Advances in RT techniques may allow for dose escalation and improved clinical outcome. A limitation of this strategy is the risk of small bowel toxicity. Little information exists to guide clinicians on appropriate bowel dose-volume constraints.

**Methods:** Dose-volume data were collected on 30 patients entered into the BC2001 phase III randomised trial from a single centre. Patients were planned with an empty bladder and allocated radiotherapy in either a single phase of 64 Gy in 32 fractions to the whole bladder (standard whole bladder radiotherapy (SRT) group) or 50 Gy in 32 fractions to the whole bladder plus concomitant tumour boost to 64 Gy (reduced high dose volume radiotherapy (RVRT) group). Dose-volume calculations were recorded and the volume of bowel receiving different doses was compared to constraints defined by Gallagher et al IJROBP 1986, utilised in our department's ongoing pelvic IMRT trial.

**Results:** The bowel volume receiving each dose increment is expressed, for example, as V45 for the volume of bowel in $cm^3$ receiving 45 Gy (Table 1). A substantial number of patients missed each dose constraint level. At each level the percentage of patients missing the constraint was less in the RVRT arm compared to the SRT arm.

Table 1

| | | SVRT n = 17 | | | RVRT n = 13 | | | All n = 30 | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Constraint ($cm^3$) | Median ($cm^3$) | Range ($cm^3$) | Missing constraint (n) | Median ($cm^3$) | Range ($cm^3$) | Missing constraint (n) | Median ($cm^3$) | Range ($cm^3$) | Missing constraint (n) |
| V45 | 158 | 98 | 32–217 | 4 | 57 | 18–173 | 2 | 79 | 18–217 | 6 |
| V50 | 110 | 90 | 26–207 | 5 | 52 | 14–155 | 2 | 66 | 14–207 | 7 |
| V55 | 28 | 85 | 21–196 | 15 | 42 | 5–147 | 8 | 50 | 5–196 | 23 |
| V60 | 6 | 63 | 9–175 | 17 | 31 | 3–118 | 9 | 38 | 3–175 | 26 |
| V65 | 0 | 12 | 0–91 | 14 | 0 | 0–21 | 8 | 7 | 0–91 | 22 |

**Conclusions:** These data suggest patients receiving bladder RT often exceed the bowel dose constraints used in other pelvic RT trials but this may occur less often if RVRT is used. Despite this, in the BC2001 trial, <6% of patients have developed ⩾grade 3 late gastrointestinal toxicity, suggesting that most patients exceeding these dose constraints do not experience excessive toxicity. A further 25 patients are undergoing analysis and dose-volumes will be correlated with prospectively collected gastrointestinal toxicity. This pilot study will be used to propose more suitable constraints for bladder RT.

**2044** POSTER

**Tumor growth inhibition and necrosis following treatment of experimental solid malignant tumors by intra-tumoral Ra-224 loaded sources**

Y. Keisari[1], T. Cooks[1], H. Bittan[2], E. Lazarov[2], S. Reitkopf[1], G. Horev[1], L. Arazi[3], R. Etzyoni[1], M. Schmidt[2], I. Kelson[3]. *[1]Tel Aviv University, Clinical Microbiology and Immunology Faculty of Medicine, Tel Aviv, Israel; [2]Tel Aviv University, School of Physics and Astronomy Sackler Faculty of Exact sciences, Tel Aviv, Israel; [3]Tel Aviv University, School of Physics and Astronomy Faculty of Exact Sciences and Althera Medical, Tel Aviv, Israel*

**Background:** Alpha radiation is a lethal form of radiation whose short range limits its use for cancer treatment. We developed a method to treat the entire tumor with alpha radiation using intratumoral wires, with radium-224 atoms fixed below their surface (Ra-wires). As Ra-224 decays, it releases into the tumor, by recoil, short-lived atoms which spread in the tumor, release their lethal alpha particles, and cause tumor necrosis. We termed this treatment Diffusing Alpha-emitters Radiation Therapy (DART).

This study examines the biological and physical effects of the Ra-wires alone or with chemotherapy, on human and mouse tumors of various histotypes.

**Methods:** Subcutaneous tumors from squamous cell carcinoma (SCC), pancreatic, colon and lung carcinoma origin were treated with stainless steel Ra-wire(s) with or without chemotherapeutic drugs, and tumor progression was recorded. Intratumoral radioactivity dose distribution was measured by the spread of Pb-212. The sensitivity of the various cancer cells was determined by their ability to form colonies after irradiation in vitro with alpha particles.

**Results:**

i. Insertion of Ra-wires into solid tumors resulted in significant reduction of tumor growth. Tumor local control was dependent on tumor size and the amount of radioactivity of the wires.
ii. An augmented level of local control was achieved when a combined treatment of Ra-wires and chemotherapy was applied.
iii. Dosimetric measurements of the intra-tumoral spread of radioactivity in different tumor models revealed biologically significant doses (>10 Gy) of Pb-212 over a region a few mm in size around the wires. The average region diameter was largest in SCC, smallest in pancreatic and intermediate for colon and lung tumors.
iv. Intratumoral tissue necrosis and tumor growth retardation were in correlation with the distribution of released alpha emitting isotopes and with the radiosensitivity of tumor cells.
v. Measurements of the mean lethal dose (D0) for human and mouse pancreatic, SCC and colon carcinomas irradiated by alpha particles, showed that SCC cells are the most radiosensitive compared to all other cell lines examined. Further attempts are made to correlate radiosensitivity with DNA repair mechanisms.

**Conclusions:** DART is an effective treatment to treat solid malignant tumors, and can be further potentiated by chemotherapy. This combined treatment modality holds significant potential for the treatment of non-resectable human cancers.

**2045** POSTER

**Demonstration of dose-response relations for a series of tumours and normal tissues after external radiotherapy**

G. Komisopoulos[1], K. Sotiriadou[2], G. Soulimioti[2], N. Papanikolaou[3], B.K. Lind[4], P. Mavroidis[4]. *[1]University Hospital of Larissa, Medical Physics, Larissa, Greece; [2]University Hospital of Larissa, Radiotherapy, Larissa, Greece; [3]University of Texas Health Sciences Center, Radiological Sciences, San Antonio Texas, USA; [4]Karolinska Institutet & Stockholm University, Medical Radiation Physics, Stockholm, Sweden*

**Background:** Radiobiological models have been developed for the performance of radiotherapy treatment plan optimization. The delivered treatment and the clinical outcome are associated by these models. It is necessary to determine the radiobiological parameters of these models from clinical patient databases, for the clinical implementation of radiobiological treatment plan evaluation. The purpose of this study is to setup a database with the parameters, which characterize the dose-response relations of different tumors and normal tissues for different radiobiological models.

**Material and Methods:** Investigation and analysis of a large number of dose-response relations for tumors and normal tissues has been performed based on data from patient materials that have been collected from the literature. The dose-response models for which radiobiological parameters were collected are the Poisson, relative seriality, k-model, LKB, critical volume and parallel. The parameters that characterize the shape of these dose-response relations are the dose, which cause response to 50% of the patients (usually denoted as $D_{50}$), the steepness of the dose-response curve (usually denoted as $\gamma$ or $m$) and the volume dependence of the tissue (usually denoted as *s-relative seriality*, $k$ or $n$). The values of these parameters are derived for a certain reference volume of the examined tissue. Since these values are related to a certain fractionation regime, the determination of the $\alpha/\beta$ ratios is also important to be performed.

**Results:** It has been reported and demonstrated that in well defined tumor stages, which are characterized by a uniform size the $\gamma$ values, are rather high. The volume of the irradiated tissue and the acceptable treatment complication rates are related to the part of the dose-response curve, which is covered by the clinical data. The volume dependence, which is related to the spatial internal structural organization of their functional subunits, affects significantly the response of normal tissues. Dose-response curves are used to illustrate the radiobiological characteristics of tumors and normal tissues. The collected radiobiological parameters are schematically expressed by these curves, which show the expected rates of tumor control or normal tissue complications for a range of uniform doses. The clinical data are plotted on these diagrams in the same approach they are registered in the patient follow-up records.

**Conclusions:** A large number of clinical factors (e.g. radiation modality, beam energy, clinical endpoint definition) influence the determination of dose-response relations. Therefore, the clinical verification and validation of reported parameters is a prerequisite for their implementation.

**2046** POSTER

**Interruptions in fractionated radiotherapy: incidence, causes and impact in tumour control probability**

M.B. Rios Pozo[1], R.E. Pacios[1], D. Guirado[1], I. Castillo[1], M.T. Delgado[1], R. Guerrero[1], J.L. Garcia-Puche[1]. *[1]Hospital Clinico San Cecilio, Oncology, Granada, Spain*

**Background:** Overall treatment time (OTT) in fractionated radiotherapy plays an important role in certain tumour types, specially in head and neck squamous cell carcinoma, cervix, lung and breast cancer. In fact, tumour control probability (TCP) can be reduced if OTT is increased. We conducted an evaluation of any potencial interruption in treatment, both scheduled and unscheduled, in terms of incidence, main causes and management of prolongation of time schedule. Finally, we propose recommendations to minimise the impact of interruptions on treatment outcomes.