Further Development of Spinal Tissue Radiotherapy Retreatment Modelling, with inclusion of Hadrontherapy.

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Purpose: Radiotherapy retreatment (radical or palliative) is useful in selected patients. Two recent publications provided methods for estimating changes in spinal radio-tolerance with time between initial radiotherapy and retreatment, but with important limitations.

Materials and methods: A model was developed to find a temporal relationship between the percentages of the tolerance biological effective doses (%BED) for two treatment courses. The primate data of Ang et al. (2010), isoeffective for a 10% incidence of myelitis, with re-treatment intervals of 1, 2 and 3 years provided the fitting parameters. As summarised in Jones and Hopewell (2014), rodent studies used shorter intervals (~6 months), spinal tissue recovery starts around 70 days after first treatment courses, and appears dose related (experiments showed little or no recovery six months after initial low dose treatments around 20-30% of %BED tolerance).

Thus recovery displays different time scales contingent on the initial dose. In the longer term, slow normal tissue turnover may allow recovery after low initial doses. This is consistent with lack of reported clinical experience of severe effects in low dose regions of the central nervous system, away from the primary target volume of the initial treatment, when compared with fully treated volumes at extended re-treatment times.

Results: The previous work is modified to incorporate the above processes to yield estimates for BED1, the %tolerance BED after an elapsed time, t, and BED, the initial %tolerance BED dose. The Probit model is used to extrapolate from primate data to the clinical situation, where the incidence of myelitis is much lower.

Conclusions: The new model allows re-treatment dose estimation within the time window of 70 days to three years after the initial course, and can be adapted for hadrontherapy. It should be used cautiously in clinical practice by choosing doses lower than predicted.

References:


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Heating caused by pulsed proton beam energy deposition generates a thermoacoustic signal. Based on time-of-flight (TOF) calculations, the arrival time of the acoustic waves can be used to verify the range of the proton beam (1, 2). The goal of this work is to assess the clinical potential of the technique by experimentally measuring the acoustic signal generated by a proton beam from a hospital-based source and to measure the accuracy of the TOF range verification.

To create a short, intense pulsed proton beam in a hospital setting, an electronic function generator was used to modulate the IBA C230 isochronous cyclotron at the University of Pennsylvania's Roberts Proton Therapy Center. A submerged hydrophone measured the acoustic emissions generated by the proton beam in water. The acoustic measurements were repeated with variable proton current and increasing distance between detector and beam. To model the expected acoustic signal, simulations were performed and compared to experimental results.

The cyclotron produced proton spills with pulsewidths of 18 µs and a maximum measured instantaneous proton current of 790 nA. The collected acoustic signal was on the order of mPa, and the pressure amplitude increased monotonically with increasing proton current. Based on the observed relationship between detector distance and acoustic arrival time, the measured signal originated in the proton beam dose deposition volume. The acoustic frequency spectrum peaked at 10-20 kHz. At a single detector position, the arrival time can be measured with a standard deviation of 0.6 µs (1 mm). The difference between simulated and measured acoustic arrival times has a standard deviation of 0.9 µs (1.4 mm).

We report the first observation of acoustic emissions generated by a proton beam from a hospital-based clinical cyclotron. Based on the methods presented, acoustic-based techniques may provide <2 mm (standard deviation) accuracy in verification of proton range.

Keywords: Proton range verification, acoustics, time-of-flight
Water based 3D optical dose imaging for particle therapy

115

fluorescent show some concentration dependent quenching. ionisation chamber, while those measured with the pure water show a good agreement with those of an allowing for high quality imaging. Bragg curves measured in approx. 50 photons/MeV were produced in the solution, visible light. In experiments with 90 MeV proton beams the proton Bragg peak with submillimeter accuracy. Medical Physics 42(2):567-574.

116

Water based 3D optical dose imaging for particle therapy

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Purpose: Scanned ion-beam delivery offers the highest confinement of target dose in external beam radiotherapy. However, fast and accurate patient-specific quality assurance is challenging. The current clinical standard for verification of dose distributions with a 2D array of ionization chambers (ICs) is slow and not very suitable for dose delivery using scanned ion-beams because the response of the ICs is not necessarily independent of beam size and position with respect to the IC.

At present, no suitable method for rapid verification of dose distributions for scanned ion-beam delivery is commercially available.

Materials/methods: We are developing a fast QA technique based on the UV light produced by swift ions in water (Fig 1A). Using fast, UV sensitive CCD cameras we measure the light distributions from which the dose distribution is reconstructed [2]. The system consist of a water tank in which ion beams are stopped and low noise, high sensitive CCD cameras (Fig 1B), which register the light distribution produced by each of the many subsequent ion beams that compose the treatment plan. Data can be taken in two modes: integral and differential (synchronized with beam delivery), thus allowing the detailed reconstruction of the contribution of each individual beam to the dose distribution.

Results: We have built a prototype optical dose imaging system to demonstrate the potential of this method for 3D dose scanning in clinical conditions (to verify actual treatment plans in particle therapy clinics). We demonstrated the feasibility of optical imaging of the full 3D dose distribution in water with a small (<1% by weight) admixture of a nontoxic, low-cost fluorescent emitting visible light. In experiments with 90 MeV proton beams approx. 50 photons/MeV were produced in the solution, allowing for high quality imaging. Bragg peaks measured in pure water show a good agreement with those of an ionisation chamber, while those measured with the fluorescent show some concentration dependent quenching.

Conclusions: The presented novel method resolves the issues of the QA techniques currently used in particle therapy: it has high position resolution in three dimensions, features direct measurement in the reference material water, and is fast as the whole dose distribution is imaged in a single dose delivery.

Keywords: particle therapy, Quality Assurance, 3D dosimetry

References:

Figure 1. A. Imaging principle: raw 2D image measured with a 360 MeV He-beam. B. Schematic drawing of the set-up with the proton gantry nozzle.

Fast dose modulation in proton therapy with continuous line scanning

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Purpose: The accuracy of scanned proton therapy suffers from respiratory or cardiac motion during irradiation: the discrete scan pattern can interfere with the induced motion of the target yielding regions of over- and underdosage [1]. Applying the same field multiple times with proportionally reduced dose – commonly referred to as rescanning – can help averagin out such interferences [2]. However, dead

References:

116

Low-dose-rate irradiation induces up-regulation of genes involved in suppression of cancer progression

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Chronic low-dose rate irradiation has been shown to be beneficial in a variety of animal models including cancer. To assess the specific transcriptional changes that tumor-bearing mice would have manifested upon LDR in comparison with that of normal mice undergoing LDR irradiation, we investigated the expression of DNA repair and damage-associated genes in the thymus of naturally occurring tumor-bearing AKR/J and normal ICR mice following low-dose-rate (LDR, Cs-137, 0.7 mGy/h, a cumulative dose: 1.7 Gy) irradiation. Thymuses were collected at 100th day post irradiation and analyzed using whole-genome microarray, quantitative reverse transcription polymerase chain (qPCR), and western blot. The thymus weight was decreased and survival rate was increased in LDR irradiated AKR/J mice while no significant changes were found in normal ICR mice.

qPCR analysis demonstrated Serpine1, Mmp3, Gzmc, Neil2, Pixin1, Rnd3, Cyp11a1, Ptg2 were specially altered in LDR-irradiated AKR/J mice but not in ICR mice. By performing Western blot, we found that Pixin1 and Rnd3, genes involved in suppression of melanoma progression, were upregulated while Cyp11a1, a gene contributes to tumor immune escape, was downregulated in LDR-irradiated AKR/J mice, but not ICR mice. These results suggest that LDR γ-radiation suppressed early stage of carcinogenesis and removed cancer cells from body by stimulating apoptosis and immune-mediated mechanisms. Therefore, LDR may offer significant benefit for the patients with solid cancer, which has traditionally been thought to be a relatively radiotherapy-resistant tumor.

Keywords: Low-dose-rate, Radiation, mice, cancer suppression, genes