Development of a Treatment Control System for IOeRT FLASH beam

PhD in *Accelerator Physics*, XXXV cycle
Sapienza University of Rome

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The IOeRT technique

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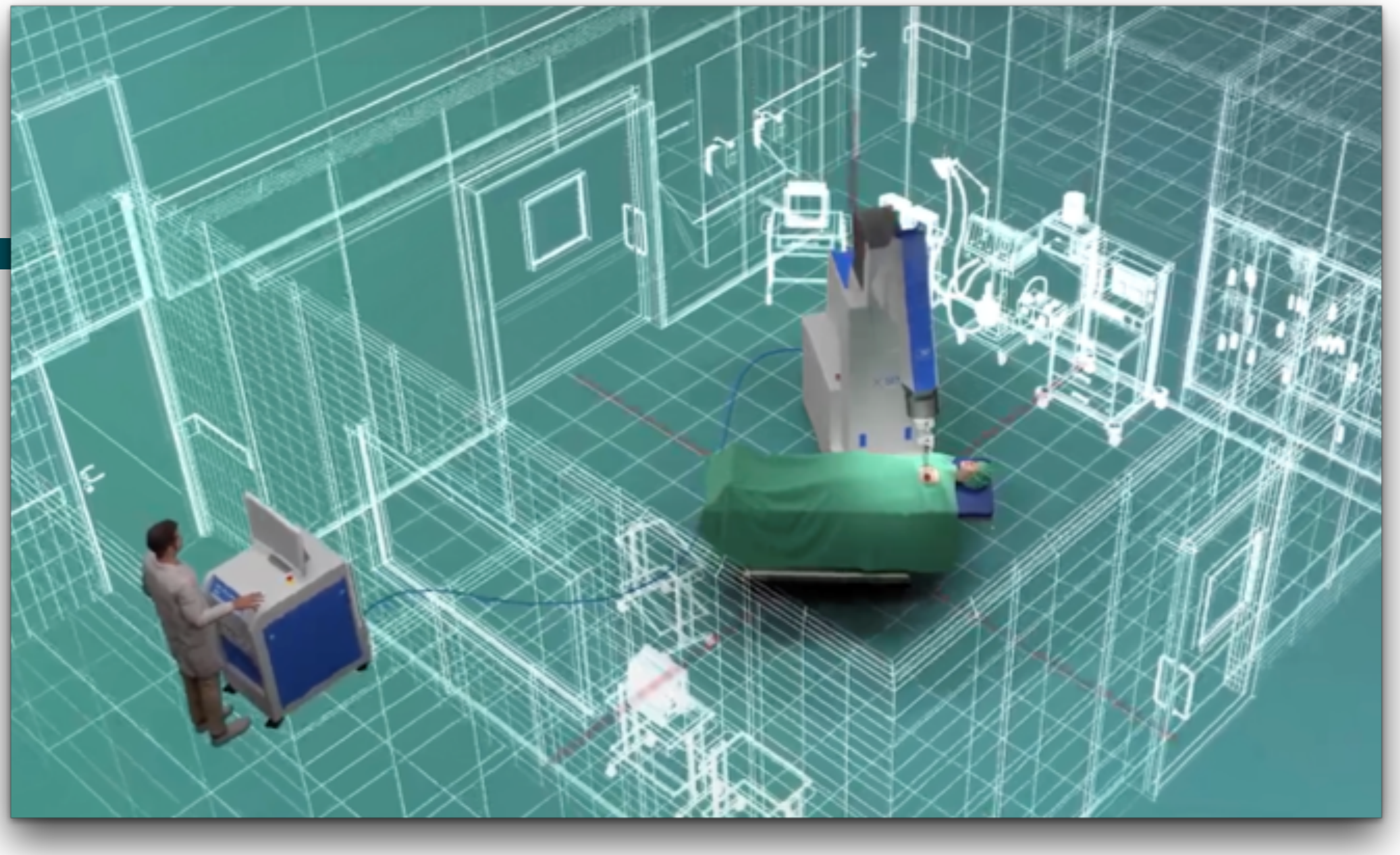

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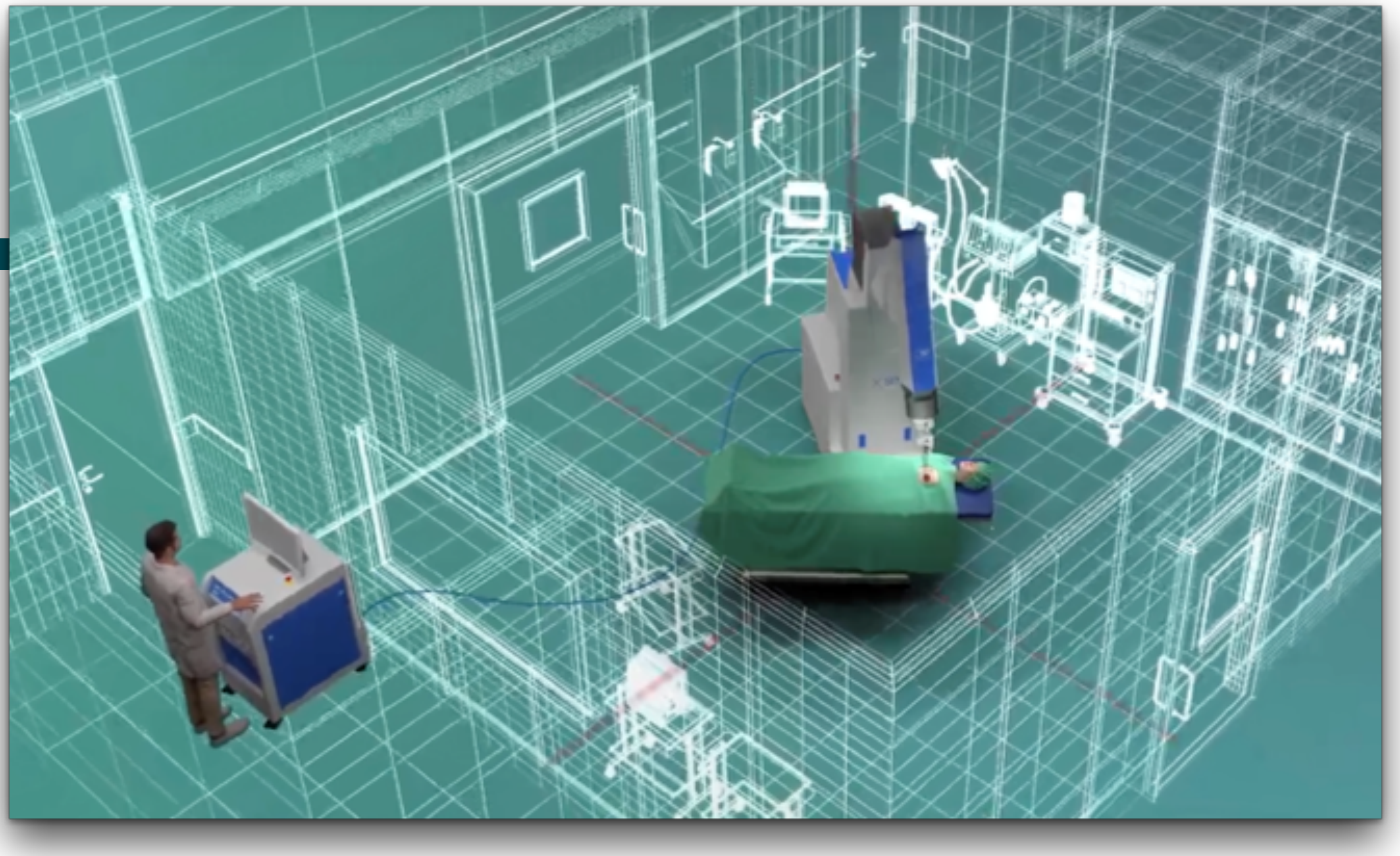

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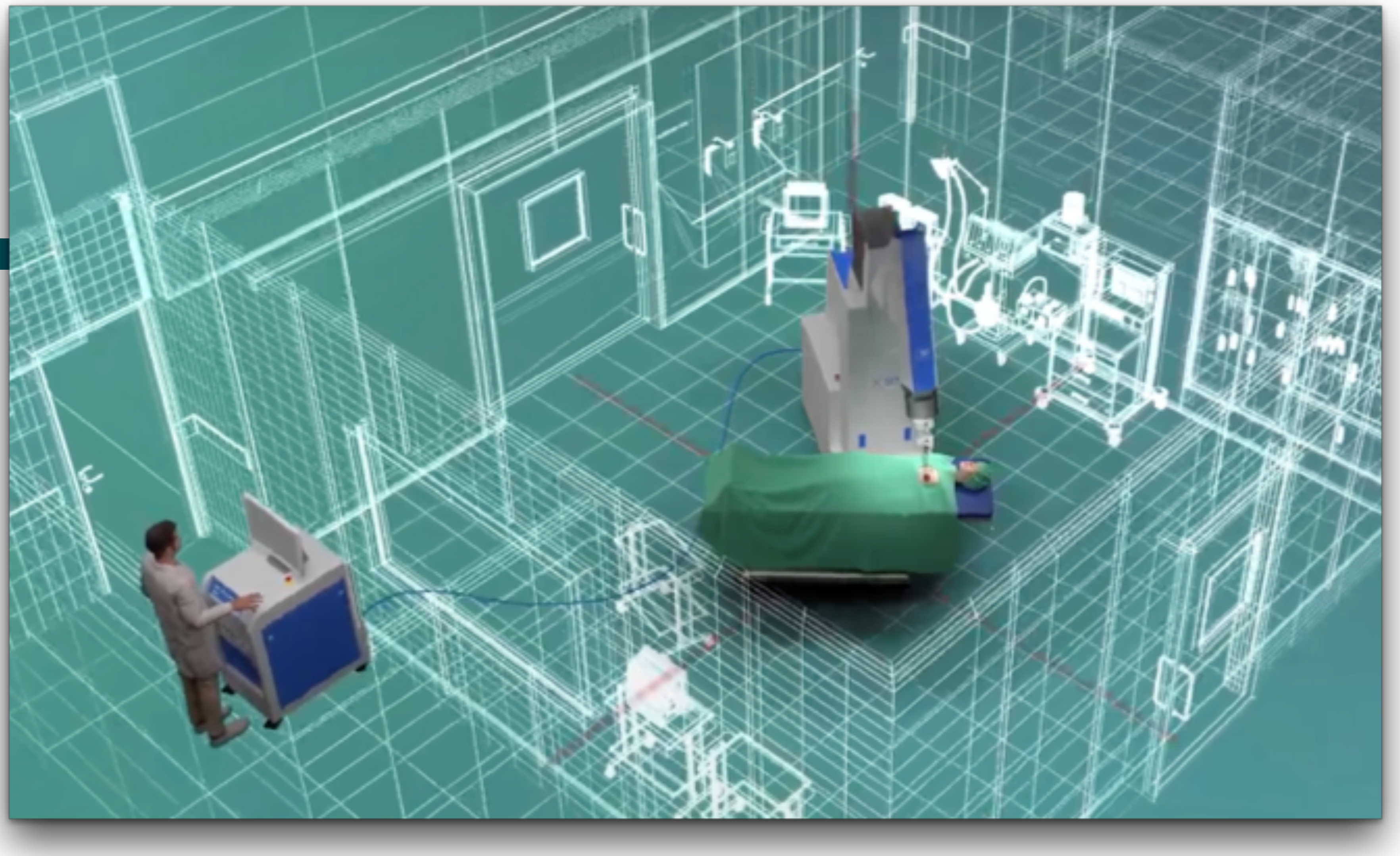

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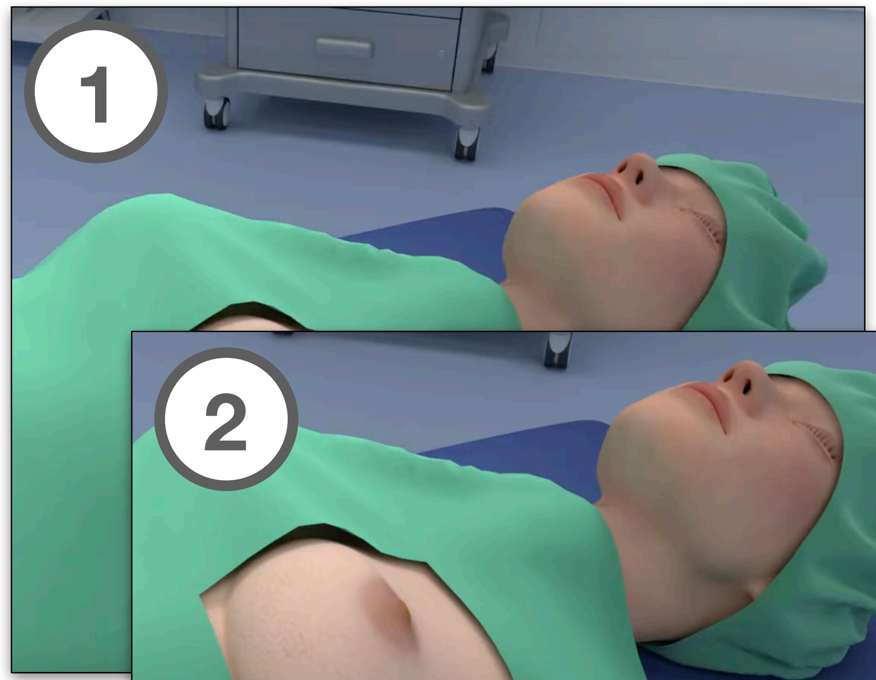

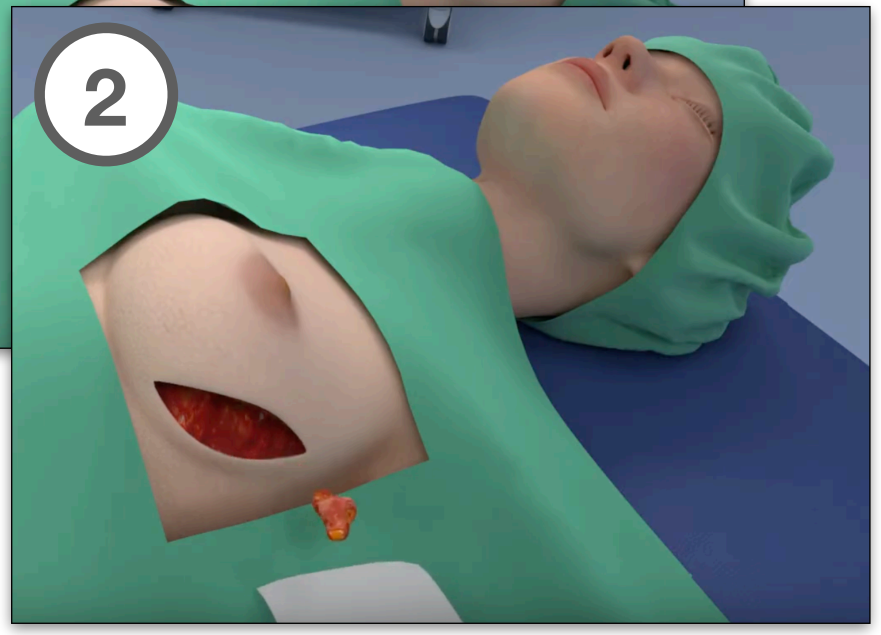

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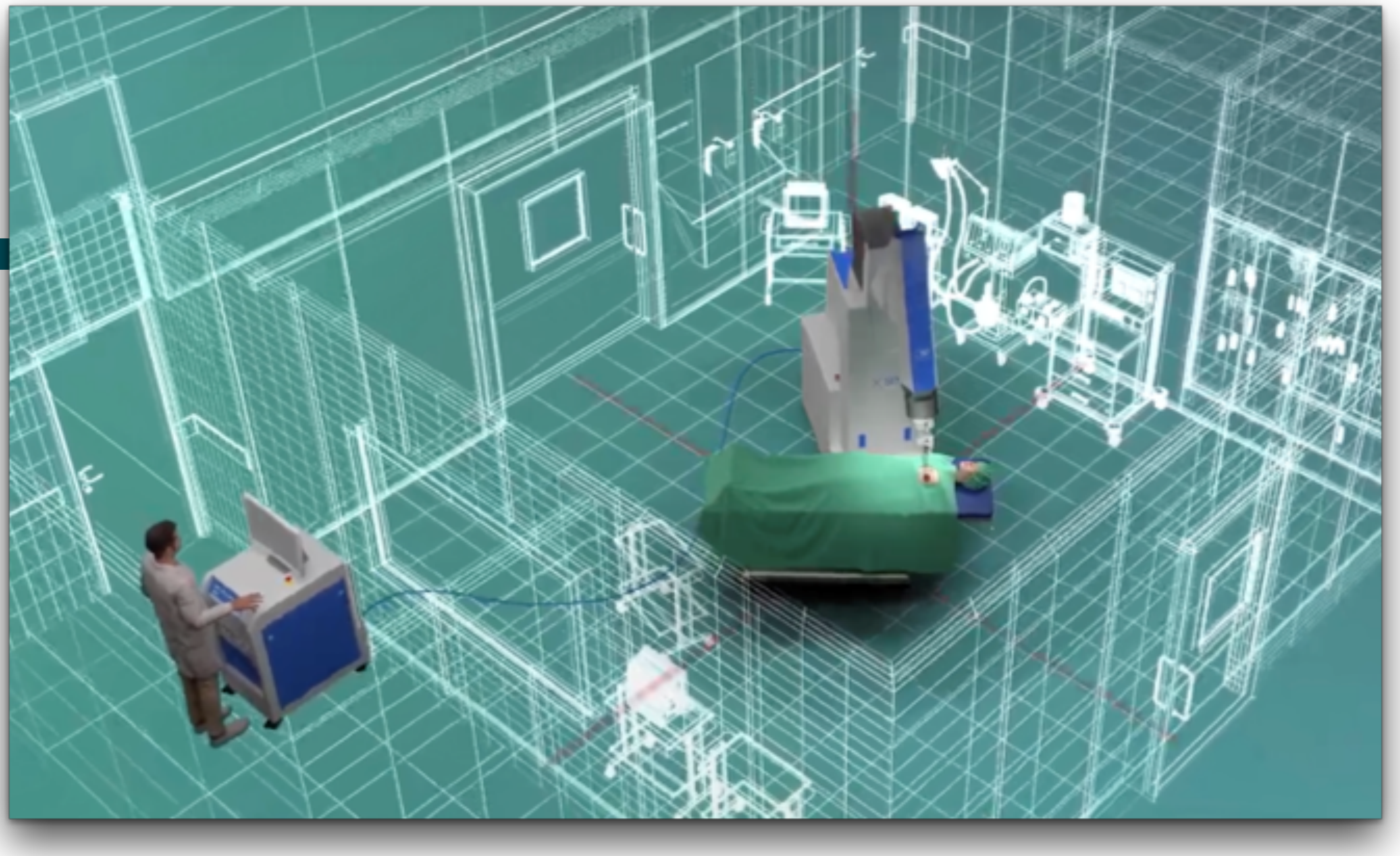

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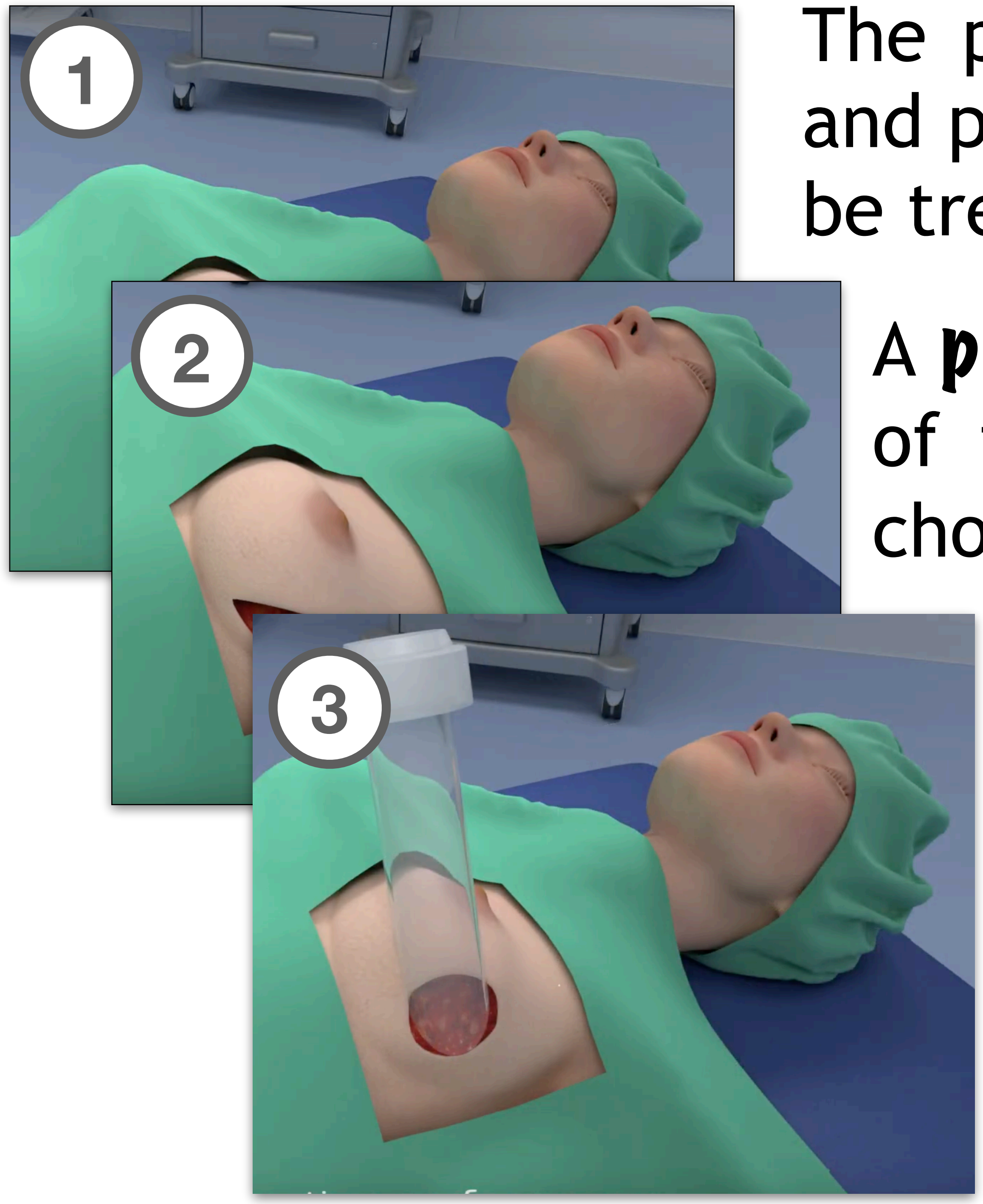

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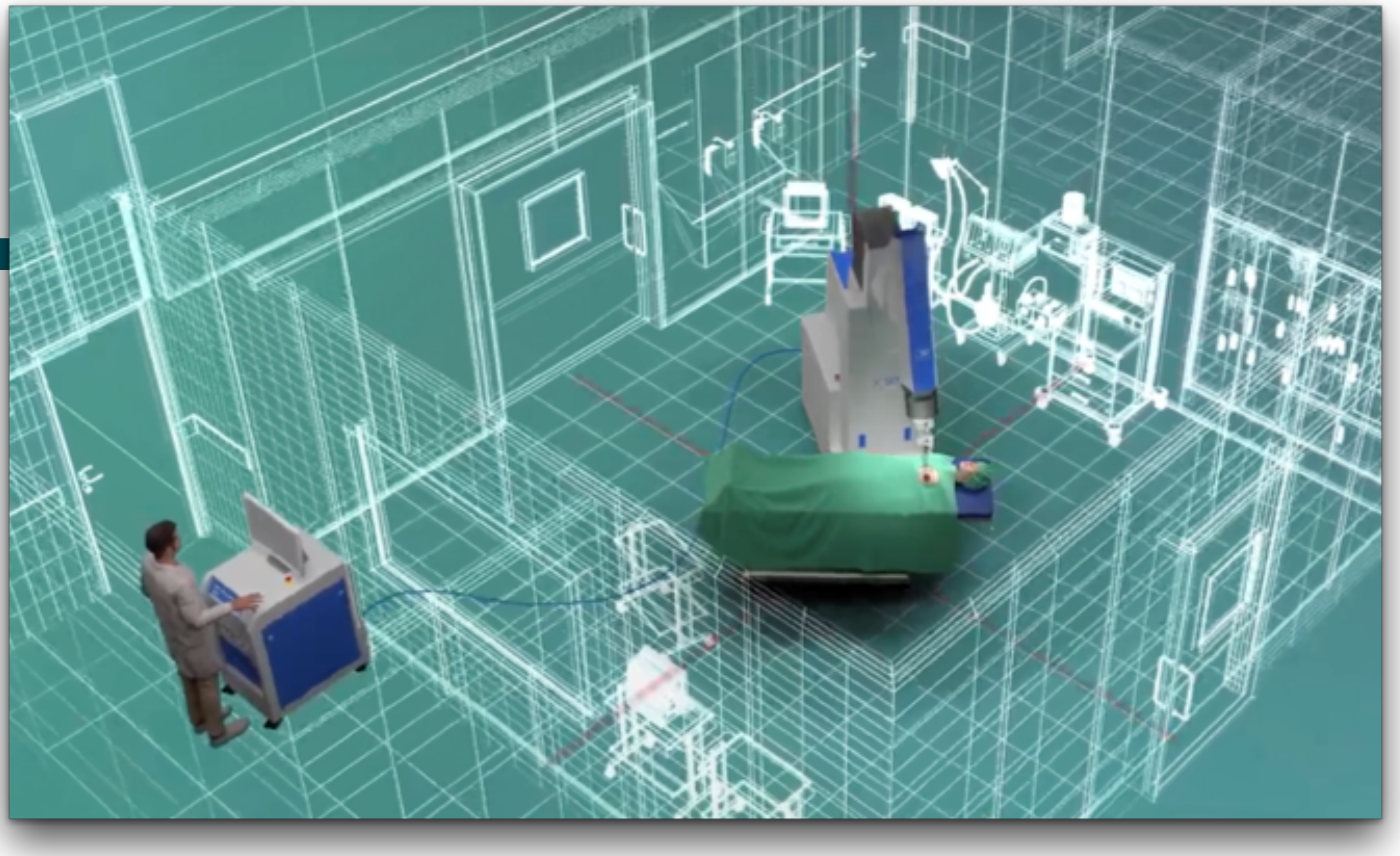

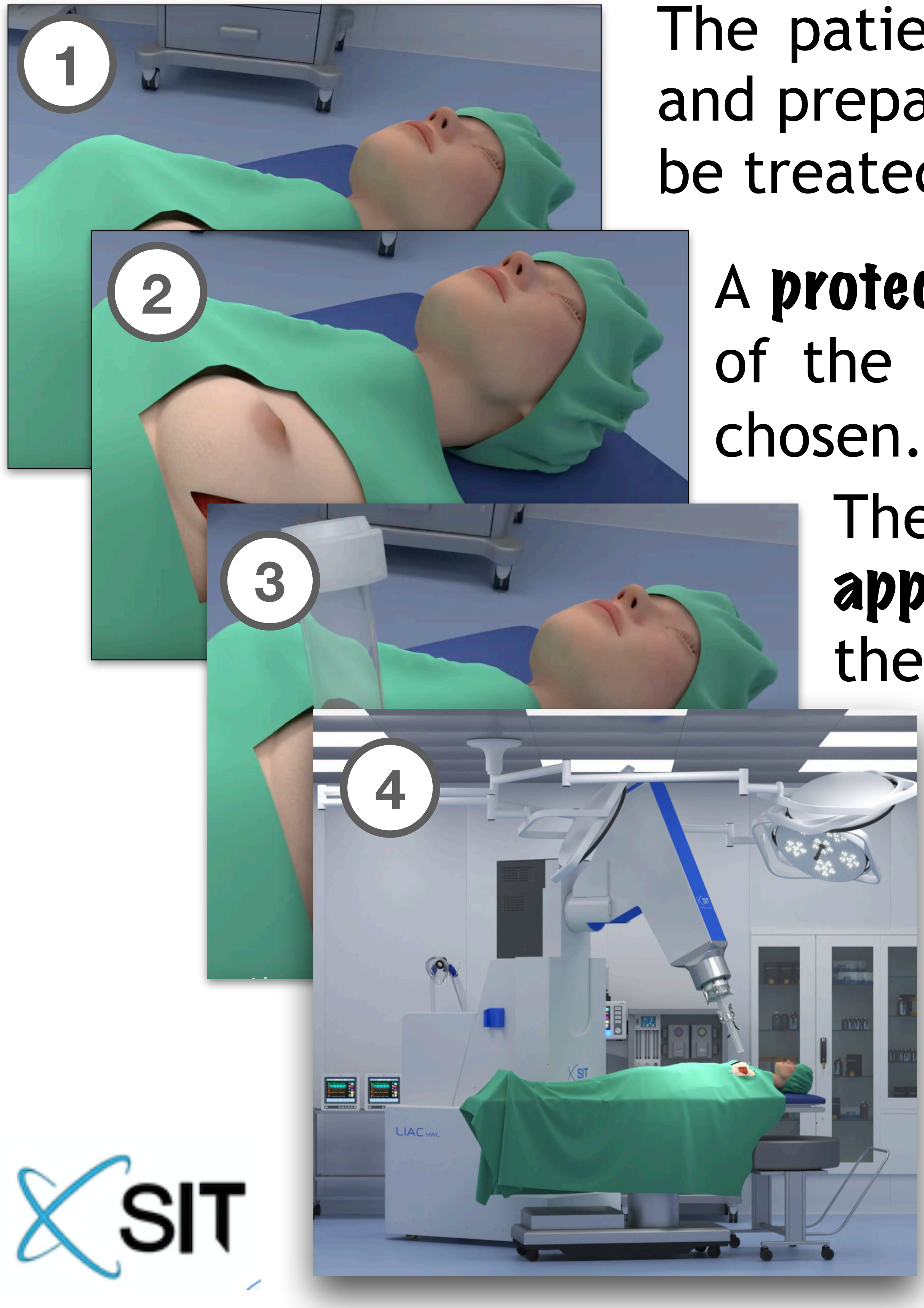

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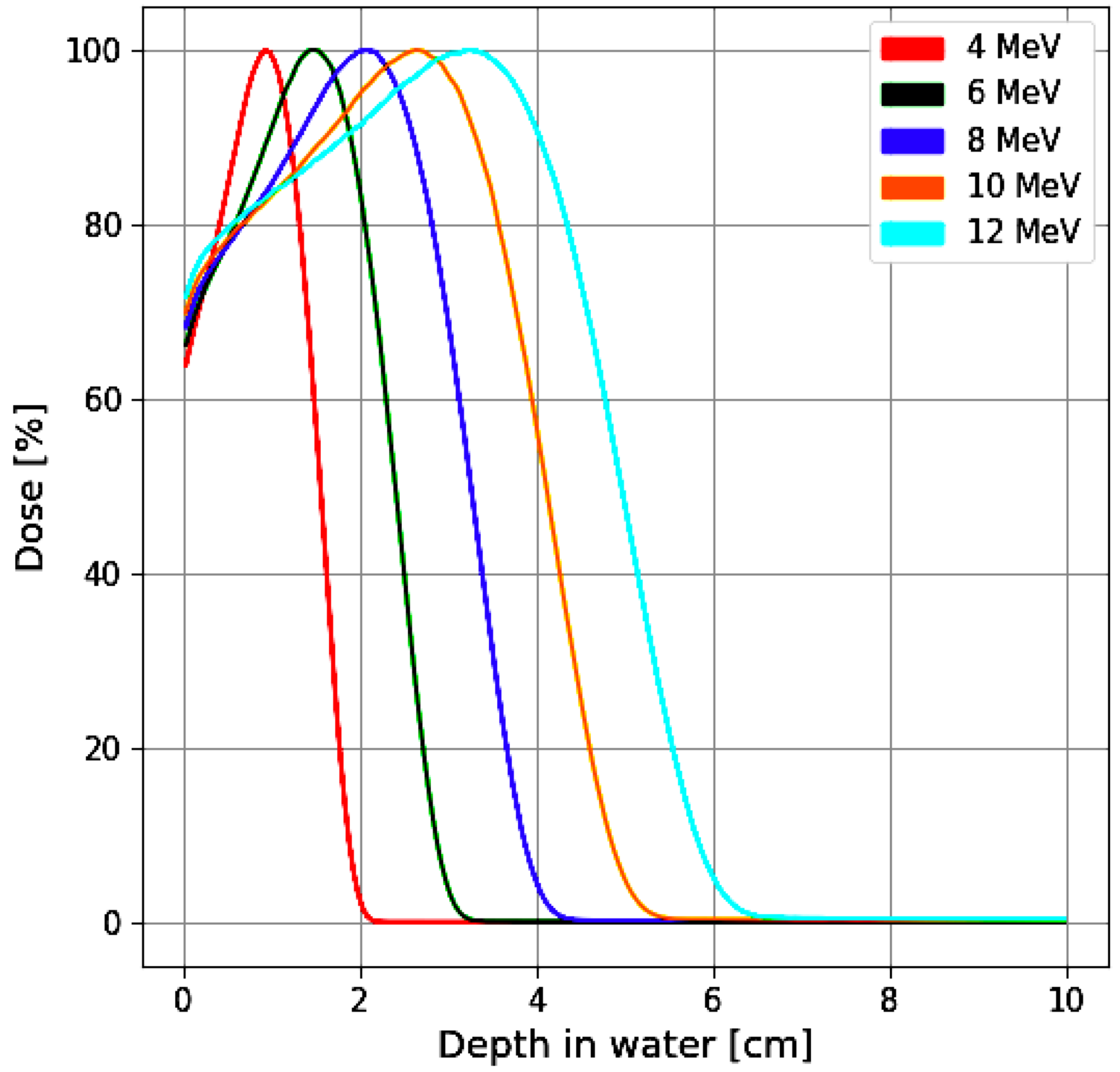

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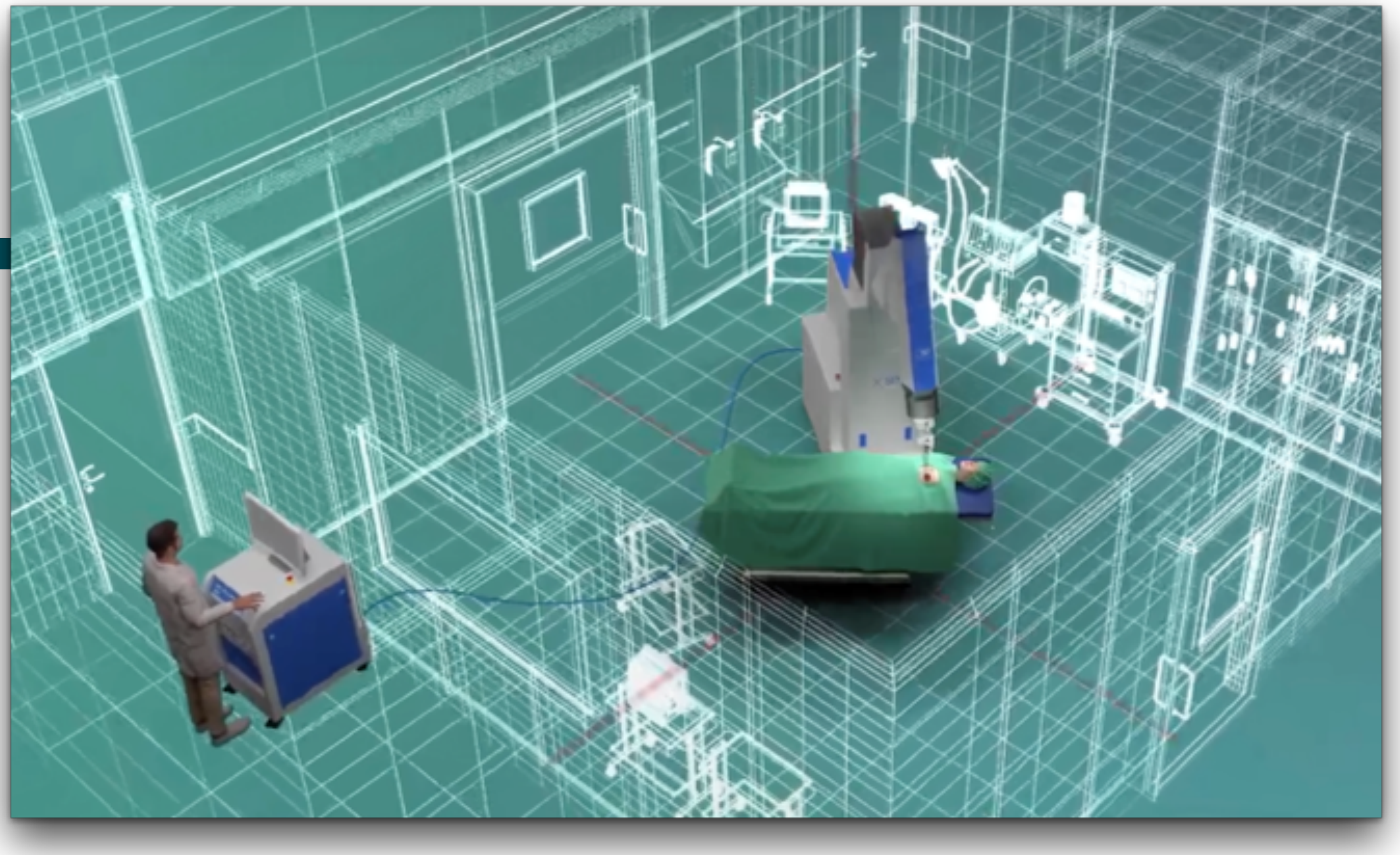

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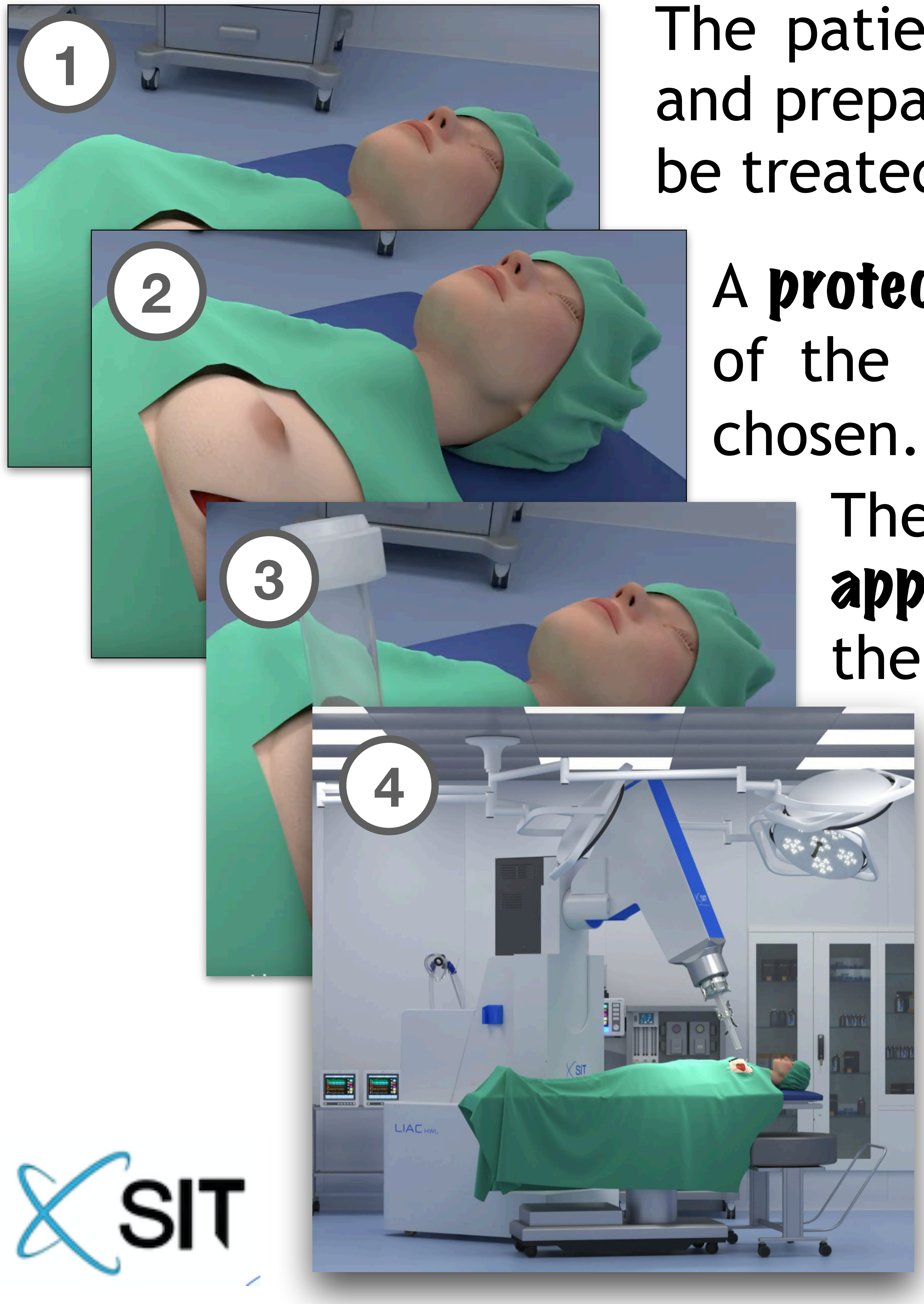

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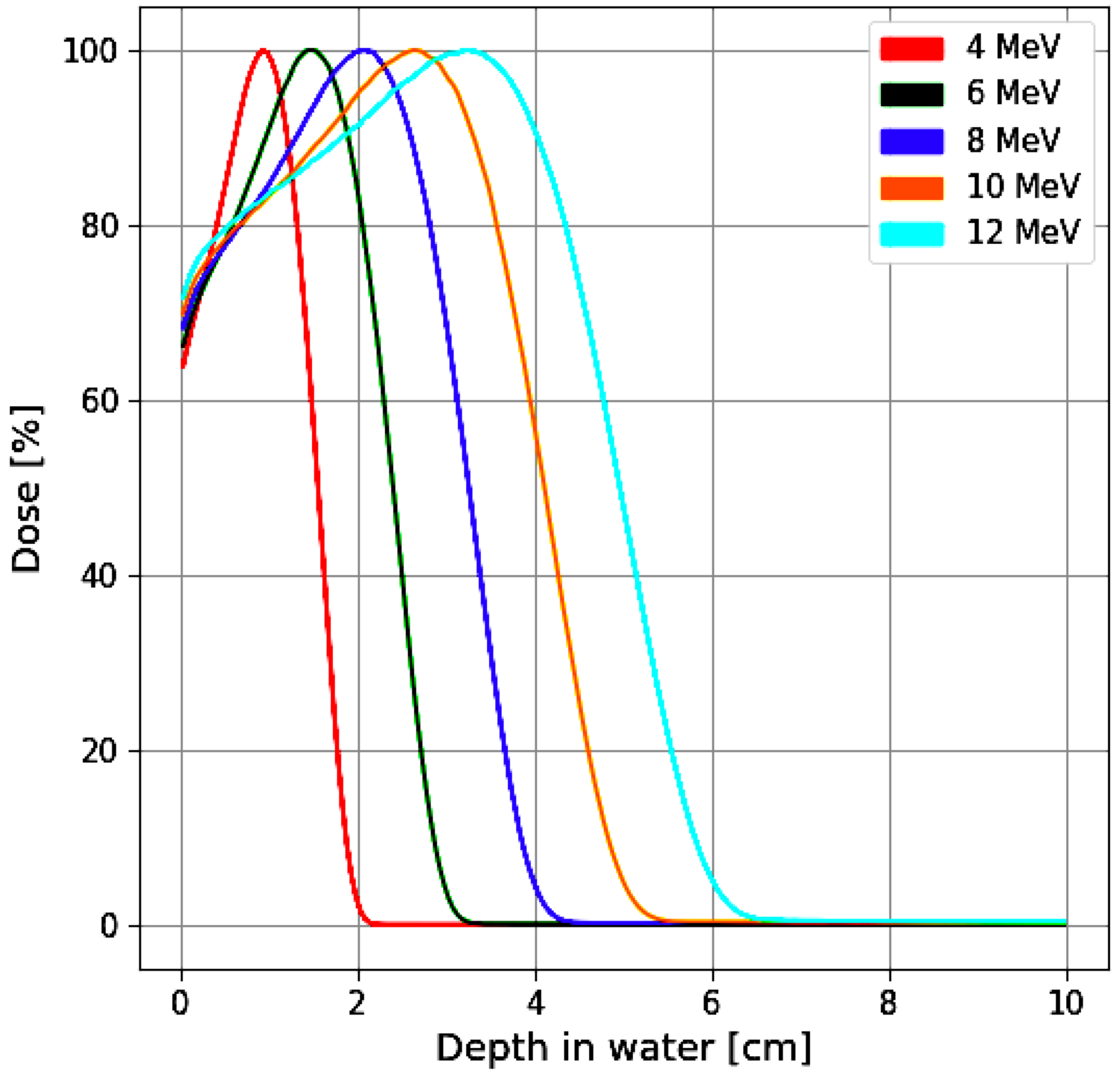


No time to perform a new patient imaging and go through the Treatment Planning System

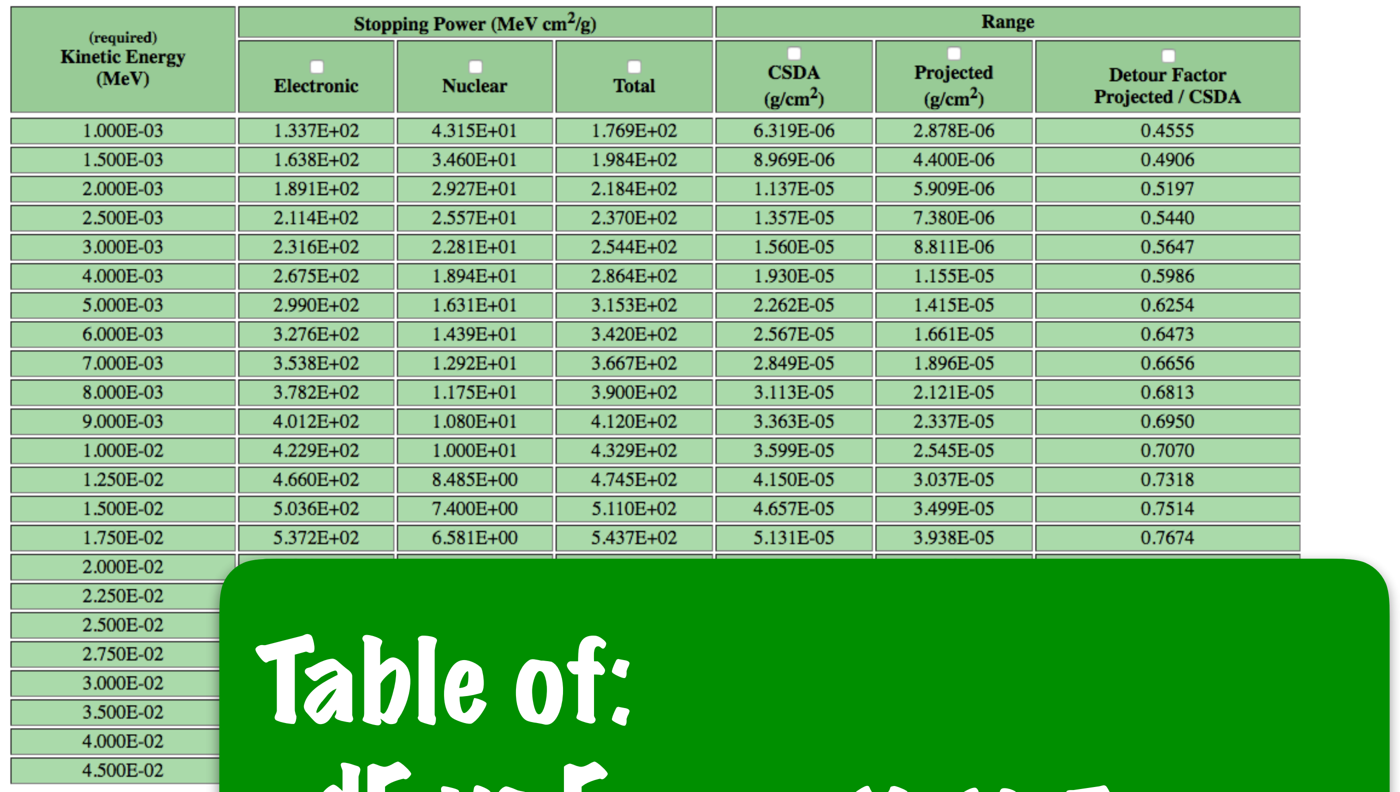
[1] Intraoperative Irradiation. Techniques and Results, Calvo FA, Gunderson LL et al., Current Clinical Oncology, Second Edition, 2011

Treatment Planning System

The Treatment Planning System (**TPS**) combines the characteristics of the particles at the energies of interest with the accelerator machine parameters to be applied in order to optimize the dose distribution to the patient. In particle therapy it can be analytic or Monte Carlo driven.

The **TPS** provides information to the beam control system:

- **Position**
- **Intensity**
- **Direction**

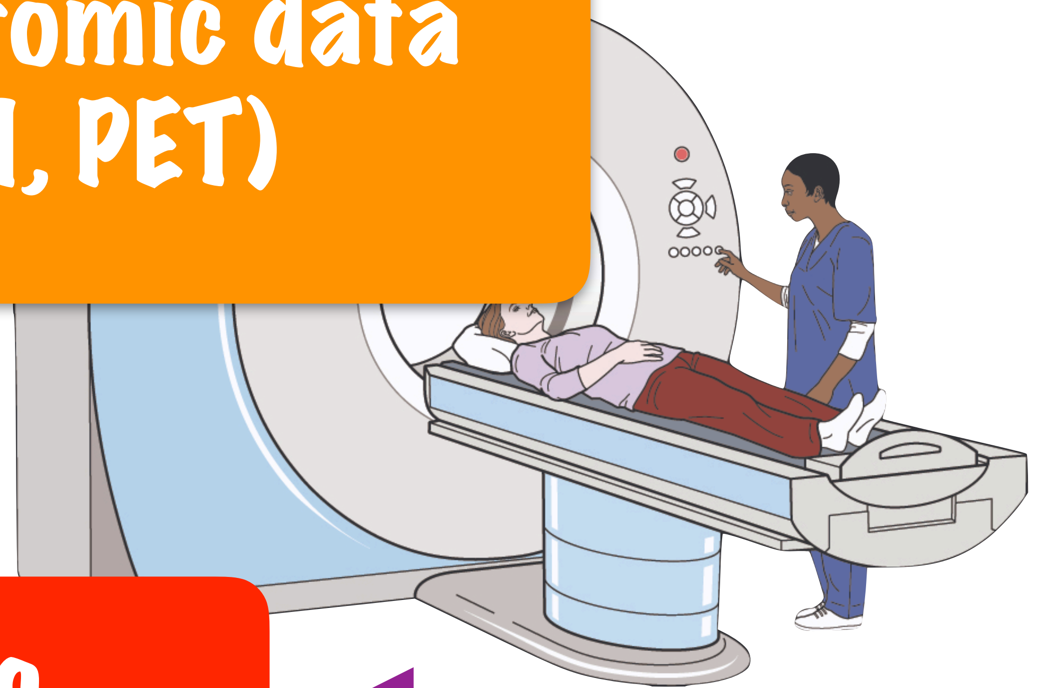


(required) Kinetic Energy (MeV)	Stopping Power (MeV cm^2/g)			Range		
	☐ Electronic	☐ Nuclear	☐ Total	☐ CSDA (g/cm^2)	☐ Projected (g/cm^2)	☐ Detour Factor Projected / CSDA
1.000E-03	1.337E+02	4.315E+01	1.769E+02	6.319E-06	2.878E-06	0.4555
1.500E-03	1.638E+02	3.460E+01	1.984E+02	8.969E-06	4.400E-06	0.4906
2.000E-03	1.891E+02	2.927E+01	2.184E+02	1.137E-05	5.909E-06	0.5197
2.500E-03	2.114E+02	2.557E+01	2.370E+02	1.357E-05	7.380E-06	0.5440
3.000E-03	2.316E+02	2.281E+01	2.544E+02	1.560E-05	8.811E-06	0.5647
4.000E-03	2.675E+02	1.894E+01	2.864E+02	1.930E-05	1.155E-05	0.5986
5.000E-03	2.990E+02	1.631E+01	3.153E+02	2.262E-05	1.415E-05	0.6254
6.000E-03	3.276E+02	1.439E+01	3.420E+02	2.567E-05	1.661E-05	0.6473
7.000E-03	3.538E+02	1.292E+01	3.667E+02	2.849E-05	1.896E-05	0.6656
8.000E-03	3.782E+02	1.175E+01	3.900E+02	3.113E-05	2.121E-05	0.6813
9.000E-03	4.012E+02	1.080E+01	4.120E+02	3.363E-05	2.337E-05	0.6950
1.000E-02	4.229E+02	1.000E+01	4.329E+02	3.599E-05	2.545E-05	0.7070
1.250E-02	4.660E+02	8.485E+00	4.745E+02	4.150E-05	3.037E-05	0.7318
1.500E-02	5.036E+02	7.400E+00	5.110E+02	4.657E-05	3.499E-05	0.7514
1.750E-02	5.372E+02	6.581E+00	5.437E+02	5.131E-05	3.938E-05	0.7674
2.000E-02						
2.250E-02						
2.500E-02						
2.750E-02						
3.000E-02						
3.500E-02						
4.000E-02						
4.500E-02						

Table of:

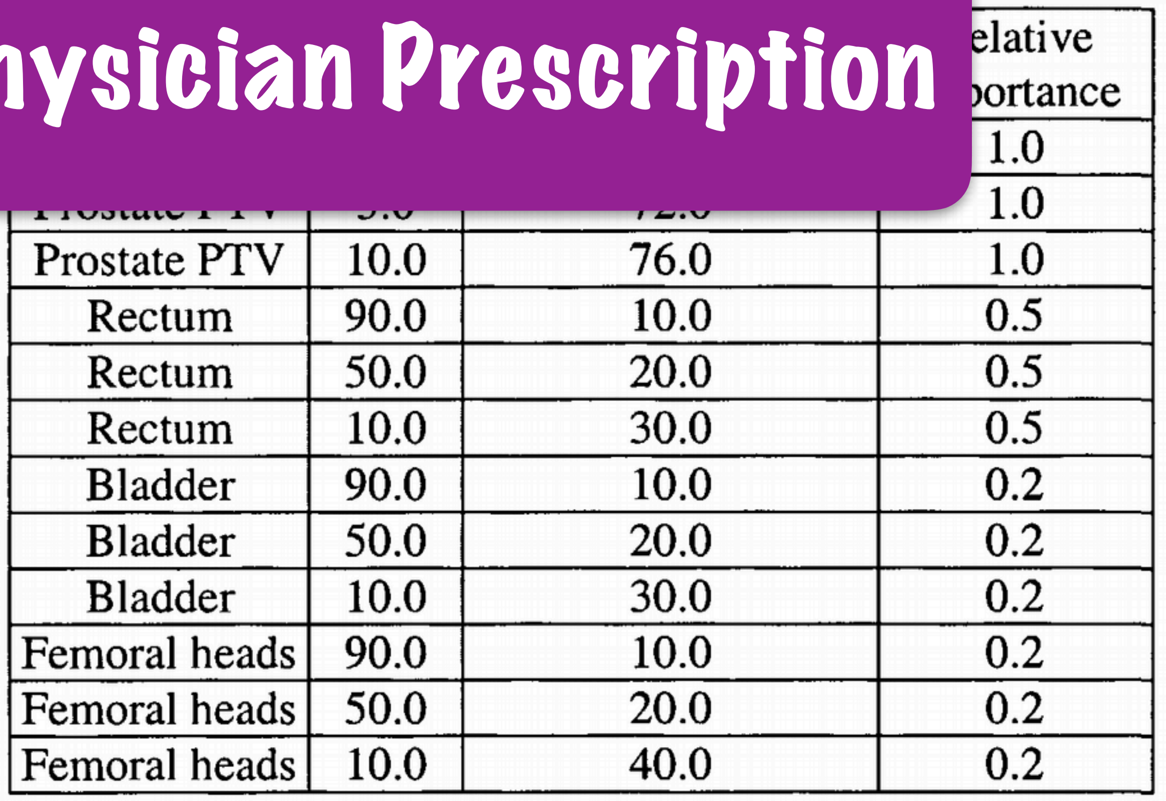
- **dE vs E_{beam}, x, y, z**
- **RBE vs E_{beam}, dE, x, y, z**

Patient anatomic data (CT, MRI, PET)

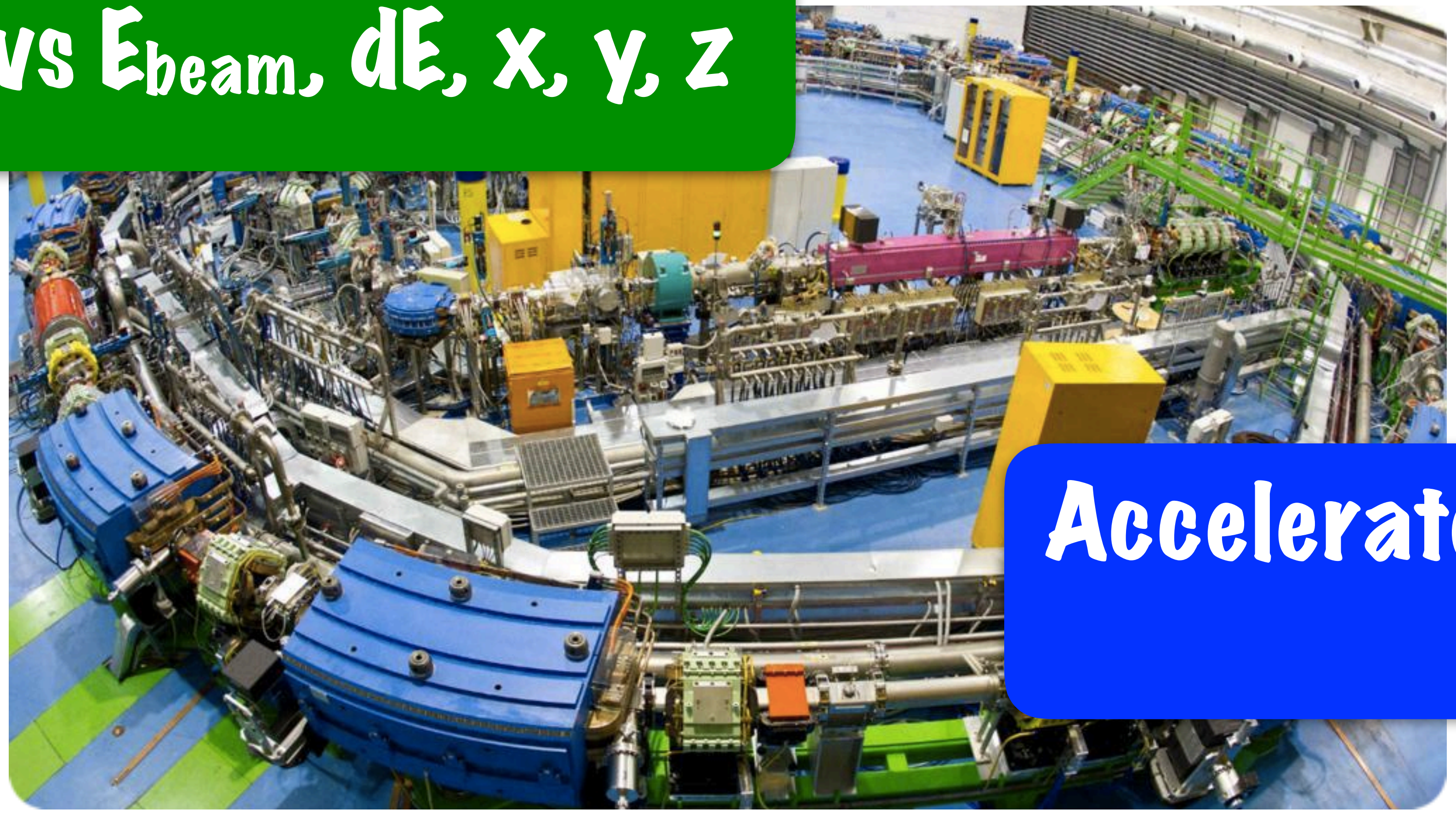


TPS

Physician Prescription



			elative portance
			1.0
			1.0
Prostate PTV	10.0	76.0	1.0
Rectum	90.0	10.0	0.5
Rectum	50.0	20.0	0.5
Rectum	10.0	30.0	0.5
Bladder	90.0	10.0	0.2
Bladder	50.0	20.0	0.2
Bladder	10.0	30.0	0.2
Femoral heads	90.0	10.0	0.2
Femoral heads	50.0	20.0	0.2
Femoral heads	10.0	40.0	0.2



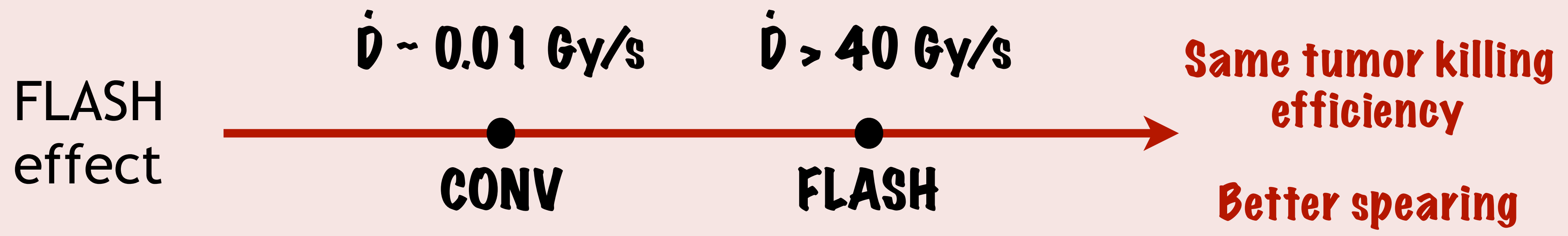
Accelerators Parameters: Fluences for each beam spot

My Ph.D. thesis challenge

The goal of my Ph.D. thesis was to address the technology gap between IOeRT and other radiotherapy techniques, by developing the **first-ever, complete TPS** dedicated to **IOeRT** treatments.

Why we need it?

- IOeRT is recommended in several *far from trivial* irradiation cases (prostate, pancreas, rectal cancer…): **Organ At Risks sparing becomes an issue**;



- **FLASH effect:** the use of mono-energetic high intensity pulses of electrons makes IOeRT the current **best candidate** for the first **clinical implementation** of the FLASH effect.

Breast IOeRT treatments scheduled in 2024

How we can do it ?

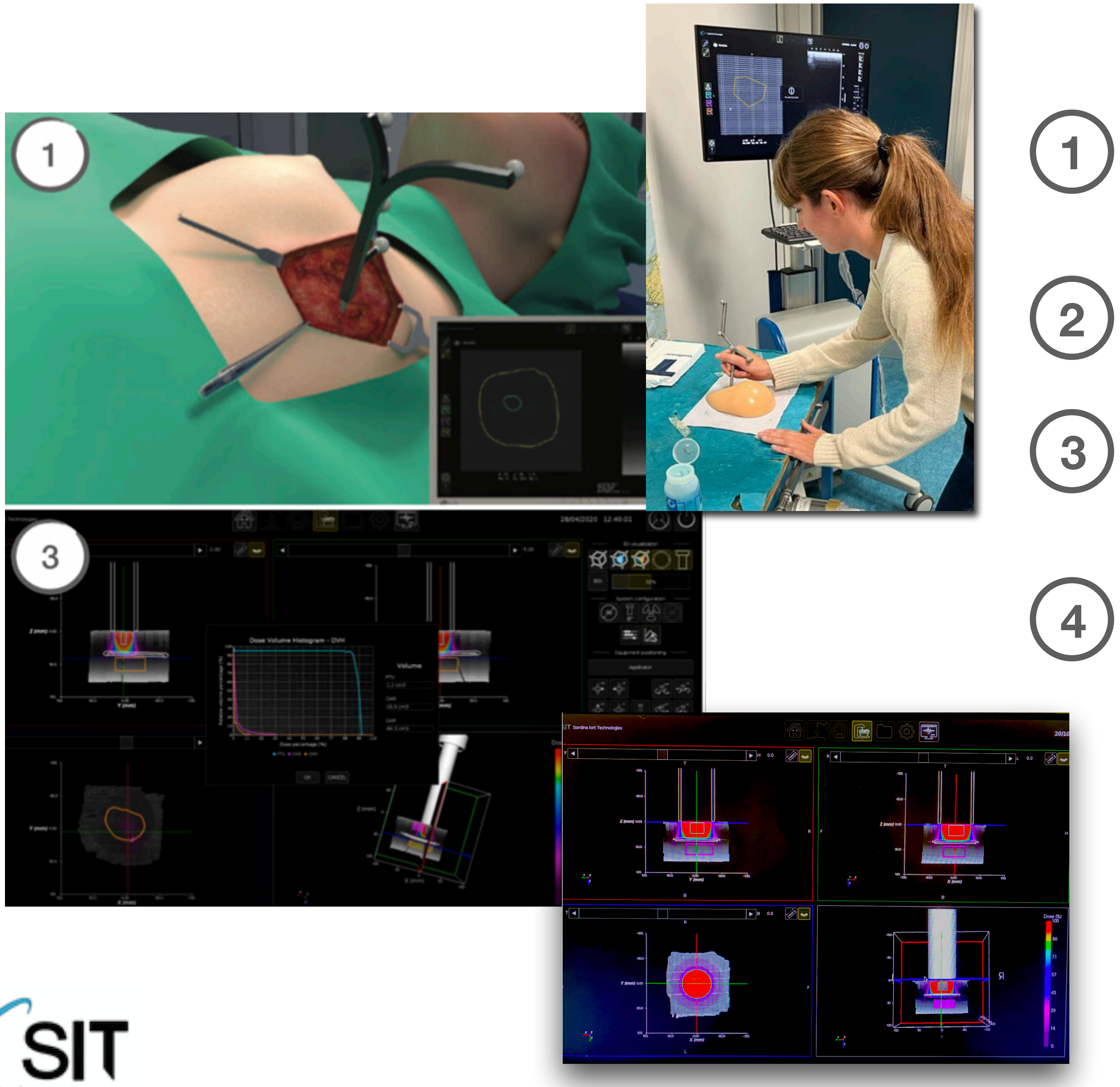
Since timing is an issue, I needed:

- **Quick imaging** after surgery;
- **Quick and accurate planning tool:** an help for the radio-therapist to choose the position, angle of the applicator and beam energy and # electrons to deliver perceived dose, to ensure a proper OARs sparing

To this aim, I collaborated with the **S.I.T. Sordina IORT Technologies S.p.A.** company

The future TPS operation

The S.I.T. company has solved the problem of providing an **online intra-operative image** by means of the ECHO imaging system, a new **3D real-time ultrasound** imaging acquisition with limited precision (capable of discriminating only significant differences in density - air, water, metal)

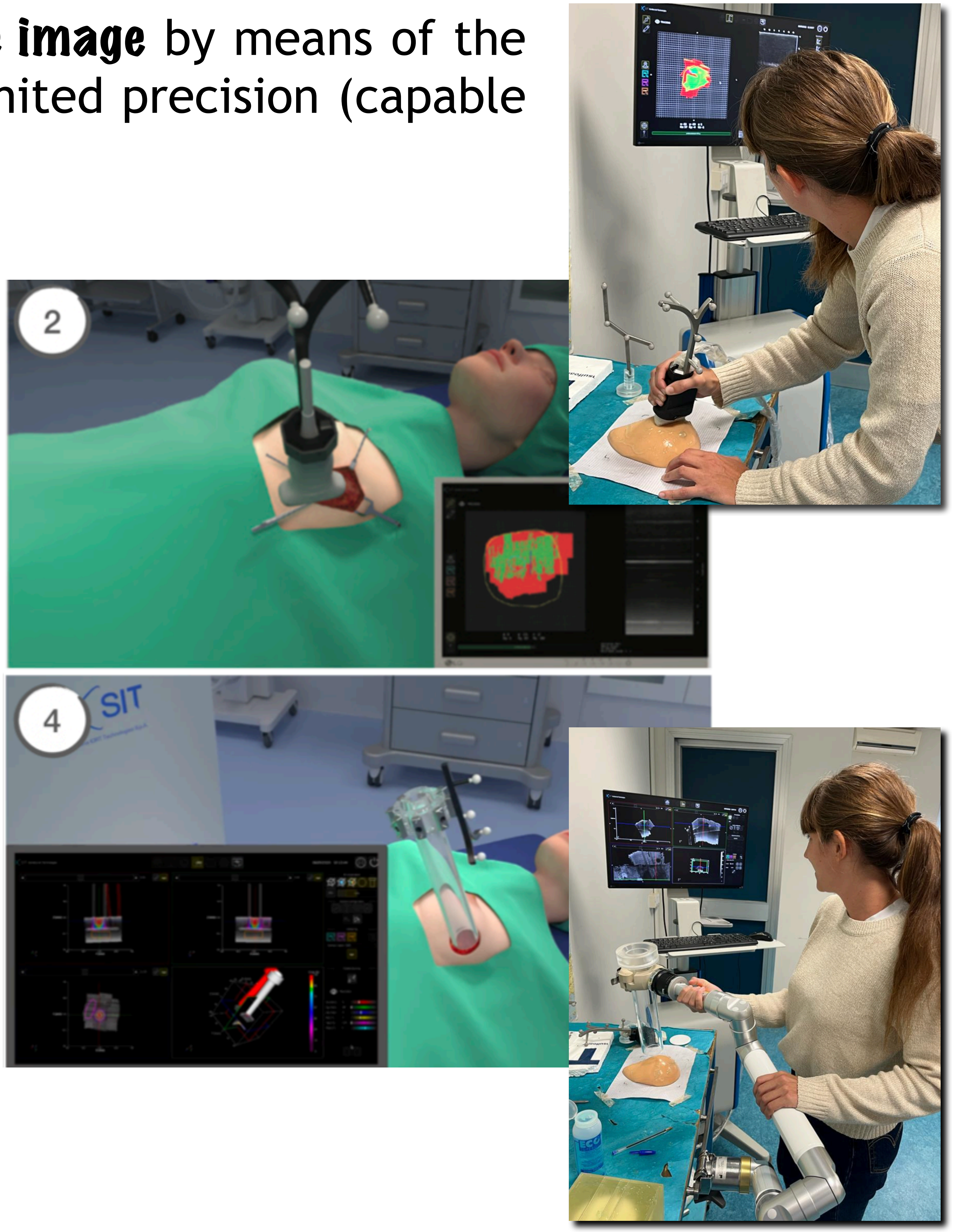


① Identification of the regions of interest (**PTV and OARs**);

② US **imaging acquisition**

③ Treatment **simulation** and optimization

④ **Image guided docking** to deliver the treatment exactly as it was planned in point 3.



Intra-operative imaging

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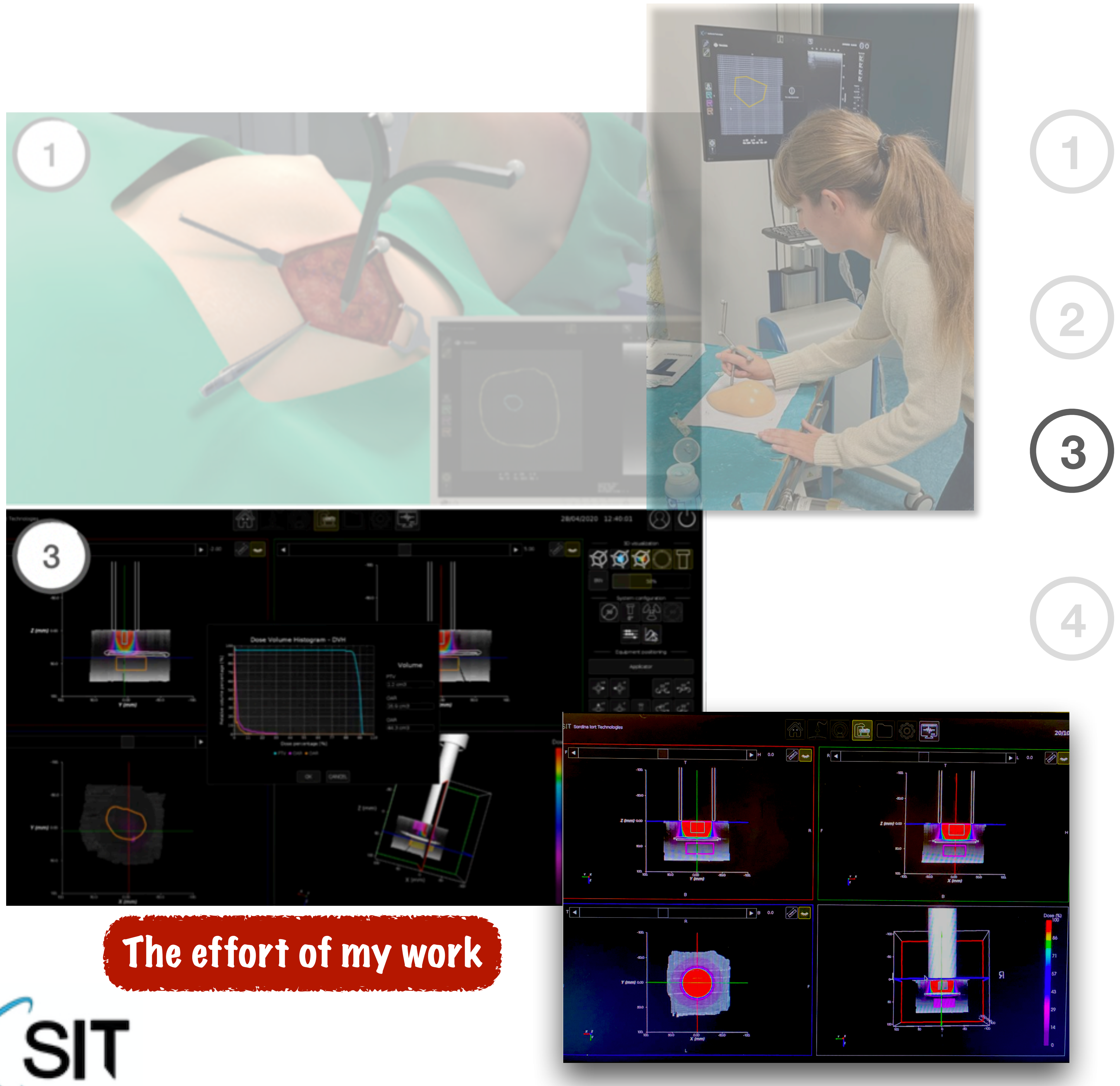

The effort of my work

① Identification of the regions of interest (**PTV and OARs**);

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③ Treatment **simulation** and optimization

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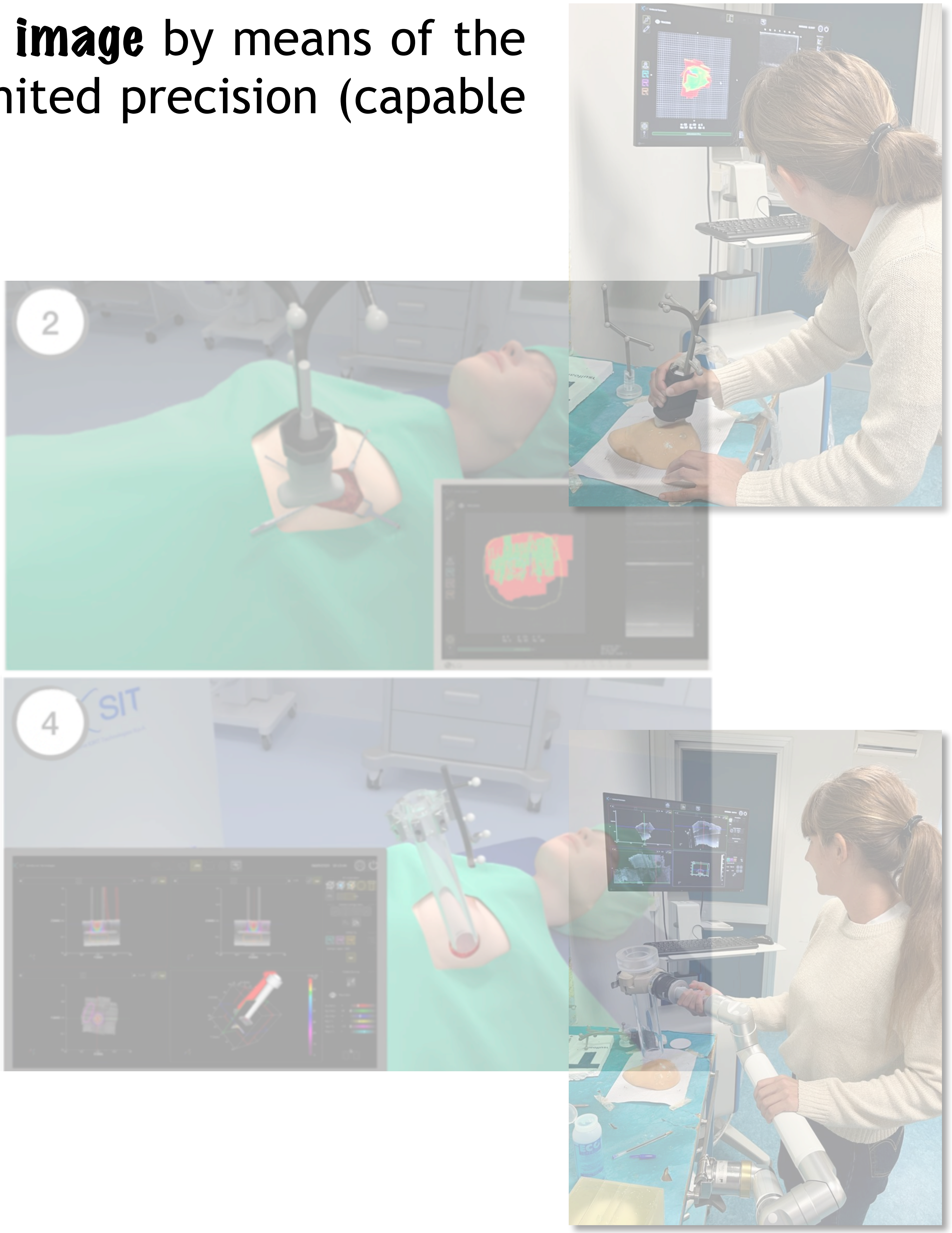
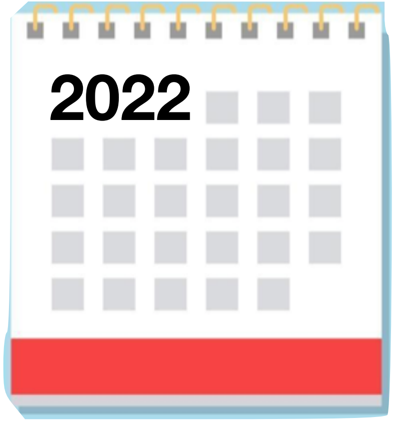


Planning tool: FRED

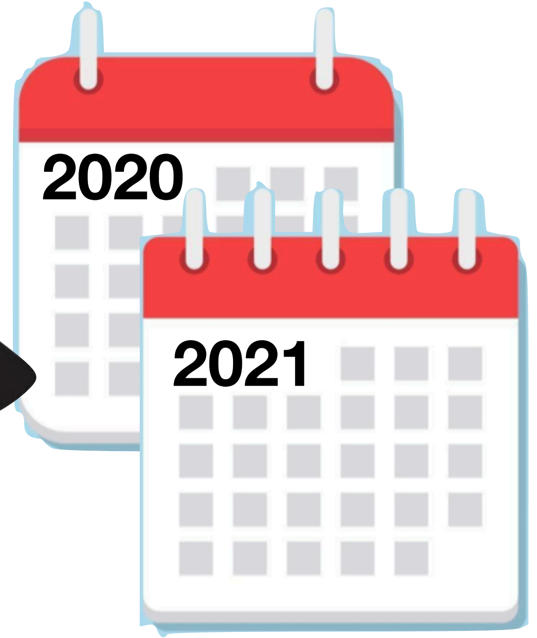
FRED (Fast paRticle thErapy Dose evaluator) is a fast dose engine based on MC code for the transport of particles in heterogeneous media that allows for a quick recalculation of the deposition of the dose. It has been developed in the context of **Particle Therapy** [4].

FRED has been developed to work on **GPU** (**Graphics Processing Unit**) and it reduces the simulation time by a factor of **1000** for proton treatments compared to a standard MC.

For the excellent results achieved with **protons** and **carbon ions** in terms of **tracking performance** and **dose accuracy**, we decided to develop the **electromagnetic** FRED model to extend the use of this MC-on-GPU-based dose engine to other radiotherapy techniques where the **time-factor is crucial**, i.e. the **IOeRT**.



My Ph.D. work thus includes both the complete **development** and test of the FRED electromagnetic model and its first **clinical application** in the context of **IOeRT**.



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[4] *A. Schiavi et al. "FRED: a GPU-accelerated fast-Monte Carlo code for rapid treatment plan recalculation in ion beam therapy" PMB 62 (2017) 18 doi:10.1088/1361-6560/aa8134*

Electromagnetic FRED model

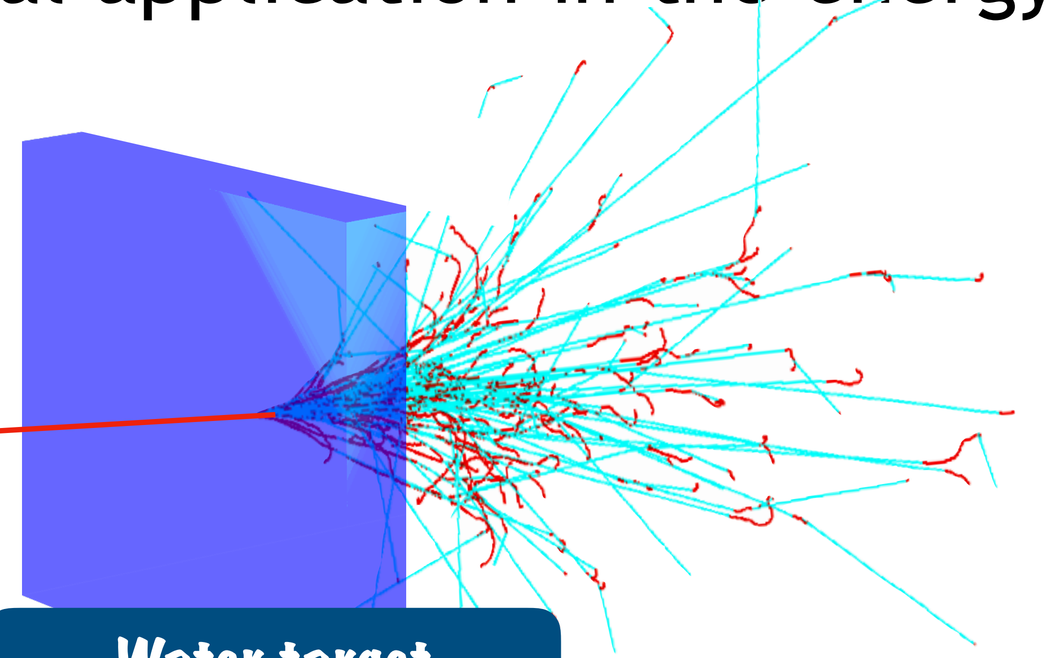
The first step was the implementation of all the electromagnetic processes relevant for medical application in the energy range of 1-200 MeV (from IOeRT to Very High Energy Electron treatments).

Continuous process (e^- e^+)

- **dE/dx** from NIST eSTAR database + **straggling** (GEANT4)
- **Multiple scattering** (doi: 10.1118/1596230).

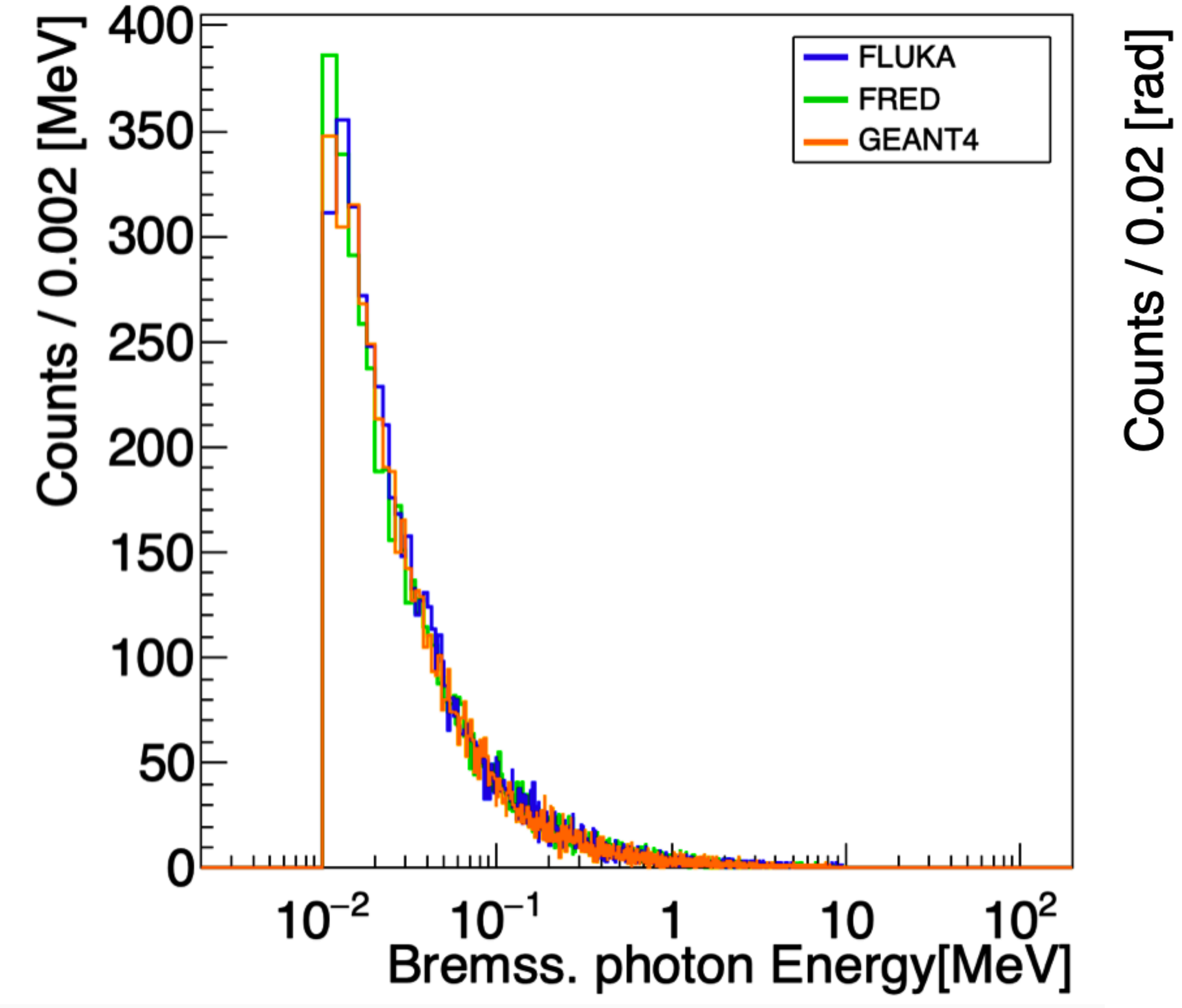
Discrete interactions (e^-, e^+, γ):

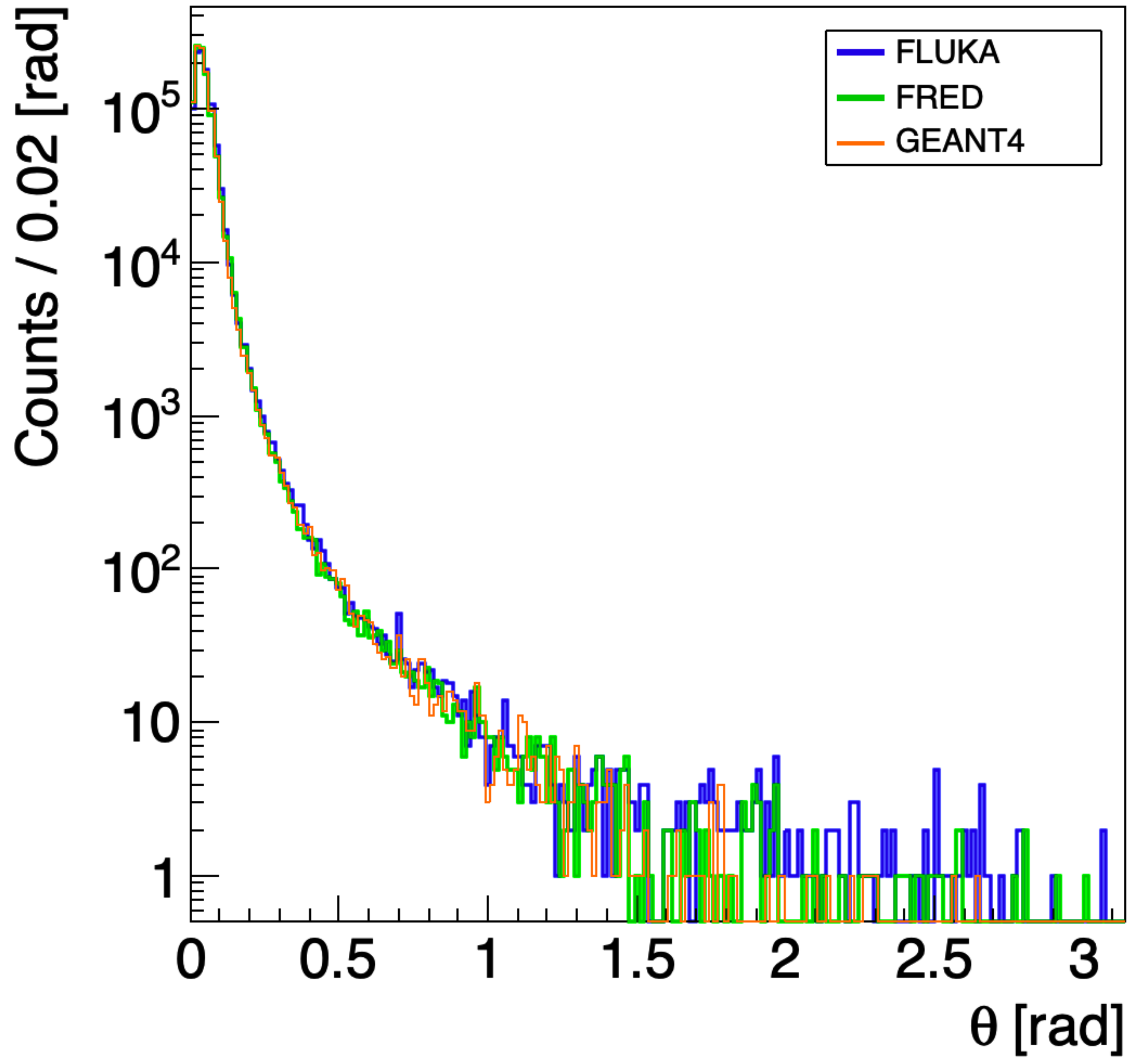
- **Bremsstrahlung** (Custom code with dσ/dk from doi:10.1016/0092-640X(86)90014-8)
- **Moller/Bhabha** scattering (GEANT4)
- **Coherent scattering** (custom code with XCOM NIST database)
- **Photoelectric** (custom code with XCOM NIST database)
- **Compton** (custom code with XCOM NIST database)
- **Pair production** (XCOM NIST database and GEANT4)
- **Positron annihilation** at rest/ in flight (GEANT4)



1e7 e^- at 10 MeV

Water target [5,5,0.05] cm^3



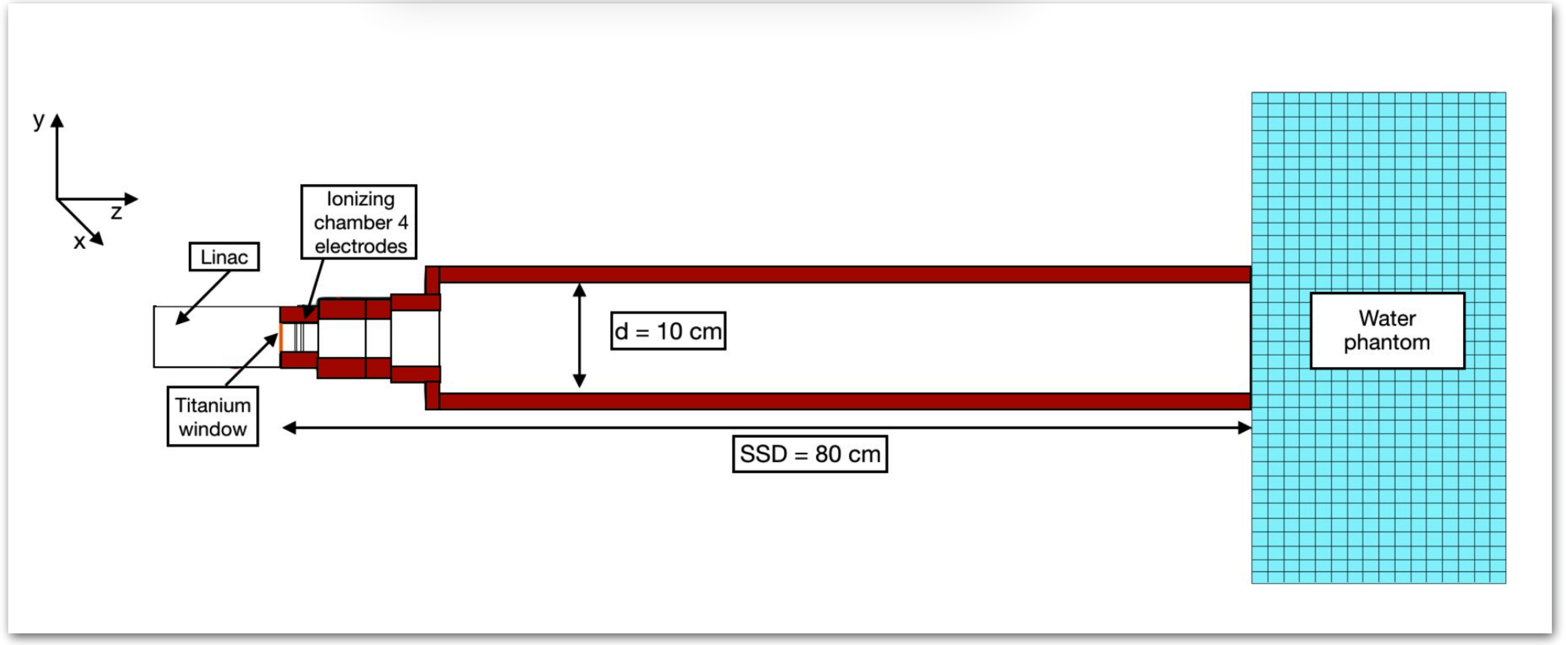


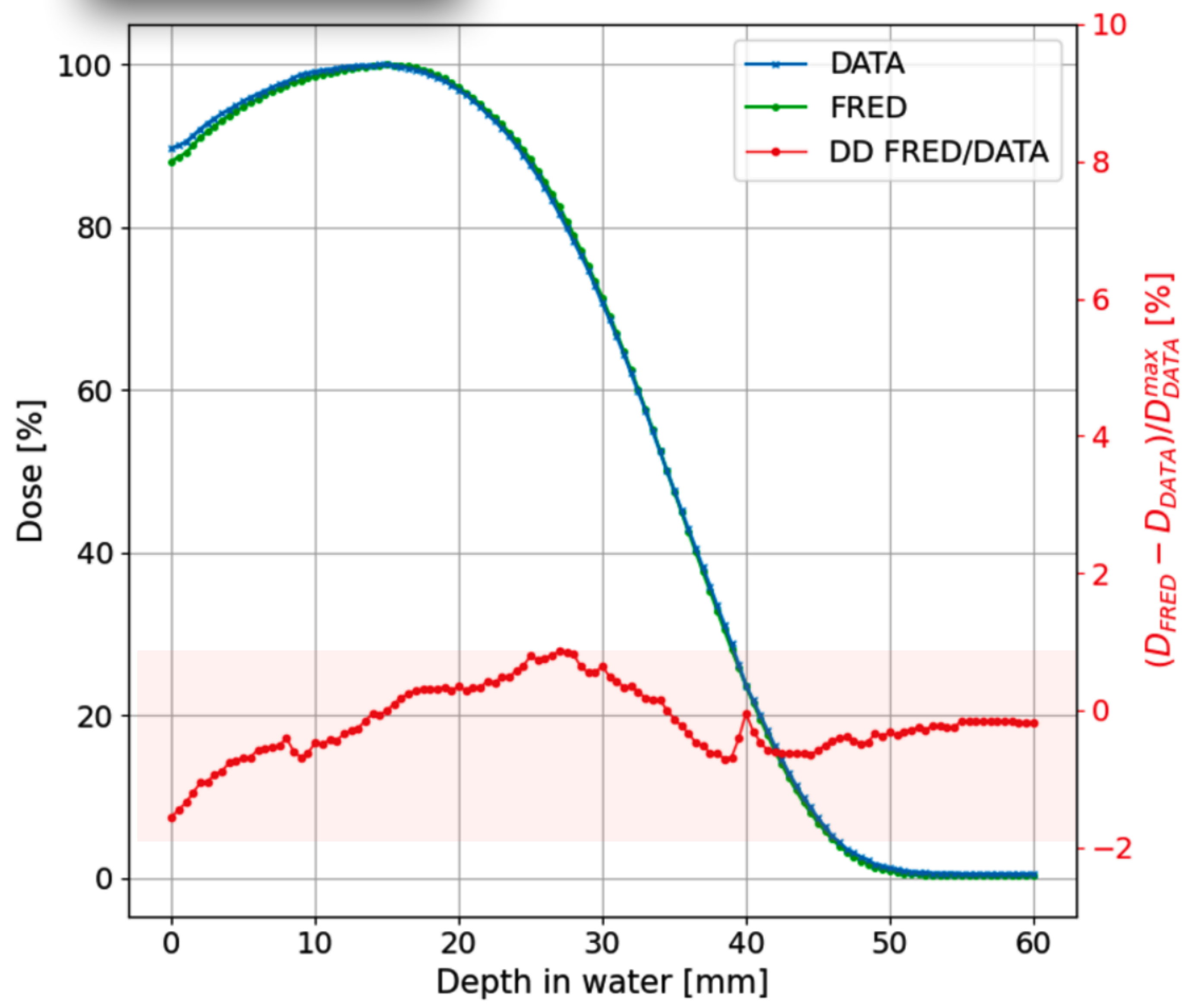
Efficiency and timing performance

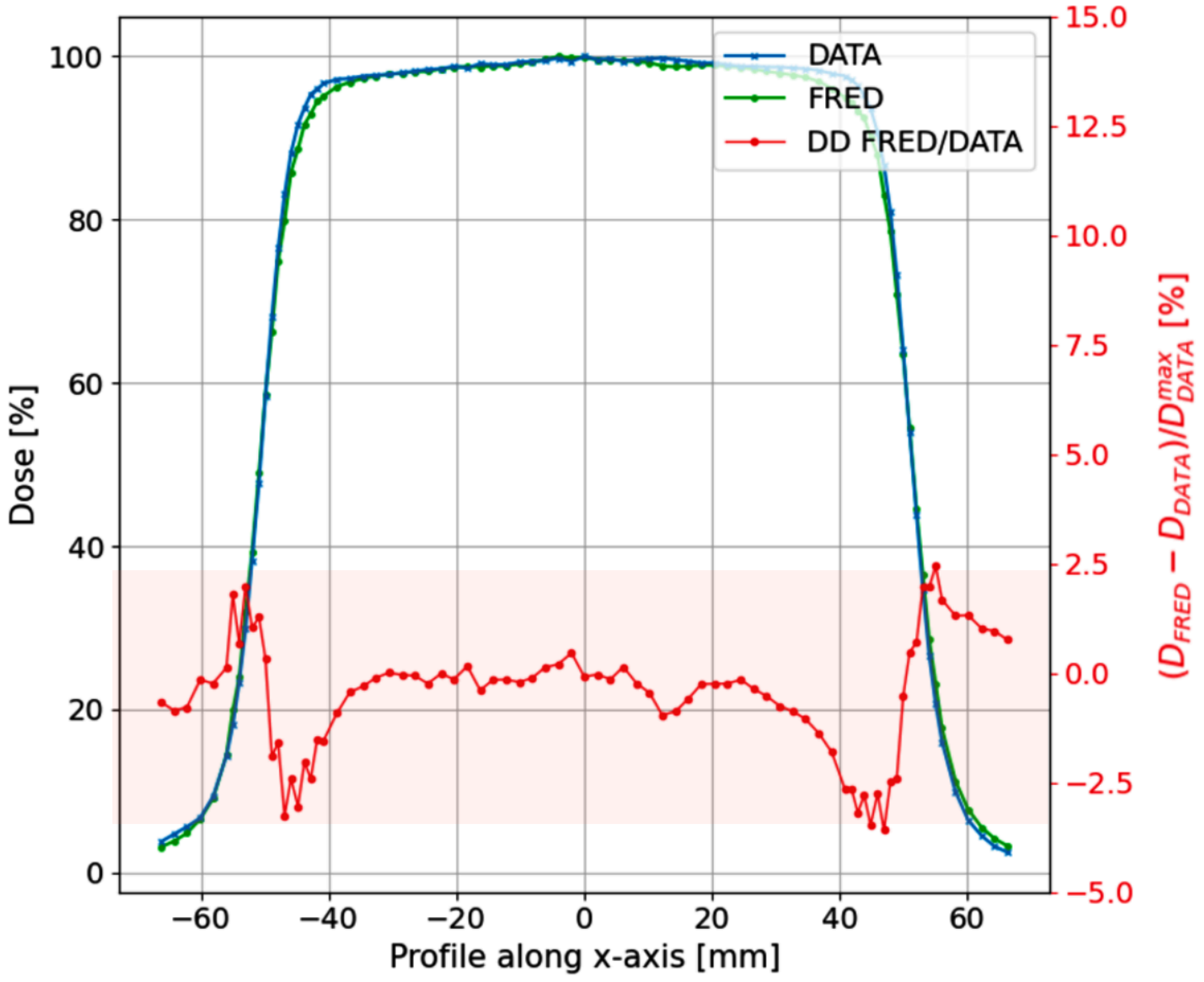
IOeRT

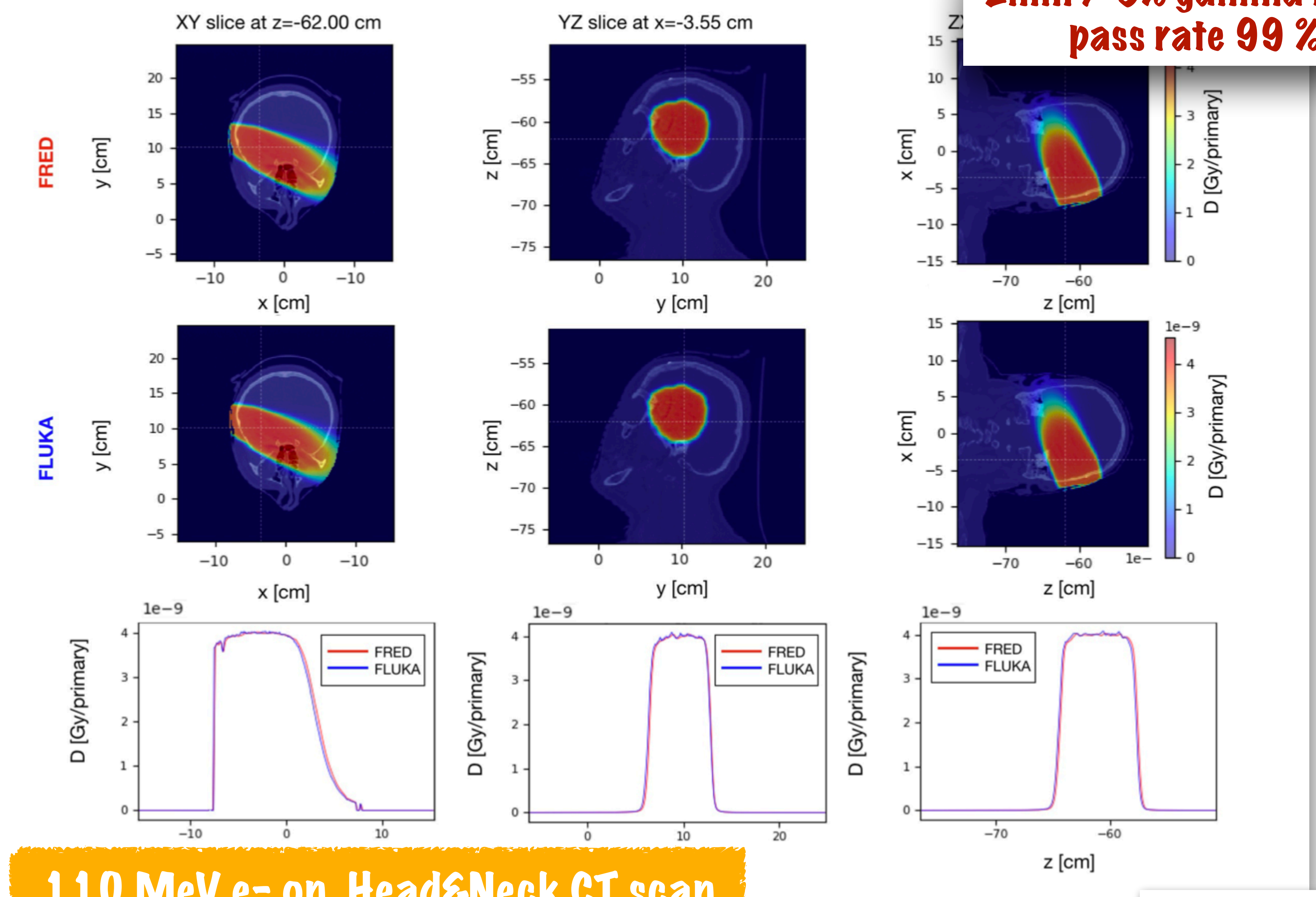
Then the **FRED** accuracy and timing performance were tested against state-of-art full MCs, such as **FLUKA** and **GEANT4**, in homogenous and **heterogenous** phantom and against **experimental data (IOeRT LINAC)** .

FRED simulation









2mm / 3% gamma index pass rate 99 %

110 MeV e- on Head&Neck CT scan

~ x1000

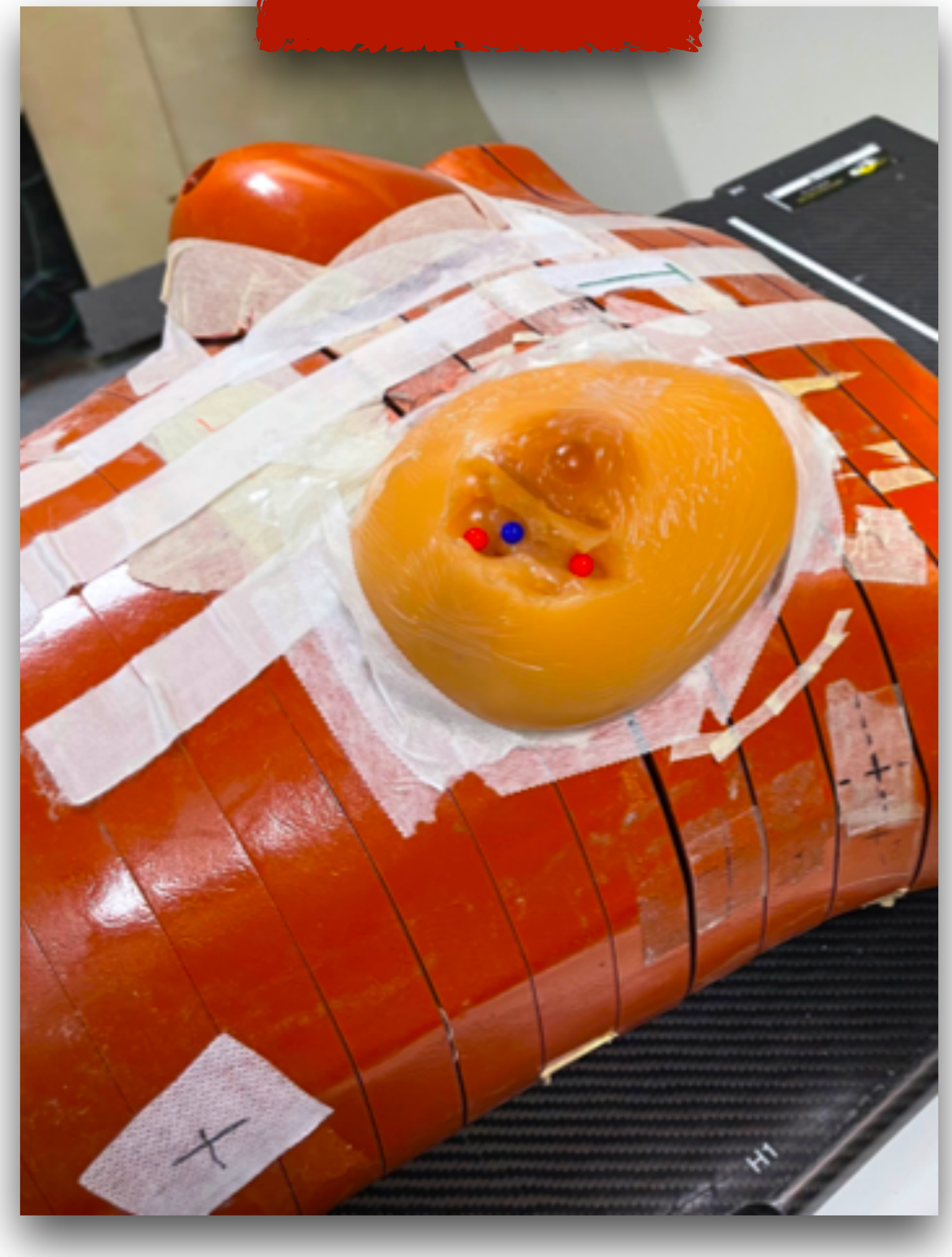
Timing Performance in water	**FLUKA**	**GEANT4**	**FRED**
e^- @ 1 MeV	1.6e4 prim/s	1.3e3 prim/s	3.0e6 prim/s
e^- @ 10 MeV	4.4e3 prim/s	2.2e2 prim/s	4.0e5 prim/s
e^- @ 100 MeV	1.1e3 prim/s	4.8e1 prim/s	7.2e4 prim/s

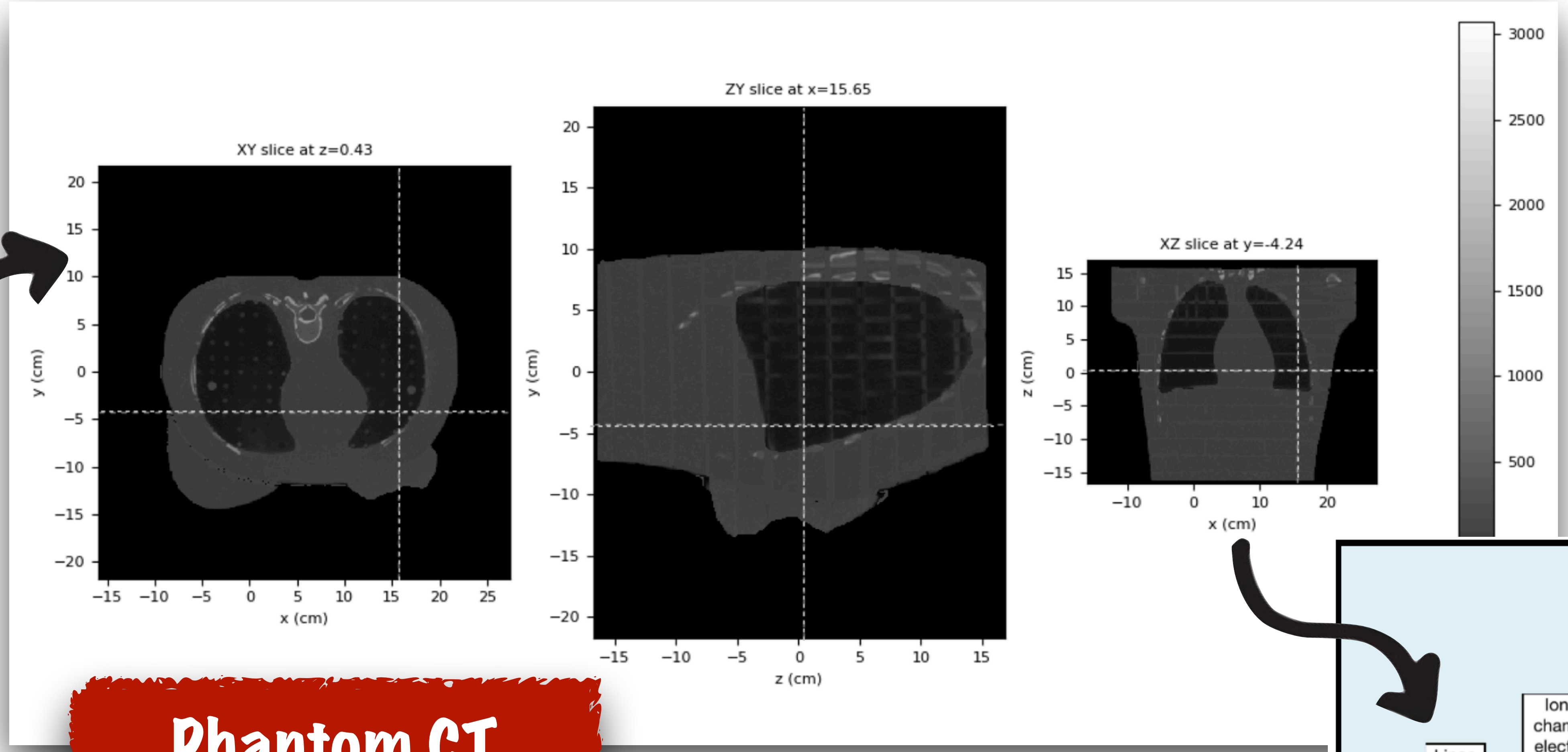
Breast cancer IOeRT TPS

Once I validated the FRED dose engine, I started working on its clinical application as a tool for treatment planning and optimization.

Since the US imaging system is today under optimization, to simulate the breast IOeRT treatment, I used a **CT** of a phantom with a **breast prosthesis** used to simulate a breast surgery attached onto it and I tried to **approximate a realistic case**.

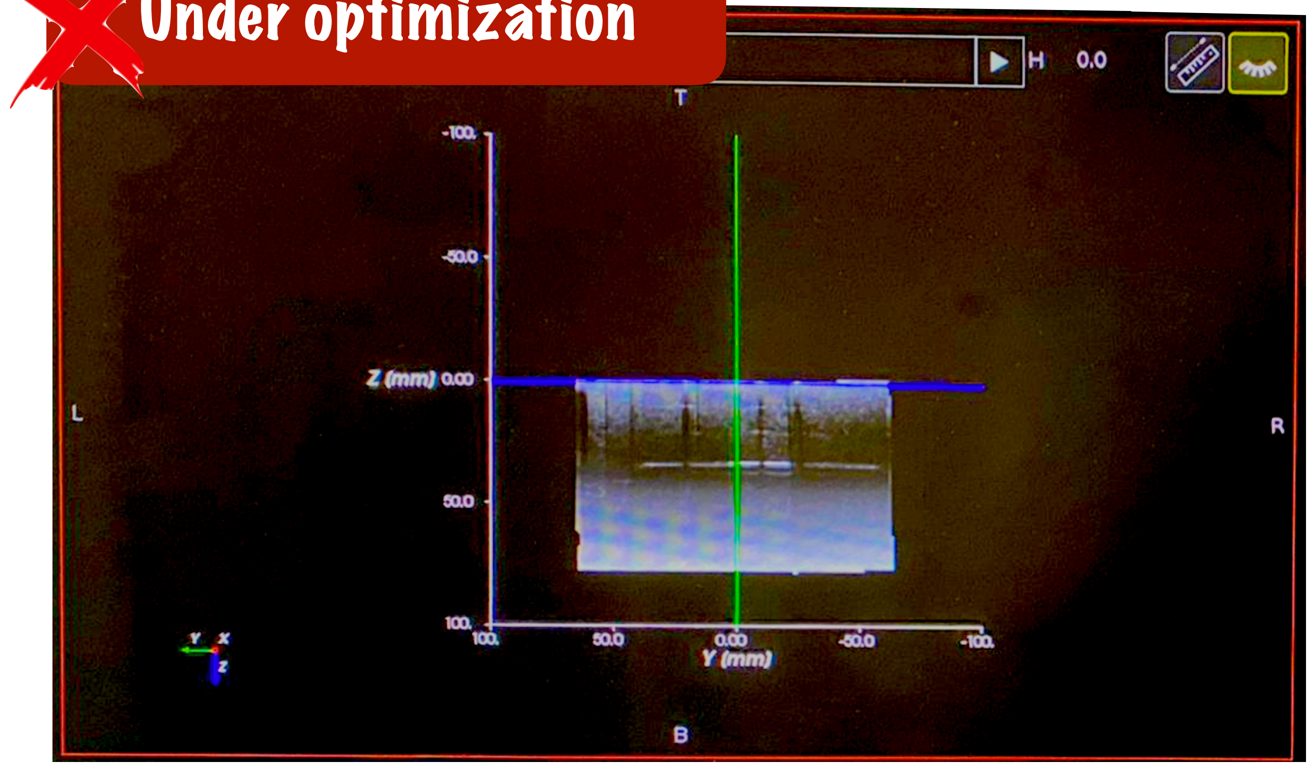
Phantom

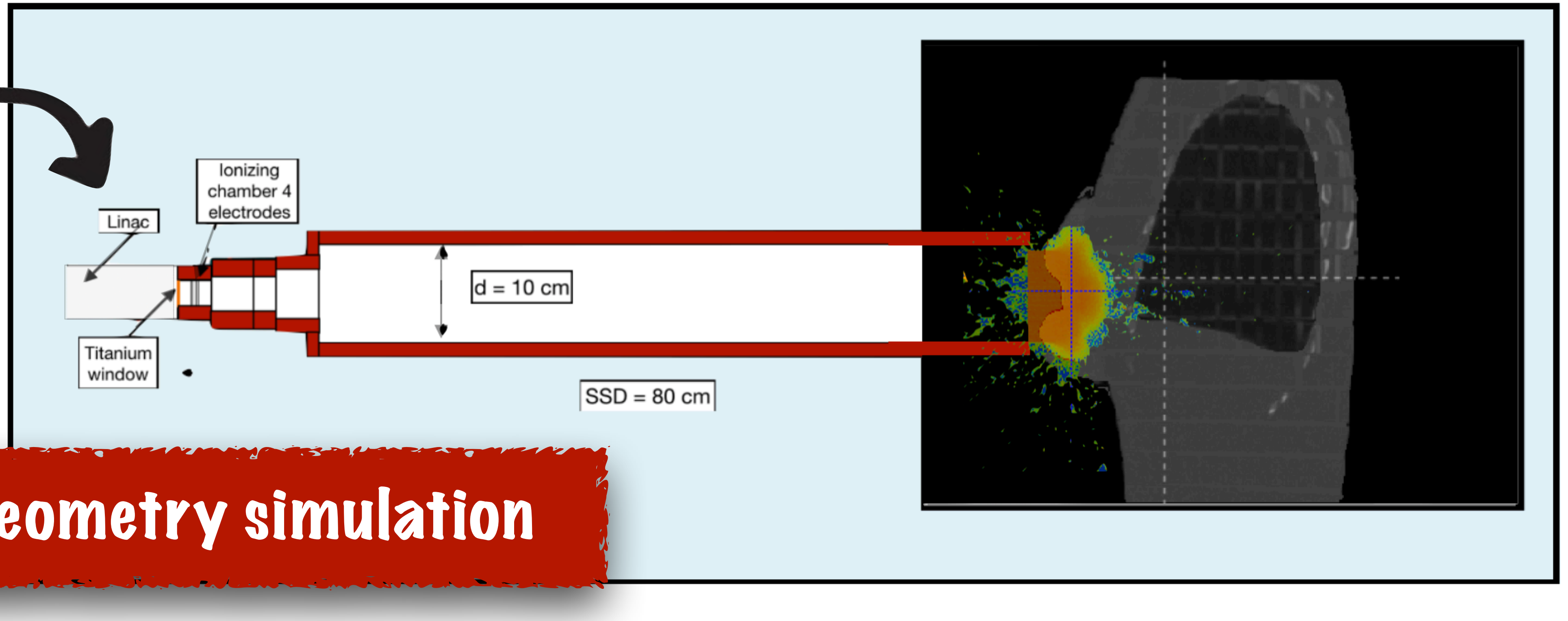




Phantom CT

Under optimization



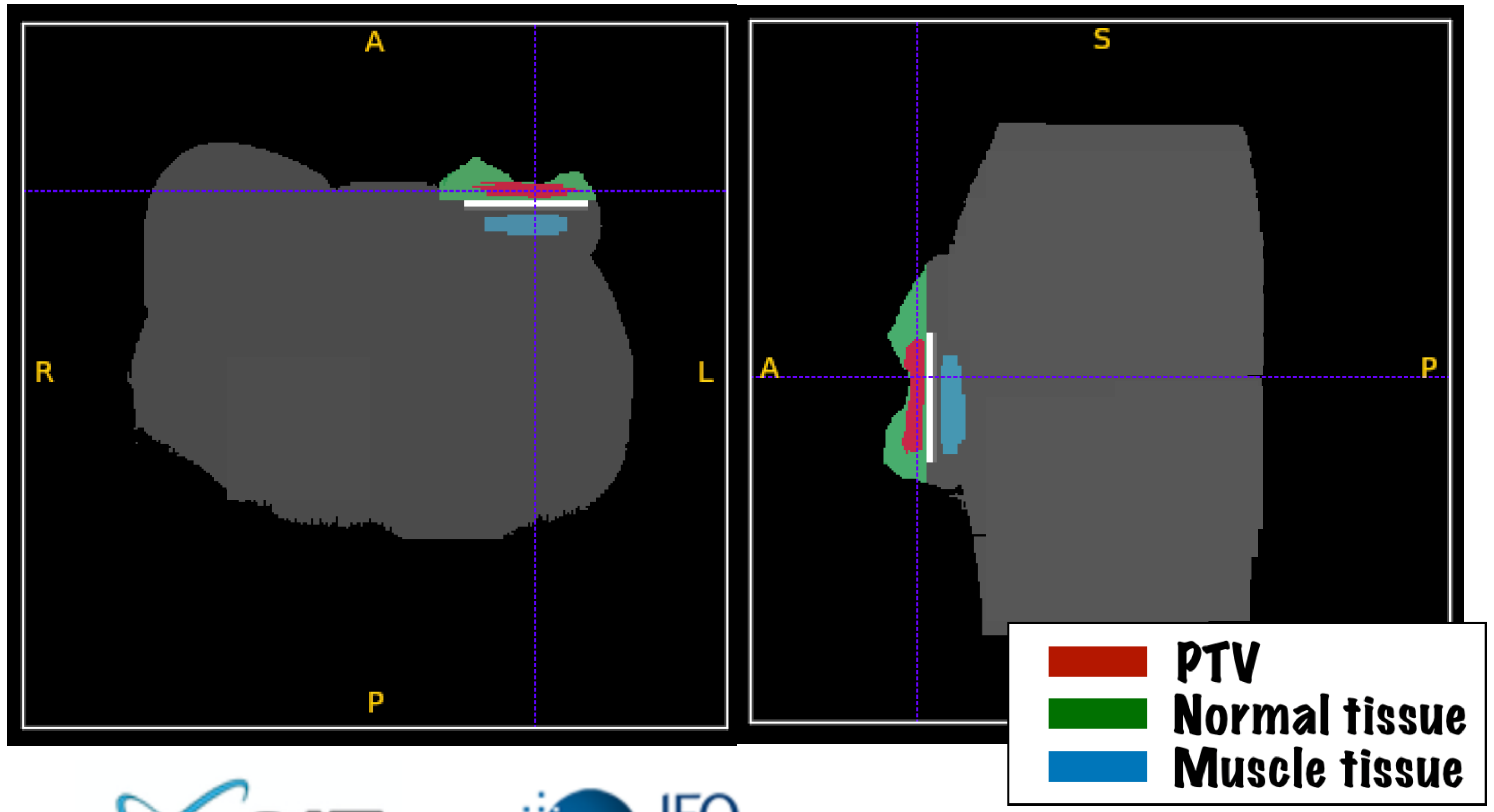


FRED geometry simulation

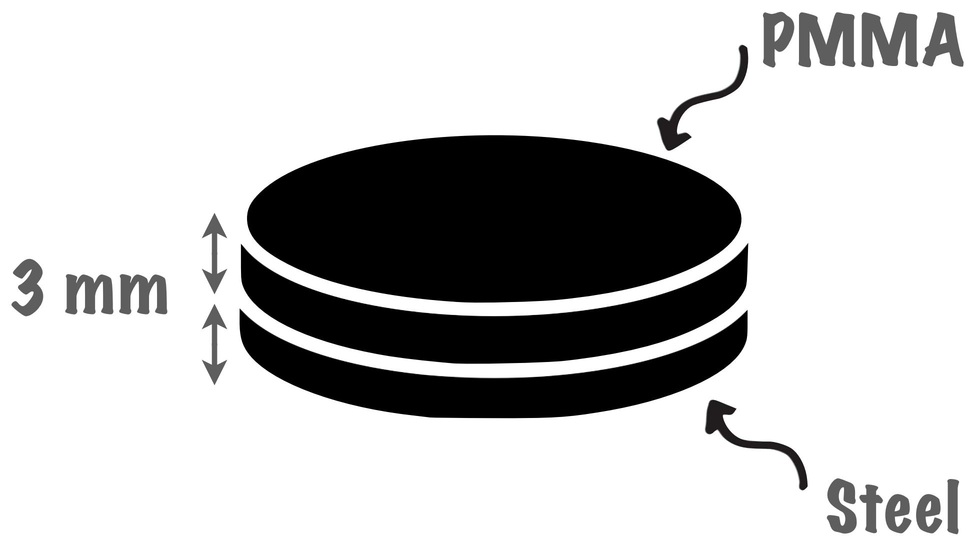
Regions of Interest (ROIs)

I then modified the CT image to meet the future US imagining resolution and identified the treatment ROIs:

- I replaced all the voxels belonging to the patient with the **water** HU value (HU=0) and the ones outside with the **air** HU value (HU=-1000);



- I inserted the radio protection disk;



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di Oncologia

- According to the US optimal viewing, I defined a reasonable **PTV** (d~6÷7cm, 1cm thick), a **Normal Tissue** region and a volume under the disk (**Muscle Tissue**) at a depth of no more than 7 cm;

Then I tried to optimize the treatment looking for the configuration that maximizes the PTV coverage and spearing of the OARs: I simulated **$5 \cdot 10^5$ electrons** (several orders of magnitude below a full treatment ~ 3.2e12), of whatever energy, beam size and position, and analyzed the **resulting Dose Volume Histograms.**

Robust results and dose calculation time ~ 7.6 s

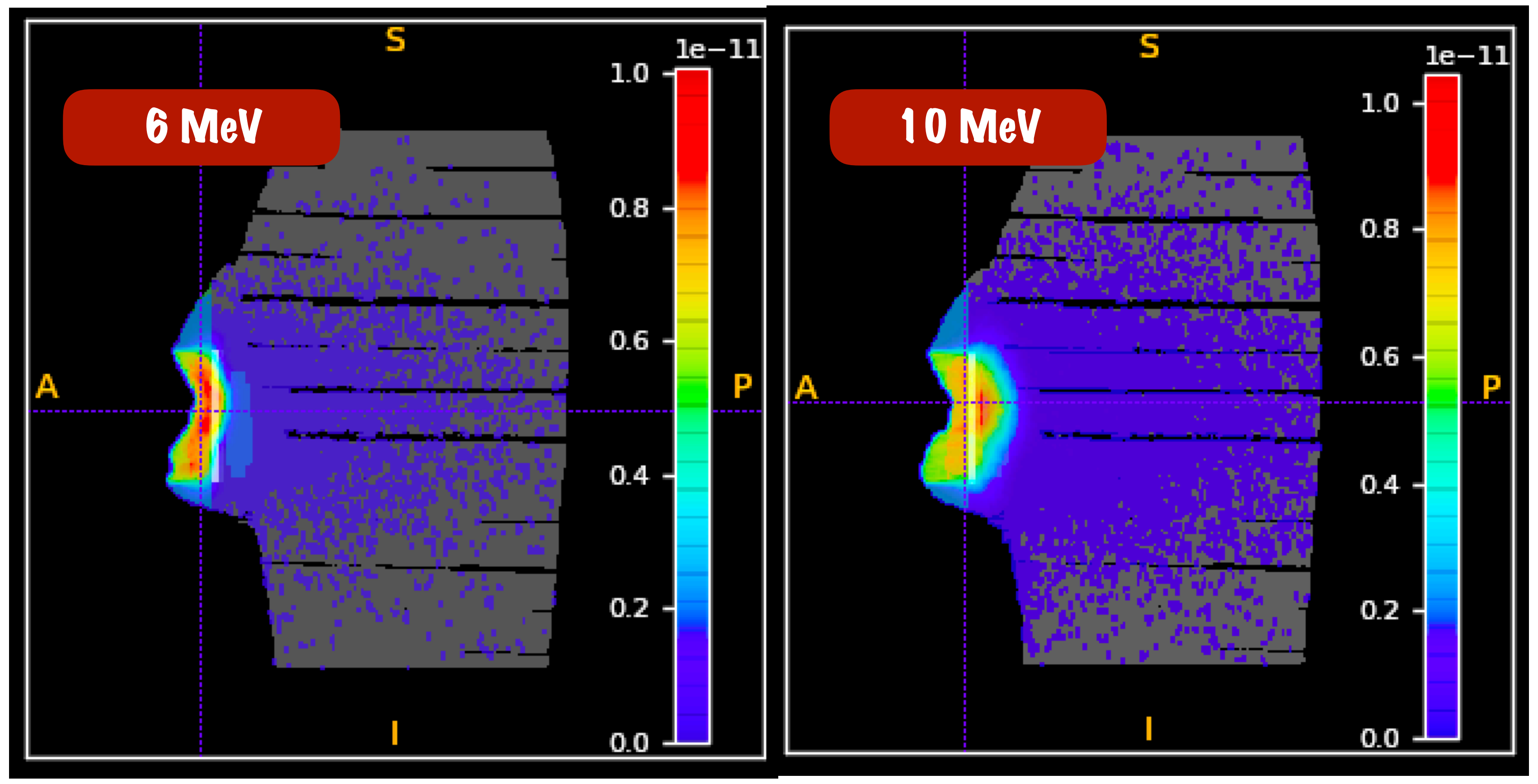
Beam energy scan

T = 23.1 s

The diameter was fixed at 80 mm and I changed only the beam energy: 6, 8 and 10 MeV were selected according to the PTV thickness.

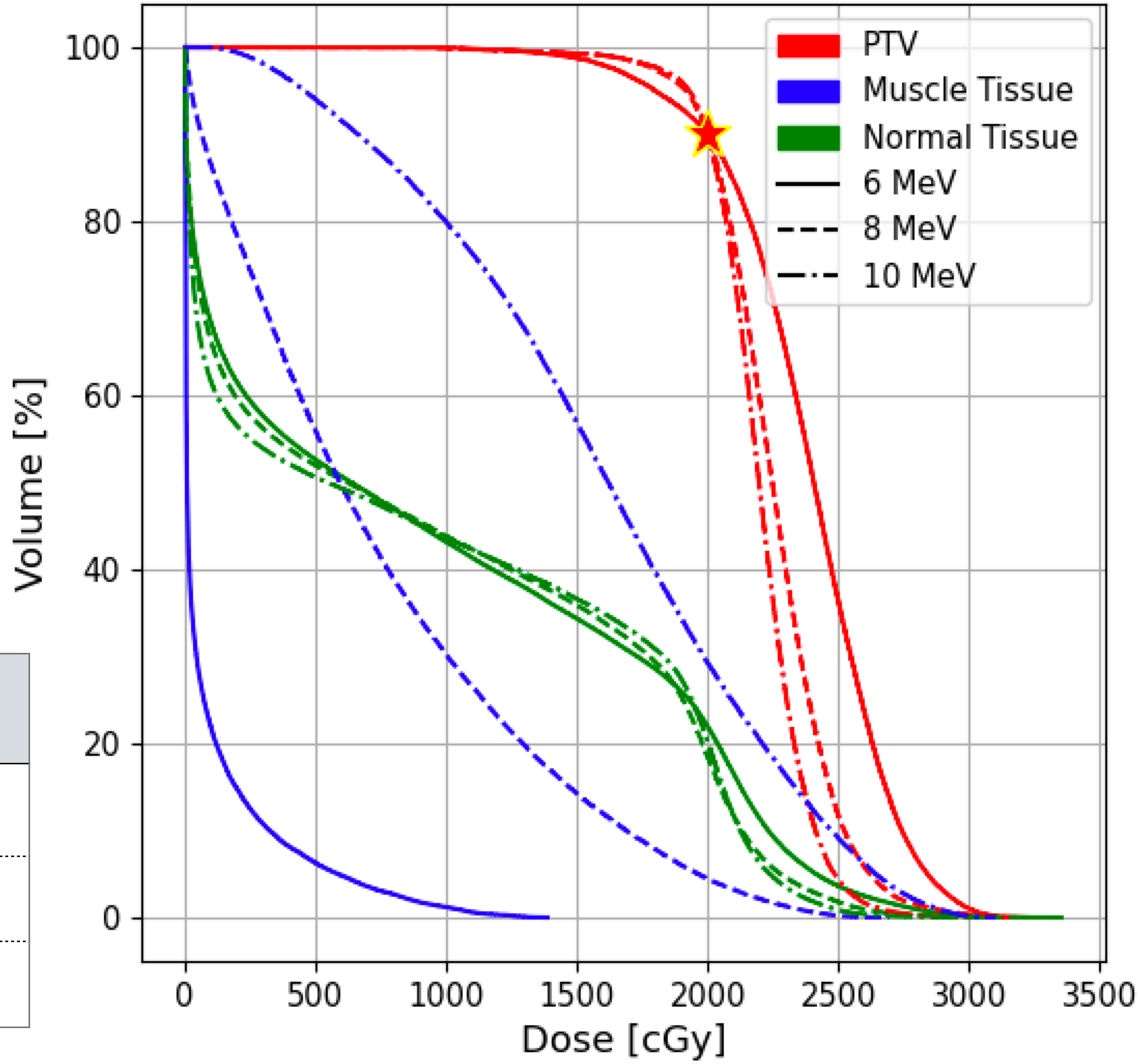
Dose prescription: ★ **20 Gy @ 90% PTV volume**

OSS: The FRED dose maps in Gy/primary units were multiplied by the **number** of **electrons** needed to **fulfill** the dose prescription: $3.26 \cdot 10^{12}$, $3.20 \cdot 10^{12}$ and $3.27 \cdot 10^{12}$ for the 6, 8 and 10 MeV simulation.



Dose mean values

D [Gy]	PTV	Muscle Tissue	Normal Tissue
6 MeV	23.7	0.9	9.6
8 MeV	22.4	7.5	9.3
10 MeV	21.9	15.9	9.1



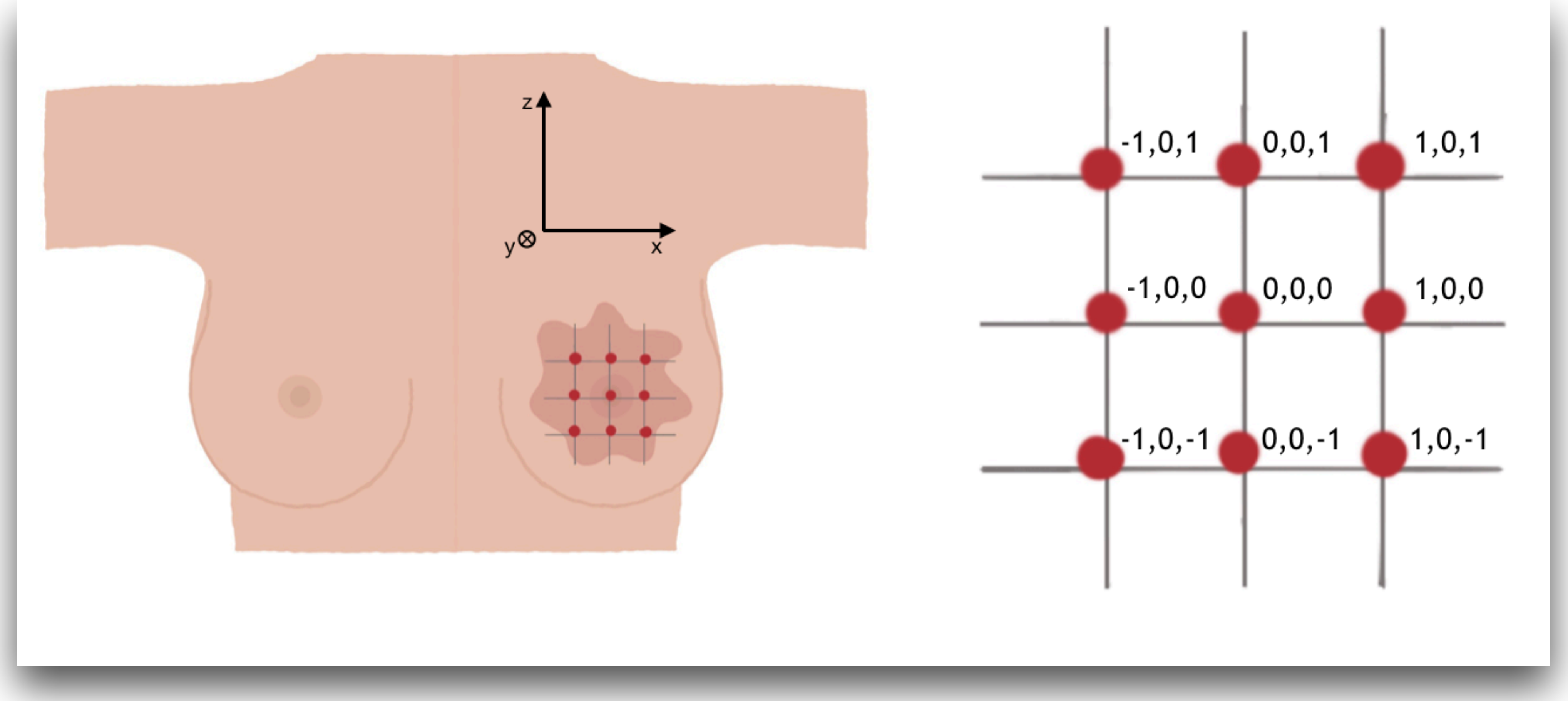
Beam position scan

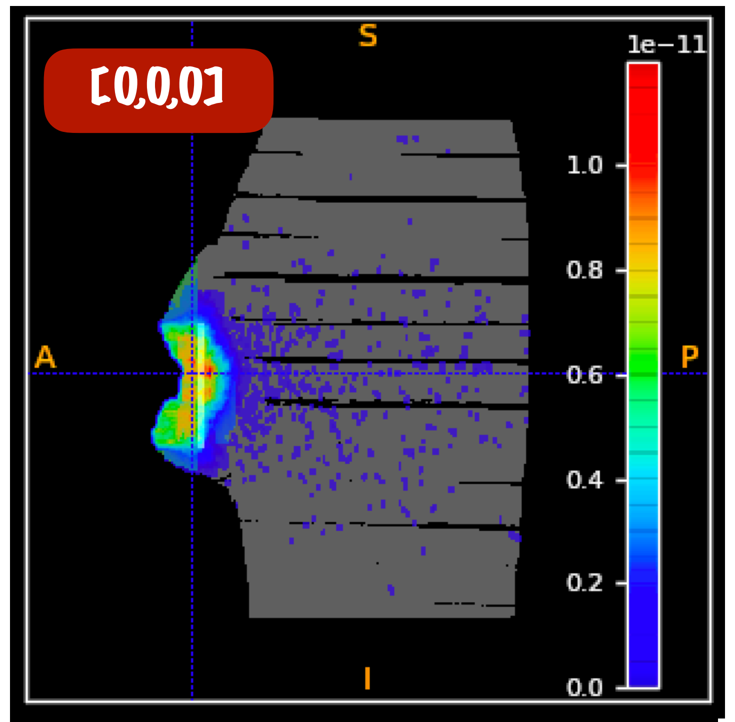
T = 60.3 s

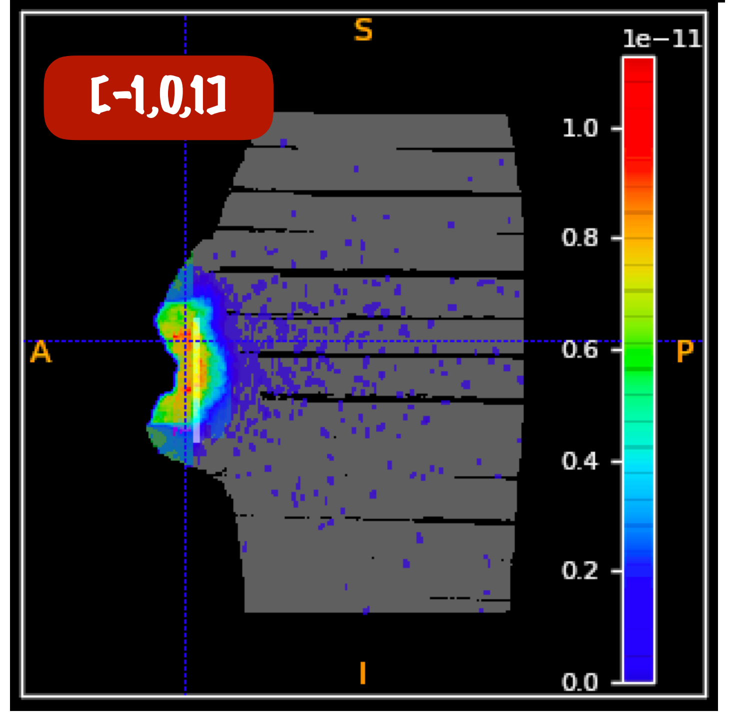
With an 8 MeV circular electrons beam with d=80 mm, I performed a position scan, moving the beam in steps of 10 mm in a **[x,z] grid**

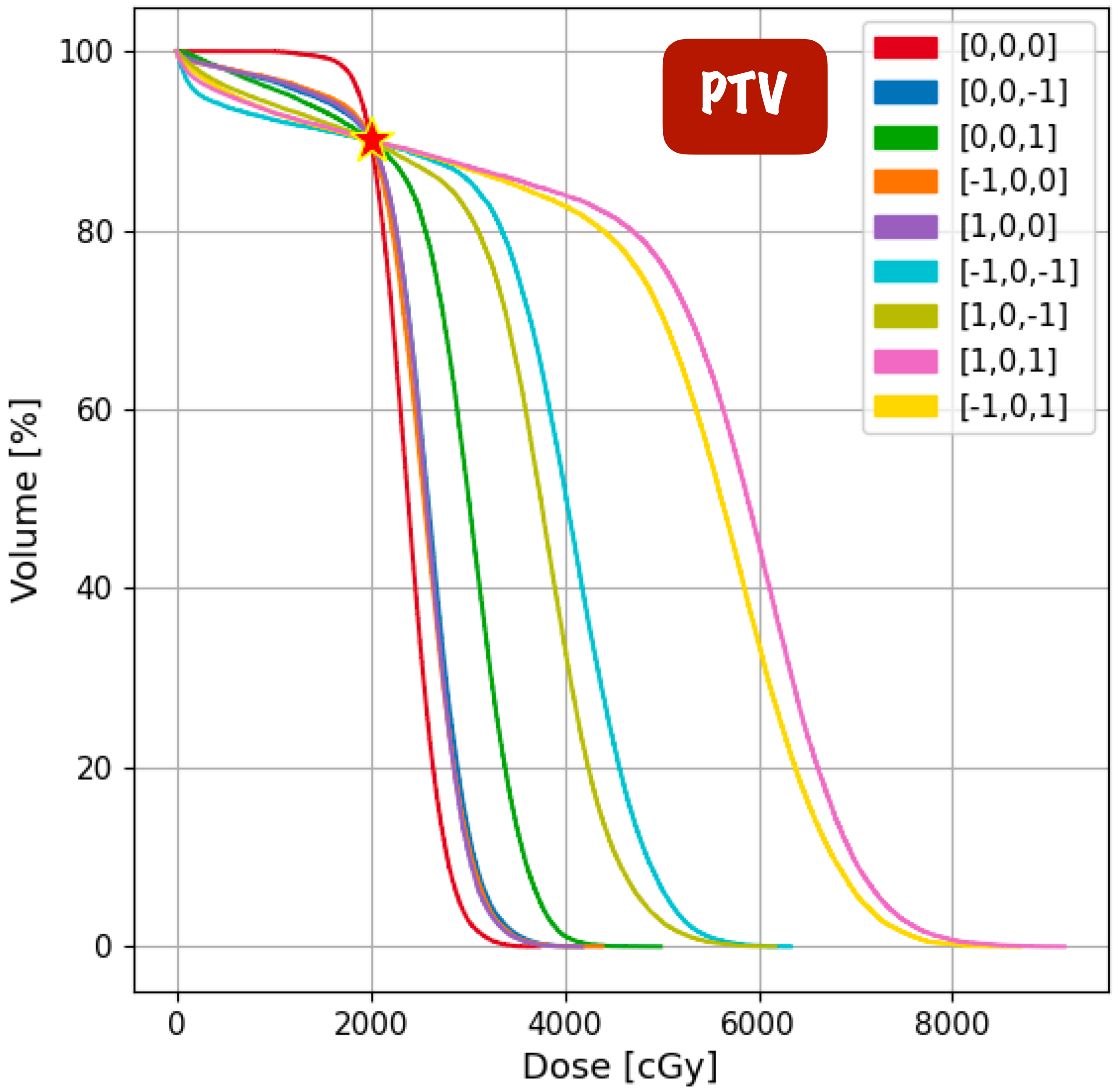
Dose prescription: ★ **20 Gy @ 90% PTV volume**

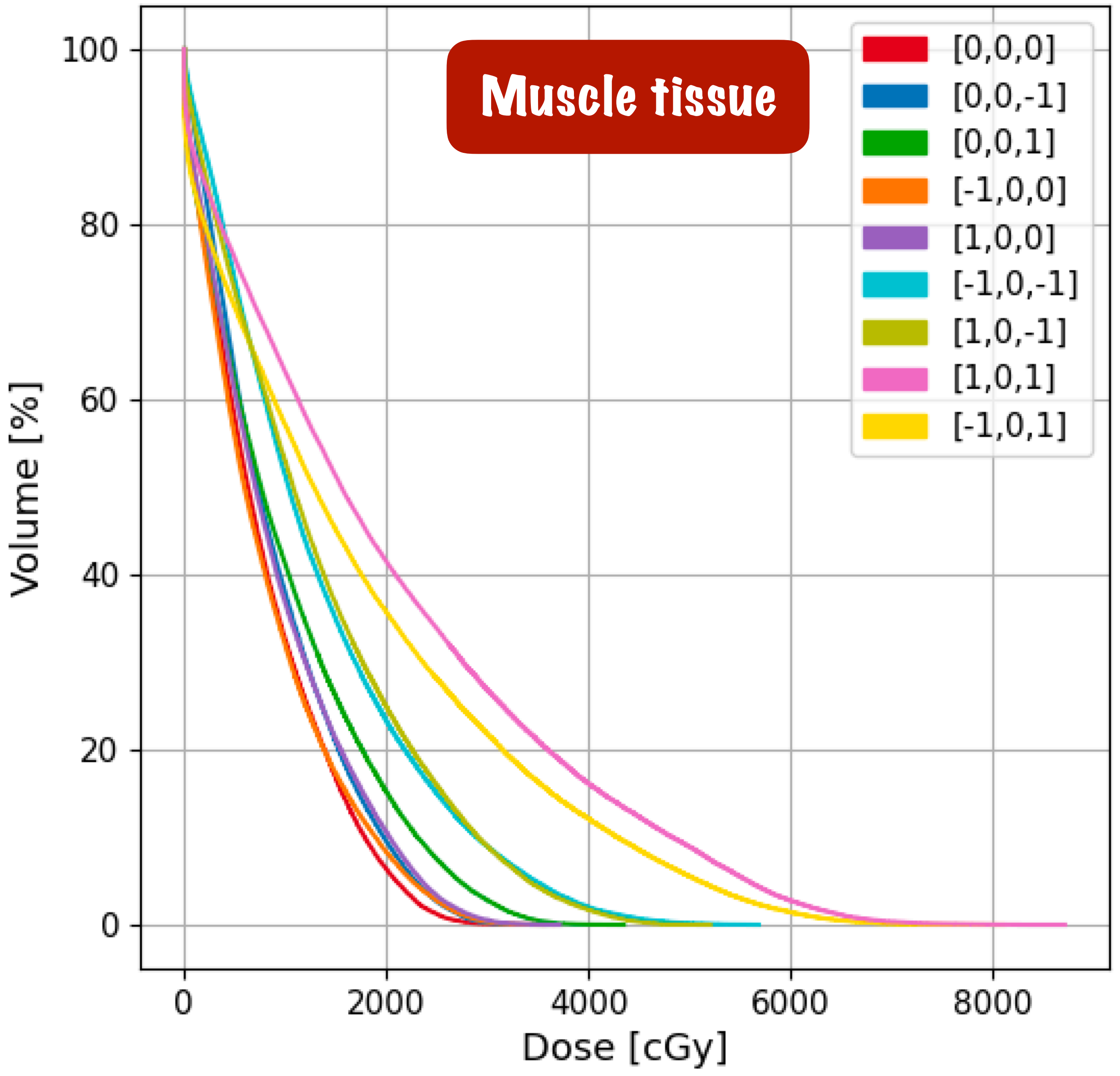
OSS: Also in this case the FRED dose maps in Gy/primary units were multiplied by the **number** of **electrons** needed to **fulfill** the dose prescription ~ 10^{12}

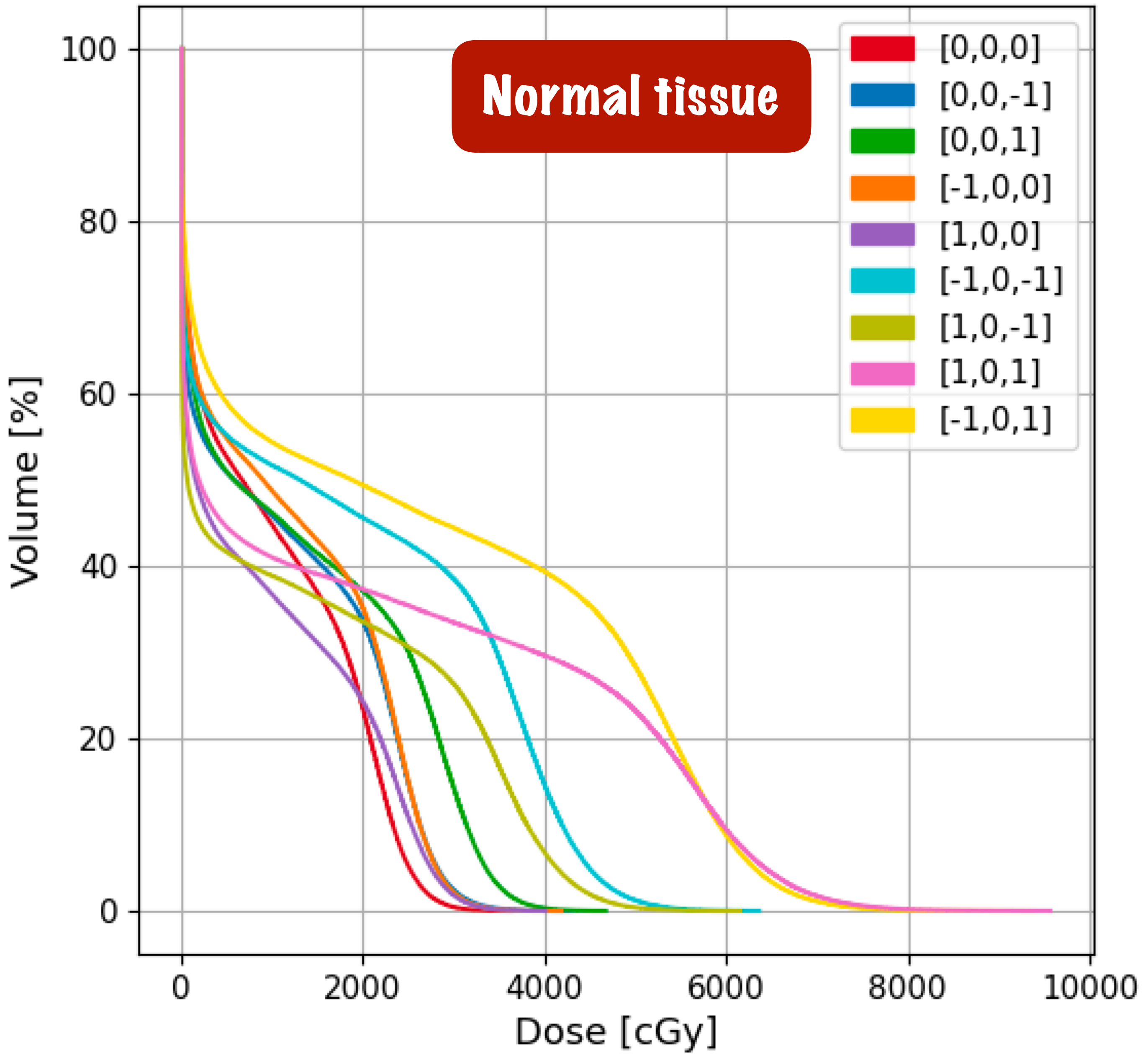










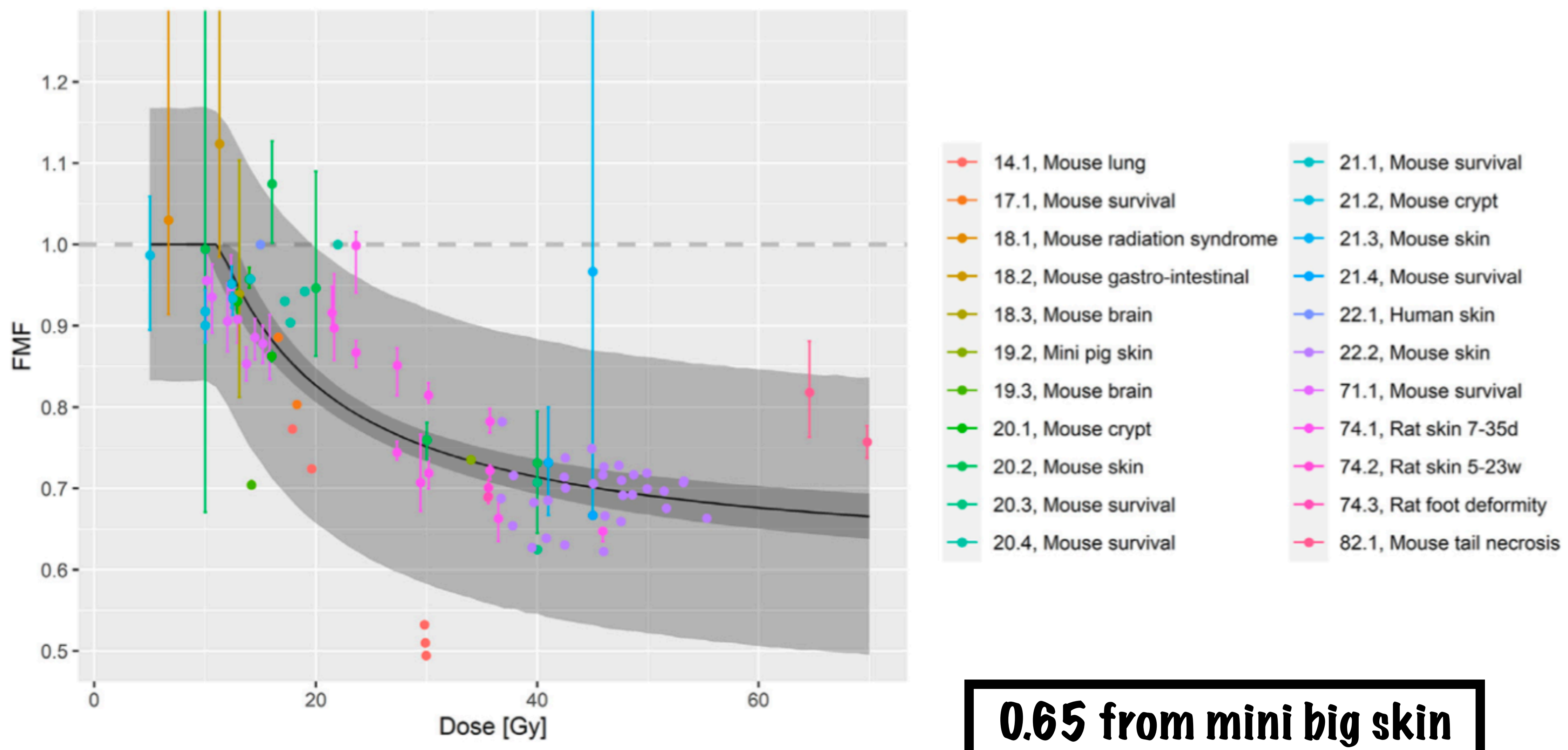


FLASH effect

FLASH irradiation provides a reduced radiation-induced toxicity in normal tissues with respect to conventional one. This effect can be parametrized by the FLASH Modifying Factor (FMF) model.

$$FMF = \frac{D_{CONV}}{D_{UHDR}}\Big|_{isoeffect}$$

FMF < 1 : greater normal tissue spearing of UHDR compared with CONV irradiation

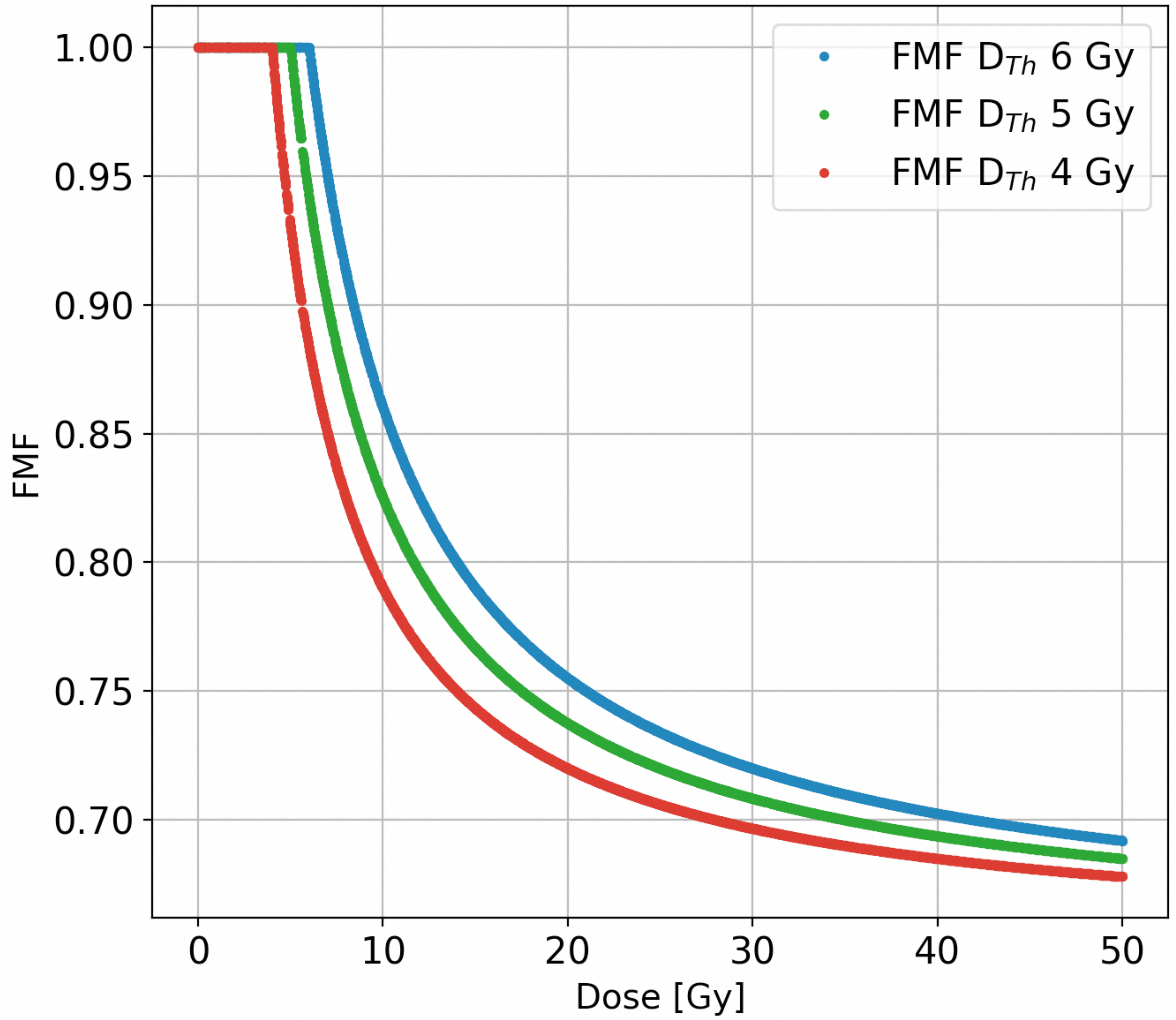


0.65 from mini big skin experiments

DOI: 10.1158/1078-0432.CCR-17-3375

$$FMF = \begin{cases} 1 & \text{for D} \leq D_{Th} \\ (1 - FMF^{min})\frac{D_{Th}}{D} + FMF^{min} & \text{for D} > D_{Th} \end{cases}$$

DOI: 10.1016/j.ijrobp.2022.05.038)



IOeRT-FLASH treatment

T = 30.8 s

Today the IOeRT presents an high probability of tumor under-dosage, due to the decision to avoid invasive surgery procedure. Therefore, the irradiated area is sometimes smaller than the the effective PTV.

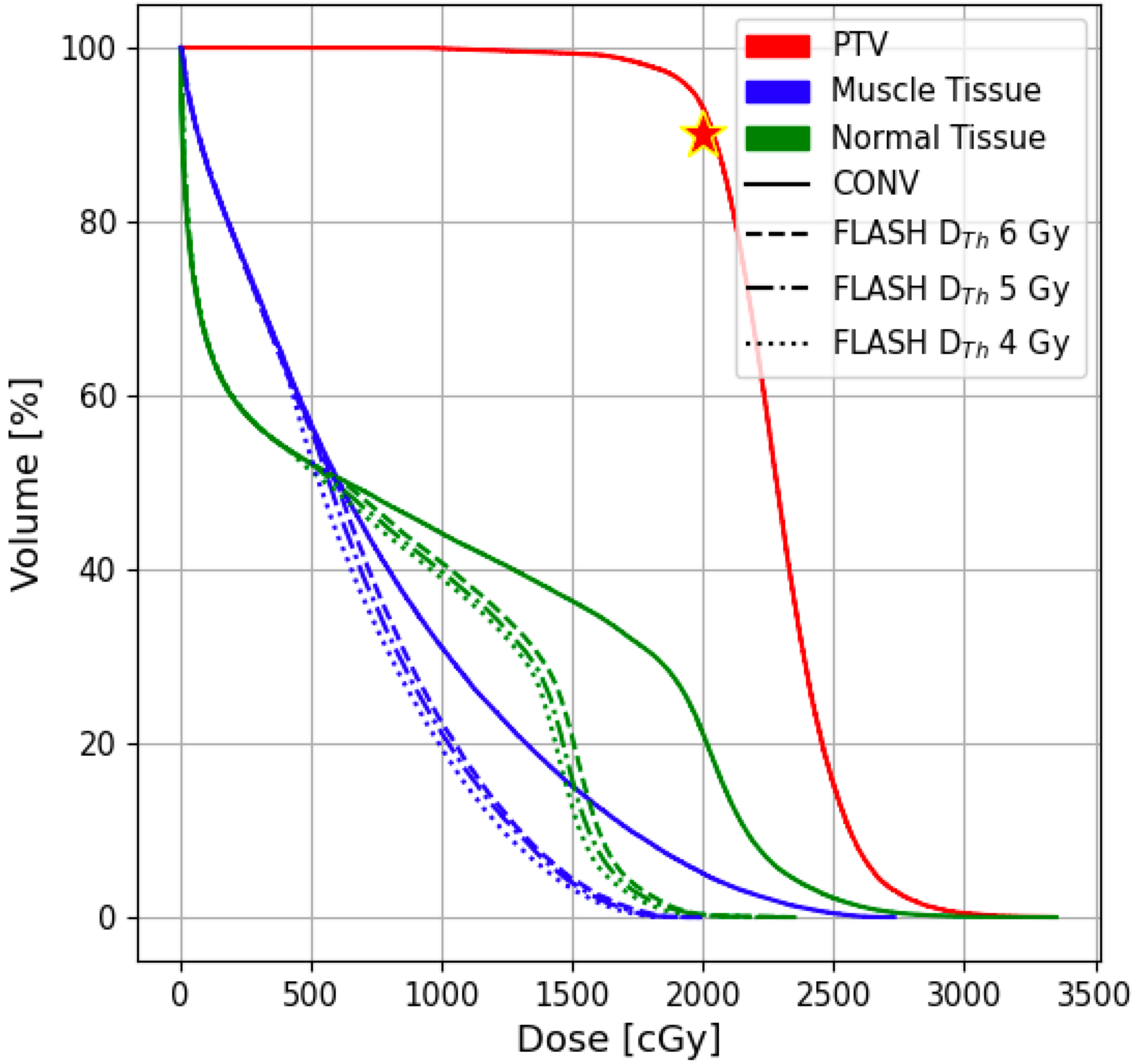
I studied the FLASH effect potential in the spearing of the superficial tissues to asses the possibility to combine **minimally invasive surgery** (small surgical breach) and a **larger electron beam irradiation** delivered at ultrahigh dose rates

This would allow to improve local tumor control (higher dose) without jeopardizing normal tissue tolerance.

An 8 MeV electrons circular beam with d=80 mm was simulated in **CONVENTIONAL** and **FLASH** regime with D_{Th} = 6, 5 and 4 Gy

Dose mean values

D [Gy]	PTV	Muscle tissue	Normal Tissue
CONV	22.4	7.5	9.5
FLASH D_{Th} = 6 Gy	22.4	6.3	7.3
FLASH D_{Th} = 5 Gy	22.4	6.2	7.1
FLASH D_{Th} = 4 Gy	22.4	5.9	6.9



Conclusion

- In this Ph.D. work I developed from scratch a fast **dose engine based on GPU-MC, crucial for the future IOeRT TPS.** It is capable of reproducing dose distributions in homogeneous and heterogeneous phantoms with an **accuracy** at the level of state-of-art full MCs and with an **impressive gain in processing time**.

- I developed an optimization tool using **FRED** which is able to produce **robust and accurate dose distributions** in about **10 seconds** that can be used for **online** treatment optimization.

- Next steps:
  - Explore a realistic case of **breast cancer** evaluating the potential of FLASH irradiation, and also **prostate** and **pancreatic applications.**
  - **Integration** of the developed treatment planning and optimization tool with **the S.I.T. software** that handles the US imaging acquisition and the graphical interface.
  - **TPS validation** against experimental data

TO DO

Thanks for your attention!

SPARE SLIDES

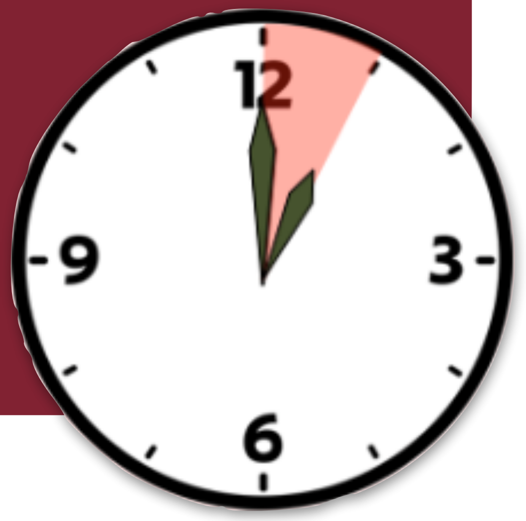
Introduction

From full to fast Monte Carlo

ANALYTICAL ALGORITHMS

- Reasonable times for calculating the TPS
- Simplified representation of the tissue: the geometry of the patient is represented in an equivalent volume of water, neglecting the real atomic composition of the tissues.
- **Not high accuracy**

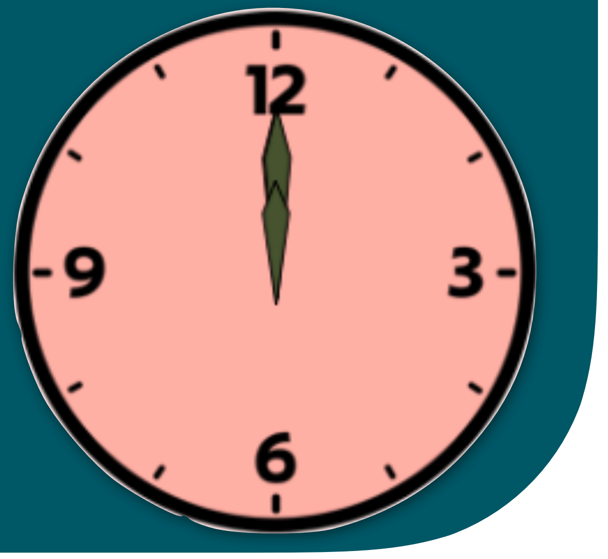
Ex. Proton TPS ~ 1 h/core



MONTE CARLO

- Realistic assessment of body composition
- Extracts accuracy in the description of the transport and the interaction of the particles with matter
- **Long times for calculating the TPS**

Ex. Proton TPS ~ days/core



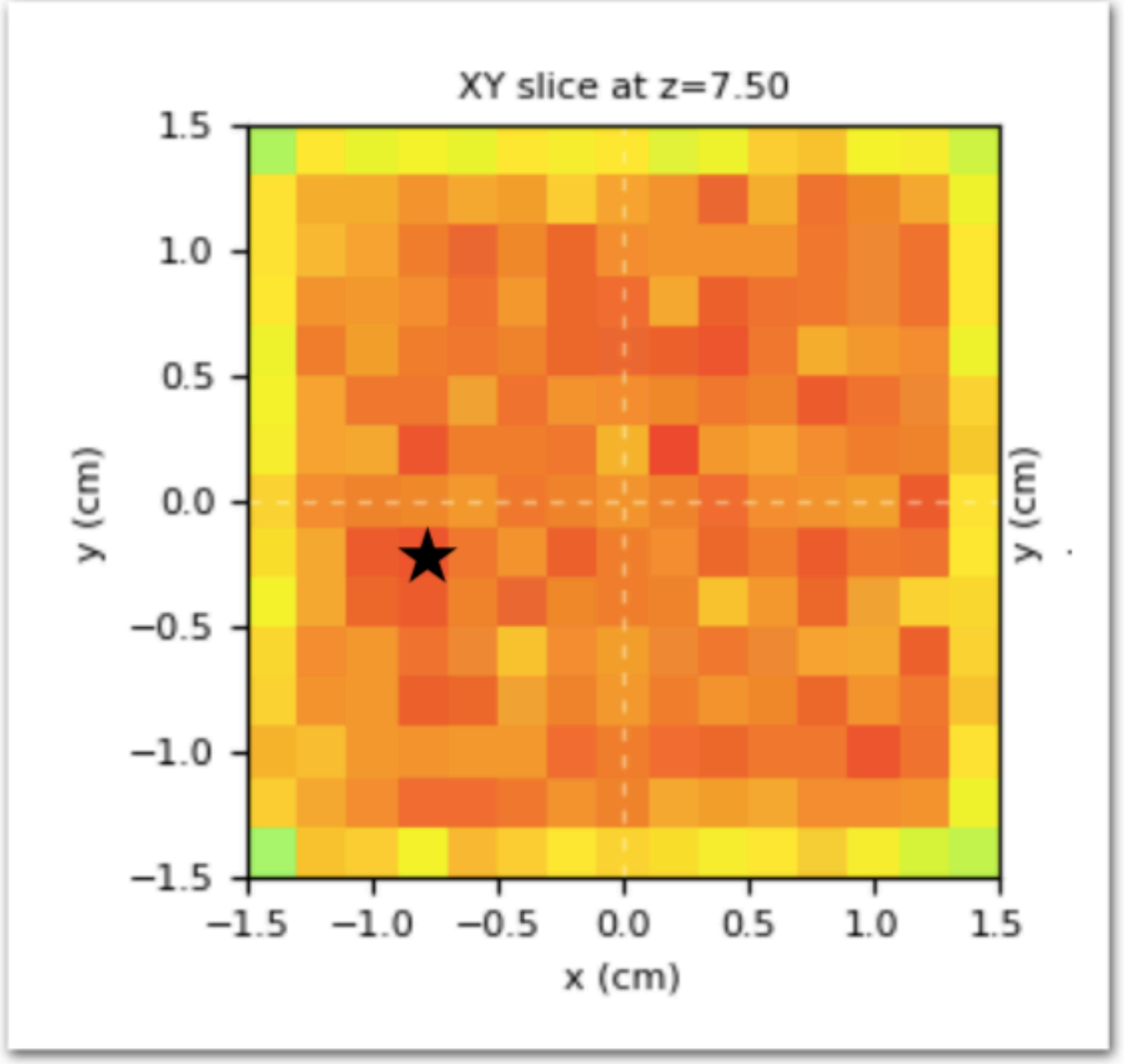
FAST MONTE CARLO

- High accuracy in the description of the transport and of the interaction of particles with matter
- Realistic assessment of body composition
- **Very fast calculation of TPS**

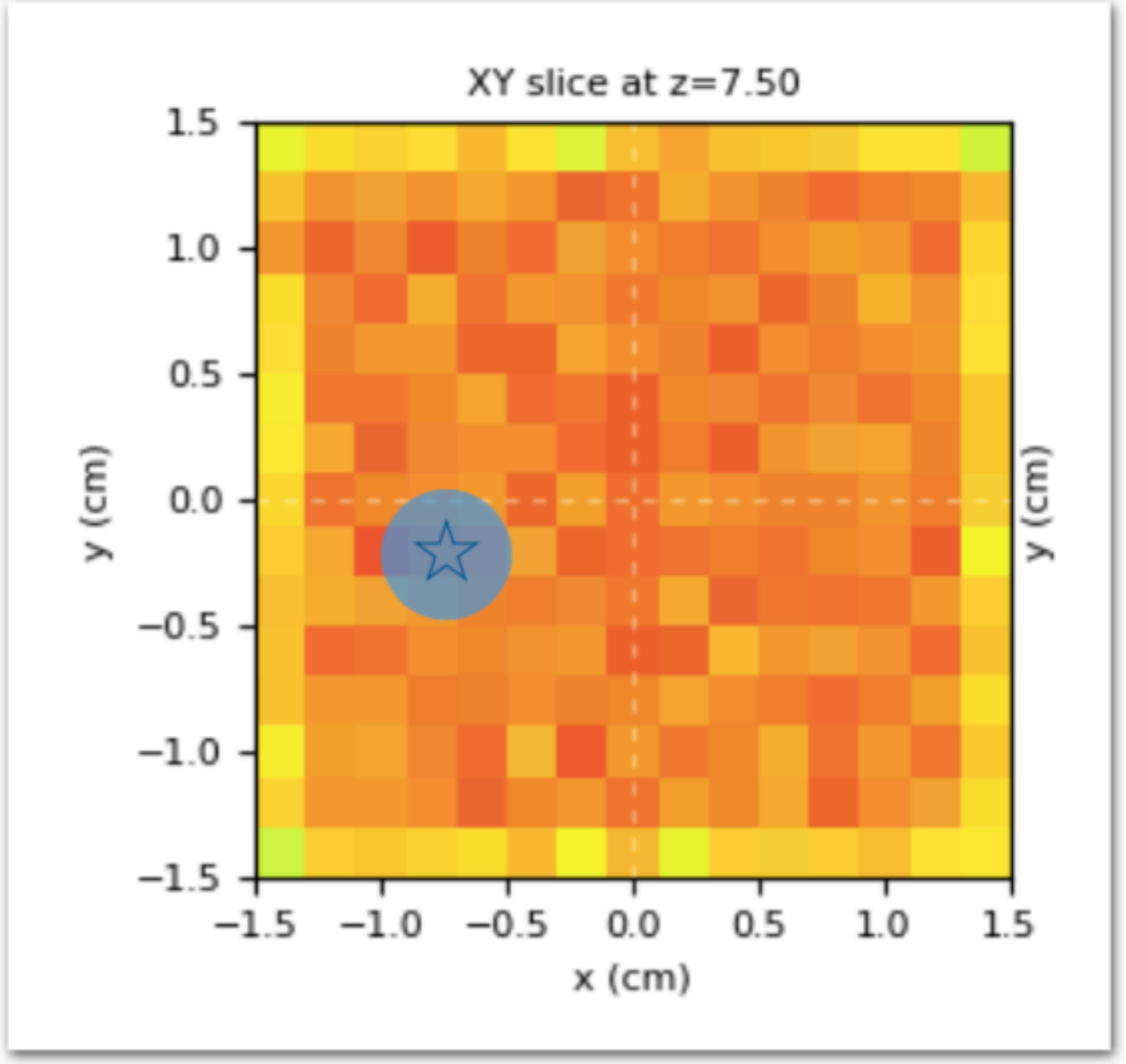
Ex. Proton TPS ~ minutes

Gamma index analysis

Reference Map



Evaluation Map



γ-index 2mm/3%

$$\Gamma(\vec{r_e},\vec{r_r}) = \sqrt{\frac{|\vec{r_e}-\vec{r_r}|^2}{\Delta r^2} + \frac{[D_e(\vec{r_e})-D_r(\vec{r_r})]^2}{\Delta D^2}}$$

D= dose (D_r of the reference map, D_e of the evaluation map)

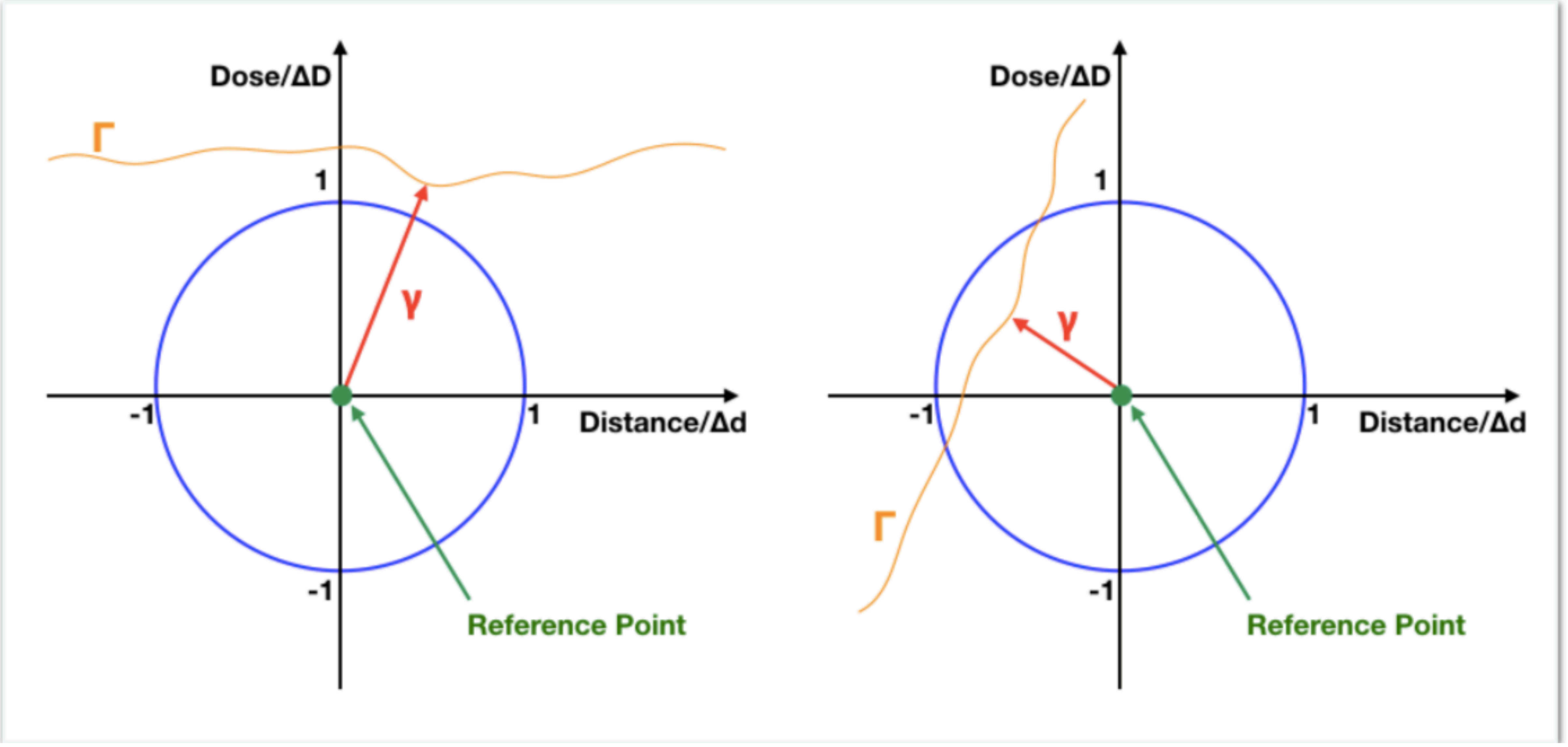
r = position of the evaluated point (r_r of the reference map, r_e of the evaluation map)

$$\gamma(\vec{r_r}) = \min\{\Gamma(\vec{r_e},\vec{r_r})\}\forall\{\vec{r_e}\}$$

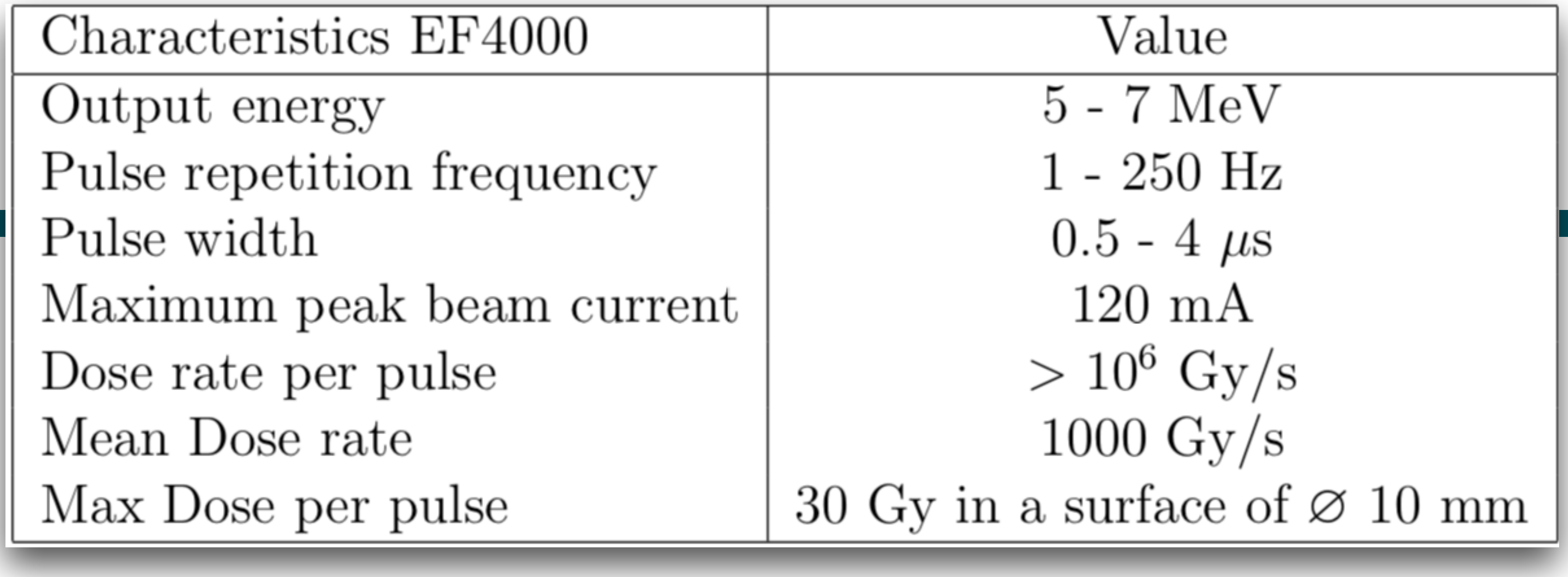
$\gamma \leq 1$ = test passed

$\gamma > 1$ = test NOT passed

pass rate ≥ 92%
clinical acceptance



ElectronFlash4000

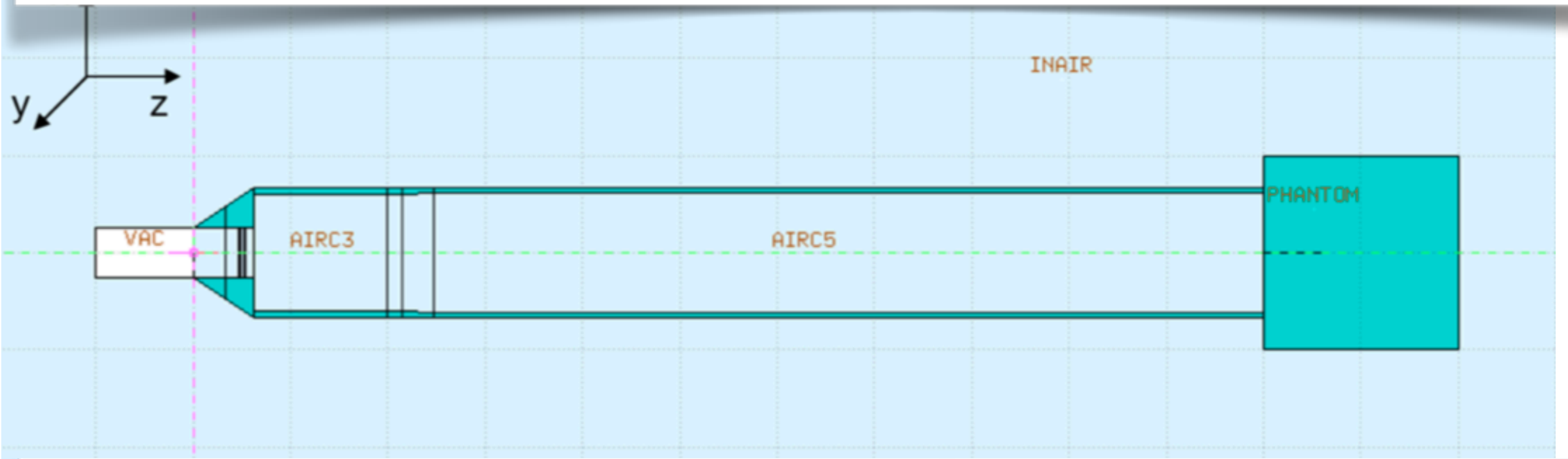


Characteristics EF4000	Value
Output energy	5 - 7 MeV
Pulse repetition frequency	1 - 250 Hz
Pulse width	0.5 - 4 μs
Maximum peak beam current	120 mA
Dose rate per pulse	$> 10^6$ Gy/s
Mean Dose rate	1000 Gy/s
Max Dose per pulse	30 Gy in a surface of ∅ 10 mm

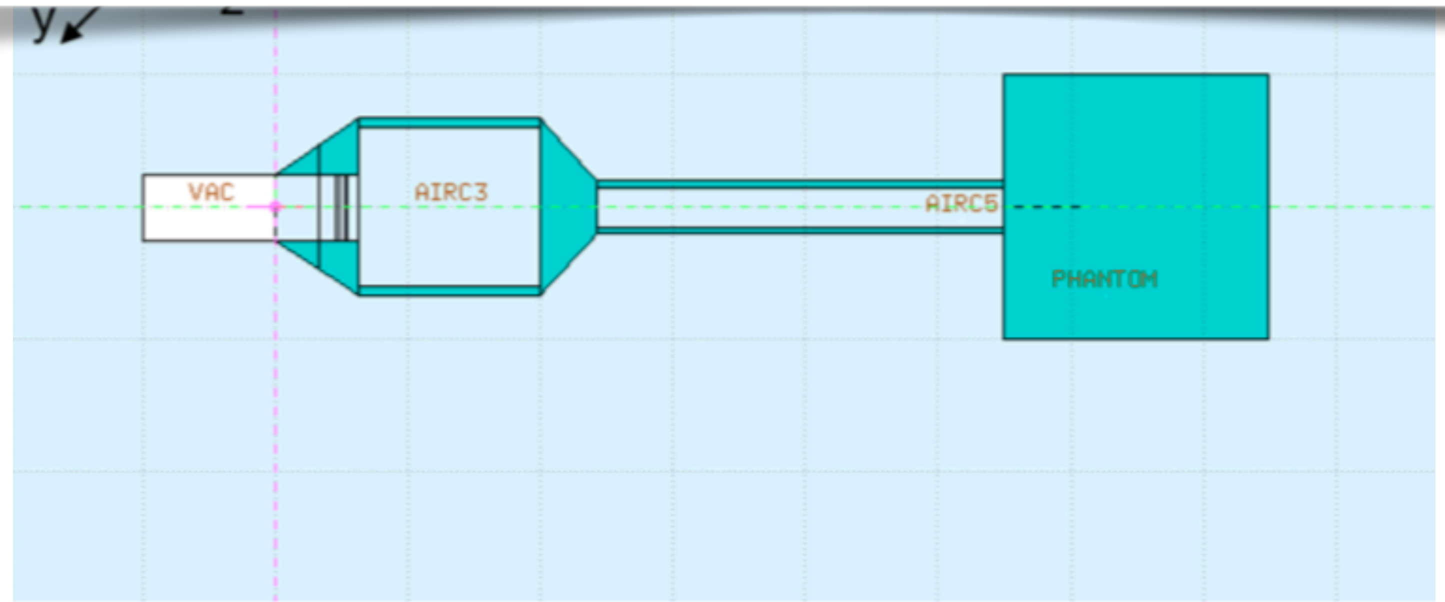
The EF4000 was commissioned by the Curie Institute and it was installed there in August 2020.

I performed the **dosimetric characterization** of the electrons beam produced by the linac by comparing the **experimental data** of the PDD and off-axis profile (Gafchromic EBT-XD films) with the ones obtained with **FLUKA**.

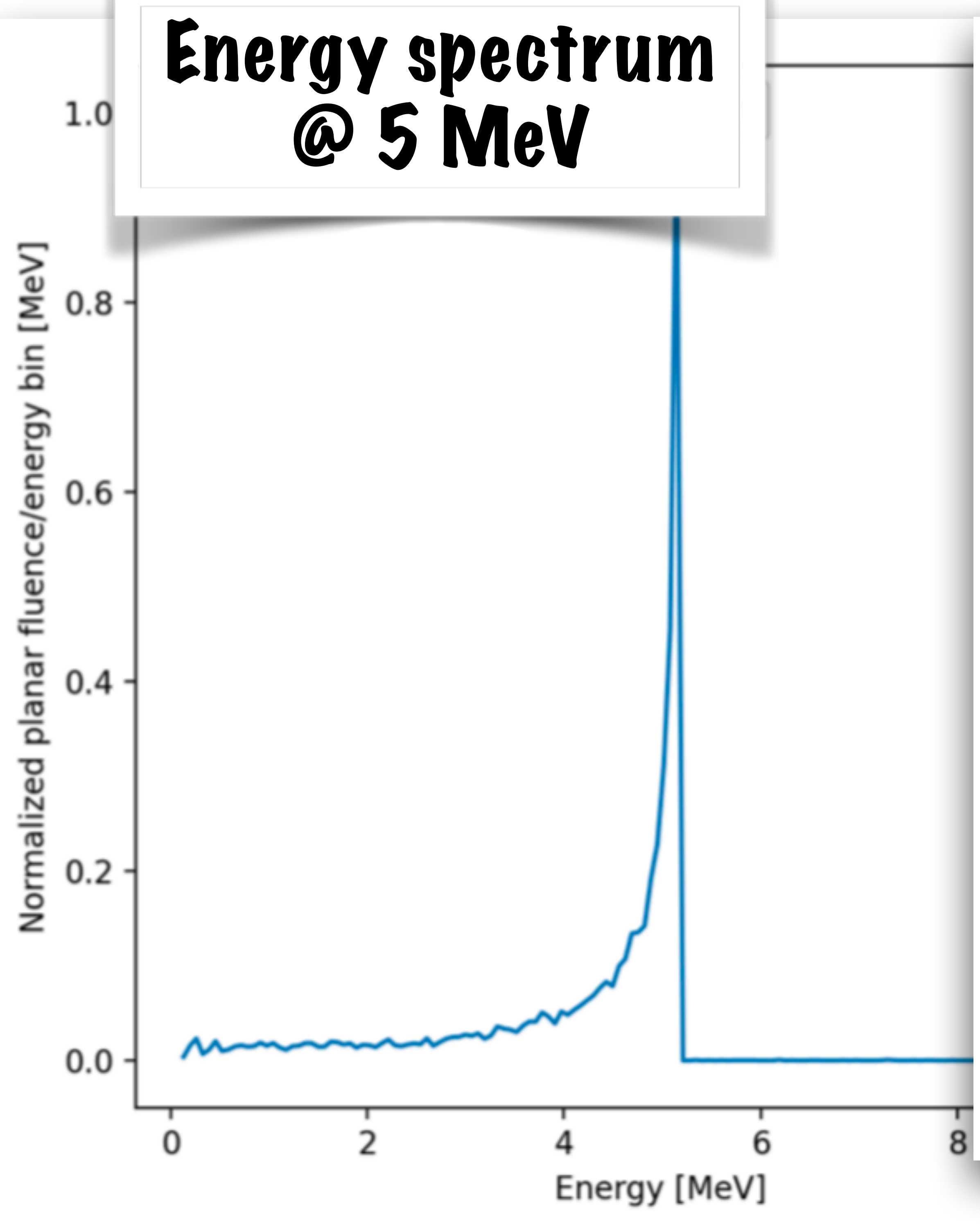
Applicator with d=120 mm and an SSD =1096 mm



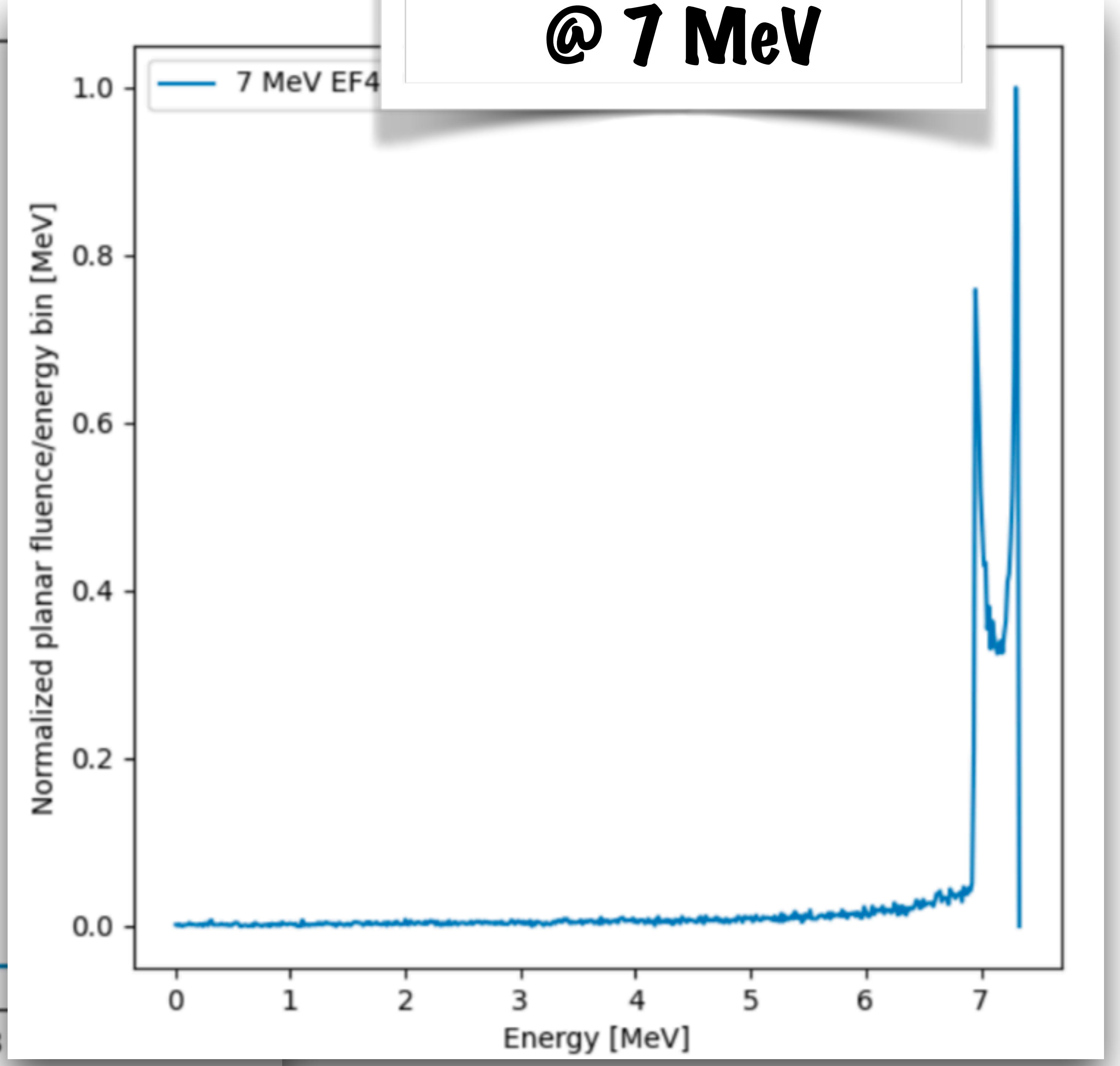
Applicator with d=30 mm and an SSD =549 mm



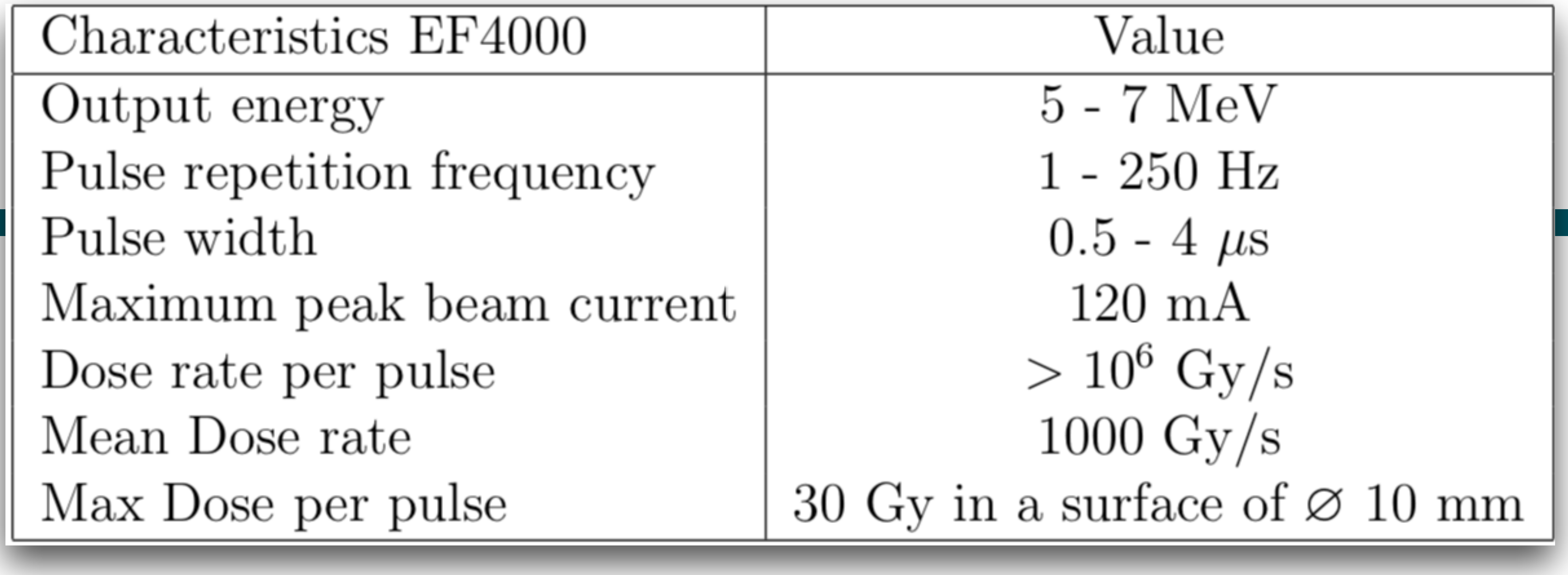
Energy spectrum @ 5 MeV



Energy spectrum @ 7 MeV

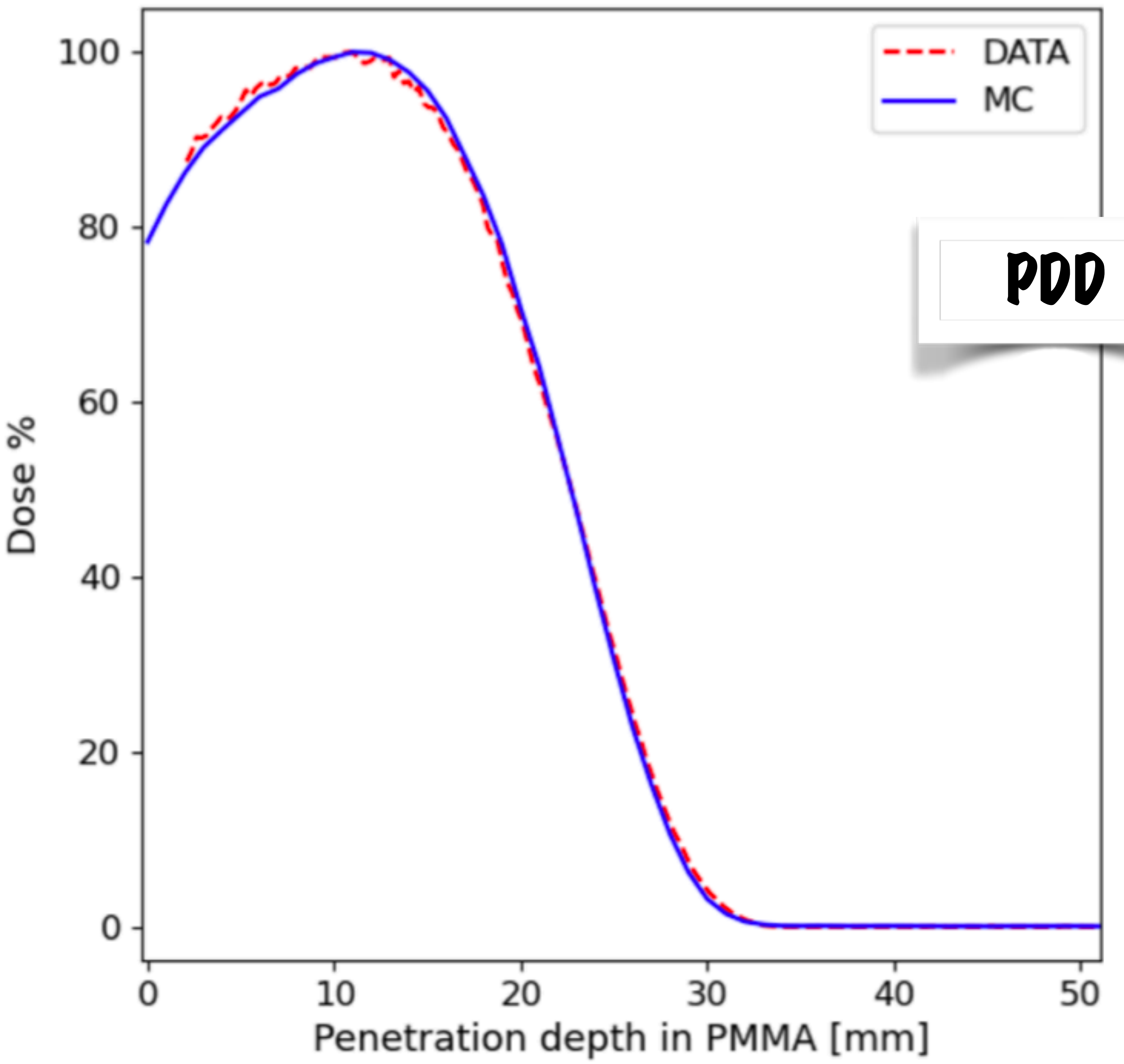


ElectronFlash4000

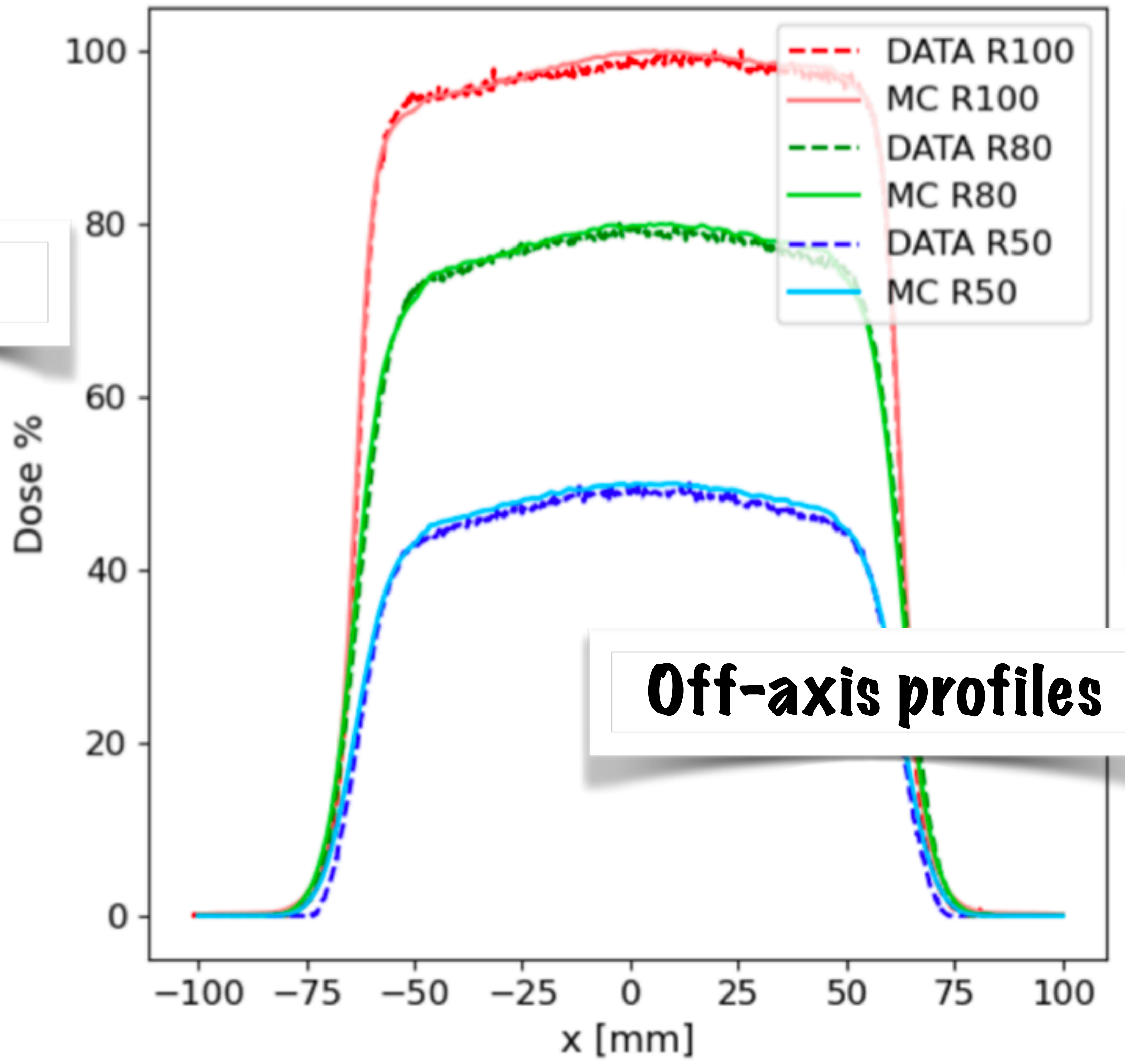


Characteristics EF4000	Value
Output energy	5 - 7 MeV
Pulse repetition frequency	1 - 250 Hz
Pulse width	0.5 - 4 μs
Maximum peak beam current	120 mA
Dose rate per pulse	$> 10^6$ Gy/s
Mean Dose rate	1000 Gy/s
Max Dose per pulse	30 Gy in a surface of ⌀ 10 mm

Example of 5 MeV collimated with the applicator with d=30 mm

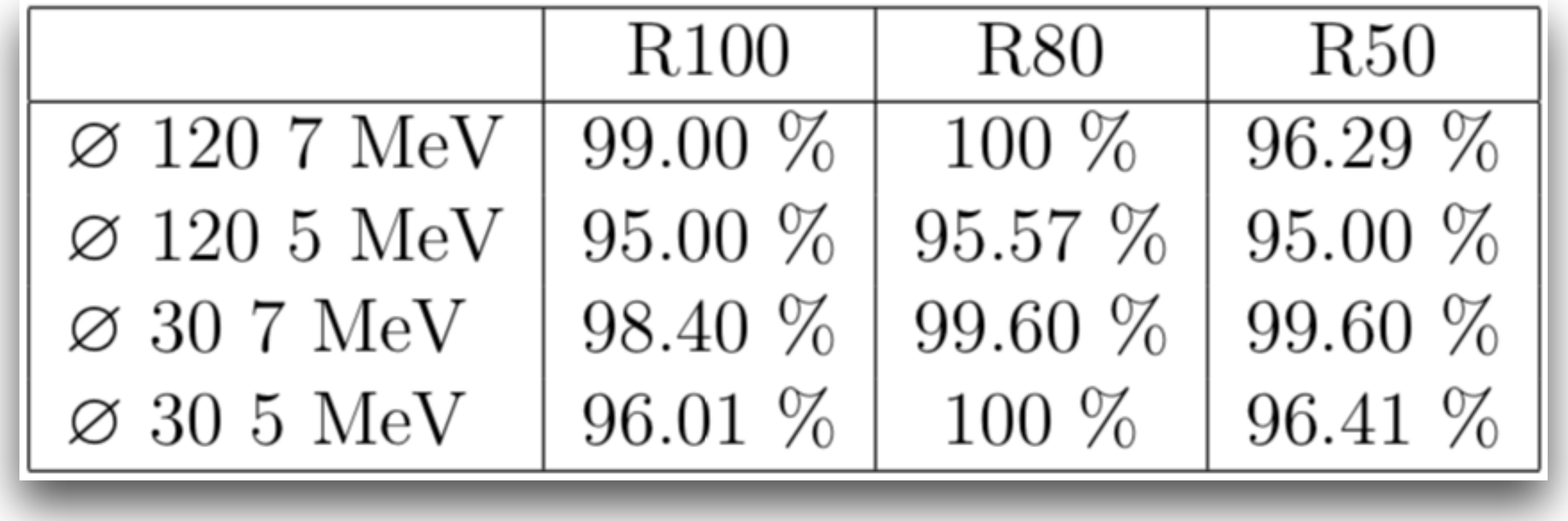


PDD



Off-axis profiles

Gamma-index 3mm/3% pass rate:



	R100	R80	R50
⌀ 120 7 MeV	99.00 %	100 %	96.29 %
⌀ 120 5 MeV	95.00 %	95.57 %	95.00 %
⌀ 30 7 MeV	98.40 %	99.60 %	99.60 %
⌀ 30 5 MeV	96.01 %	100 %	96.41 %

Conferences and Articles

Conferences

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2. **A feasibility study of IORT Treatment Planning system using a GPU based fast Monte Carlo**, plenary talk, 4th European Congress of Medical Physics, 17^{th}-20^{th} August 2022, Dublin, Ireland.
3. **A feasibility study of IORT-FLASH using a GPU-based fast Monte Carlo (FRED)**, plenary talk, International Conference on Monte Carlo Techniques for Medical Applications, 11^{th}-13^{th} April 2022, Antwerp, Belgium.
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5. **Prostate cancer FLASH therapy treatments with electrons of high energy: a feasibility study**, parallel talk, PTCOG 59 Annual Conference of the Particle Therapy Co-operative Group (ONLINE) , 4^{th}-7^{th} June 2021, Rome, Italy.

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   Paper presented at the 2019 IEEE Nuclear Science Symposium and Medical Imaging Conference,
2. G. Traini et al, *Performance of the ToF detectors in the foot experiment*
   Nuovo Cimento Della Societa Italiana Di Fisica C, 43(1).
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   Journal of Instrumentation, 15(11)
4. M. Toppi et al, *The MONDO Tracker: Characterisation and Study of Secondary Ultrafast Neutrons Production in Carbon Ion Radiotherapy*
5. M. Fischetti et al, *Inter-fractional monitoring of ^{12}C ions treatments: results from a clinical trial at the CNAO facility*
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6. G. Galati et al., *Charge identification of fragments with the emulsion spectrometer of the FOOT experiment*
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7. E. Fiorina et al, *Detection of interfractional morphological changes in proton therapy: A simulation and in vivo study with the INSIDE in-beam PET*
   Frontiers in Physics, 8
8. G. Battistoni E. et al, *Measuring the Impact of Nuclear Interaction in Particle Therapy and in Radio Protection in Space: the FOOT Experiment*
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9. M. Toppi et al, *PAPRICA: The pair production imaging Chamber—Proof of principle*
   Frontiers in Physics, 9.
10. L. Faillace et al., *Compact S-band Linear Accelerator System for FLASH Radiotherapy*
    Physical Review Accelerators and Beams (2021)
11. M. Toppi et al., *Monitoring Carbon Ion Beams Transverse Position Detecting Charged Secondary Fragments: Results From Patient Treatment Performed at CNAO*
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12. A.C. Kraan et al, *Charge identification of nuclear fragments with the FOOT time-of-flight system*
    Nuclear Instruments and Methods in Physics Research, Section A: Accelerators, Spectrometers, De-
13. G. Calvi et al., *PAPRICA: The PAir PRoduction Imaging ChAmber*
    Nuovo Cimento della Società Italiana di Fisica C, 2021, 44(4-5),147
14. S. Colombi et al., *Enhancing the understanding of fragmentation processes in hadrontherapy and radioprotection in space with the FOOT experiment*
    Physica Scripta, 2021, 96(11), 11401
15. Sarti A. et al., *Deep Seated Tumour Treatments With Electrons of High Energy Delivered at FLASH Rates: The Example of Prostate Cancer*
    Frontiers in Oncology, 2021, 11, 777852.
16. Kraan, A.C. et al., *Localization of anatomical changes in patients during proton therapy with in-beam PET monitoring: A voxel-based morphometry approach exploiting Monte Carlo simulations*
    Medical Physics, 2022, 49(1), pp. 23–40
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    Radiotherapy and Oncology, 2022, 12, 929949,.
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FLASH

FLASH effect

Several pre-clinical studies recently claimed that the toxicity in healthy tissues related to tumour treatments can be significantly reduced (from 80% down to 60%), while keeping the same efficacy in cancer killing, if the dose rate is radically increased (> 40 **Gy/s**, or even more) with respect to conventional treatments (~**0.01 Gy/s**).

Tumor response, analogous to the one obtained with conventional RT
Reduced radiation-induced toxicities in the healthy tissues

Combination of different parameters:

Mean dose rate > 40 Gy/s (total dose/total treatment time)

Total treatment time ~ 100 ms

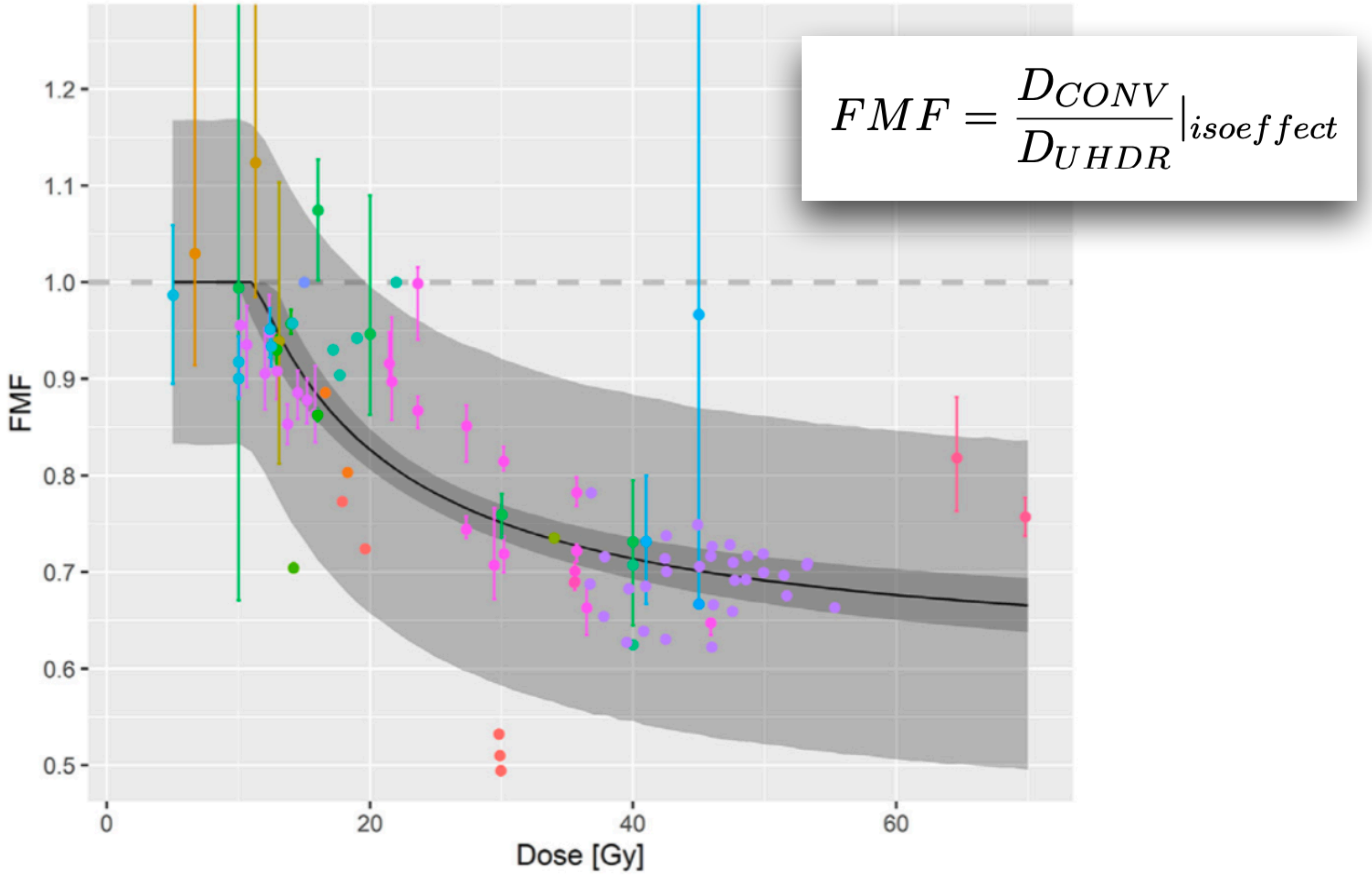
Pulse width 0.1-4 μs

Dose per pulse > 1-2 Gy

Instantaneous Dose Rate > 10^6 Gy/s (Dose / pulse width)

Dose threshold ~ 4,5 Gy

ecc..



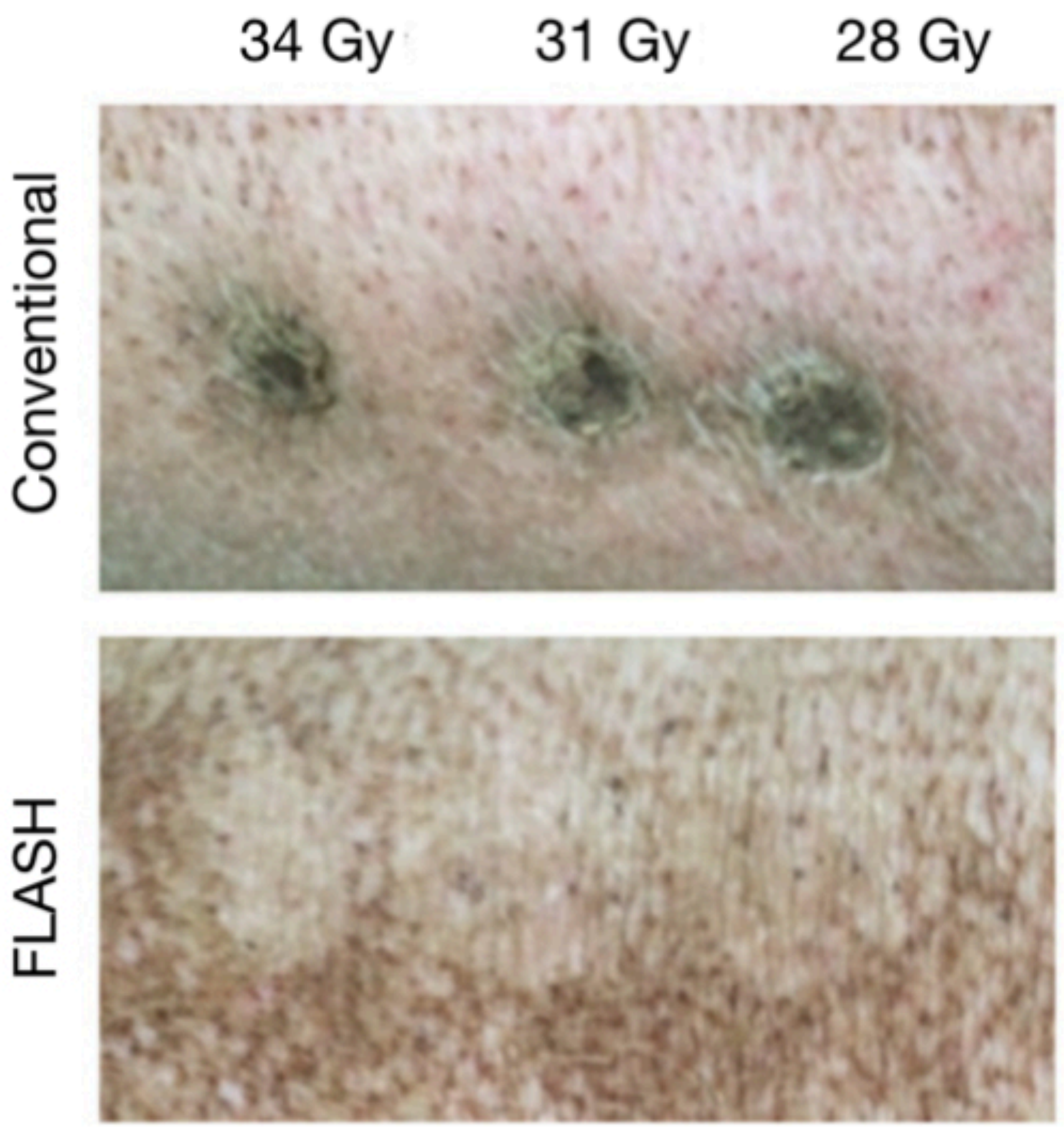
$$FMF = \frac{D_{CONV}}{D_{UHDR}}\Big|_{isoeffect}$$

The mechanism responsible for reduced tissue toxicity following FLASH radiotherapy is yet to be clarified

?Modification of the immune response ?

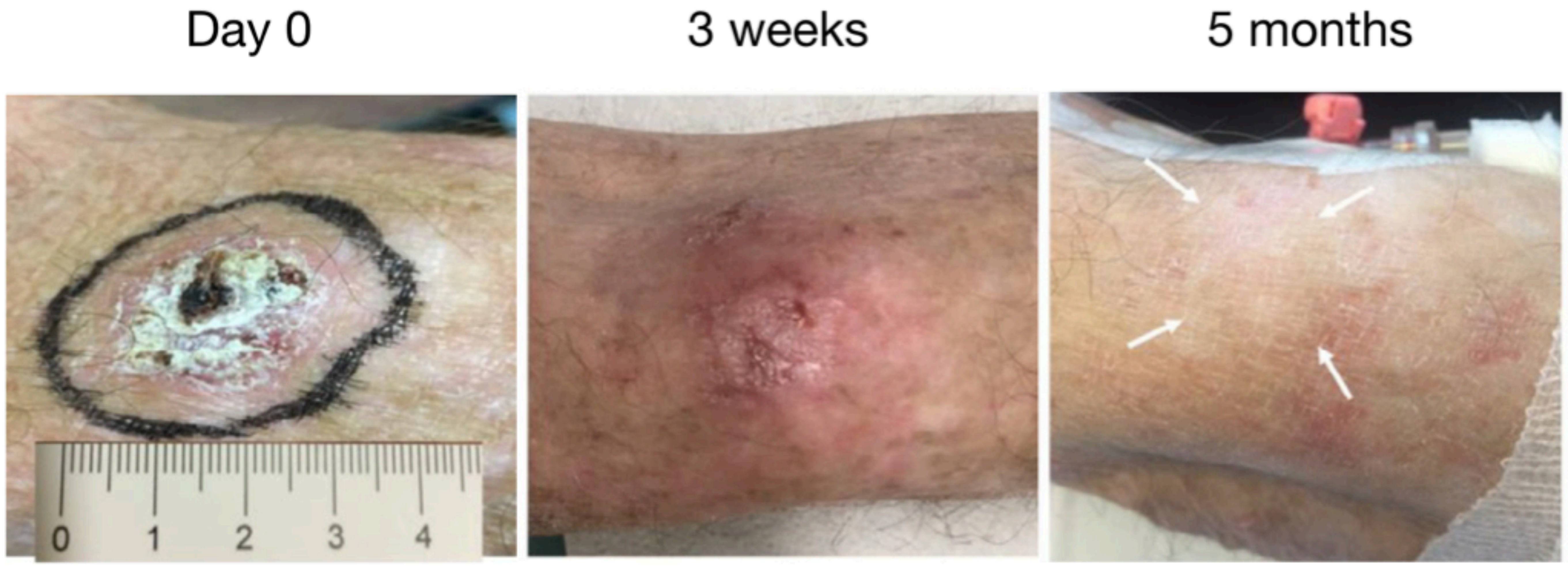
FLASH effect

Test on mini-pig skin



No skin reaction in FLASH-RT

First FLASH therapy patient



The tumor was irradiated with 6 MeV electrons. The dose releases was 15 Gy with a mean dose rate equal to 166 Gy/s

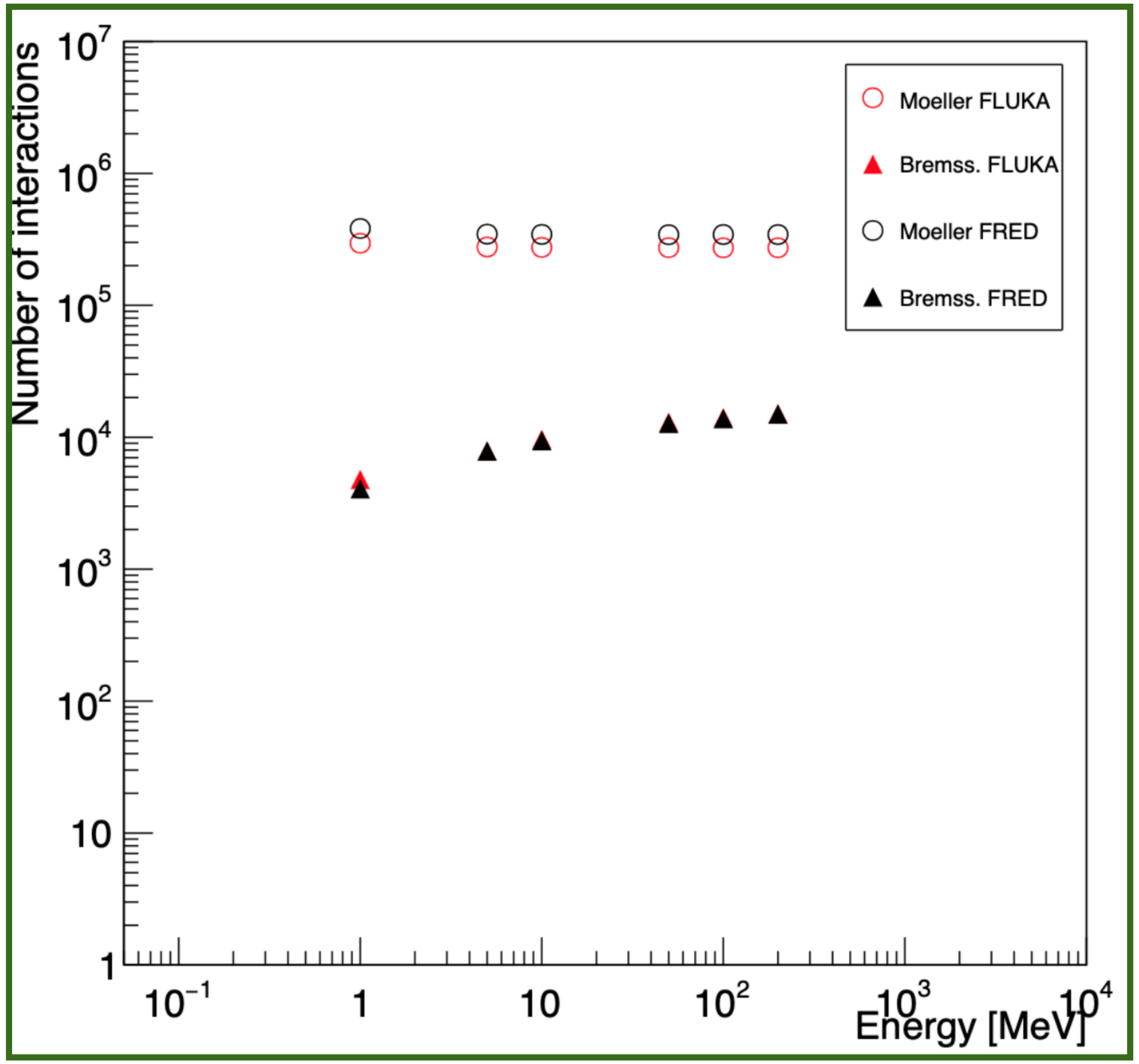
Complete tumor response at 36 days

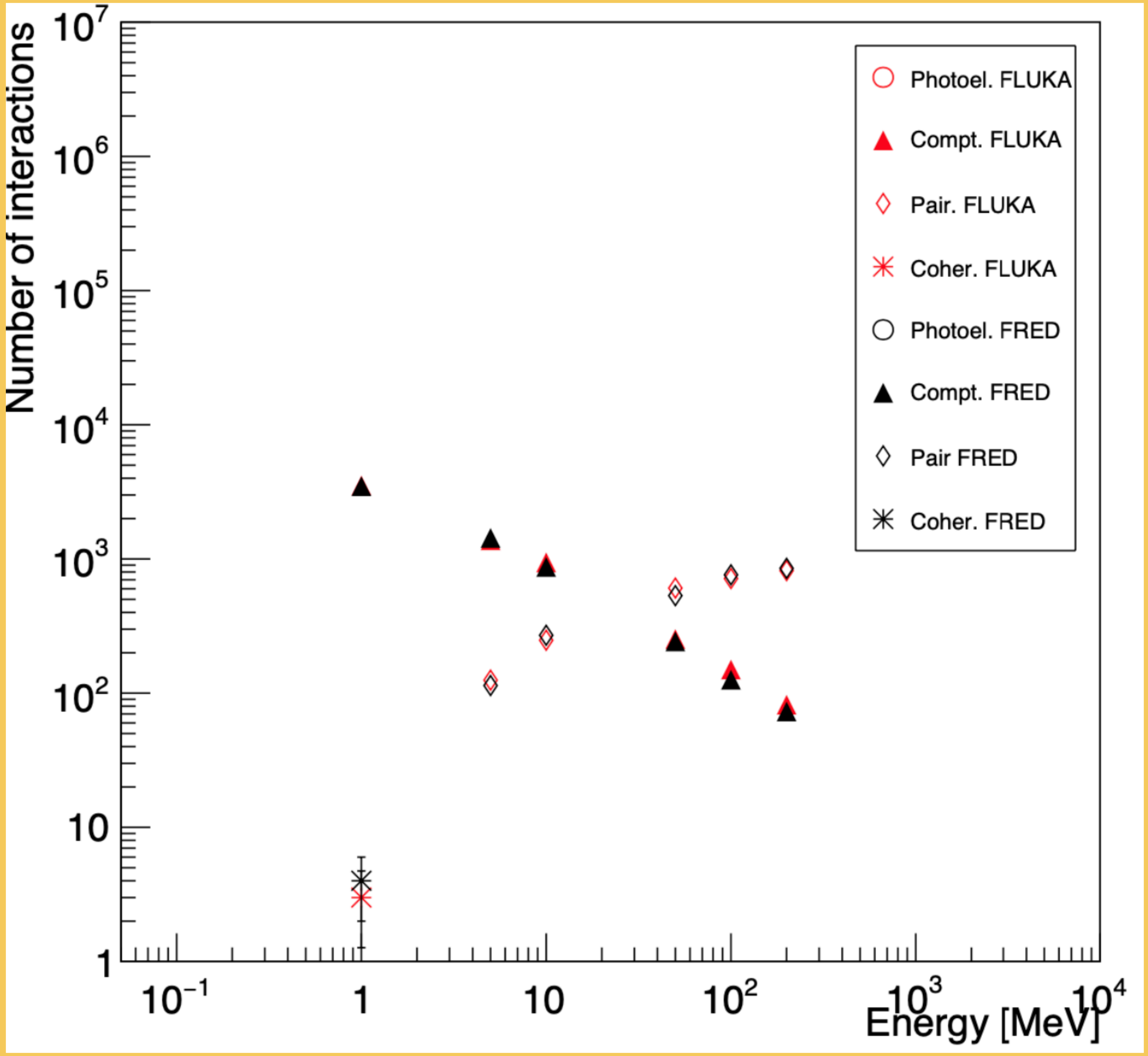
FRED

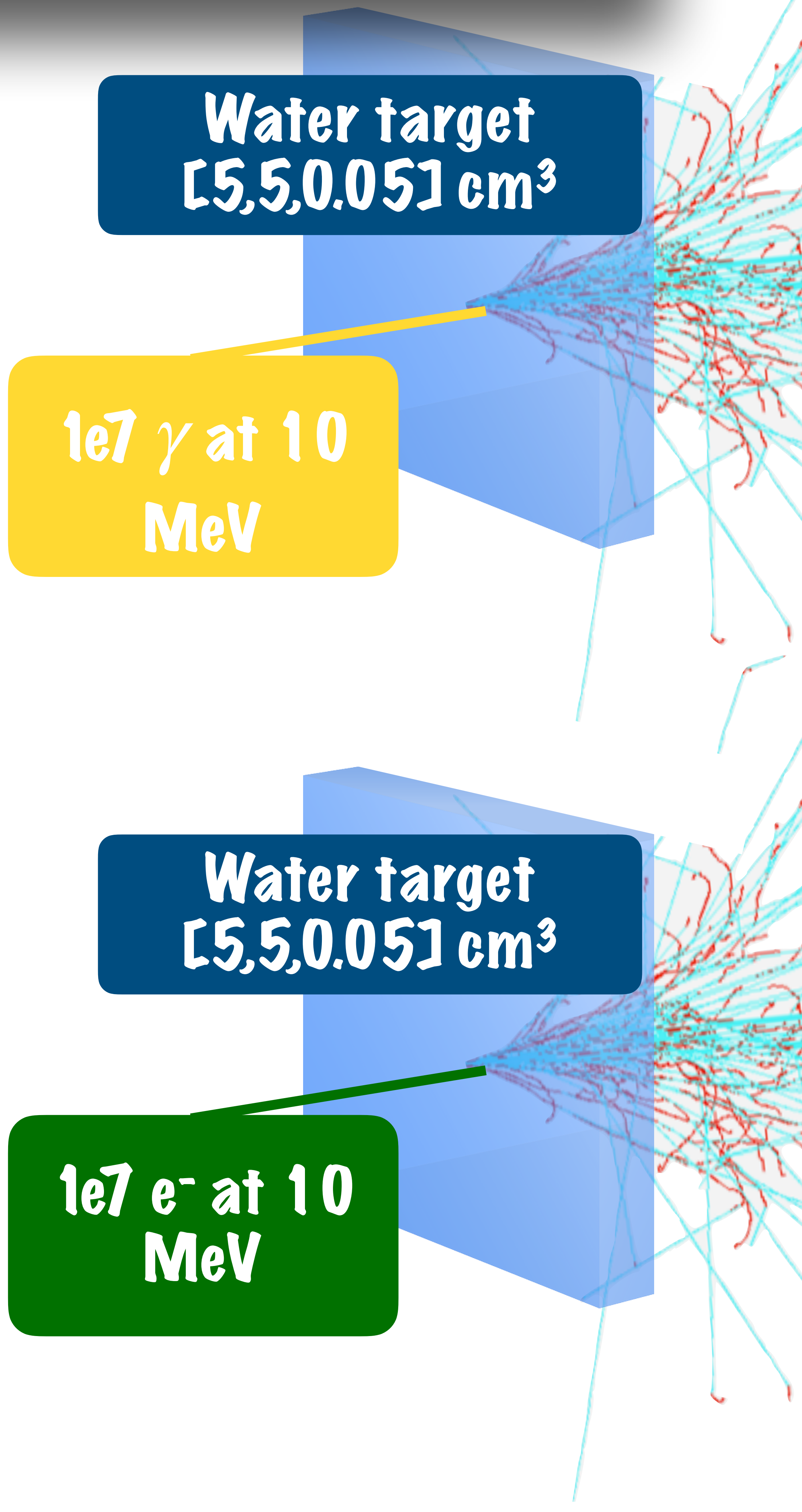
Thin target benchmark

FRED-em cross-sections

I have checked against **FLUKA** the **cross-section models** by counting the number of times a given process took place during the all simulation run.







Thin target benchmark

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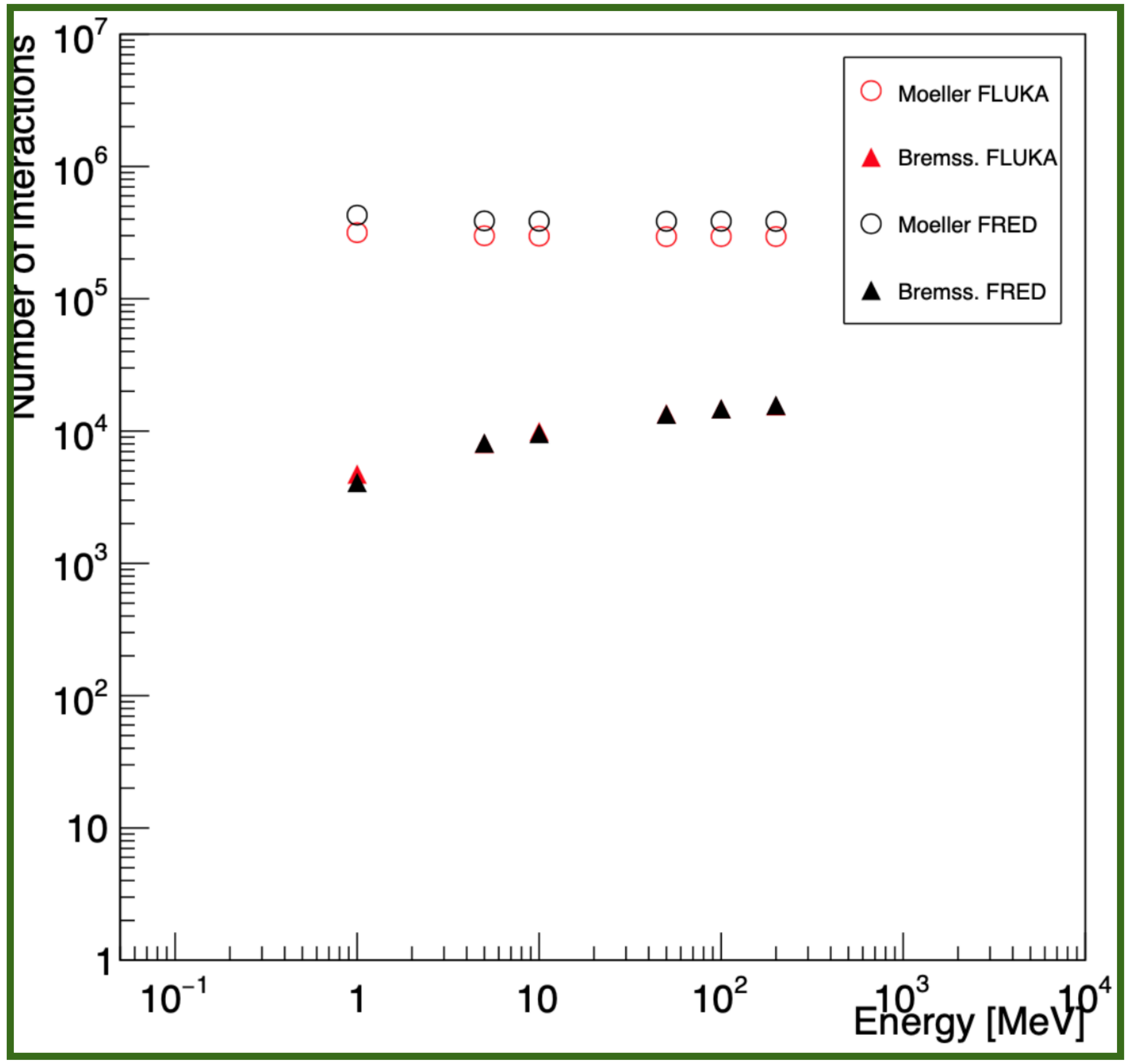
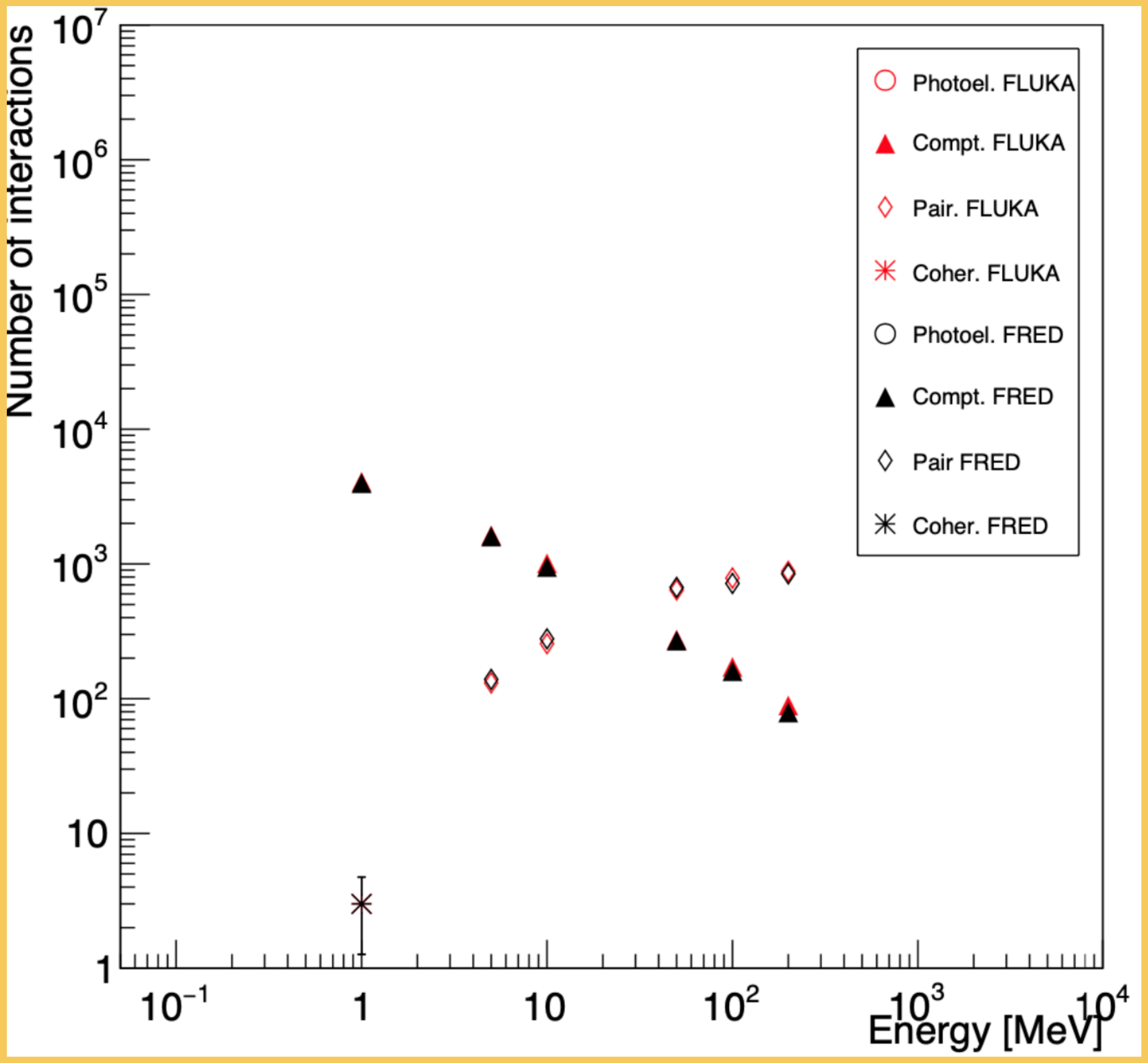
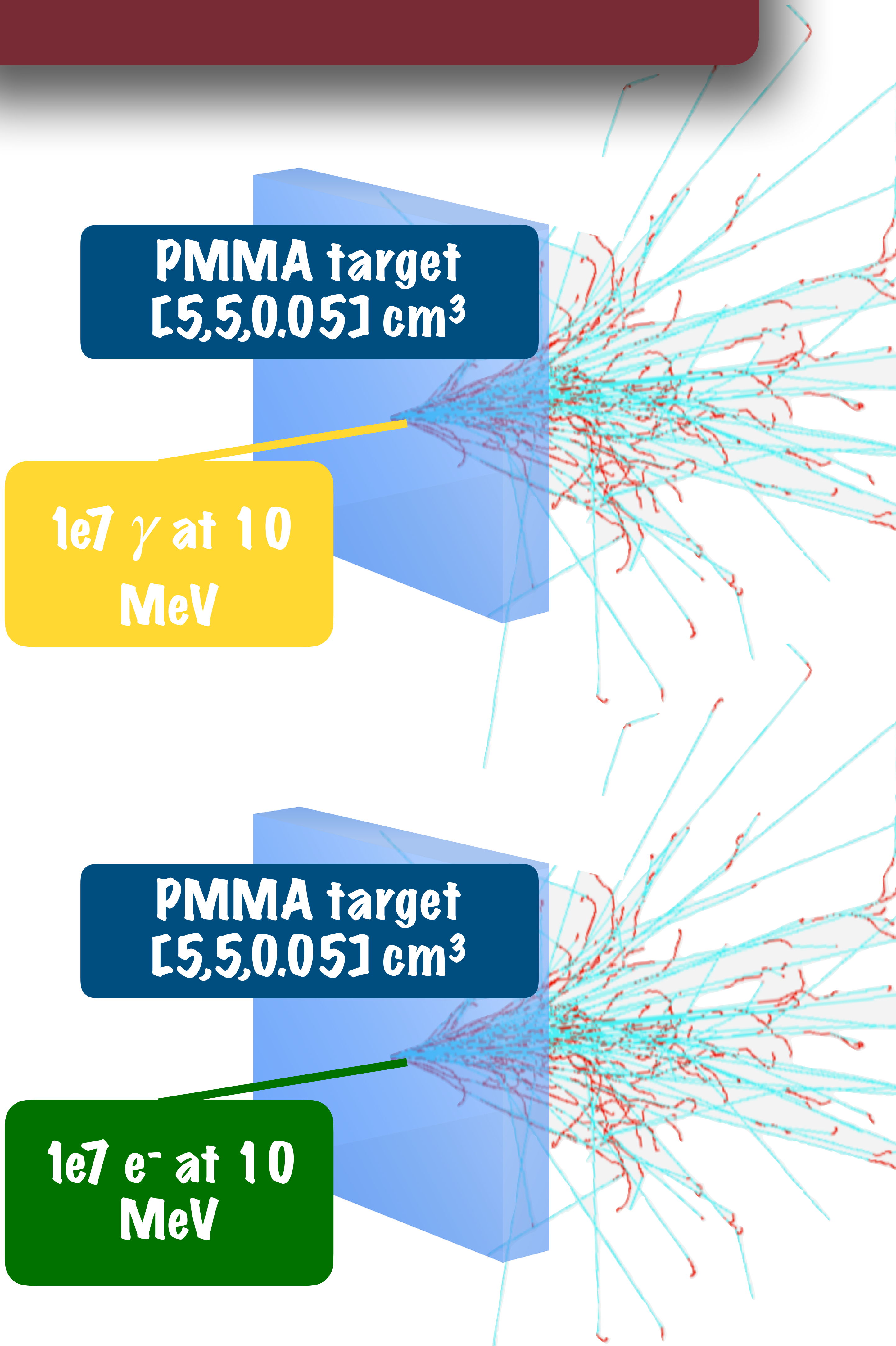
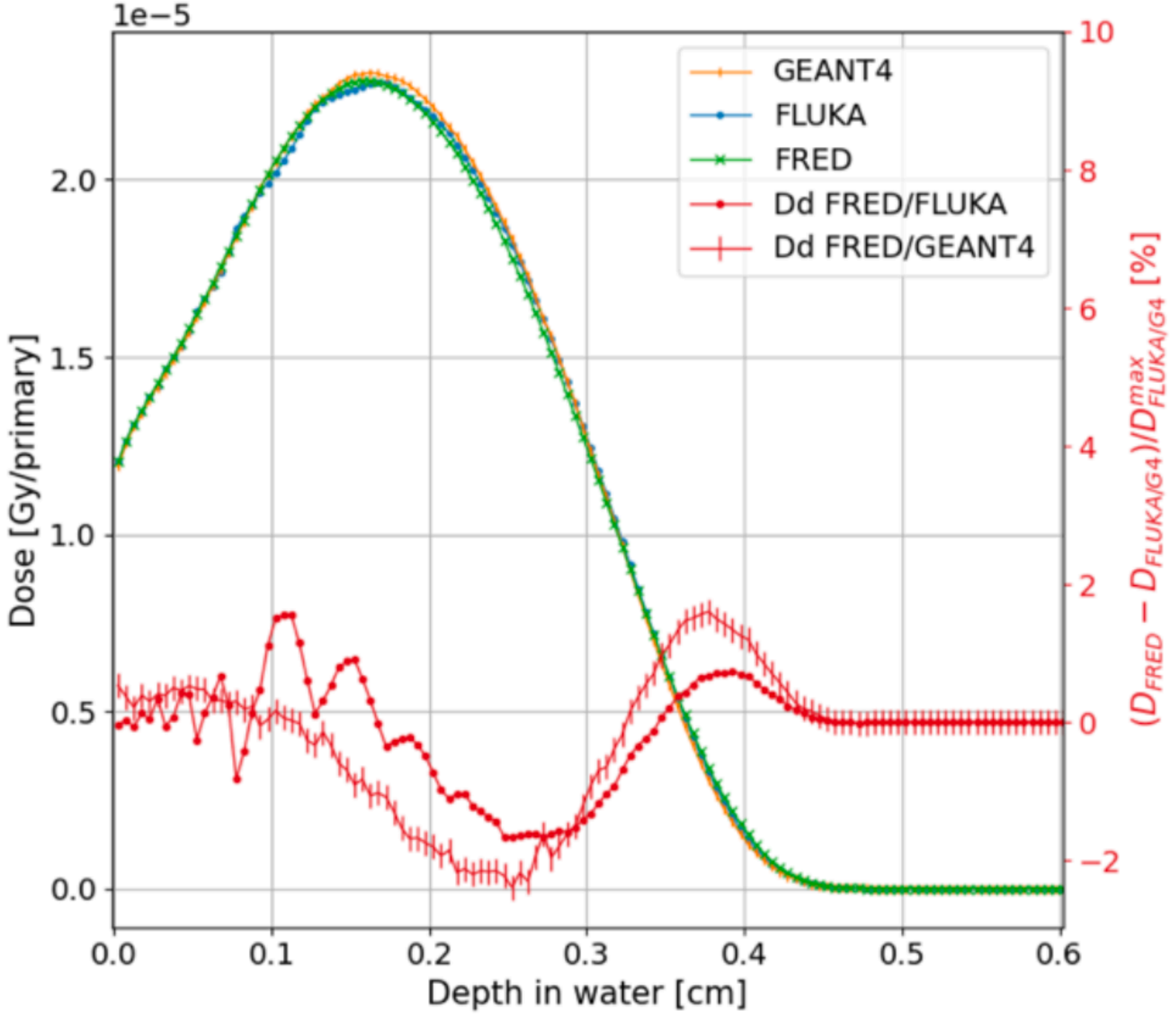
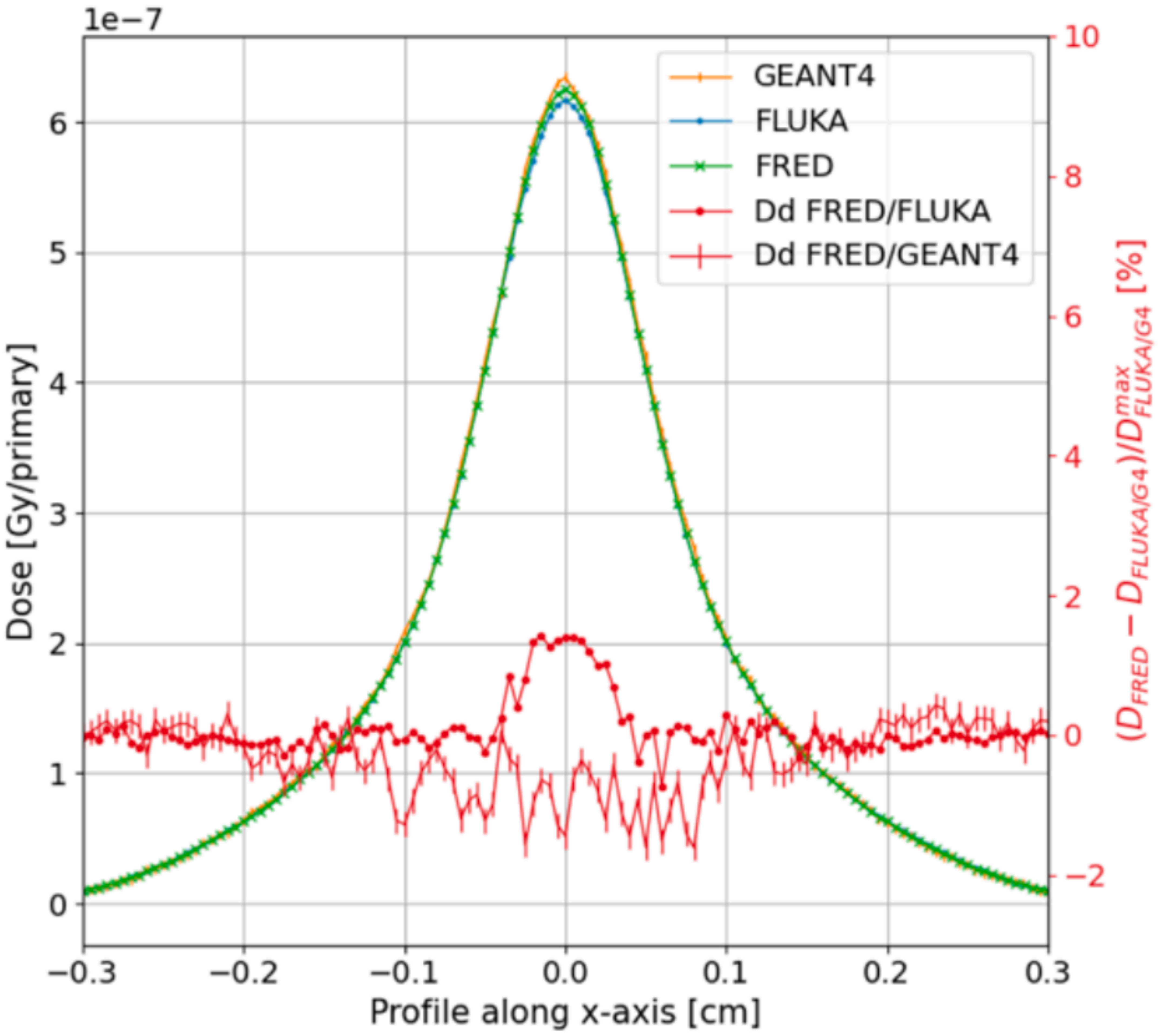




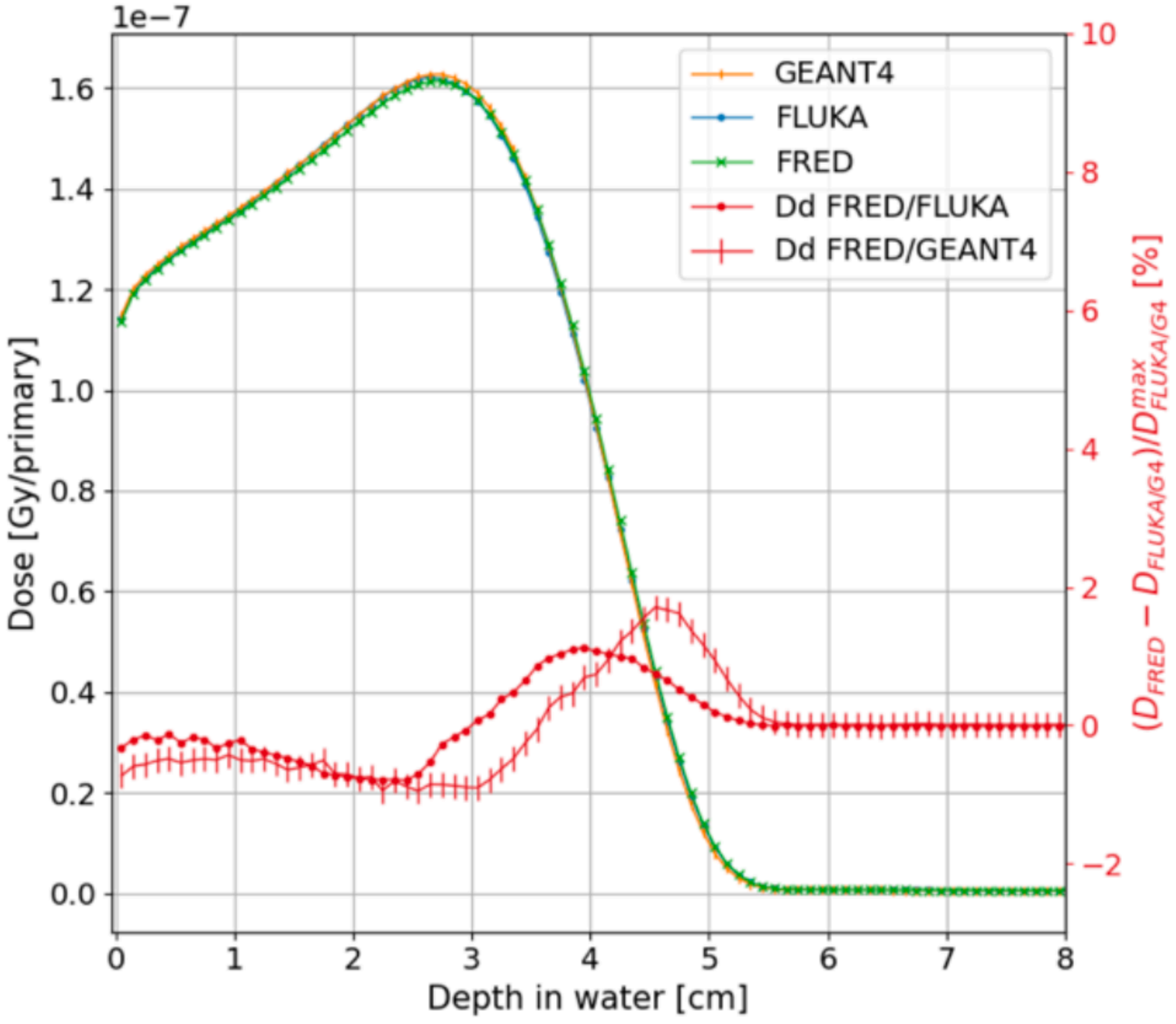


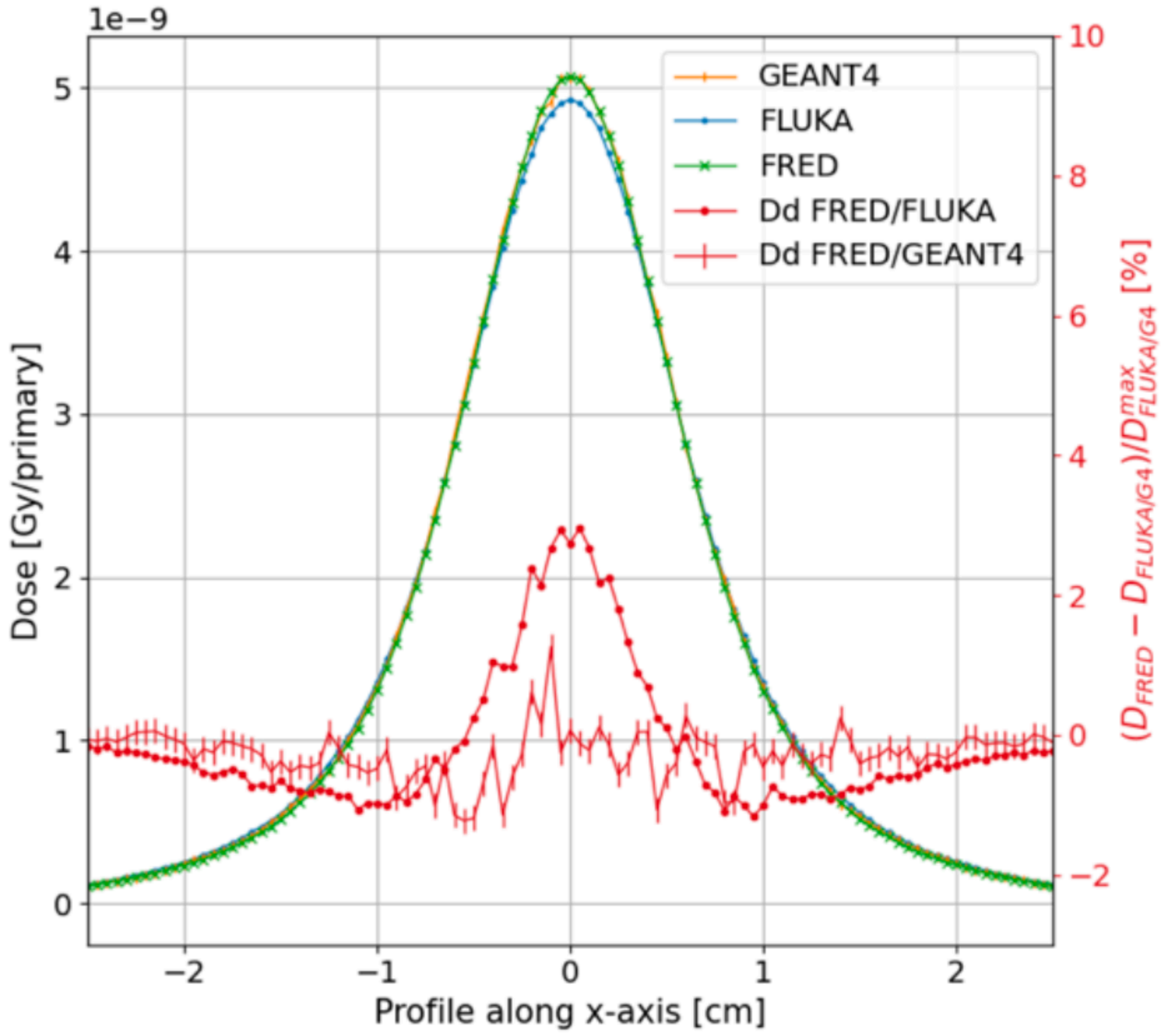
FRED-em: e^- @ 1 MeV in water



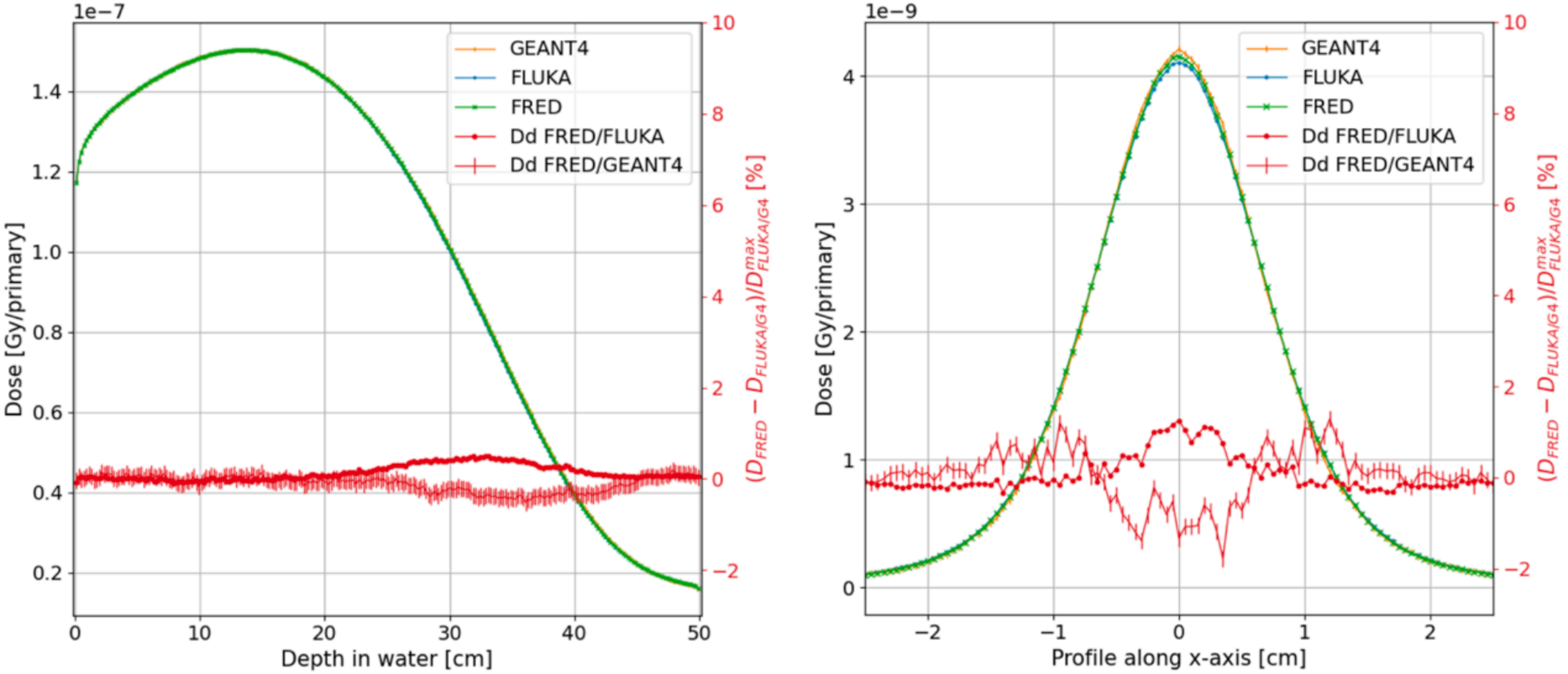


FRED-em: e⁻ @ 10 MeV in water

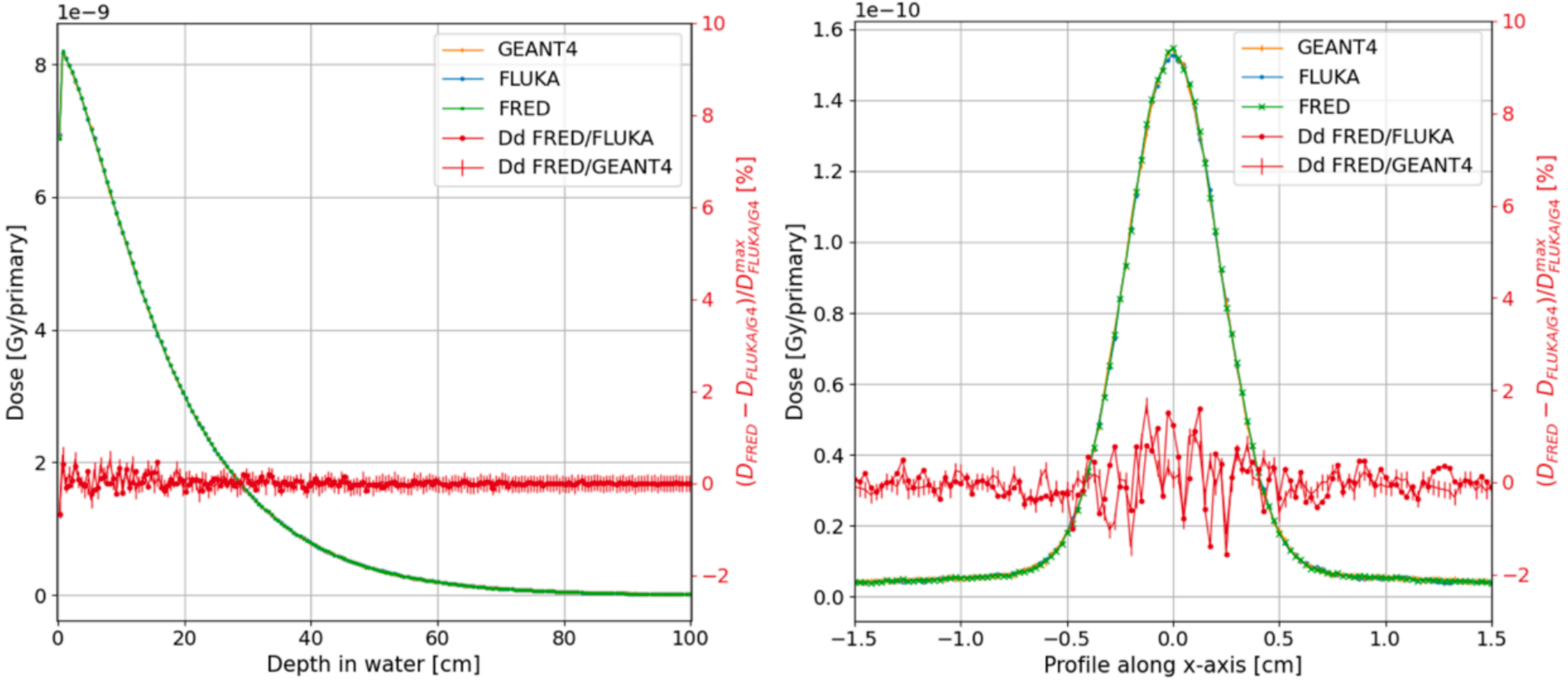




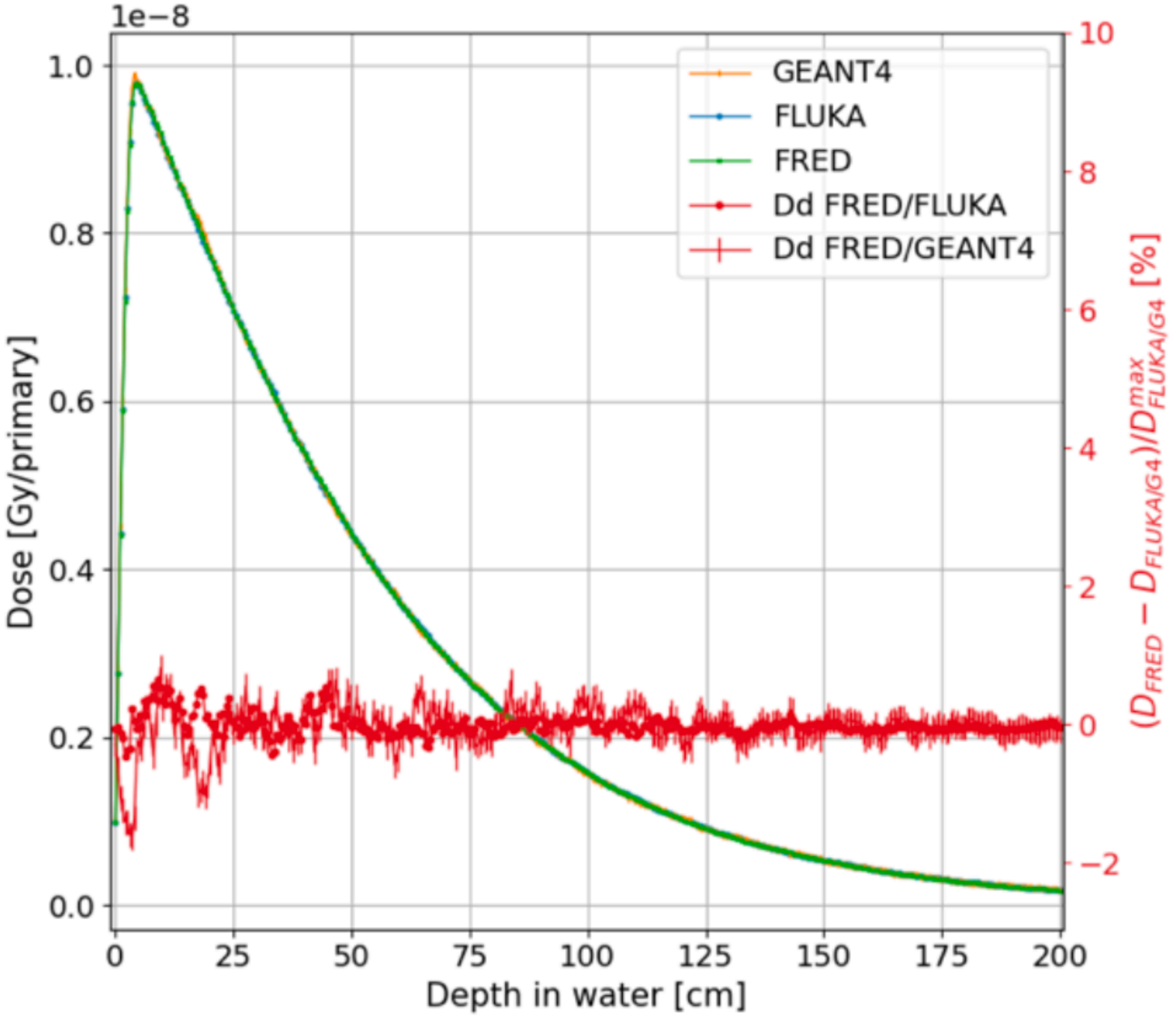
FRED-em: e$^-$ @ 100 MeV in water

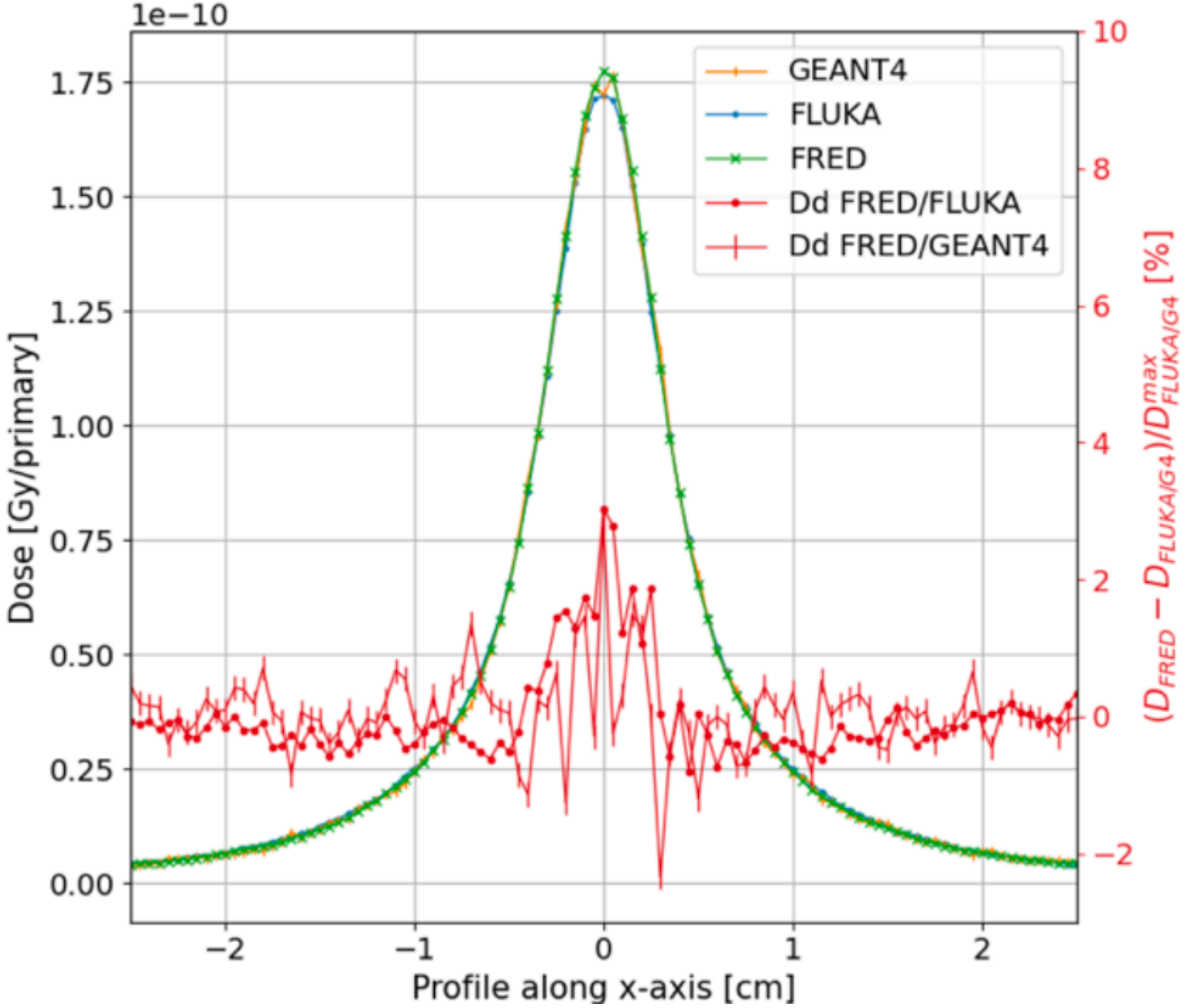


FRED-em: ph @ 1 MeV in water

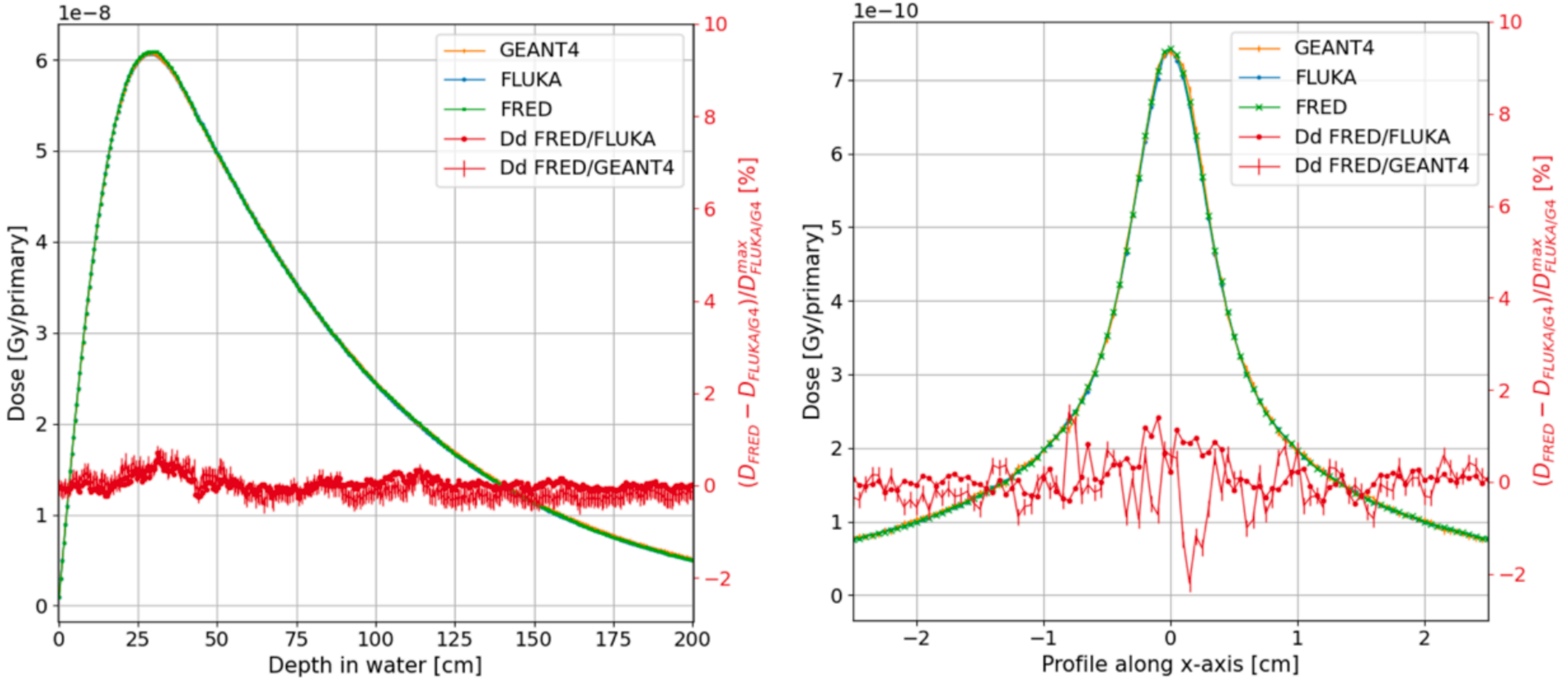


FRED-em: ph @ 10 MeV in water

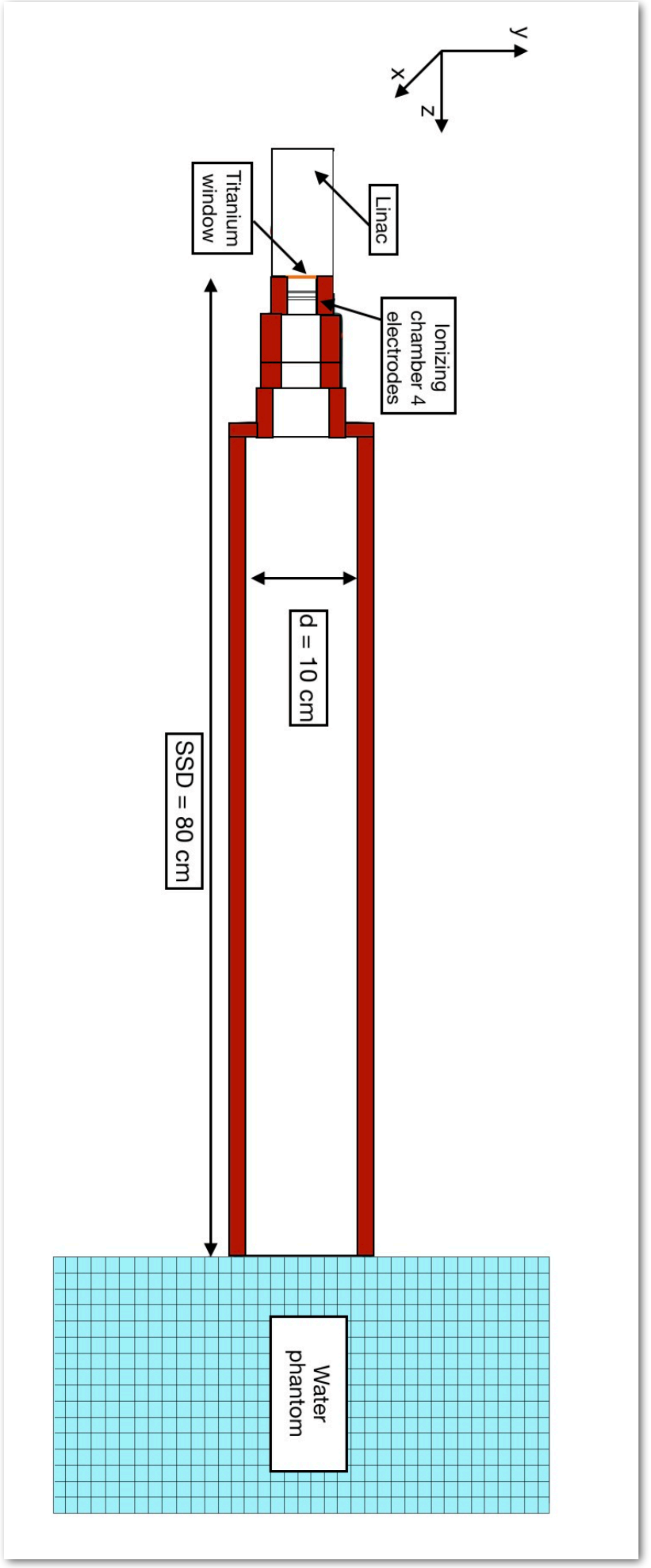


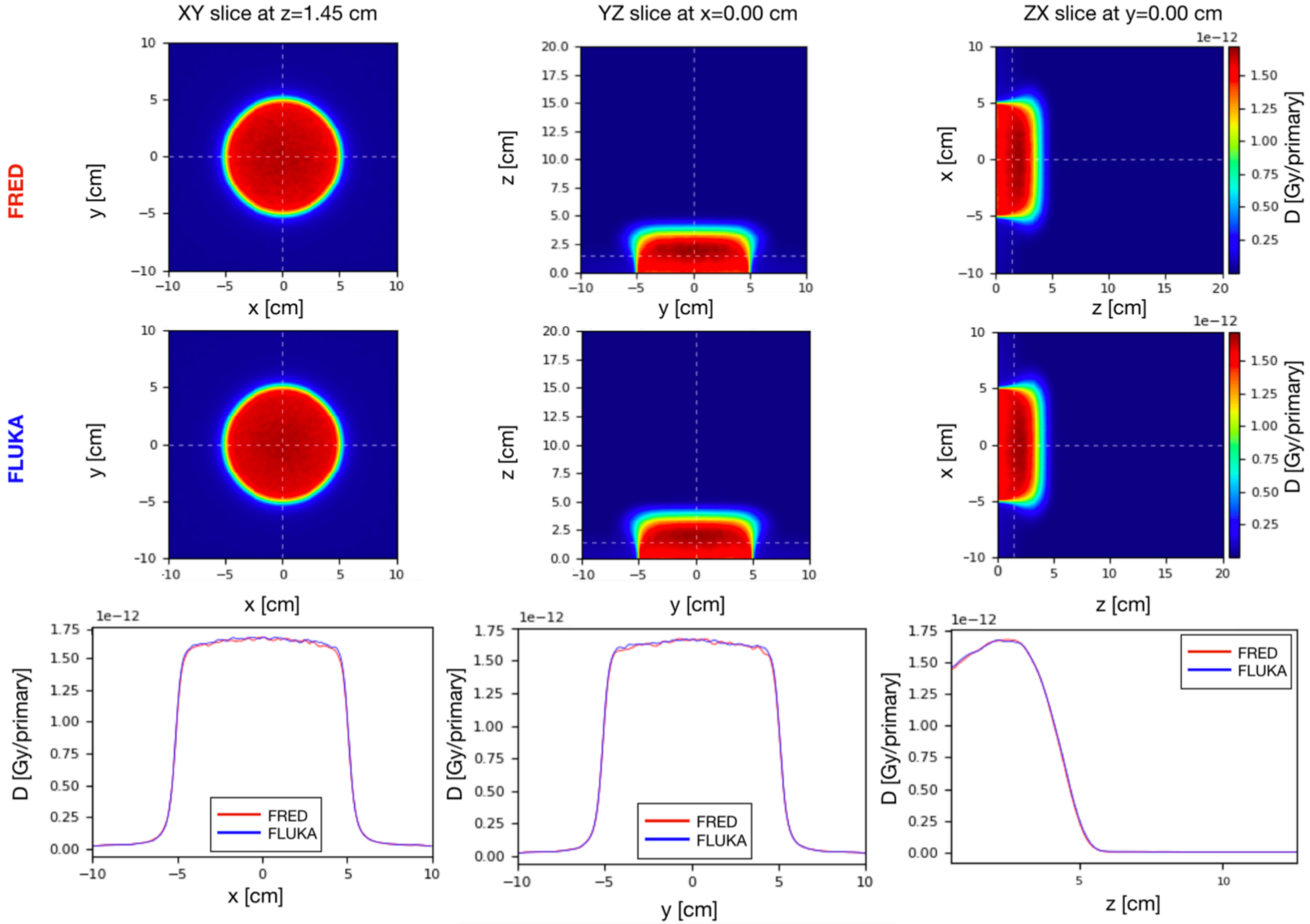


FRED-em: ph @ 100 MeV in water



FRED-em: IORT applicator

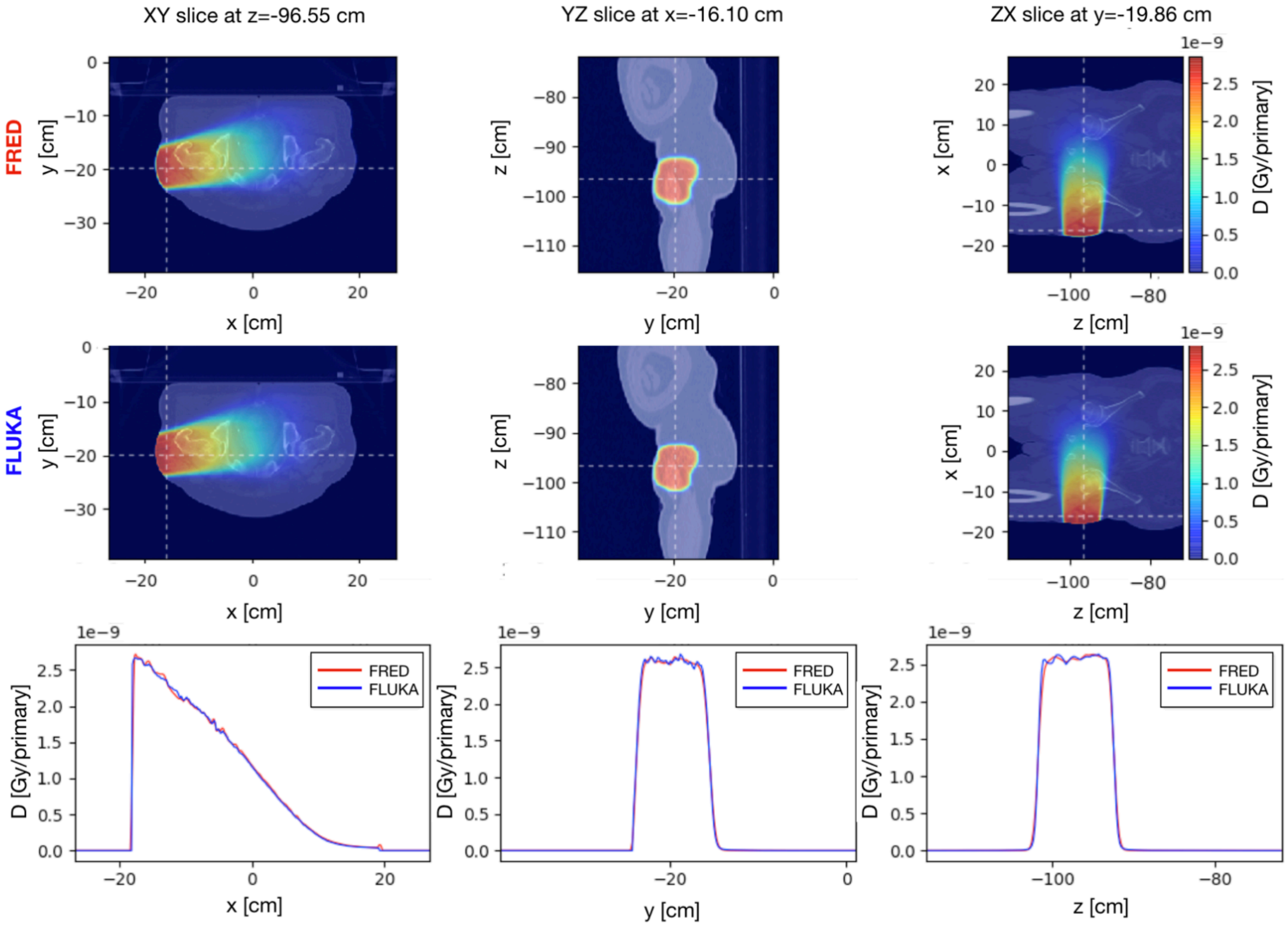




Gamma index acceptance criteria:
2 mm/3% with 5% of threshold

Gamma index pass-rate: 99.80%

FRED-em: VHEE on CT



Gamma index acceptance criteria:
2 mm/3% with 5% of threshold

Gamma index pass-rate: 99%

NOVAC 11

IORT application: NOVAC 11 accelerator

The NOVAC 11 (by Sordina IORT Technologies SpA,Aprilia, Italy) is a linear mobile electron accelerator designed for IORT application:

- Nominal energies: **4, 6, 8** and **10 MeV**;
- Able to treat targets volume with a thickness up to **2.6 cm** inside the 90% isodose;
- The device is able to successfully deliver the full treatment in only 100 seconds (up to **21 Gy at 90% isodose**).

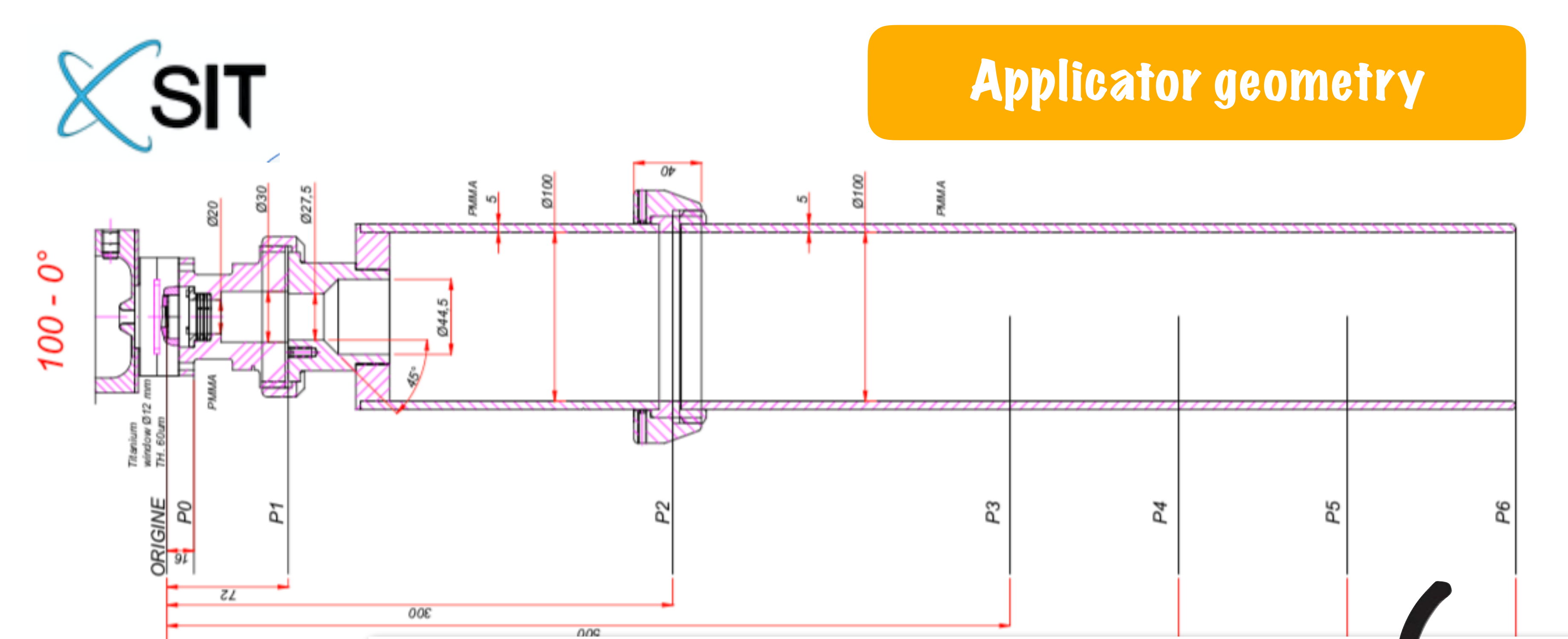
Tpulse	4.5 µs	**Beam Intensity**	1.5 mA	**Dose rate**	4-30 Gy/min

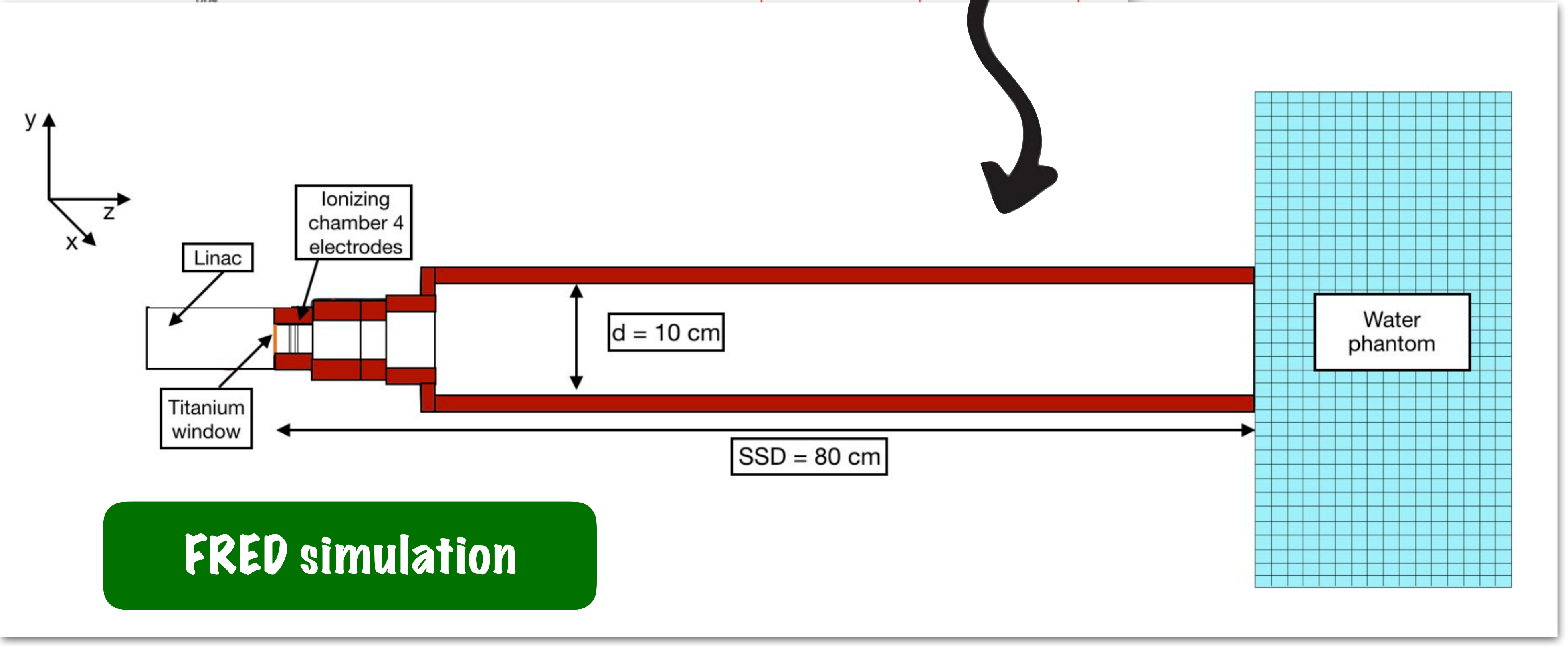
ElectronFlash

Tpulse	0.5-4 µs	Beam Intensity	100 mA	Istantaneus Dose rate	7.6×10^6 Gy/s

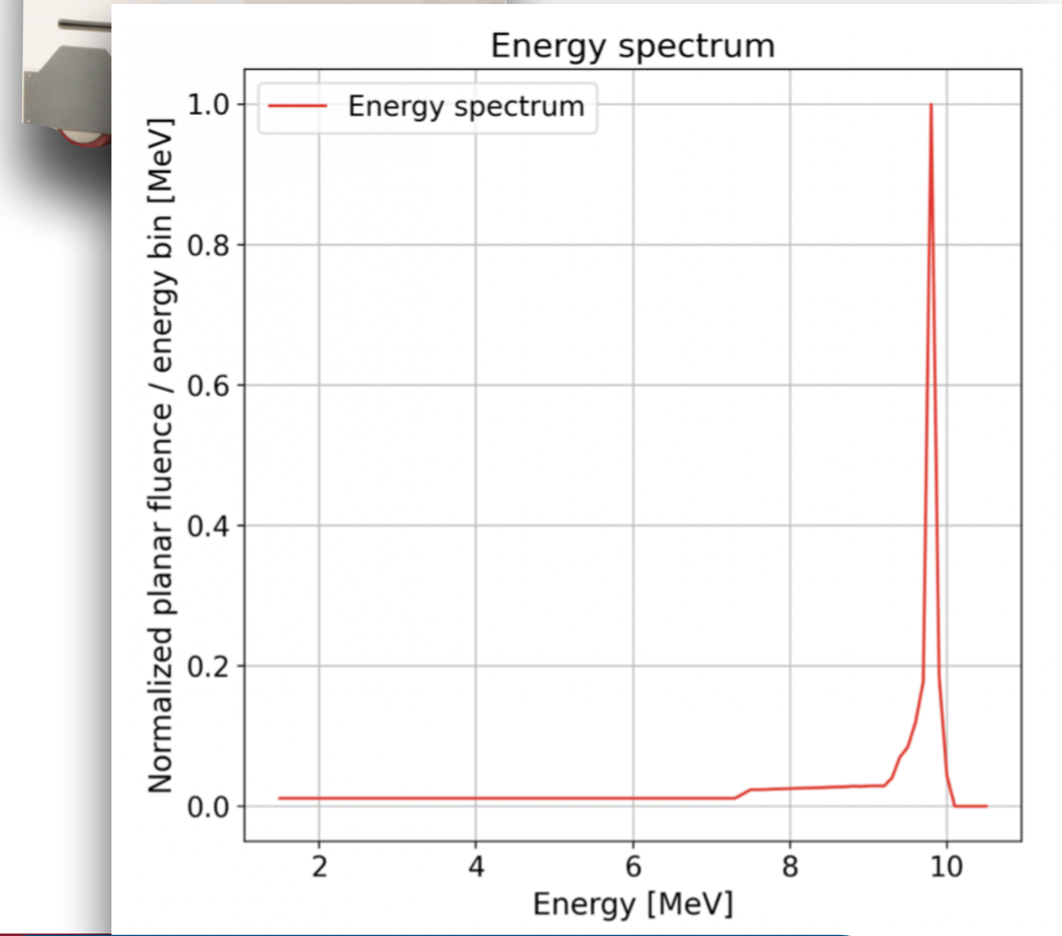
IOeRT application

To test the FRED accuracy in reproducing IOeRT dose distributions, I simulated in details the geometry of the applicators typically used during the treatments. To this aim I considered the NOVAC 11 S.I.T. accelerator and its applicators.


Applicator geometry



FRED simulation



Energy spectrum @ linac exit

Geometry setup:

1. **PMMA cylinders** with different diameters (from 20 to 100 mm)
2. Source-to-Skin Distance **(SSD)=80 cm**
3. **Titanium** window **(55 μm)**
4. **Four steel planes** of the ionizing chamber **(20 μm each)**

Simulation setup

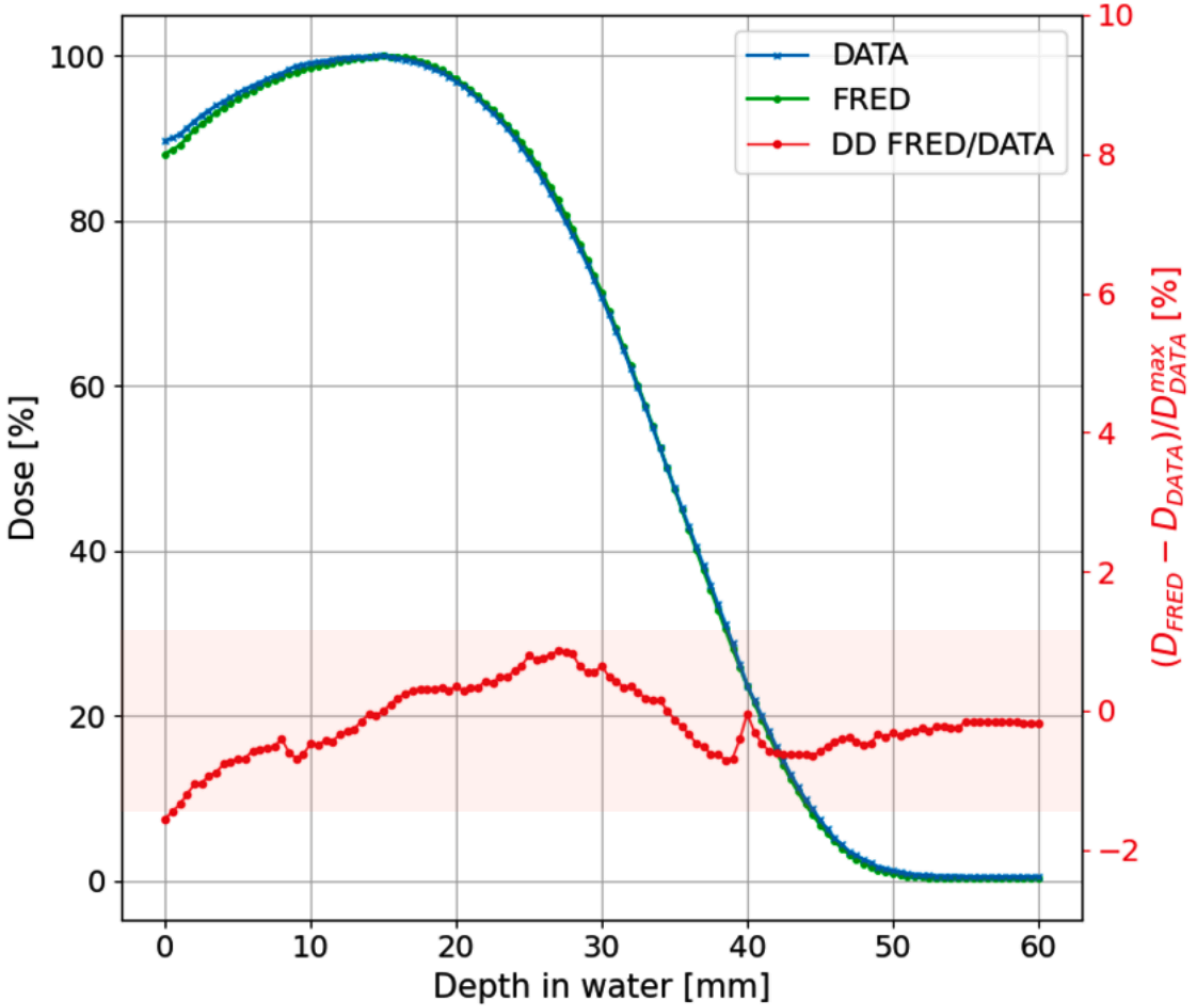
1. **~10 MeV** electrons beam;
2. Gauss section with **FWHM=0.13 cm**;
3. Transport and production energy cut = **10 keV and 50 keV** for photons and electrons respectively

I compared the FRED results against the **experimental data** of the Percentage Depth Doses (PDDs) and off-axis profiles measured in a water phantom.

IOeRT application: FRED results

Test performed on CPU

The experimental setup for relative dosimetry, i.e. PDDs and off-axis profiles measurements consisted of a 3D motorized water phantom equipped with an unshielded diode. For the MC simulation the absorbed dose was evaluated on a water target with a transverse area of 2×2 mm^2, corresponding to the sensitive are of the adopted diode



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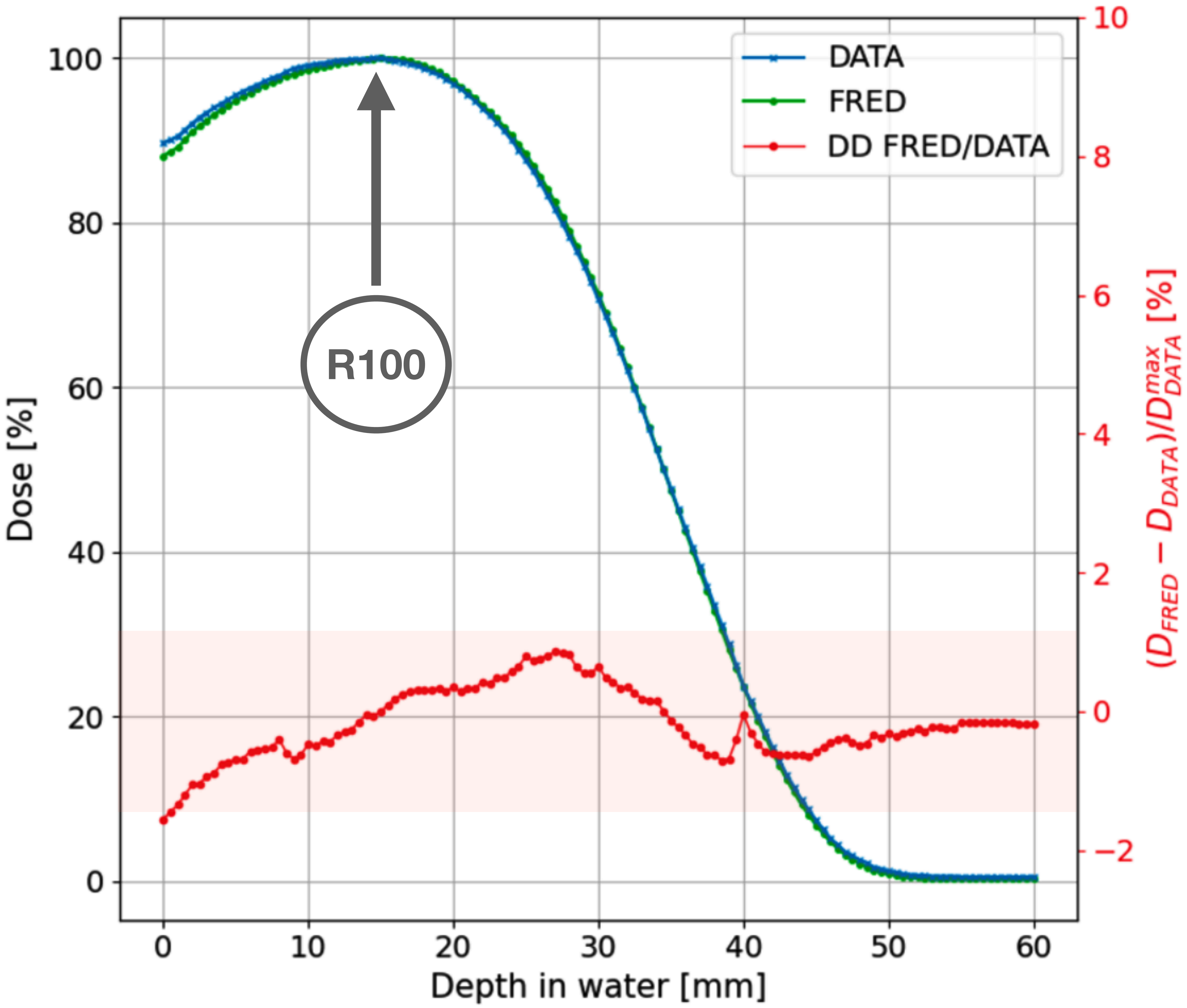

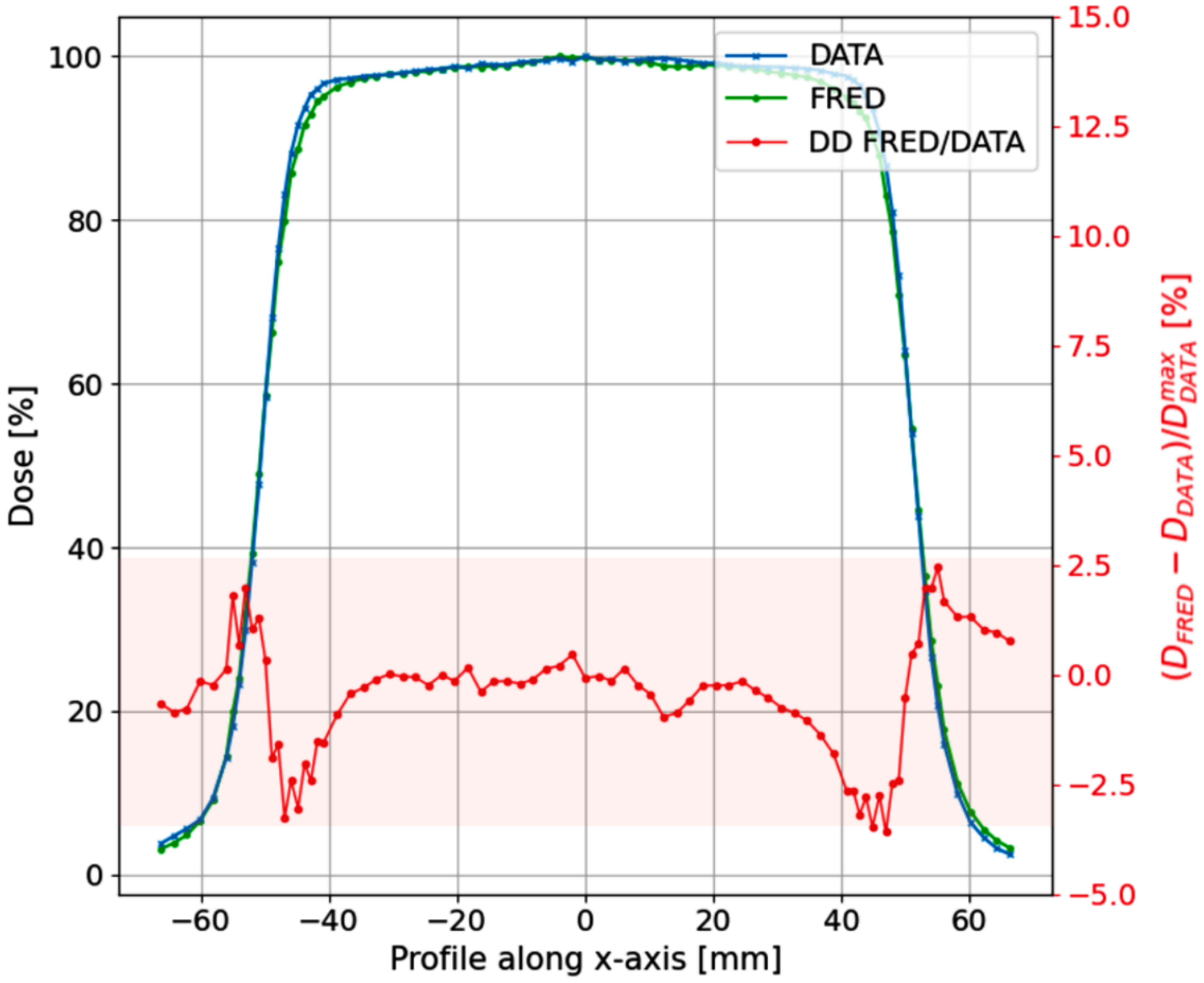

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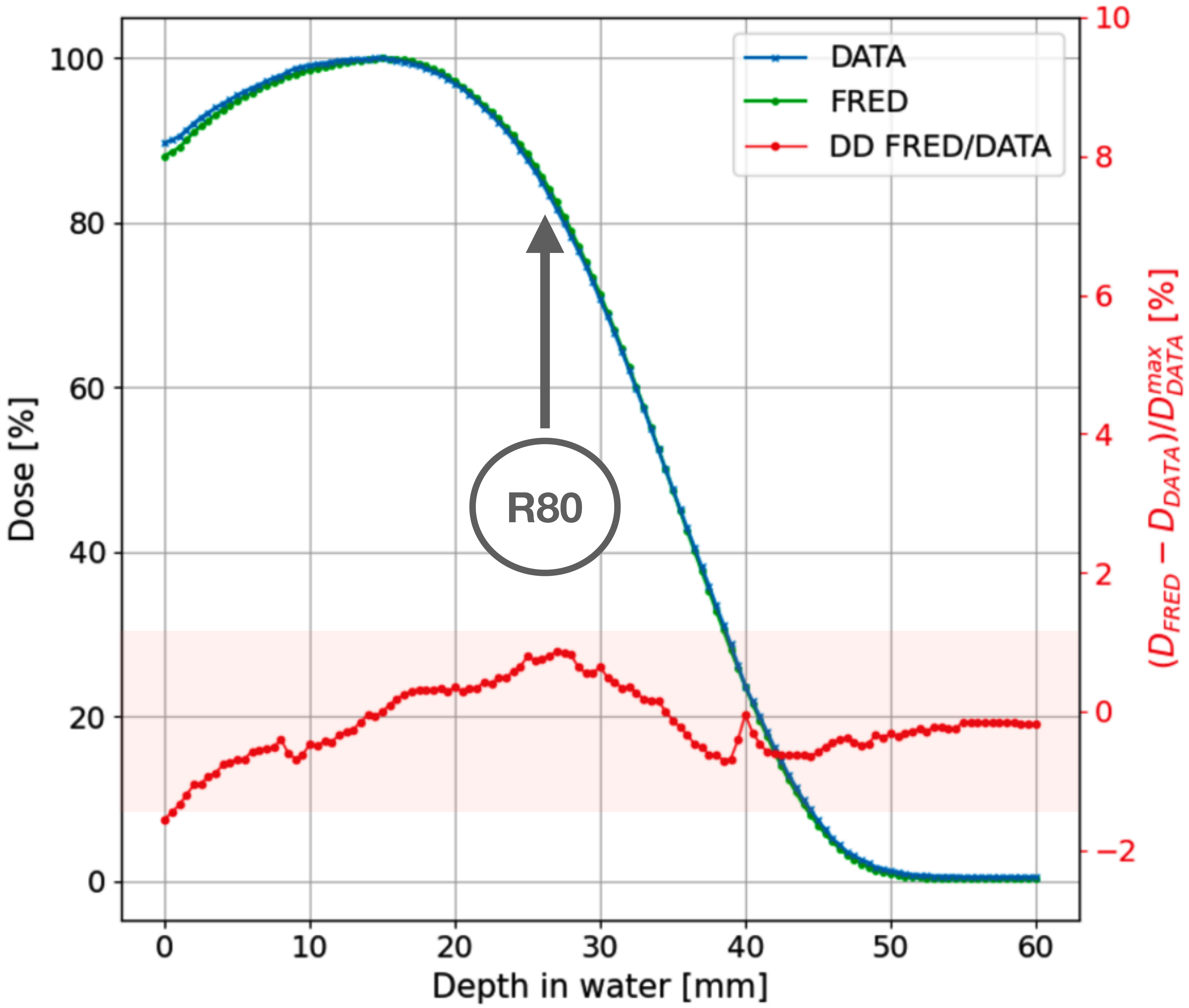

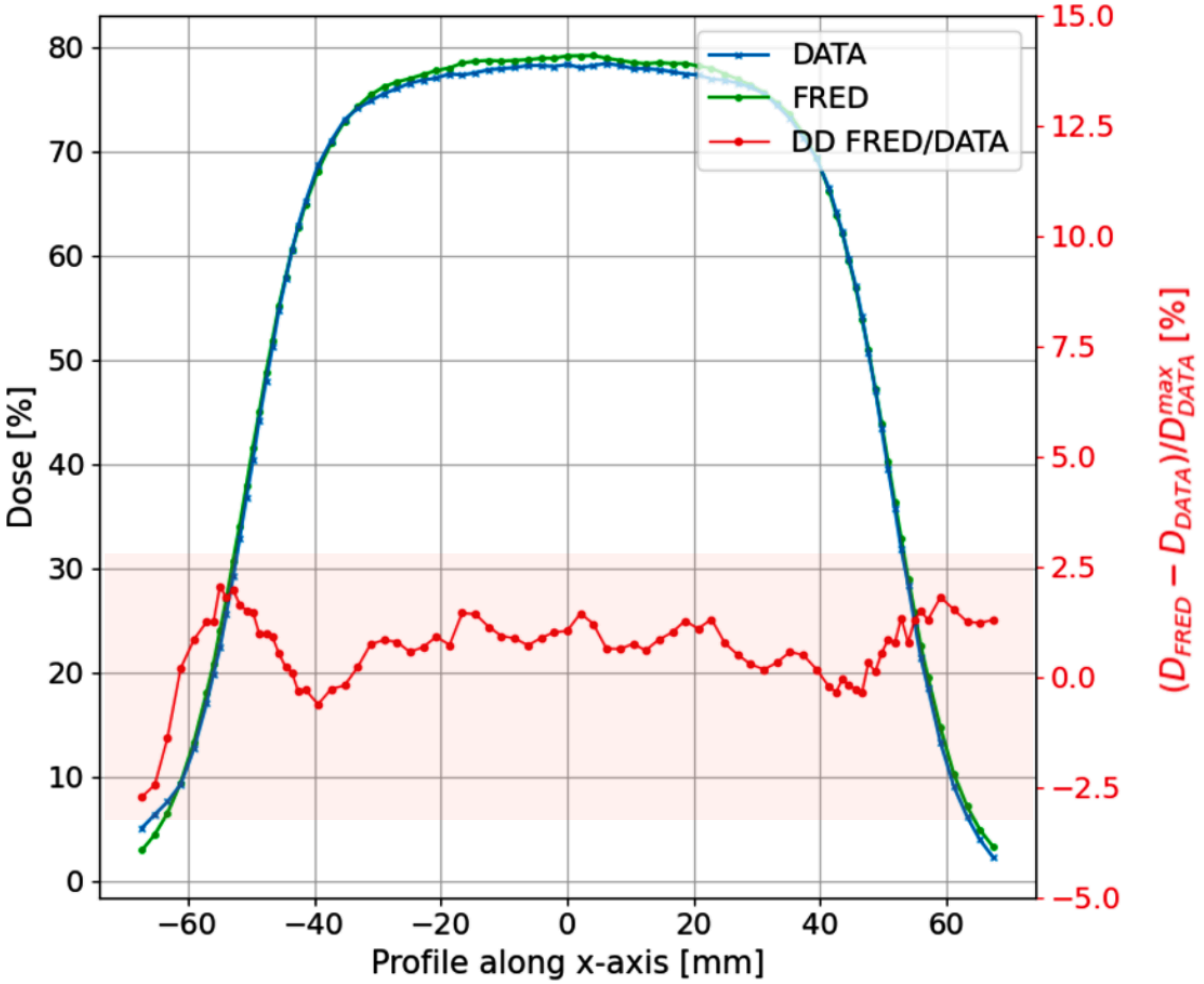

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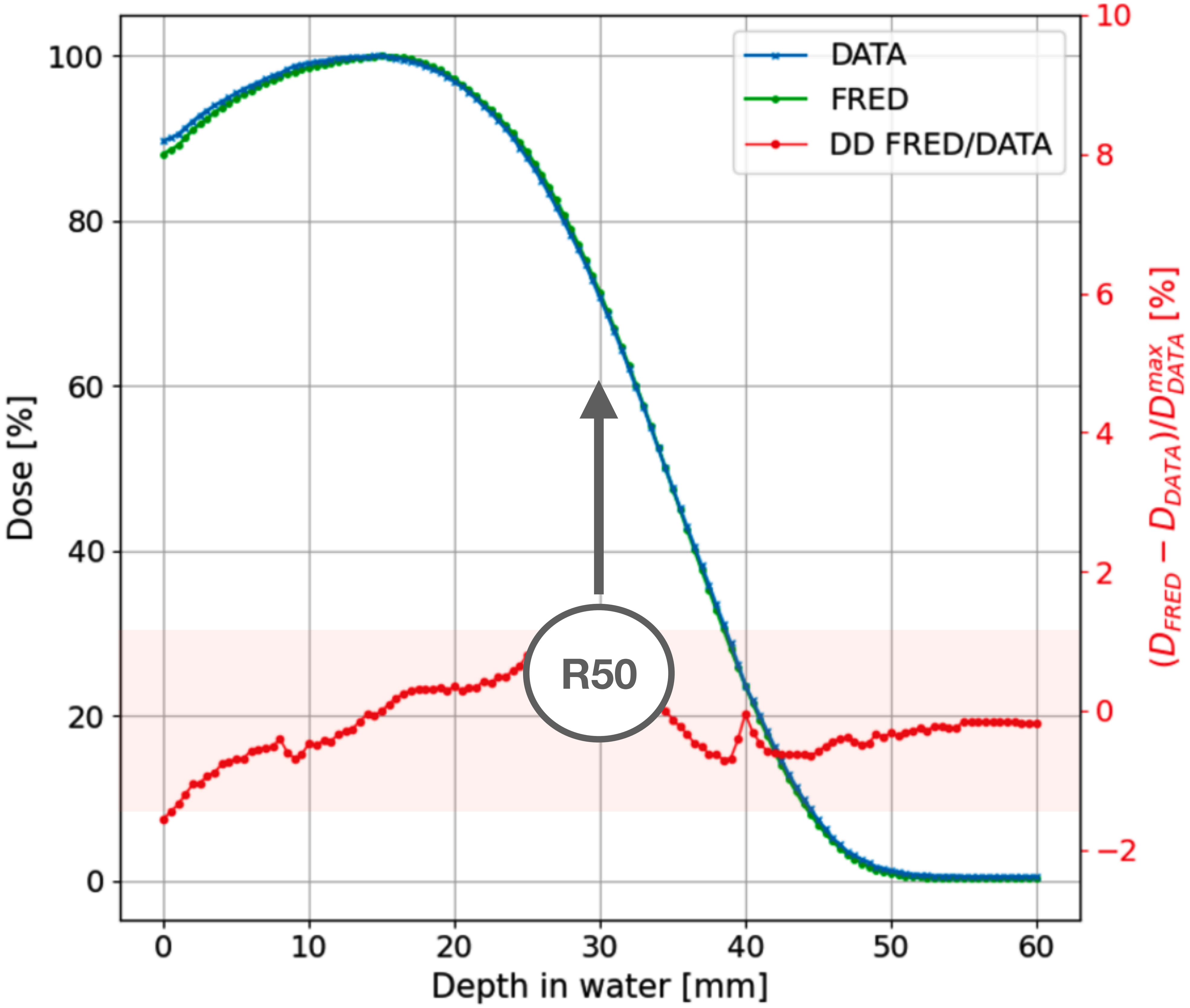
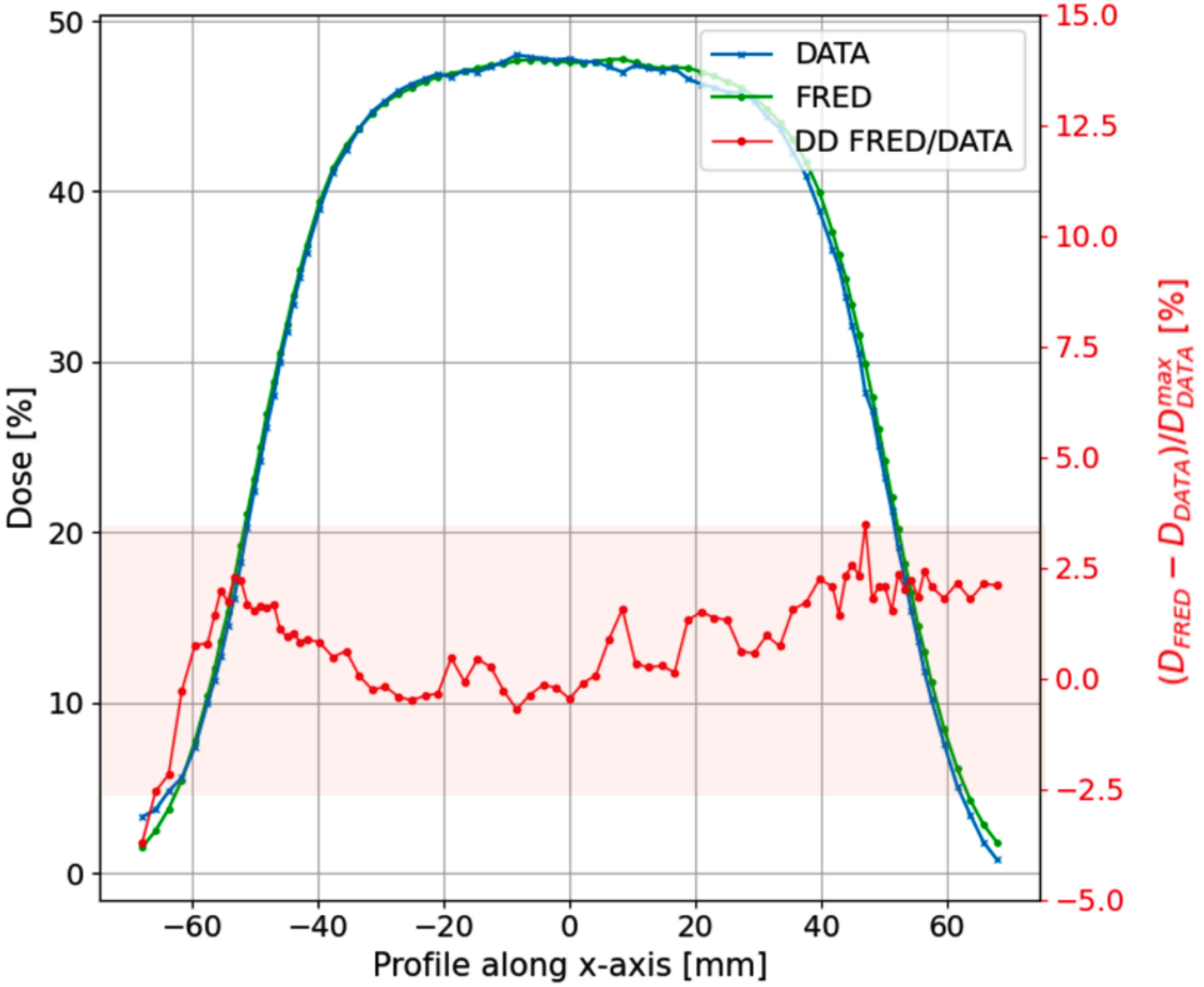




Neutrons contribution

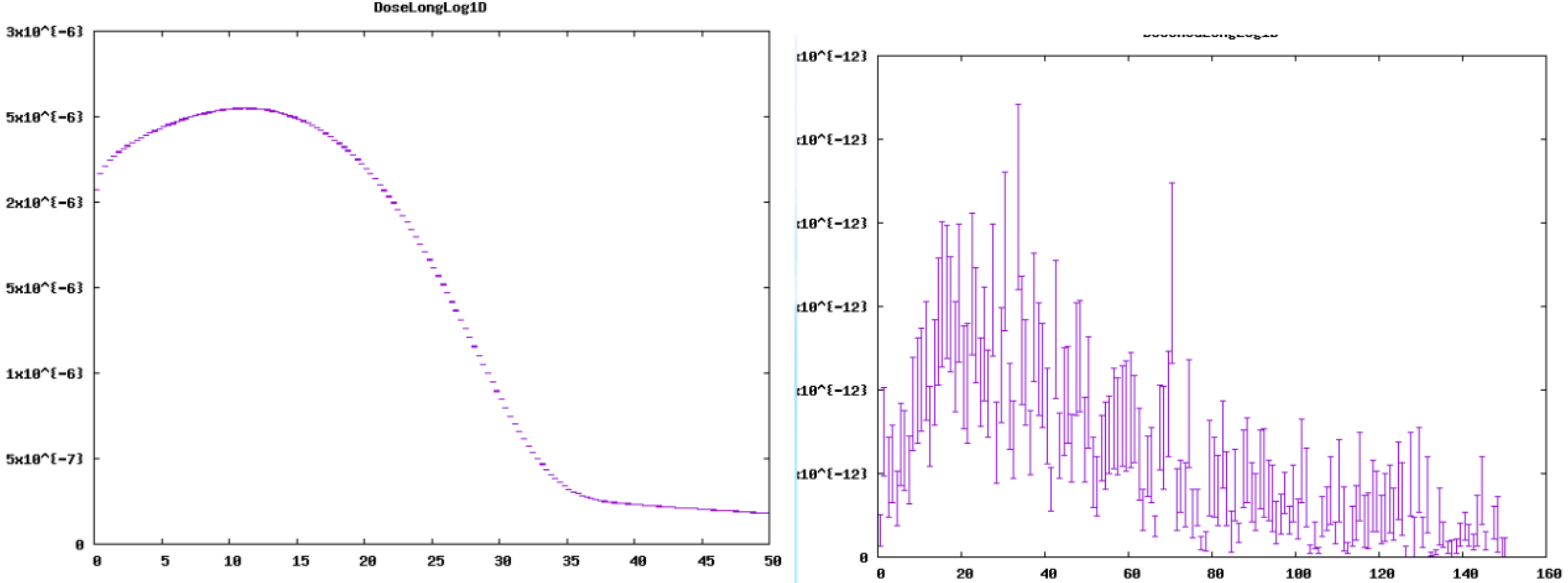
In the medical context we have two main photoneutron production processes by the high-energy bremsstrahlung photons:

1. 10 MeV < E < 30 MeV
GIANT-RESONANCE NEUTRON PRODUCTION
2. 50 MeV < E < 300 MeV
QUASI DEUTERON PRODUCTION AND DECAY

IOeRT

We are below the Giant resonance (E < 12 MeV) and thus the photoneutron production is negligible

@ 100 MeV in water



VHEE therapy

@ 150 MeV in water

Neutron yield : 0.03 n/primary e^-

Increased neutron dose: 0.2%

Increased equivalent neutron dose: 2% (w=10)

Negligible contribution


Open Access Review

Back to the Future: Very High-Energy Electrons (VHEEs) and Their Potential Application in Radiation Therapy

by Maria Grazia Ronga [1,2], Marco Cavallone [1], Annalisa Patriarca [1], Amelia Maia Leite [1,3], Pierre Loap [1], Vincent Favaudon [4], Gilles Créhange [1] and Ludovic De Marzi [1,3,*]

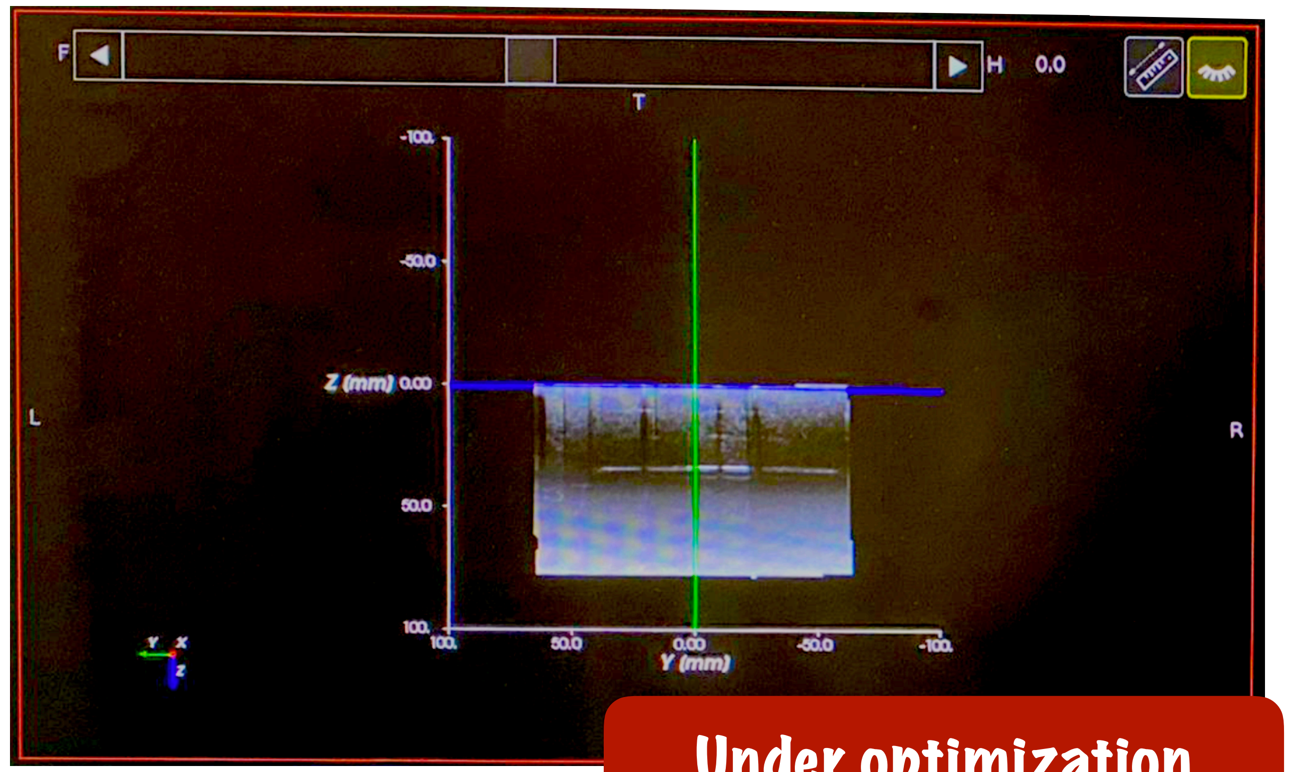
TPS

Treatment planning configuration

To give a reasonable feedback to the operator I need to be capable to 'optimize' the treatment! How can I identify the ideal energy or ideal applicator position/dimension for that **specific treatment**? Answering that question means understanding which are the constraints that have to be respected.

I developed the optimization tools and the relative algorithms, which are based on different inputs:

☒ **Ultrasound imaging input with reasonable ROIs (PTV and OAR)**



Under optimization

Currently, the US system is under optimization and thus not yet available. I used **real CT images**, modified to meet the expected US imaging resolution

☑ **Dose prescription**

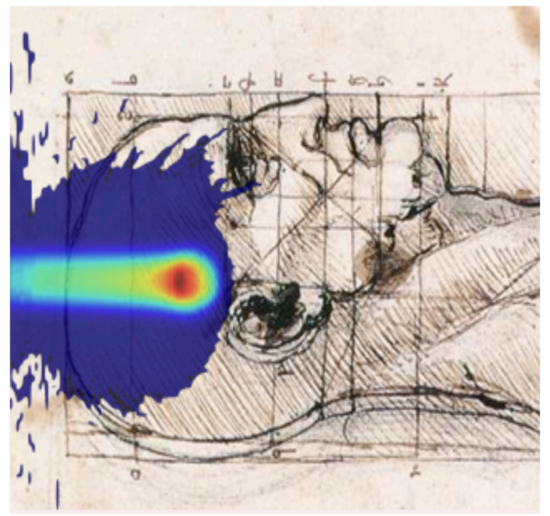
I collaborated with the IOeRT specialists of the European Institute of Oncology (Milan) to define reasonable **dose prescriptions** for the **PTV**.

SIT

IEO
Istituto Europeo
di Oncologia

☑ **Fast simulation tool**

The **FRED** timing performance is highly compatible with the time available during surgery to explore different treatment configurations (order of few minutes).



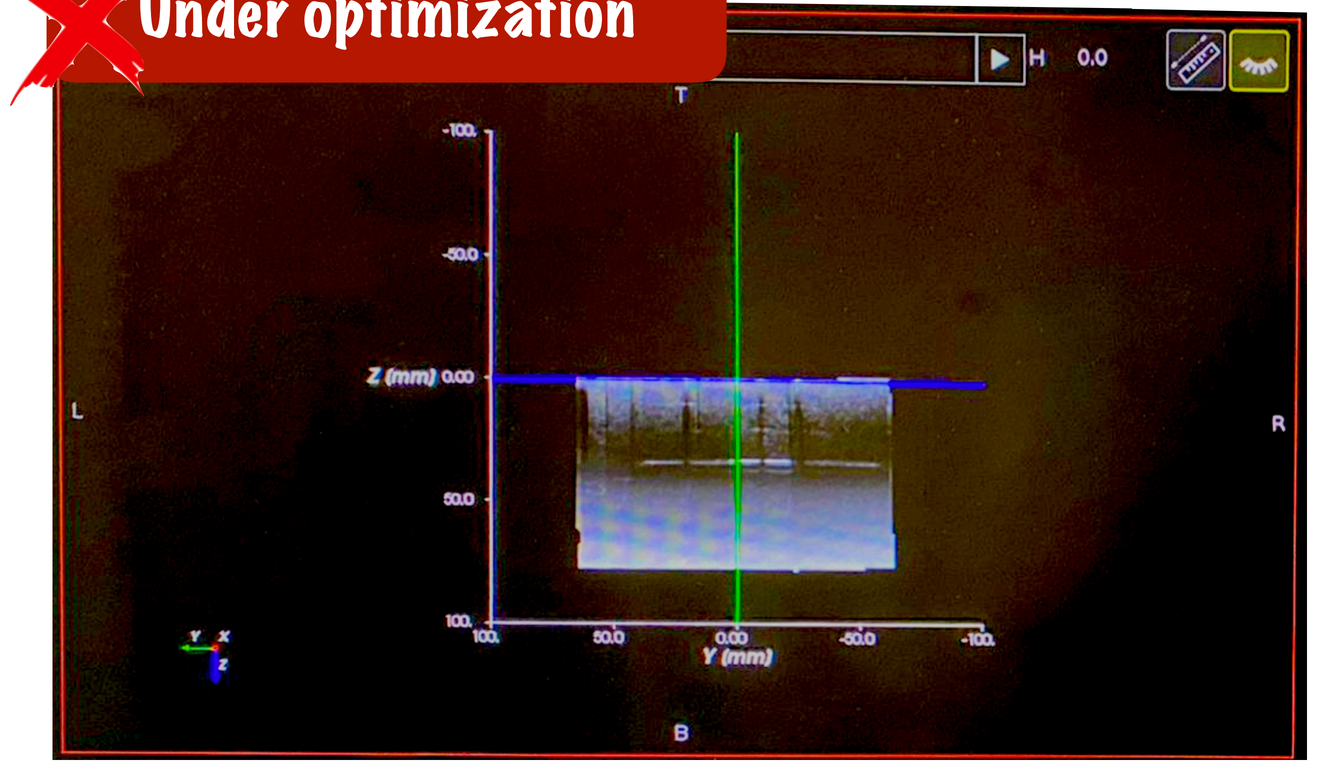
☑ **Phase-space that has to be explored**

IOeRT specialist helped me to define the energies, and the possibile beam delivery configurations (beam dimension and position)

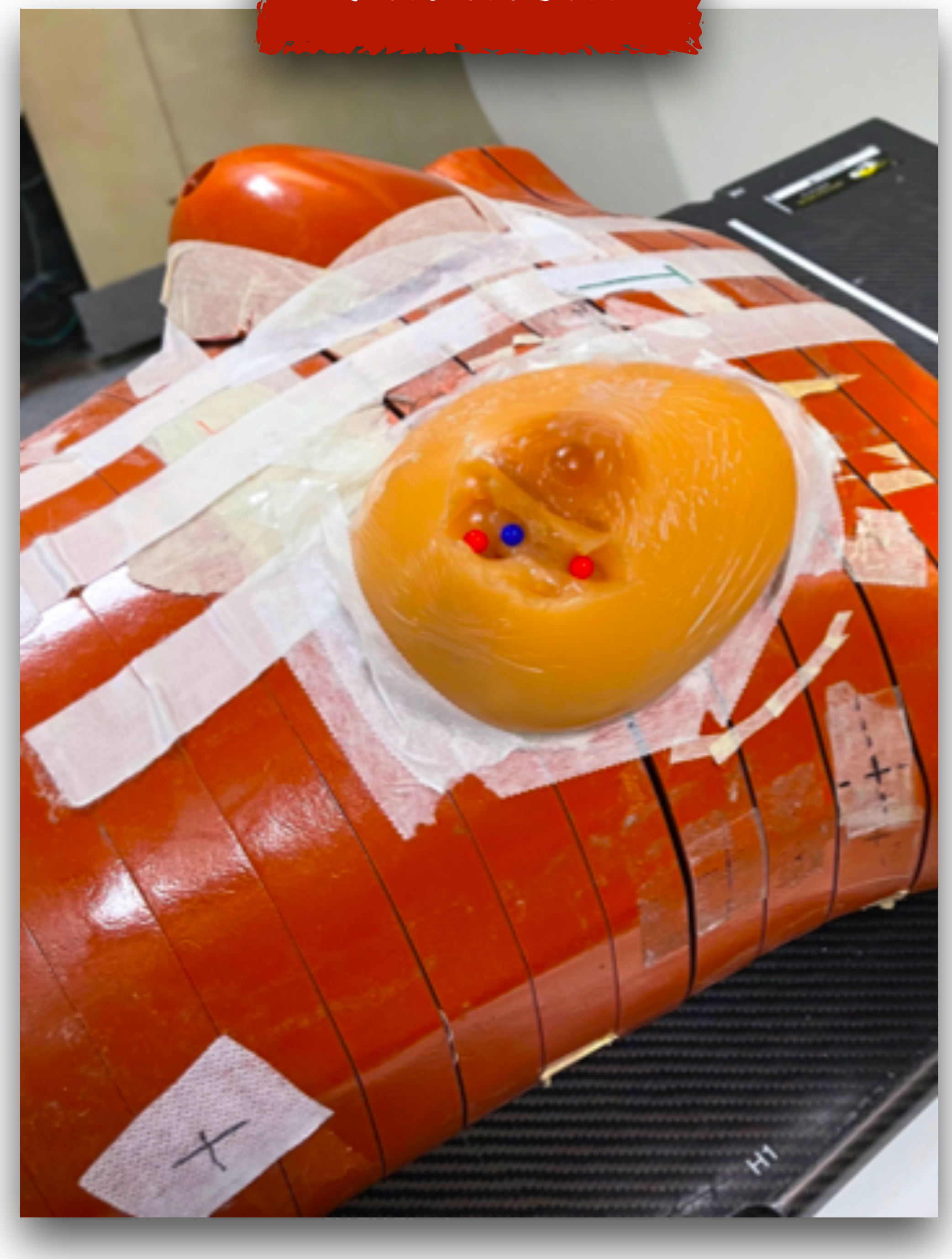
Breast cancer IOeRT TPS

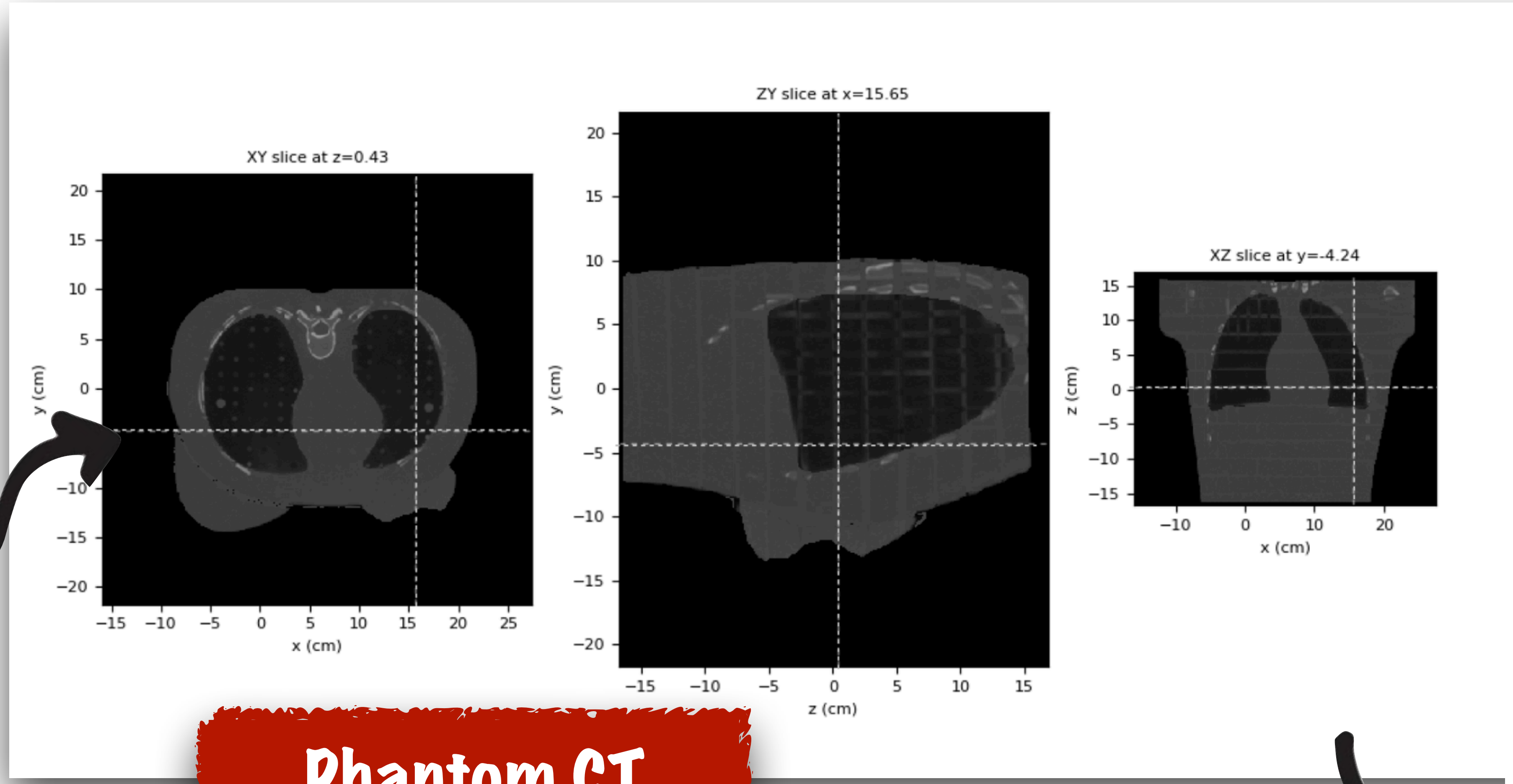
Since the US imaging system is today under optimization, to simulate the breast IOeRT treatment, I used a CT of a phantom with a **breast prosthesis** used to simulate a breast surgery attached onto it.

Under optimization

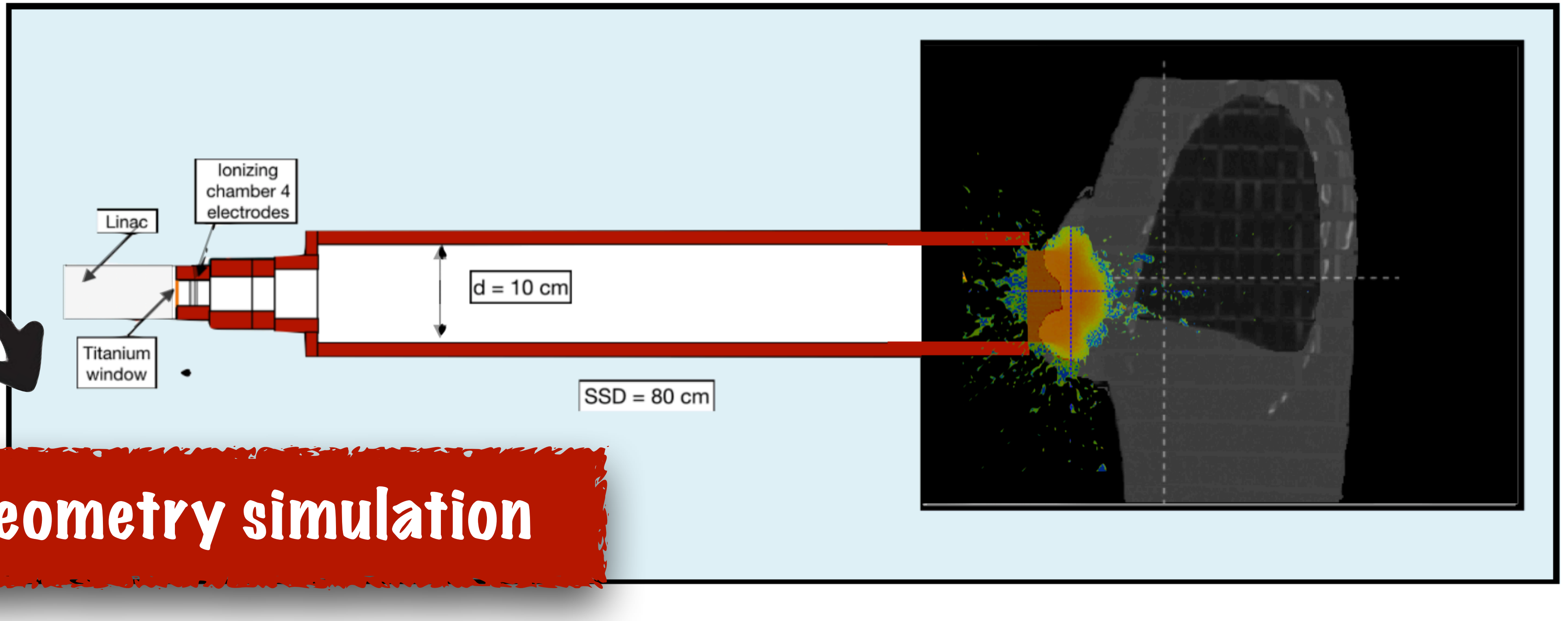


Phantom





Phantom CT



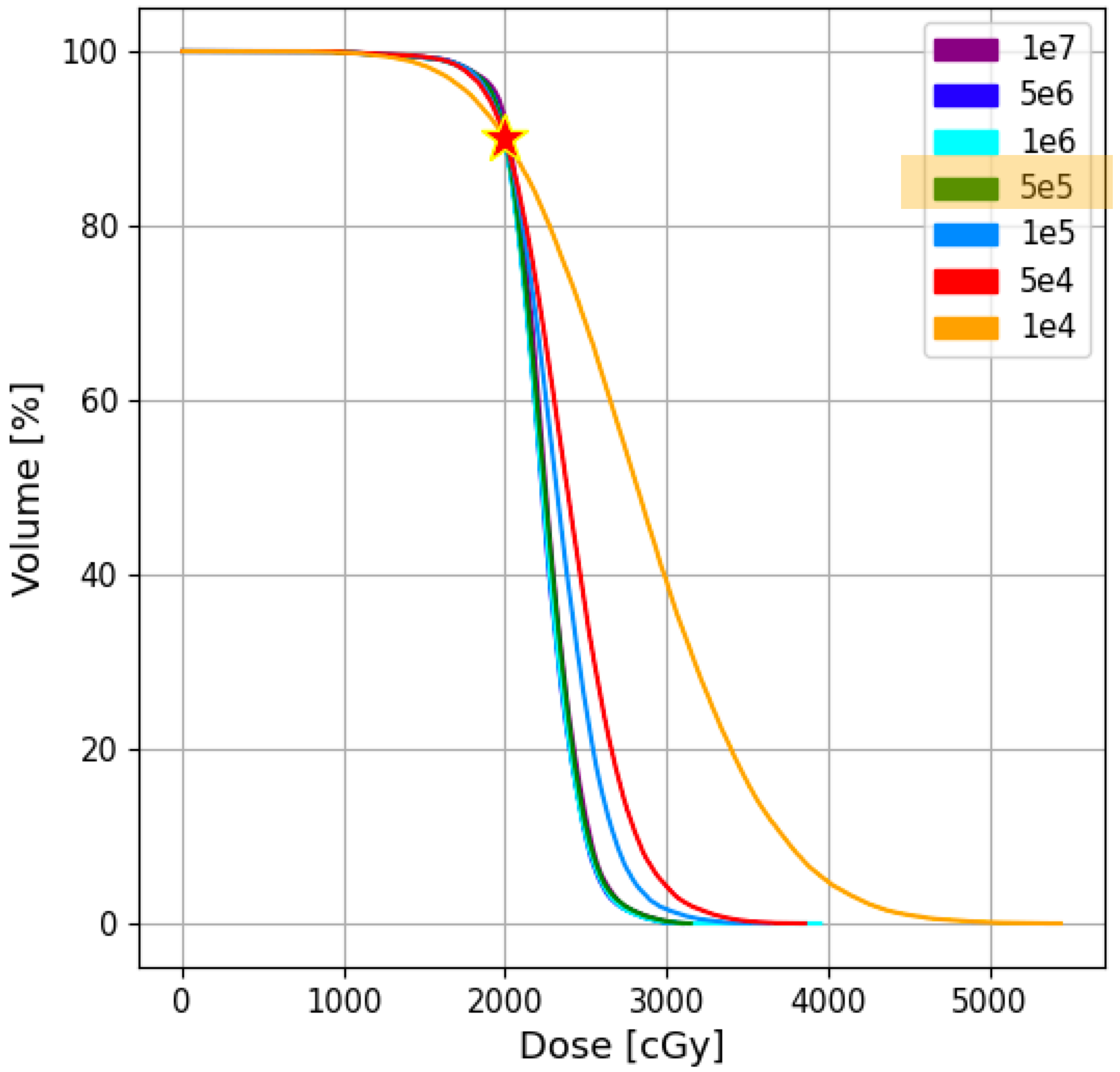
FRED geometry simulation

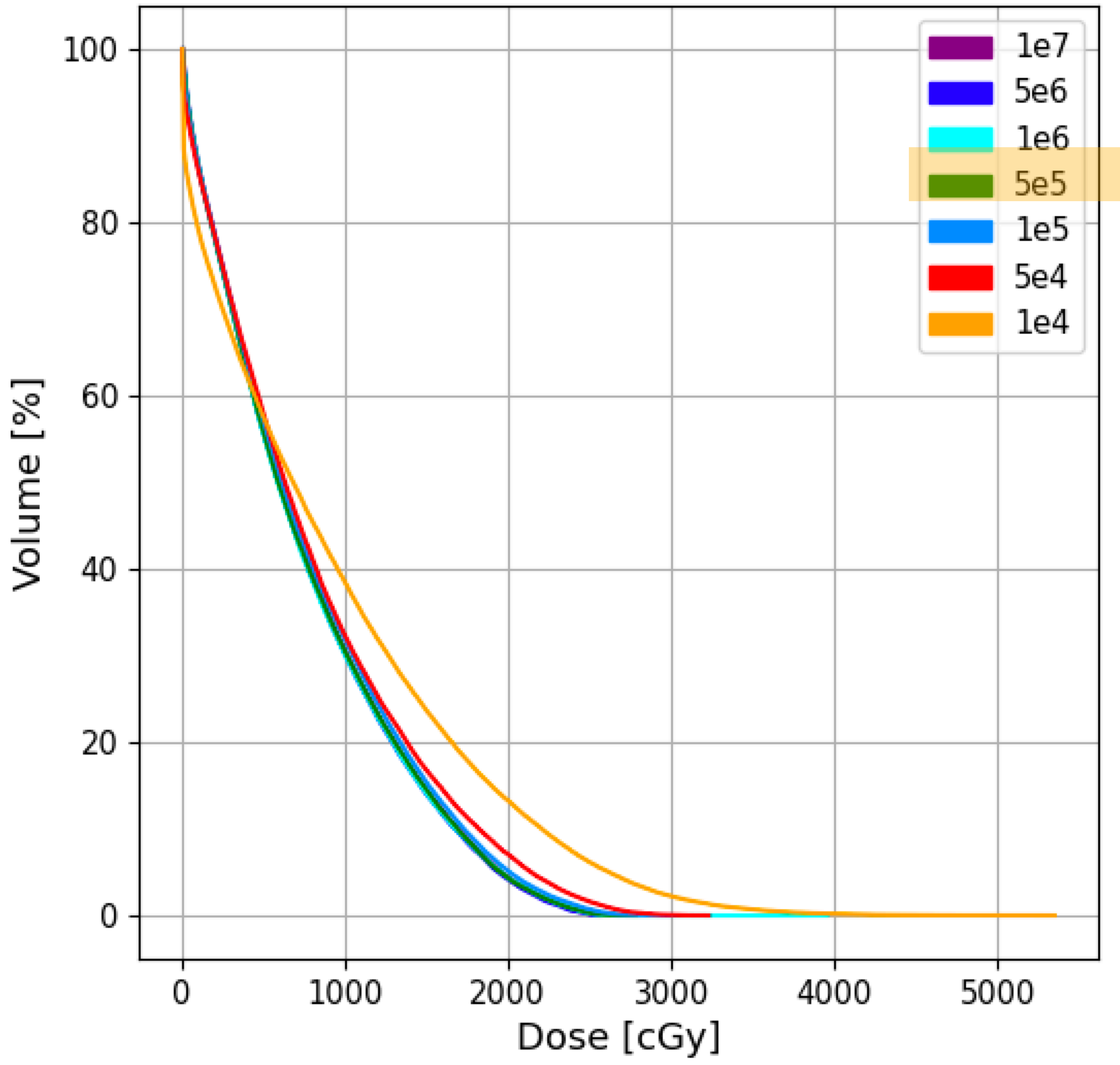
Since the applicator geometry is currently not ready on the GPU code, I simulated the uniform IOeRT irradiation at the exit of the applicator with a **circular beam** (R = available standard applicator radius) generated at ~ 1 cm from the patient skin and in a centered position with respect to the PTV.

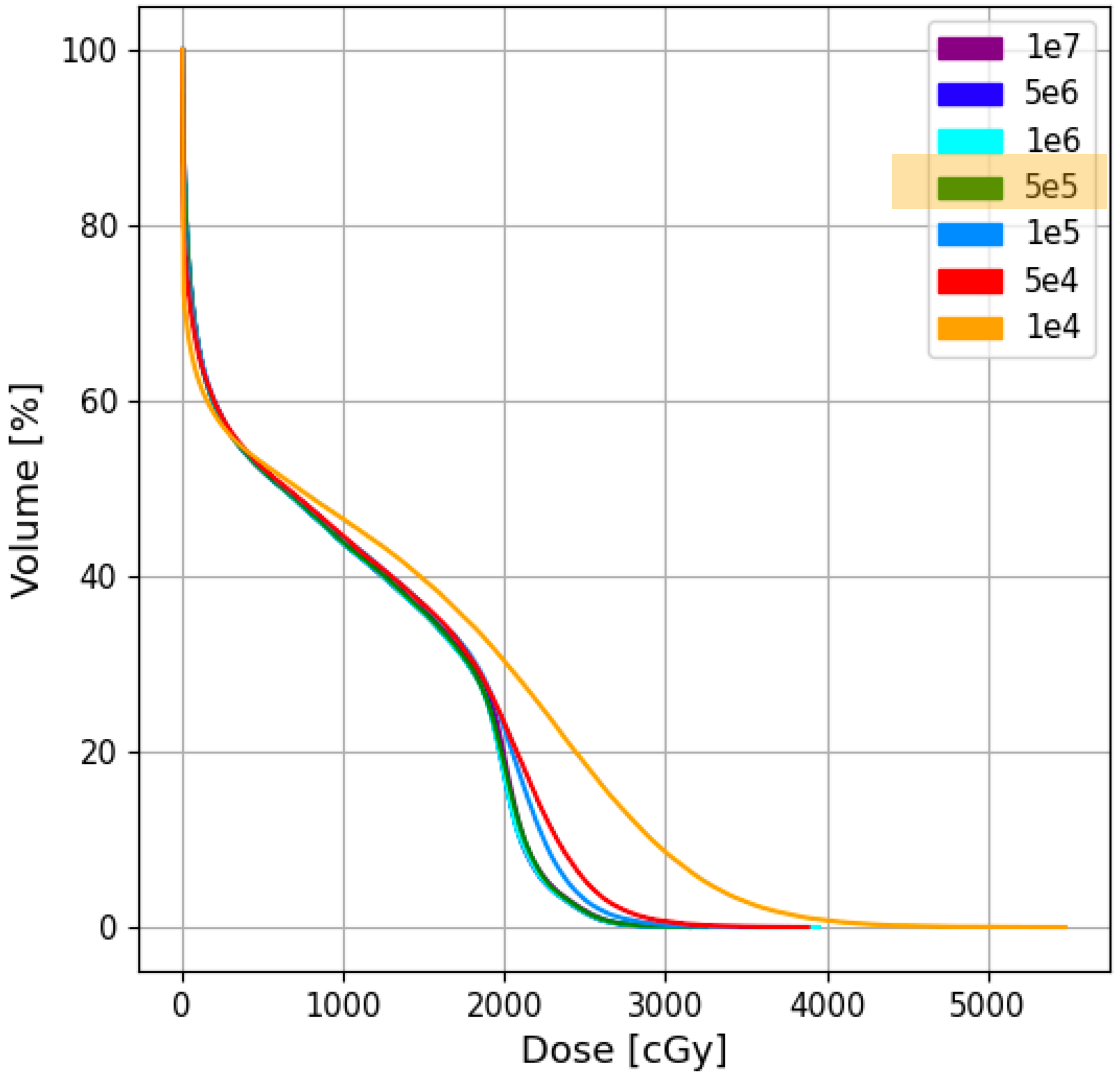
Needed statistics/GPU time

The DVHs depend not only on the "geometry considered", i.e. the volume of the PTV and OARs, but also on the simulation statistics.

I therefore performed a scan simulating different number of primaries with fixed energy and geometry to test the stability of the DVHs.







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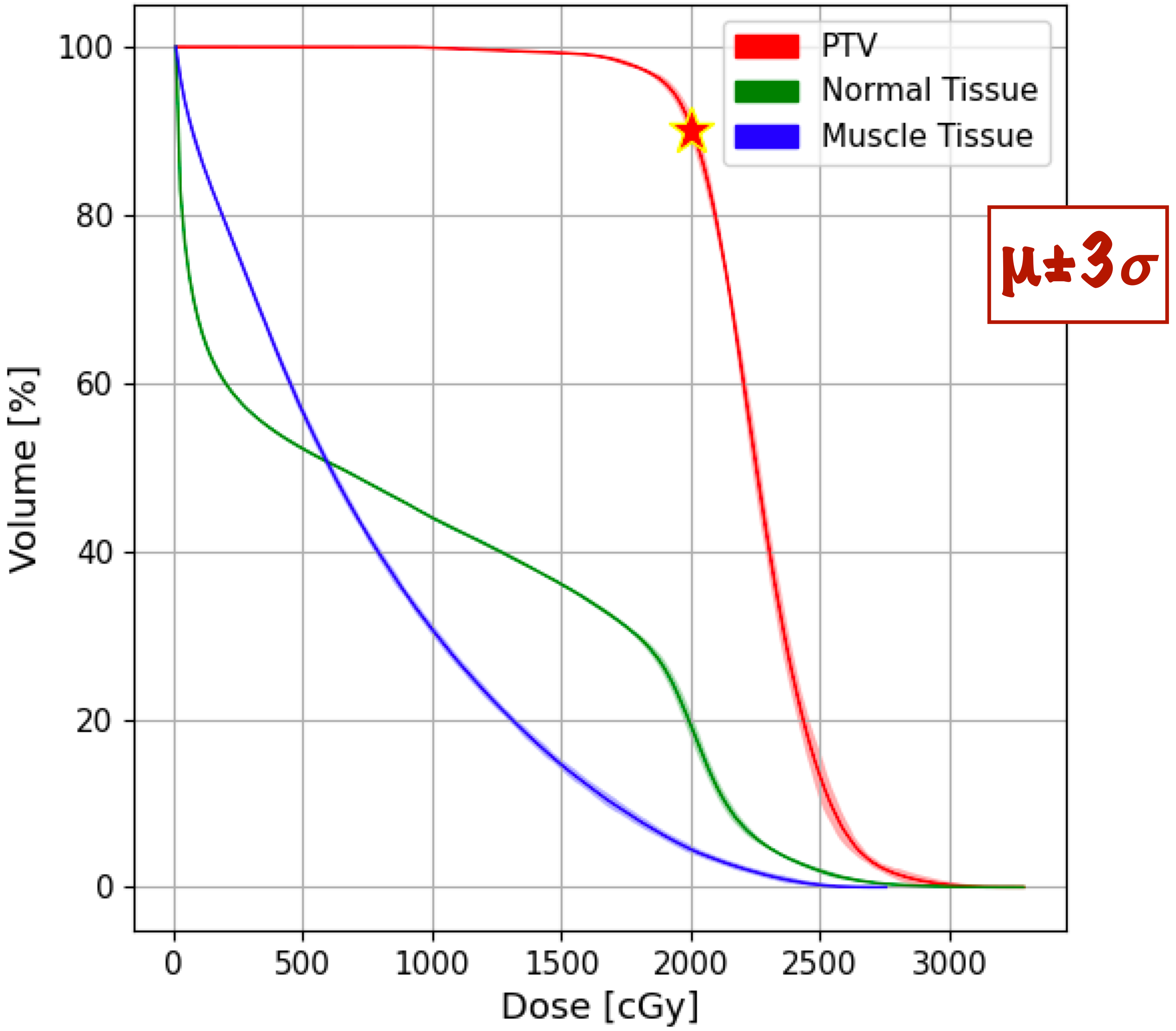


	$\mu \pm \sigma$
ROIs	D [cGy]
PTV	2256.1 ± 1.3
Muscle Tissue	746.8 ± 2.6
Normal Tissue	927.3 ± 2.8

Beam dimension scan

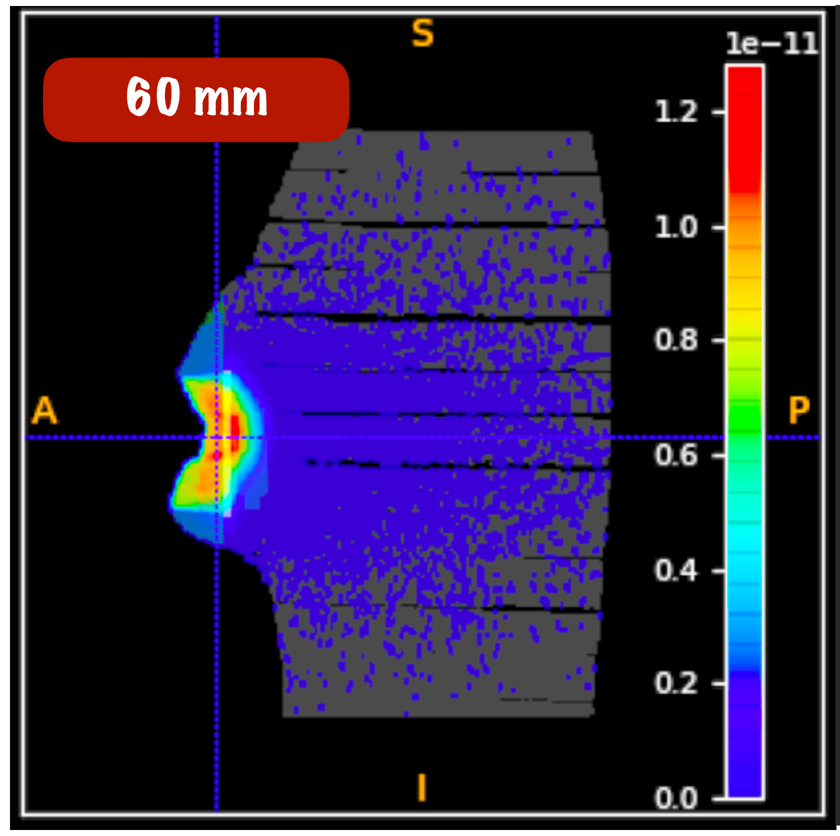
T = 23.8 s

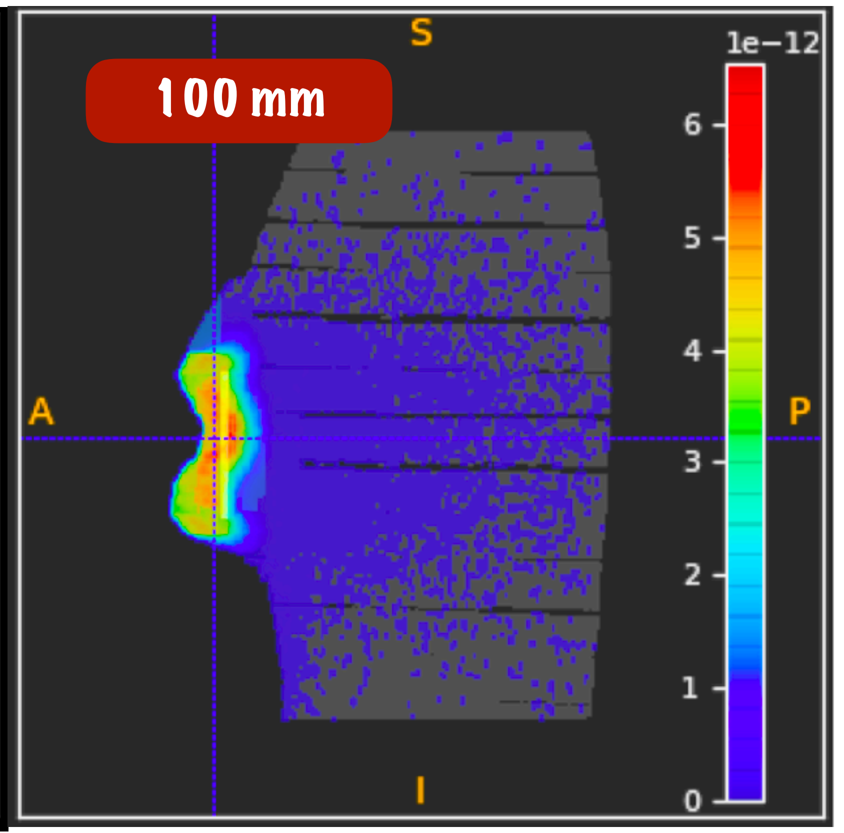
I generated a circular electron beam at ~ 1 cm from the patient skin in a centered position with respect to the PTV.

The beam energy was fixed at 8 MeV and I changed only the beam dimension: 70, 80, 90 and 100 mm were selected according to the PTV dimension.

Dose prescription: ★ **20 Gy @ 90%**

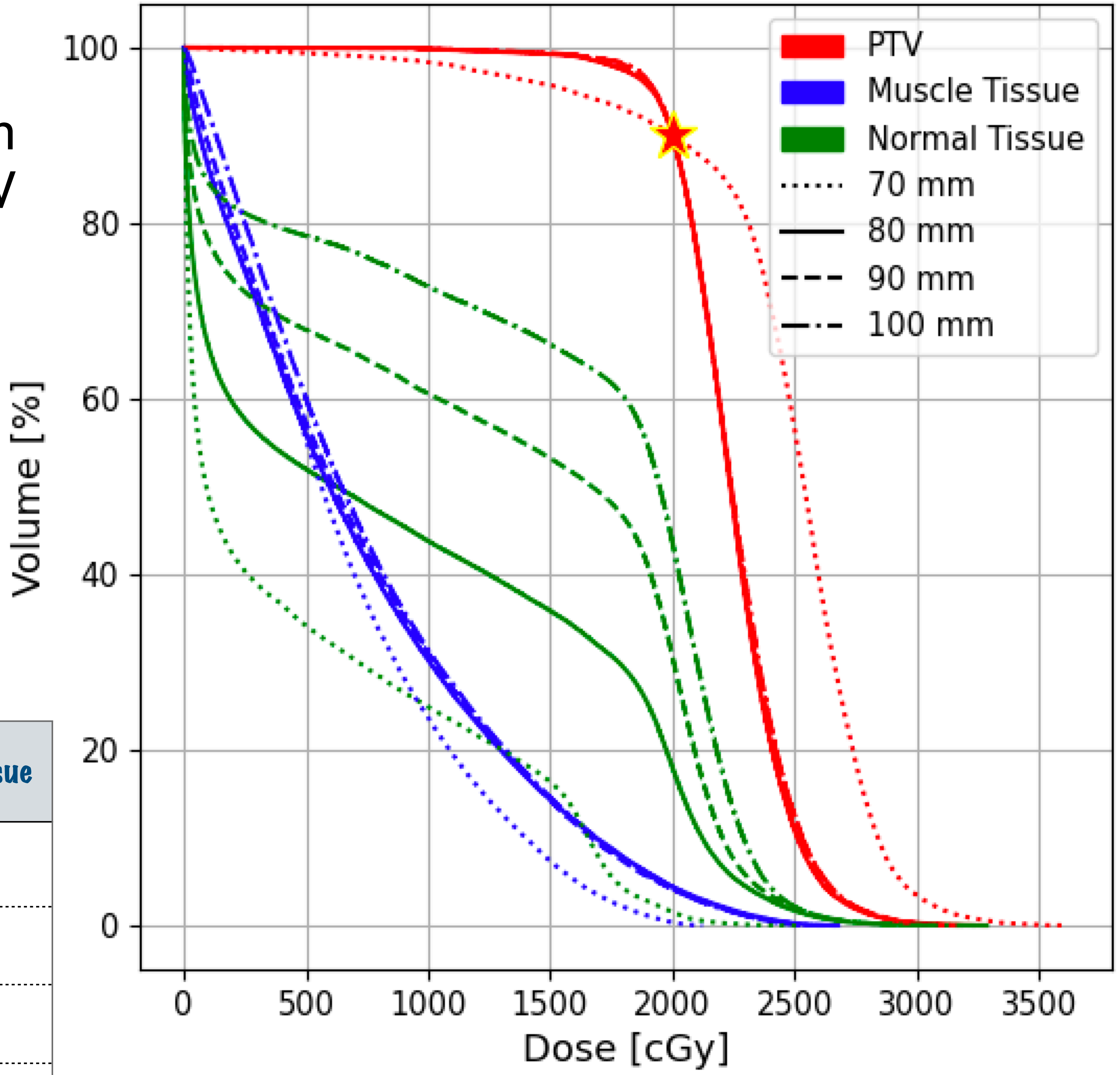
OSS: The FRED dose maps in Gy/primary units were multiplied by the **number** of **electrons** needed to **fulfill** the dose prescription: $2.85 \cdot 10^{12}$, $3.20 \cdot 10^{12}$, $4.40 \cdot 10^{12}$ and $5.20 \cdot 10^{12}$ for the 70, 80, 90 and 100 mm simulation.





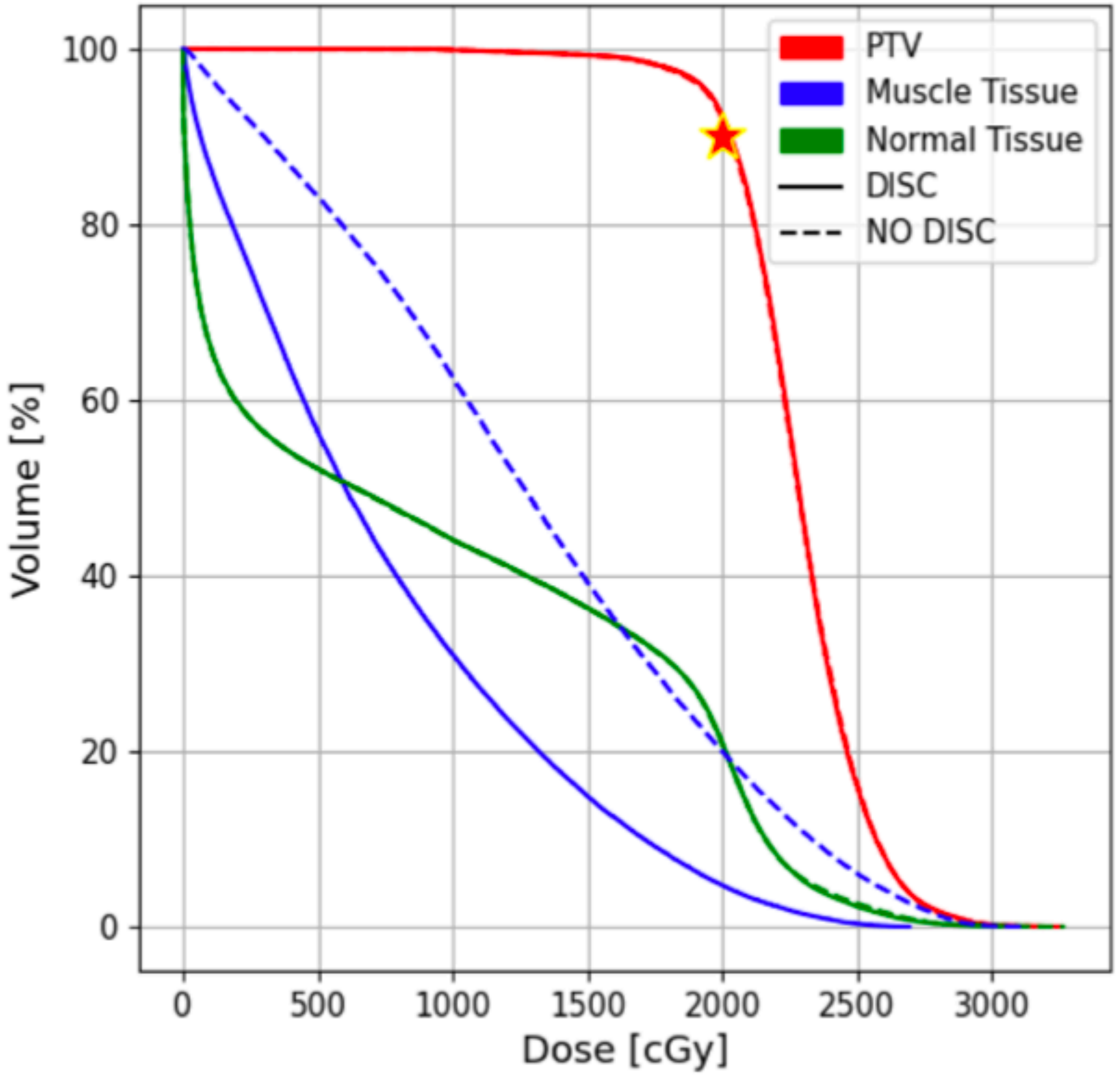
Dose mean values

D [Gy]	PTV	Muscle Tissue	Normal Tissue
70 mm	24.6	6.5	5.1
80 mm	22.4	7.5	9.3
90 mm	22.4	7.6	12.7
100 mm	22.6	7.9	15.3

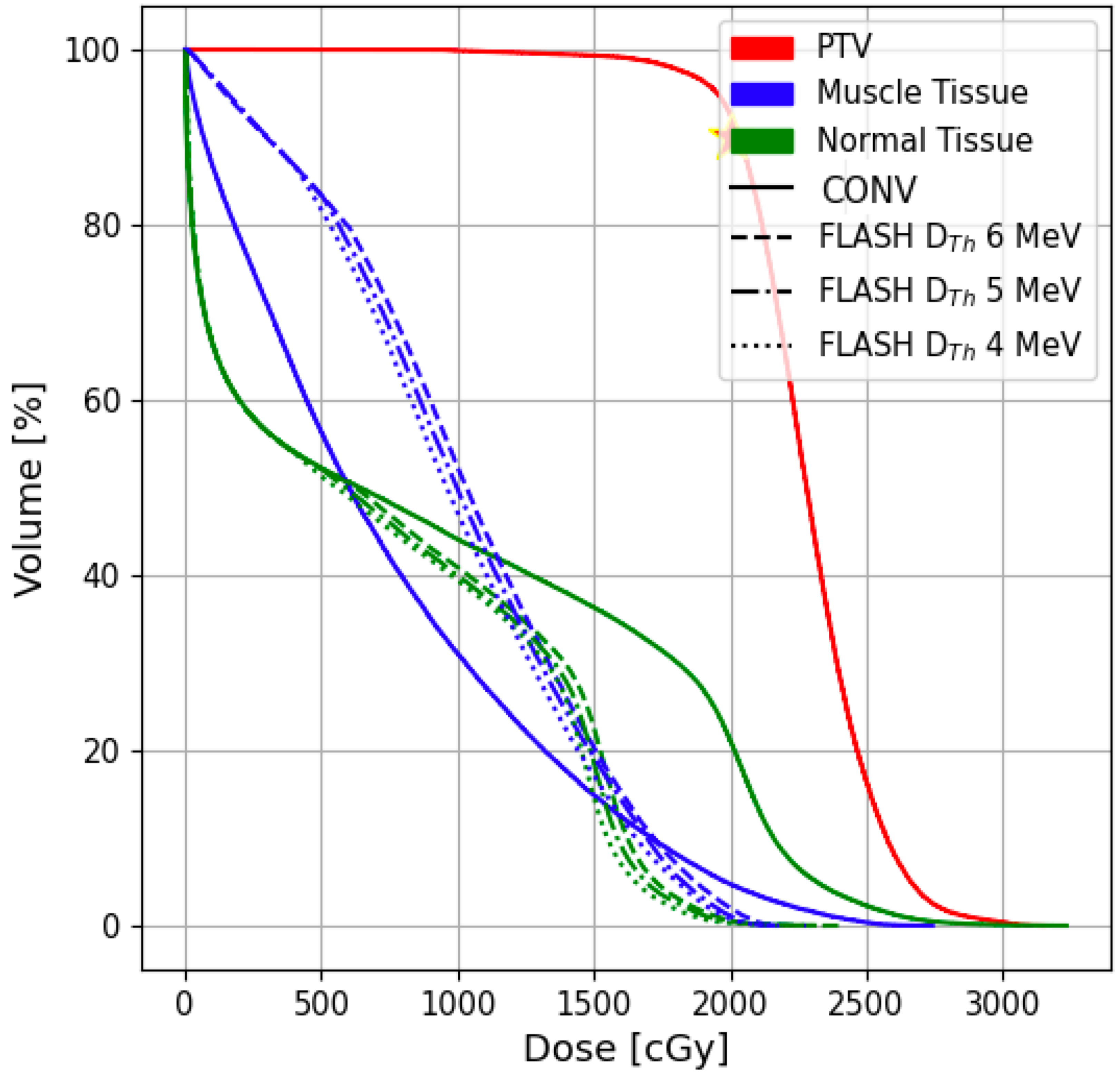


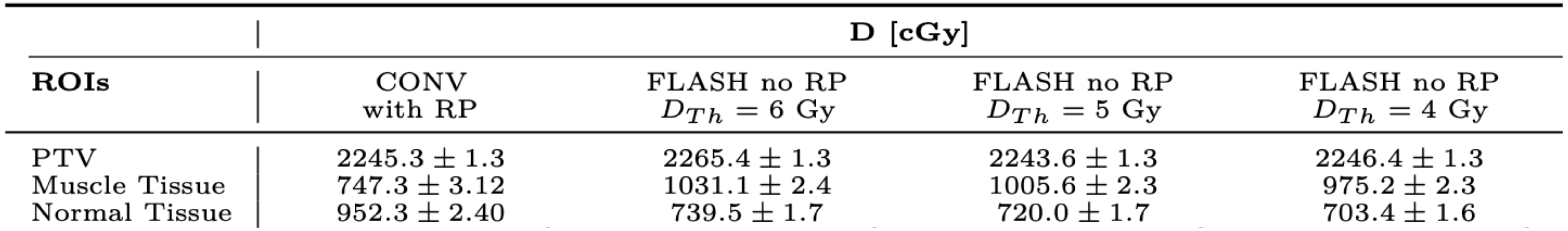
RP disc impact

	D [cGy]	
ROIs	RP disc	No RP disc
PTV	2245.3 ± 1.3	2234.2 ± 1.3
Muscle Tissue	747.3 ± 2.9	1269.5 ± 3.4
Normal Tissue	925.3 ± 2.2	928.7 ± 2.3



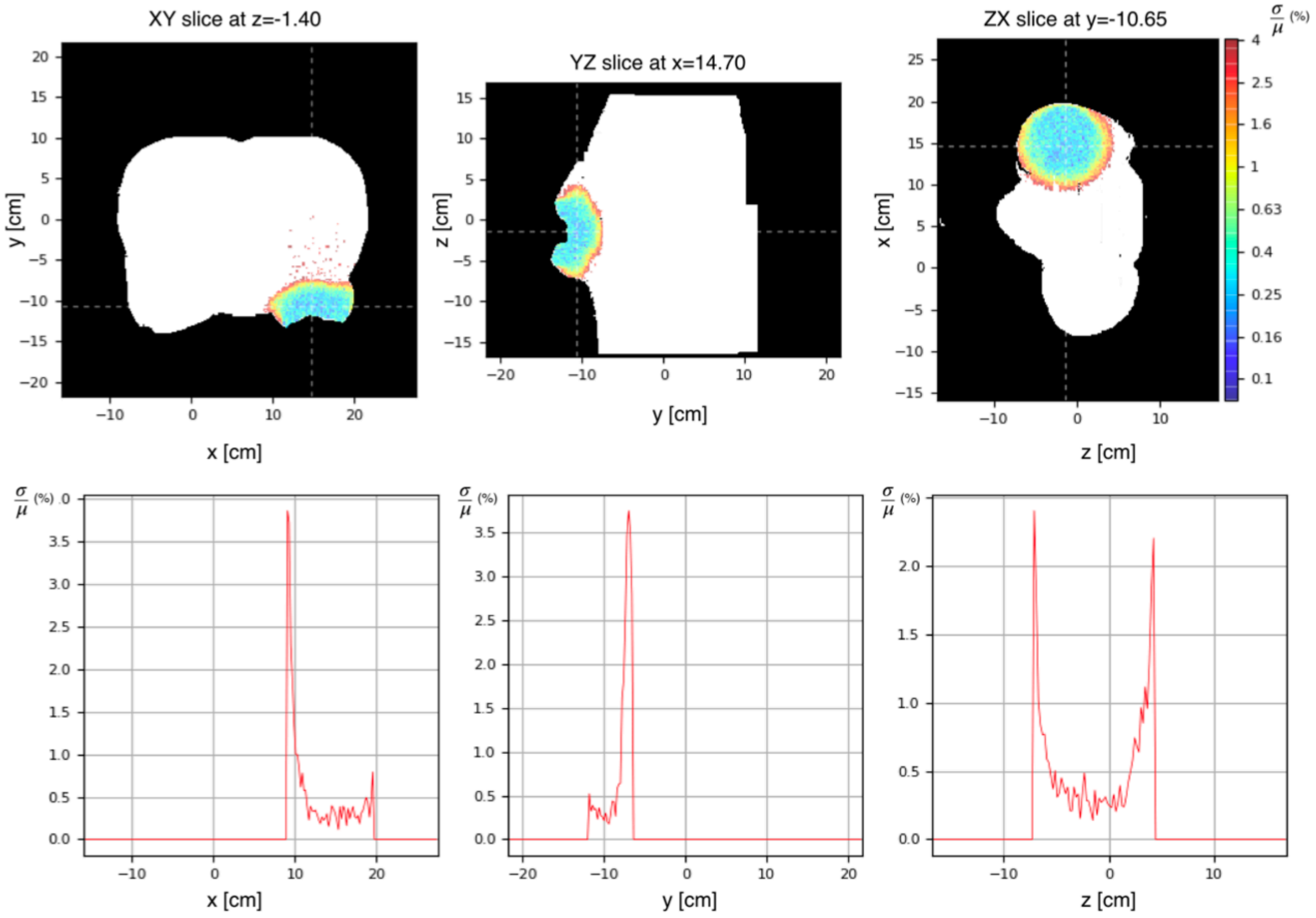
Minimally invasive surgery IOeRT-FLASH treatment





	D [cGy]			
ROIs	CONV with RP	FLASH no RP $D_{Th} = 6$ Gy	FLASH no RP $D_{Th} = 5$ Gy	FLASH no RP $D_{Th} = 4$ Gy
PTV	2245.3 ± 1.3	2265.4 ± 1.3	2243.6 ± 1.3	2246.4 ± 1.3
Muscle Tissue	747.3 ± 3.12	1031.1 ± 2.4	1005.6 ± 2.3	975.2 ± 2.3
Normal Tissue	952.3 ± 2.40	739.5 ± 1.7	720.0 ± 1.7	703.4 ± 1.6

Dose report


XY slice at z=-1.40
y [cm]
x [cm]
YZ slice at x=14.70
z [cm]
y [cm]
ZX slice at y=-10.65
x [cm]
z [cm]
$\frac{\sigma}{\mu}$ (%)
4
2.5
1.6
1
0.63
0.4
0.25
0.16
0.1
$\frac{\sigma}{\mu}$ (%)
x [cm]
$\frac{\sigma}{\mu}$ (%)
y [cm]
$\frac{\sigma}{\mu}$ (%)
z [cm]