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Modeling the FLASH mechanism on multiple scales

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The mysterious differential effectiveness of ultra-high dose rate (UHDR) irradiations, returning a protective effect on normal tissues for same antitumor efficacy as compared to conventional dose rates, the so-called FLASH effect, observed in numerous preclinical experiments, triggered in the last 3-4 years an exponentially growing number of biophysical modeling works attempting to investigate and explain it from the mechanistic point of view.

Since it was appearing that such a phenomenon should imply several physical, chemical and biological stages of the radiation action, different spatio-temporal scales were considered and analyzed in these modeling approaches.

An overview of these investigations will be concisely reported, with a focus on the ongoing joint efforts of GSI and TIFPA in this context, especially in the attempt of combining different scales.

In particular, radiation chemical based approaches, employing TRAXCHEM [1-2], the GSI radiation chemical track structure code and its specific extensions, allowing to go from the physical stage to the homogeneous chemical stage will be mentioned and a novel dedicated extension of the Generalized Stochastic Microdosimetric model (GSM2)[3-4] for UHDR regime, aiming at combining the DNA damage and repair kinetics with the chemical stages on several levels.

Impact of LET [3] and dose delivery features will be discussed as well.

REFERENCES
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