A computational tool for Radiopharmaceutical Research: *In Vitro* Monte Carlo Simulations with TOPAS

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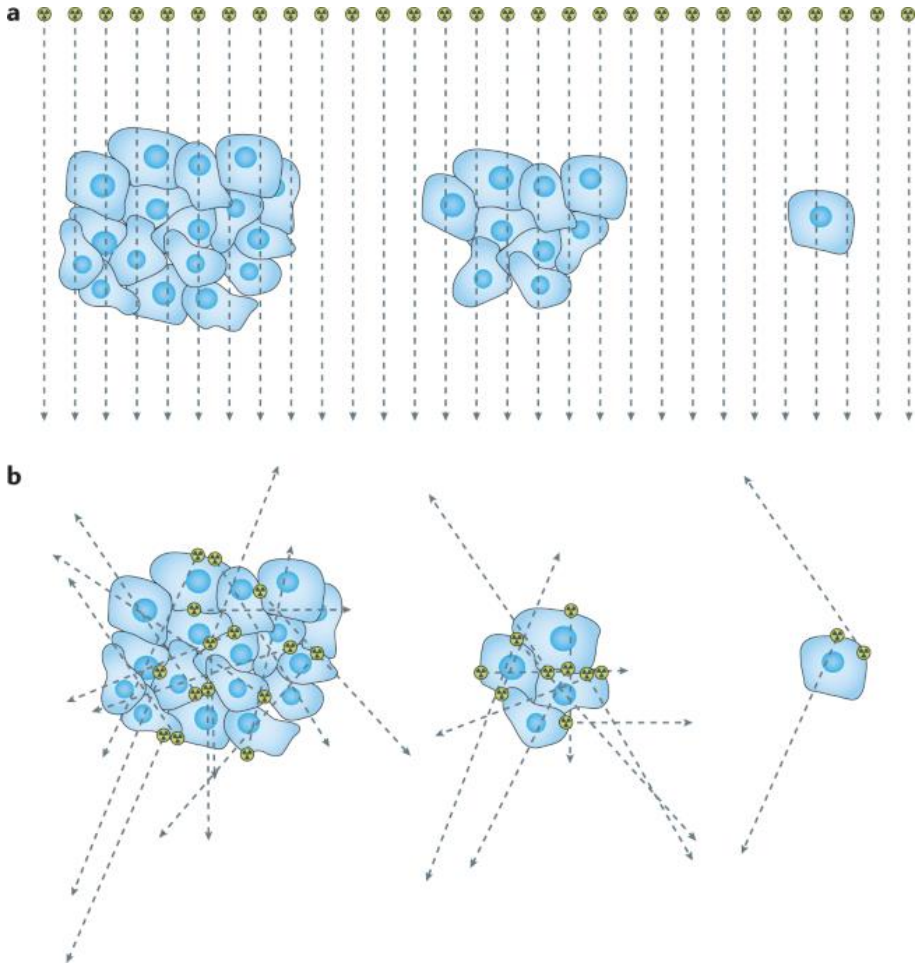
Radiopharmaceutical Therapy

Radiopharmaceutical therapy utilizes radiolabeled antibodies highly affine to antigens particularly expressed in tumor cell environments.



External beam therapy:

- Radiation beams from outside the body
- Exposes the surrounding healthy tissue
- Less invasive

Radiopharmaceutical therapy:

- Internalized radioactive substances
- Minimizes damage to healthy tissue
- Delivers a concentrated dose

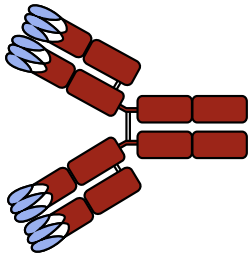
In vitro RPT experiments

Radionuclide

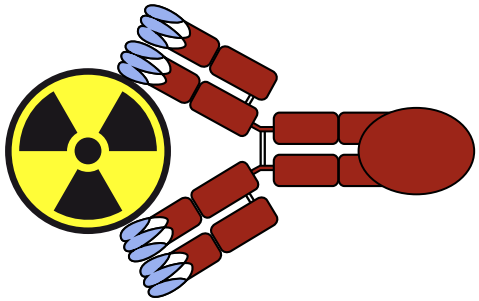
Chelate

+

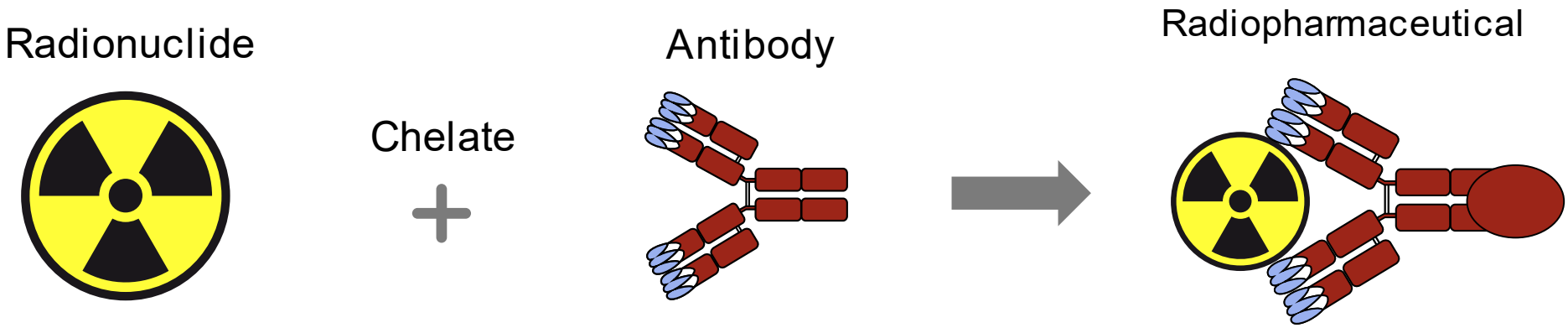
Antibody



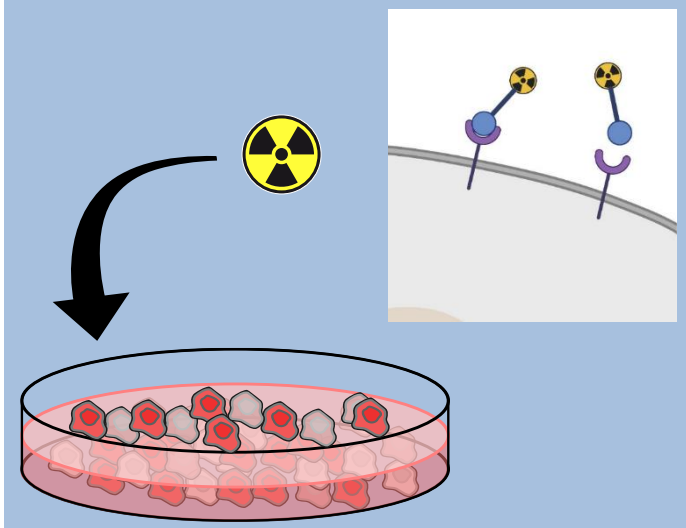
Radiopharmaceutical



In vitro RPT experiments

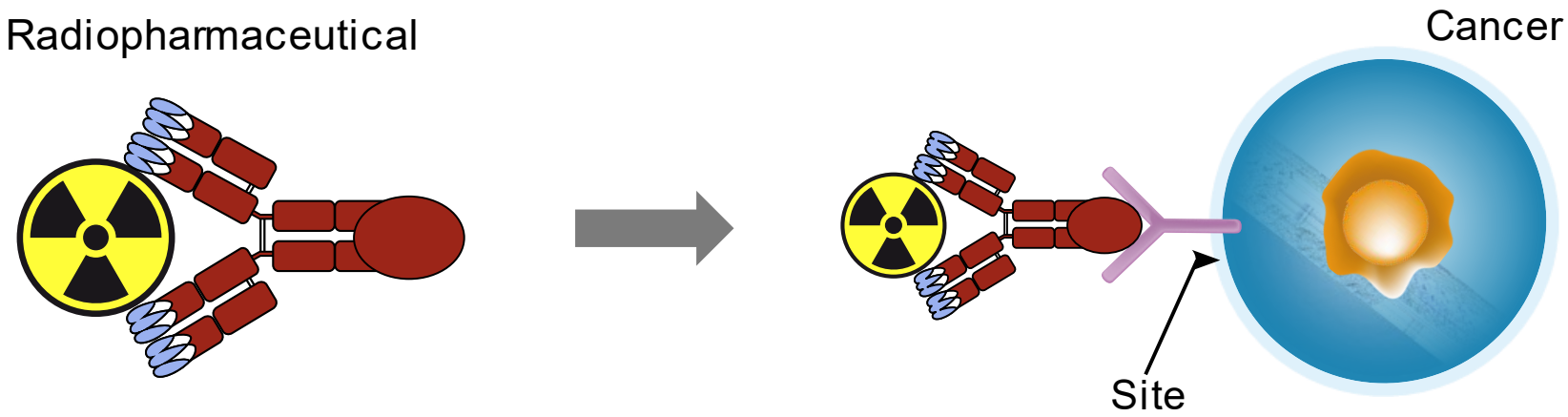


Stage 1: Injection

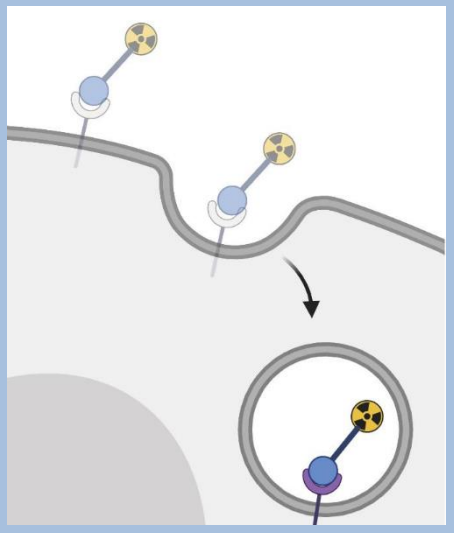


- Experiment initiates with the injection of the radiopharmaceutical into cell wells
- During this phase, the radionuclides are uniformly distributed across the medium
- After injection, they bind to cancer cells within the cell wells

In vitro RPT experiments



Stage 2: Internalization

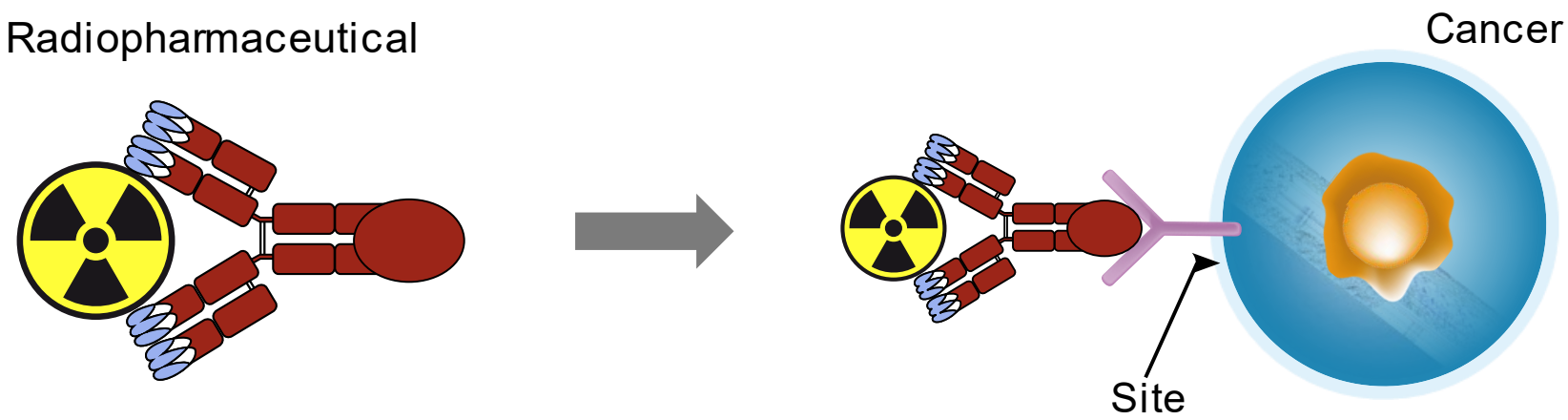


- Binding characterized by Kd

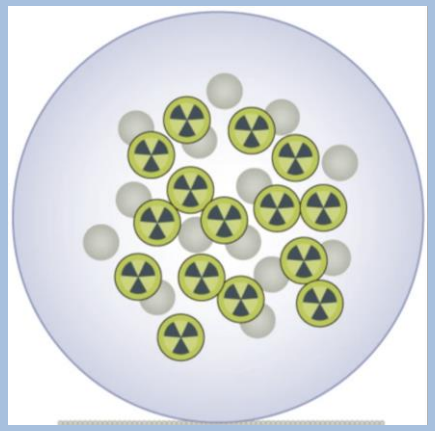
Kd: Concentration needed to have 50% of receptors bound

- Radiopharmaceuticals might internalize, i.e., pass through the membrane to the cytoplasm.

In vitro RPT experiments

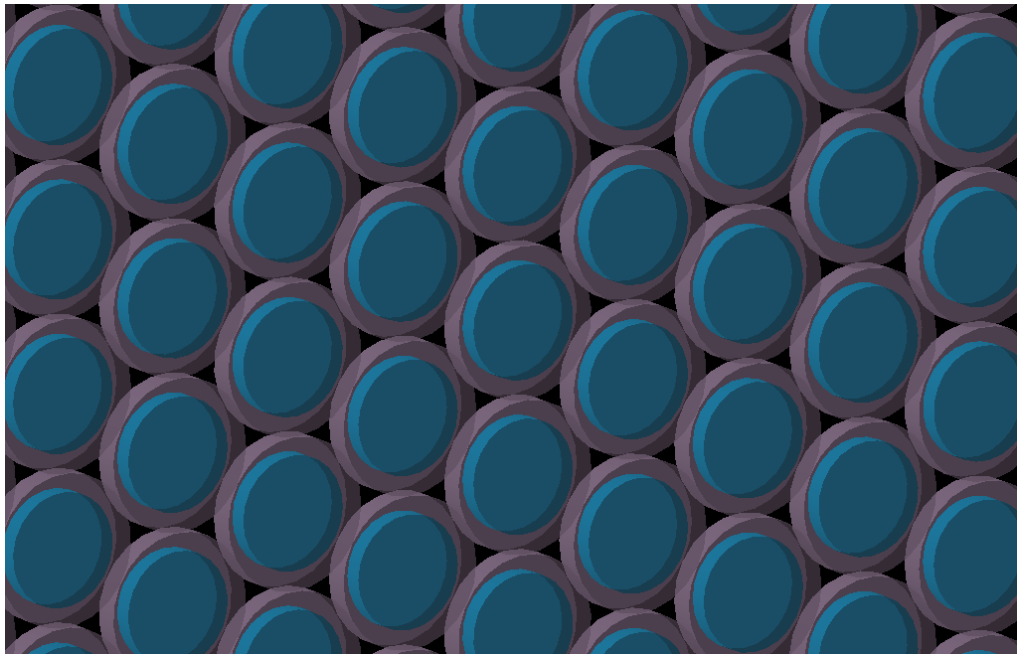


Stage 3: Already internalized

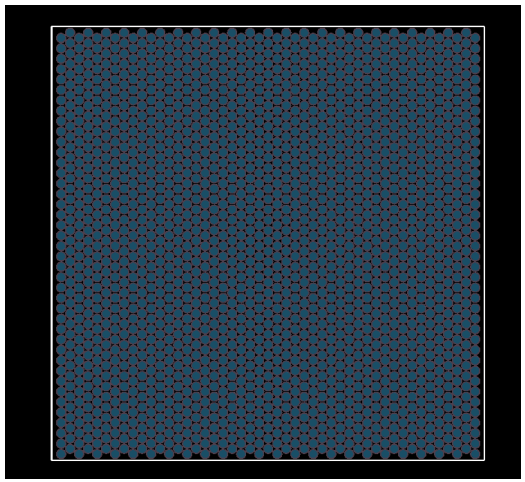


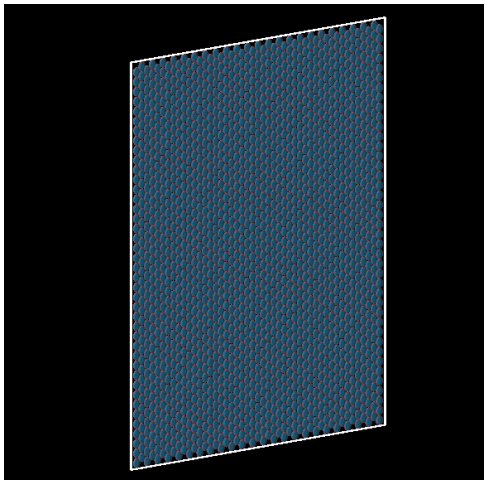
- Percentage of bound radiopharmaceutical internalizes into cytoplasm
- Radionuclide emits radiation directly from inside the cell

TOPAS tool: Geometry



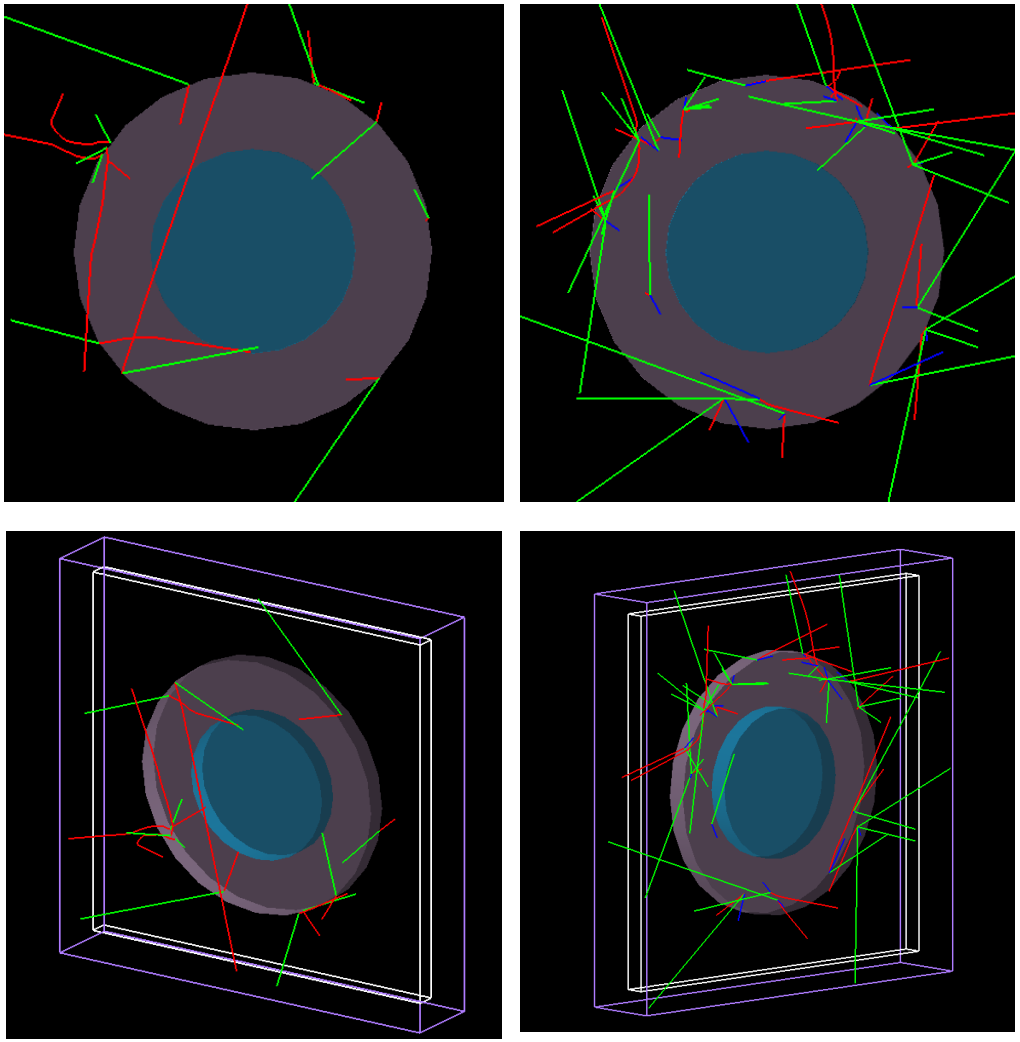
- Cell information
  - Cell radius and height
  - Nucleus radius and height





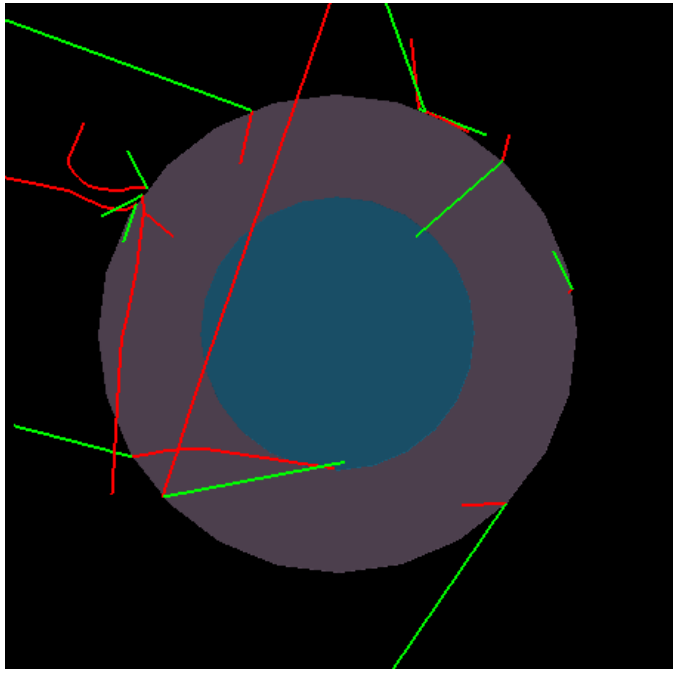
- Monolayer information
  - Monolayer dimension X, Y, Z

TOPAS tool: Source



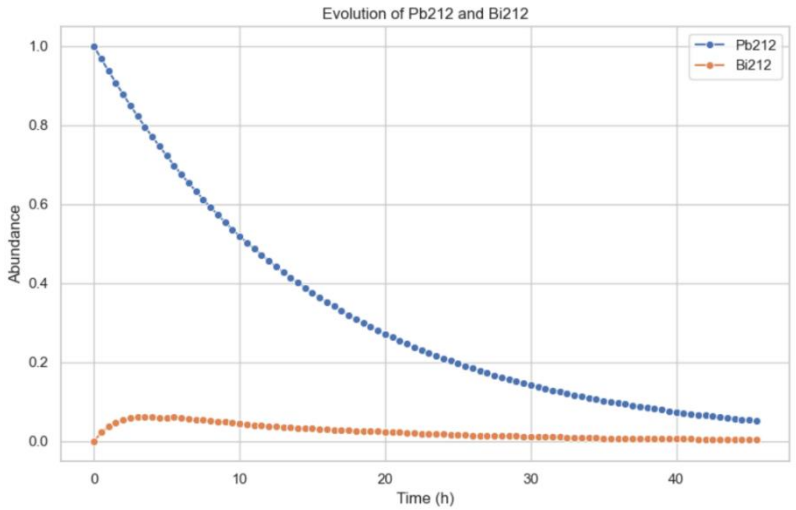
- Radionuclide
- Initial activity
- Initial and final time
- Concentration (kBq/mL)
- Nº sites/cell
- Kd
- Specific activity (kBq/mol)

TOPAS tool: Scorer

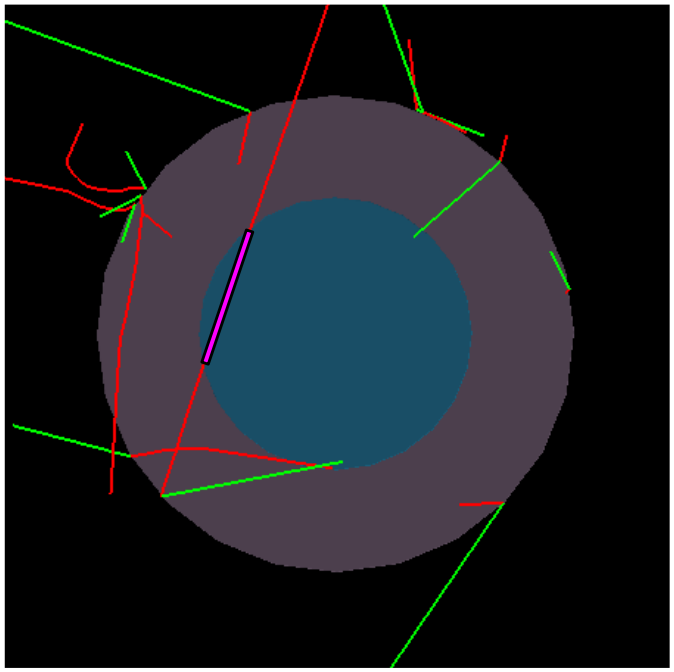


- Energy deposited in each nucleus
- Weight of each particle simulated:
  - Nº decays/Nº histories
- The output is already weighted considering abundances over time in complex decay chains.

Nucleus	Energy deposited (MeV)
2	0.02
….	….
654	1.2



TOPAS tool: Scorer



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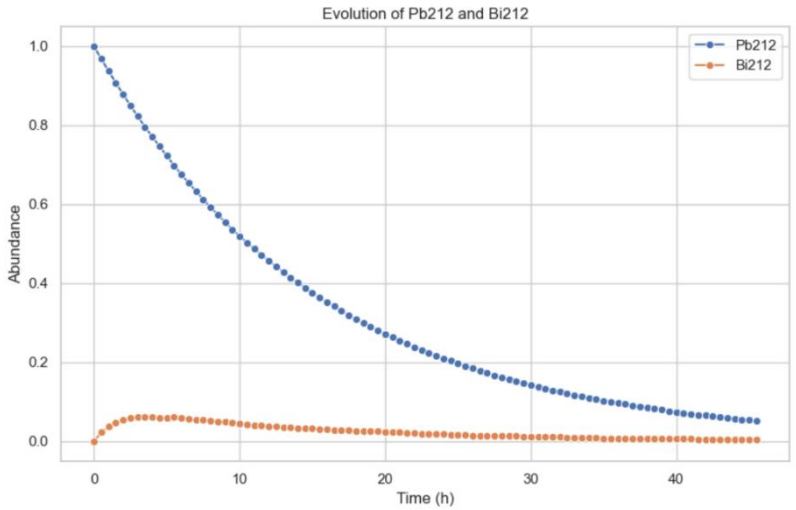
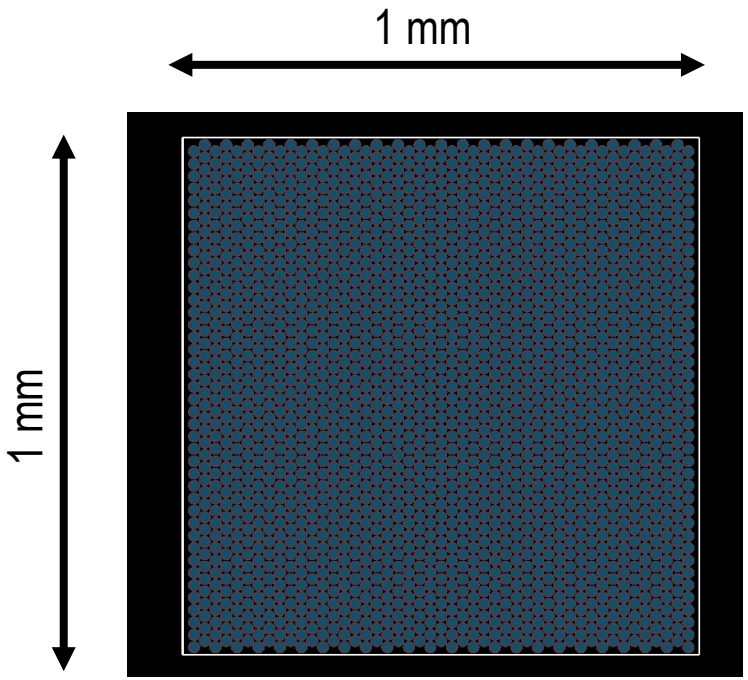
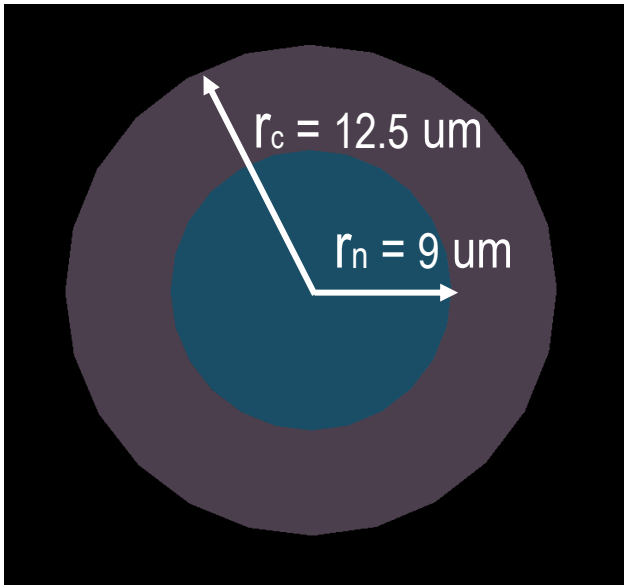


TOPAS tool: 212Pb simulations

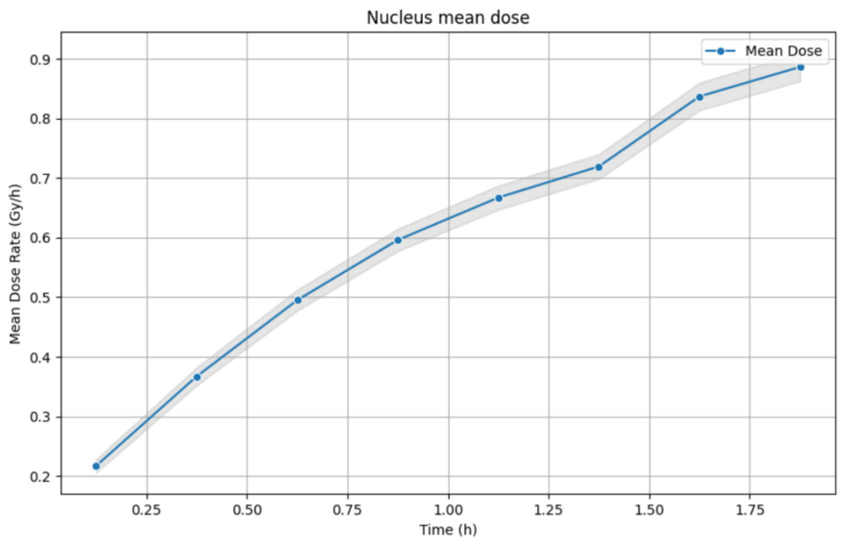


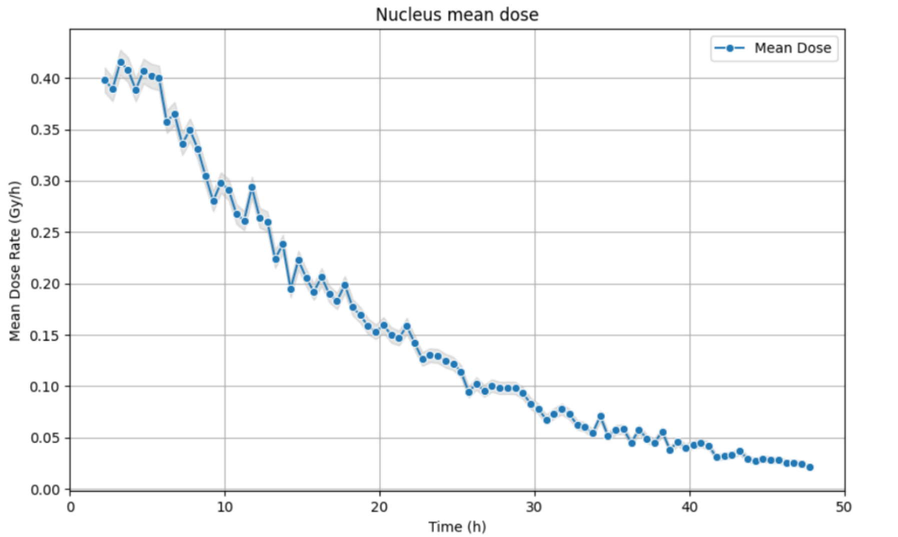


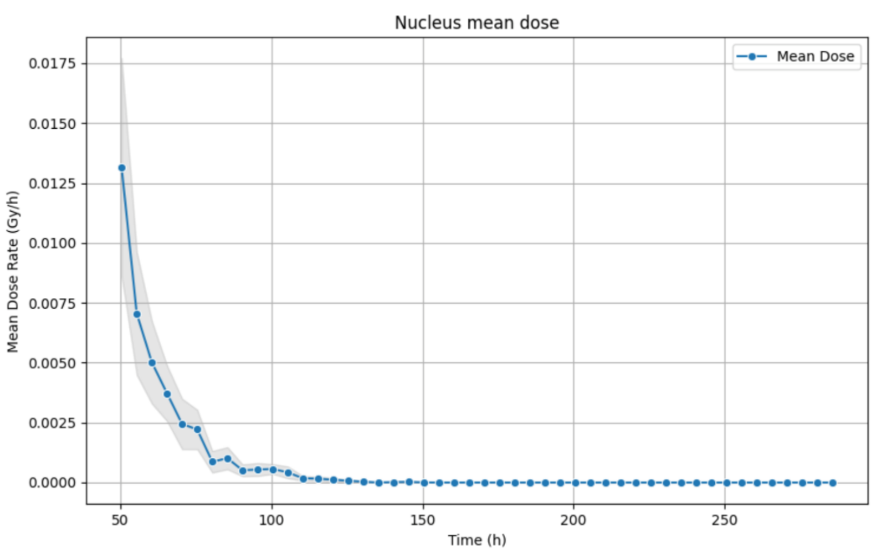
- Injection: 2h
- Internalization process: 48h
- Irradiation: 10 days

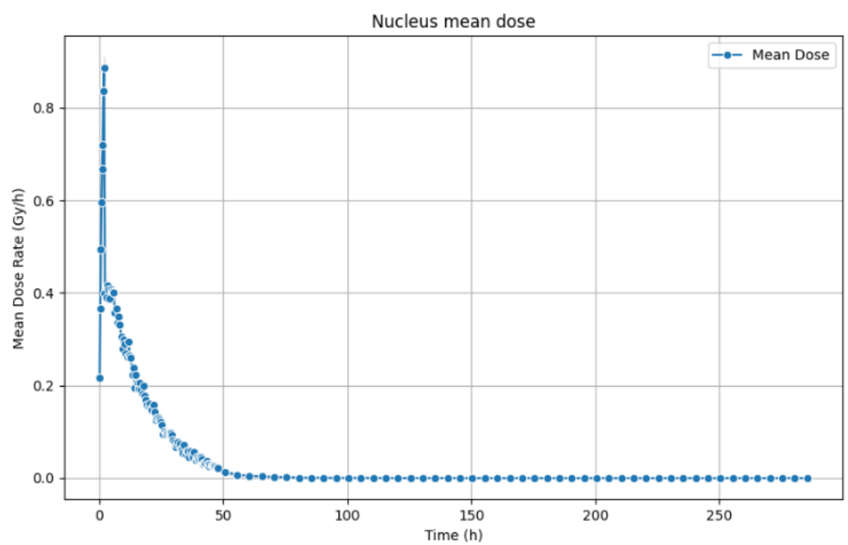
- Initial activity: 19.2 Bq
- Kd: 9 nmol/L → 14% binding
- Percentage internalized: 44%

TOPAS tool: Dose-rate vs time









Conclusions

- We have developed a computational tool to recreate *in vitro* radiopharmaceutical experiments. To our knowledge, it is the first time that:
  - An **actual time-structure** for the dose is calculated
  - All emissions from **all the decay products** are considered, ordered in the **right time and abundance**
  - It is considered the dose received **by each nucleus individually**

Future…

- To extend the tool to 3D geometries would provide capability to simulate experiment with tumor spheres.
- To implement a biological model to obtain directly the survival fraction depending on the dose delivered.

Acknowledgments

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