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RADIATION NECROSIS OF THE MANDIBLE AFTER RADIOTHERAPY OF 921 OROPHARYNX AND ORAL CAVITY CARCINOMAS

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With megavoltage radiotherapy (RT) incidence of bone radiation necrosis of the mandible (BRN) has been decreased, but it is still a serious complication. The purpose of this study was to evaluate over a 15 year period of time, incidence and predictive factors of BRN after treatment of 921 carcinomas of the oropharynx and oral cavity.

The mean age was 58.3 years. 881 were male and 40 female. RT technique was homogeneous using to lateral opposed fields treated at each session. 815 patients (pts) were treated using a Cobalt 60 unit and 46 with 10 Mv photons. Total dose ranged from 40 to 82 Gy (mean dose of 68 Gy). Dose per fraction ranged from 1.8 to 5.0 Gy. For 67 pts a boost was delivered with brachytherapy. 321 pts received chemotherapy (neoadjuvant or concomitant). For 210 pts surgical resection of the tumor was performed before RT. 303 pts were toothless, the others received fluoride applications.

60 patients (6.5%) developed BRN with a mean delay of appearance of 12.3 months (5 to 63). Surgical resection of the mandible was necessary for 28 patients (46%). Uni and multivariate analysis showed that factors associated with a high incidence of BRN were a total dose over 70 Gy, a dose per fraction > 3 Gy, a boost given with brachytherapy and a combination of surgery and radiotherapy.

We concluded that BRN is rare complication but incidence could be decreased with optimisation of technical parameters of radiation therapy.

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LOCOREGIONAL CONTROL AND DISEASE SPECIFIC SURVIVAL AFTER ACCELERATED HYPERFRACTIONATED RADIOTHERAPY IN THE TREATMENT OF SUPRAGLOTTIC CARCINOMA

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Materials and Methods: The records of 165 patients undergoing BID radiation for carcinoma of the supraglottis from 1981–1992 were reviewed. Patients received 66 to 72 Gy in 1.6 Gy bid fractions and received a planned 7 to 14 day break. Median follow-up was 56 months. Five-year actuarial local control, regional control and disease-specific survival rates are reported.

Results: For T_1, T_2, T_3, and T_4 tumors, local control was: 95%, 86%, 77% and 42%, respectively ($P = 0.002$), and disease-specific survival was: 79%, 88%, 78%, and 40%, respectively ($P = 0.0004$). For N_0, N_1, N_{2-3} disease, local control was: 86%, 73%, and 54%, respectively ($P = 0.005$), and disease-specific survival was: 86%, 53%, and 54%, respectively ($P = 0.0001$). Regional control by T and N stage was non-significant. With surgical salvage, T_1, T_2, T_3, and T_4 ultimate local control was: 95%, 92%, 88%, and 51%, respectively ($P = 0.001$). The laryngeal preservation rate for the entire group was 83% and for T_1, T_2, T_3, and T_4 tumors was: 96%, 87%, 78%, and 56%, respectively. Total treatment time greater than 43 days resulted in a decreased local control: 87% versus 70% ($P = 0.002$), and decreased disease-specific survival: 84% versus 69% ($P = 0.01$).

Conclusions: Accelerated hyperfractionated radiotherapy resulted in excellent locoregional control, disease-specific survival, and laryngeal preservation rates for T_{1-3} and node negative patients. T stage, N stage and total treatment time were predictors of outcome. T_4 tumors or node positive neck disease, even N_1, portended a poor prognosis, and therefore these patients should be entered into protocols that include adjuvant therapy.

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THE IMPORTANCE OF OVERALL TREATMENT TIME FOR THE OUTCOME OF RADIOTHERAPY OF ADVANCED HEAD AND NECK CARCINOMA IS DEPENDENT ON TUMOR DIFFERENTIATION

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Five hundred and one patients with advanced supraglottic and pharyngeal carcinoma with histopathological grading were treated with planned split-course (191 pts in the DAHANCA 2 protocol) or continuous radiotherapy (310 pts in DAHANCA 5). Irradiation were given with 2 Gy/fx, 5 fx/wk to a dose of 66–68 Gy in 91/2 or 61/2 weeks, respectively. Locoregional tumor control was significantly better in patients characterized by female sex, small T-classification, no nodes, poorly differentiated tumors and treatment given with short overall time. Overall, split-course and continuous treatment resulted in a 5-year loco-regional control of 30% and 42% ($P = 0.007$), respectively. However, the detrimental effect of split-course were only found in moderately and well differentiated tumors where the 5-year tumor control were 41% and 21% after continuous and split-course treatment, respectively ($P = 0.0009$). In contrast, poorly differentiated tumors gave tumor control values of 43% for continuous and 41% split-course treatment ($P = 0.69$). A Cox multivariate analysis confirmed that, among others, overall treatment time were a significant prognostic parameter in moderately and well differentiated tumors ($P = 0.0002$), but not in poorly differentiated ($P = 0.93$). It is suggested that the ability to accelerate repopulation may be lost by dedifferentiation. *Supported by the Danish Cancer Society*

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LARYNGEAL CARCINOMA:—TREATMENT INTERRUPTION AND OUTCOME

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Two patient groups have been identified from a data base of 965 patients with carcinoma of the larynx. One group of 393 patients had squamous cell carcinoma of the larynx arising in the glottis—no nodal involvement; the other group of 163 patients had tumours arising in the supraglottic region. The second group was a more heterogenous group some patients had nodal involvement at the time of presentation. All patients were treated on a linear accelerator. Patients were treated using a variety of dose-fraction-time schedules.

Mathematical modelling using linear quadratic equation was carried out. This shows that a break in treatment if a week reduces the local tumour rate for glottic tumours by 12% or about 25 per day. Local tumour control rates increased as the effective dose was increased. The data for tumours arising in the supraglottic region is not so convincing though it does show that prolongation of treatment time reduces local tumour control rates. The effects of longer times can be nullified by increasing the effective dose. The supraglottic subject, however, is very heterogenous, and the groups within the subset are small.

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RANDOMIZED PHASE II STUDY OF WEEKLY CISPLATIN WITH OR WITHOUT AMIFOSTINE IN PATIENTS WITH ADVANCED HEAD AND NECK CANCER

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High dose single agent cisplatin (C) regimens yield high response rates in advanced head and neck cancer (HNC) but nephro-, neuro- and ototoxicity preclude further dose escalation. In weekly C regimens bone marrow toxicity causes frequent treatment delays jeopardizing the dose intensity of C.

In this study patients (pts) with HNC are randomized between C 70 mg/m^2/wk for six weeks with or without amifostine (AMI) 740 mg/m^2. AMI is administered as a 15 min infusion directly prior to C. C is administered in 250 cc 3% NaCl as a 1-hour infusion with standard pre- and posthydration. The antiemetic schedule consists of thietylperazine, ondansetron and dexamethasone.

Up till 3/95 53 pts are randomized; 39 are fully evaluable for response and toxicity, one pt is not evaluable and 13 too early for evaluation.

Characteristics of the 39 fully evaluable pts: male:female ratio is 29:10; median age 52 years (range 36–68), median WHO performance status 1 (0–2); locally advanced disease 30 pts, locally recurrent 7 pts metastatic disease in 2 pts. Eighteen pts were randomized to C + AMI and 21 to C. In total these 39 pts received 210 C administrations, median 6 per patient (range 3–6), equal in both treatment arms. In the C alone arm 5/21 pts had treatment delays because of bone marrow toxicity versus 0/18 in the C + AMI arm. Thrombocytopenia grade 3 + 4 was