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