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

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

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.

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

I. Fraunholz[1], C. Weiss[1], K. Eberlein[1], A. Haberl[2], C. Rödel[1]. *[1]J.W. Goethe-Universität, Klinik für Strahlentherapie und Onkologie, Frankfurt (Main), Germany; [2]J.W. Goethe-Universität, Innere Medizin Klinik II, Frankfurt (Main), Germany*

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.

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

E. Topkan[1], A.A. Yavuz[1], R. Erdem[2], D. Bacanli[3], C. Onal[1], O. Yuksel[1], M.N. Yavuz[1]. *[1]Baskent University Faculty of Medicine, Radiation Oncology, Adana, Turkey; [2]Baskent University Faculty of Medicine, Pharmacology, Ankara, Turkey; [3]Baskent University Faculty of Medicine, Experimental Animals Breeding and Research Center, Ankara, Turkey*

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.

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

C. Herskind[1], F. Wenz[1]. *[1]University Medical Center Mannheim University of Heidelberg, Dept. of Radiation Oncology, Mannheim, Germany*

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.