Development of a Treatment Control System for IORT-FLASH treatment

XIX Seminar on Software for Nuclear, Subnuclear and Applied Physics
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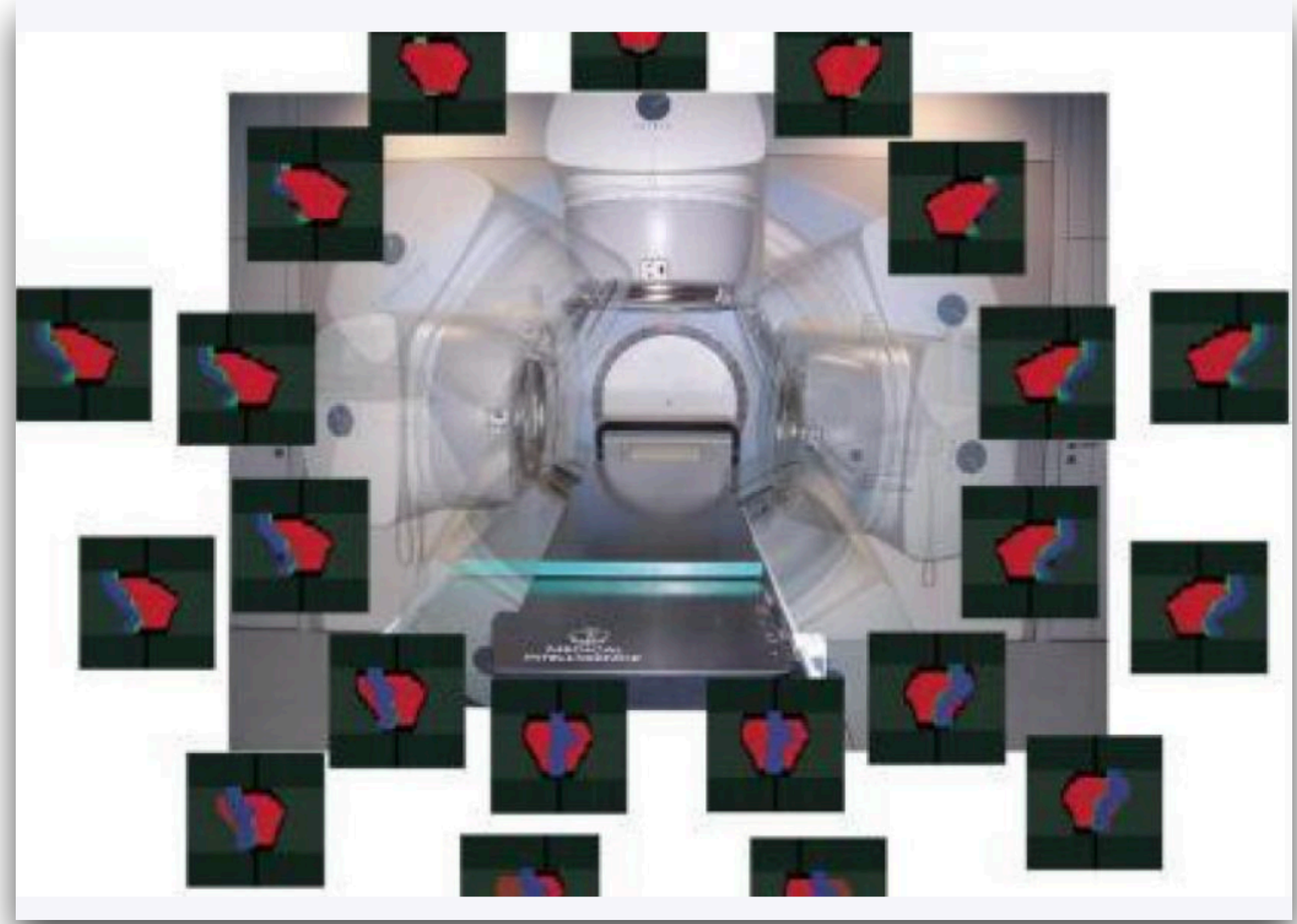
Why we need a Treatment Planning?

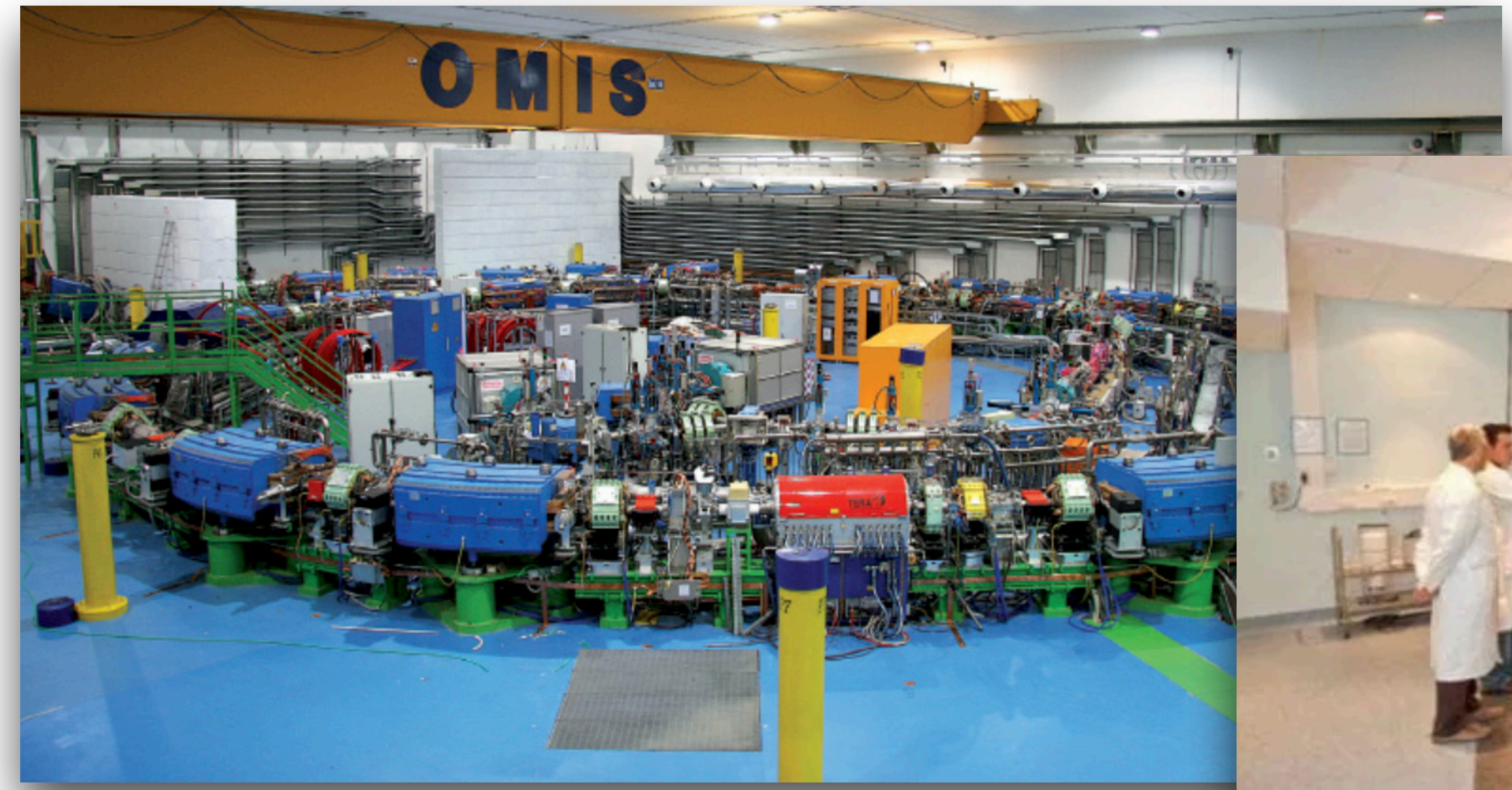
Advanced radiotherapy techniques use **complex beam delivery systems** in order to obtain:

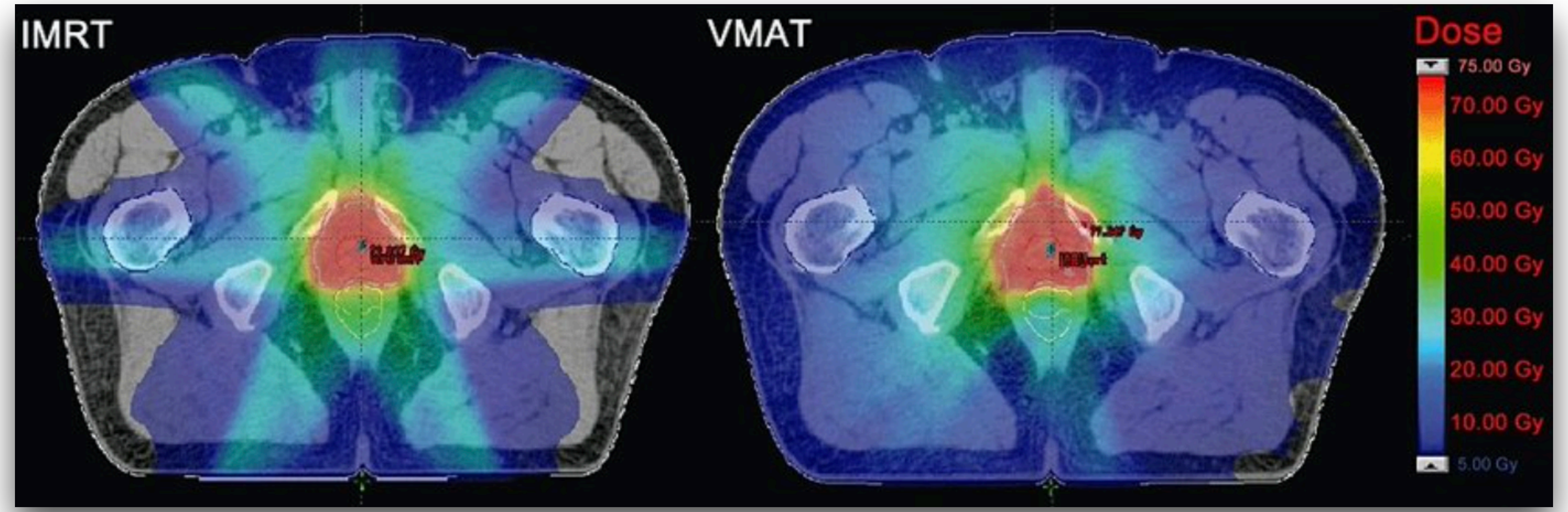
1. **high tumor control probability**
2. **reduced normal tissue complication rate**.

A perfect beam management and an accelerator control system of absolute precision are thus required.

A Treatment Planning, which has to provide to the accelerator control system the position, intensity and direction of the beams is thus crucial to achieve the patient therapeutic need







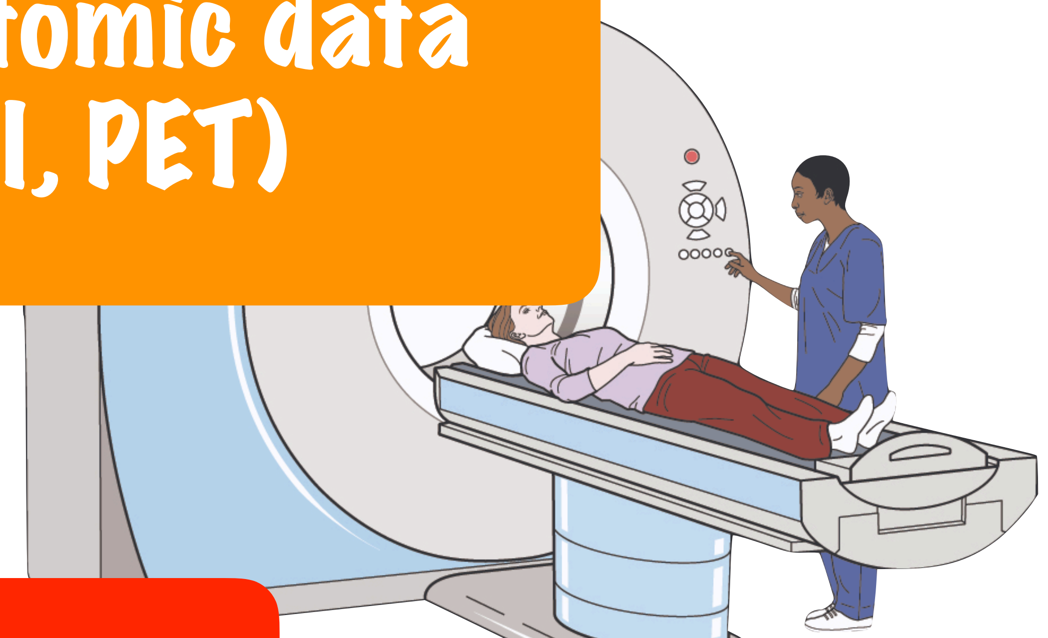
Treatment Planning System

The Treatement 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 optimise the dose distribution to the patient. In radio-particle therapy it can be analytic or Monte Carlo driven.

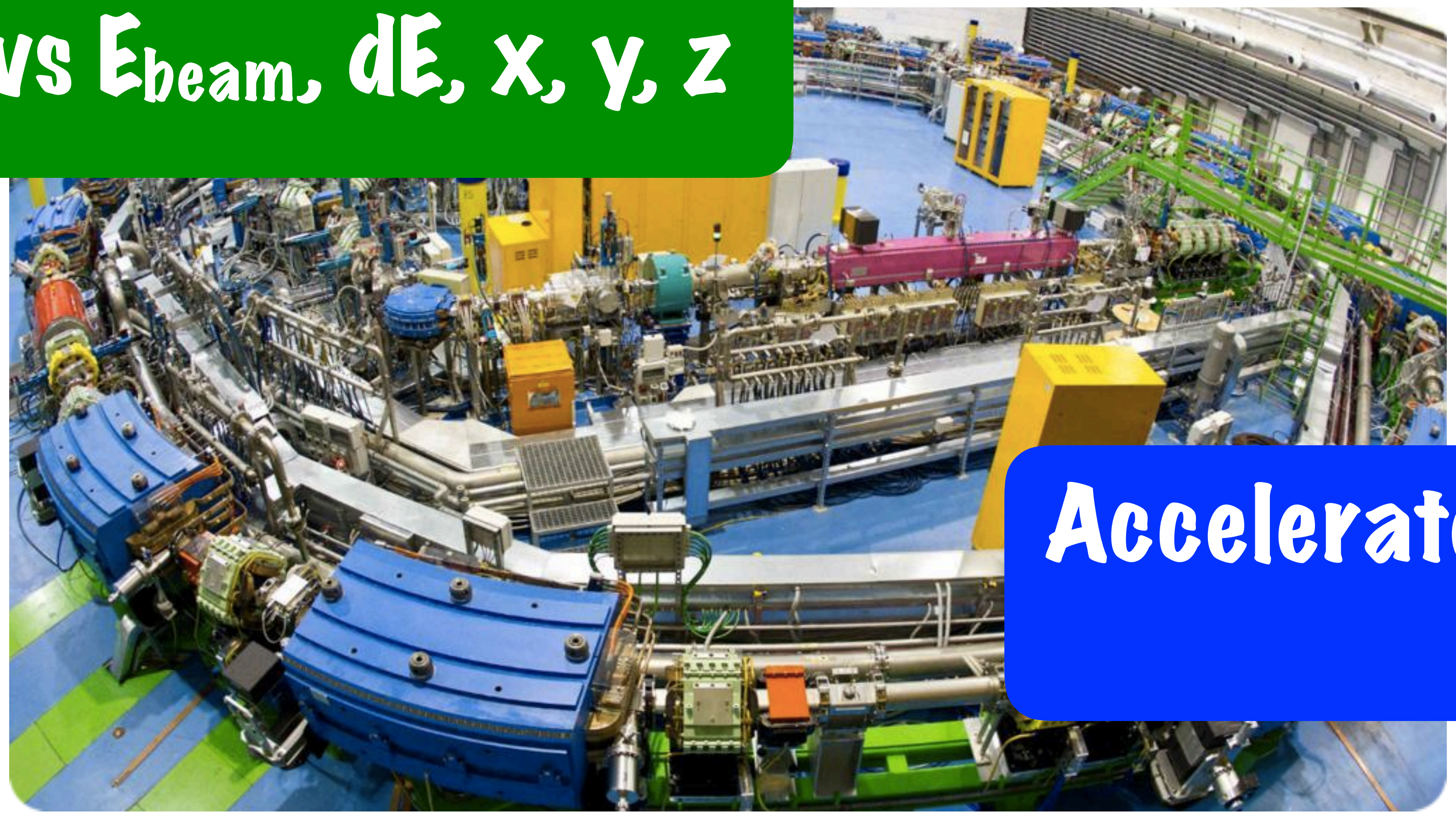
(required) Kinetic Energy (MeV)	Stopping Power (MeV cm^2/g)			Range		
	Electronic	Nuclear	Total	CSDA (g/cm^2)	Projected (g/cm^2)	Detour Factor Projected / CSDA
1.000E-03	1.337E+02	4.315E+01	1.769E+02	6.319E-06	2.878E-06	0.4555
1.500E-03	1.638E+02	3.460E+01	1.984E+02	8.969E-06	4.400E-06	0.4906
2.000E-03	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	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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



Accelerators Parameters: Fluences for each beam spot

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

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

Physician Prescription

			elative portance
Prostate PTV	100	74.0	1.0
Prostate PTV	5.0	72.0	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

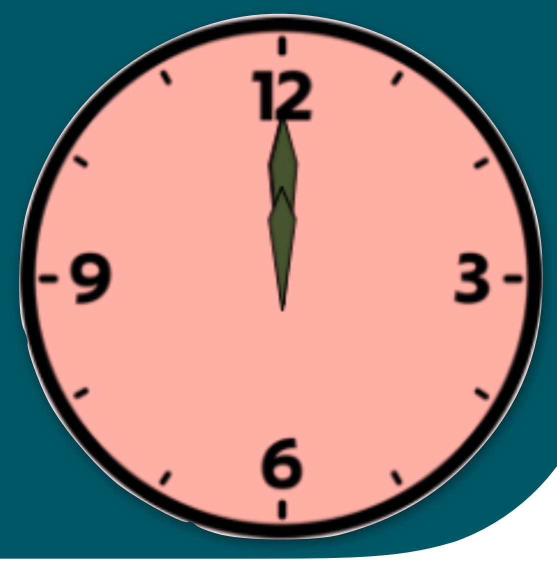
Dose kernel

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**

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**



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**

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Ex. Proton TPS
~ 1 h/core

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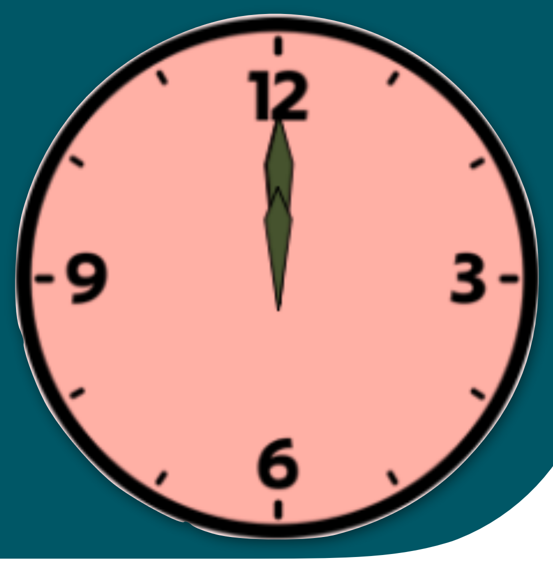
Ex. Proton TPS
~ days/core



FAST MONTE CARLO

- High accuracy in the description of the transport and of the interaction of particles with matter
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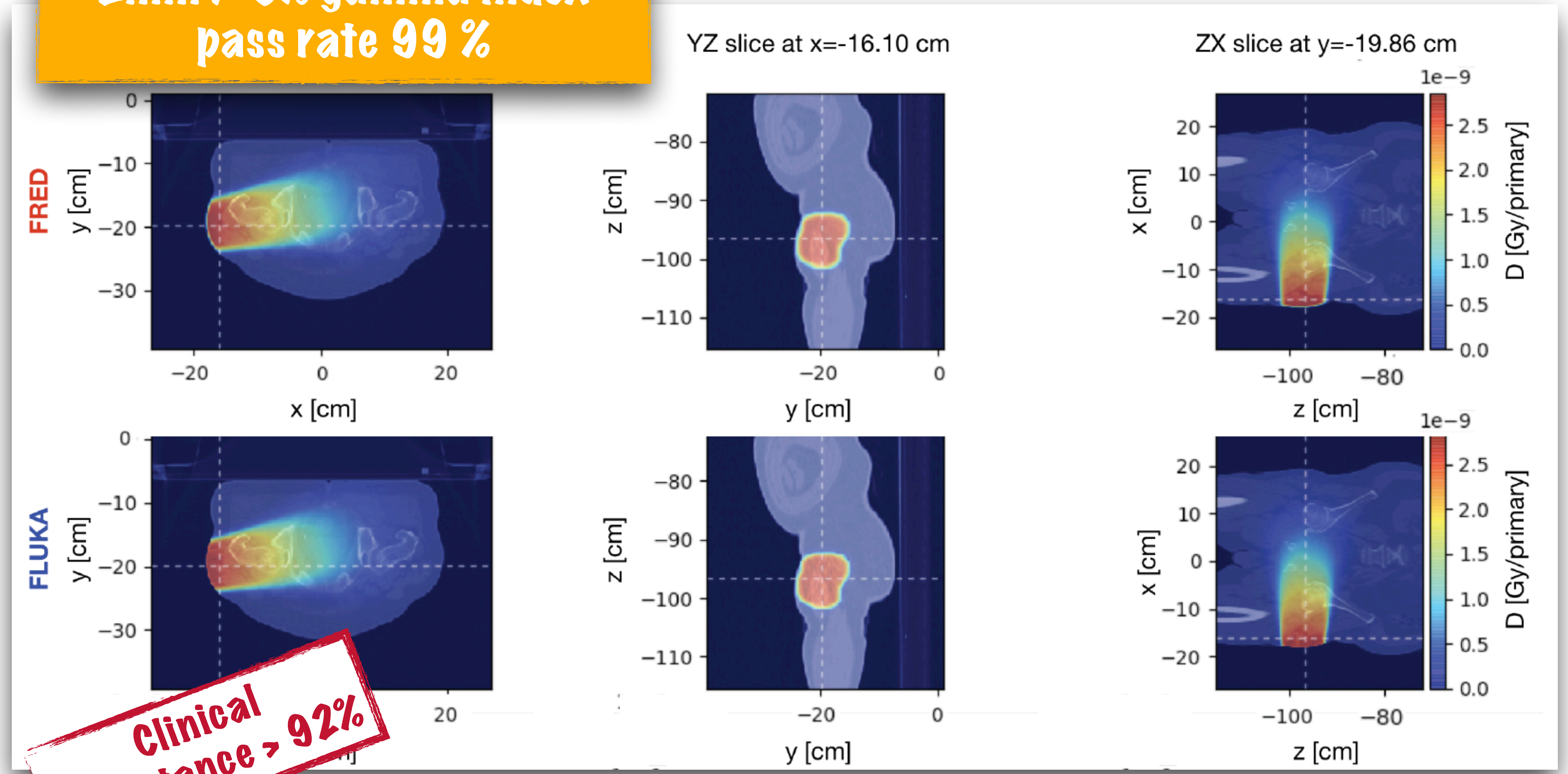
Ex. Proton TPS
~ minutes

Fast paRticle thErapy Dose evaluator (FRED)

The FRED MC has been developed to allow a **fast optimization of the TPS** in Particle Therapy, while keeping the **dose release accuracy typical of a MC tool**. Today **FRED protons** is used in various medical and research centers such as MedAustron (Vienna), APSS (Trento), Maastro (Maastricht) and CNAO (Pavia) while the **carbon ions** and **electromagnetic** models for FRED are under optimization.

2mm / 3% gamma index pass rate 99 %



Clinical acceptance > 92%

70 MeV e- on abdomen/pelvis CT scan

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.

Timing Performance in water	FLUKA	FRED
e^- @ 1 MeV	5.1e3 prim/s	3.3e6 prim/s
e^- @ 10 MeV	1.2e3 prim/s	3.5e5 prim/s
e^- @ 100 MeV	4.0e2 prim/s	3.2e4 prim/s

~ x1000

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

IOeRT Technique

The Intra Operative Radio Therapy with electron (IOeRT) is a technique that, after the surgical tumour removal, delivers a dose of ionising radiation directly to the surgery bed [1]. The goal is to eradicate the microscopic residual tumour cells that surgery was not able to remove completely.

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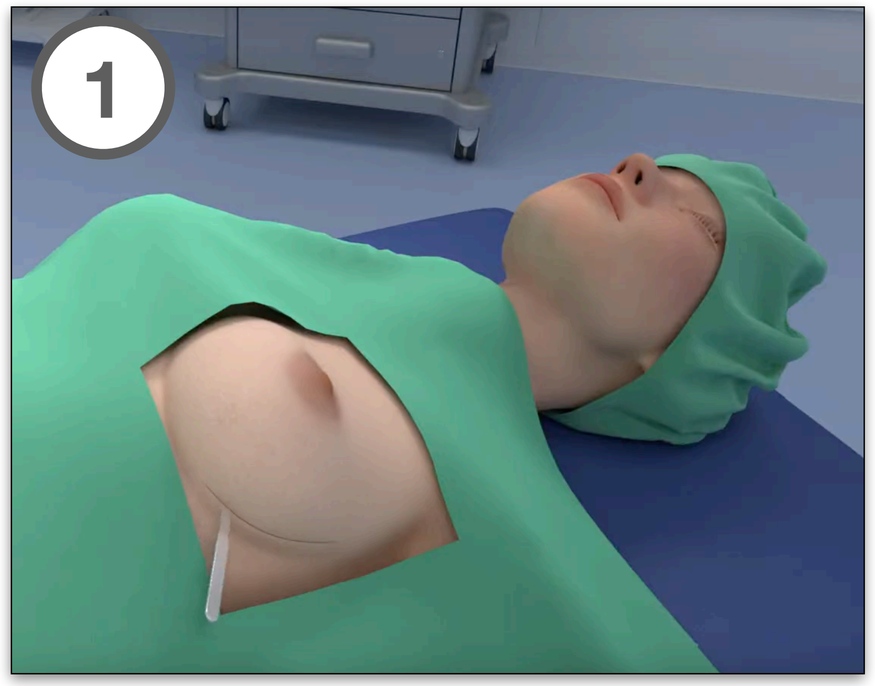

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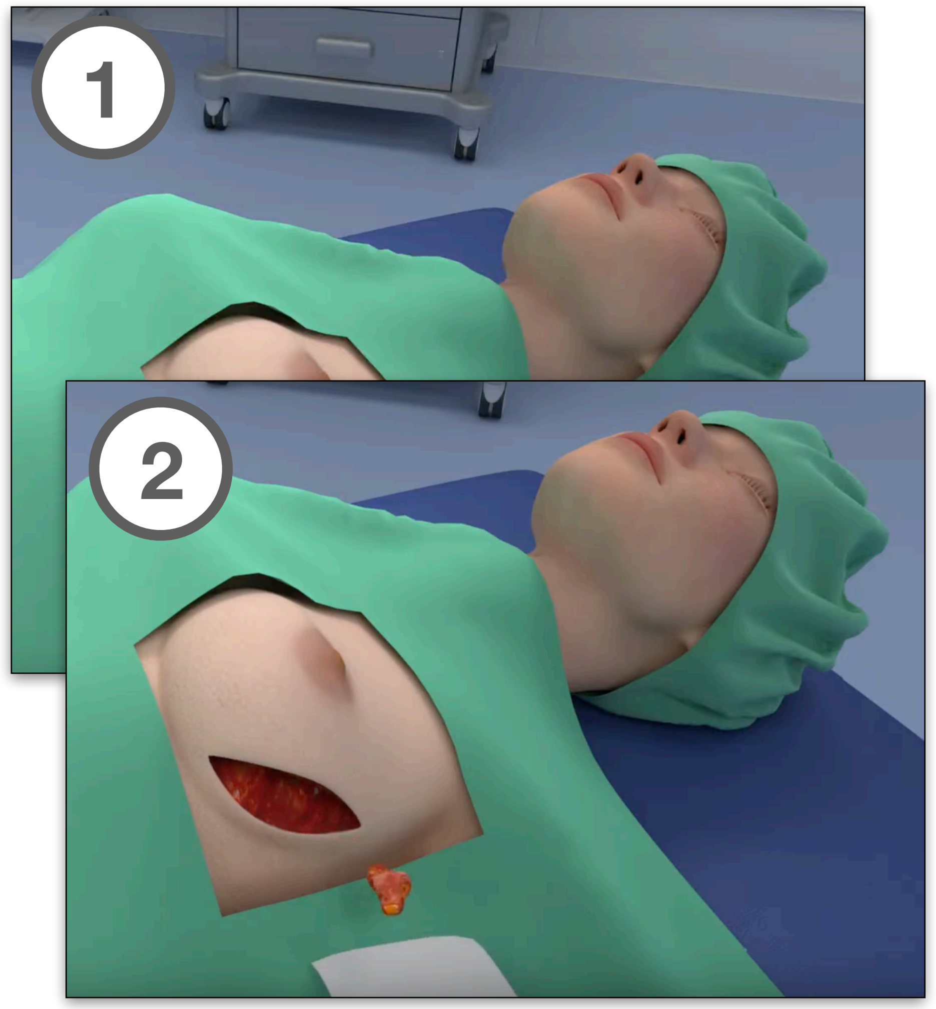

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A **protective disk** is applied in order to preserve the organs from the undesired dose. The **thickness** of the target volume is identified by means of a **needle** and thus the electron **beam energy** is chosen.

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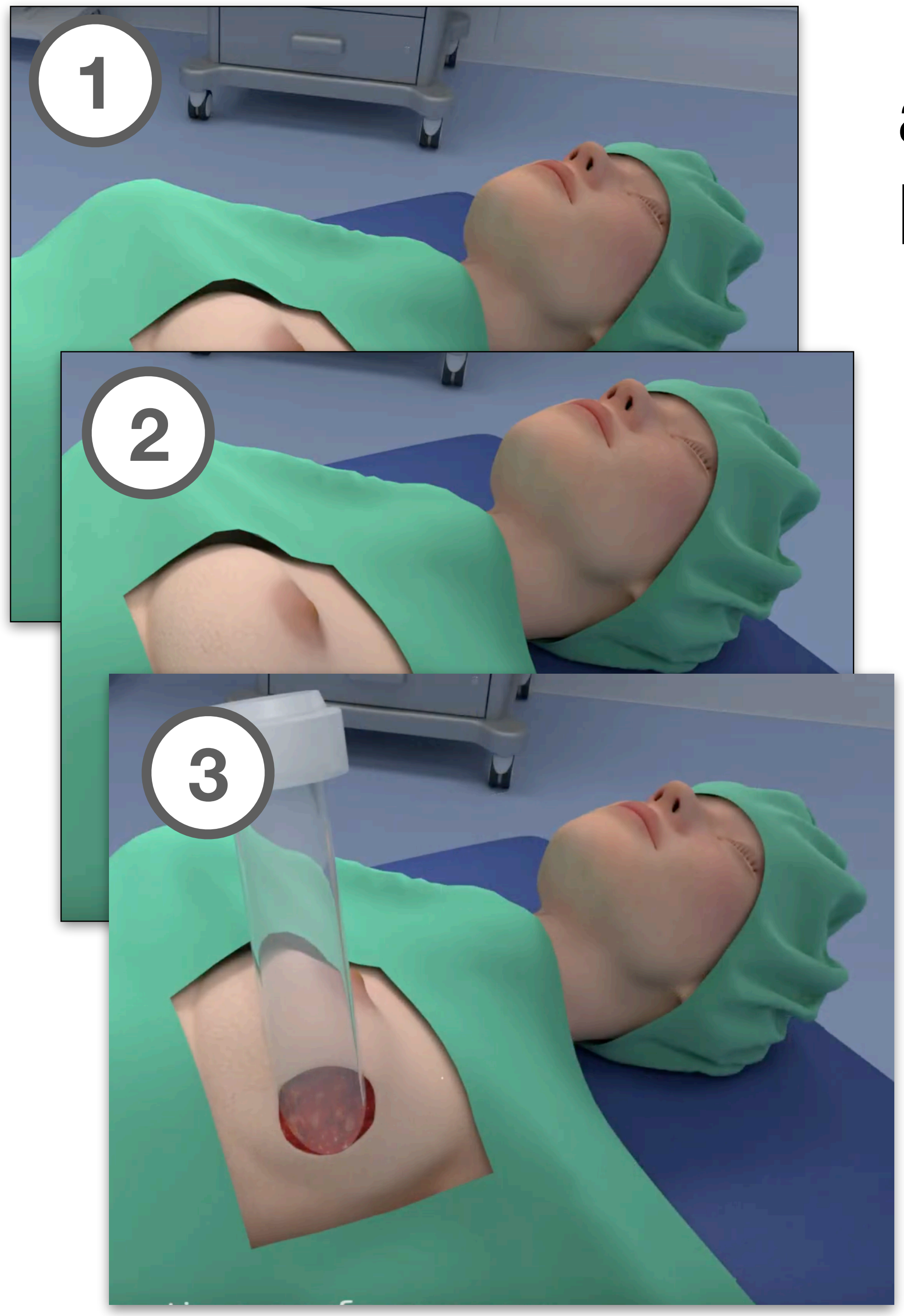

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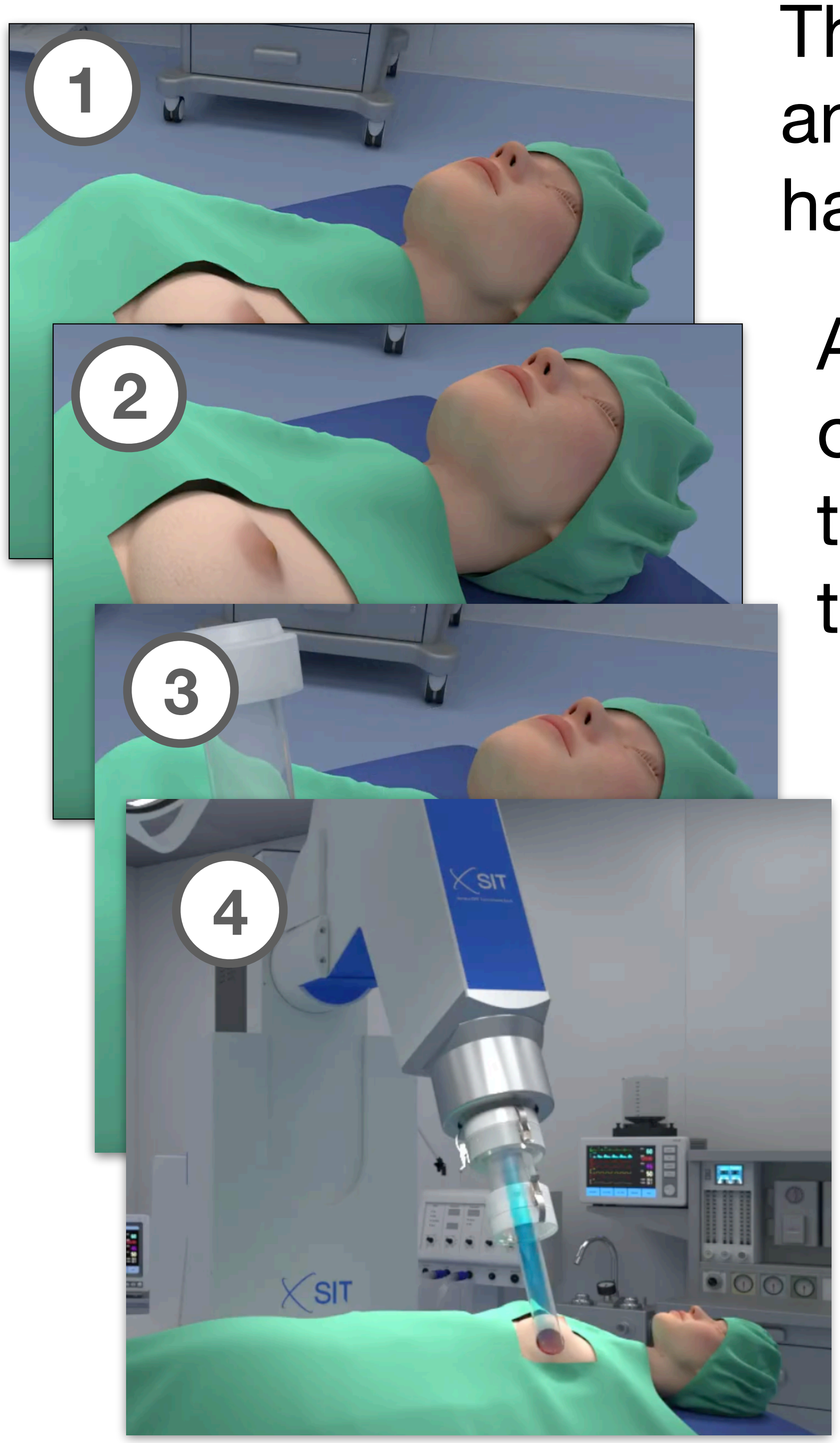

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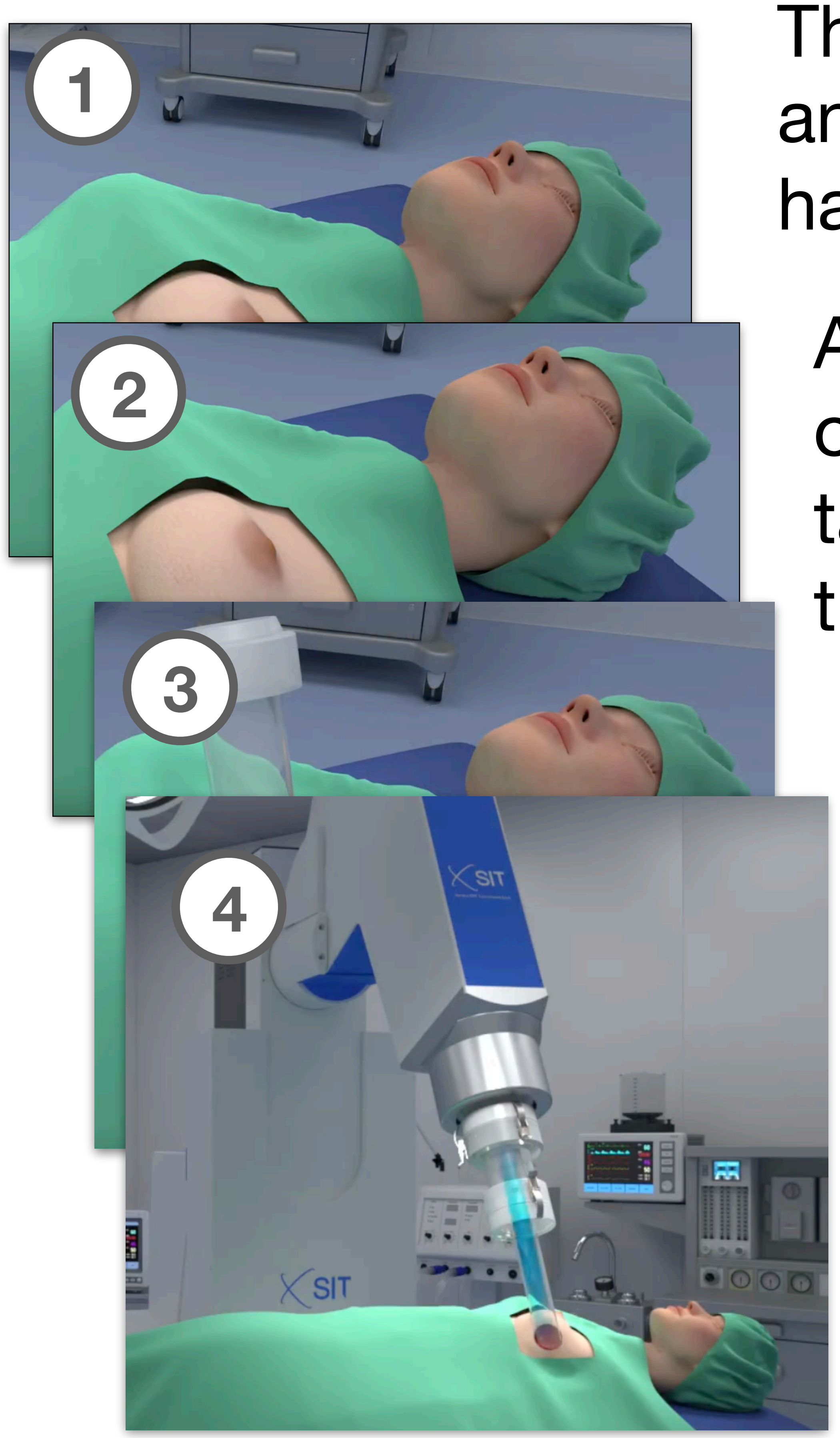

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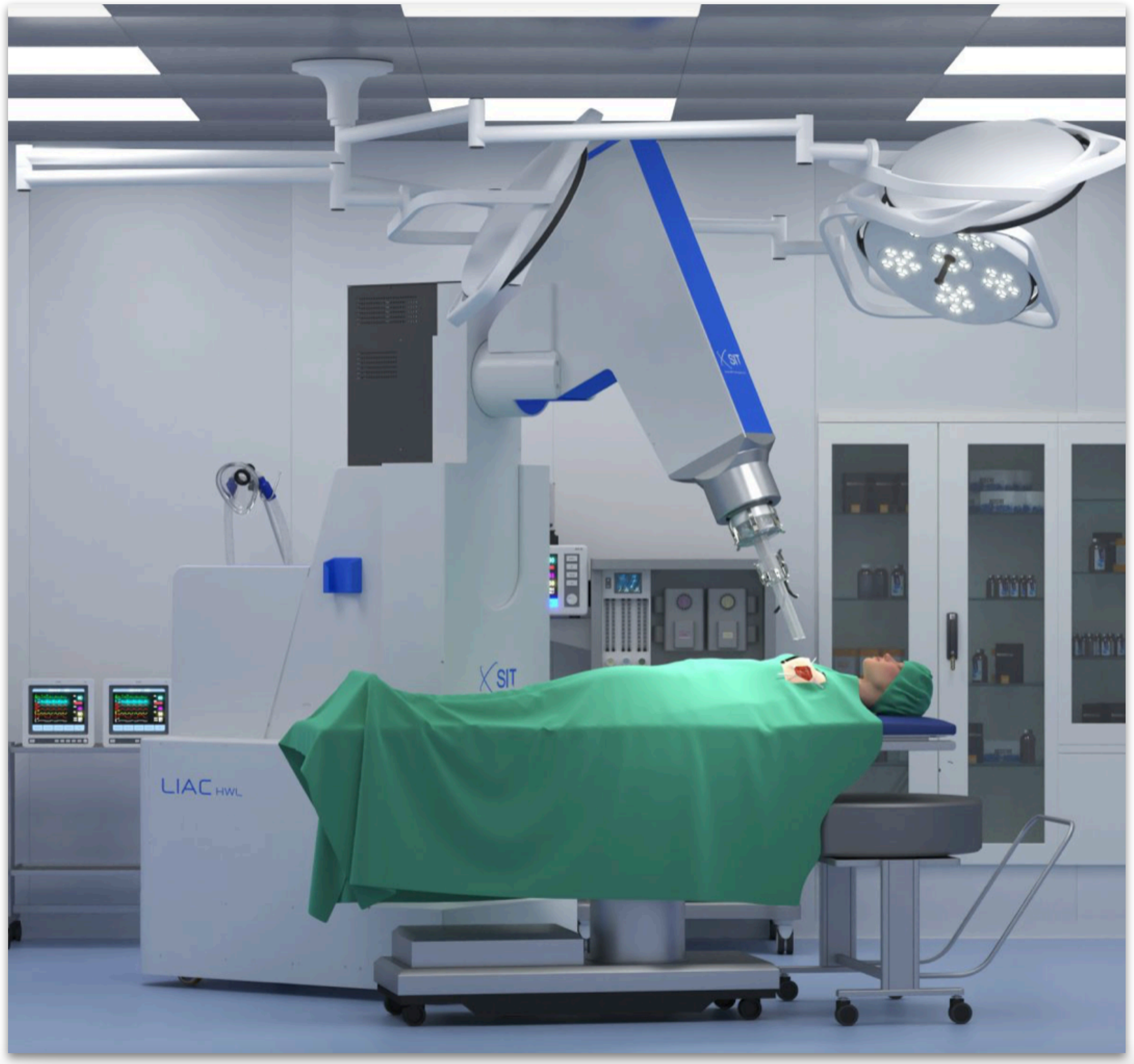


No time to obtain a new patient imagine and go through the Treatment Planning System

Why do we need a IORT planning?

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

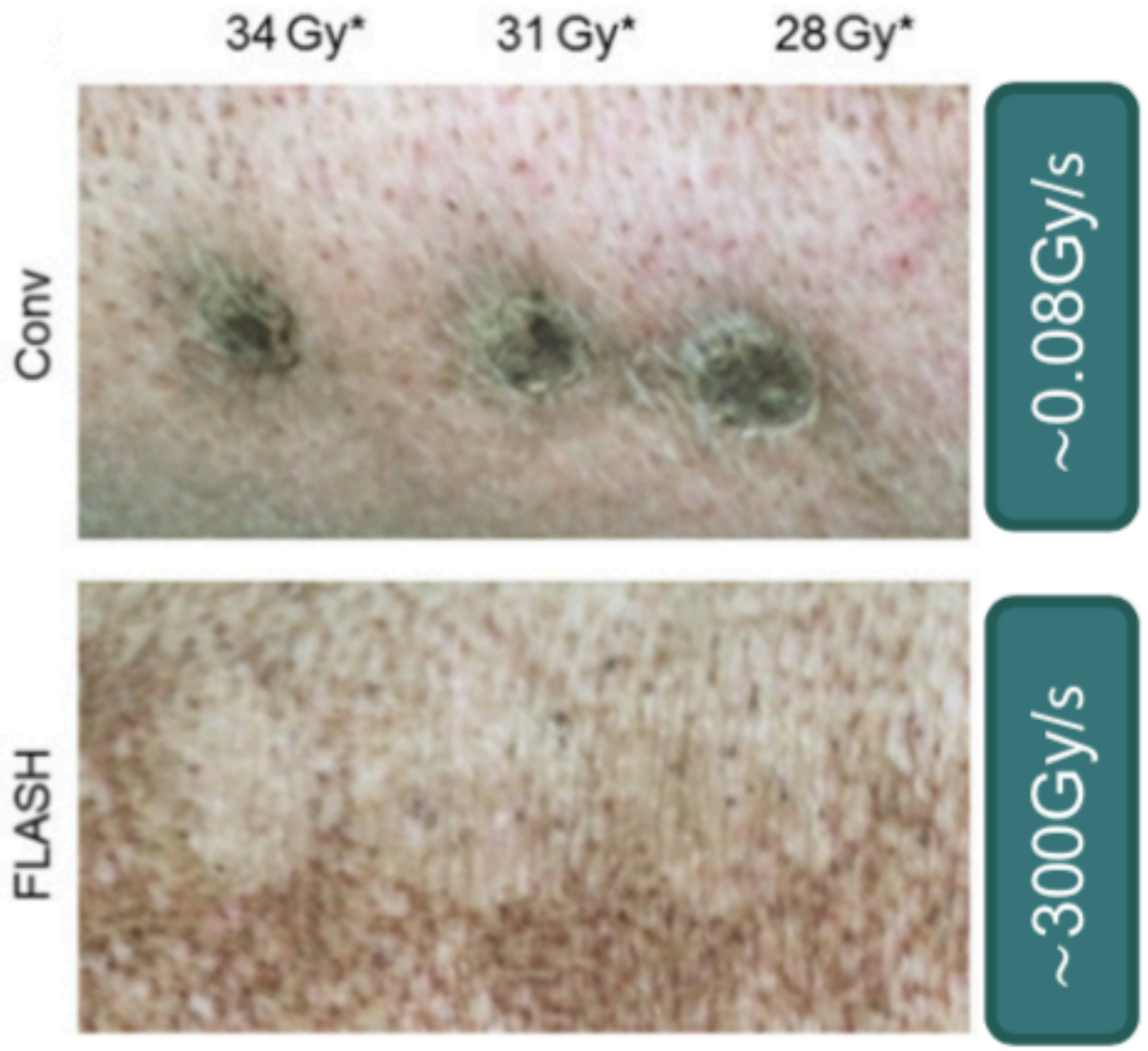
- **FLASH effect**

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 (~**100 Gy/s**, or even more) with respect to conventional treatments (~**0.01 Gy/s**).

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

Flash Effect

Test on animals



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

First FLASH human treatment

Today the use of mono-energetic high intensity pulses of electrons (mean dose rate ~ 0.5 Gy/s) makes IORT the current best candidate for the first implementation of the **FLASH effect** into the clinic.

IORT planning

Timing is an issue

1. **Quick imaging** after surgery;

2. **Quick planning:** 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

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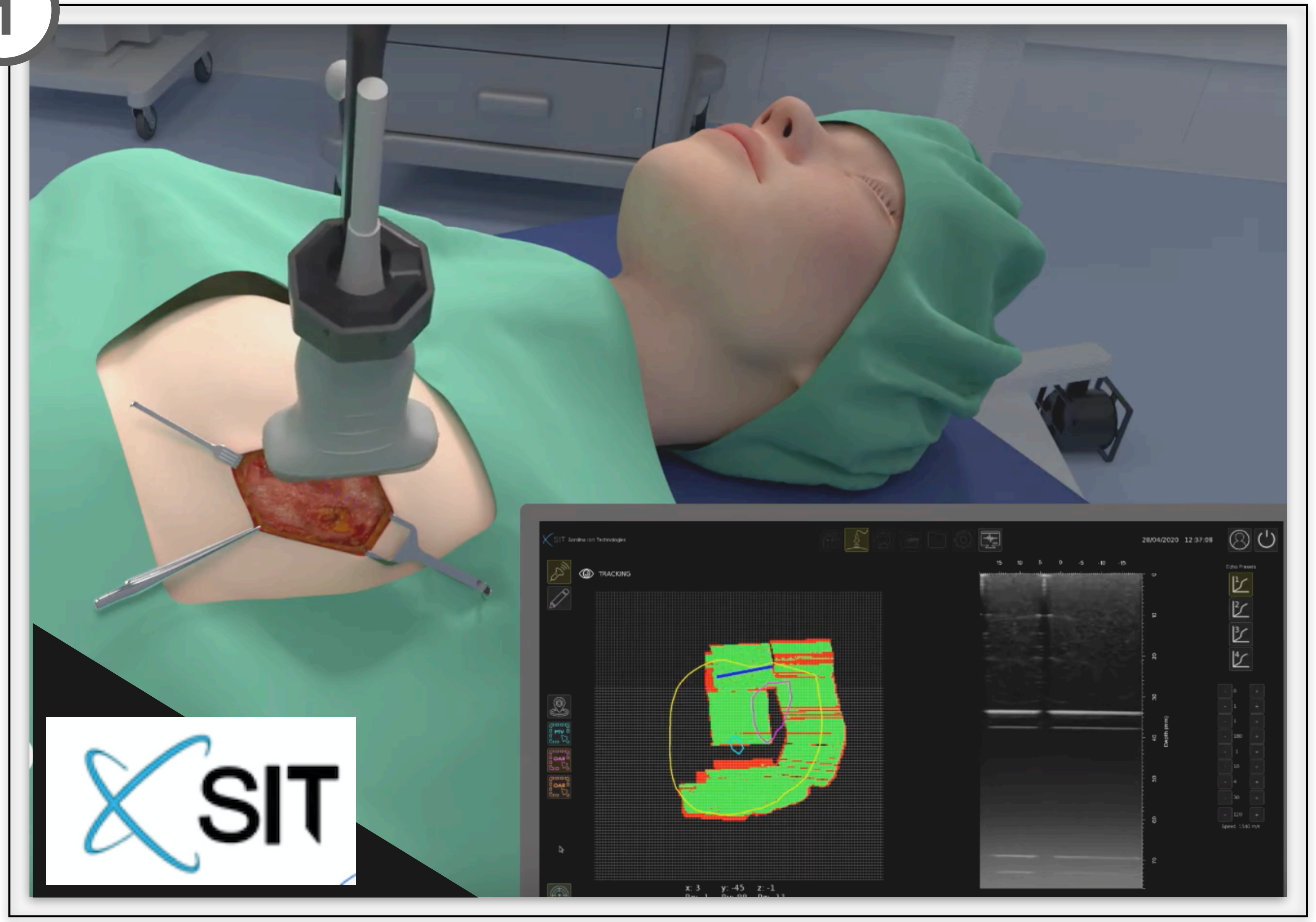


1. The SIT company (Aprilia, Italy) is exploiting a new **3D real-time echographic** imaging acquisition with limited precision (capable of discriminating only significant differences in density - air, water, metal)

2. **Quick planning:** 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

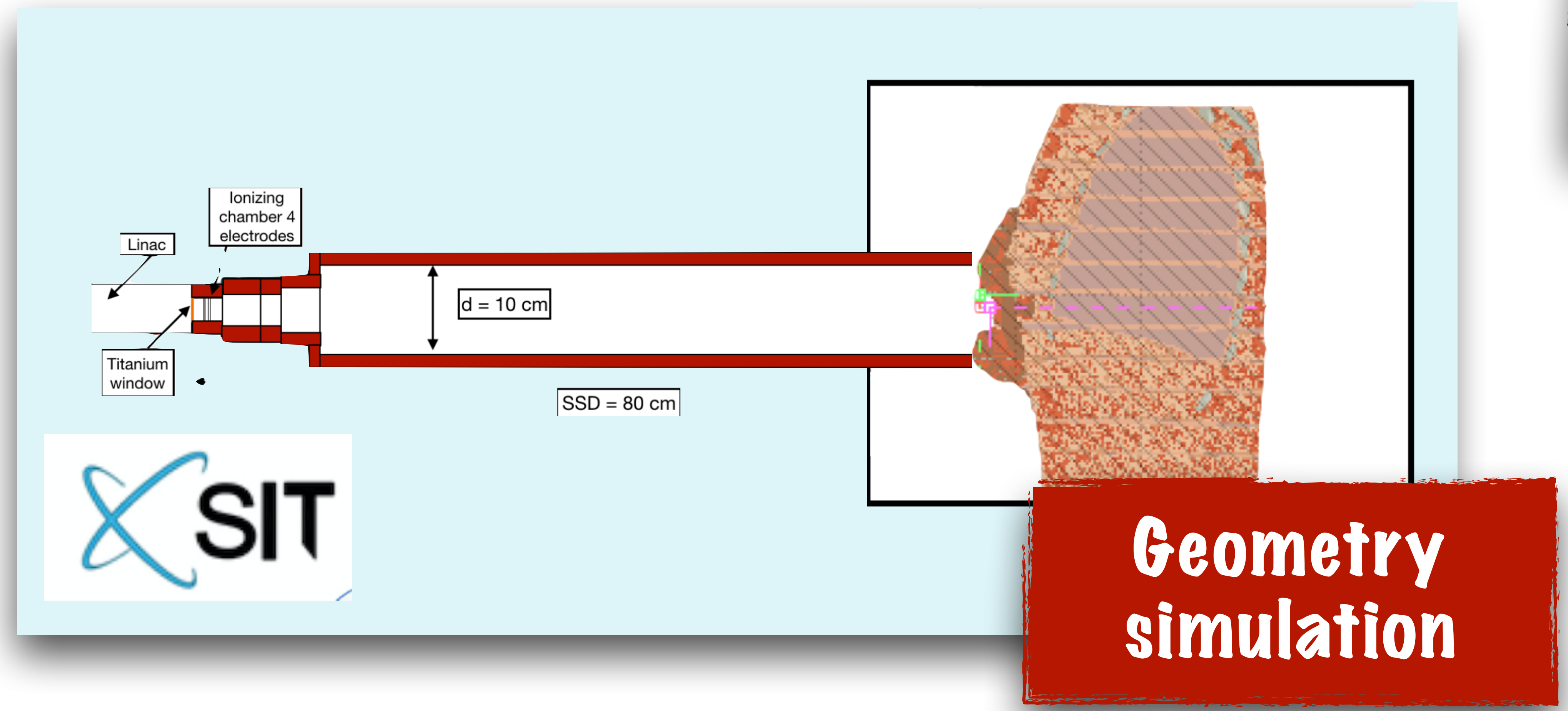
2. A full MC is needed and the GPU architecture can be exploited to speed up the planning

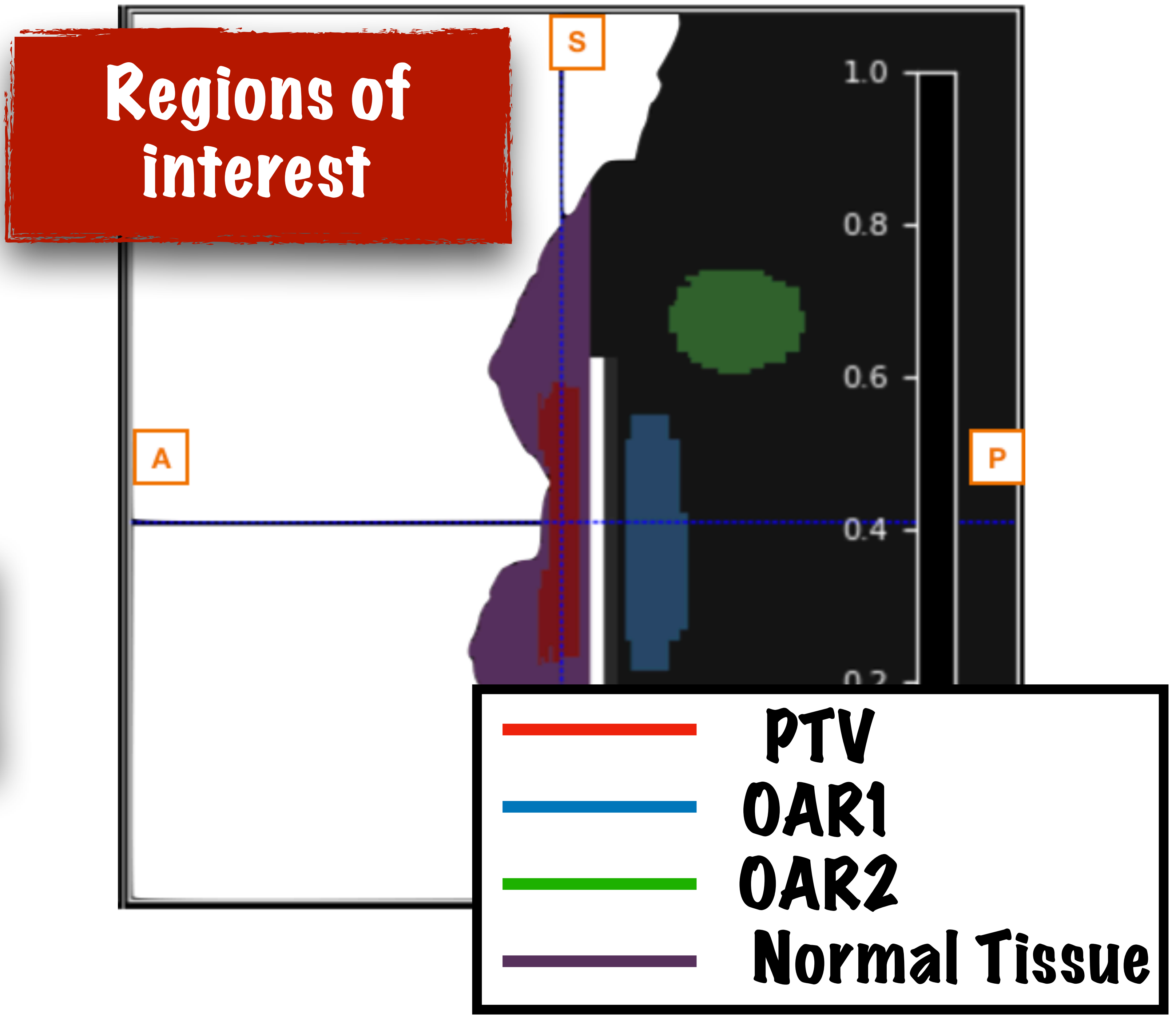
FRED

Breast cancer TPS

For the breast IORT treatment, we have used a CT of a phantom with a **breast prosthesis** used to simulate a breast surgery attached onto it and we have reproduced in detail the applicator structure of the NOVAC 11 accelerator, produced by the SIT company.

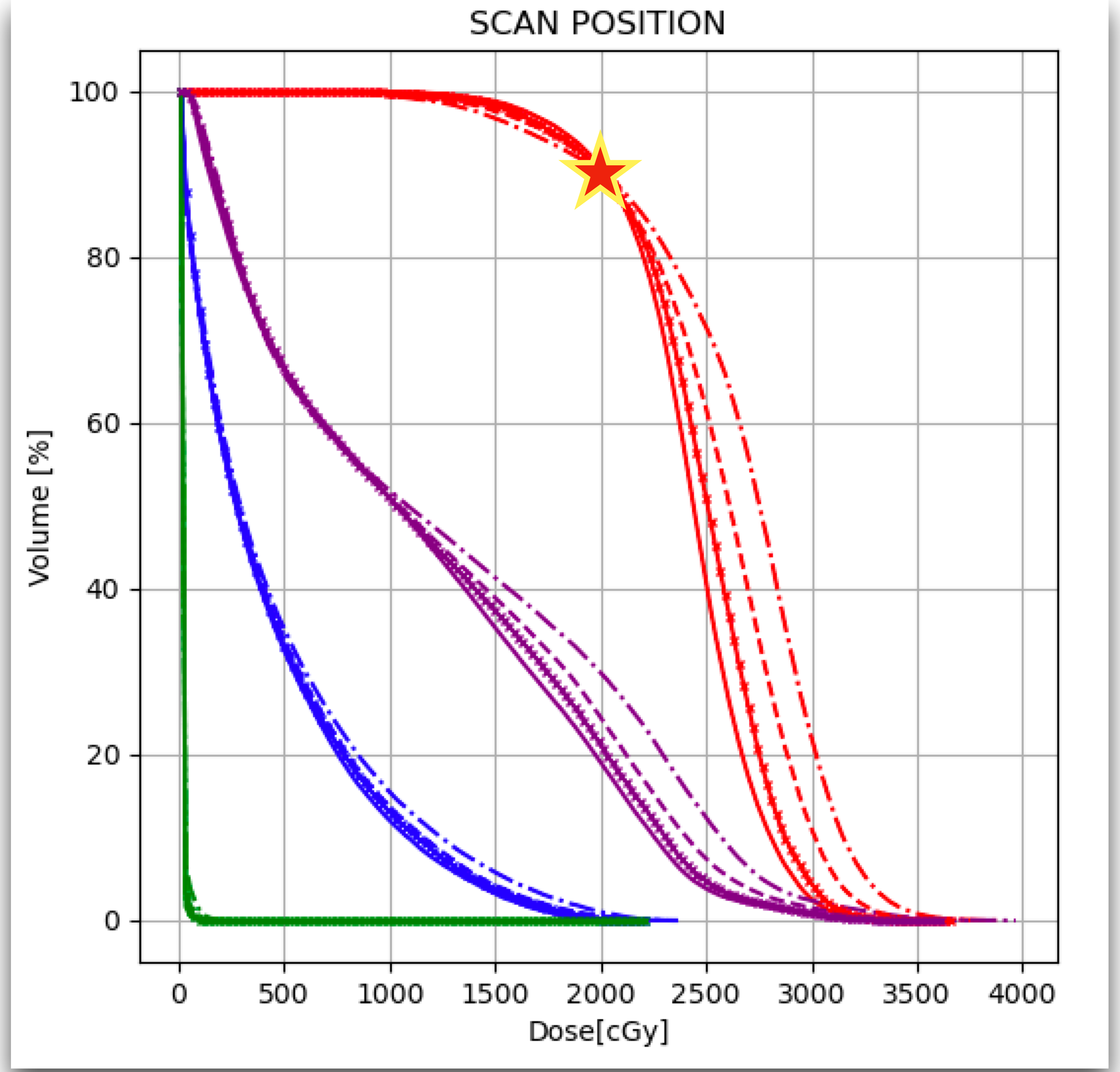
CT

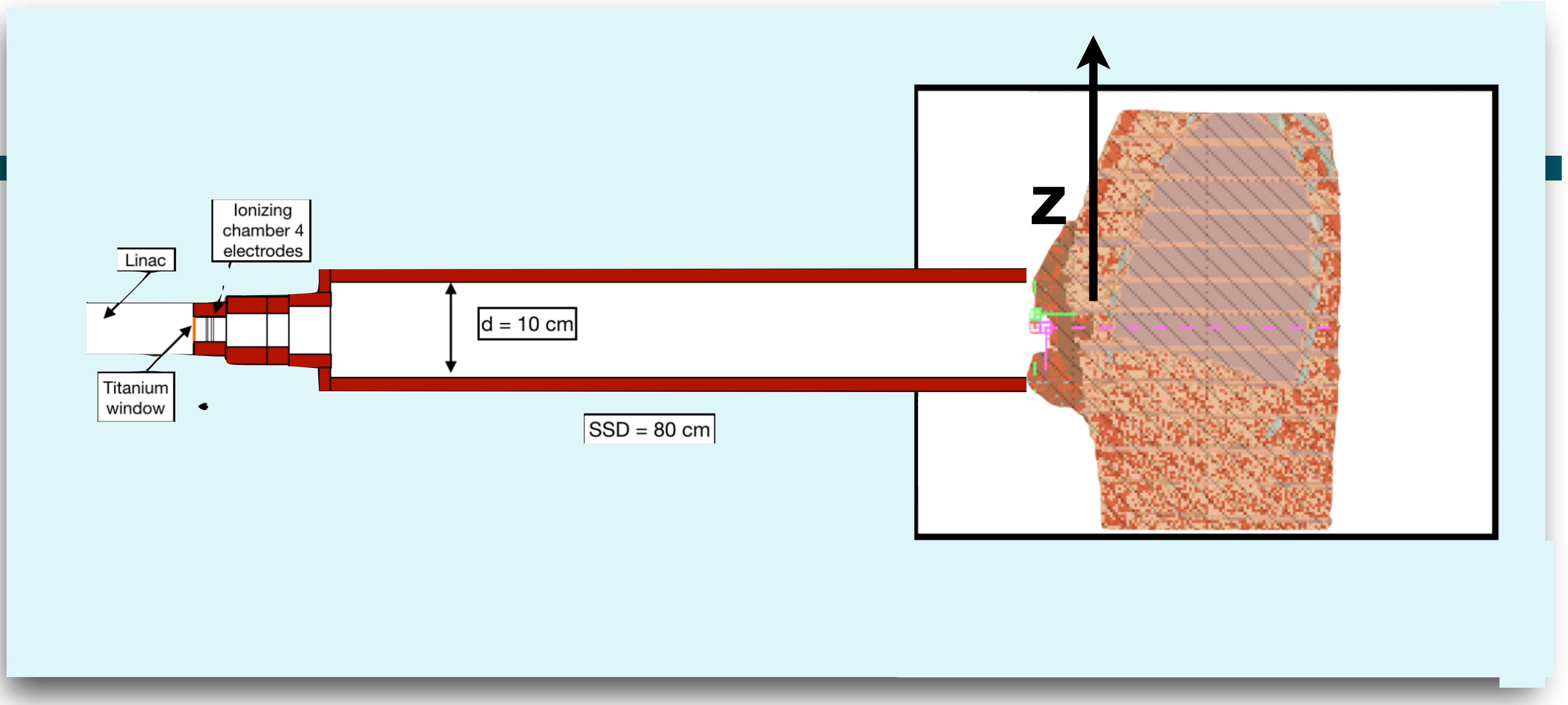




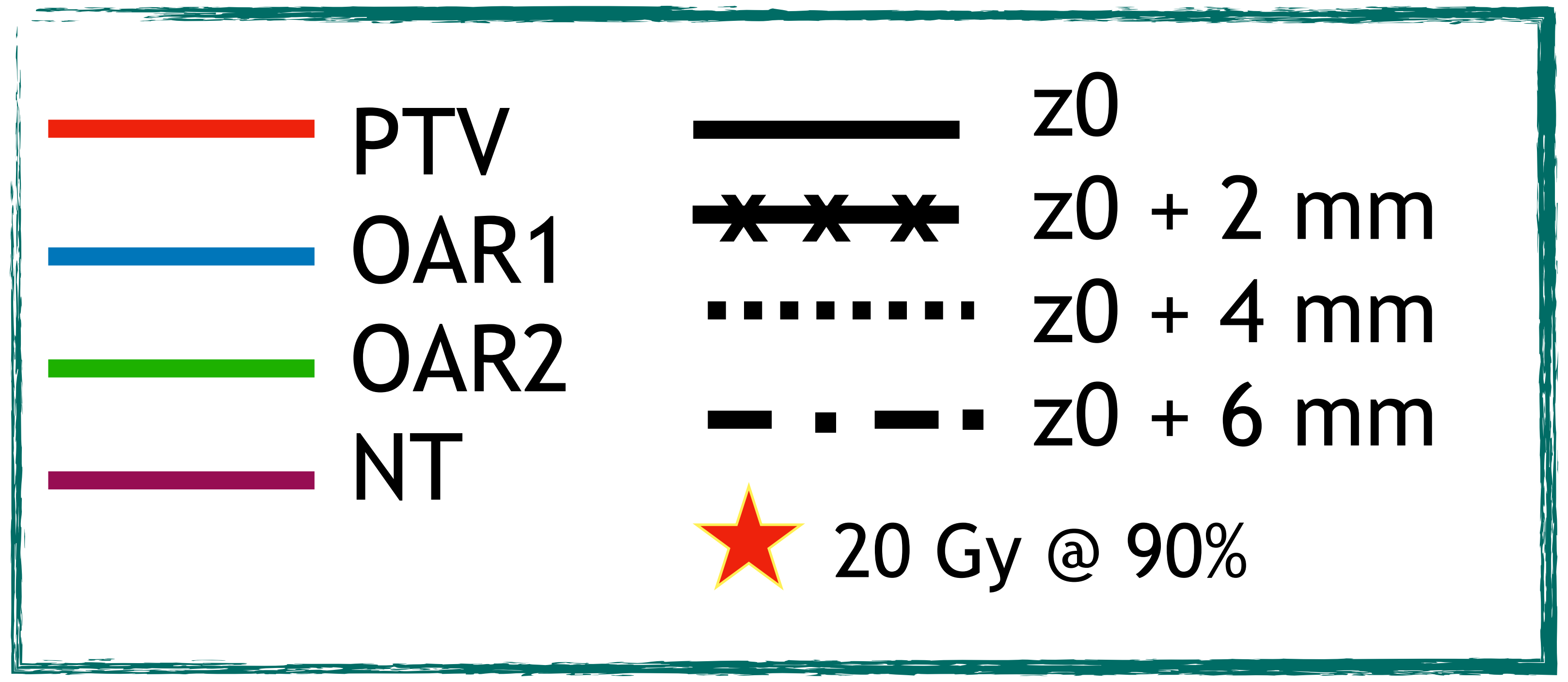
- We have inserted the **radioprotection disk**;
- We have identified a reasonable **PTV** (d ~ 6÷7 cm, 1 cm thick), two **OARs** and the **normal tissue**.
- For the optimization studies: we have shot **10^6 electrons** (several orders of magnitude below a full treatment), of different energies and with different applicator geometries and we have analysed the **resulting Dose Volume Histograms (DVHs)**.

Position scan





With an 8 MeV electrons beam and a d=70 mm applicator, we have performed a position scan, moving the applicator with 2 mm steps along the z-axis



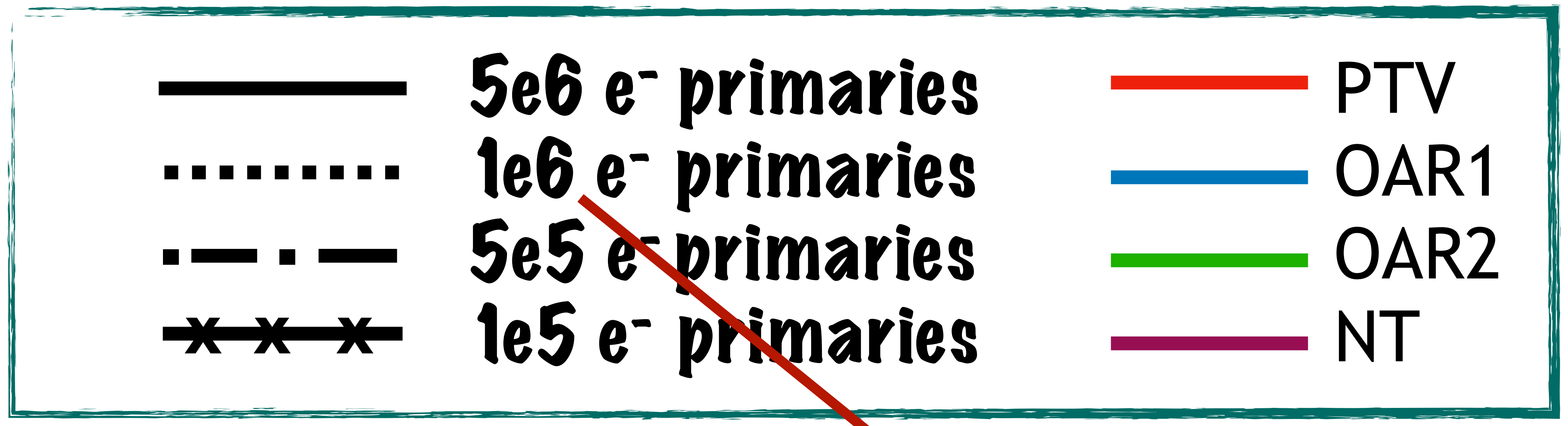
The impact of a 2mm position scan is clear both on the PTV and on the NT.

Needed statistics/GPU time

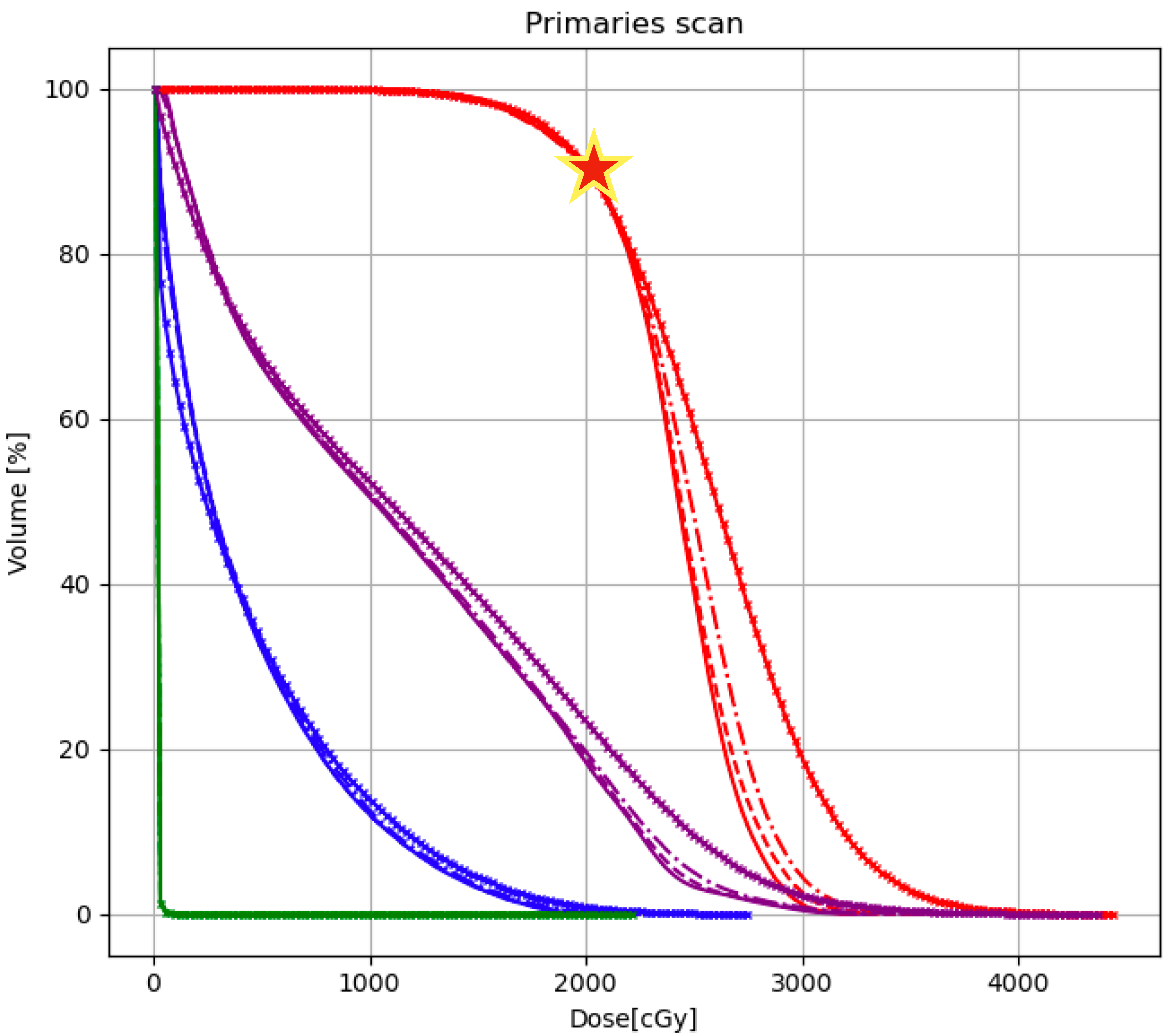
The DVHs depend not only on the "geometry considered", i.e. the volume of the PTV and OARs, but also on the simulation statistics.

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

Applicator with diameter = 70 mm
Beam energy 8 MeV



simulations takes only 10s



Conclusions and next steps

- During my PhD career I have developed from scratch a fast electromagnetic MC tool, FRED, capable of reproducing dose distributions in homogeneous and heterogeneous phantom with an accuracy at the level of state-of-art full MCs, and with an impressive timing performance.

- Using FRED I have developed an optimization tool which is able to produce with 10^6 primary electrons **robust and accurate IORT dose distributions** in about **10 seconds** that can be used for the treatment optimization. Ex: The simulation time for a preliminary IORT TPS, i.e. 3 different beam energy and for each energy 3 different applicator position, is ~ 1 minute; At the moment we need the **breast cancer specialists input** in order to progress with our study:

1. We need a more **realistic case**, i.e. a real ecographic input, a real PTV and real OARs.

2. Currently we don't have specified **dosimetric constraints.**

- Results shown so far have been obtained displaying the **physical dose**. However, the implementation of the biological dose, including the **flash effect**, will be straightforward once the DMF model will be available. We will explore the impact on the skin and in some internal organs (e.g. heart and lungs for breast cancer);

Thanks for your attention