Patterns of Local Failure in Locally-Advanced Larynx and Hypopharynx Cancers
K. Meyer, A.M. Baschnagel, A. Troeiller, D. Yan, P.Y. Chen, and D.J. Krauss; Beaumont Health System, Royal Oak, MI

Purpose/Objective(s): Intensity modulated radiation therapy (IMRT) with chemotherapy for locally advanced laryngeal and hypopharyngeal cancer provides a local control rate of 60-70%. IMRT allows for high conformity with steep dose gradients. If an area of tumor or subclinical disease is underdosed, local failure may occur. We retrospectively evaluated patients with laryngeal and hypopharyngeal cancers and investigated whether any dosimetric variations could predict for local failure.

Materials/Methods: From 2003 to 2011, 58 patients with locally advanced laryngeal (74%) and hypopharyngeal (26%) squamous cell carcinomas treated with definitive IMRT with concurrent chemotherapy with at least 6 months follow-up were analyzed. IMRT was delivered with a simultaneous integrated boost technique. A median dose of 70 Gy (range, 64.6-74.4) was delivered to regions of gross disease and 59.9 Gy to the at-risk nodal regions; both given in 35 fractions. The GTV size and the following dosimetric parameters of the PTV were reviewed: Dmax, Dmean, D99, V70 and V66. PET/CT with evidence of local failure was fused to planning CT to evaluate the relationship between site of local recurrence and treatment plan. These fusions were analyzed to determine if the recurrence fell within the PTV and received at least 95% of the prescription dose.

Results: Median follow-up was 27 months (range, 5-100 months). Stage distribution was: T1 - 10%, T2 - 34%, T3 - 36%, T4 - 19%; stage II - 10%, III - 25%, IVA - 54%, and IVB - 8%. There were 17 local failures. The one and two year actuarial local control rates were 79% and 70%; respectively. The median time to local failure was 6.2 months (range, 2.7-22.0 months). The median values of the analyzed PTV parameters were: Dmax 77.9 Gy (range, 68.9-86.2 Gy), Dmean 65.2 Gy (range, 49.1-70.1 Gy), Dmean 72.4 Gy (range, 66.4-75.2 Gy), V70 87.8% (range, 0-99), V66 98.4% (range, 75.7-100). The median GTV was 48.4 cc (range, 6.57-519 cc). T4 disease correlated with local failure (73% vs 27% for non-T4 disease, p < 0.001). There was no correlation with GTV size or treatment duration with rates of local failure. Additionally, none of the evaluated dose parameters were associated with local control rates. Nine (53%) of the local failures represented incomplete responses to radiation; the other 8 (47%) recurred after a complete response. Sixteen of the 17 (94%) local failures were within the PTV and 95% isodose line. One patient failed 2 cm away from the PTV 8 months after treatment.

Conclusions: Local control remains a concern in the management of locally advanced laryngeal cancer. In our series, local failure is not associated with lower dose to target volume and 16 of the 17 tumors failed in tissue that had received a high radiation dose. This suggests that heterogeneity in tumor biology may be responsible for local failure. Identifying biomarkers that correlate with radio resistance may allow for alternative treatment considerations, such as novel molecular targeted agents or upfront surgery.


Can It Stay or Should It Go? A Comparison of T4 Laryngeal Cancer Management
J.M. Lemons, K. Ruth, J.A. Ridge, B. Burtness, M. Lango, R. Mehra, J. Liu, and T.J. Galloway; Fox Chase Cancer Center, Philadelphia, PA

Purpose/Objective(s): It remains unclear whether T4a larynx cancer can be safely treated without a total laryngectomy (TL). We report the outcomes of T4a larynx cancer patients treated with TL or definitive chemoradiation (CRT) at a tertiary care cancer center.

Materials/Methods: We retrospectively reviewed the charts of patients with T4a laryngeal cancer treated curatively at Fox Chase Cancer Center between Jan. 2000 and Dec. 2010. T4a stage was assigned clinically in all cases. Patients treated with a TL were recommended to receive adjuvant radiation therapy +/- chemo. Overall survival (OS) was estimated using the Kaplan Meier method. Predictors of DFS and recurrence were analyzed with Cox proportional hazards regression.

Results: A total of 51 patients met inclusion criteria, 27 (53%) of whom were treated with TL and 24 (47%) with definitive CRT. TL patients were slightly older (median TL 70 yrs vs CRT 62.5 yrs, p = 0.11). There was no difference with respect to N stage (N2-3: TL 33% vs CRT 46%, p = 0.30), performance status (p = 0.41), pack-year history (p = 0.90), or histologic grade (p > 0.99). Of the 27 patients treated with a TL, 41% received adjuvant CRT and 52% received adjuvant radiation. Among the 24 patients treated with CRT, 4 (17%) received neoadjuvant chemo. Cisplatin was the most common concurrent systemic agent (74%). TL patients received a median radiation dose of 60 Gy (range, 6-70 Gy) while those treated with CRT received 70 Gy (range, 66-76 Gy) (p < 0.01). Median follow-up among all patients was 1.8 years and among living patients it was 4.2 years. Overall survival was 58% at 2 years and did not differ significantly by treatment strategy (p = 0.97). Failure patterns were similar: local/regional (TL: 15% vs CRT: 25%) (p = 0.48) and distant (TL: 11% vs CRT: 17%) (p = 0.69). There was a trend for more CRT patients to require a PEG tube overall (63% vs 48%, p = 0.30) and at 6 months (54% vs 33%, p = 0.13). Patients treated with TL tended to have more grade 3-5 toxicity (26% vs 13%, p = 0.30). No CRT patients required a laryngectomy for chondronecrosis and one patient required a permanent tracheotomy. Univariable analysis showed that patients who received any form of chemotherapy were more likely to require a PEG tube: odds ratio 5.0 (95% CI = 1.4-17.8, p = 0.013). Neither N stage, nor histology, nor performance status was found to significantly predict DFS on multivariable analysis.

Conclusions: T4 laryngeal cancer has a poor prognosis and this series shows no survival difference between treatment strategies. A trend towards increased toxicity when treated with TL was seen, although this may be related to a high utilization of adjuvant chemoradiation. The data also suggests the use of systemic therapy portends PEG tube placement. Innovative therapies to conserve the larynx, even for T4 primaries, are needed.


3DCRT and IMRT Improve Local Control Versus Opposed Lateral In Early-Stage Squamous Cell Carcinoma of the Larynx
S. Zhao, T. Strom, J. Caudell, C. Rushoven, R. Shridhar, A. Trotti, and N. Rao; Moffitt Cancer Center, Tampa, FL

Purpose/Objective(s): Early stage larynx squamous cell carcinoma has traditionally been treated with the opposed lateral radiation therapy (RT) technique. The primary purpose of this retrospective study was to evaluate locoregional control (LRC) with opposed lateral technique (LAT) versus 3-D conformal radiation therapy (3DCRT) or intensity modulated radiation therapy (IMRT).

Materials/Methods: Eighty-five consecutive patients were identified from 1998 to 2012 who were treated with definitive RT for T1-2 N0 M0 squamous cell carcinoma of the larynx. Patient demographics, tumor characteristics and radiation details were abstracted from the chart. For 3DCRT or IMRT, the GTV was contoured based on CT findings and direct laryngoscopy. The GTV was expanded by 3-5 mm for CTV and 3-5 mm for PTV. The spinal cord was limited to a maximum dose of 45 Gy. The contralateral arytenoid was spared if possible and the carotid artery was treated as an avoidance structure in selected cases. LRC was measured from the date of RT completion to the date of documented failure or censored at the last follow-up or death. The probabilities of LRC were analyzed with Cox proportional hazards regression.

Results: Median follow-up for censored patients was 32.4 months. Patients with T1 N0 M0 SCC were primarily treated to a total dose of 66 Gy in once-daily 200 cGy fractions while those with T2 N0 M0 SCC were primarily treated with either accelerated or hyperfractionated RT. Of the 85 laryngeal tumors, 60 (70.6%) were T1 and 25 (29.4%) were T2. Anterior