

# 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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Gy with 4 fractions in 4 days after precise localisation of the tumour by surgical procedure and clips.

Preliminary results, for the 146 patients that have at least one year followup, are as follows. We have observed complete tumour response in 10%, partial response in 70% and stabilisation in 20%.

Precise information about visual results and factors influencing visual results will be given.

#### 146 ORAL CHOROIDAL METASTASES: TO TREAT OR NOT TO TREAT

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The role of external beam radiation therapy (EBRT) in the management of choroidal metastases (CM) was evaluated retrospectively.

From 1970 to 1993 58 patients with CM of 80 eyes underwent EBRT with doses ranging from 20 to 53 Gy. The female to male ratio was 2.9, median age 59 years. The results of treatment measured by complete response, visual acuity improvement, retinal reattachment and eye conservation was respectively 63%, 75%, 65% and 100%.

Patient characteristics (primary tumor, histology, details of CM) will be presented.

Post-irradiation complications and related technical characteristics of the treatment will be highlighted as well as the relationship between overall survival and primary site.

From our data, EBRT is a very efficient and safe palliative treatment for CM and helps preserving a good vision, thus the quality of life in patients who have a poor overall prognosis.

#### 147 ORAL ACCELERATED RADIATION WITH CONCOMITANT CARBOPLATIN FOR GLIOBLASTOMA MULTIFORME

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The long-term efficacy and safety of postoperative accelerated fractionated radiotherapy with concomitant carboplatin was evaluated in 83 patients with glioblastoma multiforme. Patients received 2 Gy radiation three times a day for two 5-day cycles separated by 2 weeks. Prior to each radiation treatment a 2-hour intravenous infusion of 33 mg/m<sup>2</sup> carboplatin was administered. Following radiotherapy, patients were to receive procarbazine, CCNU, and vincristine, (PCV) for one year or until tumor progression. Seventy-four patients with a median age of 55 years received at least one course of PCV. Their median survival duration was 55 weeks. Covariates individually predictive of improved survival were younger age ( $P < 0.01$ ), higher Karnofsky performance status ( $P = 0.055$ ), total or subtotal resection vs. biopsy ( $P = 0.056$ ) and smaller radiation volume ( $P = 0.008$ ). Seven patients had documented therapy-induced neurotoxicity.

Accelerated fractionated radiotherapy, as used, enables concomitant full dose administration of chemotherapy or radio sensitizing agents in glioblastoma multiforme.

#### 148 ORAL CURATIVE MANAGEMENT OF RECTAL ADENOCARCINOMA WITH RADIOTHERAPY ALONE: A SERIES OF 250 CASES

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This report pools the results of two institutions using since 1970 the strategies developed in Lyon by Jean Papillon. (1) *Low and mid rectum T1 and selected T2 well differentiated adenocarcinoma* treated with intrarectal contact X-ray (ICRT) and interstitial brachytherapy (IBT). Since 1970, 200 patients (113 T1, 87 T2) were treated in Dijon and Lyon-Sud. Transrectal ultrasonography has been used for staging since 1987. Failures rates (unlimited follow-up) are local in 4.5% (T1) and 19.5% (T2), nodal in 0.9% (T1) and 9% (T2), metastatic in 3.5% (T1) and 12.5% (T2). Salvage treatment was successful in 20/24 pelvic failures. Ultimate pelvic control was obtained in 189/200 (94.5%) with preservation of a functional anal sphincter in 95% of PTS with pelvic control. No severe complication occurred. (2) *Low and mid rectum T2 and T3 adenocarcinoma* treated with external radiotherapy (30–39 Gy in 10–13 fr. and 14–17 days to the posterior pelvis. Concomitantly, ICRT delivers 60–80

Gy in 2–3 fr. After a 6- to 8-week rest period, a 20–30 Gy boost is delivered by IBT. Fifty patients were treated (34 T2, 16 T3). Twelve out of 50 (24%) had a local failure (5/12 with a subsequent surgical salvage treatment) resulting in an 82% ultimate control rate with a functional sphincter. G2 complications occurred in 16% (rectorragia/ulcer). A single patient had a G3 necrosis.

#### 149 POSTER PROGNOSTIC FACTORS IN LUNG CANCER WITH BRAIN METASTASIS

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The role of palliative cranial irradiation and relevant prognostic factors were analyzed prospectively in 103 lung cancer patients who had brain metastasis between October 1991 and December 1994. The male to female ratio was 92/11. Age range was 33–83 (median:59). Histological types were adenocarcinoma 30/103 (29%), epidermoid carcinoma 30/103 (29%), SCLC 27/103 (26%), large cell carcinoma 3/103 (3%), carcinoma without certain histopathological classification 11/103 (11%). Radiotherapy was completed in all except 8 cases. Palliation was accomplished in 92% of the cases. Palliation duration ranged between 0.5–36 months (median: 3). Median survival was 4 months. Extent of brain metastasis (solitary/multiple), presence or absence of metastasis other than brain, local symptom status at the time of brain metastasis and time of brain metastasis were the analyzed prognostic factors. Local symptom status and presence or absence of metastases other than brain were found statistically significant ( $P < 0.01$  and  $P < 0.05$  respectively).

#### 150 POSTER CONSTRUCTION AND FIRST EXPERIENCE WITH A CUSTOMIZED "BELLY BOARD" MOULD TO MINIMIZE THE VOLUME OF SMALL BOWEL IN THE IRRADIATION OF PELVIC MALIGNANCIES

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Radiation enteritis is a common complication of radiotherapy for pelvic malignancies, often requiring medical therapy, breaks of the treatment and sometimes the hospitalization or a surgical intervention.

The volume of irradiated small bowel (SB) is considered one of the most important factors in determining gastro-intestinal side effects. Numerous techniques, principally based on the reduction of the irradiated SB volume have been applied to avoid or decrease radiation enteritis. We have realized a customized "belly board" as a bowel minimization device, modifying the original technique of Shanahan (*IFROBP* 1989, 17, 187–88). We use a polyurethane foam mould to place and immobilize the patient in prone position with anterior lower abdominal wall compression. A block of polystyrene in the shape of a reverse pyramid is placed under the superior abdomen during the solidification of the mould to obtain a hole for the displacement of the SB. From October 1994 to March 1995, we have utilized such device in 28 consecutive patients irradiated for pelvic tumours. The mean high dose SB volume irradiated was 56.2 cm<sup>3</sup> (range 0–390) and the partial dose SB volume was 218.5 cm<sup>3</sup> (range 0–588). This technique permits not only the displacement of the SB (favoured also by recommended bladder distension) minimizing the irradiated SB volume, but also contribute to the immobilization of the patient in a comfortable and repeatable position.

#### 151 POSTER HYPERFRACTIONATED ACCELERATED RADIATION THERAPY IN RADICAL TREATMENT OF CANCER PATIENTS

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Total dose is just one of the factors important to the achievement of success in radiotherapy. Biological higher doses of radiotherapy to the primary site and if involved, to draining lymph nodes have produced higher response rates and suggest that higher doses may result in improved survival. Radical treatment policy in different institutions varies from conventional fractionated schedules to hyperfractionated (accelerated or not) or shorter hypofractionated ones. To achieve this goal in