Cancer Cell and Micrometastasis Dosimetry from the ^{225}Ac Decay Chain with GATE Simulations

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Introduction:

- Actinium-225 (^{225}Ac) is a promising candidate isotope for targeted alpha therapy (TAT) due to the short range and high energy of its emissions, which includes four alphas and two betas in its decay chain (Figure 1).
- TAT is well suited to highly metastasized and widespread cancers with ^{225}Ac-labelled radiopharmaceuticals that target specific cellular biomarkers.
- **Question:** How does localization of ^{225}Ac progeny at the intended target site effect the total therapeutic dose?
- **Goal:** This *in silico* study aims to quantify the dose deposition throughout the ^{225}Ac chain in individual cells and micrometastases.

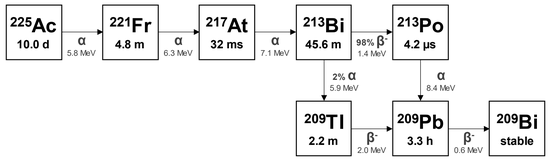

Figure 1: Decay chain of ^{225}Ac

Methods:

Simulations:

- Monte Carlo simulations were run in **GATE** (based on Geant4 toolkit) via Compute Canada servers.
- Radiative transport was simulated with a **Geant4-DNA physics** list, well validated for micro dosimetry applications.

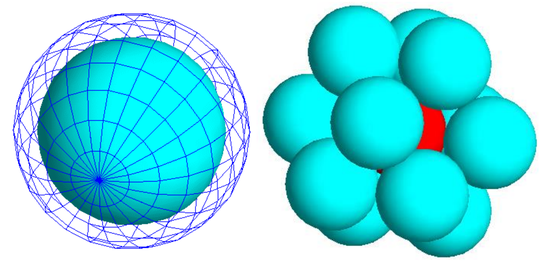

Figure 2: Cellular geometries, a cell with 10 µm cell diameter and 8 µm nucleus diameter and a cluster of cells with a centre cell (red) and neighbouring cells in a hexagonal packing structure

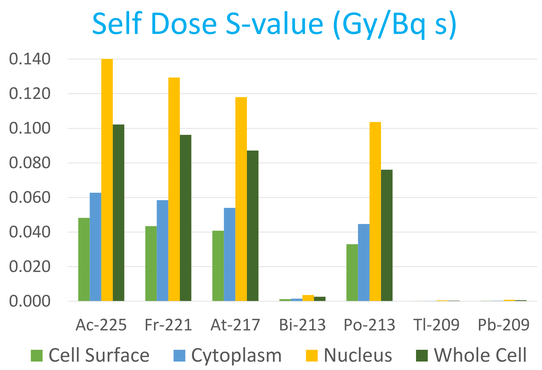

Figure 4: Self dose s-value (Gy/Bq s) to the cell nucleus for ^{225}Ac progeny radionuclides with various source distributions

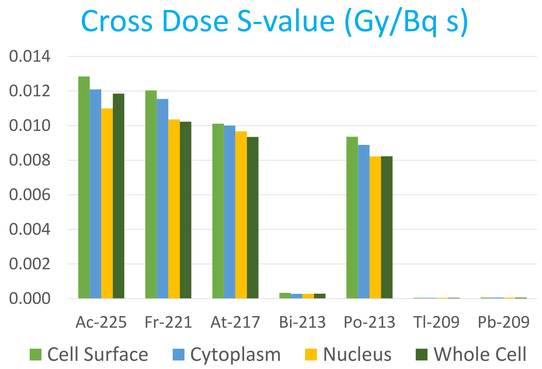

Figure 5: Cross dose s-value (Gy/Bq s) to the cell nucleus for ^{225}Ac progeny radionuclides with various source distributions

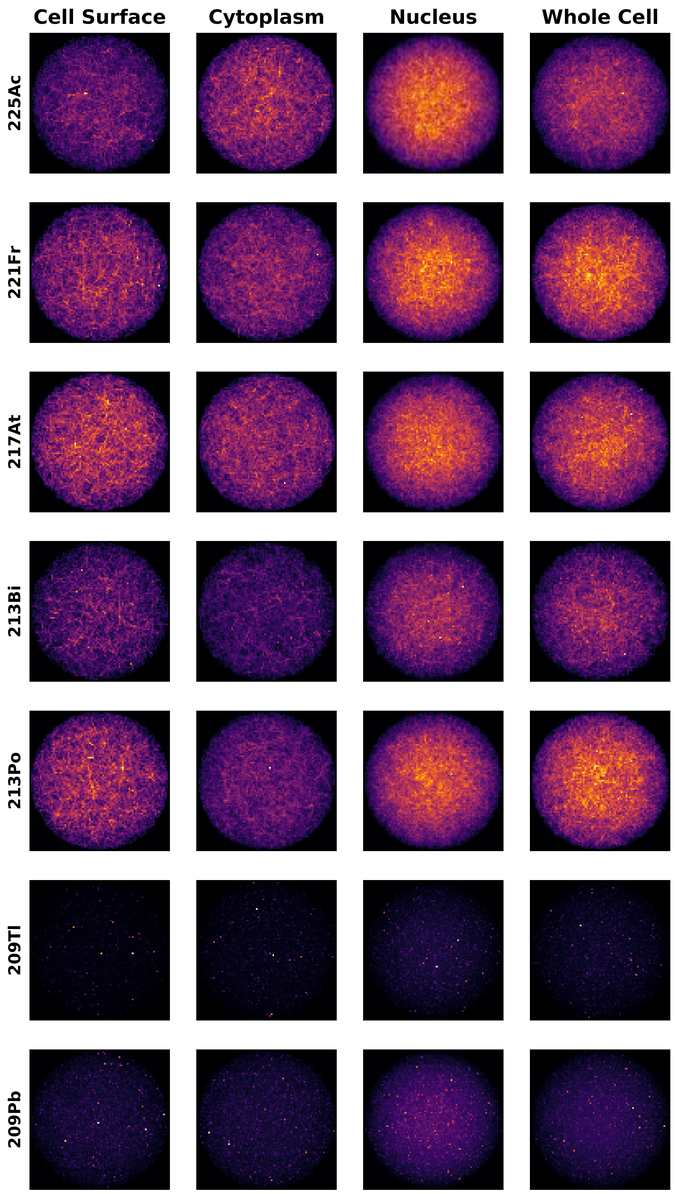

Figure 3: Cell nucleus dose maps for ^{225}Ac progeny radionuclides with various source distributions.

Cell Dosimetry:

- **Cellular geometries:** an individual cell and a cluster of cells (Figure 2).
- **Radionuclide distributions:** Cell surface, Cytoplasm, Nucleus, and Whole Cell.
- Every radionuclide in the ^{225}Ac decay chain was simulated individually to its immediate progeny.
- Scored the absorbed dose (Gy) to the cell nucleus (Figure 3).

Results:

- Throughout the ^{225}Ac decay chain, alpha emissions contribute more absorbed dose than beta emissions.
- Quantitatively, s-values (Gy/Bq s) are a measure for the absorbed dose per radionuclide decay from a source to a target.
- The self dose s-values (Figure 4) and cross dose s-values (Figure 5) are derived from single cell and cell cluster simulations, respectively.

Conclusions:

- Therapeutic dose increases with further nuclear localization. Most radiopharmaceuticals localize to the cell surface or cytoplasm, however, developing novel nuclear targeting vectors would yield significant increases in absorbed dose.
- Neighbouring cells receive similar dose depositions regardless of radionuclide localization in the source cell.
- Self dose is typically an order of magnitude greater than cross dose, supporting the notion of high target specificity with ^{225}Ac for TAT.

Discovery, accelerated