Modelization of DNA fragmentation induced in human fibroblasts by Fe-56 Ions

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DNA double-strand breaks (DSB) are widely recognized as cellular critical lesions in the pathways leading from initial energy deposition by radiation to the formation of relevant biological endpoints such as gene mutations, chromosome aberrations and cell death. Chromatin conformation and radiation track structure are expected to have a strong influence on the spatial modulation of DSB induction at the scale of the nucleosome, i.e. 100 base pairs (bp), and of the low-level chromatin fiber organization, i.e. 1 kbp. At larger scales the DNA fragmentation pattern induced by sparsely ionizing radiation approaches a scenario resulting from a random distribution of DSB. However, the pattern induced by high-LET irradiation can lead to deviation from randomness also at these scales. This feature can have important biological consequences, since spatial correlation of DSB is thought to affect their reparability. Therefore, studies on fragment size distributions induced by radiations of various qualities can help to link the physical characteristics of radiation with the cellular endpoints. This is an important issue for understanding the main mechanisms of cell damage induced by HZE particles.

In this work we have compared the pattern of DNA fragmentation (in the range 1-5700 kbp) induced in human fibroblasts by γ-rays with that induced by high-energy Fe-ions, which have biological significance for radiation protection issues during long term astronauts' travels. The study has taken into account the comparison of the experimental fragmentation spectra, their analysis performed through the implementation of a phenomenological model, and Monte Carlo simulations performed with the PARTRAC code. The phenomenological method characterizes in an approximate but simple way the non random nature of the experimental fragment distribution caused by high-LET radiation; it has the advantage to take into account in a detailed way the background fragmentation. The PARTRAC simulations, on the other hand, thanks to the accurate representation of the chromatin geometry and of the physical and physico-chemical processes associated with the energy deposition by radiation, offers the possibility to compute the spectra and to compare them with the experimental data.

Supported by European Comm. (contract no. FI6R-CT-2003-508842, "RISC-RAD")