A feasibility study of deep seated tumor treatments combining FLASH effect and Very High Energy Electron beams

Annalisa Muscato on behalf of the Rome group
Angelica De Gregorio, Gaia Franciosini,Giacomo Traini, Vincenzo Patera,Andrei Paun, Alessio Sarti, Angelo Schiavi

FRIDA meeting - 27-28 settembre 2022

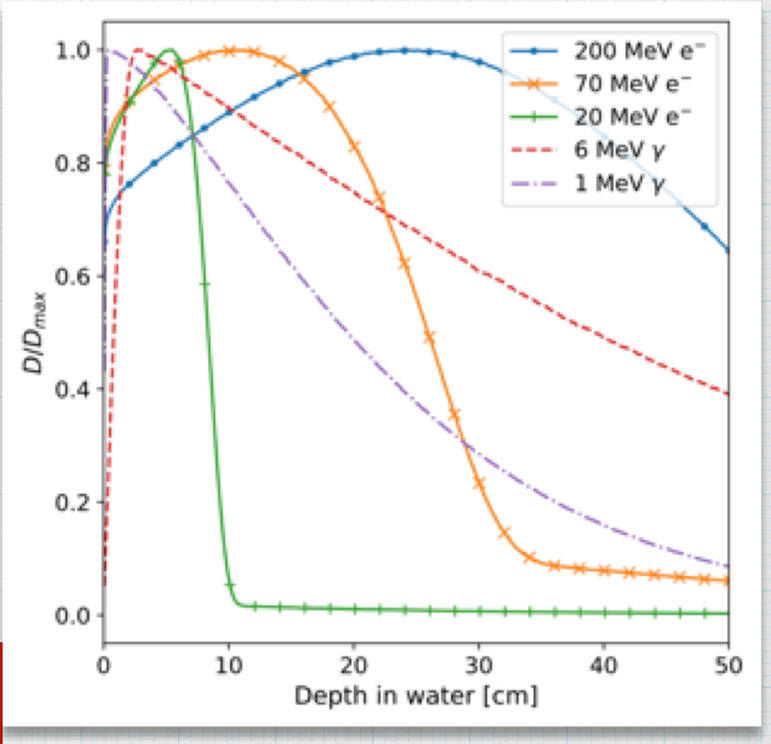
Why VHEE treatment?

Electrons have been considered already in the past as an alternative to protons and RT due to their better longitudinal sparing of OARs (charged -> BP) and reduced impact of range uncertainties (broader BP).

VHEE vs protons and photons

So far, treatments using e- have shown performances (comparable with RT or p) only at the cost of having high energies (>100 MeV) and number of fields [1].

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



Today these issues can be adressed thanks to

FLASH EFFECT:
Dose rate radically increased from~ 100 Gy/s to ~0.01 Gy/s

C-Band and X-Band technology

2.9 GHz 5.7 GHz 12 GHz

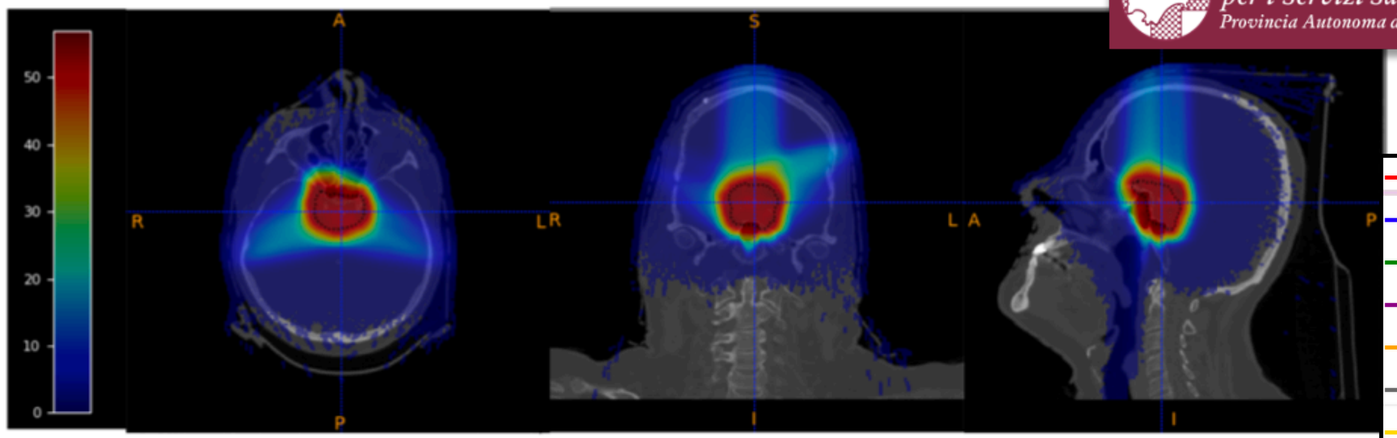
S-band G~20 MeV/m **C-band** G~50 MeV/m **X-band** G~100 MeV/m

To evaluate the feasibility of deep seated tumors VHEE treatments implementing the FLASH effect, we have investigated the case of RT and PT treatments of pancreas and head and neck cancer

Head and Neck: MI case

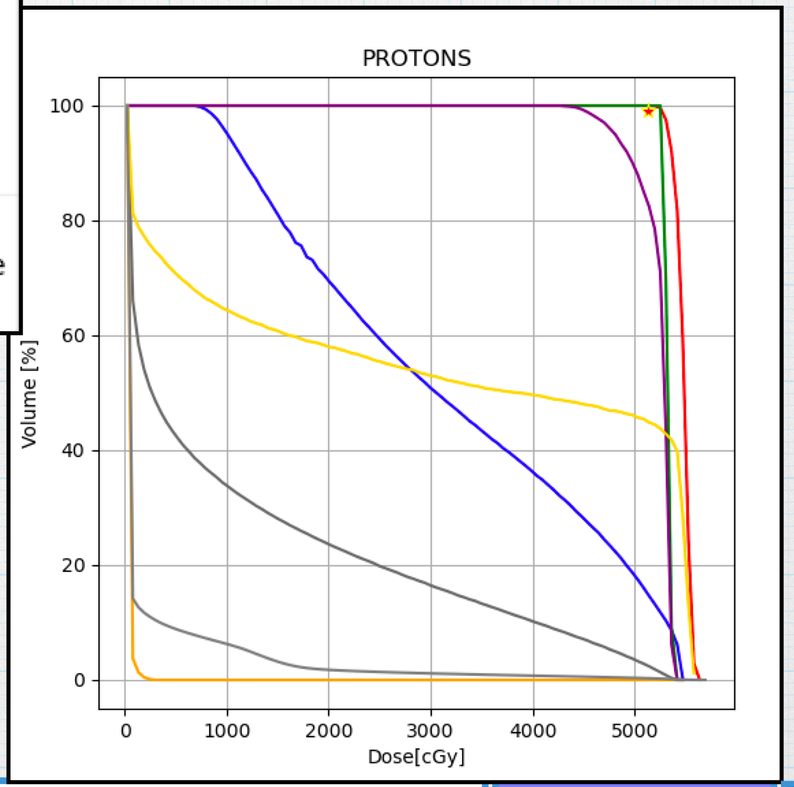
RayStation TPS optimized dose map

Real Head&Neck treatment at APSS Hospital center, Trento



- Patient with **meningioma** tumor, was treated with **54 GyRBE** in 27 fractions with **3 proton fields**;

PTV
Nervi Ottici
Chiasma
Vie Ott Post
Occhi
Tronco
Carotidi
Normal Tissue
95% 99%



Dosimetric constraints

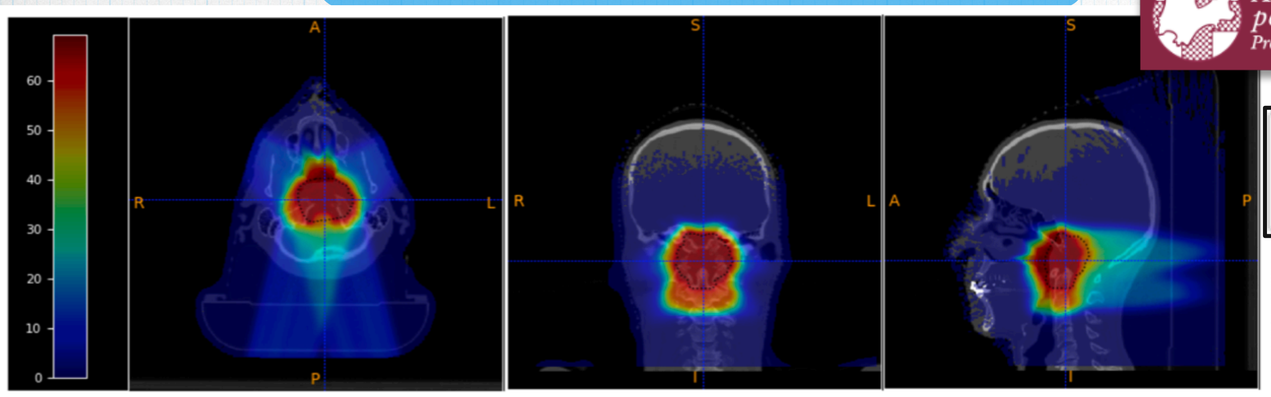
Organo	Constraints
PTV	$V_{95} > 99\%$, mai oltre il 105%
Nervi Ottici	$D_1 \leq 54$ GyRBE
Chiasma	$D_1 \leq 54$ GyRBE
Vie Ottiche Posteriori	$D_1 \leq 54$ GyRBE
Occhi	$D_1 \leq 40$ GyRBE
Tronco Encefalico	$D_1 \leq 54$ GyRBE
Carotidi	No hot spots ($< 105\%$ dose di prescrizione)

Head and Neck: C1 case

Real Head&Neck treatment at APSS Hospital, Trento

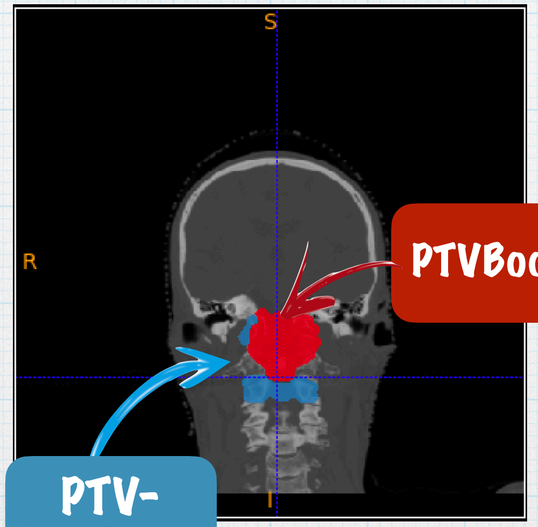
- Patient with **chordoma** tumor, was treated with proton therapy using **54 GyRBE** in 30 fractions with **4 fields**;

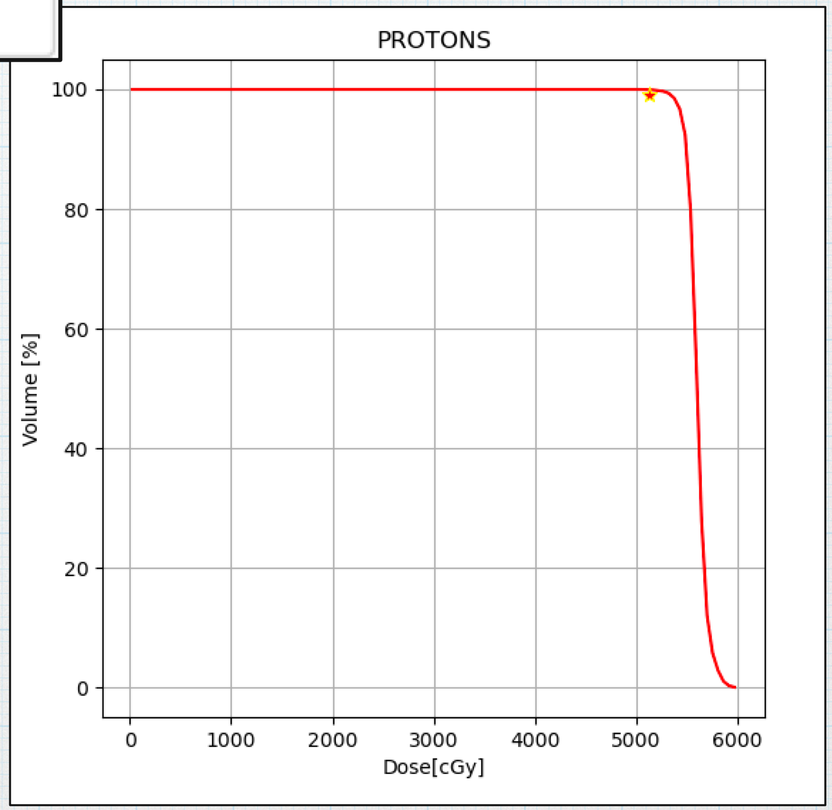
RayStation TPS optimized dose map



Azienda Provinciale per i Servizi Sanitari
Provincia Autonoma di Trento

PTV - PTVBoost
95% 99%





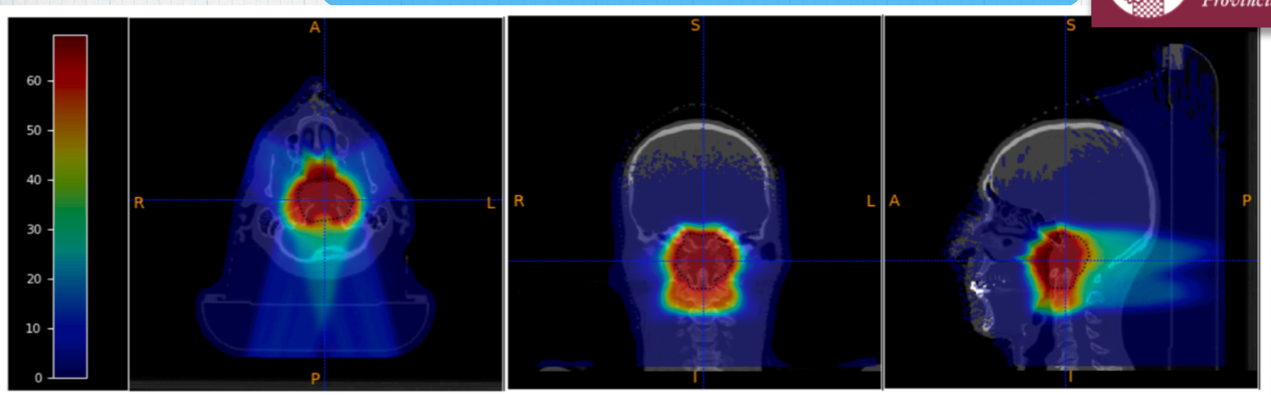
Dosimetric constraints

Organo	Constraints
PTV e PTV Boost	$V_{95} > 99\%$, mai oltre il 107%
Tronco Encefalico	$D_1 \leq 55$ GyRBE
Midollo Spinale	$D_1 \leq 54$ GyRBE
Parotidi	$D_{mean} \leq 26$ GyRBE
Canali Uditivi	$D_{mean} \leq 30$ GyRBE
Coclee	$D_{mean} \leq 35$ GyRBE

Head and Neck : C1 case

Real Head&Neck treatment at APSS Hospital, Trento

RayStation TPS optimized dose map



Azienda Provinciale per i Servizi Sanitari
Provincia Autonoma di Trento

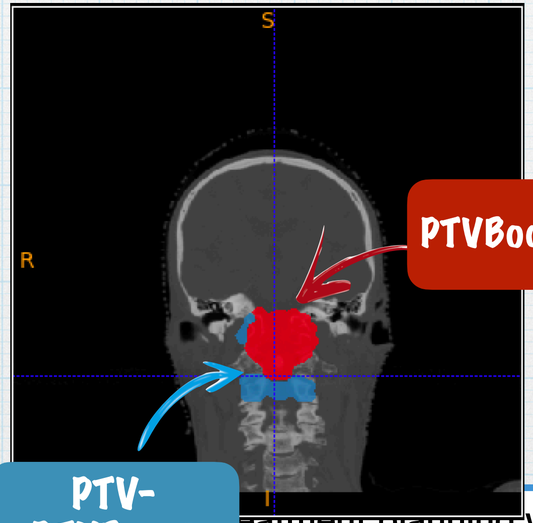
- PTVBoost
- Brainstem
- Marrow
- Parothide dx
- Parothide sin
- Ear Canal dx
- Ear Canal sin
- Cochlea dx
- Cochlea sin
- NoT
- 95% 99%

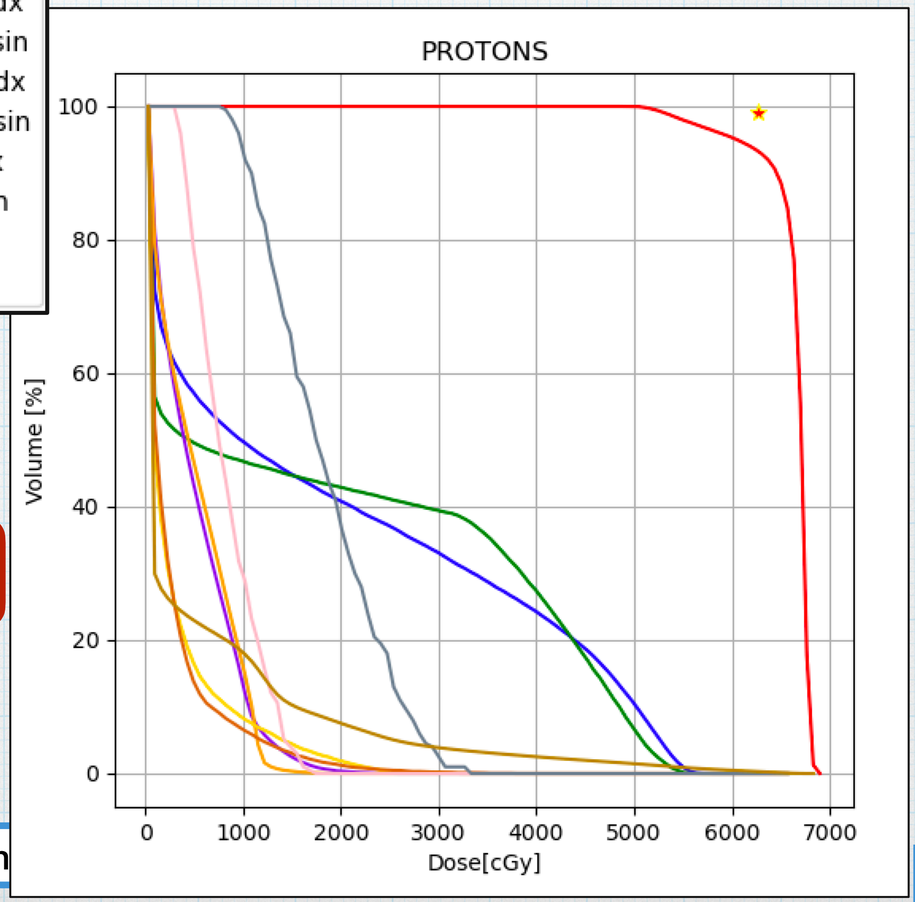
•A PTV boost was also planned on a limited region of the PTV: **66 GyRBE** in **33 fractions** with **4 proton fields**;

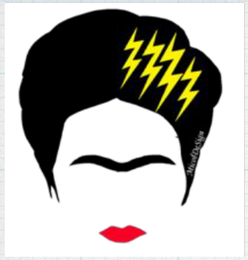
- **30 fractions** in SIB modality;
- **3 fractions** in sequential way;

Dosimetric constraints

Organo	Constraints
PTV e PTV Boost	$V_{95} > 99\%$, mai oltre il 107%
Tronco Encefalico	$D_1 \leq 55$ GyRBE
Midollo Spinale	$D_1 \leq 54$ GyRBE
Parotidi	$D_{mean} \leq 26$ GyRBE
Canali Uditivi	$D_{mean} \leq 30$ GyRBE
Coclee	$D_{mean} \leq 35$ GyRBE







Head and Neck case C1 & M1: IMRT

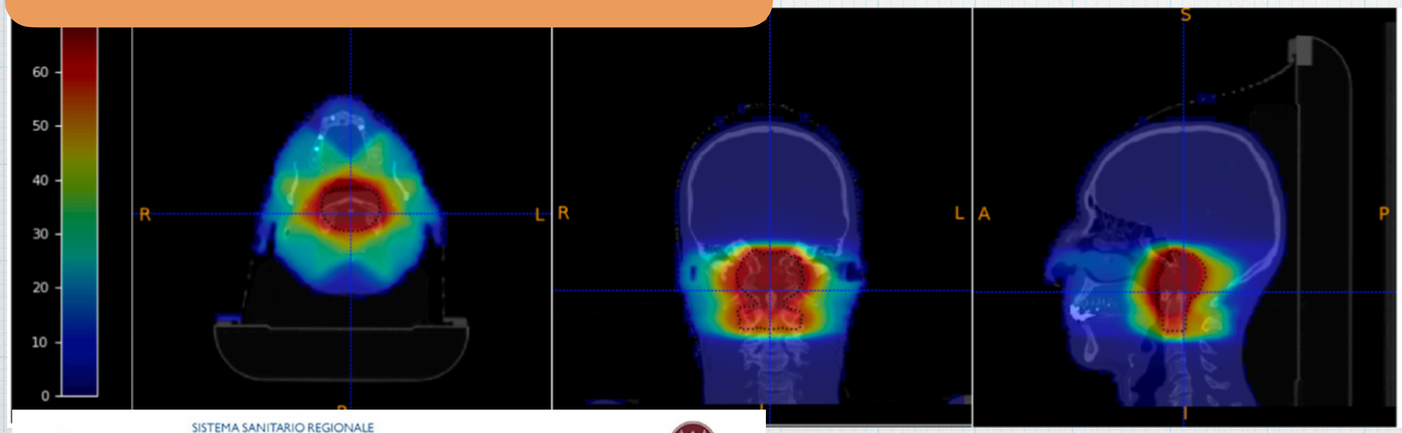
Dosimetric constraints

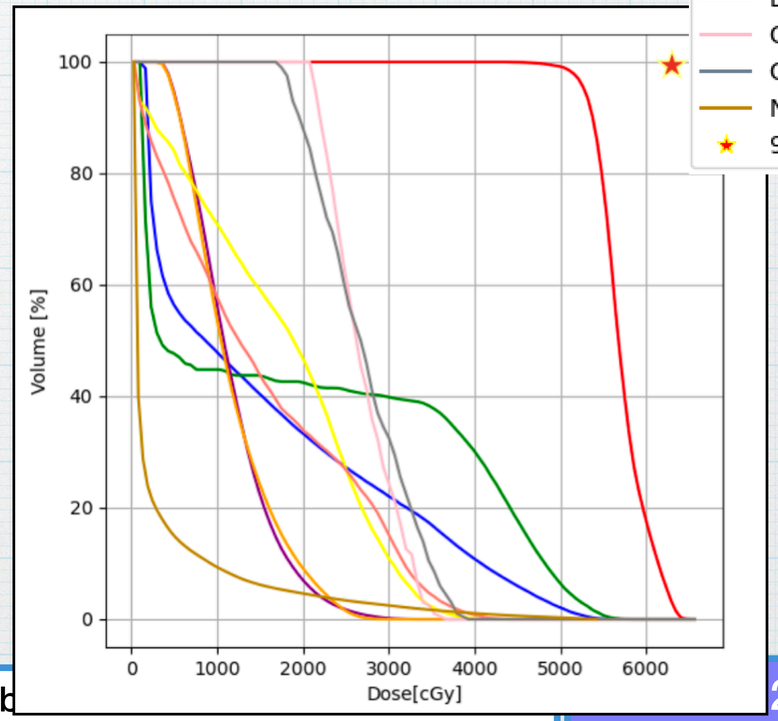
Organ	Photons
PTV	$V_{95\%}$ 86.42% $V_{105\%}$ 0.4%
Tronco	D_1 51.20 GyRBE
Midollo spinale	D_1 54 GyRBE
Can Uditivo Dx	D_{mean} 16.94 GyRBE
Coclea Dx	D_{mean} 26.37 GyRBE

•The same CT has been used by the **Policlinico Umberto I Hospital** (Rome, Italy) to plan and optimise the **photons treatment** for comparison with PT plans.

- **Primary goal**: safeguard the most critical OARs, like **Brainsteam** and **Marrow**, even at the expense of PTV coverage.

Optimized photon dose map





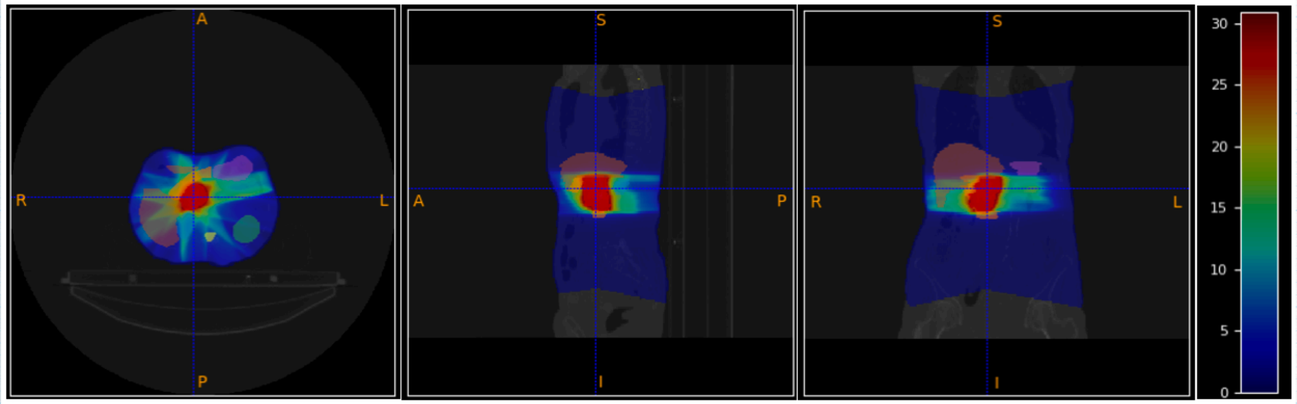
SISTEMA SANITARIO REGIONALE
AZIENDA OSPEDALIERA UNIVERSITARIA POLICLINICO UMBERTO I
SAPIENZA UNIVERSITÀ DI ROMA

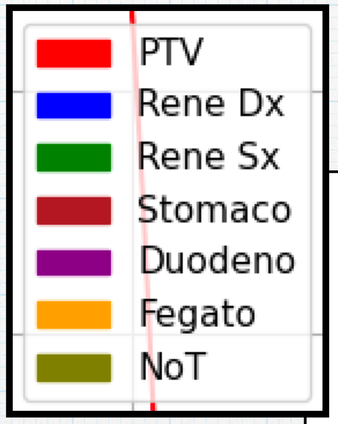
Pancreas case: IMRT

IMRT pancreas treatment at Campus Biomedico center, Rome

- Patient with **pancreas** tumor, was treated with fractionated IMRT of **30 Gy** in **5 fractions** with **7 photon fields** ;

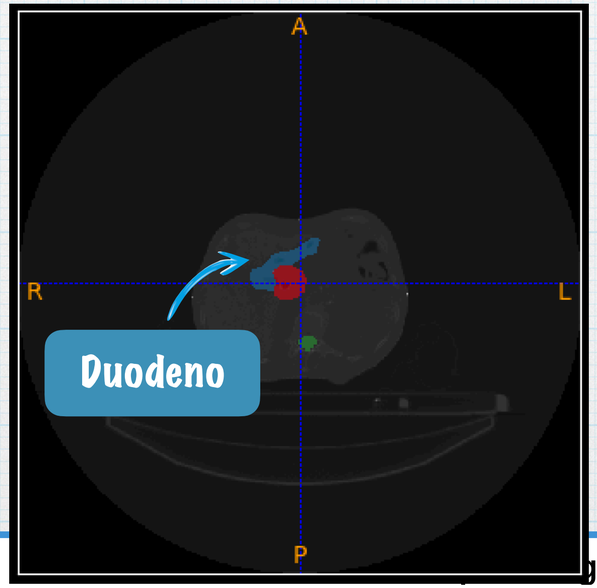
RayStation TPS optimized dose map

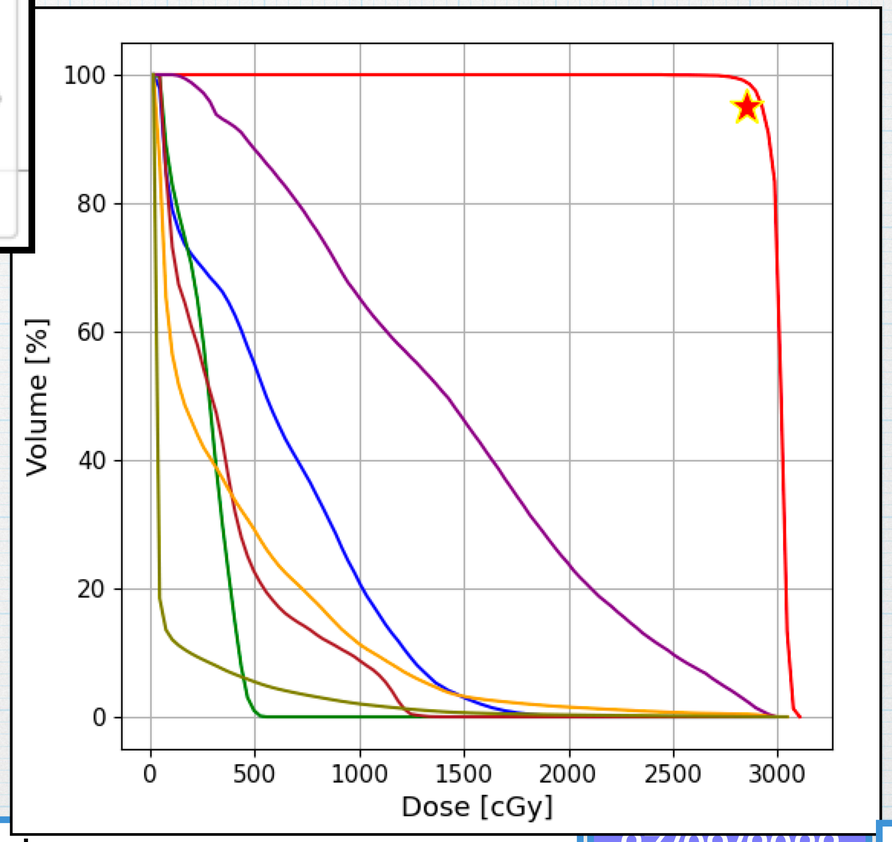


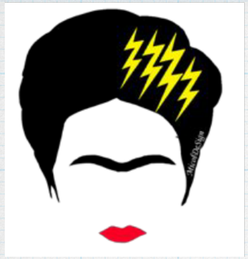


Dosimetric constraints

Organ	Dosimetric constraints
PTV	$V_{95\%}$>95% never above 107%
Rene	D_{mean}<10 Gy
Intestino	D_{max}<45 Gy
Duodeno	D_{max}<35 Gy
Midollo osseo	D_{max}<18 Gy
Fegato	D_{mean}<15 Gy



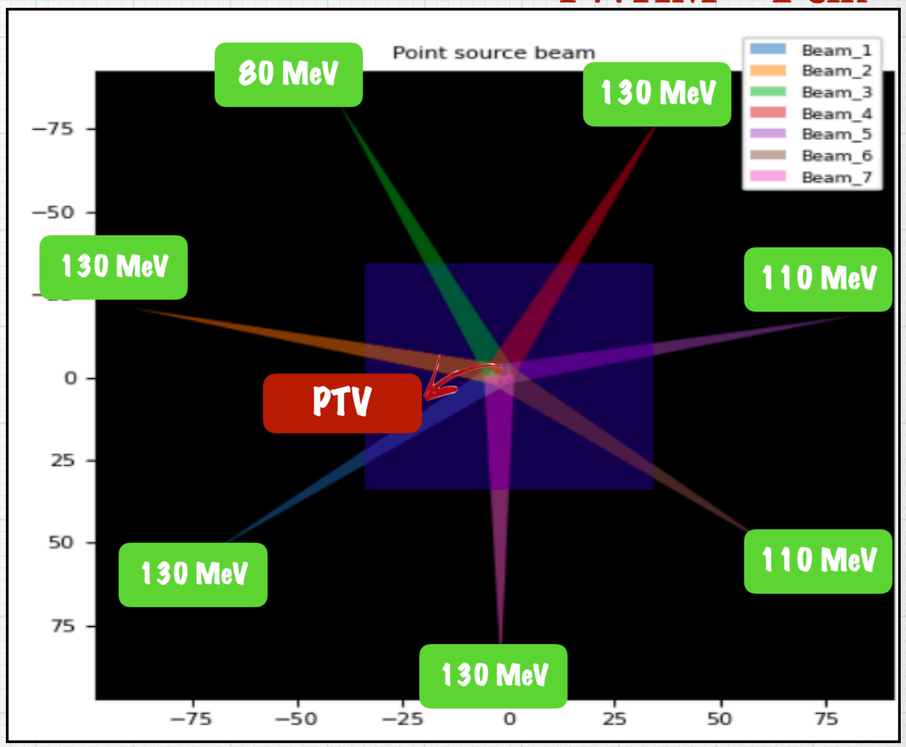




VHEE Planning: Strategy and Workflow

FLUKA MC SIMULATION

FWHM = 1 cm



To put on a solid ground the comparison in this first attempt focused on evaluating the impact of a VHEE FLASH RT:

- the same 7 equidistant fields have been used for IMRT and VHEE planning;
- VHEE beams have transverse size $O \sim$ mm and divergence $O \sim$ mrad;
- the electron "pencil beam" paints each irradiation field like in active PB scanning techniques.
- The energy of each field was chosen by centering the BP of a single PB in the PTV.

Treatment optimization

The fluence of each PB is then optimized to ensure the required PTV coverage while sparing the OARs.

FMF

The FLASH effect is modeled using the Flash Modifying Factor (**FMF**) to account for the reduced normal tissue damage

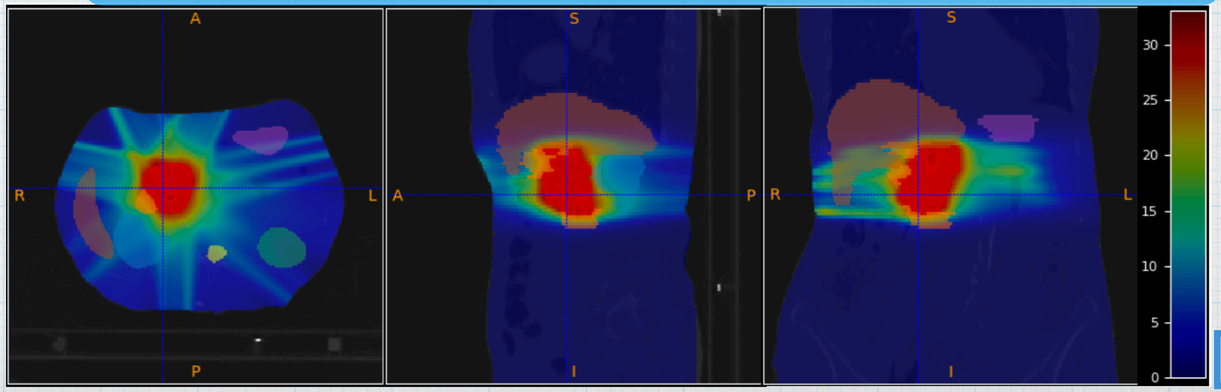
$$\mathrm{FMF} = \frac{D_{\mathrm{CONV}}}{D_{\mathrm{UHDR}}}\Big|_{\mathrm{isoeffect}}$$

Conventional

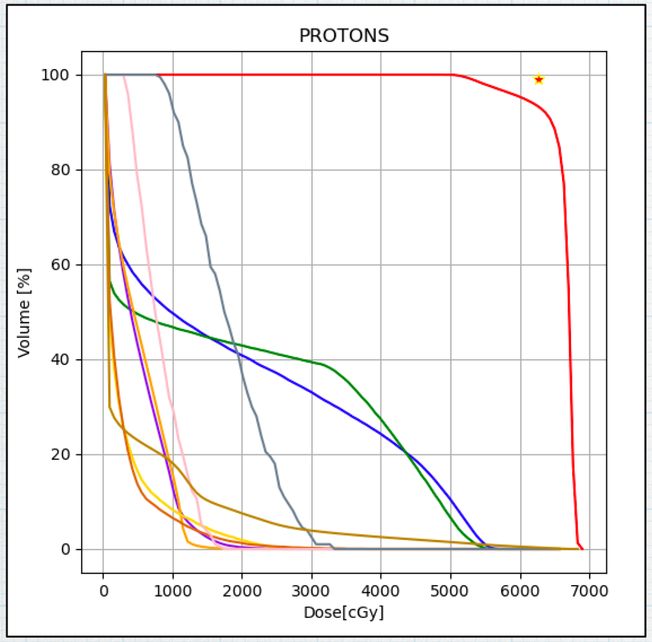
UHDR

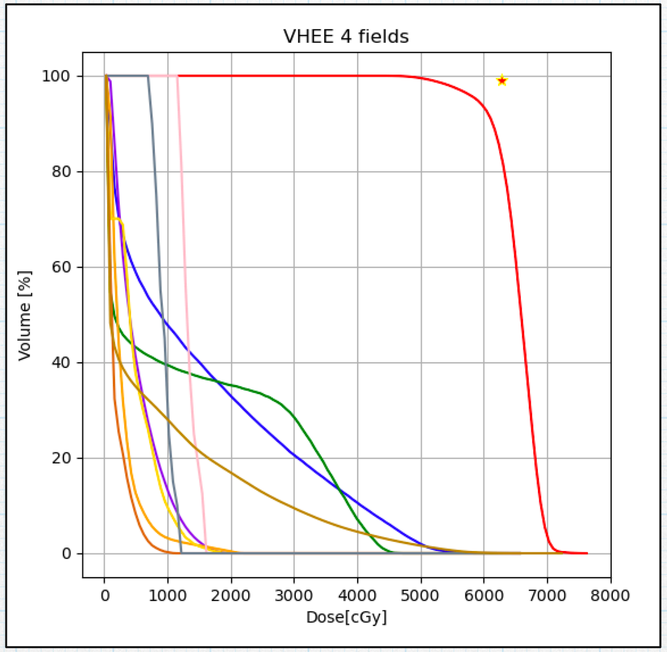
We have implmented FMF=0.9 and 0.6

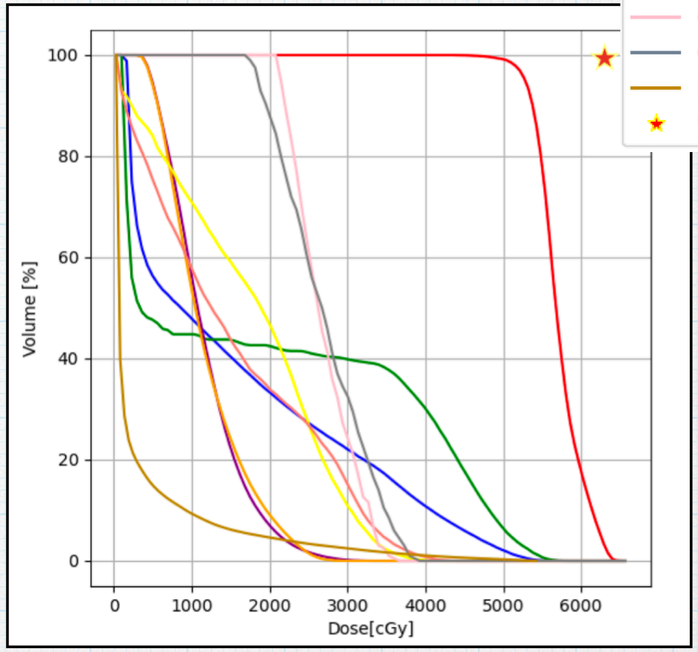
Optimazed electron dose map with NO FLASH effect

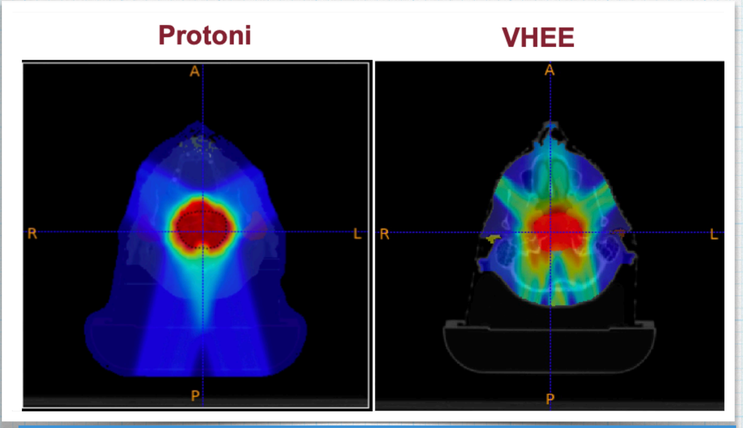


C1 case: RESULTS

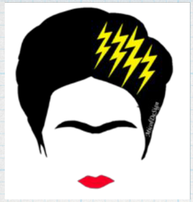




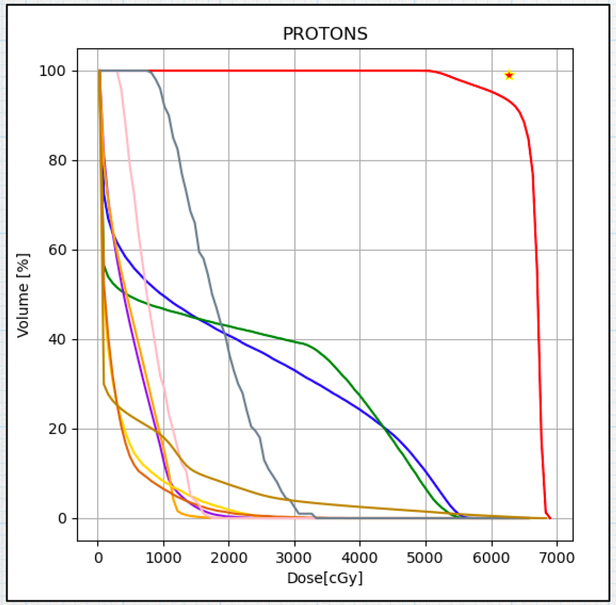


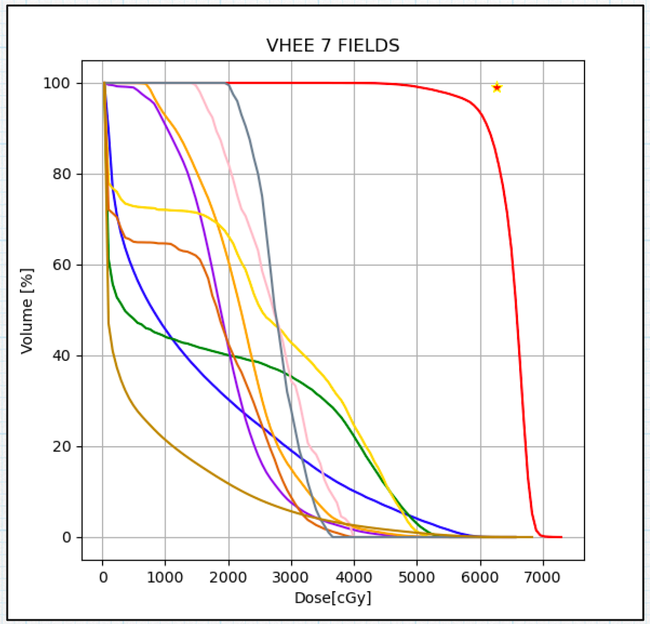


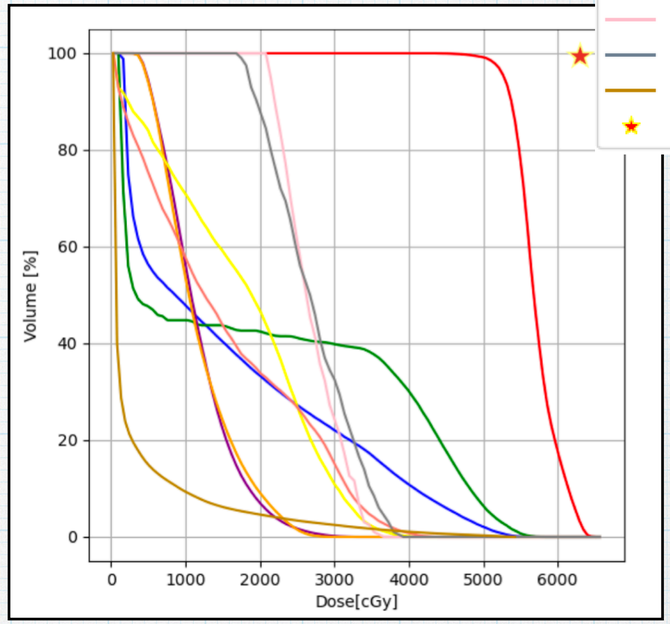
Organ	Protons	Photons	VHEE 4 field
PTV	$V_{95\%}$ 92.44% $V_{105\%}$ 0.01%	$V_{95\%}$ 86.42% $V_{105\%}$ 0.4%	$V_{95\%}$ 82.69% $V_{105\%}$ 10.18%
Tronco	D_1 54 GyRBE	D_1 51.20 GyRBE	D_1 54 GyRBE
Midollo spinale	D_1 52.75 GyRBE	D_1 54 GyRBE	D_1 42.78 GyRBE
Can Uditivo Dx	D_{mean} 2.61 GyRBE	D_{mean} 16.94 GyRBE	D_{mean} 4.13 GyRBE
Coclea Dx	D_{mean} 7.79 GyRBE	D_{mean} 26.37 GyRBE	D_{mean} 12.67 GyRBE



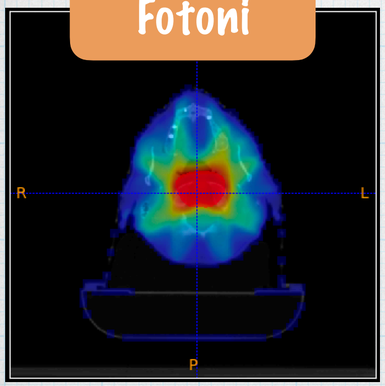
C1 case: RESULTS



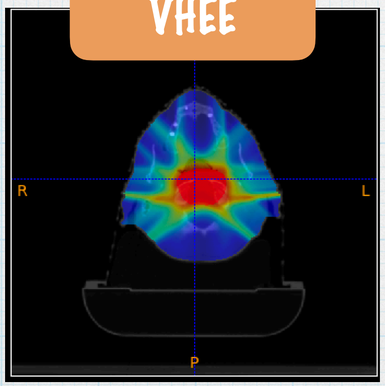




Fotoni

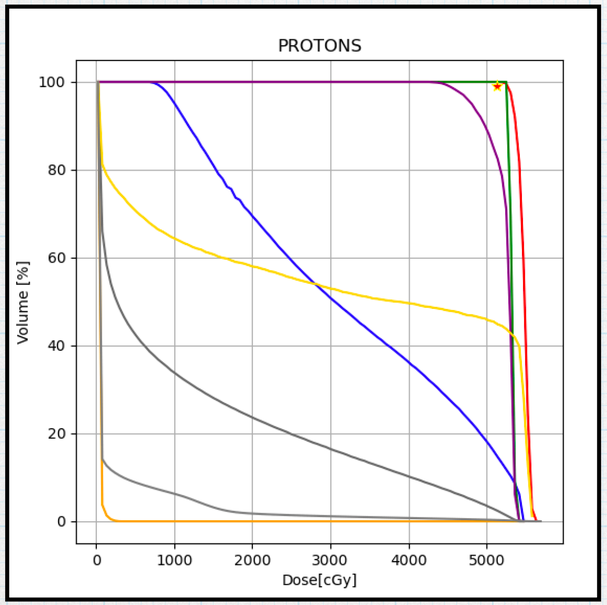


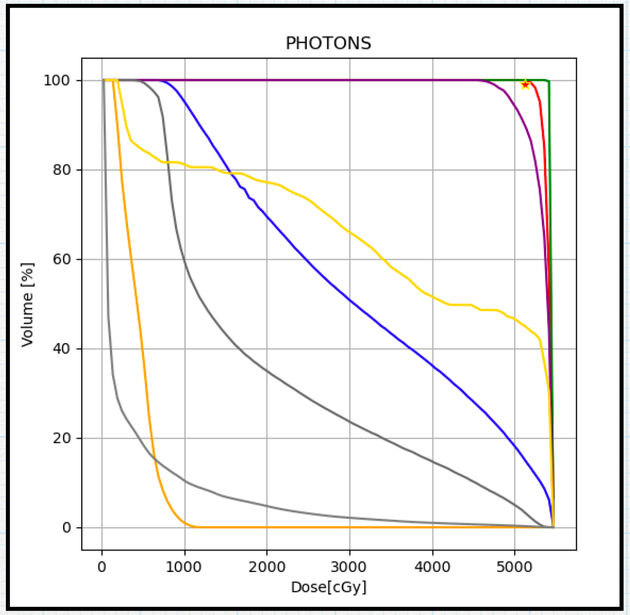
VHEE

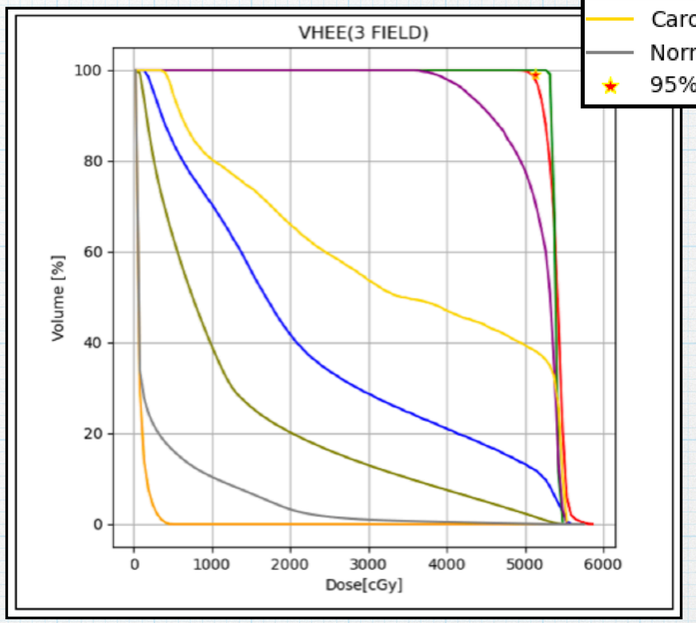


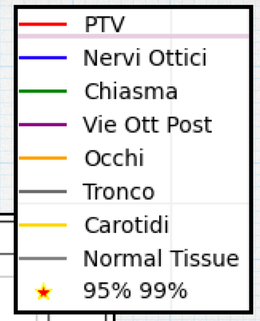
Organ	Protons	Photons	VHEE 7 field
PTV	$V_{95\%}$ 92.44% $V_{105\%}$ 0.01%	$V_{95\%}$ 86.42% $V_{105\%}$ 0.4%	$V_{95\%}$ 90.05% $V_{105\%}$ 2.28%
Tronco	D_1 54 GyRBE	D_1 51.20 GyRBE	D_1 54 GyRBE
Midollo spinale	D_1 52.75 GyRBE	D_1 54 GyRBE	D_1 49 GyRBE
Can Uditivo Dx	D_{mean} 2.61 GyRBE	D_{mean} 16.94 GyRBE	D_{mean} 21.05 GyRBE
Coclea Dx	D_{mean} 7.79 GyRBE	D_{mean} 26.37 GyRBE	D_{mean} 24.88 GyRBE

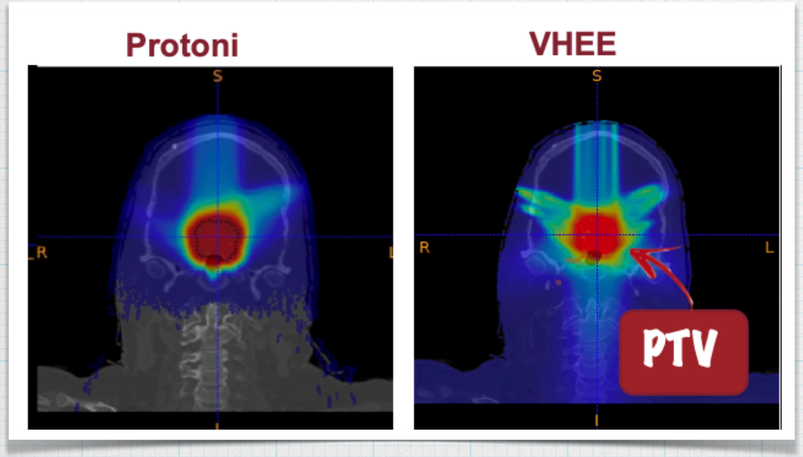
M1 case: RESULTS





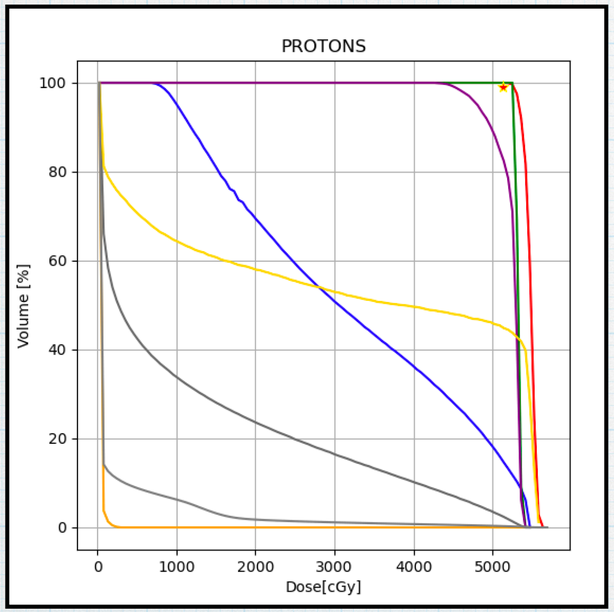


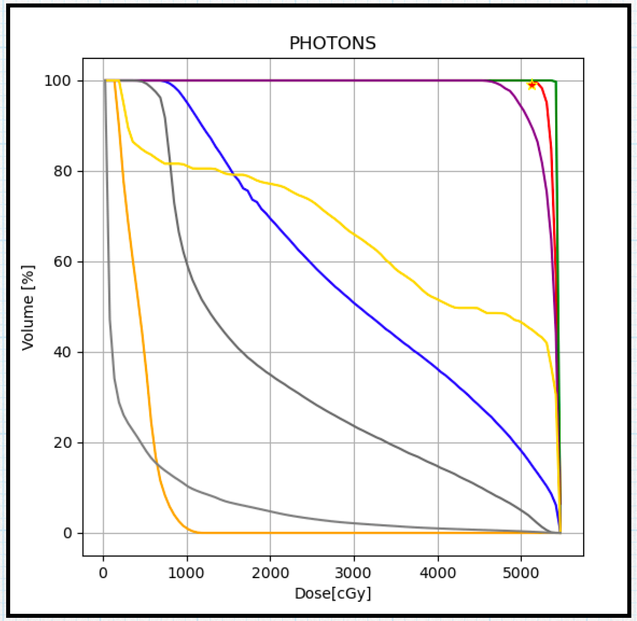


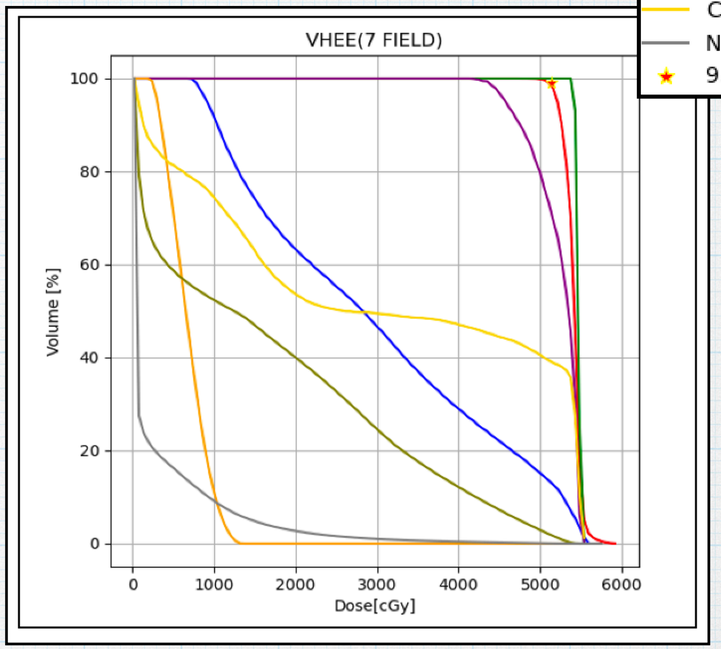


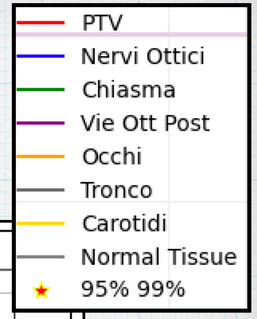
Organ	Protons	Photons	VHEE 3 field
PTV	$V_{95\%}$ 99.52% $V_{105\%}$ 0.009%	$V_{95\%}$ 99.33% $V_{105\%}$ 0.009%	$V_{95\%}$ 96.56% $V_{105\%}$ 1.12%
PRV Nervi Ottici	D_1 53.26 GyRBE	D_1 54 GyRBE	D_1 54 GyRBE
PRV Chiasma	D_1 53.43 GyRBE	D_1 53.83 GyRBE	D_1 53 GyRBE
Vie Ottiche Post.	D_1 53.55 GyRBE	D_1 53.94 GyRBE	D_1 53.53 GyRBE
Tronco	D_1 54 GyRBE	D_1 53.25GyRBE	D_1 53.14 GyRBE

M1 case: RESULTS

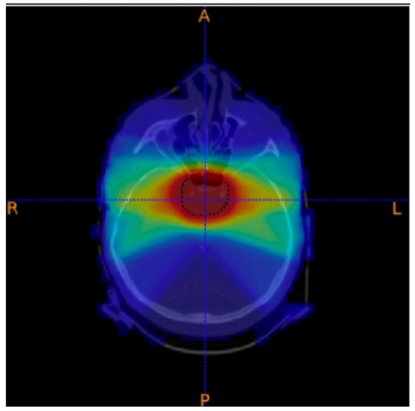




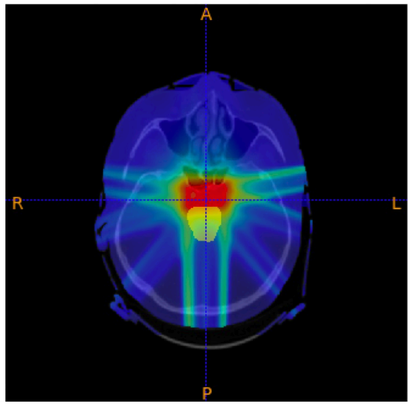




Fotoni

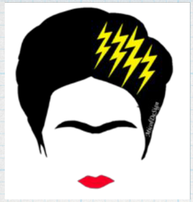


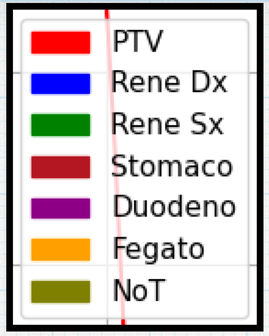
VHEE



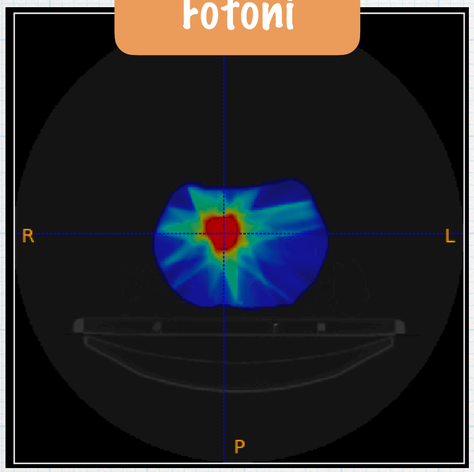
Organ	Protons	Photons	VHEE 7 field
PTV	$V_{95\%}$ 99.52% $V_{105\%}$ 0.009%	$V_{95\%}$ 99.33% $V_{105\%}$ 0.009%	$V_{95\%}$ 95.46% $V_{105\%}$ 1.25%
PRV Nervi Ottici	D_1 53.26 GyRBE	D_1 54 GyRBE	D_1 54 GyRBE
PRV Chiasma	D_1 53.43 GyRBE	D_1 53.83 GyRBE	D_1 53.02 GyRBE
Vie Ottiche Post.	D_1 53.55 GyRBE	D_1 53.94 GyRBE	D_1 53.19 GyRBE
Tronco	D_1 54 GyRBE	D_1 53.25GyRBE	D_1 51.68 GyRBE

Pancreas case: RESULTS

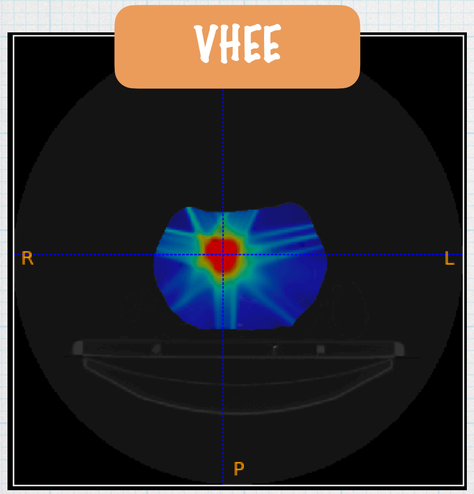




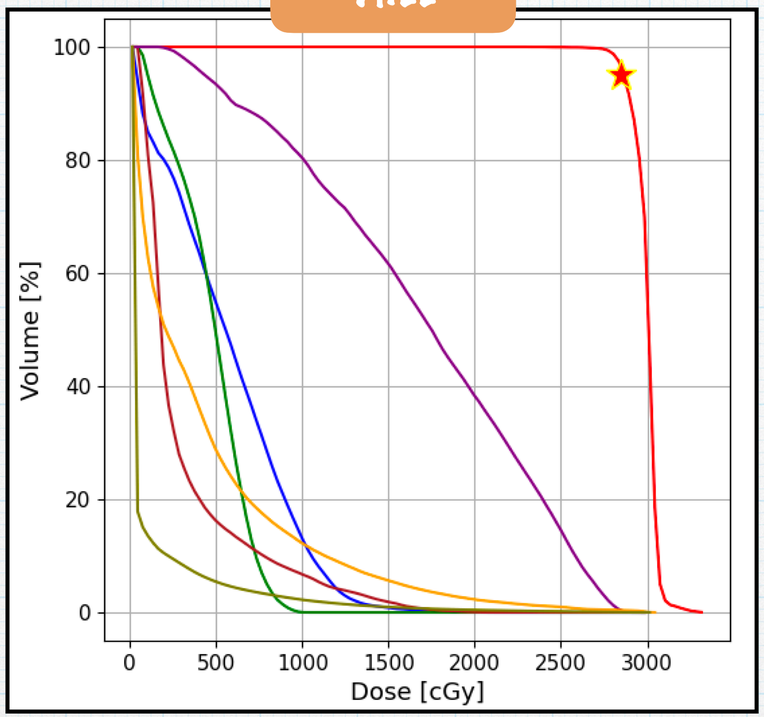
Fotoni



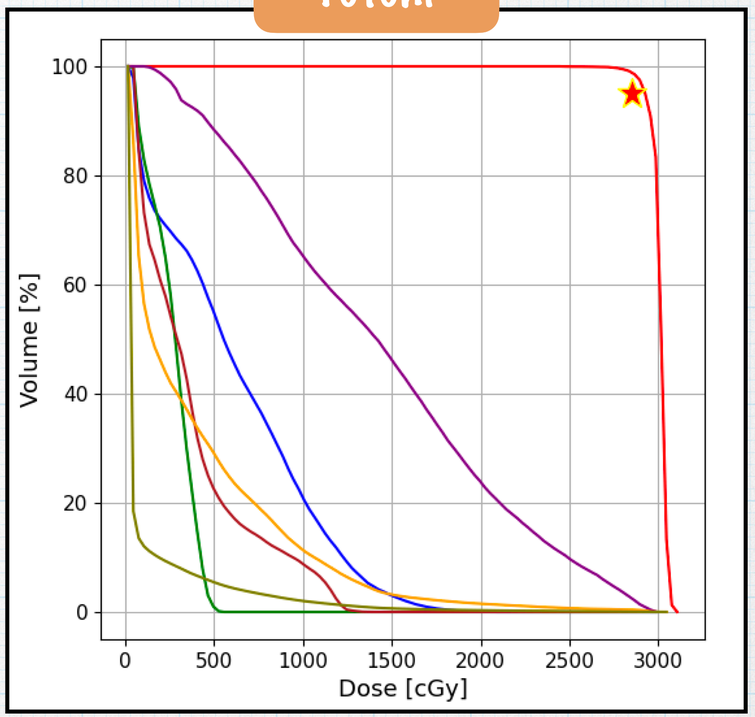
VHEE



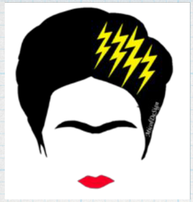
VHEE



Fotoni

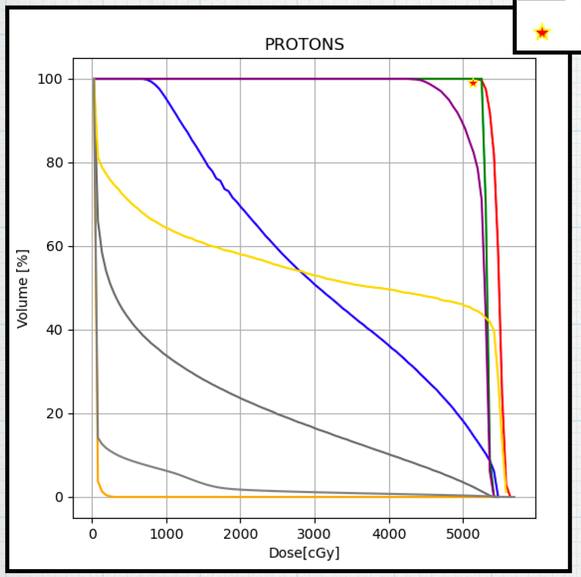


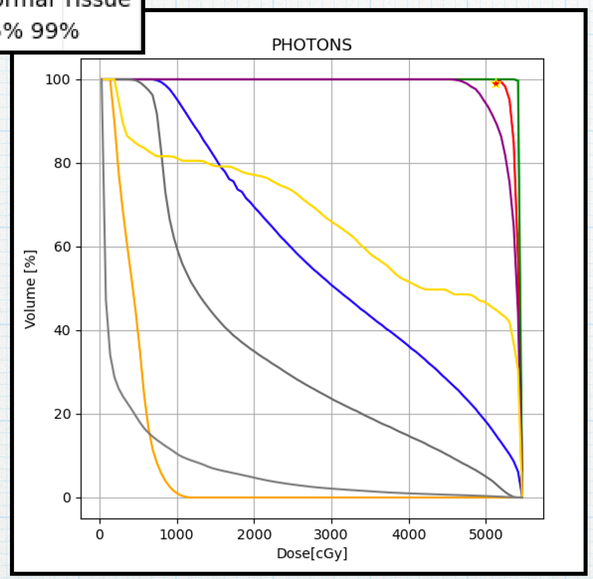
Organ	Photons	VHEE 7 field
PTV	$V_{95\%}$ 99.13% $V_{105\%}$ 83.35%	$V_{95\%}$ 98.01% $V_{105\%}$ 71.26%
Rene Dx	D_{mean} 5.88 Gy	D_{mean} 7.08 Gy
Stomaco	D_{mean} 13.65 Gy	D_{mean} 18.99 Gy
Duodeno	D_{max} 29.98 Gy	D_{max} 29.50 Gy
Fegato	D_{mean} 3.77 Gy	D_{mean} 4.08 Gy
Midollo	D_{max} 9.42 Gy	D_{max} 9.09 Gy

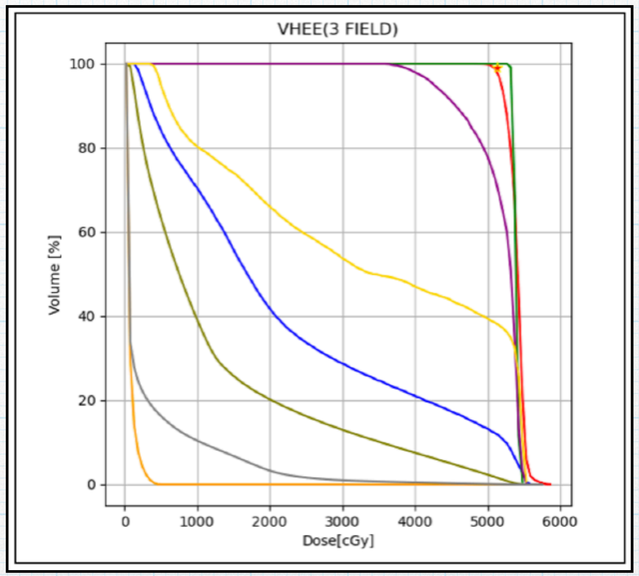


M1 case: RESULTS

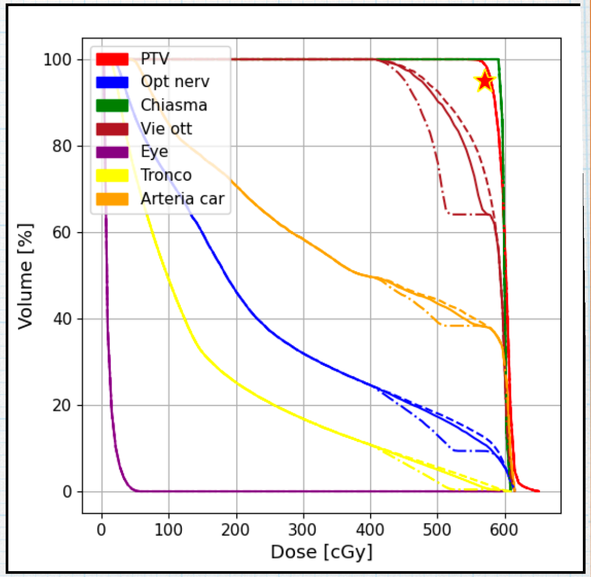
PTV
Nervi Ottici
Chiasma
Vie Ott Post
Occhi
Tronco
Carotidi
Normal Tissue
95% 99%







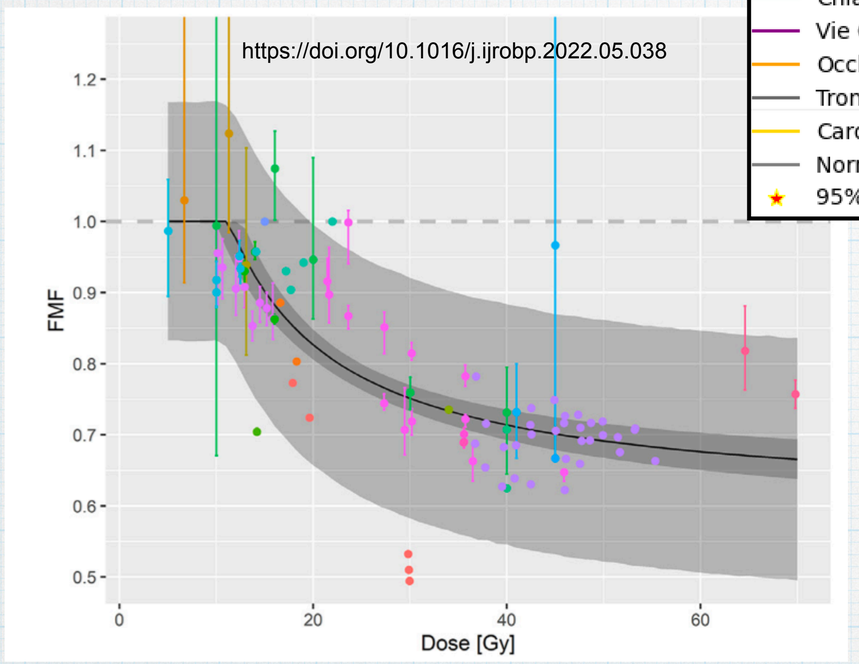
VHEE with FMF=1,0.9,0.6

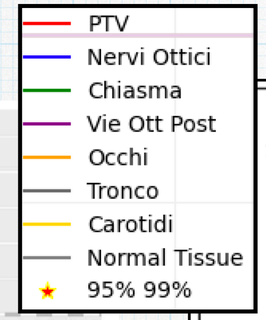


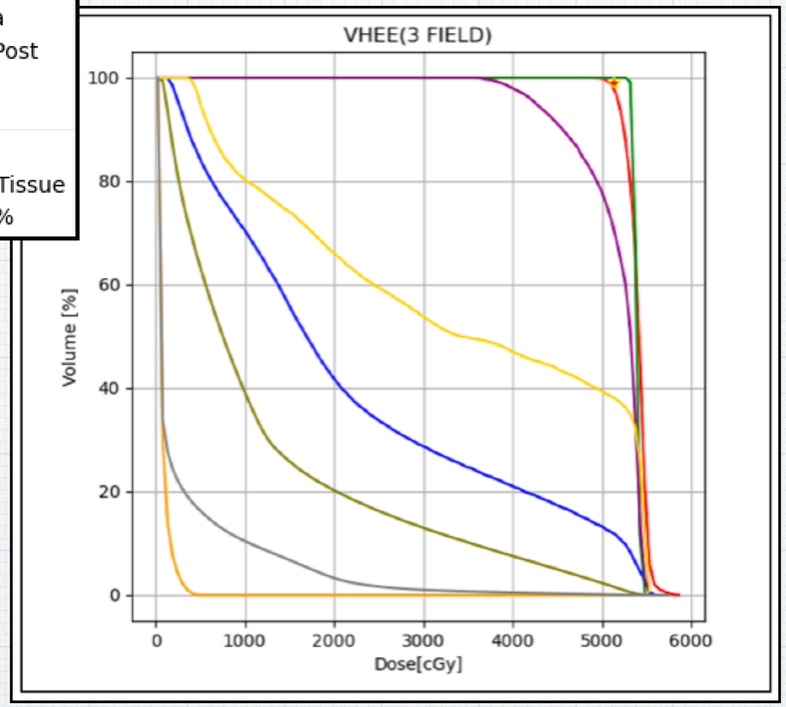
FMF 1 — FMF 0.9 — FMF 0.6

- **Without FLASH EFFECT** we obtain the needed PTV coverage and a better sparing of the OARs with respect to conventional RT;
- If a **FLASH EFFECT** is taken into account, even in the case of a small FMF, the treatment becomes competitive even with the PT one.

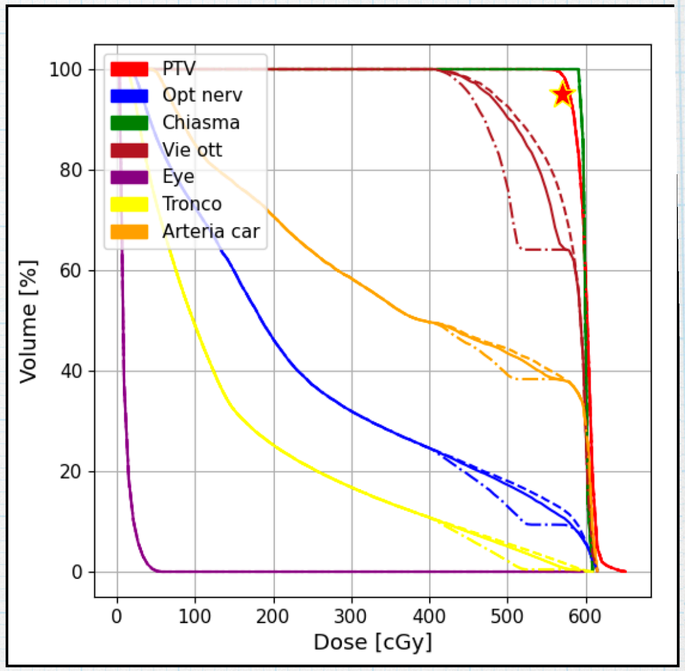
M1 case: RESULTS





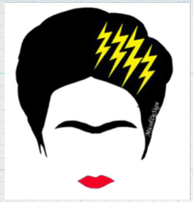


VHEE with FMF=1,0.9,0.6



FMF 1 – FMF0.9 – – FMF 0.6 – –

- **Without FLASH EFFECT** we obtain the needed PTV coverage and a better sparing of the OARs with respect to conventional RT;
- If a **FLASH EFFECT** is taken into account, even in the case of a small FMF, the treatment becomes competitive even with the PT one.



Conclusion

- A preliminary simulation study carried out in the case of **head and neck and pancreas treatment** suggests that the implementation of VHEE RT could **allow the proper PTV coverage while achieving an OARs sparing better than RT, and even p,** with a **significant improvement if the FLASH EFFECT** is introduced;

- The initial studies have been carried out without optimising the number of used fields or their direction: the **promising** results obtained are then 'conservative' in that respect;

- Development and implementation of different clinical treatments with VHEE, like **VMAT;**

- Current studies are exploring the potential for pathologies that are suited for **ipo-fractionation regime** (lung and pancreas pathologies);