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Italiadomani PIANO NAZIONALE DI RIPRESA E RESILIENZA

THE Tuscany Health Ecosystem

Preliminary evaluation of FLASH electron radiotherapy in the treatment of uveal melanoma

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Introduction

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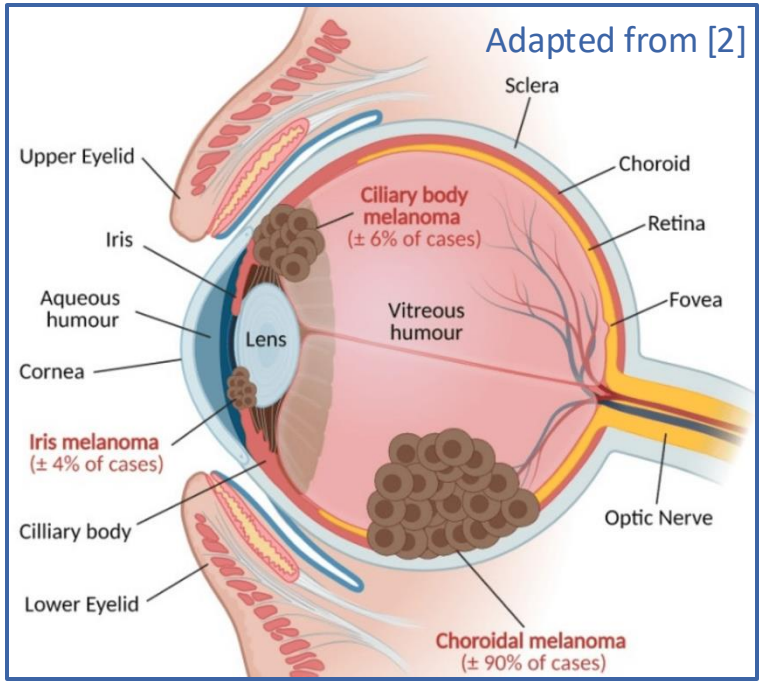
- FLASH radiotherapy (FLASH-RT) is a novel treatment modality based on **Flash effect** [1]:
  - Ultra-high dose rate (≥ 40 Gy/s)
  - Total irradiation time < 200 ms
  - **Protective effect on normal tissues** compared with conventional irradiation
  - **Isoefficacy on tumoral lesions**

- **AIM of this study:**
  → verify the possibility of using low energy electron FLASH-RT as an alternative treatment modality for **localized uveal melanoma**
    - **highly radioresistant**
    - **most common** primary intraocular malignancy in adults [2]

- **Treatment options** include [2]:
  - enucleation
  - plaque brachytherapy
  - stereotactic radiotherapy (SRS-RT)
  - particle therapy



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- FLASH radiotherapy (FLASH-RT) is a novel treatment modality based on **Flash effect** [1]:
  - Ultra-high dose rate (≥ 40 Gy/s)
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  -
  -
- **AIM**
  -
  -
- **Tr**
  - enucleation
  - plaque brachytherapy
  - stereotactic radiotherapy (SRS-RT)
  - particle therapy

irradiation

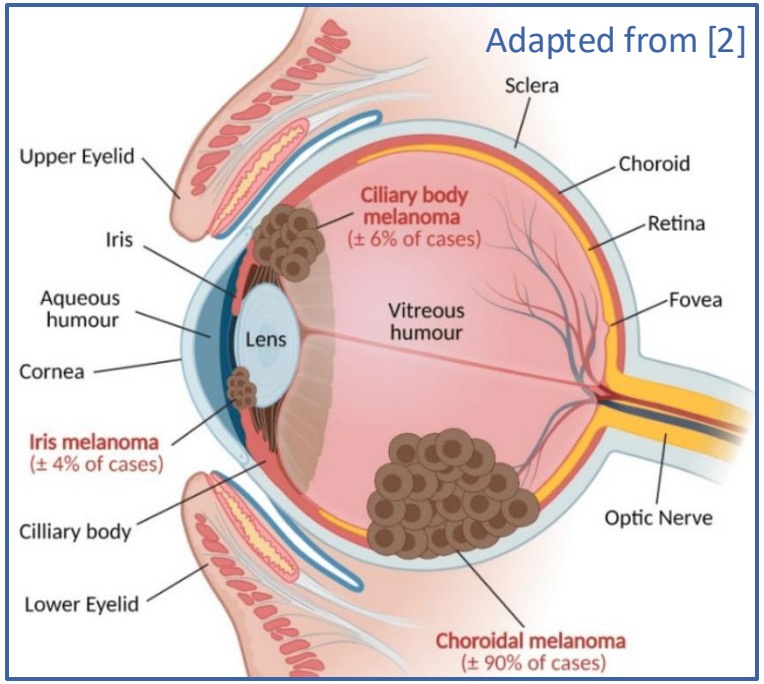
an

Main steps of the project:

i. Dose distribution evaluation and optimization (Monte Carlo tool)

ii. RBE voxel by voxel implementation + FLASH sparing effect
   - in vivo and in vitro experiments and/or literature data

iii. Evaluation of the therapeutic potential of FLASH-RT compared to SRS-RT + development of a quantitative comparison tool based on dosiomics and advanced statistics



ElectronFlash

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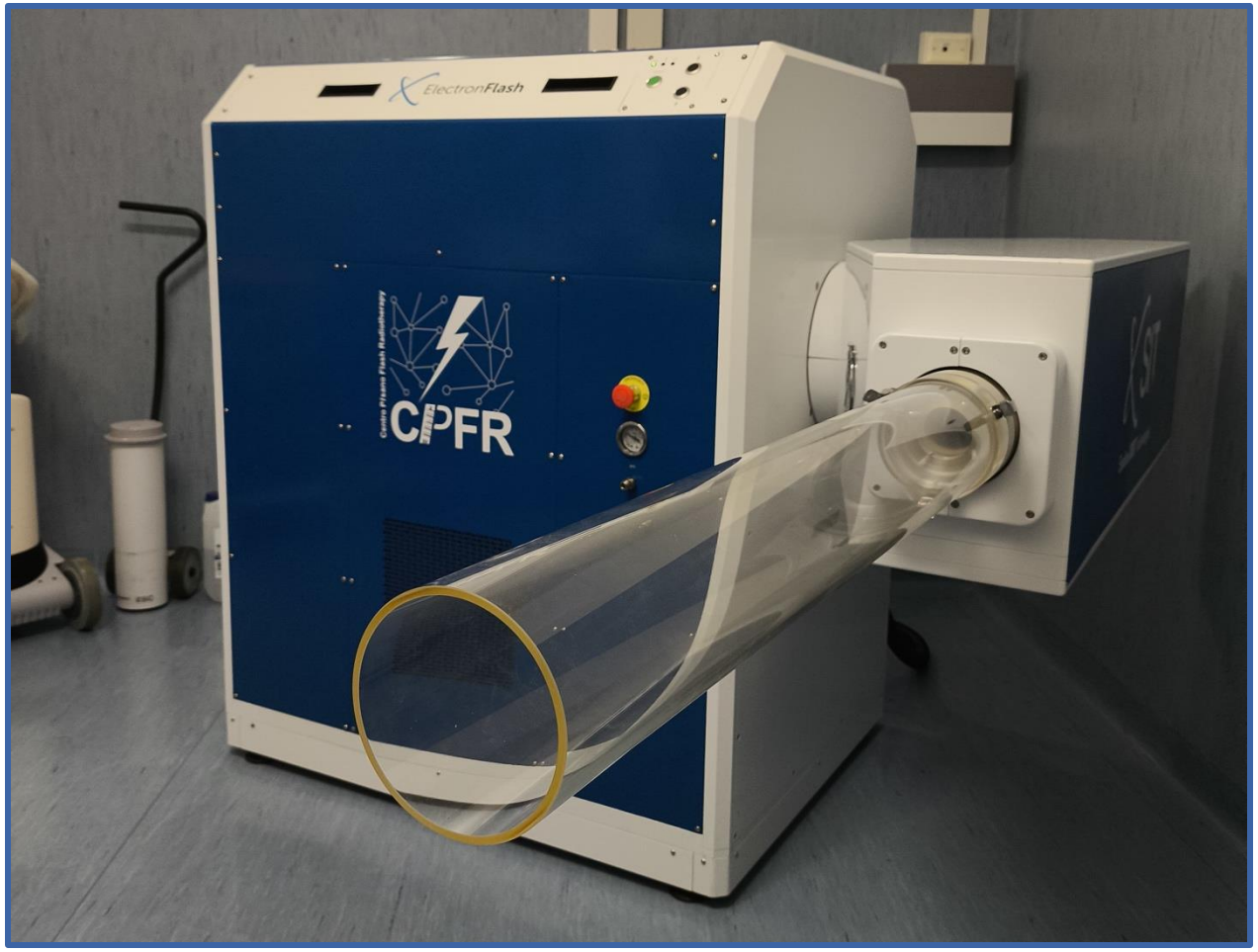
- **ElectronFlash (EF)** research LINAC installed in Pisa A.O.U.P. - S. Chiara Hospital [3]
- The system operates in electron mode only, with energies of 7 and 9 MeV [3]
- The e-beam is collimated by means of a passive beam optics + tungsten shaper [3]



ElectronFlash

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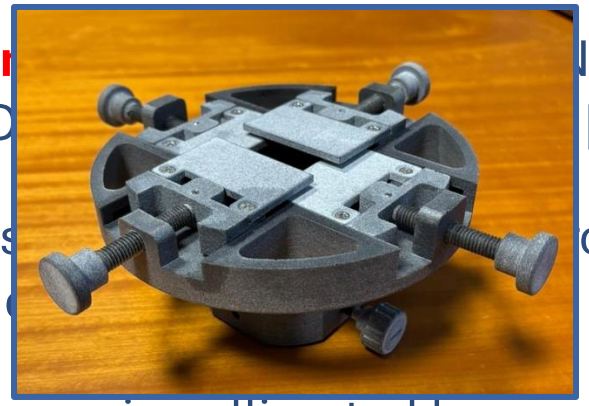

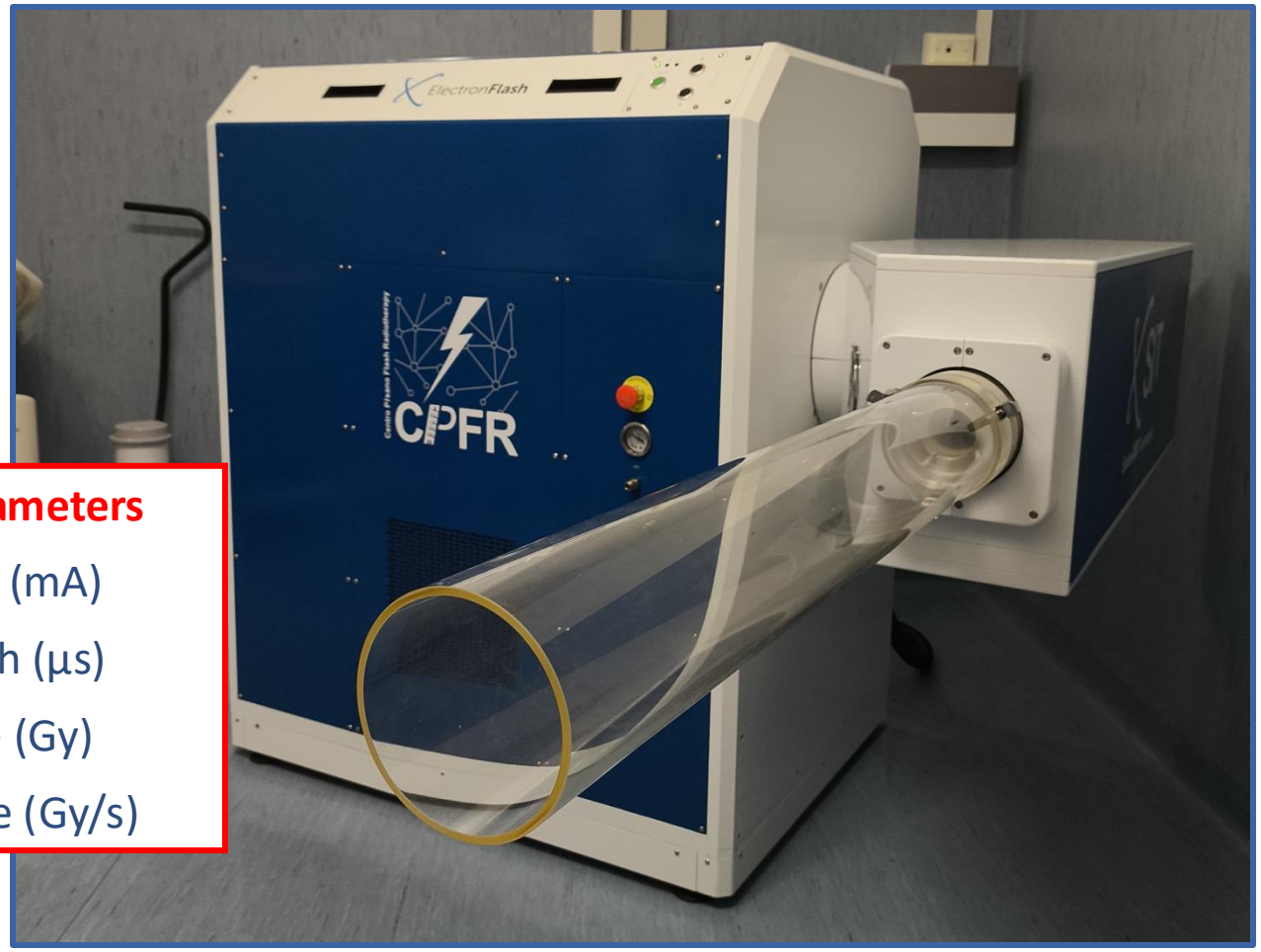

Independent parameters

e-beam current (mA)

Pulse time width (µs)

Dose-per-pulse (Gy)

Average dose-rate (Gy/s)

Simulations

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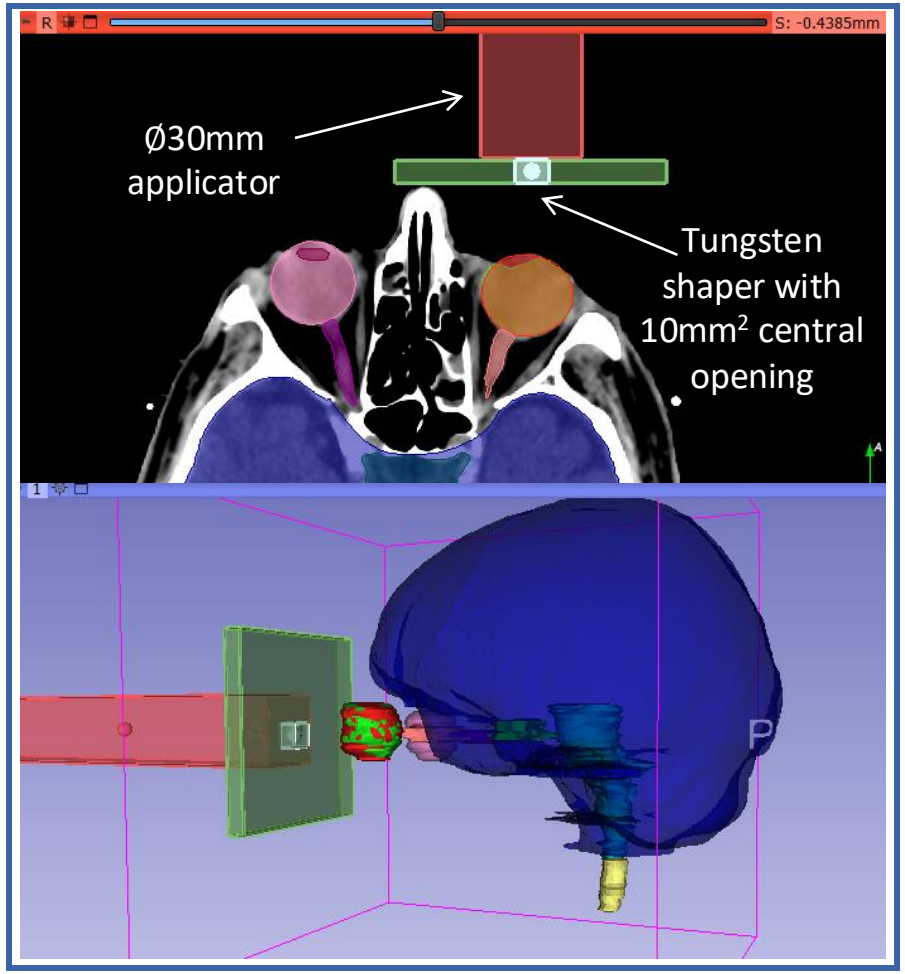
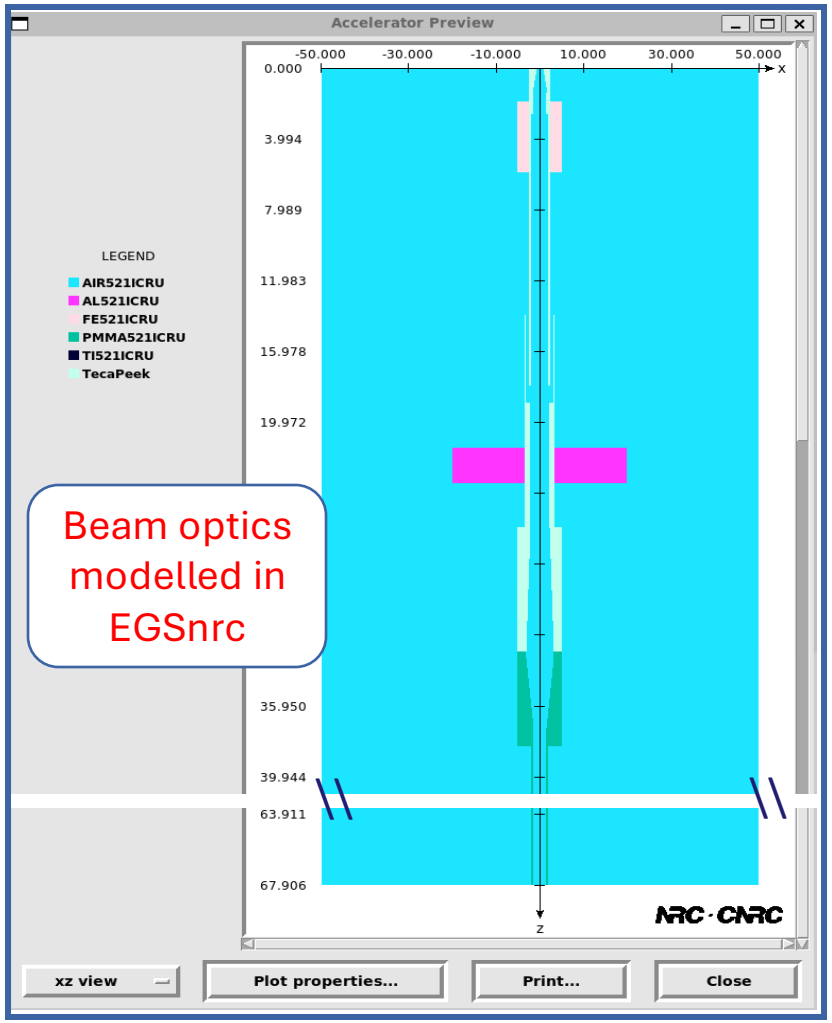
- EGSnrc Monte Carlo software
  - 9MeV electron beam
  - Ø30mm primary collimator (PMMA)
  - Tungsten shaper for further beam collimation

Part of the setup has been already dosimetrically validated!





Simulations

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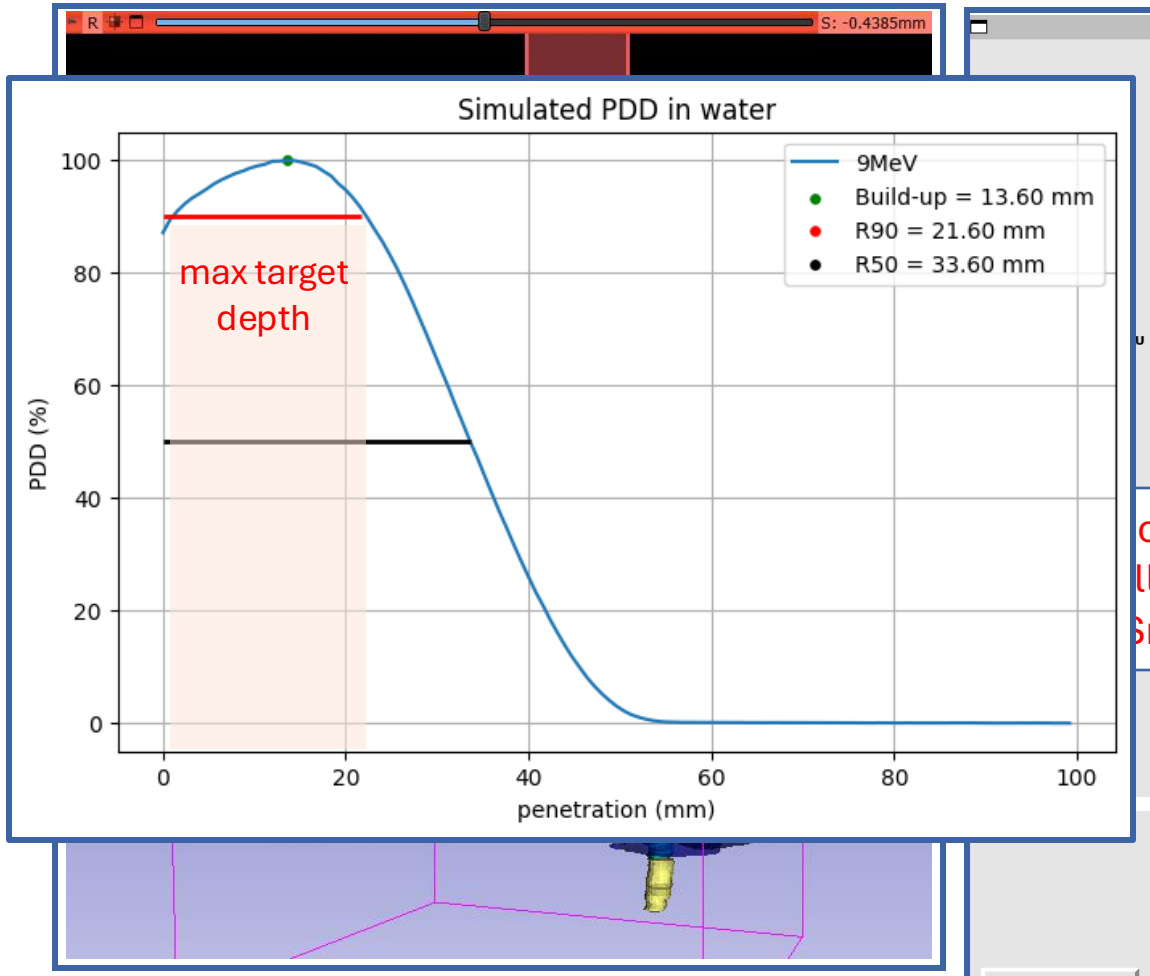
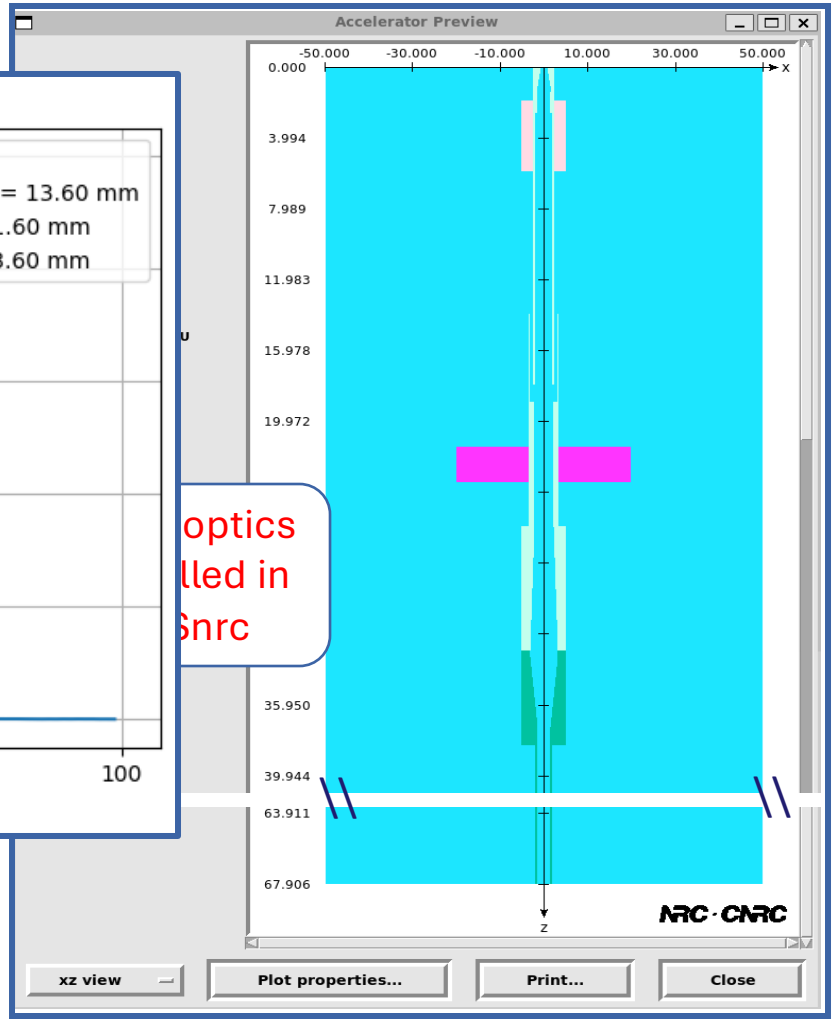
- Target coverage with beam R90
  - **limiting factor**





optics
lled in
Snrc

Patient's CTs

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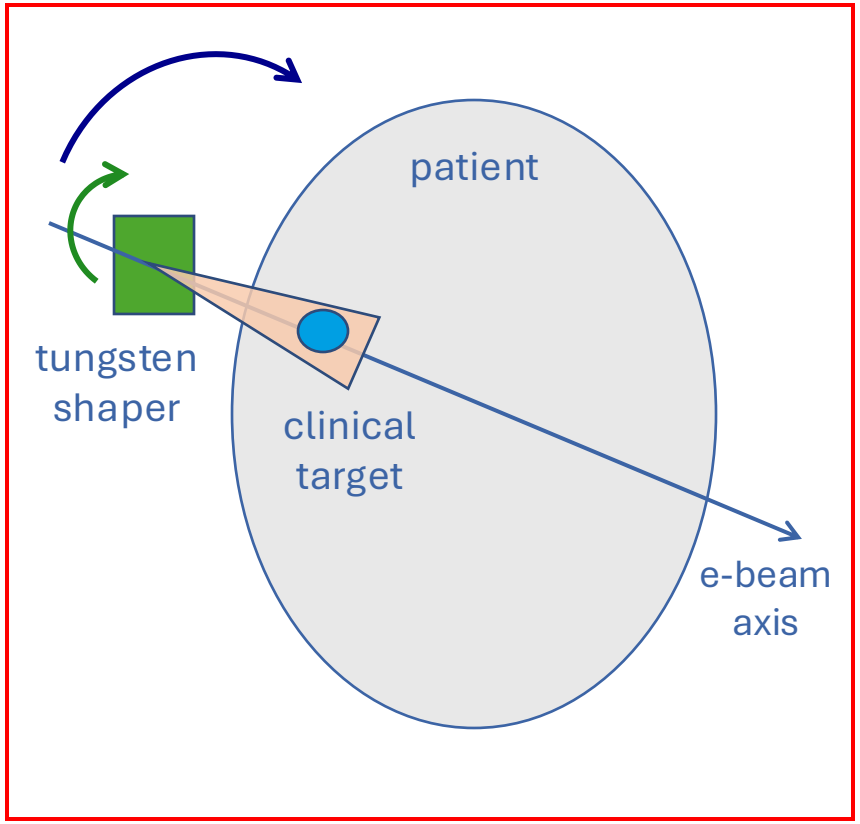
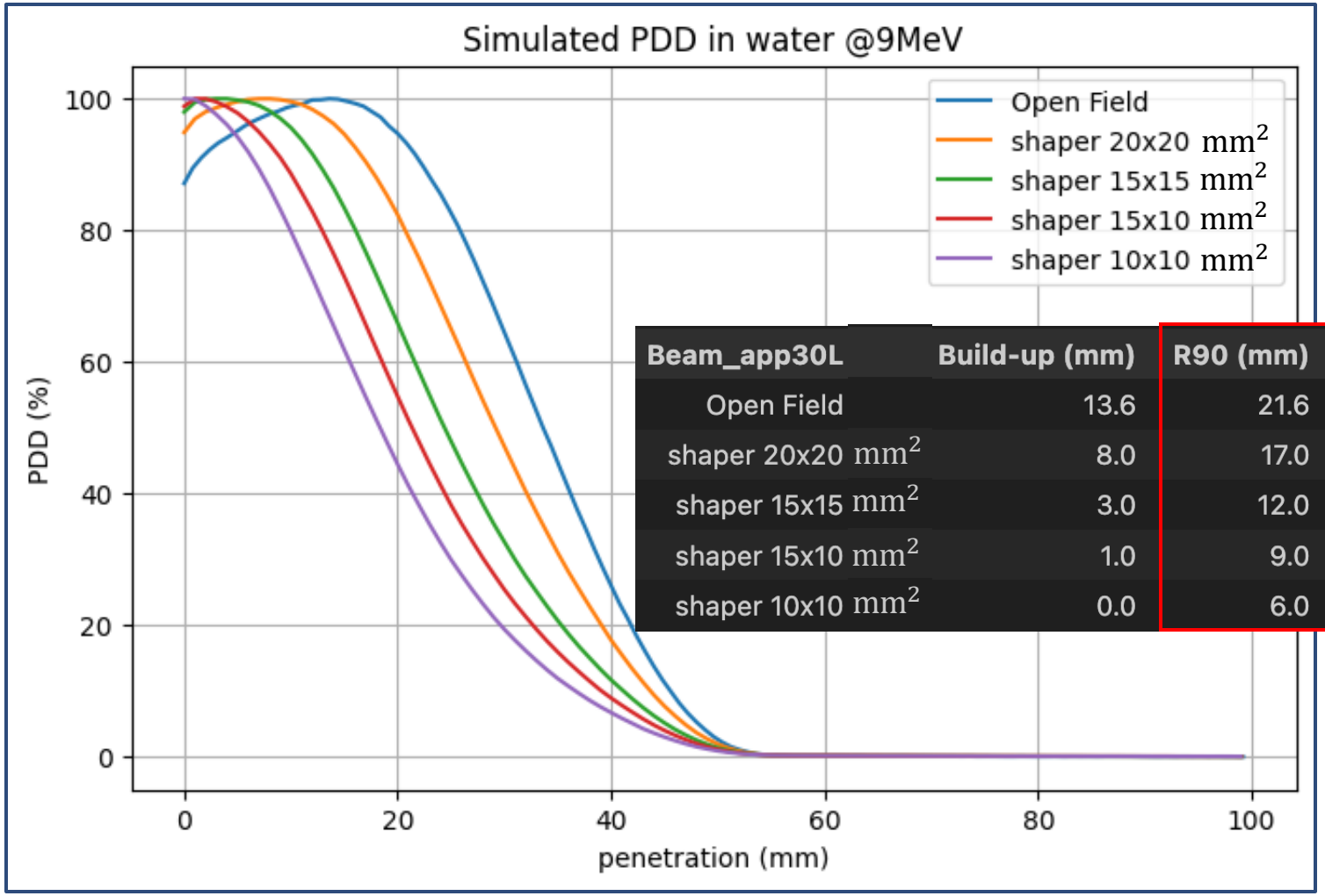
patient	max target depth (mm)	beam angle (deg)	collimator angle (deg)	tumor cross dimensions (mm^2)	configuration
P01	22	270	0	15 x 12	C1
	29	180	0	14 x 12	C2
	23	225	45	15 x 14	C3
	21	240	45	10 x 10	C4
P02	29	270	0	20 x 18	C1
	36	180	90	20 x 18	C2
	35	200	75	20 x 20	C3
P03	35	270	50	19 x 14	C1
	34	225	0	20 x 15	C2
	43	180	0	19 x 14	C3
P04	33	270	84	20 x 25	C1
	35	180	75	20 x 25	C2
	31	230	0	17 x 25	C3
	32	250	85	17 x 25	C4
P05	27	270	0	20 x 18	C1
	37	180	65	20 x 18	C2
	30	235	0	20 x 18	C3

Feasibility study



Critical issues

max target depth (mm)	tumor cross dimensions (mm^2)
22	15 x 12
29	14 x 12
23	15 x 14
21	10 x 10
29	20 x 18
36	20 x 18
35	20 x 20
35	19 x 14
34	20 x 15
43	19 x 14
33	20 x 25
35	20 x 25
31	17 x 25
32	17 x 25
27	20 x 18
37	20 x 18
30	20 x 18



Beam_app30L	Build-up (mm)	R90 (mm)	R50 (mm)
Open Field	13.6	21.6	33.6
shaper 20x20 mm^2	8.0	17.0	29.0
shaper 15x15 mm^2	3.0	12.0	24.0
shaper 15x10 mm^2	1.0	9.0	21.0
shaper 10x10 mm^2	0.0	6.0	18.0

New possibilities

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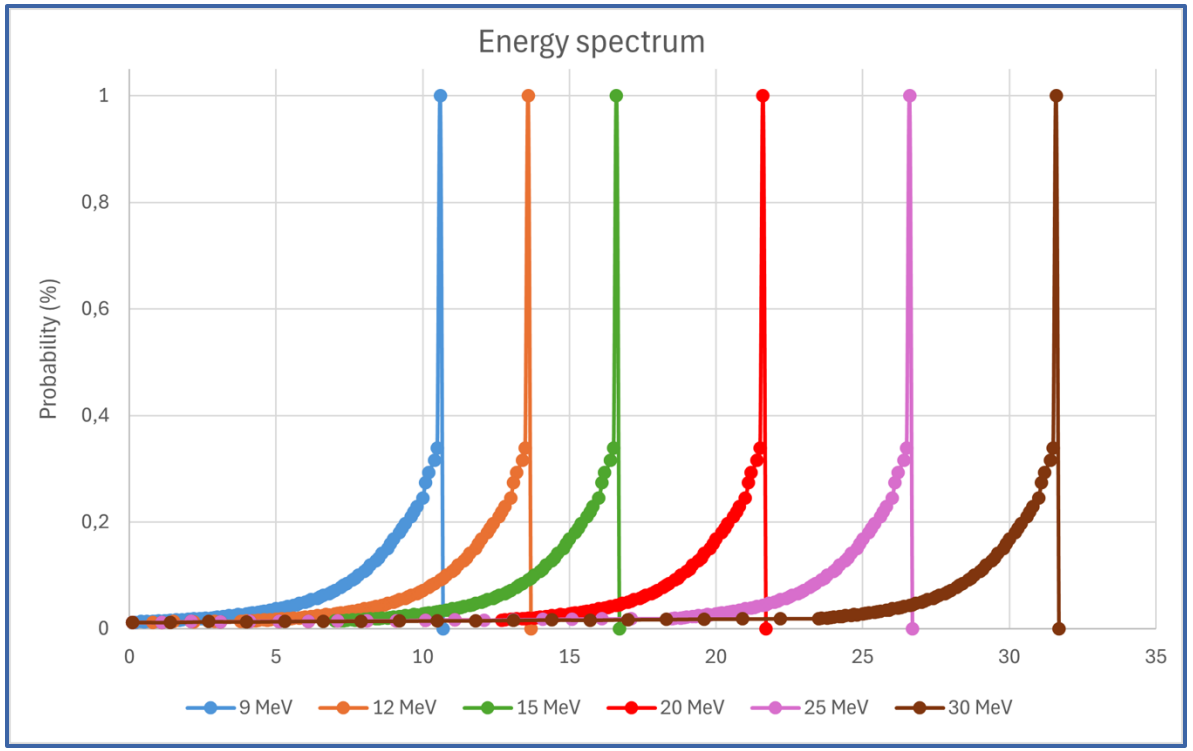
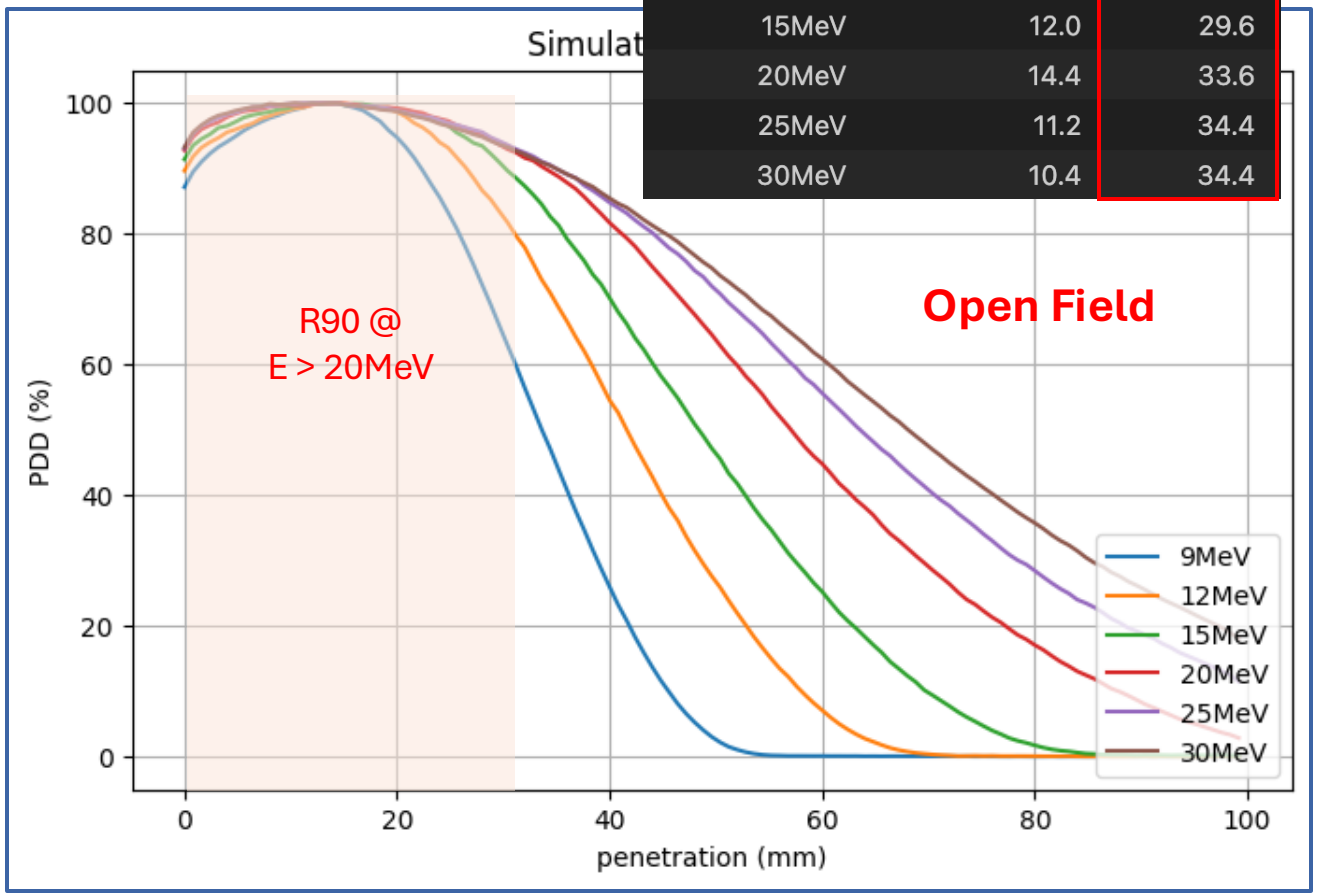


Beam_app30	Build-up (mm)	R90 (mm)
9MeV	13.6	21.6
12MeV	12.8	26.4
15MeV	12.0	29.6
20MeV	14.4	33.6
25MeV	11.2	34.4
30MeV	10.4	34.4



- Magnetron powered electron LINACs can produce **up to 30 MeV** beams [4]
  - ➢ **Can be mechanically collimated**

Example 1

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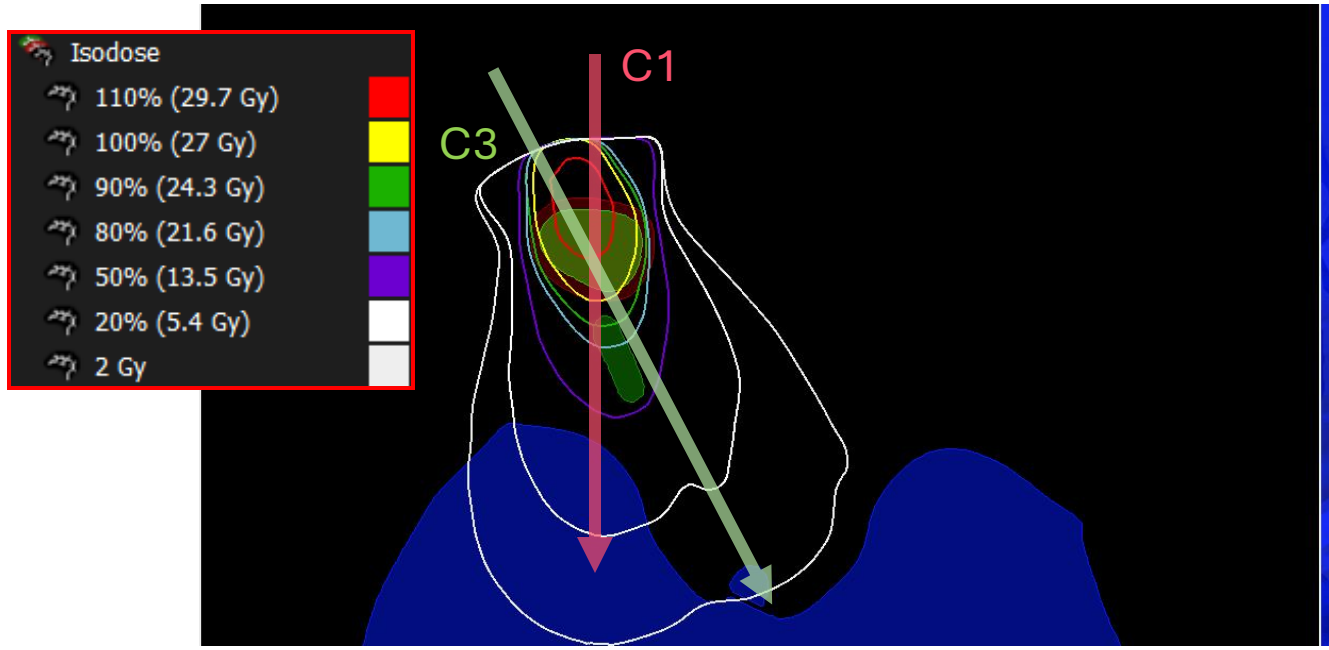
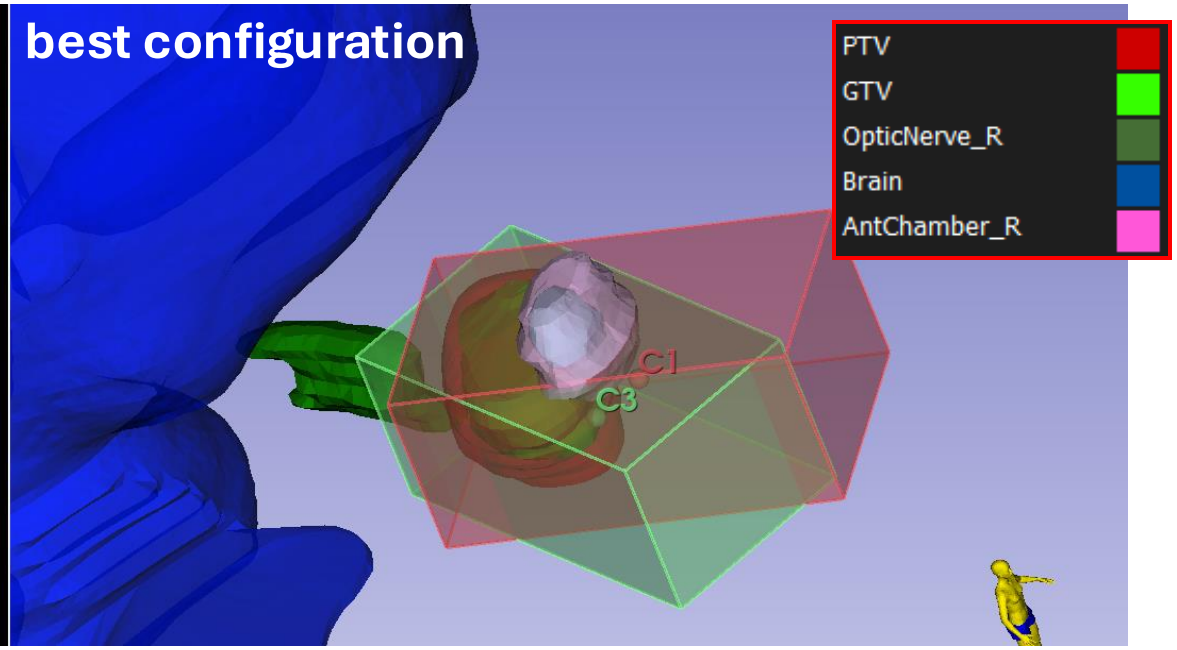
Patient 05





patient	dim voxel phantom (mm^3)	max target depth (mm)	beam angle (deg)	collimator angle (deg)	beam exit point (mm)	energy (MeV)	shaper opening (mm^2)	
P05	1.25							
		27	270	0	(-2.5, -7.7, -0.8)	20	20 x 18	C1
		37	180	65	(-6.8, -4.6, -0.8)	25	20 x 18	C2
		30	235	0	(-4.1, -7, -0.8)	20	20 x 18	C3

65% + 35% Best Configuration

Example 1

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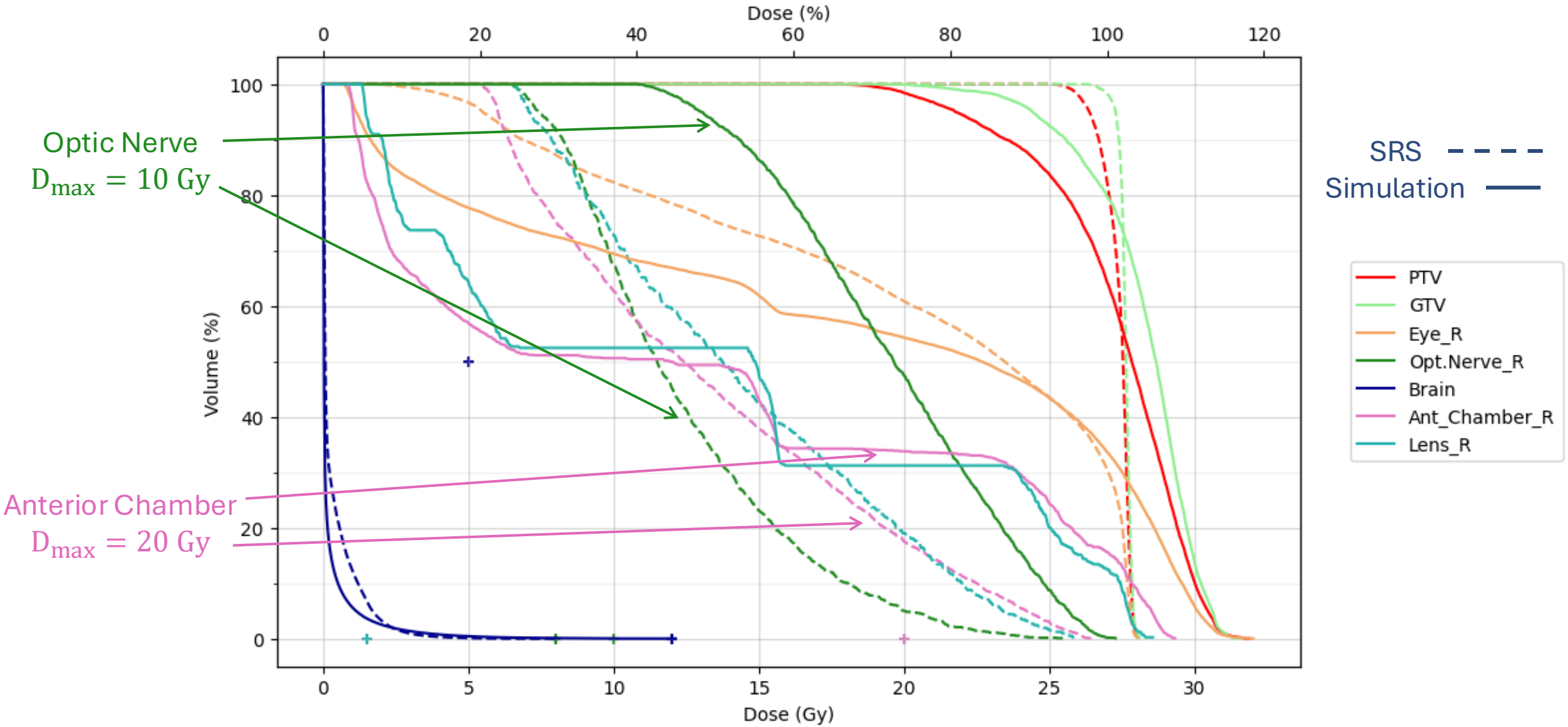

Example 1

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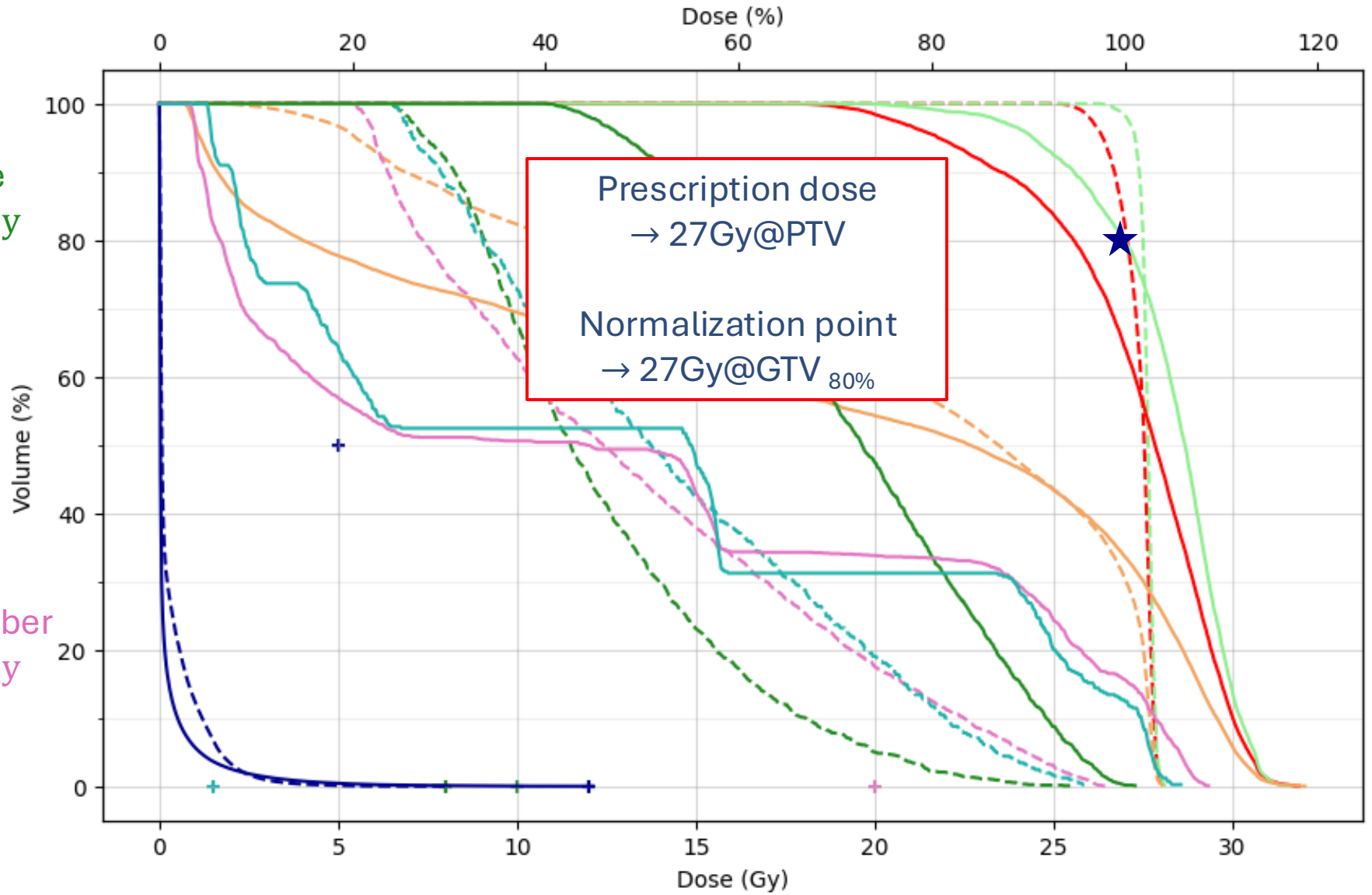
Optic Nerve
$D_{max} = 10$ Gy

Anterior Chamber
$D_{max} = 20$ Gy



Example 2

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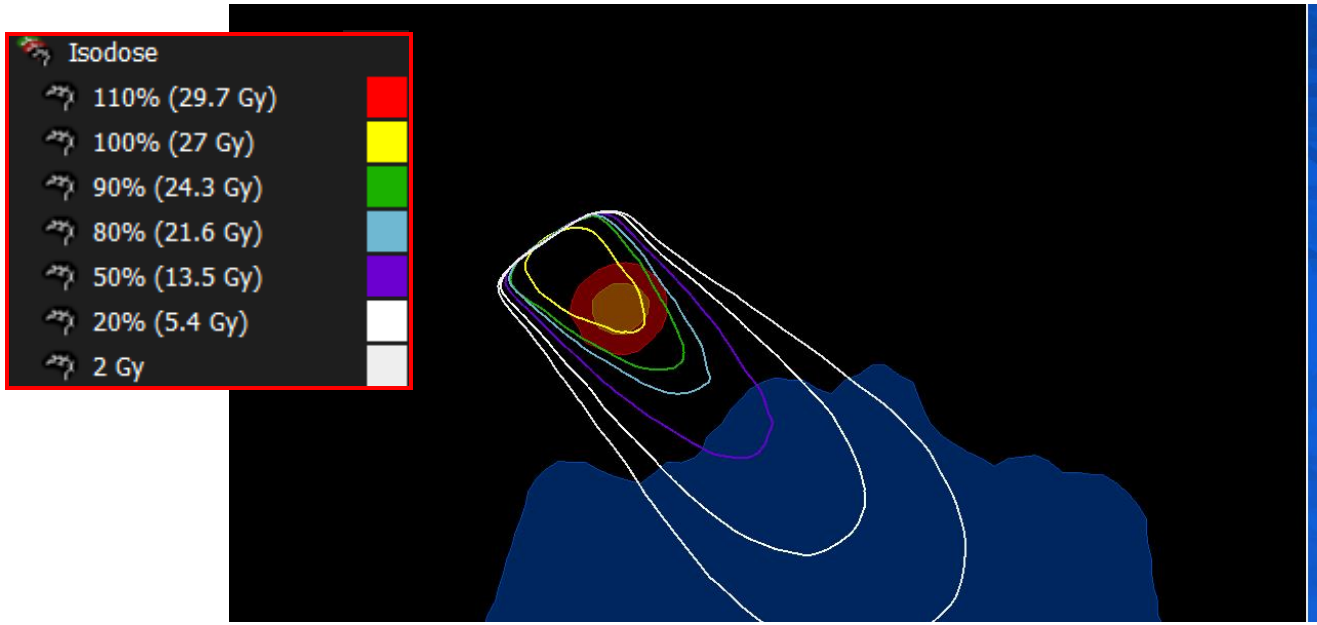
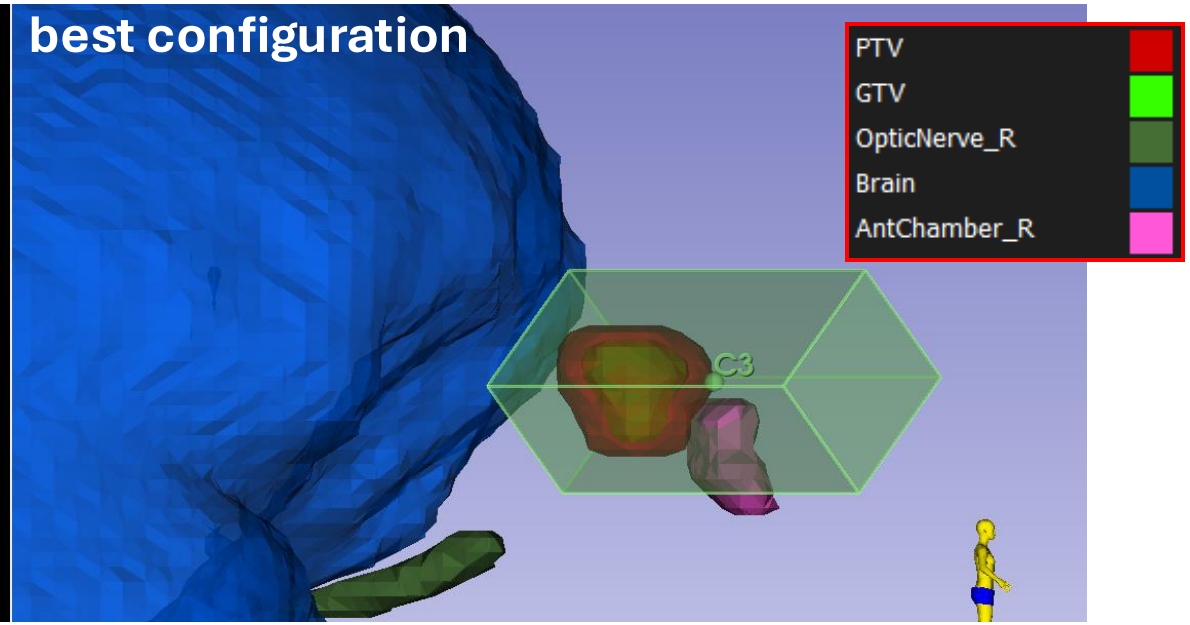
Patient 01





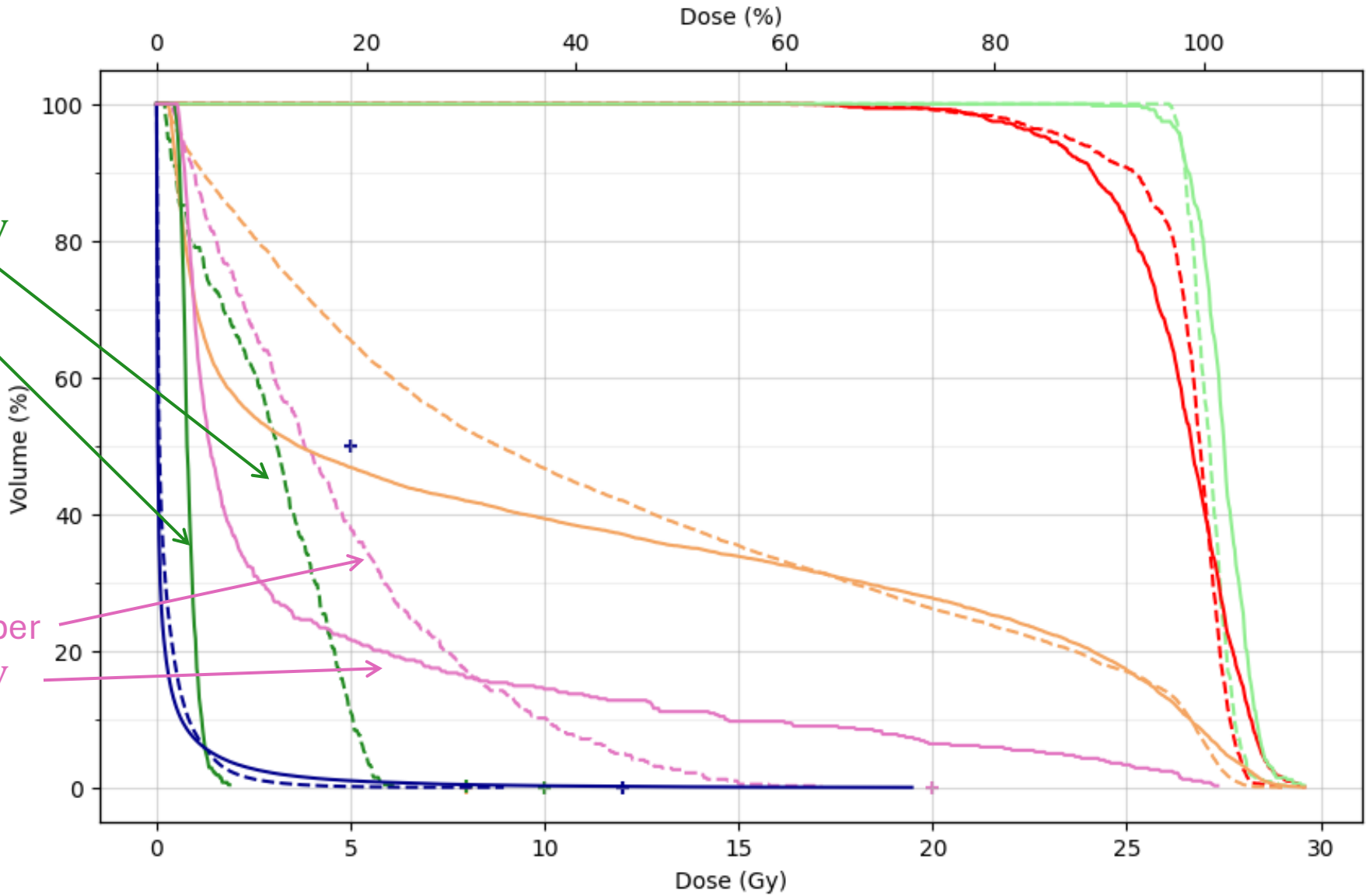
patient	dim voxel phantom (mm^3)	max target depth (mm)	beam angle (deg)	collimator angle (deg)	beam exit point (mm)	energy (MeV)	shaper opening (mm^2)	
P01	1.25							
		22	270	0	(-27, -53, 6)	20	15 x 12	C1
		29	180	0	(-60, -35, 6)	25	14 x 12	C2
		23	225	45	(-43, -50, 7)	20	15 x 14	C3
		21	240	45	(-37, -52, 7)	25	15 x 14	C4

Best Configuration

Example 2

Optic Nerve
$D_{max} = 10$ Gy

Anterior Chamber
$D_{max} = 20$ Gy



SRS – – – –
Simulation ——

PTV
GTV
Eye_R
Opt.Nerve_R
Brain
Ant_Chamber_R

Conclusions

- Final aim of this study: evaluation of the EF virtual treatment effectiveness and direct quantitative comparison with SRS-RT
- 9 MeV electron beam is not enough to cover deep targets → **virtual beam simulations**
- **Future perspectives**:
  - Quantification of flash sparing effect (radiobiological studies)
  - Combination with minibeam effect

- Bibliography:

1. Friedl, Anna A., et al. "Radiobiology of the FLASH effect." Medical Physics 49.3 (2022): 1993-2013. (https://doi.org/10.1002/mp.15184)
2. Lamas, Nuno Jorge, et al. "Prognostic biomarkers in uveal melanoma: The status quo, recent advances and future directions." Cancers 14.1 (2021): 96. (https://doi.org/10.3390/cancers14010096)
3. Di Martino, F., et al. "Architecture, flexibility and performance of a special electron linac dedicated to Flash radiotherapy research: electronFlash with a triode gun of the centro pisano flash radiotherapy (CPFR)." Frontiers in Physics 11 (2023): 1268310. (https://doi.org/10.3389/fphy.2023.1268310)
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