



SAPIENZA
UNIVERSITÀ DI ROMA



CENTRO RICERCHE
ENRICO FERMI



FLASH Radiotherapy with high
Dose-rate particle beams

Update on TPS for VHEE-FLASH

Angelica De Gregorio & Roma Group
Pisa 27 Settembre 2022



Angelica De Gregorio

Update TPS algorithm

1

THE FIRST APPROACH



- The algorithm we currently use for the optimization of a **treatment with VHEE** is based on the Proton Therapy algorithm (LOMAX) for pencil beam, rearranged for electrons.

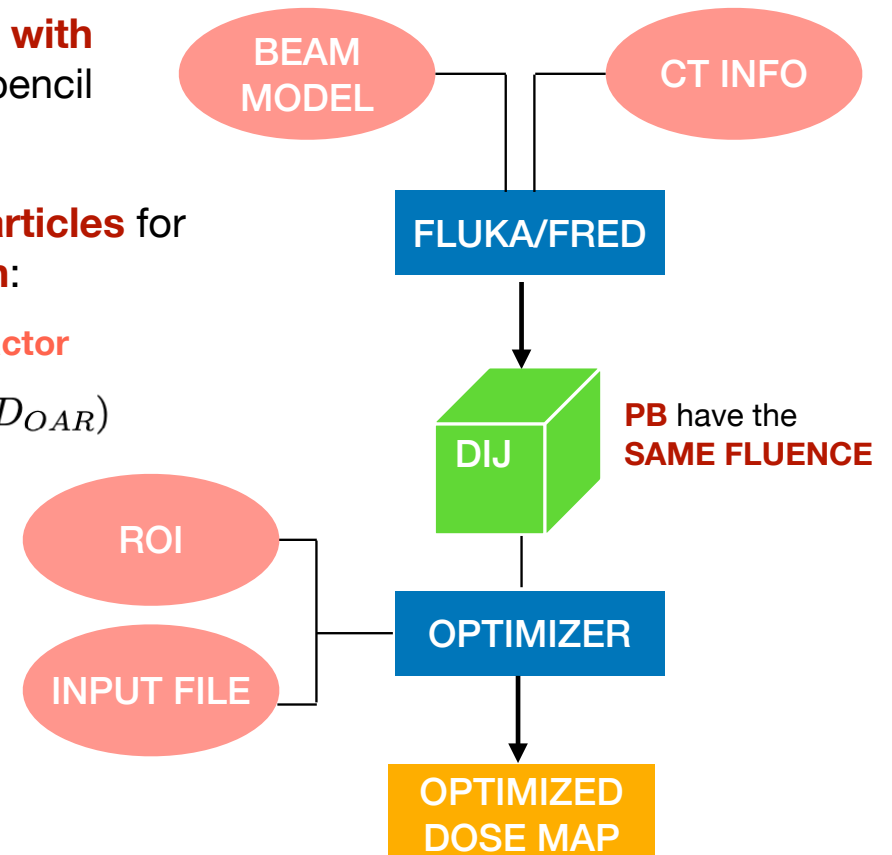
The main **goal** of the Optimizer is to select the **number of particles** for each Pencil Beam that **minimize the Cost Function**:

Voxel based

$$\chi^2 = \sum_{i \in PTV} \omega_i \frac{(d_i - D_{PTV})^2}{d_i^2} + \sum_{i \in OAR} \omega_i \frac{(d_i - D_{OAR})^2}{d_i^2} * g(d_i - D_{OAR})$$

Dose (green circle), **Dose Goal** (orange circle), **Plan factor** (red circle)

$$d_i = \sum_{j=1}^{N_j} N_j D_{ij}$$



THE FIRST APPROACH



- The algorithm we currently use for the optimization of a **treatment with VHEE** is based on the Proton Therapy algorithm (LOMAX) for pencil beam, rearranged for electrons.

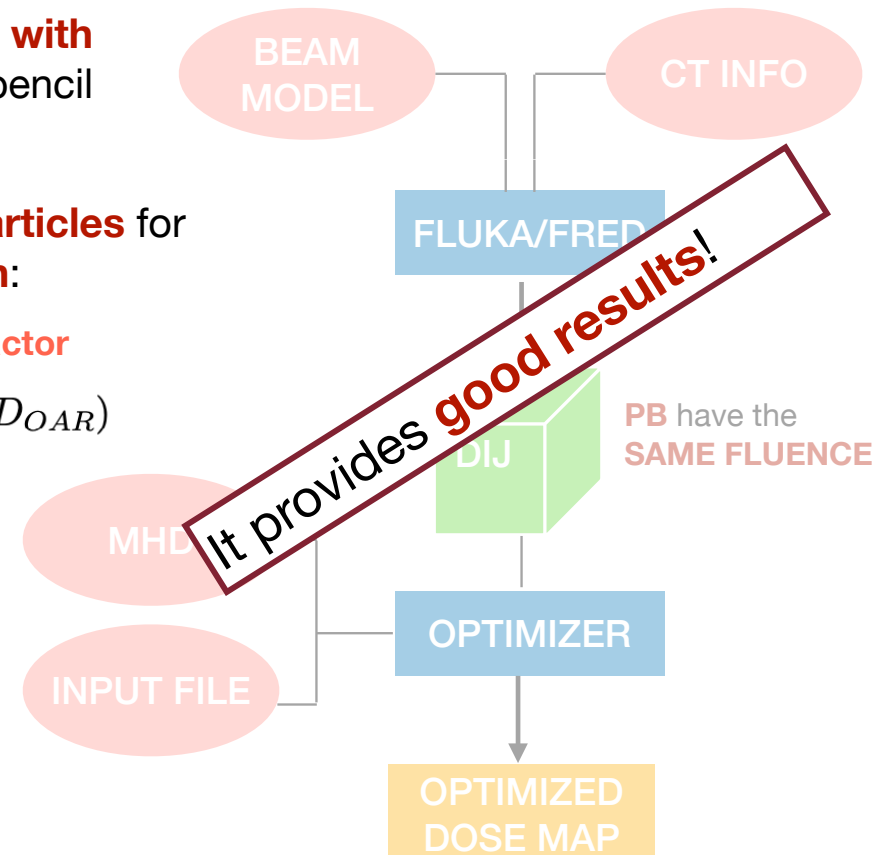
The main **goal** of the Optimizer is to select the **number of particles** for each Pencil Beam that **minimize the Cost Function**:

Voxel based

$$\chi^2 = \sum_{i \in PTV} \omega_i \frac{(d_i - D_{PTV})^2}{d_i^2} + \sum_{i \in OAR} \omega_i \frac{(d_i - D_{OAR})^2}{d_i^2} * g(d_i - D_{OAR})$$

Dose (green), **Dose Goal** (orange), **Plan factor** (red)

$$d_i = \sum_{j=1}^{N_j} N_j D_{ij}$$



THE FIRST APPROACH



- The algorithm we currently use for the optimization of a **treatment with VHEE** is based on the Proton Therapy algorithm (LOMAX) for pencil beam, rearranged for electrons.

The main **goal** of the Optimizer is to select the **number of particles** for each Pencil Beam that **minimize the Cost Function**:

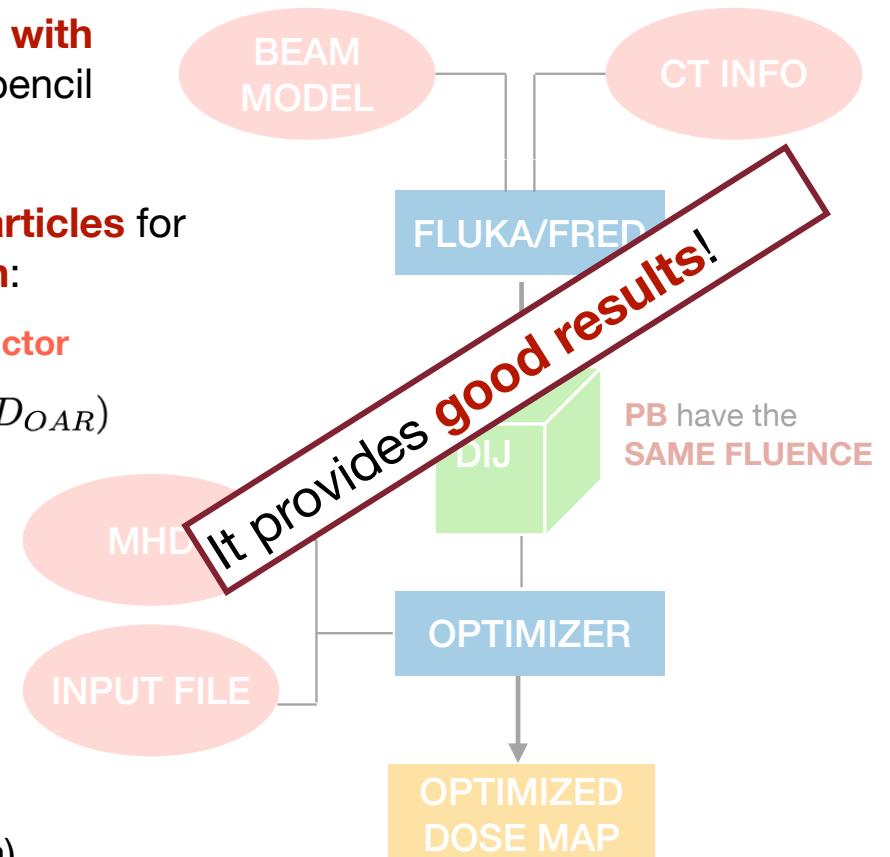
Voxel based

$$\chi^2 = \sum_{i \in PTV} \omega_i \frac{(d_i - D_{PTV})^2}{d_i^2} + \sum_{i \in OAR} \omega_i \frac{(d_i - D_{OAR})^2}{d_i^2} * g(d_i - D_{OAR})$$

Dose (green), **Dose Goal** (orange), **Plan factor** (red)

$$d_i = \sum_{j=1}^{N_j} N_j D_{ij}$$

- No tailored binning;
- Steepest descendent method**: Hessian dependent;
- Fixed PB spot setup at isocenter (FWHM = 1cm, spacing = 0.7 cm)
- No energy optimization.**



THE UPDATE



- The **features** that we would like to implement in a **VHEE/FLASH TPS** are:
 1. Optimize **field direction**;
 2. Field **Energy** and **PB flux** optimization **simultaneously**;
 3. **Dose-rate** evaluation.



- To overcome these issues and have an algorithm capable to take into account more complex constraints (volumetric constraints and dose-rate) we developed a **software** tool which implement the minimization methods called **Simulated Annealing** (SA) and **Quantum Simulated Annealing** (QSA).

THE UPDATE



- The **features** that we would like to implement in a **VHEE/FLASH TPS** are:
 1. Optimize **field direction**;
 2. Field **Energy** and **PB flux** optimization **simultaneously**;
 3. **Dose-rate** evaluation.



- To overcome these issues and have an algorithm capable to take into account more complex constraints (volumetric constraints and dose-rate) we developed a **software** tool which implement the minimization methods called **Simulated Annealing** (SA) and **Quantum Simulated Annealing** (QSA).



Less fast & memory wasteful
but more **reliable**

Able to get **out fo local minima**

THE UPDATE



- The **features** that we would like to implement in a **VHEE/FLASH TPS** are:
 1. Optimize **field direction**;
 2. Field **Energy** and **PB flux** optimization **simultaneously**;
 3. **Dose-rate** evaluation.

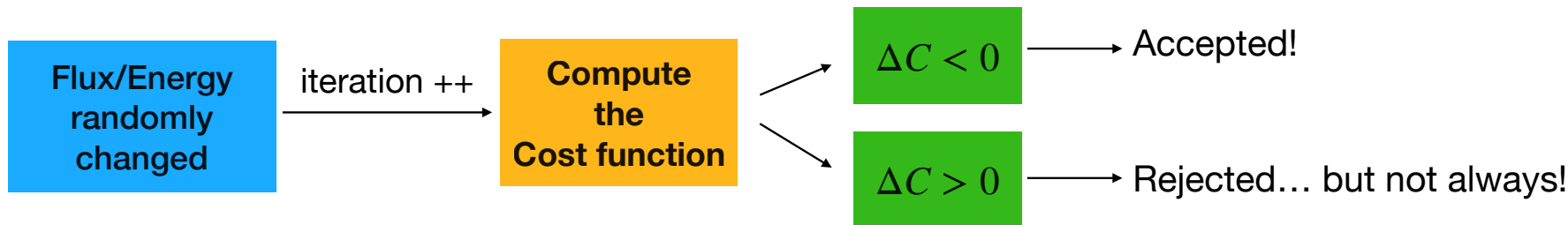


- To overcome these issues and have an algorithm capable to take into account more complex constraints (volumetric constraints and dose-rate) we developed a **software** tool which implement the minimization methods called **Simulated Annealing** (SA) and **Quantum Simulated Annealing** (QSA).

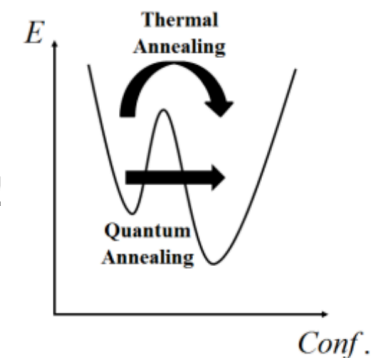


Less fast & memory wasteful
but more **reliable**

Able to get **out fo local minima**



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



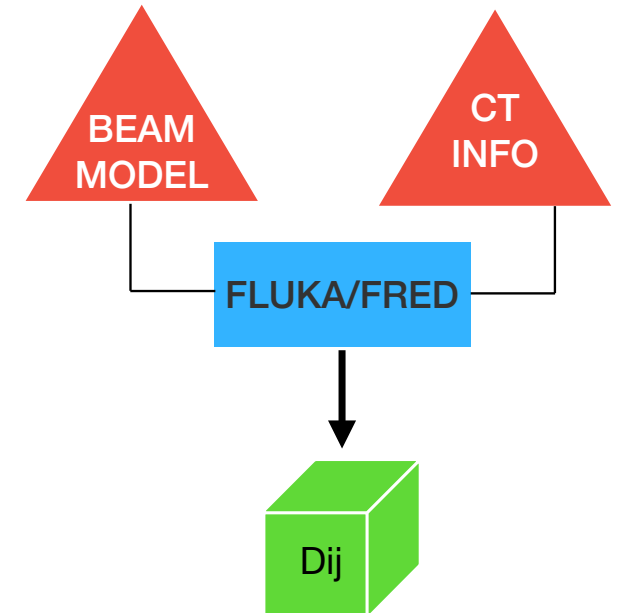


Energy optimization: the problem

- To optimize the energy we have to solve the **dose map problem**: given a PB and a voxel, which is the released dose at energy in the range [70-130]MeV?
- Using the current MC approach one could compute the Dij matrix for different energies in the range [70, 130] MeV. Using 3 MeV steps we get 21 Dij matrices: this means to put in memory the dose matrix that provide for each voxel the dose from each PB at each energy.



RAM needed $\sim 100\text{Gbyte}$





Energy optimization: the problem

- To optimize the energy we have to solve the **dose map problem**: given a PB and a voxel, which is the released dose at energy in the range [70-130]MeV?
- Using the current MC approach one could compute the Dij matrix for different energies in the range [70, 130] MeV. Using 3 MeV steps we get 21 Dij matrices: this means to put in memory the dose matrix that provide for each voxel the dose from each PB at each energy.



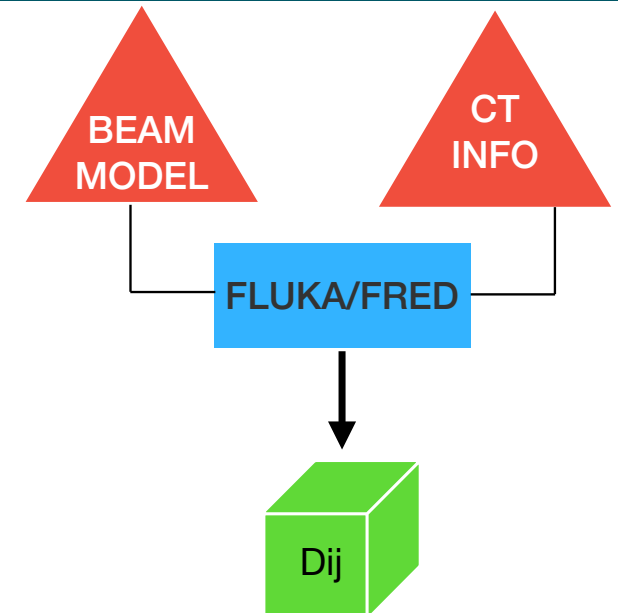
RAM needed $\sim 100\text{Gbyte}$

1)



We developed an **analytic method** for dose evaluation as a function of E_{kin} of the electrons

- We build a **libray (fluka based)** of the dose map in water of electron beam of energy from **10 to 190 MeV** built using 10^9 electrons and a FWHM = 1 cm, parametrizing the dose as a function of geometric coordinates.





Energy optimization: the problem

- To optimize the energy we have to solve the **dose map problem**: given a PB and a voxel, which is the released dose at energy in the range [70-130] MeV?
- Using the current MC approach one could compute the Dij matrix for different energies in the range [70, 130] MeV. Using 3 MeV steps we get 21 Dij matrices: this means to put in memory the dose matrix that provide for each voxel the dose from each PB at each energy.



RAM needed $\sim 100\text{Gbyte}$

1)

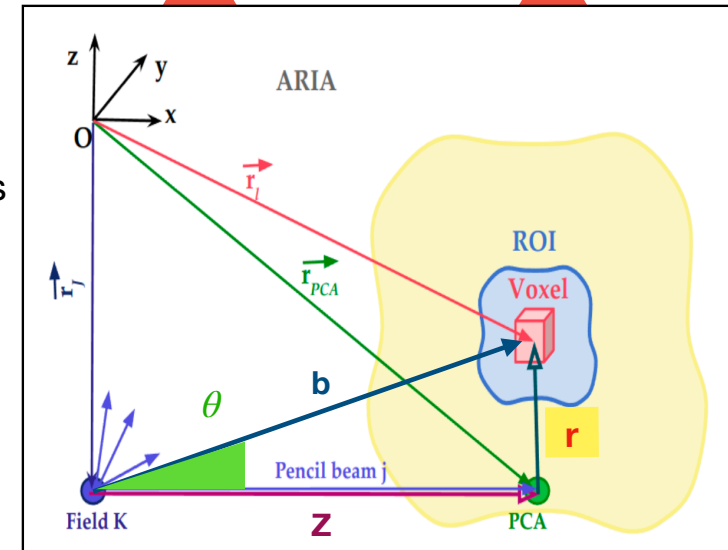


We developed an **analytic method** for dose evaluation as a function of E_{kin} of the electrons

- We build a **library (fluka based)** of the dose map in water of electron beam of energy from **10 to 190 MeV** built using 10^9 electrons and a FWHM = 1 cm, parametrizing the dose as a function of geometric coordinates.



The dose evaluation in a **non-homogeneous medium** is performed computing the water equivalent path length (ρ_z, ρ_r) or (ρ_b, θ). The dose is computed by 3th order **interpolation** in these coordinates.





Energy optimization: the problem

- To optimize the energy we have to solve the **dose map problem**: given a PB and a voxel, which is the released dose at energy in the range [70-130]MeV?
- Using the current MC approach one could compute the Dij matrix for different energies in the range [70, 130] MeV. Using 3 MeV steps we get 21 Dij matrices: this means to put in memory the dose matrix that provide for each voxel the dose from each PB at each energy.



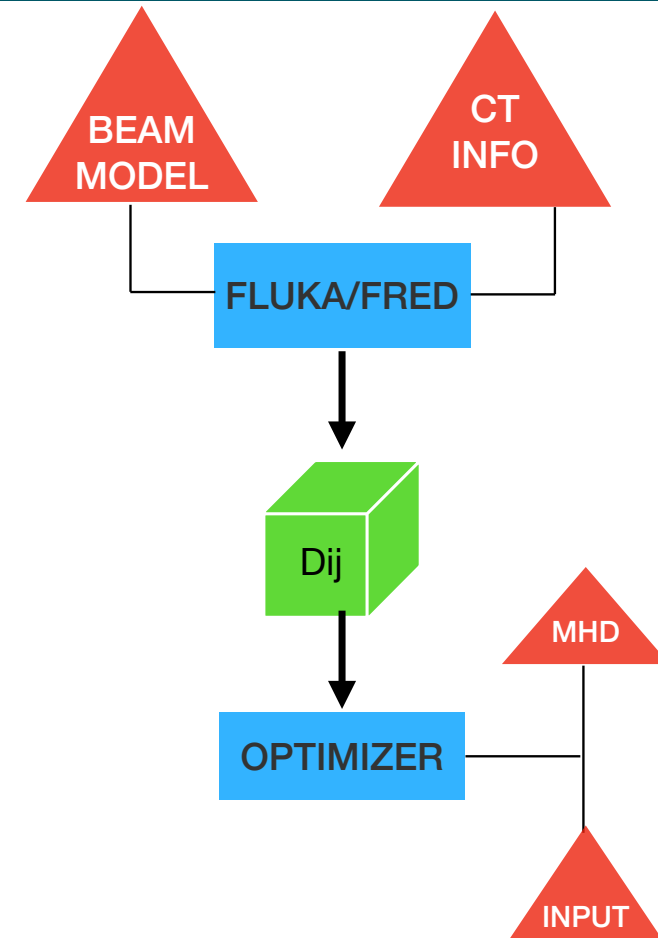
RAM needed $\sim 100\text{Gbyte}$

2)



To overcome this limitation a **rebinning algorithm** has been implemented in order to **group voxels** with similar characteristics.

- Voxels belonging to the same region (PTV or OAR) which have **similar density** are **clusterized** together. The cluster size can be adjusted from 8 (2x2x2) to 256 (8x8x8);
- The voxels near the **boundary** of the ROIs are **not grouped**.



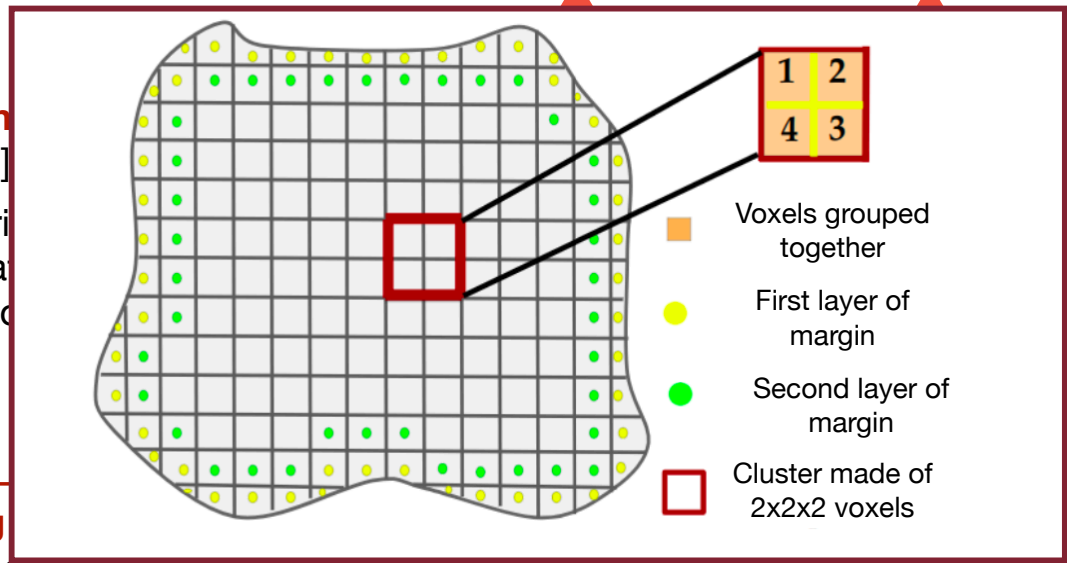
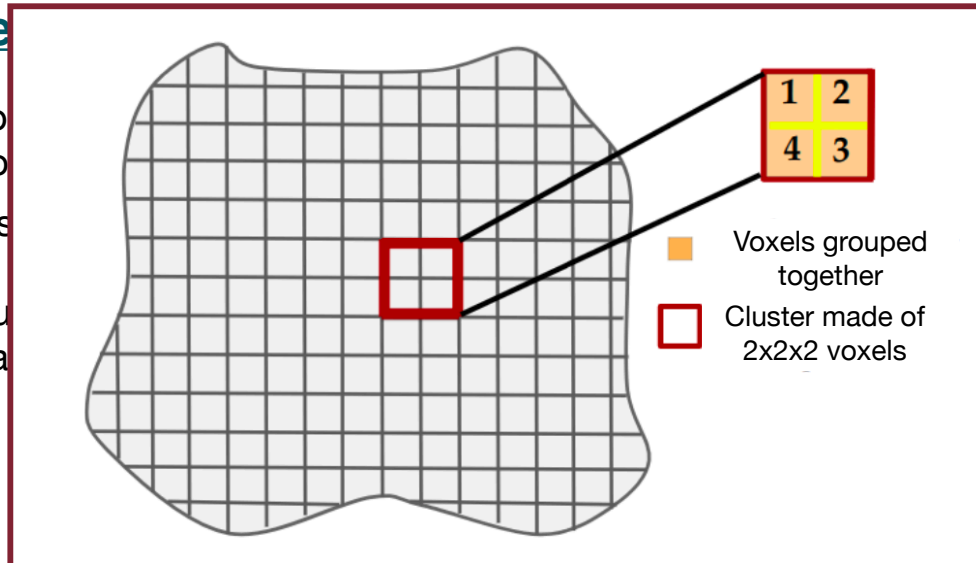
ENERGY OPTIMIZATION



Energy

- To
- vo
- Us
- in
- pu
- ea

em
30]
atri
ma
e do
e
ng



implemented in order to **group voxels** with similar characteristics.

- Voxels belonging to the same region (PTV or OAR) which have **similar density** are **clusterized** together. The cluster size can be adjusted from 8 (2x2x2) to 256 (8x8x8);
- The voxels near the **boundary** of the ROIs are **not grouped**.

In this way we go from $\sim 2 \cdot 10^5$ to $\sim 4 \cdot 10^4$ voxels (using rebin[4,4,4]) without **any loss of resolution**

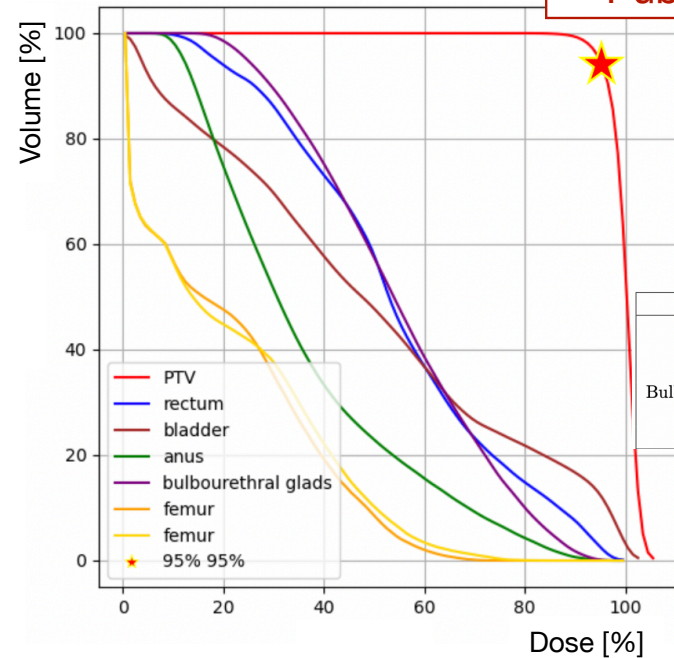
MHD

INPUT

RESULTS ON PROSTATE CASE

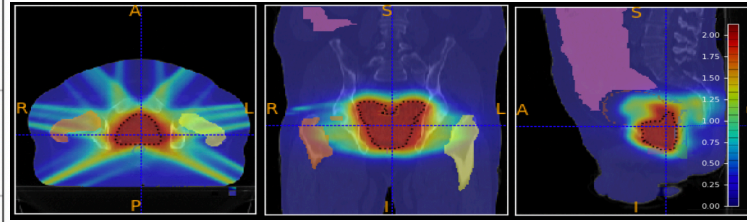


Published

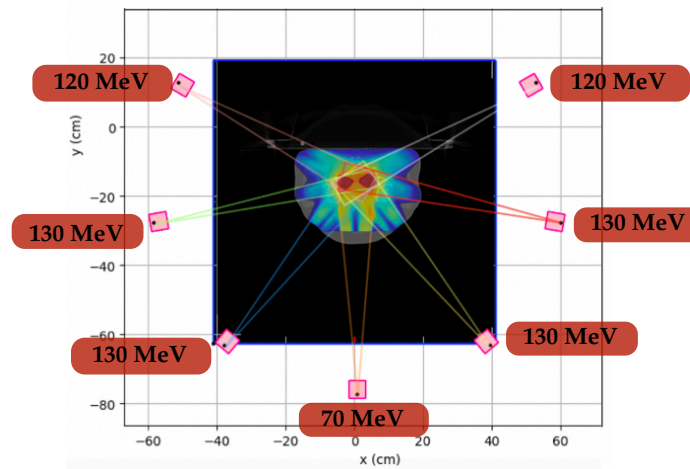


- Only PB fluences are optimized;
- The energies of the field are fixed to the ones used in the real treatment with photons;
- The dose evaluation is performed using a full MC simulation (FLUKA).

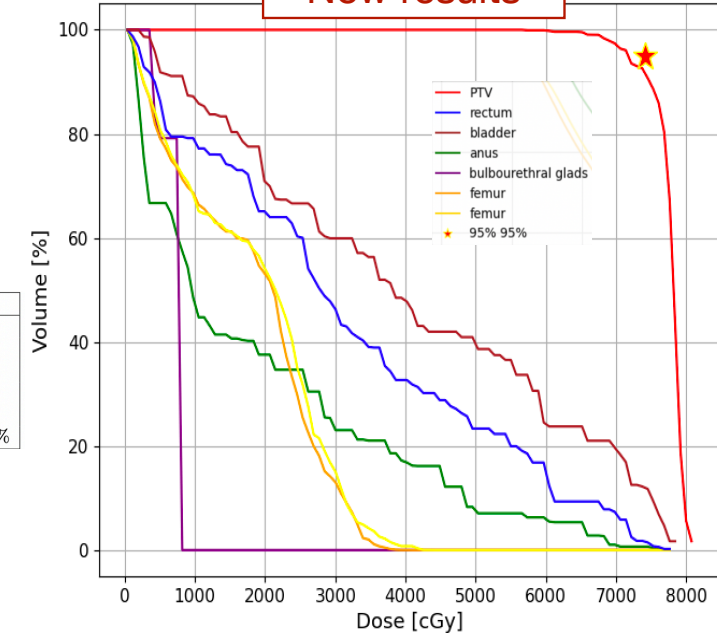
Optimized electron dose map with NO FLASH effect



Organ	DMF=1	DMF=0.9	DMF=0.8
Target volume	$V_{95\%} 96\%$ $V_{105\%} 0.2\%$	$V_{95\%} 98\%$ $V_{105\%} 0.03\%$	$V_{95\%} 99\%$ $V_{105\%} 0.04\%$
Rectum	$V_{50} 30\%$ $V_{75} 0.9\%$	$V_{50} 24\%$ $V_{75} 2.6\%$	$V_{50} 18\%$ $V_{75} 4.1\%$
Anus	$V_{30} 35\%$	$V_{30} 34\%$	$V_{30} 33\%$
Bulbourethral Glands	$\bar{D} 42$ Gy	$\bar{D} 41$ Gy	$\bar{D} 39$ Gy
Femurs	$\bar{D} 16$ Gy	$\bar{D} 14$ Gy	$\bar{D} 14$ Gy
Bladder	$\bar{D} 38$ Gy $V_{70} 17\%$ $V_{65} 20\%$	$\bar{D} 37$ Gy $V_{70} 11\%$ $V_{65} 17\%$	$\bar{D} 36$ Gy $V_{70} 9\%$ $V_{65} 9\%$



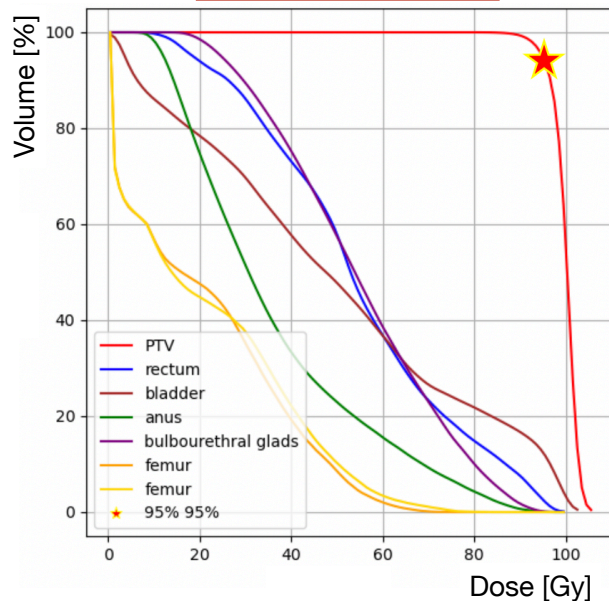
New results



- The PB fluences and the field energy are optimized, giving: [130, 130, 130, 130, 70] MeV;
- The dose evaluation is performed using the analytic method (in this case (r,z) one).
- No rebinning is performed for the comparison.

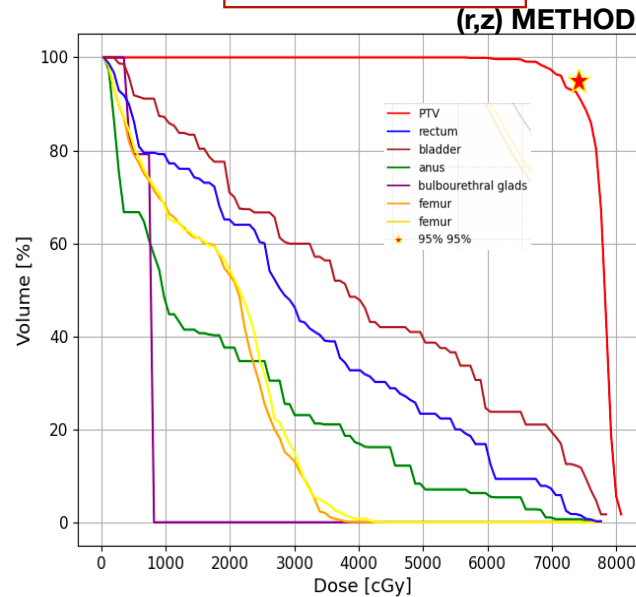
RESULTS ON PROSTATE CASE

Published



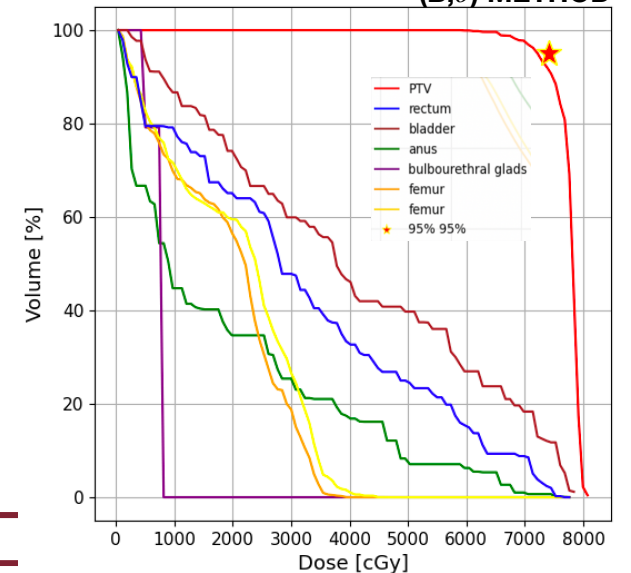
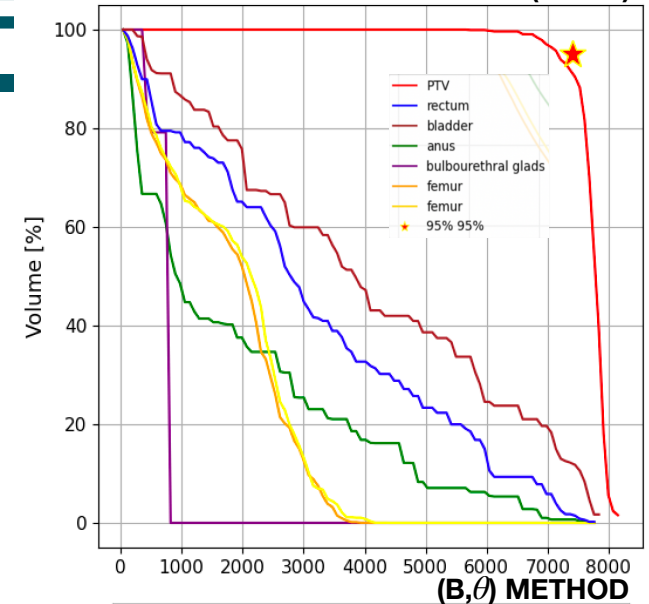
- Only PB fluences are optimized;
- The energies of the field are fixed to the ones used in the real treatment with photons: [70, 120, 130, 130, 120] MeV;
- The dose evaluation is performed using a full MC simulation (FLUKA).

New results



- The PB fluences and the field energy are optimized, giving: [130, 130, 130, 130, 70] MeV;
- The dose evaluation is performed using the analytic method.
- No rebinning is performed for the comparison.

REBIN (6X6X6)



Angelica De Gregorio

Update TPS algorithm

WHAT WE ARE WORKING ON



The **water-equivalent** dose evaluation approach is **not so accurate**. However the computational cost of the problem didn't allow us to make a more precise calculation starting from the Dij matrix given as output by a MC simulation.



With the rebinning algorithm we are able to group (6x6x6) voxels together without any loss of resolution, making possible to **reduce the computational cost**.

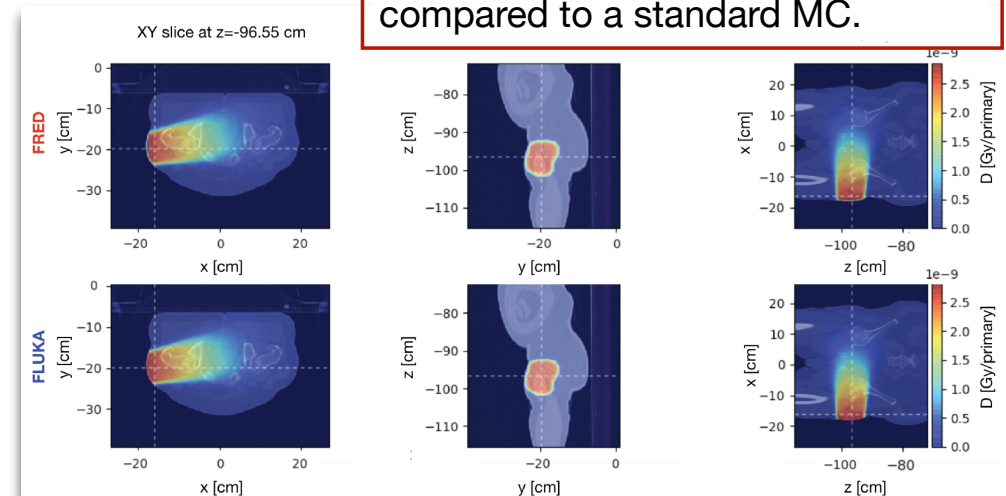
FRED has been developed to work on **GPU** (Graphic Process Unit) and it **reduces the simulation time** by a factor 1000 for proton treatments compared to a standard MC.

Dose evaluation with 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), Maastricht (Maastricht) and CNAO (Pavia) while carbon ions and electromagnetic models for FRED are under optimization.



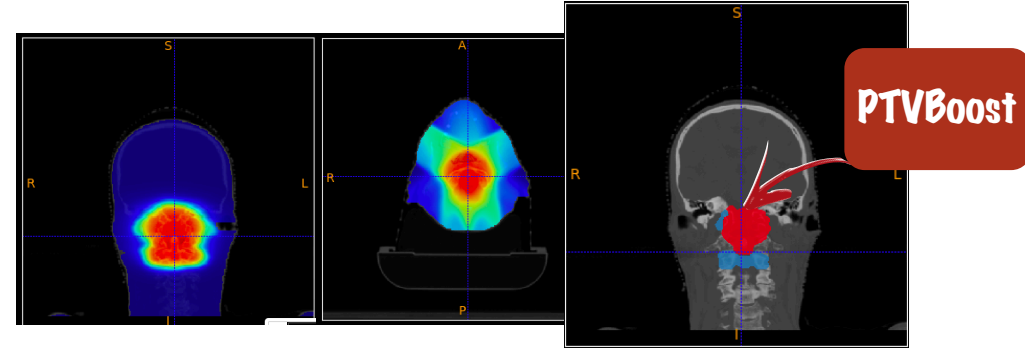
We have already done the first step: our TPS software is capable to **optimize energies and fluences simultaneously** using **Dij matrix from FRED** at energies step of 10 MeV.



NEXT STEPS

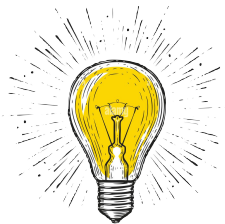


Once we are sure that the dose evaluated from the MC matrices works properly, we will study other interesting cases as the **Head&Neck district tumor**;



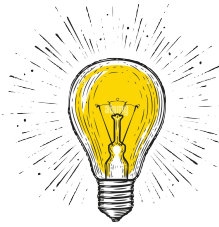
Even if the FLASH effect is already modelled using the Flash Modifying Factor (**FMF**) to account for the reduced normal tissue damage, a proper **evaluation voxel based of the Dose Rate** will be introduced as a constraint to be respected;

$$FMF = \frac{D_r}{D_t} \begin{matrix} \rightarrow \text{Conventional} \\ \rightarrow \text{FLASH RT} \end{matrix}$$

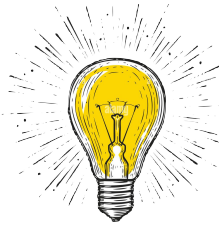
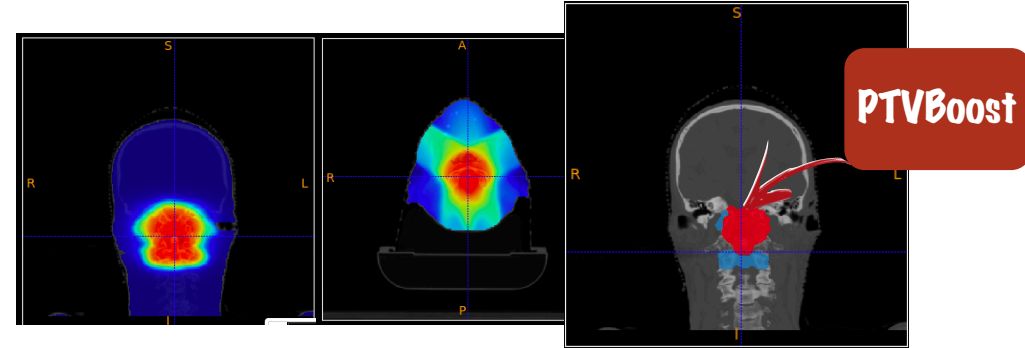


A further step will be to develop the Software on **GPU** (Graphic Process Unit) in order to reduce the execution time and make it compatible to the clinical need.

NEXT STEPS



Once we are sure that the dose evaluated from the MC matrices works properly, we will study other interesting cases as the **Head&Neck district tumor**;



Even if the FLASH effect is already modelled using the Flash Modifying Factor (**FMF**) to account for the reduced normal tissue damage, a proper **evaluation voxel based of the Dose Rate** will be introduced as a constraint to be respected;

$$FMF = \frac{D_r}{D_t} \begin{matrix} \nearrow \text{Conventional} \\ \searrow \text{FLASH RT} \end{matrix}$$



A further step will be to develop the Software on **GPU** (Graphic Process Unit) in order to reduce the execution time and make it compatible to the clinical need.

**Thank you
for the attention!**

