**1401** POSTER

**Optimization using IMRT to spare the esophagus during lung tumor irradiation: target dose escalation without increased normal lung toxicity predicted with use of more fields**

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**Background:** To evaluate whether plan optimization using increasing numbers of beamlet IMRT fields leads to tumor dose escalation for difficult lung tumor treatments without corresponding undesired effects in normal lung due to the spread of dose associated with the additional fields.
**Material and methods:** The treatment planning CT scans of 8 patients with lung tumors were used for the optimization of beamlet IMRT plans. In all cases the PTV overlapped part of the esophagus. A 3D conformal plan (3DCRT) was compared to 4 IMRT plans: one (SF) using the same fields as the 3DCRT plan and 3 additional plans with 3, 5 and 7 fields, chosen from equally spaced coaxial 5, 7 and 9 fields plans but excluding two fields each that would have entering through the opposite lung; designated, 3 of 5, 5 of 7 and 7 of 9, respectively. In the IMRT optimizations, the effective dose in the PTV was maximized using a previously described technique based on maximizing *gEUD* for the whole PTV (with a = −50) and simultaneously in a reduced PTV (PTV minus esophagus+5 mm; with a = −5). NTCP-based costlets were used to integrate the dose effects for normal tissue organs at risk, and these levels were maintained for all beam arrangements (⩽5% for heart and esophagus and 15% for normal lung). The relative ranking of the resulting plans was evaluated in terms of the absence of cold spots within the PTV, the final realized *gEUD-5* (a = −5: responsive tumor) and *gEUD-20* (a = −20: aggressive tumor) values computed for the whole PTV and besides NTCP, dose/volume parameters for lung (V13, V20 and V30).
**Results:** The isodose surface encompassing 99% of the PTV was higher in the 4 IMRT plans than in the 3DCRT plan (71 Gy, 74.1 Gy, 74.1 Gy, 74.8 Gy and 75.4 Gy, respectively, for the 3DCRT, SF, 3 of 5, 5 of 7 and 7 of 9 plans). In all cases, the IMRT plans also resulted in better gEUD-5 and gEUD-20 values. The 7 of 9 IMRT plans had the highest average gEUD-5 value (96.7 Gy) for the 8 cases (compared to 93.6, 91.7, and 89.9 Gy averages for 5 of 7, 3 of 5, and SF, respectively), with a similar trend for the gEUD-20 evaluations. Beyond maintaining equivalent NTCP, use of increasing numbers of fields also did not alter the V13, V20 and V30 values for lung.
**Conclusions:** The additional degrees of freedom associated with increasing the number of beamlet IMRT fields, for difficult cases of PTV overlapping the esophagus, appears to allow dose escalation without associated increases in lung dose V13 to V20 or lung NTCP.

**1402** POSTER

**Recruitment to the cell cycle as the fundamental mechanism of tumor cell repopulation after the combination of radiotherapy and cyclin-dependent kinase inhibitors**

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**Background:** The 5 R's (Repair, Reassortement, Repopulation, Reoxygenation, Radiosensitivity) are the basic biological processes that take place in a cell population under radiotherapy. Repair and Repopulation are also basic processes during cytostatic chemotherapy. We studied the fundamental phenomena that underlie the reentry of tumor cells in the cell cycle and constitute the repopulation.
**Methods:** We studied the cell cycle parameters in Raji (Burkitt's lymphoma) and K562 (chronic myelogenous leukemia) cell lines (distribution in cell cycle and G2 arrest, DNA synthesis and apoptosis) under the effect of olomoucine, a novel cyclin-dependent kinase (CDK) inhibitor, or gamma-irradiation or a combination of both. The laboratory assays used were flow cytometry for cell cycle distribution, BrdU incorporation for DNA synthesis and DNA electrophoresis for the estimation of apoptosis.
**Results:** 48 hours after the effect of olomoucine or gamma-irradiation or both on the above cell lines we noticed an incremented G2 fraction, decreased overall cell survival and decreased DNA synthesis in the alive cells. Olomoucine inhibited DNA fragmentation after radiation-induced DNA damage. However it also increased the fraction of G2-arrested cells and decreased BrdU incorporation in the alive fraction of the irradiated cells.
**Conclusions:** The fundamental mechanism of repopulation is recruitment of cells to the cell cycle. Targeted cell cycle therapy with CDK inhibitors can inhibit cell cycle recruitment either by the control of cell reentry to the cell cycle (CDK4/6 inhibition) or by the induction of cell cycle arrest in the G2/M checkpoint. We propose Recruitment as the 6th R in radiobiology. In addition, in the same sense, recruitment can be regarded as one of the important parameters that must be taken in account during cytotoxic chemotherapy to predict resistance to the given drugs due to cell kinetics.

**1403** POSTER

**New radiation options for patients with anal canal cancer: A comparative dose volume histogram study**

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**Introduction**: In our institution, conformal therapy was introduced in the treatment of patients with anal canal with combined chemotherapy and radiation in order to alleviate the acute toxicities and was successful in eliminating the mandatory treatment break. With the availability of IMRT, this study was mandated to estimate the differential dose volume histograms on normal tissues between conventional, conformal and IMRT techniques and treatment time and planning time were monitored respectively in order to allow for a comparative evaluation of these new options.
**Material and Methods:** 15 patients were planned at the CT simulator using gastrografin in supine position. Bone marrow, small bowel, bladder, genitals and bilateral femoral heads as well as clinical target volumes (CTV) defined as tumor bed and pelvic nodes (perirectal, inguinal, iliac nodes) were outlined. Planning was done using CadPlan software for conventional techniques using RTOG 98−11 study guidelines and for conformal technique (6-fields arrangements) while Corvus system was used for IMRT using 7-field arrangement to deliver a standard dose of 54 Gy in 30 fractions. Skin dose was measured on a Rando phantom using the EBT model GAFCHROMIC® film.

Table: Comparative DVH results

| Organ/Technique | 95% | 80% | 50% | 30% | 20% | 10% |
|---|---|---|---|---|---|---|
| **Small Bowel** | | | | | | |
| Conventional | 3022 | 3450 | 4116 | 4357 | 4517 | 4713 |
| Conformal | 305 | 495 | *1716* | 2560 | 2850 | 3073 |
| IMRT | 660 | 940 | *1470* | 1800 | 2000 | 3290 |
| **Bladder** | | | | | | |
| Conventional | 4666 | 4851 | 5114 | 5203 | 5261 | 5333 |
| Conformal | 663 | *1610* | 2871 | 3557 | 3937 | 4446 |
| IMRT | 1430 | *1810* | 2310 | 2770 | 3070 | 3430 |
| **Bone Marrow** | | | | | | |
| Conventional | *280* | 1372 | 2431 | *2952* | *3169* | 3674 |
| Conformal | *126* | 302 | 1742 | *2614* | *2891* | 3079 |
| IMRT | 460 | 790 | 1380 | 1820 | 2080 | 2450 |
| **Genitals** | | | | | | |
| Conventional | 2287 | 3707 | 4894 | 5190 | 5255 | 5316 |
| Conformal | 216 | 497 | *1320* | *2172* | *2638* | *3289* |
| IMRT | 630 | 1070 | *1820* | *2390* | *2710* | *3160* |
| **Femoral Heads** | | | | | | |
| Conventional | 1408 | 1929 | 2826 | 2940 | *2990* | *3082* |
| Conformal | 344 | 587 | *1731* | *2523* | *2826* | *3056* |
| IMRT | 1430 | 1790 | *2270* | *2620* | *2820* | *3110* |
| **Skin** | | | | | | |
| Conventional | 100 | 220 | 890 | 1620 | 2140 | 2790 |
| Conformal | 100 | 180 | 440 | 760 | 1200 | 1980 |
| IMRT | 320 | 560 | 890 | 1440 | 1780 | 2530 |
| **Perineum Skin** | | | | | | |
| Conventional | 3720 | 4380 | 4930 | 5080 | 5200 | 5350 |
| Conformal | 320 | 580 | 2800 | 4770 | 5200 | 5380 |
| IMRT | 1570 | 2290 | 3550 | 4320 | 4830 | 5300 |

Dose to the given percentage of the particular organ volume in cGy. The p values are calculated for paired t-Test distributions, and for italic ones mean values are not statistically different at 0.05 confidence level, except for the skin and perineum region where doses have been measured.

**Results:** With comparable coverage for the planned treatment volume (PTV), the results shown in the table reveal that conformal therapy and IMRT offered significantly better normal tissues sparing than conventional techniques. Integral dose for normal tissues is in favour of conformal therapy but IMRT allows better dose conformity to the PTV. Conformal therapy achieved an overall better skin sparing in particular in the perineum region, which is of clinical relevance. The overall treatment time is 6.5 hours

for Conventional, 7.5 hours for Conformal therapy, and 9 hours for IMRT, with 3 hours, 5 hours and 14 hours for planning time respectively.
**Conclusion:** Conformal therapy and IMRT are significantly superior to conventional technique to allow for normal tissues sparing. IMRT achieves better dose conformation but with higher integral dose than conformal therapy; the later is, however, best to achieve skin sparing. Finally, the overall workload is higher with IMRT than conformal therapy.

**1404** POSTER

**Performance reproducibility of intra-operative radiotherapy equipment – photon radiosurgery system**

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**Background:** Intraoperative Radiotherapy (IORT) can deliver a critical dose to the tumour bed. It is being investigated whether a single high dose of radiation will impart the same clinical benefit as a standard course of external beam therapy. Our centre has four Photon Radiosurgery Systems (PRS) currently used to treat breast and neurological sites. The PRS comprises an x-ray generator, control console, QA tools and a mobile gantry. We investigated the dosimetric characteristics of each source and its performance stability over a period of time.
**Methods:** We investigated half value layer, output decay factor, internal rate monitor (IRM) reproducibility and depth-doses in water. The half value layer was determined by the broad beam method, using high purity aluminium attenuators. To quantify beam hardening at clinical depths, solid water attenuators of 5 and 10 mm were placed between the x-ray probe and attenuators. The ion chamber current was monitored over 30 minutes to deduce an output decay factor. IRM reproducibility was investigated under various exposures. Depth-dose curves in water were obtained at distances up to 35 mm from the probe.
**Results:** The mean energies for the beam attenuated by 5 and 10 mm of solid water were derived from ICRU Report 17 and found to be 12 and 24 keV. The average output level over a period of 30 minutes was found to be 98.9%. The average difference between the preset IRM limit and the total IRM count was less than 0.5%. For breast IORT, the average difference between the calculated and actual treatment times was found to be 0.30% (0.47% for neurological IORT). The beam attenuation in water varied by approximately $1/r^3$.
**Conclusions:** The x-ray sources are stable over time. Most measurements were found to lie within the manufacturer's tolerances and an intercomparison of these checks suggests that the four x-ray sources have similar performance characteristics.

**1405** POSTER

**Radiotherapy of the skin carcinoma of the inner cantus of the eye**

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As 80% of all skin carcinomas develop on the face, the functional and aesthetic sequelae of the treatment are of paramount importance for the patient. Inner canthus of the eye is an anatomically complex region, offering slim chances for a radical excision of tumour with no undesired functional or aesthetic sequelae. Among several treatment options, surgery and radiotherapy are considered as treatment of choice. The main treatment aim is optimal cure with least possible functional and aesthetic damage. The cure rates after radiotherapy and surgery are similar, except that functional and aesthetic sequelae of radiotherapy are less mutilating.
From 1991 to 2004, we treated 61 pts (29 females, 33 males) with non-melanoma skin cancer of the inner cantus of the eye. Biopsy showed that 53 were basal-cell carcinomas, 5 squamous cell and 3 basosquamous cell carcinomas. Mean age of pts was 72, range from 43 to 88 years. All pts were trated by irradiation; 6 of them were primary treated by surgery (two of them 3 times each) and one by electrocoagulation. The follow-up ranged from at least one year to more than 10 years.
From 55 patients treated by irradiation as first treatment there was only one reccurence. In that patient tumor reccured 5 years after irradiatin and was salvaged by operation. Of 6 pts who had surgery as first treatment in 4 pts reccurence was cured by irradiation. Of remaining two, one was cured by second course of postoperative irradiation. Last patient was treated by operation 3 times, then by irradiation and was eventually salvaged by extensive operation with the removal of the eye.
In my opinion radiotherapy is the treatment of choice for skin carcinoma of the inner canthus of the eye, which is evident from the patients photograps taken before and after the treatment

**1406** POSTER

**Low acute and late toxicity with preoperative intensity modulated radiotherapy (IMRT) for rectal cancer**

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**Purpose:** to report the acute and late side effects in a group of patients with rectal cancer treated with pre-operative intensity modulated radiotherapy (IMRT)
**Methods and materials:** Forty three patients with rectal cancer with an amount of small or large bowel inside the small pelvis were treated with preoperative IMRT. Twenty six patients had a primary locally advanced rectum cancer and 17 a local recurrence. To the pelvis, a total dose of 50 Gy (2 Gy/fraction) was given to 14 patients and 44.65 Gy (2.35 Gy/fraction) to 29 patients. Five patients received a boost of 10–20 Gy because they were inoperable.
Inverse planning was performed using the module Helios of the treatment planning system Cadplan. The constraints were set to encompass the PTV within the 95% isodose line while delivering at least 100% to the isocenter. An overdose of maximum 15% was allowed. The dose to small bowel, colon and bladder was minimized. Each IMRT plan with 5 non-equispaced beams was compared with a conventional 3-field plan in order to evaluate the dose reductions of the organs at risk. The acute toxicity was scored for all patients. Twenty six patients had a follow up >6 months (median: 14; range: 6 – 32 months). Late toxicity was scored in this group.
**Results:** A median volume of 71 $cm^3$ (3–239 $cm^3$) and 11 $cm^3$ (0–99 $cm^3$) small bowel were irradiated to the 90% and 100% isodose line, resp. Conventional planning would have increased the median small bowel volumes to respectively 155 and 95 $cm^3$. For large bowel, the volume irradiated to the 90% and 100% with IMRT was 24 $cm^3$(0–178 $cm^3$) and 8 $cm^3$ (0–55 $cm^3$). The median bowel volume (small + large) to the 90% isodose line was 214 $cm^3$ (24–513 $cm^3$), IMRT reduced it to 119 $cm^3$ (15–283 $cm^3$). Overall, no acute grade 3 or 4 toxicity was reported. Twenty eight percent of the patients had a RTOG grade 1 diarrhea and 16% a grade 2. Acute side effects related to the bladder and skin were also low. Only 3 patients had late toxicity: 1 patient had RTOG grade 1 bowel toxicity, and 2 patients had RTOG grade 2 bladder toxicity.
Three of the 33 (9%) operated patients had a pathological complete response. Pathological downstaging was found in 19 of the 33 patients (57%).
**Conclusion**: With a median and maximum volume of 71 and 239 $cm^3$ small bowel to the 90% isodose line, no grade 3–4 acute and late toxicity was reported. IMRT resulted in a significant reduction of the irradiated volume of bowel and bladder. Good pathological downstaging was also found.

**1407** POSTER

**Radiotherapy for bone metastases from Hepatocellular Carcinoma: dose-response relationship between the regression of extra and intra osseous masses.**

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**Purpose:** The aim of this study was to evaluate retrospectively the palliative effect of radiotherapy (RT) for painful bone metastases and the dose-response relationship between the regression of extra soft-tissue and intra destructive osseous masses from Hepatocellular carcinoma (HCC).
**Methods and Material:** From January 2001 to June 2004, 26 patients (38 sites) with painful bone metastasis from HCC were analyzed. The patients received 8 Gy/1fr (single fraction group) in 10 sites, 20 Gy/5Ffr–30Gy/10fr (Moderate dose group) in 16 sites or 40 Gy /20f – 50 Gy/25fr (High dose group) in 12 sites. Irradiated sites were cervical spine (5), thoracic spine (6), lumbo-sacral (10), pelvis(8), long bones(5), others (4) respectively. The volume of extra-osseous soft tissue and intra-osseous masses respectively were measured both before and after radiotherapy periodically on the CT scan. Percent regression = ((pre-RT tumor volume – post-RT tumor volume) / pre-RT tumor volume)*100. Pain control was measured with self assessment questionnaire. Criteria for subjective response were as follows: CR was defined as complete disappearance of pain; PR was defined as 50% improvement in pain. NC meant that pain relief was minimal($\leqslant$50%) or absent. All patients were planning with 3D-RT planning system and were treated with 6MV-X or 10MV-X linear accelerator.
**Result:** Eighty one percent (31/38) showed some type of pain relief (CR_{PR). There were no significant differences in pain relief among the groups (Single fraction 80%, Moderate dose 82% and High dose 83%). The median duration of pain relief was 3.5 months, 5 months and 6months for Single fraction, Moderate and High dose group. High dose group had longer duration of pain relief than single fraction. ($p < 0.05$) In the median