2032 POSTER

Clinical aspects of the BEUD, EUD, Deff and gEUD biological doses

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Background: The purpose of this study is to investigate clinical aspects of the biologically effective uniform dose (BEUD), Equivalent Uniform Dose (EUD), Effective Dose (D_{eff}) and generalized Equivalent Uniform Dose (gEUD) in treatment plan optimization and treatment outcome evaluation.
Material and Methods: To investigate the way by which the different biological dose concepts handle different dose inhomogeneity levels, two types of step-wise dose distributions were utilized. For these types of dose distributions, series of different variations were produced having the same mean dose (80 Gy). The values of the BEUD, EUD, D_{eff} and gEUD were calculated for three pairs of dose distributions, which are characterized by small, medium and large target dose inhomogeneities. $D_{50} = 80$ Gy and $\gamma = 1$ or $\alpha = 0.032\ Gy^{-1}$ and $\beta = 0.0032\ Gy^{-2}$ are the radiobiological parameters that were used for the first three concepts and $a = -10$ for the gEUD concept.
Results: The target response probabilities were calculated, for the three pairs of dose distributions, and the respective values of the BEUD, EUD, D_{eff} and gEUD were cross-analyzed. Dose distributions producing the same response probabilities are associated with biological doses, which have the same value at small dose inhomogeneities (only gEUD slightly differs). The values of and EUD coincide at medium dose inhomogeneities, whereas the D_{eff} and gEUD concepts differ from the previous ones. Furthermore, for the two types of dose distributions they have different values, which however produce the same response probabilities. At large dose inhomogeneities, the same characteristics are observed but even more pronounced. Only at very large dose variations can be seen observable differences between BEUD and EUD, which stem from the differences of the Binomial and Poisson models. It is shown that different dose distributions are usually characterized by different mean target doses, D_{eff} and gEUD for the same response probability. For targets that have regions of different radiosensitivity, this problem is even more pronounced.
Conclusions: The examined radiobiological doses should be used together with the corresponding response probabilities for proper treatment plan evaluation and optimization. Furthermore, in the determination of radiobiological parameters or clinical verification of published dose-response relations these concepts should be implemented in a similar way.

2033 POSTER

Concurrent chemoradiation for anal carcinoma in HIV-positive patients with HAART

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Background: We report the clinical outcome of concurrent chemoradiation therapy (CRT) for anal carcinoma in HIV-infected patients under highly active antiretroviral therapy (HAART).
Material and Methods: Between 1997 and 2008, 21 HIV-positive patients receiving HAART were treated with CRT (50.4 Gy at 1.8 Gy/fraction plus 5.4−10.8 Gy external boost; 5-FU: 1000 mg/m^2 on days 1−4 and 29−32, mitomycin C: 10 mg/m^2 on days 1 and 29). A retrospective analysis was performed with respect to tumor response, long-term local control, anal cancer- and overall survival as well as toxicity. Immunological parameters, including pre- and posttreatment CD4-count, viral load, and AIDS-specific morbidity was also recorded during follow-up (median 53, range, 10−99 months).
Results: CRT could be completed in all patients with reduction of chemotherapy and/or RT-interruption in 5 and 5 cases, respectively, which was necessary in 7 patients (33%). Acute grade 3-toxicities occurred in 8/21 patients (38%). Complete response was achieved in 17/21 patients (81%), tumor persistence or early progression was noted in 4/21 patients (19%). Six patients (29%) died, 5 from anal cancer progression, and one from treatment-related toxicity. Five-year local control, anal cancer-specific and overall survival were 59%, 75% and 67%, respectively. The median CD4-count significantly decreased from 347.5 cells/ml before CRT to 125 cells/ml 3 to 7 weeks after completion of CRT ($p < 0.001$). In 6/19 patients (32%), a increase of the HI-viral load was noted. Both parameters returned to pretreatment values during further follow-up. Four patients had opportunistic infections after CRT, none had died from AIDS-related disease.
Conclusion: Our data confirms that in the HAART-era HIV-related anal cancer can be treated with standard CRT without dose reduction. Close surveillance of immunological parameters is necessary.

2034 POSTER

Genistein in amelioration of radiation-induced epiphyseal growth plate injury in growing rats

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Background: Genistein, is a novel radioprotective agent with antioxidant, antiproliferative and antiangiogenic properties, which is currently studied in prevention of a variety of radiation-induced tissue injuries. However, its role on prevention of radiation-induced growth plate injury (RIGPI) has not been studied yet. We planned to study the role of genistein and genistein + zinc in prevention of RIGPI in growing rats when administered prior to fractionated radiation therapy (RT).
Materials and Methods: Forty-two growing (5.5 weeks old) Sprague-Dawley rats were randomized in to one of six study groups each consisting 7 animals: Group 1 fractionated RT alone (R), group 2 genistein alone (G), group 3 zinc sulphate alone (Z), group 4 RT+G (RG), group 5 RT+Z (RZ), and group 6 RT+G+Z (RGZ). In RT (25 Gy total in 3 fractions) arms, the right rear extremity of each animal was irradiated while the contralateral leg was shielded from radiation, as a control. In drug treatment arms, 30 minutes prior to RT, 10 mg/kg genistein and/or 3 mg/kg zinc-sulphate were administered. Genistein and zinc-sulphate injections were performed via subcutaneous and intraperitoneal routes, respectively. Bone growth based on the length of the tibia, femur, and overall limb was calculated 6 weeks after the treatment by utilizing the radiographs obtained on days 0 (first day of RT) and 42 without any animal being sacrificed.
Results: In groups R, G, Z, RG, RZ, and RGZ, the mean growth loss (GL) for the overall limb was 69%, 3.3%, 3.3%, 27%, 37.4%, and 39%, respectively. The limb length discrepancies (LLD) in the same groups were 13.6%, 2.5%, 0.7%, 7%, 9%, and 9%, respectively. When compared with RT alone arm, the GL and LLD differences were significantly lower in each of pretreated arms; RG, RZ, and RGZ arms, respectively (range; $p = 0.0001-0.001$). Differences in either of mean GL and LLD were not significant between groups RZ and RGZ; however both of these groups had significantly higher GL and LLD than group RG. This finding suggests that there are no synergistic or additive actions between genistein and zinc-sulphate.
Conclusions: The results of current study revealed that the genistein has strong radioprotective actions against RIGPI, which is significantly superior to zinc-sulphate. Use of prophylactic genistein in growing children those destined to RT because of various tumors deserves to be tested in clinical trials.

2035 POSTER

Radiobiological modelling of hypofractionated accelerated partial breast irradiation (APBI) with 50 kV x rays from a miniature isotropic source

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Background: Intraoperative radiotherapy (IORT) to the tumour bed with a 50 kV miniature x ray machine (**Intrabeam®**) is applied as a single fraction during surgery or as a post-surgical procedure. However, APBI with other modalities is frequently applied in a hypofractionated scheme. The purpose was to determine isoeffective fractionated doses for late reaction compared with single-dose IORT and to model the local risk of recurrence for fractionated treatment.
Materials and Methods: Models for normal-tissue reaction and local risk of recurrence (Herskind et al., Radiat. Res. **163**:208−15, 2005; Int. J. Radiat. Oncol. Biol. Phys. **72**:1575−81, 2008) were modified to incorporate fractionation. Fractionated treatment with 10 fx in five days was assumed with dose prescription at 1 cm from the applicator surface. The increased RBE of 50 kV x rays was estimated using the linear-quadratic formalism or taken to be constant equal to 1.2 or 1.5. Based on EQD2 for the reference radiation, the risk of fibrosis and local risk of recurrence were determined from clinical dose response curves and given as function of distance from the applicator.
Results: For a 45 mm diameter applicator size, isoeffective fraction sizes yielding the same radius for 50% risk of fibrosis as single-dose IORT were $d = 1.01$ Gy with RBE estimated by the L-Q formalism and $d = 1.64$ Gy if RBE was assumed constant. At these dose levels, the influence of repair of sublethal damage during protracted irradiation was greatly reduced.

The difference in dose prescription point (applicator surface for single-dose IORT, 1 cm distance for APBI) influenced the isoeffective doses for different applicator sizes. The predicted risk of local recurrence was lower after isoeffective hypofractionation compared with single-dose IORT. The reduction was larger with $\alpha/\beta = 10$ Gy than with $\alpha/\beta = 4$ Gy for tumour cells but the size of the sphere of equivalence (within which local control is the same as for external beam RT) was larger than 10 mm in all cases.
Conclusions: All scenarios predicted a sphere of equivalence larger than the 10 mm of tumour bed tissue defined as the target volume in the TARGIT trial. Thus hypofractionated APBI should expand the therapeutic window. However, RBE estimates are sensitive to assumptions of the model at low doses, and the choice of dose depends critically on the actual value of RBE for late reaction. Therefore, the dose-effect relationship for late reaction should be tested in a phase II trial.

2036 POSTER

Potential change of ranking of competing treatment plans when combining radiotherapy with adjuvant chemotherapy: a radiobiological modeling study

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Background: To investigate if the ranking of competing radiation therapy plans with respect to the risk of radiation induced pneumonitis may change when combining radiation with chemotherapy.
Materials and Methods: Eighteen non-small cell lung cancer (NSCLC) patients previously treated with helical tomotherapy were selected for a modeling study. Three competing treatment plans were generated for each patient: the delivered tomotherapy plan, a 3D conformal radiotherapy plan (3D-CRT) and a fixed field, intensity modulated radiotherapy (IMRT) plan. The effect of chemotherapy on the normal lung was modeled as an independent cell killing process by adding a uniform, chemotherapy equivalent background dose of radiation to the entire organ at risk. The pneumonitis risk of each plan was estimated using the most common normal tissue complication probability (NTCP) models.
Results: In the case of radiation alone, NTCP values calculated using the critical volume model predict lower toxicity with both IMRT techniques than with 3D-CRT. However, this ranking order is reversed when a critical chemotherapy equivalent dose is exceeded: the modeling predicts greater toxicity with both IMRT techniques as compared to 3D-CRT. The critical dose causing the ranking to change is 5−15 Gy depending on model parameters. This dose is comparable to the chemotherapy equivalent dose derived from published clinical data. A recent clinical trial at our institution provides an indication that neoadjuvant chemotherapy does not share the risk profile of adjuvant chemotherapy applied following IMRT.
Conclusions: The addition of chemotherapy can influence the optimal choice of radiotherapy technique and planning procedures. Understanding the interaction of chemotherapy and radiotherapy will improve our ability to predict and potentially minimize the individual risk of adverse effects.

2037 POSTER

Involved node and involved field volumetric modulated arc vs. fixed beam intensity modulated radiotherapy for female patients with early stage Hodgkin lymphoma: a comparative planning study

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Background: A comparative treatment planning study was performed to compare volumetric-modulated arc (VMAT) to conventional intensity modulated (IMRT) for involved-field (IFRT) and -node (INRT) radiotherapy.
Materials and Methods: Plans for 10 early stage Hodgkin lymphoma female patients were computed for VMAT and IMRT. First, the planning target volume (PTV) coverage and organ at risk (OAR) dose deposition was assessed between the two modalities. Second, the OAR's Dose-Volume Histograms (DVHs) were computed and compared for IFRT and INRT, respectively.
Results: For IFRT and INRT, PTV coverage equally homogeneous with both VMAT and IMRT. By and large, the OAR irradiation with the IFRT planning paradigm was not significantly different between VMAT and IMRT, except for occasional dose metrics computed for the lung ($D_{33\%}$ 9.4±1.7 *vs.* 10.2±1.5 Gy; $p = 0.03$) and breast ($D_{1\%}$ 13.7±8.1 *vs.* 15.2±7.9 Gy; $p = 0.03$). For INRT, doses computed for VMAT were usually lower than those with IMRT, particularly so for the lung and breast. Compared to IMRT, the planning of VMAT leads to a significant decrease of the non-target tissue irradiation for IFRT (mean, 7.1±1.8 *vs.* 6.7±1.9 Gy; $p < 0.001$) and INRT (mean, 5.3±1.7 *vs.* 5.1±1.8 Gy; $p = 0.003$). Regardless of VMAT and IMRT modalities, a significant OAR's computed mean doses of 20 – 50% was observed with INRT when compared to IFRT.
Conclusions: VMAT and IMRT results in similar level of dose homogeneity. With INRT but not IFRT planning, the computed doses to the PTV and OAR's were usually higher and lower with VMAT when compared to IMRT. INRT when compared to IFRT planning led to a consequential decrease in OAR's computed doses.

2038 POSTER

Impact of PET-CT on radiotherapy planning and prediction of primary radiotherapy effects in non-small-cell lung cancer

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Background: PET-CT (positron emission tomography – computed tomography) is increasingly used in the clinical management of many cancers. Compared to existing diagnostic imaging modalities, the presence, location and extent of lesions may be more accurately ascertained with PET-CT. PET(-CT) is also useful to evaluate the proliferative activity of cancer tissue. We examined the impact of PET-CT on radiotherapy planning and prediction of primary radiotherapy effects in non-small-cell lung cancer.
Materials and Methods: Subjects comprised 24 patients with primary non-small-cell lung cancer. Pre-treatment PET-CT was performed in each patient, and radiotherapy was planned using a 3-dimensional radiotherapy planning system (Pinnacle$^{3\&\,®}$). All patients received radiotherapy at a total dose of 60–70 Gy.
First, chest CT was performed with the radiotherapy-planning CT and the results were sent to Pinnacle^{3}®. Next, referring to diagnostic imaging findings from other imaging modalities except for PET-CT, the location and extent of the primary lesion, regional lymph nodes were determined on Pinnacle^{3}®. Then, based on pre-treatment PET-CT findings, they were corrected. Lastly, irradiation fields were defined based on corrected lesion location and extent, and the usefulness of PET-CT on radiotherapy planning was investigated. Diagnostic chest CT was performed with each patient before radiotherapy and 4 weeks after radiotherapy to calculate the reduction ratio. Based on these values, the correlation between primary radiotherapy effects and SUV (standardized uptake value) max of pre-treatment PET-CT was determined.
Results: The primary lesion of all patients was clearly depicted by PET-CT. As far as the extent of lesion progression, which is difficult based solely on radiotherapy-planning CT scans, PET-CT made this easy to ascertain. Regarding lymph node metastasis, PET-CT was useful in identifying all lesions, including small lesions that were difficult to detect by other imaging modalities. The reduction ratio ranged from 3.4 to 87.9 percent, and SUV max of pre-treatment PET-CT ranged from 4.3 to 21.3. The reduction ratio was significantly correlated with SUV max of pre-treatment PET-CT.
Conclusions: PET-CT provided valuable information about gross tumor volume, and also detected unsuspected nodal disease. Therefore, PET-CT is very useful in radiotherapy planning for non-small-cell lung cancer. PET-CT is also useful for prediction of primary radiotherapy effects.

2039 POSTER

Comparison of conventional 3D RT for pelvis and sequential 3D boost plan for prostate versus IMRT plan for pelvis and sequential IMRT boost plan for prostate versus IMRT SIB (pelvis with prostate) versus IMRT SIB (pelvis with prostate) and sequential IMRT boost plan for prostate

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Background: To compare treatment plans in pelvis and prostate irradiation, from standard 3D conformal photon therapy versus sequential intensity modulated radiation therapy (IMRT) of pelvis and then prostate versus simultaneous integrated boost (SIB) of pelvis and prostate versus sequential SIB (pelvis plus prostate) and then IMRT (prostate only), in the radiotherapy management of high-risk prostate cancer.
Materials and Methods: We performed a planning study on a selected patient using 3DRT and IMRT Varian Eclipse 6.5 planning system. We considered: (1) the conventional 3D plan for initial whole-pelvic irradiation (50 Gy, 25×2 Gy) and sequential 3D boost plan for prostate and seminal vesicles (28 Gy, 14×2 Gy); (2) the IMRT plan for initial whole-pelvic irradiation (50 Gy, 25×2 Gy) and sequential IMRT boost plan for prostate and seminal vesicles (28 Gy, 14×2 Gy); (3) IMRT SIB (56 Gy, 35×1.6 Gy, to pelvic lymph nodes and 74.2 Gy, 35×2.12 Gy, to prostate and seminal