Simulation of radio-induced DNA damages and their repair by means of Geant4-DNA Monte Carlo Track Structure code

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Background: Monte Carlo Track Structure codes are indispensable tools to improve the knowledge of the links between the physics of ionizing radiation and its biological consequences. A first simulation chain based on Geant4-DNA was developed, capable of combining direct and indirect effects on a detailed molecular level model of the DNA content of a eukaryotic cell nucleus [1]. In this presentation we will detail the last developments brought to this simulation chain

Material and Methods: First, the geometry of the nuclear DNA target was modified according to the isochore family theory [2] that describes the distribution of hetero and eu-chromatin into segments along the genome. For the simulation of the chemical stage, the IRT-sync approach [3], has been integrated. Finally, DNA damage repair models implemented as stand-alone Geant4-DNA utils were added after the DNA damage generation to estimate several biological endpoints: cell survival rates (Two Lesion Kinetics model [4]), the time evolution of the fraction of unrejoined DSBs (Local Effect Model IV [5]), and the time evolution of γ-H2AX (Belov's model [6]). A comparison with experimental data on fibroblast cells is proposed.

Preliminary results: The new geometrical model allows the localization of damage in critical areas such as the genome core where DSB induction has been found to be more important than in the genome desert. DSB induction calculated with the IRT-sync method gives acceptable results in comparison with experimental data while the simulation performance is improved. Repair models results are in good agreement with the literature data which proves that the simulation chain can provide relevant input data for such models. All these improvements allow to make progress in the understanding of the mechanisms at the origin of the biological effects and will be made publicly available into the Geant4-DNA users community in next releases..

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