

On the use of pulsed reduced dose rate for improvement of the therapeutic ratio

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This work demonstrates three related aspects of the efficacy, delivery, and verification of pulsed reduced dose rate radiotherapy (PRDR). PRDR is a method of irradiation designed to minimize radiation-related toxicities in patients undergoing reirradiation for loco-regional recurrence of glioblastoma. PRDR uses 0.2GyX10fx daily doses delivered over a 30-minute time span. Under PRDR treatments, a subset of patients have had an unexpectedly positive response to treatment.

It was a primary goal of this project to determine if low-dose hyper-radiosensitivity was a contributor to the increased radio-response from these patients. This was done through the use of human T98G glioma and HT29 colorectal cells, and V79.379-A Chinese hamster fibroblasts with drug inhibition of the p53 and PI3K pathways. Radiation was delivered with a medical linear accelerator in either 2Gy acute doses or through PRDR. Methods used to analyze the effect of these techniques included clonogenic assay, flow cytometry, and western blots. Comparison of survival ratios demonstrated no decrease in efficacy for either the standard T98G or HT29 cell lines when using PRDR as compared to an acute dose. T98G with PI3K inhibition and V79.397-A cells demonstrated a decreased efficacy of treatment using PRDR relative to an acute dose. These results suggest an equivalency in tumor treatment with a possible improvement in normal tissue toxicities for the PRDR method.

An additional method of delivering PRDR through the use of Tomotherapy was proposed and demonstrated to be accurate. Tomotherapy planning forces the short leaf open times for individual MLC projections from low dose fractionation closed, resulting in an undeliverable plan due to the loss of a large number of usable projections. Application of a virtual grid with directional blocking allows for the output from useable segments to be above this threshold, resulting in a deliverable treatment plan.

Finally, analysis was performed on a proposed QA method for in vitro studies that can be applied to IMRT plans. This method uses a model-based conversion to electronic portal images that allows direct comparison to a water-based planar fluence. Using 188 IMRT fields, 2D diode measurements were compared to converted EPID dose planes resulting in good agreement.