FLASH-RT (Ultra-High Dose Rate) Minimizes Neurocognitive Complications and Normal Tissue Pathology Without Compromising Brain Tumor Control

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Abstract

OBJECTIVES: Radiotherapy is a major contributor for cancer cure and improving its therapeutic index remains one of the most important priorities in oncology. With the purpose of improving the therapeutic index, we have explored the potential beneficial effects of increasing the dose rate during radiotherapy.

METHODS: Our team at the CHUV/Lausanne has pioneered the development of FLASH radiotherapy (FLASH-RT), which represents an innovative modality of irradiation involving ultra-high dose rates, i.e. a thousand times higher than the conventional dose rates used in clinical practice. Using various preclinical mouse models, a prototype LINAC able to deliver ultra-high dose rates and calibrated via solid physical dosimetry was used to contrast the impact of FLASH-RT against more standard conventional (CONV) dose rate deliveries.

RESULTS: Past work has shown that FLASH-RT (> 40 Gy/s) markedly increased normal tissue tolerance to irradiation, which we termed the FLASH effect. Here we will present the collaborative work performed between UCI and CHUV, in which we explored the FLASH effect in the brain with and without glioblastoma tumors. Findings with FLASH point to significant neurocognitive sparing with reductions in neuroinflammation and a preservation of neuronal morphology when compared to CONV. The basis of these beneficial FLASH effects are in part, explained by reduced oxygen toxicity leading to radioprotection of the normal tissue but not the tumor, as FLASH and CONV were iso-efficient at tumor control.

CONCLUSIONS: FLASH provides an innovative approach for improving radiotherapy, by exploiting differences in oxygen tension between tumors and normal tissue for significant therapeutic gain.