

## Radiotherapy I

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### THE CLINICAL, PHYSICAL AND RADIOBIOLOGICAL ASPECTS OF TOTAL BODY IRRADIATION

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The current project was started with the practical aim of introducing a total body irradiation (TBI) protocol at the National Cancer Institute (NCI) of Cairo and studying the various aspects of the subject.

In the radiobiological part of the project we studied TBI-related late effects in a mouse model. The results showed that giving cyclophosphamide (CTX) after TBI and separating between the two modalities by an interval of 3 days will maximize the therapeutic gain. Combining CTX and low dose rate TBI was more toxic to the lungs than combining CTX and high dose rate. On the contrary, CTX did not affect the ability of lung tissue to repair sublethal radiation damage that occurred between fractions. The study also described a progressive and potentially fatal kidney damage occurring after TBI. There also seemed to be two waves of injury in the murine kidney after TBI. The estimated  $\alpha/\beta$  value for each wave was higher than the reported values after localised kidney irradiation. Fractionation sensitivity for cataract formation was estimated and dose-response curves for cataract after TBI were constructed.

The results from the physical part of the project enabled us to use the conventional depth dose tablets to calculate the dose in the TBI situation after proper correction for motion, the change in source skin distance and lack of back-scatter, in order to determine the dose homogeneity along the antero-posterior diameter of the patient. Homogeneity of dose along the patient's longitudinal axis of approximately 4% was achieved.

In the clinical part of the project we followed the patients treated with TBI and BMT for various late effects using different end points. TBI was used in the conditioning of more than 50 cases. Preliminary analysis of the treatment results revealed that the survival and complication rates were compatible with the international standards according to the stage of disease.

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### COMPARATIVE EVALUATION OF COPLANAR TECHNIQUES FOR PROSTATE CONFORMAL RADIOTHERAPY

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The aim of this study was to assess the relative merits of 4 different coplanar treatment techniques for conformal radiotherapy of the prostate. Twelve subjects with T1/T2 prostate cancer underwent a pelvic CT scan supine with the bladder full. The prostate and base of seminal vesicles were outlined with a margin of 10 mm. to give the planning target volume (PTV). The rectum, bladder and femoral heads were outlined as organs at risk (OARs). Isocentric plans using 3, 4, 6 & 8 fields with conformal blocks were generated and beam weights selected using a simulated annealing optimisation algorithm. The volume of each OAR within arbitrary dose bins of >50% and >80% were calculated for each plan and rectal normal tissue complication probabilities computed to determine the dose that would give a 5% complication rate (NTCP<sub>0.05</sub>). The optimised 6 & 8 field plans resulted in significantly smaller volumes of the femoral heads within both the >50% and >80% dose bins compared with the 3 & 4 field plans. There was a small but consistent advantage for the optimised 4 field plans with respect to the volume of rectum within both the >50% and >80% dose bins. The isocentric dose necessary to give the rectal NTCP<sub>0.05</sub> was up to 4 Gy higher for the 4 field plans versus the next best technique. The optimised 6 field plans consistently resulted in a smaller volume of bladder within both the >50% and >80% dose bins. We conclude that there is no universally optimal coplanar beam arrangement for conformal radiotherapy of the prostate in this sample of 12 subjects.

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### DISTRIBUTION KINETICS OF RADIOLABELLED MONOCLONAL ANTIBODIES (MAB) IN EXPERIMENTAL TUMOURS FOLLOWING INTERSTITIAL AND SYSTEMIC ADMINISTRATION

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In this study we compared the pattern of distribution of intralesional (IL) vs intravenous (IV) I<sup>125</sup> labelled MAB within a transplantable tumour (HSN), the adjacent tissue (muscle) and systemic organs. Both a specific (ALN/11/53) and non-specific control (ICR2) MAB, were evaluated to determine the importance of MAB specificity for these routes of administration. The distribution of I<sup>125</sup>I was assessed by autoradiography and gamma counting in 37 rats at 4 time points post-infusion up to 72 hours.

There was a three-fold greater regional percentage uptake/g of IL vs IV MAB (Student's t-test,  $P = 0.012$ ). Specific MAB had a 14% greater uptake than non-specific MAB following IL administration ( $P = 0.028$ ). The systemic organ uptake was lower with IL than IV administration ( $P = 0.047$ ). Up to 24 hours post-infusion, there was a prominent 'leakage' pattern of I<sup>125</sup>I within the surrounding muscle. At later time points, although the activity was not distributed across the whole tumour, there was a sharpe demarcation at the tumour/muscle junction indicating a tendency for the radioactivity to conform to the shape of the tumour.

The higher I<sup>125</sup>I activity and favourable distribution attributes suggest a role for further evaluation of intralesional radiolabelled MAB therapy in patients with localised malignancy.

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### EPR/ALANINE DOSIMETRY: JUST ANOTHER DOSE MEASURING SYSTEM?

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Electron paramagnetic resonance (EPR) dosimetry is based on a non-destructive quantitative measurement of stable free radicals in samples, induced by energy deposited by radiation. The amino acid L- $\alpha$  alanine shows favorable dosimetric properties: a linear response with dose, no energy nor dose rate dependence and no fading. The detector itself is small in size and tissue equivalent, which makes it an ideal measuring device for radiotherapy. Commercial available alanine dosimeters together with a low budget desk top spectrometer (Bruker EMS104) are tested since more than two years at our department as an *in vivo* dose measuring system. All types of dosimeters show a perfect linear dose-response, but the background level (zero dose signal) can differ significantly between different manufacturers: from 2.5 Gy to 14 Gy. Measurement precision is less than 1% (1 $\sigma$ ) if dose exceeds 10 Gy. No fading was observed over a period of one year. The reliability of alanine dosimetry for *in vivo* dosimetry will be illustrated with several case studies: dose measurements at the cervix wall during treatment of the cervix carcinoma with high and low dose rate brachytherapy, dose to the rectum wall; entry dose measurements during teletherapy. For all these very different cases correspondence of calculated and measured dose was excellent. From our experience we believe that alanine dosimetry can play an important role in clinical dosimetry in the future, combining advantages from TLD and diode dosimetry systems.

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### PRELIMINARY RESULTS OF PROTON BEAM THERAPY OF UVEAL MELANOMA

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Since September 1991, 580 patients have been treated in the centre of proton beam therapy at Orsay for choroidal melanoma.

For the 243 first patients, there were 42% men and 58% female. The mean age was 56 years. The mean tumour diameter was 13.1 mm. The mean tumour thickness was 6.3 mm. All patients were treated with 60

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