

Open questions in FLASH therapy for a successful clinical translation

Sebastien Penninckx

Radiotherapy Department, Institut Jules Bordet – Hopital Universitaire de Bruxelles, Brussels, Belgium
Radiophysics Lab, Faculty of Medicine, Université Libre de Bruxelles, Brussels, Belgium

Increasing the therapeutic ratio is one of the most significant challenges of modern clinical radiation oncology. To achieve this, there has been increasing interest in novel therapies, with the aim of selectively killing cancer cells whilst sparing normal tissues. FLASH radiotherapy (RT) is an emerging technology that involves the ultra-fast delivery of ionizing radiations at dose-rates several thousand times higher than the ones currently used in routine clinical practice. While a similar tumor cell killing efficacy was reported in both conventional and FLASH-RT, *in vivo* studies have shown that the latter limits radiation-induced damage in healthy tissues. This reduction of normal tissue toxicity enables FLASH-RT to overcome one of the main limitations of modern RT. It has the potential to revolutionize radiation oncology field by becoming a standard in future clinical practice.

Despite these promising outcomes, several key questions remain before this technique can be successfully implemented in the clinical setting. In this presentation, some of the breakthroughs we have achieved at Jules Bordet institute will be highlighted, showcasing our progress in advancing FLASH technology. The major challenges that still need to be resolved for a successful clinical translation will be discussed, including the mechanisms behind the FLASH effect, the optimization of dosimetry and the optimal fractionation schedule. By discussing these open questions, we aim to provide insights into the pathway towards the successful clinical translation of FLASH therapy and the development of this cutting-edge treatment modality.