entire neck to a dose of 45 to 50.4 Gy over 5 to 5 1/2 weeks time. The interstitial implant to original tumor volume with 2 to 3 cm margins were performed under general anesthesia 2-3 weeks after completion of external beam irradiation. An interstitial implant boost varied according to the stage of disease, 20 to 40 Gy at dose rate of 40 to 50 cGy per hour.

Results: Overall local tumor control was achieved in 90% of patients and overall neck control was achieved in 91% of patients. Five year disease-free survival (Kaplan-Meier) for stage II disease was 85%, for stage III disease 75% and for stage IV 56.25%. The overall disease-free survival as well as overall survival for the entire group at five years were 77% and 40%, respectively. RTOG grade III and IV late sequelae occurred in 7.8% and < 2% of patients, respectively. The majority of patients had excellent cosmetic and functional outcome.

Conclusion: The combined modality including limited dose of external beam irradiation followed by interstitial brachytherapy in the treatment of carcinoma of the oropharynx yields excellent long term disease control with acceptable treatment-related morbidity as well as preservation of cosmesis and functional integrity.

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Is there a prognostic influence of tumor oxygenation measured after radiotherapy in patients with SCCHN?

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Purpose: Recent experimental data in SCCHN (squamous cell carcinoma of the head and neck) in nude mice of A. Ressel et al. (IORBP, No.4; 2001) showed a good correlation between the posttherapeutical fraction of polarographically measured hypoxic values and tumor response. In our present study we retrospectively evaluated in 39 patients whether a comparable effect can be observed in the clinical situation.

Patients and methods: The oxygenation status was polarographically (Eppendorf histograph) determined 3 weeks after the onset of treatment (30 Gy) and after the end of treatment (70 Gy). Patients were treated with radiotherapy alone (5x2 Gy/week, 70 Gy, n=11) or with radiochemotherapy (5x2 Gy/week, 70 Gy, mitomycin C, 5-FU, n=28). At 70 Gy we could perform measurements in only 19 patients due to tumor shrinkage under therapy.

Results: In the univariate analysis neither the polarographic hypoxic fraction (HF<5mmHg, p = 0,6) nor the median pO2 (p = 0,8) after 30 Gy had any relevance for the overall survival of our patients. At 70 Gy also no influence of these two factors (HF<5mmHg: p = 0,4; median pO2: p = 0,4) on overall survival could be observed.

Conclusion: In contrast to the experimental findings of A. Ressel et al. we observed no influence on overall survival of the oxygenation status during and after treatment. Furthermore, Ressel et al. observed an increase of the pO2 during therapy. However, we previously described under clinical conditions a decrease of the pO2 after 30 and 70 Gy, respectively (Stadler et al. Radiother. Oncol. 1998). Therefore, we conclude that these experimental data do not reflect the clinical situation.

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CT-based target contouring of the primary site in a prospective head and neck cancer trial: significance for a resident training program

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Introduction: In meta-analyses of Head and Neck Cancer, concurrent chemoradiation and altered fractionation schemes have shown to improve locoregional control and survival at the cost of increased toxicity. 3-D CRT techniques are currently implemented in sparing of normal tissues. Radioprotectors, like Amifostine, may further increase the therapeutic ratio. However, of paramount importance for the outcome is the adequacy in delineation of the target. In Rotterdam we started a prospective clinical trial of concomitant chemoradiation, randomized for Amifostine prior to RT. Of all primary tumor sites, e.g. larynx (L), piriform sinus (PS), base of tongue (BOT), tonsillar fossa/soft palate (TF/SP), the target was delineated independently by a resident in training and two senior radiation-oncologists on CT.

Patients and Methods: A treatment protocol was designed and guidelines were given for the standardization of the CTV of the (elective) neck nodal regions. No strict guidelines were given for the delineation of the primary tumor site. Per primary tumor site 3 patients were analyzed. The CT-based (MRI-matched) delineation of the primary targets and neck nodal regions was performed by an experienced resident (MB); contours were checked and modified by the physician in charge (senior staffmember) before the start of the actual 3-D treatment planning process. For the purpose of this investigation, the initial set of contours (MB) was saved, checked and modified a second (PL) and a third (PN) time. The contouring by PL, PN, being senior H&N radiation-oncologists, was solely for comparison purposes, that is without consequence to the treatment per se. An analysis was performed regarding the 3 sets of contours (MB, PL, PN).

Results and Discussion: The common volumes of the primary target for MB, PL and PN were quite similar, with little variation per site: MB-PL 85%, MB-PN 87%, PL-PN 86%. However, it is uncertain whether the missed volume (MB-PL 13%, MB-PN 12%, PL-PN 14%) is of clinical relevance. This has to do with the poor resolution of CT/MRI in e.g. BOT and TF tumors, but also due to lack of standardization. The first problem might be very difficult to solve at this time and age. With regard to the second problem: for conformal therapy treatment it is mandatory to provide the clinician with rigid guidelines for the primary tumor site, based on CT and MRI.

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Molecular detection of tumor cells in pharyngo-esophageal brush from patients with head and neck squamous cell carcinoma

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Pharyngo-esophageal brush-capsule (Oesotest®) with cytological analysis is a simple noninvasive technique for early detection of metachronous and recurrent head and neck squamous cell carcinoma (HNSCC). Microsatellite instability (allele shift) at tetranucleotide repeat markers is a clonal marker of HNSCC. We tested whether this marker could increase the sensitivity of oesotest® for detection of rare tumor cells, compared to cytological analysis.

A series of 56 patients with untreated HNSCC had an oesotest® before initial treatment. All these patients had an oesophagoscopy during endoscopy and no additional esophageal tumor was found. Our hypothesis was that oesotest® could collect rare exfoliated cells of the primary HNSCC tumor. Microsatellite instability with marker UT5085 was observed in only 14 of 56 (25%) primary HNSCC. Cytological examination with Papanicolaou staining and molecular analysis were compared for these 15 patients.

Cytological analysis could detect tumor cells in 6 out of 14 (43%) patients. Microsatellite instability was observed in 11 out of 14 (78%) of the same sampling (p=0.03). All cytologic-positive samples were also positive with molecular analysis.

Though cytological examination remains the standard method, this study suggest that molecular analysis could greatly increase the sensitivity of oesotest®. This study also emphasizes the need of other molecular markers in HNSCC

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Late toxicity in three fractionation schedules for advanced laryngeal cancer

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Purpose: Accelerated radiotherapy may improve locoregional control in advanced laryngeal cancer, however, late toxicity may increase. We compared late toxicity between two accelerated and a conventional fractionation (fr.) schedules.

Methods: Primary radiotherapy was performed in 132 patients with advanced laryngeal cancer, follow-up is at least 6 months. Sixty patients (1981-1990) were treated with conventional fr. (Cfr: 50 Gy elective dose, 70 Gy tumour dose; 5 x 2 Gy weekly); 29 patients (1994-1997) were treated with combined hyperfractionation (week 1-3: 30 x 1.2 Gy) and accelerated fractionation (week 4-5: 20 x 1.7 Gy): HAfr. (elective dose 53 Gy, tumour dose 70 Gy in 5 weeks); 43 patients (from 1997) were treated with concomitant boost: Afr. (week 1-2: 10 x 2 Gy, week 3-5: 15 x 1.8 Gy elective field and 15 x 1.5 Gy boost field; 47 Gy elective dose, 69.5 Gy tumour dose in 5 weeks). Interval between fractions was at least 6 hours. Field sizes were comparable between the three groups.

Results: For patients with local control severe laryngeal oedema, requiring intervention, was seen in 6% for Cfr., 6% for HAfr., and 15% for