

## First test of an ionoacoustic imaging system for dose monitoring in FLASH proton therapy

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Recently, the use of ultra-high dose rates (FLASH) in radiation treatments has emerged as a new promising modality, where a pulsated ultra-high dose rate ( $>40$  Gy/s) is delivered in comparison to conventional radiation therapy ( $\sim 0.05$  Gy/s). FLASH radiotherapy has demonstrated an unprecedented ability to reduce healthy tissue toxicity while maintaining tumor control, as shown in several in vivo preclinical [1-6] and early clinical [7] studies performed mostly with electron beams. However, these studies have also revealed the associated risks FLASH-RT may have for clinical implementation without proper real-time “image-pulse” guidance to mitigate discrepancies between planned and delivered dose. The clinical translation of this technique is limited by the lack of proper dosimetric methods that can accurately measure, in real-time, the dose distribution in deep tissues as expected from modern proton to ensure its safe delivery in such high-risk mode [8,9].

On the other hand, FLASH radiotherapy using protons is expected to be the de facto therapy for deep-seated tumors and pediatric tumors, because it can combine FLASH tissue sparing with the spatial advantages of protons to shape the dose (Bragg peak) [10-12]. However, its associated higher risks with respect to conventional proton therapy without proper real-time “image-pulse” guidance results in barely a few preclinical studies [6,7] of the FLASH effect, and just one clinical study that has recently announced the completion of accrual for symptomatic bone metastases [13]. Therefore, there is an urgent need that demand investigating the unknown physical requirements (e.g., dose/pulse, dose/s, pulse width, beam size, etc.) of the proton beam to produce tumor control while sparing healthy tissues [14].

This work aims to overcome these two challenges by leveraging the concept of ionizing radiation acoustic dosimetry, where acoustic waves are generated following the absorption of pulsated high energy radiation. In this work, an ionizing radiation-induced acoustic imaging (iRAI) system has been developed to achieve real-time pulse-by-pulse 3D dose monitoring using FLASH dose rates with proton beams. Furthermore, the combination of iRAI with an ultrasound imaging system will facilitate the mapping of dose on anatomical structures [15,16].

This dual system has been tested at the Massachusetts General Hospital (USA) in tissue-mimicking phantoms. A description of the system and preliminary results will be presented. In addition, future work combining proton FLASH dosimetry and its correlation to tissue damage/toxicity response will be discussed to achieve a better understanding of the physical requirements to produce the FLASH effect during proton delivery.

### References

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