Development of a VHEE accelerator in Sapienza for the treatment of deep seated tumors: planning and radioprotection challenges of a FLASH compact machine

Ph.D. in Accelerator Physics, XXXVII cycle
Department of Physics
Sapienza, University of Rome

Thesis Advisor: Prof. Alessio Sarti

Candidate: Angelica De Gregorio

Thesis Co-advisor: Prof. Vincenzo Patera

Radiation Therapy

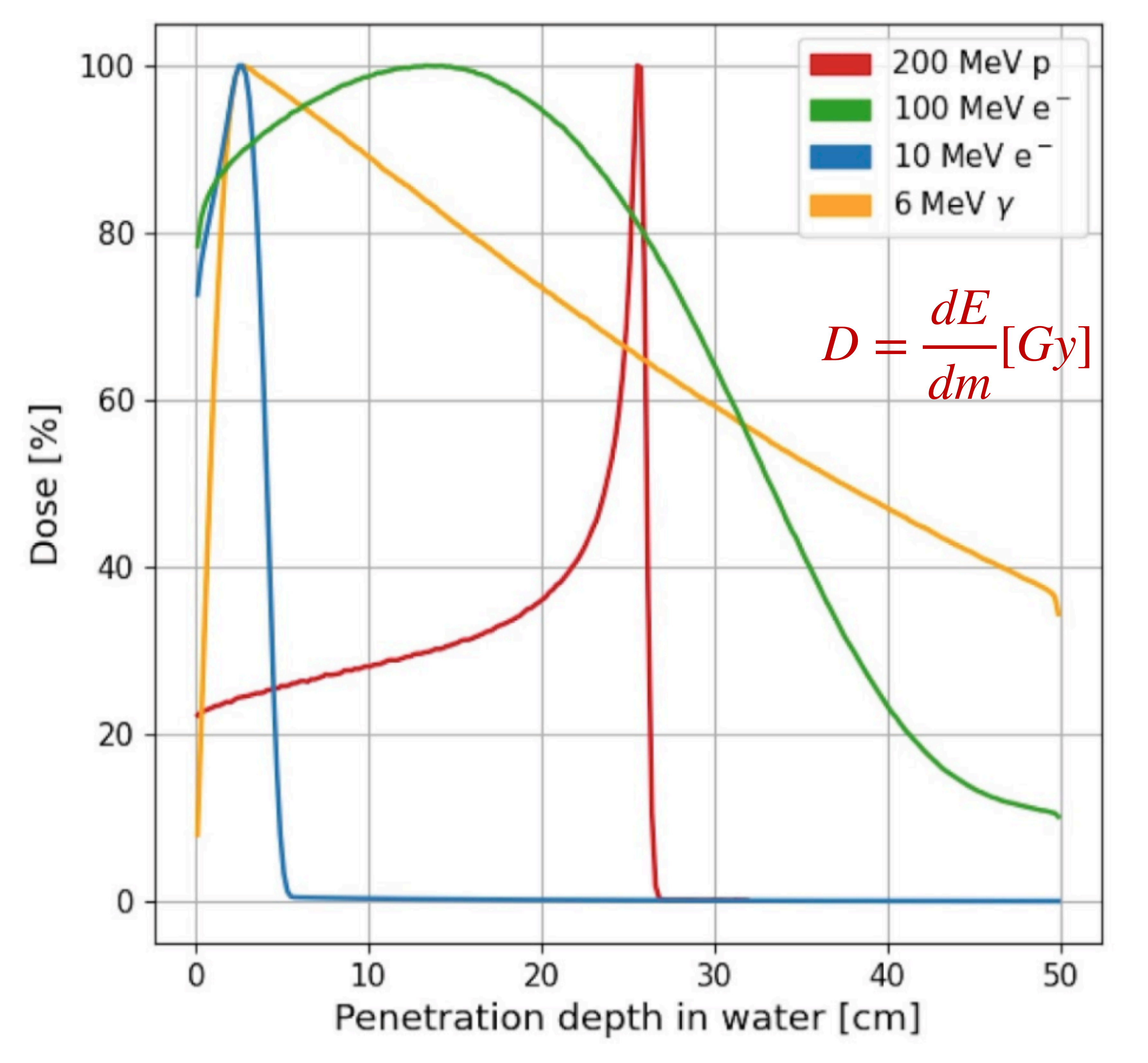
- **Radiotherapy** is a clinical technique that uses ionizing radiation to target and destroy malignant cells, primarily in cancer treatment. The principle is based on **inducing DNA damage** in tumor cells, disrupting replication and leading to cell death.

- In **External Beam Radiotherapy (EBRT)**, various radiation types are used, each with specific characteristics:

Photon Therapy: High-energy X-rays or gamma rays with deep tissue penetration, suitable for treating tumors located at various depths.

Low-Energy Electron Therapy: Shallow penetration, ideal for treating surface or near-surface tumors due to rapid dose fall-off.

Particle Therapy (proton, Carbon Ions): High precision with intense localized energy deposition (Bragg peak), maximizing damage to deep-seated tumors while sparing surrounding healthy tissues.



$$D = \frac{dE}{dm}[Gy]$$

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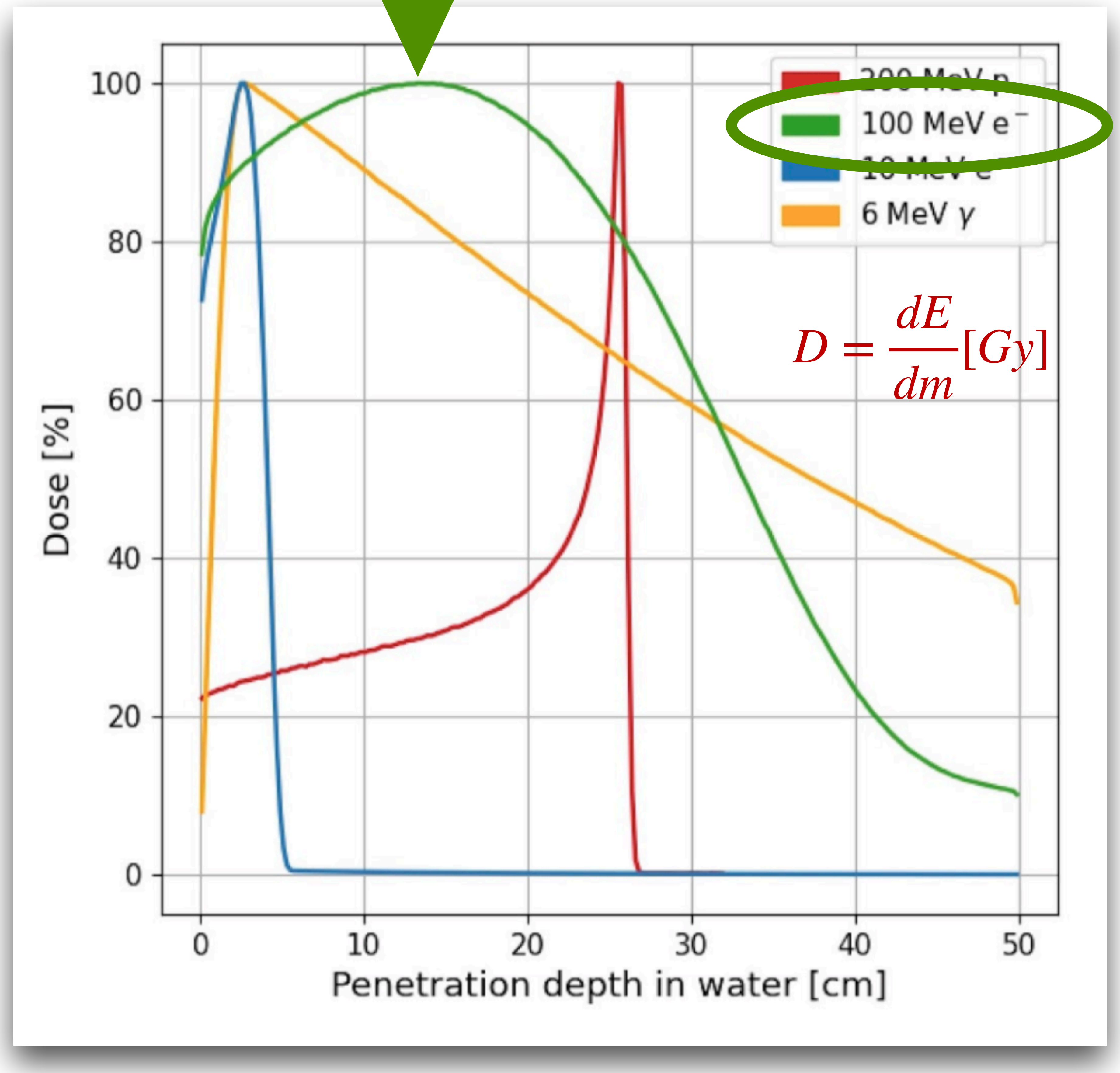
NATURAL SPREAD OUT BRAGG PEAK



$$D = \frac{dE}{dm}[Gy]$$

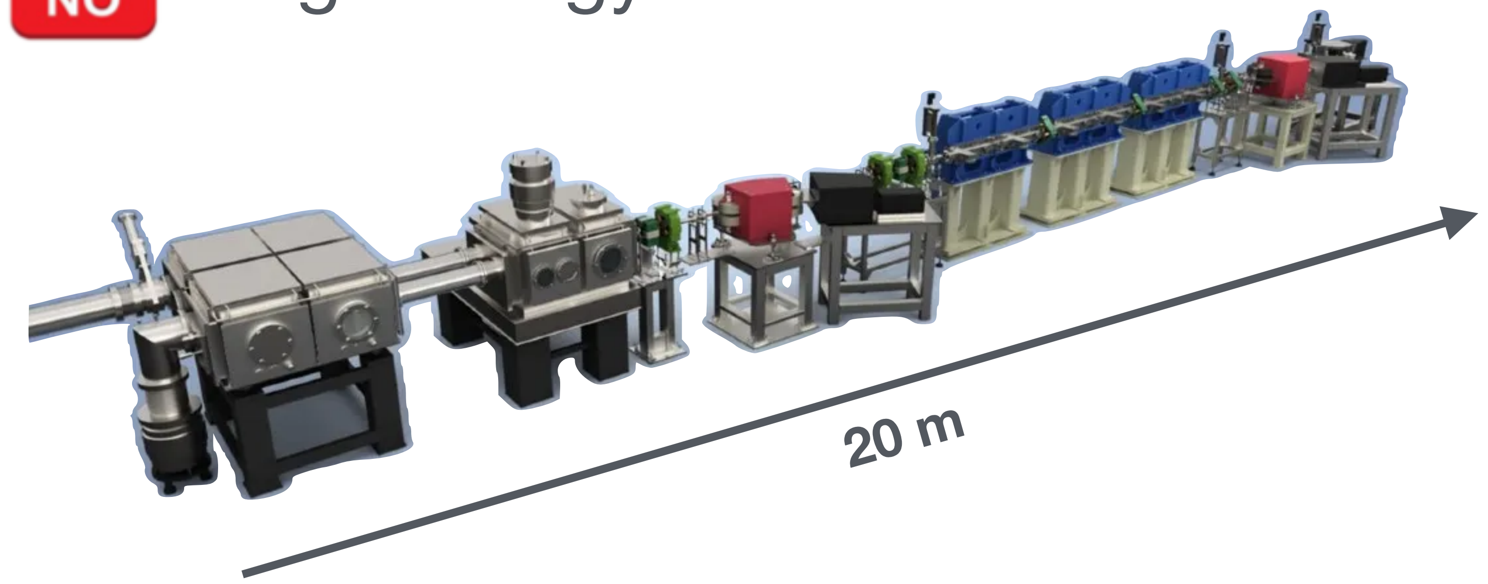
Very High Energy Electron Therapy

- Very High Energy Electrons (**VHEE**) refer to electron beams in the **50–250 MeV** energy range, which offer promising potential for treating deep-seated tumors. They have been considered already in the past as an **alternative** to protons and photon radiotherapy thanks to their **better longitudinal sparing of Organs at Risks (OARs)** and **reduced impact of range uncertainties**.

PAST

✓ **YES** High penetration capability allow for flexibility in treatment planning.

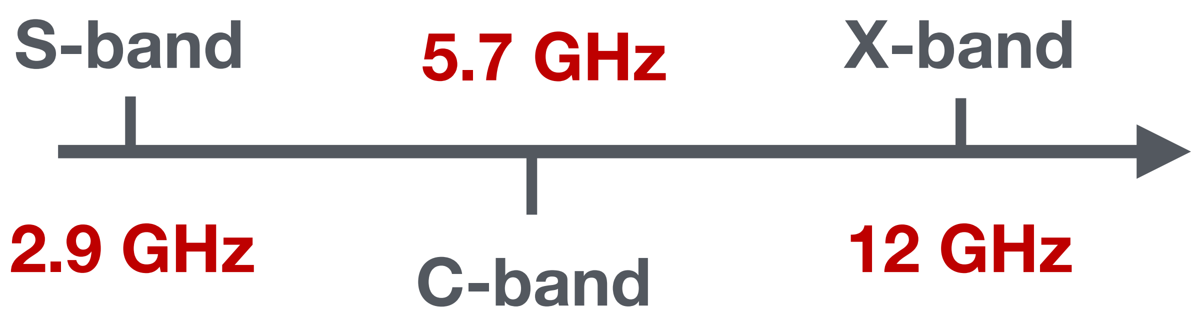
✗ **NO** Comparable performance only with high energy and multi field.



Due to cost, complexity and space (long accelerating system) VHEE have not yet reached the clinical stage.

PRESENT

Advances in C and X-band accelerators offer **higher gradient capabilities**

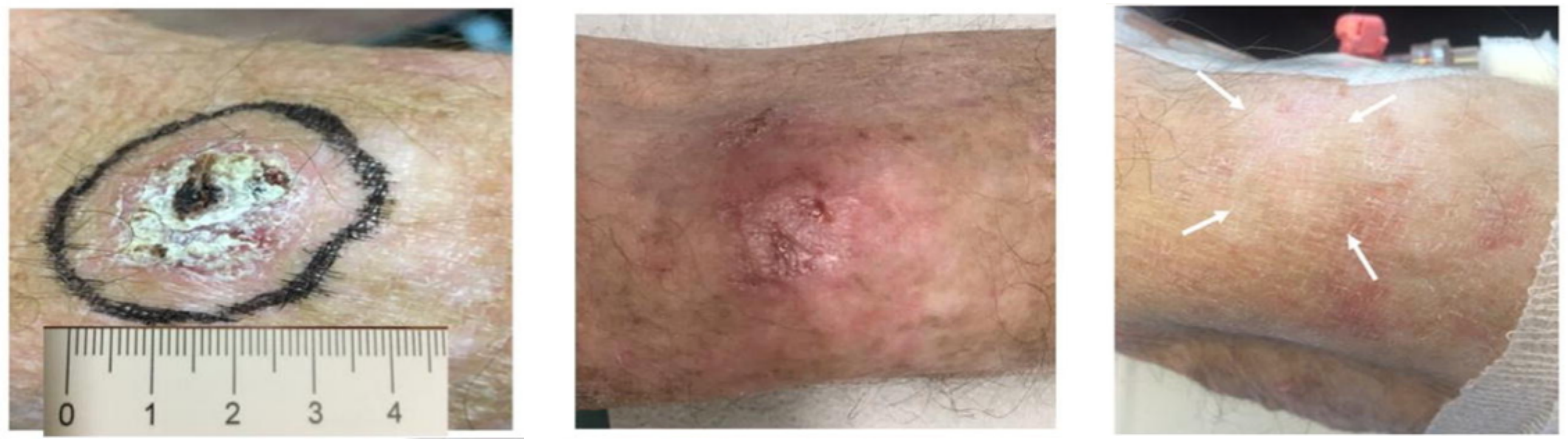


1. Compact designs;
2. Precision in dose delivery;
3. Reduced treatment times.

In 2014 the FLASH effect was discovered

Reduction of toxicity in healthy tissues (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**).

PATIENT 0



Day 0 3 weeks 5 months

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VHEE accelerators

- Translation of (FLASH) VHEE radiotherapy in clinical practice requires the development of **accelerators with a compact design** to meet the requirements for a machine suitable for the hospital environment.

The proposed VHEE source is based on a **C-band LINAC**, working at **5.712 GHz**, delivering a high intensity electron beam in FLASH regime.

PRF	$100Hz$
Pulse duration	$< 3\mu s$
Charge per pulse	$600nC$
Dose rate per pulse	$> 10^7 Gy/s$
Average dose rate	$> 10^2 Gy/s$
Pulse current	$200mA$

FRIDA

SAFEST project

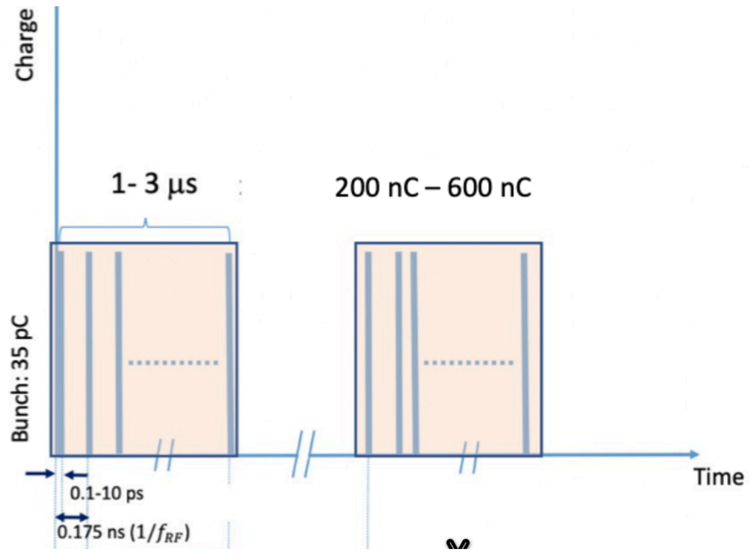
SApienza **F**lash **E**lectron **S**ource for radio-**T**herapy

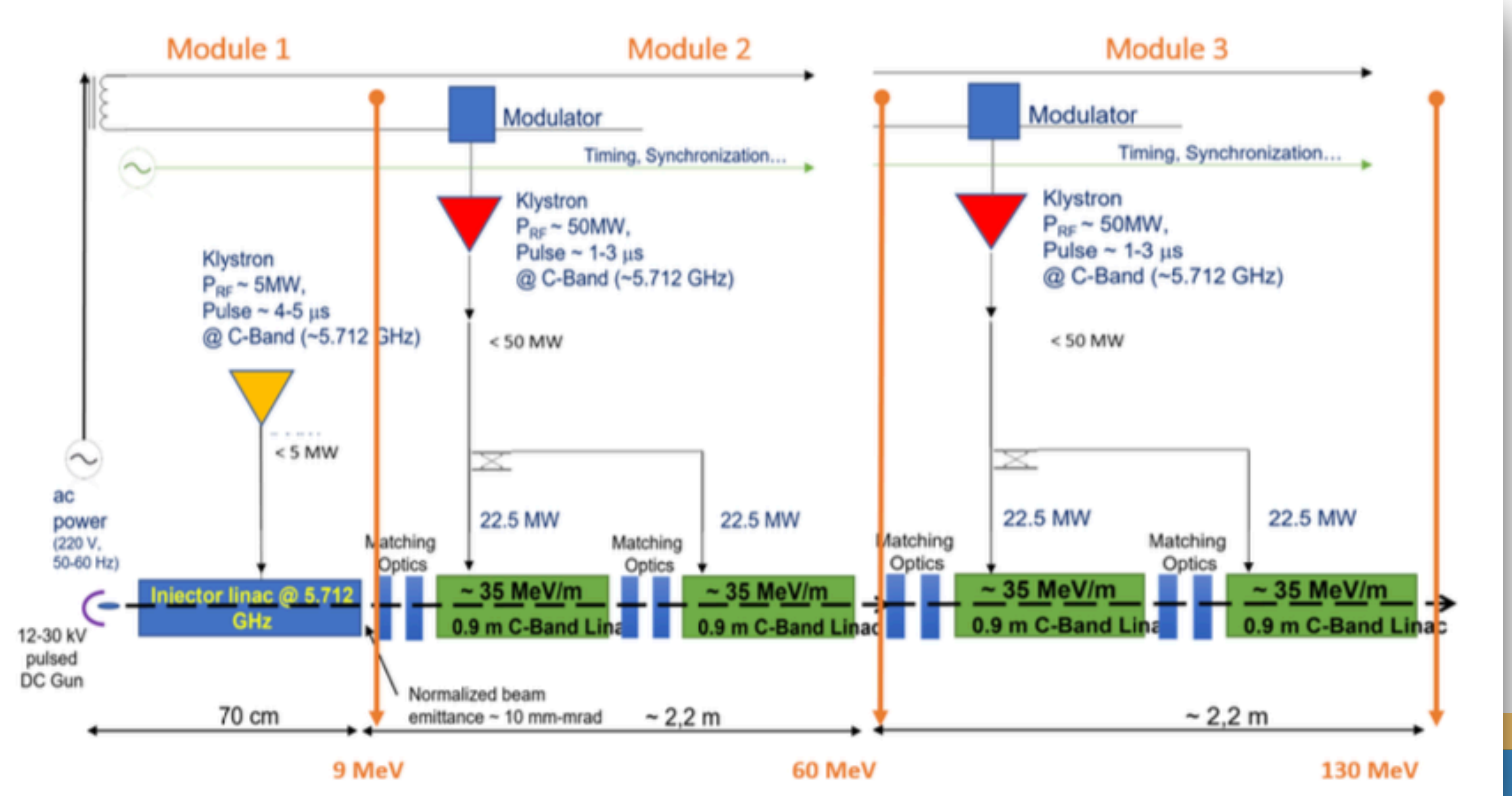
Finanziato dall'Unione europea NextGenerationEU
Ministero dell'Università e della Ricerca
Italiadomani

The high-gradient acceleration will allow to **accelerate electrons up to 130 MeV**, maintaining a good transmission efficiency of the particles, necessary to transport the high peak current.

It will be composed in **three modules**, each dedicated to different electron energies (9, 60 and 130 MeV).

1. **SW injector:** designed to accelerate a current from a pulsed DC gun to ~200 mA (energy of 9-12 MeV);
2. **Compact TW C-band:** with high gradient accelerating gradient (~ 50 MeV/m).





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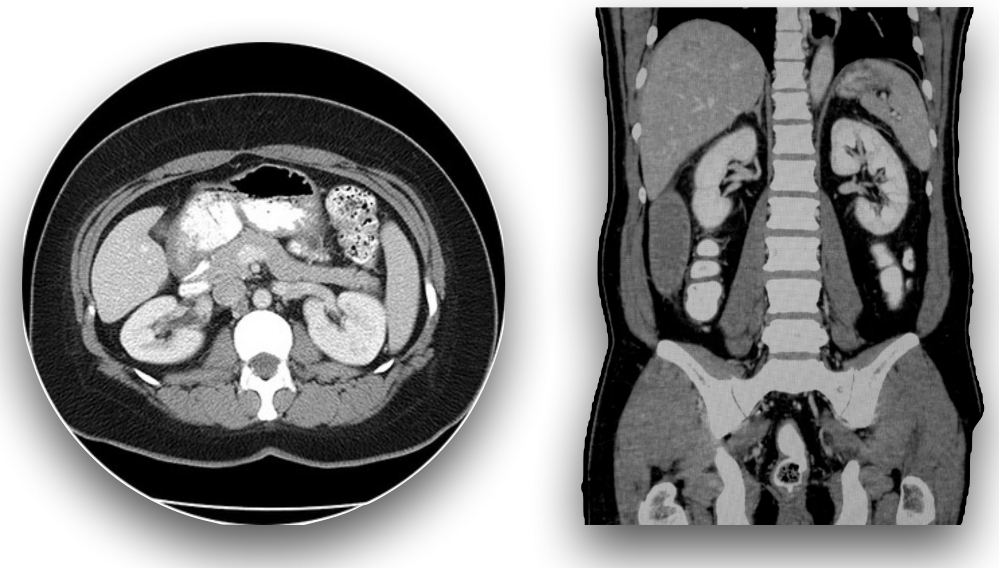
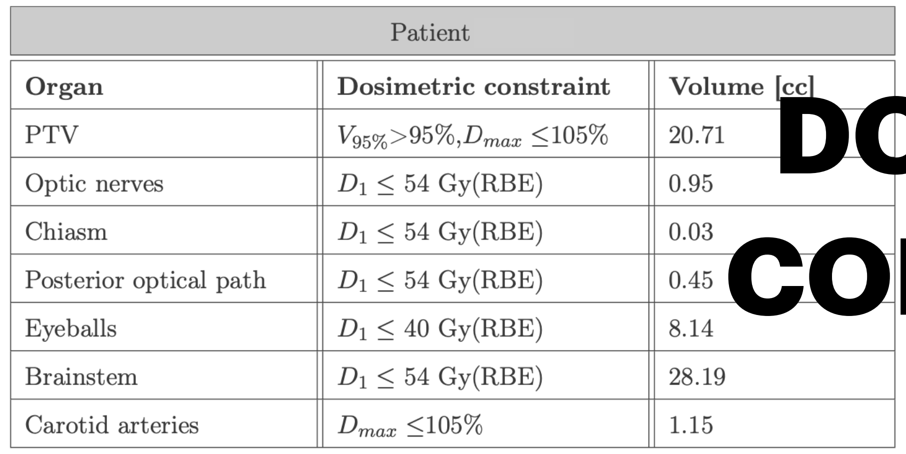
Treatment Planning Systems

- In order to finalize the machine design and to investigate the potential of VHEE based radiotherapy, a **VHEE Treatment Planning System (TPS)** is needed. TPS aims to **optimize the dose distribution** inside the patient **maximizing the tumor control** and **minimizing normal tissue complications**.

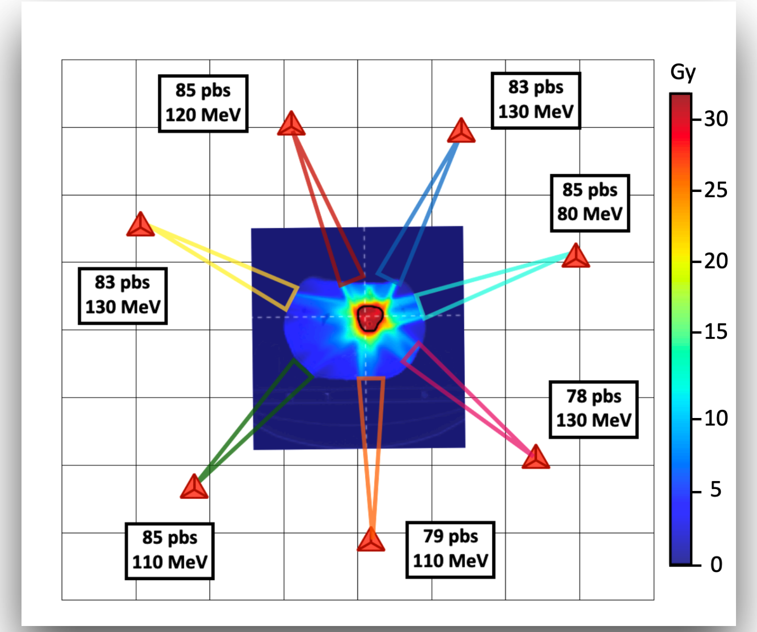


PATIENT IMAGING

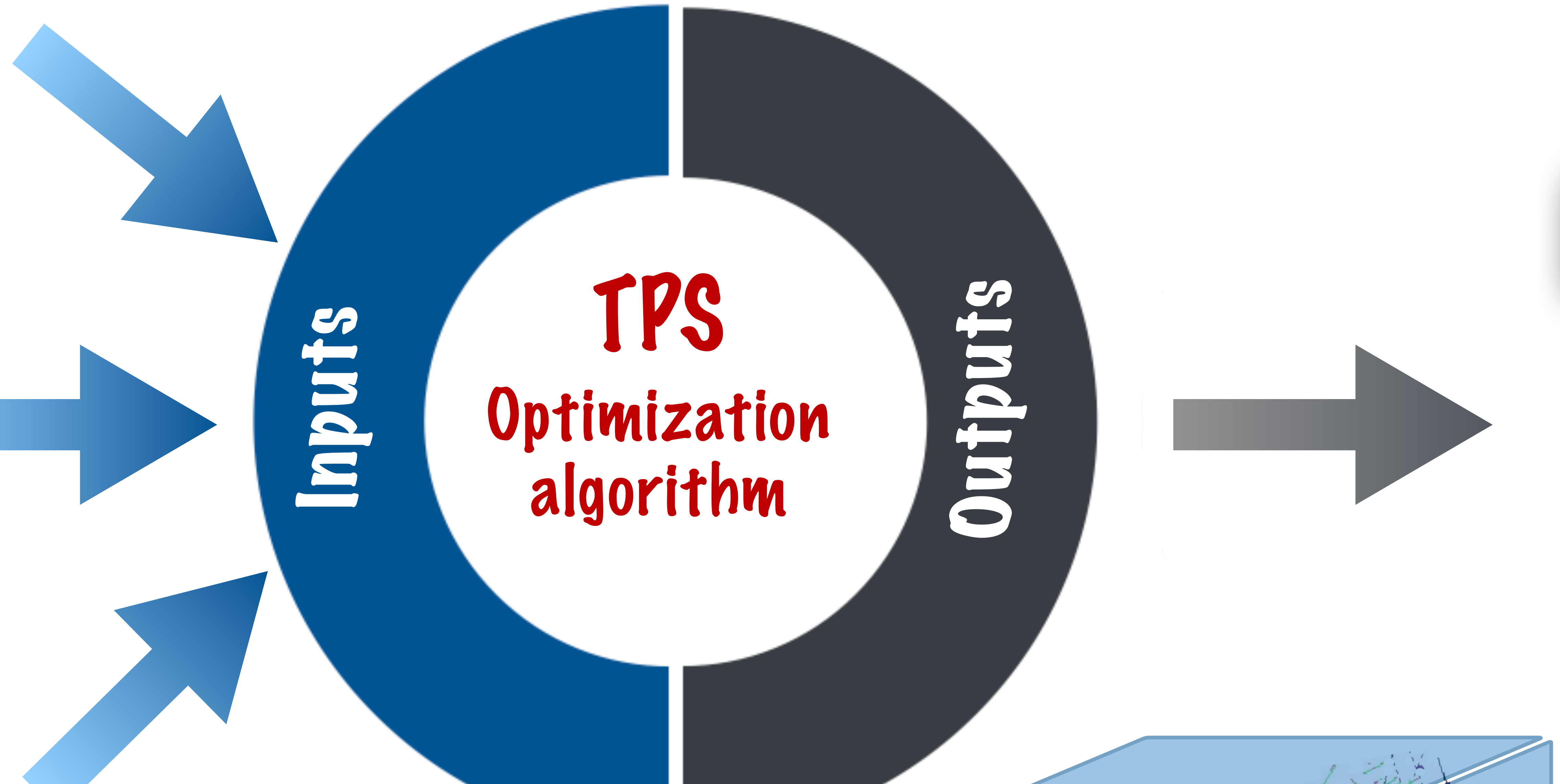


Patient		
Organ	Dosimetric constraint	Volume [cc]
PTV	$V_{95\%}>95\%, D_{max} \leq 105\%$	20.71
Optic nerves	$D_1 \leq 54$ Gy(RBE)	0.95
Chiasm	$D_1 \leq 54$ Gy(RBE)	0.03
Posterior optical path	$D_1 \leq 54$ Gy(RBE)	0.45
Eyeballs	$D_1 \leq 40$ Gy(RBE)	8.14
Brainstem	$D_1 \leq 54$ Gy(RBE)	28.19
Carotid arteries	$D_{max} \leq 105\%$	1.15

DOSIMETRIC CONSTRAINTS



PHYSICAL MODEL



Inputs

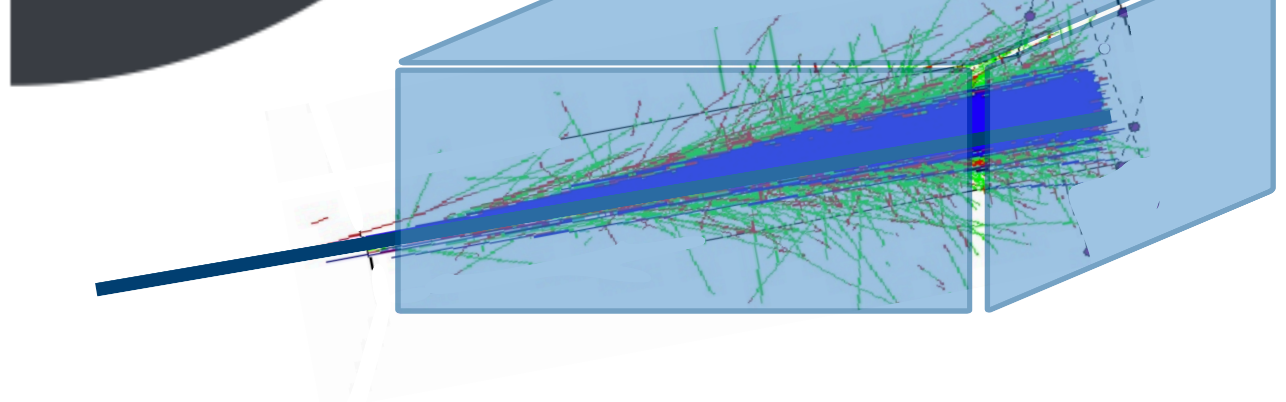
TPS

Optimization algorithm

Outputs

ACCELERATOR PARAMETERS

1. **Energy**
2. **Intensity**
3. **Direction**



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My Thesis work

- In this context the availability of a dedicated facility would allow bridging the gaps in the current knowledge and characterization of the VHEE based radiotherapy, both including or not the FLASH effect.

The aim of **my Ph.D. thesis work** was twofold: based on the VHEE LINAC designed within the SAFEST project, I focused on...

1 RADIOPROTECTION STUDIES

1. Geometry implementation and **Physics Simulations** with the Monte Carlo tool FLUKA;
2. Analysis of simulation results and **assessment of the dispersed radiation** in the LINAC's surrounding environment;
3. **Design and validation of the shielding** required for current protocols.

DEVELOPMENT OF A VHEE TPS 2

1. Implementation of **Monte Carlo dose evaluation** (using a fast MC) in place of analytical calculations;
2. Adoption of **Annealing algorithms** as minimization methods;
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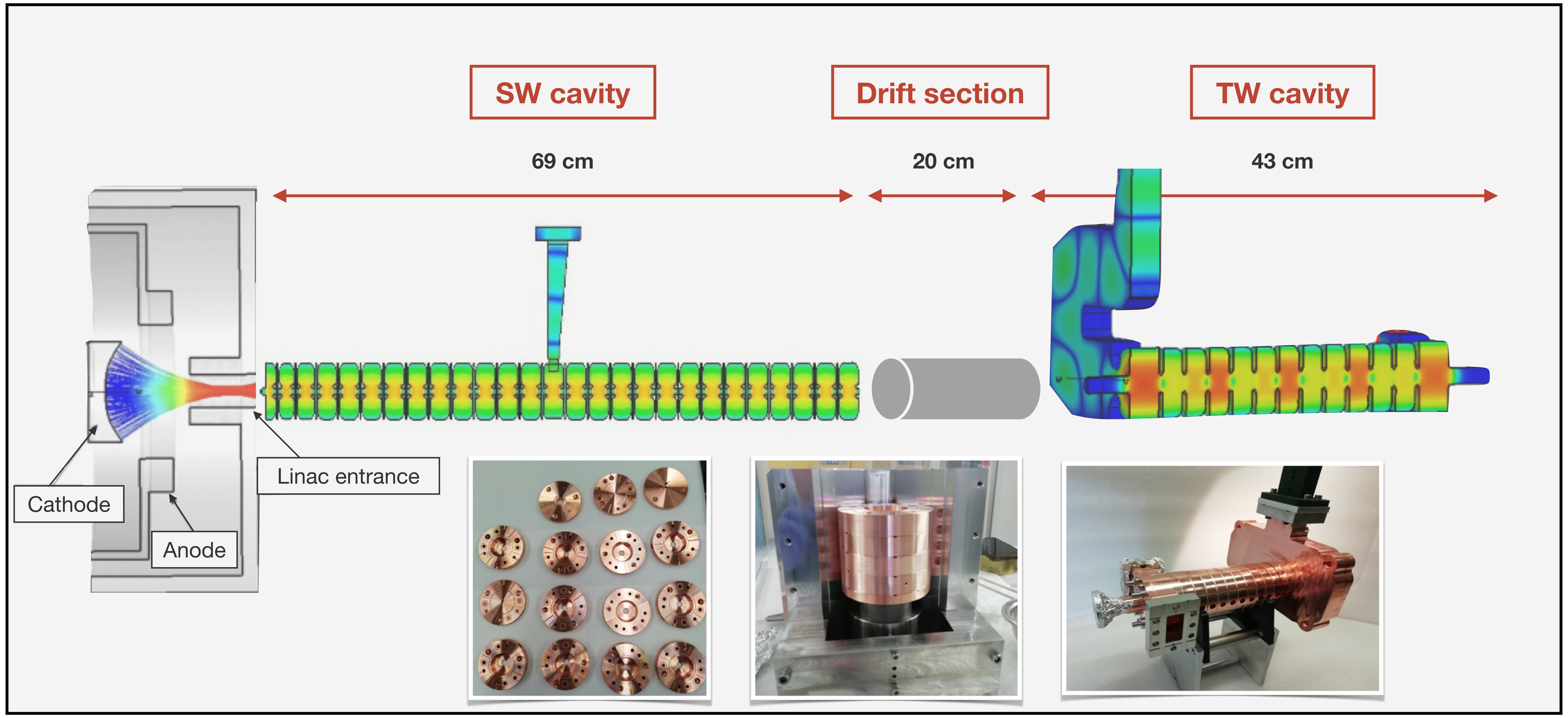
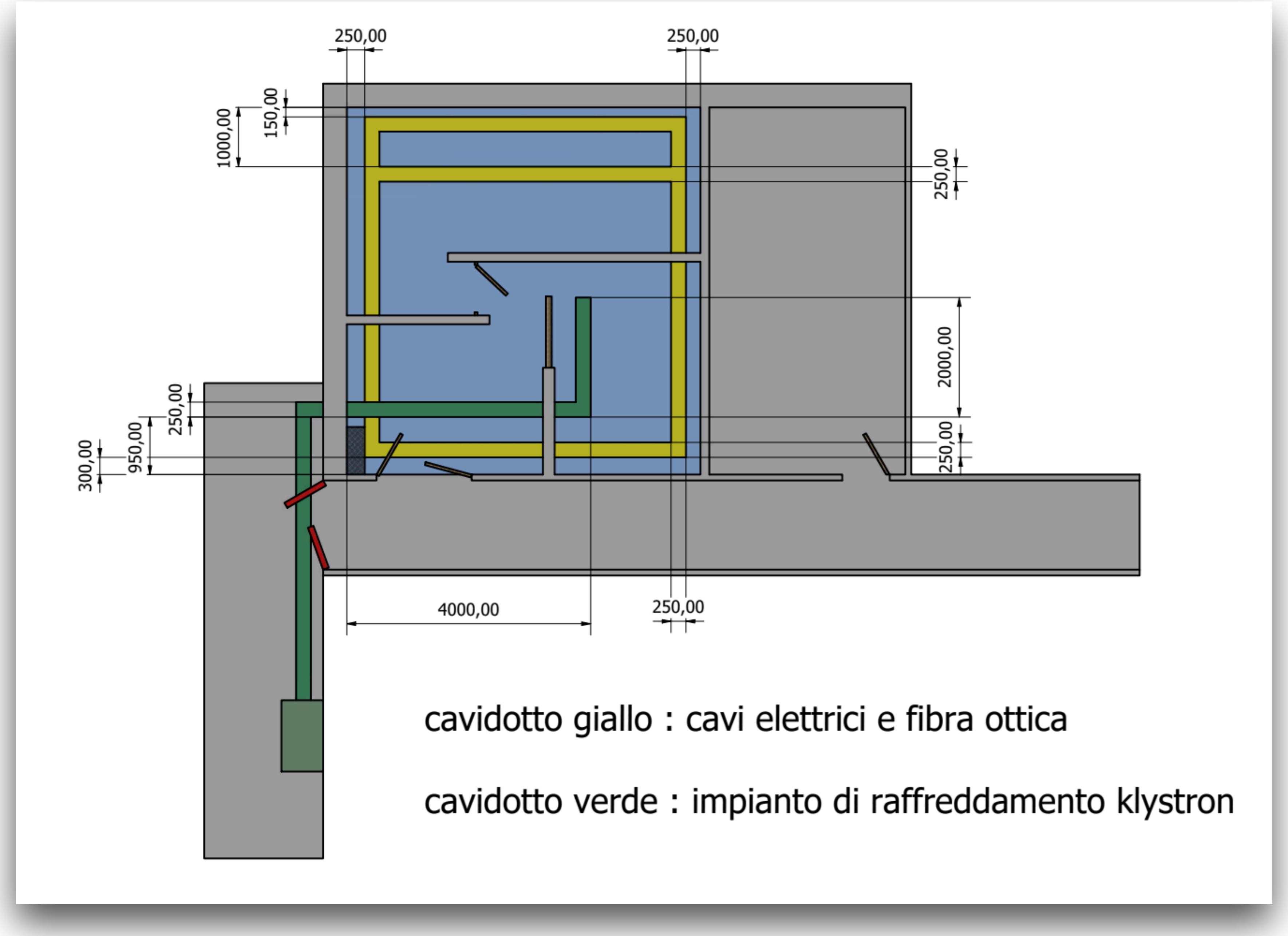
Radio-protection studies

- The **prototype** currently under construction as part of the SAFEST project is a **scaled-down version** of the proposed VHEE LINAC, designed to accelerate electron beams up to **24 MeV.**

Validate and test all components

Radiobiological experiments with 24 MeV beams





cavidotto giallo : cavi elettrici e fibra ottica

cavidotto verde : impianto di raffreddamento klystron

BUILT, TESTED AND INSTALLED IN HOUSE AT SBAI DEPARTMENT

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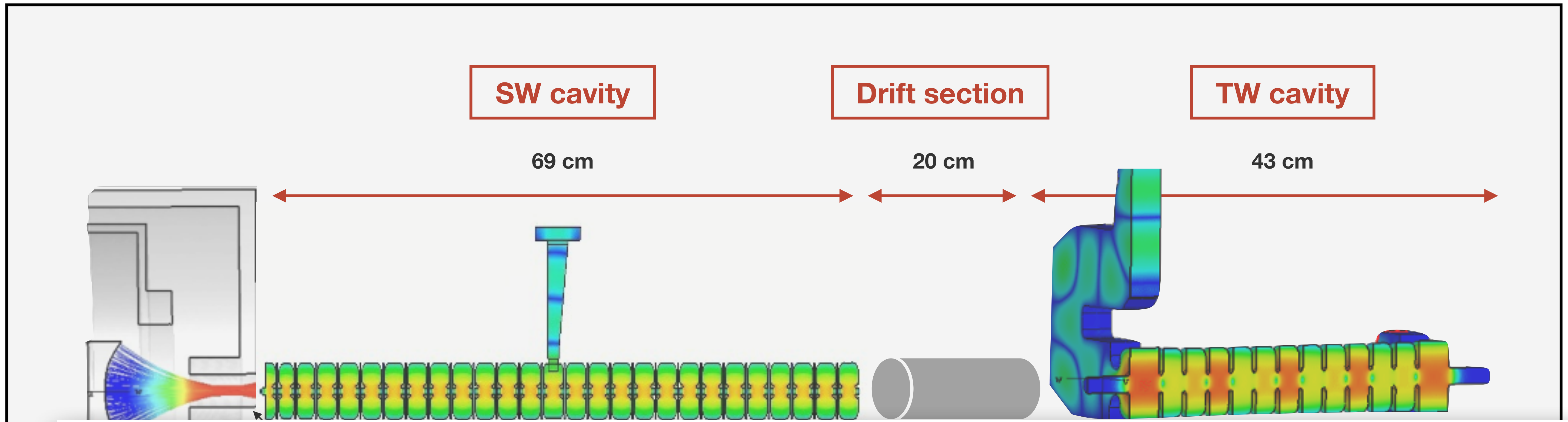

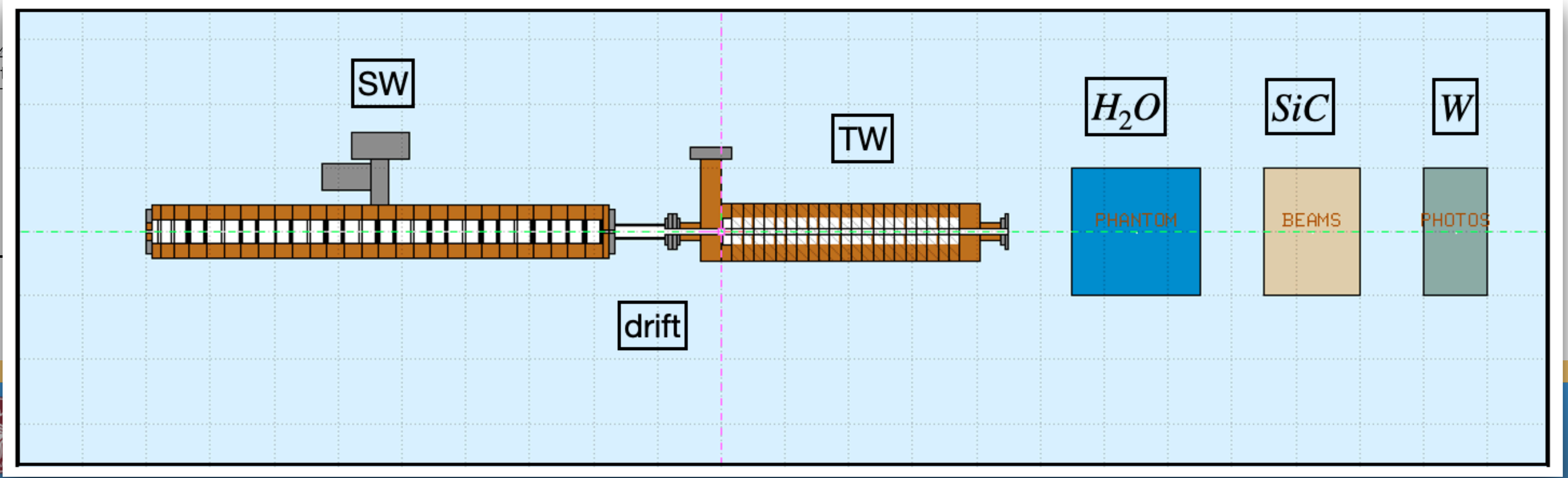

The first step was to accurately **replicate the geometry and materials** of the accelerator in **FLUKA,** both for the injection section and the high gradient cavity. Downstream, there is a:

1. **Water Phantom;**
2. **Silicon Carbide beam stopper;**
3. **Tungsten block**

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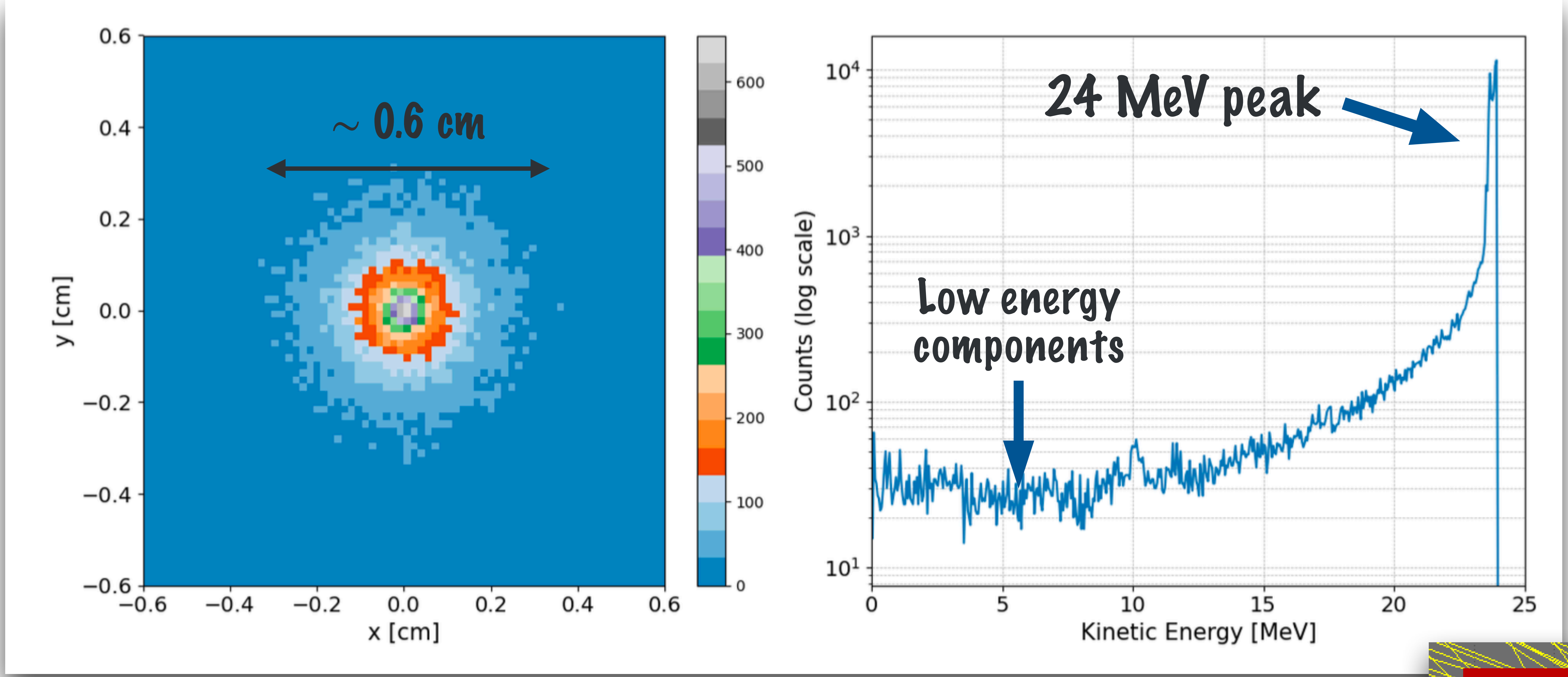
Radio-protection studies

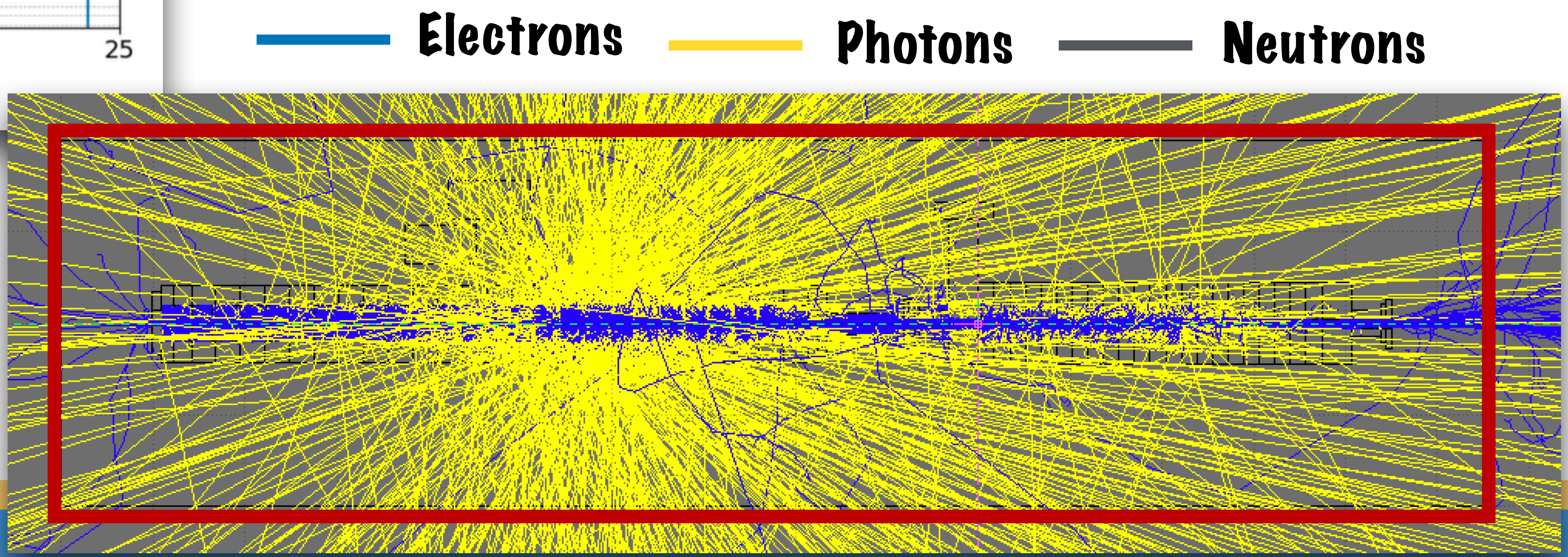
- I analyzed **electromagnetic simulations** performed using the software Parmela, that provides detailed insights into the beam dynamics and from which I **extracted the position, direction, and energy** of each individual particle.



GOAL?

Evaluate the dispersed radiation to design the needed shielding.

- **Exiting particle ~7,4 % of total**
- **Statistics 10^8 primary particles**



Analyzing the FLUKA output allowed me to characterize the **different types of radiation produced** by various interactions within the accelerator, on a scoring cylinder.

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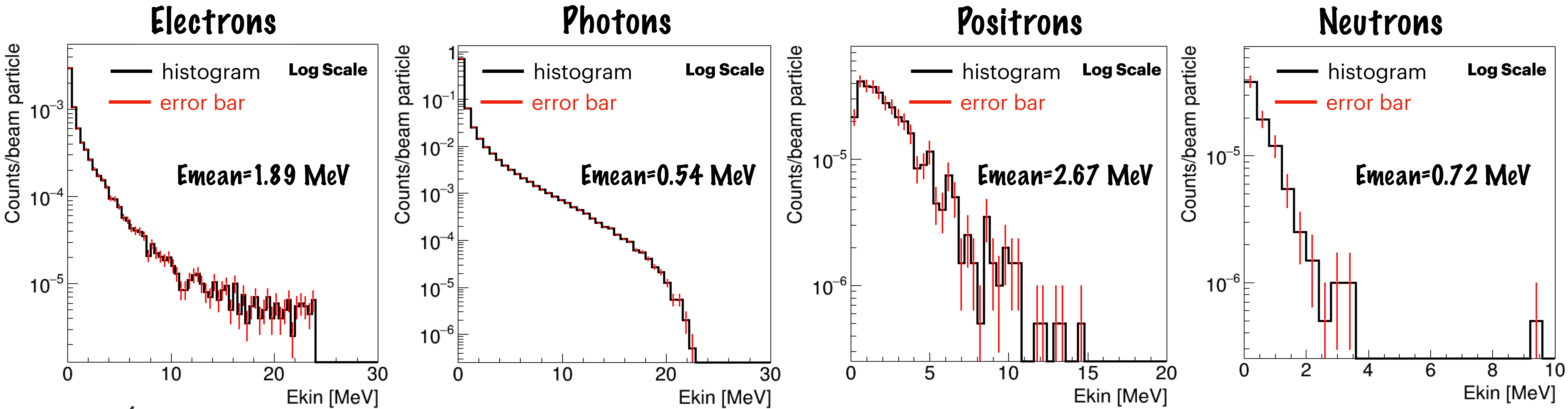
Radio-protection studies

① Energy histograms for the four main radiation products of interest



The histograms are **normalized** to the number of particles simulated with PARMELA. These results indicate the **number and energy distribution of particles** (electrons, photons, positrons, and neutrons) produced **per beam particle**.

Study on the back-scattered particle in SPARE!

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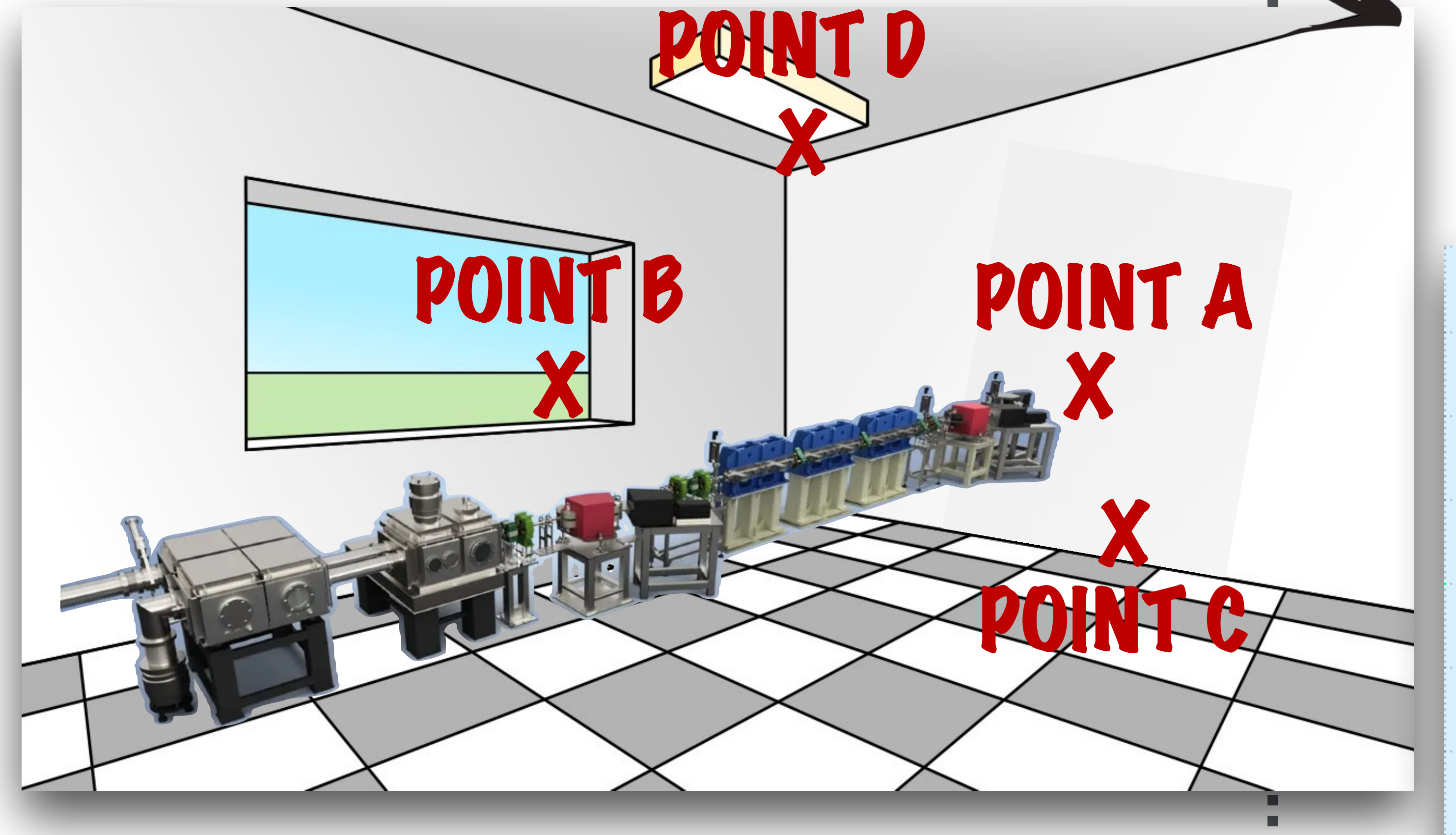
Radio-protection studies

② Dose delivered in the surrounding area

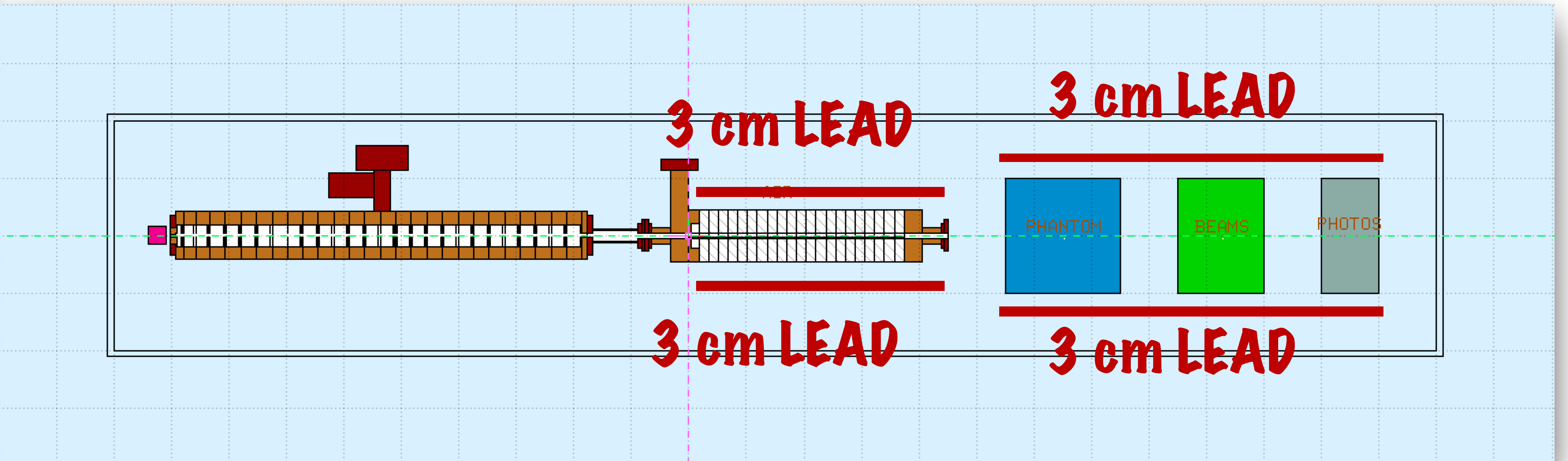
The simulation results provided insights into the **dose delivered to the surrounding air** by the particles exiting the accelerator.

- The dose was then evaluated at **4 key positions**:

- A : 180 cm from W block
- B & C: laterally 170 cm from the beam axis;
- D: 230 cm above the beam axis.



Based on these values, assuming a **workload of 3 days per week** with a number of pulses appropriate for the machine's use, **radiation shielding barriers were calculated** to reduce these values and comply with the legal limits.



	POINT A	POINT B	POINT C	POINT D
NO SHIELDING	$9.7 \cdot 10^{-18} Gy/p$	$7.3 \cdot 10^{-18} Gy/p$	$7.8 \cdot 10^{-18} Gy/p$	$3.9 \cdot 10^{-18} Gy/p$
3 cm SHIELDING	$3.7 \cdot 10^{-18} Gy/p$	$6.0 \cdot 10^{-19} Gy/p$	$8.5 \cdot 10^{-19} Gy/p$	$3.5 \cdot 10^{-19} Gy/p$

CRITICAL POINT

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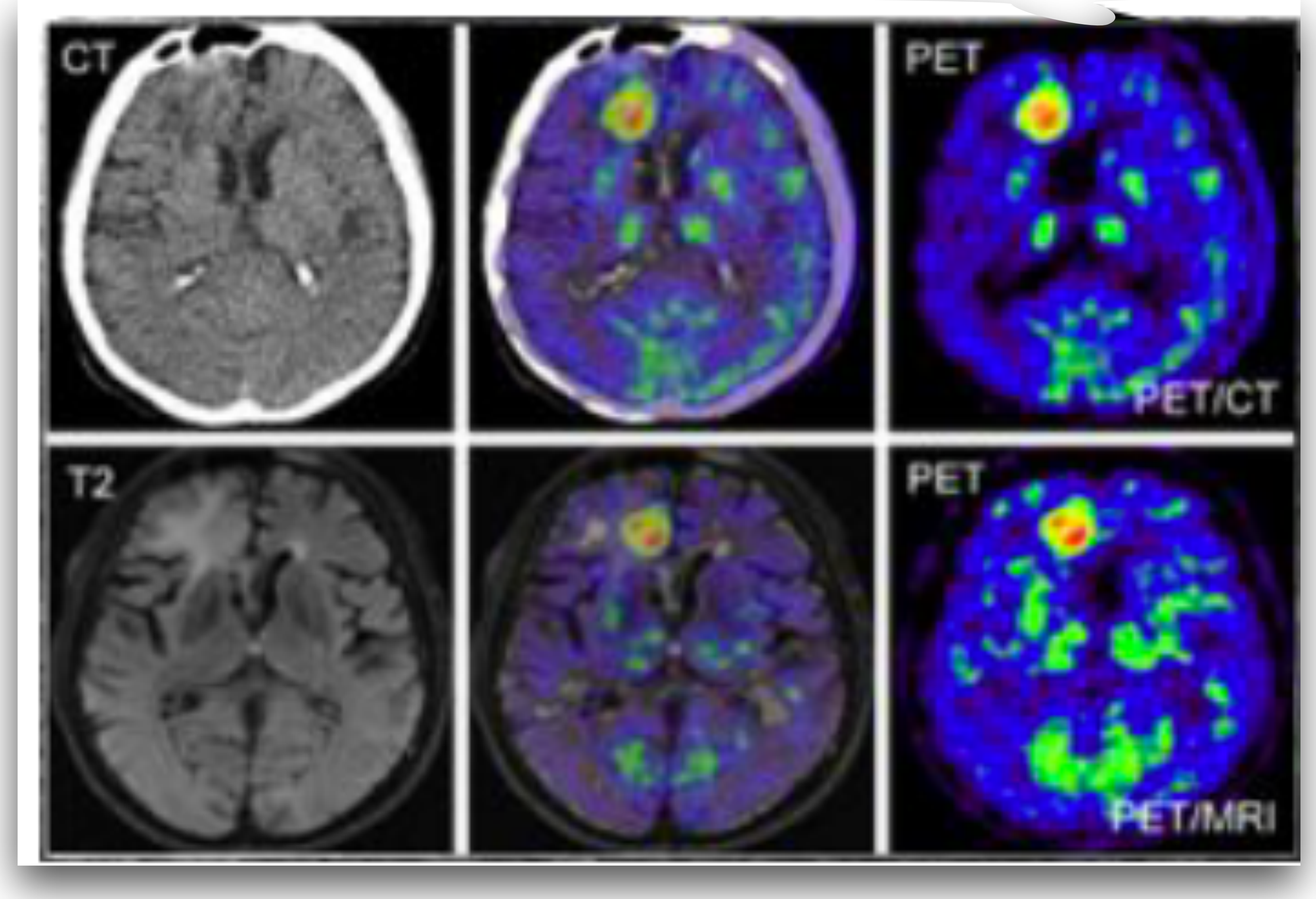
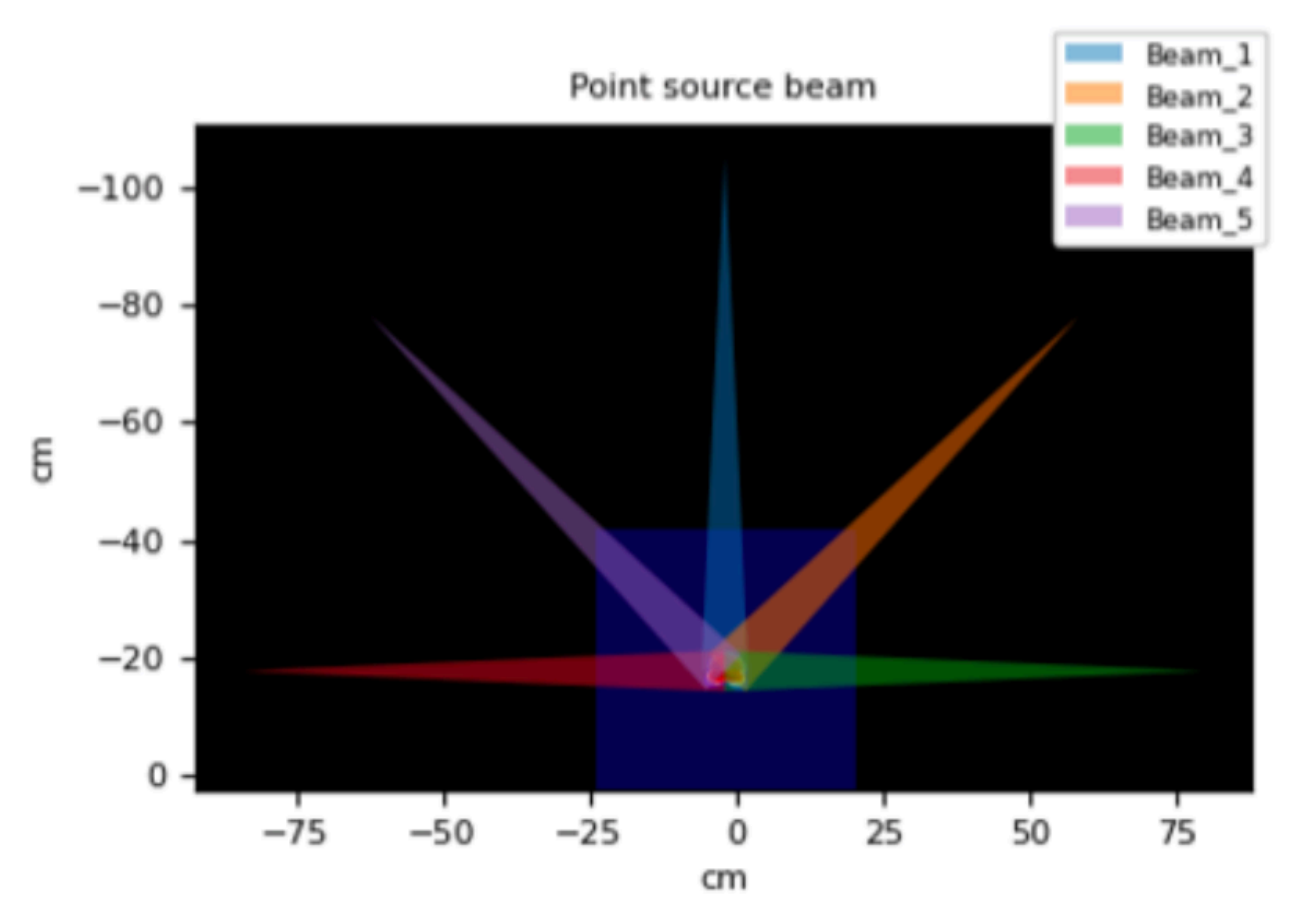
TPS for VHEE FLASH

- VHEE irradiation was simulated assuming the **compact C-band acceleration technology** which will be capable of delivering **multi-fields** with an **active scanning-like approach.**

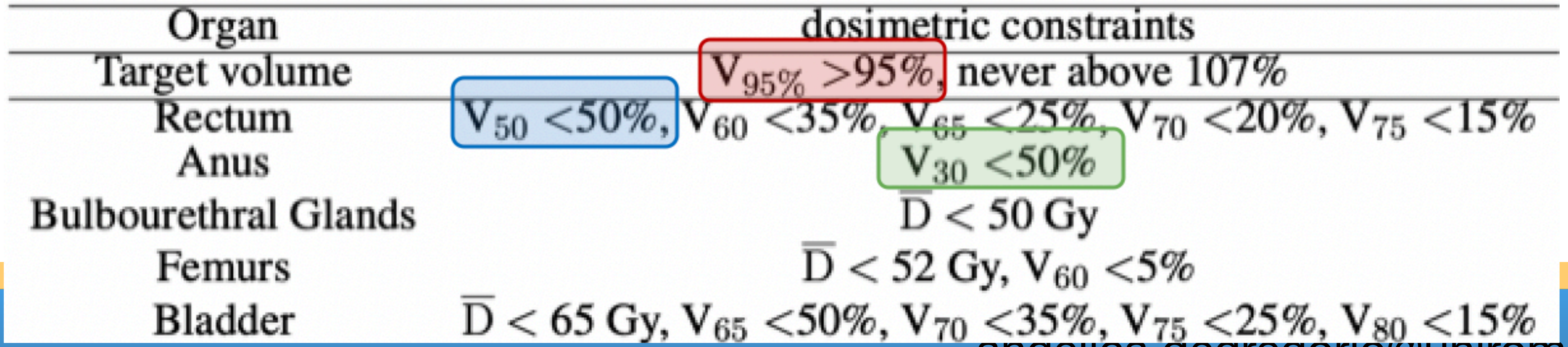
CT IMAGES & FIELD DIRECTIONS

The patient's **planning CT**, the **entry points** and the **dosimetric constraints** for each organ, together with the **prescribed dose** for the PTV, are provided by the hospital where the patients were treated.





A TPS for VHEE does not yet exist, so we derive geometric, dosimetric, and energy information from standard radiotherapy



Organ	dosimetric constraints
Target volume	$V_{95\%}$ >95%, never above 107%
Rectum	V_{50} <50%, V_{60} <35%, V_{65} <25%, V_{70} <20%, V_{75} <15%
Anus	V_{30} <50%
Bulbourethral Glands	$\bar{D} < 50$ Gy
Femurs	$\bar{D} < 52$ Gy, V_{60} <5%
Bladder	$\bar{D} < 65$ Gy, V_{65} <50%, V_{70} <35%, V_{75} <25%, V_{80} <15%

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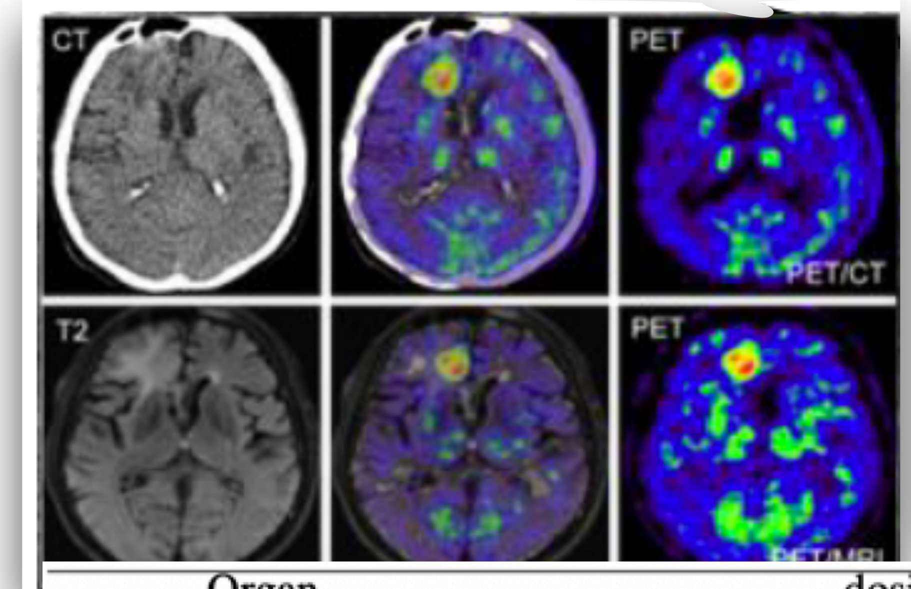

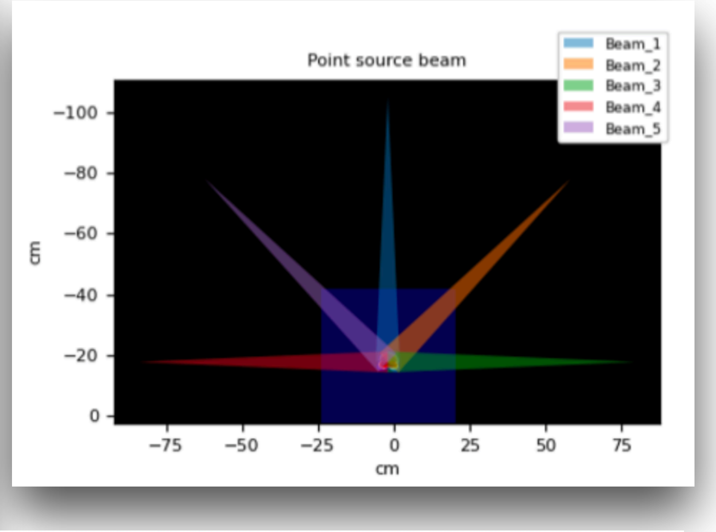

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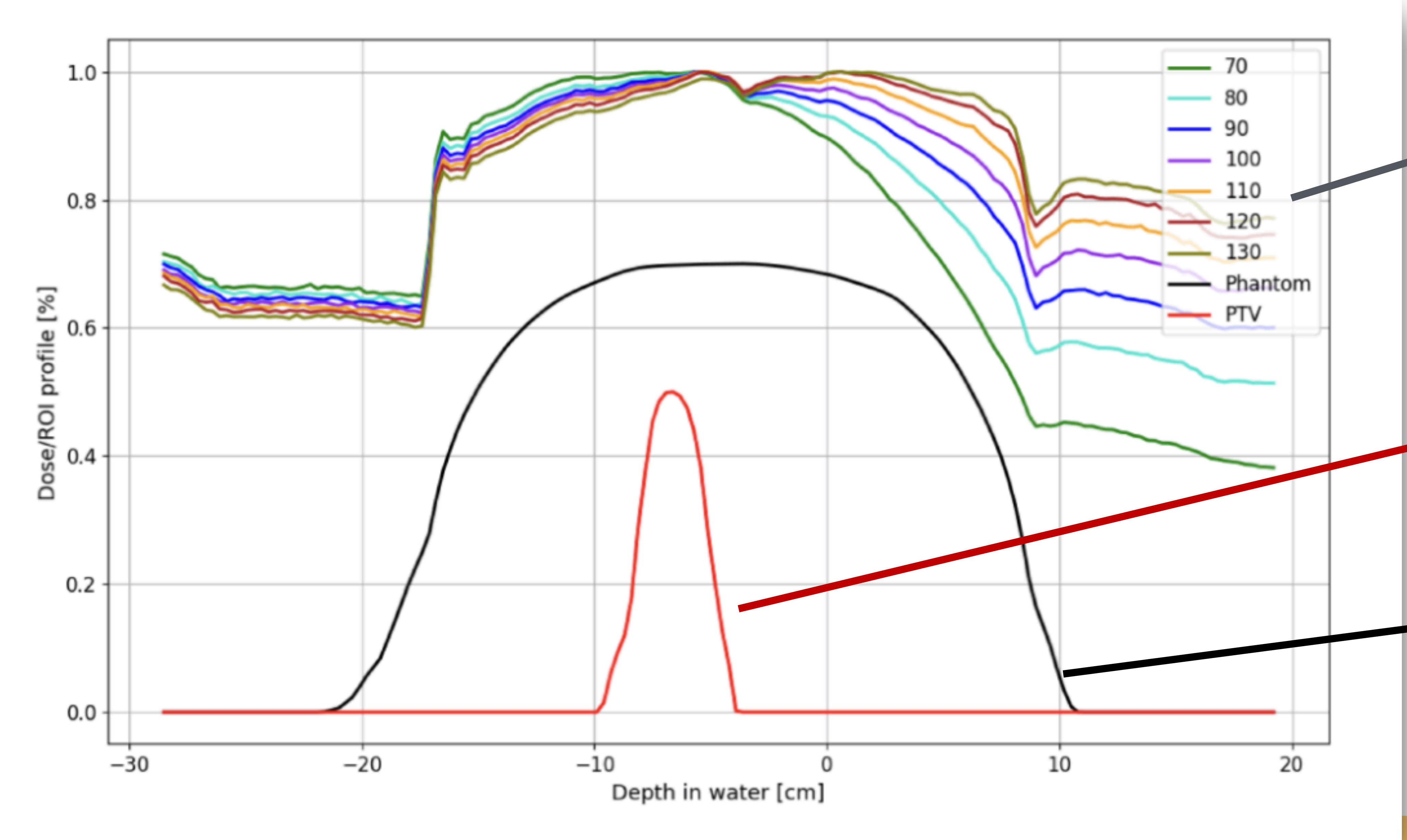
ENERGY SELECTION

The selection of the beam energies (70-150 MeV) is made looking at the dose distributions obtained **simulating a single PB delivered at the center of the PTV**.



Pb dose distribution

PTV profile

CT profile

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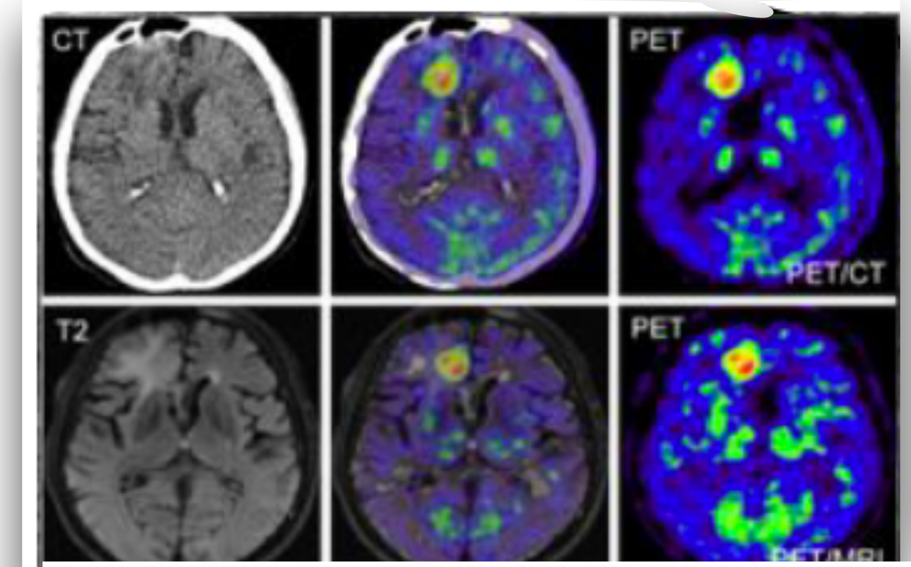

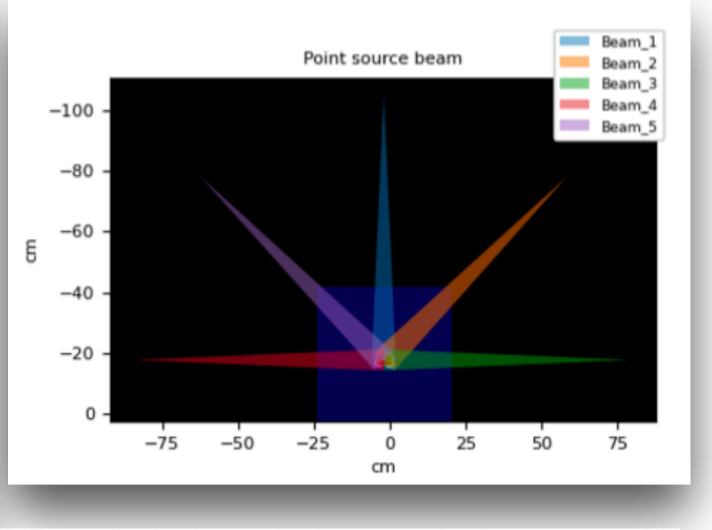

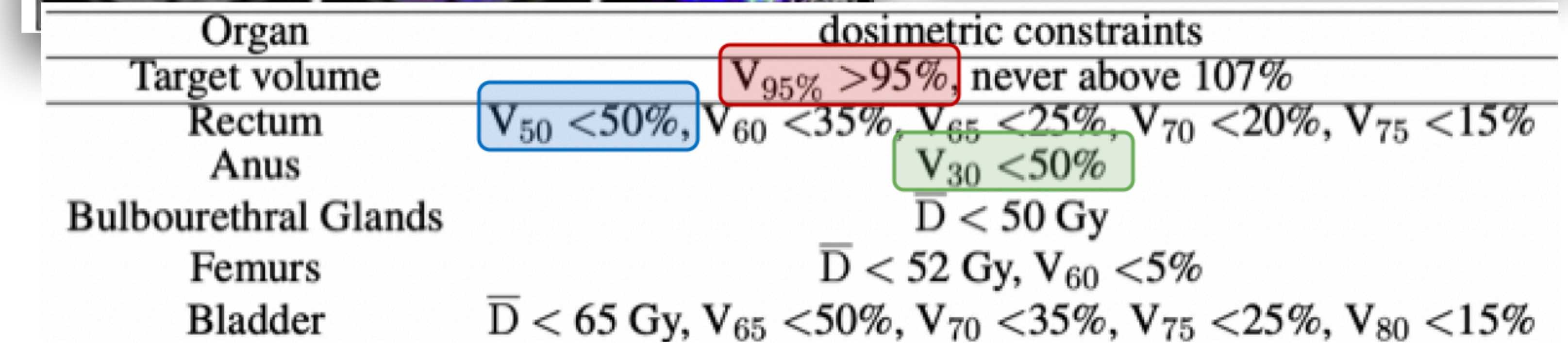

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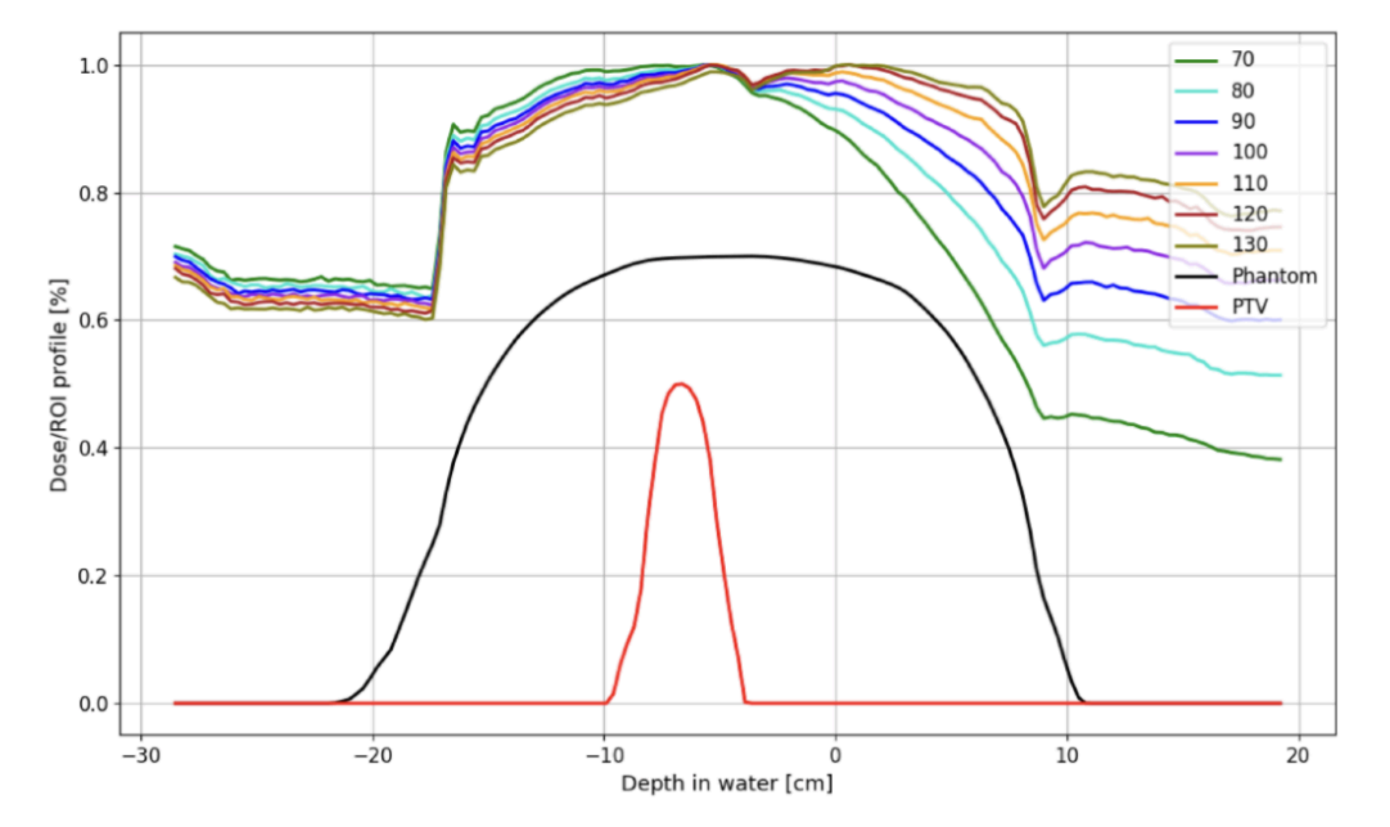
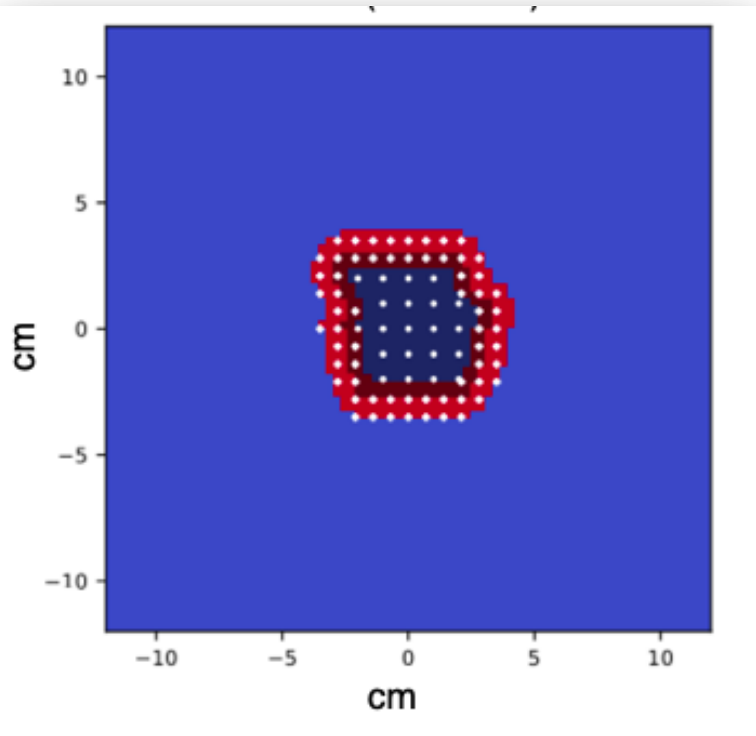


PENCIL BEAM CONFIGURATION

The **size** and **aperture of each PB** used to irradiate the PTV are defined following an approach similar to **active scanning** used in proton beam delivery.



The **spot spacing** between two adjacent PBs **varies according to the irradiation geometry**

To reduce the number of spots, and thus the computational time (**FLASH regime in mind!**)

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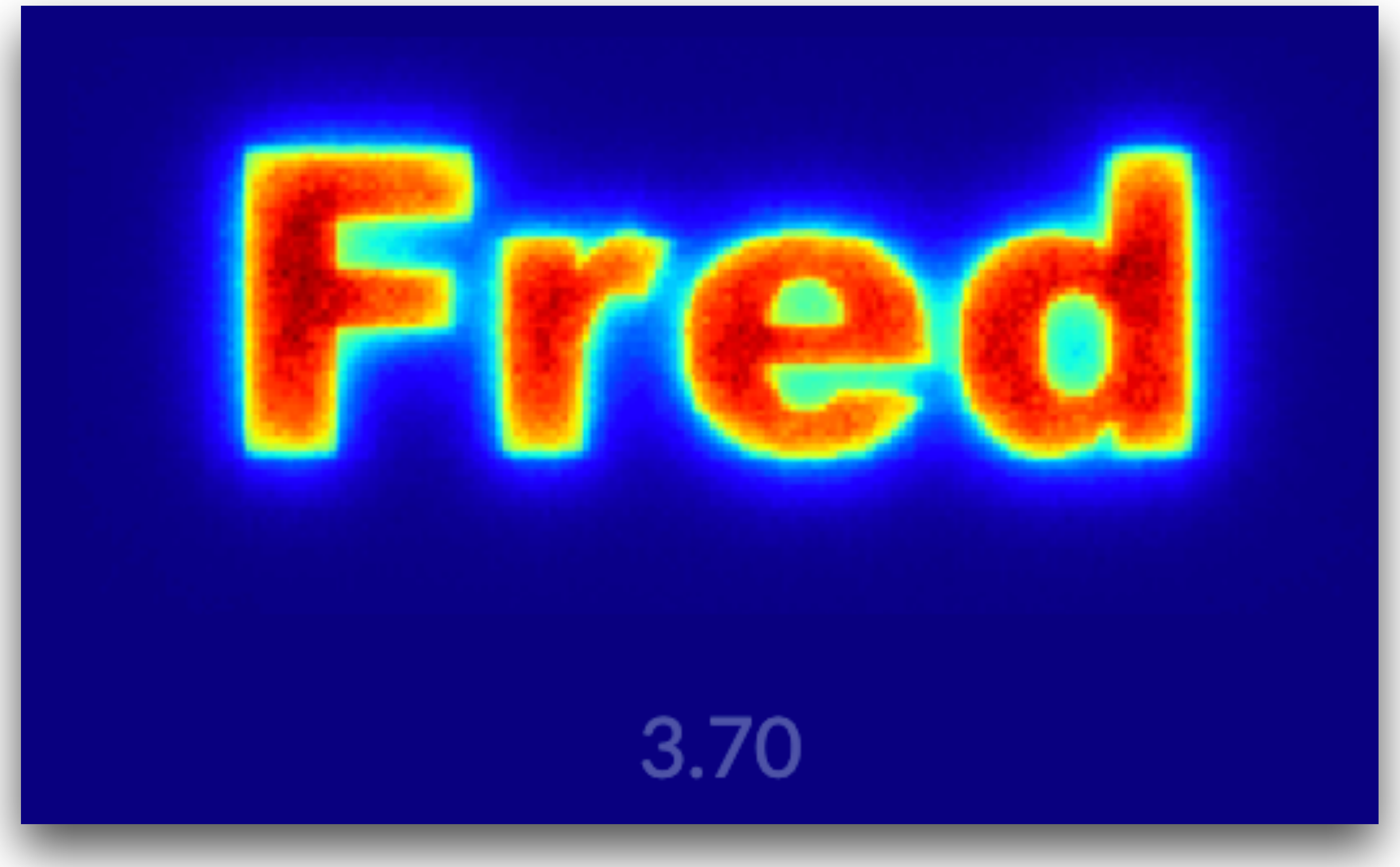
TPS for VHEE FLASH

- The majority of the TPS softwares use an **analytical** dose evaluation approach, which may be **not so accurate**. However the computational cost of the problem didn't allow so far to make a more precise calculation. Our solution is to use **FRED**.

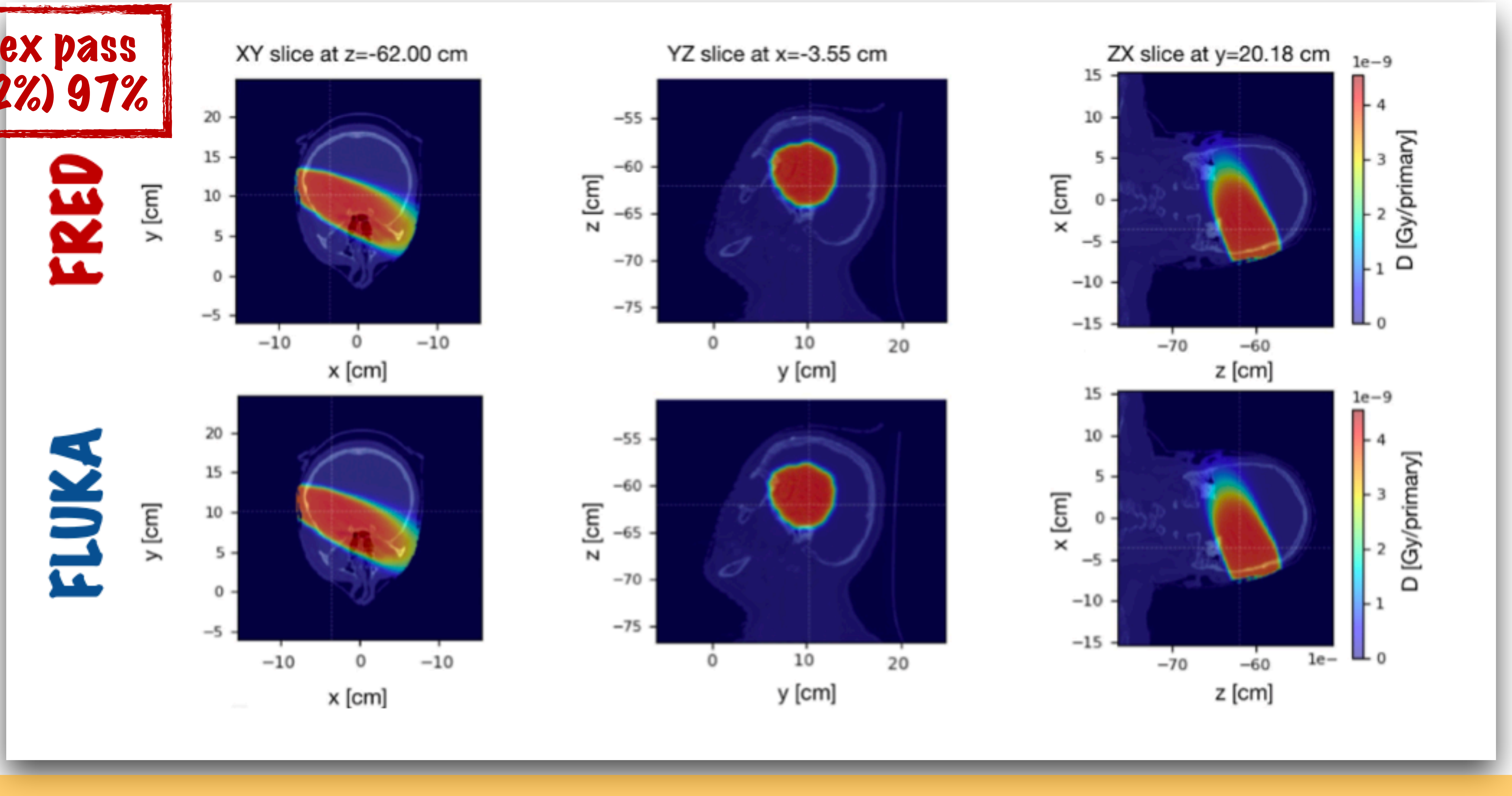
The FRED MC has been developed to allow a **fast optimization of the TPS** in Particle Therapy, while keeping the dose release accuracy typical of a MC tool. Today **FRED protons is used** in various medical and research centers: MedAustron (Vienna), APSS (Trento), Maastro (Maastricht) and CNAO (Pavia)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



Developed to work on GPU

Reduces the simulation time by a factor 1000 compared to standard MC

Gamma-Index pass rate (2mm/2%) 97%



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TPS for VHEE FLASH

GOAL? Select the **Energy of each field** and the **Intensity of each PB** of the treatment plan.

① In order to maximize tumor coverage and minimize the dose delivery to the normal tissue, the algorithm explore different set of parameters.

② Calculate the **COST FUNCTION** for a given configuration.

Dose absorbed by the voxel

Planned dose

$$\chi^2 = \sum_{i\epsilon PTV} \frac{(d_i - D_{PTV})^2}{D_{PTV}^2} + \sum_{i\epsilon OAR^j} \eta_i \frac{(d_i - D_{OARj})^2}{D_{OARj}^2} \cdot \theta(d_i - D_{OARj})$$

Heaviside function

Voxel based

③ Minimize the given cost function, with different methods.

- The TPS I developed includes **two different minimization methods**, allowing the user to select the approach depending on what is needed to be optimized:

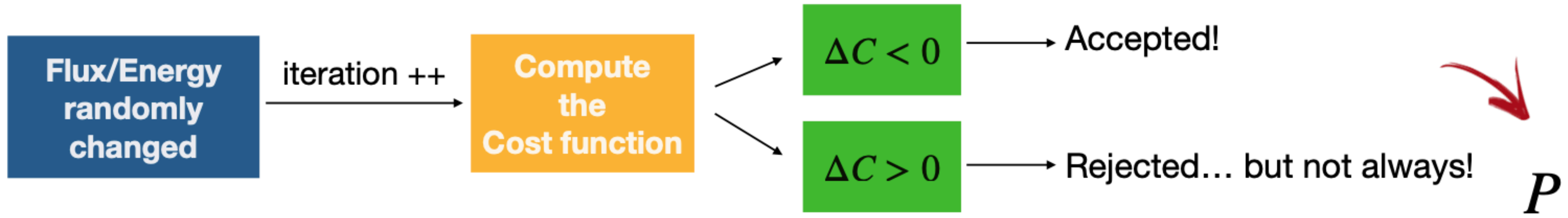
TO OPTIMIZE THE INTENSITIES OF PBs

The **Lomax algorithm** (**a conjugate gradient approach**) that effectively minimizes the cost function for **fixed beam energy** by adjusting pencil beam intensities, calculating the Hessian derivatives.

TO OPTIMIZE THE INTENSITIES OF PBs AND THE FIELD ENERGY

Simulated Annealing (**probabilistic optimization techniques**) is used for finding global minima in **high-dimensional spaces,** avoiding local minima where gradient-based methods may struggle.

Allows volumetric optimization (FLASH in mind!)


Flux/Energy randomly changed

iteration ++

Compute the Cost function

$\Delta C < 0$ → Accepted!

$\Delta C > 0$ → Rejected... but not always!

$$P = e^{-R(T)}$$

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TPS for VHEE FLASH

INPUT MODEL DOSE EVALUATION **OPTIMIZATION** RESULTS

GOAL? Select the **Energy of each field** and the **Intensity of each PB** of the treatment plan.

- The TPS I developed includes **two different minimization methods**, allowing the user to select the approach depending on what is needed to be optimized:

① In order to maximize tumor coverage and minimize the dose delivery to the normal tissue, the algorithm explore different set of parameters.

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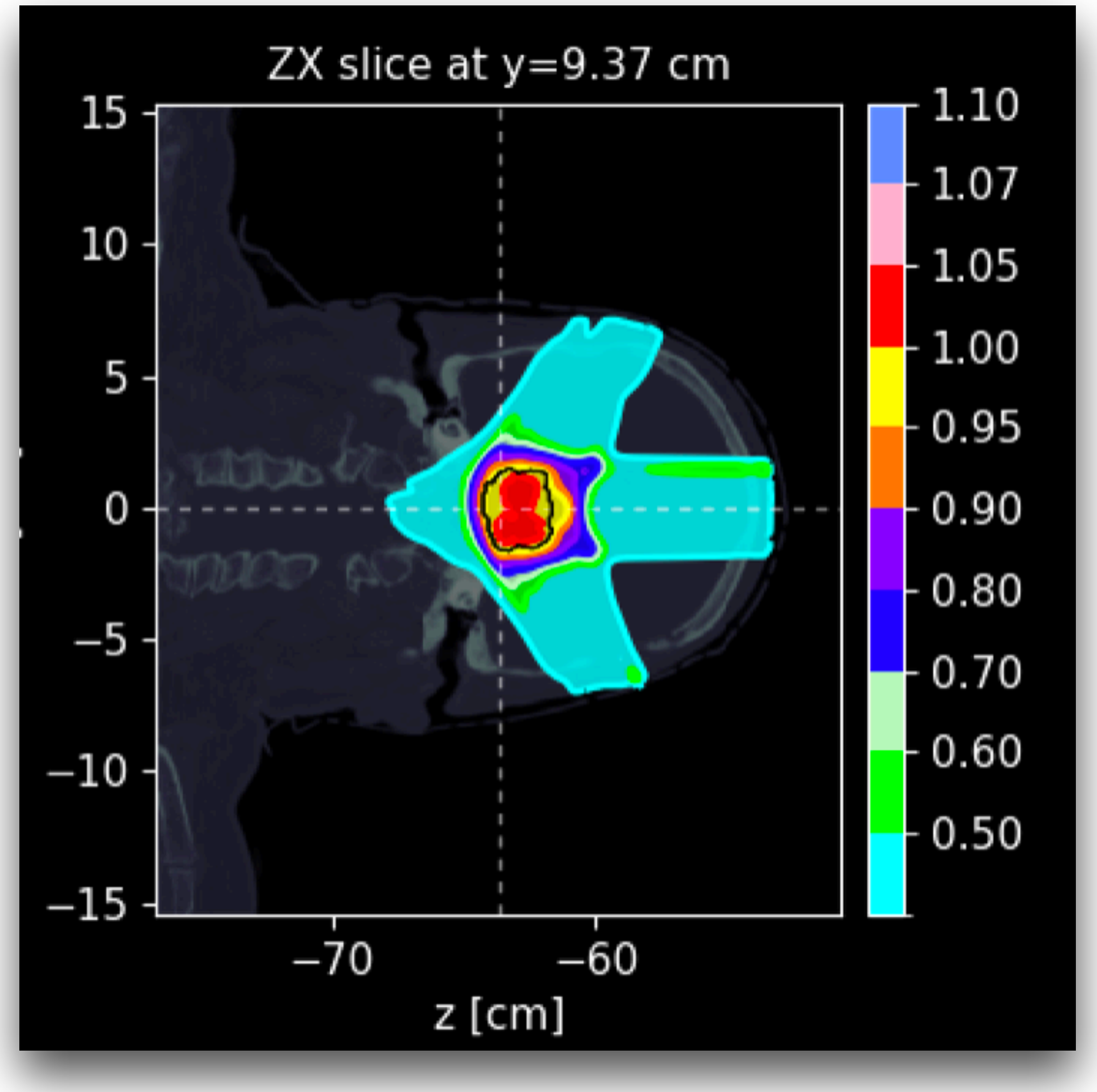
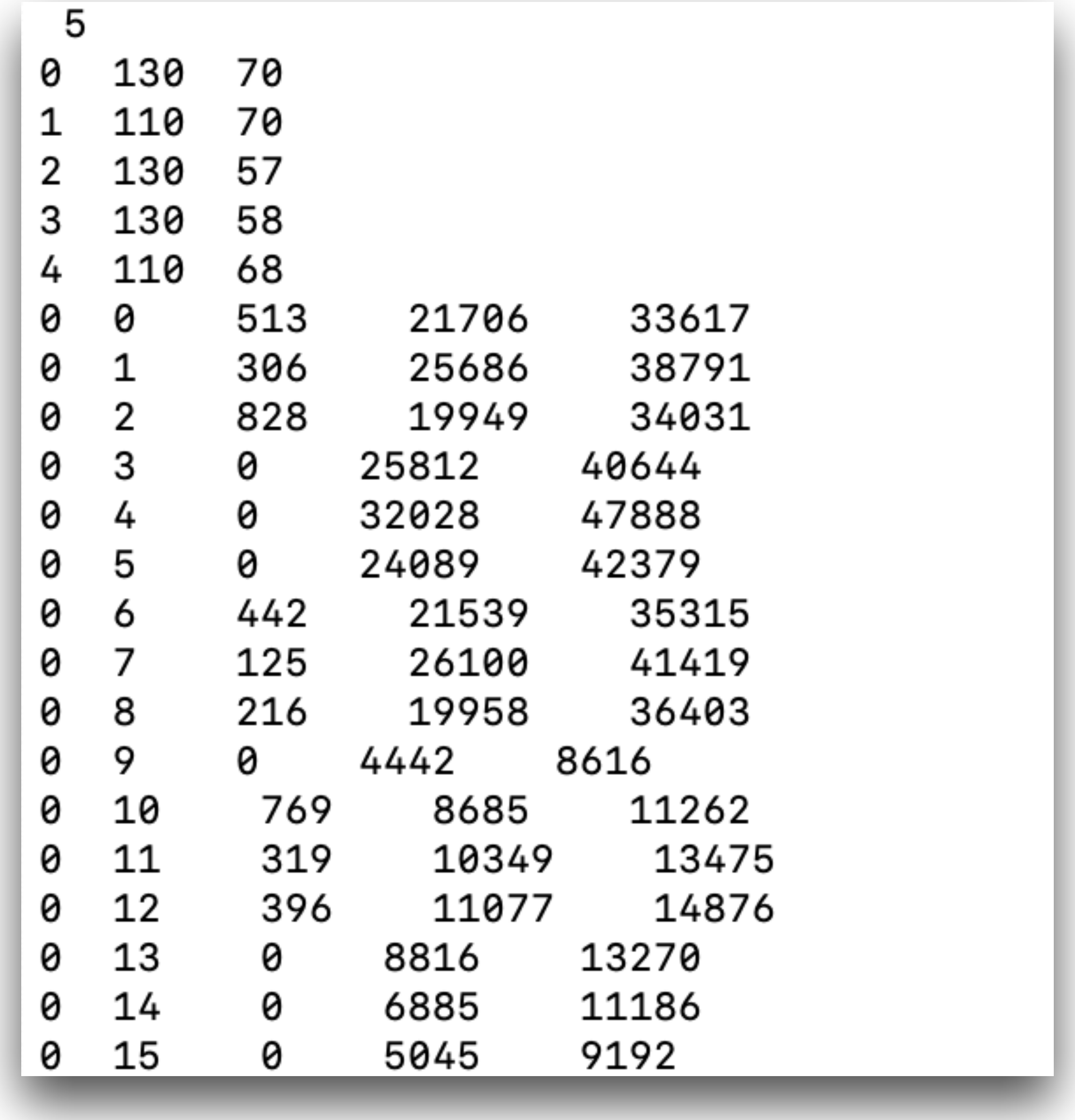
Heaviside function

Voxel based

③ Minimize the given cost function, with different methods.

The result is always:
OPTIMIZED DOSE MAP + list of
ACCELERATOR PARAMETERS





```
 5
0  130  70
1  110  70
2  130  57
3  130  58
4  110  68
0  0    513    21706    33617
0  1    306    25686    38791
0  2    828    19949    34031
0  3    0    25812    40644
0  4    0    32028    47888
0  5    0    24089    42379
0  6    442    21539    35315
0  7    125    26100    41419
0  8    216    19958    36403
0  9    0    4442    8616
0  10    769    8685    11262
0  11    319    10349    13475
0  12    396    11077    14876
0  13    0    8816    13270
0  14    0    6885    11186
0  15    0    5045    9192
```

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TPS for VHEE FLASH

- Using the TPS I have developed, I explored the potential of VHEE-based radiotherapy through **in-silico feasibility study** on **patients** with deep-seated tumors to which treatment plans were already **clinically delivered**.

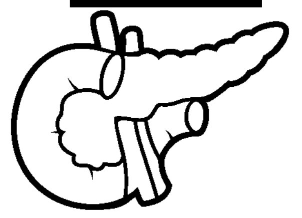
GOAL?

Compare the VHEE simulated plans with state-of-the-art conventional photon or PT treatments + **FLASH effect** exploration

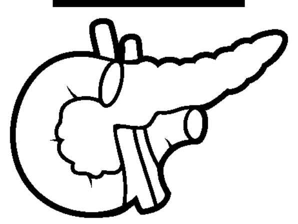
M1

C1

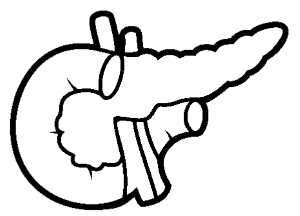
PT1



PT2



PT3



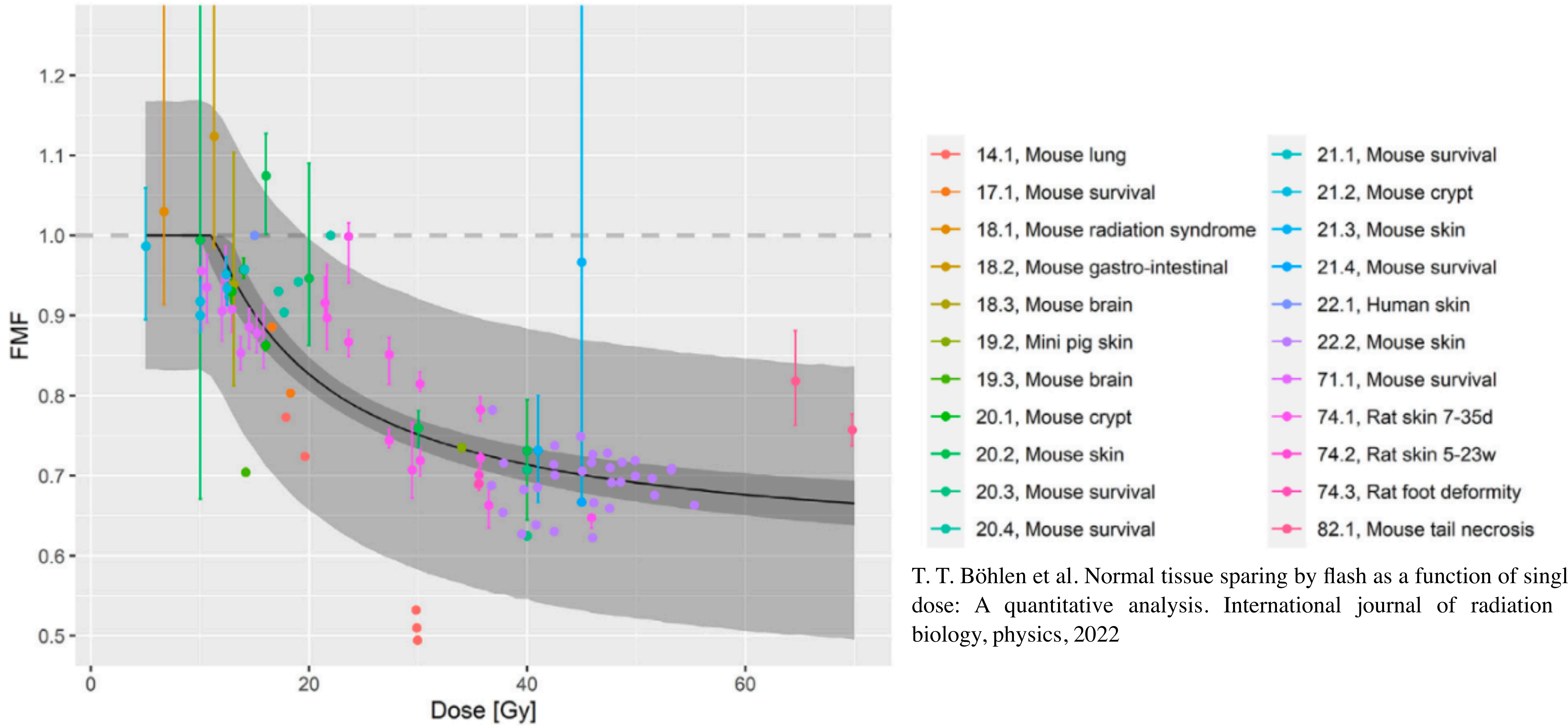
STUDY OF INTRACRANIAL LESIONS

Two patients with an intracranial lesion treated with **PT** at the Azienda Provinciale per i Servizi Sanitari (APSS) centre in Trento.

STUDY OF PANCREATIC TUMORS

Three patients with pancreatic tumor treated with **VMAT** treatments at the Fondazione Policlinico Universitario Campus Bio-Medico in Rome.

FLASH effect PARAMETRIZATION



T. T. Böhlen et al. Normal tissue sparing by flash as a function of single-fraction dose: A quantitative analysis. International journal of radiation oncology, biology, physics, 2022

The biological dose was optimized following the model:

$$D_{FMF} = FMF \cdot D \qquad FMF = \begin{cases} 1 & \text{if } D \leq D_T \\ (1 - FMF^{min})\frac{D_T}{D} + FMF^{min} & \text{if } D > D_T \end{cases}$$

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TPS for VHEE FLASH

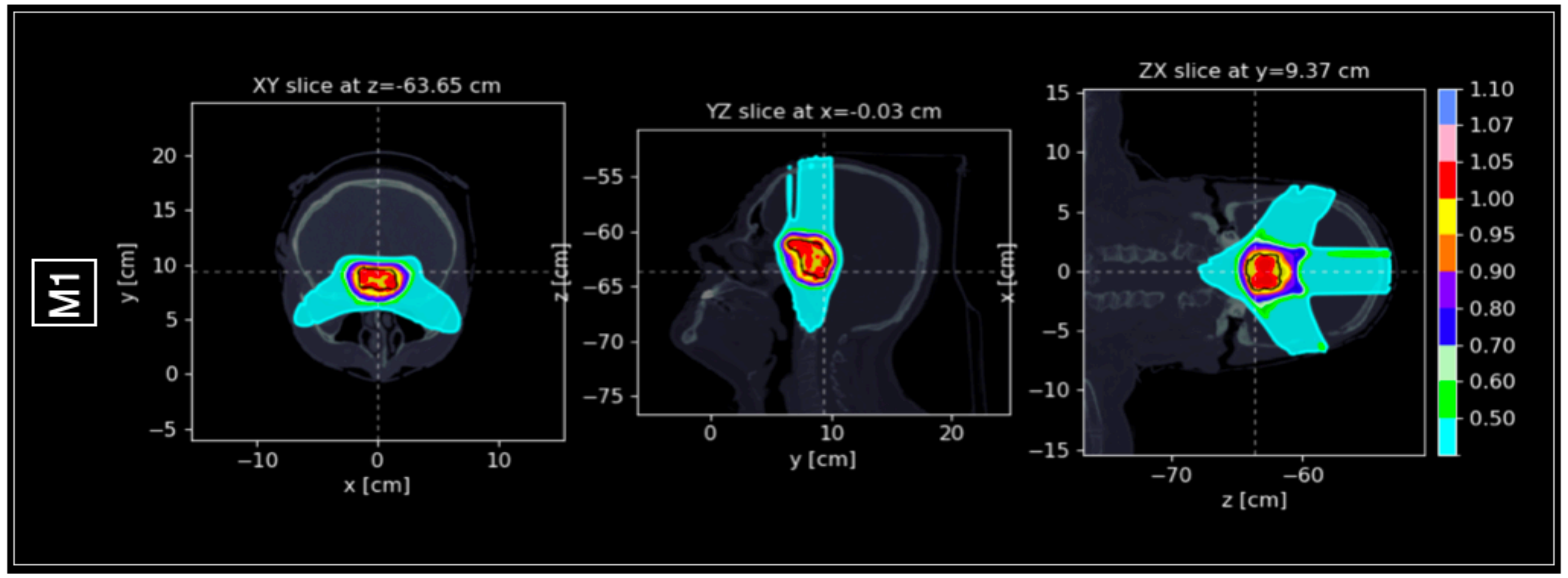
Validate VHEE treatment on DIFFICULT GEOMETRY due to the PTV position

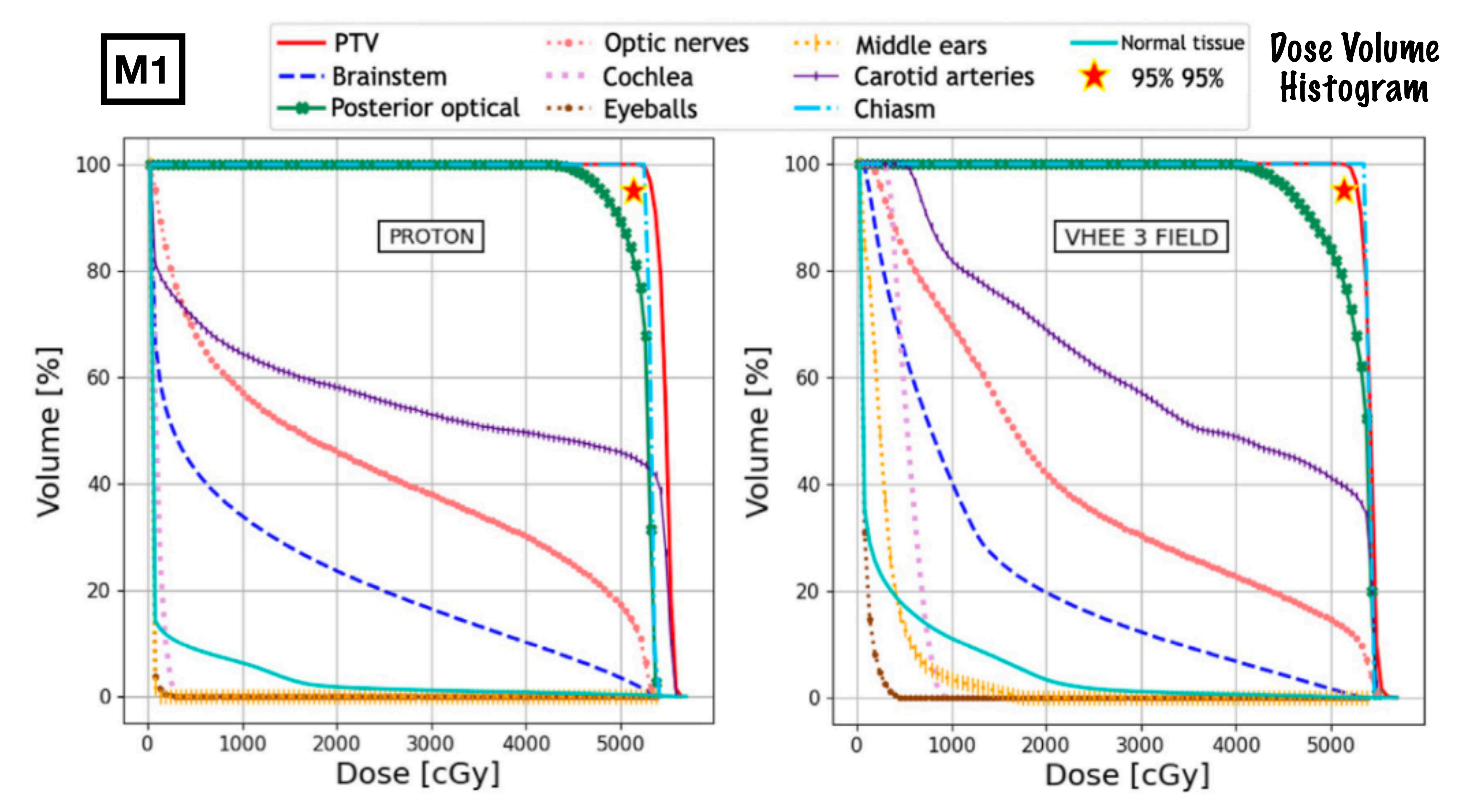
M1

- **Meningioma**: 3 fields, with a prescription to the **PTV of 54Gy(RBE)** in **27 fractions**.

C1

- **Chordoma**: 4 fields, with a prescription to the **PTV of 54Gy(RBE)** in **30 fractions**.





★ Comparing PT delivered plan and VHEE simulated plan, the DVH show **COMPETITIVE** performance.

Similar results for C1, with even more complex geometry (in SPARE!)

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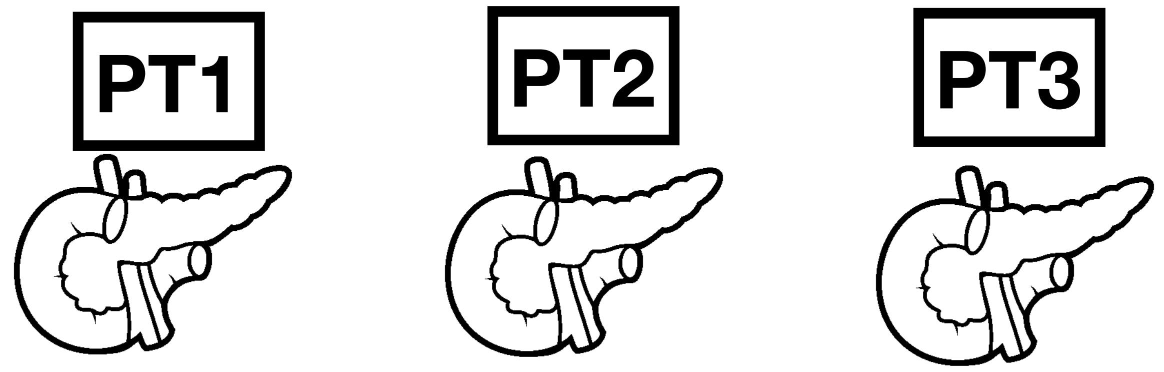
TPS for VHEE FLASH

- The TPS is crucial for pancreatic tumors as it enables precise dose delivery to the tumor while **minimizing radiation-induced toxicity to the nearby duodenum**. This approach enhances treatment efficacy by targeting the tumor effectively and reducing harmful side effects.

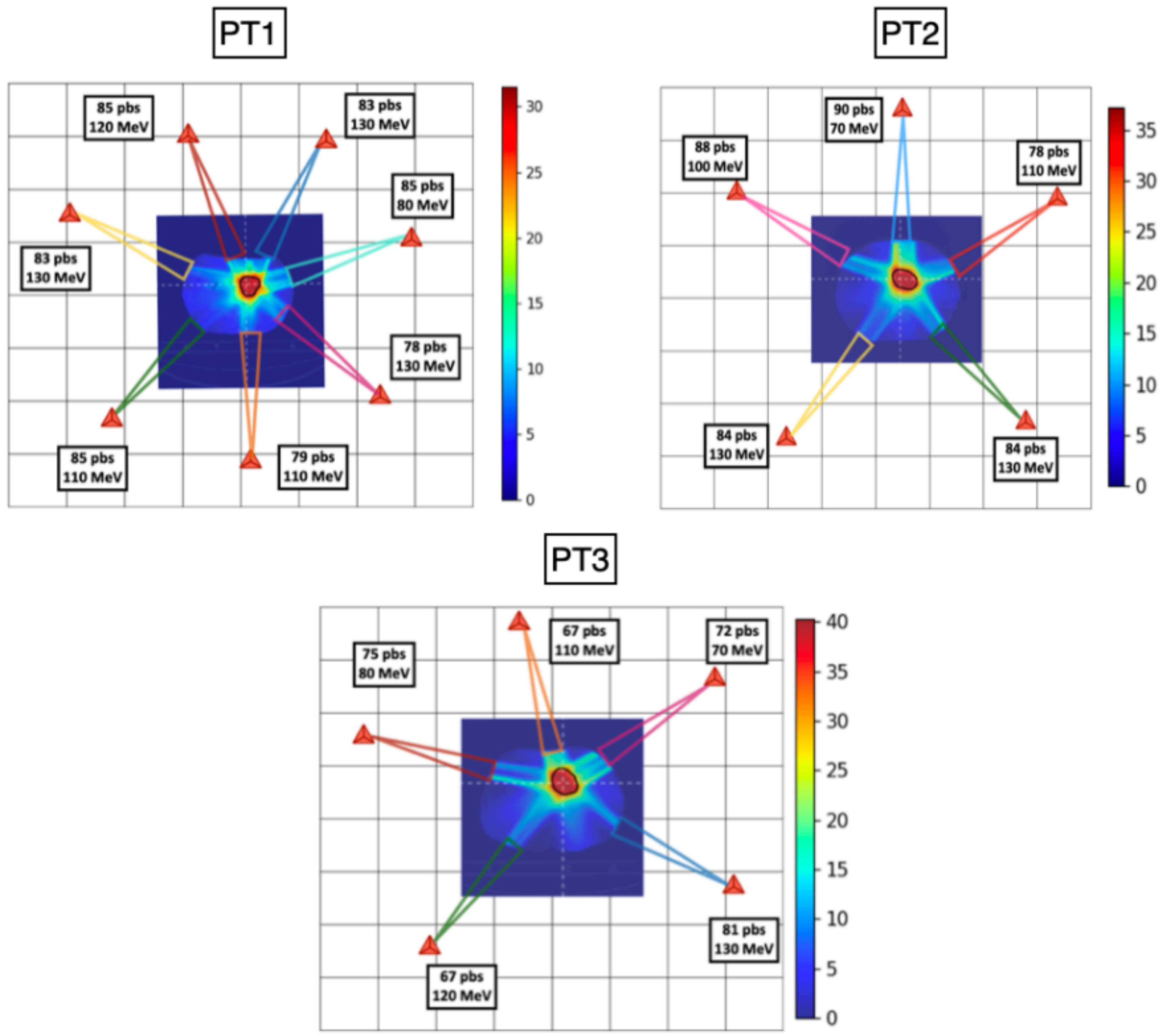
→ **GOOD CANDIDATE FOR FLASH IRRADIATION!**

PRESCRIPTIONS

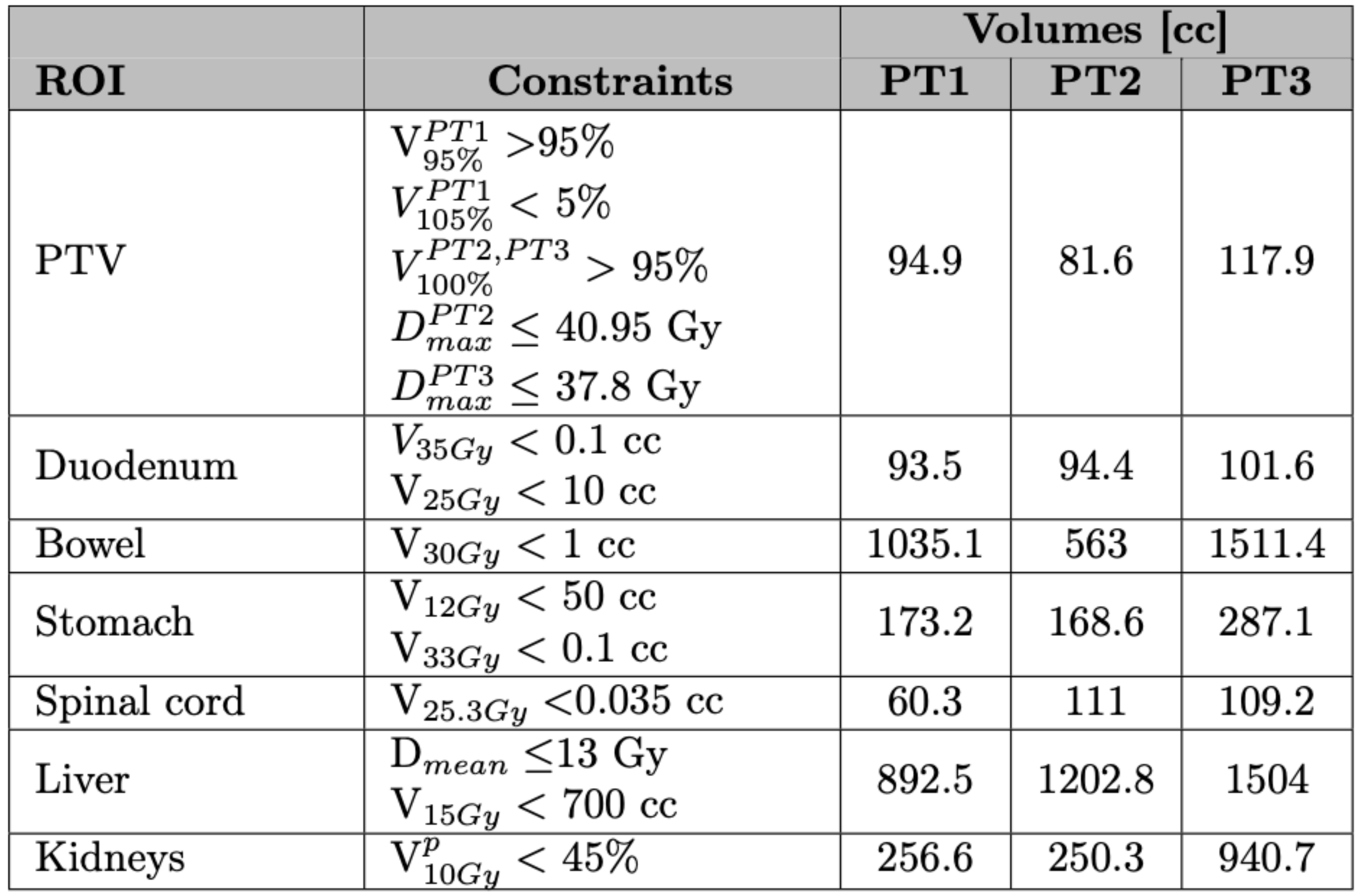


- **PT1**: seven fields were used, with a prescription to the **PTV of 30 Gy** in **5 fractions**.
- **PT2**: five fields were used, with a prescription to the **PTV of 32.5 Gy** in **5 fractions**.
- **PT3**: five fields were used, with a prescription to the **PTV of 30 Gy** in **5 fractions**.

FIELD GEOMETRY



DOSIMETRIC CONSTRAINTS



		Volumes [cc]		
ROI	**Constraints**	**PT1**	**PT2**	**PT3**
PTV	$V_{95\%}^{PT1} > 95\%$ $V_{105\%}^{PT1} < 5\%$ $V_{100\%}^{PT2,PT3} > 95\%$ $D_{max}^{PT2} \leq 40.95$ Gy $D_{max}^{PT3} \leq 37.8$ Gy	94.9	81.6	117.9
Duodenum	$V_{35Gy} < 0.1$ cc $V_{25Gy} < 10$ cc	93.5	94.4	101.6
Bowel	$V_{30Gy} < 1$ cc	1035.1	563	1511.4
Stomach	$V_{12Gy} < 50$ cc $V_{33Gy} < 0.1$ cc	173.2	168.6	287.1
Spinal cord	$V_{25.3Gy} < 0.035$ cc	60.3	111	109.2
Liver	$D_{mean} \leq 13$ Gy $V_{15Gy} < 700$ cc	892.5	1202.8	1504
Kidneys	$V_{10Gy}^{p} < 45\%$	256.6	250.3	940.7

Slightly different modalities for irradiation

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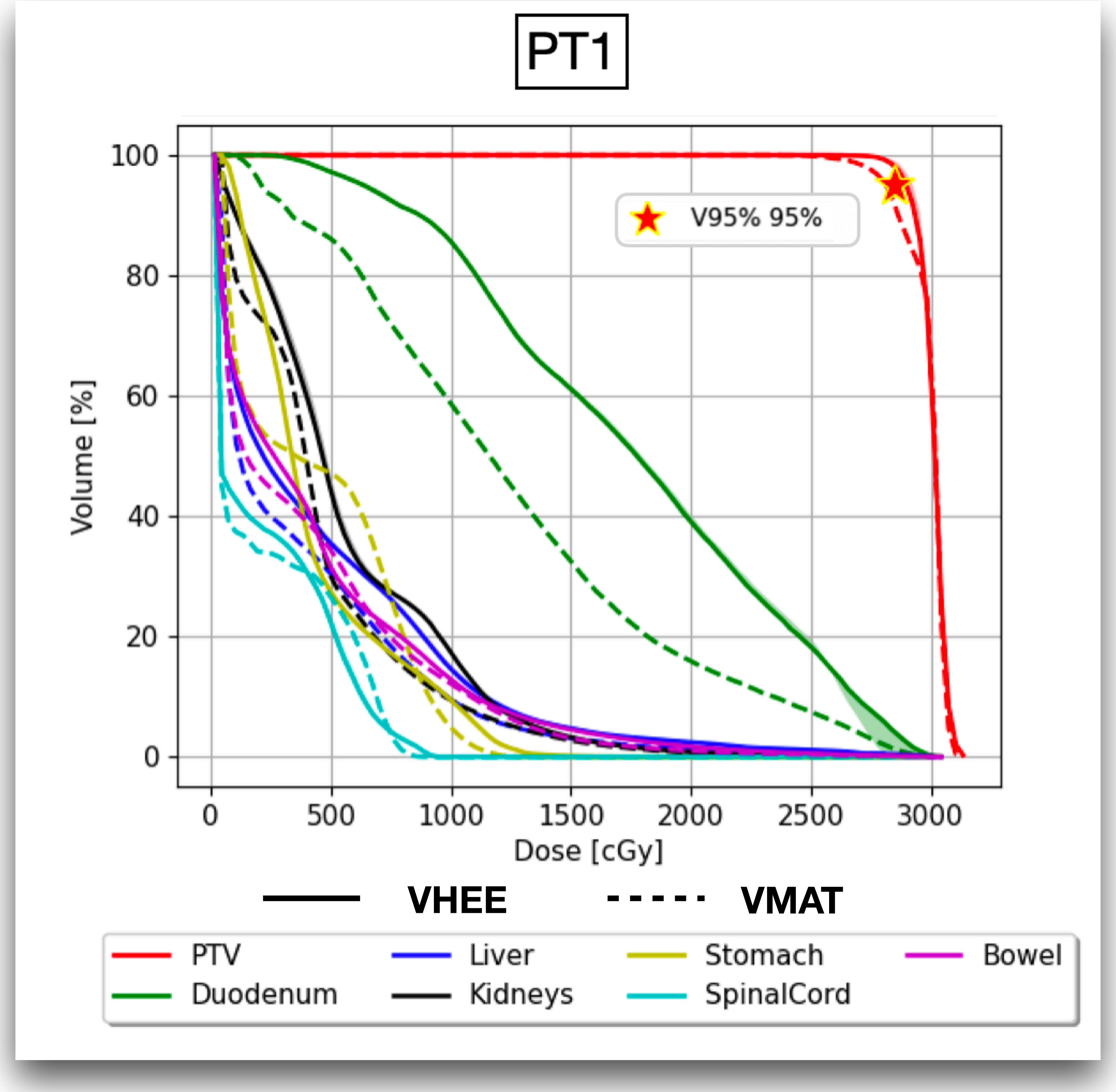
TPS for VHEE FLASH

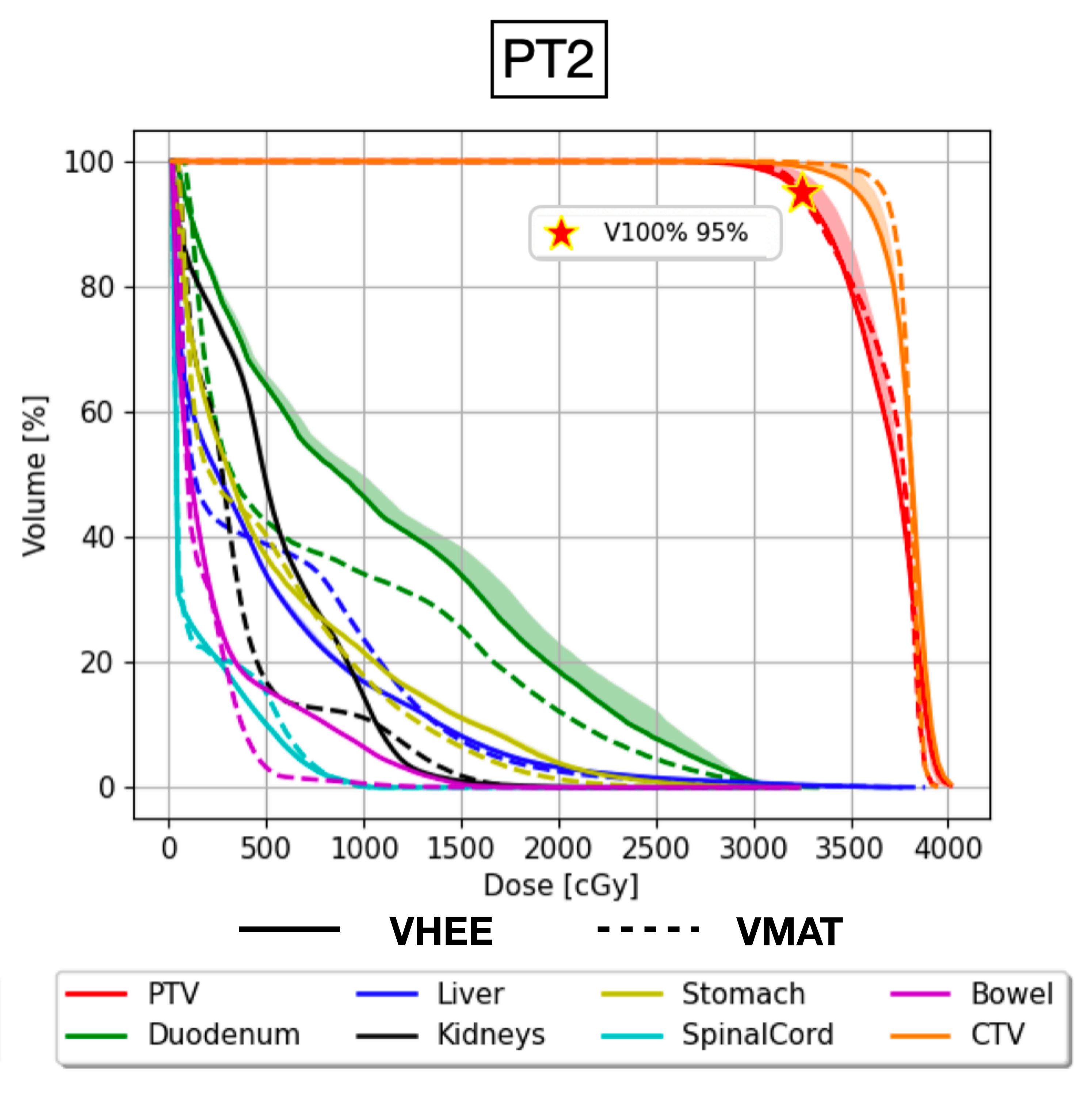
- The TPS is crucial for pancreatic tumors as it enables precise dose delivery to the tumor while **minimizing radiation-induced toxicity to the nearby duodenum**. This approach enhances treatment efficacy by targeting the tumor effectively and reducing harmful side effects.

BEST CANDIDATE FOR FLASH IRRADIATION!

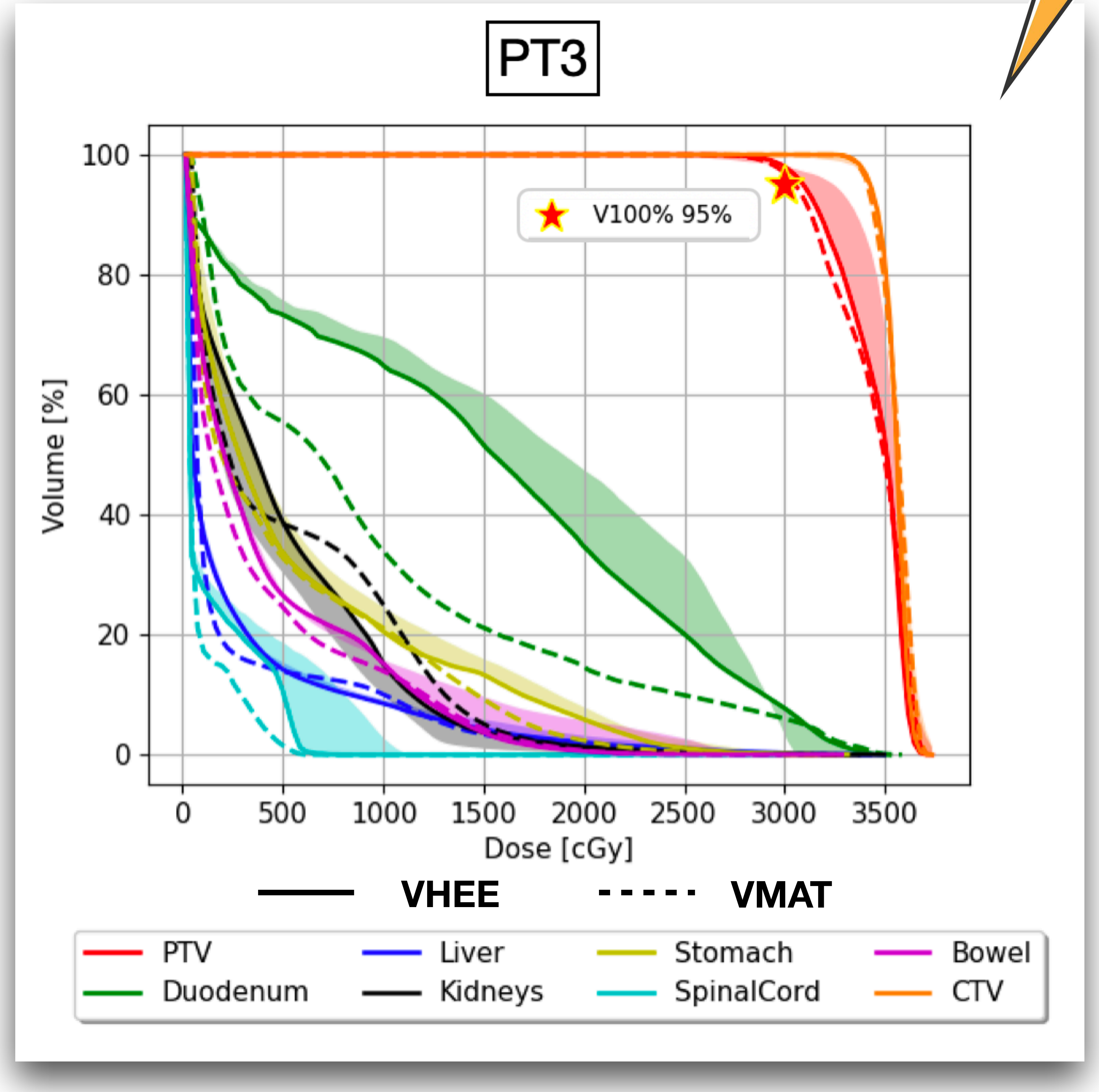
PT1



PT2



PT3

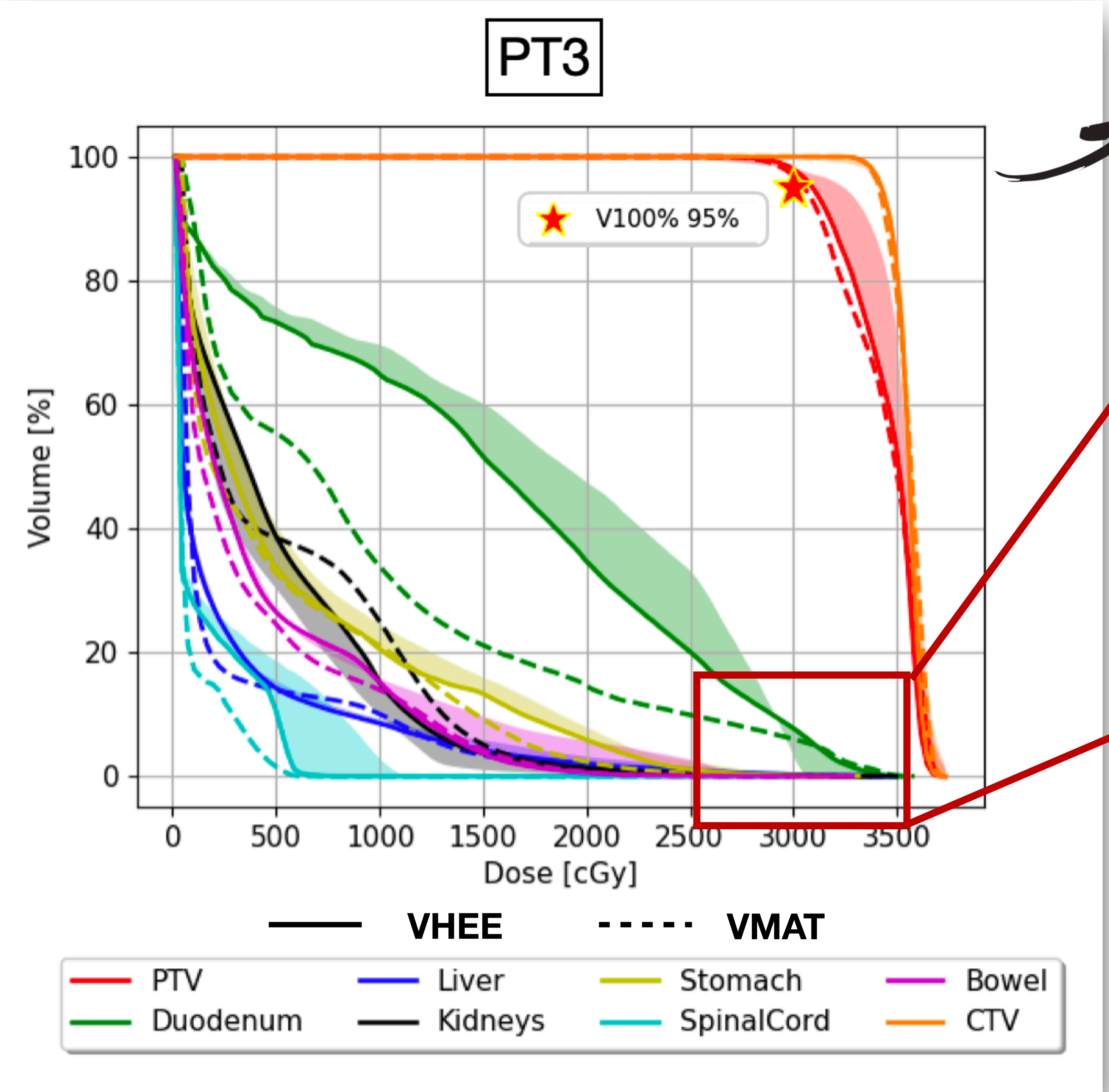


FONDAZIONE
POLICLINICO UNIVERSITARIO
CAMPUS BIO-MEDICO

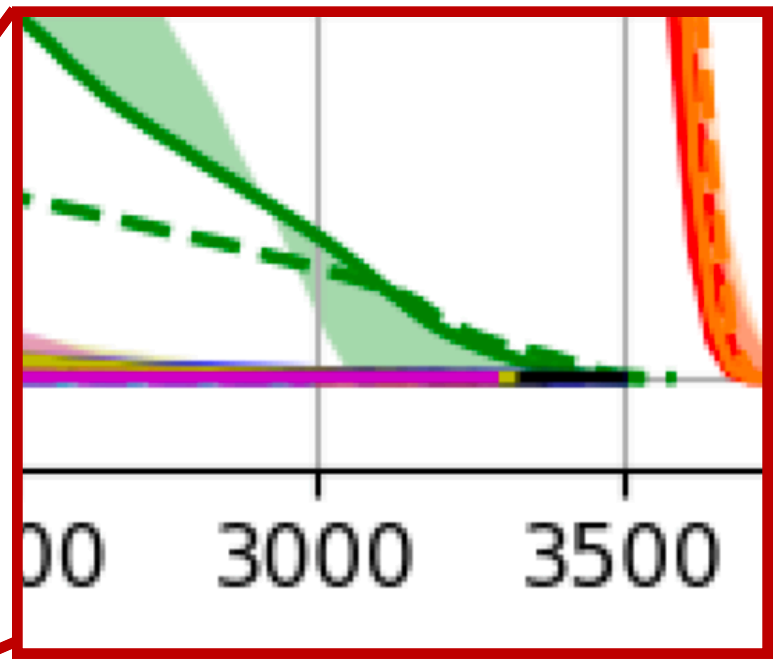
TPS for VHEE FLASH

- The TPS is crucial for pancreatic tumors as it enables precise dose delivery to the tumor while **minimizing radiation-induced toxicity to the nearby duodenum**. This approach enhances treatment efficacy by targeting the tumor effectively and reducing harmful side effects.

→ **BEST CANDIDATE FOR FLASH IRRADIATION!**



The transparent bands indicate the potential improvement if the plan is delivered in UHDR conditions.



	VMAT	VHEE	VHEE-FLASH
PTV	99%	98.32%	98.32%
Duodenum	35.88 Gy	35.11 Gy	31.06 Gy
Stomach	31.04 Gy	33.28 Gy	29.97 Gy

- FMFmin = 0.6 to 1
- Dth value of 25 Gy.

The FLASH optimization results in an **increase in the average** dose delivered to the duodenum, while **reducing its maximum absorbed dose** by approximately 4 Gy. This allows to increase the PTV coverage!

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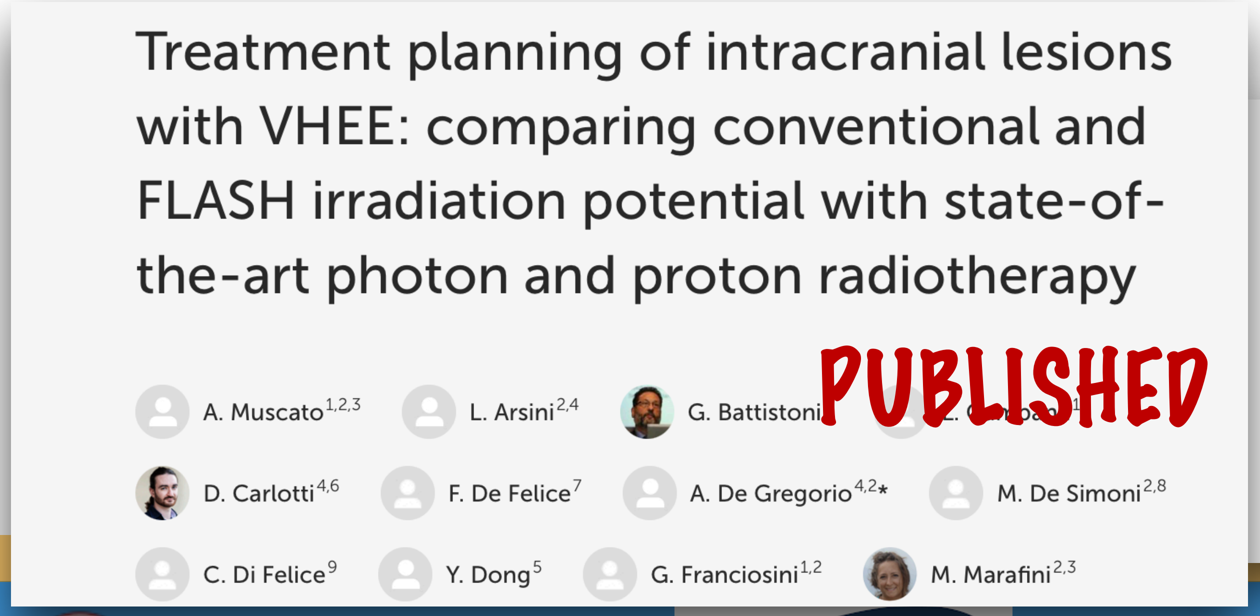
Conclusions and future steps

Over these **3 years of my Ph.D.**, my research has focused on:

1. **Radioprotection Studies for the LINAC** being constructed as part of the SAFEST project. I conducted an analysis of simulation results on interactions between the primary beam and accelerator materials to determine the shielding thickness required to reduce dose levels in the surrounding environment.

2. **Development of a TPS for VHEE in FLASH Mode:** I developed software capable of optimizing, through various methods, the dose absorbed by the tumor and surrounding healthy organs to output the accelerator's setting parameters for treatment. Several feasibility studies were conducted on patient data provided by various hospitals.

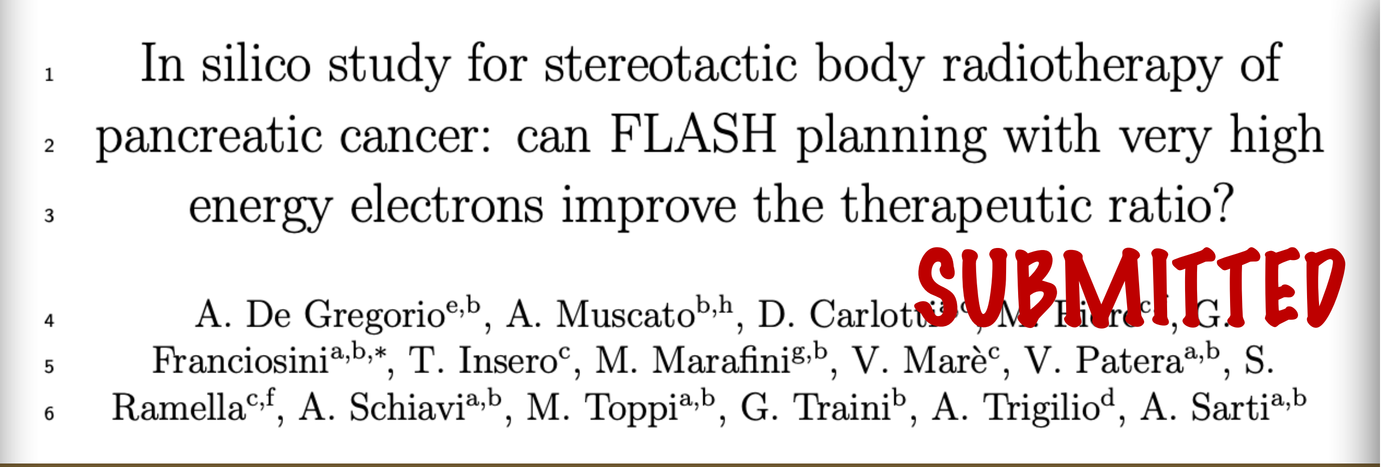
The results demonstrate the **suitability of VHEE for both intracranial lesions and pancreatic cancer treatment**. When compared to state of the art conventional radiotherapy, e.g. PT and VMAT plans, **VHEE show a comparable performance** even without reaching the UHDR regimen required to trigger the FLASH effect. Under a few plausible assumptions on the conditions required to trigger the FLASH effect, the results demonstrated that it should be possible to escalate the dose at the PTV without worsening the OARs injury.



Treatment planning of intracranial lesions with VHEE: comparing conventional and FLASH irradiation potential with state-of-the-art photon and proton radiotherapy

A. Muscato[1,2,3] L. Arsini[2,4] G. Battistoni[illegible]
D. Carlotti[4,6] F. De Felice[7] A. De Gregorio[4,2*] M. De Simoni[2,8]
C. Di Felice[9] Y. Dong[5] G. Franciosini[1,2] M. Marafini[2,3]

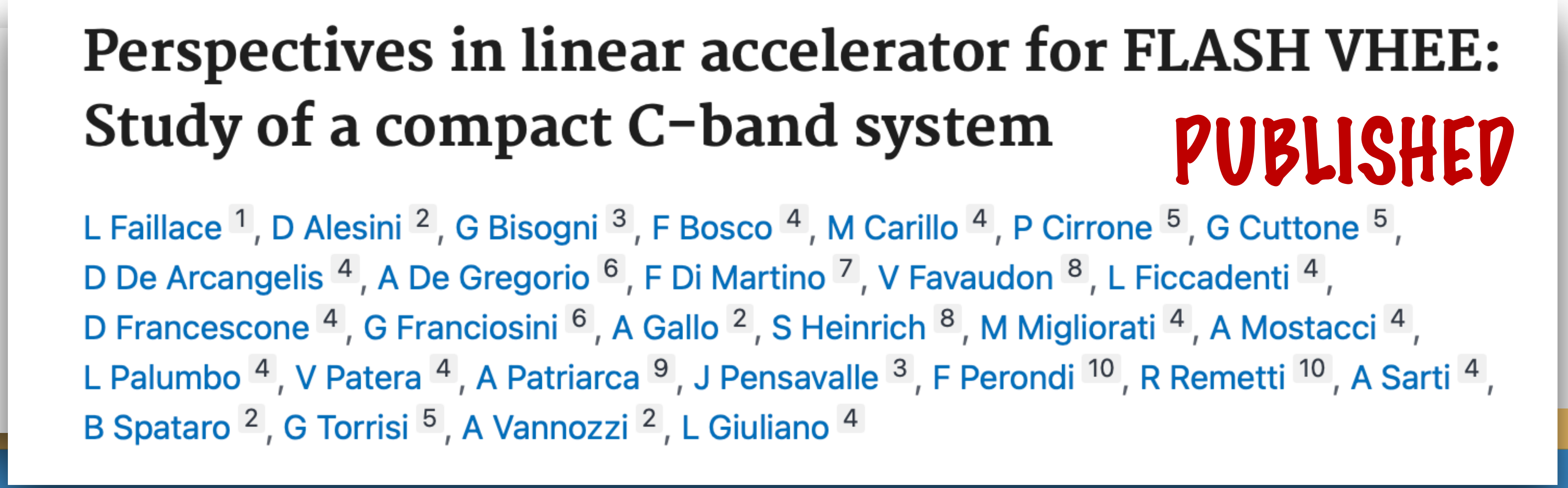
PUBLISHED



In silico study for stereotactic body radiotherapy of pancreatic cancer: can FLASH planning with very high energy electrons improve the therapeutic ratio?

A. De Gregorio[e,b], A. Muscato[b,h], D. Carlotti[illegible], G. Franciosini[a,b,*], T. Insero[c], M. Marafini[g,b], V. Marè[c], V. Patera[a,b], S. Ramella[c,f], A. Schiavi[a,b], M. Toppi[a,b], G. Traini[b], A. Trigilio[d], A. Sarti[a,b]

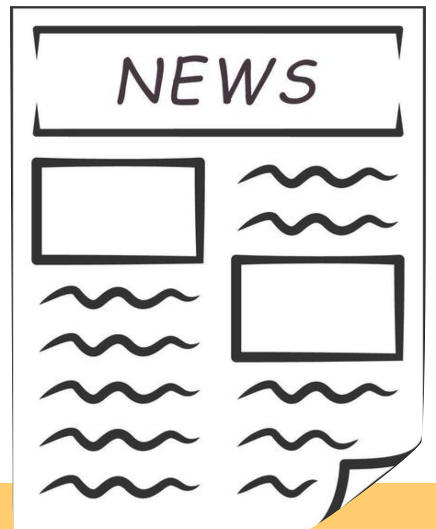
SUBMITTED



Perspectives in linear accelerator for FLASH VHEE: Study of a compact C-band system

PUBLISHED

L Faillace [1], D Alesini [2], G Bisogni [3], F Bosco [4], M Carillo [4], P Cirrone [5], G Cuttone [5], D De Arcangelis [4], A De Gregorio [6], F Di Martino [7], V Favaudon [8], L Ficcadenti [4], D Francescone [4], G Franciosini [6], A Gallo [2], S Heinrich [8], M Migliorati [4], A Mostacci [4], L Palumbo [4], V Patera [4], A Patriarca [9], J Pensavalle [3], F Perondi [10], R Remetti [10], A Sarti [4], B Spataro [2], G Torrisi [5], A Vannozzi [2], L Giuliano [4]



THANK-YOU

FRIDA

PUBLICATIONS

- A. De Gregorio et al., Measurements of the 16O cross section on a C target with the FOOT apparatus. Nuovo Cimento della Societa Italiana di Fisica C; 2022,DOI: 10.1393/ncc/i2022-22194-4
- M. De Simoni et al., A Data-Driven Fragmentation Model for Carbon Therapy GPU-Accelerated Monte-Carlo Dose Recalculation. Frontiers in Oncology; 2022,DOI:10.3389/fonc.2022.780784
- M. Moglioni et al., In-vivo range verification analysis with in-beam PET data for patients treated with proton therapy at CNAO. Frontiers in Oncology; 2022, DOI:10.3389/fonc.2022.929949
- A. Trigilio et al., The FlashDC project: Development of a beam monitor for FLASH radiotherapy. Nuclear Instruments and Methods in Physics Research, Section A: Accelerators, Spectrometers, Detectors and Associated Equipment; 2022, DOI: 10.1016/j.nima.2022.167334
- M. Toppi et al., Elemental fragmentation cross sections for a 16 O beam of 400 MeV/nucleon kinetic energy interacting with a graphite target using the FOOT ΔE-TOF detectors. Frontiers in Physics, section Medical Physics and Imaging, 2022, DOI: https://doi.org/10.3389/fphy.2022.979229
- A.C. Kraan et al., Calibration and performance assessment of the TOF-Wall detector of the FOOT experiment. Nuclear Instruments and Methods in Physics Research, Section A: Accelerators, Spectrometers, Detectors and Associated Equipment; 2023, DOI: 10.1016/j.nima.2022.167615
- L. Galli et al., The fragmentation trigger of the FOOT experiment. Nuclear Instruments and Methods in Physics Research, Section A: Accelerators, Spectrometers, Detectors and Associated Equipment; 2023, DOI: https://doi.org/10.1016/j.nima.2022.167757
- A. Alexadrov et al., Characterization of 150 μm thick silicon microstrip prototype for the FOOT experiment. Journal of Instrumentation; 2022, DOI: 10.1088/1748-0221/17/12/P12012
- L. Faillace et al., Perspectives in linear accelerator for FLASH VHEE: Study of a compact C-band system. Physica Medica; 2022, DOI: 10.1016/j.ejmp.2022.10.018
- D. Rocco et al., TOPS fast timing plastic scintillators: Time and light output performances. Nuclear Instruments and Methods in Physics Research, Section A: Accelerators, Spectrometers, Detectors and Associated Equipment; 2023, DOI: 10.1016/j.nima.2023.168277
- G. Franciosini et al., GPU-accelerated Monte Carlo simulation of electron and photon interactions for radiotherapy applications. Physics in Medicine and Biology; 2023, DOI: 10.1088/1361-6560/aca1f2
- L. Giuliano et al., Proposal of a VHEE Linac for FLASH radiotherapy. Physics in Medicine and Biology; 2023, DOI: 10.1088/1742-6596/2420/1/012087
- A. Muscato et al., Treatment planning of intracranial lesions with VHEE: comparing conventional and FLASH irradiation potential with state-of-the-art photon and proton radiotherapy. Frontiers in Physics; 2023, DOI: 10.3389/fphy.2023.1185598

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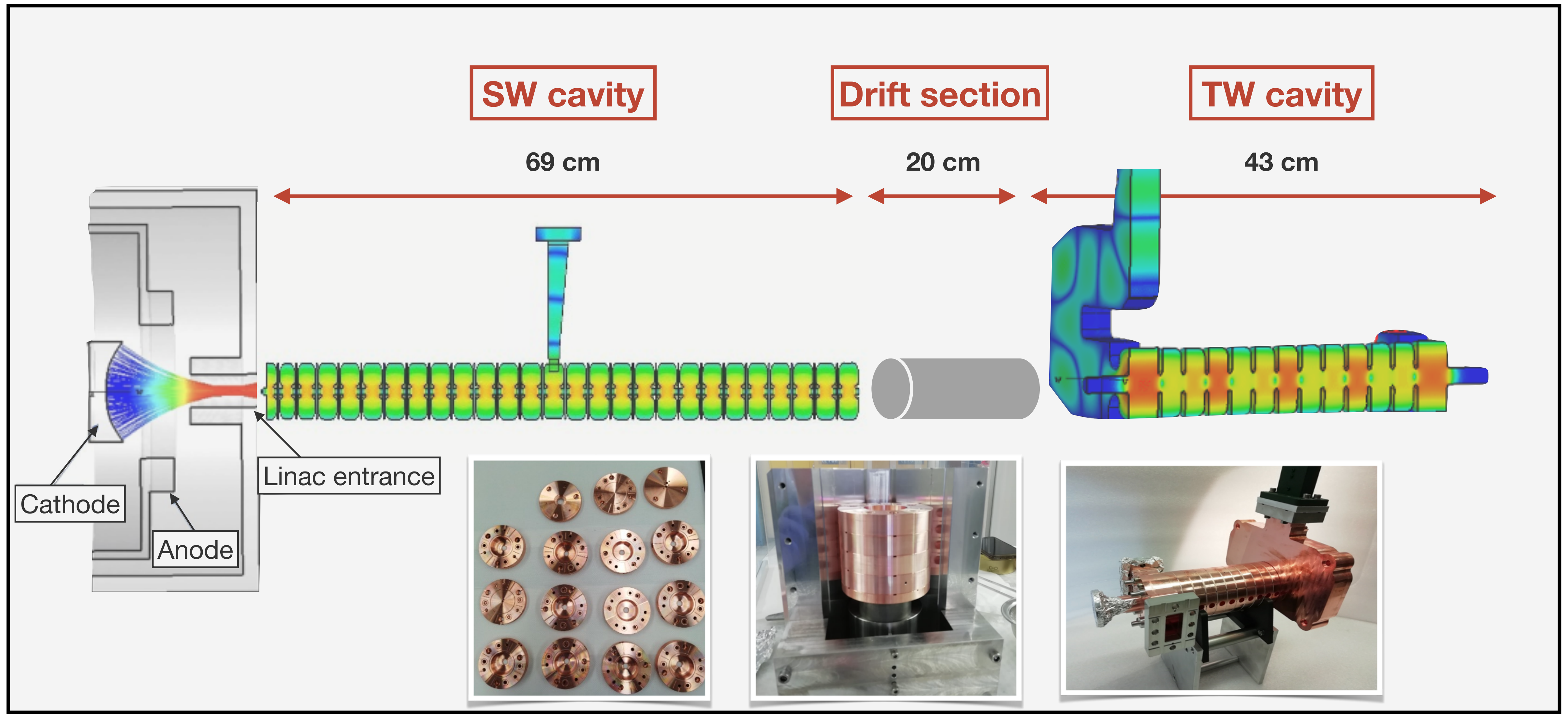
ENRICO FERMI

FRIDA

SPARE SLIDES

Radio-protection studies

- The **prototype** currently under construction as part of the SAFEST project is a **scaled-down version** of the proposed VHEE LINAC, designed to accelerate electron beams up to **24 MeV.**



	SW section	**TW section**
Shunt Impedance	103 MOhm/m	107 MOhm/m
Quality Factor	10178	10127
Energy	10 MeV	24 MeV
Pulse current	100 mA	100 mA

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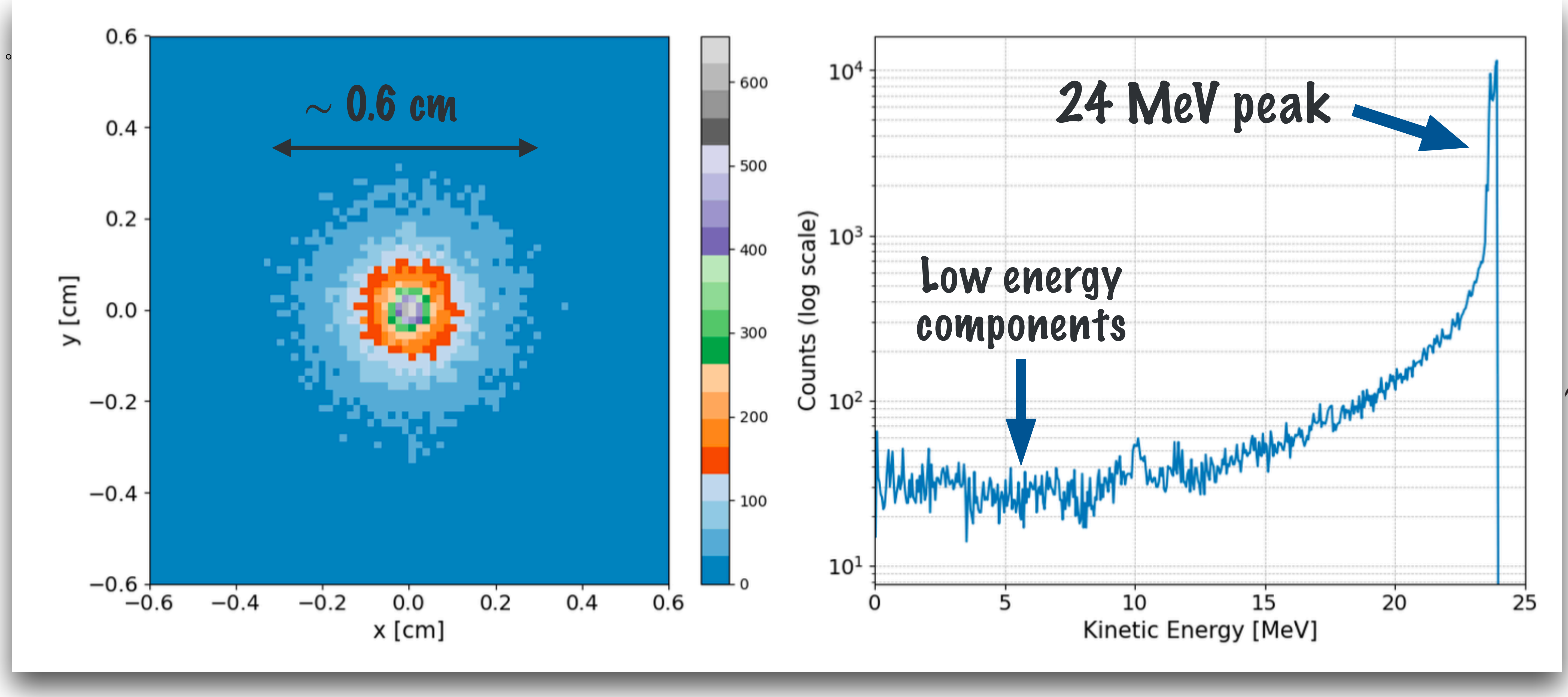
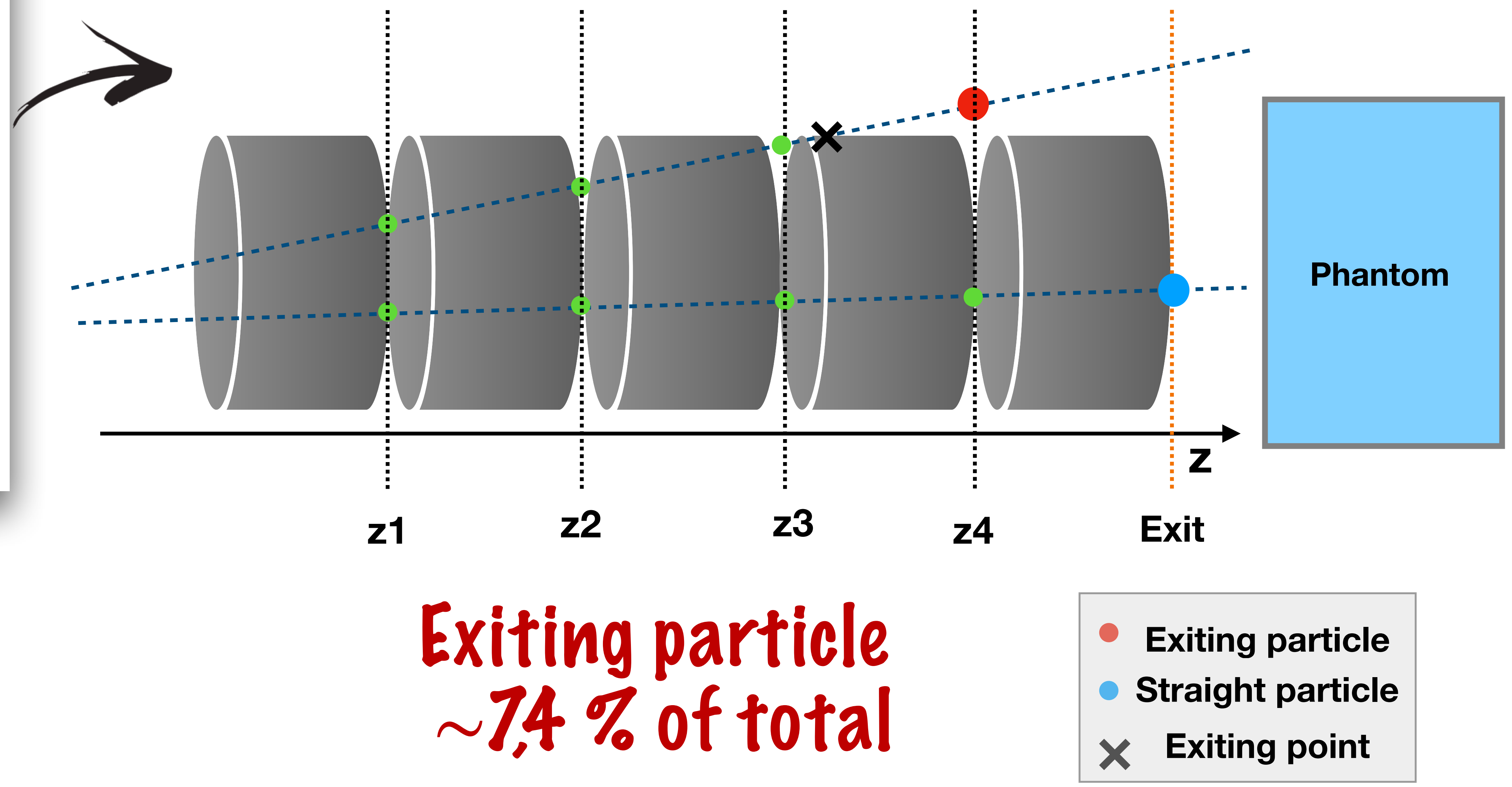
Radio-protection studies

- I analyzed **electromagnetic simulations** performed using the software Parmela, that provides detailed insights into the beam dynamics and from which I **extracted the position, direction, and energy** of each individual particle.



To **identify the electrons exiting the beam pipe** which interact with the external accelerator material (copper), I conducted a **geometrical analysis** in order to save the exit positions from the iris of the accelerator:



Exiting particle ~7,4 % of total

Radio-protection studies

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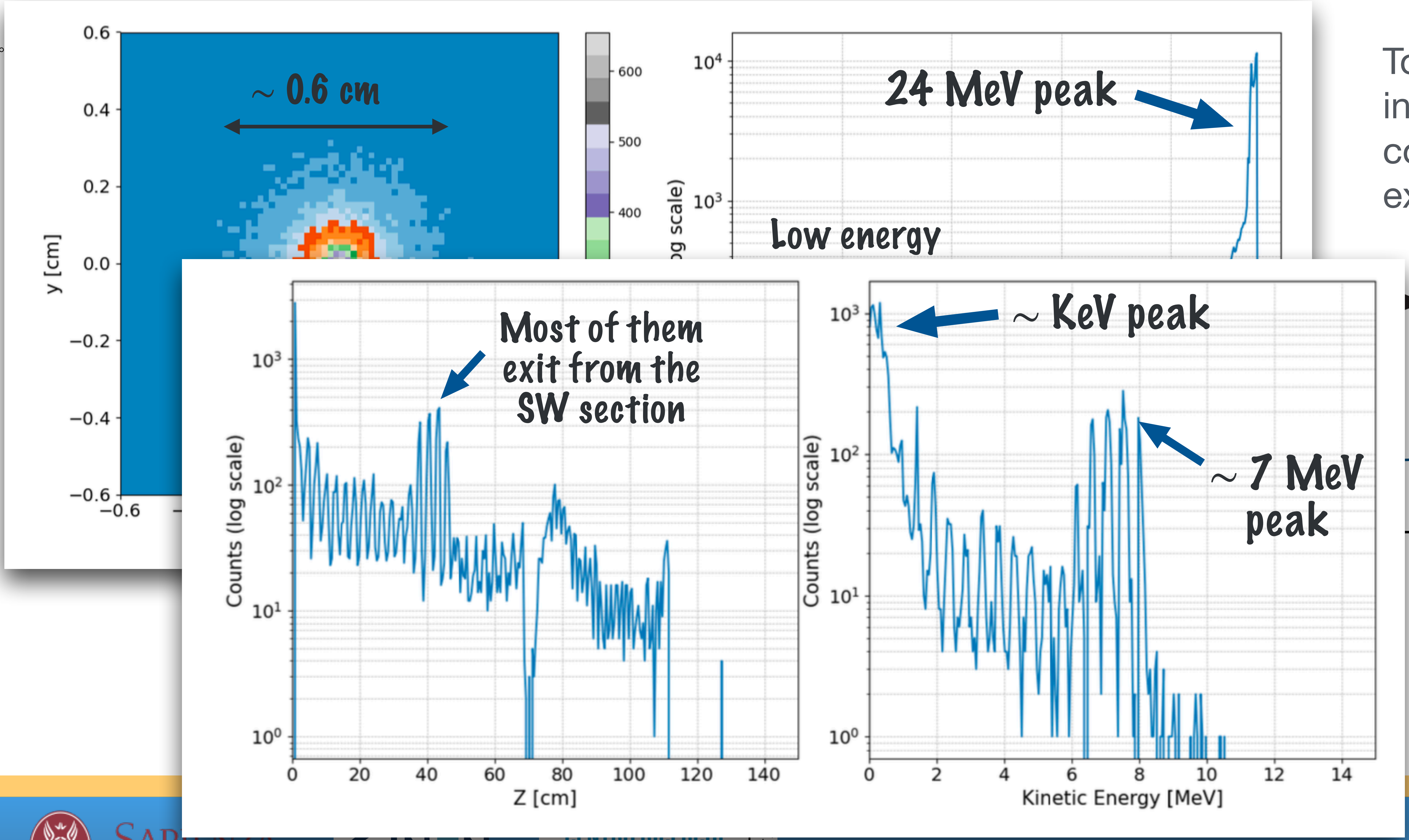

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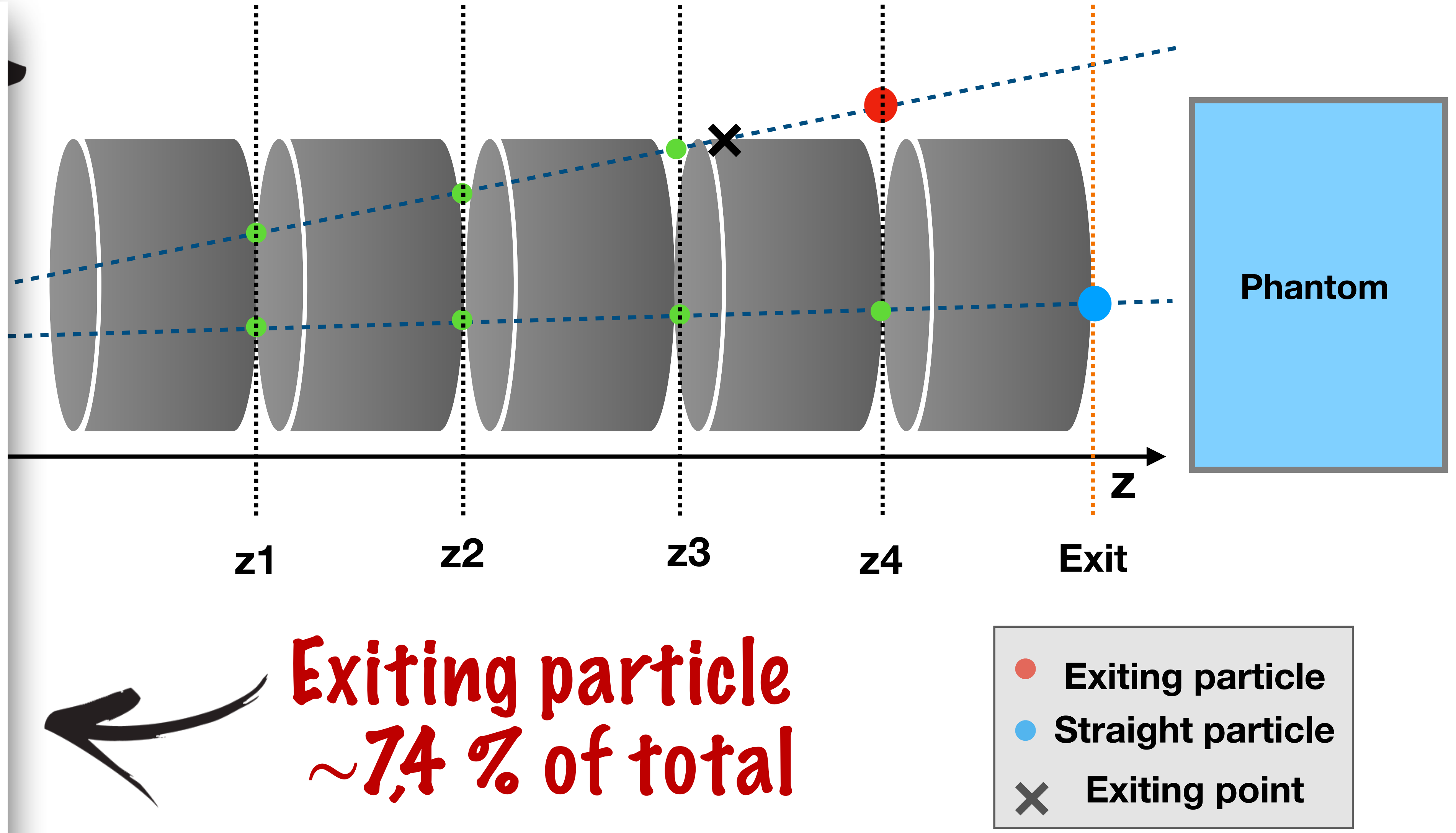

Exiting particle ~7,4 % of total

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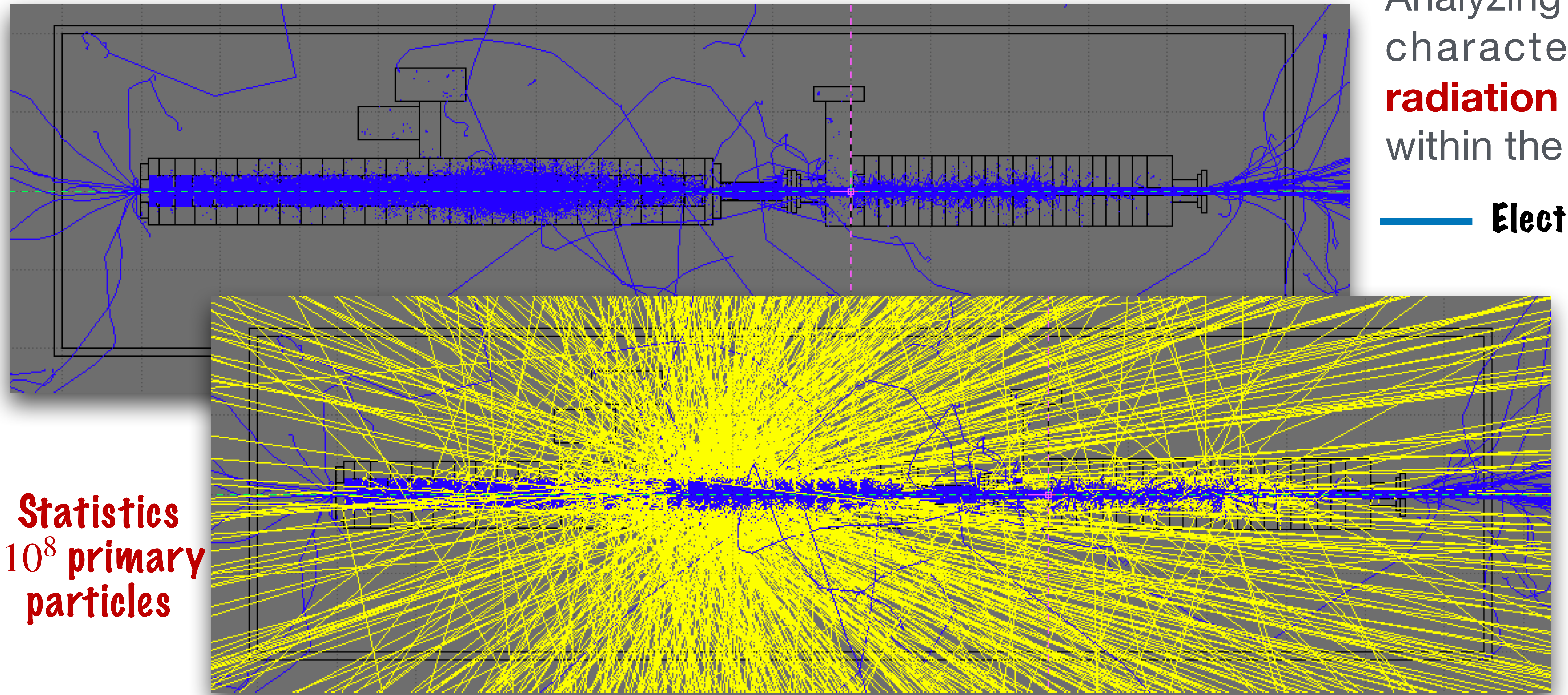
Radio-protection studies

- After identifying the coordinates at which the electrons exited the accelerator, both for the straight and scattered electrons, **further simulations were conducted using FLUKA** to model the **radiation transport** and **secondary particle production**.



Analyzing the FLUKA output allowed me to characterize the **different types of radiation produced** by various interactions within the accelerator.

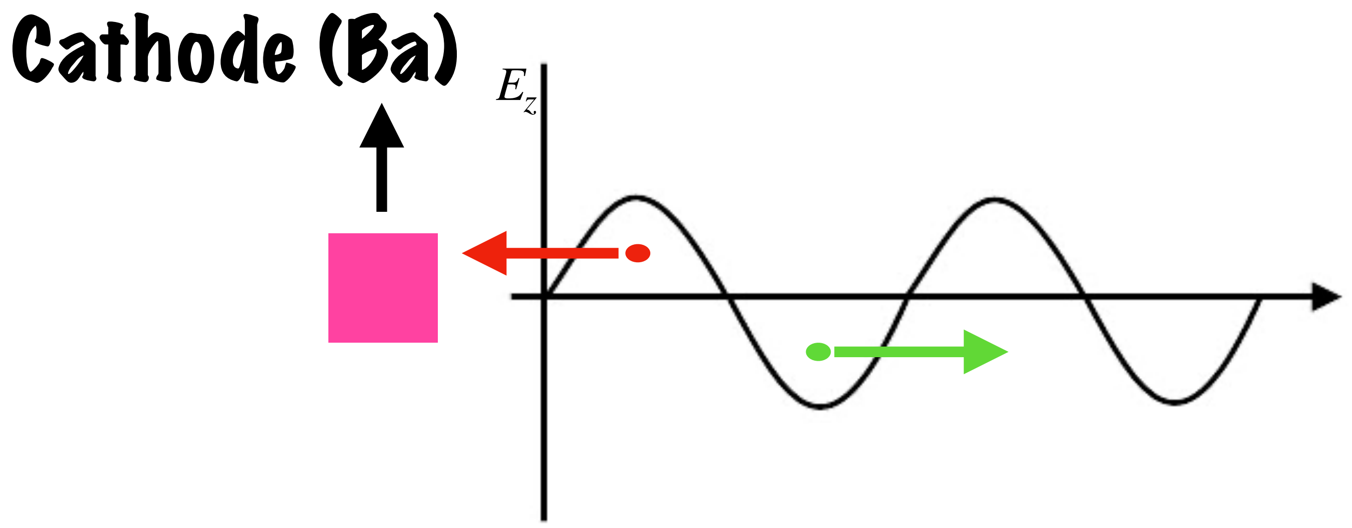
— Electrons — Photons — Neutrons

Statistics
10^8 **primary particles**

GOAL?

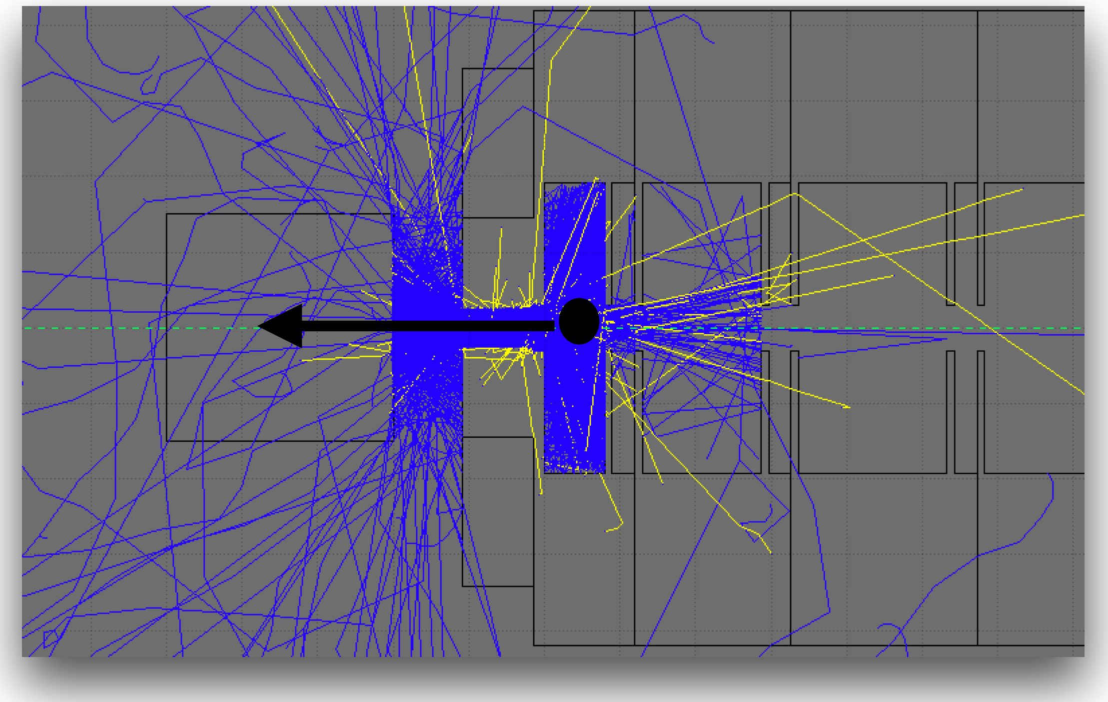
Evaluate the dispersed radiation to design the needed shielding.

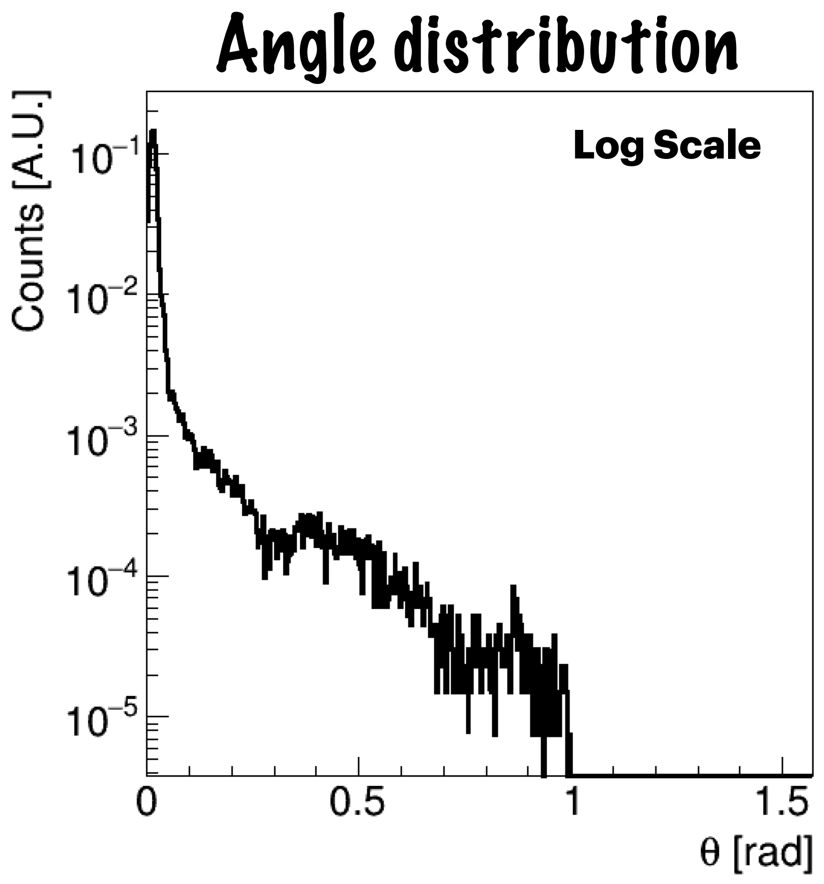
Radio-protection studies

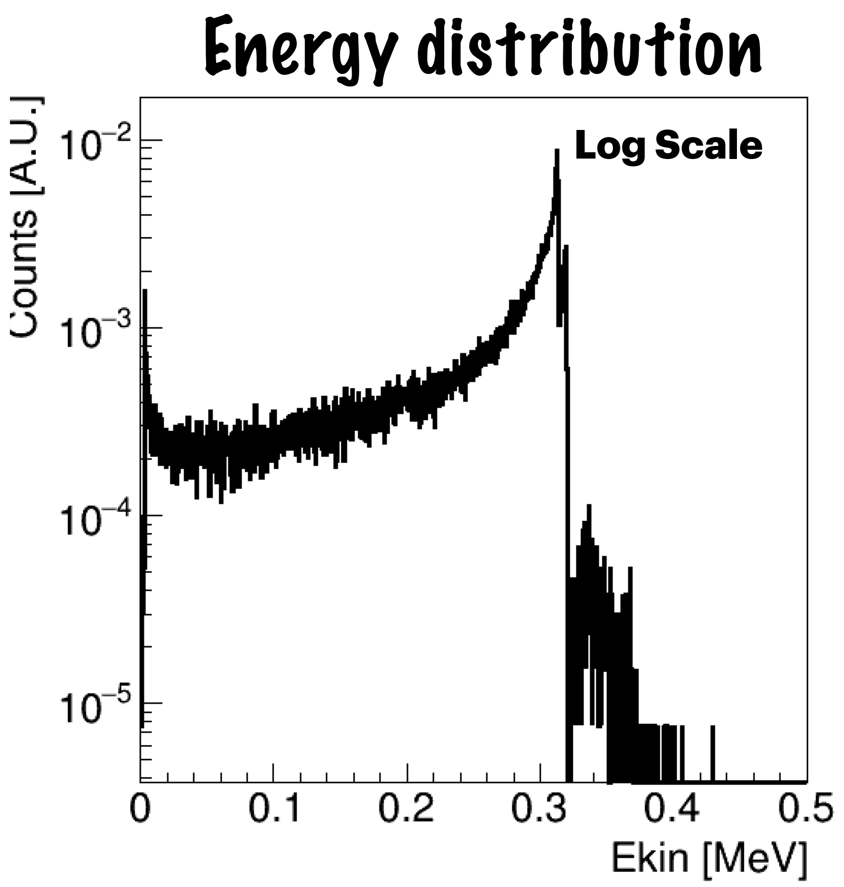


② Backscattered primaries evaluation

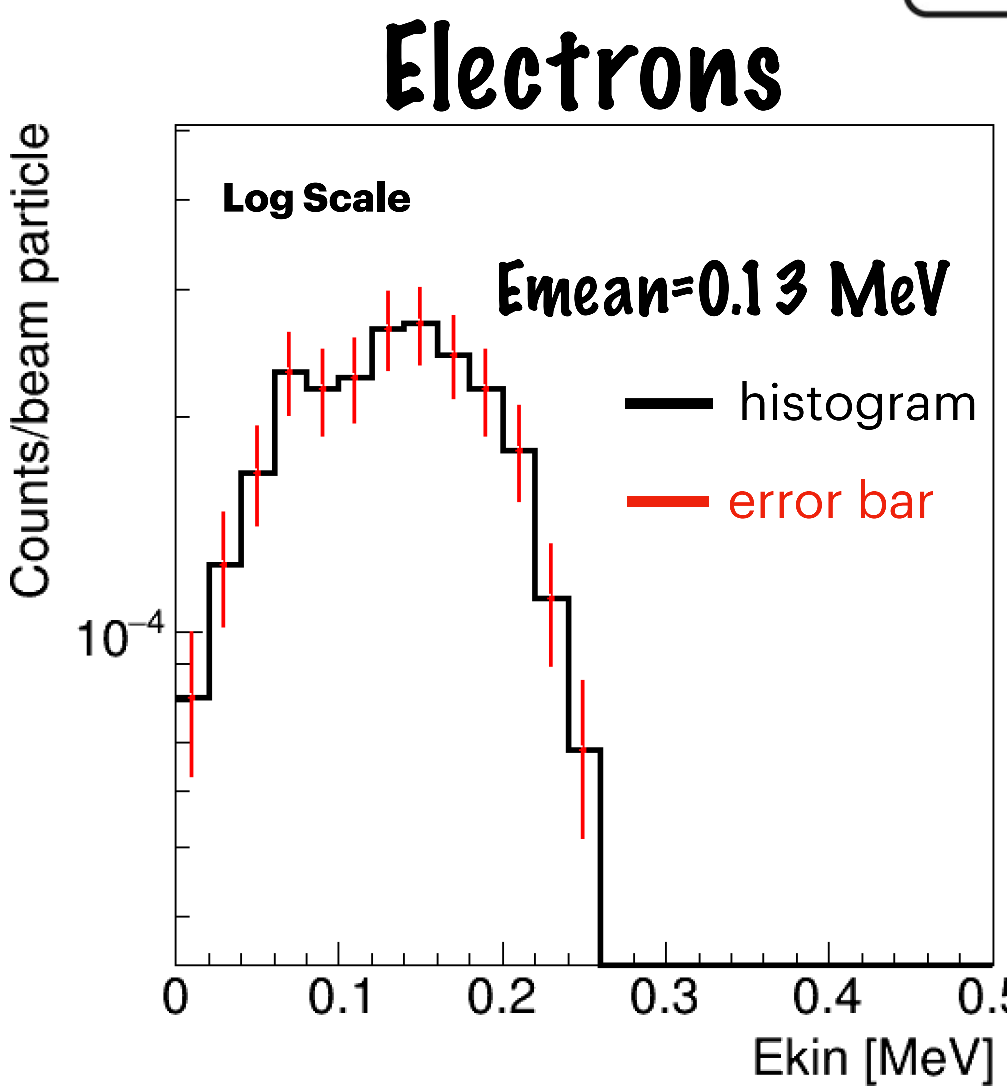
Inside the SW structure, approximately **half of the particles** within the first cell will experience a decelerating electric field and are **transported backward towards the cathode**.

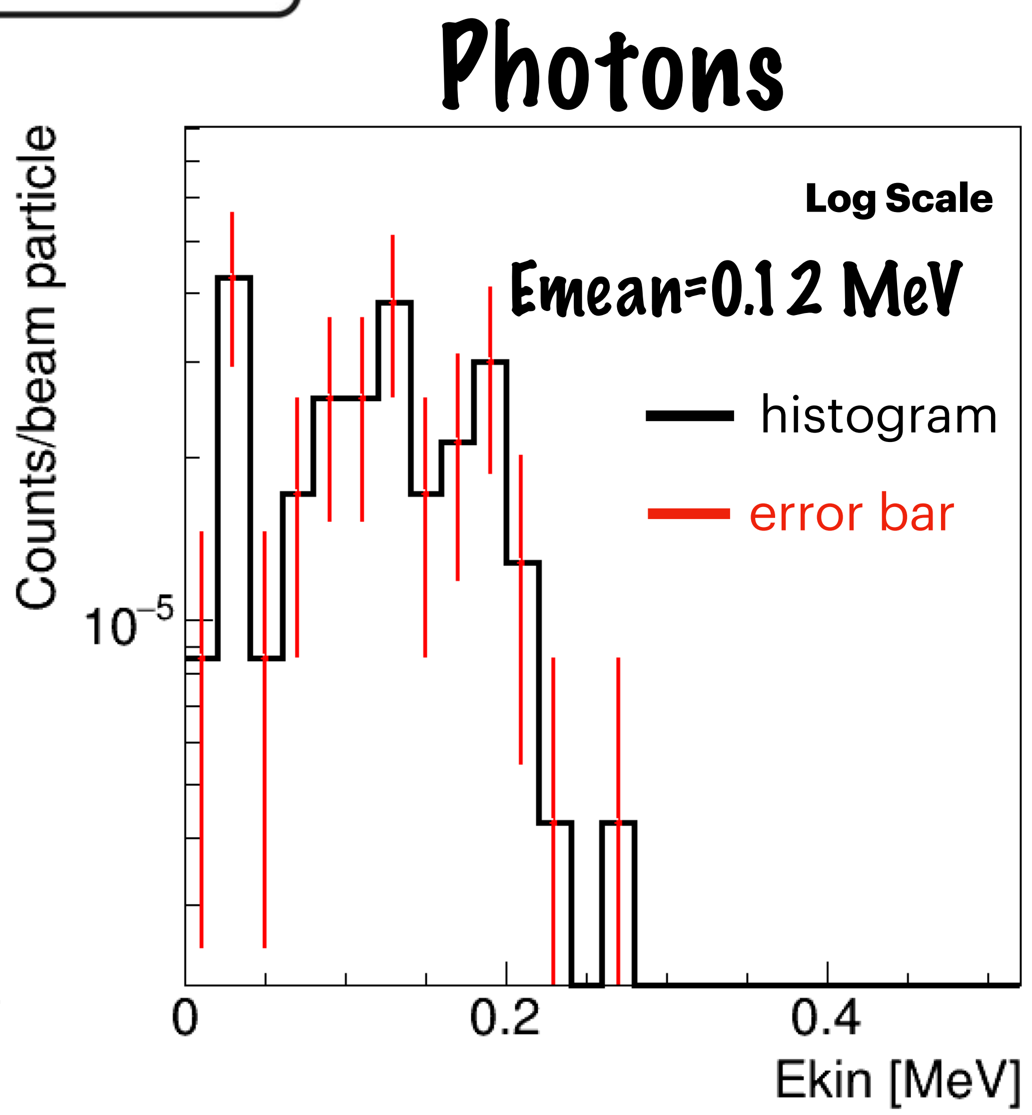






They travel in the **opposite direction** to the accelerated beam and that their **energy distribution** is, at most, that of the particles accelerated forward from the second cavity onwards.





The majority are **absorbed by the materials composing the accelerator** (copper and steel) and by the cathode (barium).

Radio-protection studies

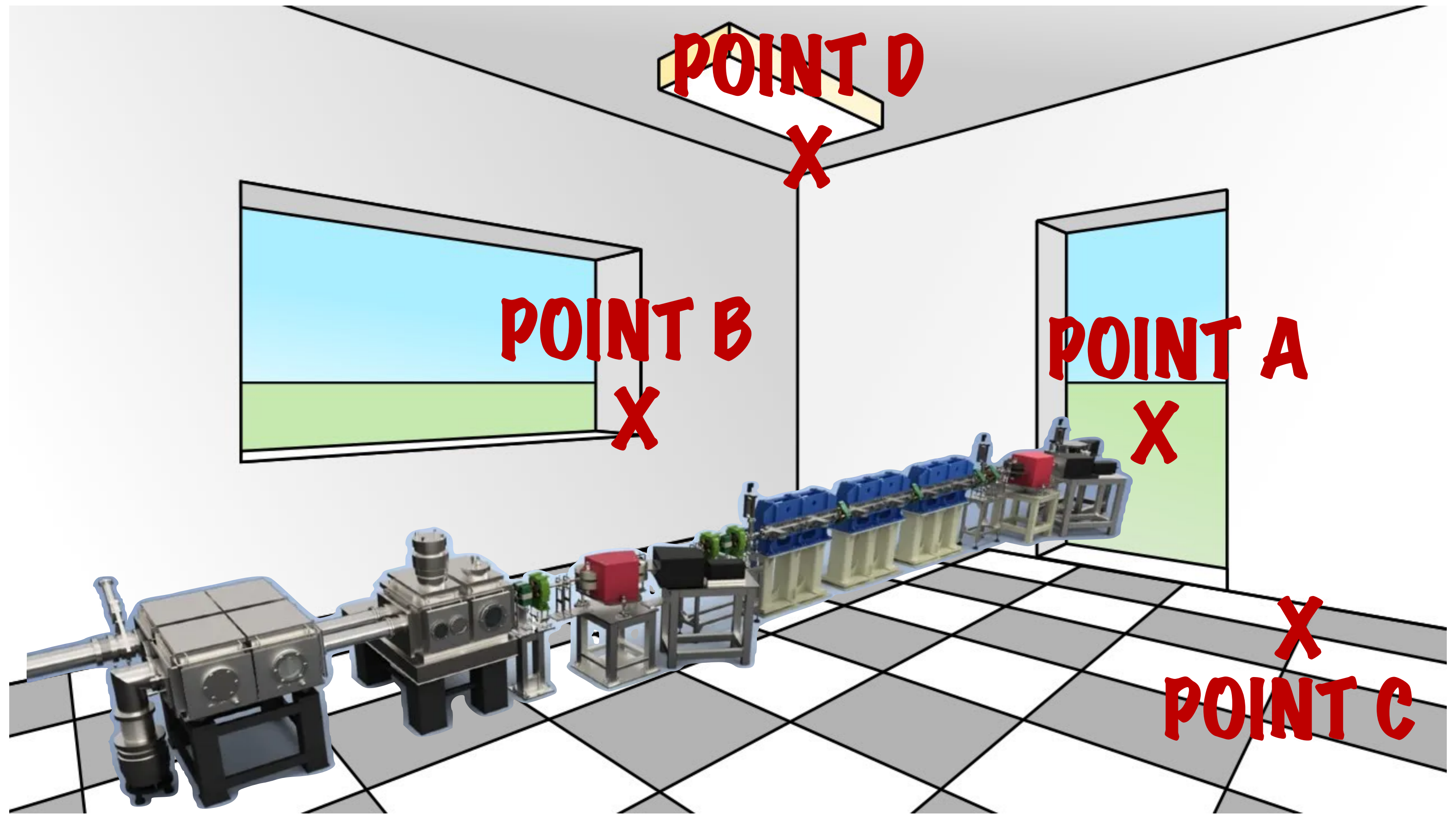
PROTOTYPE GEOMETRY **SIMULATION PROCESS** SHIELDING DESIGN

② Dose delivered in the surrounding area

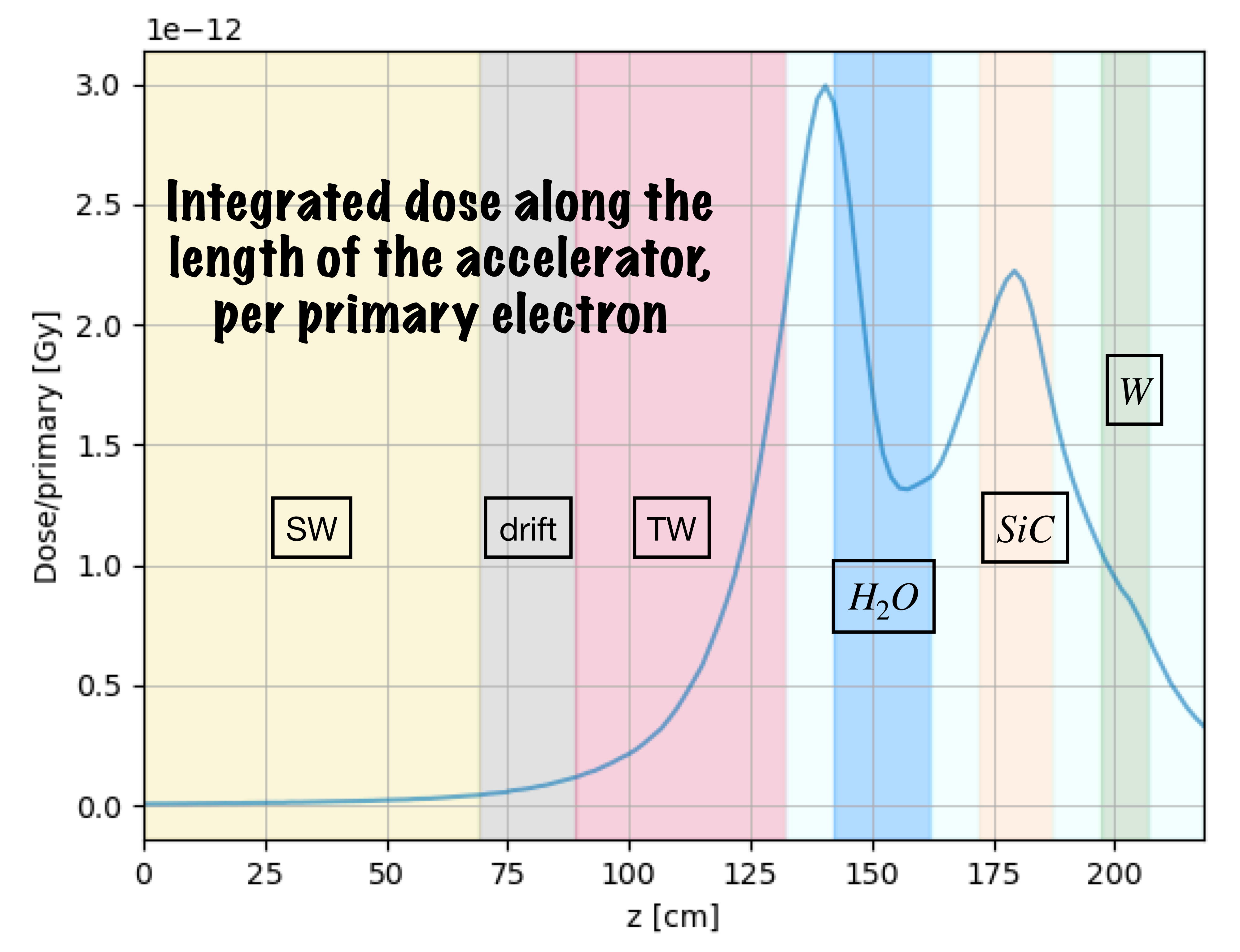
The simulation results provided insights into the **dose delivered to the surrounding air** by the particles exiting the accelerator, as well as the dose **deposited** by the focused primary beam in the region **beyond the exit window.**

The dose was then evaluated at **4 key positions**:

- A : 180 cm from W block
- B & C: laterally 170 cm from the beam axis;
- D: 230 cm above the beam axis.

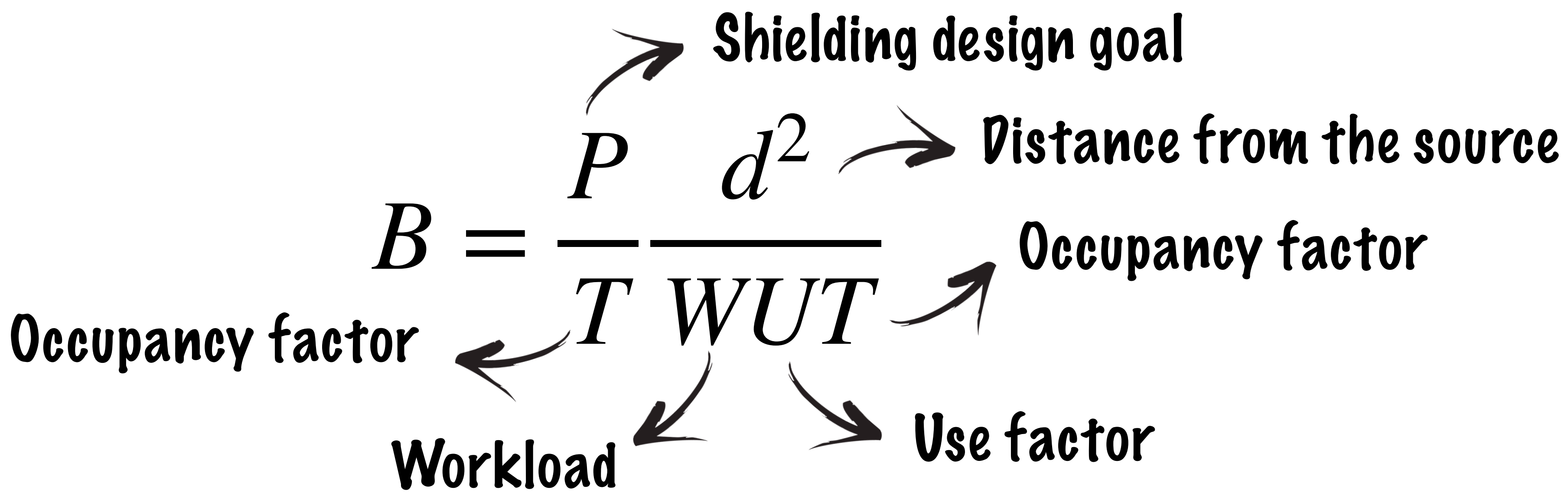


POINT A	POINT B	POINT C	POINT D
$9.73 \cdot 10^{-18} Gy/p$	$7.28 \cdot 10^{-18} Gy/p$	$7.82 \cdot 10^{-18} Gy/p$	$3.86 \cdot 10^{-18} Gy/p$



Radio-protection studies

- Based on these values, assuming a **workload of 3 days per week** with a number of pulses appropriate for the machine's use, **radiation shielding barriers were calculated** to reduce these values and comply with the legal limits.



$$B = \frac{P}{T}\frac{d^2}{WUT}$$

Shielding design goal

Distance from the source

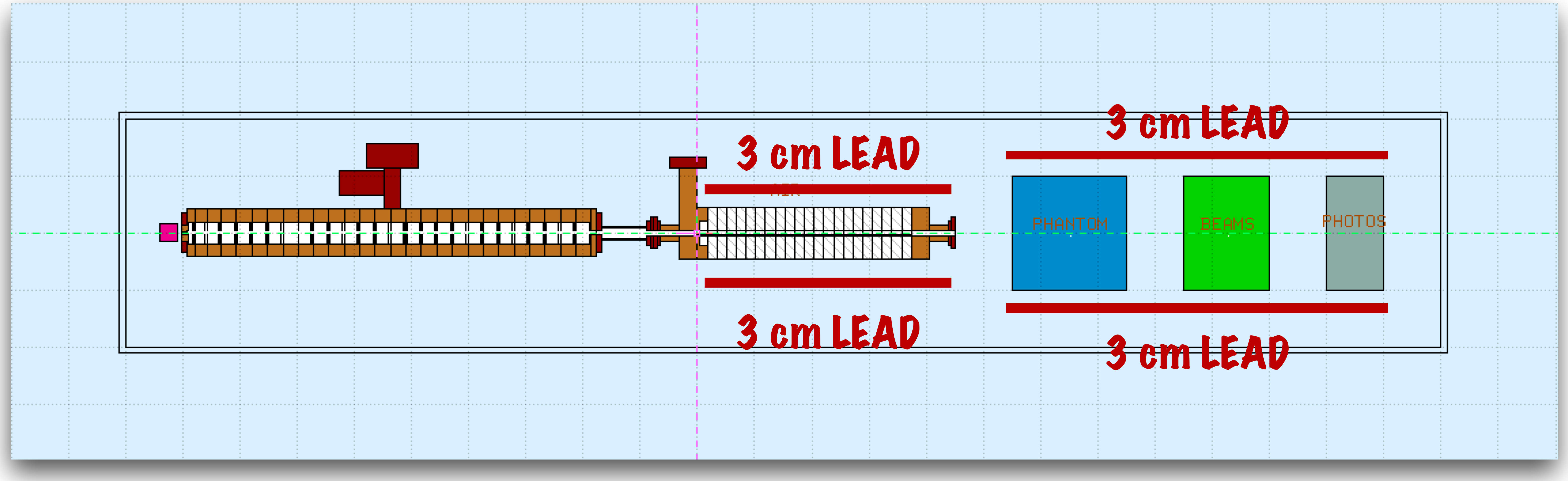
Occupancy factor

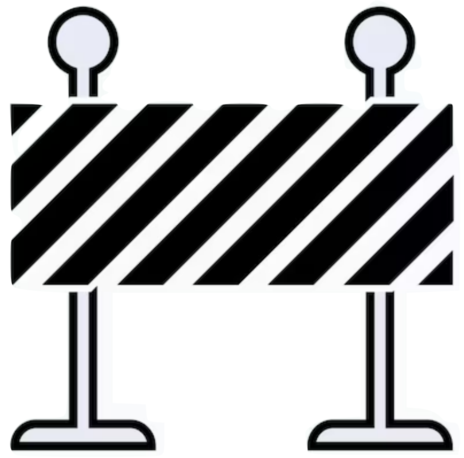
Occupancy factor

Workload

Use factor

The resulting barriers were determined to be **3 cm of lead around the final section** of the LINAC.





	POINT A	POINT B	POINT C	POINT D
NO SHIELDING	$9.73 \cdot 10^{-18} Gy/p$	$7.28 \cdot 10^{-18} Gy/p$	$7.82 \cdot 10^{-18} Gy/p$	$3.86 \cdot 10^{-18} Gy/p$
3 cm SHIELDING	$3.75 \cdot 10^{-18} Gy/p$	$5.99 \cdot 10^{-19} Gy/p$	$8.49 \cdot 10^{-19} Gy/p$	$3.48 \cdot 10^{-19} Gy/p$

CRITICAL POINT

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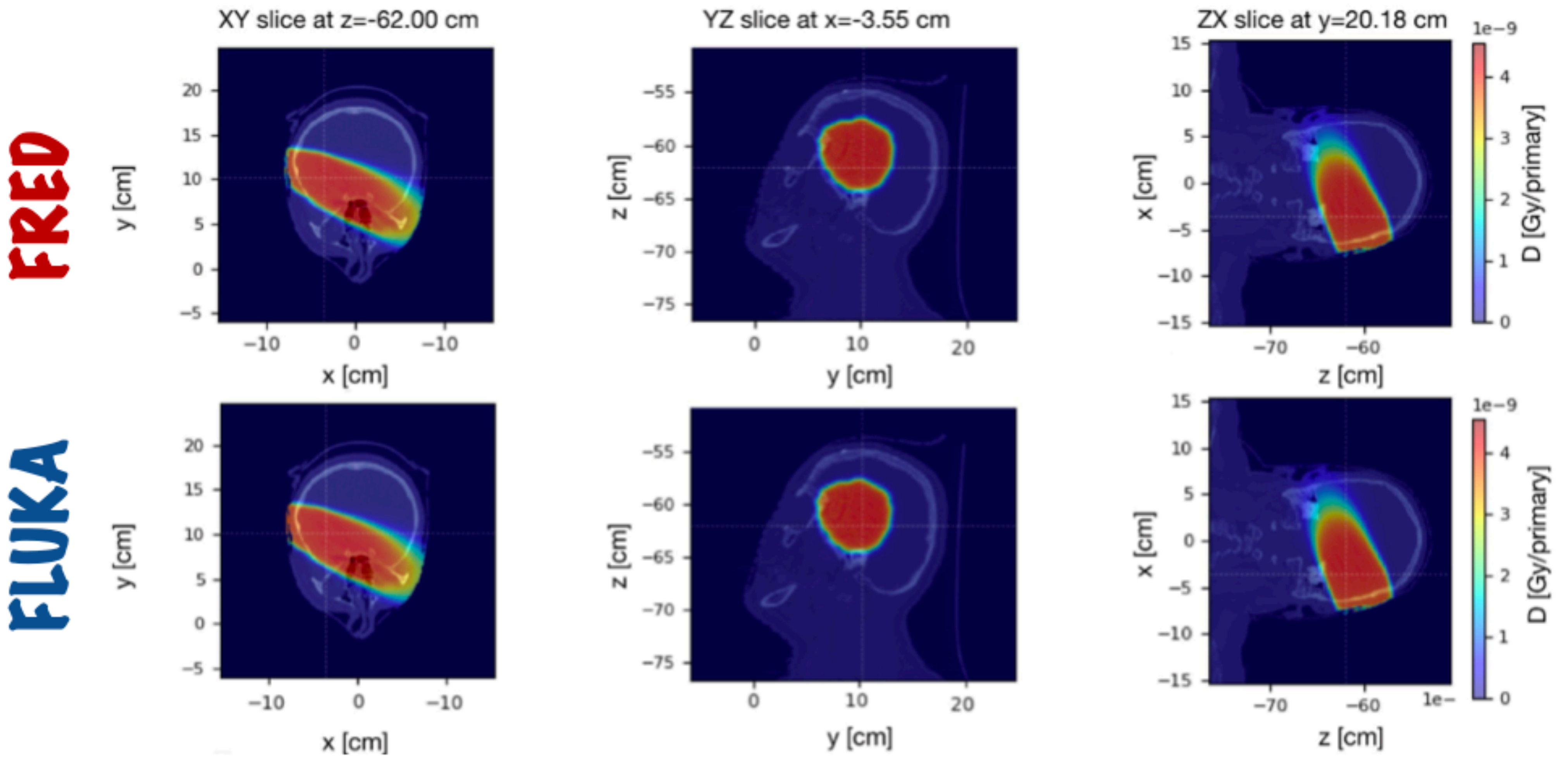
TPS for VHEE FLASH

- The majority of the TPS softwares use an **analytical** dose evaluation approach, which may be **not so accurate**. However the computational cost of the problem didn't allow so far to make a more precise calculation. Our solution is to use **FRED**.

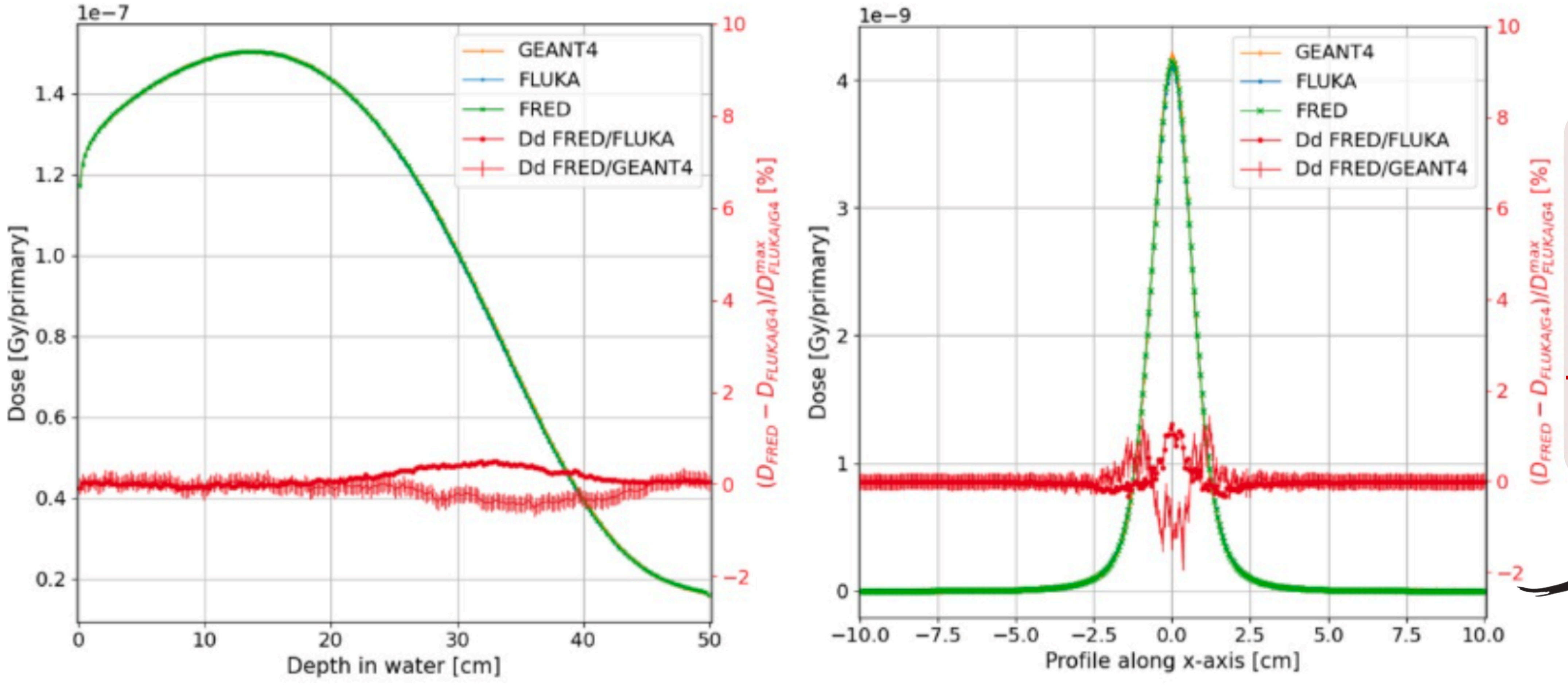
Fred

Gamma-Index pass rate (2mm/2%) 97%



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: MedAustron (Vienna), APSS (Trento), Maastro (Maastricht) and CNAO (Pavia) while **C ions and electromagnetic models for FRED are used for research purposes**.

100 MeV Electron beam



Longitudinal and lateral dose profiles

Dose difference:

• • • • FRED vS FLUKA

┼┼┼┼┼ FRED vS GEANT4

GPU **Developed to work on GPU**

Reduces the simulation time by a factor 1000 compared to standard MC

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TPS for VHEE FLASH

M1

- **Meningioma**: three fields were used, with a prescription to the **PTV of 54Gy(RBE)** in **27 fractions**.

Patient M1		
Organ	**Dosimetric constraint**	**Volume [cc]**
PTV	$V_{95\%}>95\%, D_{max} \leq 105\%$	20.71
Optic nerves	$D_1 \leq 54$ Gy(RBE)	0.95
Chiasm	$D_1 \leq 54$ Gy(RBE)	0.03
Posterior optical path	$D_1 \leq 54$ Gy(RBE)	0.45
Eyeballs	$D_1 \leq 40$ Gy(RBE)	8.14
Brainstem	$D_1 \leq 54$ Gy(RBE)	28.19
Carotid arteries	$D_{max} \leq 105\%$	1.15

C1

- **Chordoma**: four fields were used, with a prescription to the **PTV of 54Gy(RBE)** in **30 fractions**.

Patient C1		
Organ	**Dosimetric constraint**	**Volume [cc]**
PTV	$V_{95\%}>95\%, D_{max} \leq 107\%$	99.15
PTV boost	$V_{95\%}>95\%, D_{max} \leq 107\%$	71.94
Brainstem	$D_1 \leq 55$ Gy(RBE)	27.09
Spinal cord	$D_1 \leq 54$ Gy(RBE)	8.25
Parotid glands	$D_{mean} \leq 26$ Gy(RBE)	26.26
Middle ears	$D_{mean} \leq 30$ Gy(RBE)	3.80
Cochlea	$D_{mean} \leq 35$ Gy(RBE)	0.35

The clinical proton plans delivered to the patients were sent to the Medical Physics Unit of Policlinico Umberto I in Rome to carry out the **IMRT treatment planning**, together with the dose prescriptions, the details about the OARs constraints, and the CT imaging data.

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TPS for VHEE FLASH

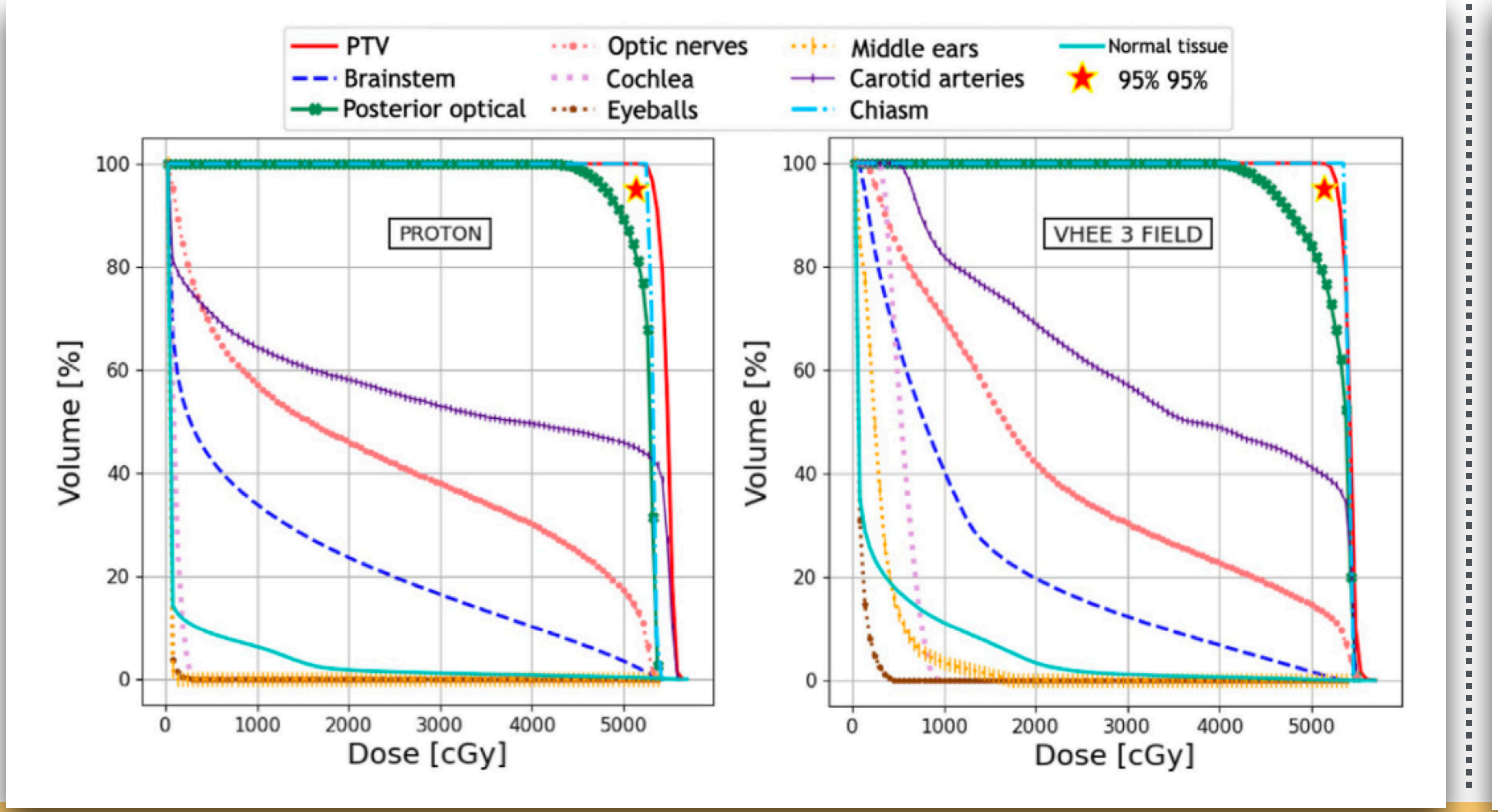
INPUT MODEL DOSE EVALUATION OPTIMIZATION **RESULTS**

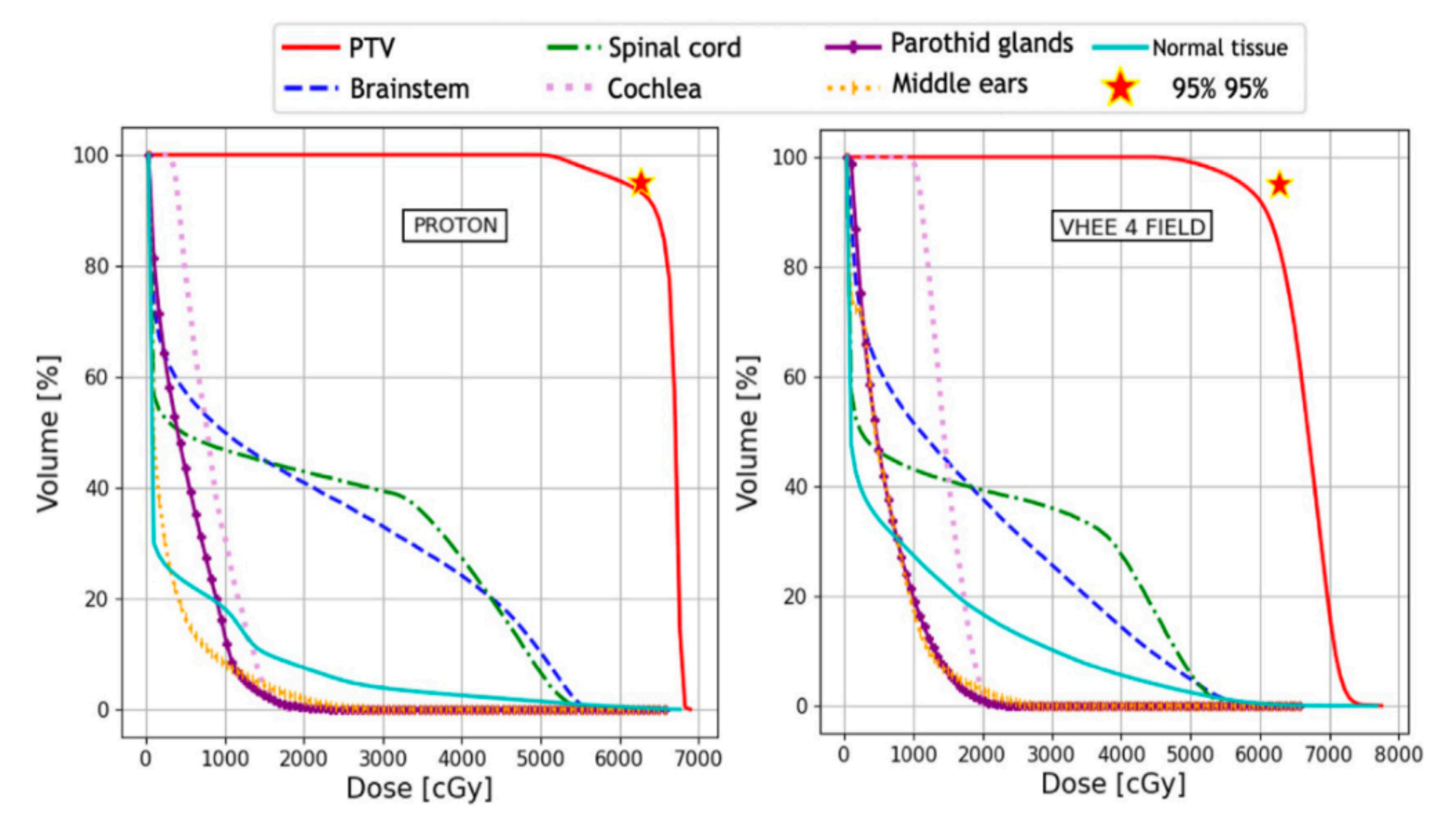
M1

- **Meningioma**: three fields were used, with a prescription to the **PTV of 54Gy(RBE)** in **27 fractions**.
- **1st configuration:** 3 fields [110, 110, 100] MeV;
- **2nd configuration:** 7 fields [90, 100, 100, 110, 100, 100, 90] MeV;

C1

- **Chordoma**: four fields were used, with a prescription to the **PTV of 54Gy(RBE)** in **30 fractions**.
- **1st configuration:** 4 fields [120, 90, 90, 120] MeV;
- **2nd configuration:** 7 fields [120, 80, 60, 60, 60, 60, 90] MeV;





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TPS for VHEE FLASH

M1

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- **1st configuration:** 3 fields [110, 110, 100] MeV;
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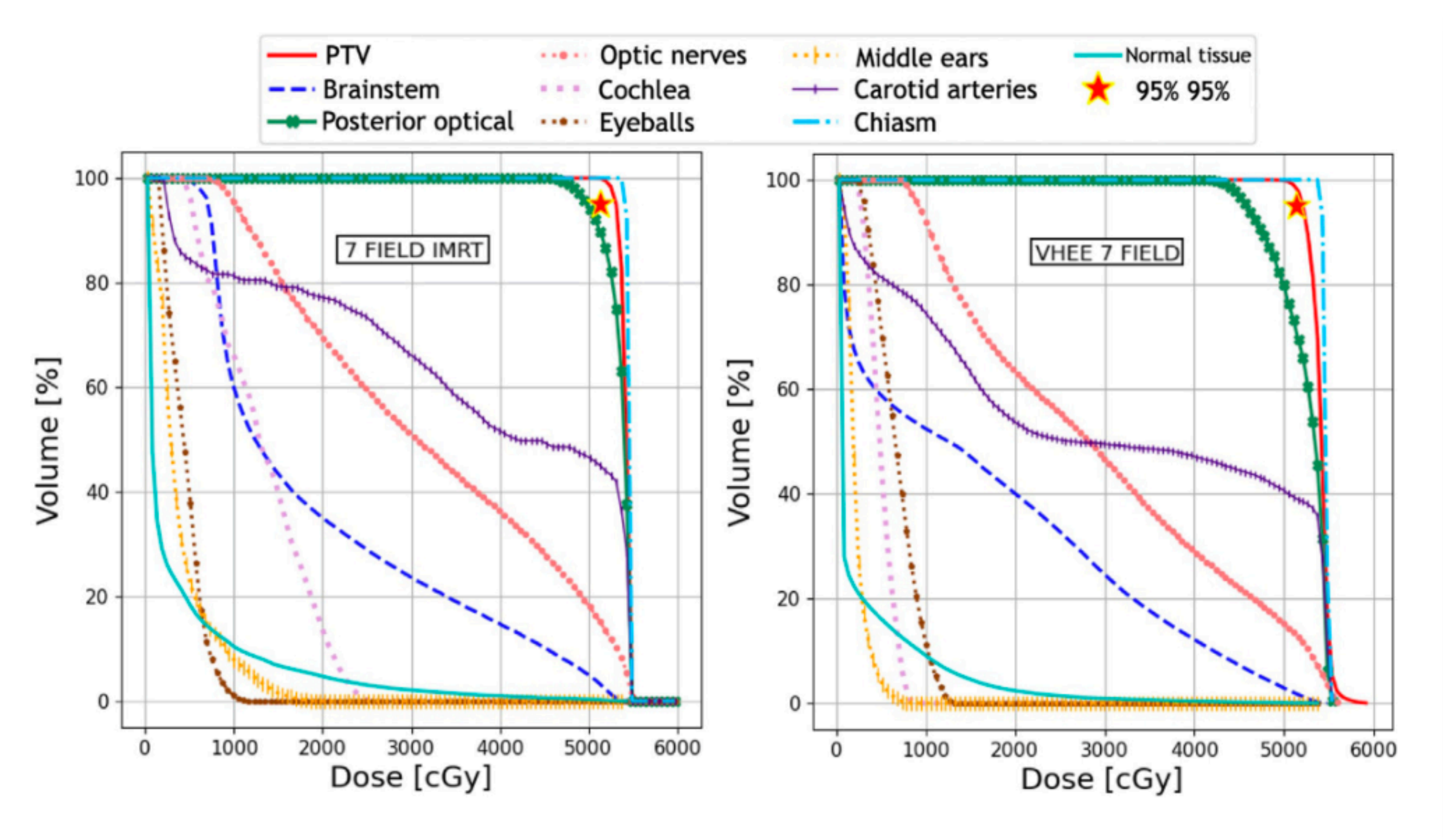
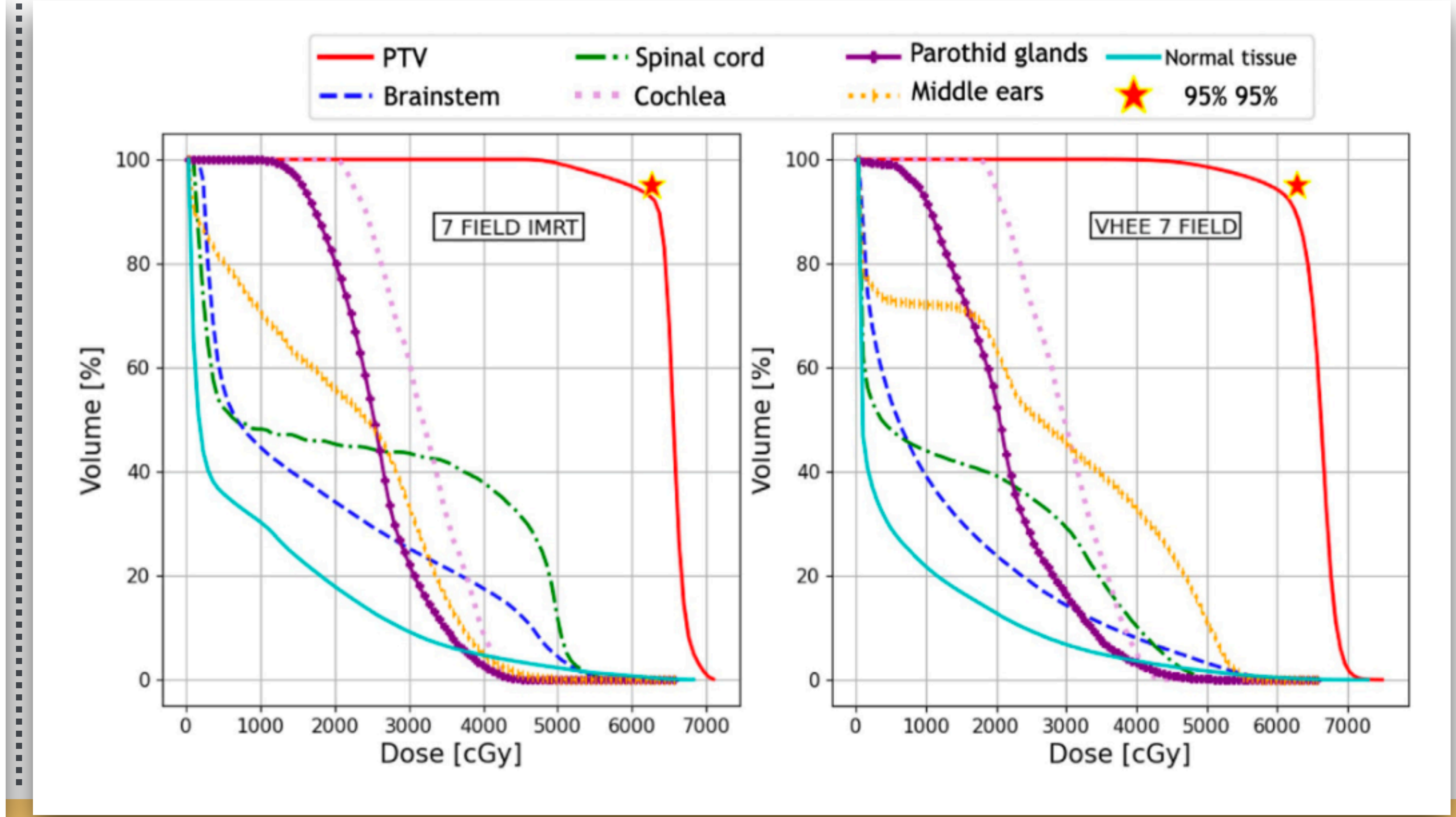


C1

- **Chordoma**: four fields were used, with a prescription to the **PTV of 54Gy(RBE)** in **30 fractions**.
- **1st configuration: 4** fields [120, 90, 90, 120] MeV;
- **2nd configuration:** 7 fields [120, 80, 60, 60, 60, 60, 90] MeV;



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TPS for VHEE FLASH

M1

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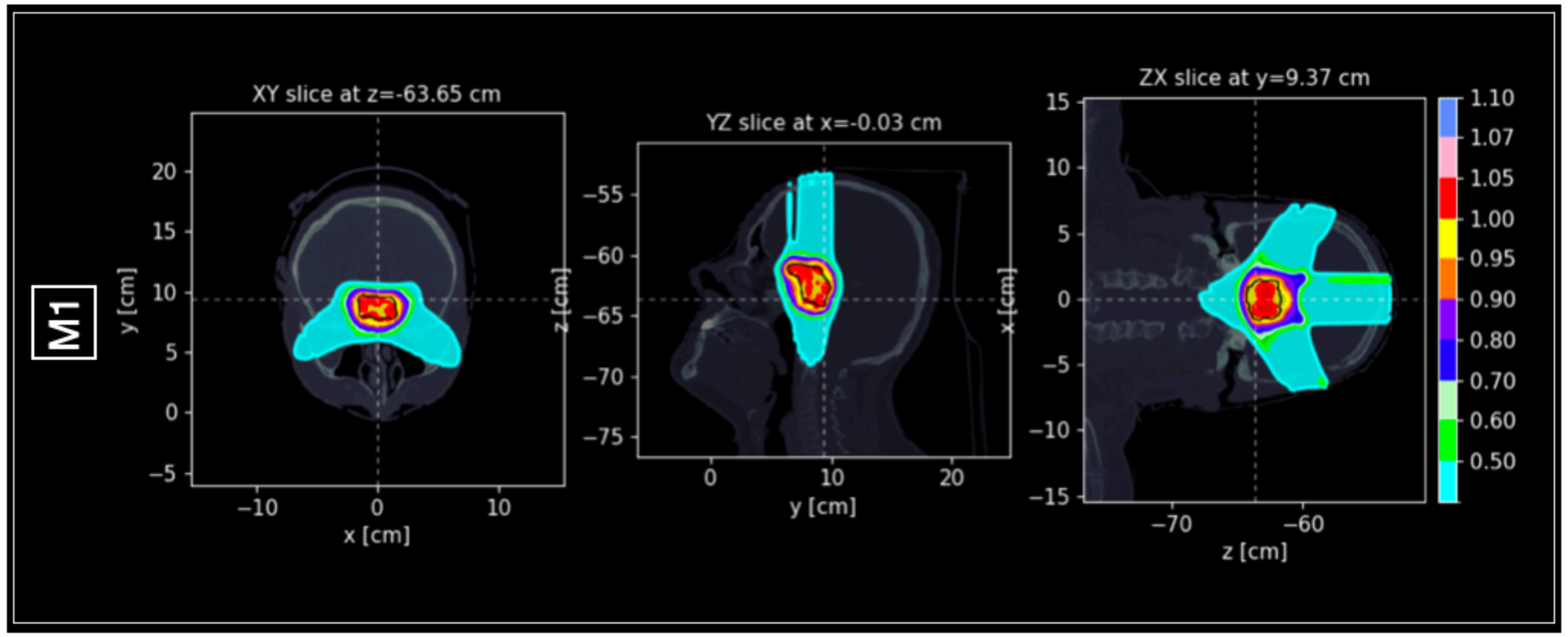
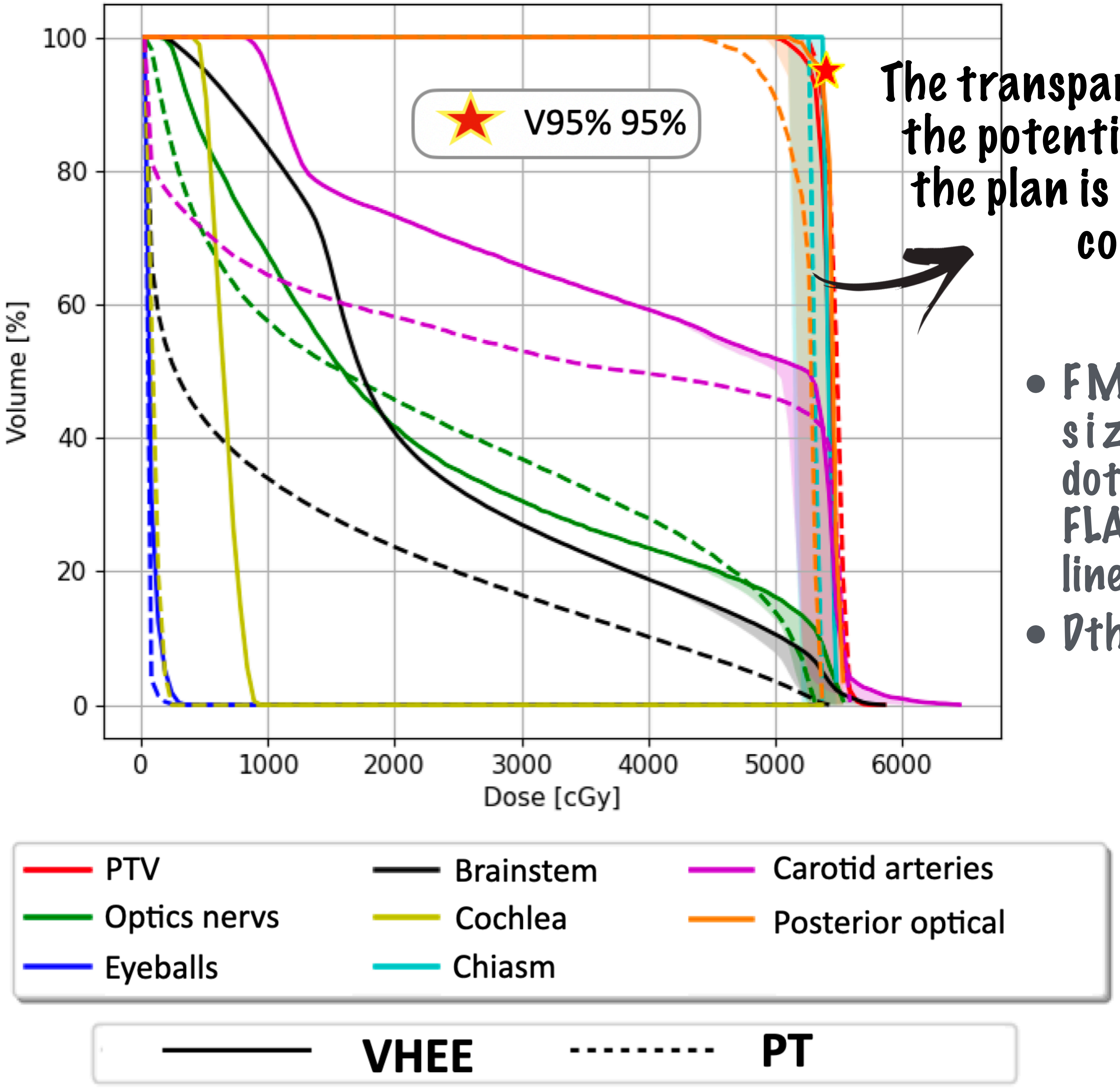
- **1st configuration:** 3 fields [110, 110, 100] MeV;
- **2nd configuration:** 7 fields [90, 100, 100, 110, 100, 100, 90] MeV;



Isodose maps are graphical representations that show curves connecting points in space where the dose is constant, in this way it is possible to display the contours of regions where the dose reaches a predefined value.

FLASH OPTIMIZATION



The transparent bands indicate the potential improvement if the plan is delivered in UHDR conditions.

- FMFmin = 0.8 (a sizeable sparing, dotted line) to 1 (no FLASH effect in solid line)
- Dth value of 40 Gy.

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FONDAZIONE
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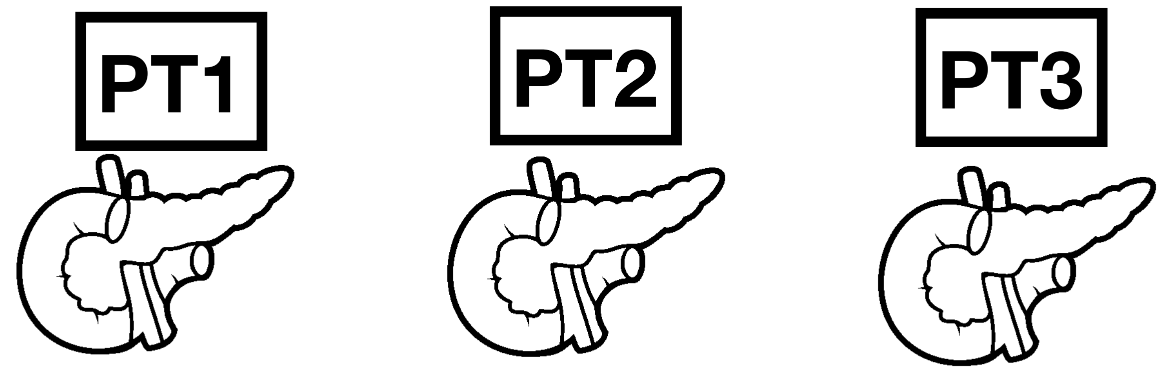
TPS for VHEE FLASH

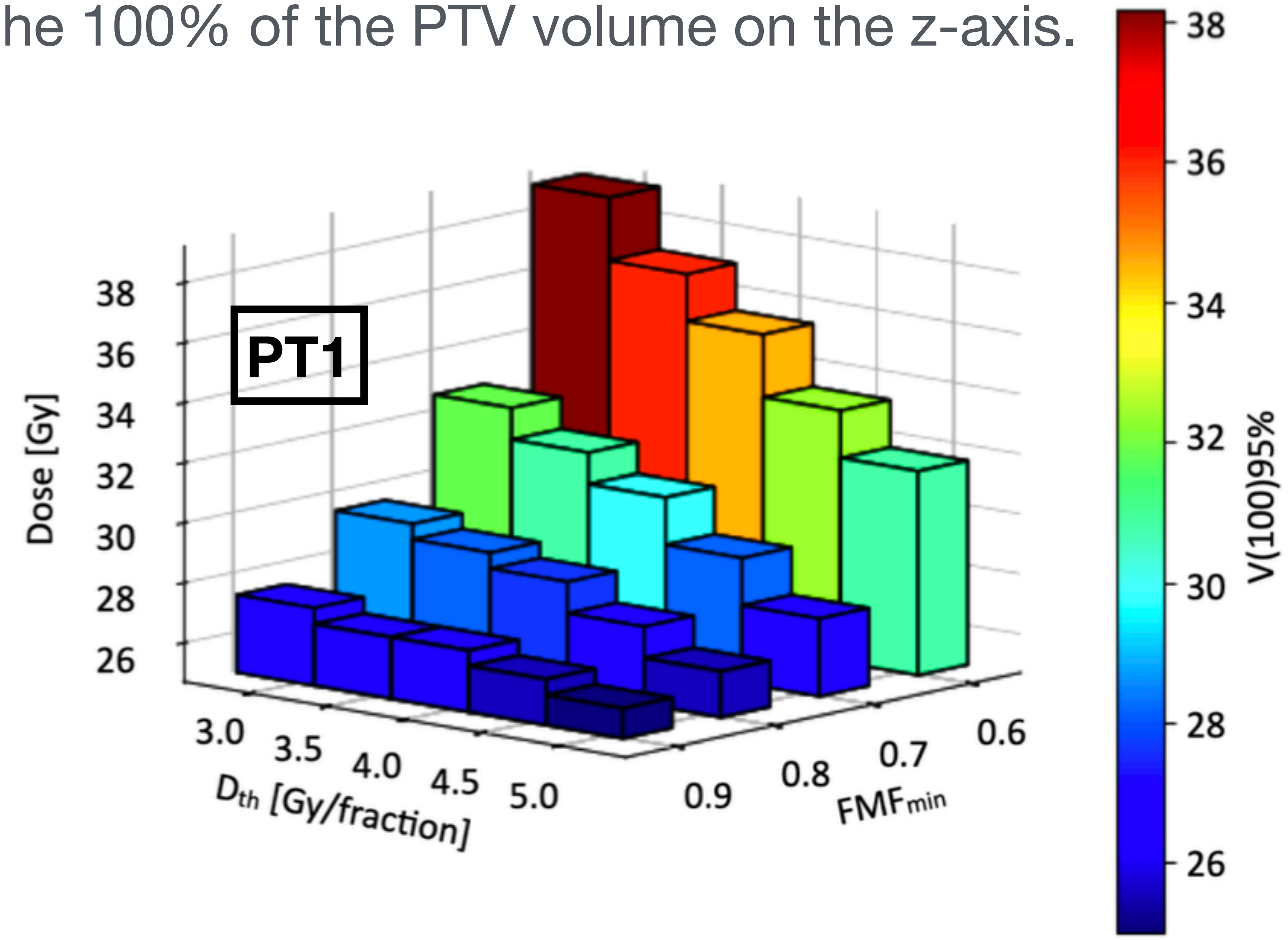
- The TPS is crucial for pancreatic tumors as it enables precise dose delivery to the tumor while **minimizing radiation-induced toxicity to the nearby duodenum**. This approach enhances treatment efficacy by targeting the tumor effectively and reducing harmful side effects.

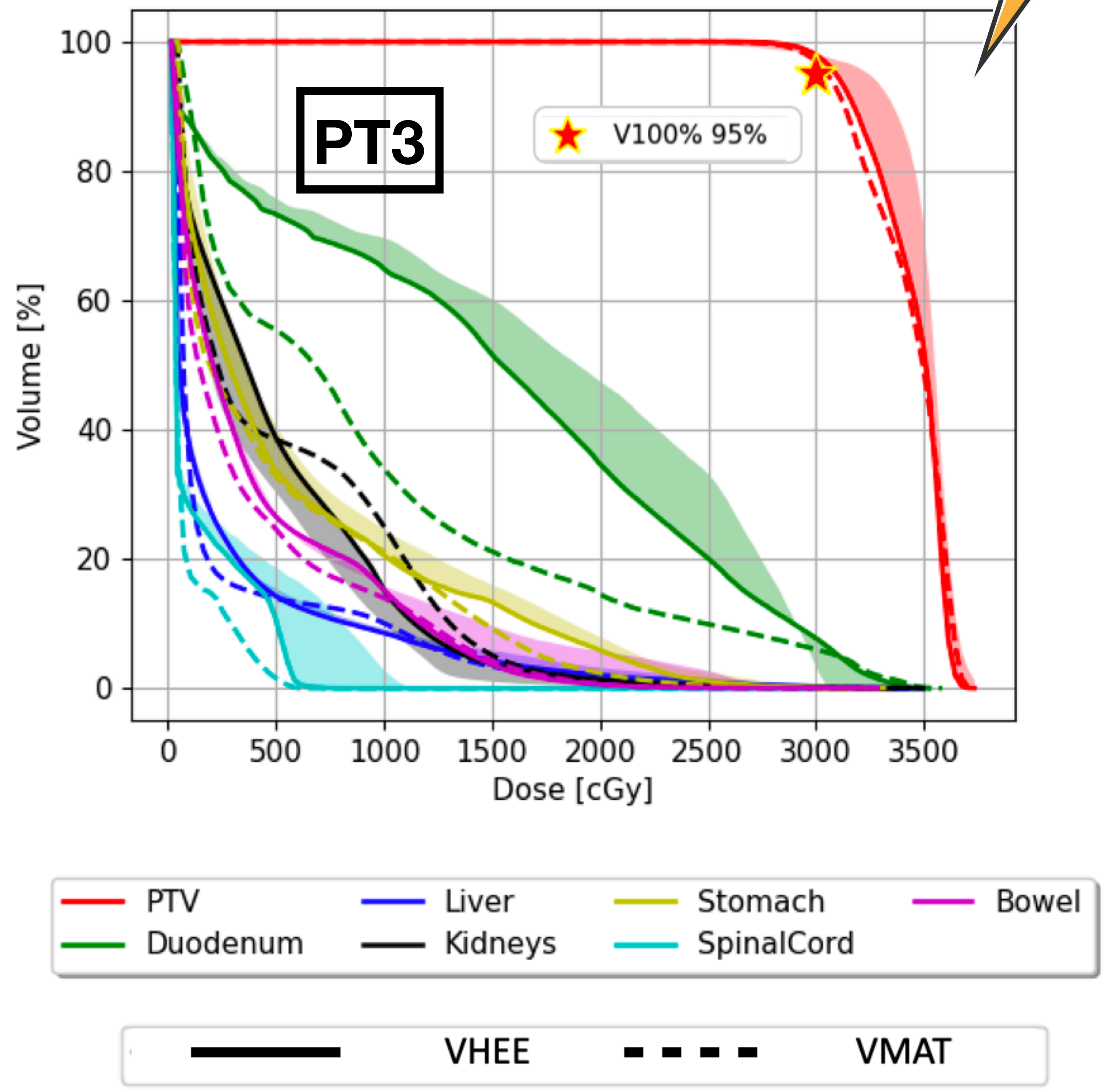
BEST CANDIDATE FOR FLASH IRRADIATION!



- **PT1**: seven fields were used, with a prescription to the **PTV of 30 Gy** in **5 fractions**.
- **PT2**: five fields were used, with a prescription to the **PTV of 32.5 Gy** in **5 fractions**.
- **PT3**: five fields were used, with a prescription to the **PTV of 30 Gy** in **5 fractions**.

- Correlation among FMF_{min} values D_{th} and the resultant increase of the 95% of the dose absorbed by the 100% of the PTV volume on the z-axis.





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