Radiotherapy II

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IN VITRO RADIOSENSITIVITY OF HEAD AND NECK TUMOUR CELLS AND FIBROBLASTS ASSESSED FROM SINGLE BIOPSIES

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The assumed selective growth of tumour cells in the soft agar clonogenic assay has formed the basis for its use to test *in vitro* sensitivity of tumours. However, studies in our laboratory have shown that also normal skin fibroblasts grow in soft agar. The present study was initiated to quantify the contaminating growth of fibroblasts in the enriched modified Courtenay-Mills soft agar assay, and to investigate ways to overcome this problem. A new colony filter-technique including immunohistochemical identification was developed, and 88–100% of the colonies obtained from 13 head and neck tumours were 5B5 Fibroblast Antibody positive, whereas 0–25% of the colonies were Cytokeratin AE1-3 positive. Thus, the present technique identifies tumour and fibroblast colonies, respectively, and it can measure the *in vitro* radiosensitivity of both tumour cells and fibroblasts. The parameter normally reported, the overall Surviving Fraction at 2 Gy (SF_2), based on the number of colonies in agar, was significantly correlated to SF_2 of fibroblasts (SF_2 F), but not to SF_2 of tumour cells (SF_2 T). The overall SF_2 was significantly different from SF_2 T in half of the examined patients. The SF_2 T was not correlated to SF_2 F. Thus, it is necessary to make a routine correction for fibroblast contamination, when studying tumour cell radiosensitivity. If this is done, the possibility of estimating both tumour cell and fibroblast radiosensitivities from a single biopsy is of interest in future clinical studies on predictive assays.

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THE PREDICITVE POTENTIAL OF TPOT FOR RADIOTHERAPY OUTCOME IN HEAD AND NECK CANCER: A META ANALYSIS

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Pretreatment potential doubling times (Tpot) of tumors have been reported to correlate with outcome after radiotherapy in some trials but not in others. Almost all the individual trials have low patient numbers. Because of the potential importance of predictors in guiding radiation oncologists in their choice of schedule, the present meta-analysis was undertaken to better define the role of Tpot. All participating centres had carried out pretreatment Tpot analyses using *in vivo* labeling with either bromo- or iodo-deoxyuridine. Those involved include one large cooperative group (EORTC), plus centres in Denmark (Danish Cancer Soc. ICR, Aarhus), Sweden (Umea Univ), U.K. (Mt Vernon Hospital, Northwood), Italy (Nat. Inst. Cancer Res, Genova; Ospidale Multizonale, Varesi), France (Gustave-Roussy, Paris) and Egypt (Nat. Cancer Inst, Cairo). This analysis concerns head and neck cancer patients treated with radical radiotherapy only, with schedules lasting at least 6 weeks. The total number of patients analyzed is over 400. The analysis considers patients with diploid and aneuploid tumors separately, since Tpot estimates are more reliable in the latter. Data are being collected at the time of writing and the analysis is expected to be complete in August 1995.

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OXYGENATION STATUS PREDICTS RADIATION RESPONSE IN ADVANCED SQAUMOUS CELL CARCINOMA OF HEAD AND NECK

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There is substantial evidence that hypoxic clonogenic cells are relatively radioresistant. The aim of the study was to correlate tumour oxygenation status and radiation response. Pretreatment oxygenation status was measured in 31 lymph nodes and 1 primary tumour from squamous cell carcinomas of head and neck using polarographic oxygen electrodes (Eppendorf, Germany). The level of hypoxia was evaluated as the percentage of measured pO_2 values $\leq$ 5 mmHg ($\%pO_2 \leq 5$ *mmHg*). All patients were treated by conventional external radiotherapy 66–68 Gy in 33–34 fractions. The median follow up was 21 month. So far 15 patients had locoregional tumour recurrence. Among these 15 patients the median of the $\%pO_2 \leq 5$ *mmHg* was 49% (range 6–100%) as compared to the 17 patients without failure, who had a median of 18 $\%pO_2 \leq 5$ *mmHg* (range 0–84%). The means of these two groups were significantly different (Students t-test, $P < 0.022$). When dividing all patients into tertiles by $\%pO_2 \leq 5$ *mmHg* and comparing the actuarial tumour control at 2 years using Kaplan Meier estimates the most hypoxic third had significantly lower tumour control ($P < 0.004$, Logrank test). Also by Cox multivariate analysis the $\%pO_2 \leq 5$ *mmHg* as continuous variable was found to be significant ($P = 0.03$). In conclusion these results suggest that tumour oxygenation is predictive of radiation response.

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HYPOXIA IN CERVIX CANCER—PRELIMINARY RESULTS WITH THE EPPENDORF ELECTRODE

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Hypoxia is an important factor predicting tumour relapse following radiation therapy. To assess the magnitude of hypoxia prior to treatment, 23 new patients with cervix cancer were evaluated during examination under anesthesia using a polarographic oxygen electrode. Tumours were of FIGO stages IB to IIIB and maximum tumour size ranged from 2 to 10 cm. Six patients had repeat oxygen assays performed prior to brachytherapy following external beam radiation of 45–50 Gy. Median pO_2 values prior to treatment ranged from 0 to 93.8 mm Hg with a median of 4.7 mm Hg. Thirteen of 23 patients had median pO_2 values of $<$ 10 mm Hg. The proportion of pO_2 values $<$ 5 mm Hg in each tumour ranged from 2.2 to 99% with a median of 52%. In two patients the median pO_2 improved following external radiation, in two other patients there was a drop in oxygen tension and in the remaining two there was no significant change. PO_2 measurements using this technique are feasible and demonstrate that over 50% of tumours have significant levels of hypoxia.

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ACUTE TOXICITY IN ELDERLY WITH HEAD AND NECK CANCER

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Elderly are often treated less agressively to preserve quality of life with regard to toxicity. Yet, there are few data regarding the toxicity of radiotherapy (RT) in elderly patients (pts). From 1975 to 1994, 1588 pts with head and neck cancers enrolled in EORTC trials received RT and were available for analysis on RT toxicity. Pts above 65 years are in excess of 20%. Age and acute objective mucosal reactions were available for 1307 pts and 1288 had toxicity $>$ grade 1. Age and acute functional mucosal reactions were registered for 838 pts and 760 pts had toxicity $>$ grade 1. Bodyweight alteration was available in 1252 pts, it increased in 153 pts and decreased in 1099 pts. Toxicity was examined in different age ranges from 50 years to 75 years and more. A trend test (χ^2) was performed to assess any difference in occurring toxicity. There was no significant difference in acute objective mucosal reactions ($\chi^2 < 0.0001$, 1 df, $P = 0.1$) and in loss of weight $> 10\%$ ($\chi^2 = 12.052$, 1 df, $P = 0.441$). In contrast, older pts had more functional acute toxicity ($\chi^2 = 19.184$, 1 df, $P = 0.0001$) than younger.