Monte Carlo Simulation for personalized dosimetry in radionuclide therapy

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Overview

- Introduction
  - Molecular Radiotherapy (MRT)
  - Internal dosimetry
  - Dosimetrical approaches
- Personalized dosimetry
- Results presentation
- Conclusion & future perspectives

Molecular Radiotherapy

- **Molecular radiotherapy (MRT)** is a treatment that deliver dose to a tissue through the administration of radiopharmaceuticals that interacts with a molecular receptor.
- To perform dosimetry calculation for MRT it is necessary:
  - quantitative imaging of the patient at certain time points;
  - modelling the distribution of activity within the patient over time from these images;
  - converting this cumulated activity in different regions into an absorbed dose.

Lu-177

Electrons		Photons	
Avg. Energy [keV]	Electrons per 100 disint.	Energy [keV]	Photons per 100 disint.
47.6	**11.6**	71.6	1.7E-1
78.6	0.01	**112.9**	**6.2**
111.7	**9.1**	136.7	4.7E-2
149.4	**79.3**	**208.4**	**10.4**
		249.7	2.0E-1
		321.3	2.1E-1

Thera-nostic

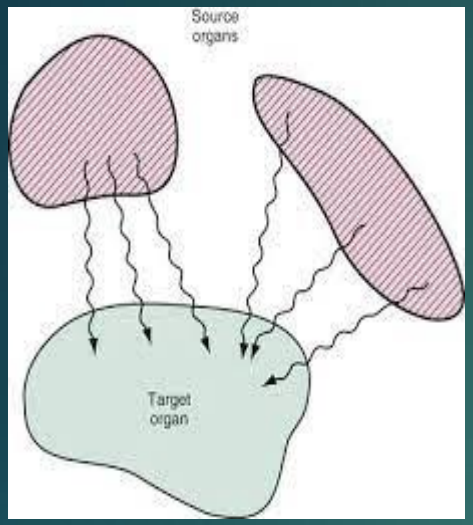
- In this study, we present how we have approached to the dosimetry evaluation for:
  - 177Lu-Dotatate is a radiolabelled peptide designed to target and suitable for neuro-endocrine tumours (NETs)

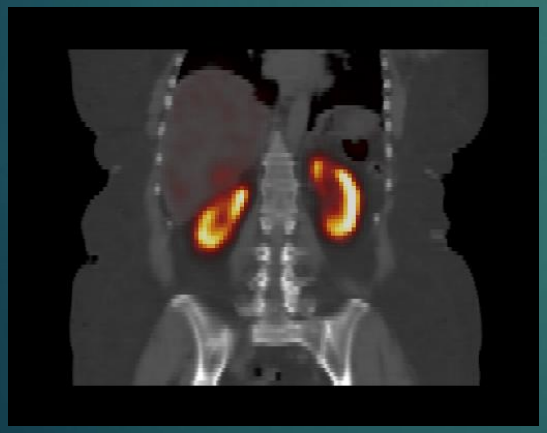
Dosimetric methods

Method	Advantages	Drawbacks
S value approach	Easy, fast, commonly used and generally accepted	Phantom-based, spherical approximation for targets.
Dose kernel approach (voxel dosimetry)	Patient-specific, tissue inhomogeneities are taken into account	S values must be calculated for each nuclide and each tissue.
Monte Carlo simulations	Very accurate	Time-consuming, not applicable for clinical routine.

- Different softwares are able to perform dose estimations, according to these methods:
  1. **HMS® OLINDA/EXM 2.0** (*S values approach model-based*);
  2. **MIM® MRT** (both *S values* and *dose kernels approach image-based*);
  3. **DOSIsoft PLANET® Onco Dose** (*MIRD schema image-based*)

MIRD dosimetry

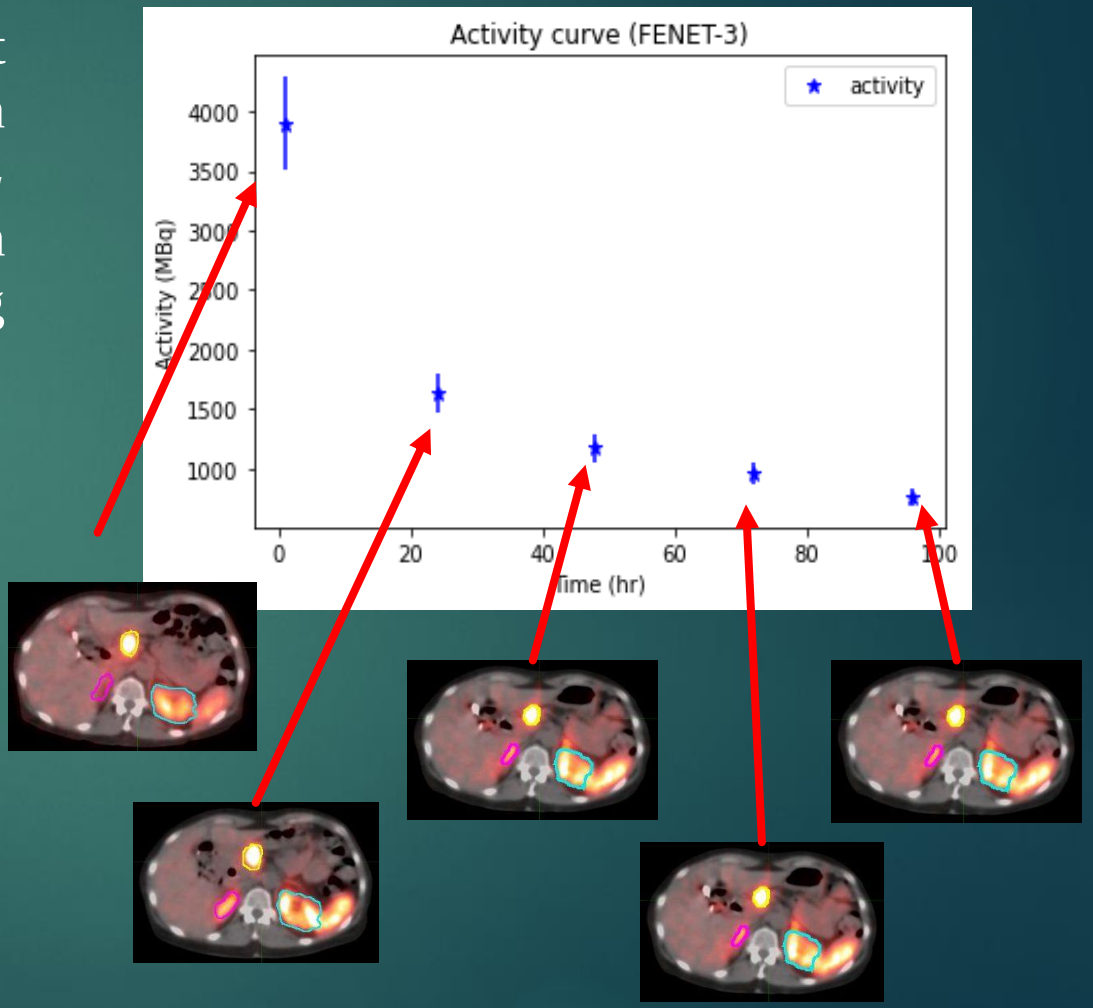




- According to MIRD pamphlet n° 21 [**2**], mean absorbed dose is defined in the following way:
  - $\bar{D}(r_T) = \sum_{r_S} \int_0^{+\infty} dt\, A(r_S, t) \cdot S(r_T \leftarrow r_S\,, t)$
- where S values are defined in the following way:
  - $S(r_T \leftarrow r_S, t) = \frac{1}{m(r_T,t)} \sum_i E_i Y_i \phi(r_T \leftarrow r_S, E_i, t)$
- and $A(r_S, t)$ is activity ($m(r_T, t)$ is target region mass, E_i is the energy per decay, Y_i is number of i-th nuclear transitions per nuclear transformation and ϕ is absorbed fraction).
- In nuclear medicine, **SPECT/CT images** are used to provide activities at each time point.

S values approach (MIRD method)

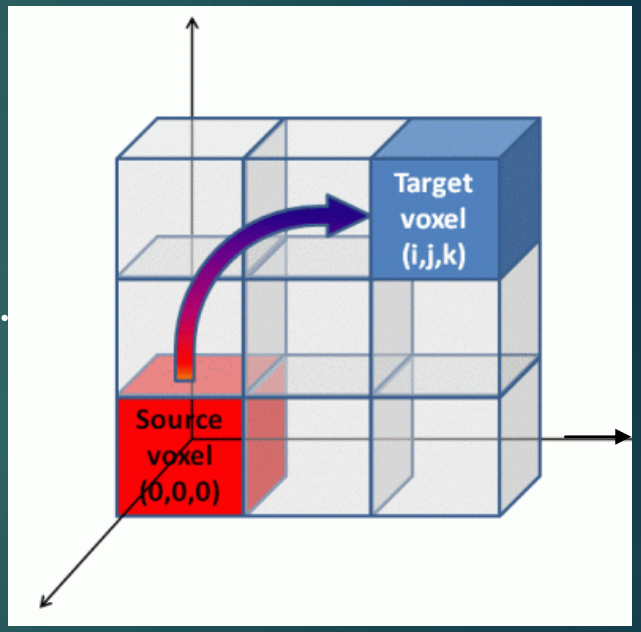
- **If we assume S values to be time-indipendent**, then they can be brought out of the integral in time, and mean absorbed dose [**1**], by a target region r_T due to the presence of a source region r_S, can be calculated with the following equation:
  - $\overline{D} = \sum_{r_S} \tilde{A}(r_S) \cdot S(r_T \leftarrow r_S)$
- where $\tilde{A}(r_S)$ is the cumulated activity:
  - $\tilde{A}(r_S) = \int_0^{t_D} dt\, A(r_S, t)$
- S values are obtained with Monte Carlo simulations, performed on phantoms.



Dose kernel approach (voxel dosimetry)

- In the limit of continuos space, the summation over r_S becomes an integral:

$$\bar{D}(r_T) = \int_0^{+\infty} dt \int d^3 r_S \; A(r_S, t) \cdot S(r_T - r_S, t) = \int_0^{+\infty} dt \, \dot{D}(r_T, t)$$



- That's why it's also called «***convolution method***».
- SPECT/CT returns activity distribution with 3D matrix (voxel).
- Convolution calculation is performed for each voxel.

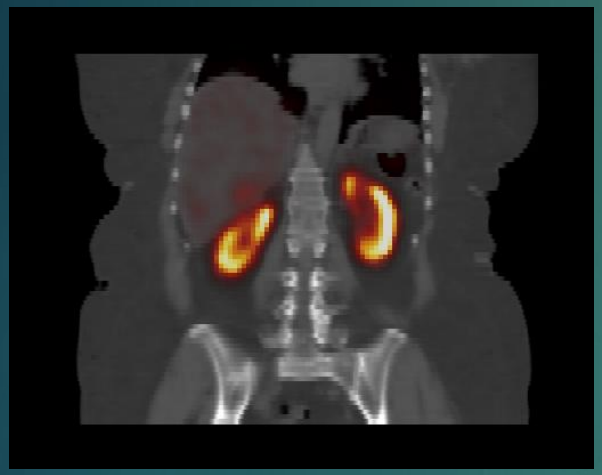
- Actually, from voxel dosimetry we get **dose rates**
- Data must be fitted, and the function is then integrated, in order to get doses.

Personalized dosimetry

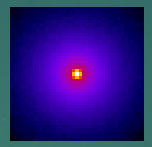
- **To develop a patient-specific dosimetry**:
  - **Dose kernels approach**, to provide doses in volumes of interest (kidneys & target).
  - **Monte Carlo code** (dosimetry gold standard), in order to get doses in the same regions.

- Ensemble made up of 7 patients (FENET sperimental protocol, 5 SPECT/CT images, for each one).
  - To validate dose kernel results with Monte Carlo ones.

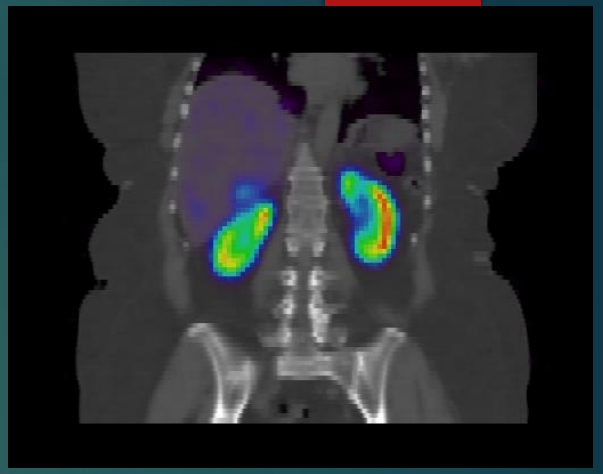
SPECT/CT data



DVK-GATE



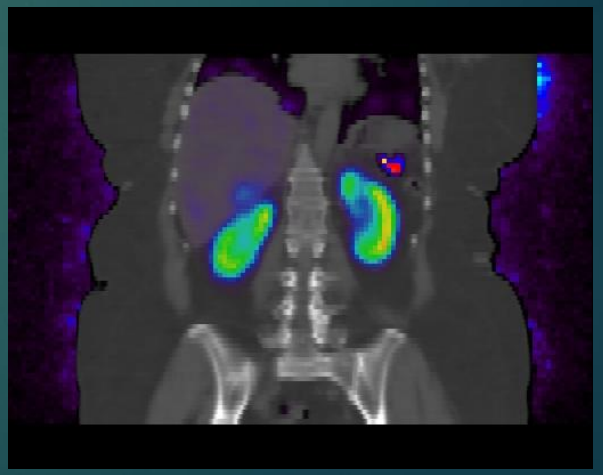
Lu-177 DVK in water



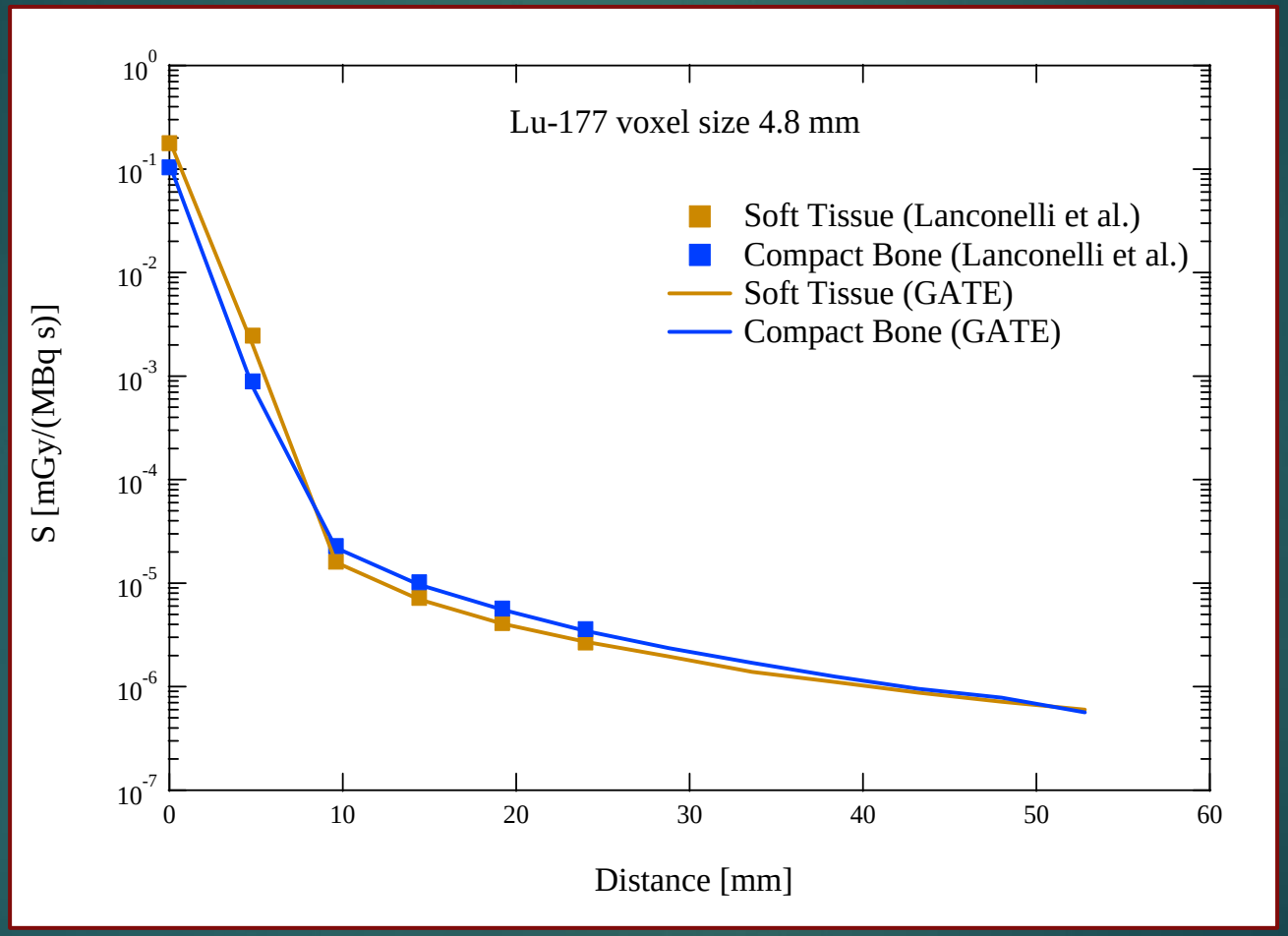
Dose Rate 3D distribution on CT data

MC-GATE

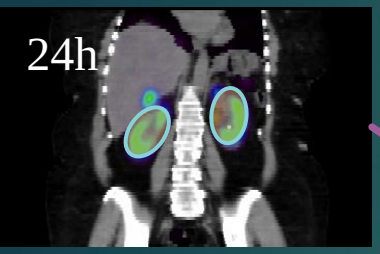
Photons and electrons tracking

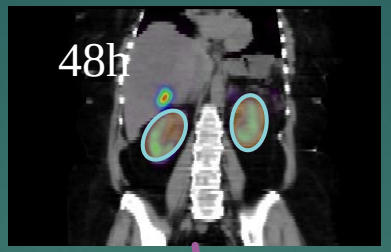


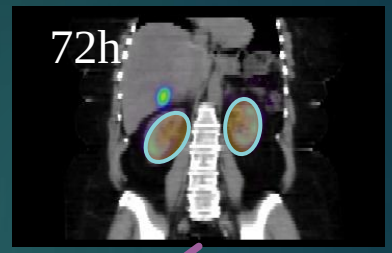
Results: GATE DVK calculation (1)

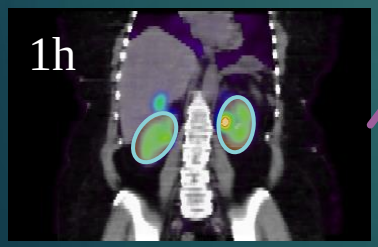


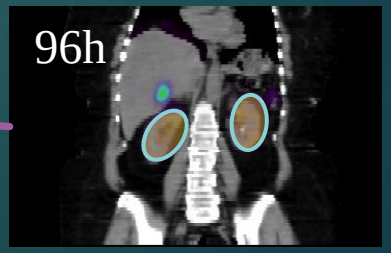
Results: GATE DVK calculation (2)

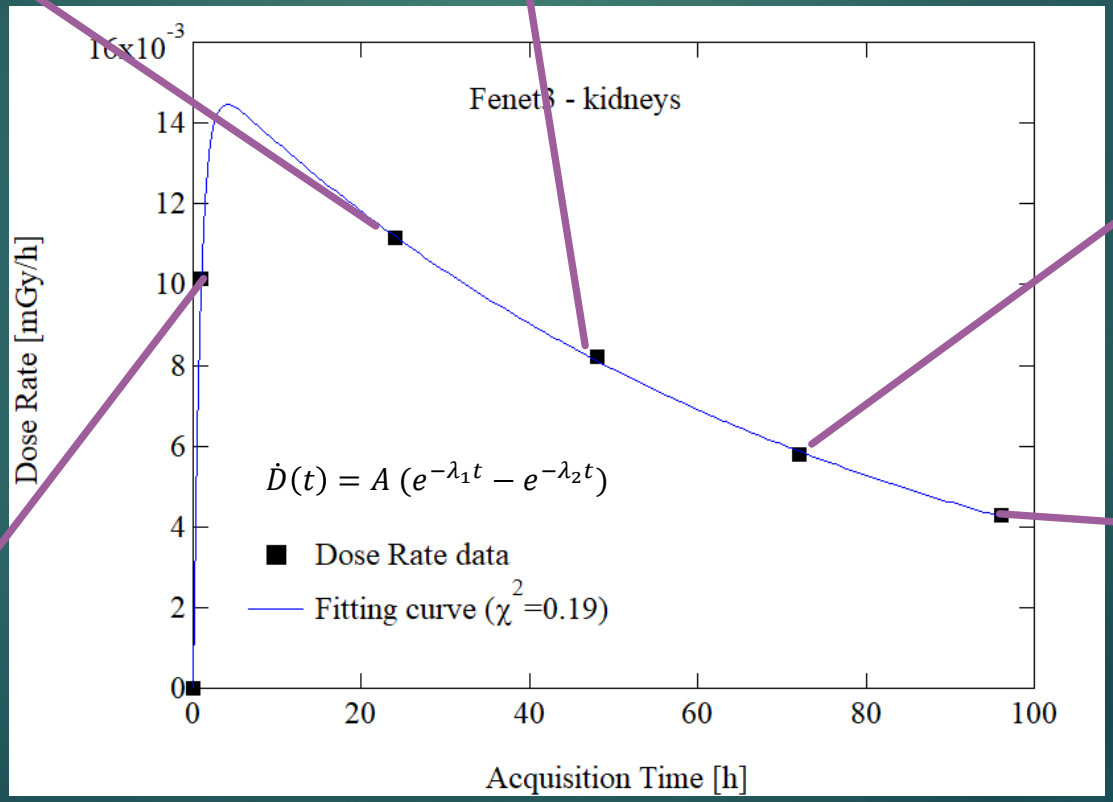








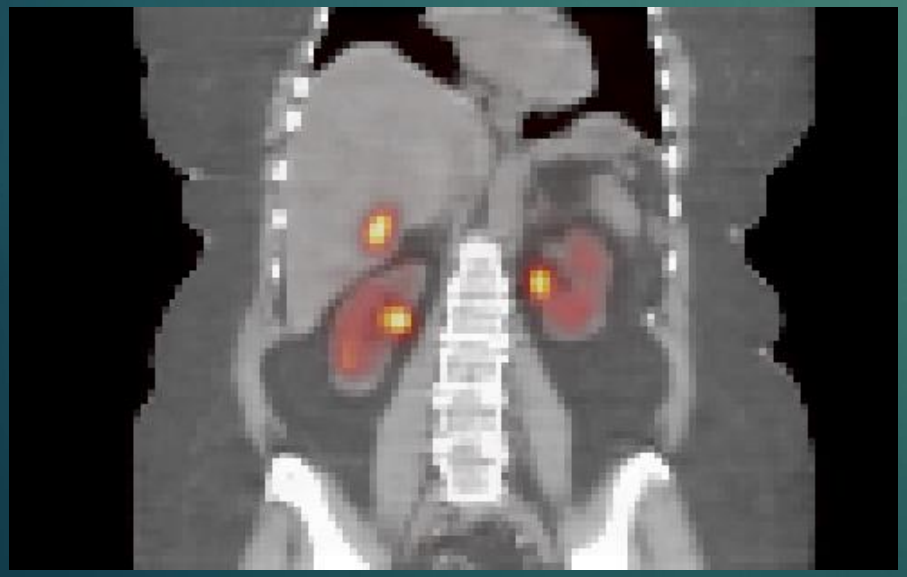




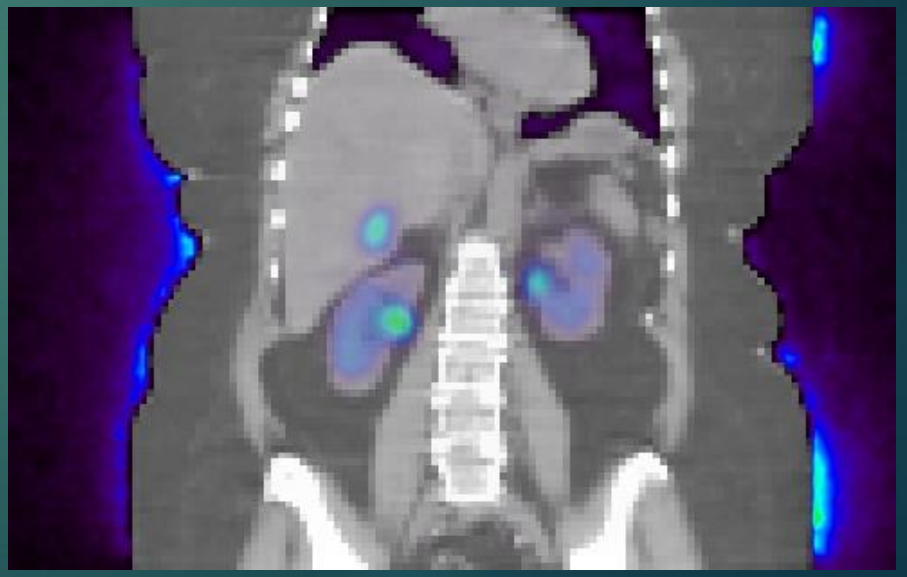
Results: GATE MC simulations (1)

- GATE is able to perform dose calculations by simply simulating Lu177 decay within human body.
- SPECT/CT images must be given, as input, to the simulator: SPECT image will define where actually is the radiation source confined; CT image with which materials is the radiation interacting.

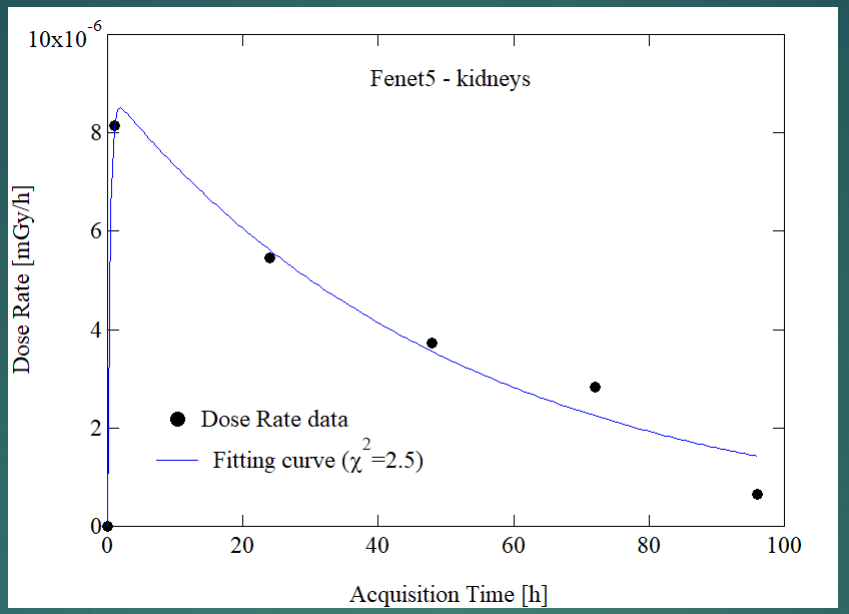
GATE inputs: CT and SPECT volumes



GATE ouput: 3D Dose distribution

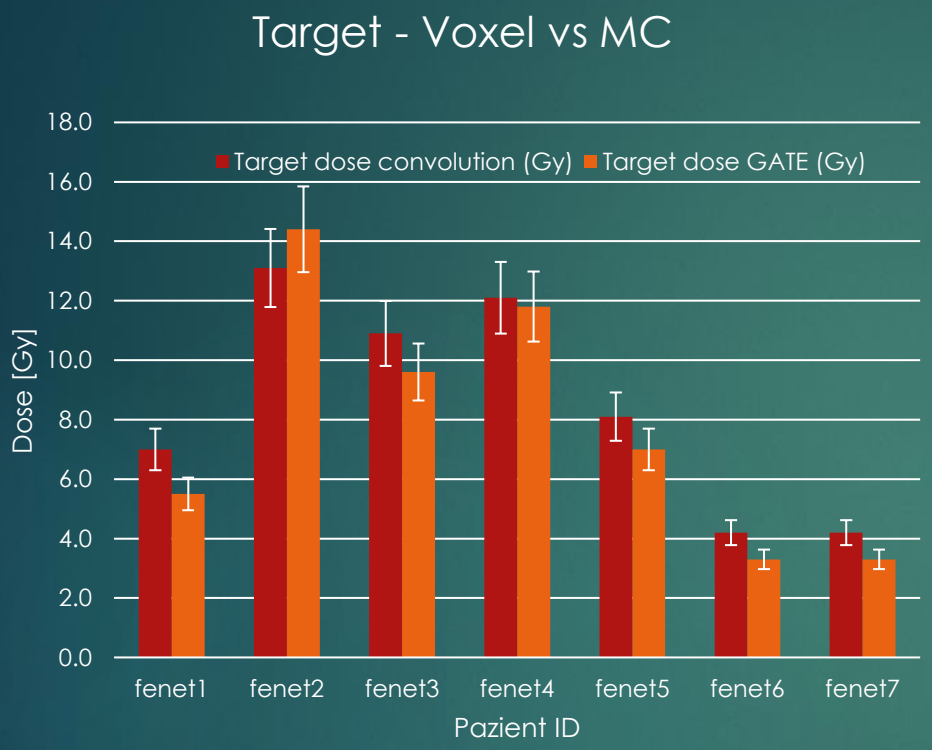


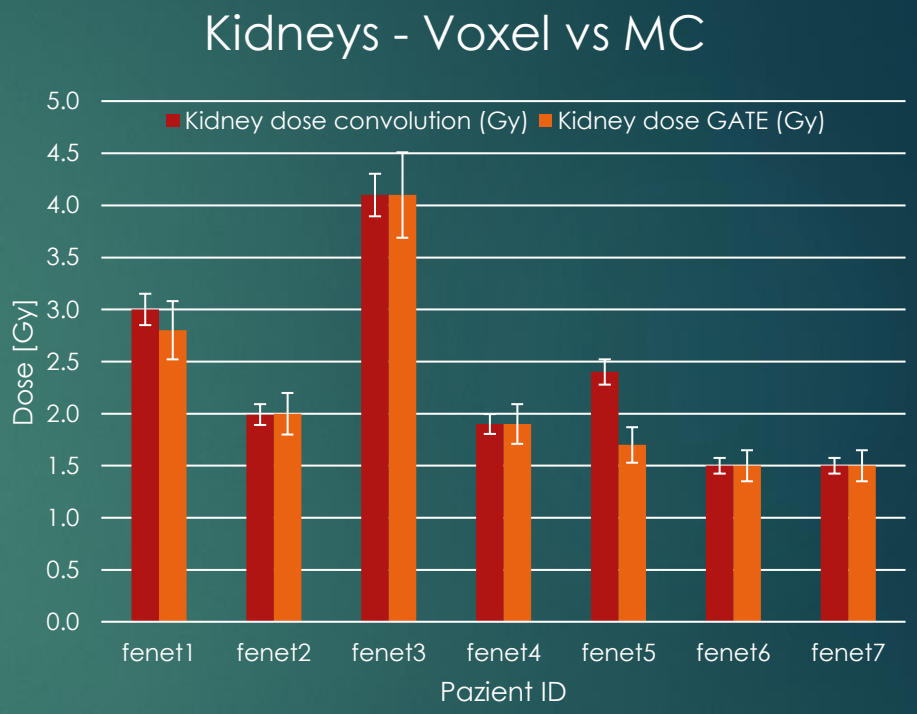
Results: GATE simulations (2)



- From dose rate data, we can get dose estimations in ROIs by calculating the area under a fitted curve.
- Usually, it is assumed that the function, which fits data, is a linear combination of two decreasing exponentials:
  - $\dot{D}(t) = A\,(e^{-\lambda_1 t} - e^{-\lambda_2 t})$
- Integrating the function, we finally get doses in kidneys and target.

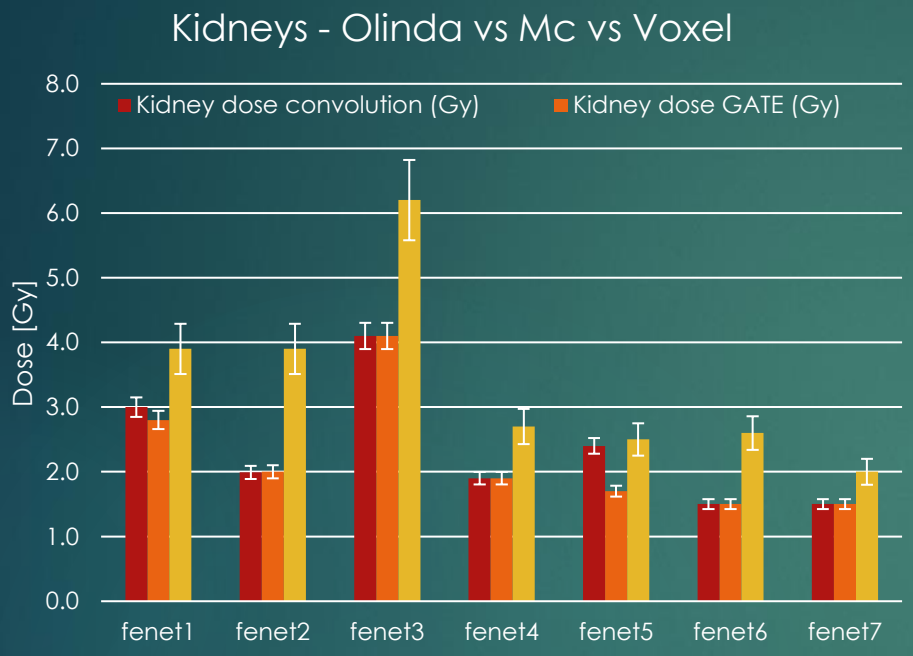
Results: dose kernel approach (voxel dosimetry) (2)

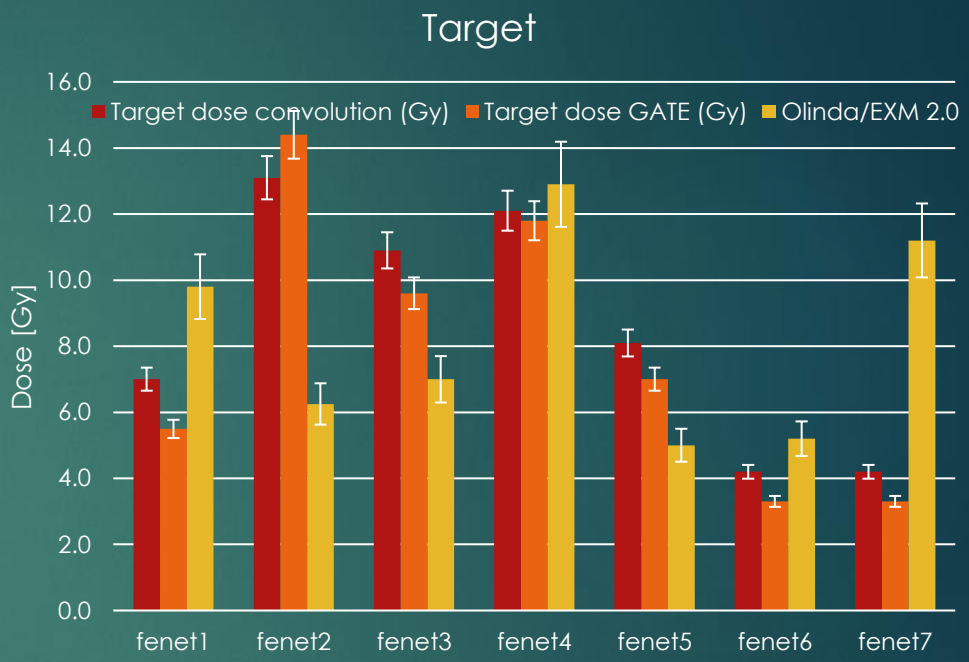




- After dose rate maps are obtained, basically the workflow is identical to GATE one.

Results: comparison with platforms (2)





- Agreement between dose kernel approach and GATE.
- HMS® OLINDA/EXM 2.0 is **not always** in agreement with voxel dosimetry and Monte Carlo simulations.
- Difficulties arise when dealing with small targets.

Conclusions & future perspectives

- Results obtained with voxel dosimetry approach and GATE are in agreement, both for kidneys and targets.
  - On average, HMS® OLINDA/EXM 2.0 is **not** in agreement with these two approaches.
- This approach can be used, in principle, also for whatever nuclide → feasible way to provide precise dose estimations.
- Image-based dosimetry allows a patient specific dose estimation → planning and providing personalized treatments.