AG GDR Mi2B 2026

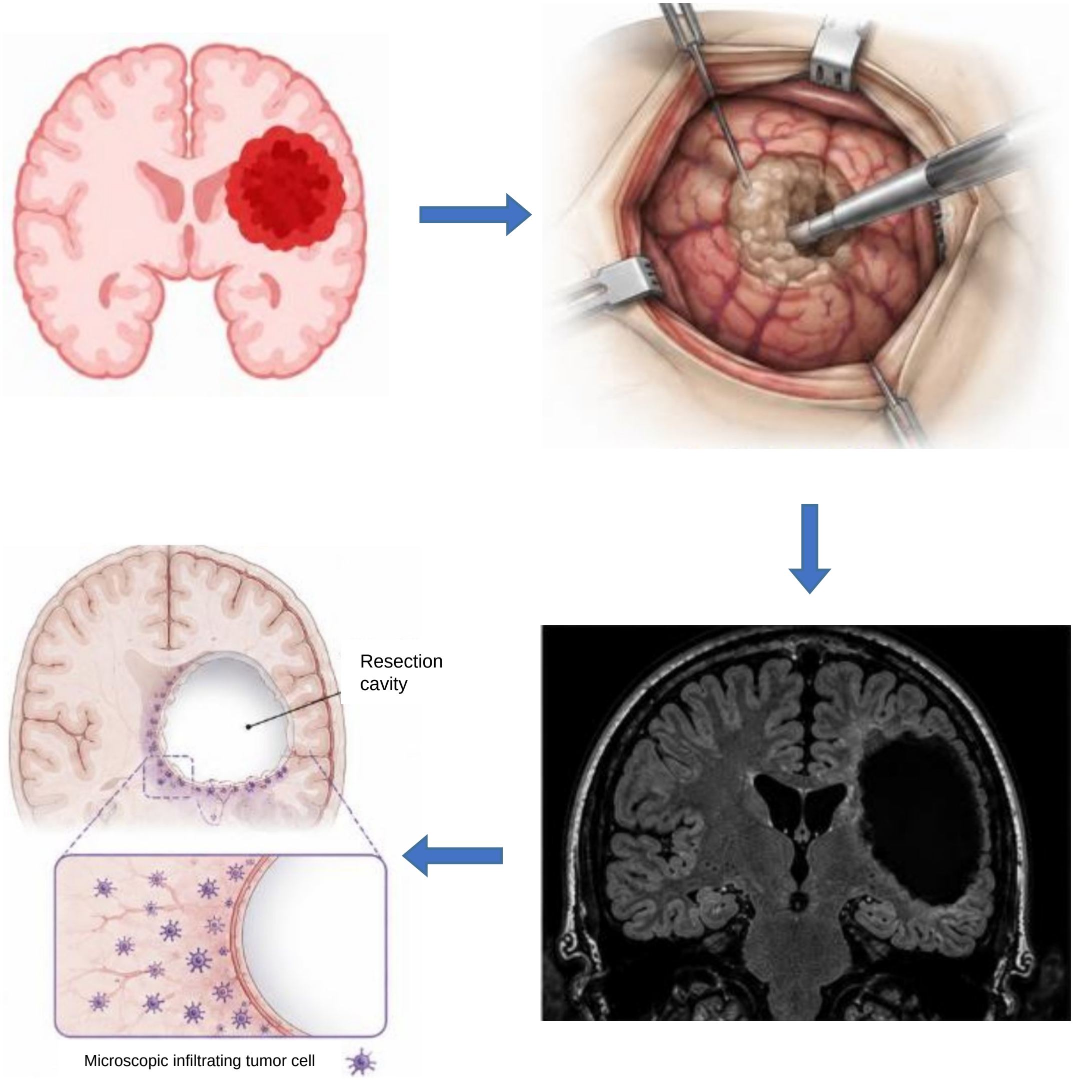
30/06/2026

IRHydroBRAIN project: IRT for glioblastoma treatment with α and β emitters

Alicia Garnier

Context: Glioblastoma

- Commonest primary **malignant brain tumor** in adults.
- 5-year survival **below 5%.**
- Current treatment → Surgical resection followed by external radiotherapy (RT).
- Issue: remnant infiltrating tumor cells → **local recurrence.**



Schematics representing the surgical resection of the GBM and the microscopic infiltrating tumor cell responsible for the local recurrence.

Context: Glioblastoma

- Commonest primary **malignant brain tumor** in adults.
- 5-year survival **below 5%.**
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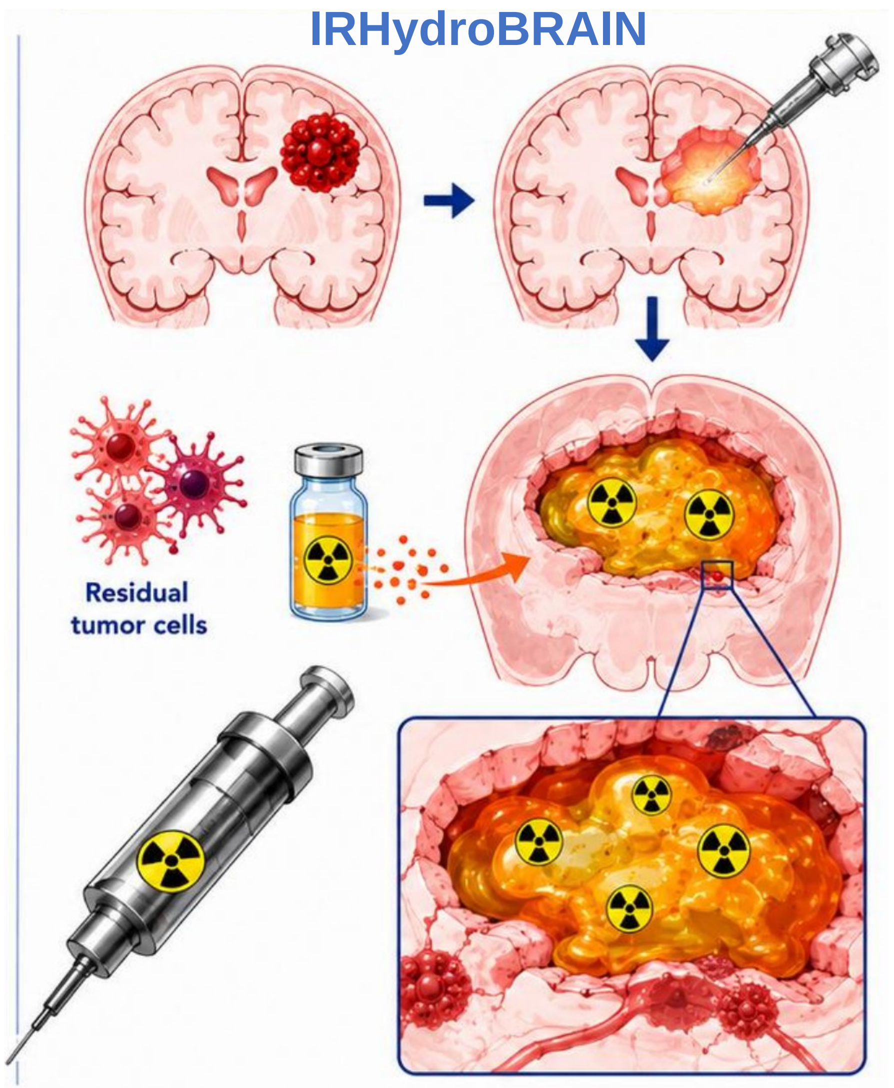
Solution proposed: Using a radiolabeled chitosan hydrogel in the resection cavity after surgery for **internal RT** in addition to the external RT.

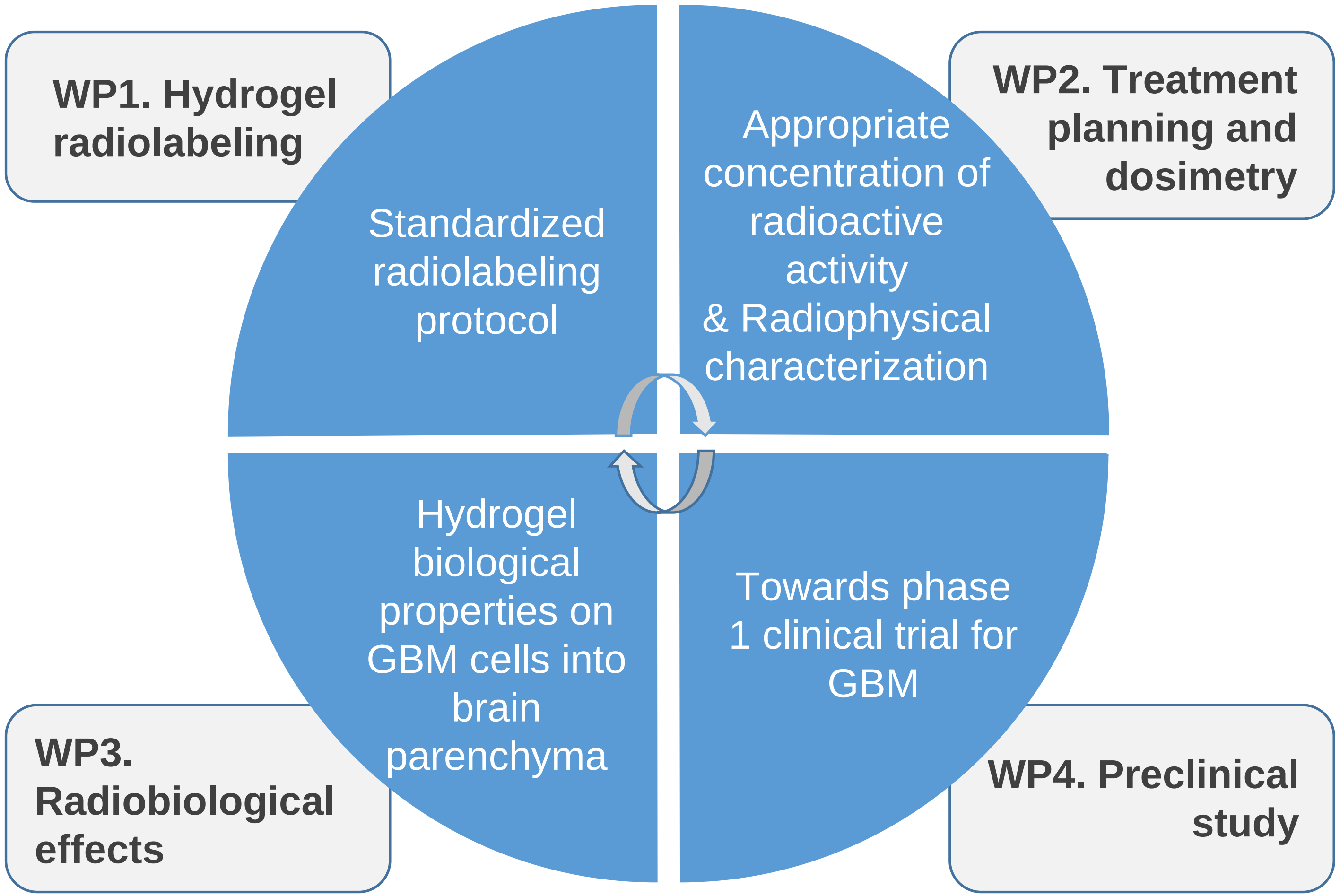


Surgical resection followed by the administration of the hydrogel in the cavity for internal RT.

IRHydroBRAIN project

Organization of the **IRHydroBRAIN** project in 4 work packages divided between three organisms :

- Nano-H (Lyon)
- The CRAN (Nancy)
- The **LPCA** (Clermont-Ferrand)



Main objectives of the IRHydroBRAIN project.

IRHydroBRAIN project

Organization of the **IRHydroBRAIN** project in 4 work packages divided between three organisms :

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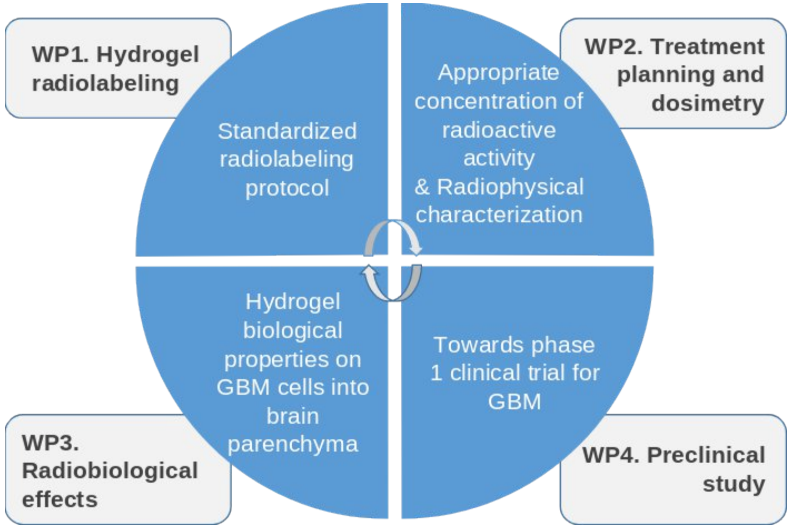
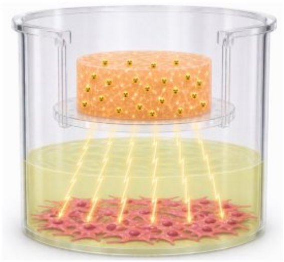
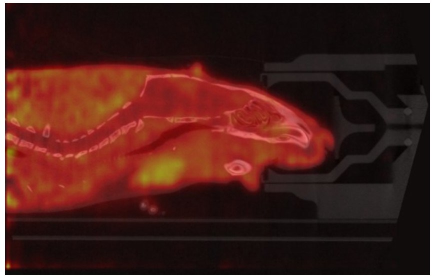


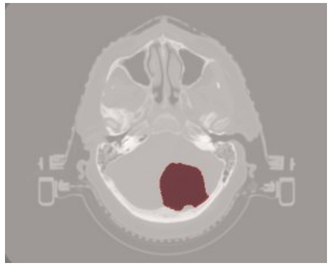
Main objectives of the IRHydroBRAIN project.



In-vitro study of the radiobiological effects at the cellular level.



In-vivo study of efficiency on the Fisher rat operated with a F98 glioblastoma.



Dosimetric study on human head CT after surgical resection (activity between 1 and 5 MBq).

Patient dosimetry: isotopes

Gate simulation

- Version: **Gate 10.4**
- Source: isotope (β or α emitters), voxelized

Isotopes	Y-90	Lu-177	Tb-161	Ac-225	At-211
Decay type	β	β	β	α	α
Half-life	2.7 days	0.3 days	6.9 days	9.9 days	7.2 hours
Mean energy	0.93 MeV	0.13 MeV	0.15 MeV	5.79 MeV	5.87 MeV
Mean range (soft tissue)	4.024 mm	0.233 mm	0.296 mm	0.048 mm	0.049 mm

Table describing the characteristics of different isotopes studied to be used with the hydrogel.

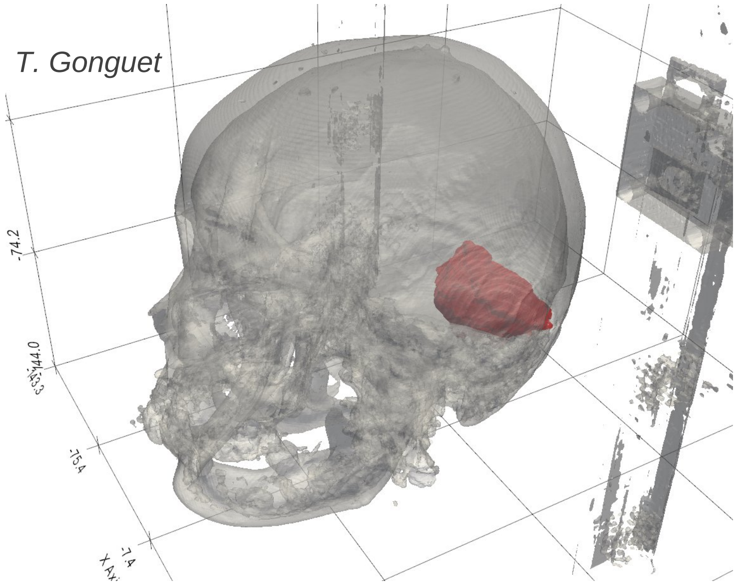
Patient dosimetry: patient CT

Gate simulation

- Version: **Gate 10.4**
- Source: isotope (β or α emitters), voxelized
- Placement: in the **GTV**
- Target: patient head CT
- Activity: **100MBq** or **1GBq** to limit statistical fluctuations

```
# Physics list choice
sim.physics_manager.physics_list_name = "QGSP_BIC_EMZ"


# Placement of the source in the selected ROI
source = sim.add_source("VoxelSource", "source")
source.attached_to = sim_volume.name
source.particle = particle
source.image = str(mask_file_path)
source.energy.type = "spectrum_histogram"
source.energy.spectrum_histogram_interpolation = None
source.activity = (activity / number_of_threads) * Bq
gate.sources.utility.set_source_energy_spectrum(source, spectrum)
```

T. Gonguet



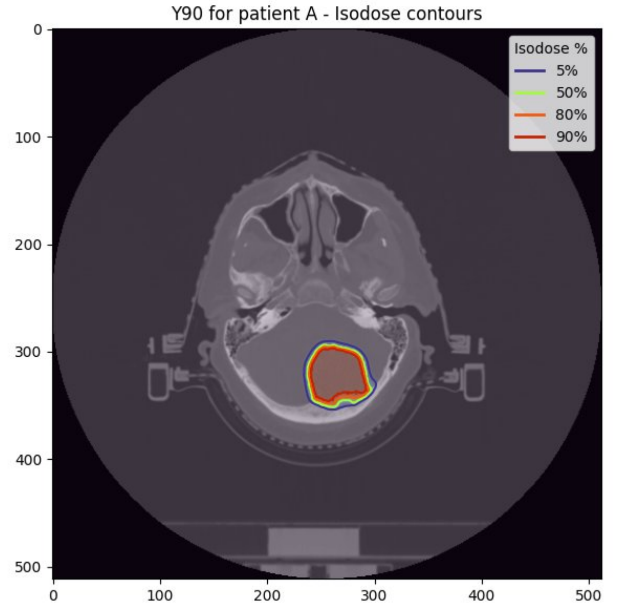
3D representation of the patient, with the GTV highlighted in red.

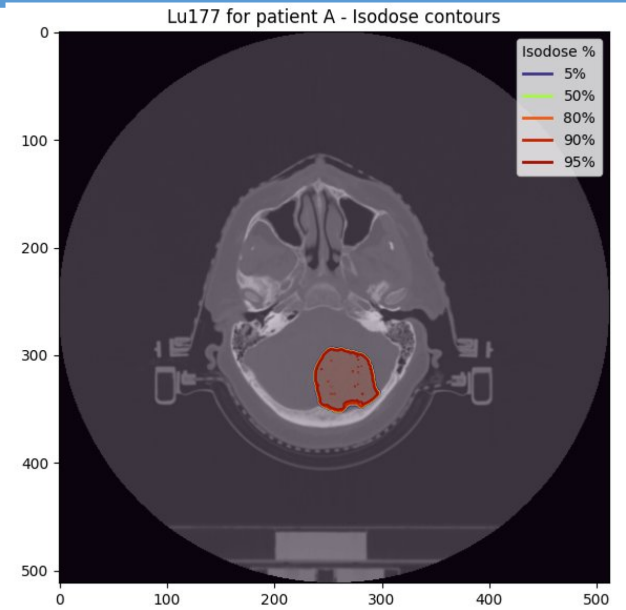
```
# Read patient volume from CT data
reader = sitk.ImageSeriesReader()
reader.SetFileNames(ct_files)
volume = reader.Execute()
volume.name = f"{rtstruct_path.stem}_CT_volume"

# Dose actor
dose = sim.add_actor("DoseActor", "dose")
dose.attached_to = sim_volume.name
dose.output_filename = str(output_file)
```

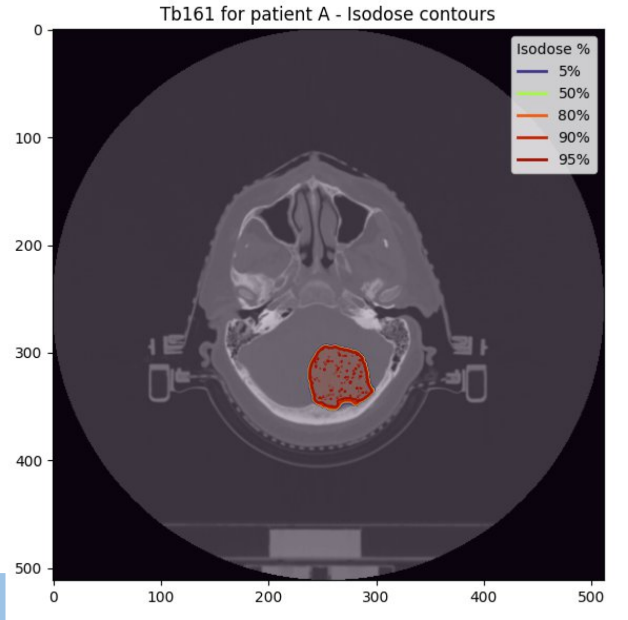
T. Gonguet

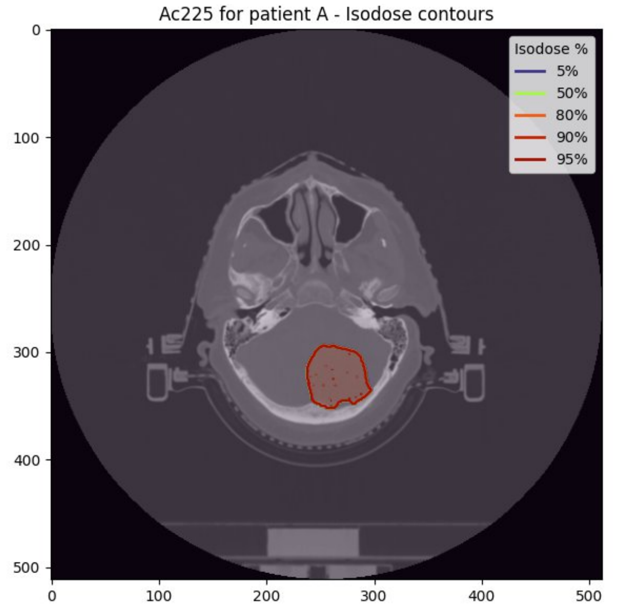
Patient dosimetry: Isodoses - Patient A

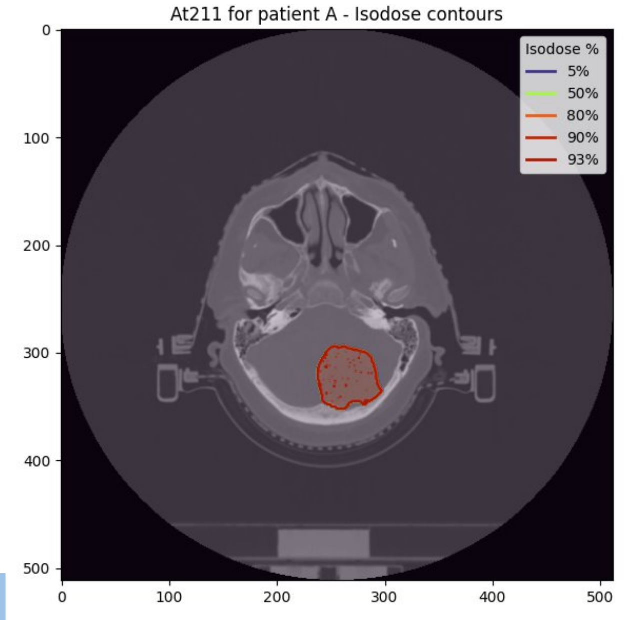
Isotopes comparison:
Yttrium-90 is used for now but several isotopes can be considered.







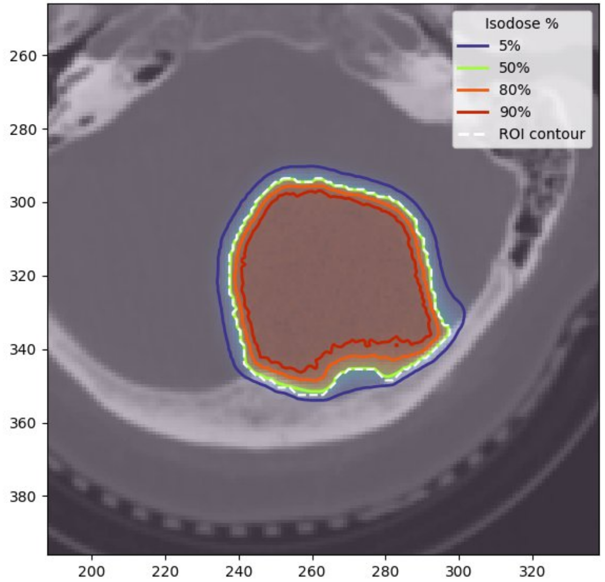




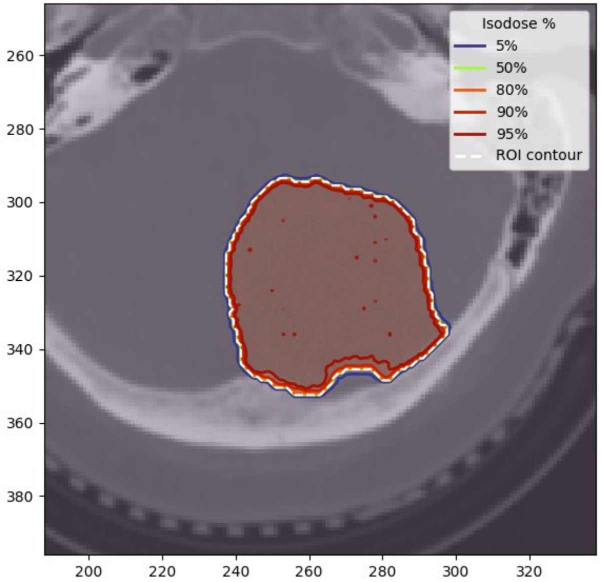
Patient dosimetry: Isodoses - Patient A (ROI)

Isotopes comparison:
Yttrium-90 is used for now but several isotopes can be considered.

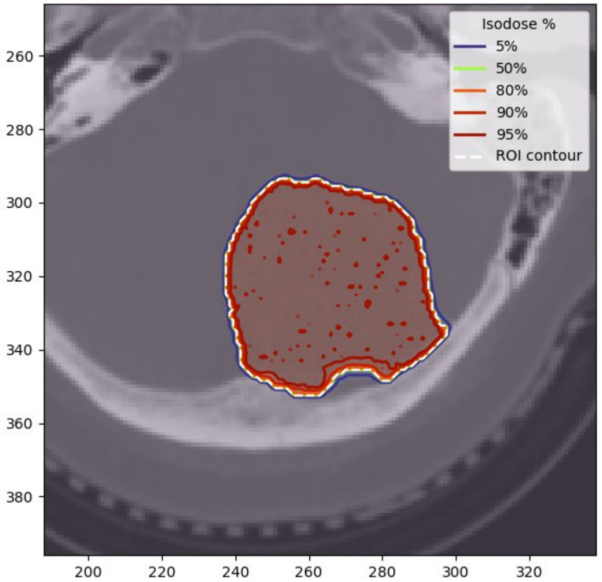
Y90 for patient A - Isodose contours zoom



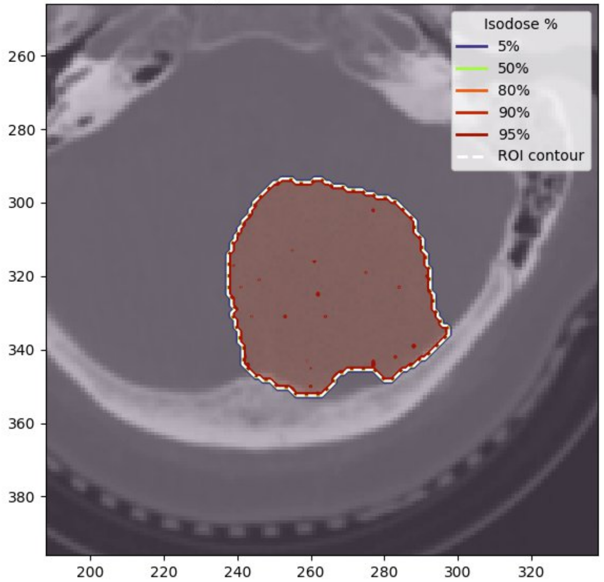
Lu177 for patient A - Isodose contours zoom



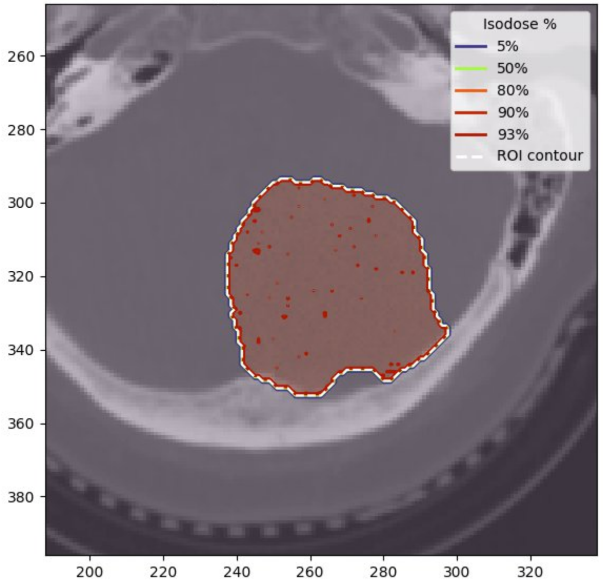
Tb161 for patient A - Isodose contours zoom



Ac225 for patient A - Isodose contours zoom



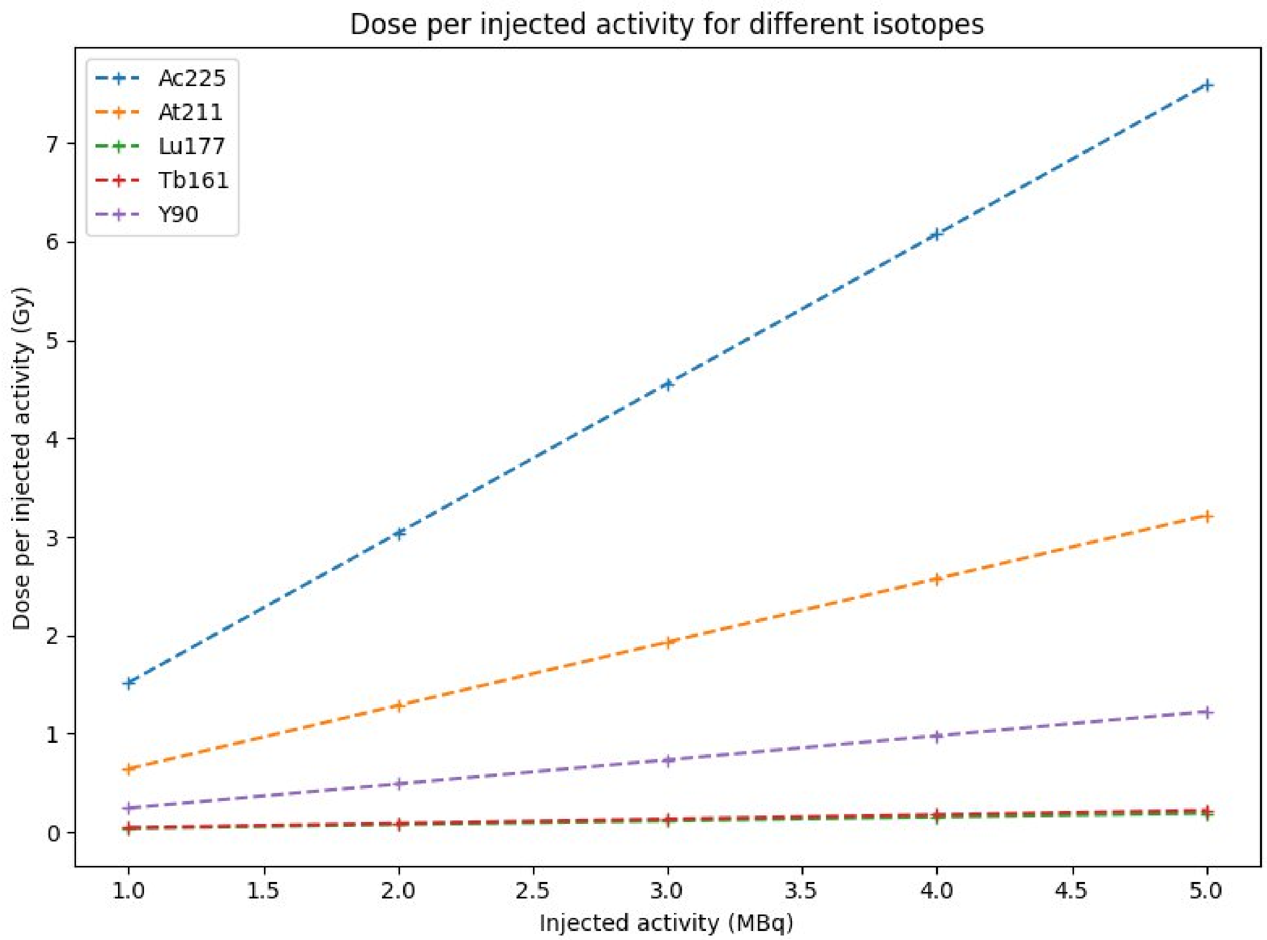
At211 for patient A - Isodose contours zoom



Patient dosimetry: Dose per injected activity

Isotopes comparison:
Yttrium-90 is used for now but several isotopes can be considered.

Injected activity considered : 1, 2, 3, 4, 5 MBq.
6 times more dose absorbed using **Ac-225** rather than **Y-90** for the same activity injected.

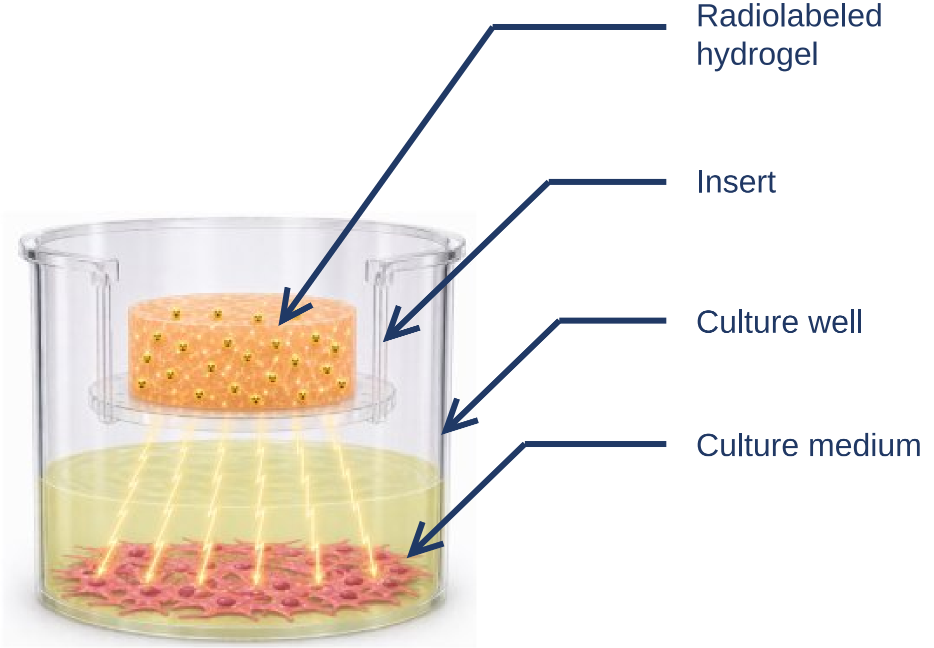


Need to consider the dose on the edges of the GTV, where the microscopic infiltrating tumor cells would be.

In-vitro characterization

In-vitro experiment to characterize the radiobiological effects of the chitosan hydrogel radiolabeled with ^{90}Y.

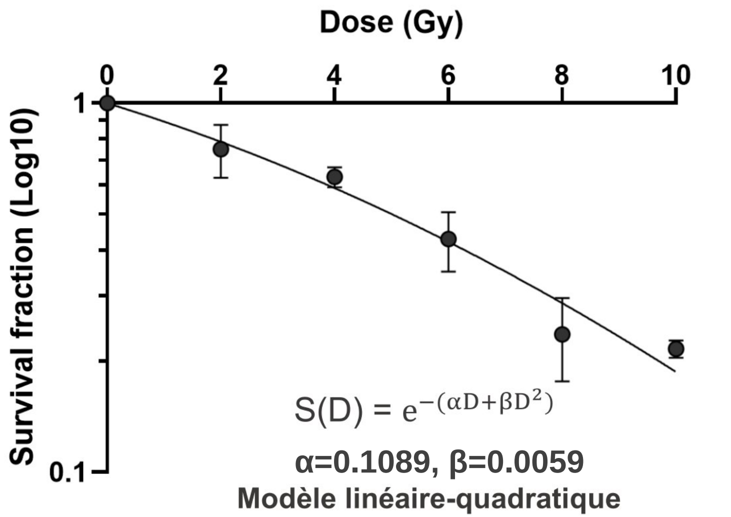
Irradiation of a culture medium with **HYdro-90Y** for 48 hours (about 10 Gy of dose deposition).
Analysis of the changes that occur in the medium : reactive oxygen species (ROS) quantification, DNA damage, cell membrane, etc.



Schematics of the in-vitro experiment.

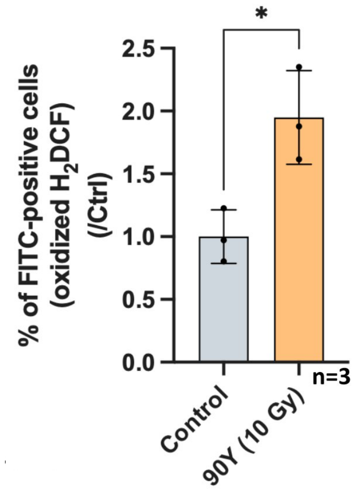
In-vitro experimental data

Survival curves: predominance of the direct lethal damages.



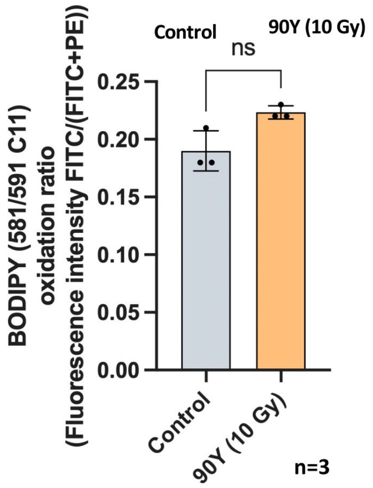
Intracellular ROS quantification measured using H_2DCFDA by cytometry

→ **significant increase of the ROS production after irradiation.**



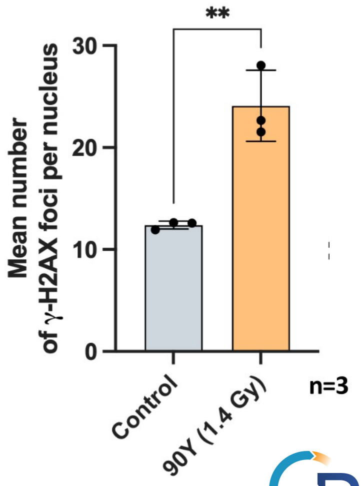
Lipid peroxidation quantification measured by cytometry using the BODIPY 581/591 C11

→ **increase of the lipid peroxidation compatible with the ROS production.**



Double strand DNA damage quantification using the γ-H2AX immunocytofluoresence

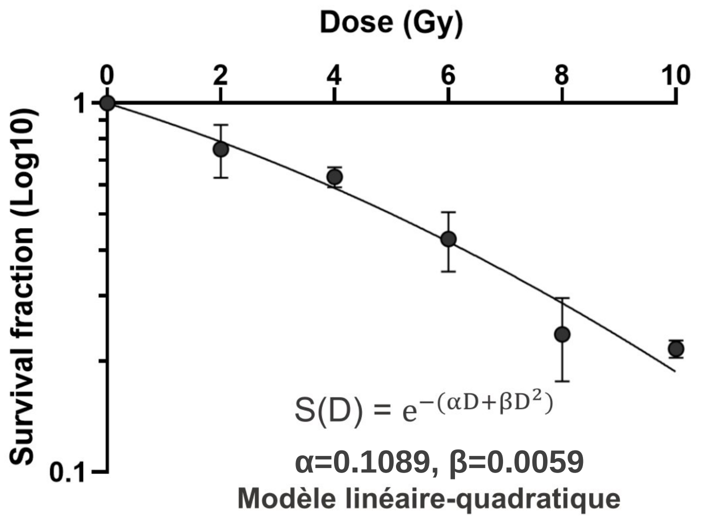
→ **double strand breaks after irradiation.**



In-vitro experimental data to simulation

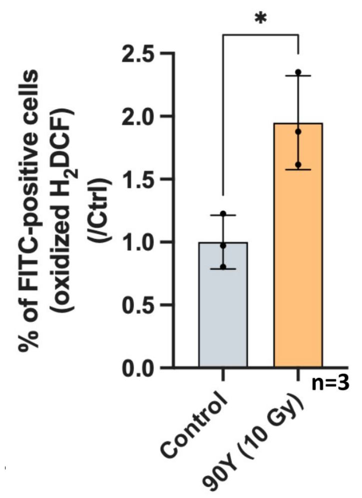
Survival curves:

→ **Gate biodose actor (needs to be adapted for e-)**



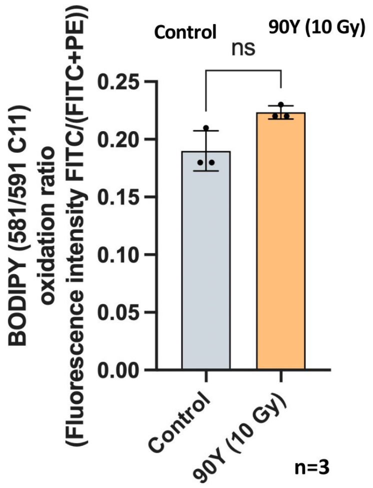
Intracellular ROS quantification

→ **ROS yield with Geant4-DNA (especially H_2O_2)**



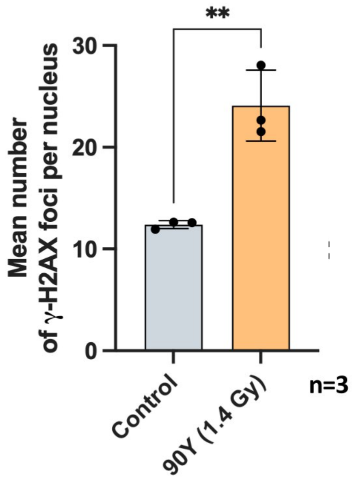
Lipid peroxidation quantification

→ **Geant4-DNA implementation of the reaction and impact on the lipid membrane**



Double strand DNA damage quantification

→ **Geant4-DNA: molecularDNA example and fractalDNA package**



In-vitro experimental data to simulation

Survival curves:

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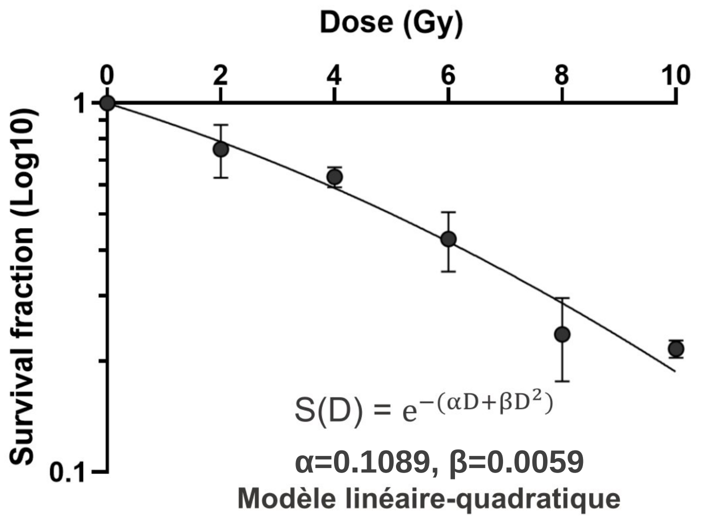

Intracellular ROS quantification

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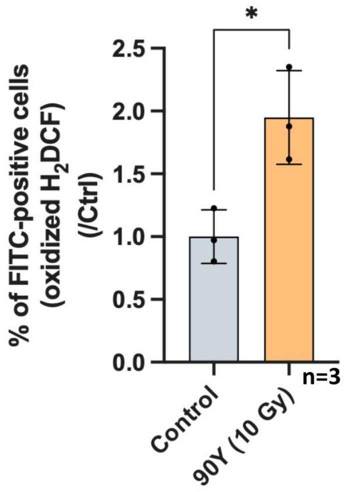

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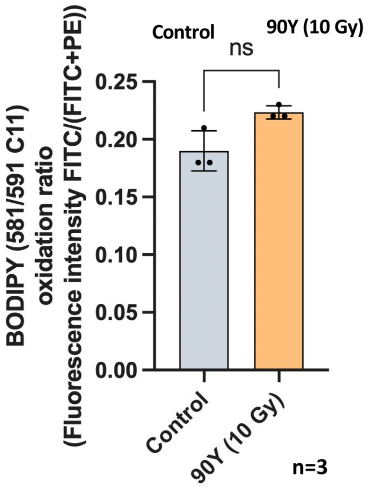
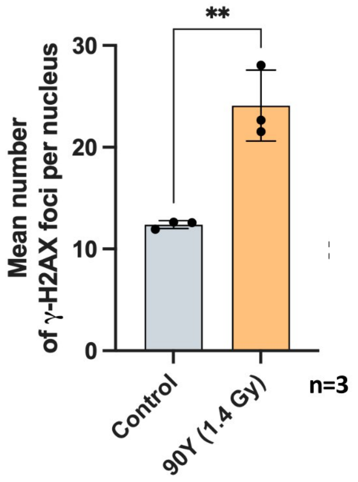


Double strand DNA damage quantification

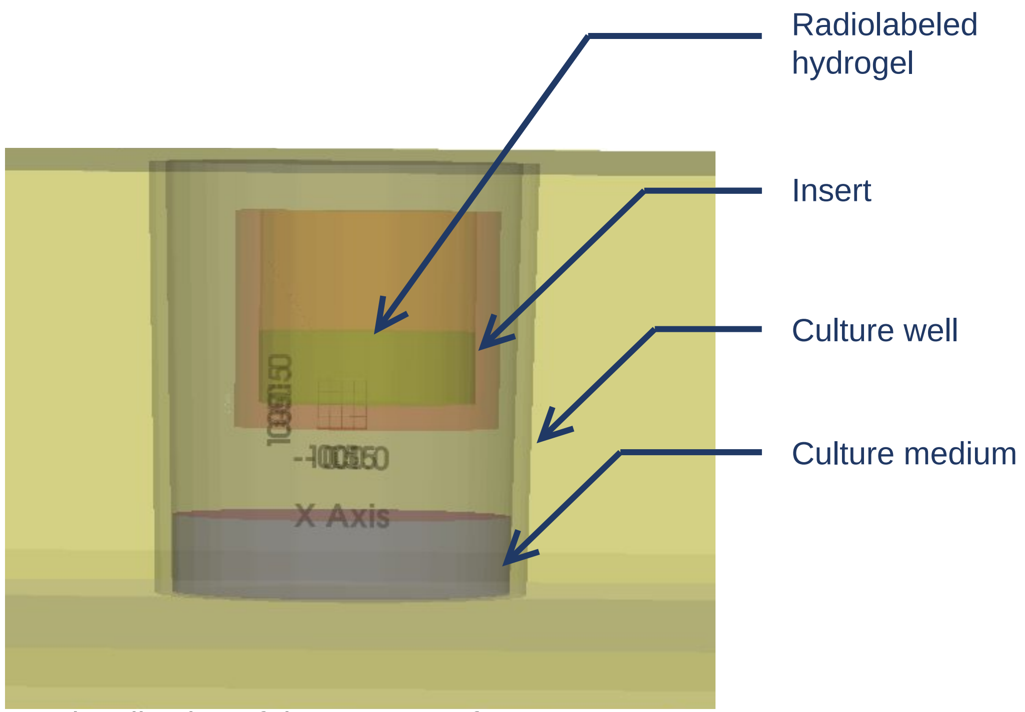
→Geant4-DNA: molecularDNA example and fractalDNA package



In-vitro simulation

Simulation of the in-vitro experiment using Gate (v10.4).

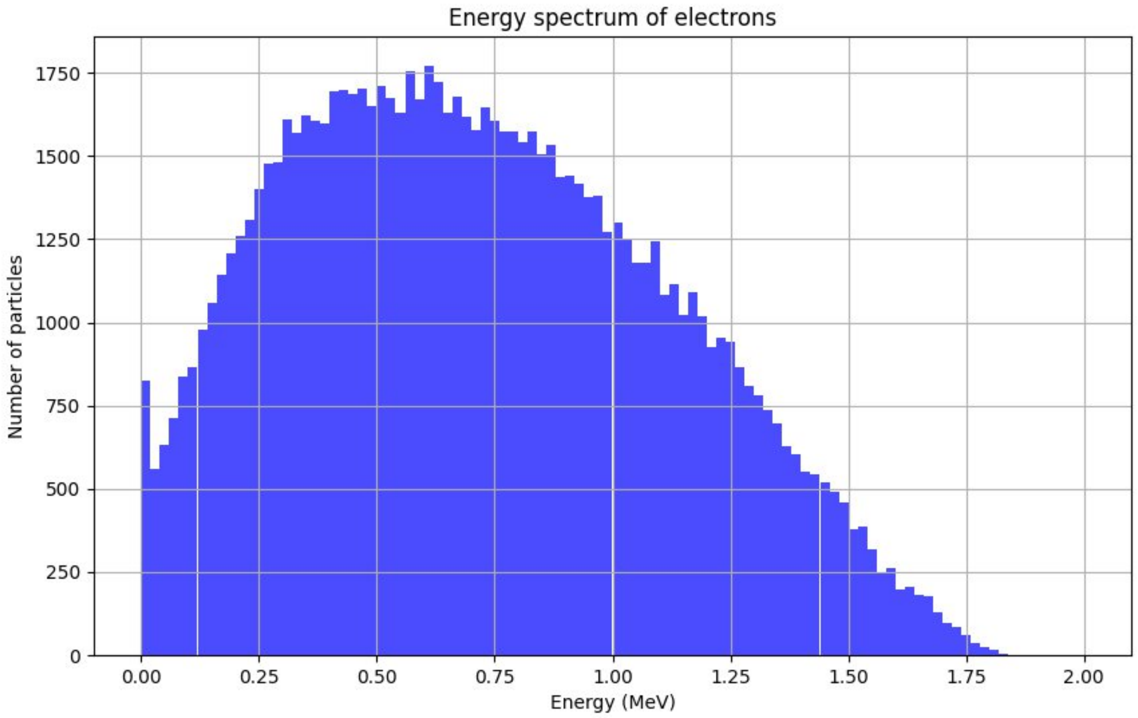
- Source: **^{90}Y** placed in the insert
- Activity: **100MBq** (enough to limit statistical fluctuations)
- Actor: **phase space** placed at the surface of the culture medium (dz = 0.1 um)
- Attributes saved:
  - **Energy**
  - Particle type
  - Particle position
  - ...

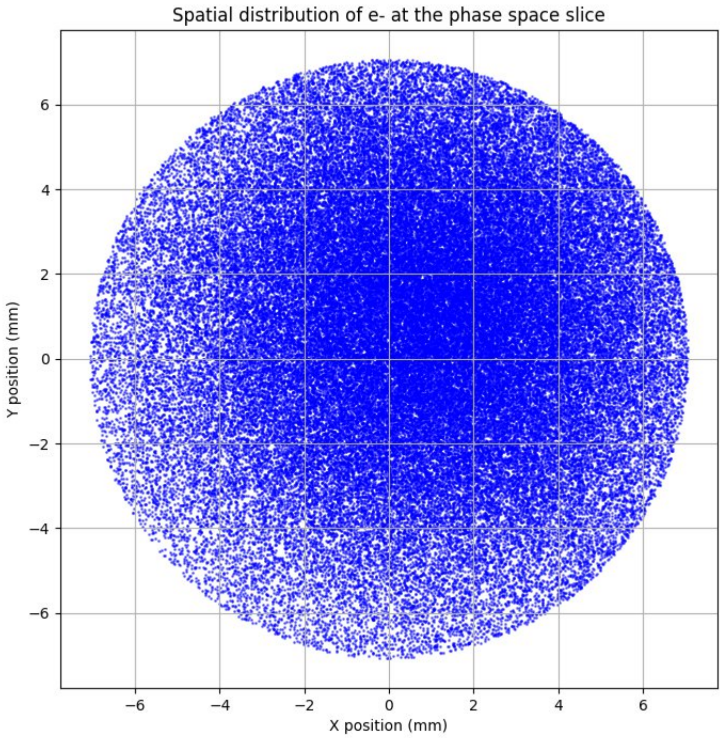


Visualization of the geometry from Gate.

In-vitro simulation: phasespace data

Analysis of the phase space data.
Energy spectrum (e-) and spatial distribution extracted from the phasespace.
Use of the mean and standard deviation of the energy spectrum for the chemistry analysis in Geant4.





Chem6 example

- **Geometry**: 7.065 x 7.065 x 3.2 mm^3 (dimensions of the phase space)
- **Source**: e- (at the center)
- Gaussian energy distribution (using the mean and standard deviation from the spectrum)
- Around **100 events**

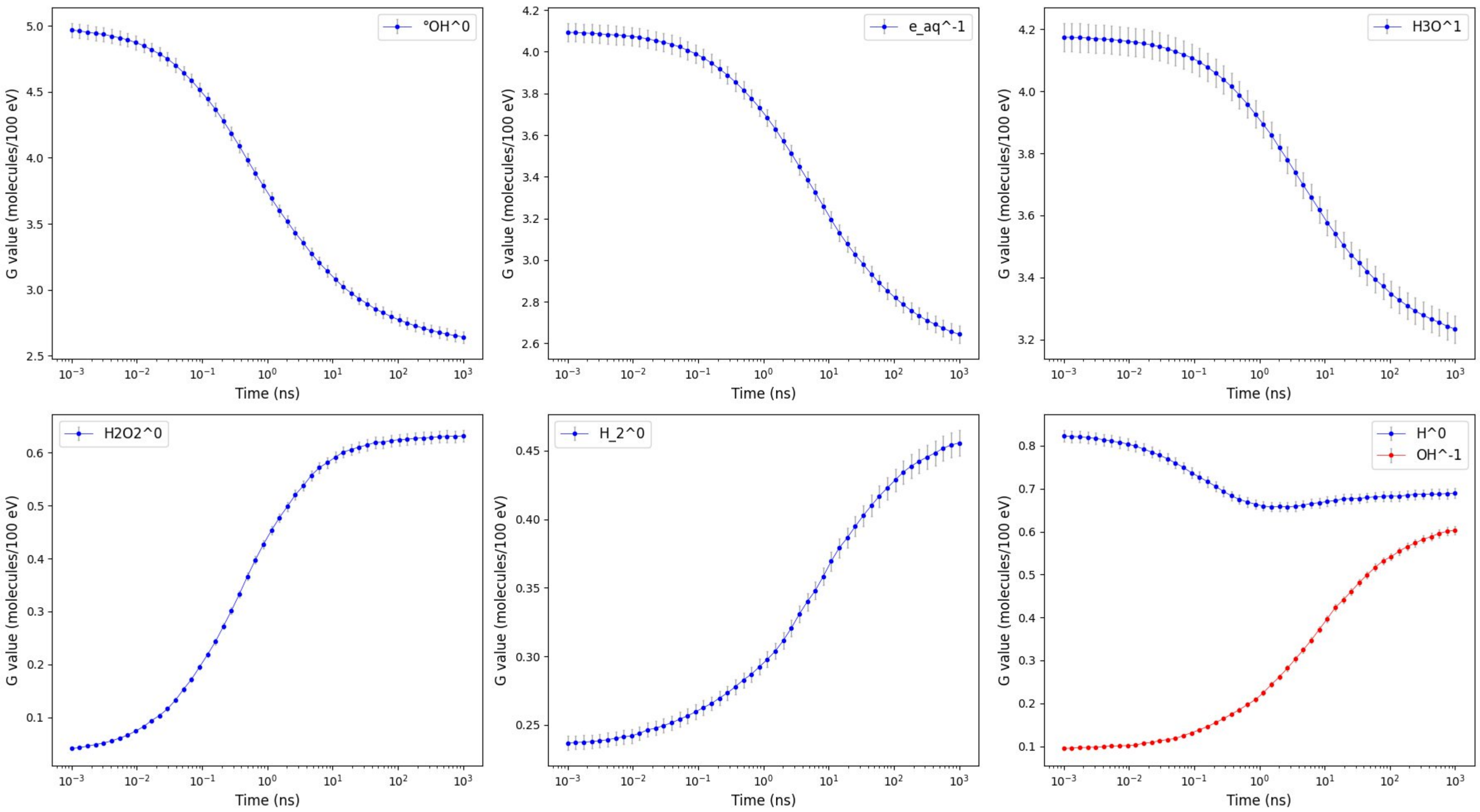
```
Number of chemical species involved in reactions = 6
Reaction                                                     Reaction Rate [dm3/(mol*s)]
-----------------------------------------------------------------------------------------
H3O^1 + OH^-1 -> No product                                   1.13e+11
-----------------------------------------------------------------------------------------
H3O^1 + e_aq^-1 -> H^0                                        2.11e+10
-----------------------------------------------------------------------------------------
°OH^0 + H^0 -> No product                                    1.55e+10
-----------------------------------------------------------------------------------------
°OH^0 + °OH^0 -> H2O2^0                                     5.5e+09
-----------------------------------------------------------------------------------------
°OH^0 + e_aq^-1 -> OH^-1                                     2.95e+10
-----------------------------------------------------------------------------------------
e_aq^-1 + H^0 -> H_2^0 + OH^-1                                2.5e+10
-----------------------------------------------------------------------------------------
e_aq^-1 + e_aq^-1 -> H_2^0 + OH^-1 + OH^-1  6.36e+09
-----------------------------------------------------------------------------------------
e_aq^-1 + H2O2^0 -> OH^-1 + °OH^0           1.1e+10
-----------------------------------------------------------------------------------------
H^0 + H^0 -> H_2^0                                            5.03e+09
-----------------------------------------------------------------------------------------
```

Chem6 example: G_values

Results
G_values as a function of time for different radicals

Gaussian beam
mean : 0.7 MeV
Stdev : 0.3

Geometry
7.065 x 7.065 x 3.2 mm³



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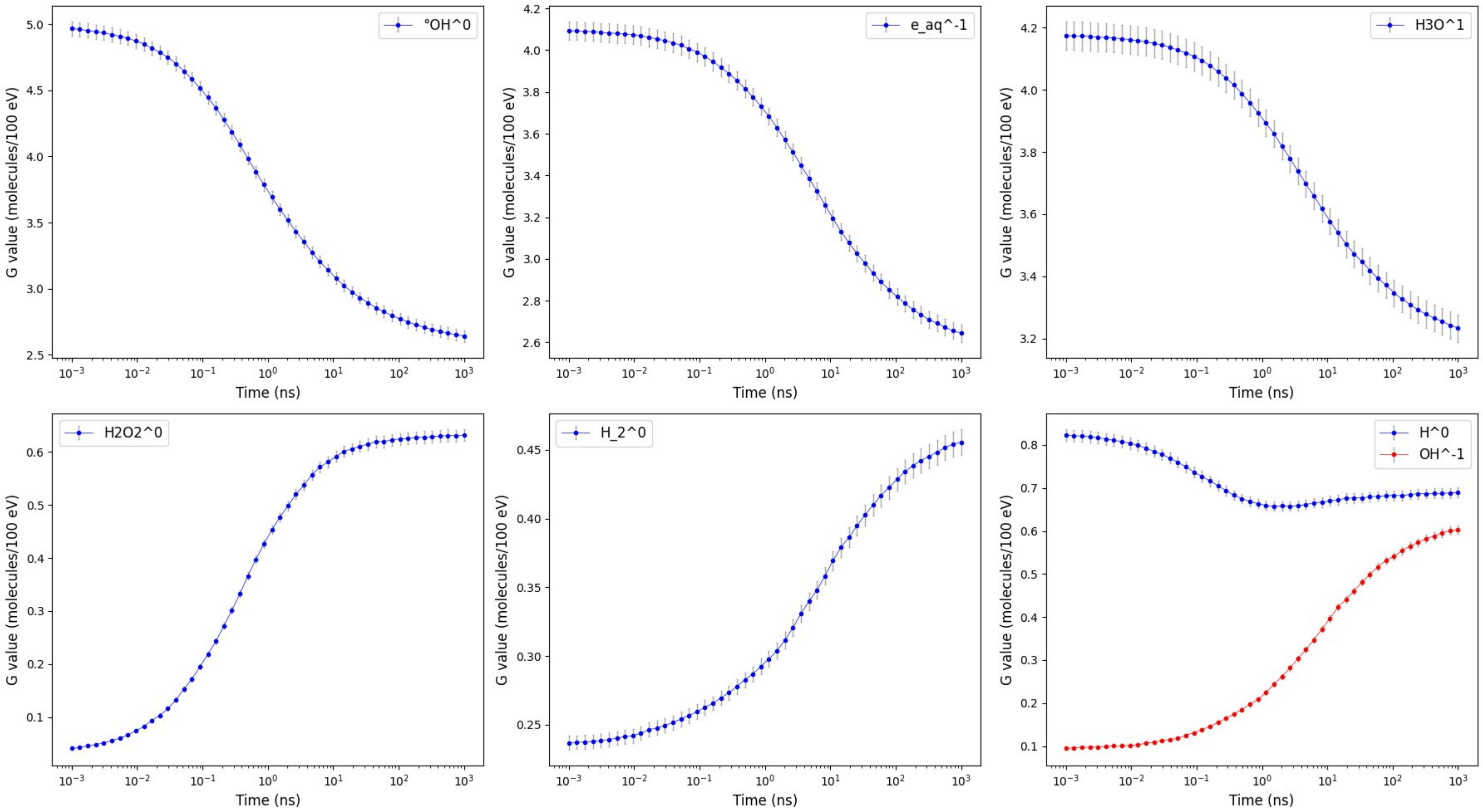
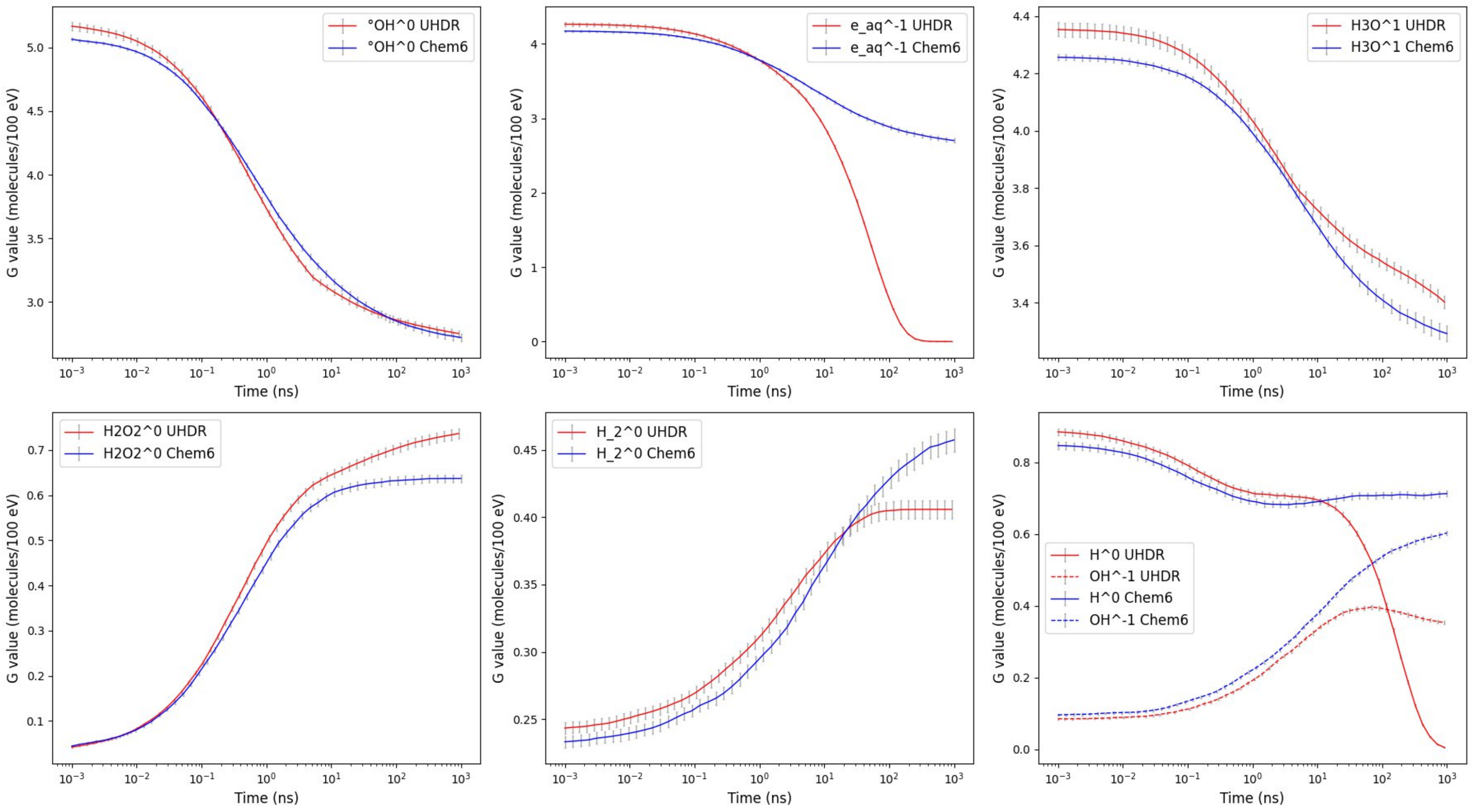


Issue: no possibility to control the experiment conditions with chem6

UHDR example

Simulation conditions:

- Geometry : 3.2 um³
- **ph = 7.2**
- **O_2 level: 21%**
- **CO_2 level: 5%**
- Particle source: e-
- Energy: 0.7 MeV
- beamOn: 100



Differences observed between the examples.
Could be caused by the different conditions but also by the different reactions involved.

Conclusions and perspectives

Conclusion:

- Analysis of the different radio-isotopes for the hydrogel.
- Gate simulation of the in-vitro experiment.
- H_2O_2 yield obtained for the in-vitro simulation in Geant4-DNA (with both the chem6 and UHDR example).

Perspectives:

- **Patient dosimetry**: microdosimetric analysis on the edge of the cavity at the millimetric and micrometric scale.
- **In-vitro simulation**:
  - Find the relation between the cytometric data and the yield for the ROS
  - Simulations with Geant4-DNA to quantify the DNA damage, lipid peroxidation etc.
- **Dosimetric study on the small animal** (Fischer rats)

Thank you for your attention

Questions?

Patient dosimetry: Dose per injected activity

Isotopes comparison: Yttrium-90 is used for now but several isotopes can be considered.

Y90	
Injected activity (MBq)	Dose in ROI (Gy)
1	0.2448
2	0.4896
3	0.7344
4	0.9792
5	1.224

Lu177	
Injected activity (MBq)	Dose in ROI (Gy)
1	0.0382
2	0.0764
3	0.1146
4	0.1528
5	0.191

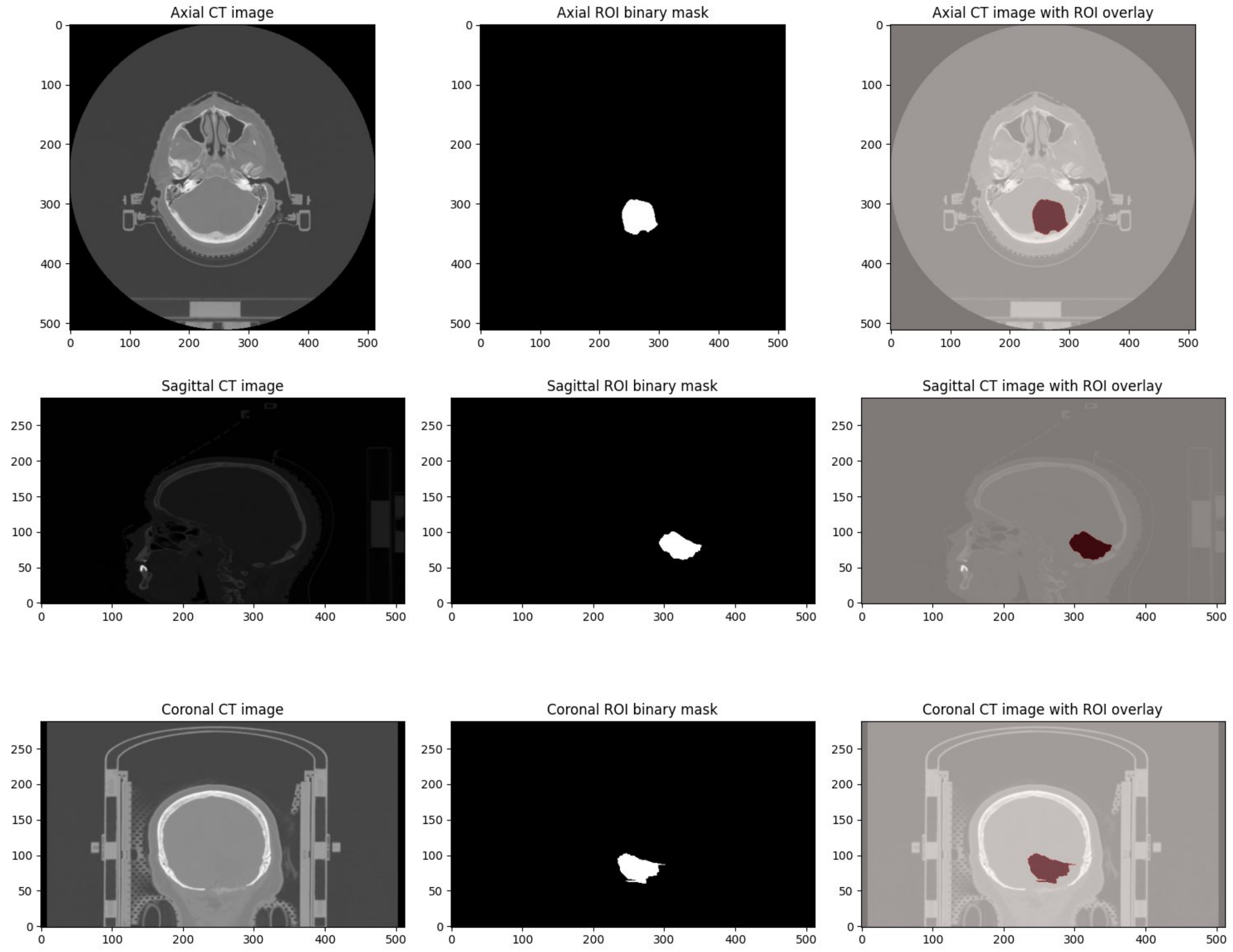
Tb161	
Injected activity (MBq)	Dose in ROI (Gy)
1	0.0442
2	0.0884
3	0.1326
4	0.1768
5	0.221

Ac225	
Injected activity (MBq)	Dose in ROI (Gy)
1	1.5186
2	3.0372
3	4.5558
4	6.0744
5	7.593

At211	
Injected activity (MBq)	Dose in ROI (Gy)
1	0.6436
2	1.2872
3	1.9308
4	2.5744
5	3.218

Patient dosimetry: patient CT

Gate simulation
- Version: **Gate 10.4**
- Source: isotope (β or α emitters), voxelized
- Placement: in the **GTV**
- Target: patient head CT
- Activity: **100MBq** or **1GBq** to limit statistical fluctuations



First column: *Patient CT image.* ***Second column***: *creation of the binary mask delimiting the GTV.* ***Third column***: *Overlap between the CT image and the mask.*

Patient dosimetry: Isodoses - Patient A (zoom)

Isotopes comparison:
Yttrium-90 is used for now but several isotopes can be considered.