Ruprecht-Karls-Universität Heidelberg
Medizinische Fakultät Mannheim
Dissertations-Kurzfassung

The Radiochemical Basis of FLASH and Minibeam Radiotherapy: Investigating H_2O_2 Production and Diffusion

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Background: FLASH and minibeam radiotherapy (MBRT) have emerged as promising approaches to enhance the therapeutic ratio in radiation therapy by selectively sparing normal tissues while maintaining effective tumor control. Despite their potential, the underlying radiochemical mechanisms remain incompletely understood, particularly regarding hydrogen peroxide (H_2O_2) production and diffusion under ultra-high dose rate (UHDR) conditions.
Purpose: This dissertation investigates the radiochemical basis of FLASH and MBRT, focusing on the dose-rate dependency of H_2O_2 production and its diffusion dynamics in both pure water and biological-relevant tissues. By elucidating these processes, this work aims to provide insights into radiochemical mechanism and advancing the clinical implementation of these novel radiation therapy modalities.
Methods: H_2O_2 production was quantified under different radiation sources—including electron, X-ray, and carbon-ion beams—across UHDR and conventional dose rates (CONV). And the impact of scavengers, carbon dioxide (CO_2), and multiple UHDR pulses on H_2O_2 kinetics was also examined. Additionally, a novel diffusion-absorption model was developed to simulate the H_2O_2 distribution under MBRT, and compared with previous aniaml experiments.
Results: The findings revealed a significant dose-rate dependency in H_2O_2 production, with UHDR irradiation leading to lower H_2O_2 yields than CONV. This effect was attributed to the enhanced removal of hydroxyl radicals (•OH) under UHDR, mediated by solvated electrons. Experimental results also demonstrated that CO_2 presence increased H_2O_2 production, further influencing radiochemical kinetics. In MBRT, H_2O_2 diffusion played a crucial role in dose homogenization over time, with the refined diffusion model accurately predicting its various MBRT treatment outcome.
Conclusion: This dissertation provides novel insights into the radiochemical foundations of FLASH and MBRT, particularly concerning H_2O_2 production and diffusion mechanisms. The results contribute to refining theoretical models and optimizing treatment strategies for these emerging radiotherapy techniques. Future research should focus on validating these findings in preclinical and clinical settings to facilitate the translation of FLASH and MBRT into routine clinical practice.