

# Towards particle treatment planning with Ionization Detail

Simona Facchiano, PhD student  
Division E0404, Department of Medical Physics in Radiation Oncology, DKFZ  
simona.facchiano@dkfz-heidelberg.de  
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## Contents of the presentation

- *From Ionization Detail to Cluster dose* Mathematical model  
Why is it important?
- *My PhD project* The main idea  
Starting point: protons
- *Future outlook* Heavier ions  
Treatment planning

## What is cluster dose? Analogy with the physical dose

### Dose

- Energy deposited per unit mass;
- Biological models are necessary to study the effect of the deposited dose;
- Biological model depends on the source particle, and also several models exist for the same source;

### Cluster Dose

- Number of ionizations per unit mass;
- Physical model describing the distribution of ionization clusters;
- Related to the number of DSB (double strand breaks) in the DNA, expected same biological effect in volumes with same cluster dose value;

## Mathematical model

1. Frequency ICSD (ionization cluster size distribution)

Number of clusters of size  $v$   
 $f(v)$

2. Ionization parameter

Condensed ID information  
 $I_p$

3. Cluster dose

Generalized  $I_p$  per unit mass  
 $g_j^{I_p}$

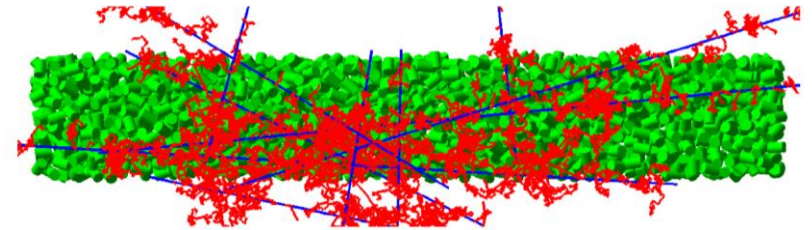


Illustration taken from Ramos-Mendez et al. 2018

The ICSD describes the Ionization Detail (ID), i.e. the spatial distribution of ionization along a particle track

## Mathematical model

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Number of clusters of size  $\nu$   
 $f(\nu)$

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Generalized  $I_p$  per unit mass  
 $g_j^{I_p}$

Number of ionizations:  $N_k$

$$N_k^c = \sum_{\nu=k}^{\infty} \nu f^c(\nu)$$

Number of clusters:  $F_k$

$$F_k^c = \sum_{\nu=k}^{\infty} f^c(\nu)$$

Ionization parameter  $I_p$

$$G_p : f^c(\nu) \rightarrow I_p^c$$

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Generalized  $I_p$  per unit mass

$$g_j^{I_p}$$

The cluster dose is the fluence-weighted sum of the  $I_p$  in a macroscopic bin.

$$g_j^{(I_p)} = \frac{1}{\rho_0 V_j} \sum_{c \in \mathcal{C}_j} t_j^c I_p^c$$

$$\phi_j^c = \frac{t_j^c}{V_j}$$

$$g_j^{(I_p)} = \frac{1}{\rho_0} \sum_{c \in \mathcal{C}_j} \phi_j^c I_p^c$$

## Mathematical model

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Number of clusters of size  $\nu$   
 $f(\nu)$

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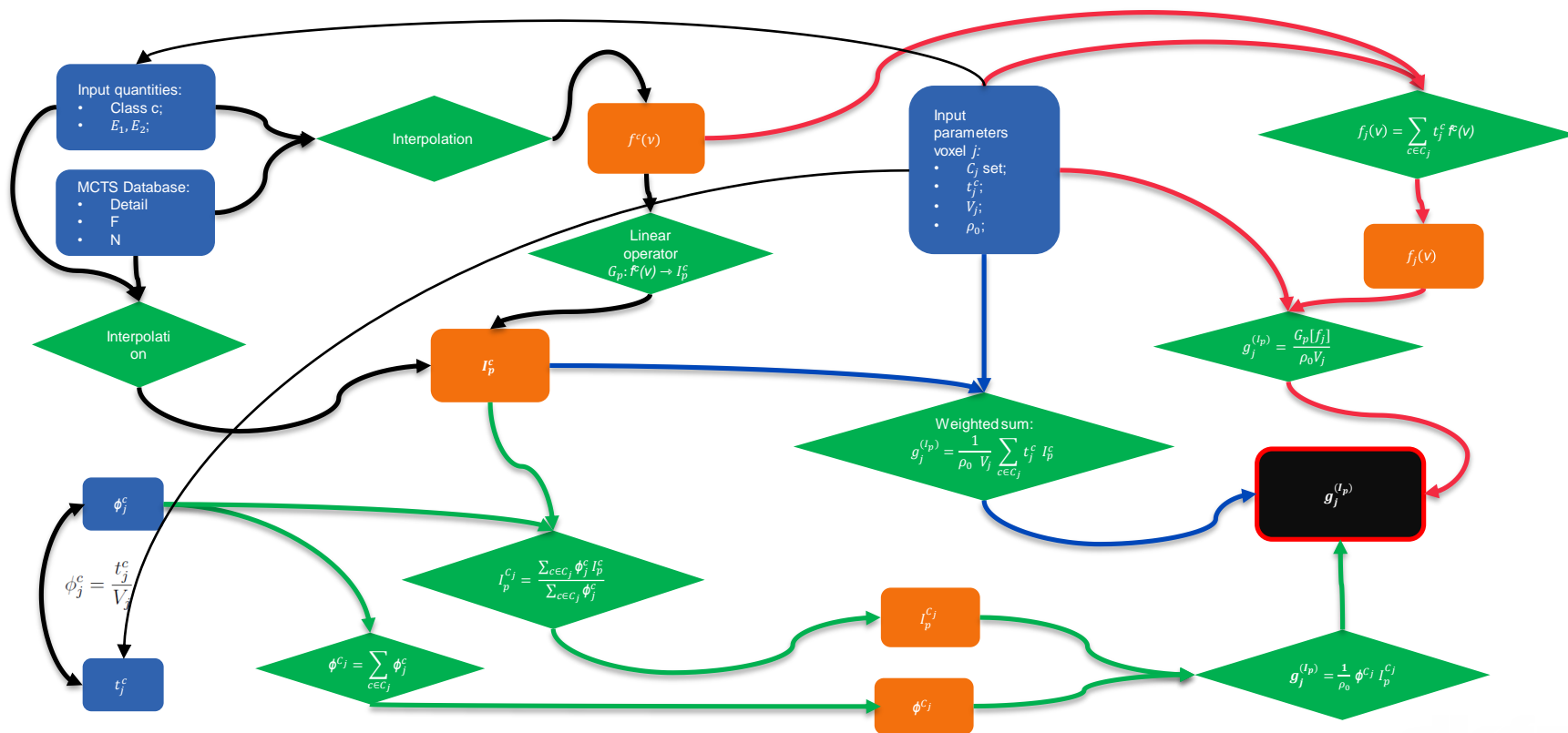
Condensed ID information  
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3. Cluster dose

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 $g_j^{I_p}$

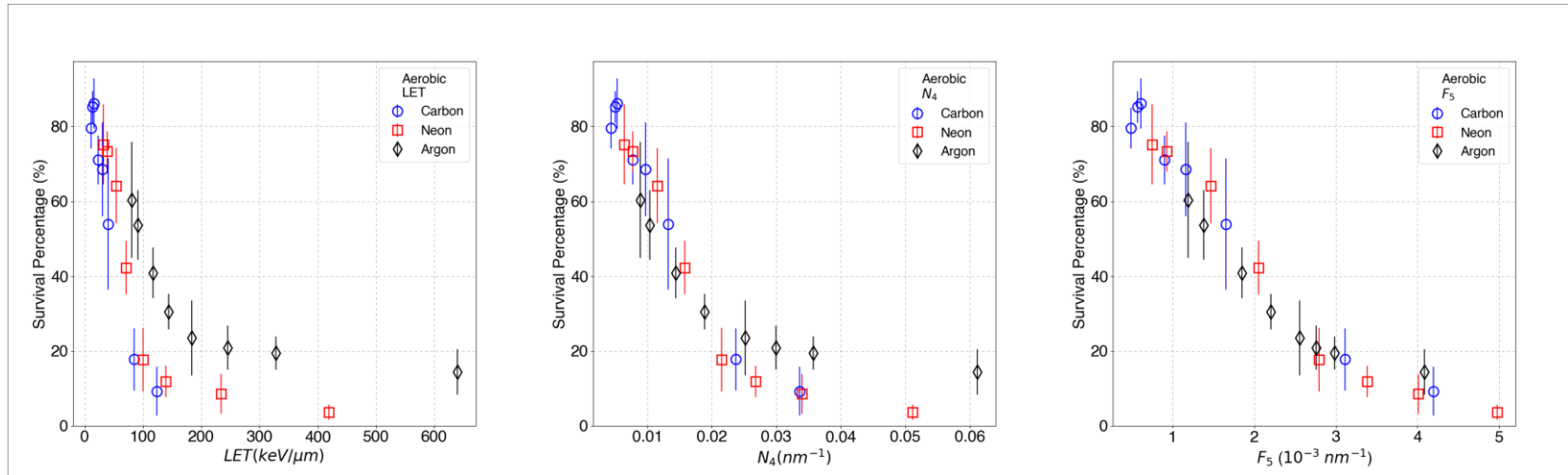
$$\begin{array}{c}
 f^c(\nu) \\
 \downarrow G_p \\
 I_p^c = G_p[f^c(\nu)] \\
 \downarrow \Sigma \\
 g_j^{(I_p)} = \frac{1}{\rho_0 V_j} \sum_{c \in C_j} t_j^c I_p^c
 \end{array}$$

## Mathematical model: the overview





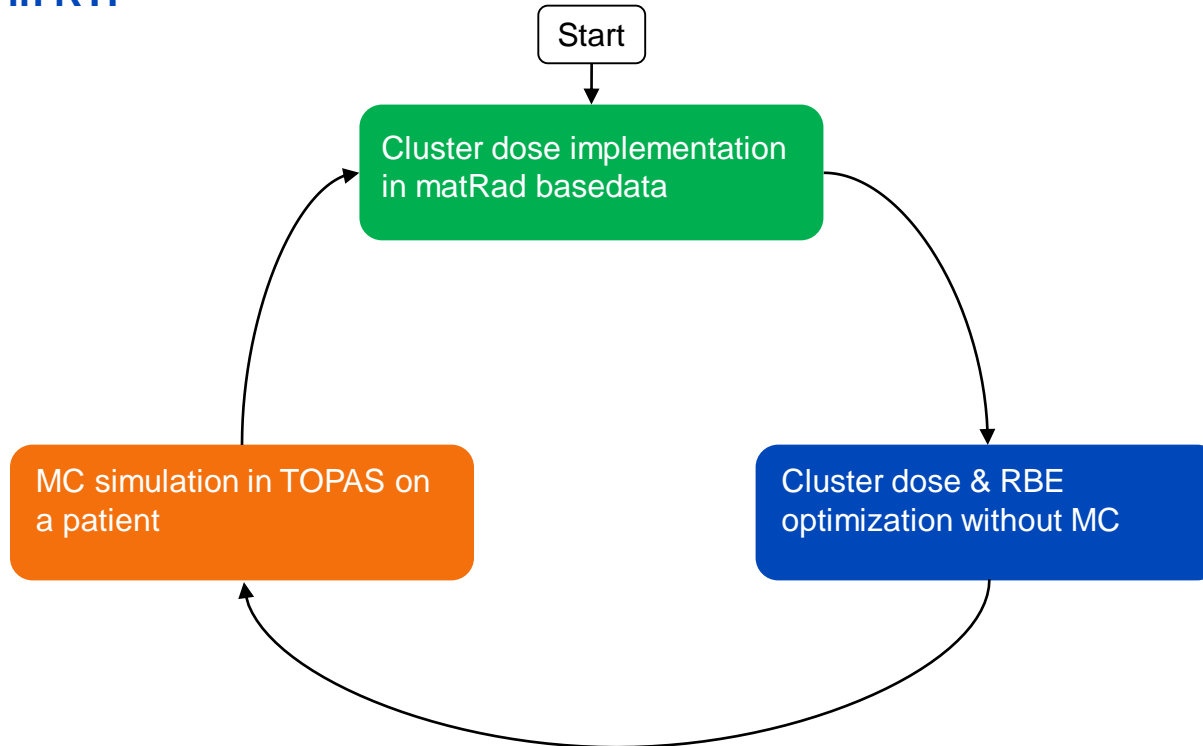
## Why is cluster dose remarkable?



The association of cell survival measured under aerobic conditions with LET (left), N<sub>4</sub> (middle) and F<sub>5</sub> (right).

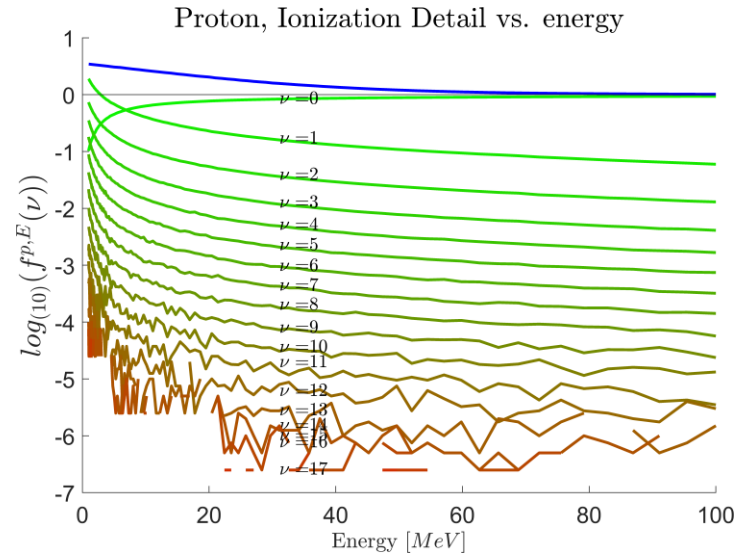
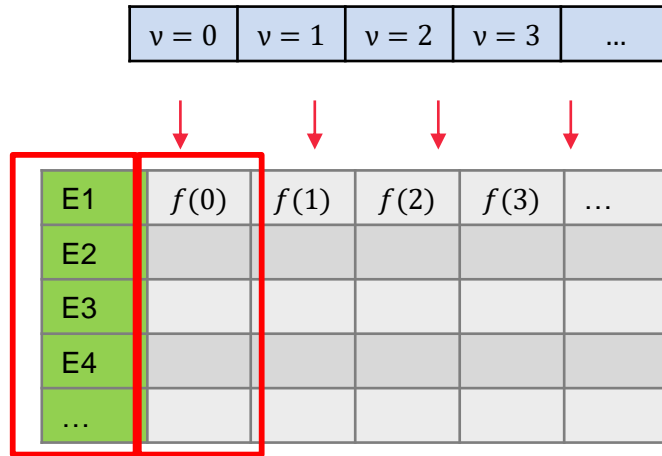
Taken from "Ionization detail parameters and cluster dose: A mathematical model for selection of nanodosimetric quantities for use in treatment planning in charged particle radiotherapy" Faddegon et al. 2023 (accepted PMB)

## The main idea: Introducing the Cluster Dose optimization in RTP



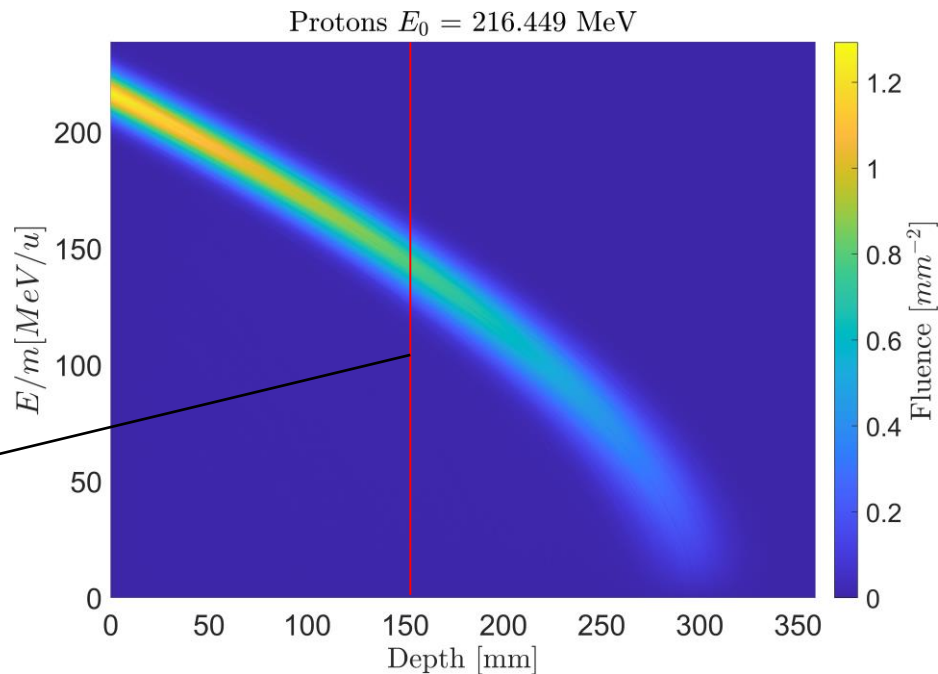
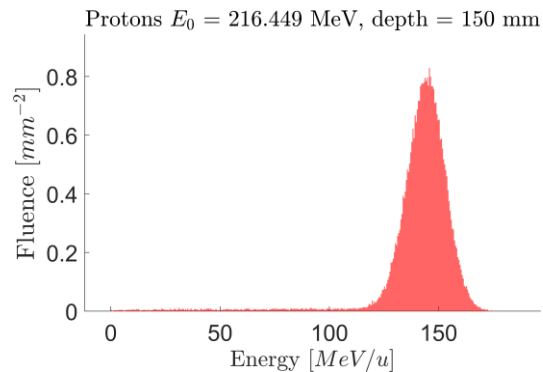
## How can I compute the cluster dose?

- MCTS UCSF database format



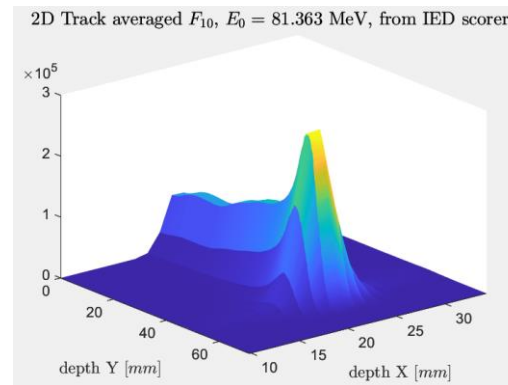
## How can I compute the cluster dose?

- MCTS UCSF database;
- TOPAS simulations:  
Fluence matrix scoring;



## How can I compute the cluster dose?

- MCTS UCSF database;
- TOPAS simulations:  
Fluence matrix scoring;
- TOPAS IED scorers: score the track weighted sum of  $I_p$  for each particle, and for each voxel;



Weight Accumulation

$$\sum_{c \in C_j} t_j^c$$

Ionization Detail

$$\sum_{c \in C_j} t_j^c f^c(v)$$

IonizationIDsF and IonizationIDsM

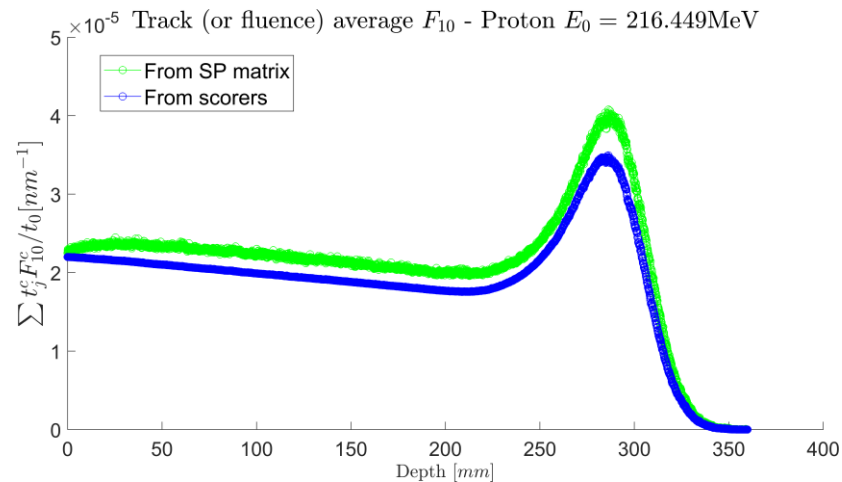
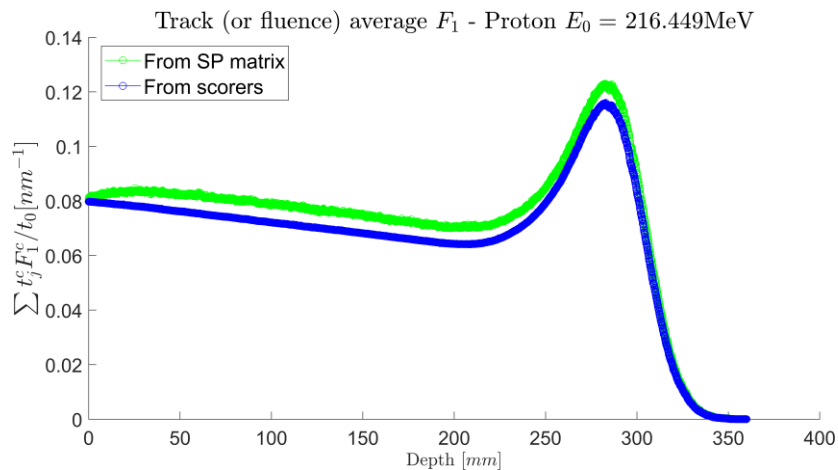
$$\sum_{c \in C_j} t_j^c F_k^c$$

$$\sum_{c \in C_j} t_j^c N_k^c$$

Total, primary, secondary

## Starting point: protons

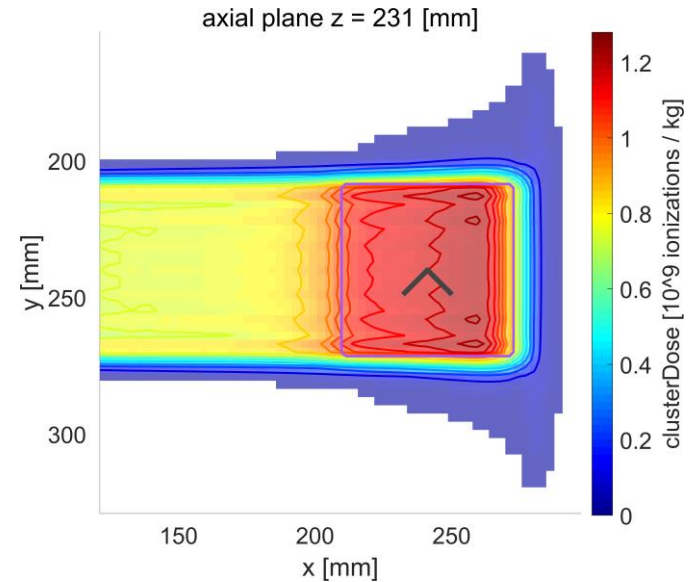
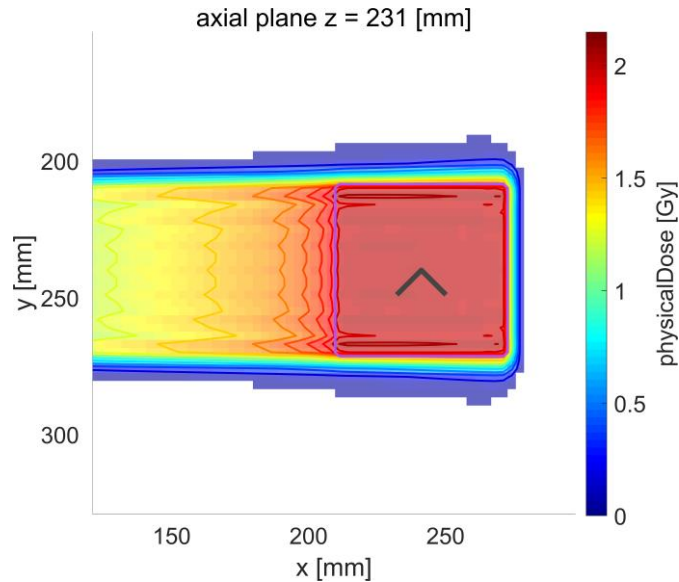
matRad cluster dose implementation based on fluence-energy kernels in water



## Starting point: protons

What I can do with the basedata:

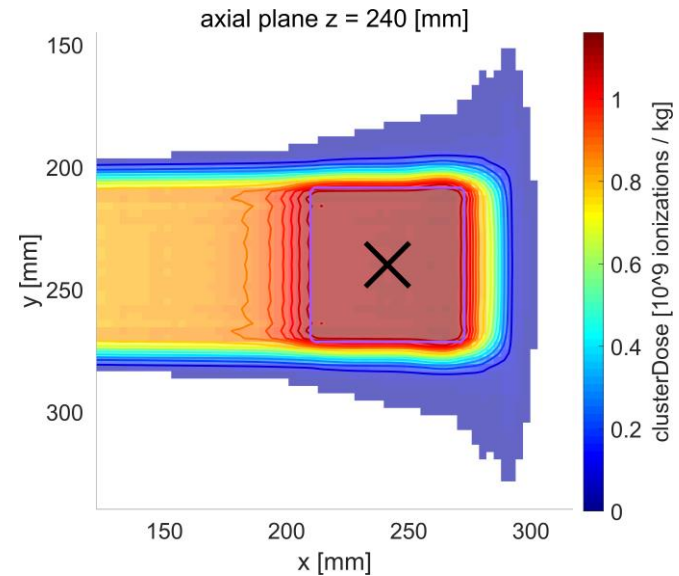
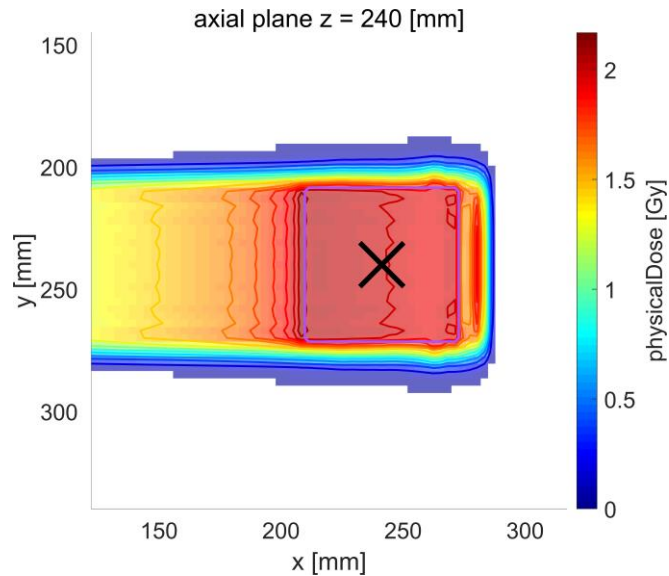
- **Physical dose optimization in a box phantom;**
- Cluster dose and physical dose optimization in a box phantom;



## Starting point: protons

What I can do with the basedata:

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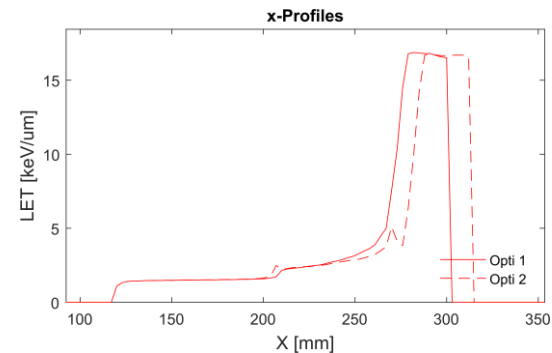
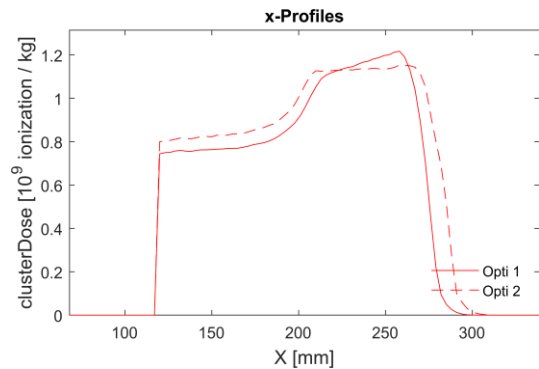
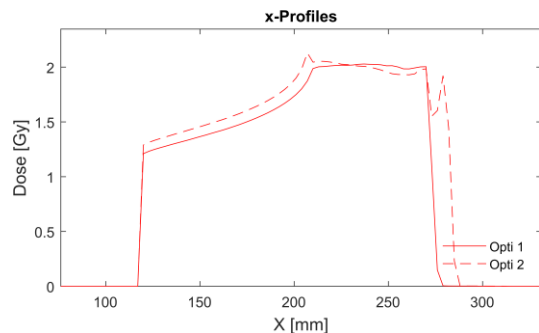


## Starting point: protons

Results compared

Opti 1: Physical dose optimization;

Opti 2: Cluster dose and physical dose optimization;

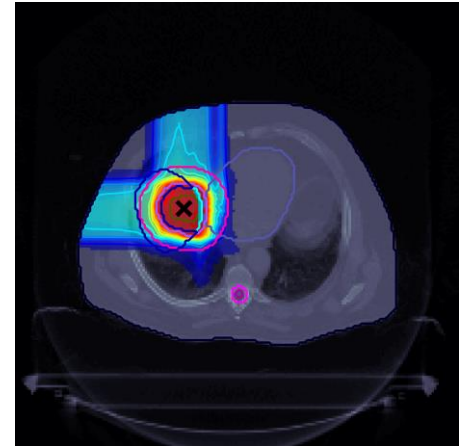


## Summary

- Cluster dose vs. depth curve with fluence kernel in water;
- Comparison with scored 3D cluster dose;
- Cluster dose implemented in dose computation in matRad;
- Cluster dose objective implemented and optimization on a boxphantom;

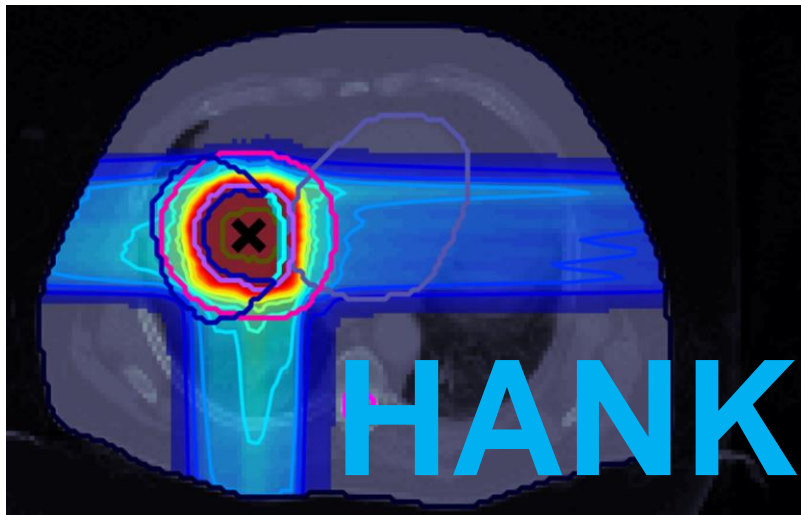
## Future outlook

- Extend the cluster dose computation to heavier ions and fragments;
- Extend the basedata for cluster dose – depth and lateral profiles;
- Implement new objectives and constraints in cluster dose optimization with matRad;
- Patient RTP with RBE and cluster dose combined optimization;



## My PhD project

The end (for now).



**YOU.**