presented at the meeting) are awaited in order to make a decision about further trials with this regimen.

383 POSTER

Exclusive high-dose-rate brachytherapy for oral cavity carcinomas

M. Jolicoeur[1], N. Brochet[2]. [1] *Université De Montréal, Radiation Oncology, Montréal, Canada;* [2] *Montréal, Radiation Oncology, Montréal, Canada*

Purpose: The important role of brachytherapy in the treatment of oral cavity tumors is well established. However, there is still a lot of controversy about the use of high-dose-rate brachytherapy (HDRBT) for head and neck carcinomas. In this prospective study, we evaluated the efficacy and safety of exclusive HDRBT in patients with oral cavity carcinoma.

Methods and Materials: Were eligible patients with a biopsy proven grade 1 or 2 squamous cell carcinoma or adenocarcinoma of oral cavity stage Tis, T1 or T2, N0, M0. HDR Ir-192 afterloading system was used delivering dose of 40.2 Gy in 12 fractions over 98 hours. The implants technique and dosimetry followed the rules of Paris system with optimisation allowed.

Results: 17 patients were included, 6 of which presented with a lower lip tumor, 4 with carcinoma of the floor of the mouth, 3 with oral tongue tumor, 2 with cancer of the buccal mucosa, one with lower alveolar ridge tumor and one with soft palate tumor. The tumor mean diameter was 2.37 cm. Eleven were T1, 5 were T2 and 1 Tis. All cases were proven by biopsy and there were 16 squamous cell carcinomas and one adenocarcinoma. Of the 16 invasive carcinomas, 12 were grade 1 and 4 were grade 2. In only 4 patients was HDRBT used for a prior treatment failure. For all the others, HDRBT was the first and exclusive treatment.

At the last follow-up, 11 patients were alive without evidence of disease and no toxicity, 1 patient was alive with toxicity, 2 patients were alive but developed a second cancer and 3 patients were deceased (of whom two from atherosclerotic disease). With a median follow-up of 30 months, late toxicity was found in three patients (17.6%): one patient experiencing soft tissue necrosis, one patient suffering a bone necrosis and one other patient neuropathic pain. The soft tissue necrosis was successfully treated with hyperbaric oxygenotherapy.

The local control rate and locoregional control rate are 88.2% and 76.5% respectively. The disease-free survival, the overall survival and the disease-specific survival are respectively 76.5%, 82.4% and 94.1% at 2 years.

Conclusion: In this series, exclusive HDRBT for oral cavity cancers bears no higher risk of toxicity when compared to than LDRBT series. So far, control rate and survival also seem similar.

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Regionally advanced nasopharyngeal carcinoma (NPC): patterns of failure after sequential chemotherapy (CT) and radiotherapy (RT)

M. Palazzi[1], L. Licitra[2], M. Possanzini[3], C. Grandi[4], M. Guzzo[4], S. Tomatis[5], A. Cerrotta[1], G. Cantu'[4]. [1] *Istituto Nazionale Tumori, Radiotherapy, Milan, Italy;* [2] *Istituto Nazionale Tumori, Medical Oncology, Milan, Italy;* [3] *Universita' Degli Studi, Milan, Italy;* [4] *Istituto Nazionale Tumori, H&N Surgery, Milan, Italy;* [5] *Istituto Nazionale Tumori, Med. Physics, Milan, Italy*

Purpose: To evaluate clinical outcome and pattern of failure in 61 patients (pts) with regionally advanced NPC treated with sequential CT and RT.

Methods: In 1990 a Phase II trial was designed to evaluate feasibility and activity of a regimen including sequential CT and RT. Inclusion criteria: pathological confirmation of NPC; stage (UICC 1987) T-any, N2-3, M0; ECOG PS 0-1. Treatment: 3 cycles of induction CT with epirubicin 70 mg/m2 d1 and cisplatin 100 mg/m2 d1 (recycle 21 d) followed by radiotherapy to nasopharynx (64-70 Gy) and neck (50-70 Gy), with conventional fractionation (1,8-2 Gy/fr, 5 frs/week).

Results: Sixty-one patients were accrued from 2/1990 to 9/1996. Stage according to UICC 1997 was IIb in 13%, III in 33% and IV in 54% of pts. Sex: male 75%; age: median 44 y (range 17-72 y); histology: WHO type 1-2 (11%), WHO type 3 (89%). Sixty pts received 3 cycles of CT, 1 pt 2 cycles due to no response. Toxicity was moderate with minor dose reductions in 4 pts. RT was given to 60 pts. (1 pt. had distant M+ after CT): total dose ranged from 60 to 71.6 Gy (median 66.9 Gy), total duration 40-65 d (median 51 d). Acute toxicity was acceptable with a split prescribed in 26% pts. With a median follow-up of 5.3 y (range 3.6-10.2 y) 44 failures have been observed in 29 pts. Initial failure was local in 10%, regional in 18%, local and regional in 1.6% and distant in 18% of pts. Seven pts were dissected for a neck nodal failure, and 4 were re-irradiated to the primary site for a local failure. At 5 years local control was 83%, regional control 74% and freedom from M+ 70%; overall survival was 62% and disease-free survival (DFS) 52%. Frequently reported late effects included xerostomia in the majority of patients and significant hearing loss in 18 pts.

Conclusions: In our series, freedom from distant metastases and overall survival were similar to values reported recently with more aggressive regimens of combined modality treatment; regional control and DFS were relatively worse probably due to inclusion criteria (N2-N3).

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Analysis of mandibular dose distribution in radiotherapy (RT) for oropharyngeal cancer

B.A. Jereczek-Fossa[1,3], G. Catalano[1], C. Bocci[4], C. Garibaldi[2], A. d'Onofrio[2], M. Ciocca[2], M.C. Leonardi[1], H.R. Marsiglia[1], R. Lazzari[1], R. Orecchia[1,5]. [1] *European Institute of Oncology, Radiation Oncology, Milan, Italy;* [2] *European Institute of Oncology, Medical Physics, Biostatistics, Milan, Italy;* [3] *Medical University of Gdansk, Oncology and Radiotherapy, Gdansk, Poland;* [4] *S Maugeri Foundation, Radiation Oncology, Pavia, Italy;* [5] *University of Milan, Radiotherapy, Milan, Italy*

Purpose: Relationship between RT dose and the risk of osteoradionecrosis is well known. However, the dose to the mandible is not routinely assessed in RT for head and neck cancer. Our aim was to analyze the mandibular dose distribution in patients (pts) administered RT for oropharyngeal cancer.

Methods: We examined RT plans in 18 pts treated with bifractionated RT for stage II-IV M0 oropharyngeal cancer. In 17 pts RT dose prescribed in the ICRU point was 74.4 Gy/62 fractions (1.2 Gy bid, 6 h interfraction interval) and 1 pt received 75.6 Gy. The whole dose to the mandibular region was delivered with 6 MV photons. The mandible was contoured manually on CT scans and the point doses at the both mandibular condyles, ascending ramus, mental symphysis, molar and retromolar regions were assessed. Cumulative dose-volume histograms (DVH) were evaluated.

Results: The highest doses were observed in the retromolar regions. The mean percentage doses at the right and left retromolar regions were 101.3% ± 3.8% (range, 90.2-109.1%) and 101.7% ± 2.5% (range, 95.2-105.8%), respectively. Lower doses were seen in ascending ramus (mean right and left ramus: 97.3% ± 8.5% and 97.8% ± 7.6%, respectively), the molar regions (mean right and left molar region: 86.0% ± 13.5% and 88.1% ± 12.9%, respectively), and at the mandibular condyles (mean right and left condyle 72.6% ± 18% and 77.0% ± 16.5%, respectively). The mandible volume ranged from 60.1 cm3 to 110.1 cm3 (mean 82.3 cm3). In all pts the maximum dose absorbed in the mandible was higher then the dose prescribed in the ICRU point and the mean maximum dose absorbed in the mandible was 105.7% ± 2.1% (range 102.4-110.6%). The percentage of mandibular volume receiving a dose higher than prescribed was 28.6% ± 14.9% (range 10.2-58.1%). The DVH area, maximum mandibular doses and retromolar doses did not appear to statistically depend on use of wedge or mandibular volume.

Conclusions: RT for oropharyngeal cancer is associated with high doses to the retromolar mandibular regions (the dose can be higher then prescribed in the ICRU point), ascending ramus and molar regions. Lower doses are absorbed at the condyles and mental symphysis. The single dose point (for example, the ICRU reference point) could be not representative for the mandibular dose.

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Low-dose paclitaxel radiosensitization in locally advanced head and neck cancers

J. Lövey[1], K. Koronczay[2], É. Remenár[3], O. Csuka[4], G. Németh[5]. [1] *National Institute of Oncology, Dept. of Radiotherapy, Budapest, Hungary;* [2] *National Institute of Oncology, Dept. of Radiotherapy, Budapest, Hungary;* [3] *National Institute of Oncology, Dept. of Head and Neck Surgery, Budapest, Hungary;* [4] *National Institute of Oncology, Dept. of Pathogenetics, Budapest, Hungary;* [5] *National Institute of Oncology, Dept. of Radiotherapy, Budapest, Hungary*

Introduction: Combined modality treatment with chemotherapy and radiotherapy in locally advanced head and neck cancers is an effective and often the only treatment with a chance of cure. These schedules are usually very intensive and therefore hardly be executed in patients with impaired general condition. An alternative is to use chemotherapeutic agents in low dose as radiosensitizers. In this study we examined the radiosensitizing effect of low dose paclitaxel (Taxol, Bristol-Myers Squibb) in locally advanced head and neck cancer.

Patients and methods: 26 patients with locally advanced squamous cell carcinoma of the oral cavity and the oropharynx were treated with external beam radiotherapy up to doses of 66-70 Gy and received concomitantly 2 mg/m2 paclitaxel intravenously after appropriate premedication three times a week 1 hour prior radiotherapy. Response rates according to WHO criteria, side effect according to the National Cancer Institute Common Toxicity Criteria and overall and progression free survival were evaluated.

Results: All of the patients completed the therapy. Median radiation dose was 66 Gy, paclitaxel dose 40 mg/m2 and treatment duration 54 days. 12 weeks after completion of therapy complete response was 30,8%, partial response 34,6%, stable disease 11,5% and progressive disease 23,1%. The median follow-up time was 25 months (9-36). At two years 13 (50%) of the patients was alive 10 (38,4%) without evidence of disease, 1 of whom with a secondary oesophageal cancer. The estimated median overall survival was 22 months (CI 14,2-34,6) the median progression free survival 12 months (CI5,2-18,8). We observed four grade 4, fourteen grade 3 and a number of grade 1-2 side effects. There was no treatment related death.

Discussion: Our regimen resulted a worse response rate than the aggressive chemoradiation protocols treating the same disease however the two-year survival is comparable with the results of other studies. The advantages of our schedule are that it is well tolerated, easy to perform on an outpatient basis, resource effective and do not deteriorates the general condition of the patients, therefore successive therapy can be carried out immediately if necessary. We intend to evaluate the effectivity of this treatment in a study comparing radiotherapy with paclitaxel sensitisation versus radiotherapy alone.

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Prognostic impact of complete remission after radical radiotherapy of oropharyngeal cancer. A retrospective study of the Cancer Centre in Warsaw data, 1984-1995

Z. Szutkowski, A. Kawecki, A. Hliniak, E. Kraszewska. *Cancer Center, Head & Neck Cancer, Warszawa, Poland*

This retrospective study was done to estimate the outcomes of patients with squamous cell carcinoma of oropharyngeal region treated in the Department of Radiotherapy, Cancer Centre in Warsaw, Poland, between February 1984 and December 1995 with radical irradiation.

The importance of tumour remission for patients overall survival and time to progression were analysed. 241 patients with histologically proven squamous cell carcinoma of the oropharynx were treated with definitive megavoltage therapy. The follow-up time was at least 5 years.

The median total dose was 66 Gy delivered with 2.0 Gy fraction 5 times weekly. The great part of clinical material consist of advanced cases T3,T4 =152 patients [63%] and N2,N3 = 89 patients [41%]. The complete remission [CR] at the end of treatment was observed in 175 [73%] patients. 5 years overall survival probability for the whole group of patients was 27%. Probability of 5 years survival for patients with CR was 36% and for patients with non CR 2% $p<0.0001$. Analysis of time to progression or death of patients showed for CR patients 32% 5 years probability and for non-CR 0% $p<0.0001$. N-stage end hemoglobin concentration were significantly important for overall survival $p= 0.002$, $p< 0.001$ respectively. Interruption during the treatment reduced 50% probability of CR at the end of treatment $p=0.04$.

Conclusion: The strongest clinical predictor of survival and time to progression was the degree of tumour remission at the end of radiotherapy. Patients with poor response to radiotherapy should be recommended for salvage surgery.

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Alternating radio-chemotherapy with docetaxel/DDP and involved field radiotherapy for recurrent, inoperable, and previously irradiated head & neck cancer

T. Hehr, W. Budach, C. Belka, J. Classen, F. Paulsen, M. Bamberg. *Eberhard-Karls University, Radiation Oncology, Tuebingen, Germany*

Purpose: Loco-regional recurrences of head&neck cancer after adjuvant irradiation or primary radio-(chemo)therapy represent a therapeutic dilemma. Median survival with symptomatic therapy is 4 months. The major cause of death is uncontrolled local tumor growth. In most cases, a second course of high dose radiotherapy cannot be delivered due to limited normal tissue tolerance. Response to simultaneous chemo-radiation protocols is generally high, but considerable problems with mucositis occurred. To decrease oral toxicity an alternating chemo-radiation protocol was tested.

Methods: 21 pat. with inoperable, and previously irradiated head&neck cancer, SCC, GII-III, average tumor diameter 4.6cm (range 2-12cm), underwent alternating radio-chemotherapy with docetaxel 60mg/m2 d1 + DDP 15mg/m2 d2-5 in 1st, 4th, and 7th week and involved field irradiation with 5x 2.0Gy in 2nd-3rd and 5th-6th week to 40.0Gy total dose (ICRU50). Reduction of docetaxel to 50mg/m2 in pat. 13 to 21. Median age 56 years, 17 male, KI ≥70%, 15x nutritional deficiency, pre-treatment: 5x primary accelerated radio-(chemo)therapy 70.6Gy, 15x adjuvant irradiation 60-66Gy.

Results: Docetaxel/DDP chemotherapy was given in 46/41 of 63 planed courses, reduced doses in 7/5 courses, respectively. Chemotherapy was interrupted due to DDP induced renal toxicity WHO°II in 2 pat., 1x ForrestII bleeding of ulcus duodeni, and 1x docetaxel hypersensitivity. Alternating radio-chemotherapy was interrupted due to one large bowel perforation (deceased at home 2 months later for unknown reason), and in 2 pat. with rapid tumor shrinkage resulting in a pharyngocutaneous fistula and 1 lethal tumour bleeding. WHO °III-IV toxicity occurred in 9/18 evaluable pat.: 3/18 mucositis, 8/18 leukopenia (twice with neutropenic fever). Anemia WHO°II required blood transfusion in 5/18 pat. Response in 18 eligible pat.: 7x CR, 7x PR, and 4x SD. Median time to local progression was 12 months, and median disease specific survival 9 months. 9 pat. died of progressive local tumor, 3 due to distant metastasis, 1 lost to follow up 7 months after therapy with NED.

Conclusion: Alternating radio-chemotherapy in inoperable, recurrent, and previously irradiated head&neck cancer resulted in a 78% overall response rate (14 of 18 patients with CR or PR) with acceptable oral toxicity. However substantial systemic toxicity was observed with docetaxel 60mg/m2 d1 + DDP 15mg/m2 d2-5, requiring a dose reduction of docetaxel to 50mg/m2.

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Hyperfractionated irradiation with concurrent chemotherapy (Carboplatinum) for locally advanced head and neck cancer

O. Pradier[1], P. Ambrosch[2], H. Schmidberger[1], C. Hess[1]. [1] *University, Radiotherapy, Goettingen, Germany;* [2] *University, Othorhinoralyngoloy-Head and Neck Surgery, Goettingen, Germany*

Background: Radiotherapy is often the primary treatment for advanced head and neck cancer, but the rates of locoregional recurrence are high and survival is poor. We investigated whether hyperfractionated irradiation plus concurrent chemotherapy (combined treatment) is effective.

Methods: 66 patients with advanced head and neck cancer who were treated with hyperfractionated irradiation and Carboplatinum at the university of Goettingen between August 1987 and May 1994. The chemoradiotherapy schedule was composed of two fractions per day, separated by 6 h. intervals. Each fraction consisted of 210 cGy preceded by a dose of 50 mg/m2 carboplatinum i.v. daily. A total radiation dose of 5670 cGy was applied in 6 weeks as a split course regimen. A break of 2 weeks was planned between the 2 first weeks and the 2 last weeks. Treatment was given 4 days a week. Both the neck and the primary tumour were treated up to 5670 cGy.

Results: All patients in both treatment groups had unresectable disease. At two years the rate of overall survival was 20 percent and 10 percent at 10 years. Confluent mucositis developed in 80 percent of the patients. Skin fibrosis occurred in three patients. Our results are inferior compared to published studies. There are several explanations for this. The radiotherapy fractionation was not optimal with a long break (2 weeks) during the treatment, which could allow for tumour cell repopulation. Furthermore, the patient selection has been less favourable compared to published prospective studies. In our institution, all patients who were medically operable have been treated with local CO2-laser resection. Therefore the group of patients treated with a combination of primary radiation with chemotherapy are representing a selected group with unfavourable risk factors, such as bad general bad condition, concurrent diseases, advanced tumours ineligible for laser resection. Patients with N2 or N3 disease represented 85% of our population.

Conclusions: This combined treatment with daily high dose radiotherapy for advanced head and neck cancer is less efficacious than conventional combined radio- and chemotherapy.