22 to 196 cc, while the post-CRT tumor volumes ranged from 9 to 124 cc. The mean relative decrease in tumor volume size after CRT in all patients was 49% (range, 29% to 75%) and the mean absolute volume of shrinkage was 37 cc (range, 12 to 79 cc). There did not appear to be a difference in GTV shrinkage between TPF and carboplatin/taxol (IC mean decrease 45% vs. 49%, respectively). After limited follow-up (mean 5 months), there has been 1 locoregional failure. This patient had an initial tumor volume of 36.1 cc that decreased to 17.6 cc (51%) after CRT. **Conclusions:** CRT results in significant tumor volume reduction of approximately 50%. Longer follow-up and larger patient numbers will provide data to determine if the relative or absolute volume amount of tumor shrinkage correlates with chemotherapy regimen, smoking history, p16/HPV status, and ultimately locoregional control.

**Author Disclosure Block:** V. Gupta: None. R. Cotter: None. S. Blacksburg: None. K. Misiukiewicz: None. E. Genden: None. P. Som: None. M. Posner: None.
a marker of unfolded protein response. Results: At data cut-off (August 12, 2011), 103 patients had been enrolled (dose escalation [n=23], expansion [n=80]). Median age was 58 years (range 29-80). The MTD was determined as 1.76 mg/m². MTD expansion cohorts included NSCLC (n=20), sarcoma (n=20), head and neck carcinoma (n=15), prostate cancer (n=8), and tumor biopsy (n=17). Patients received a median of 2 cycles (range 1-11). Common AEs included fatigue (53%), nausea, thrombocytopenia, and vomiting (each 39%). Grade ≥3 drug-related AEs were seen in 50% of patients and included thrombocytopenia (22%), fatigue (7%), maculo-papular rash (5%), and dehydration (5%). Two patients had drug-related grade ≥3 peripheral neuropathy, one of whom discontinued. Serious AEs included pneumonia and thrombocytopenia (each 7%). Of 66 response-evaluable patients, one with head and neck carcinoma treated at MTD achieved a partial response observed throughout 8 cycles. 23 patients had stable disease, including two with renal cell carcinoma who had measurable tumor shrinkage. Change in AST-3 levels post treatment was observed in 5 patients with tumor biopsy samples, indicating proteasome inhibition in tumor tissue. Preliminary PK data showed multi-exponential plasma disposition and terminal half-life of ~4-8 days post day 11 dose. Exposures increased proportionally with increasing dose from 0.5 to 2.34 mg/m². At MTD, maximal 205 proteasome inhibition in blood was approximately 60% at 0.08 hours. Whole blood PD effect was immediate and dose dependent. Conclusions: These data suggest that MLN9708 has a generally manageable safety profile and may have clinical utility in patients with head and neck carcinoma. This study is ongoing.


204 Phase II Trial of Docetaxel (D) with Oxaliplatin (O) followed by Cetuximab, in Patients with Recurrent or Metastatic Squamous Cell Carcinoma of Head and Neck (SCCHN)

C. Huang1*, C. T. Hsuheh1, P. Neupane1, S. Williamson1, S. Taylor1, A. Allen1, S. Spencer1, P. J. VanVeldhuizen1,1,1,1, Un of Kansas, Kansas City, KS, Loma Linda University, Loma Linda, CA, Veteran’s Administration Medical Center, Kansas City, MO

Purpose/Objective(s): Recurrent and metastatic SCCHN have poor prognosis with median survival in the range of 5 to 7 months and invariably have been exposed to prior cisplatin. Oxaliplatin is active in several solid tumor types, including cisplatin/carboplatin refractory cancers. We initiated a phase II trial to test the activity of DO in patients with recurrent SCCHN. We also sought to determine role of sequential cetuximab in patients with initial response to DO. The primary objective was to determine the response rate after 2 cycles of DO in SCCHN. The secondary objective was to assess time to progression of patients who received Cetuximab after initial chemotherapy. Material / Methods: The trial had a 2 stage design with the stopping rule at 16 patients if less than 3 patients responded in the first stage. Oxaliplatin was given at 130 mg/m2 and docetaxel at 60 mg/m2 over 1 hour, both IV every 21 days. After 4 cycles, patients with stable disease or response by RECIST would be treated with sequential cetuximab weekly for total of 12 weeks. Patients with recurrent or metastatic SCCHN who had prior surgery and/or chemoradiation, performance status of 0-1 and adequate bone marrow, hepatic and renal function were eligible. Results: 16 caucasian male patients with median age of 66 were entered in the initial phase of the study. We gave a total of 44 cycles of DO (7 had 4 cycles, 1 had 3 cycles, 5 had 2 cycles, and 3 had 1 cycle) We observed 2 partial response (12.5%), 6 stable disease (37.5%) with a control rate of (50%). We did not observe further response among 4 patients who received sequential cetuximab therapy. The median progression free survival (mPFS) was 30 days and median overall survival (mOS) was 180 days. Among 4 patients treated with sequential cetuximab, they had mPFS of 145 days and mOS of 250 days. Toxicities related to the treatment were: Grade 3 leukopenia (5), fatigue (5), neutropenia (3), fever (2), anorexia (2), pneumonia (2), dehydration (1), confusion (1), hypokalemia (1), anemia (1), syncope (1), dysphagia (1), Grade 4 neutropenia (1), aspiration (1), leukopenia (1), febrile neutropenia (1), hypokalemia (1), non-infection pneumonia (1); Grade 5 sepsis (1), multi-organ failure (1). Conclusions: In this first stage of the trial, the study did not achieve the predetermined response rate to warrant further investigation. Patients treated with sequential cetuximab seems to have longer mPFS and mOS. The approach using sequential chemotherapy followed by cetuximab may be eligible to select patients that are most likely to benefit from sequential single agent cetuximab.


205 Hypofractionated Radiotherapy Alone is Efficacious Treatment for Head and Neck Cancers

J. Gentile*, M. Mierzwka*, W. Barrett*, University of Cincinnati, Cincinnati, OH

Purpose/Objectives: Although definitive chemoradiotherapy has become standard therapy for many head and neck cancers, many patients can not undergo 7 weeks of radiation with concurrent chemotherapy. We reviewed patients treated at the University of Cincinnati with hypofractionated RT alone. Patients treated with this regimen typically included patients with multiple comorbidities, elderly patients, far distance for patient travel and/or inability to tolerate chemotherapy. Methods: Chart review of 26 consecutive patients treated with radiotherapy alone to 50 Gy in 25cGy fractions for squamous cell carcinoma of the head and neck using 3DC or IMRT technique with sequential boost. Initial fields received 35 GyG with boost to 50 Gy after a week break. Outcomes recorded included locoregional control (LRC), distant metastasis free survival (DMFS), cause specific survival (CSS), overall survival (OS) and toxicities graded by RTOG criteria. Results: Sixteen patients were treated definitively for C2-4N0-3M0 cancers of the oropharynx, larynx, paranasal sinus or nasal cavity. Ten patients were treated post-operatively for squamous cell carcinoma of the oral cavity, larynx or paranasal sinuses. Median followup was 26 months (range 1-79), with minimum follow-up of 21 months for living patients. 2 year LRC was 73%, DMFS 65%, CSS 65 % and OS 55%. Toxicities of radiotherapy included acute grade 1-2 mucositis in 80%, grade 3-4 in 14%. Acute grade 1-2 skin toxicities occurred in 90% and grade 3-4 in 8%. One patient required G tube insertion during definitive radiotherapy, and 4 patients had G tubes placed intraoperatively prior to post-operative RT. One patient required hospital admission related to RT toxicity. In patients with longer than 2 yrs of follow-up, 11% and 8% of patients had late ≥ grade 3
mucosal and skin toxicity, respectively. Conclusions: As historically reported, this hypofractionated radiotherapy regimen is a safe and well-tolerated with LRC and CSS similar to chemoradiotherapy. The efficacy of this regimen may have a biologic basis in that treatment is completed prior to the development of accelerated repopulation.

Author Disclosure Block: J. Gentile: None. M. Mierzwa: None. W. Barrett: None.

206 Improved Mandibular Dosimetry with Intensity-Modulated Radiotherapy Compared to Conventional Radiotherapy for Patients Treated Definitively for Oropharyngeal Cancer

T. Chapman*1, S. Stanic*2, M. Mathai*2, J. A. Purdy*2, A. M. Chen*2, 1Tufts University School of Medicine, Boston, MA, 2University of California Davis Cancer Center, Sacramento, CA

Purpose/Objective(s): Osteoradionecrosis (ORN) is a significantly debilitating complication associated with the treatment of head and neck cancer patients with radiotherapy. In particular, its incidence has been associated in a number of studies with dose to the mandible. This analysis sought to determine how the use of intensity-modulated radiotherapy (IMRT) impacts mandibular dosimetry compared to non-IMRT techniques in the management of oropharyngeal cancer.

Material/Methods: Three patients with locally advanced oropharyngeal cancer treated with definitive radiotherapy to a total prescribed dose of 70 Gy for cancers using IMRT constituted the study population. The original IMRT treatment plans were retrieved and total mandibular volume, minimum dose, maximum dose and mean dose to the mandible were obtained. The volumes of the mandible receiving 74, 70, 66 and 60 Gy were recorded. The maximum and mean doses to the temporomandibular joint (TMJ) were recorded. The patients were then re-planned using conventional radiotherapy (CRT) consisting of initial opposed lateral fields matched to a low anterior neck field, and the same data were collected for comparison.

Results: The maximum and mean dose with IMRT and CRT was similar (p>0.05, for both). However, the volumes of the mandible receiving 74 and 70 Gy were reduced with the use of IMRT: 0.1 cc +/-0.2 vs. 11.5 cc +/-19.9 at 74 Gy and 2.6 cc +/-4.2 vs. 27.2 cc +/-24.9 at 70 Gy for IMRT and 3D-CRT respectively. In addition, while the maximum dose to the TMJ was similar in both plans, IMRT reduced the mean dose to this structure: 31.8 Gy +/- 5.4 with IMRT vs. 44.8 Gy +/- 13.8 with CRT.

Conclusions: Dosimetry to the mandible is fairly similar in both IMRT and CRT plans in patients receiving definitive radiation for the treatment of cancers of the oropharynx. However, further analysis demonstrates that significantly lower volumes of mandible are exposed to high doses (74 Gy and 70 Gy) classically associated with ORN when patients are treated with IMRT. This provides a potential explanation for the recent decline in the incidence of ORN with the advent of IMRT. Further studies are under way to examine the causative relationship implied in this study.


207 Impact of Social Support and Patient Characteristics on Head and Neck Cancer US Treatment Patterns and Outcomes

B. Murphy*1, F. J. Malinoski*2, M. Botteman*2, M. Corral*4, K. L. Covello*5, A. Saylors*2, G. Carter*6, E. Pennella*7, E. Pennella*: Vanderbilt Ingram Cancer Center, Nashville, TN, 2Medical Data Analytics, Parsippany, NJ, 3Pharmerit International, Bethesda, MD, 4Bristol-Myers Squibb Co., Plainboro, NJ, 5Bristol-Myers Squibb Co., Cookeville, TN, 6Eli Lilly and Company, Indianapolis, IN

Purpose/Objective(s): This study explored the relationship between pt characteristics, clinical outcomes, and resource utilization in squamous cell cancer of the head and neck (SCCHN) in the non-experimental, routine clinical setting. Material/Methods: This was a nationally-representative, retrospective, stratified multicenter observational longitudinal medical chart review study. A random sample of 139 oncologists each abstracted medical charts of <10 SCCHN pts diagnosed between 01/01/2005 and 12/31/2009. By protocol, half of pts sample enrolled had to have been diagnosed with local/regional advanced disease (LAD, n=785) and the other half with recurrent or metastatic disease (RMD, n=752). Pts identified for chart abstraction were randomly selected within each stratum using pre-defined criteria. Descriptive statistics, univariate and bivariate analyses were conducted on key variables, including baseline clinical and demographic characteristics; living arrangements/caregiver support; treatment outcomes, and healthcare resource utilization. Results: At diagnosis, patients were 64 years old; mostly male (77.5%), Caucasian (70.4%), with the remainders African-American (AA) (20.0%), Hispanic (5.2%), and Asian (3.8%); living alone (25.9%); on Medicare (42.5%), Medicaid (11.9%), or fee for service (7.3%). Only 37.8% and 20.7%, respectively, of LAD and RMD pts were working. In LAD pts, increasing age, AA race, tobacco and heavy alcohol use were associated with a decrease in performance status; female gender, tobacco use and AA race were associated with disease progression; age and tobacco use were associated with risk of death. In pts with RMD, tobacco use, AA race, and heavy alcohol use were associated with performance status; tobacco and heavy alcohol use were associated with disease progression; tobacco use, AA race and heavy alcohol use were associated with risk of death. In pts with LAD, 3.3% of all pts required a nursing home facility for cancer related reasons. This increased to 6.2% in pts >75 years of age, 5.4% in current smokers, 8.9% in AAs and 6.6% in heavy alcohol users. Emergency room (ER) visits related to LAD was 12.0% overall, increasing to 17.1% in pts >75 years of age. In pts with RMD, nursing home use was associated with age >75; highest rate of ER visits was among Hispanics; hospitalization was associated with Hispanic ethnicity and smoking history; use of ancillary services was associated with AA race, Hispanic ethnicity, smoking history, and heavy alcohol use.

Conclusions: Preliminary results indicate that in both LAD and RMD, several sociodemographic characteristics are associated with worse clinical outcomes, performance status, and increased resource utilization. Early identification and aggressive social support may improve outcomes.

Purpose/Objective(s): To study the safety and toxicity of concurrent Gefitinib and Intensity Modulated Radiation Therapy (IMRT) with or without concurrent weekly cisplatin in locally advanced HNSCC. Material/Methods: Patients with inoperable stage III or IV squamous cell carcinoma of the head and neck were enrolled and received Intensity Modulated Radiation Therapy(IMRT) along with Gefitinib 250 mg orally once a day starting a week prior to commencement of radiotherapy. Patients fit for chemotherapy received concurrent chemotherapy with weekly Cisplatin (40 mg/m2). Patients were monitored during treatment period for tolerance of therapy. Clinical and radiological assessment was done six weeks after completion of radiotherapy. Results: Eighteen patients were enrolled and 17 were available for evaluation; 8 patients had Gefitinib alone with IMRT (GEF arm) and 9 patients had chemotherapy in addition to Gefitinib and IMRT (GEF-CHEMO arm). Of the 17 patients, only 4 patients had treatment related break (febrile neutropenia and persistent grade 3 mucositis). Toxicity profile observed was similar to those reported in literature. There was no incidence of grade 3/4 toxicity for symptoms such as dysgeusia, hoarseness of voice, cough, vomiting or asthenia. No patient had a pain score of over five on a numerical scale. Nasogastrectomy tube placement for feeding was required in 47% of the patients (more in the GEF-CHEMO arm - 55.5%). Grade 3/4 acute toxicities included skin rash (GEF / GEF-CHEMO - 12% / 12%), mucositis (50% / 55%), neutropenia (0% / 44%) and liver enzyme elevation (12.5% / 0%). There was no incidence of grade 3/4 diarrhoea, while grade 1/2 diarrhoea was observed (37.5% / 55.5%). At the end of RT, 11 patients (68.75%) did not have any residual disease. At 6 weeks follow up, the response rate (CR + PR) was 71% (100% in the GEF-CHEMO arm and 50% in the GEF arm). Conclusions: IMRT with Gefitinib alone and in combination with chemotherapy was well tolerated with favourable safety profile and no clinically significant grade 3/4 toxicity. Further follow up of patients is essential to report on the efficacy of this novel combination of IMRT, concurrent chemotherapy and molecular targeted therapy.

Author Disclosure Block: N. Balaiyya: B. Research Grant; Christan medical college & Hospital, Vellore, Tamilnadu, India, Dr Reddy's Laboratories limited, Hyderabad, India. S. Das: None. R. Isiah: None. S. John: None. S. Pat: None. P. Solomon: None. R. Balakrishnan: None. S. Backianathan: None. 

Purpose/Objective(s): Primary thyroid lymphoma is rare and the published literature includes patients treated by various approaches over many decades. Indeed, the ability to optimize current management decisions is difficult. Herein, we report outcomes for this cohort of patients using current diagnostic and therapeutic techniques. Materials/Methods: This is a retrospective review of prospectively collected multi-center data for 19 patients (15 female, 4 male, age 41-89, median 68 years) with primary thyroid lymphoma who underwent treatment between 2004 and 2011. All 19 patients had B-cell lymphoma. Hypothyroidism, thyroiditis or goiter was present in 32%. Staging included contrast CT in all curative patients, PET/CT in 10 and marrow biopsy in 7. Eighteen patients were treated for cure and one was treated for airway palliation; all curative pts were stage I or II. Results: Initial intervention was by surgery resulting in: total thyroidectomy (n=6, 32%), subtotal thyroidectomy (n=5, 26%), wide excision (n=2) or needle biopsy alone (n=3, 16%). Two patients had regional nodal dissection. Multicycle, multiagent chemotherapy was delivered to 13 patients (68%), most commonly: CHOP/Rituxan (32%) or CHOP alone (16%). Consolidative external beam radiation (XRT) followed in 12 patients (63%) with concomitant XRT in 1 patient. Six patients (32%) underwent XRT alone. Radiation field size was the thyroid bed alone in 7 patients (37%) and thyroid plus regional nodes in 12 (63%). Dose delivery was by IMRT in 6 patients (50%). Thyroid bed prescribed dose ranged from 30 to 50 Gy (mean 36); nodal prescribed dose ranged from 30-50 Gy (Mean 35.4). Notably, of 7 stage I pts treated by XRT directed to the thyroid only, 5 also had chemotherapy. The 6 stage I pts who underwent XRT as definitive therapy (no chemotherapy) had fields that included regional nodes in 4 cases. Patients have been followed up to 52 months (median 15) with no local failures noted. One patient who presented with a bulky 7 cm tumor succumbed to systemic disease, however no other deaths have been attributed to lymphoma. Radiation morbidity was mild (grade I-II) and most commonly included dysphagia in 42% and dermatitis in 32%. Conclusions: Primary thyroid lymphoma is rare and we report the largest multi-center series to date. Most patients undergo CHOP based chemotherapy followed by consolidative XRT which results in high tumor control rates. Radiation dose was also variable but no local failures were noted at 30 Gy, though the mean dose was 36 Gy. Of the 10 pts undergoing PET/CT only 2 had evidence of nodal spread and this imaging modality may serve as a means to better define radiation treatment planning and delivery.


Is Tumor and Nodal Volume Important Clinical Parameter in Patients with Nasopharyngeal Cancer? 5-year Results of Radiation Therapy and Evaluation of Treatment Toxicity


Purpose/Objective(s): To evaluate impact of tumor and nodal volume on the effectiveness and toxicity of radiotherapy alone or radiochemotherapy for patients with nasopharyngeal cancer - 5-year results of treatment. Materials/Methods: Fifty seven patients irradiated
between 2002 and 2006 because of newly diagnosed nasopharyngeal cancer have been analyzed. In majority (66%) advanced stage (IV) was diagnosed. In all patients tumor and nodal volume was evaluated precisely with MRI and CT scan before treatment. In 35 patients radiotherapy and chemotherapy were used together. 22 patients were treated with radiotherapy alone. 33 patients were irradiated with IMRT and 24 with classic conformal 3-D technique. Median follow-up was 5 years. To evaluate tolerance of treatment acute mucosal reactions (according to EORTC/RTOG and Dische scores) and late toxicity (according to CTC v3.0) were examined. Results: Primary tumor volume was observed in very wide range between 2.7 and 257 cm³ (mean value 62.6 cm³ for whole group). Metastatic nodal volume in whole group of patients was also in wide range between 1 and 236.2 cm³. There was no correlation (r=0.03) between primary tumor volume and metastatic neck nodes volume in patients with squamous cell cancer. For patients with undifferentiated tumors this correlation was high (r=0.61). 5-year local control (LC) and nodal control (NC) was 72% and 90% respectively. 5-year disease free survival (DFS) was 58% and distant metastasis free survival (DMFS) 88%. Moderate, but significant correlation was observed between primary tumor volume and LC (r=-0.30). There were better results of LC for patients treated with chemo- and radiotherapy than for radiotherapy alone (84% vs. 52%, p=0.009). No correlation between metastatic nodal volume and NC was observed (r=0.08). No difference in LC results between classic 3-D and IMRT was observed (p=0.9) and acute mucositis was comparable between both techniques (p=0.21). Only five patients (9%) temporarily had to break treatment because of acute radiation toxicity. Moderate correlation (r=0.33) between Gross Tumor Volume (primary tumor and nodal) and intensity of acute mucosal reaction was observed.

211 Clinical Outcomes of Non-esthesioneuroblastoma Sinonasal Malignancies of Neuroendocrine Origin Treated with Multi-Modality Therapy


Purpose/Objectives: To report the multi-modality treatment outcomes of patients with non-esthesioneuroblastoma (non-ENB) sinonasal malignancies of neuroendocrine origin. At our institution we have favored preoperative chemoradiotherapy (CRT) followed by definitive surgery. Methods and Materials: We conducted an IRB approved, retrospective chart review of 19 biopsy proven non-ENB sinonasal neuroendocrine carcinomas diagnosed between 1997 and 2010 composed of 15 sinonasal undifferentiated carcinomas (SNUC), 3 sinonasal neuroendocrine carcinomas (SNEC), and 1 small cell carcinoma (SCC) treated with multi-modality therapy. 16/19 (84%) tumors were clinically staged T4. 11 (58%) had definitive surgery: 5 craniofacial resection, 5 sinonasal endoscopic resection, and 1 had a bilateral maxilectomy with preoperative CRT (n=9) or postoperative CRT (n=2). Eight (42%) patients received definitive CRT. The median preoperative, postoperative, and definitive CRT radiation doses were: 59.4 Gy (range: 50.4-64), 53.6 Gy (range: 53.2-54), and 70 Gy (range: 46-74), respectively. All patients received chemotherapy; 17 (90%) platinum based. 6 patients received neoadjuvant and 17 received concurrent CRT. Kaplan-Meier estimates of local control (LC), distant metastases free survival (DMFS), and overall survival (OS) were calculated. Responses to neoadjuvant chemotherapy and CRT are also presented. Results: The median follow-up was 39 (5 to 95) months. The 3 year LRC, DMFS, and OS for all patients was 53%, 50%, and 63%, respectively. 3 year OS was similar for patients treated with definitive surgery vs. definitive CRT (59% vs. 70%; p=0.97). Recurrences were seen in 10 patients: 3 local, 1 local and regional, 3 distant, 3 local and distant, and 2 locally and distantly. In 6 patients receiving neoadjuvant chemotherapy, partial radiographic responses were noted in 1/4 SNUC and 2/2 SNEC. The other SNUC had stable or progressive disease. All 9 patients receiving preoperative CRT and had at least a pathological partial response: 3/7 SNUC and 2/2 SNEC had complete responses. All 5 patients with a pathological complete response are alive without disease at a median follow up of 37 (29 to 61) months. The 4 patients with a pathologic partial response obtained negative margins during surgery. The radiation dose for these patients ranged from 50 to 60 Gy and 4/5 received cisplatin/etoposide. Conclusions: Clinical outcomes for non-ENB sinonasal malignancies of neuroendocrine origin are modest and similar for patients treated with definitive surgery versus definitive CRT. Having a complete response to CRT was a favorable prognostic indicator.

212 Cutaneous Metastatic Squamous Cell Carcinoma: Prognosis and Management

B. Saltman*, D. Frank*, D. L. Schwartz*, Hofstra North Shore-LIJ School of Medicine, New Hyde Park, NY

Purpose/Objective: Metastatic lymphadenopathy from cutaneous Squamous Cell Carcinoma occurs quite rarely. Because of the rarity of this event and the generally poor prognosis of patients it has generally been thought of as the hallmark of very aggressive disease. Our goal is to share our experience with this disease including treatment modalities, pathologic characteristics and prognosis. Materials/Methods: A retrospective chart review was performed of the two faculty head and neck surgeons in the Division of Head and Neck Surgery, Department of Otolaryngology at Hofstra Northshore-LIJ Medical School. All patients with squamous cell carcinoma of the parotid gland or metastatic squamous cell carcinoma to the head and neck regional lymphatics with a known cutaneous squamous cell carcinoma were eligible. Results: 17 patients were identified with an average age of 78. Two patients were lost to follow-up. Of the 15 remaining patients, 1 had a positive SCC fine needle aspiration biopsy of the parotid gland without an identified cutaneous primary tumor. All patients with one exception had undergone adjuvant radiation therapy to the primary site as well as to the regional lymphatics. The average follow up was 14.6 months. At the time of last follow-up 3 patients were alive with disease (AWD) and 12 had no evidence of disease recurrence (NED). Two out of the three of these (2/3)
had extracapsular spread of disease (ECS). With three exceptions all patients underwent resection of both parotid and cervical lymphatics. Six patients (6/17) were found to have extracapsular spread (ECS) and 5/17 were found to have perineural invasion (PNI). Of the patients who had a parotid and neck dissection for a primary parotid lesion (14/17), four (4/14) had metastases to the cervical lymphatics. **Conclusions:** Metastatic cutaneous squamous cell carcinoma is a rare occurrence. While the literature supports a poor prognosis, with a relatively short follow up, comprehensive lymphadenectomy and radiation therapy, we have found a relatively low recurrence rate of 20%.


213 Response to Salvage Treatment in Head and Neck Squamous Cell Carcinoma (HNSCC) Patients who Failed Neoadjuvant Chemotherapy with Docetaxel/Cisplatin/5-Fluorouracil (TPF)

R. Leon-Ferre*, T. Abu Heijeh*, A. Wehbe*, University of Iowa Hospitals and Clinics, Iowa City, IA

**Purpose/Objective(s):** Neoadjuvant TPF followed by concurrent carboplatin with radiation is an effective regimen for patients with locally advanced HNSCC. However, a subset of those tumors show resistance to TPF that warrants switching to a different treatment regimen. Response and survival outcomes to salvage regimens are note well established. **Materials/Methods:** After obtaining approval by the institutional review board (IRB), we retrospectively reviewed the electronic medical charts of HNSCC patients who received TPF at University of Iowa Hospitals and Clinics between 2007 and 2009. Nine patients were identified. Of those, six patients were switched to a different treatment regimen due to poor response (less than 25%) or adverse reactions to TPF. Demographic and clinical variables were collected and analyzed on those patients. **Results:** Five patients (83%) were males and one (17%) was female. Median age at diagnosis was 60.5 years (55-71). All patients had a smoking history >10 pack/year and 3 (50%) also had heavy alcohol consumption. The anatomic site of HNSCC was: lip/oral cavity in 3 (50%), oropharynx in 1 (17%), hypopharynx in 1 (17%) and glottis in 1 (17%). TNM subclasses were: T4: all patients, N0: 1 (17%), N2: 2 (33%), N3: 3 (50%). M0: all patients. Tumor was moderately differentiated in 3 (50%), poorly differentiated in 2 (33%) and unknown in 1 (17%). 4 patients (67%) received 1 cycle of TPF and 2 (33%) received 2 cycles. Reasons for discontinuing TPF were disease progression/no response in 3 (50%) patients and adverse events due to TPF in 3 (50%) patients. 5 patients (83%) were switched to concurrent chemoradiotherapy and 1 (17%) was switched to radiation alone. The chemotherapies used included: cetuximab: 2 (33%), high-dose cisplatin: 1 (17%), carboplatin: 1 (17%) and both docetaxel and cisplatin: 1 (17%). Median radiation dose was 70.1 Gy. Responses to the salvage regimen in the subset of patients who did not respond to TPF were: no response (NR) in 2 (33%) and partial response (PR) in 1 (17%). However, responses of the patients who stopped TPF due to side effects were: complete (CR): 2 (33%) and PR: 1 (17%). None of the patients had salvage surgery. Regarding survival, 4/6 (67%) patients were deceased by the time of data collection. Median survival for all patients was 8.9 months (4.7-29.8). Median survival for the patients who did not respond to TPF was 7.5 months (4.7-9.8). **Conclusions:** HNSCC patients who fail to respond to TPF are probably more resistant to other chemotherapy regimens even if administered concurrently with radiation. Additionally, survival seems to be poor in that subpopulation. Although scientifically plausible, these results need to be confirmed in larger cohorts.

Author Disclosure Block: R. Leon-Ferre: None. T. Abu Heijeh: None. A. Wehbe: None.

214 Stereotactic Body Radiation Therapy for Treatment of Primary and Recurrent Salivary Malignancies

S. D. Karam*, J. Snider*, M. Wooster*, K. Newkirk*, B. Davidson*, J. Deeken*, H. Wang*, K. Harter*, Georgetown University Hospital, Dept. of Radiation Oncology, Washington, DC, Georgetown University Hospital, Dept. of Otolaryngology-Head and Neck Surgery, Washington, DC, Georgetown University Hospital, Dept. of Hematology and Oncology, Washington, DC, Georgetown University Hospital, Dept. of Biostatistics, Bioinformatics, and Biomathematics, Washington, DC

**Purpose/Objective:** To evaluate the role of fractionated stereotactic body radiation therapy (SBRT) for definitive treatment of primary and recurrent tumors of the salivary glands. **Materials and Methods:** Between September 2003 and March 2011, 29 patients with salivary gland malignancies received SBRT. Treatment groups were divided into primary SBRT and reirradiation SBRT. The reirradiation group consisted of 18 patients, all with recurrent tumors. The primary group consisted of 11 patients who either declined or were ineligible for conventional treatment and had adverse pathologic features postoperatively. Median age was 68 for all patients and for the SBRT reirradiation group, and 78 years for the primary SBRT group. The majority of tumors in all groups were of major salivary glands, treated postoperatively, with either gross disease or positive margins. Twenty one percent of all patients had N2 disease with 28% in the reirradiation group and 9% in the primary SBRT group. The median cumulative dose was 30 Gy for all patients and the primary SBRT group, and 91 Gy for reirradiated patients. Primary endpoints were progression-free survival (PFS), locoregional control (LC), and overall survival (OS). Toxicity was a secondary endpoint. Log rank and Cox regression analyses were conducted to evaluate the association between clinical factors and each survival outcome. Logistic regression was used for toxicity analysis. **Results:** The median followup was 11.5, 18, and 15 months for all patients, SBRT reirradiated group, and primary SBRT patients, respectively. The respective OS, PFS, and LC were 18, 5, and 6 months for all patients, 11.5, 3.5, and 5.5 months for the SBRT reirradiated group, and 20, 14, and 18 months for the primary SBRT group. The respective 2-year OS, PFS, and LC rates were 44%, 34%, and 67% for all patients, 39%, 24%, and 53% for the SBRT irradiated group, and 51%, 51%, and 89% for the primary SBRT group. In all patients, surgery, age, nodal stage, and cumulative dose were predictors of OS (p<0.05). Nodal stage was a strong predictor of OS, PFS, and LC in all patients (p<0.05). Presence of gross disease was a positive predictor of OS in all groups (p<0.05). For the primary SBRT patients, surgery, tumor size, age, nodal status, and presence of gross disease all correlated with OS (p<0.05). Long term toxicity analysis revealed that 22% of patients in the reirradiated group developed soft tissue necrosis, which was strongly correlated with cumulative dose (p=0.01). **Conclusions:** Fractionated SBRT is feasible to use in patients with salivary gland malignancies who are ineligible or decline conventional therapy and for reirradiation of recurrent disease. Our data show association between patient outcome and advanced nodal disease, surgical resectability, and cumulative dose.

**Erlotinib Given Intermittently During First Line Platinum Based Chemotherapy for Metastatic and Recurrent Head and Neck Squamous Cell Carcinoma.**

H. Alì*, G. Divine*, , Henry Ford Hospital, Detroit, MI

**Purpose/Objectives:** Metastatic and recurrent head and neck cancer (MRHNC) has a moderate response to combination chemotherapy. Platinum-based chemotherapy is the standard. The combination of Paclitaxel(T) and platinum(P) has a response rate of 35% as first line therapy. The epidermal growth factor receptor (EGFR) is involved in the regulation of essential biological processes such as cell proliferation and survival. MRHNC over-express EGFR in 43-62% of patients. Erlotinib is a small-molecule inhibitor of EGFR tyrosine kinase. In preclinical models the combination of chemotherapy with EGFR inhibitor appeared synergistic. Randomized Clinical trials explored the combination in the setting of first line therapy for metastatic lung cancer, but did not improve responses or survival. We hypothesize that the antagonism observed clinically with combination regimens given in a continuous fashion may be reversed by giving the drugs intermittently. We designed a regimen in which platinum-based paclitaxel therapy was given intermittently with erlotinib, paclitaxel/platinum given day 1 and erlotinib day 3-17 starting with a loading dose, cycle length was 21 days. The study was a phase II trial, the goal was to enroll 15 patients with a primary endpoint of response rate. 6 patients were enrolled in the study, the study was stopped because of slow accrual. 5 patients received TP(cisplatin) and one patient received TP(carboplatin). 3 of 6 achieved PR, none achieved CR, 2 had SD. 35 cycles were delivered. The median number of cycles was 6 (2-10). All cycles were delivered at full dose, one cycle was delayed because of patient request. The regimen was well tolerated. Grade 3 toxicity was observed as follows; 2 patients lymphopenia, 2 neutropenia, 2 anemia, 1 neutropenic fever and 1 hearing loss. 1 grade 4 lymphopenia was observed. All other adverse events were grade 1 or 2. **Conclusions:** The combination of paclitaxel and platinum-based therapy given intermittently with erlotinib is a well tolerated regimen, further study is needed to determine the true response rate.

H. Alì: D. Speakers Bureau/Honoraria; genentech, eisai, celgene, genomic health. G. Divine: None.

**Ipsilateral Neck Proton Radiotherapy for Lateral Head and Neck Cancers Using a Matched Field Technique**

J. I. Kang*, R. S. Grover*, D. A. Bush*, J. D. Slater*, , Loma Linda University Affiliated Hospitals, Loma Linda, CA

**Purpose/Objective(s):** Well-lateralized head and neck cancers have a low risk for contralateral neck recurrence and can be treated with definitive or adjuvant radiation therapy to the ipsilateral neck. Proton radiation offers a dosimetric advantage when treating these tumors by eliminating any significant radiation dose to the contralateral organs at risk and substantially reducing dose to the oral cavity, spinal cord, brain stem and other midline organs at risk. To assess feasibility and follow outcomes of lateral head and neck cancer patients (parotid, lateral oral cavity/oropharynx, etc.) treated with ipsilateral proton radiation therapy using a matched field technique. **Materials/Methods:** Between 2007 and 2010, 14 patients with various well-lateralized head and neck cancers were treated with an ipsilateral neck proton radiation therapy technique using a pair of matched superior and inferior fields with feathered match lines to the primary and elective ipsilateral neck. Generally, a superior posterior oblique or lateral field was matched inferiorly to an anterior field. Two sets of these match fields with a match line moved by 5 mm were treated on alternating days to deliver a dose of 50 Gy(Elective neck) or 60 Gy (post-operative neck) at 2 Gy per fraction per day. High risk regions or gross disease were then boosted with proton radiotherapy to 66-70 GyE as indicated. **Results:** Using CTCAE 4.0 descriptions, there were no grade 4-5 acute toxicities reported. Three patients reported grade 3 acute dermatitis radiation and/or oral mucositis, and one patient reported grade 3 dysphagia requiring the use of temporary tube feedings. All patients reporting grade 3 toxicity were treated with concurrent chemotherapy. All other acute toxicities were grades 1-2 or not reported. With a median follow up of 25 months, there have been no in-field local recurrences. There have been no reported in-field ipsilateral neck failures including at or near the proton field matchline. There have been no reports of grade 3 or higher soft tissue fibrosis particularly at or near the matchline. There were 2 patients with local-regional recurrence beyond initial treatment fields in base of skull and supraclavicular regions respectively. One patient had simultaneous supraclavicular recurrence outside initial field and mediastinal metastases. **Conclusions:** Protons delivered effective ipsilateral radiation treatment providing local control with acceptable acute toxicity and minimizing contralateral radiation dose. Field size limitations addressed with matched proton fields showed no failures or disabling soft tissue fibrosis at potential cold or hot spots at or near the matchline.

Author Disclosure Block: J.I. Kang: None. R.S. Grover: None. D.A. Bush: None. J.D. Slater: None.

**The Use of Combined Cetuximab and Daily Cisplatin Chemotherapy in Conjunction with Radiation for the Treatment of Head and Neck Cancers**

V. I. King**, D. O. Hartshorn**, D. N. King**, M. R. Hancock**, , 1Western Colorado Radiation Oncology, Grand Junction, CO, 2Colorado West Otolaryngologists, Grand Junction, CO, 3St. Mary’s Hospital, Grand Junction, CO

**Purpose/Objective(s):** Cisplatin (CDDP)/RT and Cetuximab/RT have been shown to be effective regimens for control of head and neck cancers. In many disease sites, combination therapy has proven to be more effective than single agent treatment. In addition, the standard high dose Cisplatin (every 3 weeks for 3 cycles) is difficult to administer due to toxicity. The purpose of this analysis is to assess efficacy and safety in a group of patients receiving daily Cisplatin, weekly Cetuximab, and concurrent IMRT. **Materials/Methods:** Prescribed treatment for 36 patients (29 males, 7 females) was IMRT with CDDP (6mg/m² daily) and Cetuximab (250mg/m² weekly) between 11/1/2008 and 7/1/2011. Ten patients were treated postoperatively. Thirty-one had stage IV, 4 had stage III, and 1 had stage II disease. Radiation dose was 60 to 66 Gy for post-op patients, and 69.3 Gy (at 2.16Gy/fraction) for all others. Actual radiation dose delivered was reduced in 6 patients. Median age was 59 and median follow up was 11 months. All patients had squamous cell cancer: 20 oropharyngeal, 6 unknown primary, 5 laryngeal, 4 oral cavity, and 1 hypopharyngeal. HPV data was available on 19 patients, of which 7 were positive. PET scans were ordered 3 months after therapy to assess treatment response. **Results:** No patient died of progressive disease during the study period, 3 patients required post chemoradiation neck dissection for residual PET positive disease, and one larynx cancer patient had a neck recurrence 1.5 years after treatment. One patient
developed neutropenic sepsis and subsequent aspiration pneumonia and died during treatment. Three patients died of non-cancer related causes 5, 8, and 20 months after treatment. Patient toxicity included: moist skin desquamation in 14 patients, average weight loss of 11 pounds during treatment (6%), and average pain level of 5.6 (scale 1-10). Hematological toxicities included neutropenia in 7 patients (ANC < 1,500), thrombocytopenia in 3 patients (96k, 65k, 98k), hypomagnesemia in 8 patients (Mg < 1.6), and a mean hemoglobin reduction of 5%. Of the patients with neutropenia, 2 required Cisplatin dose reduction. During treatment, creatinine levels were stable in 11 patients, decreased in 12 patients, and no patients developed abnormally elevated levels. Five patients (14%) were hospitalized during treatment for neutropenia, stroke, pain management, intractable diarrhea, pulmonary embolus, and general clinical deterioration. **Conclusions:** The use of CDDP/Cetuximab/RT and salvage surgery as needed for head and neck cancer treatment appears to produce high rates of local control and disease free survival. The toxicity of this approach appears less than other approaches.

**Author Disclosure Block:** V.J. King: None. D.O. Hartshorn: None. D.N. King: None. M.R. Hancock: None.

---

### 218 Volumetric-modulated Arc Radiotherapy for Skull-base or Non-skull-Base Head and Neck Cancer: A Treatment Planning Comparison with Fixed Beam IMRT

**Purpose/Objective(s):** To compare the dose distribution, delivered monitor units (MUs) and radiation delivery time between volumetric-modulated arc therapy (VMAT) and step-and-shoot (S&S) intensity modulated radiotherapy (IMRT) plans in skull-base and non-skull-base head and neck cancer (HNC).

**Materials/Methods:** CT datasets of 8 skull-base and 7 non-skull-base HNC were identified. IMRT and RA plans were generated for each case. The prescription dose ranged 45-70Gy (1.8-2.2 Gy/fraction). The Eclipse 8.9 treatment planning system (Varian Inc.) was used to generate both plans. The radiation delivery time was measured on the linear accelerator when the VMAT plans were delivered to the patients. The S&S treatment time was generated by delivering the plan on a phantom. Comparison of dose-volume histogram data, MUs, and treatment times were performed separately for skull base and non-skull-base cases using T-test. **Results:** Both planes yield similar target volume coverage, homogeneity, and conformity. In skull-base cases, VMAT plans generated significantly lower maximum chiasm (41±15Gy vs. 32±11Gy, P=0.026) and mean ipsilateral middle ear dose (43±9 Gy vs. 38±10Gy, P=0.020) than S&S plans and a trend for lower optic nerve, temporal lobe, parotid, temporal-mandibular joint and oral cavity dose. In non-skull-base cases, doses to normal tissues were similar between the two plans except for a trend for lower contralateral parotid dose favoring S&S. There was a substantial reduction in MUs {486 ± 95 vs. 1614 ±931, p < 0.001} and radiation deliver times (3.0 ± 0.6 vs. 11.0 ± 3.3 min, p < 0.001) favoring VMAT. **Conclusions:** VMAT appears to spare more normal tissues for skull-base tumors compared to S&S. Dosimetrically, both approaches were equivalent for non-skull-base tumor with exception of VMAT using fewer monitor units and short radiation delivery time.

**Author Disclosure Block:** J. Chen: None. E. Mok: None. L. Wang: None. C. Chen: None. Q. Le: B. Research Grant; GSK, Amgen, Varian.

### 219 Comparison of Carotid Sparing Radiation Treatment Approaches for Early Laryngeal Cancers: VMAT vs. IMRT

**Purpose/Objective(s):** Volumetric-modulated arc therapy (VMAT) is a technique in which the gantry rotates continuously around the patient with gantry speed, leaf speed, and dose rate simultaneously modulated. VMAT offers reduced treatment times compared to static field treatments. IMRT (intensity-modulated radiation therapy) has been shown to provide greater carotid sparing in early glottic cancers compared to 3D techniques, but is associated with increased heterogeneity, which may increase the risk of complications. Here, we compare larynx dose homogeneity, carotid sparing, and treatment time with VMAT and IMRT.

**Material/Methods:** Using CT data sets from 5 previously treated patients, we contoured the larynx (cricoid to the base of the epiglottis, with the exception of the posterior-lateral portions of the thyroid cartilage, where it approached the carotid arteries), as well as organs at risk (OARs) including the spinal cord and carotid. Carotids were contoured 1 cm above and below the PTV and both carotids were included in a single volume for dosimetric calculations. Plans were generated on Pinnacle v. 9.0 using both static IMRT and VMAT for direct comparisons. Dose distributions to the targets, OARs, and treatment times were compared. Dose homogeneity was compared using the ratio of D5%/D95%. Treatments were simulated on a Varian Trilogy linear accelerator to determine treatment times. We used SPSS-18 for statistical analysis with paired T-test to compare means and Kruskal-Wallis test to compare dose homogeneity ratios. **Results:** The mean carotid dose using IMRT was 18.0 Gy (range 17.0-19.2 Gy) compared to 17.0 Gy with VMAT (p<0.001; range 16.0-17.9 Gy). The mean maximum dose to the carotids using IMRT was 50.6 Gy (range 45.3-55.3 Gy) vs. 47.3 Gy with VMAT (p=0.08; range 40.5-54.8 Gy). Mean V10 and mean D50% of the carotids were not statistically different comparing VMAT and IMRT. Mean V10 favored VMAT (IMRT 0.43 cc vs. 0.28 cc with VMAT, p = 0.038) but both techniques resulted in small volumes receiving 35 Gy. Mean max dose to the PTV, mean dose to the spinal cord, and mean monitor units required for treatment were not statistically different. One VMAT plan showed a hot spot of 69.7 Gy, or 110.6% of prescribed dose, which was higher than max dose in the IMRT plans. Mean treatment time favored VMAT, 200 seconds vs. 242 seconds (p=0.04). Mean dose homogeneity was significantly improved with VMAT, 1.033 vs 1.052, (p=0.028). **Conclusions:** In this dosimetric study, VMAT showed statistically significant improvements in treatment time, laryngeal dose homogeneity, and mean carotid dose compared to IMRT plans. VMAT did not resolve high max doses to the PTV with inverse planning. We demonstrated that VMAT can be utilized to treat early stage laryngeal cancer, and offers advantages over other treatment techniques.

**Author Disclosure Block:** J.A. Cox: None. J.D. Sturgeon: None. E.C. Endres: None. J. Clewlow: None. T.A. Swanson: None. L.R. Wiederhold: None.
Clinical Outcome According to p16 Status and Treatment Modalities in Oropharyngeal Cancer (OC) Patients (PTS)

F. Valduga*, A. Caldara*, V. Vanoni*, E. Bragantini*, E. Magri*, E. Vattemi*, A. Bolner*, C. Grandi*, L. Tomio*, E. Galligioni*, S. Chiara Hospital, Trento, Italy

Purpose/Objective(s): To analyze the correlation between p16 status, radiotherapy technique and outcome for OC and to evaluate toxicity in the concomitant treatment. Materials/Methods: Between September 2005 and September 2008, 62 patients with OC were treated at our department with exclusive primary radiotherapy +/- chemotherapy or cetuximab. Thirty-five pts (56.5%) had stage IV disease (all M0); 17 pts (27.4%) had base of tongue cancer and 34 pts (54.8%) had tonsillar cancer. Seventeen pts (27.4%) were treated with 3D-planned simplified conventional three field-RT (3D-S), 22 (35.5%) 3D advanced conformal (3D-A) and 23 (37.1%) IMRT with simultaneous integrated boost (SIB). In 30 pts (48.4%) RT was combined with concomitant systemic treatment (in 23 cisplatin 100 mg/m² q 21, in 2 weekly cisplatin 30 mg/m² and in 5 cetuximab). HPV status was analyzed by p16 immunohistochemistry (CINtec Histology V-Kit) and molecular biology. Results: Mean follow-up was 28 months (range 5-61). 27 pts (43.5%) were p-16 positive, and 34 (54.8%) negative. P16-positive and p16-negative groups had similar distribution of stages and treatment modalities. 3y-DFS for p16-positive and p-16-negative group was 76.2% and 58.4%, respectively (p=0.03). 3y-OS was 68.2% and 44.1% respectively (p=0.002). In the p16-positive group, no statistically significant differences were found for the three different RT techniques regarding 3y-DFS, while, for p16-negative pts, 3y DFS for 3D-S, 3D-A and IMRT was 30%, 63% and 87% respectively (p=0.05). We also analyzed toxicity in the subgroup of concomitant treatment. In cetuximab pts we did not observe worse side effects than expected with RT alone, except for cutaneous toxicity (G1 in 2 pts, G2 in 1, G3 in 1). In the chemotherapy subgroup we pointed out: haematological toxicity in 7 pts (≥ G3 in only 3 pt), G1 renal failure in 3 pts, neurosensorial toxicity in 2 pts (both G2). Is interesting to observe that in the IMRT subgroup the association with systemic treatment (in 8 pts) had not to lead to increase of locoregional toxicity. Conclusions: IMRT with SIB appeared to be more relevant for outcome in p16-negative pts. Toxicity of concomitant treatment was generally manageable. Particularly the association between IMRT and systemic treatment seemed to be feasible.

Author Disclosure Block: F. Valduga: None. A. Caldara: None. V. V Canonii: None. E. Bragantini: None. E. Magri: None. E. Vattemi: None. A. Bolner: None. C. Grandi: None. L. Tomio: None. E. Galligioni: None.

Toxicity to Moderately Hypofractionated Accelerated IMRT and Concomitant Chemotherapy in Locally Advanced Head and Neck Cancer

D. R. Fernandez*, L. Guzman**, P. Garcia***, S. B. Zunino****, Instituto Privado de Radioterapia Oncologica, Cordoba, Argentina, **Hospital Privado, Cordoba, Argentina

Purpose/Objective(s): To evaluate toxicity and time to complete recovery after moderately accelerated radiotherapy with concurrent chemotherapy in advanced head-and-neck squamous cell carcinoma. Materials/Methods: For this study we have selected 16 patients with non-operated head-and-neck epidermoid carcinoma, admitted at the Radiotherapy Institute-Marie Curie Foundation between August 2008 and November 2010. All were irradiated with a Primus accelerator with MLC Optifocus Siemens. The IMRT planning was done with TPS KonRad. A total dose of 70 Gy in 30 fractions were delivered to primary tumor and involved nodes >15 mm, 60 Gy in 30 fractions to high-risk nodal areas, and 54 Gy in 30 fractions to low-risk nodal areas. All patients were planned to receive concurrent cisplatin 100 mg/m² with or without neoadjuvant chemotherapy. During the chemoradiotherapy, the follow-up was close in order to control and manage the hematological and mucosal toxicities. All patients required medication for pain, mycosis and other infections, as well as nutritional complements guided by nutritionists. Results: Of the 16 patients, 8 were women and 8 men, the median age was 54 years (34-69 years). The primary tumor location was: oral cavity in 3, cavum in 3, oropharynx in 3, hypopharynx in 1 and larynx in 6. The mean follow-up time was 8 months (range 2-30 months). The total dose to the 95% of GTV was 72.4±1.6 Gy in 30 fractions in six weeks. The median dose to the contralateral parotid, in oropharynx and oral cavity, was 27±1.1 Gy. In hypopharynx and larynx the mean dose of both parotids was 24.5±4 Gy. 15 patients completed two cycles of chemotherapy (DDP 100mg/m² every 21 days) as planned and two patients received 2 cycles of chemotherapy with taxanes. One patient completed only one cycle due to gastrointestinal toxicity. 8 patients had an average of 1.8 days of treatment interruption; the other 8 did not have any treatment interruption. The duration of the treatment was 41±1.5 days on average. Six of nine patients (67%) in the group with oral cavity, oropharyngeal and nasopharyngeal tumors, had mucositis grade 3. Five of sixteen patients (30%) had dysphagia grade 3. Two of sixteen (12.5%) had dermatitis grade 3, nine of sixteen (56%) had dermatitis grade 2. The median time to the complete recovery of acute toxicity was 35 days (range 15-70). Conclusions: Despite the high rate of toxicity with this treatment, there was adherence by the majority of patients and the time to complete recovery was acceptably short. More follow up on this fractionation regimen is necessary for further assessment of its efficacy and toxicity.


Modified Sequential Chemoradiation for Stage IVA/B HPV-Positive Head and Neck Squamous Cell Carcinoma (H&NSCC)


Purpose/Objective(s): HPV-positive H&NSCC tumors are known to be more sensitive and respond better to treatment with chemotherapy and radiation than HPV-negative tumors. This is leading some to propose dose de-escalation for these patients. Given the potentially higher cure rates in HPV+ disease, dose intensification may be more appropriate. Sequential chemoradiotherapy is a combination of induction chemotherapy, typically with cisplatin, docetaxel, and infusional 5-FU (TPF), followed by radiation with concurrent carboplatin (CB). Two phase III trials (TAX 323 and TAX 324) used different dosages of TPF during three or four cycles of induction, and only TAX 324 used concurrent CB. The TPF induction regimen is associated with high toxicity, which may delay or impact on the delivery of definitive radiotherapy. Materials/Methods: Patients with HPV+ Stage IVA/B (nodal status ≥2a) H&NSCC were treated with 2 cycles of TPF (per TAX323 dosing: cisplatin...
75mg/m2, docetaxel 75mg/m2, and 5-FU 750mg/m2/day for 4 days, with pegfilgrastim on D5, repeated q21 days). After 2 cycles, patients went on to receive standard fractionation IMRT radiation with weekly CB (2AU0). HPV status was determined using p16 IHC and/or PCR. Patients with residual adenopathy by exam or scan underwent neck dissection. After treatment, patients were followed clinically and with serial CT/PET scans. Patients were assessed for response rate, disease-free, and overall survival (DFS, OS), **Results:** Between 11/08 and 3/11, eight (8) patients with HPV+ disease were treated using this modified sequential schedule. Primary sites were oropharynx (n=7) and supraglottis (n=1). The mean time from cycle 1 of TPF to radiation start was 42 days (range 36 to 49) and mean duration of radiation was 58 days (range 56 – 61). Average radiation dose was 7510 Gy (range 7200–7560). Two patients did not receive infusional 5-FU. One patient required a change to carboplatin (6AUC) for C2 of induction therapy due to cisplatin toxicity. Three patients underwent neck dissection, none of which had any residual disease at the time of surgery. The complete response rate to chemoradiation was 100%. After a mean follow up of 19 months (range 6 - 33 mos), no patients have experienced disease recurrence, with a DFS and OS rate of 100%. **Conclusions:** Using this modified sequential chemoradiation approach in patients with advanced stage HPV-positive H&NSCC was well tolerated, with impressive response and survival results in this small patient cohort. A larger clinical trial is warranted.

**Author Disclosure Block:** J. Deeken: None. J. Qi: None. R. Comstock: None. B. Davidson: None. K. Newkirk: None. A. Jay: None. G. Esposito: None. K. Steadman: None. W. Harter: None.

### 223 Intensity Modulated Radiation Therapy (IMRT) or External Beam Radiation Therapy (EBRT) with Fractionated Stereotactic Body Radiation Therapy (SBRT) Boost in the Treatment of Salivary Gland Tumors with High Risk Features


**Georgetown University Hospital, Washington, DC**

**Purpose and Objective:** To evaluate the role of intensity modulated radiation therapy (IMRT)/external beam radiation therapy (EBRT) with fractionated stereotactic body radiation therapy (SBRT) boost in the treatment of salivary gland tumors with adverse features.

**Materials/Methods:** Between 2003 and 2011, 10 patients with salivary gland tumors received primary or adjuvant IMRT/EBRT with fractionated SBRT boost. Three patients received primary radiation therapy, while 7 underwent treatment post-operatively. All of the patients with adjuvant treatment had adverse pathological features such as gross residual disease or positive margins. Nine patients received IMRT and 1, EBRT, followed by SBRT to a median of 13.8 Gy following a median interval to reirradiation of 23.5 days. SBRT was delivered in 3 to 7 fractions. This approach produced a median cumulative dose of 78.5 Gy. Six patients received concurrent chemotheraphy with radiation. Histologies included 3 patients with adenocarcinoma, 1 adenoid cystic carcinoma, 2 squamous cell carcinoma, 1 poorly differentiated carcinoma, 1 carcinoma ex pleomorphic adenoma, 1 pleomorphic adenoma, and 1 adenocarcinoma with adenoid cystic features. Eight lesions were derived from salivary primaries, 1 metastatic from dermal primary, and 1 from unknown primary. **Results:** Three females and 7 males with a median age of 59 years were enrolled. Median follow-up was 16.5 months with a mean of 26.5 months and a range of 3 to 93 months. Median overall survival was 16.5 months (mean of 26.1 months). Two patients died of disease, each at 6 months following therapy. Median locoregional control was 16.5 months (mean of 25.6 months). Only one patient had locoregional progression. Median progression free survival was 16.5 months (mean of 25.4 months) with three noted to have disease progression. Five year actuarial rates for overall survival, locoregional control, and progression free survival were 0.78 (95% CI 0.51-1.05), 0.88 (95% CI 0.67-1.1), and 0.56 (95% CI 0.14-0.97), respectively. Seven patients experienced complete radiographic responses, and one patient had a partial response to therapy. Stable disease and progression were seen in the final two patients. Common toxicities included mucositis and xerostomia. Two patients suffered sensorineural hearing loss and trismus. One patient experienced osteoradionecrosis requiring surgical reconstruction and hyperbaric therapy. **Conclusions:** In this population, IMRT/EBRT followed by SBRT boost appears to be an effective locoregional therapy in patients with high risk pathologic features.


### 224 Pulsed Reduced-Dose Rate (PRDR) Re-irradiation for Recurrent Head and Neck Carcinoma Following Concurrent Chemoradiation

S. Russo*, M. Asher*, M. Williams*, F. Silver*, R. Ove*, University of South Alabama Mitchell Cancer Institute, Mobile, AL

**Purpose/Objective(s):** Locoregional recurrences developing within or near previously irradiated fields in patients who received chemoradiation for head and neck cancer (HNC) presents a clinical challenge. Reirradiation is an established approach in patients who are medically or technologically inoperable, but is associated with significant toxicities which may affect quality of life and poor survival. Smaller retreatment volumes and reduced doses are used to minimize toxicity but potentially reduce efficacy. Pulsed reduced dose rate radiation (PRDR) is a technique that allows for enhanced repair of radiation damage in normal tissue while maintaining a therapeutic dose to the tumor. Conventionally fractionated radiation using doses of 2 Gy delivered at a dose rate of 4-6 Gy/min results in generation of free radicals, but this interval is insufficient for normal tissue repair to have clinical effects. PRDR reduces the effective dose rate by increasing the interval during which 2 Gy is delivered, allowing sublethal damage repair to occur during radiation. A dose-rate between 0.01 and 1 Gy/min has been shown to demonstrate the most effect. We describe our early experience with PRDR as an alternative to standard dose rate fractionated for the re-treatment of recurrent HNC. **Materials/Methods:** Reirradiation to sites of tumor recurrence with 3D-CRT a series of 0.2 Gy pulses separated by 3 minute time intervals was delivered, creating an apparent dose rate of 0.0667 Gy/min. A total dose of 44 Gy over 22 fractions with concurrent weekly radiosensitizing carboplatin and paclitaxel was delivered. **Results:** Complete clinical response was achieved by the end of treatment. Complete radiographic and metabolic response was demonstrated by PET-CT 3 months after completion and there is no evidence of recurrence at 4 years followup. Acute treatment-related toxicities were limited to grade 1 vocal cord toxicity, grade 2 erythema and grade 2 dysphagia, resolving within 2 weeks. Late toxicities include grade 3 subcutaneous tissue fibrosis, grade 2 atrophy of the pharyngeal mucosa, and grade 3 swallowing dysfunction improved with rehabilitation and V-STIM. **Conclusions:** Reirradiation using PRDR should be considered for patients with recurrent HNC who may not be ideal candidates to tolerate with standard fractionation approaches. Late toxicities may be exacerbated by
radiosensitization effects of concurrent chemotherapy and short intervals to retreatment. The PRDR technique warrants further investigation with and without concurrent chemotherapy with objective evaluation long term toxicities and of quality of life.


Identification of Sensitizers of Cisplatin Response in Head and Neck Cancer Cell Lines
S. Cervantes*, 1, R. L. McCall*, 2, L. Young**, I. M. Gonzales*, 1, M. L. Hinni*, 1, R. E. Hayden*, 1, D. O. Azorsa*, 1, F. Arora*, 1, 2, Translational Genomics, Phoenix, AZ; 2 Mayo Clinic, Phoenix, AZ

Purpose/Objective(s): While the majority of cancers have enjoyed decreased mortality rates over the last 40 years, head and neck cancer (HNC) unfortunately has not, despite advances in basic science and clinical research. Almost 75% of patients present late when the cancer has advanced to stage III-IV. While early stage cancer may be adequately treated with radiation or surgery alone, advanced head and neck cancers require combination therapy including surgery, radiation therapy, and chemotherapy such as platinum-based therapy. Most of the head and neck cancers that initially respond to platinum-based therapy develop acquired resistance. The use of RNAi-based screening is a powerful platform for the identification of genes whose silencing can increase the sensitivity of cancer cells to the effects of chemotherapeutic drugs. Thus, the objective of the current study was to use this innovative functional genomics approach based on a high-throughput RNA interference (HT-RNAi) phenotypic screening approach to identify sensitizing targets of cisplatin in HNC cells. Materials/Methods: We investigated the efficacy of chemotherapeutic targets, including cisplatin on nine HNC cell lines using drug dose response (DDR) experiments. Two of these cancer lines (SCCO90 and UM5CC47) are also known to be HPV-positive. A siRNA library against the human “apoptome” with ~500 genes is used for the HT-RNAi screening to identify sensitizers of cisplatin response. Each gene is represented by four different siRNA sequences in the library. Results: Using DDR assays and inhibitory concentration (IC) calculations, we have identified cisplatin-sensitive HNC cell lines (UMSCC14C and SCC090) and cisplatin-resistant HNC cell lines (SCC9, SCC15, and SCC090). We are serially-treating the sensitive HNC cell lines with increasing doses of cisplatin until these lines become drug resistant. This will be used to compare cell characteristics and genomic changes before and after cisplatin resistance. Next, we are performing HT-RNAi experiments on cisplatin-resistant cell lines (SCC9 and SCC15) using a siRNA library against the human “apoptome” (targeting the apoptosis related genes) to identify sensitizers of cisplatin response in resistant HNC cell lines. Confirmation of gene silencing and validation of drug modulation will be done on a subset of target genes. Conclusions: Chemo-radiotherapy with cisplatin-based regimens offers the possibility of cure to a subset of patients with surgically non-resectable HNCs, but acquired drug resistance frequently limits outcome, so it will be immensely helpful to identify sensitizing targets that can potentiate cisplatin response in head and neck cancer.


The Value of PET Scan in the Routine Follow-up of Patients with Squamous Cell Carcinoma of the Head and Neck
Y. Rudha*, 1, A. Aref*, 1, P. Chuba*, 1, K. O’Brien*, 1, St. John Hospital / Van Elslander Cancer Center, Grosse Pointe Woods, MI, St. John Macomb Hospital, Warren, MI

Purpose/Objective(s): To evaluate the utility of PET/CT in the routine follow up of patients treated for squamous cell carcinoma of the head and neck. Materials/Methods: Cases of head and neck cancer (n=234) treated with chemoradiation between 2006 and 2010 and having post-therapy PET/CT scan were identified as part of an IRB approved study. Retrospective chart review was performed for cases achieving clinical no-evidence-of-disease (NED) status at the time of the imaging (n=45). Positive findings indicated on PET/CT were correlated with ensuing pathology findings and/or other radiological studies. Cases were then coded as true positive or false positive depending on the result of further clarifying tests. Results: Post-therapy PET/CT identified 15 patients with abnormality requiring further evaluation. Of these, eight cases (53%) were proven to have malignancy based on biopsy findings. Six out of 8 cases showed occult persistent disease at the primary site; one additional case was diagnosed with regional lymph node recurrence and in one case a colon cancer was identified. All patients who had negative PET/CT scan remained free from local-regional relapse at the time of last follow up. In the remaining seven cases, imaging findings were shown to represent false positive results with unnecessary work-up and/or biopsy evaluation. Hence for this population the true positive rate for routine PET/CT surveillance in head and neck cancer patients is estimated as 8/15 = 53% and the false positive rate as 7/15 = 46%. Conclusions: The routine use of PET/CT scan in the follow up of patients with squamous cell carcinoma of the head and neck may be useful for the detection of local-regional recurrences before they become clinically apparent. This in turn may improve the outcome of salvage therapy. The routine use of PET scan however is associated with a high false positive rate. This should be considered when ordering radiological exams and biopsies. A negative post therapy PET scan appears to be an excellent predictor of freedom from future loco-regional recurrence.

Author Disclosure Block: Y. Rudha: None. A. Aref: None. P. Chuba: None. K. O’Brien: None.

A Quantitative Evaluation of Deformable Image Registration as a Surrogate for Target Definition for Adaptive Radiotherapy in Head and Neck Cancers
S. Sekaran*, W. A. Gray*, J. A. Tanyi*, J. M. Holland*, Oregon Health and Science University, Portland, OR

Purpose/Objective(s): To quantitatively evaluate the feasibility of deformable image registration (DR) algorithm as a surrogate for manual target and organs-at-risk treatment planning contours for adaptive radiotherapy (ART), and to compare with rigid scale (RC) and rigid-only methods of structure propagation in headandneck cancer. Materials/Methods: Two headandneck cancer patients underwent an initial planning CT and adaptive re-planning CT approximately 5 weeks into treatment due to tumor shrinkage and weight. The planning CT images (moving images) of these patients were registered to adaptive CT images (fixed images) via three image registration methodologies in the following sequential order: rigid-only; rigid plus scale (RC), and deformable image registration (DR). Region-of-interest (ROI) contours drawn on
the planning CT were propagated onto their corresponding adaptive CT images. The Dice coefficient was used as a measure of similarity between the registered contours and manually delineated contours. Results: For target volumes, up to 40% (mean/median Dice coefficient of 0.85/0.88) improvement in the agreement between DR contours and manual contours were observed over rigid-only and RC image registrations techniques. Similarly, up to 27% (mean/median Dice coefficient of 0.81/0.85) improvement in the agreement between DR contours and manual contours were observed for organs-at-risk. Conclusions: Deformable image registration provides better agreement with manually delineated contours than rigid-only or rigid plus scale image registration techniques. The DR technique is a promising tool for automatic target delineation, and, hence, may be useful in adaptive radiation therapy, saving physician contouring time and allowing potential online ART.

Author Disclosure Block: S. Sekaran: None. W.A. Gray: None. J.A. Tanyi: None. J.M. Holland: None.

228 Implications of Dental Artifacts on Radiotherapy Planning for the Head and Neck
W. Gray*, S. Sekaran*, J. A. Tanyi*, J. M. Holland*, Oregon Health and Science University, Portland, OR

Purpose/Objective(s): High density materials such as dental amalgams can lead to extensive streaking artifacts on computed tomography (CT) scans. These artifacts obscure the underlying anatomy, leading to uncertainty in the delineation of the target volumes and potentially compromising the integrity of the density representation that is crucial for accurate dose calculation. The purpose of this current study is to quantitatively evaluate the effect of dental artifact on the delineation of target volumes and normal structures in treatment planning for head and neck cancers, and the ensuing dosimetric implications. Materials/Methods: Three patients with pharyngeal carcinoma form the basis of the current study. Each patient had two computed tomographic scans; a pre-extraction scan with evidence of dental artifacts and a post-extraction scan with little or no streak artifacts. Each post-extraction image set (moving image) was deformably co-registered onto its corresponding pre-extraction CT (stationary image), allowing for auto-propagation of planning target volume and organ-at-risk (OARs) contours on the latter image set. Slices of the propagated contours were deleted at the level of the streak artifacts, termed the region of interest (ROI). Two physicians with experience in head and neck cancer were asked to delineate target volumes and OARs on these slices, with difference between them attributed to the presence of the artifacts. The Dice coefficient was used to quantify inter-observer variability in terms of contours at the ROI, as well as the entire contours of the selected organs. In addition, inter-observer dosimetric differences were quantified for both the ROI cases and the full contour scenario. Results: Mean Dice coefficient difference between observers ranged from 1.3% to 13.4% when considering the entire contour set, and 13.8% to 64.3% when only evaluating the ROI. Inter-observer-induced mean dosimetric differences in mean target and OAR doses were as much as 7% (for the ROI) and 4.5% (when considering the entire contour). The largest discrepancies were observed in disease of the soft palate, and the least in disease of the base of the tongue. Conclusions: Dental artifacts can affect physician target and OAR delineation accuracy with potential significant implications on therapy.

Author Disclosure Block: W. Gray: None. S. Sekaran: None. J.A. Tanyi: None. J.M. Holland: None.

LBPV5 Gene Expression Profiling Predicts Non-responders to Chemoradiation in HPV16 Positive Head and Neck Squamous Cell Carcinoma

Purpose/Objective(s): Human papillomavirus (HPV) has been shown to have a causal role in the development of Head and Neck Squamous Cell Carcinoma (HNSCC). In one study, 22% of tumors were HPV+, with 87% being of the HPV16 subtype. HPV+ HNSCC is associated with a better response to radiation and prognosis. However, approximately 15% of patients do not respond favorably to radiation or chemoradiation, thus suffering unnecessary morbidity and delay to treatment. Genes over-expressed in complete responders. RNA from prospectively collected, pre-treatment tumor specimens were subjected to gene expression analysis using Affymetrix Human Exon 1.0ST arrays. HPV-status was confirmed by detection of HPV16 E7 with RT-PCR. Results: ANOVA (p≤0.05) and a 2-fold cutoff were used to identify 118 altered genes, including 112 genes over-expressed in the complete responders compared to the non-responders. Genes over-expressed in the complete responders included genes associated with T cell proliferation (PTPRC, ITGAL, IL6ST, CD3E, CORO1A) and antigen processing/presentation (HLA-F, HLA-DRA, HLA-DQA2, PSMB9, ERAP1, CD74). Utilizing Ariadne Pathway Studio to characterize the data, changes in gene expression were enriched in genes encoding proteins involved in regulating cell processes such as presentation of endogenous peptide antigen, lymphocyte adhesion, and T-cell related processes. Further, genes associated with the Gene Ontology group “response to virus” are up-regulated in complete responders. Conclusions: Our gene expression analysis suggests that differences in gene expression related to chemoradiation therapy are related to immune response prior to treatment. These data can potentially lead to an assay that can be used clinically to predict HPV+ HNSCC patients that will not benefit from chemoradiation, thus helping clinicians to lower morbidity and get selected patients to surgery faster.


LBPV6 Volumetric Variations in Target and Organs at Risk During Adaptive Radiotherapy of Head and Neck Cancer: Evidence From a Prospective Clinical Trial
S. K. Mullapally*, B. K. Mohanty*, M. A. Laviraj*, V. Subramani*, S. Bhaskar*, S. PANDIT*, R. M. Pandey*, G. K. Rath*, All India Institute Of Medical Sciences, New Delhi, India

Purpose/Objective(s): To identify the volumetric changes that occurs in target and organs at risk during adaptive radiotherapy (ART) of head and neck squamous cell carcinoma (HNSCC) and to assess the need for adaptive RT planning in HNSCC.
Materials and Methods: A prospective randomized clinical trial on adaptive image guided RT in HNSCC was conducted in our institute from August 2009 to Dec 2010 after institutional ethics committee approval. 41 patients of HNSCC (oropharynx, larynx, hypopharynx) were randomized into two arms: 3DCRT arm and IGRT arm. The treatment plan was decided by tumor clinic as RT or Chemo-radiation with RT dose of 70 Gy in 35 fractions over 7 weeks. Each patient was planned by 3DCRT in Pinnacle TPS (version 8) based on baseline planning CECT (week 0).

The treatment was executed in Elekta Synergy linac. Weekly EPID was done for 3DCRT arm and CBCT was done for IGRT arm and error more than 3 mm was corrected. At week 5, after 22 fractions of RT, Midcourse CECT was done for all the patients and adaptive replanning was done on fusion CT images (with baseline planning CT). The target volumes (GTV, CTV, PTV) and Organs at Risk (OAR) including parotids, submandibular glands, oral cavity, constrictors, soft palate, glottis, supraglottis etc. were delineated in both baseline (week 0) and Midcourse CT (week 5) and the volumetric and dosimetric differences were measured. Statistical analysis was done using STATA software, Version 9.

Results: The baseline (week 0) GTV0 and CTVO mean volumes (in cc) for 3DCRT arm were 18.31(1.73-60) and 20.60(8.73-73) whereas at Midcourse (week 5), the adaptive GTV5 and CTVO mean volumes were 6.90(3.31-37) and 66(30.4-111.4) with p=0.0001. In IGRT arm, the GTV0 and CTVO mean volumes (in cc) were 20.60(8.73-3) and 8.20(49.4), p=0.0003 whereas CTVO and CTV5 volumes were 102.9(268.8) and 82.2(9.5-260), p=0.047. The mean volumes (in cc) for OARs [week 0; week 5; p value] for the total patients (n=41) were right parotid [23.2(11.5-40.3);17.7(10.1-42.8); p=0.0000], left parotid [22.8(9.9-45.8);18.1(8-9.9); p=0.0000], right submandibular [9.0(9.3-13.53);6.4(0-9.5); p=0.0000], left submandibular [8.7(5-12.9);6.6(1.9-9.9); p=0.0000], superior constrictor [10.1(4.4-16.7);12.5(6.4-20.8);p=0.003 and inferior constrictor [5.9(1.9-11.6);6.6(0.8-10.2); p=0.03].

Conclusions: There are significant volumetric changes in the target volumes (GTV, CTV) and Organs at risk between the baseline CT and the Midcourse CT (week 5) during RT in HNSCC. There is significant tumor shrinkage during RT and volume loss in parotids and submandibular glands whereas in constrictors, an increase in volume is seen. These volumetric variations necessitate adaptive RT in head and neck cancer for optimum target coverage and normal tissue sparing. This is the largest adaptive volumetric data till date from a prospective study.


LBPV7 Preliminary Monte Carlo Simulation of Developments of Zr-89 PET Imaging Protocols for Head and Neck Cancer
K. Alzimami 1,2, S. A. Sassi 3,4, N. M. Spyrou 1,2, 1King Saud University, Riyadh, Saudi Arabia, 2University of Surrey, Guildford, United Kingdom, 3Riyadh Military Hospital, Riyadh, Saudi Arabia

Purpose/Objective(s): Immuno-position emission tomography (PET), the combination of PET with monoclonal antibodies (mAbs), is an attractive novel option to improve diagnostic tumor characterization and to guide mAb-based therapy in certain cancers such as head and neck cancer in comparison to 18F-deoxyglucose (18F-FDG). Zirconium-89 (89Zr) has recently drawn significant interest to be a promising metallo-radionuclide for use in immuno-PET due to favorable decay characteristics. Despite all efforts that have been done over the last few years in the development of procedures for large scale production and purification of 89Zr and its stable coupling to mAbs as well as successful preclinical and clinical 89Zr immuno-PET studies, there is still gap for exploring the optimal imaging protocols for 89Zr PET. This preliminary study aims to characterize 89Zr PET imaging performance compared to 18F and to investigate the optimal energy window settings for 89Zr PET imaging.

Materials/Methods: For this study, the Siemens Biograph 6 PET scanner geometry, which consists of 24,336 ISO crystals, was modelled using GATE. More the Physics processes were modelled using the low energy electromagnetic processes package including Rayleigh, photoelectric and Compton interactions. GATE allows modeling signal processing including energy and timing resolution blurring and coincidence sorting. A paralyzable dead-time model of 800 ns in order to simulate the dead time at the singles level was applied. Scans were made with energy windows of 425-580, 425-650, and 425-750 keV, in 3D mode. The ROOT output (V.5.14), providing list mode of the detected single events including energy deposited and coordinates of detection within the modelled scanner geometry for each single event, was used to calculate the scatter fraction (SF) and noise equivalent count rate (NECR) results. The SF and NECR measurements were simulated by modeling the NEMA NU-2001 scatter phantom uniformly filled with a solution of water and 89Zr or 18F.

Results: Although, the energy window 425-750 keV gave the highest NECR, it significantly increases the SF. Using the narrowest energy window (425-585 keV) significantly improves image contrast by reducing the SF by 25% and slightly reduces NECR by 6.8% in comparison to the energy window setting of 425-650 keV.

Conclusions: This preliminary study suggests that 89Zr isotope seems to be promising radionuclide for immune-PET imaging as its physical characteristics fulfill immune-PET imaging requirements in comparison to 18F. Further simulation investigations including tomographic spatial resolution and NEMA image quality phantom are required to find the optimal energy window settings of 89Zr PET image quality.

Author Disclosure Block: K. Alzimami: None. S.A. Sassi: None. N.M. Spyrou: None.

LBPV8 Antitumor Effects of Combined Therapy with Radiation and Intratumoral Injection of Mesenchymal Stem Cells Expressing Interleukin-12 on Hypopharynx Carcinogenesis in Balb/c- Nude Mice
C. Kim 1, Y. Ji Young 1, Y. Kim 1, C. Kwang-Jae 1, M. Kim 1, 1Department of Otolaryngology-HNS Uijongbu St. Mary's Hospital, Uijongbu City, Kyonggi-Do,480-130, Korea, Korea, Republic of, 2POSTECH-CATHOLIC biomedical engineering, 222 Seocha-Gu Seoul City , Korea, Korea, Republic of, 3POSTECH-CATHOLIC biomedical engineering institute, 222 Seocha-Gu Seoul City,Korea, Korea, Republic of, 4Department of Otolaryngology-HNS,Seoul St.Mary's Hospital, 222, Seocha-Gu,Seoul City,137-701,Korea, Korea, Republic of

Purpose/Objective(s): It has been reported that intratumor injection of mesenchymal stem cell expressing modified interleukin-12(MSCs/IL-12M) exhibit strong antitumor effect. The purpose of this study was to evaluate more potent antitumor effects of combined therapy with MSCs/IL-12M and radiation for hypopharynx carcinoma in BALB/c- nude mice.

Materials/Methods: Sixteen BALB/c- nude mice were inoculated with FaDu cell(a hypopharyngeal carcinoma cell line) via subcutaneous injection. Four groups were randomly divided into control, irradiation only, MSC/IL-12M intratumoral injection only, and combined treatment group with irradiation and MSCs/IL-12M intratumoral injection. 4 weeks after the xenograft model formation. Both radiation therapy and intra-tumour injection of MSCs/IL-12M were performed on days 0, 7, 14, and 21 following the initial injection.
BALB/c-nude mice were irradiated 4 times every 3 days by dose of 2 Gy/min. 4 mice were intratumorally injected with 2×10^6 MSCs/IL-12M cells/50 ul PBS. 4 mice of combined treatment group were irradiated first, followed by being received intratumoral injection of MSCs/IL-12M. Tumor volume was calculated and IL-12 levels were measured in sera of tumor-bearing mice. Immunohistochemistry of xenograft tumors were performed for Ki-67, casp-3, and VEGF. Results: There were no significant differences in hypopharynx carcinogenesis among 4 groups (p > 0.05) but showed more antitumor effect in combined treatment group when measuring tumor volume. Also, even though no statistical significance, combination treatment tended to more increase the level of IL-12 than single treatment groups. On immunohistochemistry of caspase-3, the most intense staining was shown in combined treatment group. However, Ki-67 and VEGE were more weakly stained in combined treatment group than single treatment groups. Conclusions: We demonstrated that combination treatment of radiation with intratumoral injection of MSC/IL-12M and radiation exhibited the potent antitumor effect for hypopharynx carcinogenesis by preventing angiogenesis and inducing cell apoptosis in BALB/c-nude mice.

Author Disclosure Block: C. Kim: None. Y. Ji Young: None. Y. Kim: None. C. Kwang-Jae: None. M. Kim: None.

LBPV9 Non-invasive Intraoperative Angiography for Reconstruction of Head and Neck Defects
S. Daram1, J. M. Sacks2, M. E. Kupferman2, 1Baylor College of Medicine, Houston, TX, 2Johns Hopkins University - Department of Plastic Surgery, Baltimore, MD, 3University of Texas MD Anderson Cancer Center - Department of Head and Neck Surgery, Houston, TX

Purpose/Objectives(s): Reconstruction of head and neck defects can be accomplished with local random flaps, pedicled fascio- or musculocutaneous flaps or free flaps. Flap failure, while rare, is often caused by vascular insufficiency and venous congestion to the graft, and may be increased by factors such as prior radiation or surgical treatment to the area, cardiovascular disease, and smoking history. Fluorescence laser angiography using near-infrared wavelength with Indocyanine Green (ICG) has the ability to detect perfusion deficits in flaps intraoperatively, which when recognized early, may result in lower failure rates. While this technology has been validated in other fields, this has yet to be demonstrated in the head and neck literature. We present 3 representative cases that successfully apply this technology to evaluate head and neck tissue flaps.

Materials/Methods: Three cases utilizing differing, but representative, flaps were chosen. The three cases involved a local rotated flap, a pectoralis myofascial flap, and a radial forearm flap. Each of the patients had risk factors that increased flap failure. ICG angiography was employed intraoperatively to design grafts and evaluate vascular flow to the flaps after placement. Each patient was followed for 9 months post-operatively for evidence of flap dehiscence or failure. Results: In all cases, ICG angiography was successfully utilized to design the flaps and ensure vascular flow to all areas of the graft, especially its periphery, perioperatively. No complications secondary to graft failure were noted postoperatively or during the 9-month follow-up. Conclusions: Flap reconstruction is the standard of care for repairing tissue defects secondary to H&N cancer resection. While graft failure typically begins almost immediately after graft placement, it progresses insidiously, and unfortunately becomes apparent a few days to a week post-operatively. Thus, by the time graft failure is recognized, it has already developed, and may result in lower failure rates. While rare, failure rate can be increased by several risk factors. H&N surgeons can employ this technology with high-risk patients to minimize failure rates by identifying critical vascularization to the graft before harvest and ensuring adequate vascular flow after inset. This reduces morbidity and costs associated with flap failure and corresponding re-operation.


LBPV10 A Randomized, Open-label, Phase II Study of Afatinib (BIBW 2992) vs. Cetuximab in Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck - Final Data
T. Seiwert*, J. Fayette*, D. Cupissol*, J. Del Campo*, P. Clement*, J. Tourania*, M. Degardin†, W. Zhang*, E. Ehnmooth*, E. Cohen*, 1University of Chicago Medical Center, Chicago, IL, 2Centre Léon Bérard, Lyon, France, 3Centre Val d’Aurelle, Montpellier, France, 4Hospital Universitario Vall D’Hebron, Barcelona, Spain, 5Katholieke Universiteit Leuven, Leuven, Belgium, 6Université De Poitiers, Chu De Poitiers, France, 7Centre Oscar Lambret, Lille, France, 8Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, 9Boehringer-Ingelheim, Danmark A/S, Denmark

Purpose/Objectives(s): In this open-label, randomized, Phase II study, afatinib (BIBW 2992), an oral, irreversible Erbb-family blocker was compared with cetuximab in patients with metastatic or recurrent head and neck squamous cell carcinoma (HNSCC) after failure of a platinum-based therapy. Materials/Methods: Eligible patients were randomized to afatinib 50 mg daily, or weekly cetuximab 400 mg/m^2 loading dose followed by 250 mg/m^2/week, until disease progression or treatment-related AEs (Stage 1); they could then opt to cross over treatment arms (Stage 2). Response (RECIST 1.0) was assessed 8 weekly. Primary endpoint was tumor shrinkage (maximal reduction in the sum of the longest diameters of the target lesions compared to baseline) at the end of Stage 1. Results: Patients (n=124, median age 58.0 years, 87.1% male) were equally randomized. At Stage 2, 68 patients crossed over arms (32 from afatinib; 36 cetuximab). For Stage 1, mean tumor shrinkage (adjusted mean percentage change from baseline [standard error]) was -10.4% (5.07) vs. -5.4% (4.86) for afatinib and cetuximab (p=0.46) by investigator review and -16.6% (4.60) vs. -10.1% (4.67) by independent central review (ICR) (p=0.30). Investigator assessed confirmed objective response rates (ORRs) were 16.1% (afatinib) and 6.5% (cetuximab) for intent-to-treat (ITT) patients (p=0.09) and 19.2% vs. 7.3% for evaluable patients. ICR ORRs were ITT: 8.1% afatinib, 9.7% cetuximab (p=0.78); evaluable patients: 9.6% vs. 11.1%. Median PFS was 15.9 weeks (95% CI: 10.3-17.1) for afatinib and 15.1 weeks (95% CI: 8.3-19.3) for cetuximab (p=0.93) by investigator review, and 13 weeks (95% CI: 8-20) and 15 weeks (95% CI: 8-31.7) by ICR (p=0.39). For Stage 2, disease control rate (DCR) by investigator review was 38.9% (afatinib as second treatment) vs. 18.8% (cetuximab second) and 33.3% vs. 18.8% by ICR. Duration of DC was 20.2 weeks vs. 20.7 weeks per investigator assessment and 17.3 weeks vs. 16.6 weeks per ICR. Most common treatment-related AEs in Stage 1 for afatinib (n=61) were diarrhea, 48 (78.7%) vs. 12 (20.2%) for cetuximab (n=60) and rash/ acne, 48 (78.7%) vs. 46 (76.6%), respectively. There were 29.5% and 3.3% of patients with AEs leading to dose reduction, and 37.7% and 16.7% leading to discontinuation in the afatinib and cetuximab arms. Conclusions: Afatinib has at least comparable anti-tumor
activity to cetuximab in HNSCC that is refractory to platinum-based therapy: DCR results in Stage 2 were particularly notable for afatinib. Both drugs showed safety profiles characteristic of EGFR/HER2 inhibitors and the number of patients observed with diarrhea was higher in the afatinib group.

**Author Disclosure Block:**

**T. Seiwert:** B. Research Grant; Boehringer Ingelheim, Genentech, Ariad. F. Consultant/Advisory Board; Boehringer Ingelheim.  
**J. Fayette:** None.  
**D. Cupissol:** None.  
**J. DelCampo:** None.  
**P. Clement:** None.  
**J. Tourani:** None.  
**M. Degardin:** None.  
**W. Zhang:** A. Employment; Boehringer Ingelheim.  
**E. Ehrnrooth:** A. Employment; Boehringer Ingelheim.  
**E. Cohen:** F. Consultant/Advisory Board; Boehringer Ingelheim.
Abstract Presenter Index

Alphabetical by Last Name

<table>
<thead>
<tr>
<th>Name</th>
<th>Last Name</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdul Razak, Albiruni Ryan</td>
<td>Abdul Razak</td>
<td>6</td>
</tr>
<tr>
<td>Alabi, Sulyman</td>
<td>Alabi</td>
<td>119</td>
</tr>
<tr>
<td>Ali, Haythem</td>
<td>Ali</td>
<td>215</td>
</tr>
<tr>
<td>Alizadeh-Kashani, Moein</td>
<td>Alizadeh-Kashani</td>
<td>131</td>
</tr>
<tr>
<td>Alzimami, Khalid, LBPV7</td>
<td>Alzimami</td>
<td>193</td>
</tr>
<tr>
<td>Ampil, Federico</td>
<td>Ampil</td>
<td>143</td>
</tr>
<tr>
<td>Anderson, CArryn</td>
<td>Anderson</td>
<td>102</td>
</tr>
<tr>
<td>Arora, Shilpi</td>
<td>Arora</td>
<td>123</td>
</tr>
<tr>
<td>Bahig, Houda</td>
<td>Bahig</td>
<td>156</td>
</tr>
<tr>
<td>Bairati, Isabelle</td>
<td>Bairati</td>
<td>134</td>
</tr>
<tr>
<td>Balaiyya, Naveen Kumar</td>
<td>Balaiyya</td>
<td>193</td>
</tr>
<tr>
<td>Batth, Sukhjeet</td>
<td>Batth</td>
<td>134</td>
</tr>
<tr>
<td>Beadle, Beth</td>
<td>Beadle</td>
<td>4</td>
</tr>
<tr>
<td>Bedi, Manpreet</td>
<td>Bedi</td>
<td>186</td>
</tr>
<tr>
<td>Beitler, Jonathan</td>
<td>Beitler</td>
<td>150</td>
</tr>
<tr>
<td>Bensalem, Assia</td>
<td>Bensalem</td>
<td>114</td>
</tr>
<tr>
<td>Bensalem, Assia</td>
<td>Bensalem</td>
<td>195</td>
</tr>
<tr>
<td>Blakaj, Dukagjin</td>
<td>Blakaj</td>
<td>183</td>
</tr>
<tr>
<td>Bradley, Julie</td>
<td>Bradley</td>
<td>152</td>
</tr>
<tr>
<td>Caudell, Jimmy</td>
<td>Caudell</td>
<td>173</td>
</tr>
<tr>
<td>Caudell, Jimmy</td>
<td>Caudell</td>
<td>191</td>
</tr>
<tr>
<td>Caudell, Jimmy</td>
<td>Caudell</td>
<td>12</td>
</tr>
<tr>
<td>Cervantes, S Santino</td>
<td>Cervantes</td>
<td>225</td>
</tr>
<tr>
<td>Champ, Colin</td>
<td>Champ</td>
<td>198</td>
</tr>
<tr>
<td>Chang, Zheng</td>
<td>Chang</td>
<td>106</td>
</tr>
<tr>
<td>Chapman, Tobias</td>
<td>Chapman</td>
<td>206</td>
</tr>
<tr>
<td>Chasen, Martin</td>
<td>Chasen</td>
<td>125</td>
</tr>
<tr>
<td>Chen, George</td>
<td>Chen</td>
<td>103</td>
</tr>
<tr>
<td>Chen, Allen</td>
<td>Chen</td>
<td>148</td>
</tr>
<tr>
<td>Chen, Chuangzhen</td>
<td>Chen</td>
<td>190</td>
</tr>
<tr>
<td>Chen, Jianzhou</td>
<td>Chen</td>
<td>218</td>
</tr>
<tr>
<td>Chow, Laura</td>
<td>Chow</td>
<td>203</td>
</tr>
<tr>
<td>Christensen, Michael</td>
<td>Christensen</td>
<td>196</td>
</tr>
<tr>
<td>Cohen, Ezra</td>
<td>Cohen</td>
<td>122</td>
</tr>
<tr>
<td>Comstock, Richard</td>
<td>Comstock</td>
<td>118</td>
</tr>
<tr>
<td>Cooper, Jay</td>
<td>Cooper</td>
<td>1</td>
</tr>
<tr>
<td>Cox, John</td>
<td>Cox</td>
<td>219</td>
</tr>
<tr>
<td>Daram, Shiva</td>
<td>Daram</td>
<td>134</td>
</tr>
<tr>
<td>De Almeida, John</td>
<td>De Almeida</td>
<td>177</td>
</tr>
<tr>
<td>Deekken, John</td>
<td>Deekken</td>
<td>222</td>
</tr>
<tr>
<td>Dobrosotskaya, Irina</td>
<td>Dobrosotskaya</td>
<td>157</td>
</tr>
<tr>
<td>Dominello, Michael</td>
<td>Dominello</td>
<td>11</td>
</tr>
<tr>
<td>Ellis, Janet</td>
<td>Ellis</td>
<td>11</td>
</tr>
<tr>
<td>Feldman, Rebecca</td>
<td>Feldman</td>
<td>105</td>
</tr>
<tr>
<td>Fernandez, Diego</td>
<td>Fernandez</td>
<td>221</td>
</tr>
<tr>
<td>Finkelstein, Steven</td>
<td>Finkelstein</td>
<td>209</td>
</tr>
<tr>
<td>Frank, Douglas</td>
<td>Frank</td>
<td>187</td>
</tr>
<tr>
<td>Fried, David</td>
<td>Fried</td>
<td>211</td>
</tr>
<tr>
<td>Galloway, Thomas</td>
<td>Galloway</td>
<td>165</td>
</tr>
<tr>
<td>Ganly, Ian</td>
<td>Ganly</td>
<td>181</td>
</tr>
<tr>
<td>Gentile, Jamie</td>
<td>Gentile</td>
<td>205</td>
</tr>
<tr>
<td>Giese-Davis, Janine</td>
<td>Giese-Davis</td>
<td>124</td>
</tr>
<tr>
<td>Name</td>
<td>Page</td>
<td></td>
</tr>
<tr>
<td>-----------------------</td>
<td>------</td>
<td></td>
</tr>
<tr>
<td>Ryan, Michael</td>
<td>127</td>
<td></td>
</tr>
<tr>
<td>Sales, Lindsay</td>
<td>144</td>
<td></td>
</tr>
<tr>
<td>Saltman, Ben</td>
<td>212</td>
<td></td>
</tr>
<tr>
<td>Schwartz, David Louis</td>
<td>142</td>
<td></td>
</tr>
<tr>
<td>Schwartz, David Louis</td>
<td>197</td>
<td></td>
</tr>
<tr>
<td>Seiwert, Tanguy</td>
<td>LBPV10</td>
<td></td>
</tr>
<tr>
<td>Sekaran, Shreya</td>
<td>227</td>
<td></td>
</tr>
<tr>
<td>Sheets, Nathan</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Shetti, Madhu</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>Siddiqui, Farzan</td>
<td>154</td>
<td></td>
</tr>
<tr>
<td>Skinner, Heath</td>
<td>174</td>
<td></td>
</tr>
<tr>
<td>Smith, Valerie</td>
<td>117</td>
<td></td>
</tr>
<tr>
<td>Snider III, James</td>
<td>223</td>
<td></td>
</tr>
<tr>
<td>Stenson, Kerstin</td>
<td>130</td>
<td></td>
</tr>
<tr>
<td>Stricker, Thomas</td>
<td>LBPV3</td>
<td></td>
</tr>
<tr>
<td>Stucken, Chaz</td>
<td>189</td>
<td></td>
</tr>
<tr>
<td>Swisher-McClure</td>
<td>Samuel</td>
<td>116</td>
</tr>
<tr>
<td>Terakedis, Breanne</td>
<td>153</td>
<td></td>
</tr>
<tr>
<td>Terhaard, Chris</td>
<td>138</td>
<td></td>
</tr>
<tr>
<td>Thomas, Kimberly</td>
<td>194</td>
<td></td>
</tr>
<tr>
<td>Tun, Nay Min</td>
<td>175</td>
<td></td>
</tr>
<tr>
<td>Valduga, Francesco</td>
<td>220</td>
<td></td>
</tr>
<tr>
<td>Vanderwalde, Noam</td>
<td>176</td>
<td></td>
</tr>
<tr>
<td>Vlacich, Gregory</td>
<td>133</td>
<td></td>
</tr>
<tr>
<td>Vlasman, Renske</td>
<td>136</td>
<td></td>
</tr>
<tr>
<td>Vora, Nayana</td>
<td>202</td>
<td></td>
</tr>
<tr>
<td>Wilson, George</td>
<td>LBPV5</td>
<td></td>
</tr>
<tr>
<td>Wirth, Lori</td>
<td>171</td>
<td></td>
</tr>
<tr>
<td>Wolf, Gregory</td>
<td>101</td>
<td></td>
</tr>
<tr>
<td>Wolf, Gregory</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Wong, Steven</td>
<td>146</td>
<td></td>
</tr>
<tr>
<td>Wong, Stuart</td>
<td>170</td>
<td></td>
</tr>
<tr>
<td>Wygoda, Andrzej</td>
<td>210</td>
<td></td>
</tr>
<tr>
<td>Yang, Samuel</td>
<td>120</td>
<td></td>
</tr>
<tr>
<td>Yao, Min</td>
<td>162</td>
<td></td>
</tr>
<tr>
<td>Zhang, Hong</td>
<td>113</td>
<td></td>
</tr>
<tr>
<td>Zhu, Guopei</td>
<td>180</td>
<td></td>
</tr>
</tbody>
</table>
ADVOCACY DAY
March 25-27, 2012 • The Liaison Capitol Hill, Washington

SPRING REFRESHER COURSE
April 13-15, 2012 • Westin Chicago River North, Chicago
www.astro.org/springrefresher

STATE OF THE ART TECHNIQUES IN IMRT, IGRT, SBRT, PROTON AND BRACHYTHERAPY:
Emphasis on Quality and Safety
May 4-6, 2012 • Encore at Wynn Las Vegas, Las Vegas
www.astro.org/stateofthearttechniques

2012 CHICAGO MULTIDISCIPLINARY SYMPOSIUM IN THORACIC ONCOLOGY
September 6-8, 2012 • Chicago Marriott Downtown Magnificent Mile, Chicago
www.thoracicsymposium.org
Co-sponsors – ASCO, ASTRO, IASLC and The University of Chicago

ASTRO ANNUAL MEETING
October 28-31, 2012 • Boston Convention and Exhibition Center, Boston
www.astro.org/annualmeeting

RADIATION ONCOLOGY BENEFIT MANAGERS (ROBM)
March 15, 2012, 3:00 p.m. Eastern time
Speakers: Brian Kavanagh, MD, MPH, and Alex Khariton, RTT, MBA
Learn how radiation oncology benefit management companies impact your practice and patient care.

PHYSICIAN VALUE BASED PURCHASING
June 14, 2012, 3:00 p.m. Eastern time
Speakers: Ajay Bhatnagar, MD, and Sheila Madhani, MA, MPH
An overview of Medicare value based purchasing initiatives will be presented along with a discussion of the challenges this creates for radiation oncologists and how you can meet the demands of this new payment environment.

Visit www.astro.org/webinars for more information.
thank you

Special thanks to the 2012 Multidisciplinary Head and Neck Cancer Symposium Educational Grant Supporters.

Gold

Bristol-Myers Squibb  Lilly

General

AMGEN  Varian medical systems

A partner for life