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DIRECT INTRATUMORAL INJECTION OF COLLOIDAL ^{32}P IN ADDITION TO CONVENTIONAL RADIOTHERAPY FOR ADVANCED HEAD AND NECK CANCER: A PILOT STUDY

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A new technique of infusional brachytherapy, developed by Order, using macroaggregated albumin followed by chromic phosphate ^{32}P, allows the selective irradiation of the tumor at very high doses. In order to improve the treatment of locally advanced unresectable or recurrent head and neck cancer, this technique was studied to deliver a continuous extra radiation dose to the tumor, in addition to conventional fractionated radiotherapy.

Nine patients were included in the study. Bremsstrahlung imaging, performed for direct tumor quantification and dosimetry, showed the ^{32}P activity at the injection sites, up to 70 days post-injection ^{32}P activity was found to be insignificant in the blood (<0.00001% ID/ml) as well as in the saliva (<0.001% ID/ml).

Except for facial edema in 2 patients, regressing with corticosteroids administration, no acute treatment-related, hematological or mucosal, toxicity was observed. Significant tumor regression was noted for three out of five patients evaluable, treated by combined intratumoral colloidal ^{32}P infusion and external irradiation. Thus, this technique of infusional brachytherapy by colloidal ^{32}P may be a valuable adjunct to conventional radiotherapy to boost the dose in locally advanced head and neck cancer. Our phase I/II study is currently in progress.

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RISK FACTORS FOR OSTEORADIONECROSIS AFTER RADIOTHERAPY FOR ORAL CANCER

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57 risk factors for osteoradionecrosis (ORN) in the dental, surgical and radiotherapeutic areas were analyzed. *Patients and methods:* 168 patients with oral cancer were irradiated as follows: 55 patients: total dose 60 Gy, 2.0 Gy daily, BED 90 Gy_4, 61 patients: 70 Gy (BED 105 Gy_4). 52 patients: total dose 82.8 Gy, 1.2 Gy twice daily, (BED 108 Gy_4). *Results:* The frequency of ORN was 8.6% (conventional RT) but 22.9% (hyperfractionated RT, $P = 0.029$). Significant risk factors (total dose 50–70 Gy) were deep paradontitis ($P = 0.023$) and bone surgery in the lower jaw ($P = 0.05$), but not BED. Comparing conventional to hyperfractionated radiotherapy BED was the most important risk factor ($P = 0.008$), furthermore age ($P = 0.042$), T-stage ($P = 0.042$) and deep paradontitis ($P = 0.016$). *Conclusion:* Applying total doses up to 70 Gy the frequency of ORN seems independent from dose. The dose–effect relationship fitted from our results shows that a total dose of 82.8 Gy applied hyperfractionally is equivalent to a dose of 76 Gy applied conventionally. The high rate of necrosis is thus attributable to overdosage.

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CONVENTIONAL RADIOTHERAPY VERSUS ACCELERATED HYPERFRACTIONATED RADIOTHERAPY VERSUS CONVENTIONAL RADIOTHERAPY AND CONCOMITANT CHEMOTHERAPY IN ADVANCED OROPHARYNGEAL CARCINOMA: A RANDOMIZED CLINICAL TRIAL

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In January 1993 a phase III randomized trial (ORO-01) was activated comparing conventional radiotherapy—RT–(arm A) versus accelerated hyperfractionated RT (arm B) versus conventional RT plus concomitant chemotherapy—CT (arm C). Previously untreated patients affected with epidermoid carcinoma of the oropharynx, stage III–IV M0 (according to UICC 1987) with the exclusion of T1N1 and T2N1, with KPS $\geq$ 70 and aged $\leq$ 70 are considered eligible. In the arm A a total tumor dose (TTD) of 66–70 Gy are given in 33–35 fractions over 6.5–7 weeks. In the arm B a TTD of 64–67.2 Gy is given in 40–42 fractions, two fractions of 1.6 Gy a day separated by 6 hours; a two-week split is planned after delivering 38.4 Gy. In the arm C RT is given in the same way as in the arm A: CT is administered according to the following schedule: carboplatin 75 mg/sqm bolus in days 1–4, 24–32, 57–59 and 5-FU 1000 mg/sqm in with continuous infusion over 96 hours (days 1–4, 29–32, 57–59). The first two cycles are given concomitantly with RT. Between January 1993 and January 1995 104 patients were accrued in 18 participating centers. Full information about participating centers will be given. The distribution of patients by treatment arm, according to age, gender and stage has been balanced in the three arms. Particularly for the stage the distribution has been the following: ARM A ST III 9, ST IV 26; ARM B ST III 12, IV 23; ARM C III 10, IV 24. The study is still on going. Preliminary data concerning clinical response at two months after the end of the treatment and also treatment compliance will be reported.

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A PHASE II TRIAL OF DOCETAXEL IN SQUAMOUS CELL CANCER OF THE HEAD AND NECK

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Docetaxel was given as a 100 mg/m^2 intravenous injection, once every 3 weeks; in patients with metastatic or recurrent squamous cancer of the head and neck. Patients were pretreated with steroids and antihistamines. Twenty eight patients were entered. All had previous radiotherapy and 9 had cisplatinum/FUra based induction chemotherapy > 12 months previously. The remaining 19 had no prior chemotherapy. There was a 50% response rate (4 CR and 10 PR) among all patients. Response among patients treated with prior induction chemotherapy was 40%. The median duration of response was 4 months. 43% of the patients experienced leukopenia (WBC < 1000) resulting in dosage reduction. Hypersensitivity reaction occurred in 2 patients and one was retreated. One patient died of unknown causes during the first course of therapy. Pleural effusions occurred in 2 patients and were not clearly related to therapy. Grade II stomatitis and grade III neurotoxicity were rare (4% and 1% respectively). Significant grade III fatigue occurred in 5 patients but resolved with continued therapy in all but one. We conclude that docetaxel is highly effective in squamous cell carcinoma of the head and neck and warrants testing in combination chemotherapy programs. Docetaxel appears to be an effective, simple palliative therapy for recurrent disease.

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HOW TOLERABLE ARE THE ACUTE REACTIONS OF ACCELERATED RADIOTHERAPY IN HEAD AND NECK CANCER

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It has been reported that if a radical dose is to be achieved with accelerated radiotherapy schedules, a gap in treatment is required. However, several groups have shown that effective total doses can be given without a gap. We have analysed the acute morbidity data in 99 patients with head and neck cancer treated with CHART between 1985 and 1990.

All patients developed mucositis by week 3, with complete resolution in 60% and 82% by weeks 12 and 16 respectively. Symptoms of dysphagia mirrored these clinical findings, with 92% of patients developing moderate or severe dysphagia at week 3 which disappeared in 80% by week 12. Nasogastric feeding was required in 7 patients. Thirteen patients were hospitalised for between 1 and 4 weeks, for reasons relating to mucositis (6 patients) or suspected infection. Skin reactions were less of a problem. Maximum intensity of erythema was seen at week 3 but was severe in only 13%. Moist desquamation developed in 20% of patients between weeks 3 and 4 but in only 5% did it involve more than 25% of the treated field. In conclusion, the acute morbidity associated with this type of accelerated regimen is not unduly severe thus obviating the need for a gap in treatment.