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Correlation between dosimetry quantities and cell survival for microbeam radiation therapy

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Spatially fractionated radiation therapy (SFRT) has shown promise in increasing the therapeutic window compared to conventional irradiation techniques. However, which dose parameter best correlates highly modulated dose distributions with cellular and clinical endpoints remains unresolved. The aim of this work was to determine the predictive value of several physical and biological dose quantities with regard to cell survival. A human fibroblast cell line (MRC5) and two tumor cell lines (LN18 and A549) were irradiated with 225kV x-rays over a range of doses with uniform and microbeam radiation therapy (MRT). The MRT field had a slit width of 50μm and a center-to-center spacing of 400μm. Cell survival for uniform and MRT irradiation were analyzed in terms of average dose, peak dose, valley dose and the equivalent uniform dose (EUD). Dose uncertainties were evaluated through measurements and error modeling. Cell survival plotted as a function of EUD matched uniform irradiation within the estimated uncertainties and was the most predictive quantity followed by the valley dose. Average and peak doses showed poor correlation with invitro cell survival. Enhanced cell killing was observed for both tumor cell lines (1.1 for LN18 and 1.3 for A549 at 8 Gy EUD) for MRT compared to uniform irradiation. Normal human fibroblasts showed reduced cell killing for MRT relative to uniform irradiation (0.6 for MRC5). Modeling revealed that EUD uncertainties are strongly dominated by valley dose uncertainties, especially at high doses, highlighting the importance of accurate dosimetry. EUD is preferred over physical dose quantities for comparisons of SFRT and uniform irradiation. The results suggest an increase in survival of normal-human fibroblast cells and reduced survival for both tumor cell lines after SFRT relative to uniform irradiation. Further work is required to independently confirm these findings for different beam types and MRT geometries.

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