

decrease in the overall oxygenation of the tumors. The dramatic increase in very low oxygen measurements may reflect selective survival of radio- or chemoresistant hypoxic tumor cells.

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PUBLICATION

Concurrent cisplatin and concomitant boost accelerated radiotherapy (CBAR) in advanced head and neck (H&N) cancer

Roumen Gabrovski¹, Jordan Todorov², Margit Tzanev¹, Georgi Dimov¹.

¹Radiother. Dep. Regional Hospital, Shoumen; ²Radiother. Dep. University Hospital "Queen Giovana" Sofia, Bulgaria

Purpose: To evaluate feasibility and efficacy of concurrent cisplatin and CBAR in advanced H&N cancer.

Methods: Forty one previously untreated patients with unresectable squamous cell H&N cancer were enrolled between 3/95–9/98, 36 (88%) of whom had IV stage disease. Primary and subclinical disease was irradiated to 54 Gy in 30 fractions for 5.5 weeks, with two daily fractions during the first two days. Gross tumour was boosted during the last 2.5 weeks to 72 Gy with a second daily fraction of 1.5 Gy. Continuous I.V. infusion of Cisplatin 20 mg/m²/24 h was administered for 5 consecutive days in I and V week of the basic treatment. The median follow-up for the surviving patients was 19 months (range, 4–45). The median dose and treatment duration were 72 Gy (range, 67–74) and 41 days (range, 36–47). Ten patients (24%) did not have a second chemotherapy course.

Results: Grade 3 (RTOG) dysphagia (12%), weight loss (average 9%), grade 3–4 mucositis (66%) and grade 3 myelosuppression (5%) were the most important acute side effects. Two of the patients died during 2 months following the treatment. Soft tissue necrosis was observed in 3 patients (7%), 4–10 months after treatment. The tumour response was impressive: 85% (33/41) CR. The 2-year actuarial loco-regional control was 60% and the overall survival was 53%.

Conclusions: Although longer follow-up is needed for a definitive evaluation, we conclude that this schedule is feasible and appears to be effective.

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PUBLICATION

The efficacy of Xialine in patients with xerostomia resulting from radiotherapy for head and neck cancer (a pilot study)

A.P. Jellema¹, J.A. Langendijk¹, L. Bergenhengouwen¹, W.A. van der Reijden², Ch.R. Leermans³, L.E. Smeele⁴, B.J. Slotman¹. ¹University Hospital Vrije Universiteit, Radiation Oncology, Amsterdam; ²Academic Centre for Dentistry, Amsterdam; ³The University Hospital Vrije Universiteit, Otolaryngology/Head and Neck Surgery, Amsterdam; ⁴University Hospital Vrije Universiteit, Oral and Maxillofacial Surgery and Oral Pathology, Amsterdam, Netherlands

Objectives: The aim of the study was to evaluate the changes in subjective sensations due to xerostomia, and quality of life (QoL) before and after use of Xialine, a xanthan gum-based saliva substitute, in patients with xerostomia as a result of radiation therapy in the head and neck area.

Methods: The effect of Xialine was evaluated by the EORTC questionnaires QLQ-C30 and the QLQ-H&N35 in a double-blinded, placebo-controlled, cross-over design in 30 patients with xerostomia. Seventy-five percent of the volume of the parotid glands received at least 50 Gy or more during previous radiation therapy. Patients received Xialine or placebo for one week, followed by a wash-out period of one week and another week placebo or Xialine. The composition of the placebo was similar to Xialine, but did not contain xanthan gum.

Results: After administration of Xialine a decrease of problems with speech and 'smell and taste' was noted (–7 and –6 respectively on a 0–100 scale), while a minimal decrease with regard to these endpoints was noted after placebo (–1 and –2). Global QoL increased with 4 on the same scale after Xialine, while a reduction of 3 was noted after placebo. Although not statistically significant in this small group, these changes were regarded as clinically relevant. Xerostomia in general decreased with Xialine as well as with placebo to approximately the same degree (–17 versus –16). No differences between Xialine and placebo were noted with regard to other domains.

Conclusion: problems with speech, 'taste and smell' and the global QoL in patients with xerostomia resulting from radiation therapy for head and neck cancer. A larger study will be initiated to confirm the trends observed in this pilot.

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PUBLICATION

Prognostic impact of the steroid receptor level in head and neck cancer

E. Remenár, M. Kásler, I. Számel, B. Budai, Zs. Orosz, O. Csuka. *National Institute of Oncology, Budapest, Hungary*

Purpose: The aim of our study was to investigate steroid receptor contents and expression of Bcl2 in head and neck cancer (HNSCC) and to compare them with known predictors of outcome as age, tumor size, differentiation and lymph node status.

Methods: Oestrogen and progesterone receptor contents of tissue samples of 61 HNSCC and the neighbouring healthy mucosa were determined by radio ligand assay as well as Bcl2 levels of 46 of the same tumors by Western blot analysis.

Results: We found that steroid receptor positivity was significantly more common in tumour tissues than in the healthy mucosa for both receptors ($p < 0.05$). The rate of tumour free survival was significantly higher in oestrogen receptor positive cases ($p < 0.05$). There was a positive correlation between Bcl2 and oestrogen receptor content and between Bcl2 and lymph node status. However, there was no relationship between tumor size, differentiation and survival.

Conclusions: Our results suggest that oestrogen receptor positivity might be of prognostic value in HNSCC as well, but we could not prove the independent prognostic impact of Bcl2 expression.

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PUBLICATION

Supracricoid partial laryngectomy in advanced laryngeal cancers

M. Kim¹, D. Sun¹, W. Yoo¹, H. Kim¹, S. Cho¹. ¹The Catholic University of Korea, Otolaryngology-HNS, Seoul, South Korea

Purpose: Supracricoid partial laryngectomy (SCPL) has been shown satisfactory oncological outcome and postoperative functional results. In this study we evaluated the efficacy of this procedure as a primary surgical modality in advanced laryngeal cancers and the functional results according to the type of the surgery for the successful functional rehabilitation.

Methods: Thirty nine patients with laryngeal cancers were managed by this procedure between 1993 and 1999, and the tumors were glottic and supraglottic in origin in 32 and 7 patients, respectively. To evaluate the efficacy of this procedure in locally advanced cancer, sixteen patients monitored for at least more than one year and over than T2b stage were reviewed. For the functional evaluation, voice parameters were analyzed by CSL program and swallowing analysis was performed by modified barium swallow test.

Results: Local recurrence was found in 4 (25%) cases and all of them was pathologically T4. Among them 2 patients were successfully managed by salvage operation but 2 patients showed distant metastasis. Voice parameters were different from normal speaker, but the patients were allowed for the social interaction successfully. Normal deglutition was achieved in 38 patients, but one patients had total laryngectomy because of intractable aspiration. Aspiration was associated with faulty backward tilting and improper position of epiglottis and inadequate movement of base of tongue. Silent aspiration was observed more frequently in extended procedures and delayed decannulation cases.

Conclusion: The SCPL could be considered as a primary surgical modality in selected advanced laryngeal cancers with good oncologic and functional results.

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PUBLICATION

Neoadjuvant cisplatin (P) 5-fluoracil (5-FU) and radiation therapy (RT) for organ preservation in squamous cell carcinoma of the head and neck: A single institutional experience

C. Carracedo, R. Travezan, J. Postigo, P. Sanchez, M. Zaharia, S. Santillana, L. Casanova, W. Rodriguez, H. Gomez, J. Leon, C. Vallejos. *INEN, Medicine, Av. Angamos Este 2520, Lima 34, Peru*

The use of neoadjuvant Cisplatin – 5-Fluoracil followed by radiation therapy is an effective method for organ preservation in squamous cell carcinoma of the head and neck. We developed a phase II study with P 100 mg/m² over 3 hours d1, 5FU 1000 mg/m² over 24 hours d1–5, followed by (XRT) 60–70 Gy, as preservation organ strategy. Tumor response assessment was done after the 2nd cycle and after the end of neoadjuvant treatment. Between february 92 and november 97, 56 patients (pts) were admitted to the trial.

With mean age 57 years, M/F 69/31%, Larynx and Hypopharynx were the most common primary sites. Only T3-T4, N0-N3, M0 pts. were treated. After 2 two cycles we obtained an overall response (OR) of 79% (33/42) with 7% of CR. At the end of neoadjuvant chemotherapy (3 cycles) 9/29 were in PR and 16/29 CR (55%) with OR of 86%. After consolidation radiotherapy a total of 64% (16/25) obtained CR with organ preservation. Main toxicity was grade 1-2 mucositis and neutropenia with no treatment related deaths. With a median follow up of 21 months (6-105), 44% (6/16) have relapsed, median disease free survival was 59 months (IC 95% - 32-85%) and the median overall survival was 71 months (IC95% 44-99%). With this strategy we were able to preserve organ in an important group of patients, however future research should include more efficient neoadjuvant treatments.

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PUBLICATION

Results of simultaneous radiochemotherapy vs. concomitant boost radiation in patients with inoperable cancer of the head and neck

P. Schueller¹, U. Schaefer¹, O. Micke¹, N. Willich¹. ¹Univ. of Muenster, Radiotherapy, Muenster, Germany

Purpose: This prospective but not randomised study compares the results of simultaneous radiochemotherapy (RCT) to those of radiation alone (concomitant boost therapy, CBT) in the first-line therapy of inoperable head and neck cancer.

Methods: From 1/93 to 3/99, 76 patients were treated with a combined-modality therapy containing cis-DDP and 5-FU plus 70.2 Gy (accelerated split-course); from 1/95 to 3/99, additional 28 patients with contraindications against chemotherapy received accelerated radiotherapy alone (CBT) to a total dose of 72 Gy. Toxicities were prospectively recorded using a standardised RTOG/EORTC compatible form.

Results: Median follow-up amounted to 10 months. Most tumours responded well to therapy (CR + PR: RCT: 67%, CBT: 56%). 2-year recurrence free survival was 36% (RCT) resp. 30% (CBT); $p = 0.28$; after remission, 2-year recurrence free survival was 39% (RCT) resp. 35% (CBT); $p = 0.82$. 2-year tumour-specific survival was 40% (RCT) resp. 33% (CBT); $p = 0.60$. Acute and late toxicities did not differ significantly in both arms. 6/76 RCT pats. and 1/28 CBT pats. experienced grade III fibrosis, 3/76 and 0/28 grade III xerostomia. Grade IV late effects remained casuistic (1 fistula).

Conclusion: Both therapy concepts yield high remission rates with moderate toxicity. Nevertheless, median time to recurrence remains short. We were not able to demonstrate any difference between both schemes concerning toxicity (except chemo-associated), local control and survival.

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PUBLICATION

Analyses of cervical lymph node metastases in oral squamous cell carcinoma

T. Moriyama¹, M. Nakazawa¹, S. Iwai¹, I. Kato¹¹, M. Sakuda¹. ¹Osaka Univ., Oral & Maxillofacial Surg., Osaka, Japan

Purpose: We studied the influence of regional lymph node metastases in patients with oral squamous cell carcinoma (SCC) on their prognosis.

Method: A clinicostatistical investigation was carried out in 349 patients with oral SCC in our hospital from 1978 through 1992. Of all 349 patients, metastases to the cervical lymph node were histologically confirmed in 99 patients (28%).

Result: The 5-year survival rate of all patients was 74%, and that of patients with lymph node metastases was 49%. However, the 5-year survival of patients with metastases limited to sub-mandibular nodes was 61%.

Conclusion: Neck node level is important in prognosis.

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PUBLICATION

Preoperative concurrent paclitaxel, carboplatin and radiotherapy in advanced operable cancer of the oropharynx and oral cavity: A phase II evaluation

A. Eckhardt¹, I. Wildfang², J.H. Karstens². ¹Department of Oral and Maxillofacial Surgery; ²Department of Radiation Oncology, Hannover Medical University, Hannover, Germany

Purpose: Taxol and carboplatin have both demonstrated excellent radiosensitization through two mechanisms, namely cell blockage in G2-M phase and inhibition of DNA repair respectively. A prospective Phase II evaluation was initiated using Paclitaxel and carboplatin (CBDCA) with concurrent

conventional fractionated external beam radiotherapy followed by surgery of the primary tumor and the regional neck nodes.

Methods: From 6/98-2/99, 12 patients received 5 cycles of weekly Paclitaxel (40 mg/m²), CBDCA (AUC of 1.5) with conventional radiotherapy (40c Gy). Within three to four weeks after chemoradiotherapy, resection of the tumor with neck dissection in those patients with palpable lymph nodes was performed. The patient characteristics were as follows: Men 9, women 3; mean age 54 (range 40-71); Stage III 3, Stage IV 9. Site: oropharynx 4, oral cavity 8.

Results: Twelve patients were evaluable for toxicity and response. The clinical response was as follows: Complete response (CR) 7/12 (58%); partial response (PR) 5/12 (42%). Nine patients (75%) were evaluable for pathologic response after surgical resection. The pathological response was as follows: pCR 5/9 (55%); pPR 4/9 (45%). CTC grade 2 or 3 mucositis occurred in all twelve patients. Other grade 2 or 3 toxicity include skin 50%, leucopenia 17%.

Conclusion: Concurrent Paclitaxel, carboplatin and radiotherapy as pre-operative treatment resulted in excellent clinical and pathological responses. The study is ongoing with a projected number of 30 patients.

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PUBLICATION

3-D conformal radiotherapy for nasopharyngeal carcinoma: Parotid gland sparing technique

J. Lim¹, G.E. Kim¹, K.C. Keum¹, S.W. Lee¹, W. Park¹, H.C. Park¹, C.O. Suh¹, S.H. Lee¹, J. Yeo¹. ¹Yonsei Cancer Center, Radiation Oncology, Seoul, South Korea

Purpose: We conducted this study to explore a new parotid gland sparing technique in 3-D conformal radiotherapy (3-D CRT) in an effort to prevent the radiation-induced xerostomia.

Methods: We performed three different planning for four clinically node-negative nasopharyngeal cancer patients with different location of tumor, and intercompared the plans.

Total prescription dose was 70.2 Gy to the isocenter. For plan I, 2-D parallel opposing fields, a conventional radiotherapy technique, were employed. For plan II, 2-D parallel opposing fields were used up until 54 Gy and afterwards 3-D non-coplanar beams were used. For plan III, from the beginning of the treatment 54 Gy was delivered by 3-D conformal 3-port beams (AP and both lateral ports with wedge compensator; shielding both superficial lobes of parotid glands at the AP beam using BEV) and early spinal cord block (at 36 Gy). And bilateral posterior necks were treated with electron. After 54 Gy, non-coplanar beams were used for cone-down plan. We intercompared dose statistics and dose volume histograms (DVH) of tumor and normal tissue and NTCP of parotid glands for the three plans.

Results: For all patients, plan III was comparable to the other plans in target volume dose statistics but it has more homogenous target volume coverage. Plan III was most superior to the other plans in parotid glands sparing (mean volume receiving 46 Gy; 99%, 97%, 66% for each plan I, II and III). Plan III showed the lowest NTCP of parotid glands in all patients (range of NTCP; 82-100%, 76-100%, 44-73% for each plan I, II and III).

Conclusion: The new technique employing 3-D conformal radiotherapy at the beginning of radiotherapy and cone down using non-coplanar beams with early spinal cord block is highly recommended to spare parotid glands for node-negative nasopharyngeal cancer patients.

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PUBLICATION

Prophylactic selective neck dissection in oral cancer

Chun-Ta Liaw, Shu-I Tu, Chun-Ming Chen, Joseph T. Chang, Hong-Ming Wang, I-How Chen. Chang Gung Memorial Hospital Linkou, Taiwan

Purpose: To evaluate the role of prophylactic neck dissection in early staged oral cancer and the contribution to neck control.

Methods: From January 1996 to June 1998, 207 clinical staged T1-2N0 oral cancer patients receiving primary radical operation (OP) in Chang Gung Memorial Hospital-Linkou were recruited for study. 125 of them also received prophylactic supra-omohyoid neck OP. The numbers of the patients according to cancer anatomic sites were tongue 99, mouth floor 6; lip 24; buccal 58; gum 6, hard palate 8 and retromolar 6. When grouping with treatment modalities, 202 patients received OP alone, 4 patients with pathologically diagnosed neck lymph node metastasis received OP and post-OP radiotherapy, and 1 patient with lymph node metastasis and extracapsular spreading received OP and postOP concomitant chemoradiotherapy. The median follow up time for oral cancer patients was 1.5 years (from 0.6 to 2 years).