

PhD Thesis Title: Facilitating the Clinical Translation of Flash Radiotherapy Through Dosimetry Development and Beam Parameter Optimization

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ABSTRACT:

Radiation therapy (RT) is a cornerstone of cancer treatment, used in over half of U.S. cancer patients. Its aim is to cure disease by maximizing the therapeutic index—effectiveness against tumors while minimizing damage to normal tissues. A promising development, ultra-high dose-rate (UHDR) RT—delivered at ≥ 40 Gy/s in ≤ 200 ms—has shown the ability to spare normal tissue without compromising tumor control, a phenomenon known as the FLASH effect.

While multiple preclinical studies have demonstrated the FLASH effect, inconsistencies in outcomes suggest that the current definition—based solely on mean dose rate and total treatment time—is insufficient. These discrepancies are likely due to underreported and variable beam parameters, compounded by limitations in existing dosimetry systems that struggle to capture UHDR-specific metrics.

To address these gaps, we propose a comprehensive approach to improve measurement accuracy and systematically characterize the FLASH effect. Our goals are to establish reliable real-time monitoring, develop next-generation dosimetry tools, and optimize beam parameters for therapeutic gain. The project includes three specific aims:

- **Aim 1:** Implement real-time beam monitoring for electron UHDR RT. We will use beam current transformers (BCTs) calibrated to dose-rate independent dosimeters (e.g., Gafchromic film, OSLDs/TLDs) to measure key parameters (e.g., dose, dose per pulse, mean/instantaneous dose-rate). We hypothesize that this system will achieve dose uncertainties $< 5\%$.
- **Aim 2:** Develop ion chambers optimized for UHDR dosimetry. In collaboration with Standard Imaging Inc., we will engineer ion chambers with reduced electrode spacing and high electric fields (≥ 1000 V/mm) to minimize recombination and polarity effects, enabling accurate measurements (within 5 %) for dose per pulses of up to 5 Gy.
- **Aim 3:** Determine optimal beam parameters for maximizing the FLASH effect. Through controlled in vivo experiments, we will assess how variations in dose, dose per pulse, instantaneous dose rate, and radiation type influence tissue sparing and tumor control. We aim to identify beam settings that minimize GI toxicity without sacrificing therapeutic efficacy.

Impact: This work will define essential beam parameters for the FLASH effect, establish infrastructure for accurate UHDR dose measurement, and guide future FLASH RT clinical trials and mechanistic studies. It represents a crucial step toward safely translating FLASH RT into clinical practice.

References to author publications that relate specifically to the dissertation:

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