Pencil Beam Scanning FLASH Radiotherapy Increases Acute Gastrointestinal Toxicity

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Current radiotherapy treatment for abdominal and pelvic cancers typically results in some form of acute gastrointestinal (GI) toxicity in patients. X-ray irradiation to deep-seated abdominal tumors typically results in notable damage to normal tissue preceding it. Recent studies suggest that ultrahigh dose rate "FLASH" radiotherapy (~40 Gy/s) reduces normal tissue toxicity using electron beam and proton radiation. However, prior proton FLASH studies used clinically inapplicable delivery methods. Hence, in this study, we utilized pencil beam scanning (PBS) FLASH proton irradiation, which has already been implemented in recent clinical trials, to investigate the effects on the GI tract. PBS FLASH and conventional (CONV) proton irradiation had been exposed to mouse intestinal tissue. Immunohistochemistry, immunofluorescence, complete blood counts (CBCs), crypt microcolony assays, and FITC-dextran assays were performed on isolated intestinal tissue samples. No significant differences were observed in the immunohistochemistry and immunofluorescence. CBCs revealed a significant decrease in circulating white blood cells between the control and irradiation groups ($p<0.05$). Furthermore, the FITC dextran assay revealed no significant difference in fluorescence intensity within the PBS proton irradiated group ($p> 0.05$). With this being the first study to investigate the effects of PBS FLASH irradiation on GI toxicity, it should be noted that PBS FLASH may result in increased acute GI toxicity in comparison to PBS CONV which does not depend on direct crypt cell killing.