A Preclinical Research Platform for FLASH and Spatially Fractionated Radiation Treatment

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Objectives: Spatial and temporal factors have long been known for their impact on modifying the therapeutic ratio of tumor control over normal tissue sparing in radiation treatment. FLASH radiotherapy (RT) and SFRT are two RT techniques that modulate radiation delivery in time and space, respectively. Despite transformative potential of these techniques, their clinical translation has not been broadly implemented, mainly due to limited systematic studies to understand underlying biological mechanisms and the impact of dosimetric and geometric parameters on the biological response. The significant hurdle for the systematic laboratory investigations has been the reliance on advanced irradiation systems that are less accessible to the community. To overcome this obstacle, we have developed a novel preclinical platform for FLASH RT (i.e., FLASH-SARRP) utilizing two high capacity x-ray sources in a parallel-opposed geometry. This study aims to evaluate the feasibility of implementing x-ray pencil beam scanning (PBS) capability on the FLASH-SARRP for effective, systematic laboratory investigations of spatial fractionation and FLASH RT, alone or together.

Methods: Dosimetric performance of the x-ray source (RAD44, Varex) used for FLASH-SARRP was characterized at the close distance (61 mm SSD) to x-ray focal spot. A micrometer driven 0.1 mm x 40 mm slit beam was scanned across the x-ray source to establish nominal center of focal spot with respect to the mechanical center of x-ray tube outlet. X-ray PBS will be facilitated using small circular and slit aperture beams with openings of 0.5 mm and larger, fabricated from tungsten collimator plate. Measurements were made by EBT3 films and TLD calibrated at the ADCL at University of Wisconsin. The dosimeters were placed at diffirent depths in a 20-mm thick kV plastic water phantom. Measured dose profiles were reconstructed by the superposition of the single beam data, simulating SFRT capability by scanning a single pencil beam.

Results: Our measurement shows that center of focal spot is within 1 mm from the mechanical center of the RAD44. Uniformity of beam intensity within a 1.0 mm diameter of the nominal source position is < 3% for a single beam and < 1% for the parallel-opposed beams arrangement. This high degree of uniformity relaxes the alignment tolerance of parallel-opposed apertures. A wide range of peak-to-valley dose ratios from 1.3 to > 50 can be achieved at both FLASH and conventional dose rates for an extended range of field sizes from 0.5 mm to > 5 mm. Peak dose rate from a single x-ray source for 1-mm circular aperute were 56.5, 40.5, and 32.0 Gy/s at 1, 5, and 10 mm depths in the phantom, respectively. For parallel-opposed sources, the corresponding dose rates were 74.6, 61.7, 64.9 Gy/s. This data suggests that a single x-ray source can be utilized for superficial and shallow-depth targets (< 5 mm), and parallel-opposed sources are appropriate for deeper targets (10 mm) in FLASH-SFRT.

Conclusion(s): The dosimetric results support the feasibility of x-ray PBS system on the FLASH-SARRP. A computer-controlled robotic positioning system will be implemented to facilitate PBS by translating a mouse bed in 3D Cartesian motion, with appropriate range of motion, speed, and positioning accuracy.