

included the GTV-T, N remaining after the first phase of chemoradiation with 1-cm margin and was treated to 33.6 Gy.

Results: Between Jan-01 and Aug-04, sixteen patients were recruited with an average age of 52 years. Two patients had stage III and 14 patients stage IV tumors. Tumor site: Oropharynx (50%), Hypopharynx-larynx (22%), Nasal cavity-paranasal sinuses (11%), Parotid Gland (6%) and Unknown primary site (6%). Grade III-IV acute events noted were mucositis in 14 patients (87%), esophagitis in 5 patients (31%), epilitis in 2 patients (12%) and leukopenia in 3 patients (18%). Twelve patients (75%) required hospital admission for control of symptoms and nutritional support. The response observed at the end of the chemoradiation program has been complete in 75% and partial in the rest. Three patients underwent salvage cervical lymph node dissection for residual neck disease after chemoradiation. Locoregional control of the disease was achieved in 14 of the 16 patients (87%). With an average follow-up of 21 months (range, 5–36) 13 patients remained alive and free of locoregional disease, 2 patients died with locoregional disease and one patient died from massive hemorrhage after carotid blowout. The 3-year overall survival was 80%.

Conclusions: Simultaneous administration of 3DCRT with weekly Cisplatin-Paclitaxel yields response and locoregional control in more than 80% of the cases but at the expense of a high toxicity. Studies with more accrual and longer follow-up are required to confirm these data. Tolerance must be improved through the use of sophisticated irradiation techniques which allow more healthy mucosal tissue to be spared.

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POSTER

Sonographic maximal malignancy criteria count (MMCC) of lymph nodes predicts progression and survival in H&N cancer stage IVA – a new prognostic factor

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Background: Inoperable head-and-neck cancer is usually treated with aggressive radiochemotherapy though survival is often poor. A tool that identifies subgroups of patients according to their prognosis would be highly desirable. We present a non-invasive method of strong prognostic value.

Material and Methods: Systematic high-resolution B-scan and colour-coded duplex-sonography was applied prospectively on neck lymph nodes of 50 pts. with inoperable H&N cancer stage IVA 05/99–01/02 before start of definite radio-chemo-therapy. 710 lymph nodes were identified. In 219 >1.5 cm the fulfilling of the following 8 malignancy criteria was counted: inhomogeneity of echotexture, irregular surface, lack of hilar sign, spherical form, matting, aberrant intranodal vessels, infiltration of surrounding tissue and intranodal cystic necrosis. The maximal malignancy criteria count in a single lymph node (MMCC) was taken as a representative for that tumor and correlated with follow-up data (overall survival=OS, locoregional recurrence-free survival=LRFS, metastatic-free survival=MFS, disease-free survival=DFS).

Results: Follow-up was 2.3–5.3 years for 11 survivors, 39 pts. have died. Median OS was one year. Pretreatment MMCC was the strongest predictor for overall survival: 26 pts. with a low MMCC (1–6) had a median OS of 24.7 months vs. 8.1 months for 24 pts. with a high MMCC (7–8), $p = 0.0004$ (logrank). Estimated 1- and 3-year-OS were 69% and 41% for low MMCC and 25% and 8% for high MMCC. Ten out of eleven living patients had a low MMCC.

Outcome in pts. with a low vs. high MMCC differed significantly for all endpoints, 3yr-LRFS was 46% vs. 26%, MFS 81% vs. 57% and DFS 35% vs. 11%.

Anaemia with a pretreatment hemoglobin level <13 g/dl was associated with poor LRFS and OS; N-stage ($\leq 2b$ vs. $\geq 2c$) or grading (G1–2 vs. G3–4) did not reach significance in univariate testing. In multivariate Cox analysis MMCC and anaemia were independent prognostic factors for LRFS, and MMCC remained the only significant prognostic factor for OS, MFS and DFS.

Conclusions: In conservative management of head-and-neck cancer standardized ultrasonography of neck lymph nodes should be integrated into pretreatment work-up, not only for its diagnostic, but also for its prognostic properties, as the MMCC is a powerful prognostic factor for all tumor-related endpoints. It seems to resemble the aggressiveness of tumor biology beyond UICC-stage and may be of help to individualize treatment strategy.

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POSTER

Concurrent chemoradiation followed by interstitial brachytherapy boost and neck dissection for T4 base of tongue cancer

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Background: Concurrent chemoradiation and brachytherapy implant boost both improve outcomes compared to external beam radiation alone for base of tongue (BOT) cancers. Limited data exist regarding the feasibility and efficacy of adding a brachytherapy boost after definitive chemoradiation (CT/RT) for advanced base of tongue cancers. We report our experience treating T4 BOT cancer with concurrent chemoradiation followed by planned neck dissection and brachytherapy.

Methods and Materials: From 4/98–12/04, 18 patients with T4 (1997 AJCC stage) BOT cancer were treated by conventional fractionated external beam radiation therapy followed by brachytherapy. 17 of the 18 patients received concomitant platinum-based chemotherapy. The median dose of external beam radiation delivered was 6660 cGy (5040–7440 cGy) (1 patient received hyperfractionation). Planned neck dissection and interstitial Iridium-192 brachytherapy boost were performed at median time of 5 weeks after CT/RT. The median dose of brachytherapy: 1200 cGy (range: 1000–3000 cGy). Patient characteristics were as follows: median age: 60yrs (range 40–78yr), 17 were male. Nodal stage: N0 (1/18), N1 (2/18), N2 (12/18) and N3 (3/18).

Results: At a median follow up of 23 months (6–75 months), the crude local control rate (LC) was 83% (15/18), regional control (RC): 100%, incidence of distant metastasis (DM): 28% (5/18), disease free survival (DFS): 61% (11/18), and overall survival (OS): 94% (17/18). The two-year actuarial estimates of LC, RC, LRC, DM, DFS and OS were 84%, 100%, 84%, 36%, 50% and 100%, respectively. The one patient who did not receive chemotherapy failed locally.

The incidence of acute RTOG/NCI grade 3 toxicity was 69% (11/16) primarily consisting mucositis (6/15), dysphagia (6/15), and leukopenia (6/16). There were three patients with grade 4 toxicity: 2 hematologic and one aspiration pneumonia prior to his implant. There was no treatment-related mortality. The incidence of late grade 3 or greater toxicity was 24% of 17 patients evaluated.

Conclusion: Concomitant chemoradiation therapy followed by an interstitial brachytherapy boost and a planned neck dissection provides excellent local and regional control for T4 base of tongue cancers and is well tolerated. Despite the addition of concurrent platinum-based chemotherapy, distant metastasis remains significant and is the dominant mode of failure.

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POSTER

Short hairpin RNA directed against the human telomerase reverse transcriptase produces apoptosis in Hep-2 Cells

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Background: More and more researches approve that suppressing telomerase RNA and telomerase reverse transcriptase mRNA both can reduce telomerase activity restrain the growth of cancer cells in short-term. Here we investigate the effect of short hairpin RNA (shRNA) by targeting human telomerase reverse transcriptase mRNA (hTERT mRNA) on Hep-2 cells.

Materials and Methods: shRNA expression vectors targeting the mRNA of hTERT were constructed. Cells were treated with shRNA expression vectors directed against two different hTERT sites, or control vectors including mismatched shRNA or without shRNA. At 24, 48 and 72 h, the expression of hTERT mRNA and the activity of telomerase was measured. After one and two days shRNAs administrations, apoptosis was evaluated using the TUNEL assay and transmission electron microscope respectively.

Results: Hep-2 cells treated with shRNA against hTERT showed a remarkable inhibition of the mRNA expression of hTERT, the telomerase activity and a profound induction of programmed cell death. After one or two days of transfection, special shRNA caused profound cell death in the Hep-2 cells. All of these effects were seen regardless of hTERT target site, and shRNA control showed none of them.

Conclusions: The results suggest that inhibition of telomerase activity in Hep-2 cells by short hairpin RNA treatment against the mRNA of hTERT result in apoptotic cell death. RNA interference may be a promising strategy for the treatment of laryngeal cancer.