14.
SEARCH FOR IMPROVEMENT OF THE THERAPEUTIC RATIO IN RADIOTHERAPY FOR NON-SMALL CELL LUNG CANCER (NSCLC)

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There are several approaches under investigation in view of improvement of the therapeutic ratio of NSCLC radiotherapy in our Department:

1/ Dose escalation above 70 Gy using conformal radiotherapy techniques, 2/ accelerated radiotherapy with or without induction chemotherapy addressed to III stage tumours, 3/ conformal postoperative radiotherapy to total minimum dose in PTV of 50 Gy addressed to completely resected III stage tumours.

Ad 1/ From XI 1998 to XI 2000 43 patients were included in dose escalation study. Doses from 70 to 74 Gy were delivered. Apart from one toxic death, due to radiation pneumonitis, toxicity was acceptable. Since 1999 for N0 patients the study of omission of elective irradiation is conducted. By the time being 10 patients were irradiated with omission of elective fields. There was no relapse in non-treated "elective areas". The actuarial 1-, 2- and 3-year survival were respectively 84-, 64-, and 42%. There were 14 local relapses in 19 progressions observed in the entire group. In spite of encouraging results a high level of local relapses shows the limits of moderate dose escalation using conformal techniques and conventional fractionation in improvement of local control of NSCLC.

Ad 2/ From III 1999 two different accelerated radiation therapy schedules are investigated for III stage tumours. Forty patients were enrolled in the study: 26 were irradiated according to accelerated hyperfractionated radiotherapy (57 Gy in 40 fractions [first week: elective fields - 1.2 Gy x 2 per day, 3 remaining weeks 1.8 Gy to elective fields and 1.2 Gy boost to tumour] during 26 days), 14 were irradiated according to accelerated conformal radiotherapy with concurrent boost (56.7 Gy in 21 fractions and 26 days: all treatment was conformally planned and delivered: 1,9 Gy per fraction to the limited elective field and 0.8 Gy as a concurrent boost to the GTV). There was no difference on compliance with treatment plan, toxicity and response rate (80- and 72%) in the both investigated groups.

Ad 3/ From I 1999 eleven patients were enrolled in the phase II study of postoperative conformal radiotherapy of the region of the highest probability of microscopic invasion by the disease to the minimum dose of 50 Gy in PTV. The study is conducted in view of the future design of randomised study addressing question of the value of postoperative radiotherapy using modern techniques in management of NSCLC.

15.
RADIATION SURVIVAL AND COLONY SIZE OF HUMAN EPIDERMAL KERATINOCYTES IN THE PRESENCE OF KERATINOCYTE GROWTH FACTOR (rhKGF)

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The capacity of recombinant human keratinocyte growth factor (rhKGF) to ameliorate the radiation response of mouse oral mucosa and other epithelial tissues was recently reported. However, the exact mechanisms of action of KGF remain unclear. The aim of the present study was to investigate the effect of rhKGF on survival and colony size of normal human epidermal keratinocytes in vitro. Primary human neonatal keratinocytes (HEKn) were irradiated with doses of 0 Gy and 2 Gy (200 kV X-rays) and incubated in the presence or absence of 100ng/ml rhKGF. Plating efficiency (PE) and surviving fraction (SF2) were determined in a clonogenic assay. In cell cultures without rhKGF the mean PE was 4.6%. Irradiation with 2 Gy resulted in a SF2 of 51%. In cell cultures with rhKGF, the mean PE was identical (4.6%). After irradiation with 2 Gy, a similar SF2 of 54% was observed, indicating that KGF did not change the survival characteristics of HEKn keratinocytes. Individual colony size, however, in all cultures incubated with rhKGF was significantly increased compared to incubation without rhKGF. The number of extremely large colonies (□2 mm) was clearly higher (p=0.0000) with rhKGF-