

MONTRÉAL, QUEBEC AUGUST 27 - 30, 2023



17TH INTERNATIONAL CONGRESS FOR RADIATION RESEARCH



Influence of the Bragg peak on average vs instantaneous dose rate for proton FLASH biological studies

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Due to technical limitations in modulating spot energy to maintain Ultra-High Dose Rates (UHDR), the FLASH effect in proton beams has recently been studied in the plateau region delivered at maximal energies (250 MeV). This type of delivery has limited clinical applications, since it sacrifices the dose escalation property of Bragg peaks and maintains a uniform exit dose that irradiates all normal tissues both upstream and downstream of the tumor. Plans to exploit the FLASH effect in proton therapy naturally expect to capitalize on the Bragg peak by modulating the proton energy across the tumor site.

In this study, a plastic scintillator based optical fiber dosimeter capable of ultra-fast time resolution (2.5 ms) was used to measure the percent depth dose of 250 MeV proton beam scanned across a small area $(3.5 \times 3.5 \text{ cm}2)$. The scintillator was shown to be repeatable and linear with dose, though there was a small but reproducible decrease (~30%) in response at low energies. More importantly, as the scintillator can be used to measure the precise proton beam delivery times at various depth, one can calculate the average (*D*) and maximum instantaneous dose rate (*D*max) as a function of depth. This is particularly beneficial in the Bragg peak.

Our results show that as the proton spot becomes wider with depth, the time to deliver the entire dose increases by a factor of ~1.7 between the entrance dose (3 cm) and the Bragg peak. The average dose rate consequently varies from 52.7 Gy·s-1 at the entrance to 29.3 Gy·s-1 at mid-depth, to 70.4 Gy·s-1 at the Bragg peak. While the impact of the increase in delivery time on average dose rate is mitigated by the increase in the dose at the Bragg peak, the maximum instantaneous dose rate decreases from 472 Gy·s-1 near the entrance to 236 Gy·s-1 at the Bragg peak.

Since the literature shows that the FLASH effect is typically only observed at dose rates ≥40 Gy·s-1, this has profound implications on the ability of investigators to maintain the UHDR necessary to trigger the FLASH at or near the Bragg peak. While these results would be improved overall by increasing beam current, the fact remains that the highest instantaneous dose rates are seen near the beam entrance. Furthermore, dose rates near the Bragg peak, where organs at risk would normally be situated, will see the least benefit from the FLASH effect.



Figure 1. Difference in the time-dose profiles for the dose delivered at mid-plane (left) vs the Bragg peak (right). UHDR delivery at the Bragg peak takes nearly twice as long to execute, and the instantaneous dose rate is generally lower than that at shallower depths.