Istituto Nazionale di Fisica Nucleare
LABORATORI NAZIONALI DI LEGNARO

Laboratori Nazionali di Legnaro – INFN

Image-based cell dosimetry using Geant4

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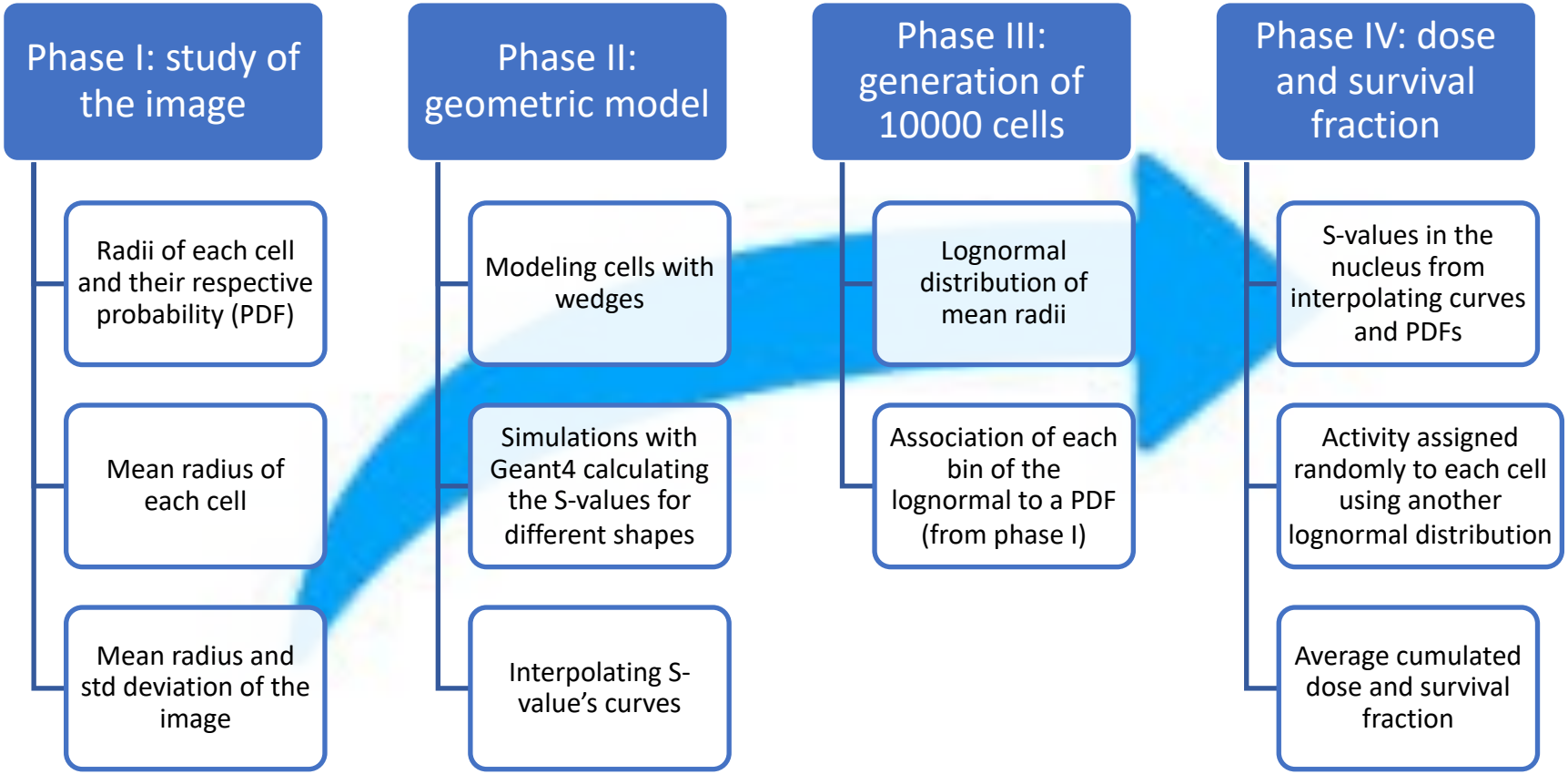
My thesis work in a nutshell

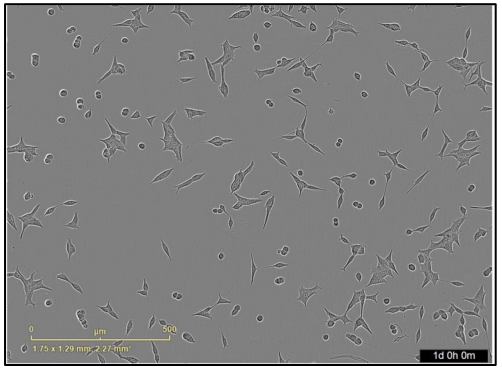
- Image of cells (LNCaPs)
- Development of a geometric model
- Simulations with Geant4
- Determination of absorbed dose and of survival fraction in a colture irradiated with Ag-111

Work flow


Phase I: study of the image
Radii of each cell and their respective probability (PDF)
Mean radius of each cell
Mean radius and std deviation of the image
Phase II: geometric model
Modeling cells with wedges
Simulations with Geant4 calculating the S-values for different shapes
Interpolating S-value's curves
Phase III: generation of 10000 cells
Lognormal distribution of mean radii
Association of each bin of the lognormal to a PDF (from phase I)
Phase IV: dose and survival fraction
S-values in the nucleus from interpolating curves and PDFs
Activity assigned randomly to each cell using another lognormal distribution
Average cumulated dose and survival fraction

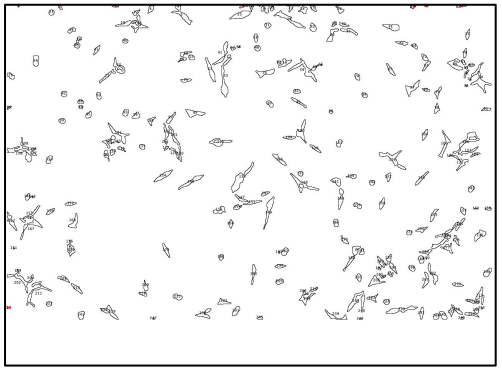
Phase I: image analysis with ImageJ

1)



2)

3)



4)

```
Cellula numero  1
r_ 1 = 1.6866   p_ 1 = 0.08333
r_ 2 = 1.9159   p_ 2 = 0.08333
r_ 3 = 2.1452   p_ 3 = 0.08333
r_ 4 = 2.3744   p_ 4 = 0.08333
r_ 5 = 2.6037   p_ 5 = 0
r_ 6 = 2.833   p_ 6 = 0
r_ 7 = 3.0622   p_ 7 = 0.25
r_ 8 = 3.2915   p_ 8 = 0.1667
r_ 9 = 3.5208   p_ 9 = 0.1667
r_ 10 = 3.75   p_ 10 = 0.08333
Mean radius [um]= 2.8809   Dev std [um]= 0.6332
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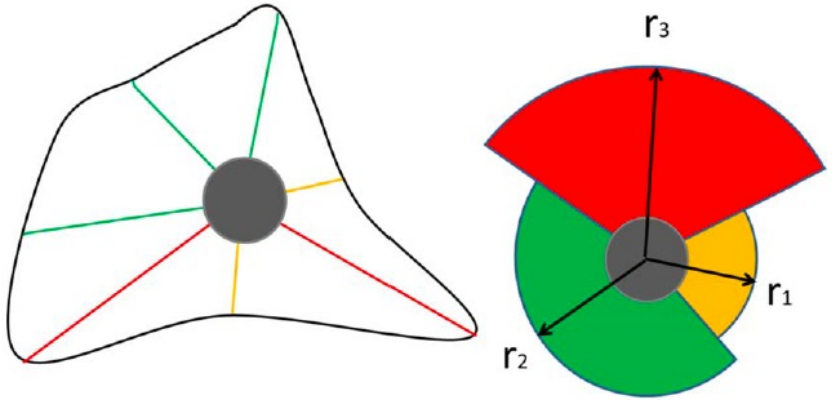
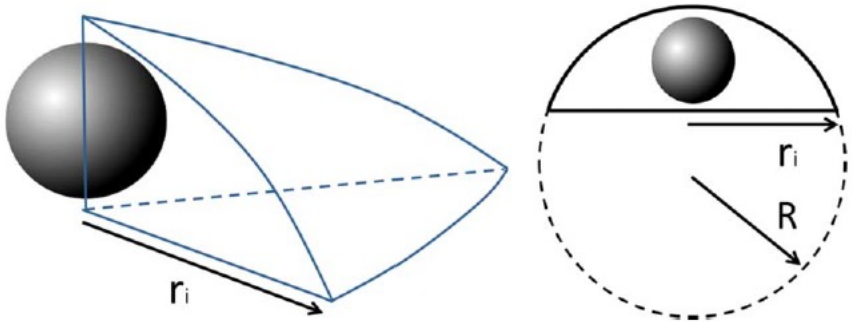
Phase II: geometric model



A 3-bin histogram representation

In 3 dimensions

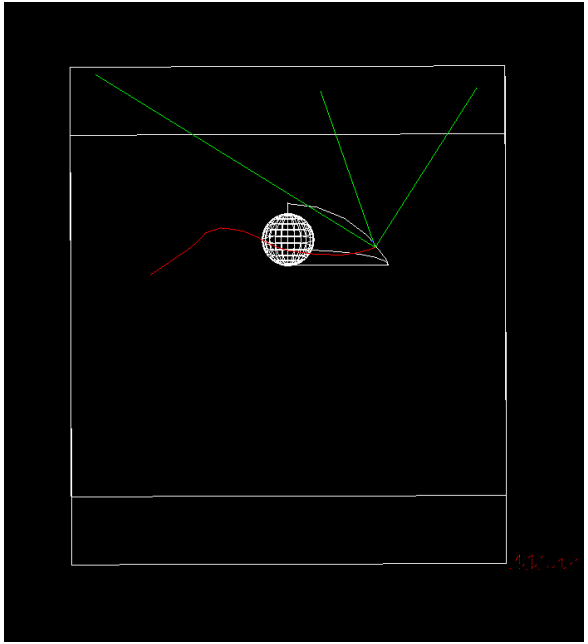
Spherical cap representation of wedge



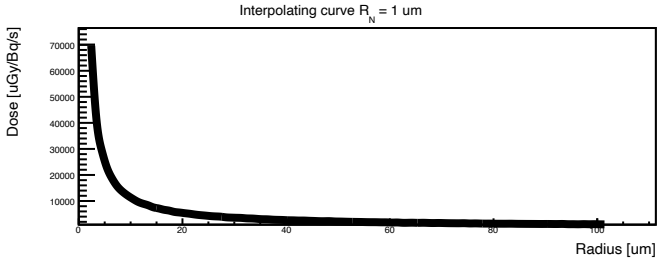
Simulations with GEANT4

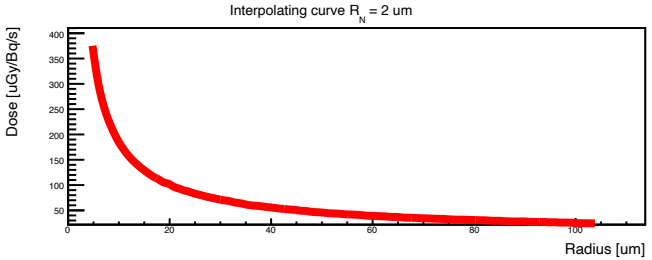
A SIMULATION TOOLKIT

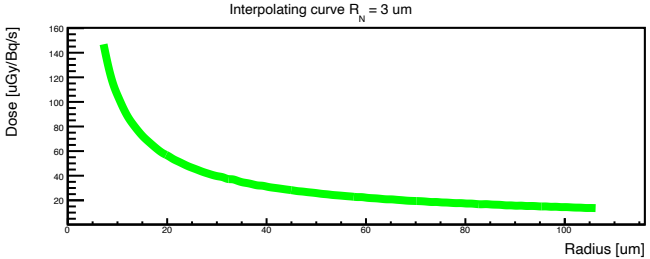
- Simulations of this geometry changing the radius of the sphere and of the nucleus
- Calculation of the S-value for 100 radii and 5 radii of the nucleus

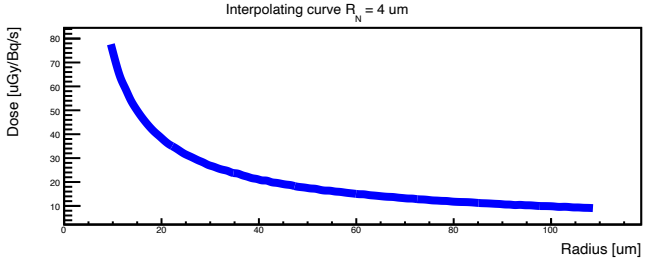


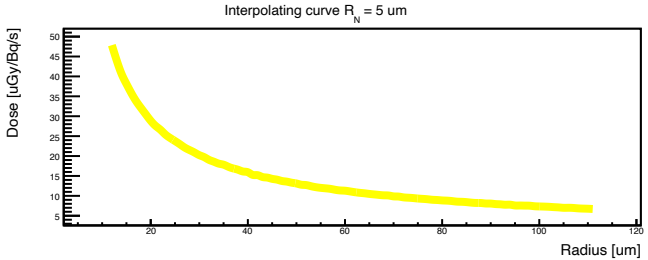
S-values curves







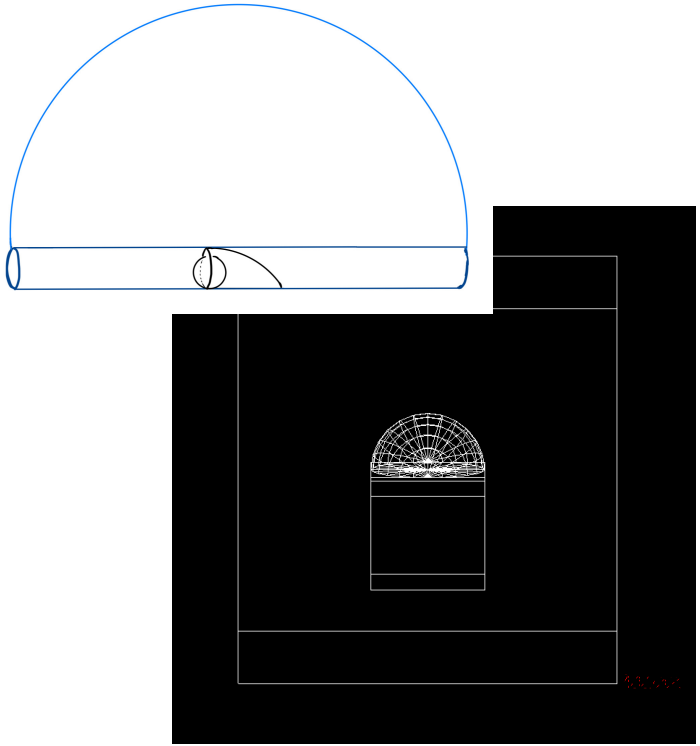




Source: membrane
Target: nucleus

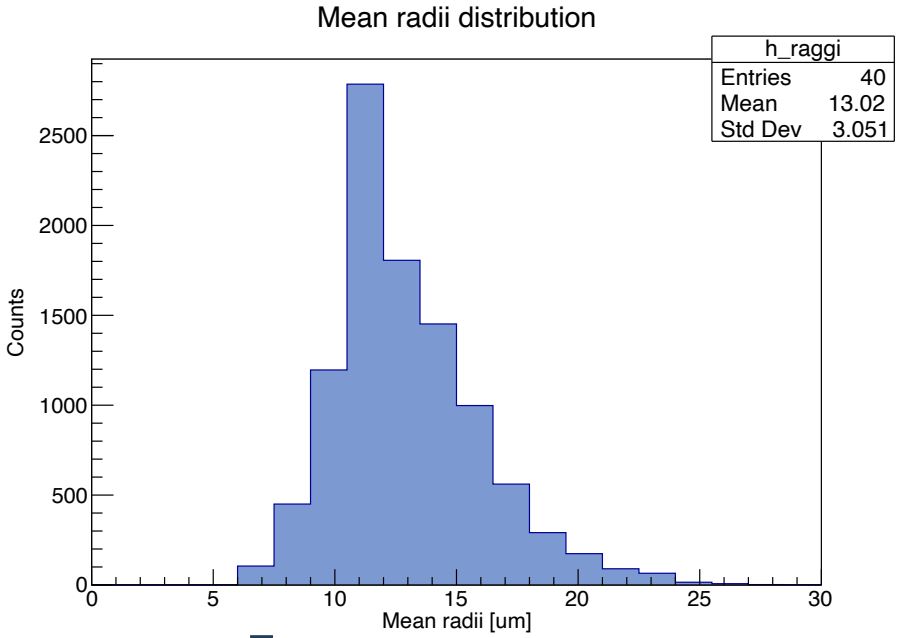
Environment and cross dose

- Emisphere (water) of radius 3 mm
- Cylinder (water) of height $\sim 15\ \mu m$
- Box (polystyrene) of height 1 mm
- Box (steel) of height 5 mm



Phase III: generation of 10000 cells

- 10000 cells of different mean radii
- Lognormal distribution
- Each bin of the distribution is associated with a PDF

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Phase IV: S-value calculation

$$D_{tot} = \sum_{r_i}^{\#bins} D(m \rightarrow n)\,(r_i) \cdot p_i + D(cy \rightarrow n)(r_i) \cdot p_i$$

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S-value from the interpolating curves:

- source: membrane
- target: nucleus

Phase IV: S-value calculation

$$D_{tot} = \sum_{r_i}^{\#bins} D(m \rightarrow n)\,(r_i) \cdot p_i + \boxed{D(cy \rightarrow n)(r_i)} \cdot p_i$$

S-value from the interpolating curves:

- source: cytoplasm
- target: nucleus

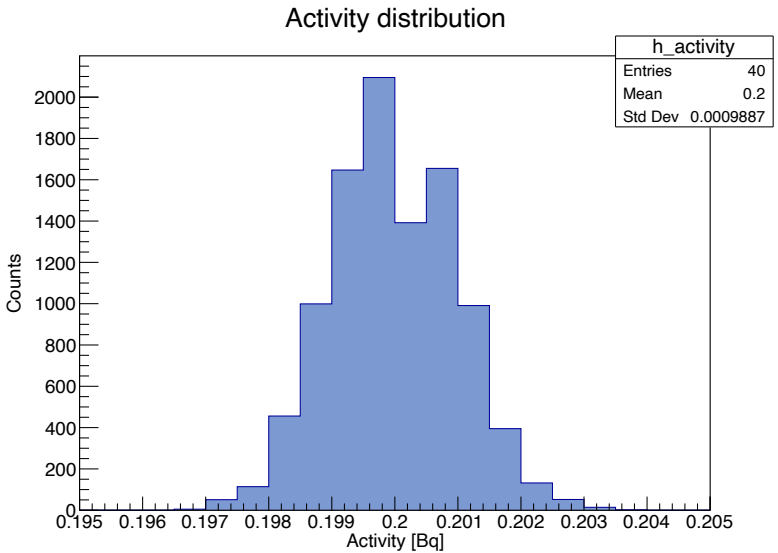
Phase IV: S-value calculation

$$D_{tot} = \sum_{r_i}^{\#bins} D(m \rightarrow n)\,(r_i) \cdot p_i + D(cy \rightarrow n)(r_i) \cdot p_i$$

Probability of the radius r_i

Implementation of the activity

- The activity is assigned randomly to each cell using a lognormal distribution

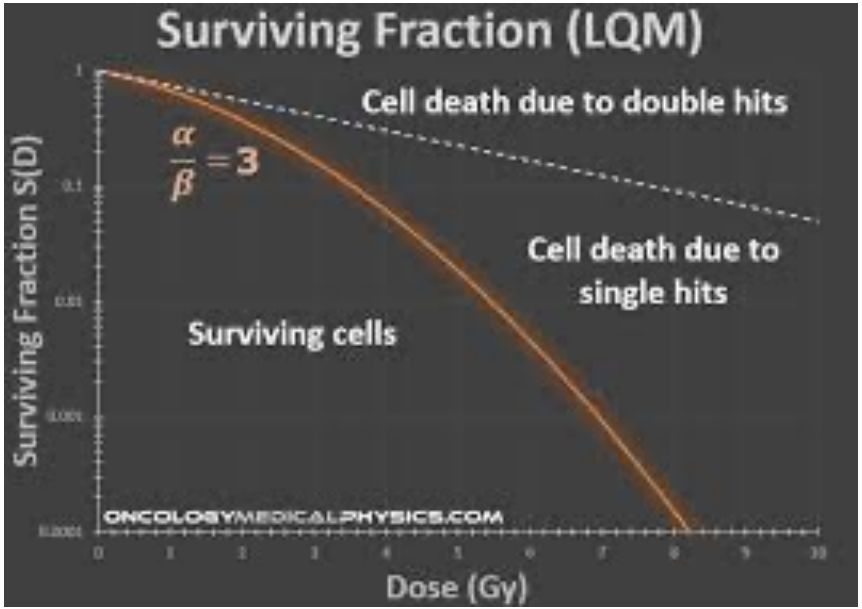


Hypothesis

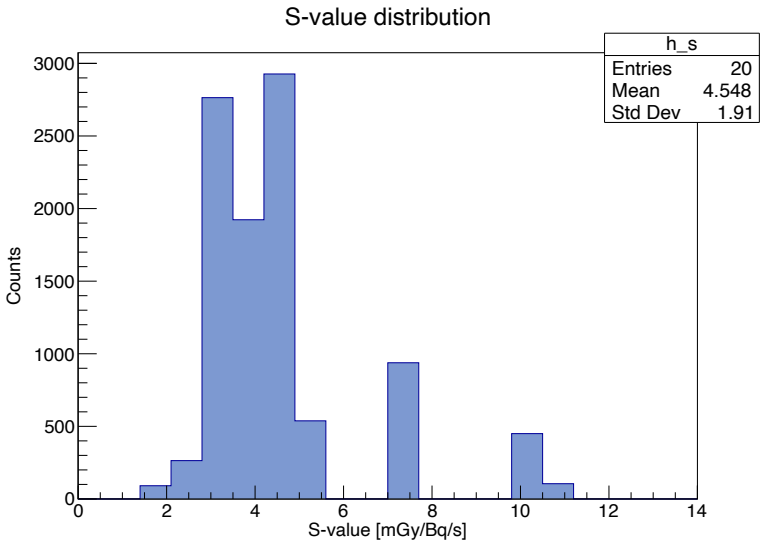
- Applied activity: 100 kBq
- Uptake: 2%
- In the cytoplasm: 60%
- In the membrane: 40%

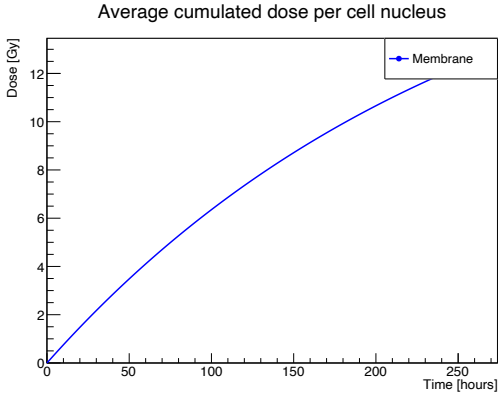
Cell survival probability

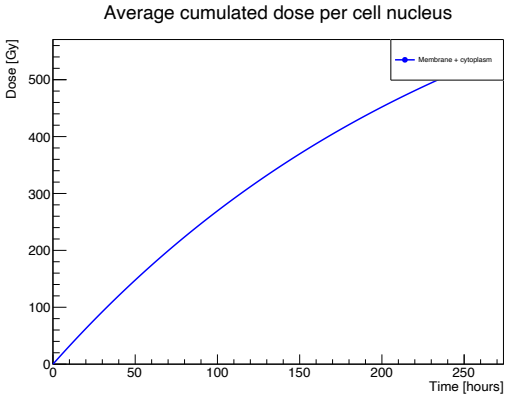
- LQ model: $P = e^{-\alpha D - \beta D^2}$
- A cell is alive if $\xi < P$, for $\xi \in [0, 1]$
- Average survival probability: N_{alive}/N_{cells}



First results



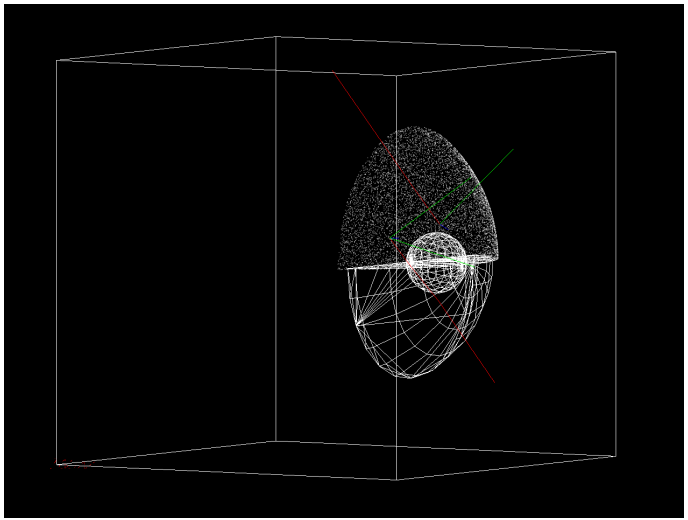


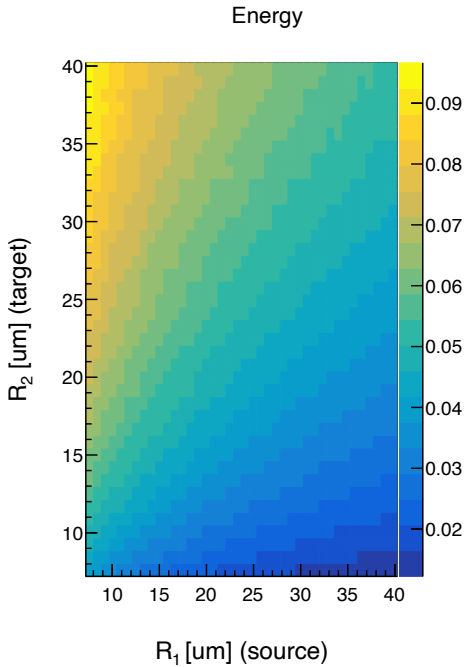


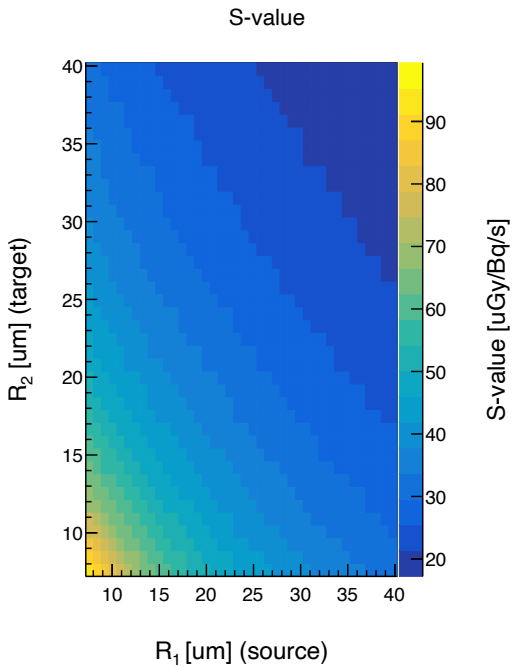
- Great dose released in the nucleus from the cytoplasm
- Average surviving fraction after 4 days: $\sim 0\ \%$

$D(cy \rightarrow cy)(r_i)$

- Two wedges: one is the source, the other is the target







Conclusions: what's next?

- Predictions on how the cumulated dose and the surviving fraction change with the applied activity
- Predictions on how the cumulated dose and the surviving fraction change with the uptake
- Compare the results with experimental data from the next experiment in May
- Implementing angular extension in the study of the target cytoplasm
- Therapy simulations with Geant4-DNA with Lu-177 in collaboration with Brescia hospital.

Thanks for your attention!