## MINAS TIRITH: a Geant4-DNA-based tool for modeling damage at the cell population scale

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**Background:** Linking a radiation-induced DNA damage topology to a beam quality can be achieved by coupling realistic nuclear geometries [1] to nanodosimetric simulations with the Geant4-DNA toolkit [2]. Currently, these simulations are performed on a single cell nucleus while results are validated with experimental data from irradiated cell populations [3]. We propose here a modeling tool, so-called MINAS TIRITH that allows the calculation of the damage topology at the cell population scale, conditioned by the micro-dosimetric characteristics of the beam [4], for e<sup>-</sup>, p<sup>+</sup> and  $\alpha$  from 1 keV to 20 MeV.

**Material and Methods:** First, the MINAS TIRITH tool distributes the tracks in the nucleus population to reach a given absorbed dose considering the microdosimetric spectrum  $f_l(z)$ . This spectrum is obtained thanks to interpolations and convolutions of precalculated spectra from a database built with Geant4-DNA microdosimetric simulations. In a second step, each track is associated to a damage topology, according to its specific energy *z*, by interpolation and sampling in a second database built with Geant4-DNA based nanodosimetric simulation chain [2].

**Preliminary results:** The MINAS TIRITH tool has been verified by comparing its results with those obtained directly with the Geant4-DNA simulation chain [2]. Considering the typical experimental data uncertainty on DNA damage, we consider that MINAS TIRITH answers favorably to the verification tests (Figure 1). The advantage is the significant time savings of MINAS TIRITH compared to track structure codes.



Figure 1: Mean number of DSB as a function of LET

[1] Y. Thibaut *et al.*, Int. J. Mol. Sci., 23 (2022) 3770.

- [2] S. Meylan *et al.*, Comput. Phys. Commun., 204 (2016) 159-169.
- [3] N. Tang et al., Int. J. Mol. Sci., 20 (2019) 6204.
- [4] G. Gruel et al., Plos One, 11 (2016) e0145786.