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Monte Carlo track structure simulations and the biophysical model NanOx in targeted radionuclide therapy

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Targeted radionuclide therapy (TRT) is seen nowadays as a promising therapeutic technique against several types of tumors. The selection of the appropriate carrier molecule and radionuclide are two critical aspects of TRT. Regarding the nature of the radionuclides, particular attention has been given to Auger electron and α-particle emitters, because these particles would provide a localized irradiation ideal for eradicating single tumor cells and micrometastases. However, appropriate simulation tools are needed to carry out preclinical studies to determine the true potential of these radionuclides. Monte Carlo track structure (MCTS) codes are useful for this purpose because they provide a detailed cartography of the energy deposited by ionizing radiation down to the nanometric scale.

We recently applied the MCTS codes EPOTRAN [1], TILDA-V [2] and its dosimetric module, CELLDOSE [3, 4], to investigate the relative performance of several Auger electron and α-particle emitters for irradiating single tumor cells and micrometastases. The comparison of the radionuclides was made in terms of S-values (Gy· Bq−1·s−1) and normalized absorbed doses, considering a spherical geometry for the cell and taking the cell nucleus as the critical target for radiation-induced cell death. We analyzed the effect on S-values of different radionuclide dis- tributions within the cell (i.e. on the cell surface, intracytoplasmic, intranuclear, and a uniform whole cell distribution). Moreover, in the case of α-particle emitters, we studied the contribution to the total energy deposited in the cell of the radiations emitted directly by the parent radionuclide, as compared to the radiations emitted by its full decay series. The results were in excellent agreement with the predictions of other codes (MIRDcell [5], PHITS [6]), and with similar calculations found in the literature [7].

While the latter study was limited to the physical phase of radiation action, which may serve to es- timate the direct DNA damage, other numerical tools also describe the processes taking place during the subsequent physico-chemical and chemical phases, responsible for indirect DNA damage mechanisms. By having the spatial distribution of energy transfers and that of the physico-chemical events associated to a given irradiation, it is then possible to provide this information as input to biophysical models, which can be integrated into treatment planning systems for estimating the biological dose. In this context, the recently developed NanOx biophysical model [8] has been successfully applied to hadrontherapy. NanOx (as most biophysical models), currently considers the cell nucleus as the only sensitive structure to radiation damage. While this assumption may be justified for hadrontherapy, the application of NanOx in the fields of TRT and boron neutron capture therapy (BNCT) requires a deeper understanding of the impact of cell geometry and the microdistribution of the radionuclides on the biological dose calculations. Thus, NanOx has to be extended to consider extra-nuclear radiation sensitive sites in the cell. This work is currently underway, as one of the main goals of the PICTURE (Planning Innovative Cancer Therapies Using RadioElements) project, a joint endeavor of researchers at the Institute of Physics of the 2 Infinities (Lyon) and the Laboratory of Subatomic Physics and Cosmology (Grenoble).

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Keywords

• Targeted radionuclide therapy • Monte Carlo track structure • Auger electrons • α-particles • Cellular dosimetry • NanOx biophysical model

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