FLASH Radiotherapy - How Ultrafast Treatment Modalities Stand to Revolutionize Cancer Care

Charles Limoli, PhD, Marie-Catherine Vozenin, PhD

Fractionation schedules have evolved over the decades to minimize normal tissue toxicities that dictate the maximum tolerated doses used for curative intent. While advancements in tumor imaging and targeted beam delivery have improved the therapeutic ratio, recent data implementing ultra-high dose rate FLASH radiotherapy (FLASH-RT) may soon provide clinicians with enhanced capabilities to control tumor growth while greatly limiting normal tissue injury. The realization that dose rate can be an effective and adjustable parameter in the clinic has surprised the field of radiation oncology, and has mobilized investigators to rationalize the mechanistic basis underlying the "FLASH effect". Recent data from others and us have pointed to the importance of oxygen in modulating the FLASH effect, and theoretical arguments have implicated divergent radiochemical mechanisms that may account in part, for the divergent response of normal tissues to ultra-high versus more conventional dose rates. Data will be presented that demonstrates the differential impact of oxygen tension on tumor response and normal tissue toxicities using preclinical models exposed to FLASH or conventional dose rate irradiation.