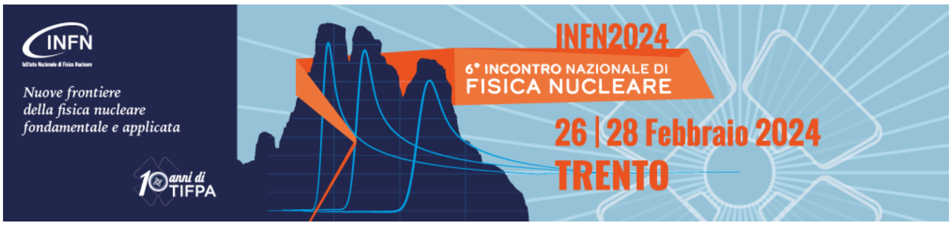

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A unique model to accurately describe low and high LET particle beam biological response

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Assessing the biological impact of radiation relies on understanding the fundamental interactions between radiation and matter. This is particularly essential in various fields, including radiotherapy cancer treatment. To link the physics of radiation to its biological effect, mathematical mechanistic models have been proven powerful tools. Consequently, developing an accurate and reliable model for predicting cell killing from specific irradiation patterns becomes imperative for improving our knowledge of the biological effectiveness of radiation.

Current mechanistic radiobiological models face limitations in offering a comprehensive description across a diverse spectrum of particle species and energies. Different ions with distinct energies yield various biological responses due to significant differences in the underlying radiation patterns. One of the most relevant situations is verified in the case of extremely high Linear Energy Transfer (LET), defined as energy deposited per unit length. In this regime, the overkill effect is observed, where there is a decrease in the biological effect as the LET increases. This contrasts with the conventional relationship where an increasing LET typically results in a higher biological response.

The Generalized Stochastic Microdosimetric Model (GSM2) [2,3] has been developed as a new mechanistic and probabilistic model, which describes the time-evolution of the DNA damages in a cell nucleus by considering the stochastic description of energy deposition. Among the most relevant strengths is the capability to efficiently treat several levels of spatiotemporal stochasticity in a broad range of particle species and energies [4].

In this study, we predict the Cell Surviving Fraction (SF) of an irradiated cell culture from the experimental work conducted by [1] using GSM2. First, an extensive study is conducted about the impact of the sensitive target volume size on the radiation-induced damage predicted by GSM2. This leads to a two-scale description of the radiation-induced damage. The experimental irradiation conditions have been accurately reproduced with Monte Carlo codes simulations, using TOPAS [5,6] as the MC toolkit. Then, the SF curves are predicted for two different cell-culture lines and three kinds of radiation quality: protons, Helium ions, and Carbon ions. The strength of the model is exploited with matching predictions for all three types of radiation fields in a completely general way and a very wide range of LET. This range covers two orders of magnitude: from 1 keV/μm to around 100 keV/μm (Figure 1). Moreover, the model's power is fully displayed with a natural mechanistic prediction of the overkill effect directly from radiation physics.

We show the complete generality and ability to successfully predict the SF considering the stochasticity inherently given by the nature of radiation fields interacting with matter.

[1] Bronk et al. Cancers (2020)
[2] Cordoni et al. Phys.Rev.E (2021)
[3] Cordoni et al. Rad.Res. (2022)
[4] Cordon et al. International Journal of Radiation Biology (2023)
[5] Hongyu Zhu et al. Physics in Medicine & Biology (2019)
[6] Perl et al. Medical Physics (2012)

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