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Tumour growth in waiting time for radiotherapy in head and neck cancer

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Aim: Waiting time prior to radiotherapy is a major problem. The aim of this study is to determine the impact of waiting time on tumour growth in an unselected population of patients with head and neck cancer referred to primary radiotherapy.
Material and methods: In a consecutive cohort of head and neck cancer patients referred to the Head and Neck Centre in Aarhus from 2000 to 2003, medical records were searched to identify patients with a diagnostic scan (MR or CT) and a CT scan for treatment planning. Thirty-three patients were identified having comparable scans. Tumour size, size and number of metastatic lymph nodes were measured by a skilled radiologist.
Results: Median waiting time between the two scans was 28 days (5–124 days). Nineteen patients (58%) developed an increase in total tumour volume with a 14% median volume increase (3–315%). Evaluated by the RECIST Criteria 18% had progressive disease (>20% increase in largest tumour diameters). Three patients (9%) developed lymph node metastasis and 5 patients (15%) progressed to a higher stage during the waiting time.
Discussion: Several studies have shown that the prognosis depends on tumour size, lymph node metastasis and stage. This study thereby indicates a negative prognostic effect of waiting time. In Denmark a significant increase in professional delay (from first visit to a doctor until beginning of treatment) for head and neck cancer patients has been reported, from 50 days in 1992 to 70 days in 2002. In the present work we focused only on a minor part of this delay. The impact of the total waiting time can be expected to be fare above the present findings.
Conclusion: Delay in the initiation of radiotherapy does significantly increase tumour size, tumour volume and the risk of lymph node metastasis in a substantial part of patients with head and neck cancer, resulting in worse prognosis. It is therefore important to emphasise that waiting time should be hold as short as reasonable achievable.

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Herpes simplex virus-1 (HSV-1) infection during head and neck radiotherapy. Incidence and therapeutic considerations

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Background: The aim of the study was to investigate the incidence and role of herpes simplex virus-1 (HSV-1) infection in mucositis during head and neck cancer radiotherapy.
Patients and Methods: Sixty patients with malignant head and neck tumor, eligible to receive radiotherapy entered the study. Thirty-one patients received fluconazole antifungal prophylaxis and 29 did not. Median total dose was 60 and 66 Gray respectively in each patient cohort. Sixteen patients (26.6%) received concomitant chemotherapy. Mucositis was recorded weekly. Smears from the ulcers of mucositis were stained with Papanicolaou and APAAP immunocytochemical method to identify HSV-1.
Results: Forty-eight patients developed ulcerative mucositis. Twenty-three patients (38%) completed radiotherapy with severe mucositis. Nine patients interrupted RT due to mucositis. Smear was available from 29 patients. HSV-1 infection was identified in 14/29 patients (48.2%). Mucositis healed or was reduced after one week of antiviral treatment in 11 of those 14 patients. Ulcerations recurred after quitting antivirals.
Conclusions: The incidence of HSV-1 infection was 29.1% (14 HSV-1 positive of 48 patients with ulcerations). Healing or reduction in the grade of mucositis after one week of antivirals supported the hypothesis that HSV-1 infection aggravated radiation mucositis. Dose and duration of antivirals during radiotherapy need to be further evaluated.

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A dose-volume histogram analysis of the PTV in patients with advanced head and neck cancer treated with concomitant chemoradiotherapy

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Background: Irradiated volume and delivered dose are considered as major factors for acute toxicity in head and neck cancer (HNC). We investigated the relationship between various parameters derived from planning target volume (PTV) dose-volume histogram (DVH) analysis and the risk of acute toxicity in patients undergoing concomitant radio-chemotherapy (RT-CT) for advanced HNC.
Material and method: From September 2001 to December 2003, 80 stage III and IV HNC patients were treated with a concurrent association of RT-CT to a prescribed target dose of 70 Gy in 35 daily fractions. Chemotherapy consisted of an association of carboplatin and 5 fu at weeks 1, 4 and 7. Acute toxicity according to the RTOG scoring system was prospectively recorded throughout the course of treatment. 3-D treatment planning based on computed tomography was done in all patients with contouring of gross tumour volume (GTV) consisting of primary tumour and involved lymph nodes. The PTV was defined by a 5–10 mm margin depending on clinical condition and tumour location. DHV were calculated for the PTV.
Results: The mean PTV volume was 79.5 cm^3 (range 11.2 – 255.6) without significant difference between tumour locations ($p = 0.56$) but with a significant trend ($p < 0.0001$) towards higher AJCC stages. Maximal dose (Dmax) deviation from ICRU dose in PTV ranged between 0 and 7% in 17 patients (pt) and was >7% in 63 pt. Mean dose (Dm) deviation ranged between −5% and <0% in 17 pt, *0% and $\leqslant$7% in 57 pt and >7% in 6. There were no differences in Dmax and Dm deviations between AJCC stages. Only weight loss during treatment was significantly correlated with higher PTV volume ($p = 0.01$) but objective mucosal reactions ($p = 0.029$) and xerostomia ($p = 0.04$) increased significantly with AJCC stage. Objective and functional mucositis, epithelitis, xerostomia, weight loss and Karnofsky index changes during treatment were not correlated with Dmax and Dm deviations.
Conclusion: A partial relationship between acute toxicities and irradiated volume was demonstrated by analysing DVH. Homogeneity in dose distribution obtained with 3-D conformal radiotherapy approach could have minimised toxicity variations due to differences in delivered dose.

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Radiochemotherapy comparing with radiochemotherapy and local hyperthermia in patients with unrecectable pharynx and larynx cancer: a phase I study

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Patients with primary advanced head and neck cancer not amenable to surgery require more aggressive regimes of radiation- and chemotherapy, or use of radiomodification. The purpose of the study was to test the hypothesis that radiochemotherapy in combination with local microwave hyperthermia (RCT-HT) leads to a better loco-regional control in patients with stage III-IV of squamous cell cancer of pharynx and larynx with lymph nodes metastases than radiochemotherapy (RCT) alone.
Methods: From December 2002 to May 2004, 65 patients with III-IV stage of squamous cell cancer of pharynx, hypopharynx and larynx with involved neck nodes were included into a prospective non-randomized study. The treatment protocol in the first group consisted of three courses of chemotherapy (5-FU+cisplatin) given in the 1-st, 5-th and 11-th week and conventional split radiation therapy (6–9 and 12–14 week), a total dose 68–72 Gy. In the second group, besides, patients were performed 6–8 sessions of local hyperthermia (915 MHz, 60–75 Wt). Heat was delivered for an hour up to 41.5–43^{0}C in the tumor after irradiation. 35 patients treated with radiochemotherapy were compared with 30 patients treated with radiochemotherapy and local microwave hyperthermia. Adverse effects (skin and mucosa toxicity, dysphagia, xerostomia and hematologic toxicity) were scored according to RTOG/EORTC criteria.
Results: CR+PR rate, achieved in one month after treatment, was 31 patients (88.5%) in the first group and 28 patients (93.3%) in the second group, respectively ($p = 0.16$). Progression was observed in 4 patients (11.5%) in the first and 2 (6.7%) in the second group. The 1-year progression-free survival was 54.2% and 60% ($p = 0.24$). RCT-HT patients more often developed 3+4 grade mucositis (45.5% vs 28%, $p = 0.034$)