laboratoire commun CEA/DRF CNRS/IN2P3

Dosimetry in preclinical radiotherapy

Anne-Marie Frelin

Introduction

▶ Preclinical investigations in radio-oncology

Reproducibility of experiments → Comparison between experiments/treatments

Translation to clinical application → Relevance of preclinical studies

▶ Improving the relevance and the translation of preclinical results

- Relevance of biological models (cancerous cell lines…)
- Relevance of experimental setups (delivered dose, schedule…)
- Calibration and dosimetry of irradiations
- Details and accuracy of the methods and results description

Small animal RT

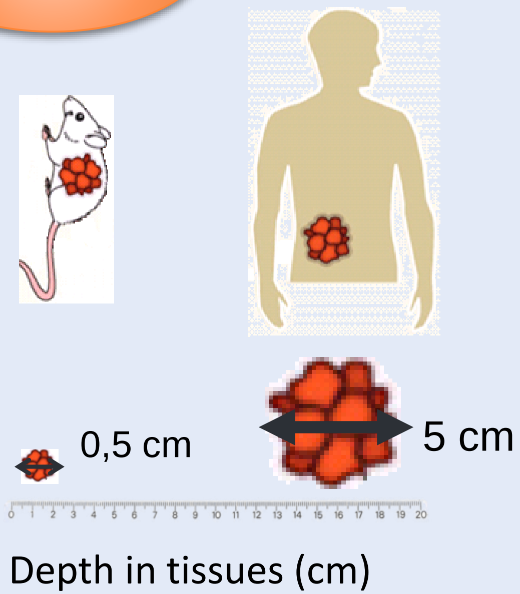
In vitro assessment of TAT

Small animal radiotherapy

Downscaling clinical RT to animal size

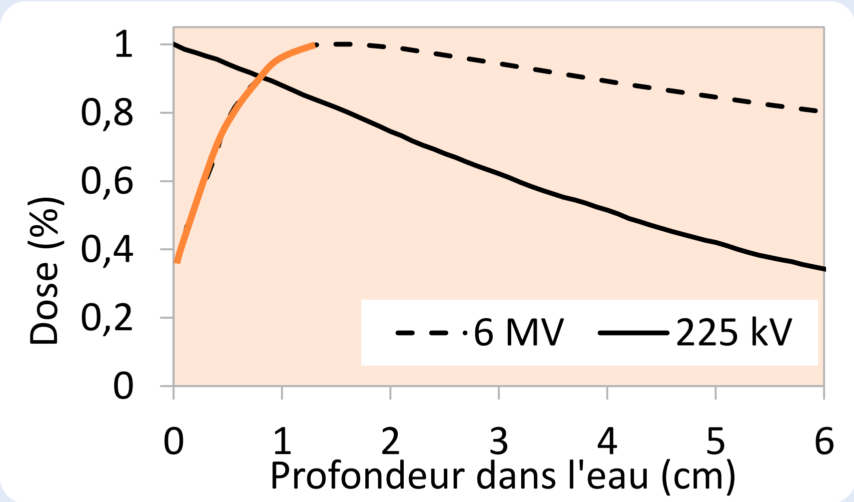
→ Reduction of beams size

cm → mm



→ Reduction of beams energy

1-25 MeV → <300 keV



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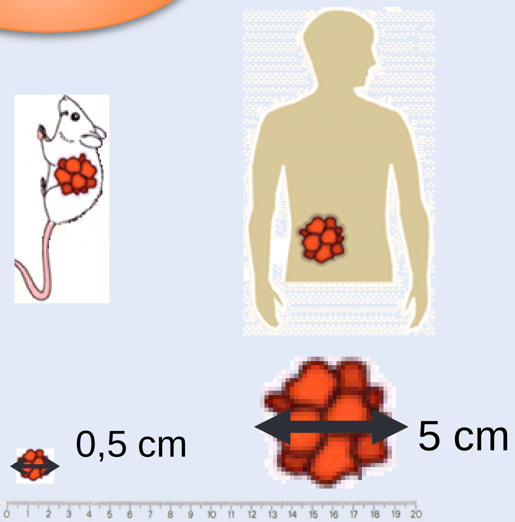
Small animal radiotherapy

Downscaling clinical RT to animal size

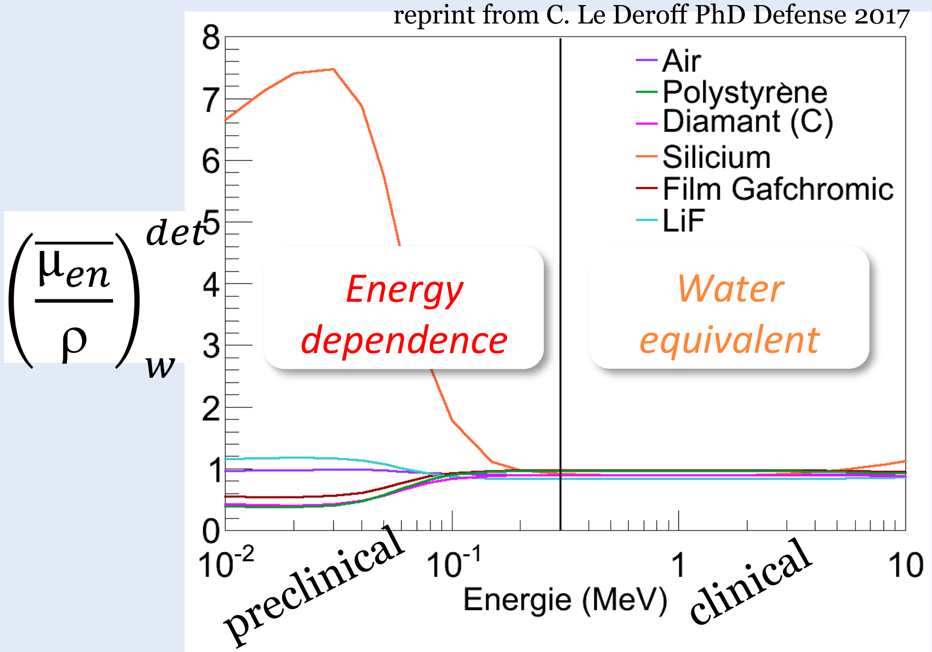
→ Reduction of beams size

cm → mm



→ Reduction of beams energy

reprint from C. Le Deroff PhD Defense 2017



- Photoelectric effect
- Compton scattering

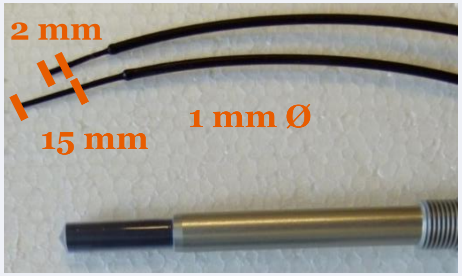
Small animal radiotherapy

Preclinical scintillating fiber dosimetry

Material non-equivalence + mm beam size → suitable detector ???

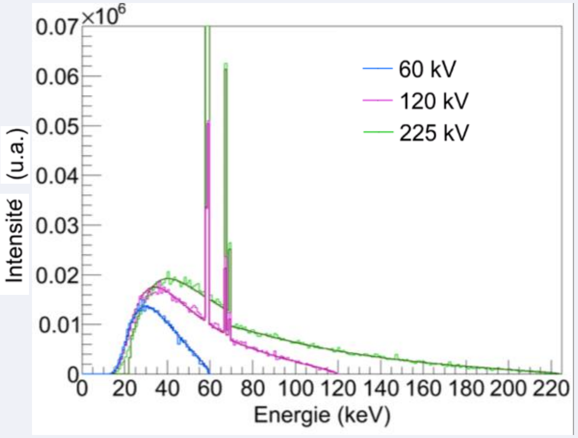
No clinical dosimeter answer all requirements

Scintillating fiber dosimeter called **DosiRat**



- Composition close to tissue (PS, PMMA)
- Small dimension (∅ 1 mm to 0.5 mm)
- Allow direct reading

X-RAD 225Cx



Energy dependence study with a preclinical irradiator (wide range of energy spectra)

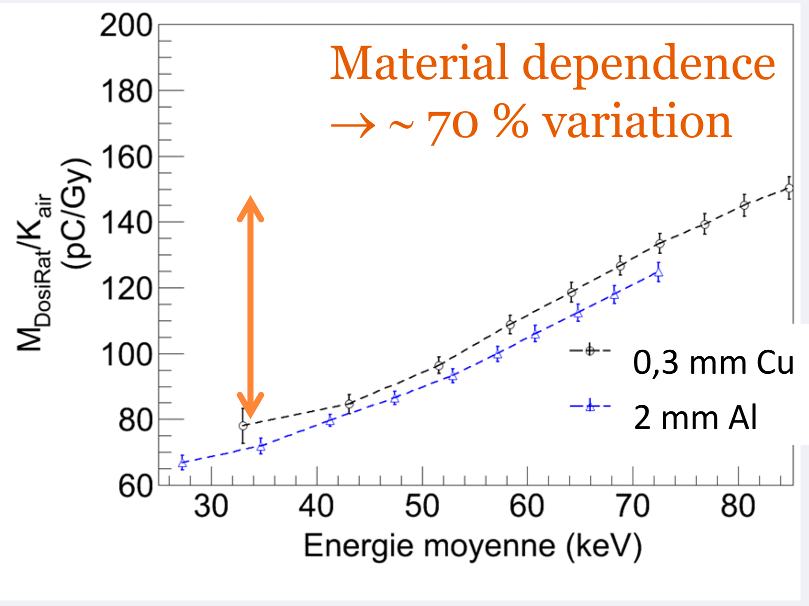
Small animal radiotherapy

Energy dependence assessment

DosiRat response vs. Kerma measured in air

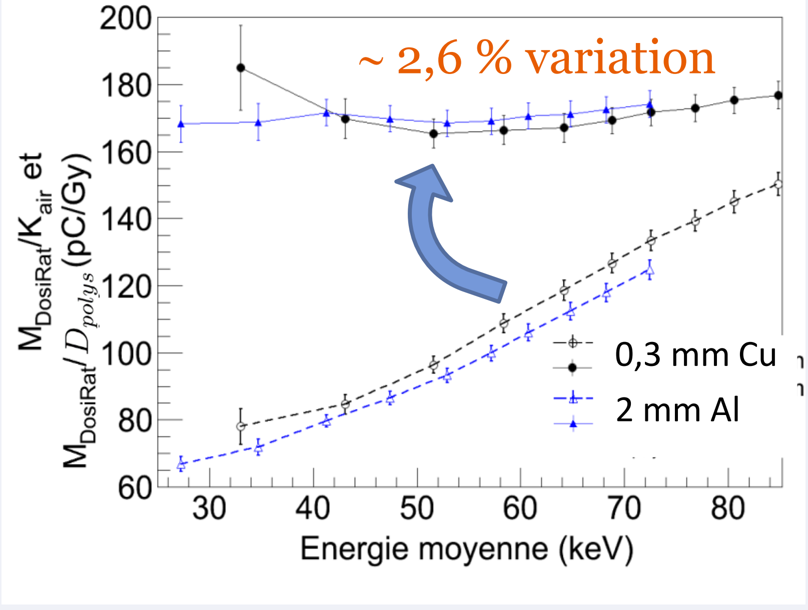
DosiRat response vs. Dose in polystyrene

Measurements: $\frac{M_{DosiRat}}{K_{air}}(\Phi)$



$\frac{M_{DosiRat}}{D_{polys}}(\Phi)$

Scintillation quenching



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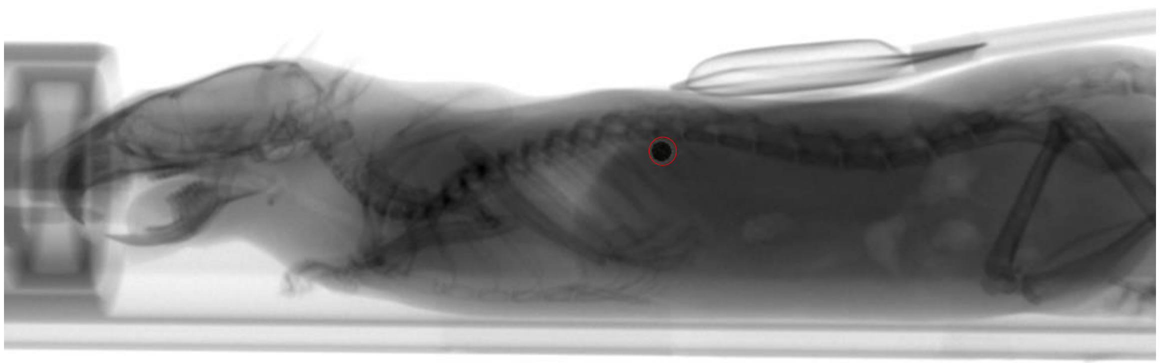
Small animal radiotherapy

Small animal *in vivo* dosimetry

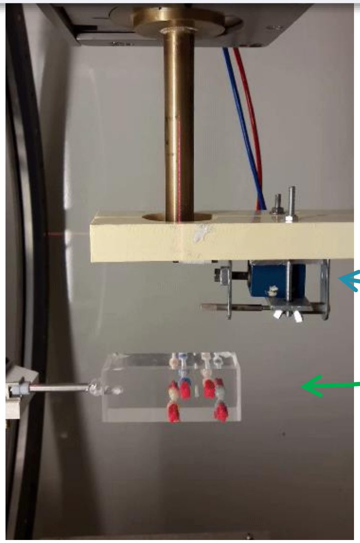
→ Implementation of ***in vivo* dosimetry** in the case of mobile tumor

- Target volume (lung tumor) + millimeter motion
- How to achieve a homogeneous dose distribution ?
  - Implementation of respiratory gating → Dosimetry tools needed



DosiRat → dose rate

EBT3 Film → spatial distribution



- Dynamic phantom
- Synchronized beam shutter

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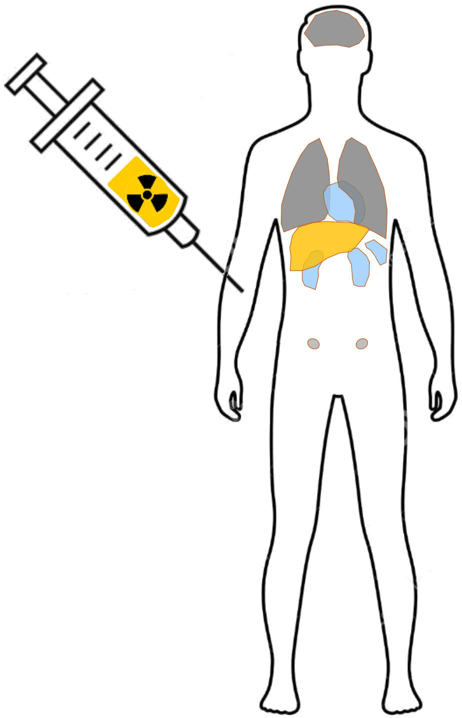
Dosimetry for *in vitro* assessment of Targeted Alpha Therapy (TAT)



- α-particle short range
- High Linear Energy Transfer (LET)
- Hypoxia

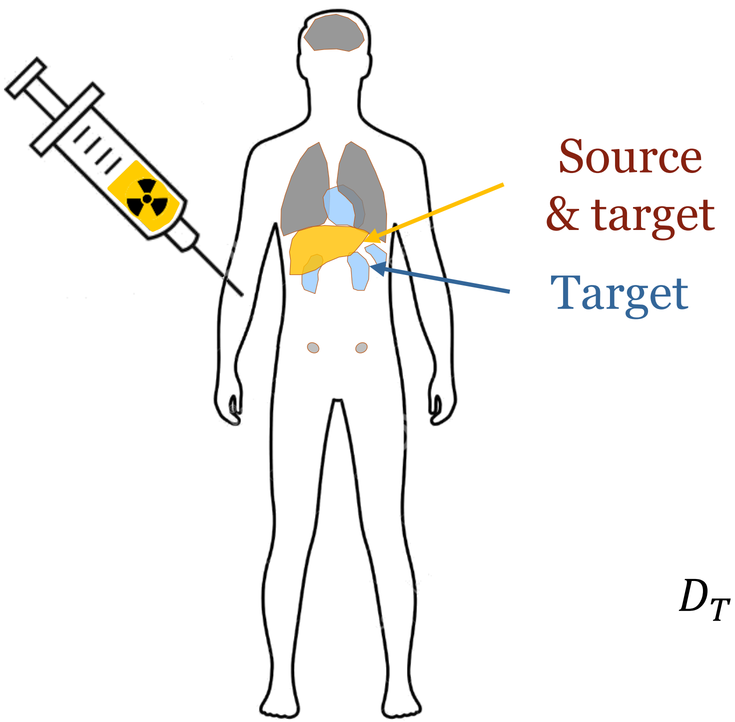
- Preclinical evaluation

- Quantification of biological effect
  → Generally administered activity
  → That easy with α-particles ?

- Comparison with other treatments
  → Pb: different irradiation techniques, different particles
  → No solution but dose measurement

Dosimetry for *in vitro* assessment of Targeted Alpha Therapy (TAT)

Dosimetry: MIRD Formalism



$$D(Gy) = \frac{E(J)}{m(kg)}$$

In radionuclide therapy:

Nb of radionuclide decays in a particular volume $\tilde{A}_S$

× energy emitted per decay E_0

× fraction of emitted energy absorbed by a particular (target) mass $\varphi_{T \leftarrow S}$

$$D_T = \frac{\tilde{A}_S \cdot E_0 \cdot \varphi_{T \leftarrow S}}{m_T}$$

S value

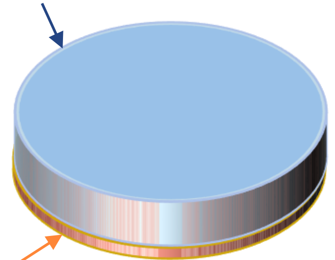
depends on the activity distribution, the type of particle, the target geometry…

Dosimetry for *in vitro* assessment of Targeted Alpha Therapy (TAT)

Dosimetry: MIRD Formalism

$$D(Gy) = \frac{E(J)}{m(kg)}$$

Case of *in vitro* irradiation



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$$D_T = \frac{\tilde{A}_S \cdot E_0 \cdot \varphi_{T \leftarrow S}}{m_T}$$

???

Max range in water = 90 µm

⇨ *a small fraction of radionuclides is "seen" by the cells. HOW MUCH ???*

⇨ *cell thickness ?*

1) Determining the spatial (and temporal) activity observed by the target
2) Determining the fraction of energy left by radiations in the target

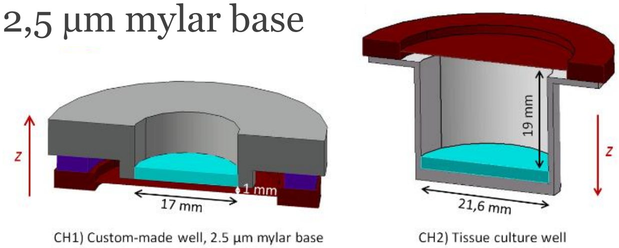
Dosimetry for *in vitro* assessment of Targeted Alpha Therapy (TAT)

Spatial and temporal distribution

- Experimental setup:

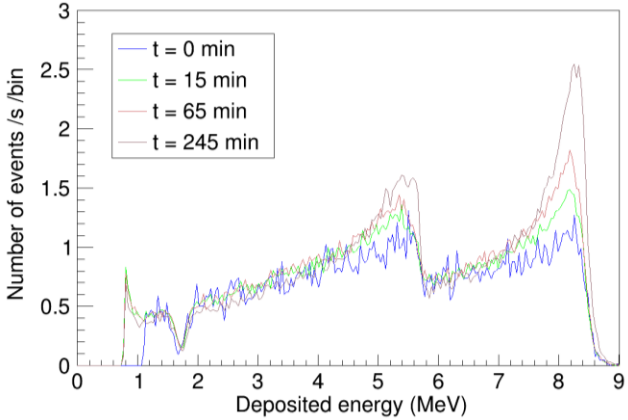
Silicon detector
⇩
Time of interaction
& Deposited energy

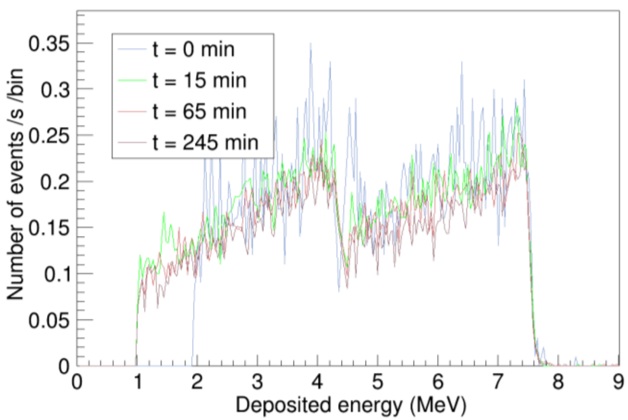
Custom-made plastic well
2,5 µm mylar base



1,8 mm of culture medium
+15 kBq of vectorized isotopes

Experimental energy spectra

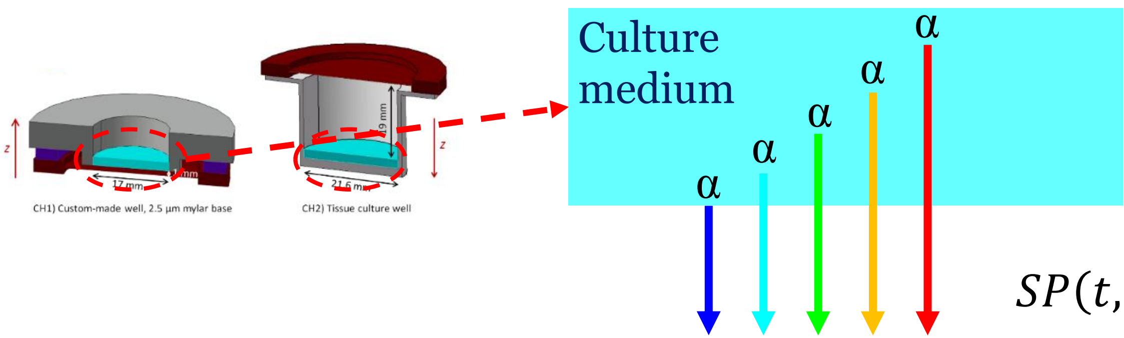




Dosimetry for *in vitro* assessment of Targeted Alpha Therapy (TAT)

Spatial and temporal distribution

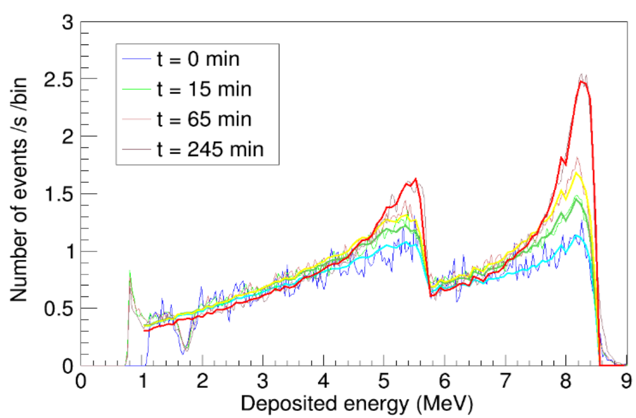
- Monte Carlo simulations vs Experimental spectra:

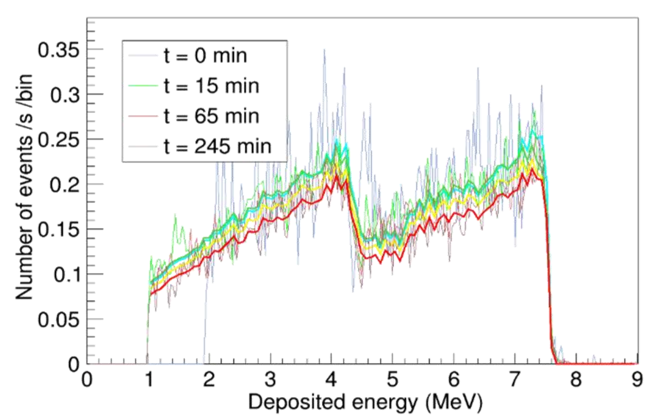


χ^2 minimization for each spectrum

$$SP(t,E) = \sum_i A(t,z_i) \cdot SP_{MC}(z_i,E)$$

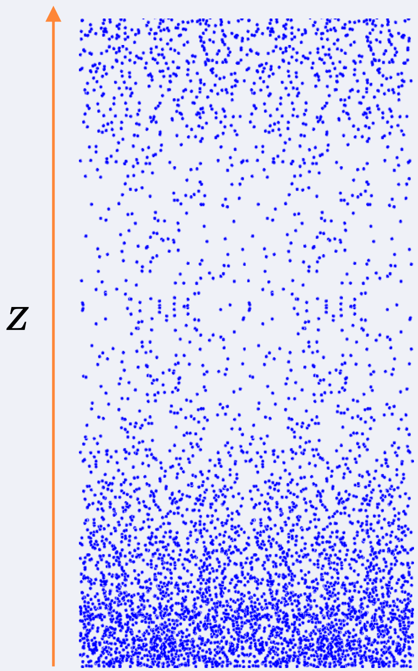
Convoluted energy spectra



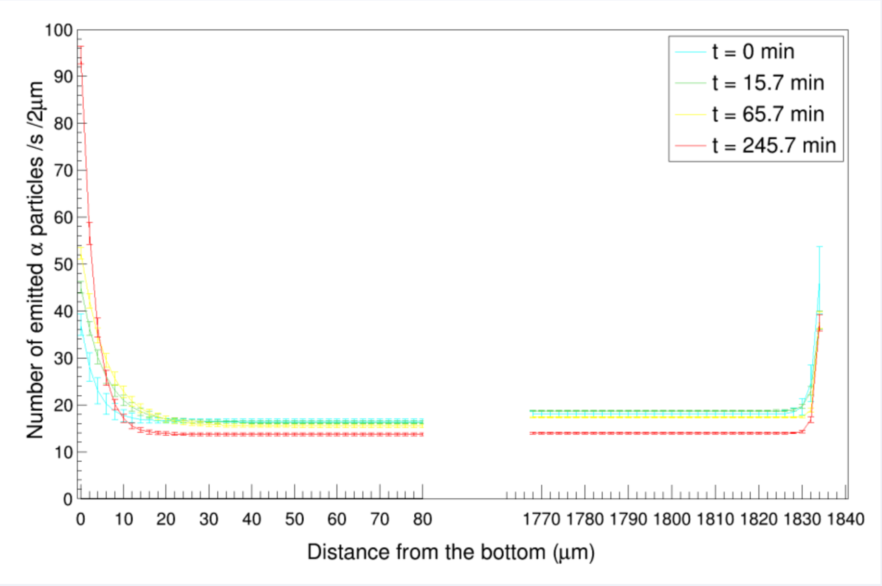


Dosimetry for *in vitro* assessment of Targeted Alpha Therapy (TAT)

Spatial and temporal distribution



$$A(t, z_i) = h(t) + a(t) \cdot e^{-b(t) \cdot z_i}$$



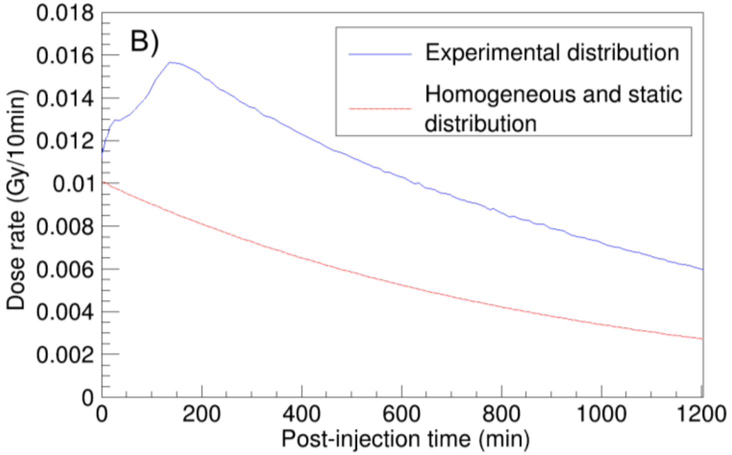
Spatial distribution of isotopes in the medium at different post-injection times

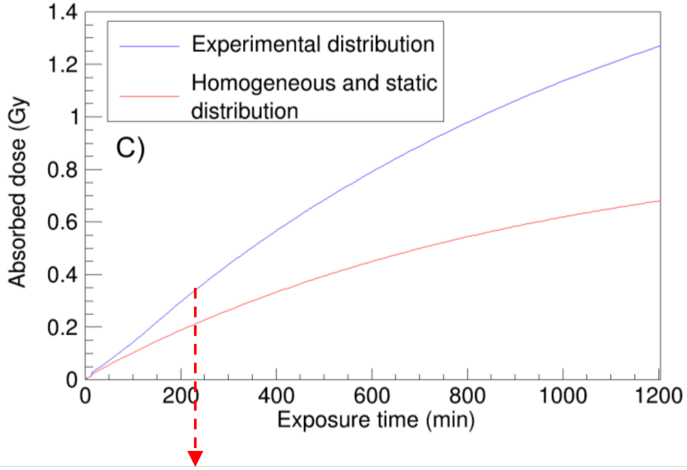
Dosimetry for *in vitro* assessment of Targeted Alpha Therapy (TAT)

2) Dose calculation

$$A(t, z_i) = h(t) + a(t) \cdot e^{-b(t) \cdot z_i}$$

$$\frac{dD}{dt}(t) = \sum_i A(t, z_i) \cdot S(z_i)$$





0,35 Gy

0,20 Gy

Error of 43% !

Almost a factor 2 in biological effect interpretation

Conclusion

- Preclinical dosimetry
  - Necessary to compare studies/treatment
  - Specific
  - Conventional methods not always adapted
    - Energy dependence in small animal RT
    - Spatial distribution of radionuclides in *in vitro* assessment
  - Requires knowledge and competences in Physics: instrumentation, MC simulation…
  - Require close collaboration between different disciplines