“ Impact of intracellular radionuclide distribution in Targeted Alpha Therapy : a Monte-Carlo biophysical study in 3D multicellular model “

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Background: To understand and predict the therapeutic efficiency of targeted alpha therapy, nano/micro-dosimetry are needed by considering the very heterogeneous dose deposition at cell level. The objective of this study is to evaluate theoretically the importance of radionuclide cell internalization on relevant dosimetric and biological endpoints.

Material and Methods: The treatment with ^{211}At of mono-cells or microtumors was simulated. The Monte Carlo CPOP [1] code, based on Geant4, was used to generate realistic deformable 3D multi-cellular geometries, and was adapted to generate the radionuclide source distributions in various internalization cases (membrane, cytoplasm, cytoplasm + nucleus and nucleus only) and collect the physical outputs needed for the biophysical calculations. Physical absorbed doses in cell nuclei of ovarian cancer cell line OVCAR-3, have been calculated, in addition to therapeutic indexes like Tumor Control Probability (TCP), using the biophysical model NanOx [2], which considers in the current version that the cell nucleus is the unique sensitive volume.

The impact of cell packing, tumor size, alphas energy and radionuclide daughter diffusion after fixation were studied, under the hypothesis that all cells are labeled with alpha particles.

Preliminary results: With 42 alpha particles per cell, radionuclide cell internalization has very little impact on physical dose and TCP, except if radionuclides are internalized in the nucleus. However, when the number of alphas per cell is reduced below 10, TCP decreases below 1. For instance, with 5 alphas per cell, TCP were equal to 0.06, 0.16 and 0.66 when the sources were distributed, respectively, in membrane, cytoplasm and nucleus only.

[1] Maigne, L., et al. Phys. Med. 89 (2021) 41-50
[2] Cunha, M. et al. Phys. Med. Biol. 62 (2017) 12-48