With mean age 57 years, M/F 69/31%, Larynx and Hypopharinx 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.

658 PUBLICATION

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

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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 survi-val 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.

659 PUBLICATION

Analyses of cervical lymph node metastases in oral squamous cell carcinoma

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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.

660 PUBLICATION

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

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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/m^2), 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 4071); 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 preoperative treatment resulted in excellent clinical and pathological responses. The study is ongoing with a projected number of 30 patients.

661 PUBLICATION

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

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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 nasopharygeal cancer patients.

662 PUBLICATION

Prophylactic selective neck dissection in oral cancer

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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).

Results: For all patients, neck recurrence was found in 22 patients, and 3 of them accompanied with local recurrence. Local recurrence was only found in 6 patients. One patient developed distant metastasis but no local regional failure. Neck recurrence was found 6.6% (7/125) in those who received neck OP, but 18.3% (15/67) in those who did not receive neck OP. The difference was significant (p = 0.004). Among tongue cancer patients, neck recurrence was 36% (8/22) in neck OP patients, but 4.5% (3/66) in those without neck OP. The difference was significant (p = 0.003). Among buccal cancer patients, neck recurrence was 13.6% (3/22) in neck OP patients, and 3.1% (1/32) in those without neck OP. Primary tumor stage, tumor invasion depth and tumor margins were not related to neck recurrence.

Conclusion: We will suggest prophylactic supraomhyoid neck dissection as part of treatment to staged T1-2N0M0 of tongue cancer patients to improve the tumor control. However, longer follow-up and larger sample size are needed in order to understand the role of prophylactic neck dissection on the other subsite of oral cancers.

663 PUBLICATION

Tumor perfusion studies using fast magnetic resonance imaging in head and neck cancer treated with radiotherapy

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Purpose: This study investigated sequential changes in tumor perfusion and assessed significance in the prediction of outcome of patients with head and neck cancer treated with radiotherapy.

Methods: MRI perfusion studies were performed in 14 patients with head and neck cancer. Three sequential studies were obtained in each patient; immediately before radiotherapy, after a dose of 20 Gy (early therapy), and after completion of radiotherapy. Perfusion imagings of tumors were obtained using T1-weighted gradient-echo (Fast SPGR) imaging. During bolus injection of Gd-DTPA, dynamic MRI images were recorded from the same slice. Tumor perfusin was evaluated by a maximum signal intensity of tumor (SImax; maximum value of SI in tumor/SI of background).

Results: Tumor with SImax increments (SImax (20 Gy)/SImax (pretherapy) $\geq$ 1.3) in the early therapy had a good radiosensitivity.

Conclusion: High tumor perfusion early during the course of therapy demonstrates good radiosensitivity. This phenomenon may be reflected to reoxygenation of the tumor during early radiation therapy (before 20 Gy).

664 PUBLICATION

Long-term follow up of larynx leukoplakia under treatment with retinyl palmitate and prospective impact of proteolytic enzyms

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Purpose: Retinoic acid derivatives have gained interest because of their efficiency in suppressing carcinogenesis and because of some promising results of chemoprevention in clinical trials. In our study for the first time patients with larynx leukoplakia were treated with high dose retinyl palmitate.

Methods: This study had two phases. In the first phase, all patients underwent induction therapy with a high dose of retinyl palmitate (A-Mulsin Hochkonzentrat™, Mucos Pharma, Geretsried, GERMANY) 300,000 IU/day for the first week up to 1,500,000 IU/day, in patients with resistent lesions, in the fifth week. Patients whose lesions progressed during this period were withdrawn from the study. In the second phase, patients whose lesions responded to the treatment or remained stable were then assigned to a maintenance therapy of 150.000 IU/day.

Results: We observed a remission rate of 75% (15 out of 20 patients). Among the 5 patients with partial response, 3 relapsed. The median duration of treatment and follow up was 18 months (range 12–24 months).

Conclusion: Because of the positive results we observed with retinyl palmitate in larynx leukoplakia we started four years ago a double blind study using retinyl palmitate and proteolytic enzyms in head and neck cancer, in order to diminish local recurrences and metastases.

665 PUBLICATION

'Tomudex' (raltitrexed) and cisplatin in the treatment of patients with locally advanced or metastatic head and neck cancer (HNSCC): A Phase I/II study

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Objectives: A combination of infusional 5-fluorouracil and cisplatin is the standard treatment for patients (pts) with advanced or metastatic HNSCC. However, 'Tomudex' (raltitrexed) in combination with cisplatin has a more favourable infusion regimen and may be less toxic. To assess the toxicity, maximum tolerated dose (MTD), and activity of different doses of 'Tomudex' in combination with a fixed dose of cisplatin, an open, dose-escalation Phase I/II study has been initiated.

Methods: Pts with advanced or metastatic HNSCC were treated with a 3-weekly cycle of 'Tomudex' (15-min infusion) followed by cisplatin 100 mg/m[2] (4-h infusion). Dose escalation with 4 doses of 'Tomudex' (2.0, 2.5, 3.0, 3.5 mg/m[2]) was planned for sequential groups of at least 3 pts and dose-limiting toxicity (DLT) was assessed after the first 2 cycles. The recommended dose level will be expanded to include 6 pts to further evaluate efficacy and toxicity.

Results: 6/9 treated pts were evaluable for toxicity and efficacy. The mean age was 57 years (51–71 years), mean Karnofsky score was 90 (80–100), and mean number of cycles per patient was 3.2 (range 1–5). The first two dose levels have not been associated with any DLT. Mild nausea, vomiting, nephrotoxicity, and WHO grade II–III leucopenia were each observed in 3 pts and grade II thrombocytopenia in 1 pt. In 3 of the first 5 pts treated, creatinine clearance decreased by 40–70% with partial recovery (not expressed in WHO criteria). 1 pt with persisting serious renal failure was withdrawn from the study. The cisplatin dose has now been reduced to 80 mg/m[2] due to the observed cisplatin-induced nephrotoxicity. To date, 2 pts have entered the third dose level ('Tomudex' 3.0 mg/m[2] and cisplatin 80 mg/m[2]). At the first two dose levels partial response was observed in 3/6 pts and stable disease in 3/6 pts.

Conclusion: Preliminary results suggest that this combination of 'Tomudex' and cisplatin has promising therapeutic activity in pts with HNSCC. Pts are currently being recruited and the MTD has not yet been reached. Final results will be presented at this meeting. 'Tomudex' is a trade mark, the property of Zeneca Ltd.

666 PUBLICATION

A randomised trial of opioid versus tricyclic antidepressants for radiation induced mucositis pain in patients with head and neck cancer

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Purpose: Patients who receive radiotherapy for head and neck malignancies develop painful mucositis. The pain is characterised as burning or stinging sensations much like neuropathic pain sensations. The purpose of the study was to compare the analgetic effect of a tricyclic antidepressant (TC), commonly used in the treatment of neuropathic pain, and opioid on radiation induced mucositis pain.

Materials and Methods: Fourty-two patients receiving 66–68 Gy external radiation according to guidelines in the Danish Head and Neck Cancer Association underwent randomisation to either morphine 5 mg × 6/day or TC 25 mg × 2/day when their pain was insufficiently managed with weak analgetics. Patients with insufficient pain management, received supplementary medicine from the opposite treatment arm. The pain was evaluated weekly using a VAS-scale and related to the degree of mucositis.

Results: Twenty-one patients entered each treatment arm. Two patients in each arm were non-evaluable. Eight patients in the TC arm managed with TC alone, but for 11 patients it was necessary to add morphine. The 19 evaluable patients in the morphine arm required no additional treatment.

Conclusion: Some of head and neck cancer patients with radiation induced mucositis pain, seem to have sufficient pain control on TC alone, which might be an advantage in patients with relative contraindications to opioid-treatment.