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POSTER

# Free ileocolic autograft – the preferable method of reconstruction following advanced hypopharyngeal tumor resection

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**Background:** Patients with carcinoma of the hypopharynx or cervical esophagus usually undergo total laryngectomy with hypopharyngoesophagectomy. They, consequently, lose the ability to swallow and speak. Free-tissue transfers using microvascular anastomoses have been used progressively to restore swallowing, but some of them to restore speaking also.

**Material:** The medical records of 12 patients who underwent immediate reconstruction of circumferential hypopharyngeal defect after ablative surgery for the advanced squamous cell carcinoma were reviewed to analyze the results, complication rates, and success of early and late functional results.

**Methods:** Twelve patients underwent free ileocolic autograft reconstruction with microvascular anastomoses in the neck. Digestive tract was restored by the caecum and ascending colon, while the last ileal loop, protected by the Bauhini valve for food aspiration, was anastomosed to the cervical trachea. Patients were monitored to assess complications and recovery of satisfactory swallowing and speech. The statistical significance of differences in rates for selected complications and parameters were determined by t-Student, Fisher's exact, and Mann-Whitney tests. Cumulative autograft survival rates were calculated by Kaplan-Meier method and analyzed by Wilcoxon's and Cox-Mantel tests.

**Results:** The most common complication after surgery was autograft necrosis due to vessel thrombosis. It resulted in graft removal in two patients. In other patients we observed no anastomotic fistulas. The patients started an oral food intake on 10–15 postoperative day. The medium length of their hospital stay was 27 days. Two-year survival rate for ileocolic transfers was 66.7%. The power of speech was restored in all patients with free ileocolic flap reconstruction due to Bauhini valve vibration. **Conclusion:** This study revealed that free ileocolic transfer could be considered as a good alternative option for pharyngoesophageal reconstruction, offering an immediate restoration of swallowing and good voice function.

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# Socio-economic study of mortality in patients undergoing curative radiation therapy (RT) for squamous cell carcinoma (SCC) of the head and neck

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**Purpose:** Socioeconomic conditions such as race may be related to cancer treatment outcomes, but the reasons are not well understood. This study analyzes prognostic factors for mortality among patients undergoing curative RT for SCC of the head and neck at a large urban hospital.

**Materials/Methods:** In 2000–2002, 203 head and neck cancer patients were seen in the department of radiation oncology at the Medical Center of Louisiana at New Orleans. Among 186 charts available for review, 108 patients with SCC were treated with curative intent. Survival was determined from the date of the last radiation treatment. The following variables were analyzed for association with mortality using a Cox proportional-hazards model: dose, time, age, gender, race, financial class, 1997 AJCC stage, larynx primary, post-op RT, pre-RT feeding tube, chemotherapy, completion of prescribed radiation, and residence.

**Results:** The median follow-up was 22 months (0–57) and median actuarial survival was 27 months. The median primary dose/fractions/time was 70 Gy (2–79)/35 fractions (1–66)/50 days (1–204). The median age was 56 years (30–90), 88% were male, and 59% and 37% were African- and Caucasian-American, respectively. Patients with VA care, free care, Medicaid and Medicare comprised 41%, 30%, 12% and 4%, respectively. The distribution of stages was: Stage I: 11; II: 7; III: 16; IV: 69. Larynx primaries accounted for 40%, post-op RT was delivered in 28%, a pre-RT tube was placed in 41%, chemotherapy was delivered in 54% and radiation was completed in 87%. Patients living in New Orleans accounted for 45%.

Single variables significantly associated with increased mortality were: dose ( $p < 0.0001$ ), post-op RT ( $p = 0.03$ ), RT completion ( $p < 0.0001$ ), and larynx primary ( $p = 0.03$ ); those with decreased mortality were: pre-RT tube ( $p = 0.006$ ) chemotherapy ( $p = 0.04$ ) and stage ( $p = 0.007$ ). In a multivariate model, dose ( $p = 0.004$ ) and post-op treatment ( $p = 0.001$ ) associated with decreased mortality and stage ( $p < 0.0001$ ) and African-American race ( $p = 0.05$ ) associated with increased mortality.

**Conclusions:** African-American race may be independently associated with increased mortality in patients treated with curative RT for SCC of the head and neck at a large urban hospital. The reasons for this are complex and require further investigation.

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# Combined chemo-irradiation for locally advanced nasopharyngeal cancer

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**Purpose:** This retrospective study tried to evaluate the effectiveness of combined treatment using radiation therapy and cisplatin based chemotherapy in the management of locally advanced nasopharyngeal cancer.

**Materials and methods:** From March 1988 to August 2002, 104 patients of locally advanced nasopharyngeal cancers (AJCC stage II, III, IV) were treated curative radiation therapy (total 70–82.8 Gy; median 70 Gy) and cisplatin based chemotherapy. Follow-up ranged from 5.5 to 201 months (median 50.8 months). Forty two patients (40.4%) were treated with induction chemotherapy using cisplatin 100 mg/m<sup>2</sup> for 1 day and 5-fluorouracil 1 g/m<sup>2</sup> for 5 days followed by radiation therapy. 45 patients (43.3%) were treated with cisplatin concurrent chemoradiation (CCRT) using cisplatin 100 mg/m<sup>2</sup> on D1, D22, and D43 and 17 patients (16.3%) were treated with induction chemotherapy followed by CCRT.

**Results:** Seventy three (70.2%) patients achieved clinical complete response and 24 (23.1%) patients showed partial response. Patterns of failure were as follows: locoregional recurrence 22.7% and distant metastasis 17.0%. Among these patients, 6 patients (5.7%) failed locoregionally and distantly. Five years overall survival rate (OS) was 53.5% and 5 years disease-free survival rate (DFS) was 51.5%. AJCC stage and response to chemoradiation were significant prognostic factor for OS and DFS ( $p < 0.05$ ). According to treatment group (induction chemotherapy followed by radiation vs CCRT vs induction chemotherapy followed by CCRT), there were no significant OS and DFS difference. The grade 3–4 mucositis, nausea/vomiting and hematologic toxicity were noted in 43.6%, 12.7% and 12.7% respectively. Major prolongation of radiation therapy duration (>2 weeks) was inevitable in 26.5%. Thirty six patients (58.1%) completed planned 3 courses of cisplatin and 19 patients (30.6%) received 2 courses of cisplatin.

**Conclusions:** Combined cisplatin based chemoradiation therapy in locally advanced head and neck cancer showed high response rate, reasonable locoregional control, and survival rate. As expected, acute toxicities were increased, but compliance to treatment was acceptable. Our study could not show survival benefit in concurrent chemoradiation compare to induction chemotherapy followed by radiation. But limitation of retrospective study, further accrual and follow-up were required.

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# Initial results of a prospective clinical study of cisplatin/paclitaxel-based hyperfractionated chemoradiation (3DCRTHF) in squamous cell head and neck cancer (HNC) stages III-IV

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**Background:** It is well established that chemoradiotherapy produces better results than radiotherapy alone in some subsets of LAHNC. However, few studies have examined the combination of Cisplatin and Taxanes with 3DCRThf. In this study we have analyzed the tolerance, response and patterns of recurrence of a cohort of Stage III-IV HNC patients prospectively treated with simultaneous Cisplatin/Paclitaxel-based chemotherapy and 3DCRThf.

**Materials and methods:** The treatment regimen included 3DCRThf (74.4 Gy/1.2Gy.b.i.d./62Rx) with weekly Cisplatin (30 mg/m<sup>2</sup>) and Paclitaxel (50 mg/m<sup>2</sup>). The PTV1 included the GTV-T, CTV-T, GTV-N, and elective nodal areas with 1-cm margin and was treated to 40.8 Gy. The PTV-2

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%), epitelitis 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.