



The Henryk Niewodniczański  
Institute of Nuclear Physics  
Polish Academy of Sciences

# An Overview of FRED: A GPU-based Monte Carlo Tool for Proton Therapy

**A Rucinski<sup>1\*</sup>**, J Baran<sup>1</sup>, G Battistoni<sup>2</sup>, M Durante<sup>3</sup>, J Gajewski<sup>1</sup>, M Garbacz<sup>1</sup>, C Granja<sup>\*</sup>, R Kopec<sup>1</sup>, N Krah<sup>4</sup>, G Mierzwinska<sup>1</sup>, N Mojzeszek<sup>1</sup>, C Oancea<sup>\*</sup>, V Patera<sup>5</sup>, M Pawlik-Niedzwiecka<sup>1</sup>, E Pluta<sup>6</sup>, I Rinaldi<sup>7</sup>, E Scifoni<sup>8</sup>, A Skrzypek<sup>1</sup>, F Tommasino<sup>8</sup>, A Schiavi<sup>5</sup>

(1) Institute of Nuclear Physics PAN, Krakow, Poland

(2) INFN, Milan, Italy

(3) GSI Helmholtzzentrum für Schwerionenforschung, Technische Universität Darmstadt, Germany

(4) University Lyon, CNRS, CREATIS UMR 5220, Centre Lyon Berard, Lyon, France

(5) Sapienza University of Rome, Rome, Italy

(6) M. Sklodowska-Curie Institute OC, Krakow, Poland

(7) ZonPCT/Maastro clinic, Maastricht, Netherlands

(8) TIFPA, Trento, Italy

(\*) Advacam, Prague, Czech Republic



# Outline:

- FRED Monte Carlo code
- Automated implementation of the beam model phase space
- FRED validation
- FRED applications
- Current developments
- Conclusions



# Krakow proton beam therapy centre, Poland



- IBA Proteus C-235
- Clinical operation from Oct 2016    **Eclipse TPS v.13.6**
- 2x Gantry (~200 H&N patients treated)
- Eye treatment room
- Experimental hall



# Krakow proton beam therapy centre, Poland



- IBA Proteus C-235
- Clinical operation from Oct 2016 **Eclipse TPS v.13.6**
- 2x Gantry (~200 H&N patients treated)
- Eye treatment room
- Experimental hall

# FRED, GPU-accelerated Monte Carlo code

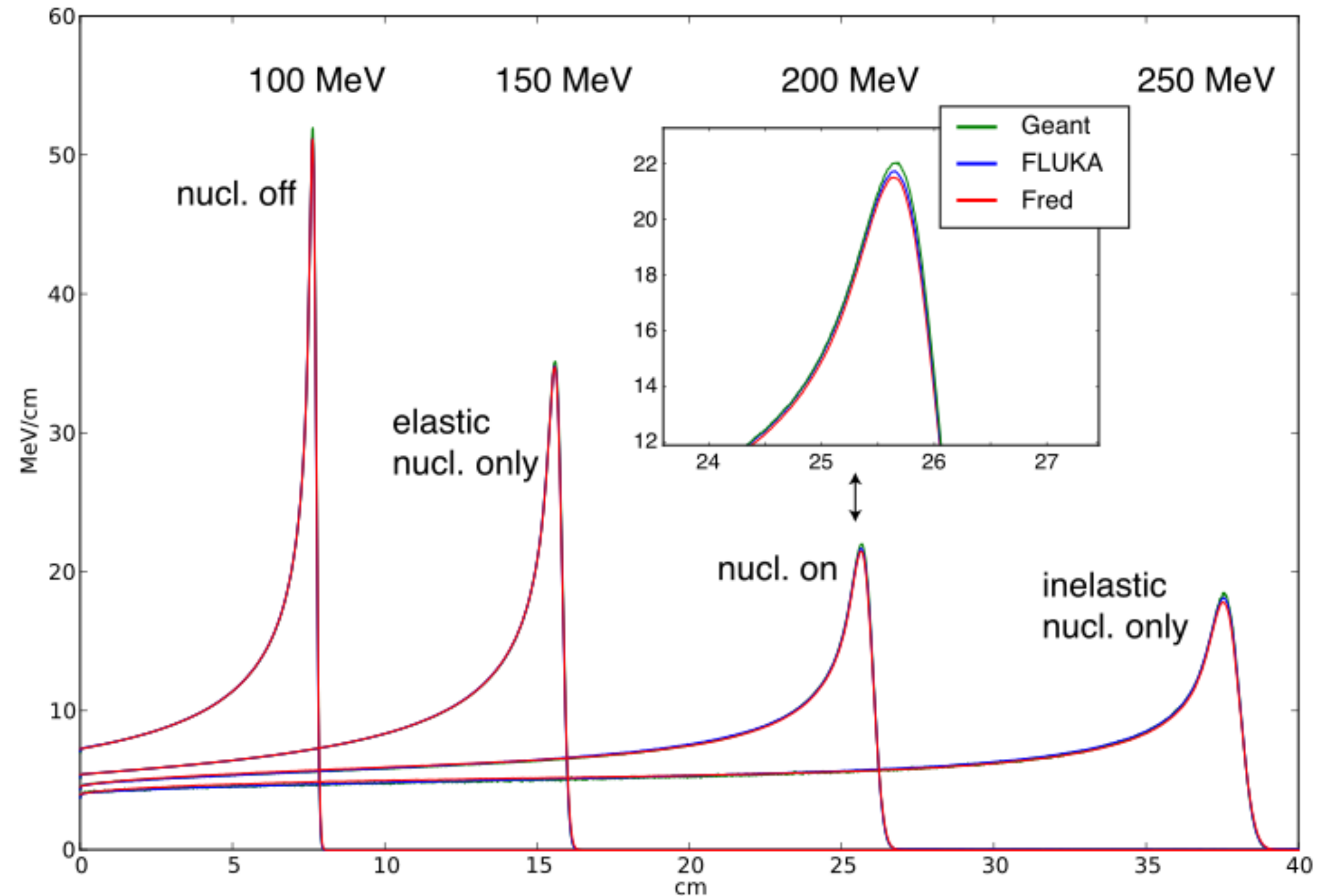
[Schiavi et al. 2017, PMB]



- In-house developed at Sapienza University of Rome
- Condensed history for continuous processes (dE/dx, MCS, energy loss fluctuations)
- Single steps for nuclear events
- **Acceleration x1000 (tracking rate  $10^6$  p<sup>+</sup>/s):**
  - x10 - physics processes mainly contributing to the proton dose deposition
  - x100 - parallelisation on GPU.

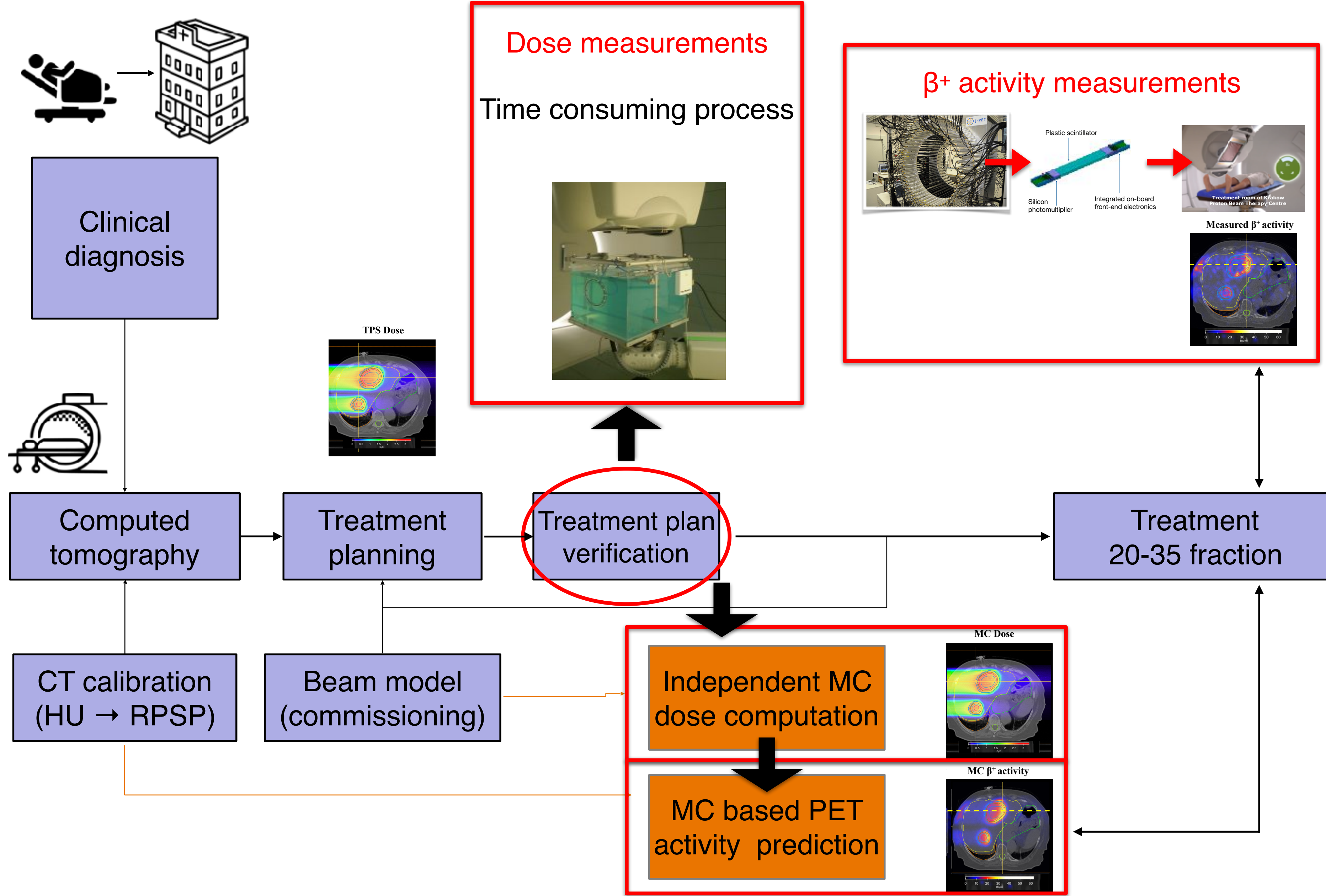


# FRED, GPU-accelerated Monte Carlo code



[Schiavi et al. 2017, PMB]

# Proton therapy treatment



# Automated implementation of the beam model phase space library in FRED



# Commissioning

Input:

Facility  
commissioning  
measurements  
(in 10 MeV steps)

**Commissioning**

**Input:**

Facility  
commissioning  
measurements  
(in 10 MeV steps)



**Phase space library characterisation:**  
(in 10 MeV steps)

**Step 1: Fitting emittance parameters**  
( $\epsilon_x, \alpha_x, \beta_x, \epsilon_y, \alpha_y, \beta_y$ )

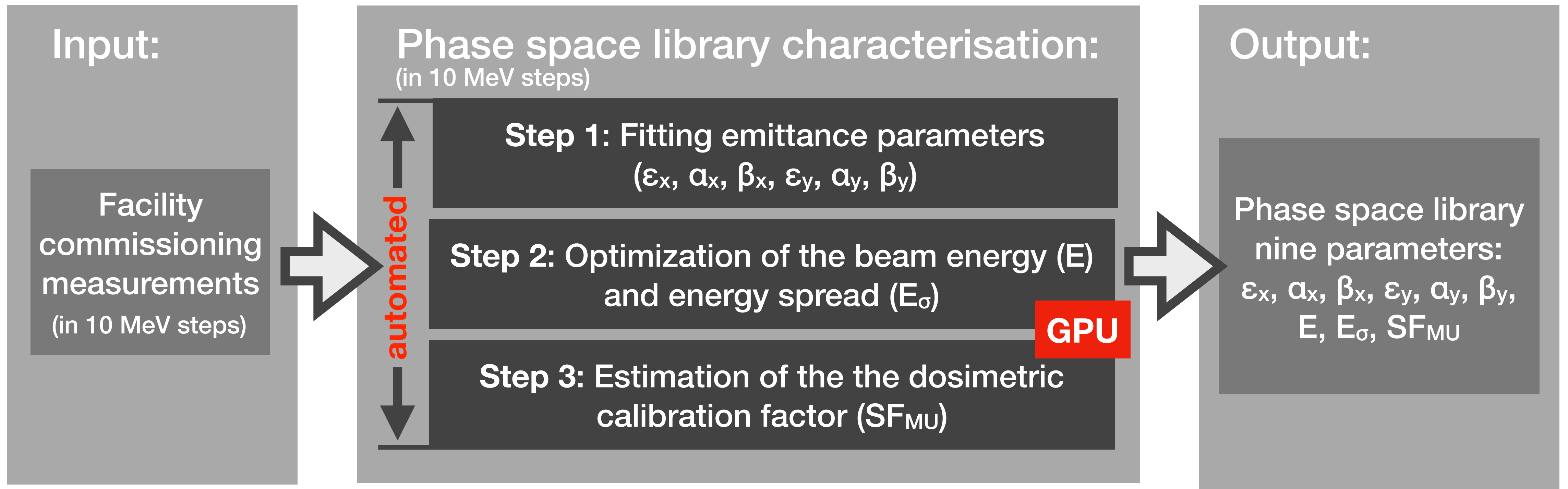
**Step 2: Optimization of the beam energy (E) and energy spread ( $E_\sigma$ )**

**Step 3: Estimation of the the dosimetric calibration factor ( $SF_{MU}$ )**

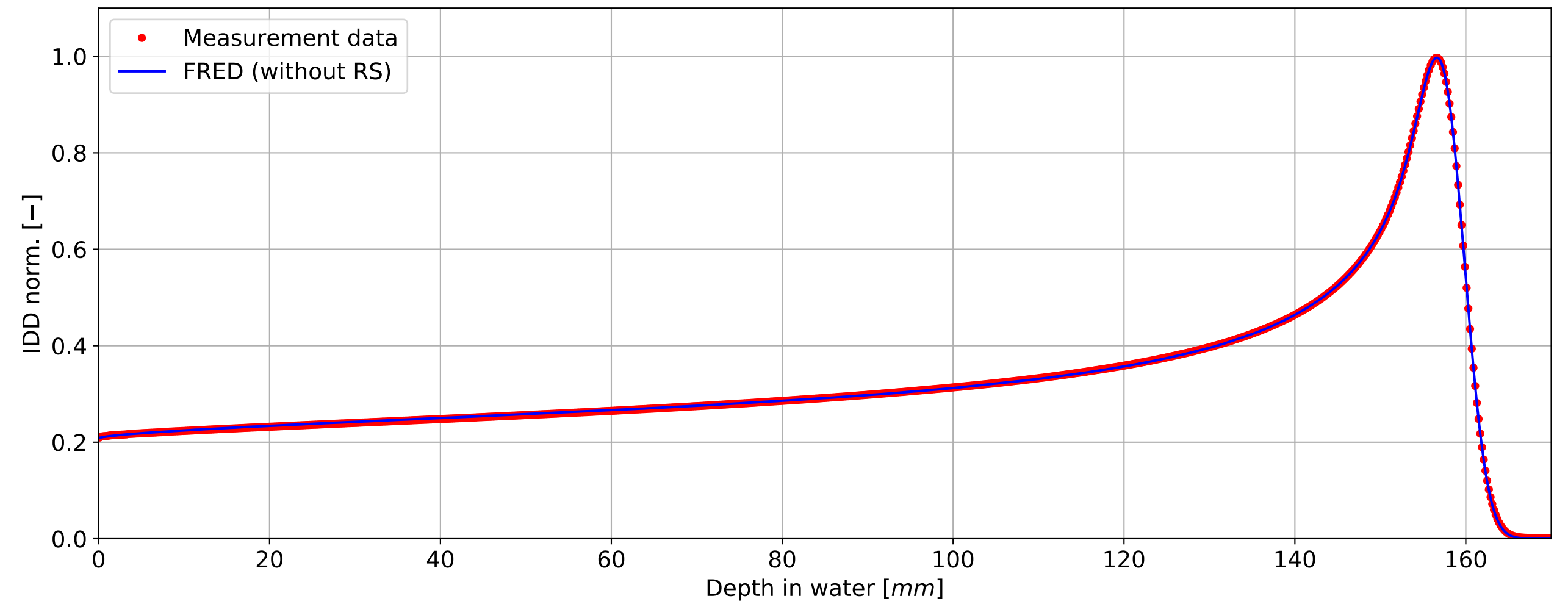
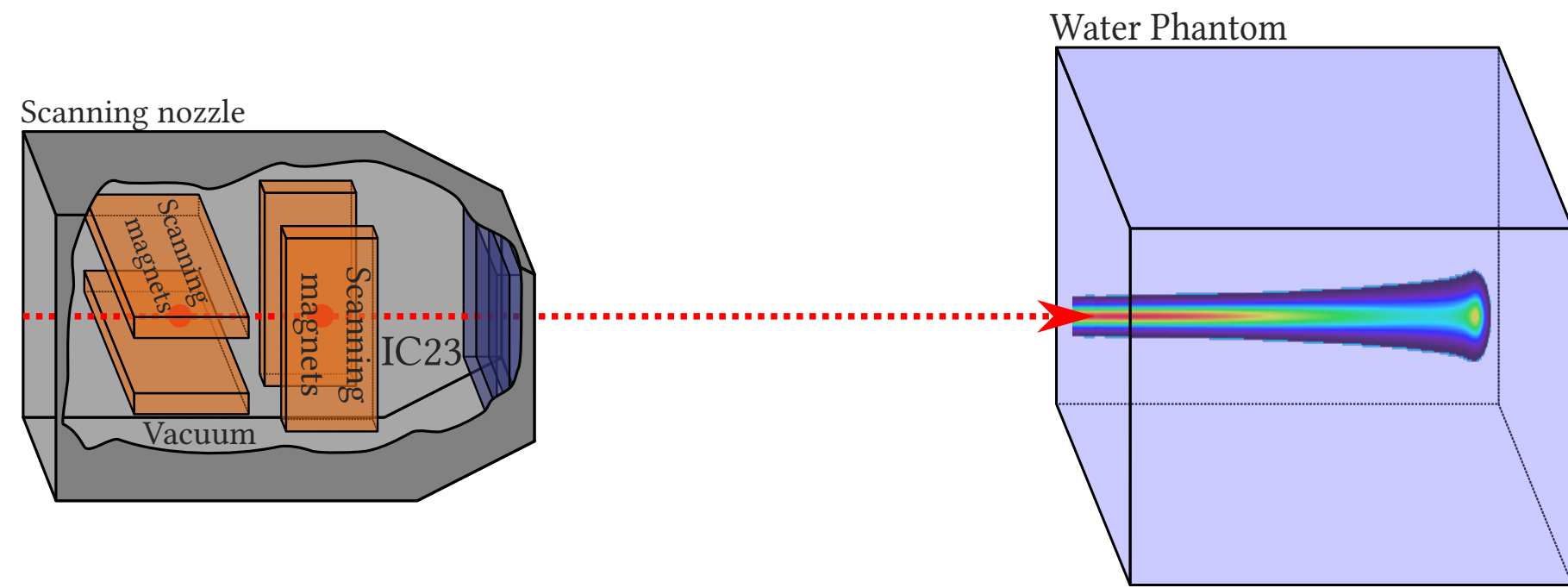
**GPU**

**automated**

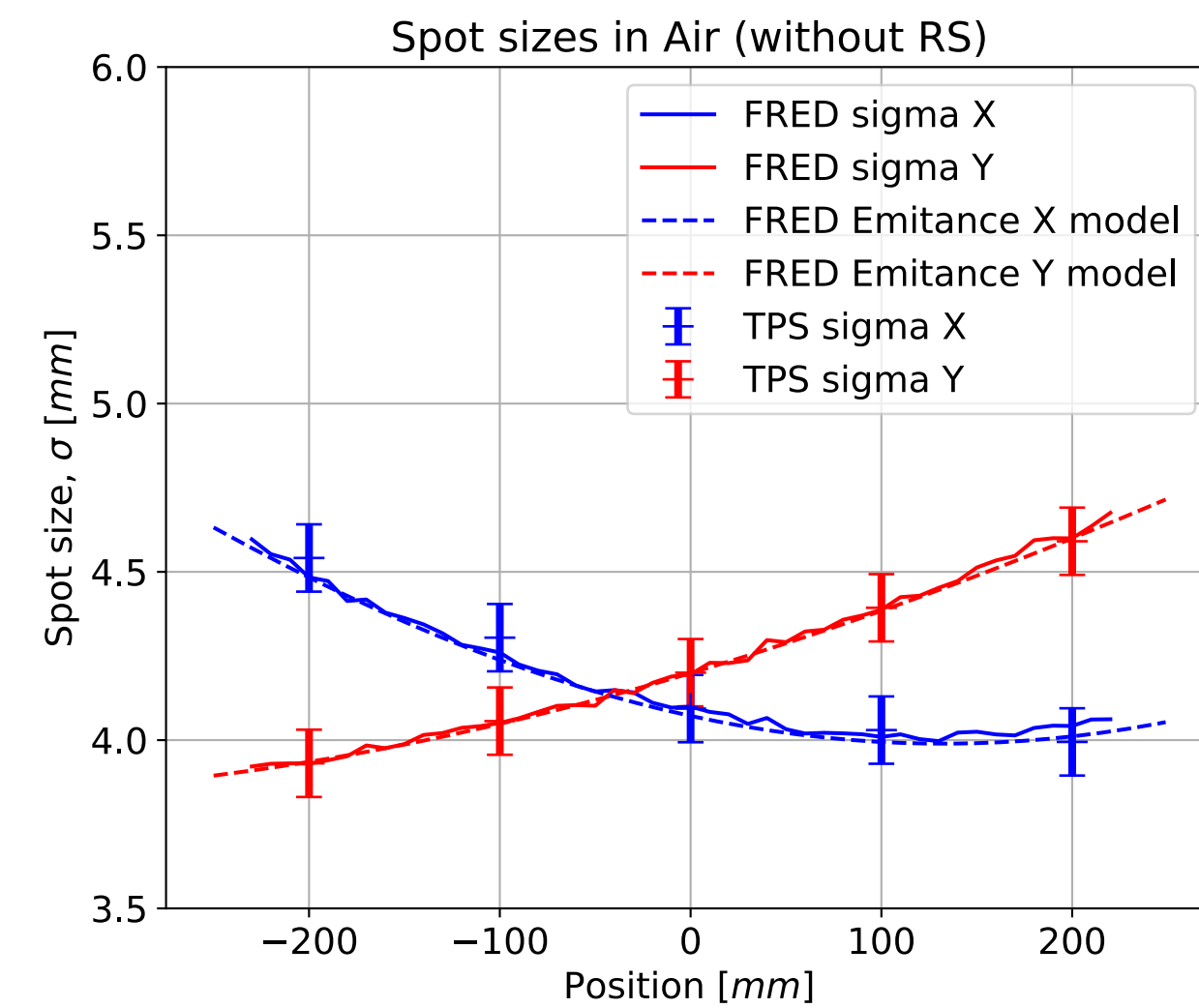
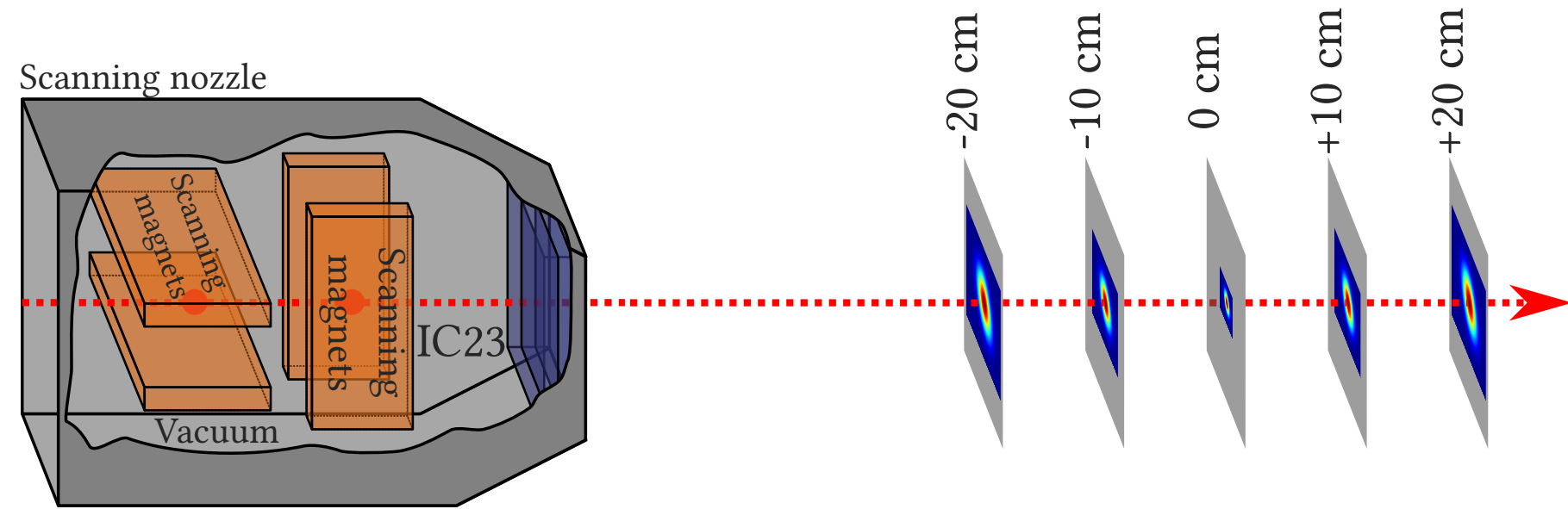
**Commissioning**



# Beam model phase space library in FRED



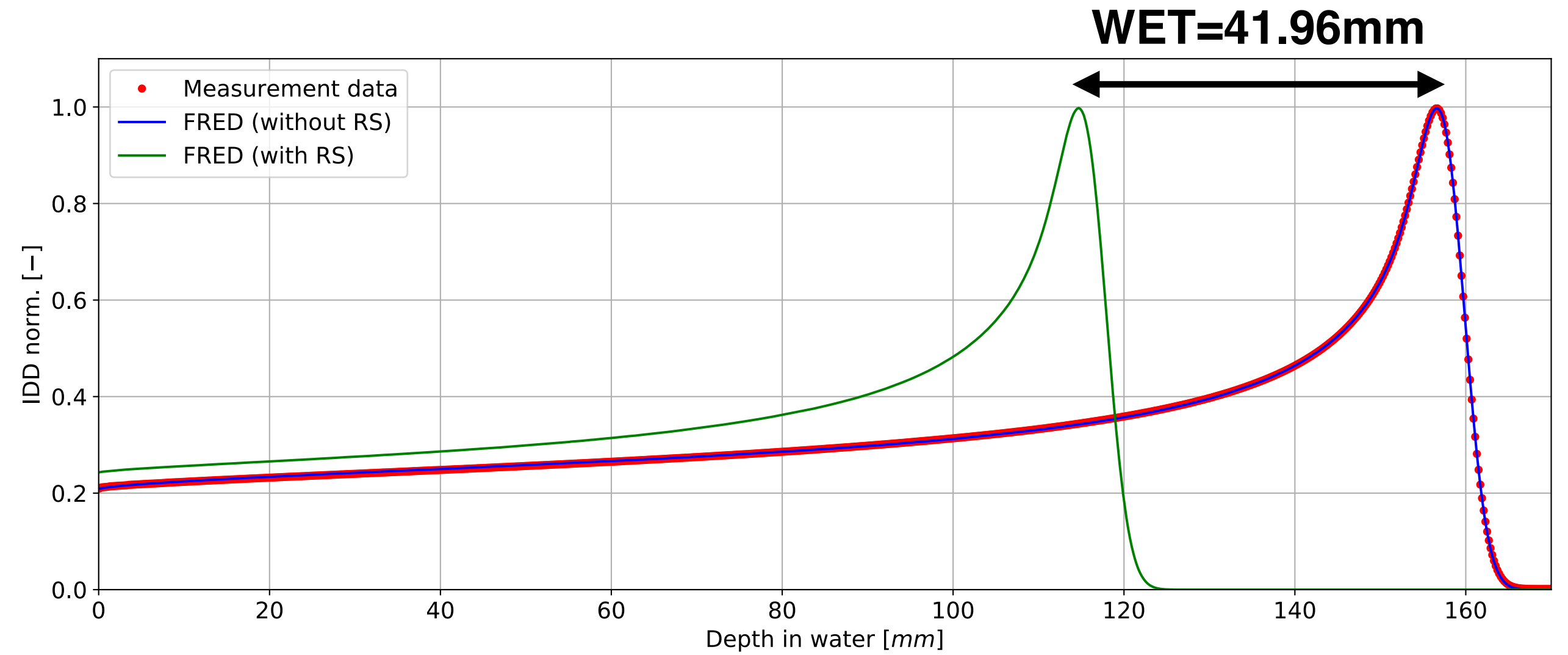
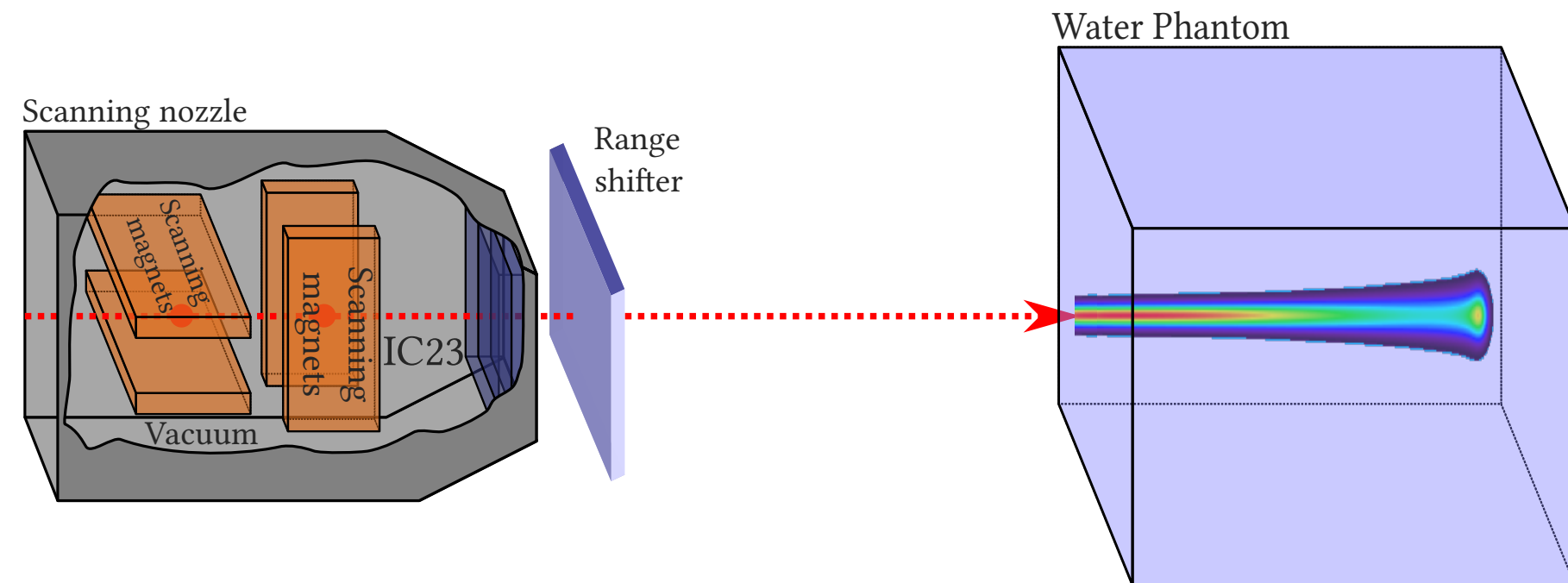
**p+ @150 MeV**



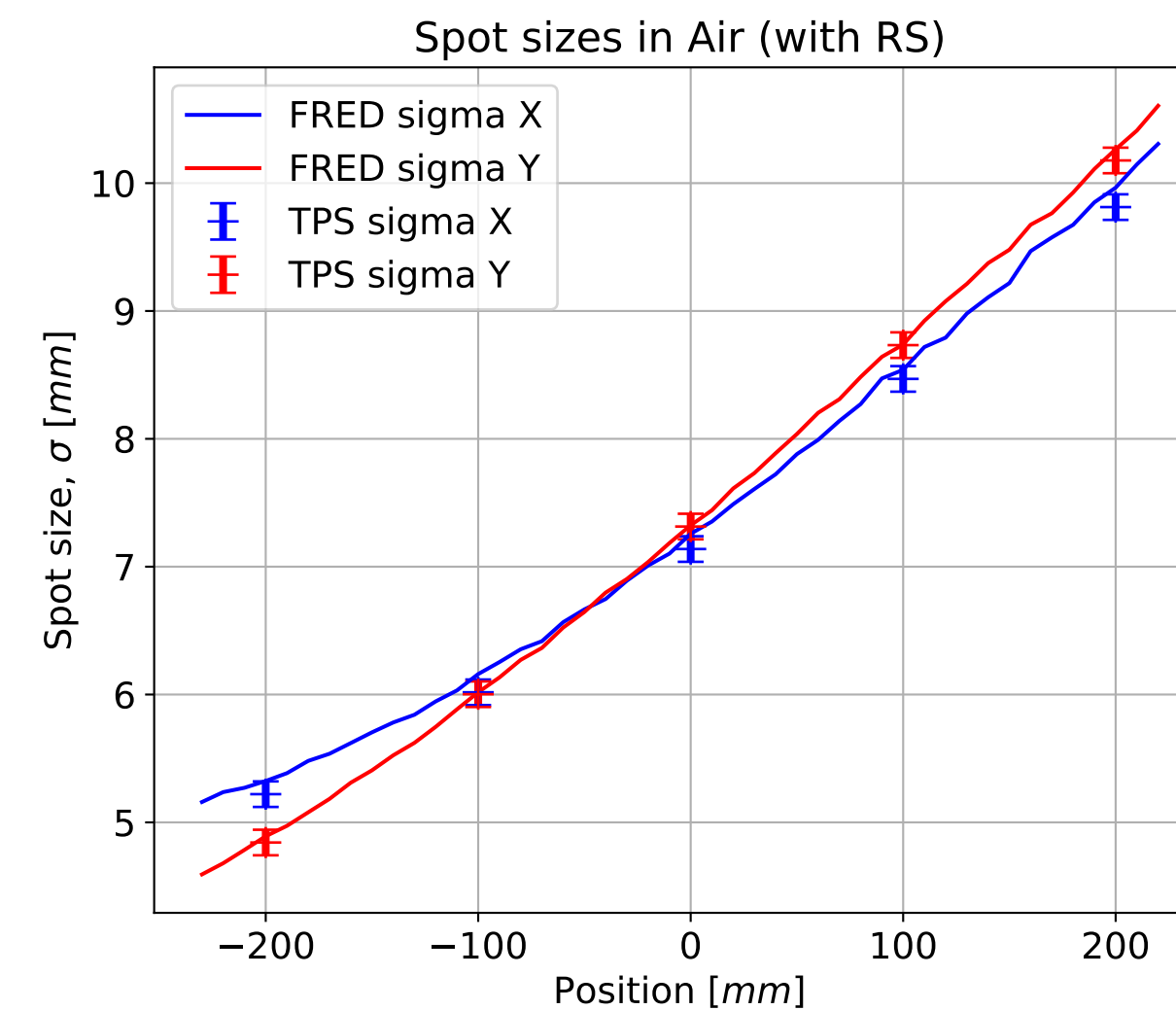
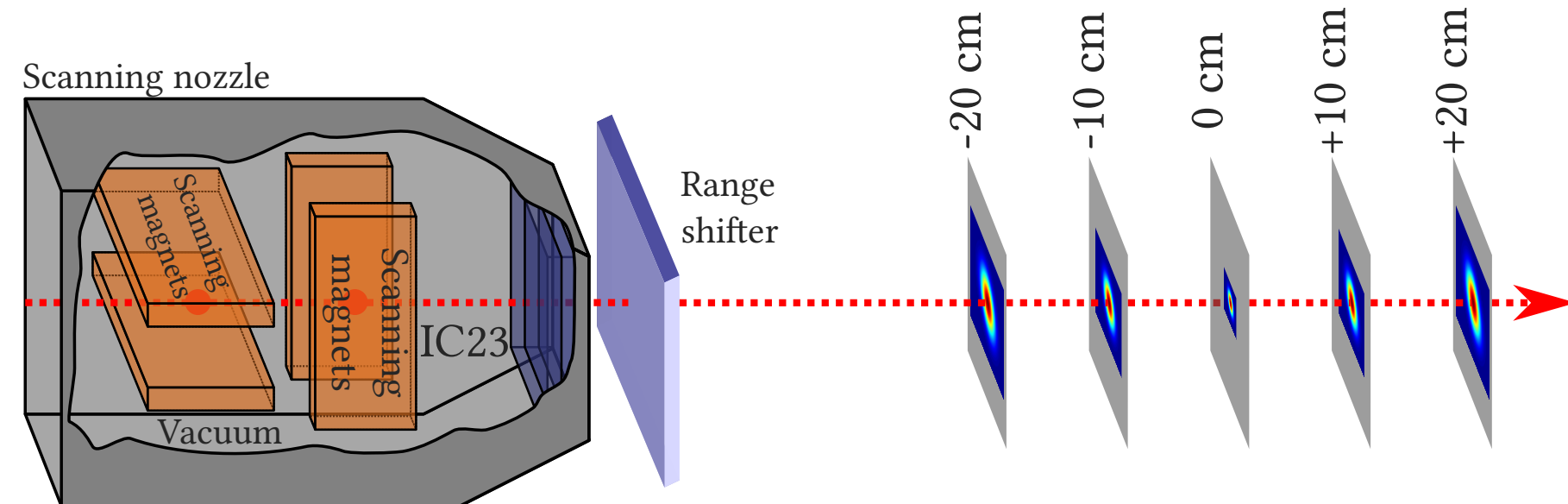
**Submillimeter agreement**

# Beam model phase space library in FRED

## Range Shifter



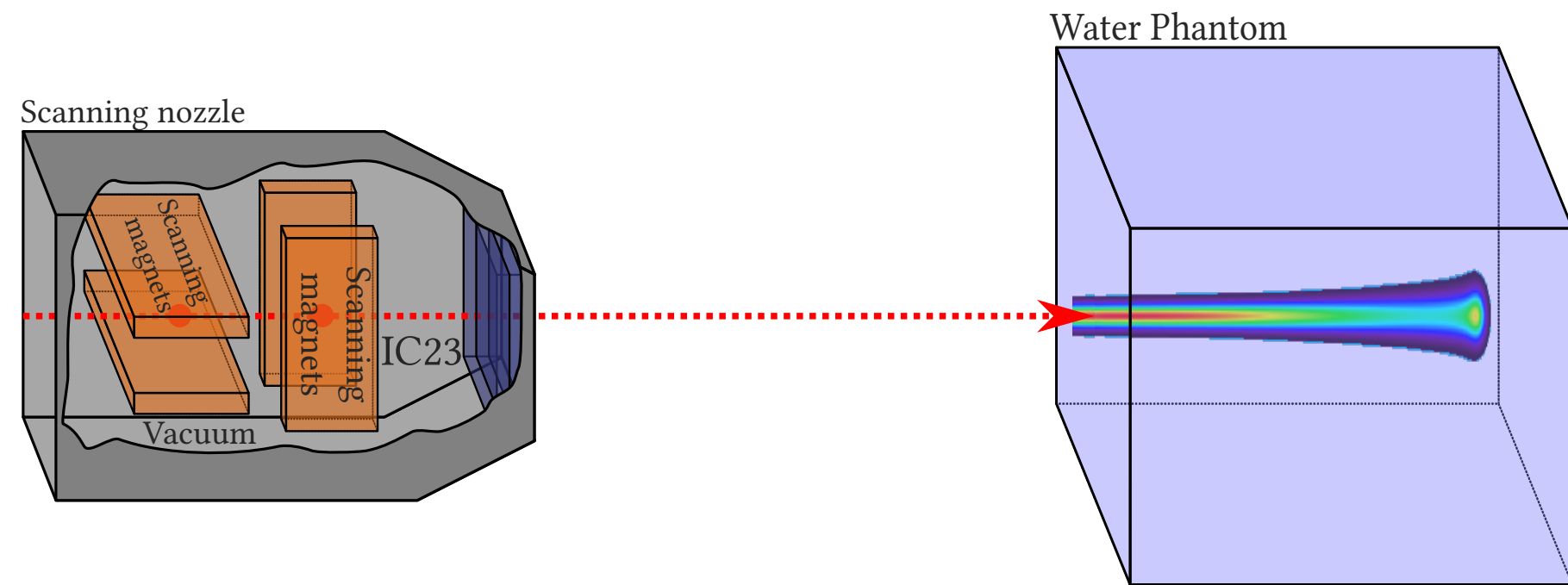
## p+ @150 MeV



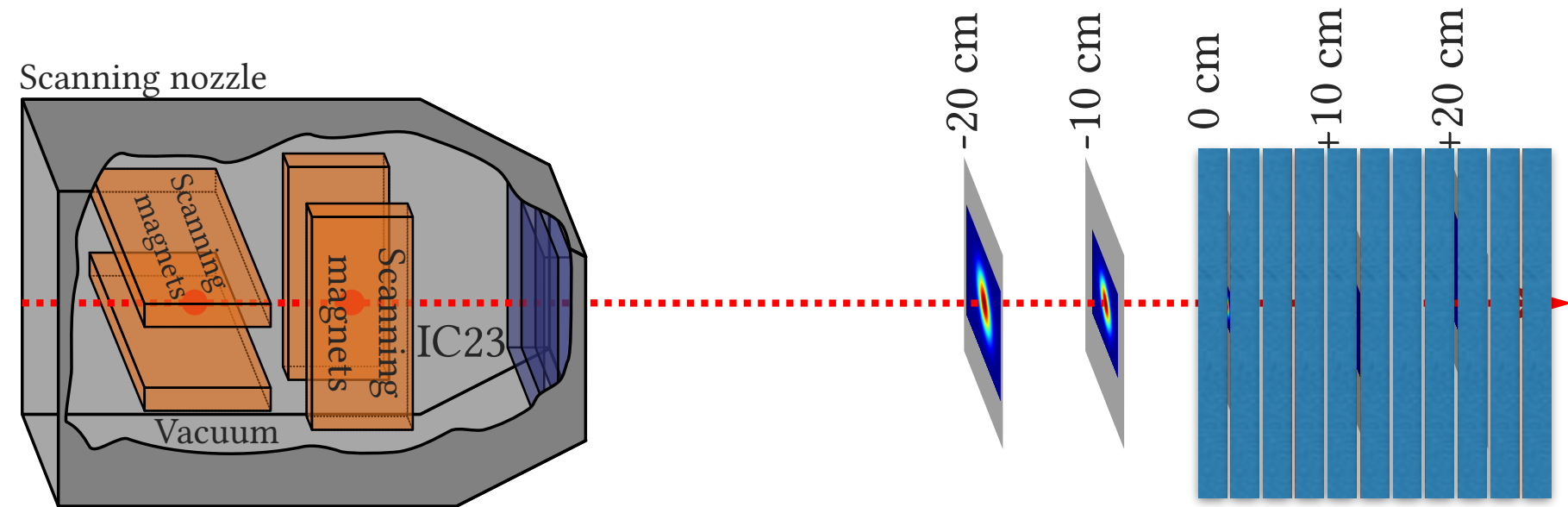
**Submillimeter agreement**



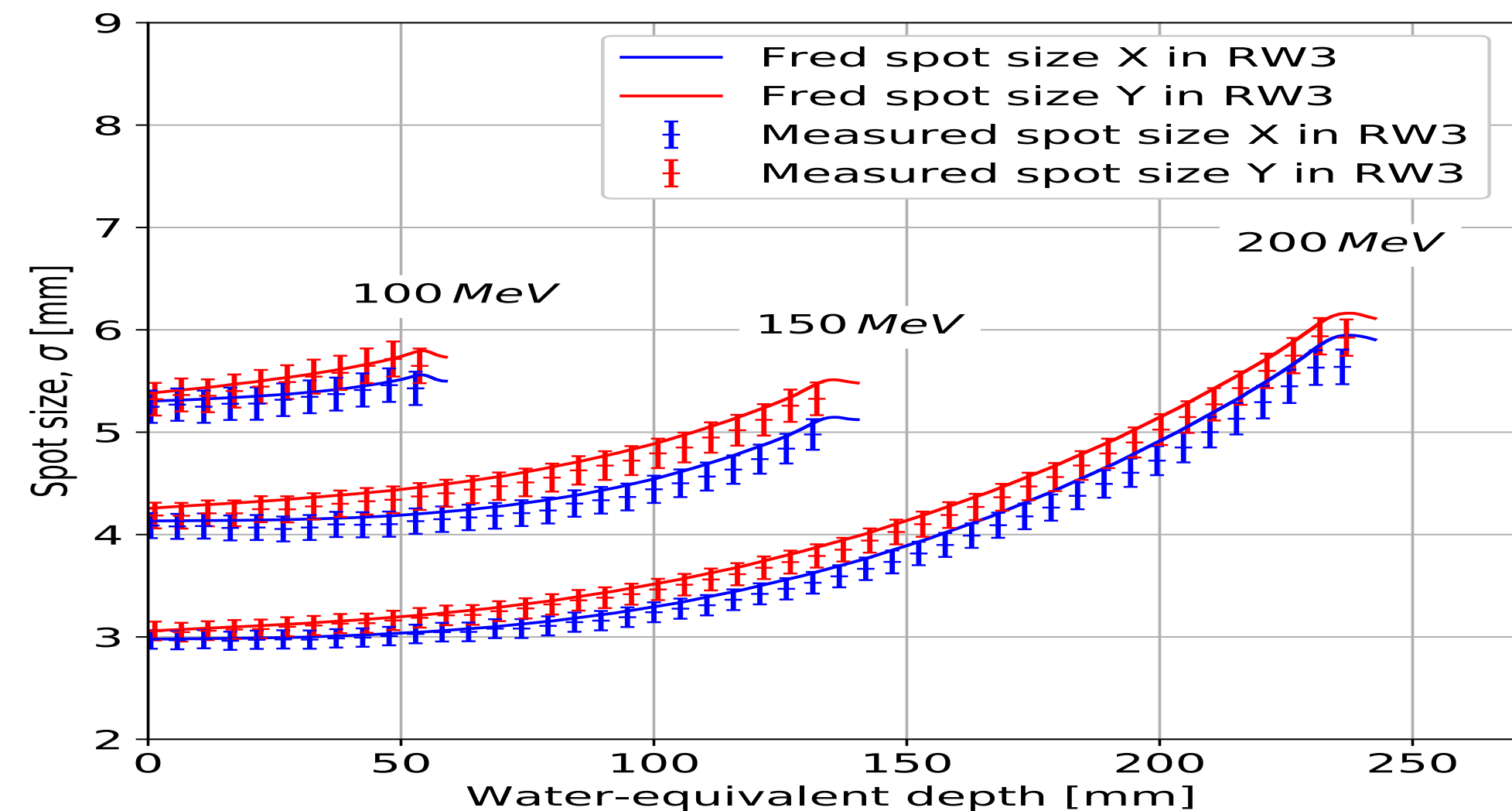
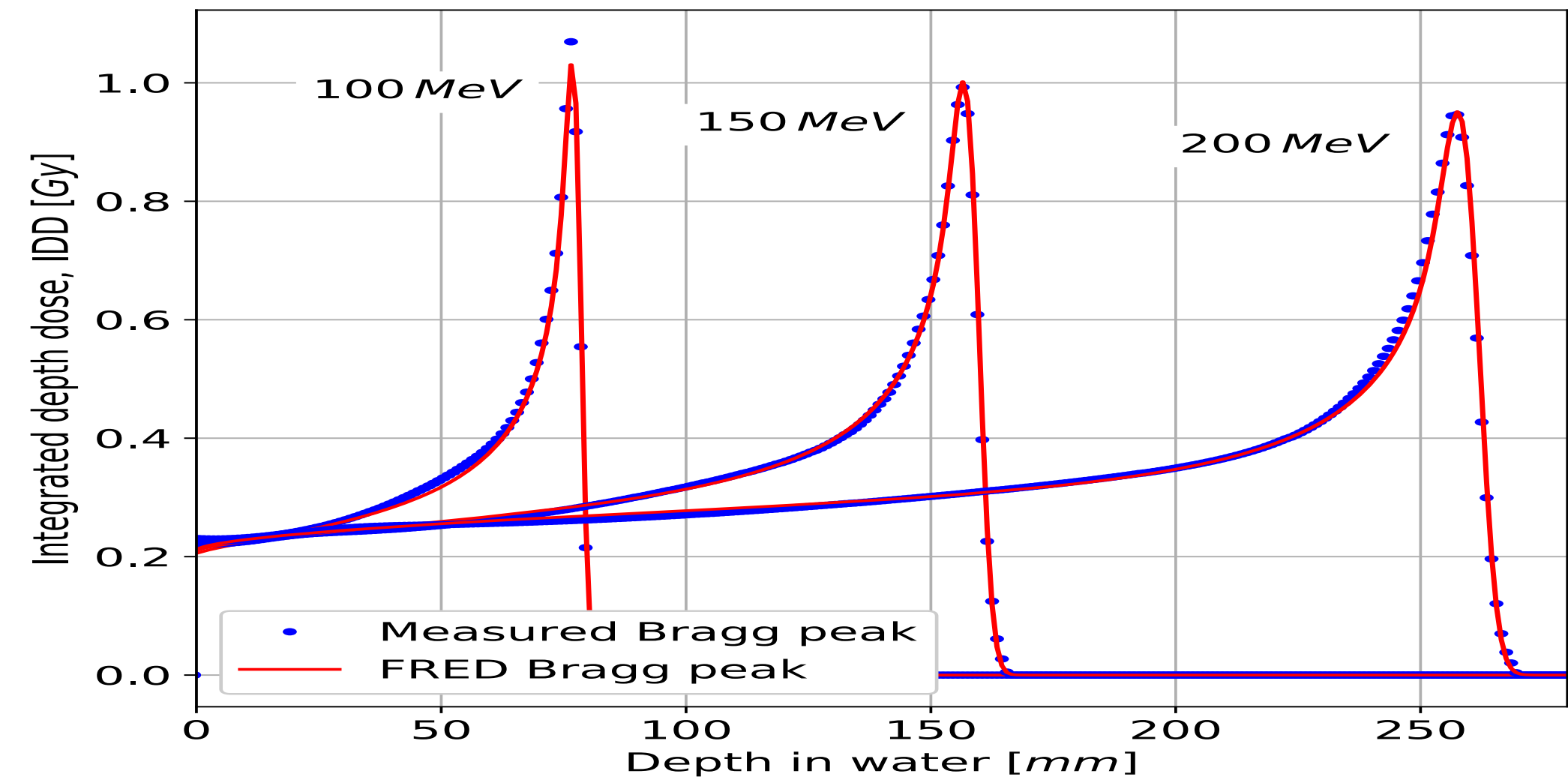
# Beam model phase space library in FRED



**p<sup>+</sup> @ 100, 150, 200 MeV**

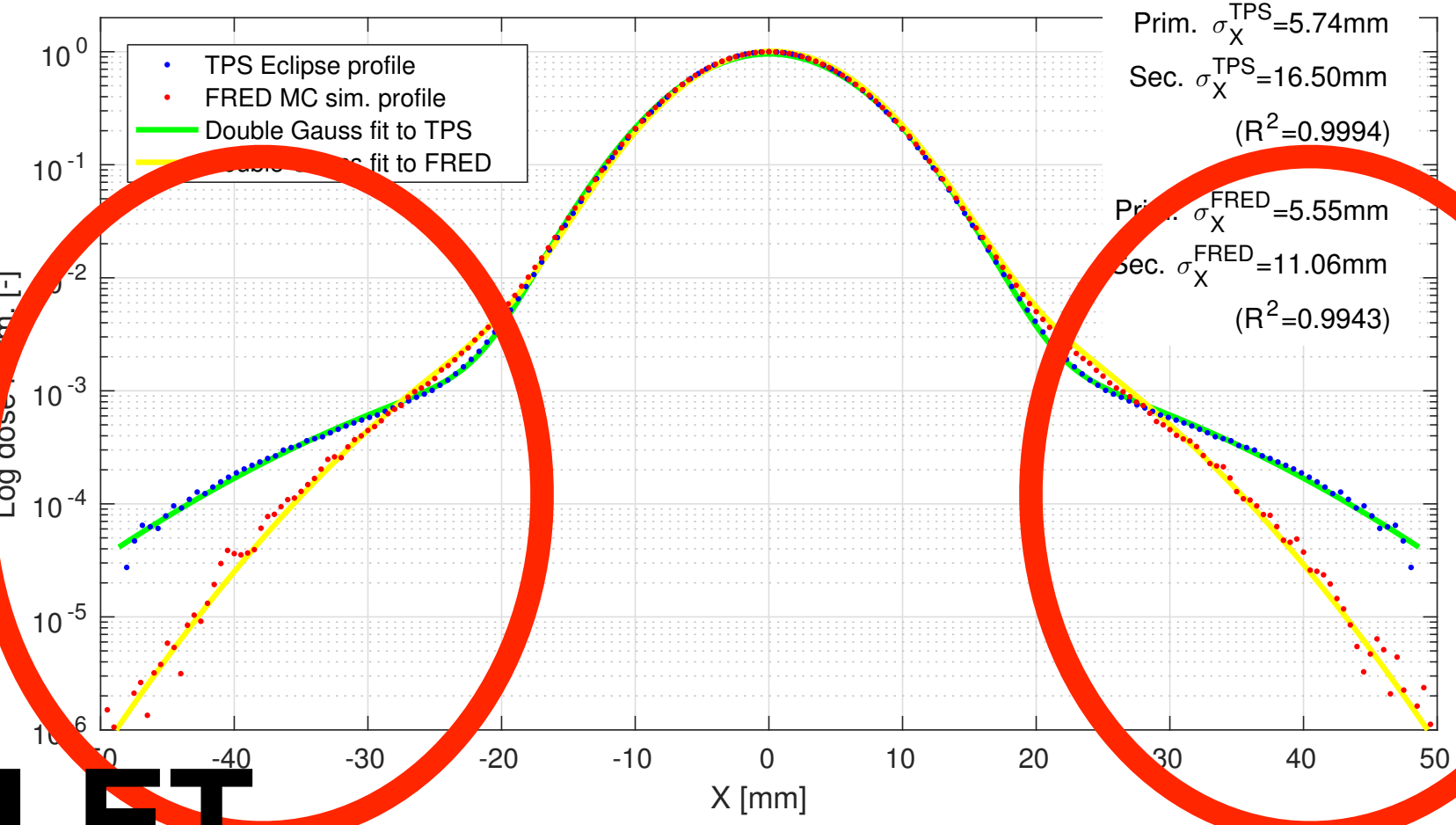
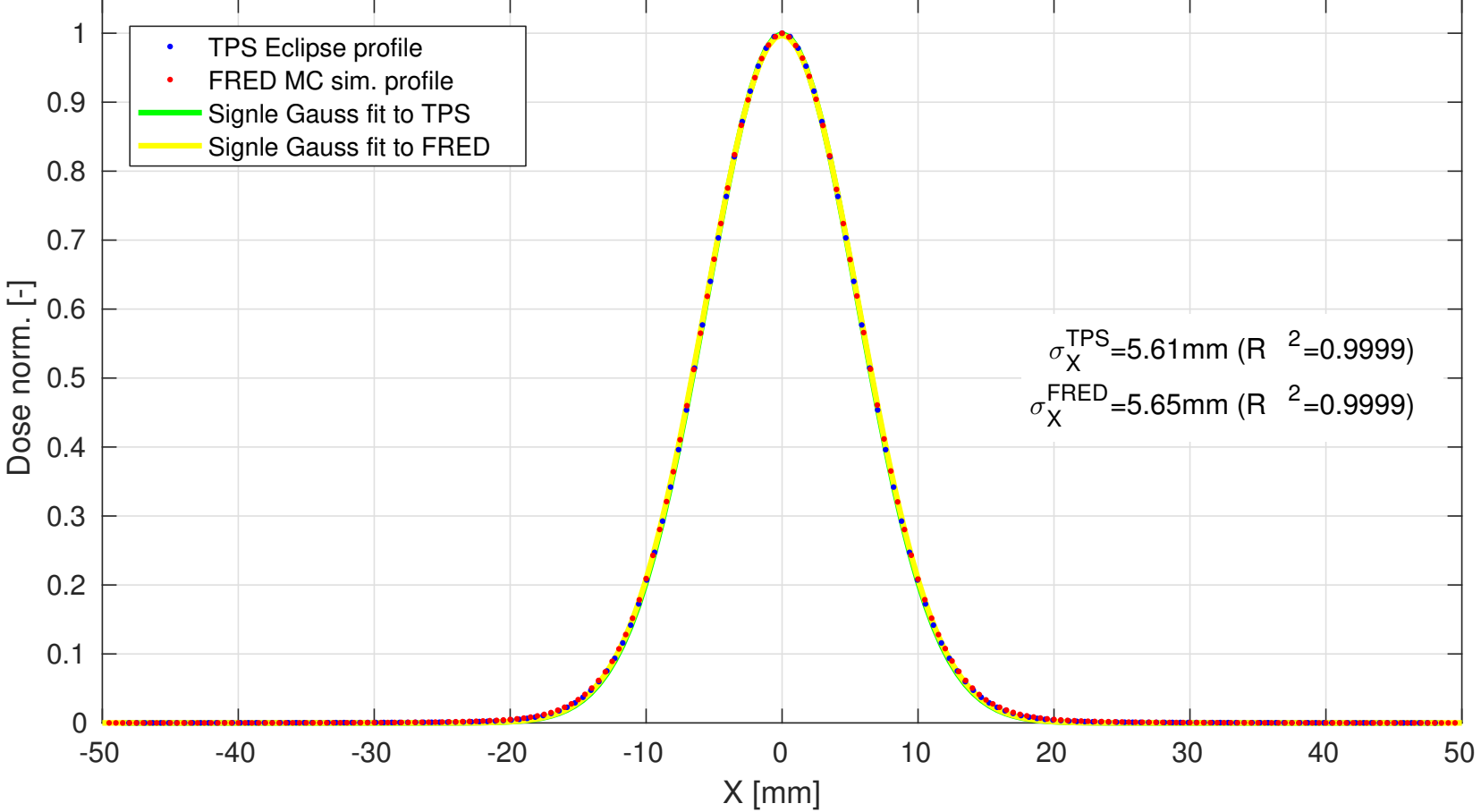
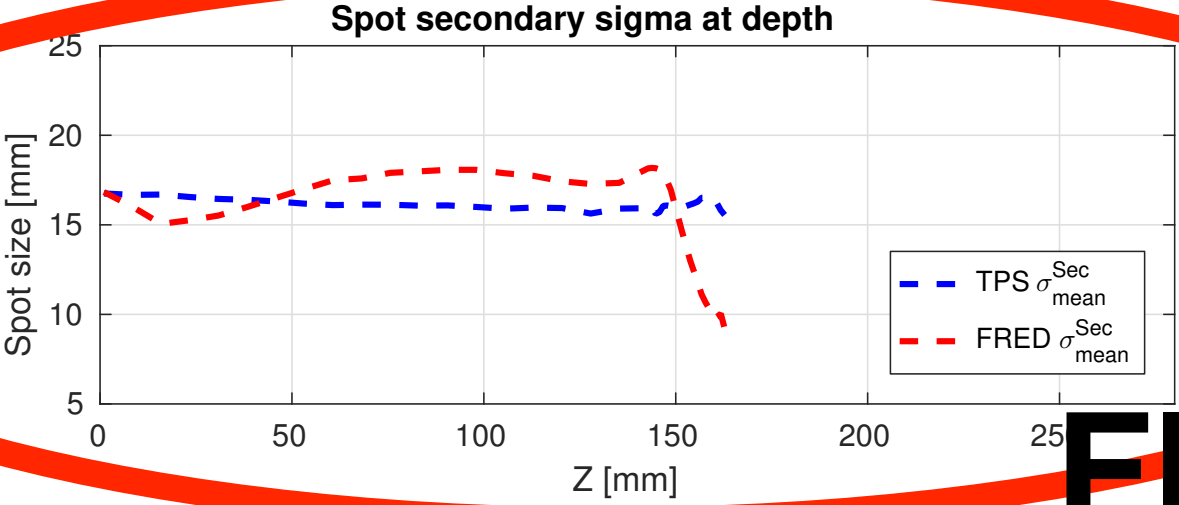
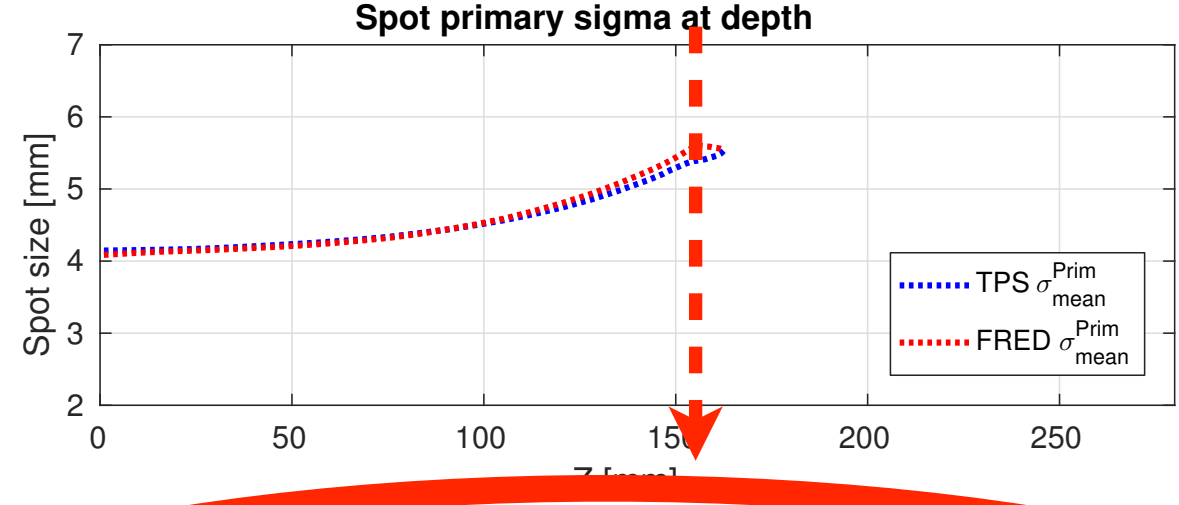
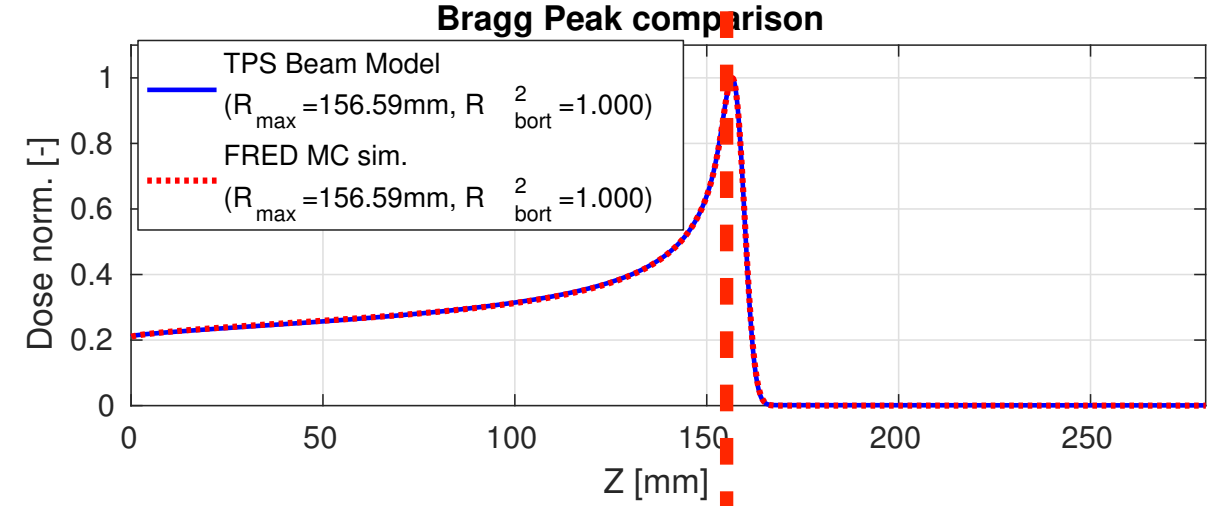
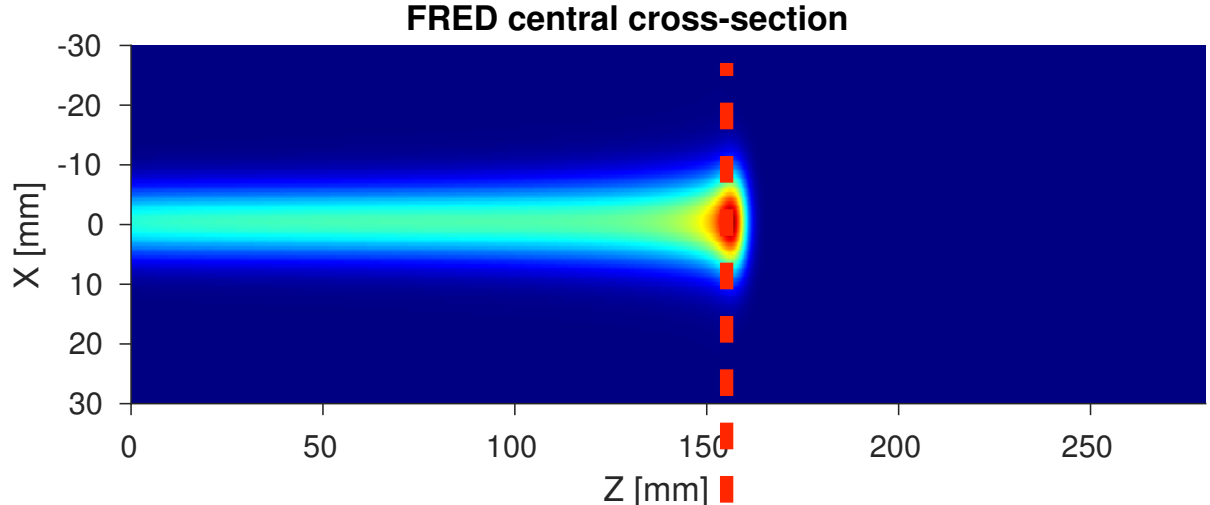


**RW3 slab phantom**



# What about the secondary sigma?

**p+ @150 MeV**



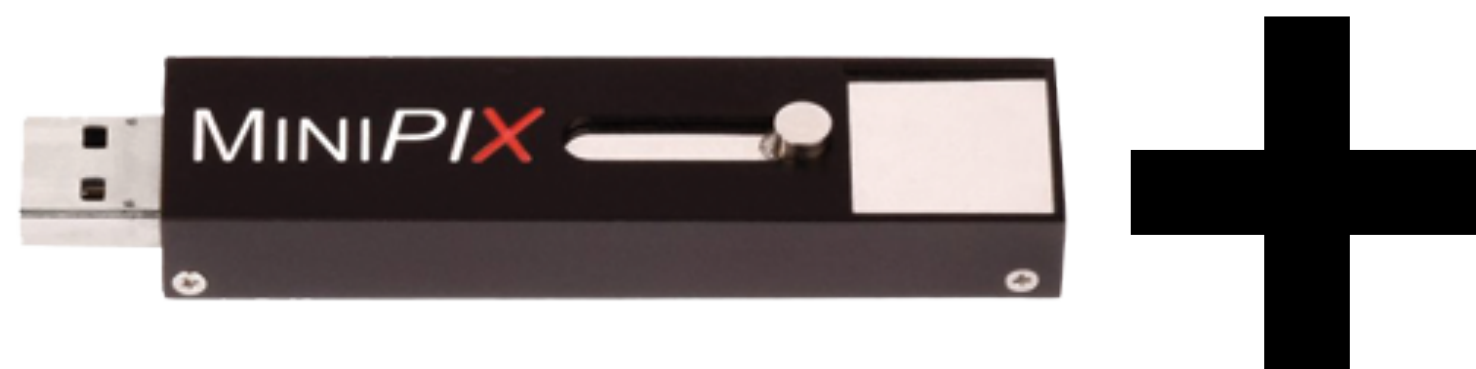
**Fluence, LET**



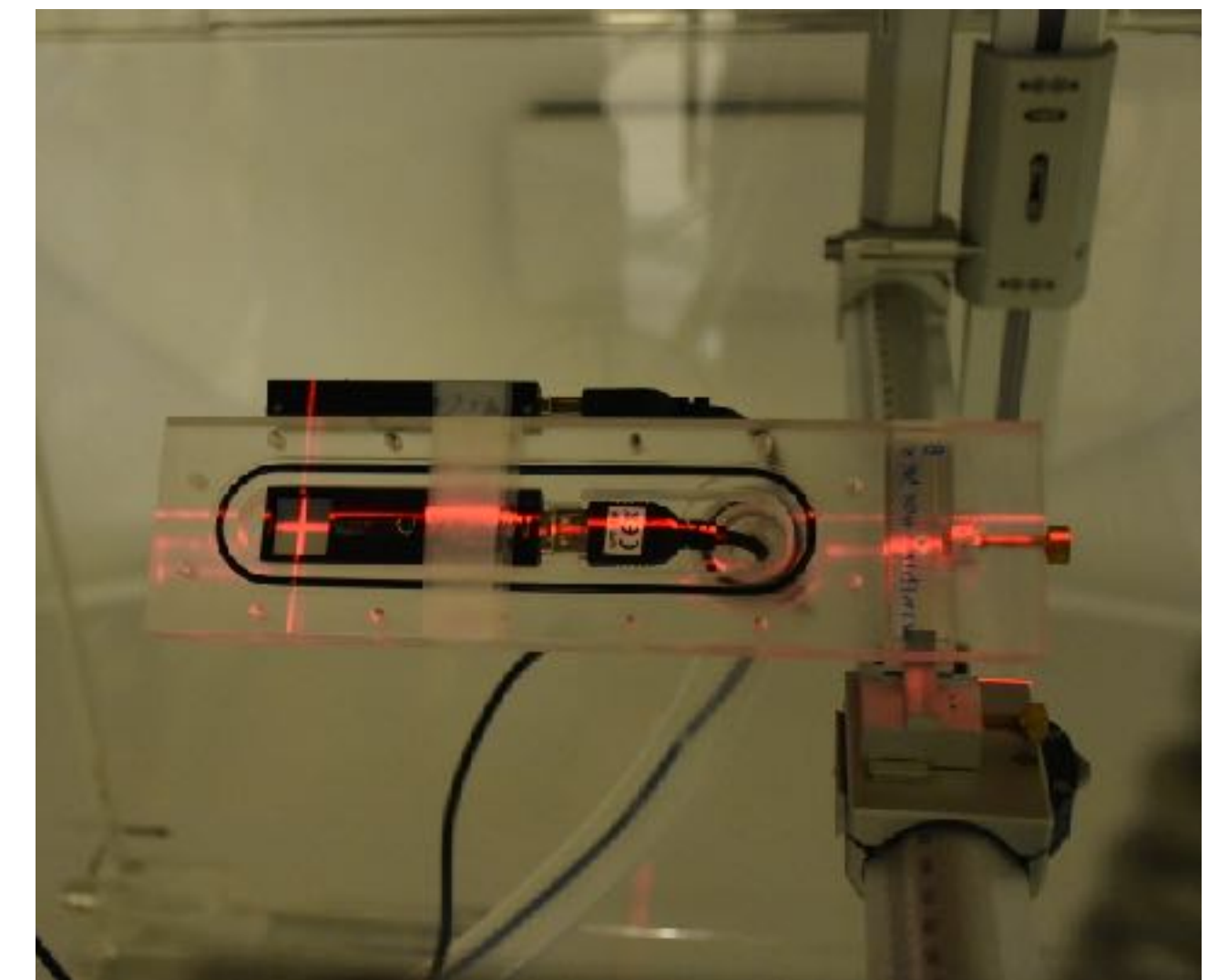
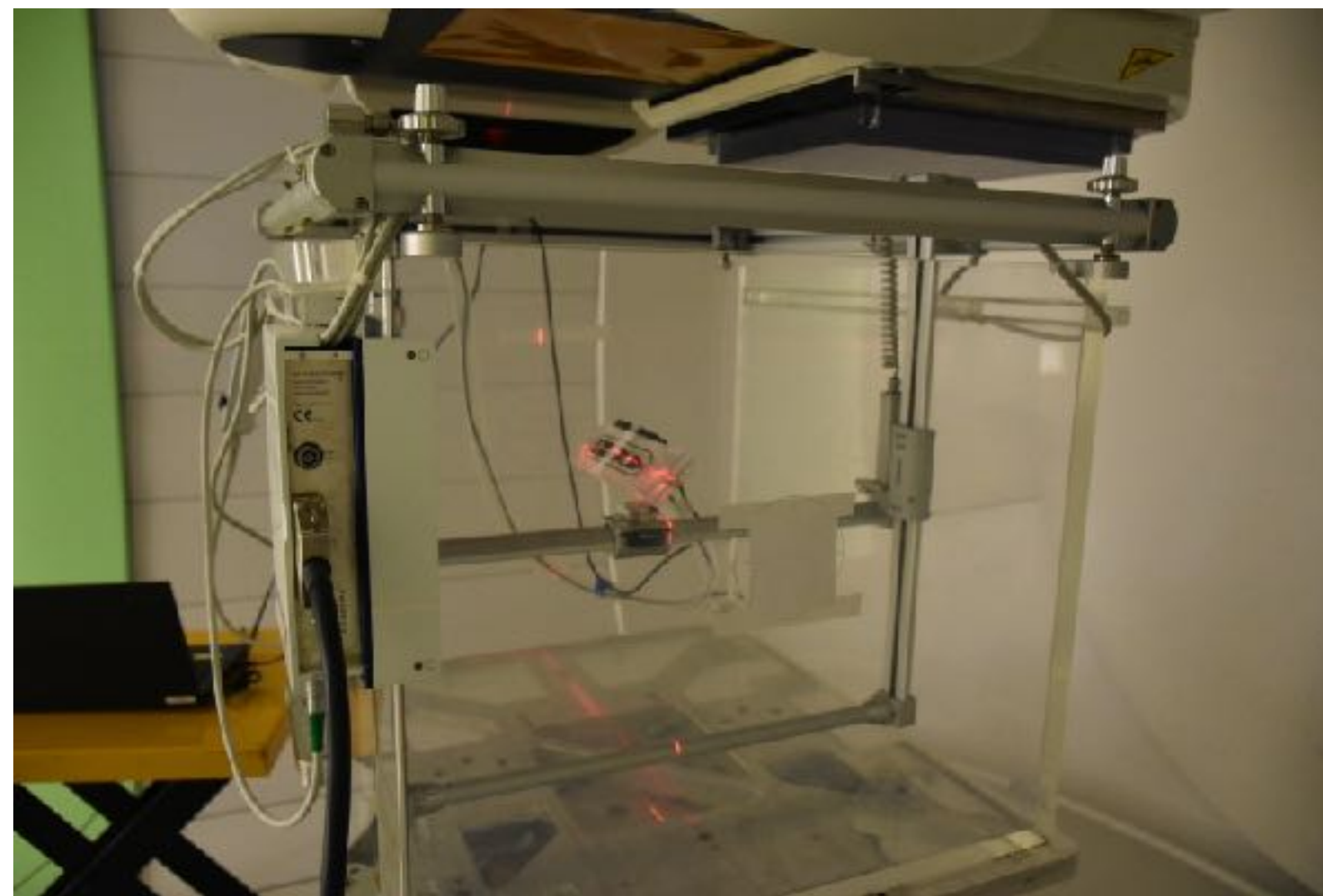
# What about the secondary sigma?

MiniPix TimePix  
from Advacam

Water phantom  
+  
Submarine

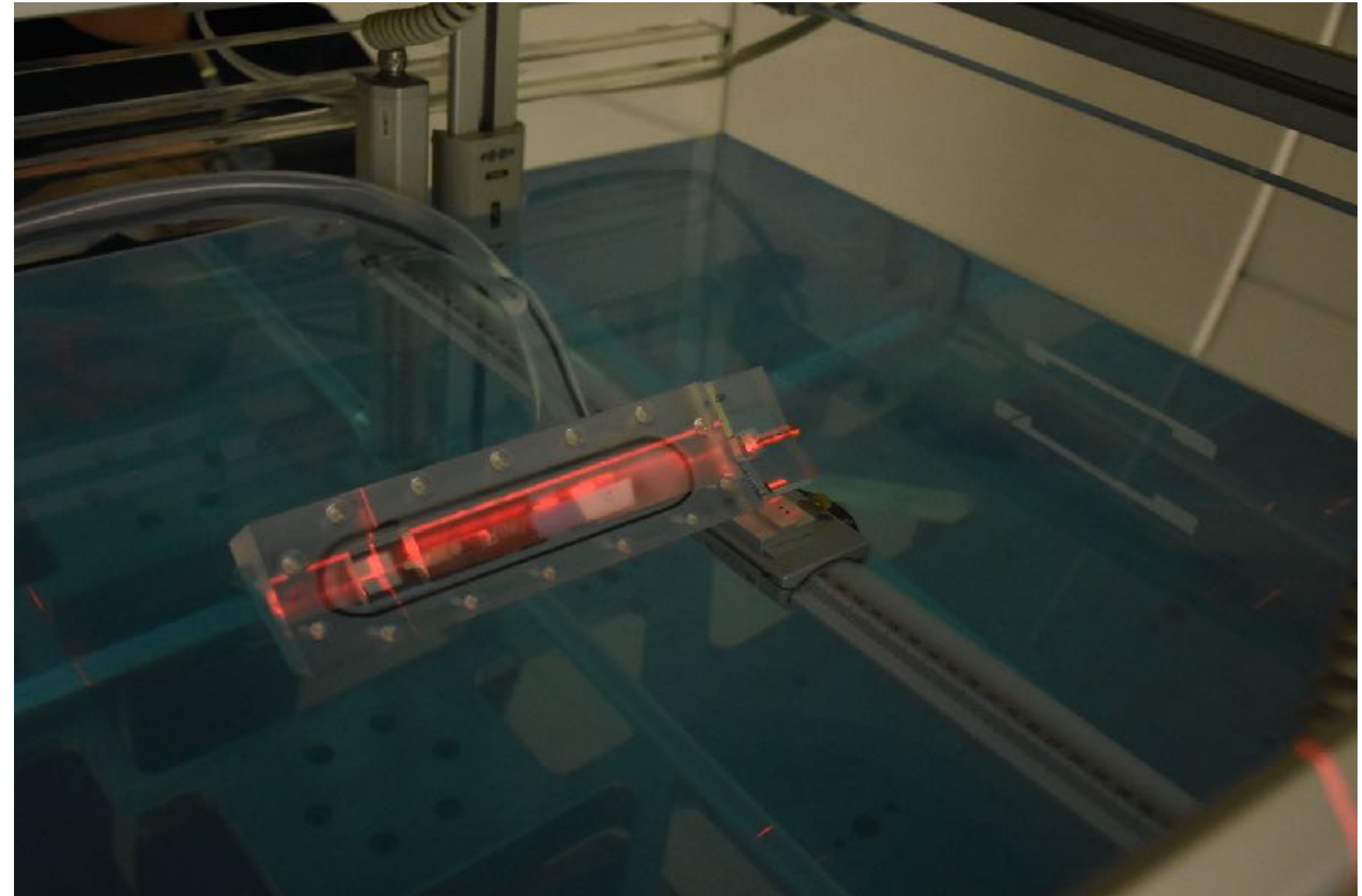
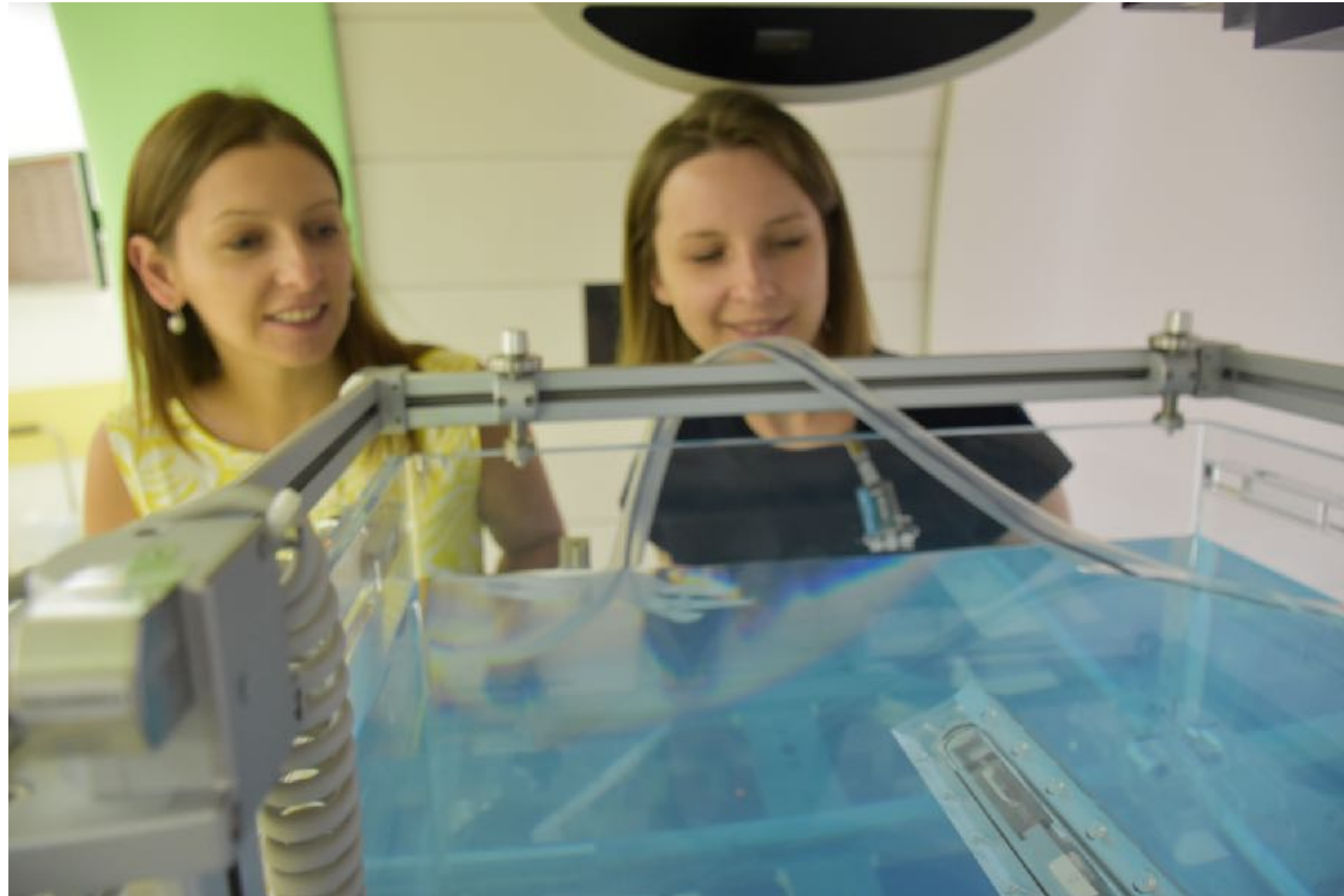


Sensor Thickness: 300  $\mu\text{m}$  for Si  
Sensitive Area: 14 mm x 14 mm  
Number of Pixels: 256 x 256  
Pixel Pitch: 55  $\mu\text{m}$   
Readout Speed: 45 frames/s





# Proton beam characterisation in water



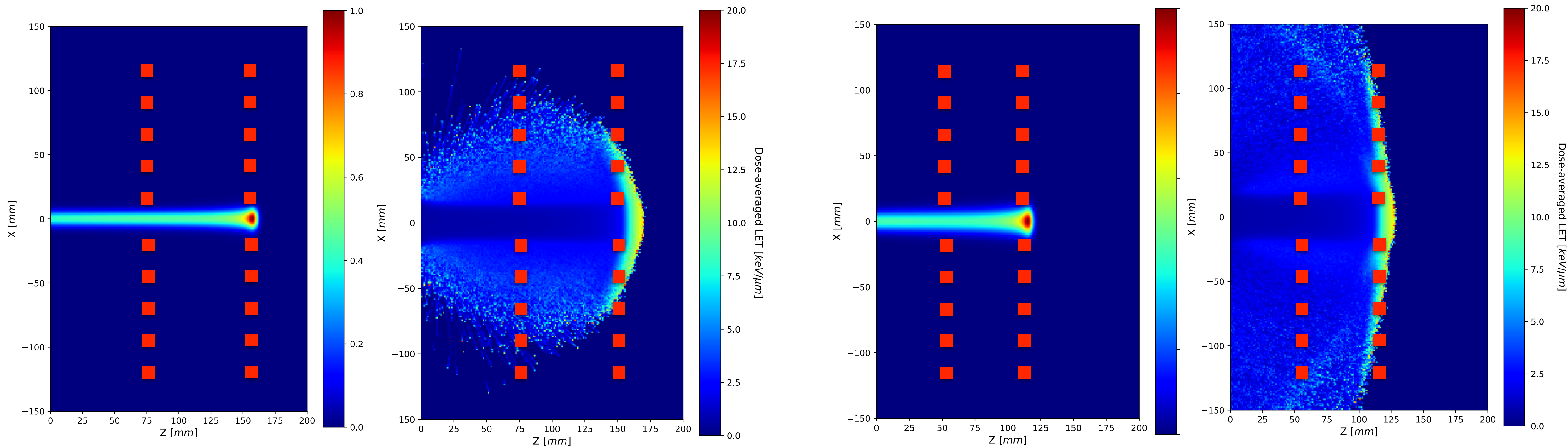


# Proton beam characterisation in water

$p^+$ , 1nA, clinical mode, 150 MeV

no Range shifter

Range shifter



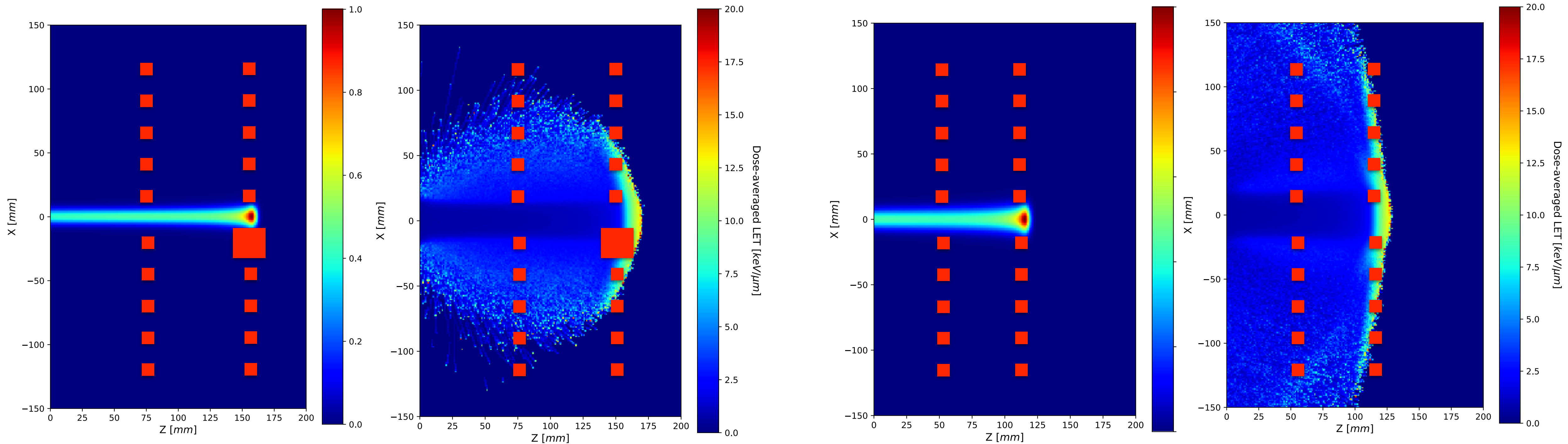


# Proton beam characterisation in water

$p^+$ , 1nA, clinical mode, 150 MeV

no Range shifter

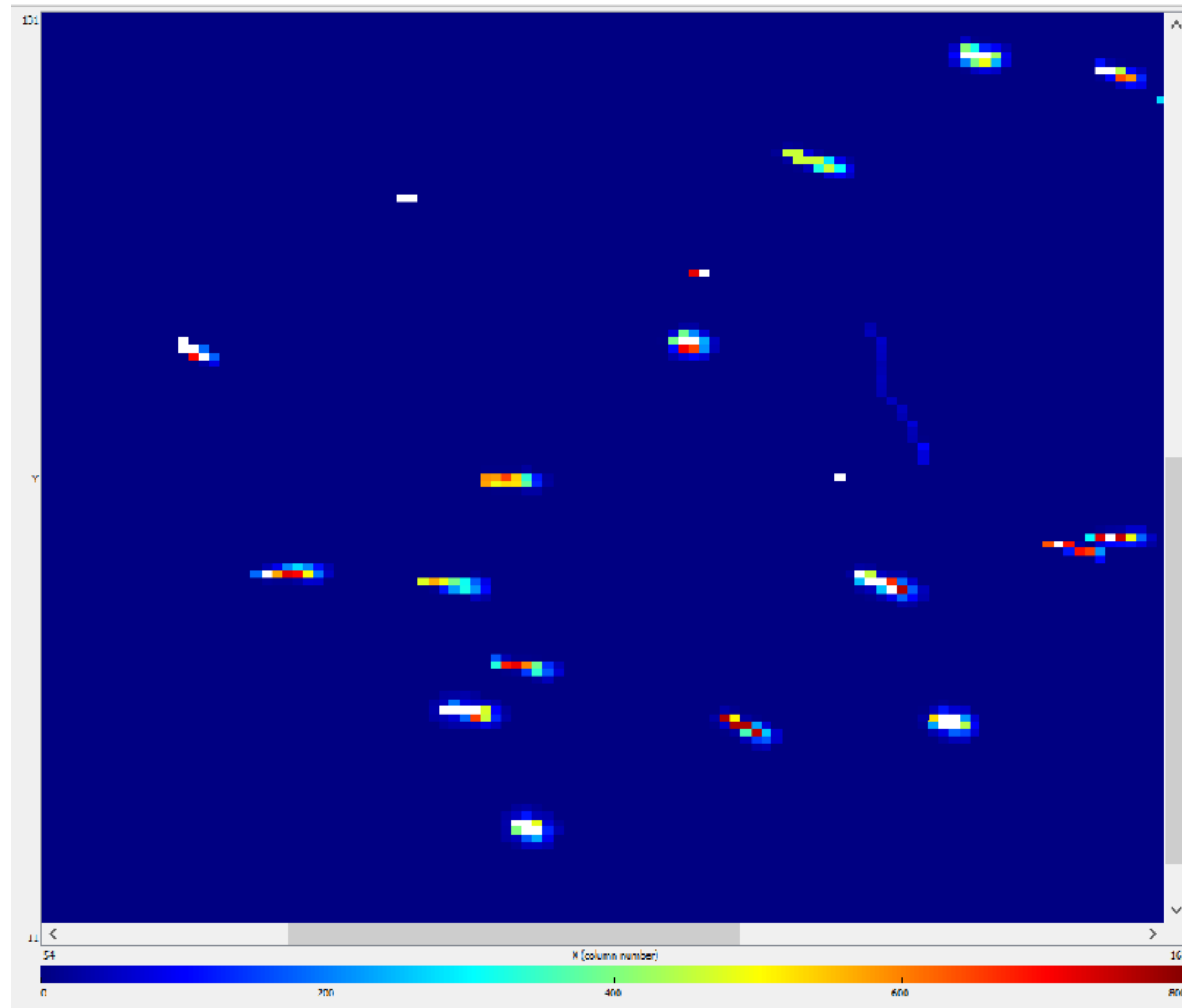
Range shifter





# Pixel detectors Timepix

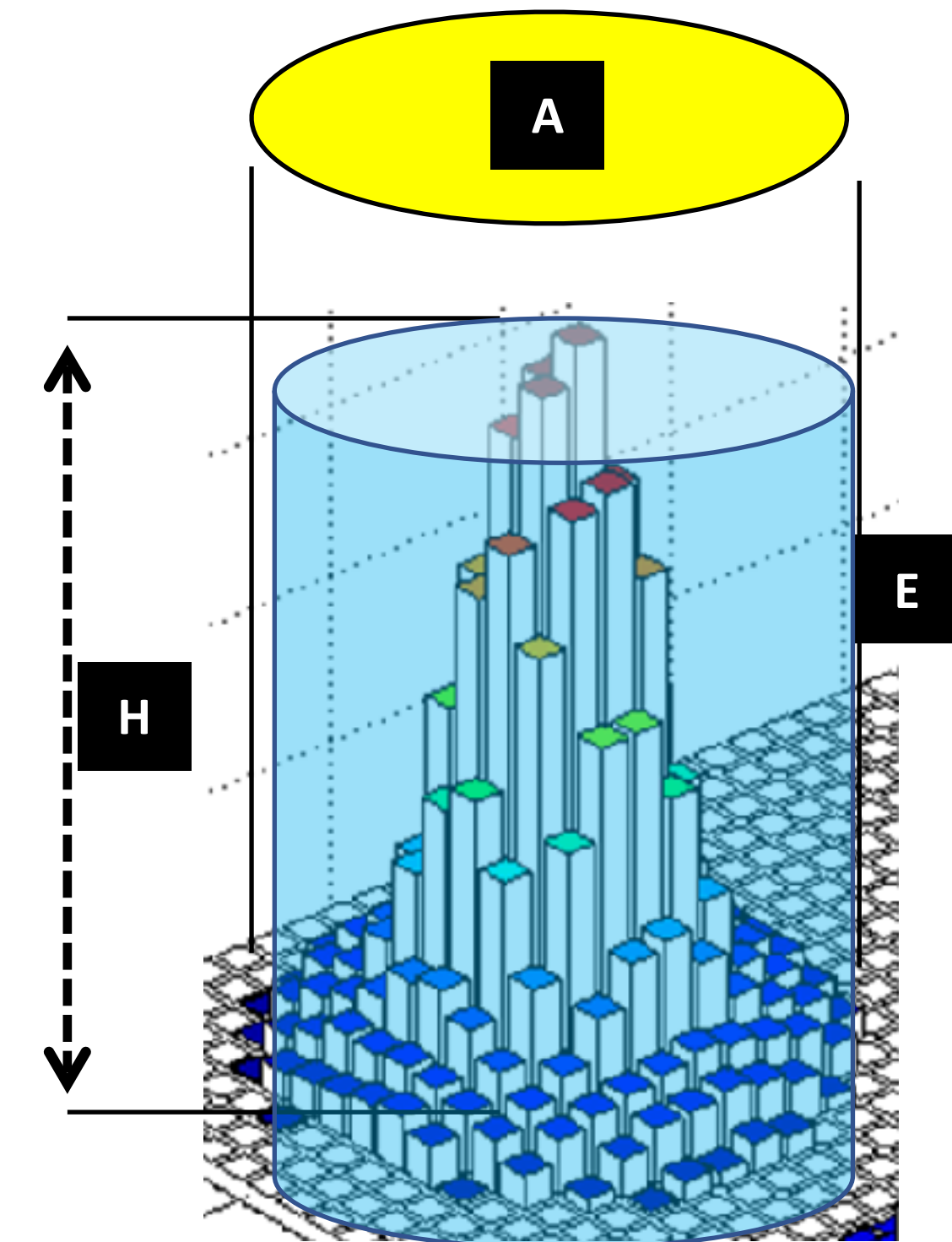
Events display: Mixed Field



## Cluster parameters:

- Height [keV],  $H$
- Area [px],  $A$
- Energy [keV/px],  $E$

## Pixel cluster analysis



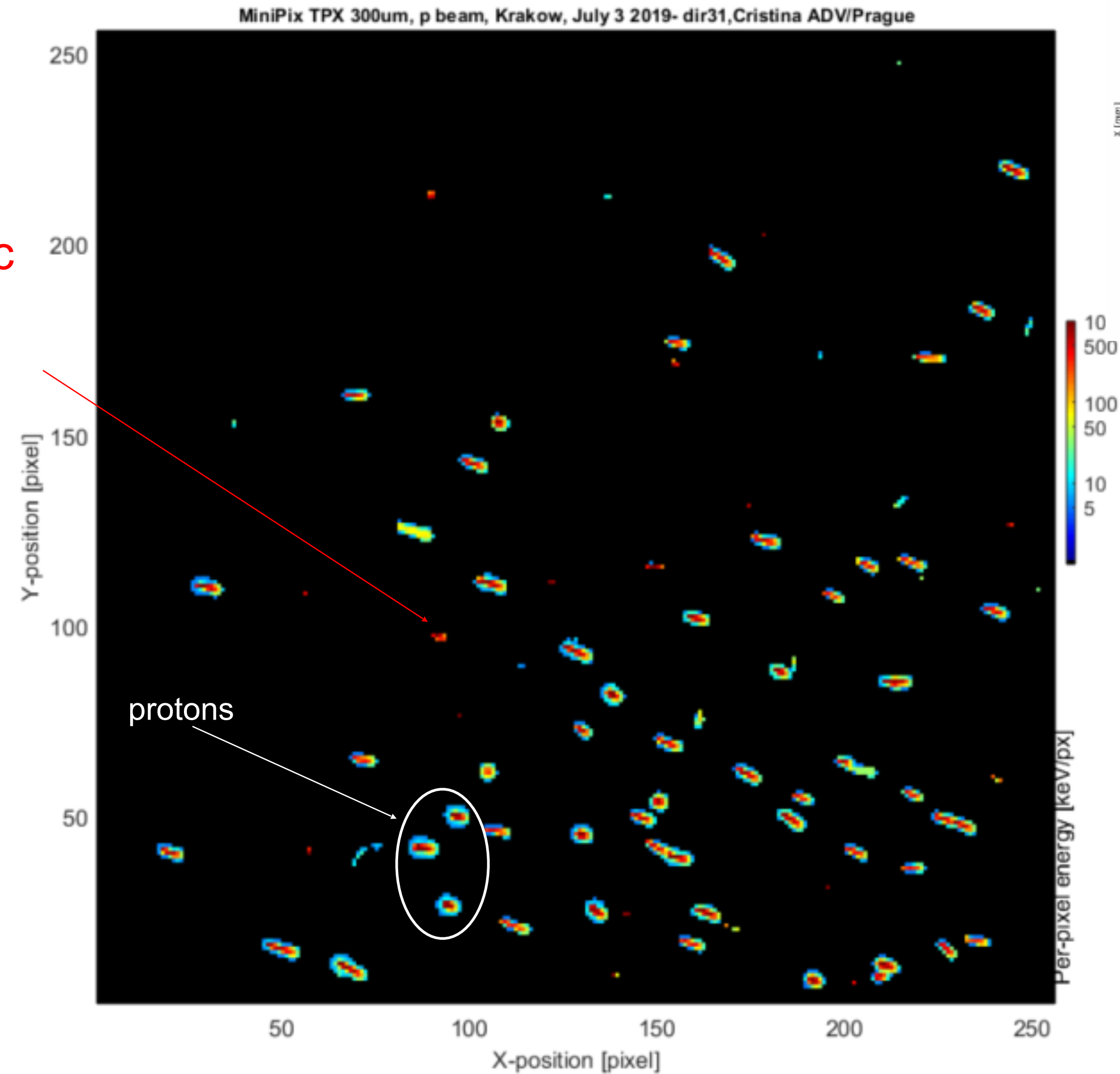


## 2D visualization of Cluster Energy

dir 31  
Close to the proton beam spot  
Minipix Timepix 300 $\mu$ m Si sensor

- Detector placed close to the proton beam spot
- Dir 31
- 1 frame
- 256x256 pixels, 14 mm x 14 mm
- Per-Pixel energy deposited
- Mixed field

Highly energetic charged particles



All events

All data no filters

Events A

Height filter **200 to 650 keV**  
for the 1<sup>st</sup> peak

Events B

Height filter **800 to 1100 keV**  
for the 2<sup>nd</sup> peak

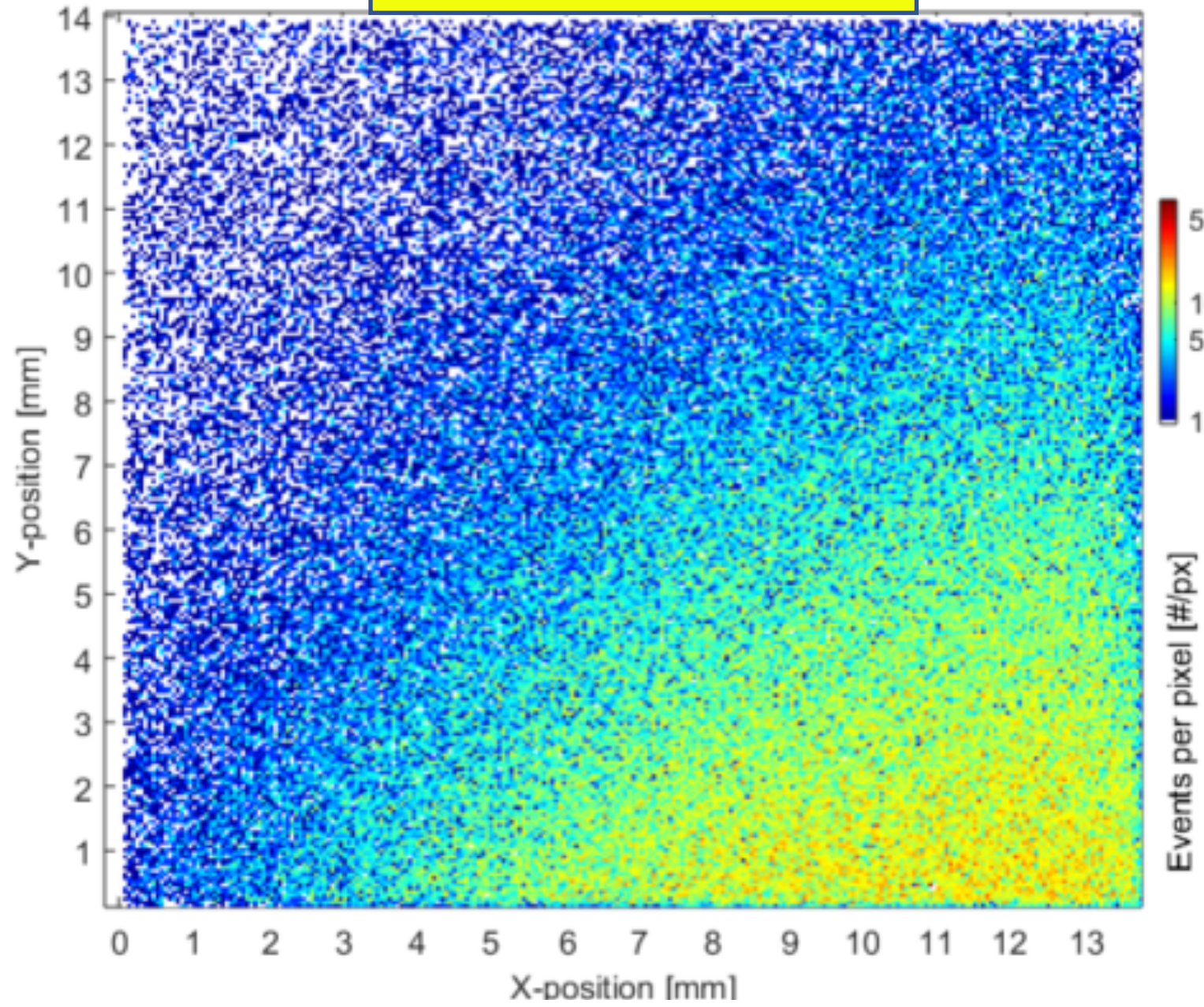




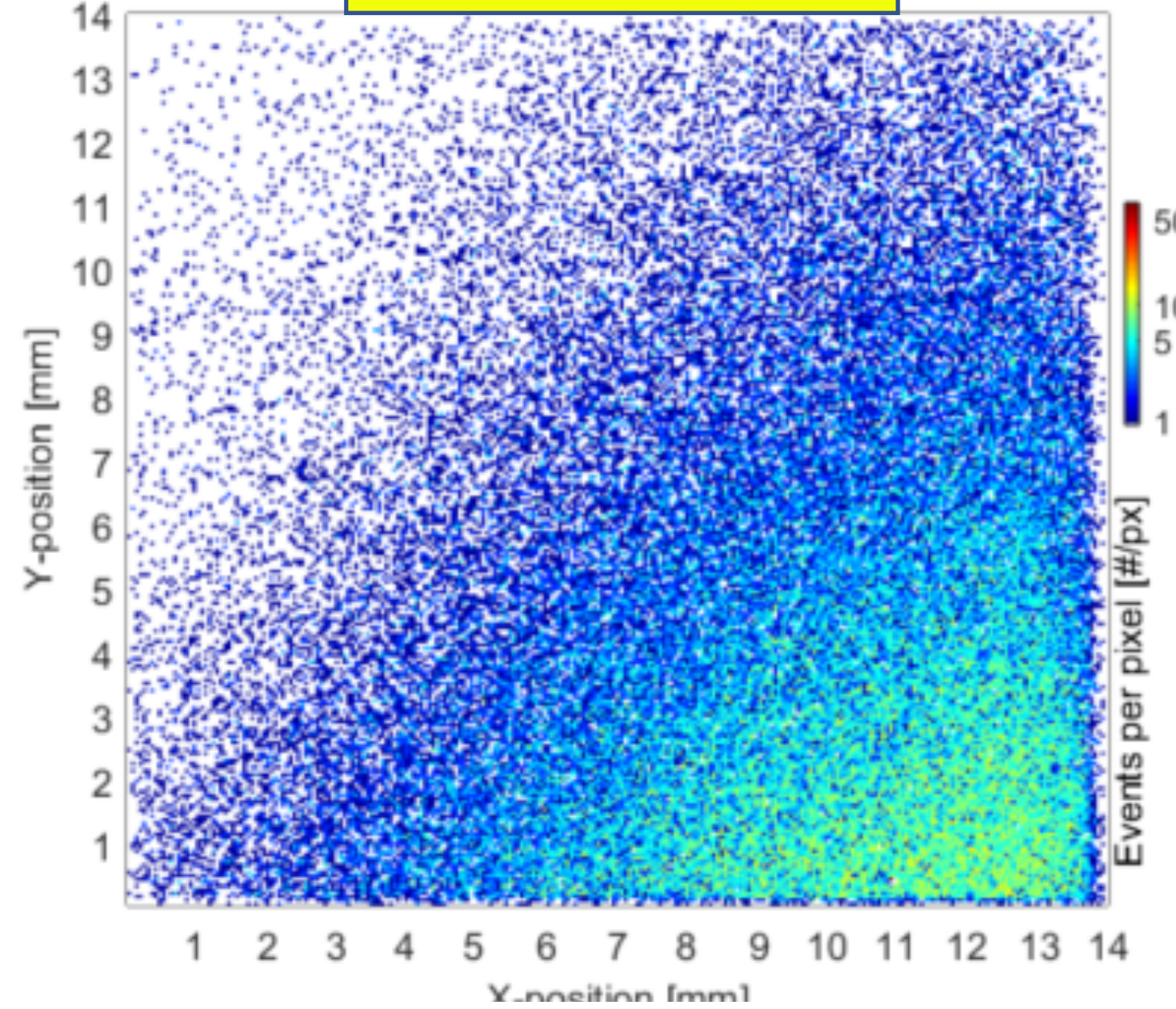
# Spatial distribution of Event counts

Close to the proton beam spot  
Minipix Timepix 300 $\mu$ m Si sensor

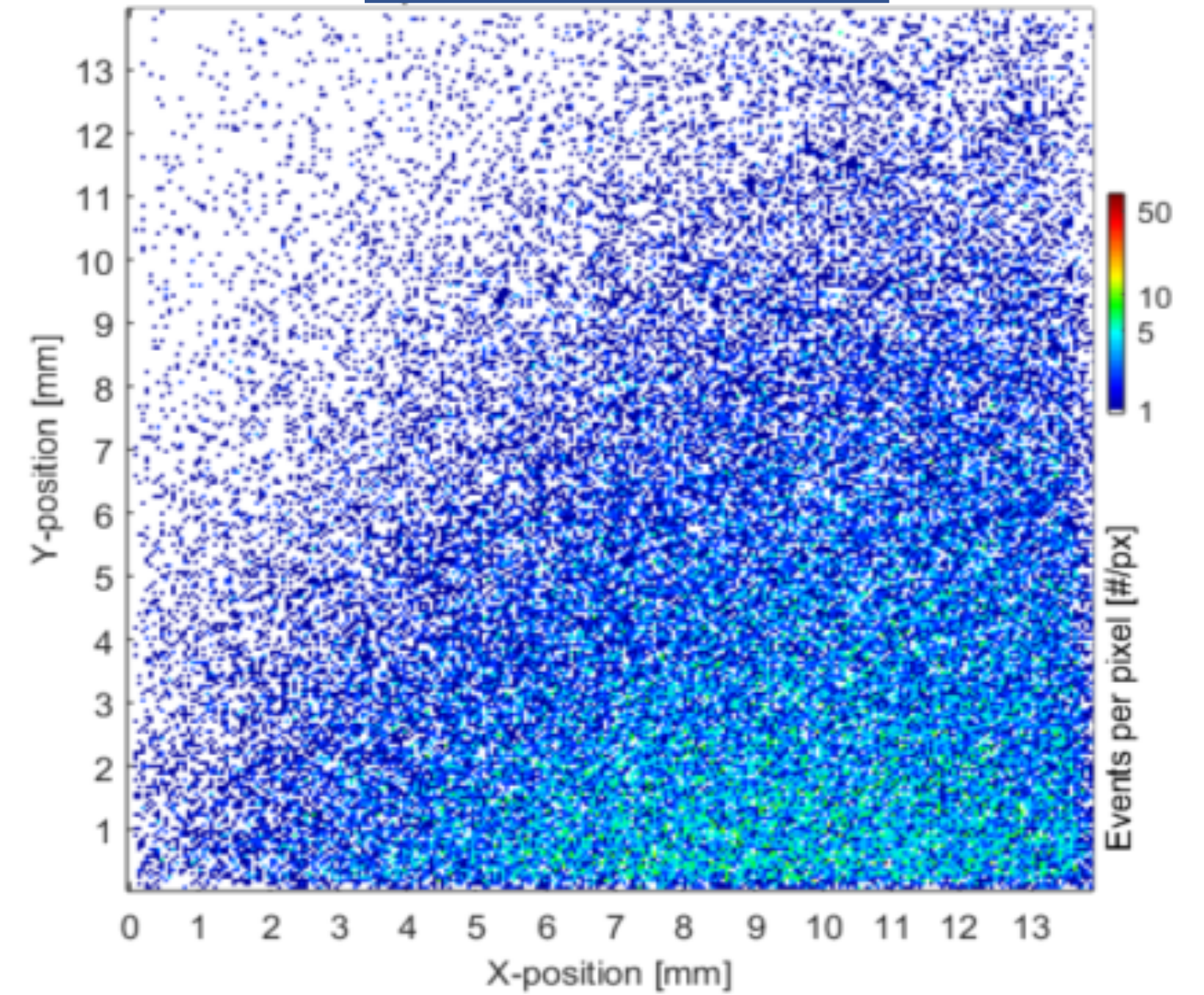
All events



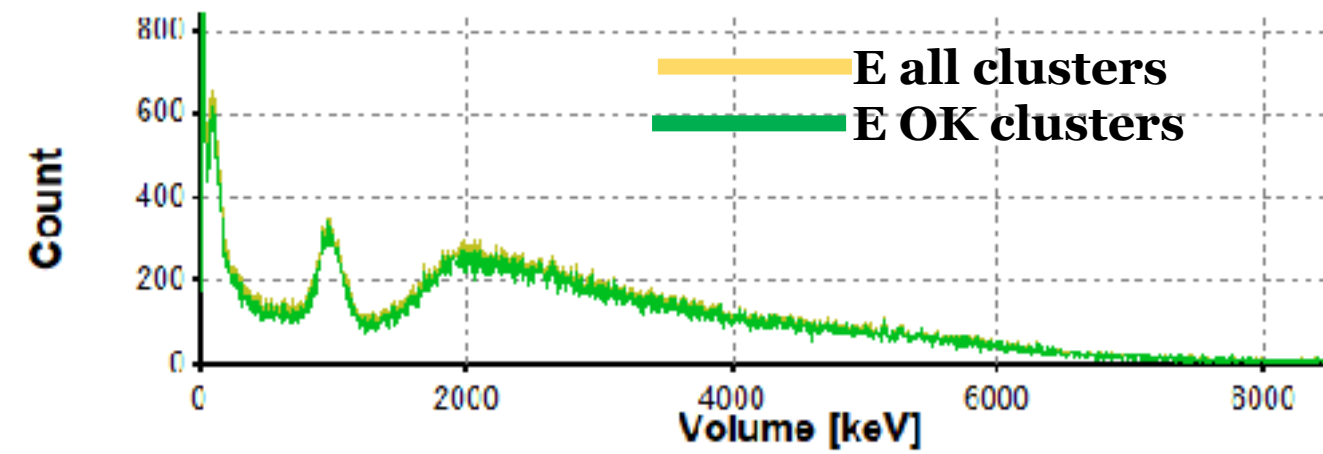
Events A



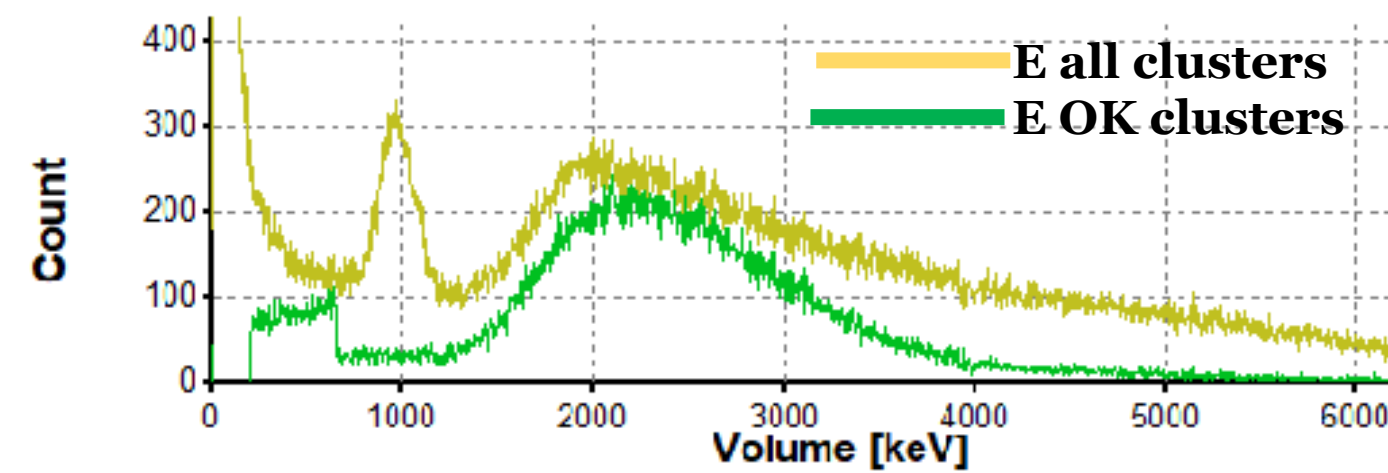
Events B



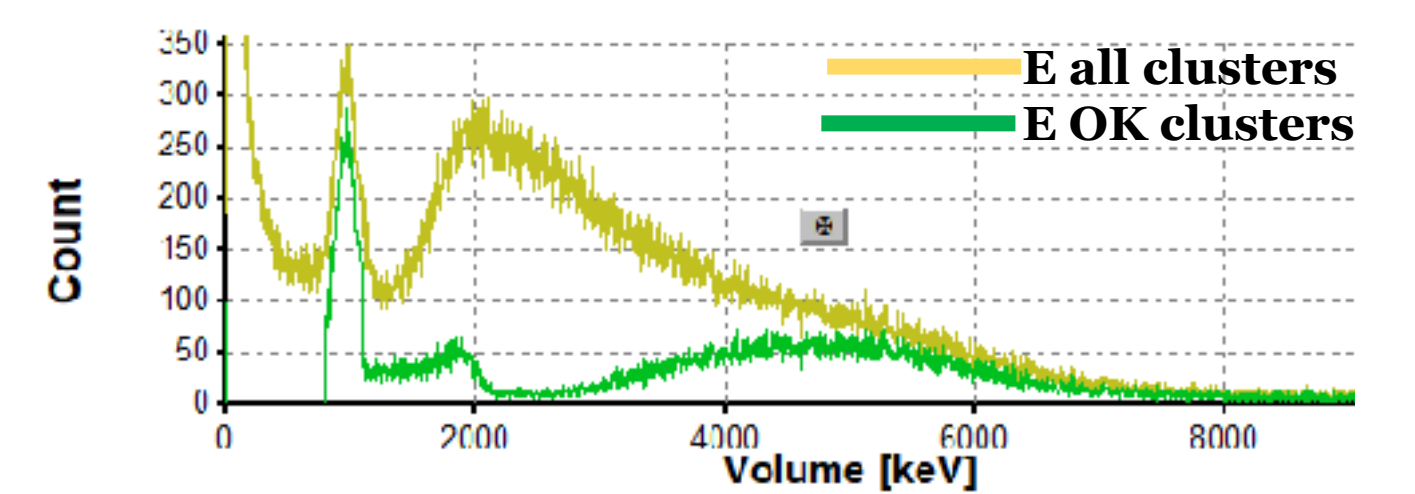
Cluster Energy distribution



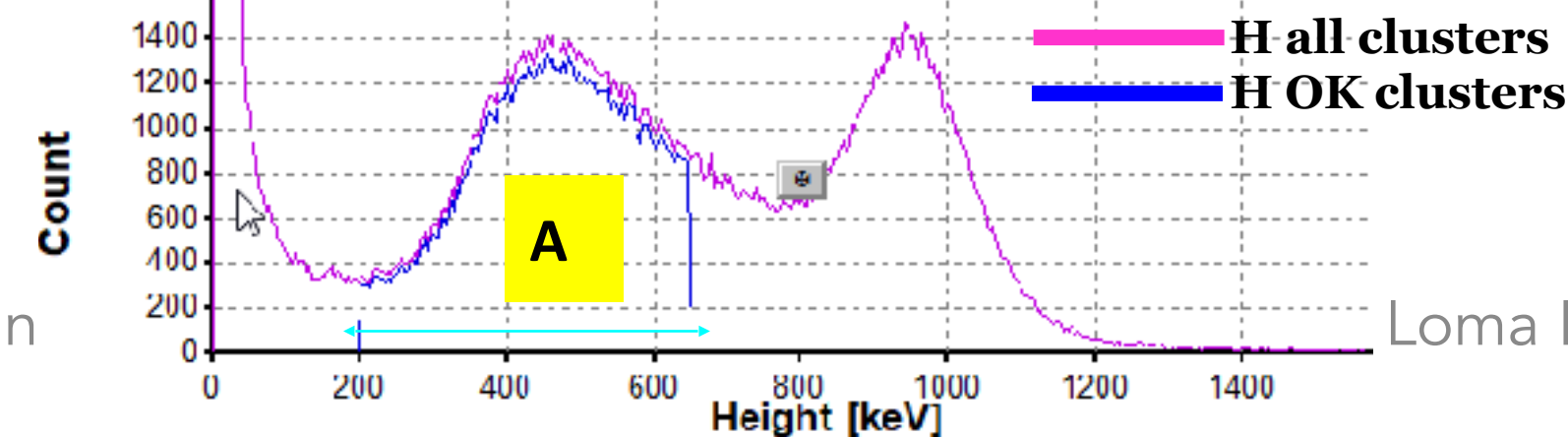
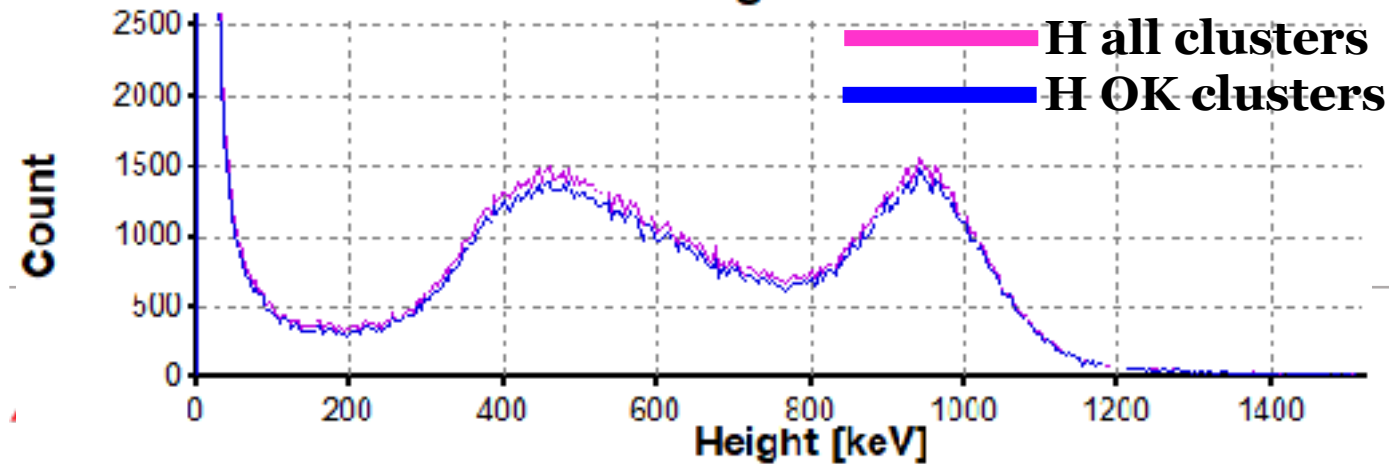
Cluster Energy distribution



Cluster Energy distribution

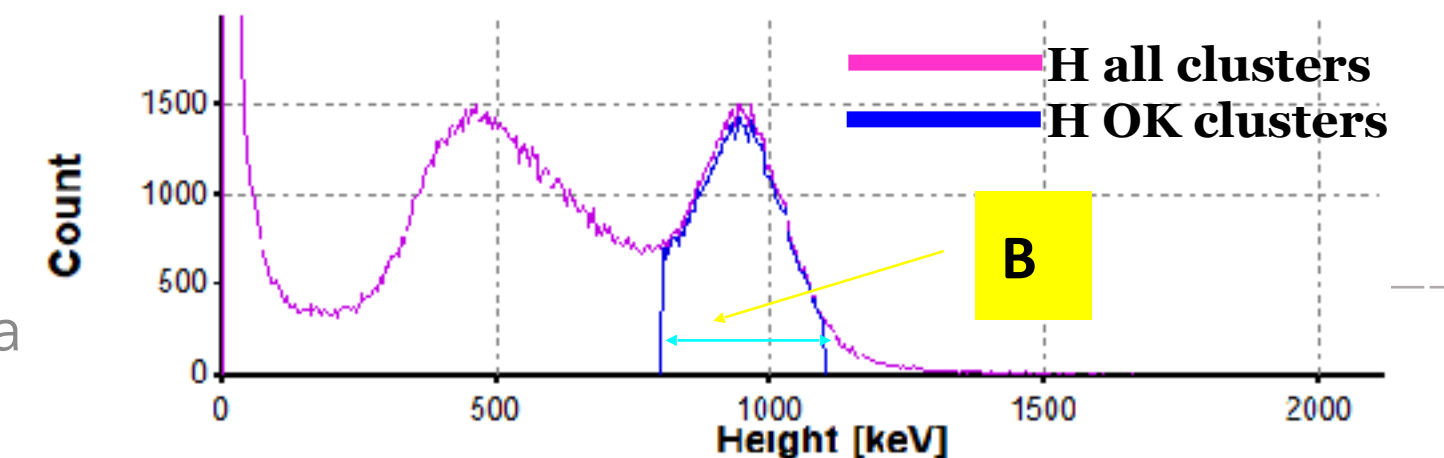


Cluster height distribution



Cristin

Loma Linda

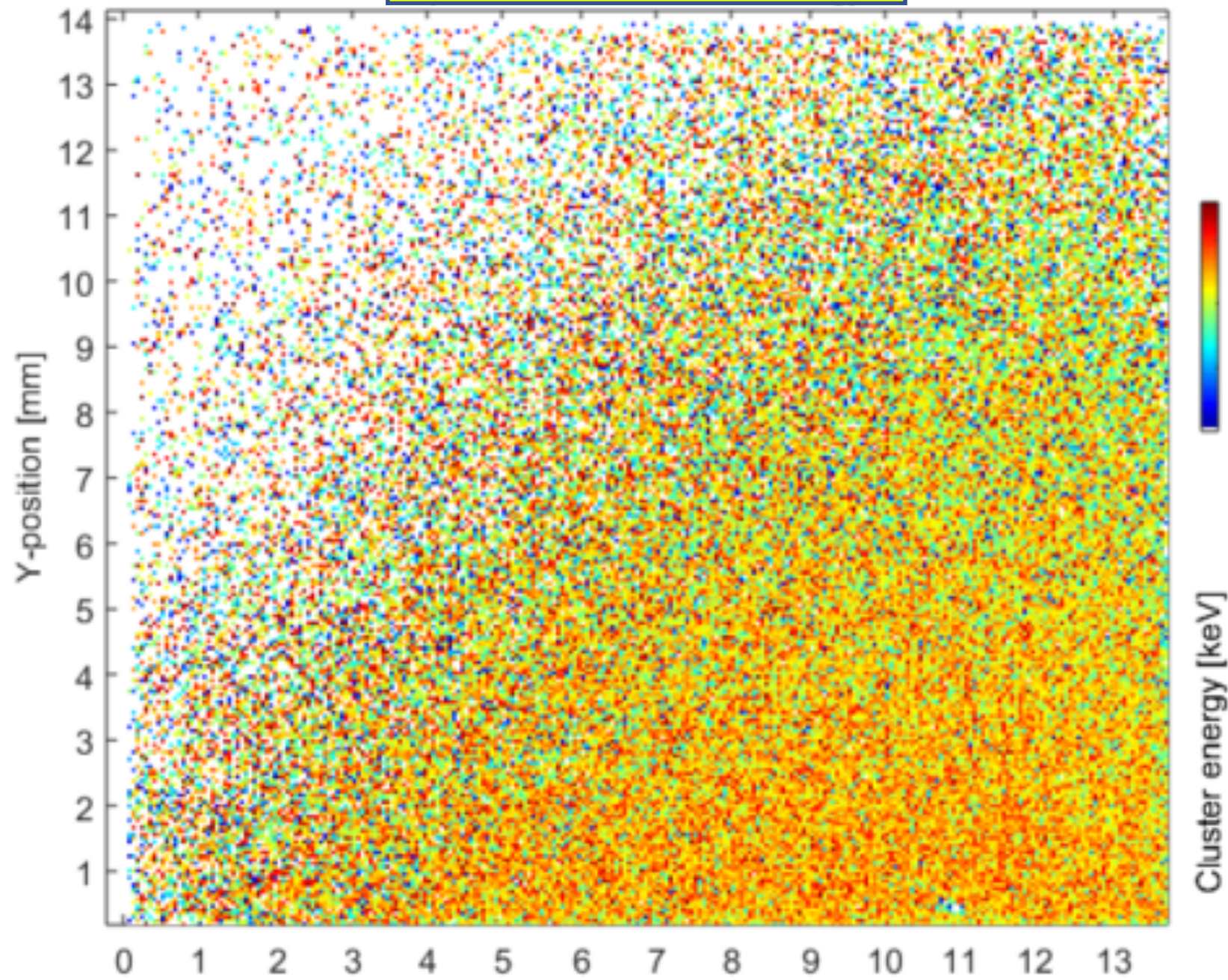




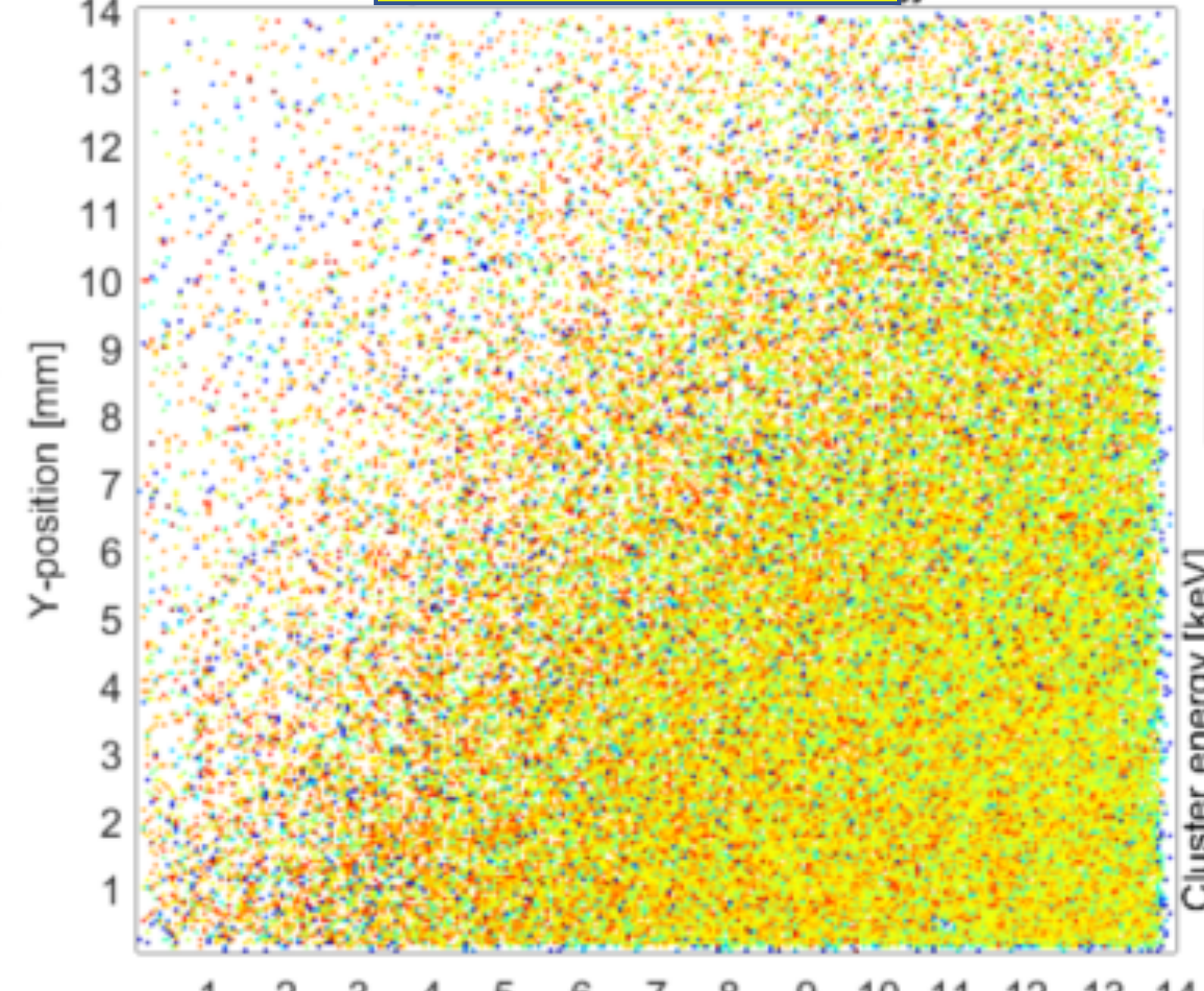
# Spatial distribution of events Energy (deposit

Close to the proton beam spot  
Minipix Timepix 300 $\mu$ m Si sensor

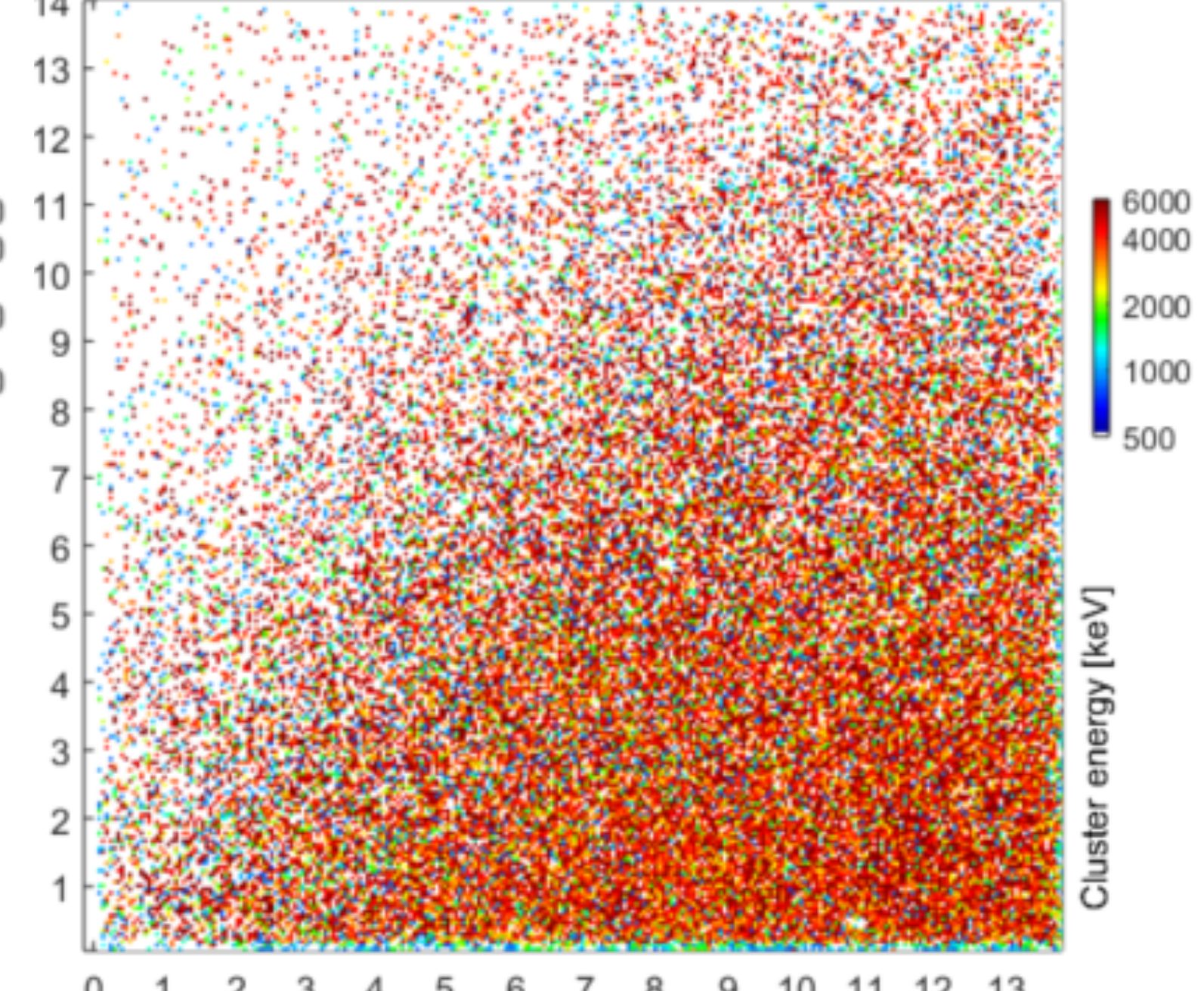
All events



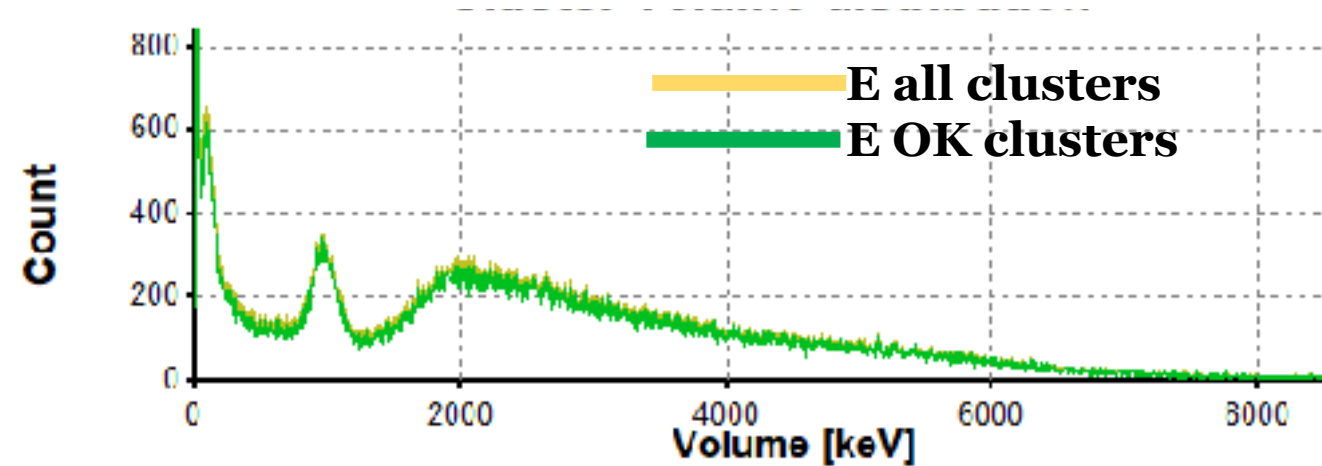
Events A



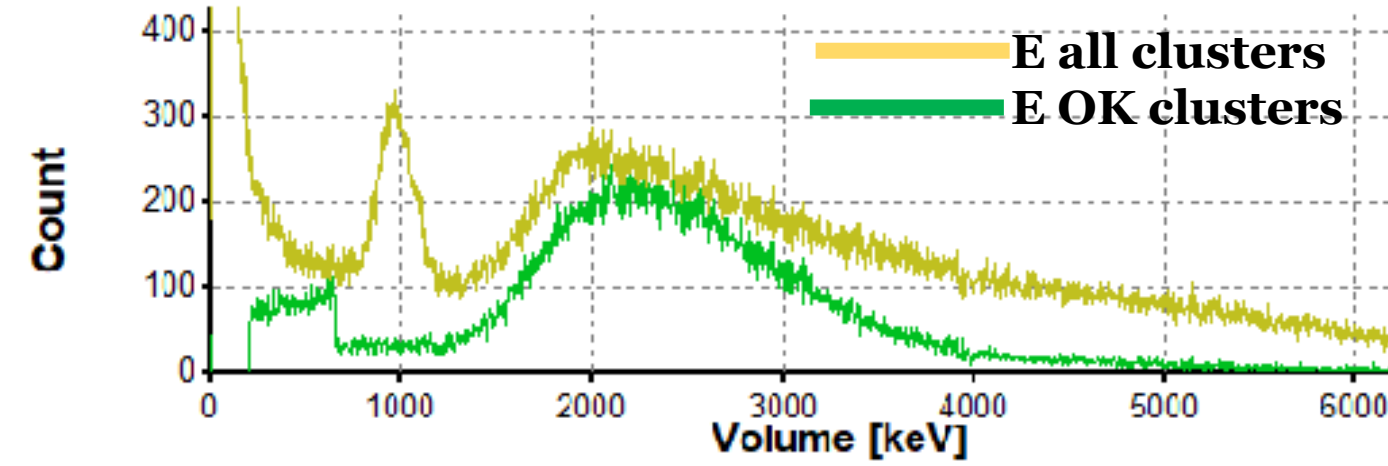
Events B



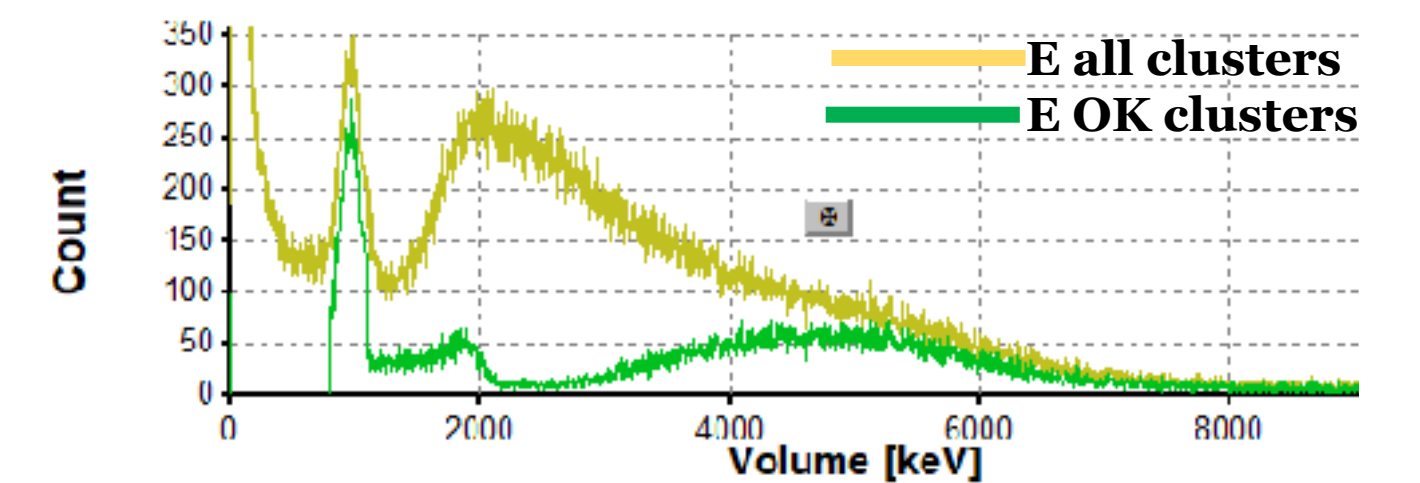
Cluster Energy distribution



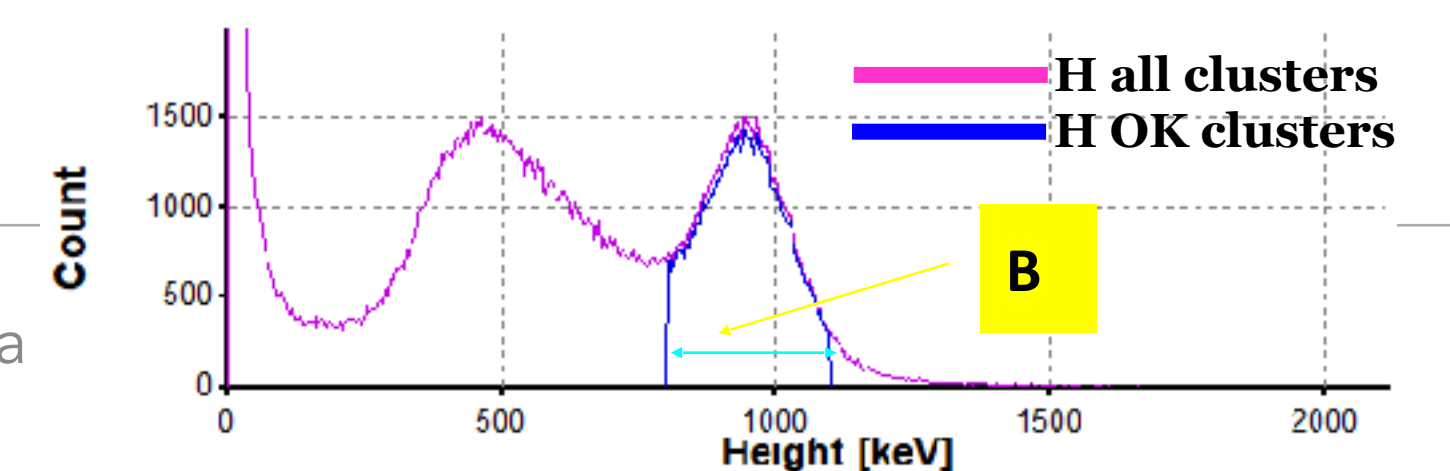
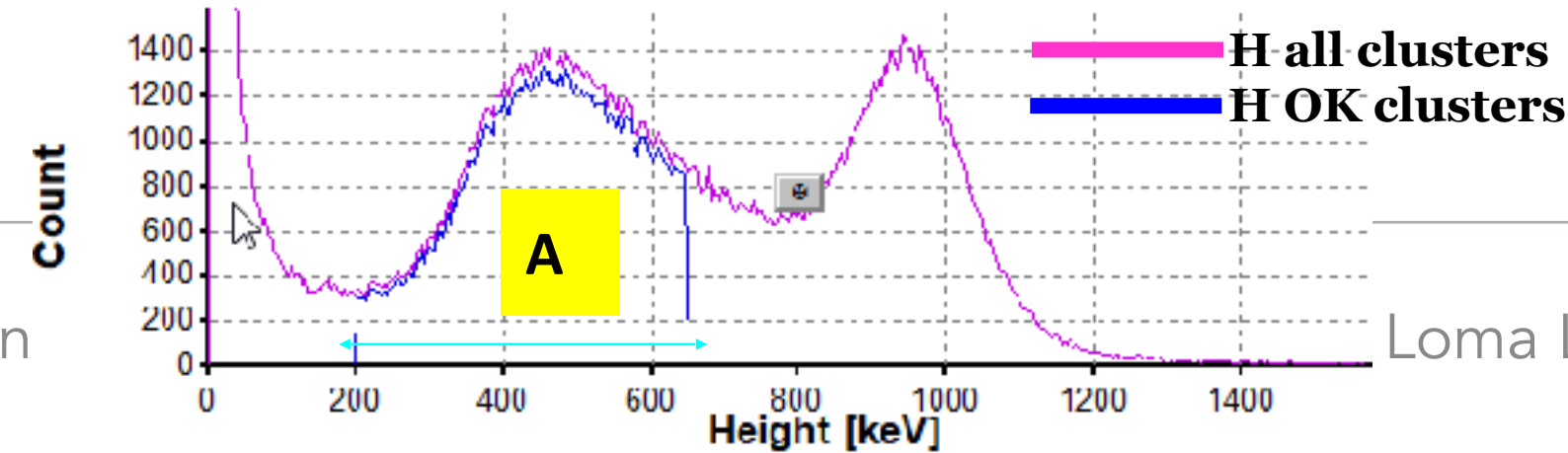
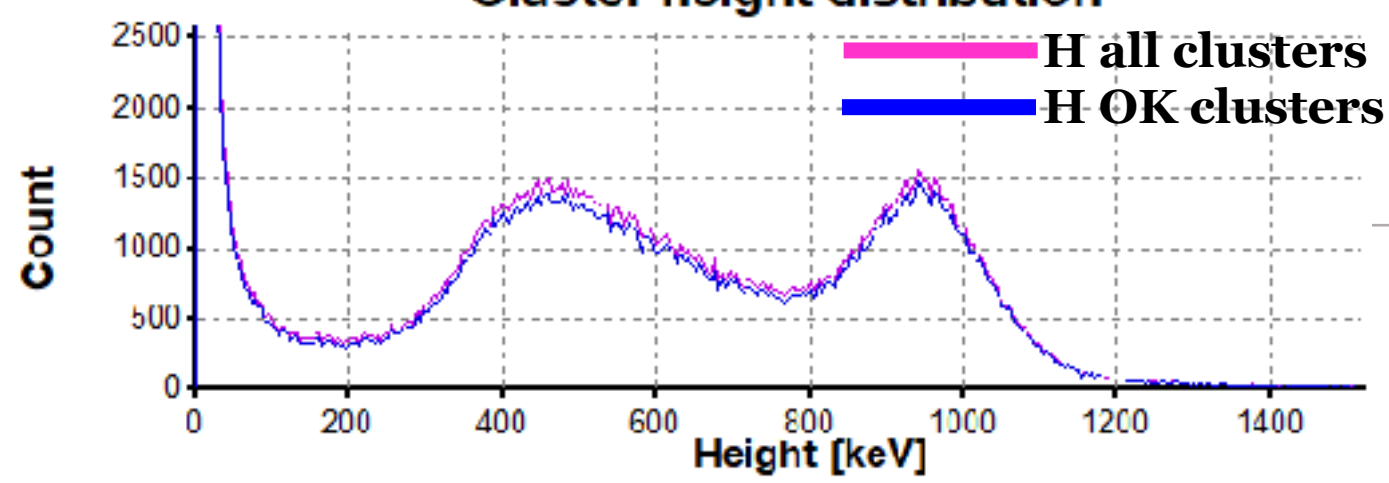
Cluster Energy distribution



Cluster Energy distribution



Cluster height distribution



Cristin

Loma Linda





protons

## 2D visualization of Cluster Energy

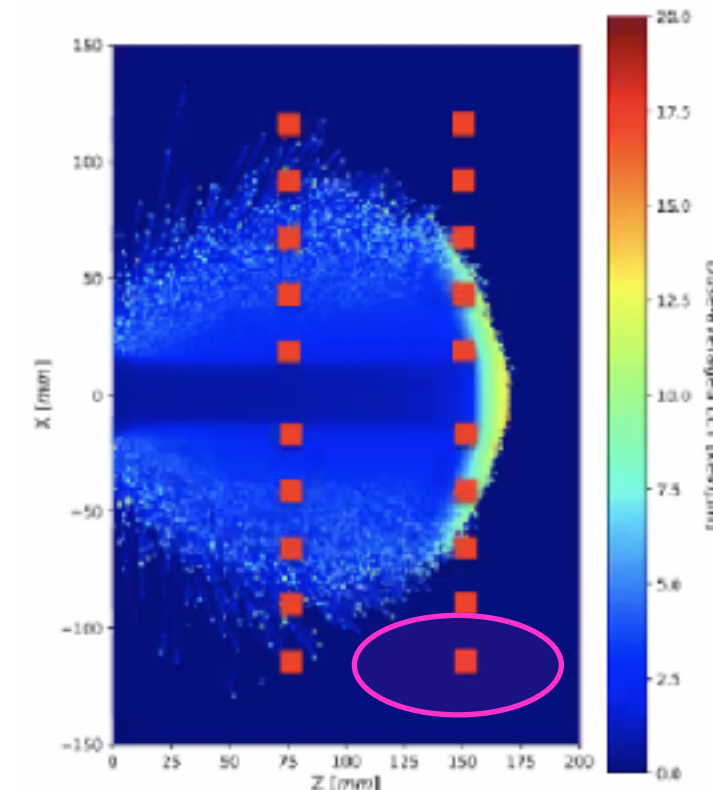
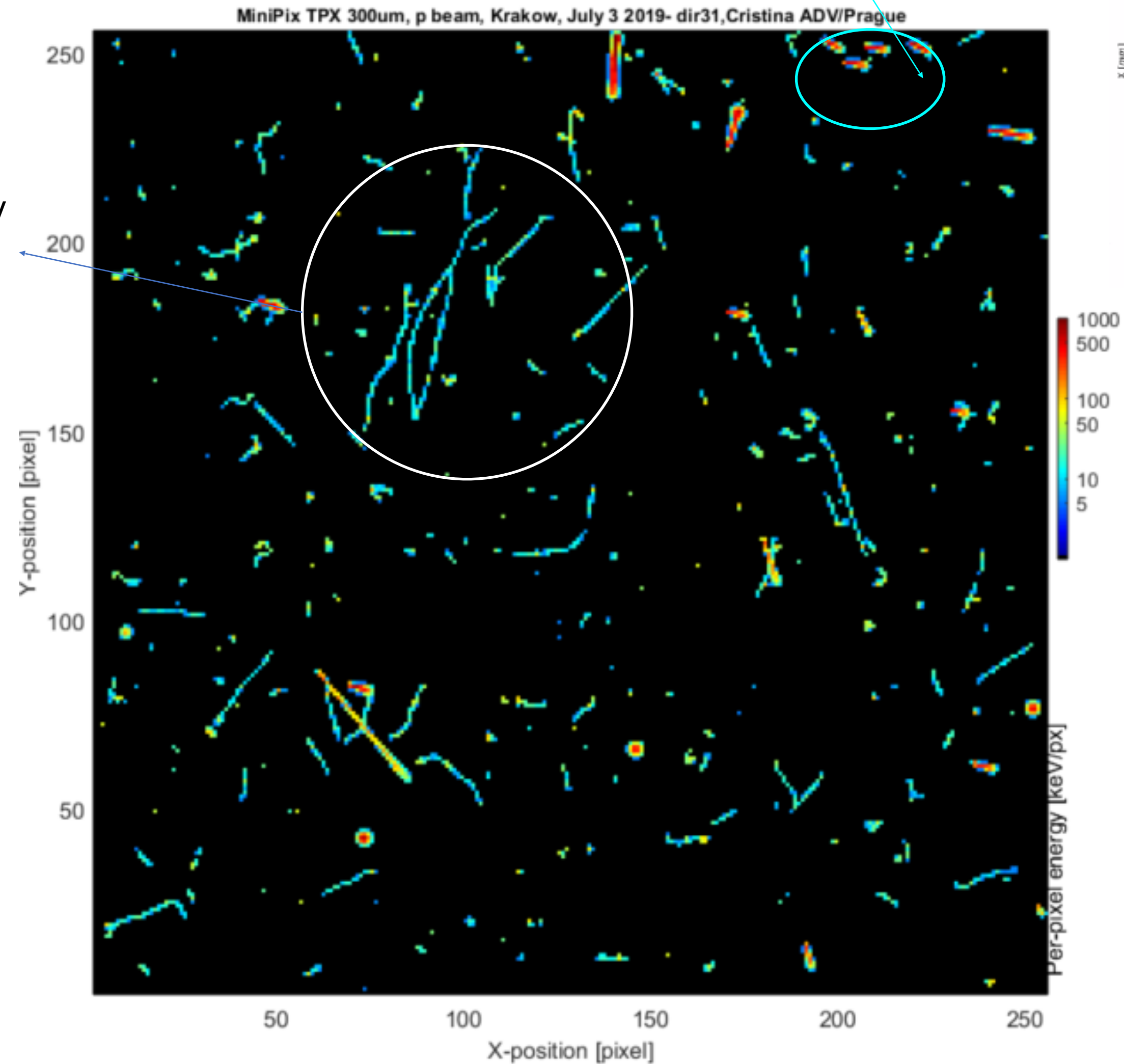
- Detector placed far from the proton beam spot
- Dir 35
- Minipix Timepix Si sensor, 300 µm
- 4 frame
- 256x256 pixels, 14 mm x 14 mm
- Per-Pixel energy deposited
- Mixed field

**All events** All data no filters

**Events A** Height filter **1 to 11 keV**  
for the 1<sup>st</sup> peak

**Events B** Height filter **12 to 200 keV**  
for the 2<sup>nd</sup> peak

Secondary particles







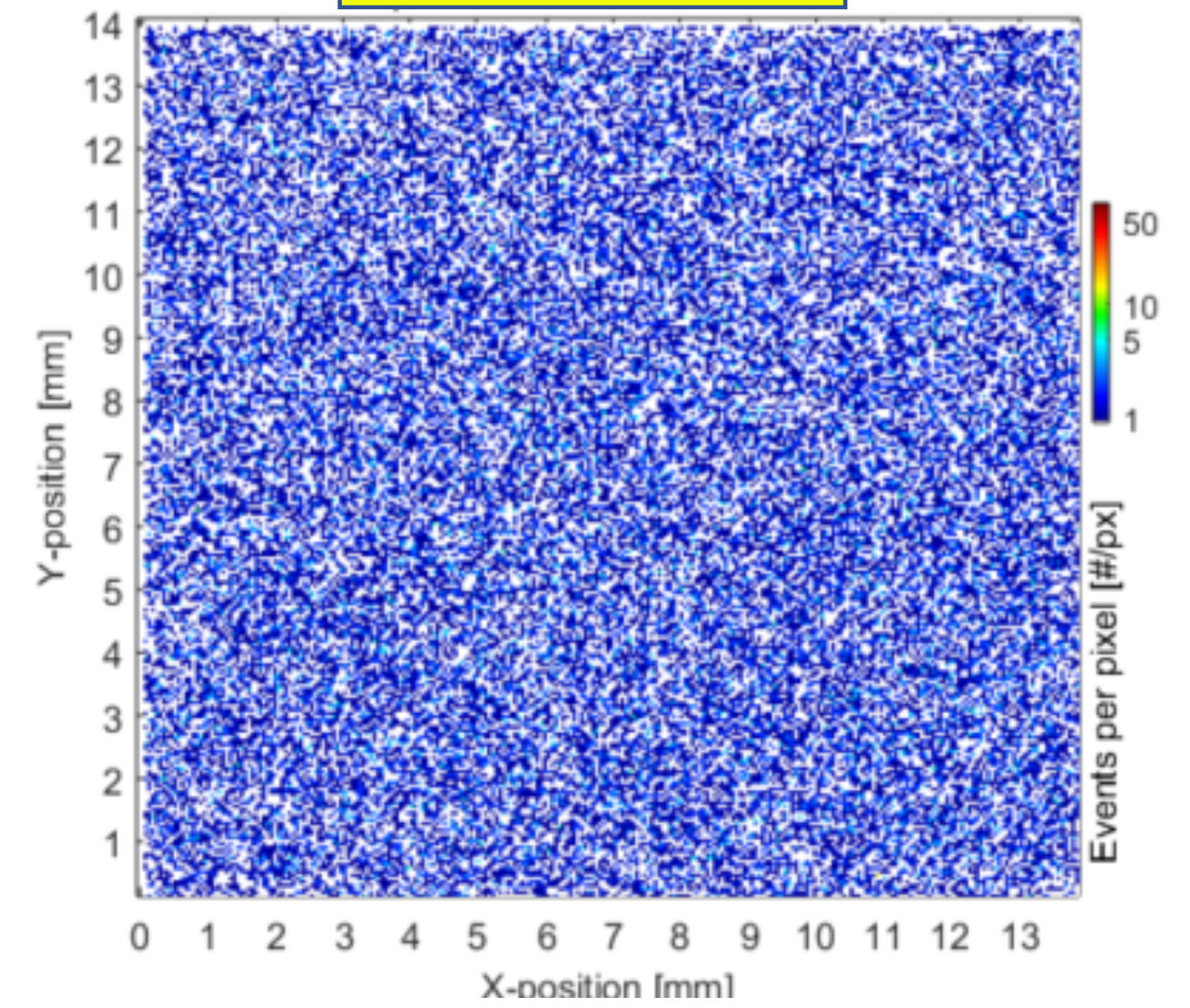
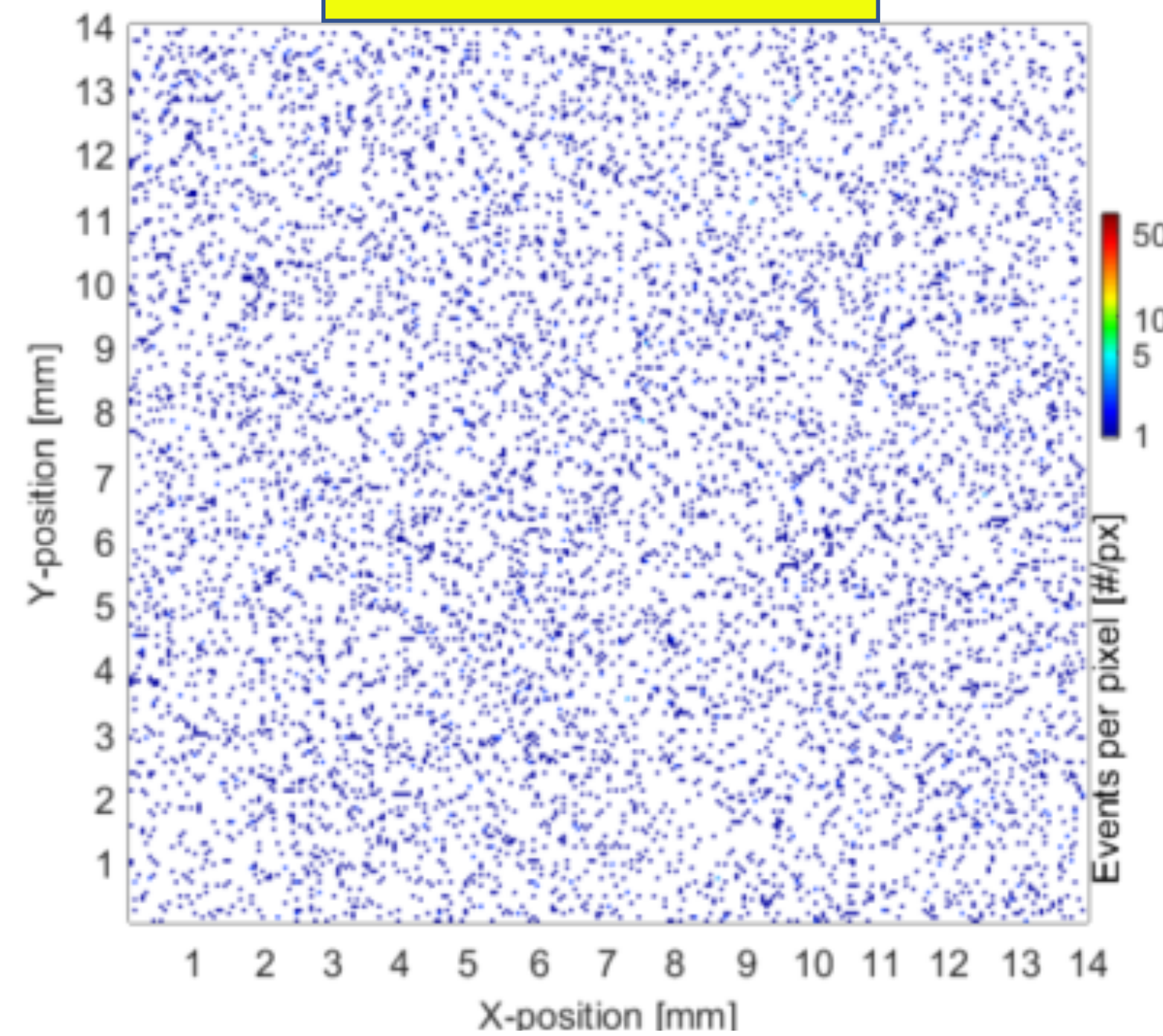
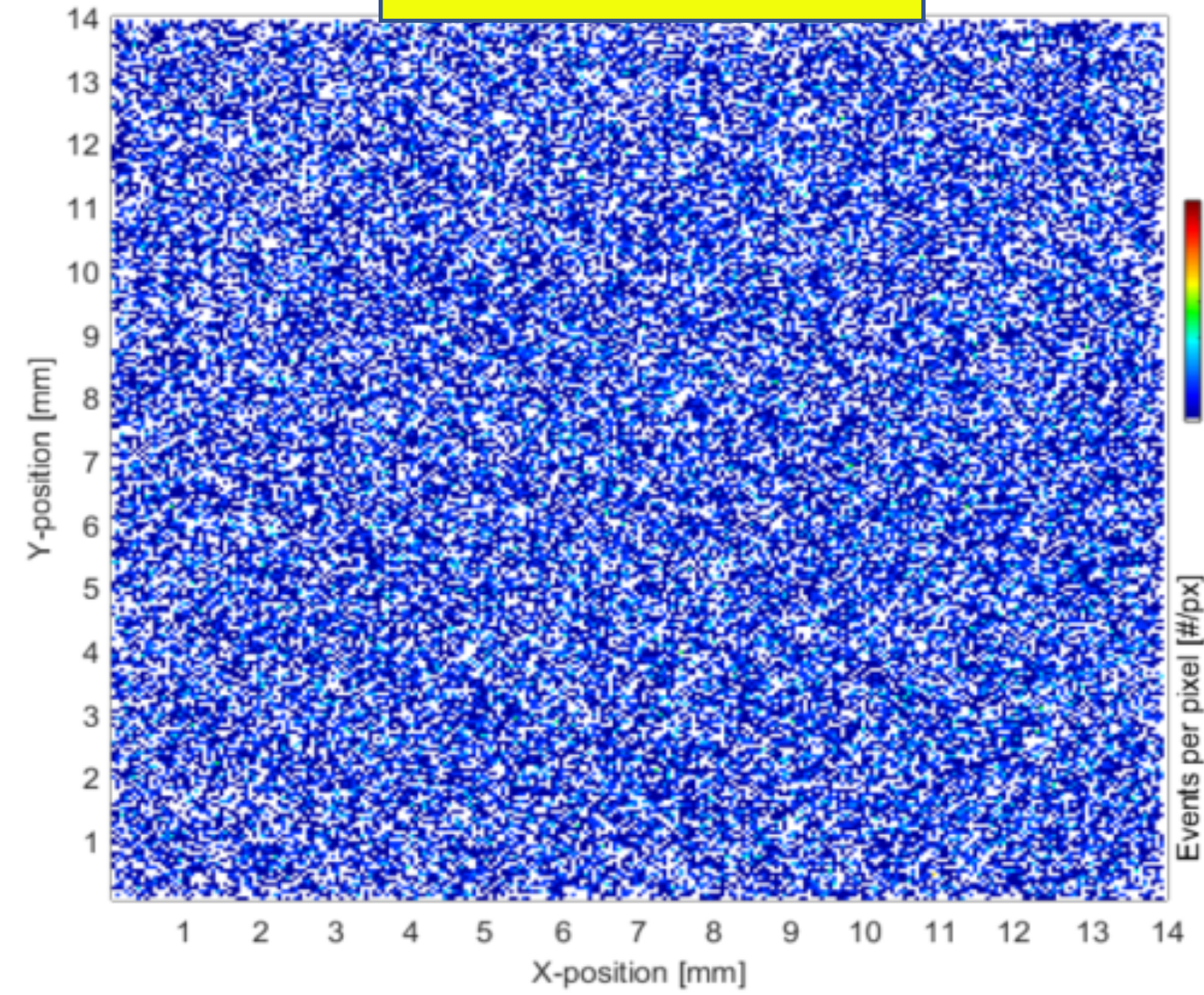
# Spatial distribution of Event counts

Far from the proton beam spot  
Minipix Timepix 300 $\mu$ m Si sensor

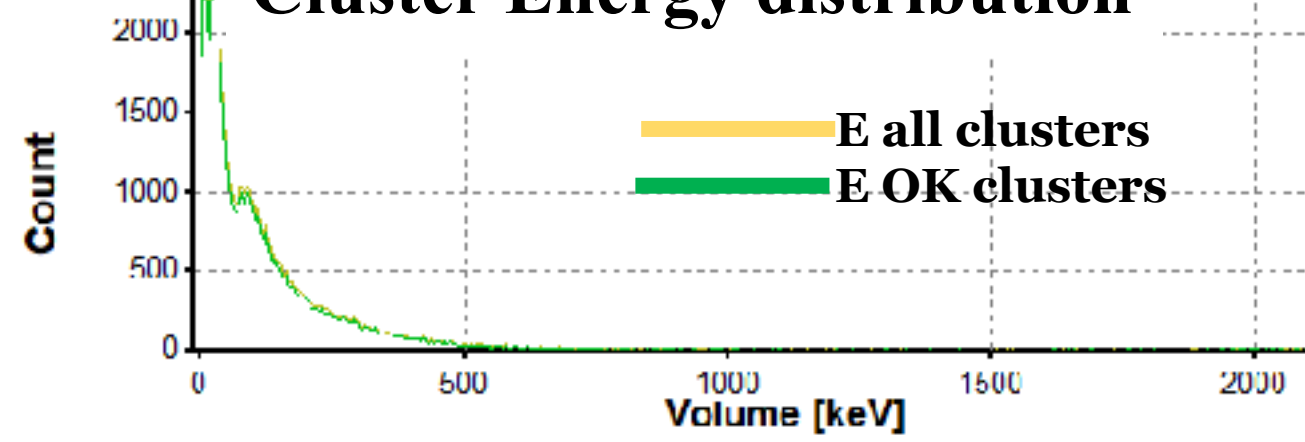
All events

Events A

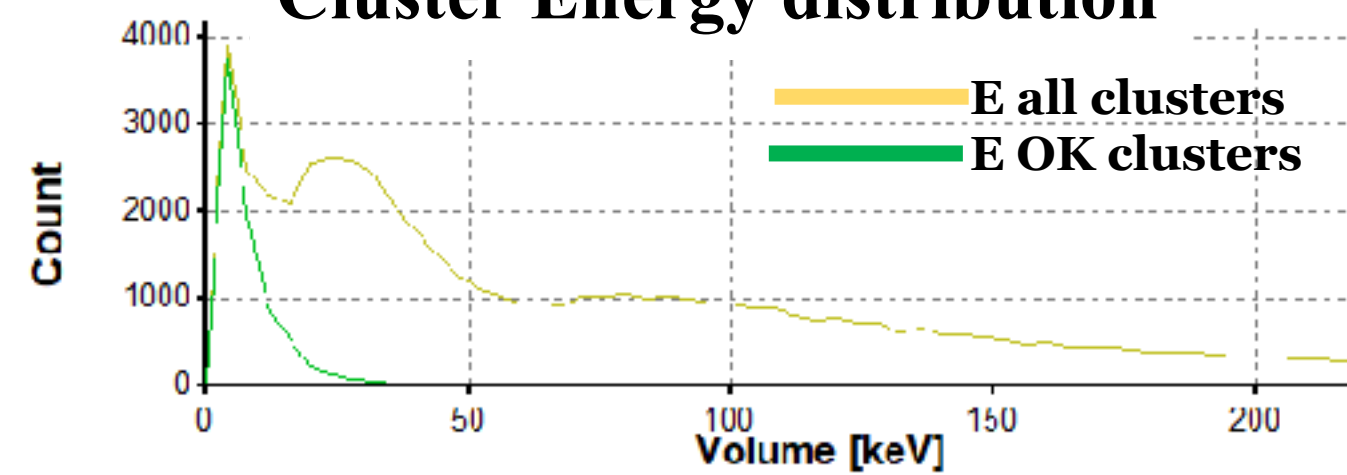
Events B



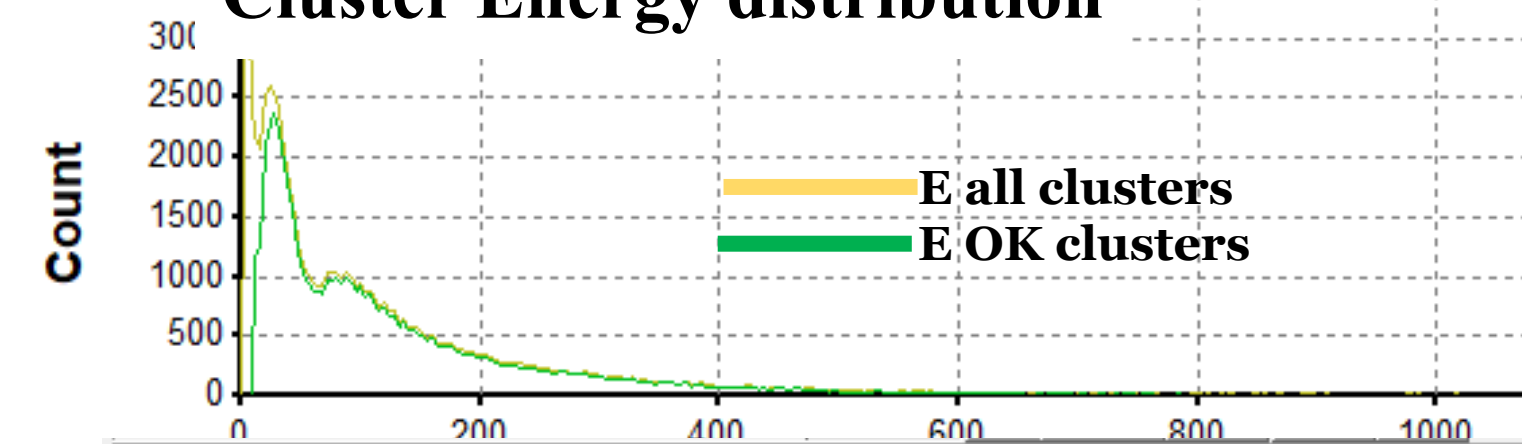
Cluster Energy distribution



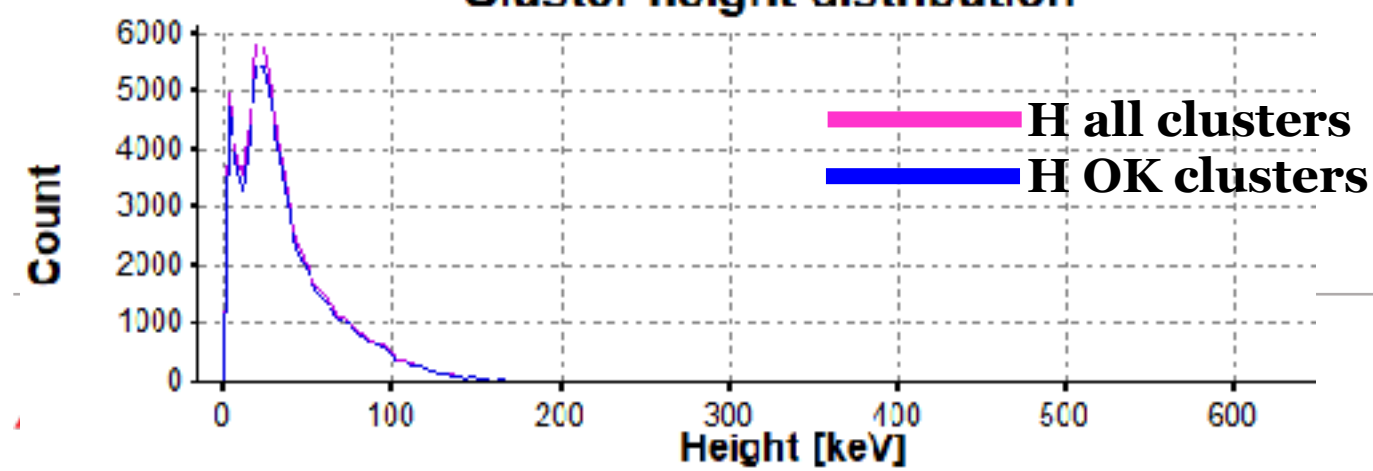
Cluster Energy distribution



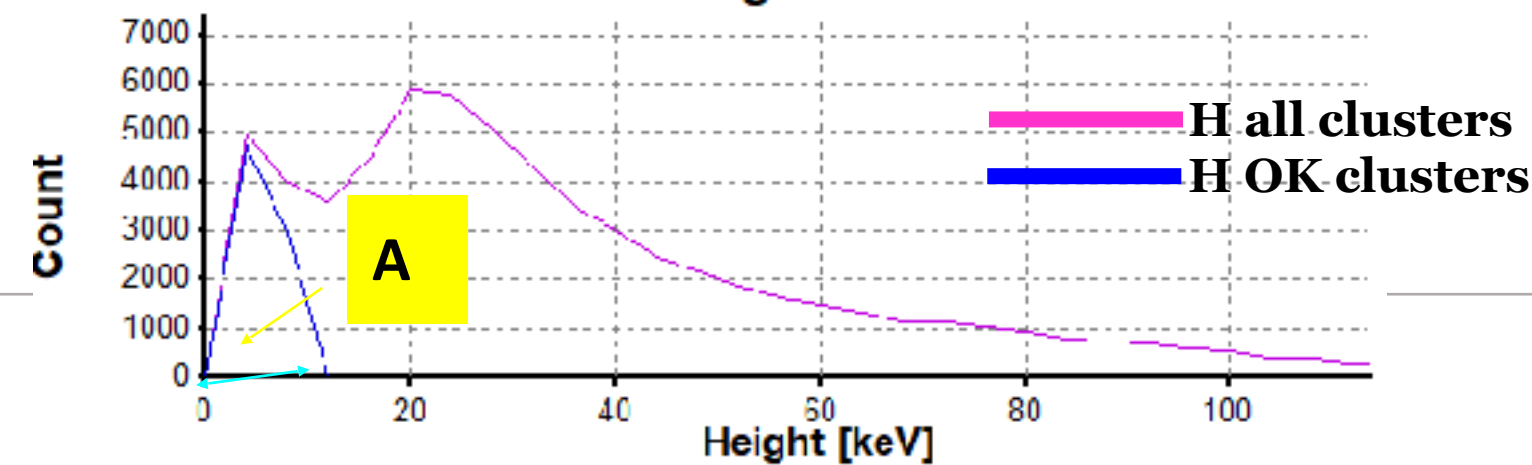
Cluster Energy distribution



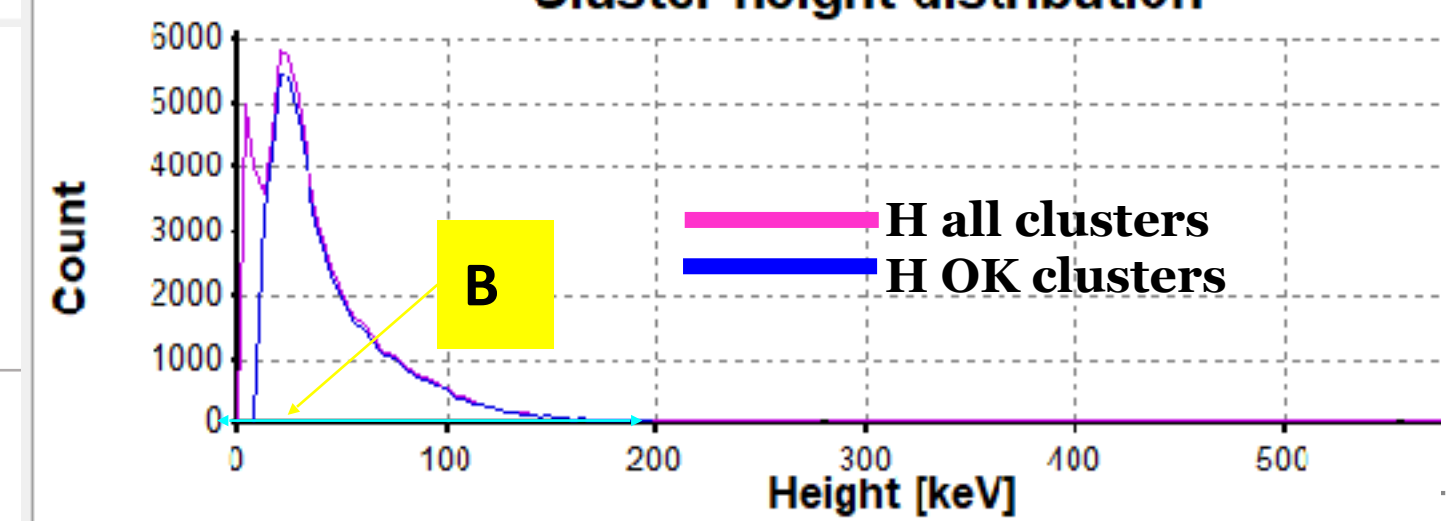
Cluster height distribution



Cluster height distribution



Cluster height distribution

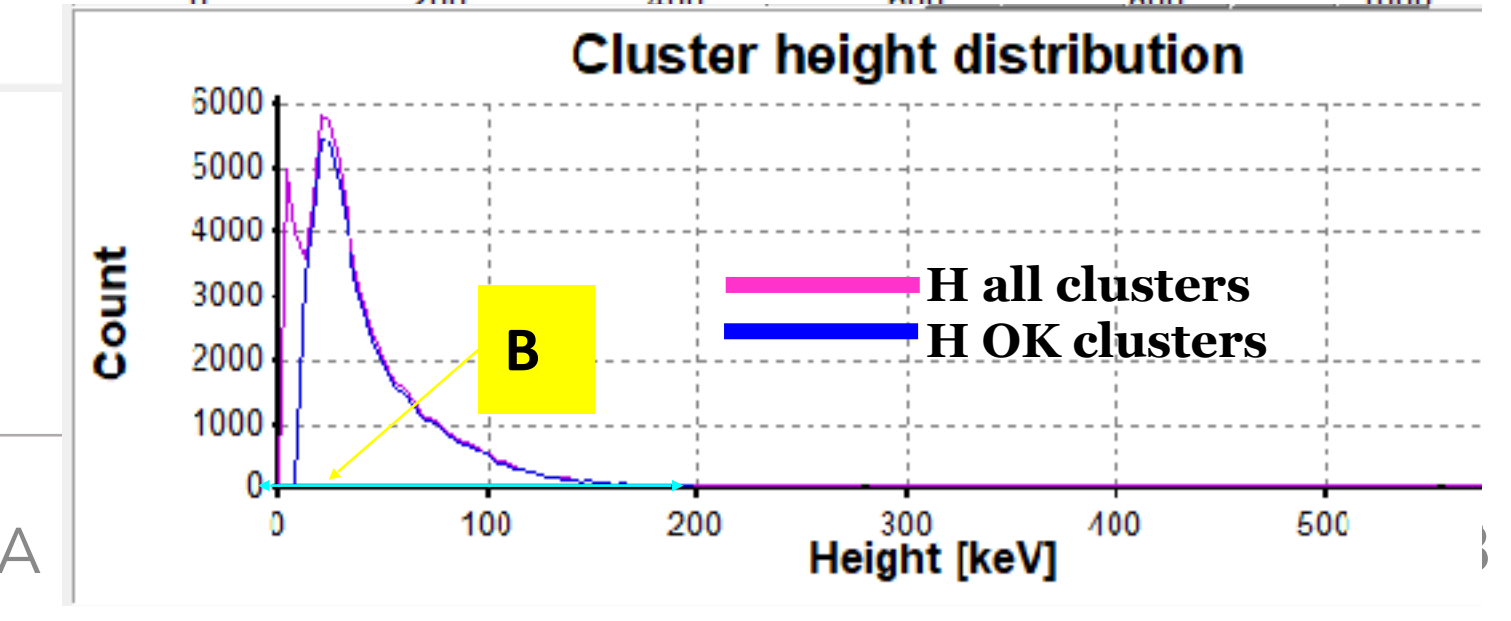
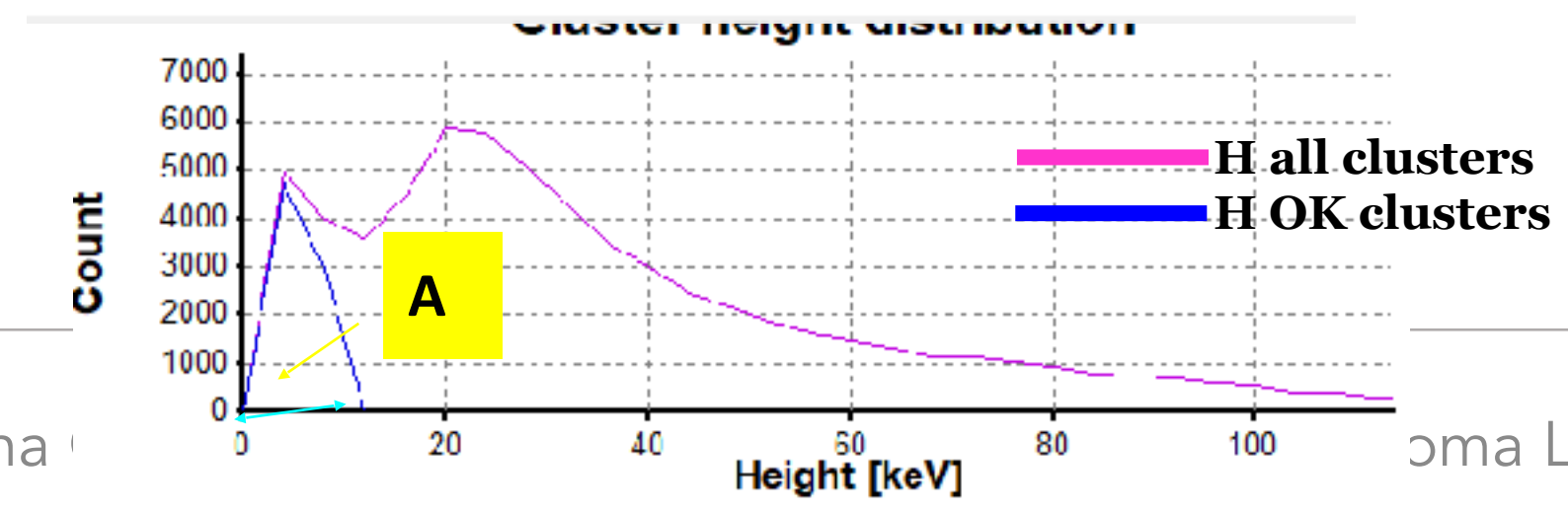
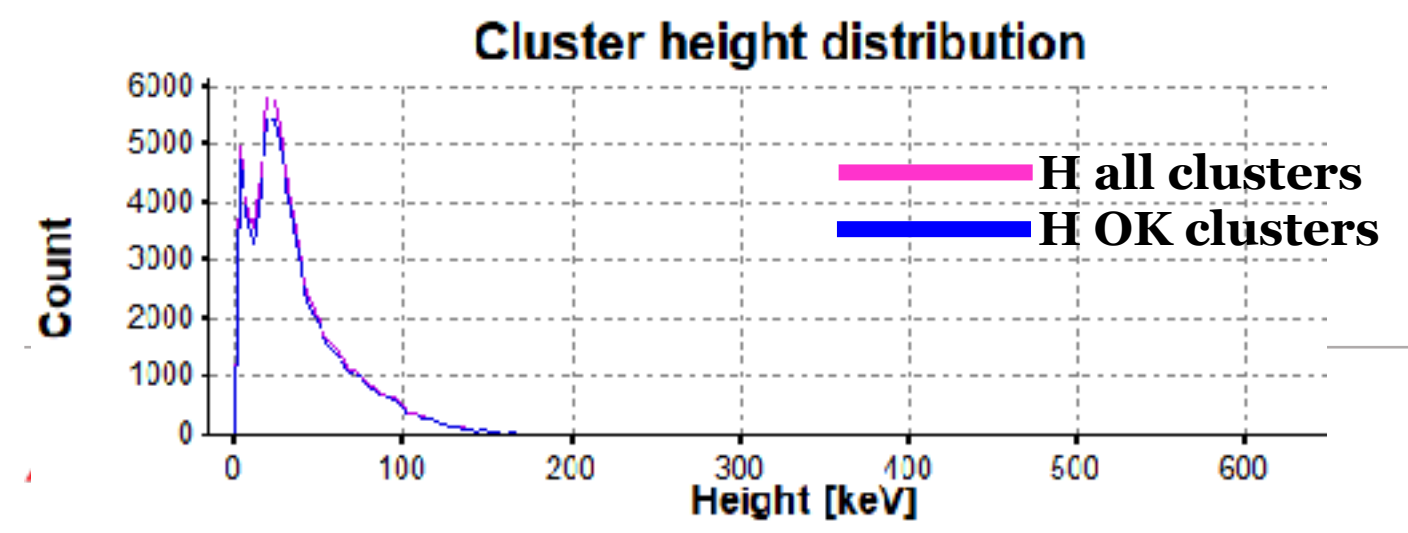
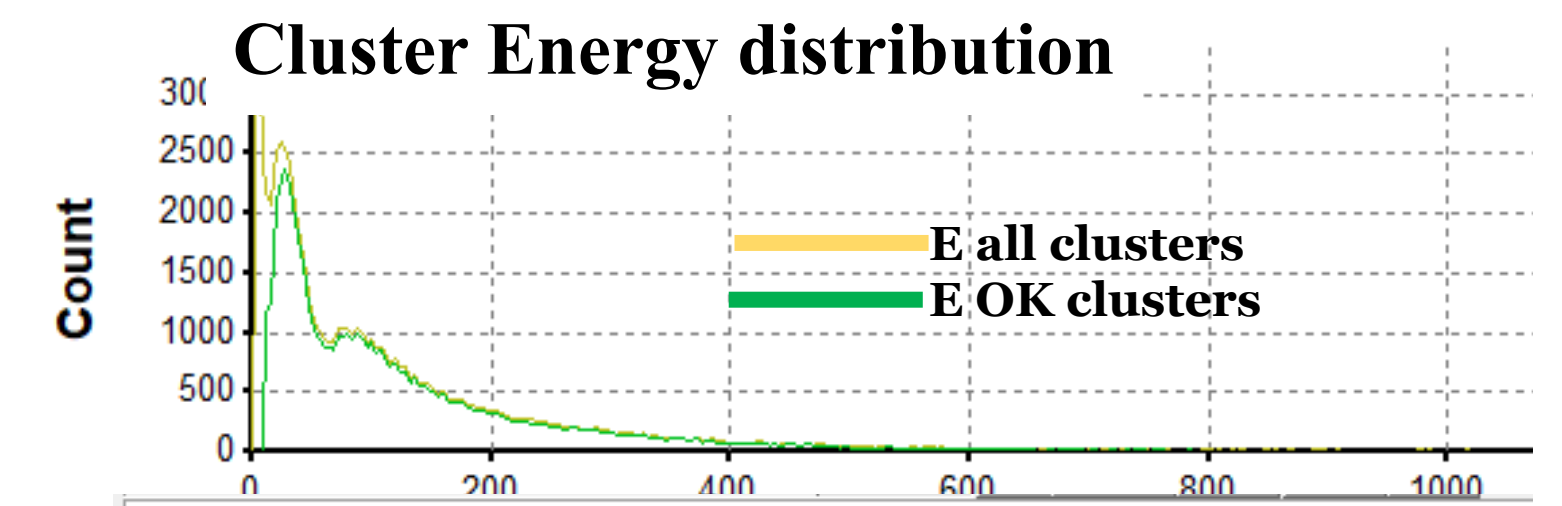
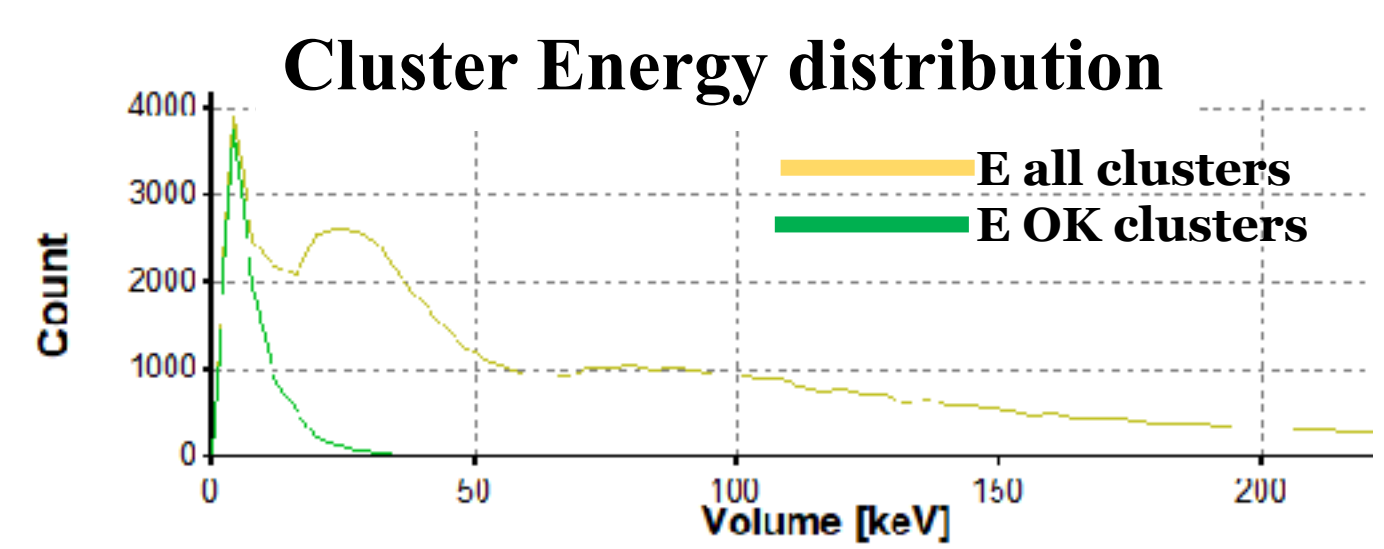
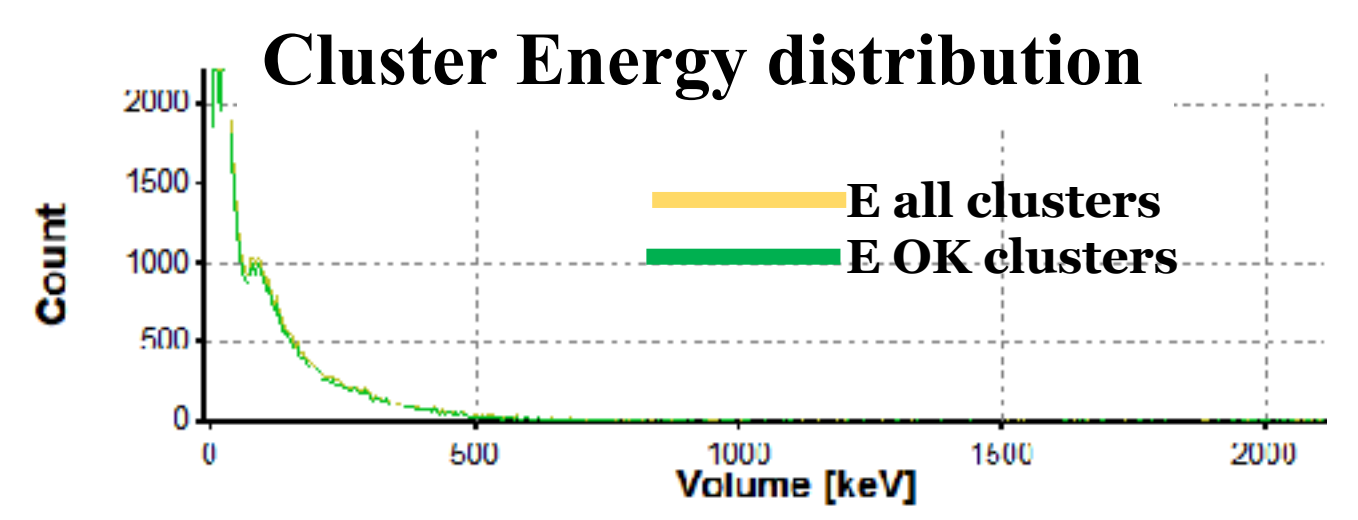
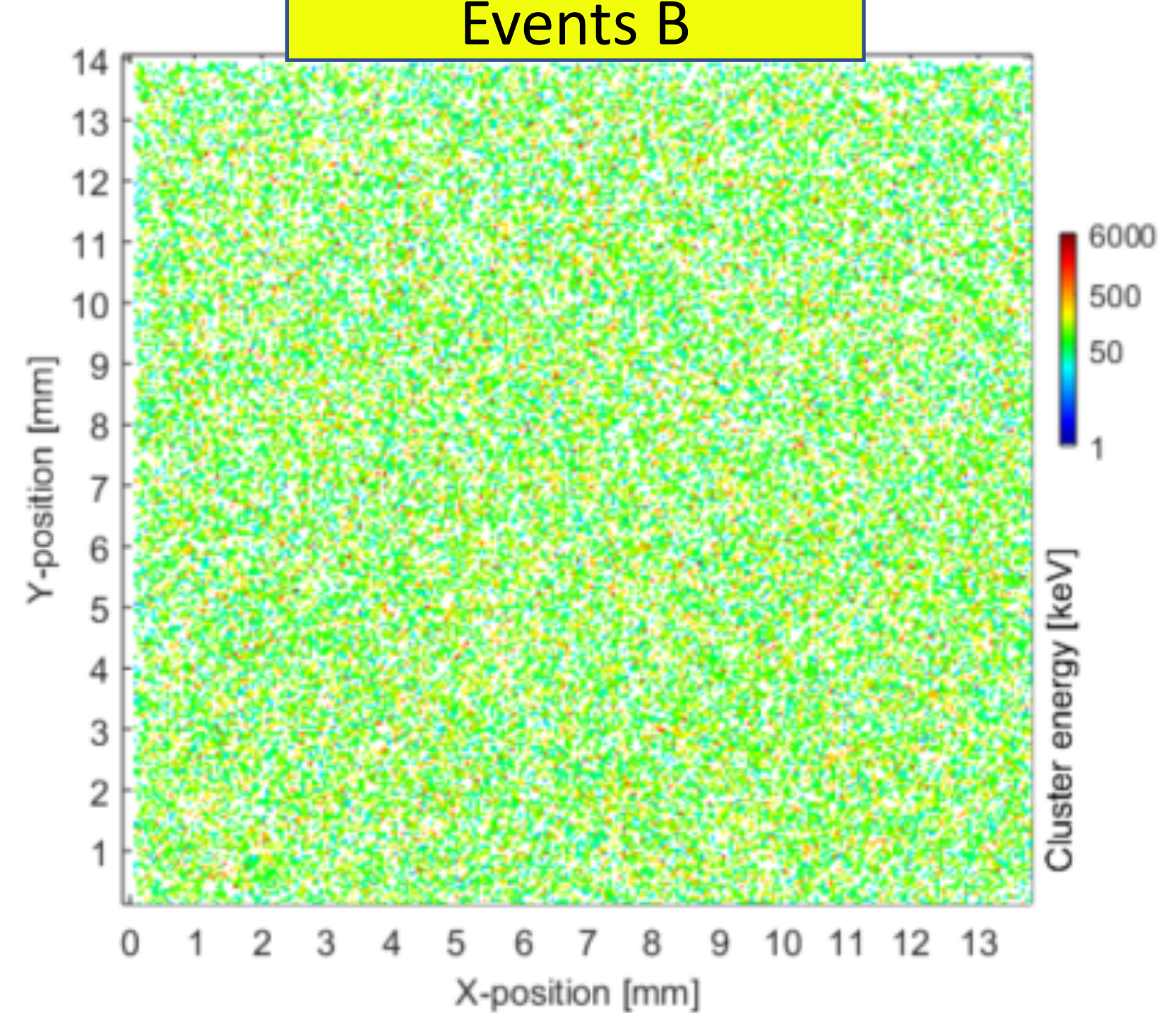
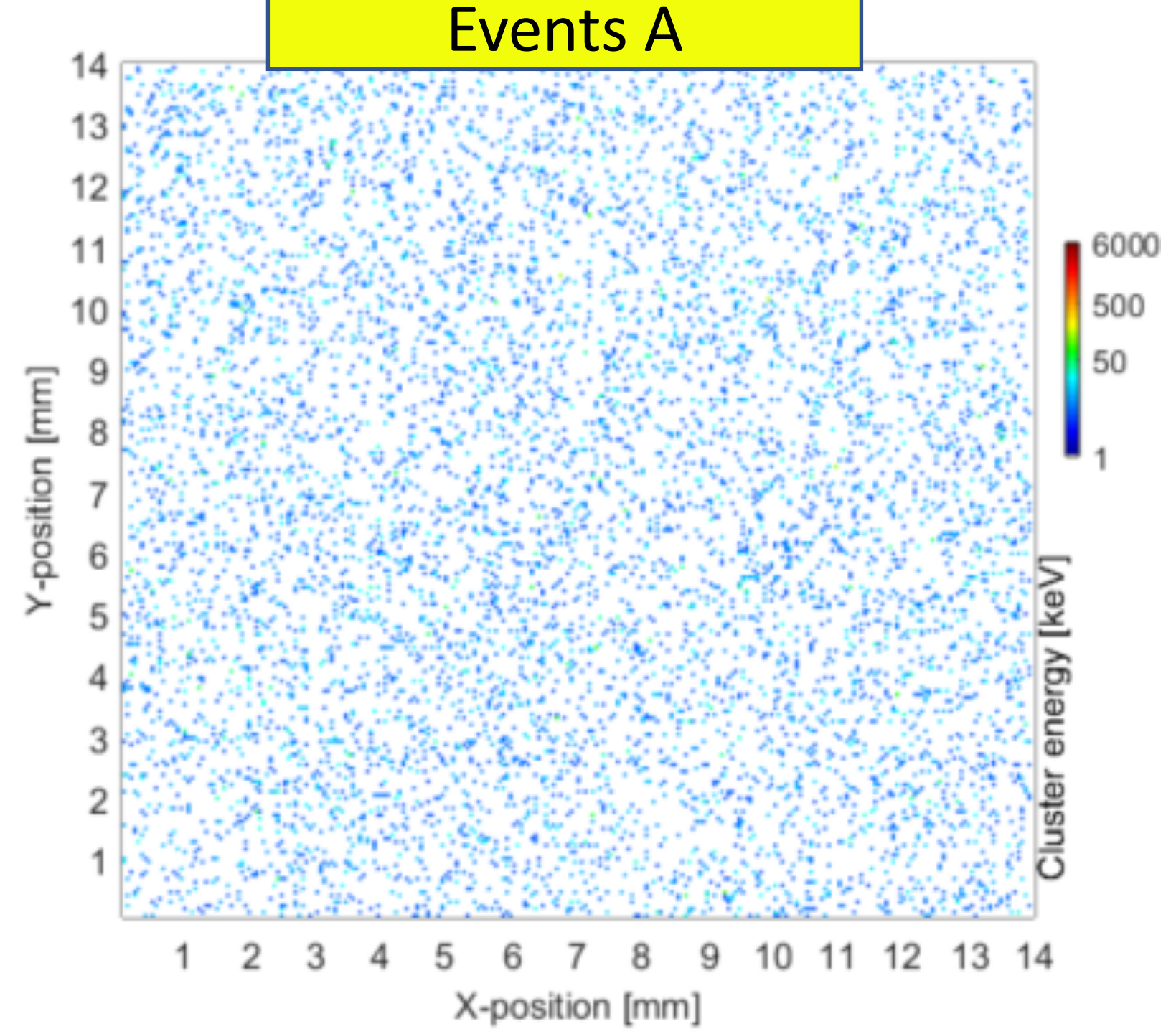
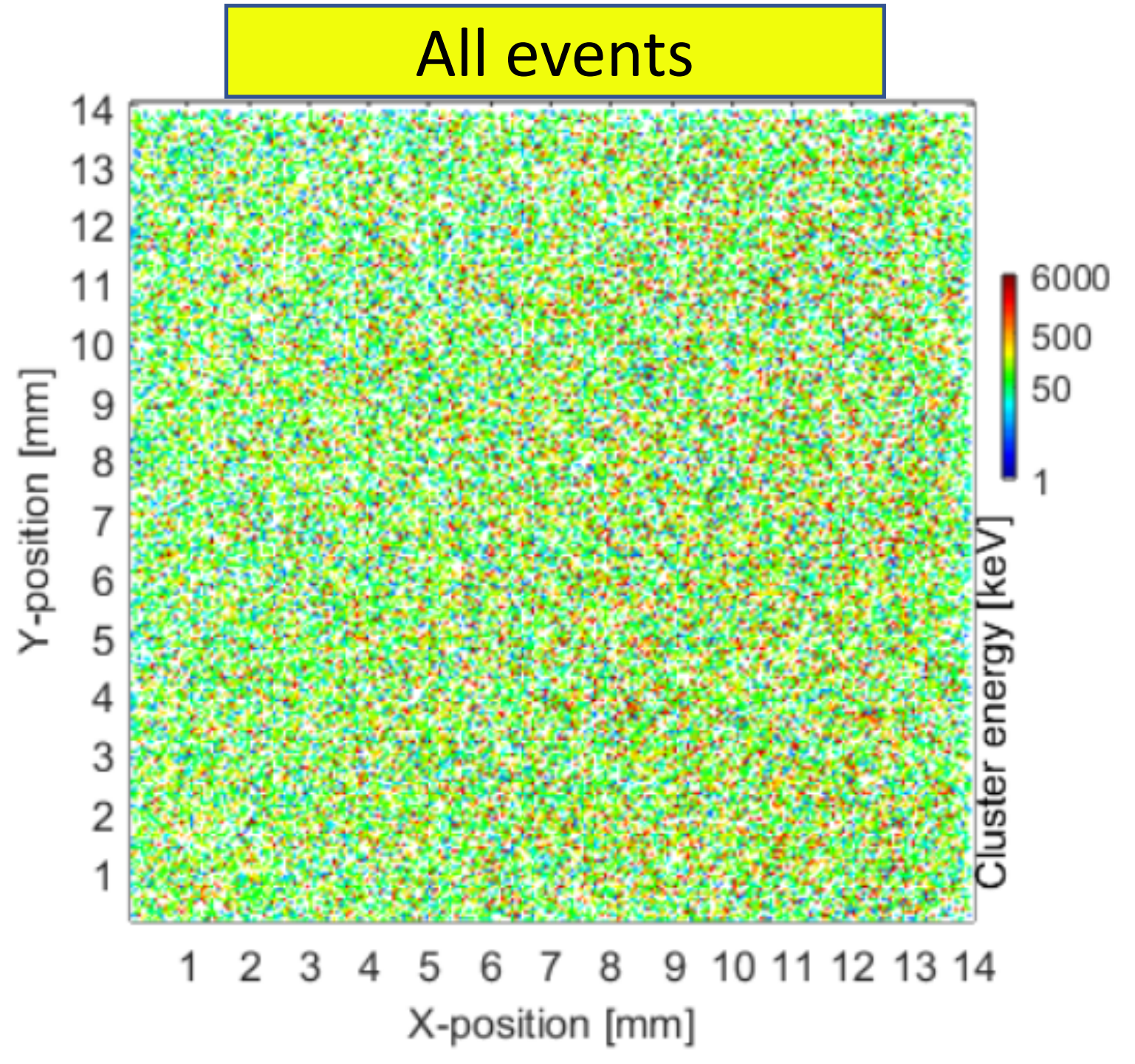






# Spatial distribution of Event Energy (deposition)

Far from the p beam spot  
Minipix Timepix 300 $\mu$ m Si



Cristina

oma Linda USA



**Commissioning**

**Input:**

Facility commissioning measurements (in 10 MeV steps)

**Phase space library characterisation:**  
(in 10 MeV steps)

**Step 1: Fitting emittance parameters**  
( $\epsilon_x, \alpha_x, \beta_x, \epsilon_y, \alpha_y, \beta_y$ )

**Step 2: Optimization of the beam energy (E) and energy spread ( $E_\sigma$ )** **GPU**

**Step 3: Estimation of the the dosimetric calibration factor ( $SF_{MU}$ )**

↑ automated ↓

**Output:**

Phase space library nine parameters:  
 $\epsilon_x, \alpha_x, \beta_x, \epsilon_y, \alpha_y, \beta_y, E, E_\sigma, SF_{MU}$

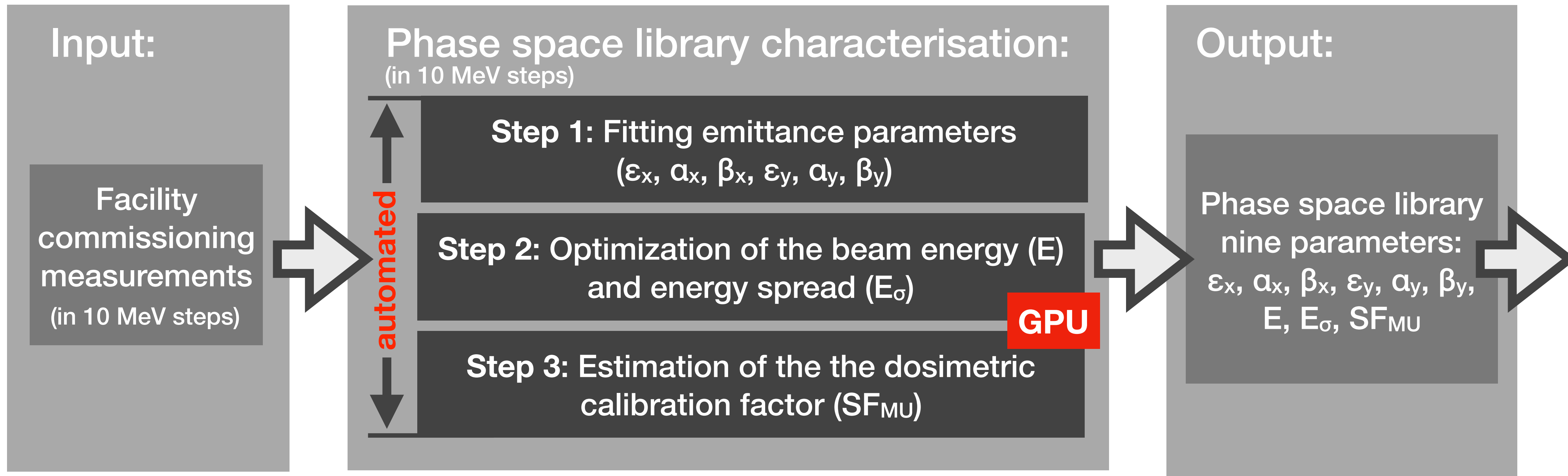
**Validation**

**Input:**

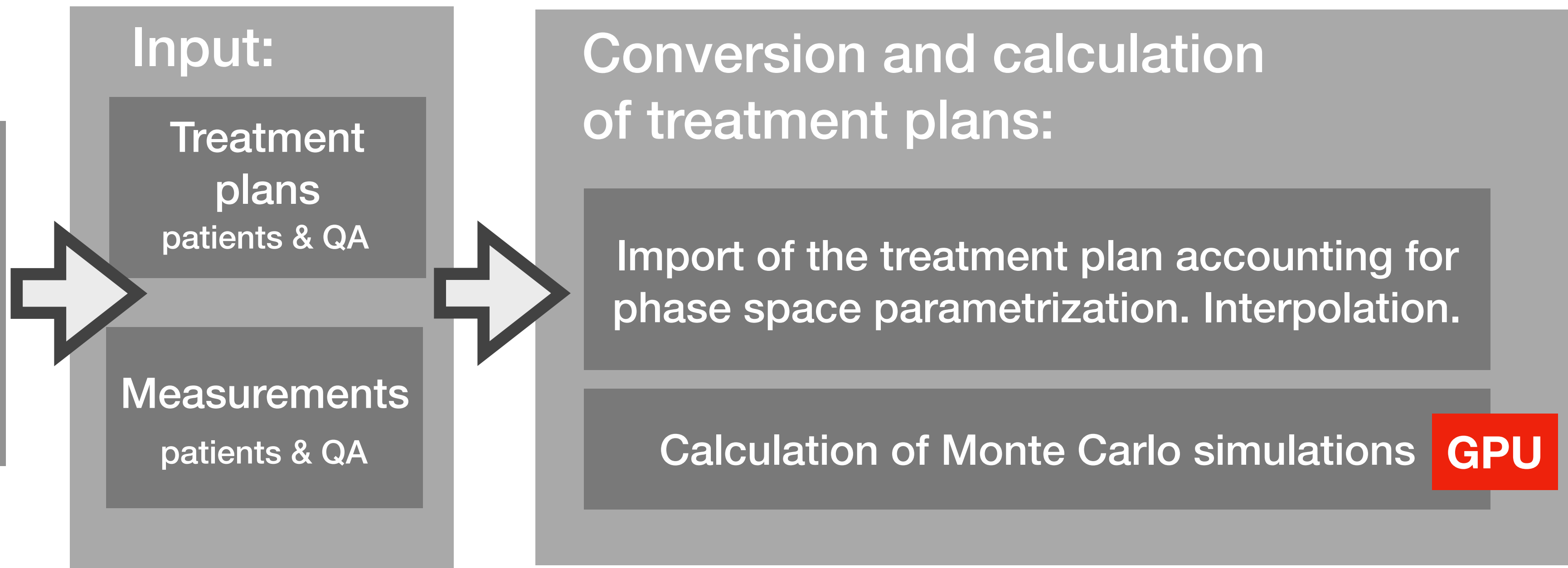
Treatment plans patients & QA

Measurements patients & QA

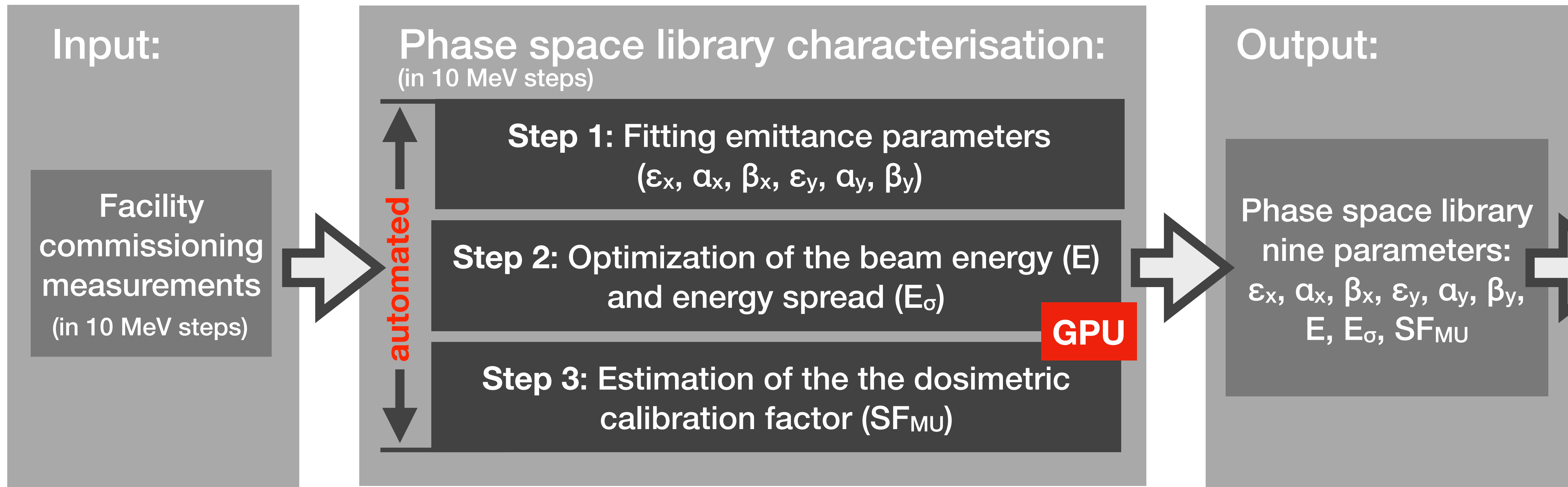
**Commissioning**



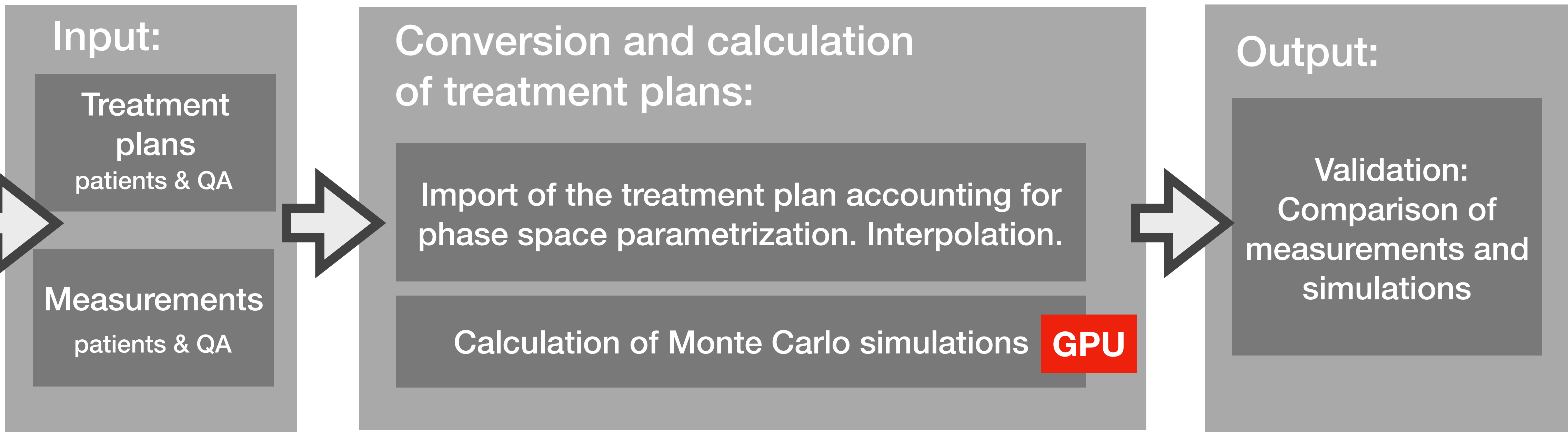
**Validation**



**Commissioning**

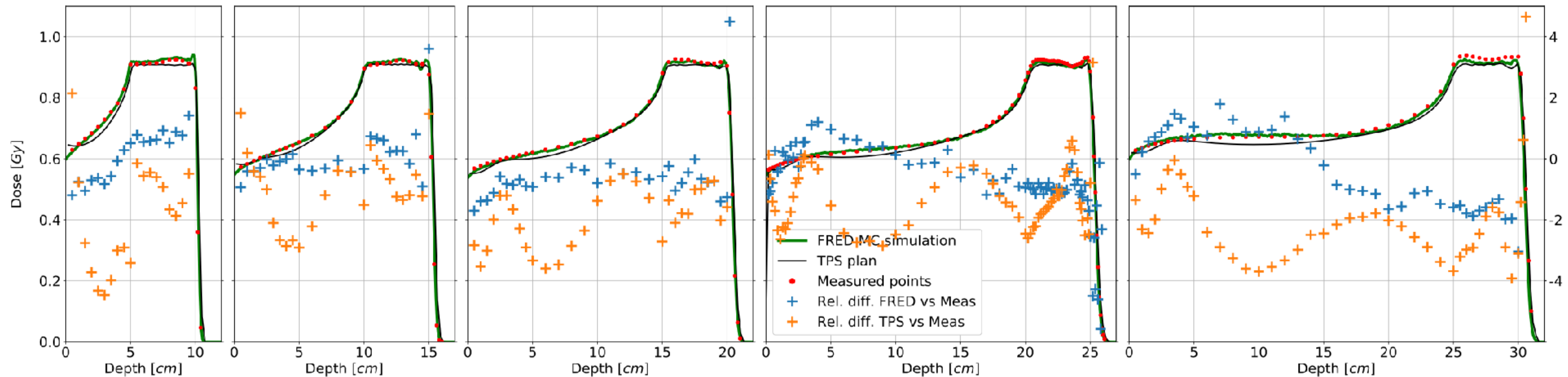


**Validation**





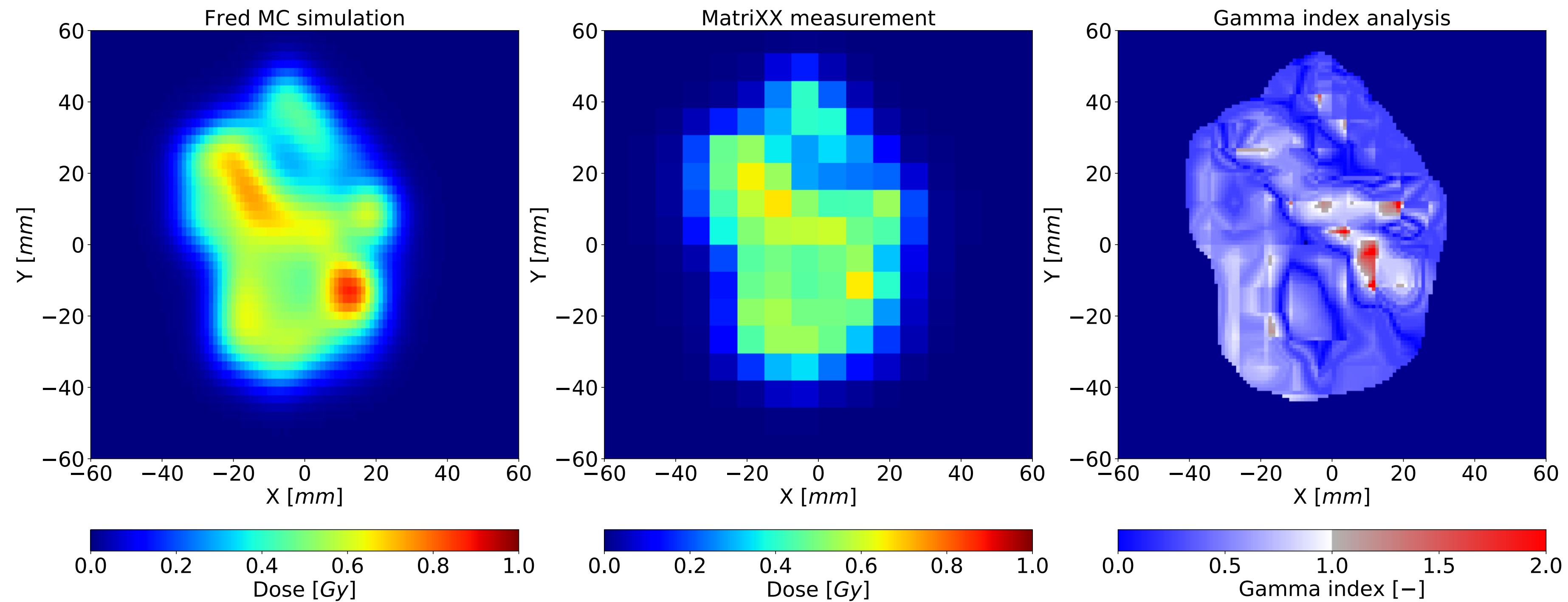
# Phase space validation in water



FRED vs Measurements:  $\leq 2\%$   
TPS vs Measurements:  $\leq 4\%$

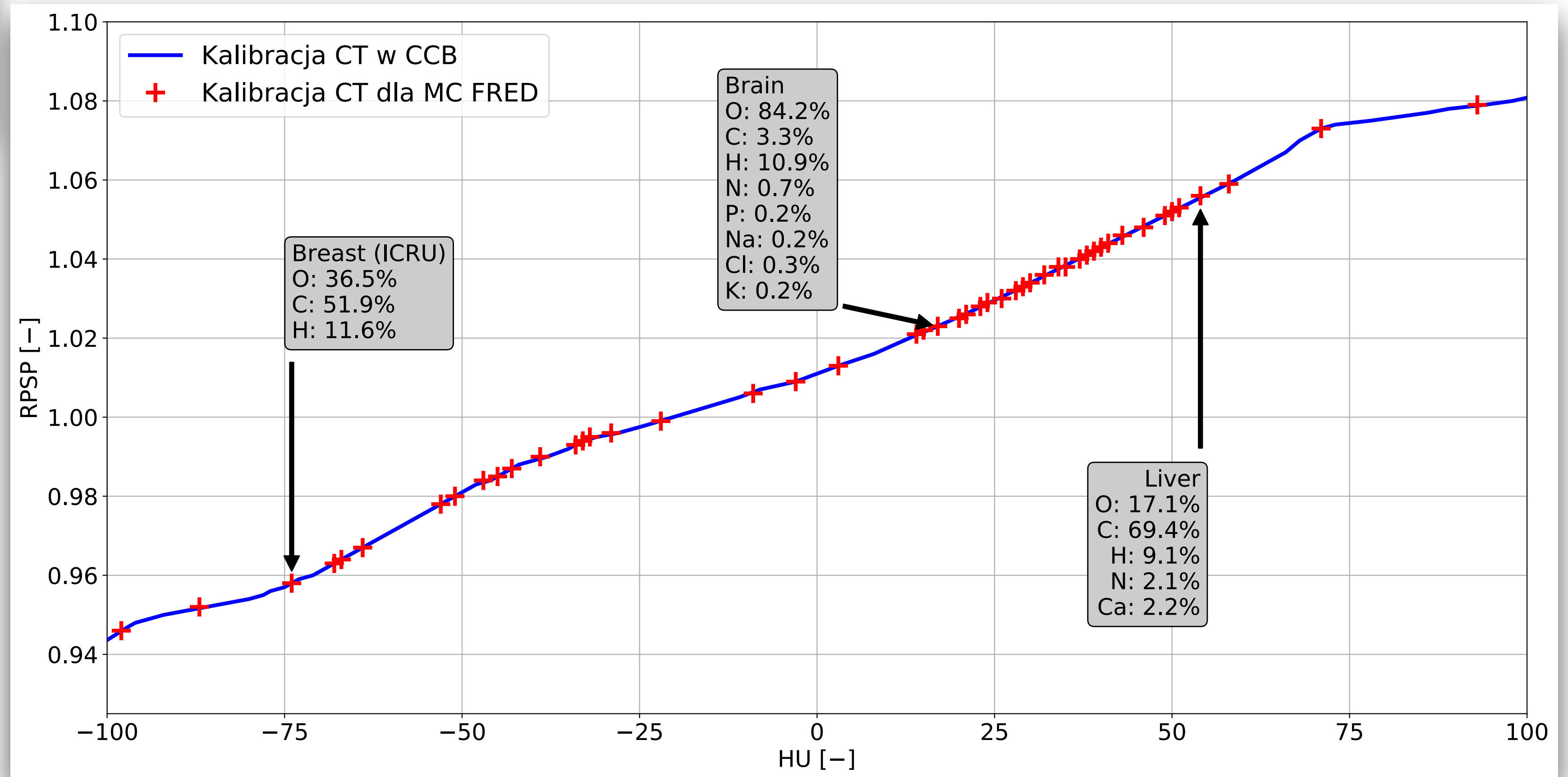
# 182 simulated and measured layers of verification plans in water

2D plane through the isocenter



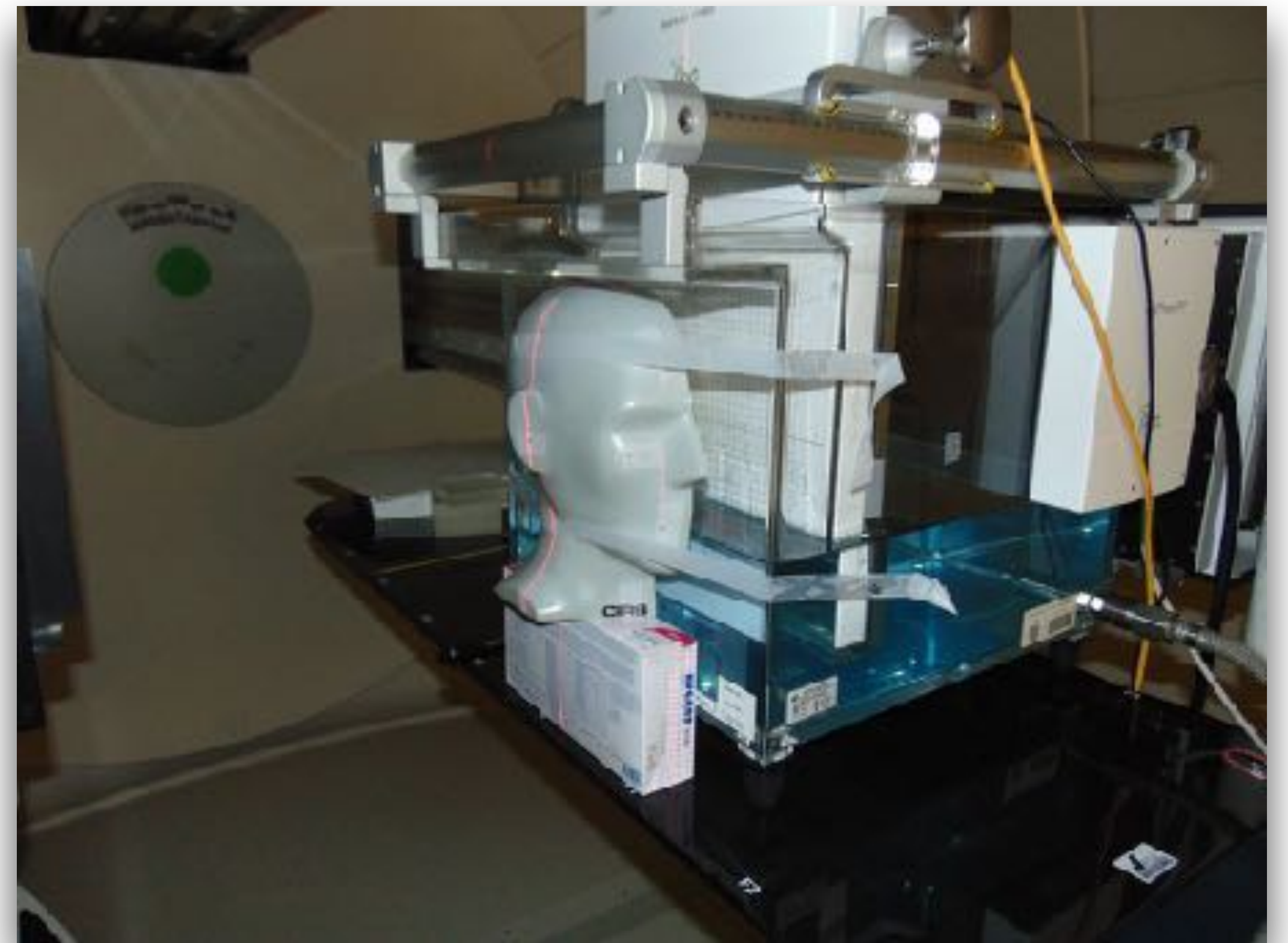
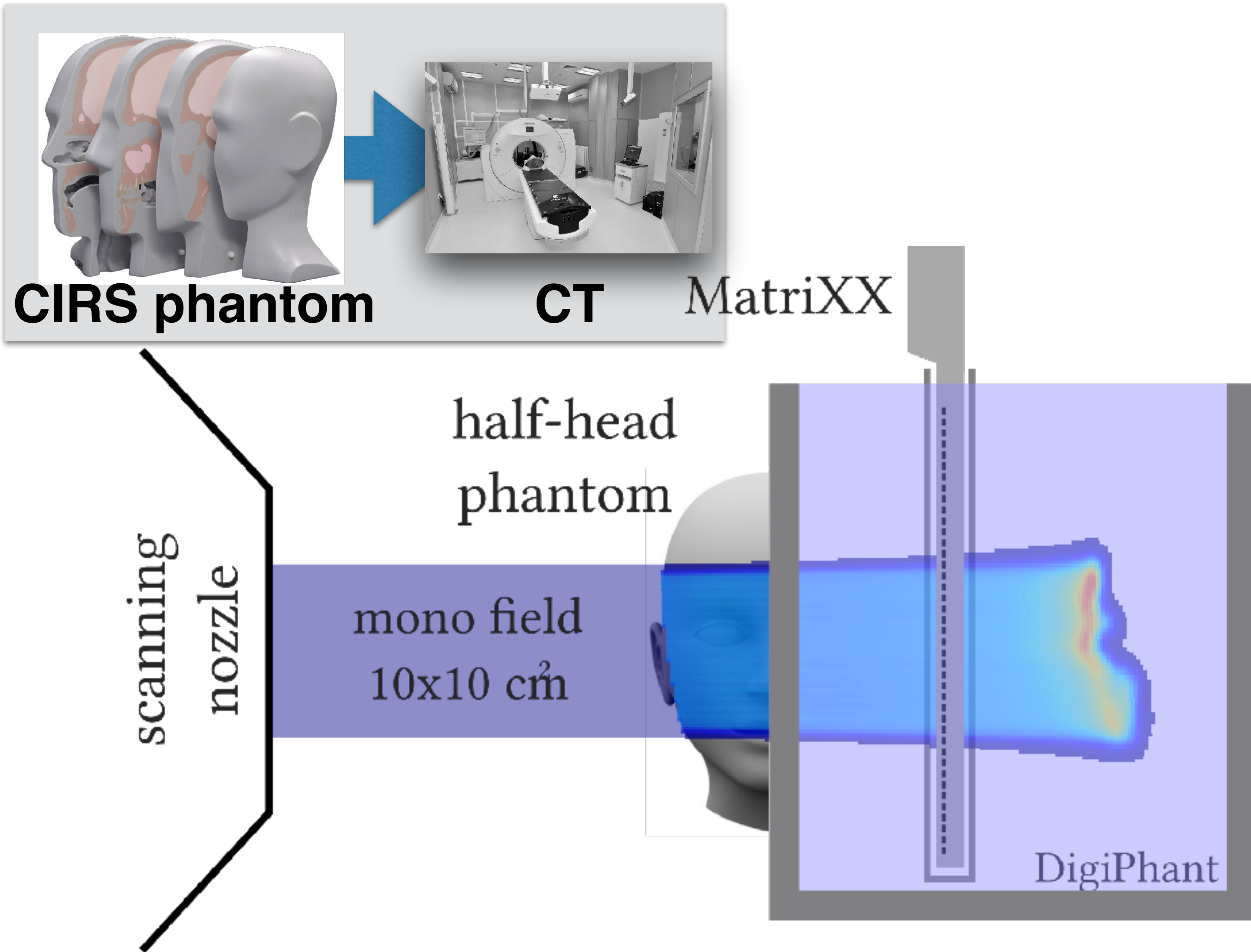
$\langle \text{GI pass rate} \rangle$  (2mm/2% criteria) = **96.3(3.3)%**

# CT calibration





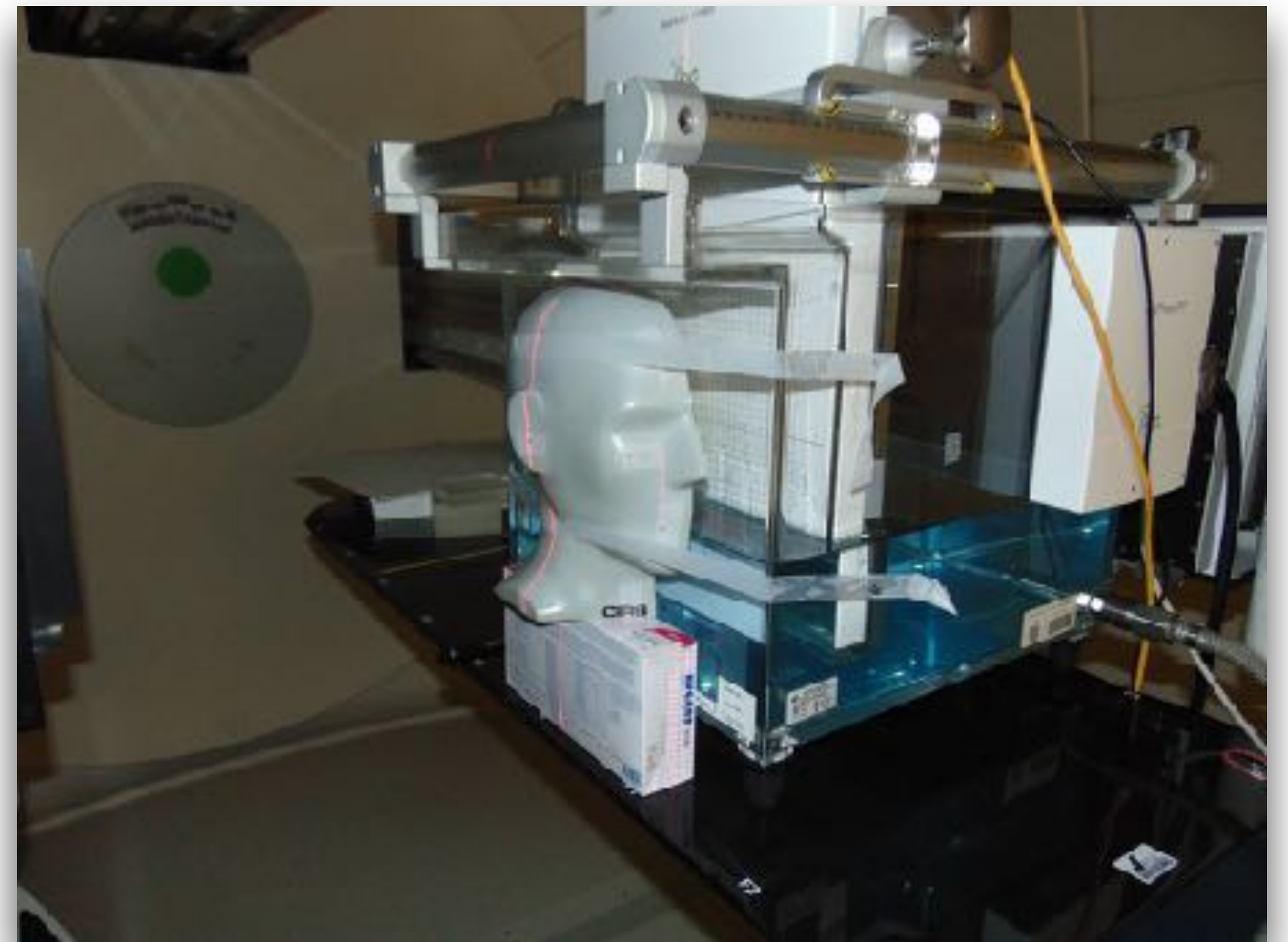
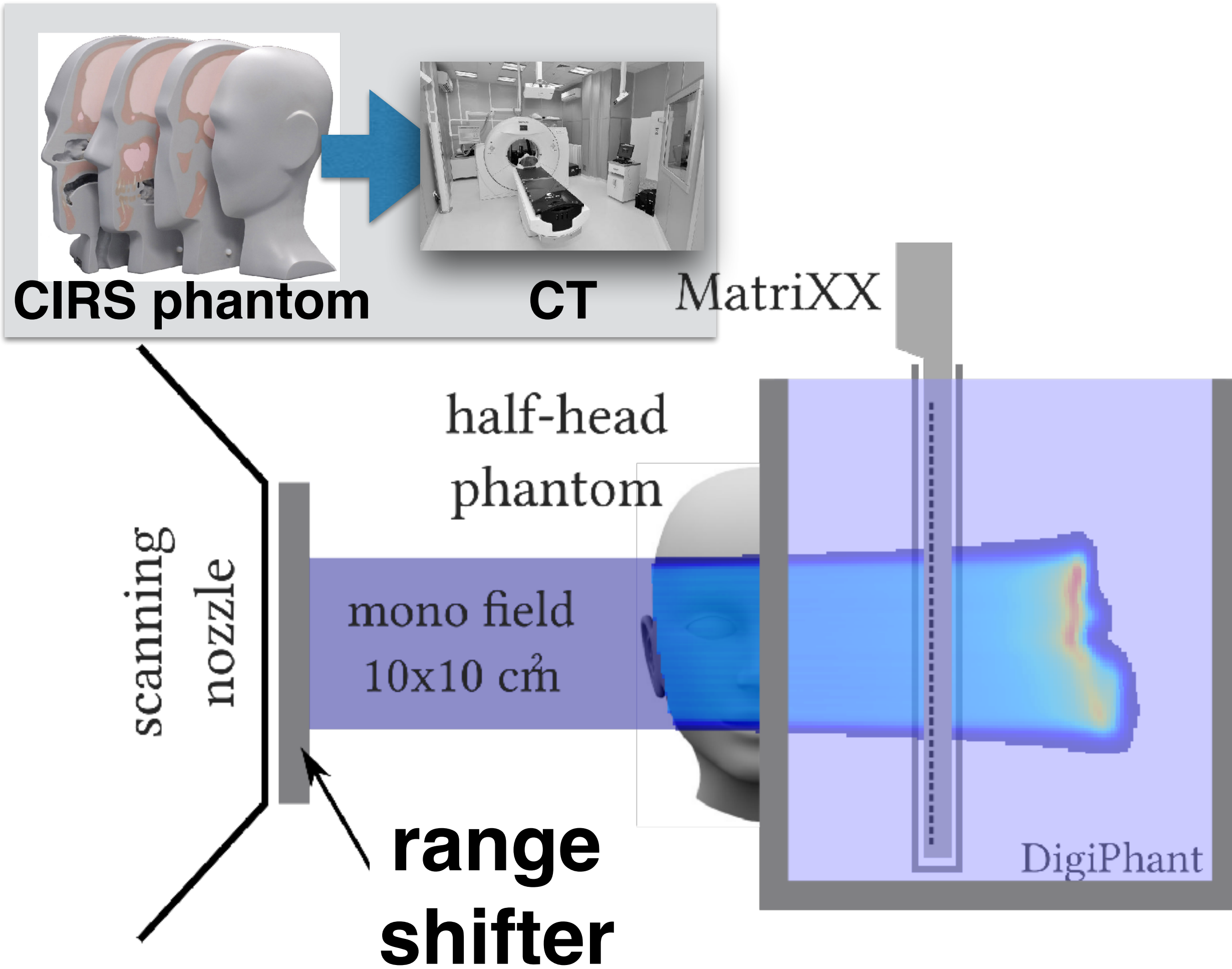
# Phase space validation in heterogenous phantom



Mono-energetic p<sup>+</sup> field: 150 MeV, 10x10cm<sup>2</sup>



# Phase space validation in heterogenous phantom



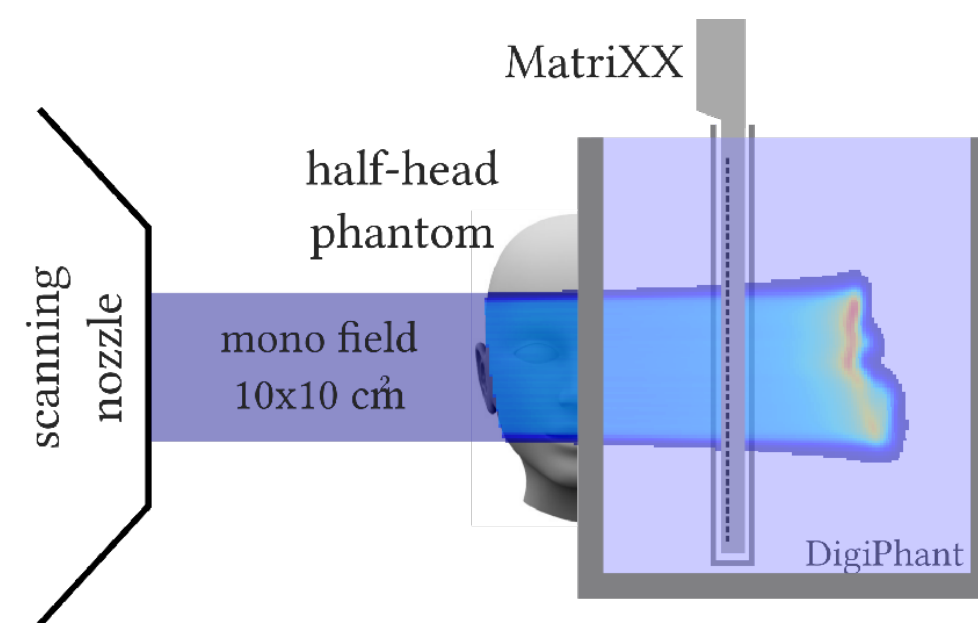
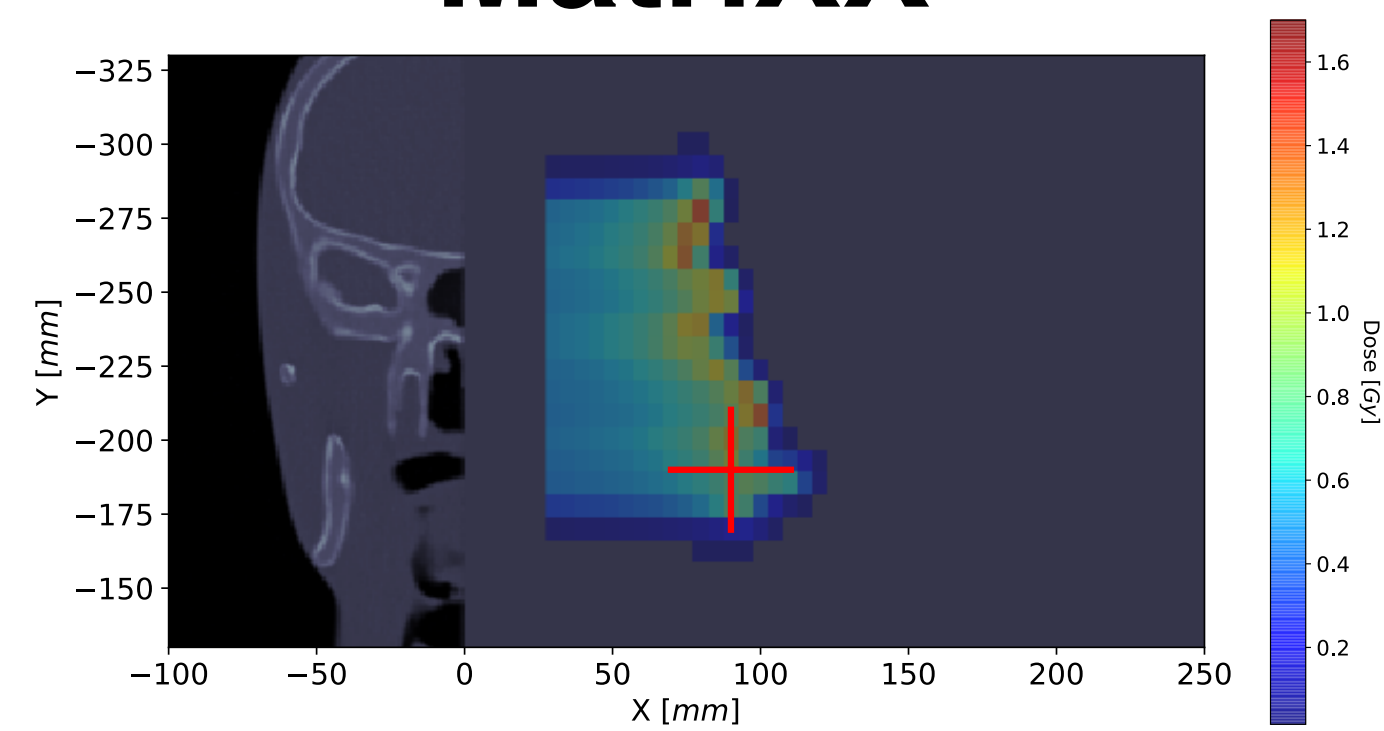
Mono-energetic p<sup>+</sup> field: 150 MeV, 10x10cm<sup>2</sup>



# Phase space validation in heterogenous phantom

## Measurement

### MatriXX



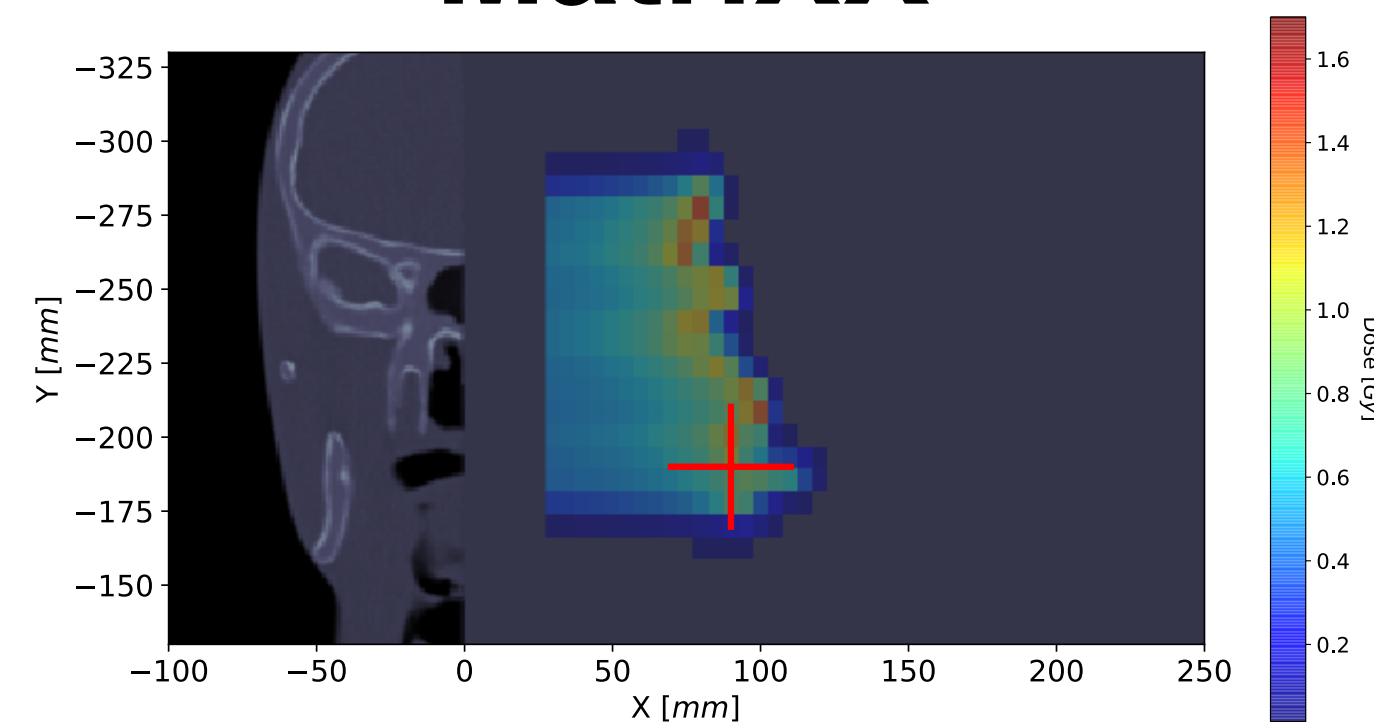
Mono-energetic  $p^+$  field: 150 MeV,  $10 \times 10 \text{ cm}^2$



# Phase space validation in heterogenous phantom

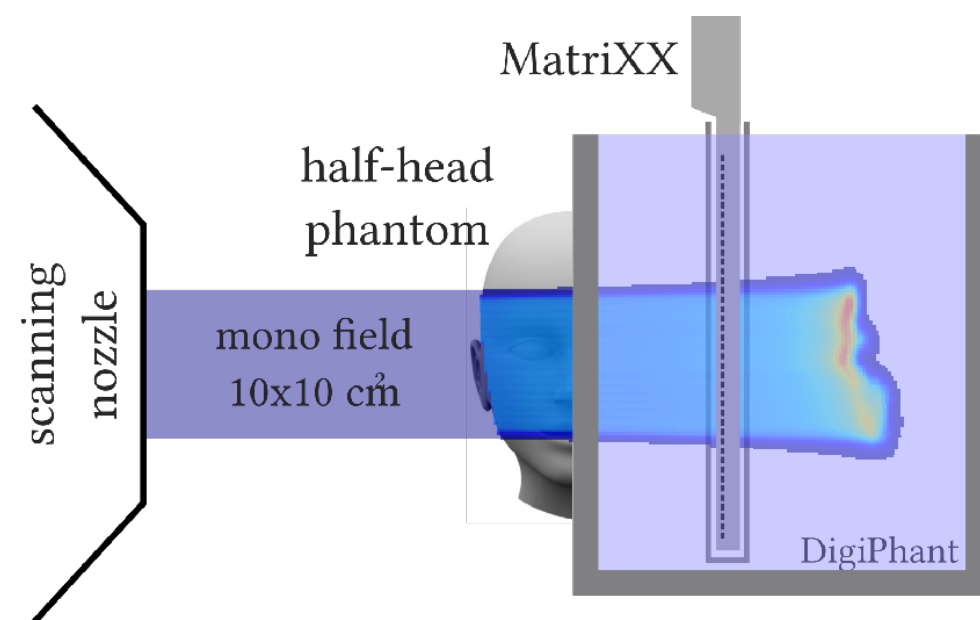
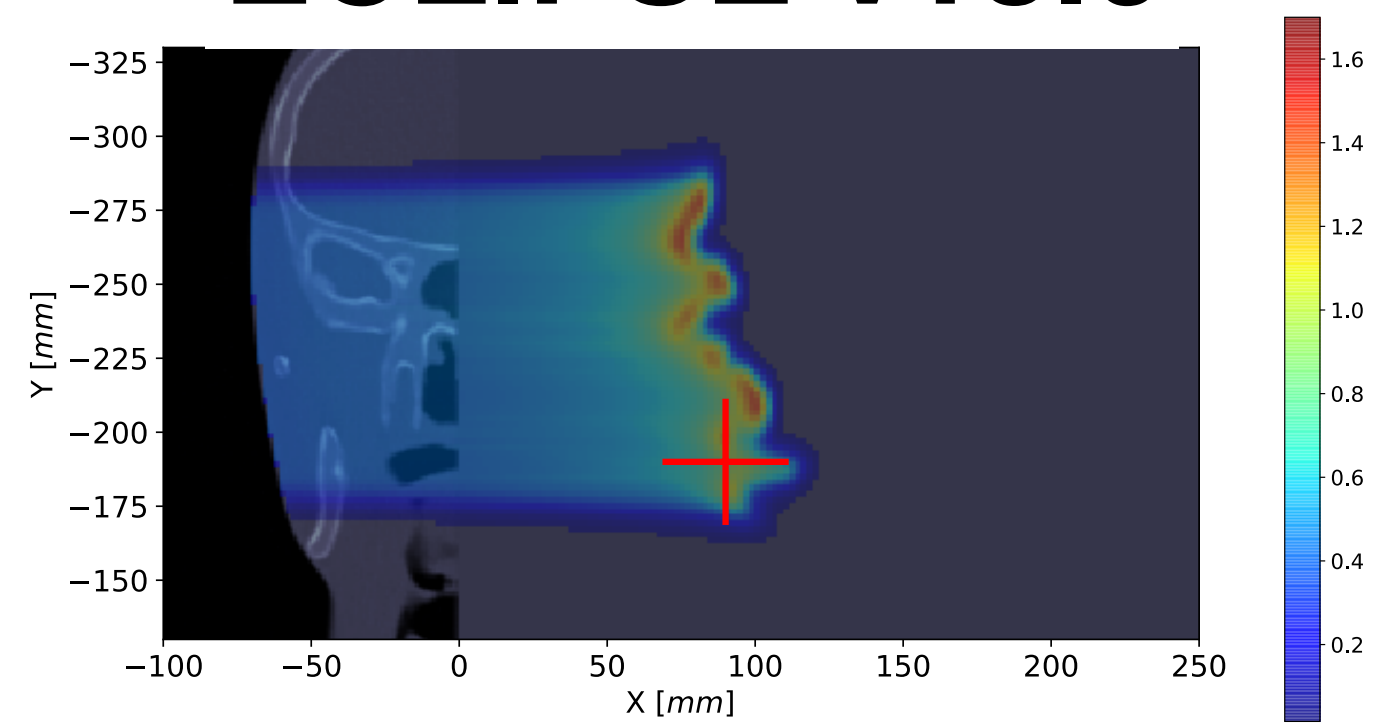
## Measurement

### MatriXX

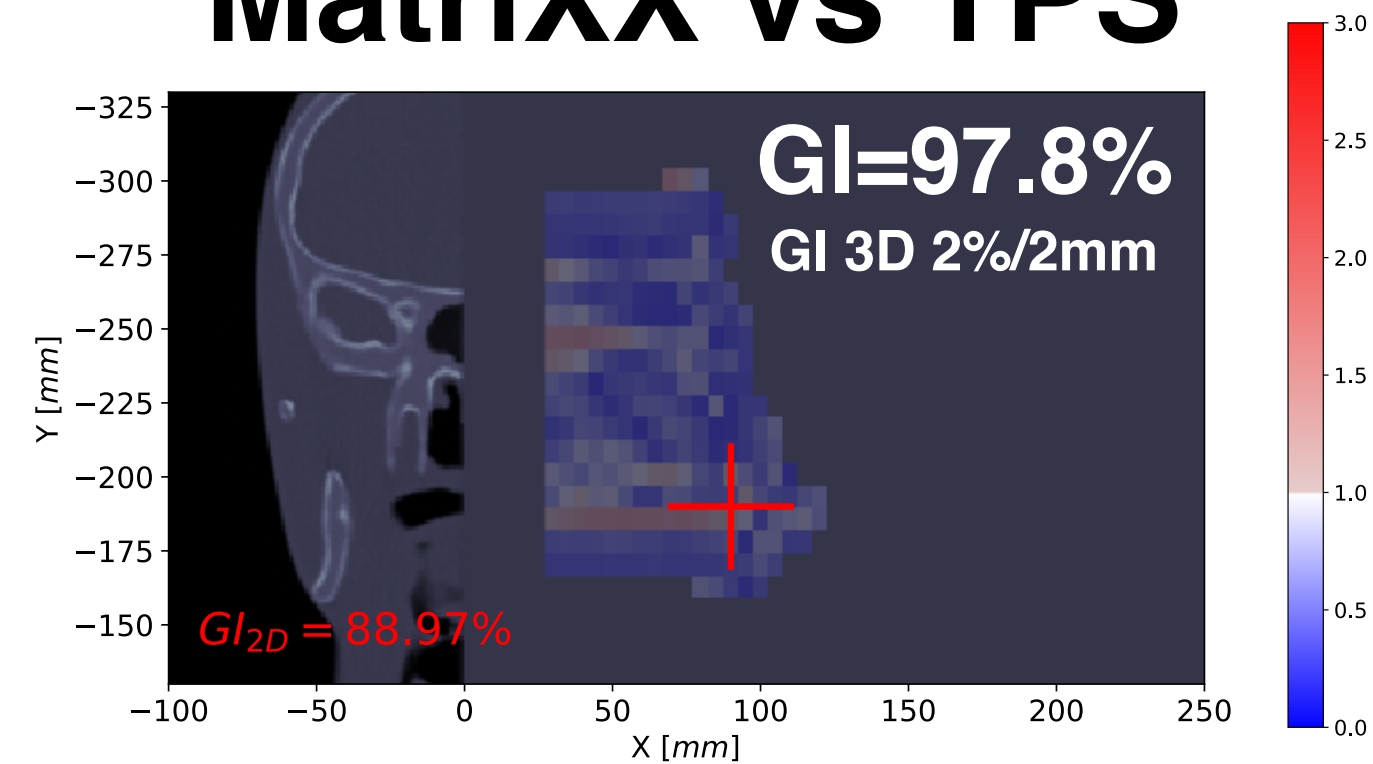


## TPS calculation

### ECLIPSE v13.6



## MatriXX vs TPS



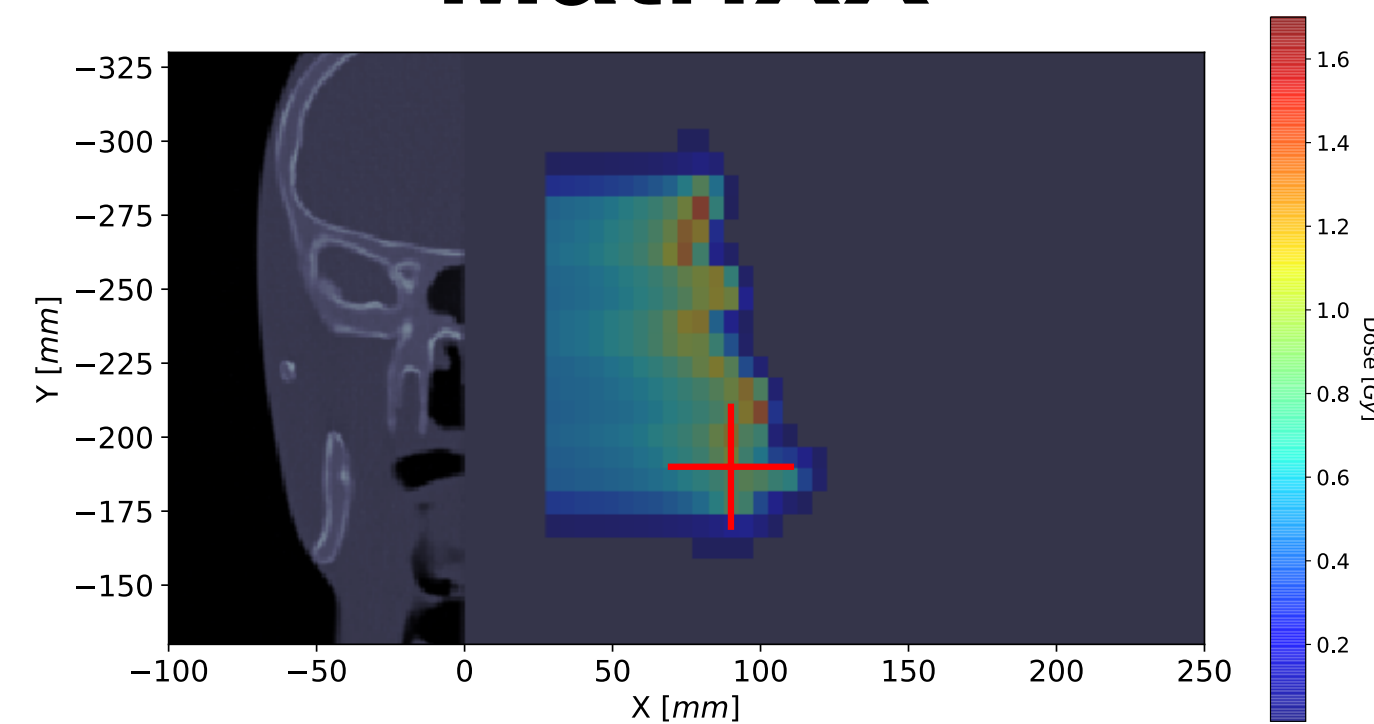
Mono-energetic p<sup>+</sup> field: 150 MeV, 10x10cm<sup>2</sup>

Gamma Index tools: <https://pymedphys.com>

# Phase space validation in heterogenous phantom

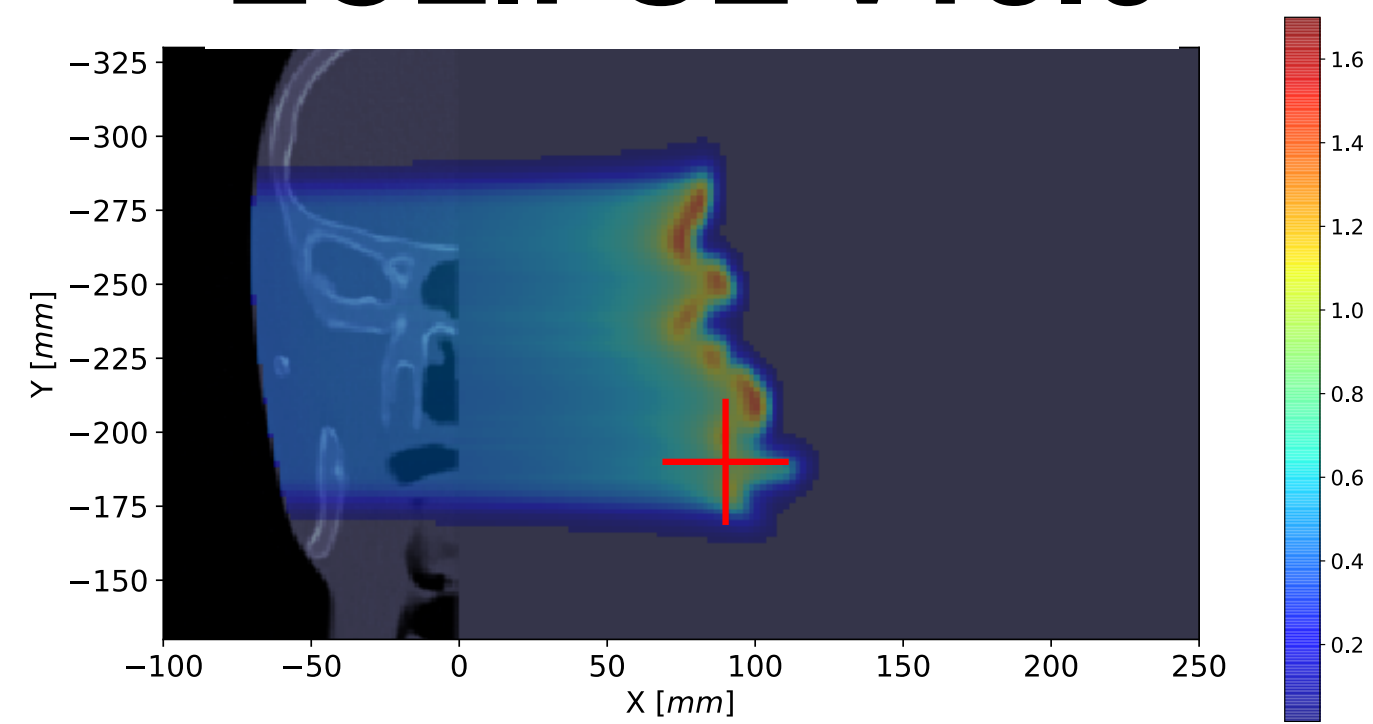
## Measurement

### MatriXX



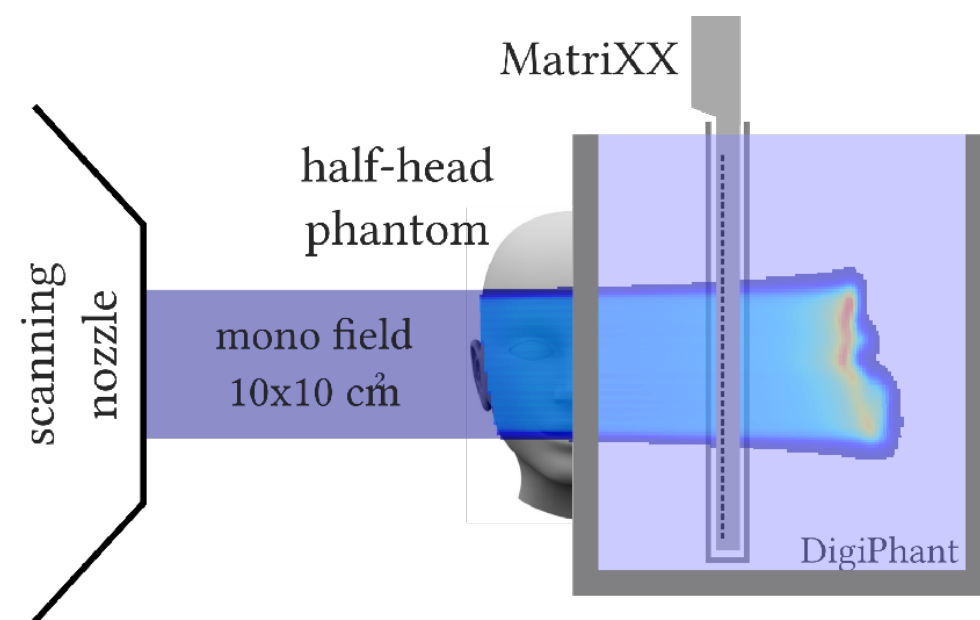
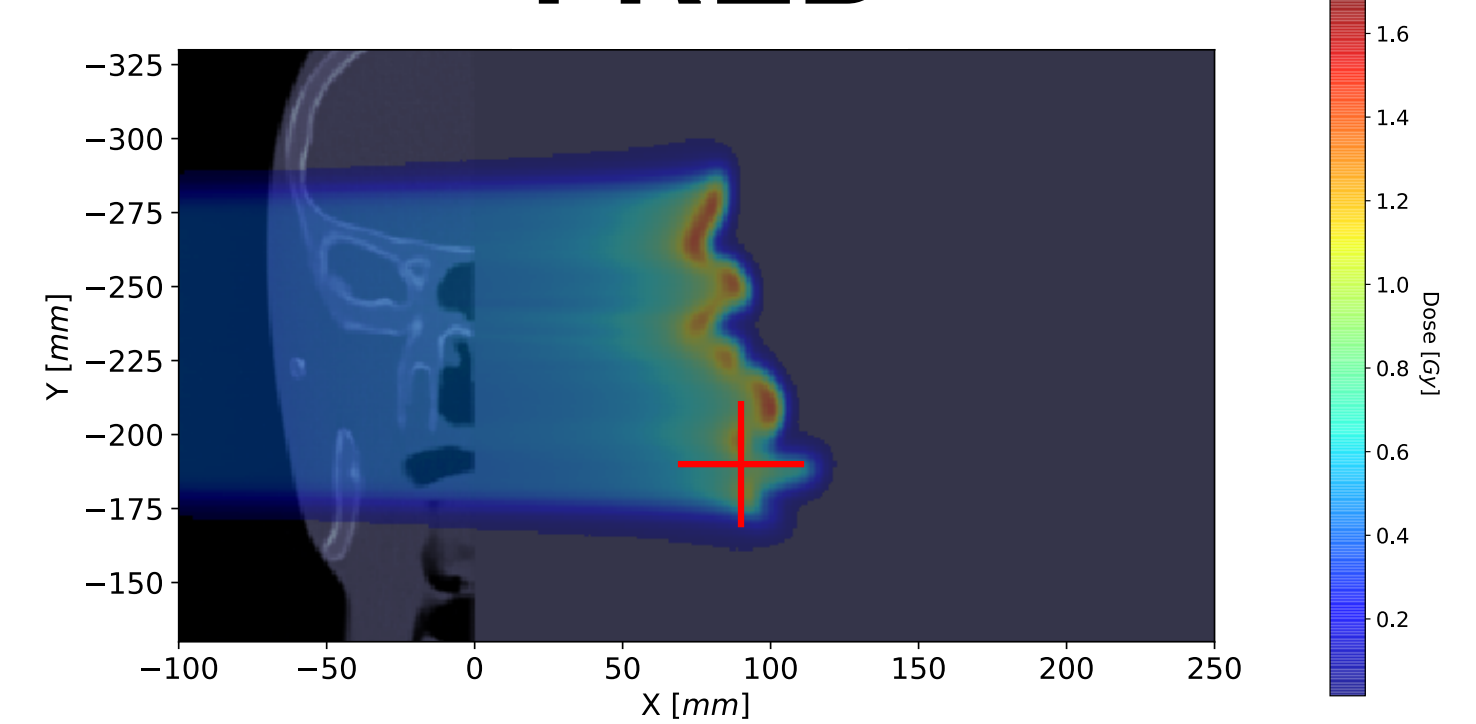
## TPS calculation

### ECLIPSE v13.6



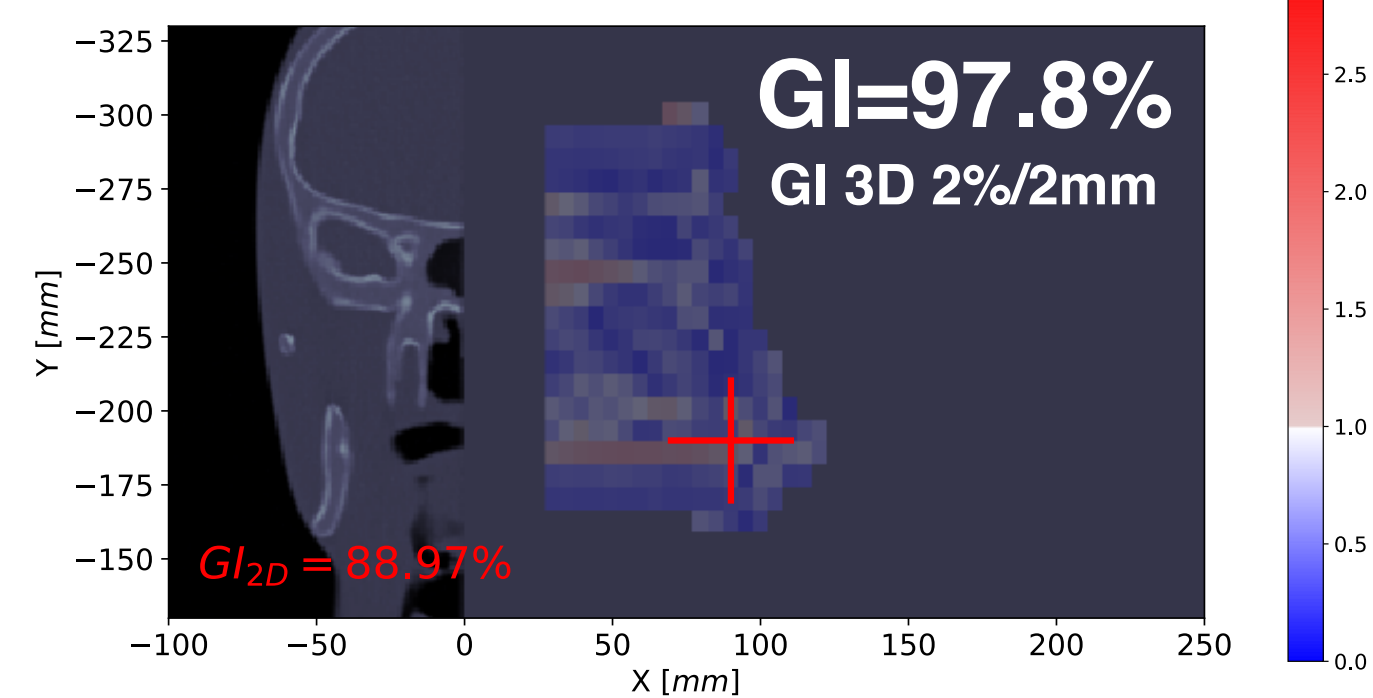
## FRED calculation

### FRED

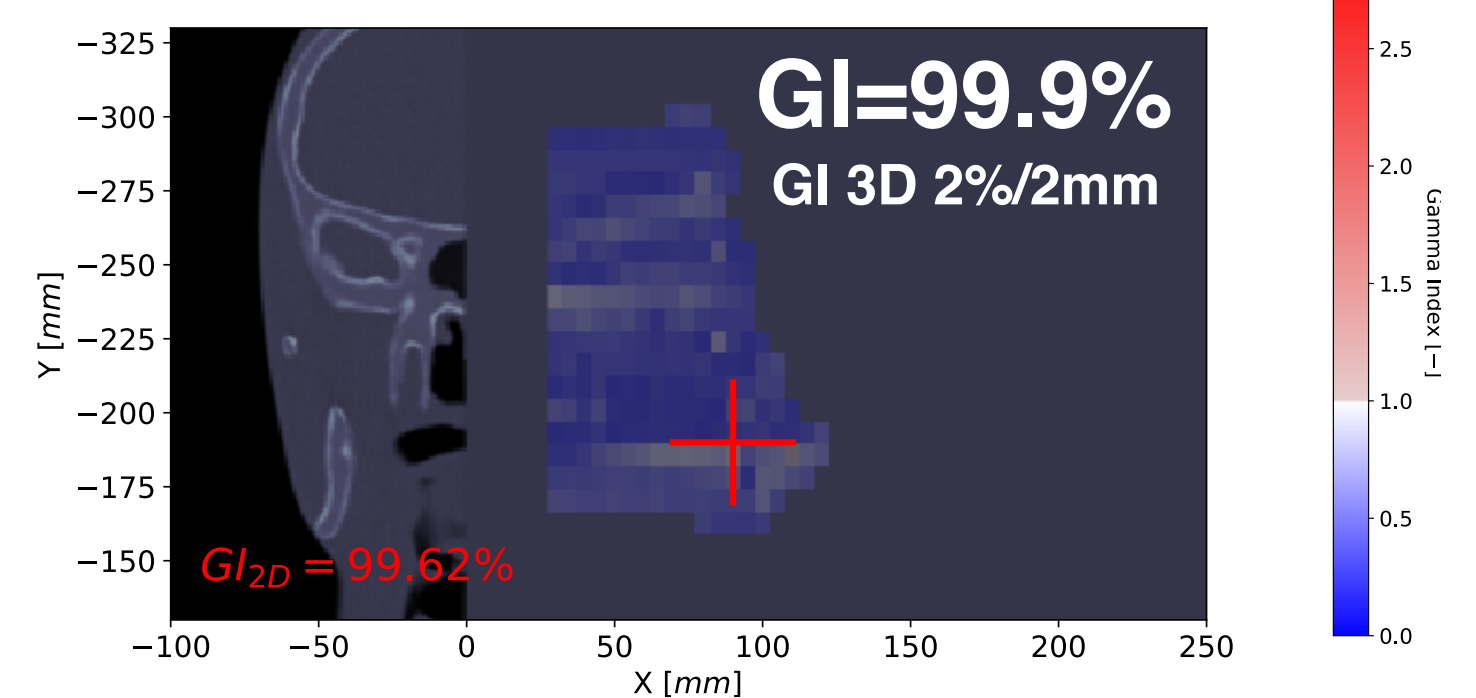


Mono-energetic p+ field: 150 MeV, 10x10cm<sup>2</sup>

## MatriXX vs TPS



## MatriXX vs FRED



Gamma Index tools: <https://pymedphys.com>

10<sup>5</sup> p+/spot , total sim. time 2'

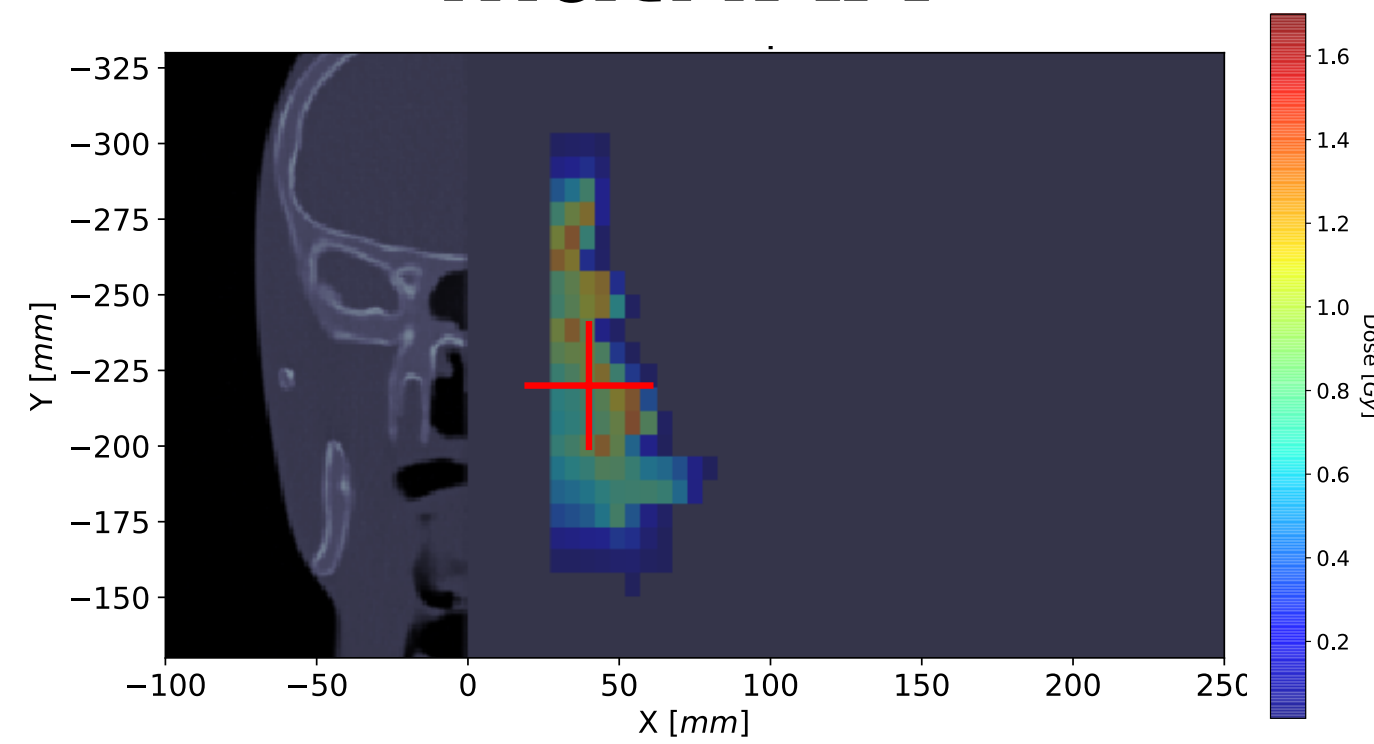


# Phase space validation in heterogenous phantom

Range shifter

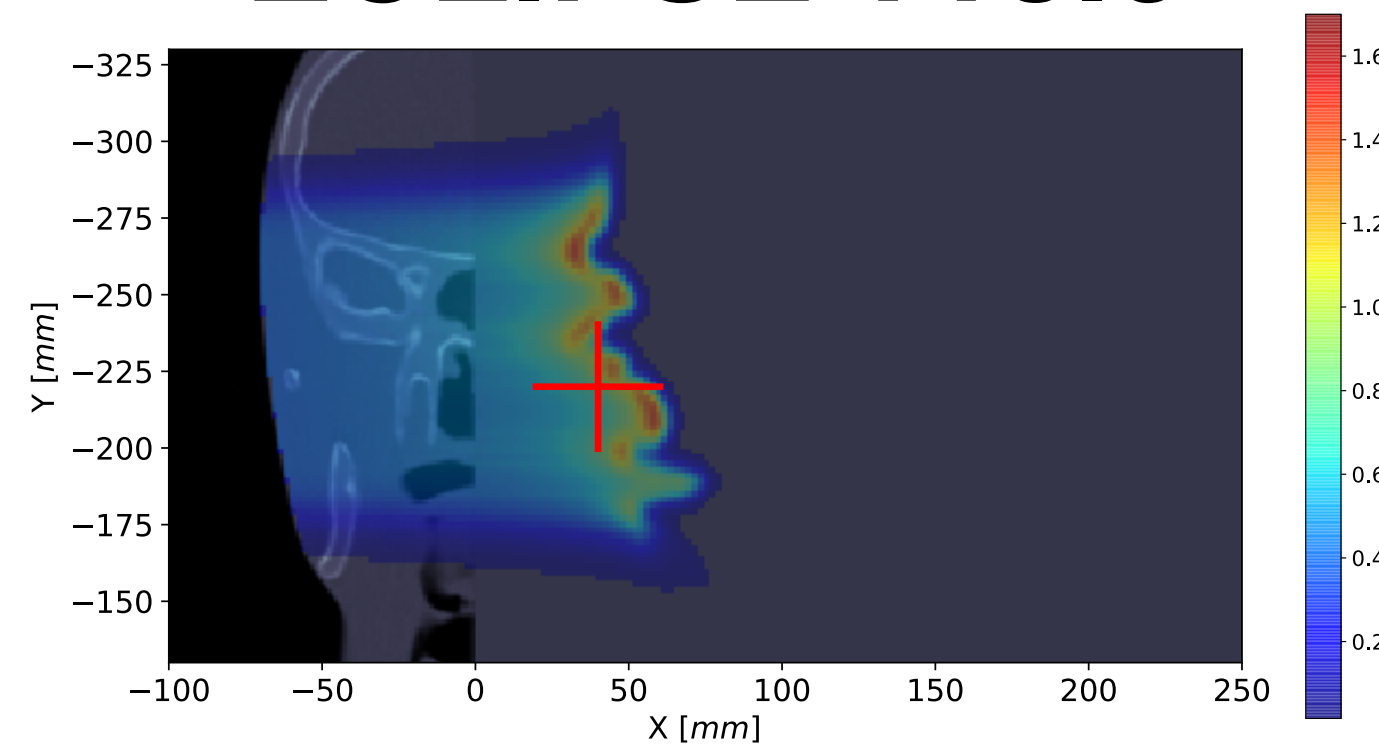
Measurement

MatriXX



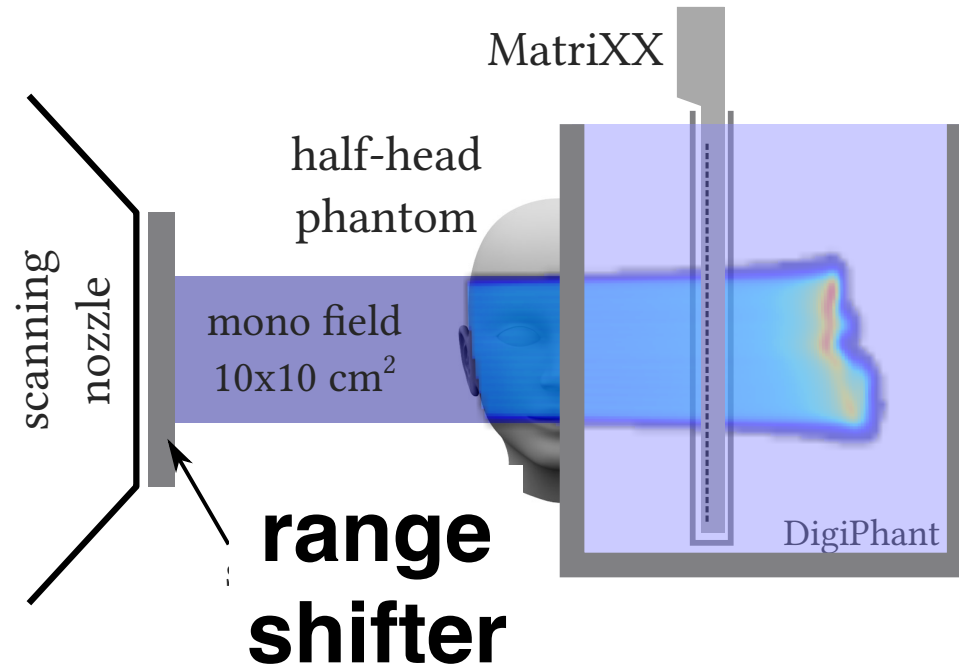
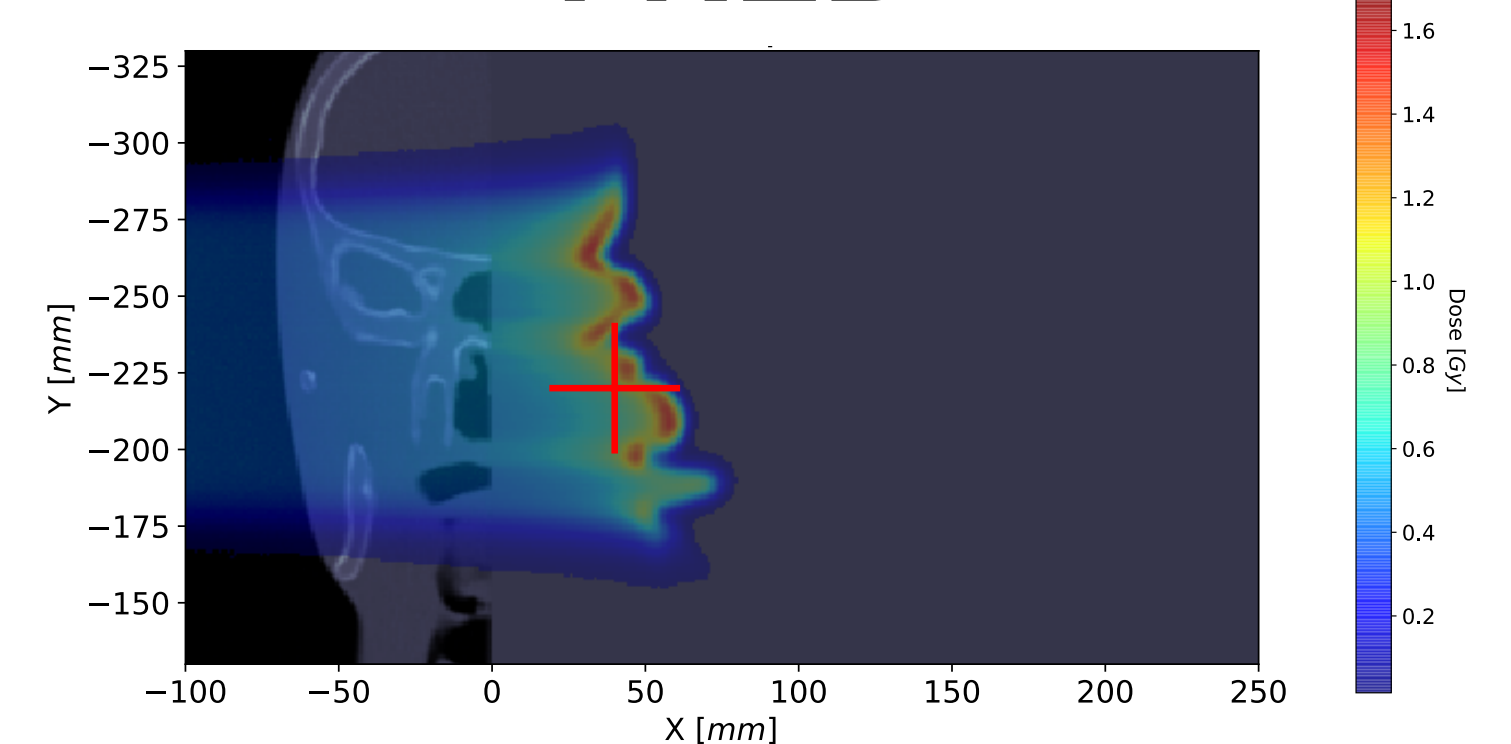
TPS calculation

ECLIPSE v13.6



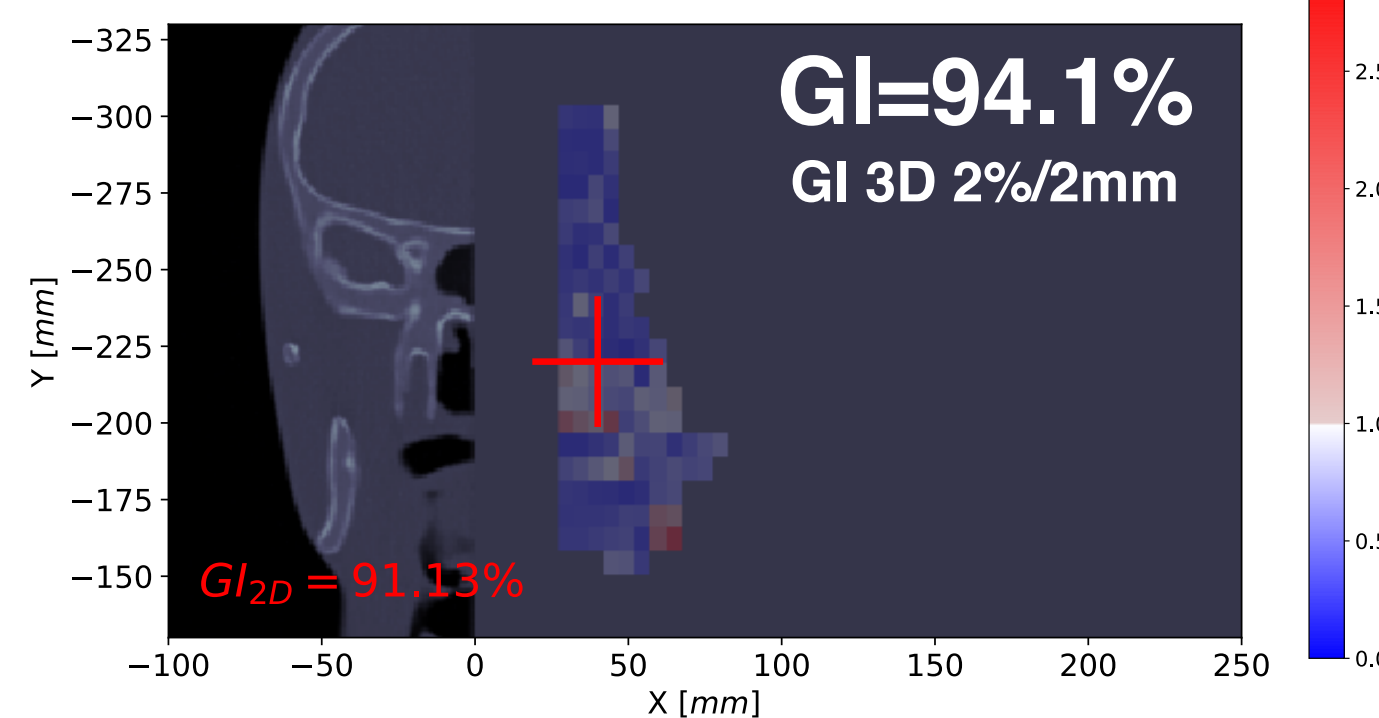
FRED calculation

FRED

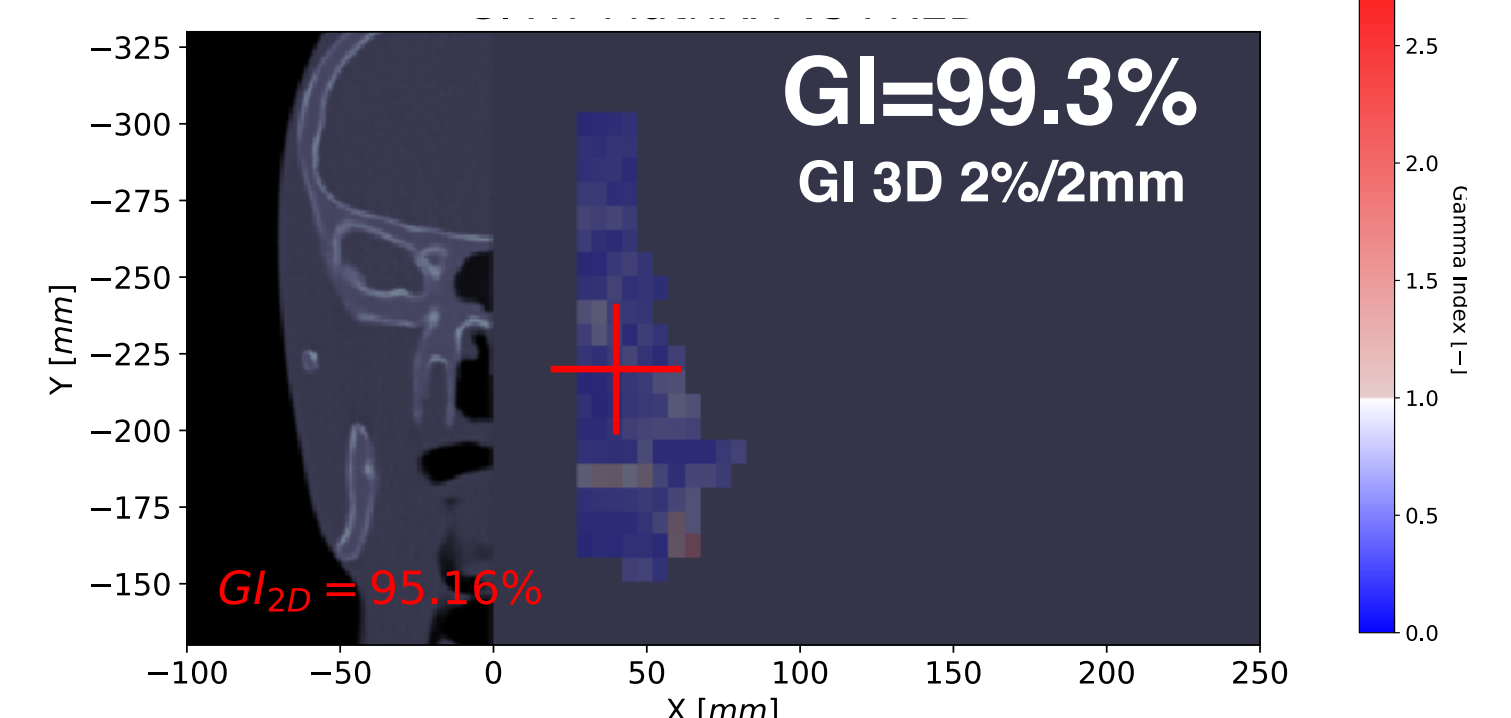


Mono-energetic p<sup>+</sup> field: 150 MeV, 10x10cm<sup>2</sup>

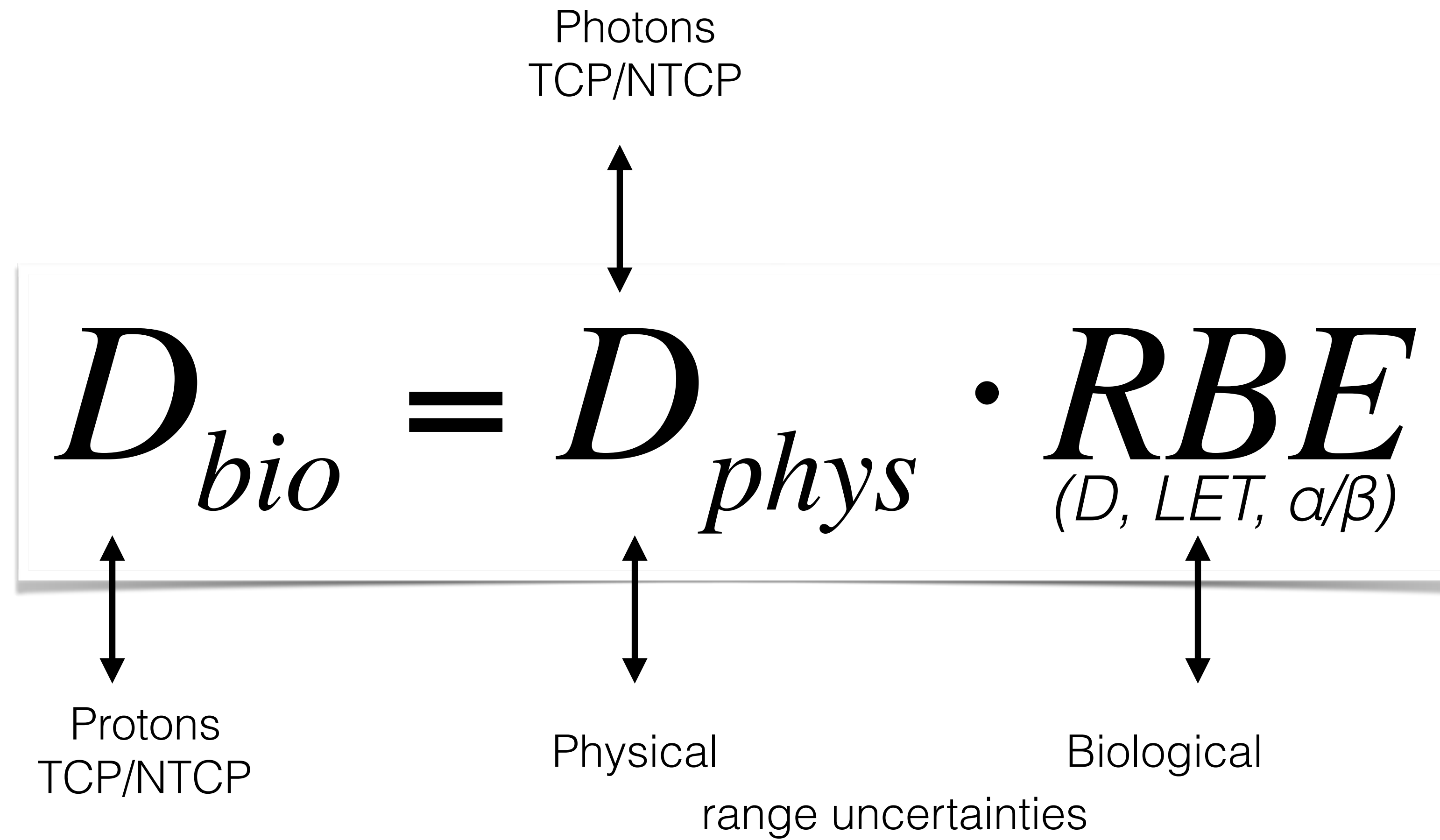
MatriXX vs TPS



MatriXX vs FRED

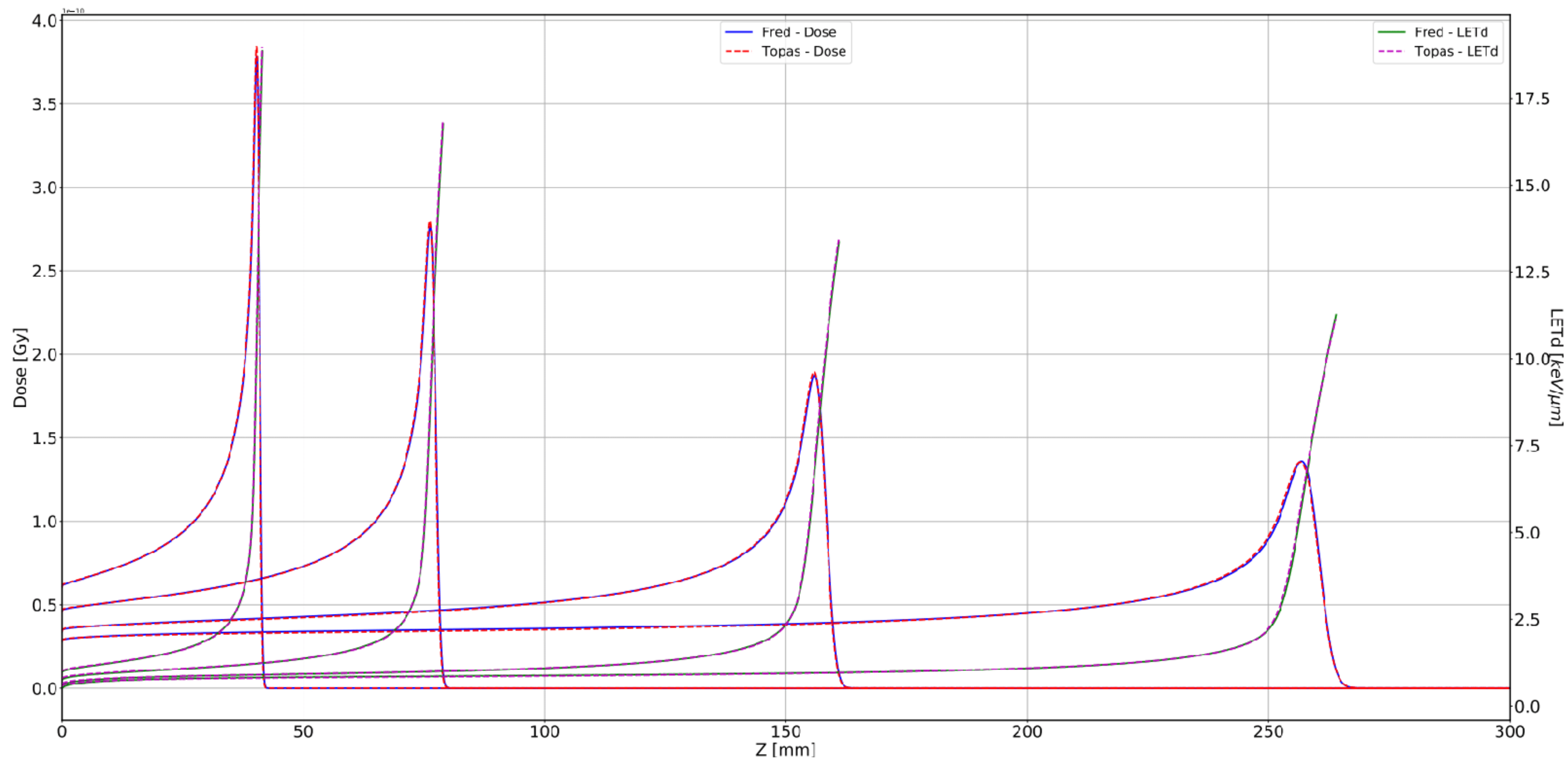


Gamma Index tools: <https://pymedphys.com>



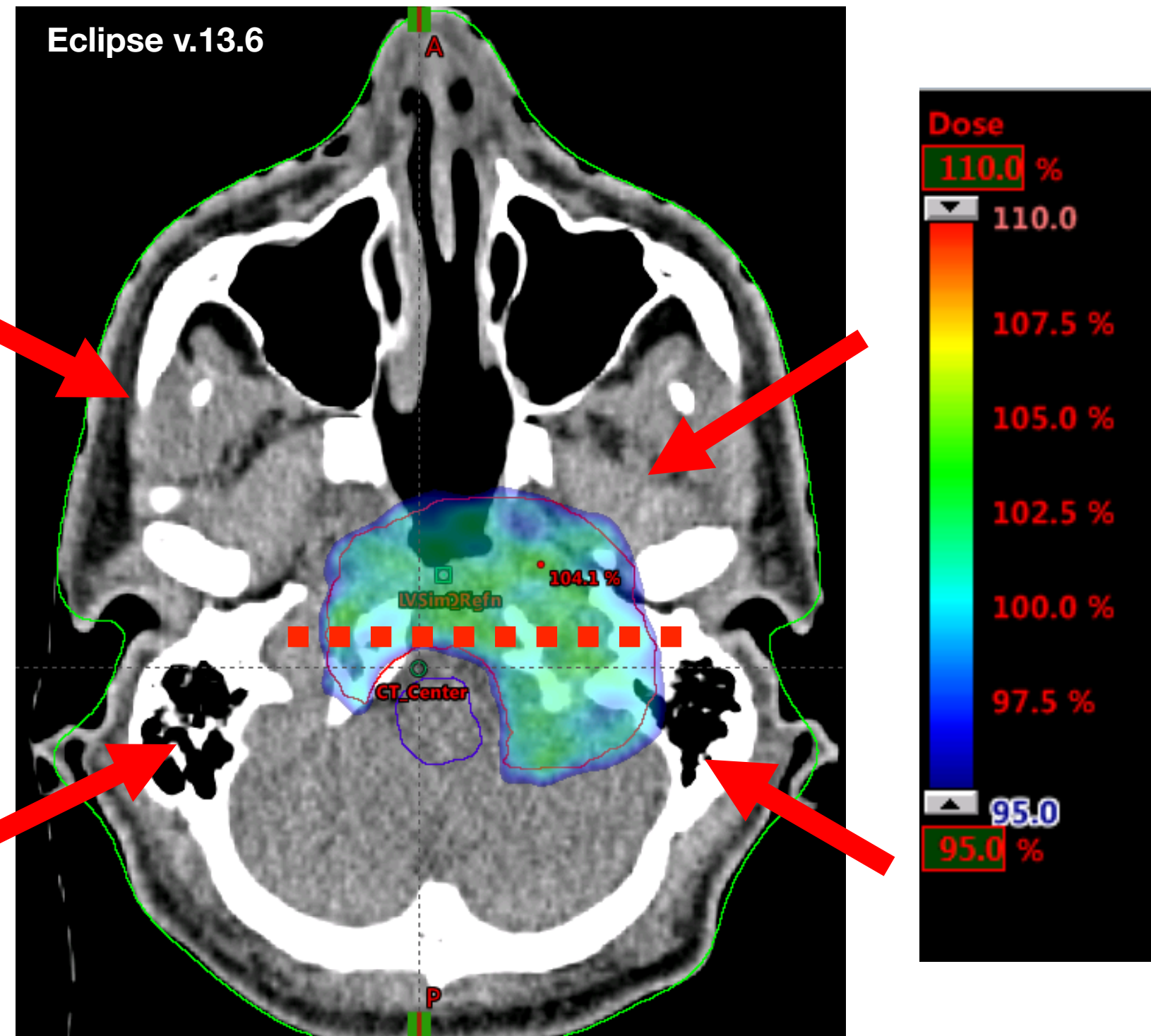


# LET validation: FRED vs TOPAS

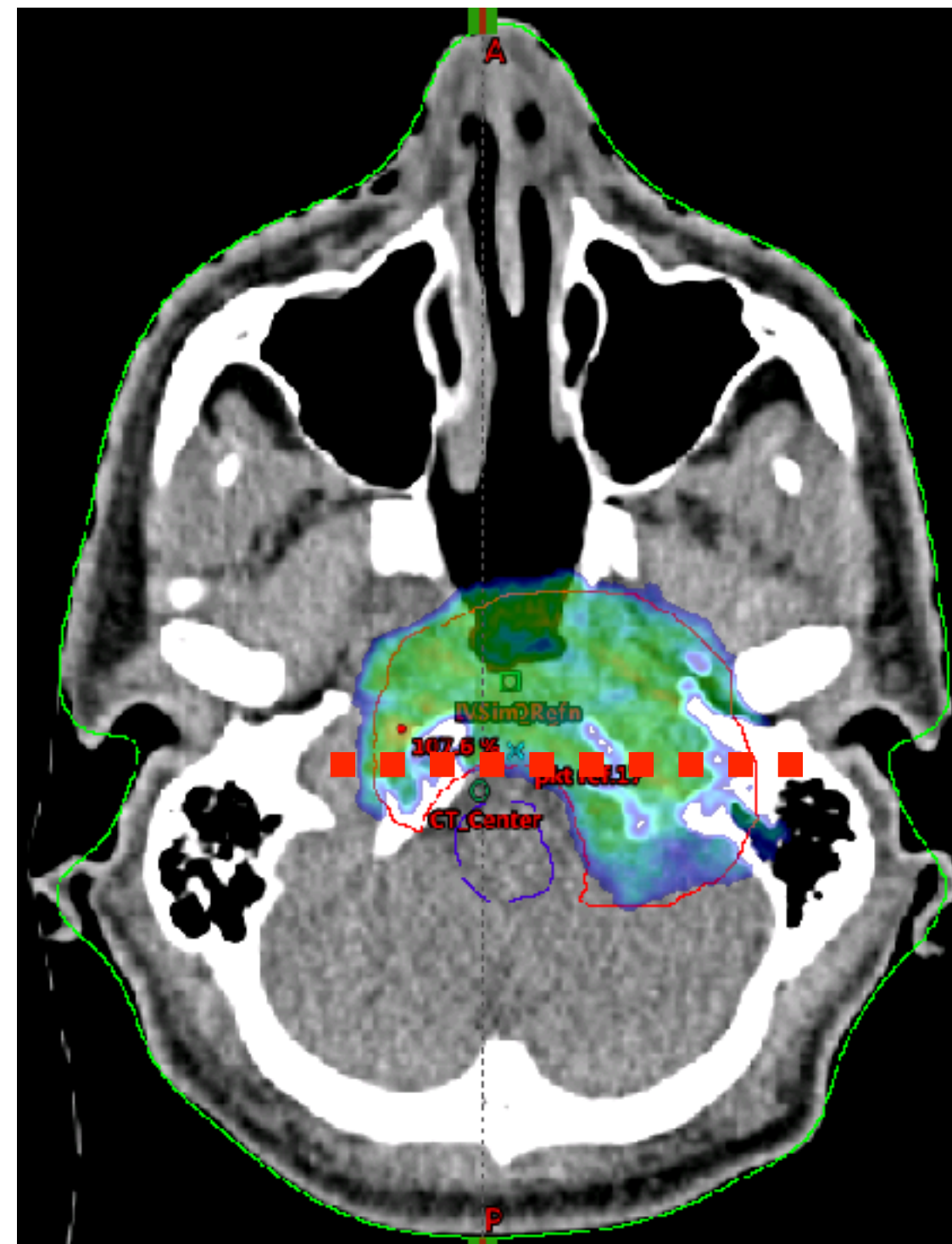


# FRED for independent dose calculation and treatment planning studies

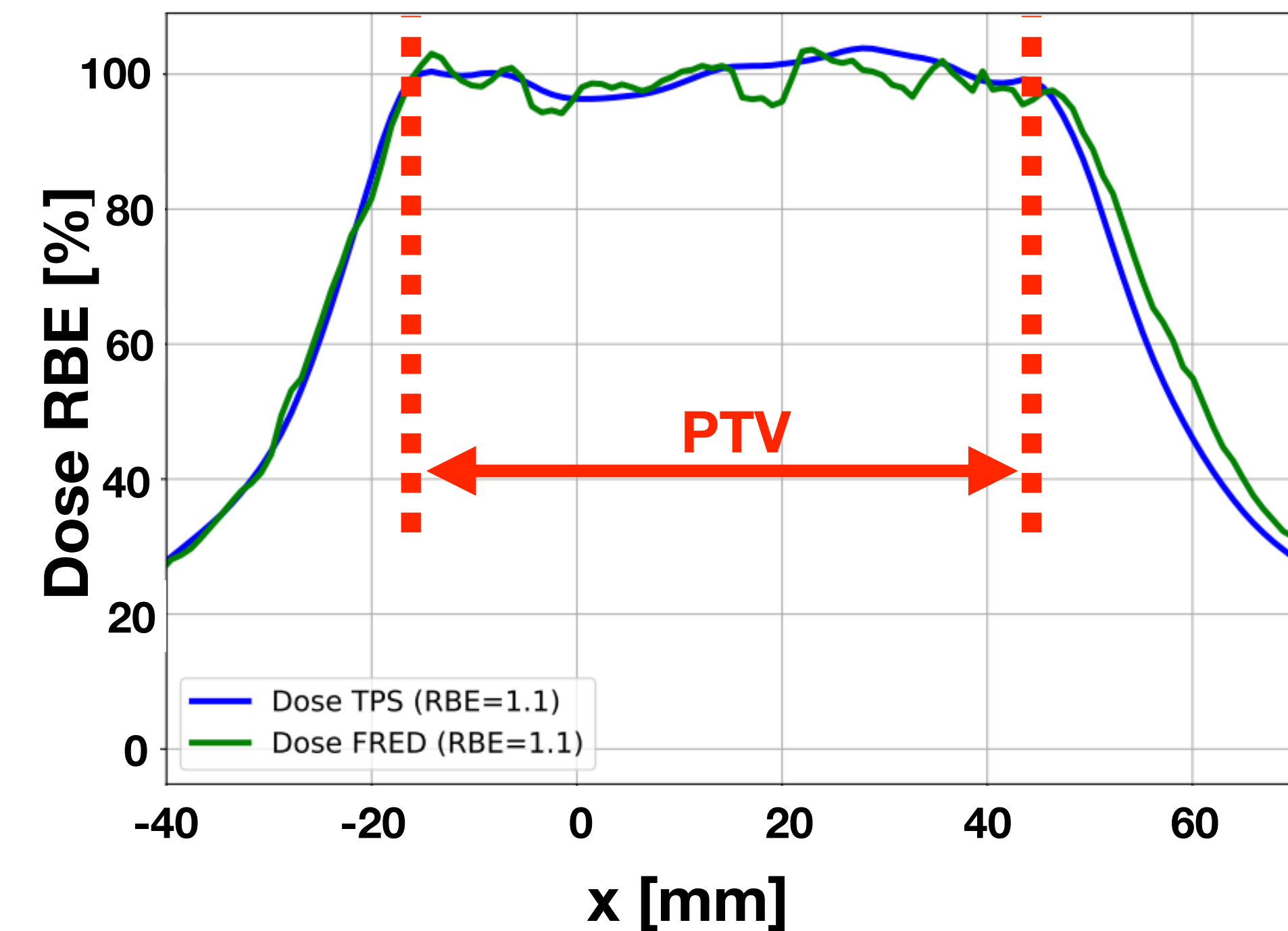
Radiobiological dose  
TPS RBE=1.1



Radiobiological dose  
FRED RBE=1.1



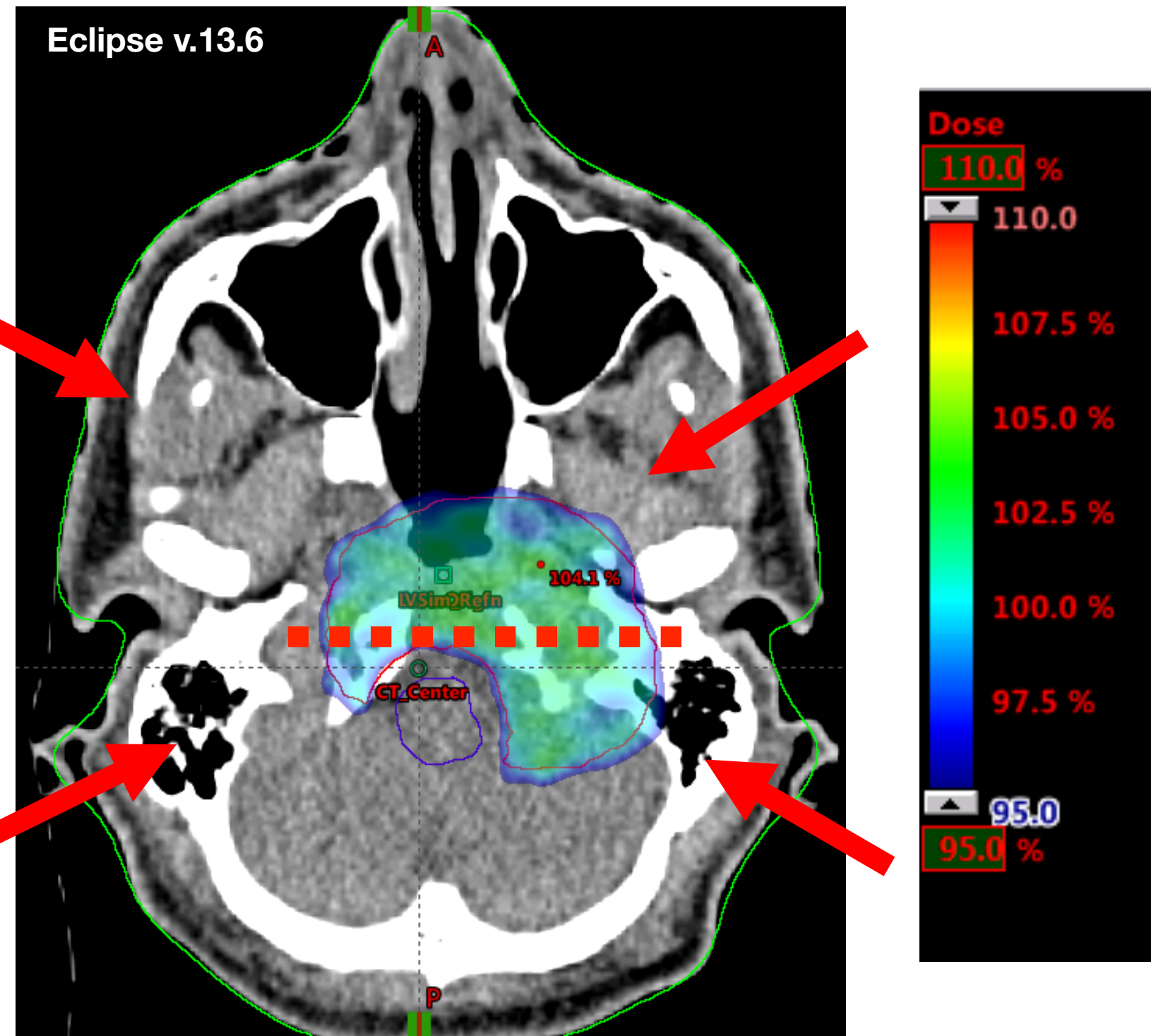
TPS<sub>RBE=1.1</sub> VS FRED<sub>RBE=1.1</sub>



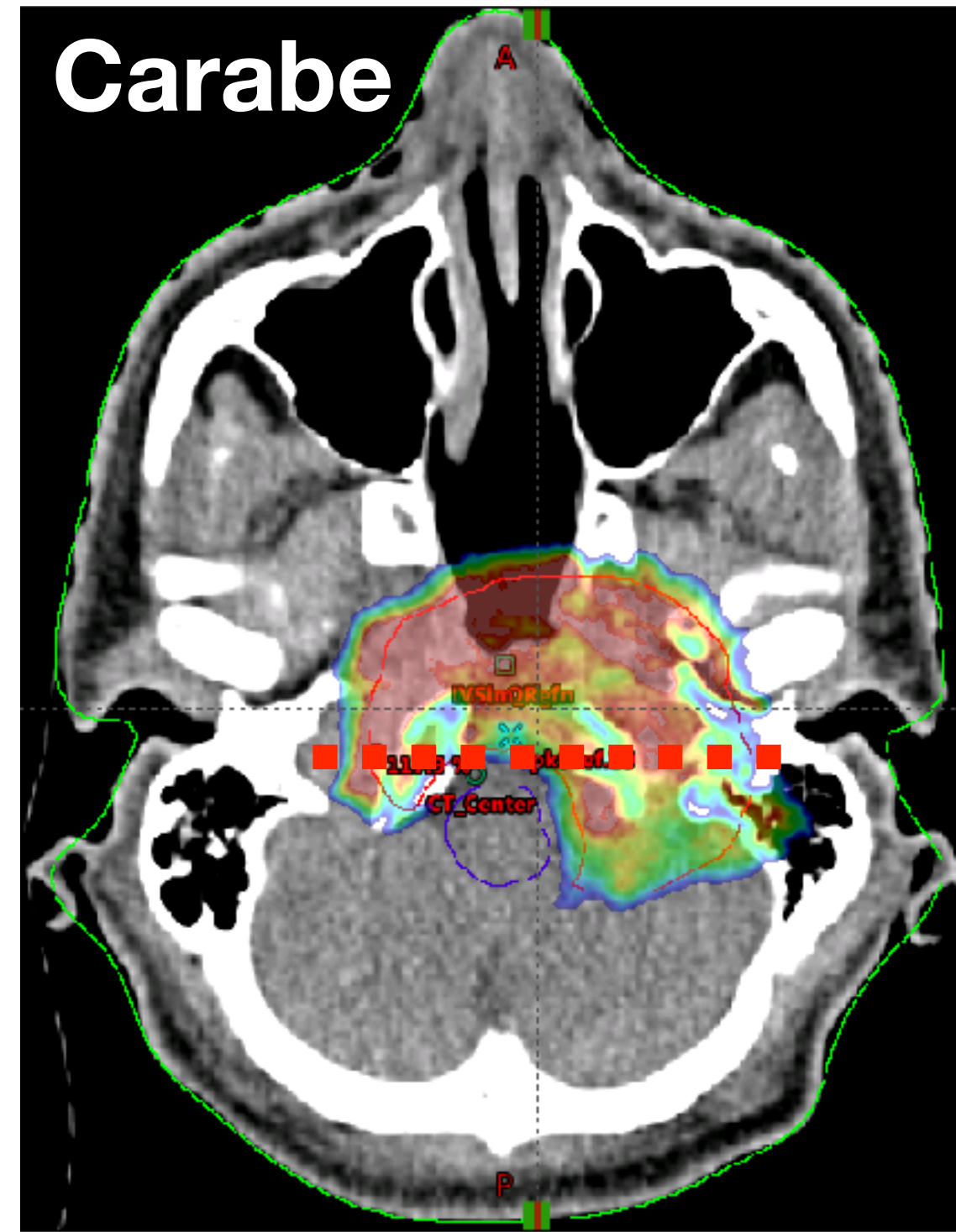


# FRED for independent dose calculation and treatment planning studies

Radiobiological dose  
TPS RBE=1.1

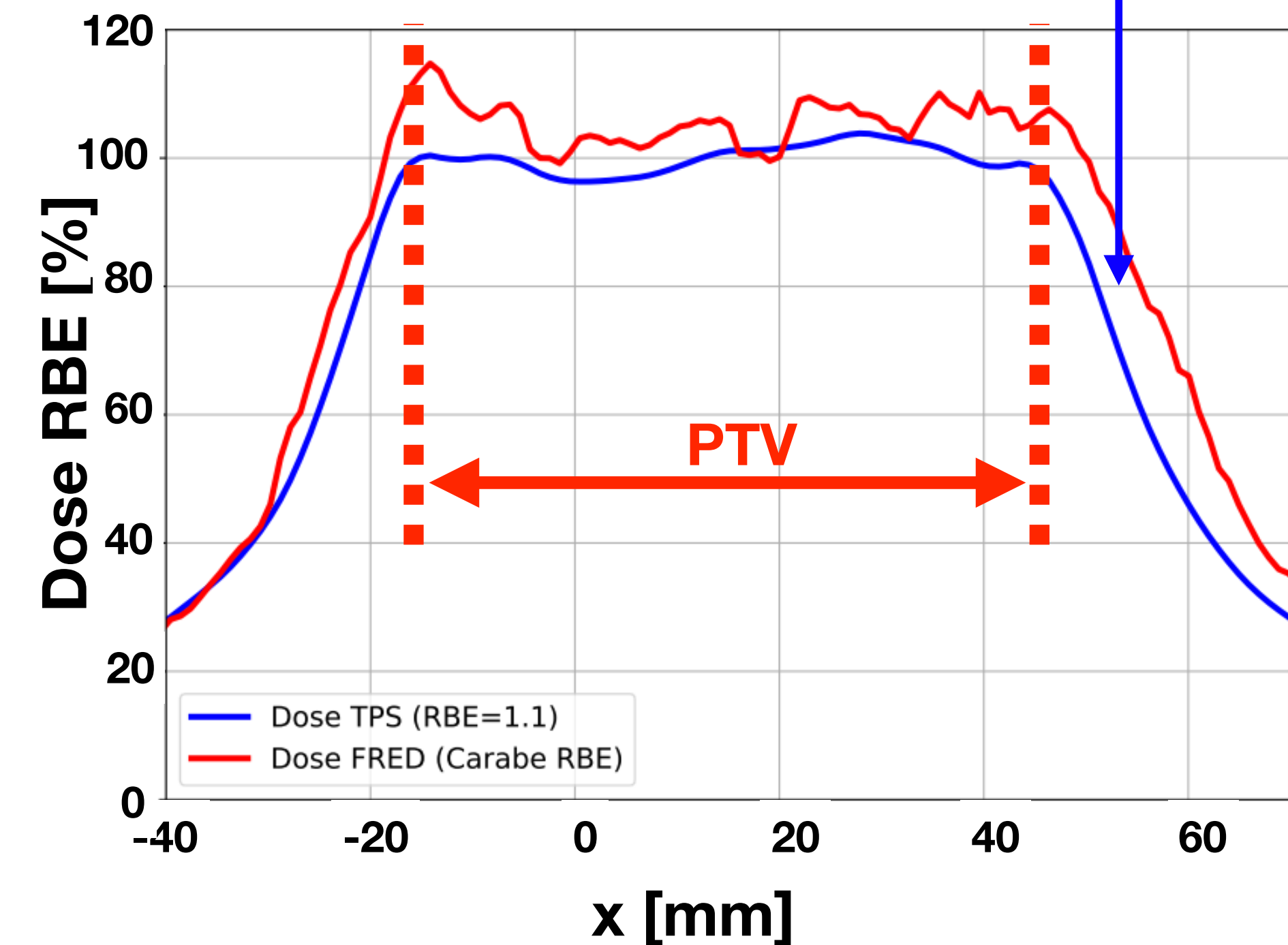


Radiobiological dose  
FRED variable RBE



5mm range difference

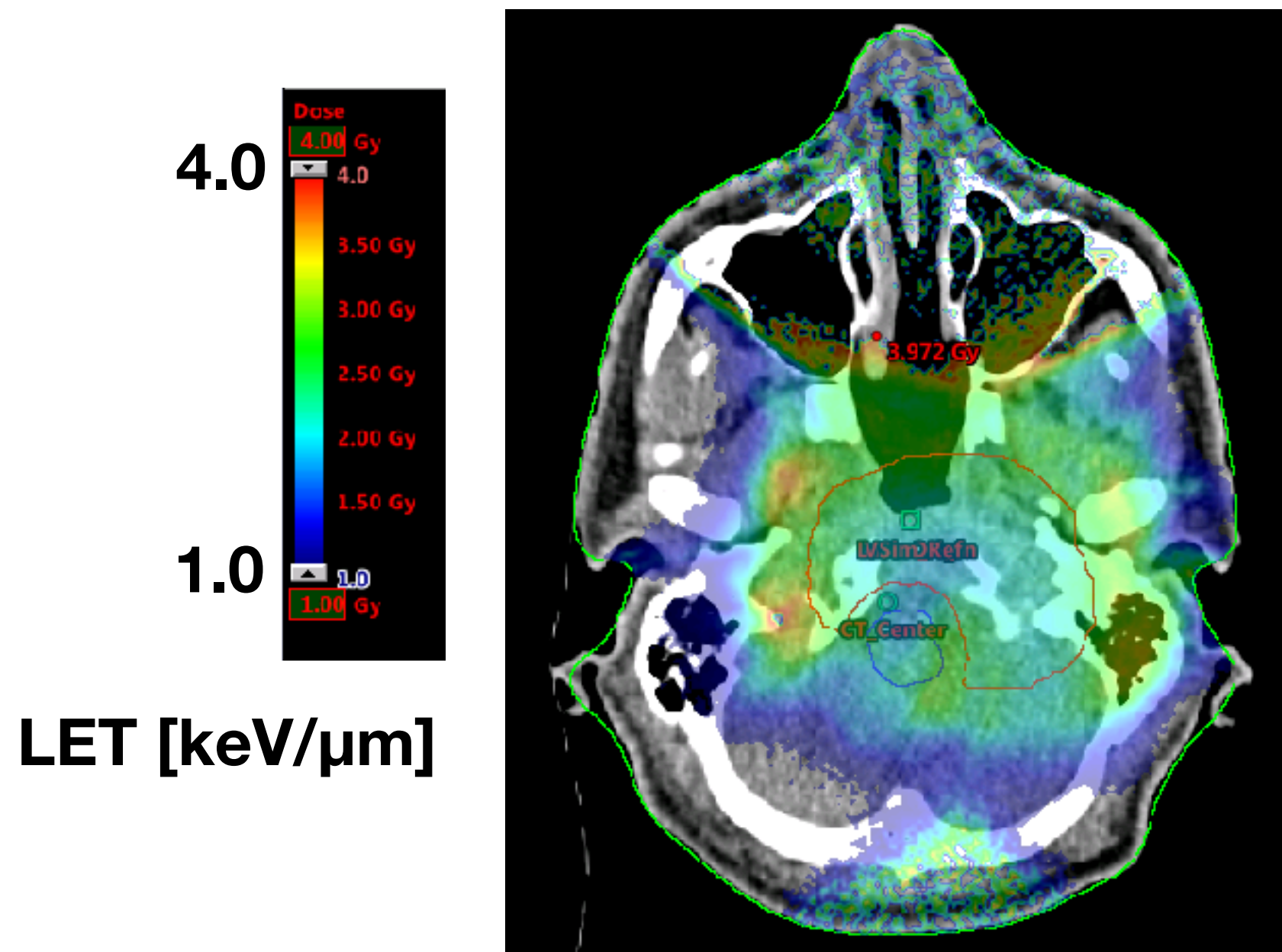
TPS<sub>RBE=1.1</sub> VS FRED<sub>RBE(Carabe)</sub>



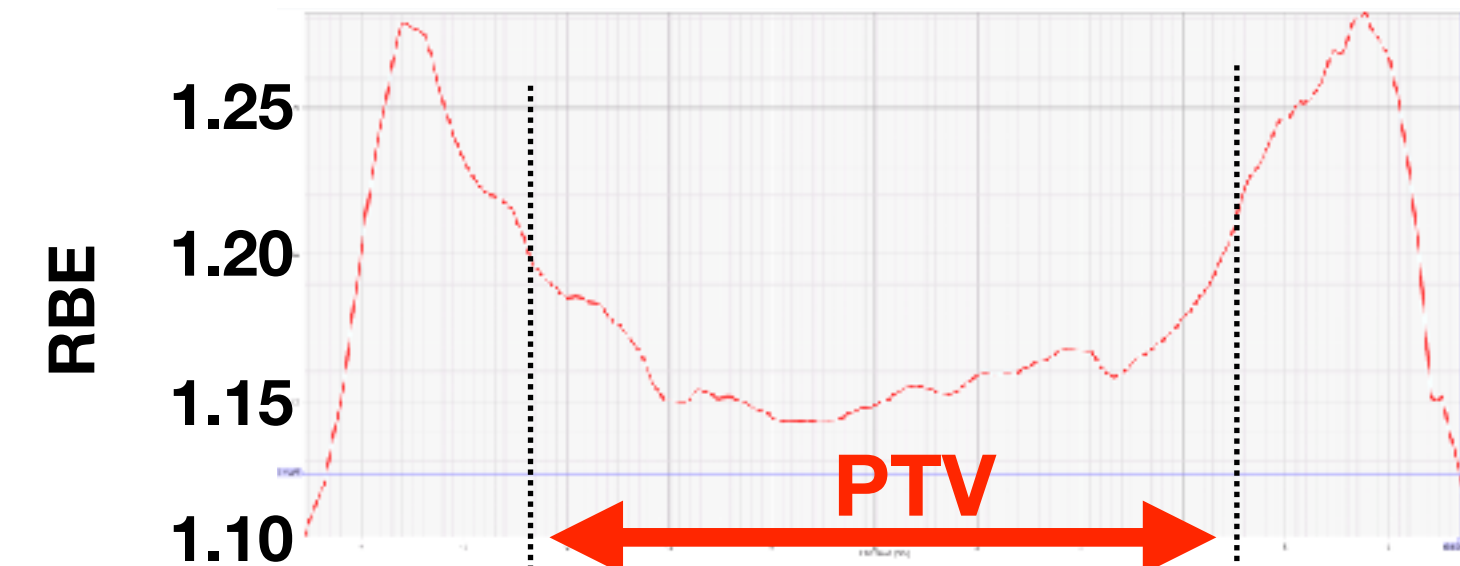
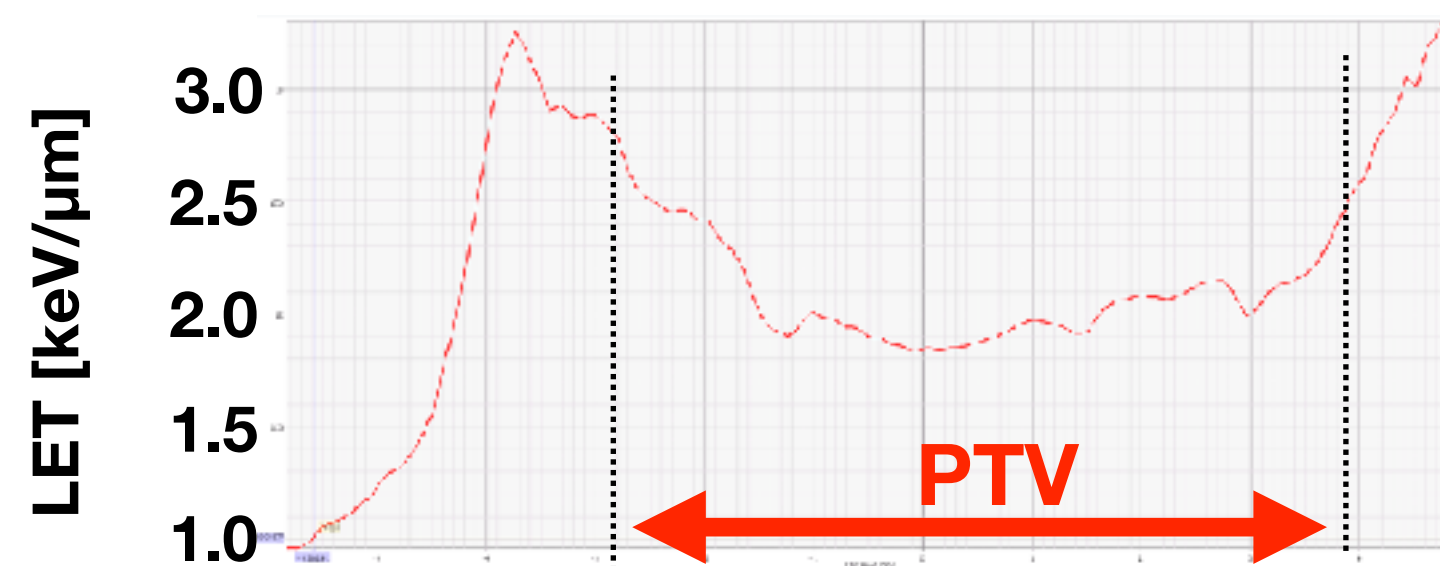
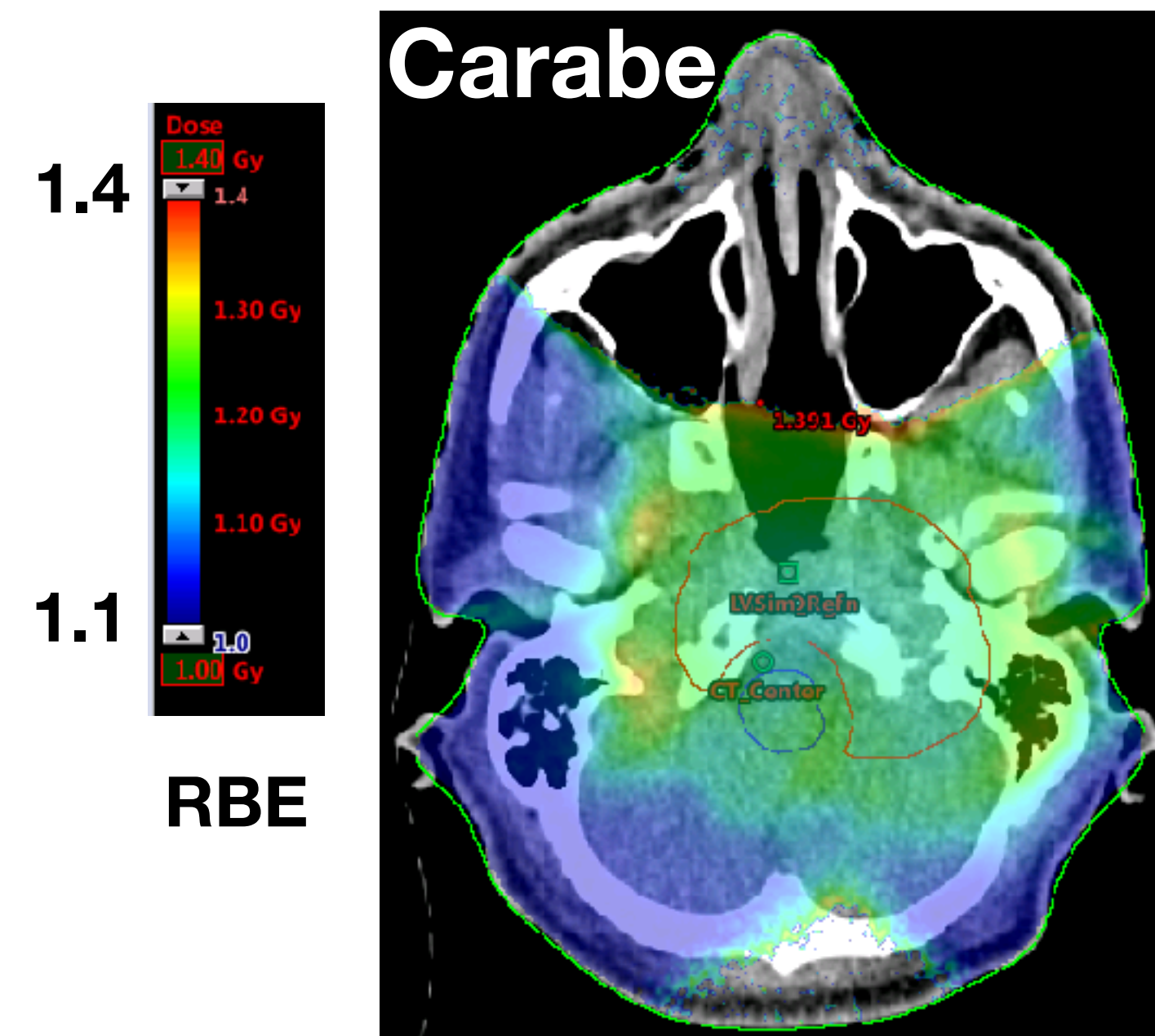


# LET and RBE distributions for variable RBE dose calculations

## LET distribution



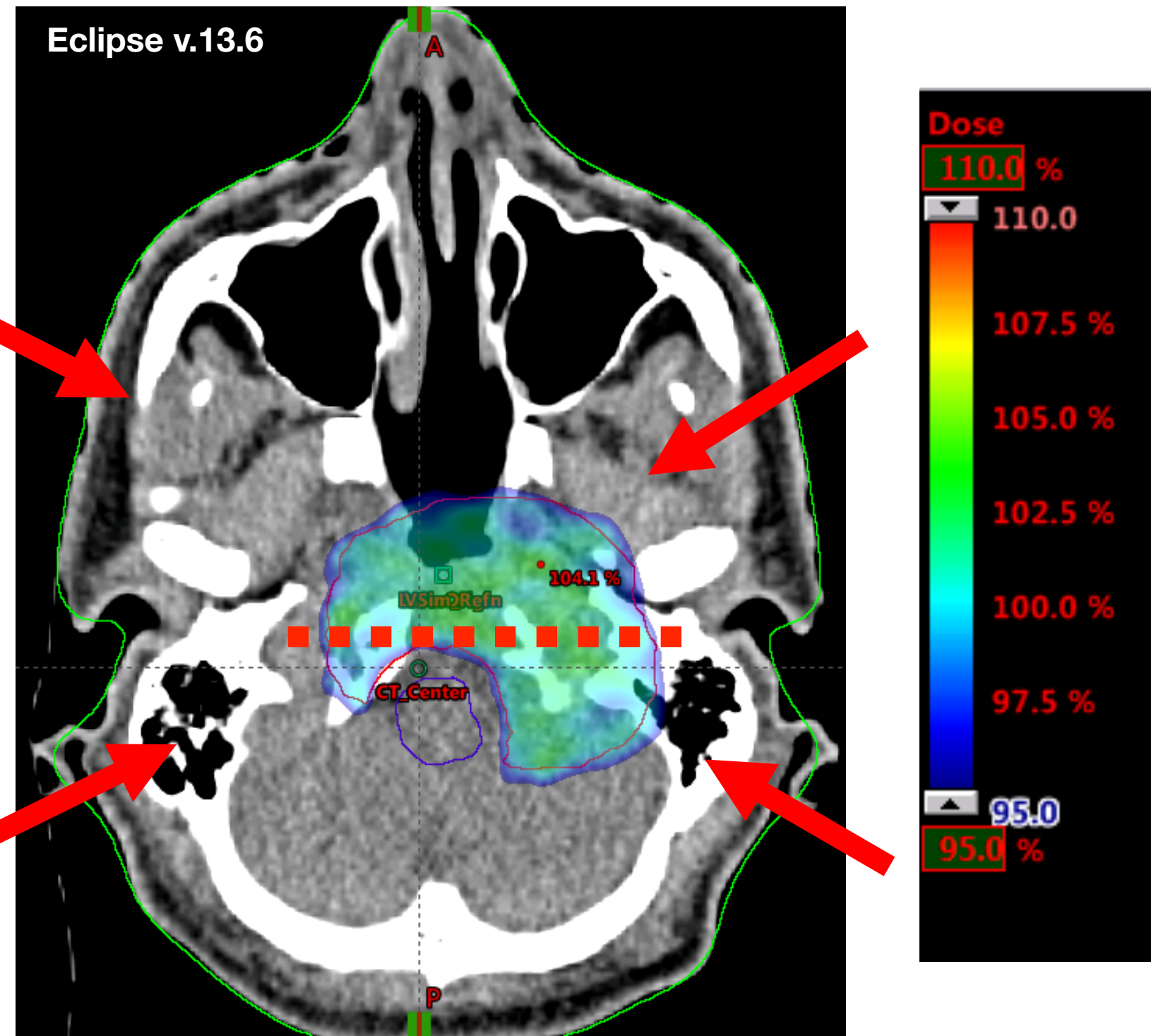
## RBE distribution



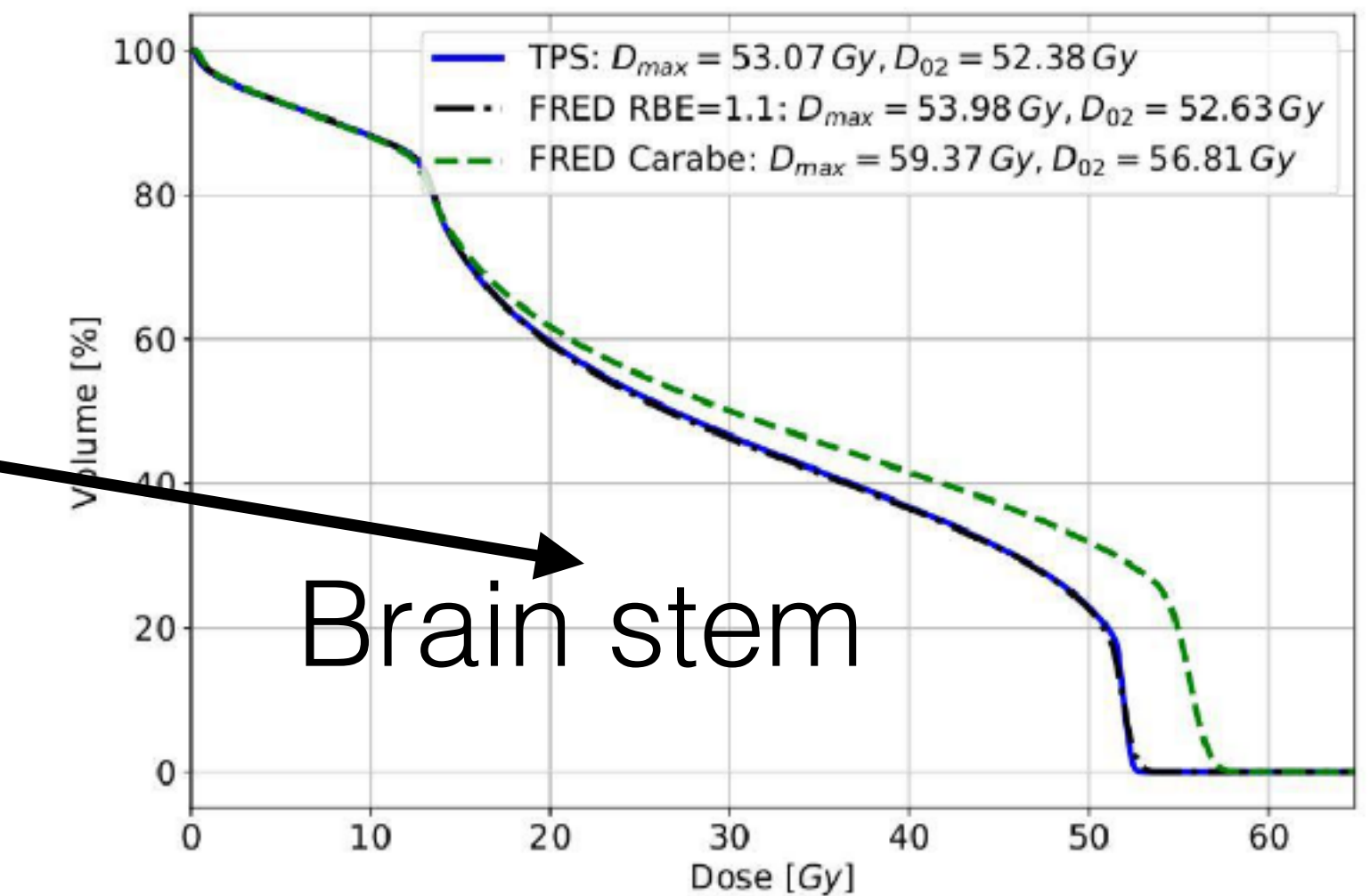
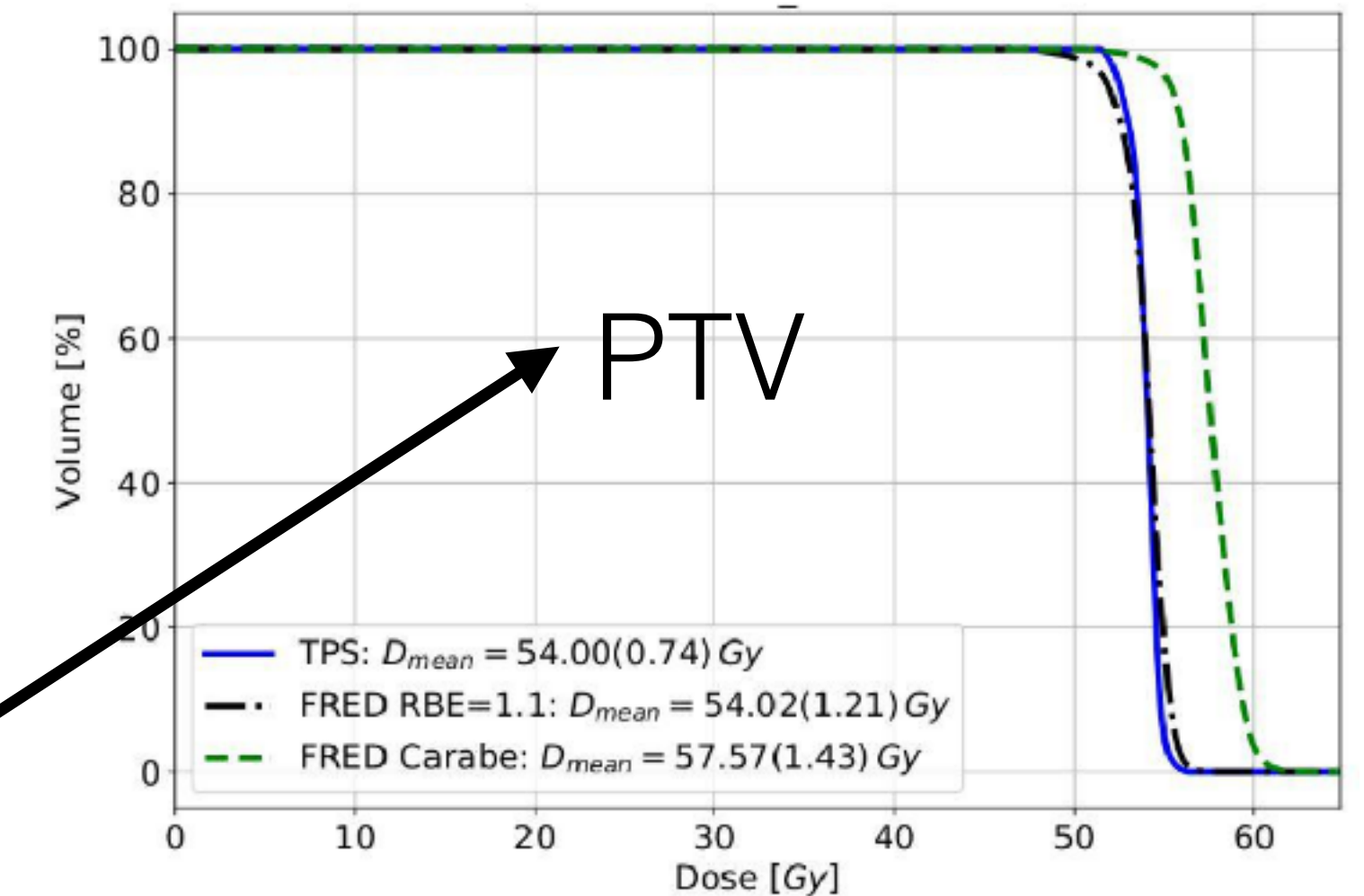
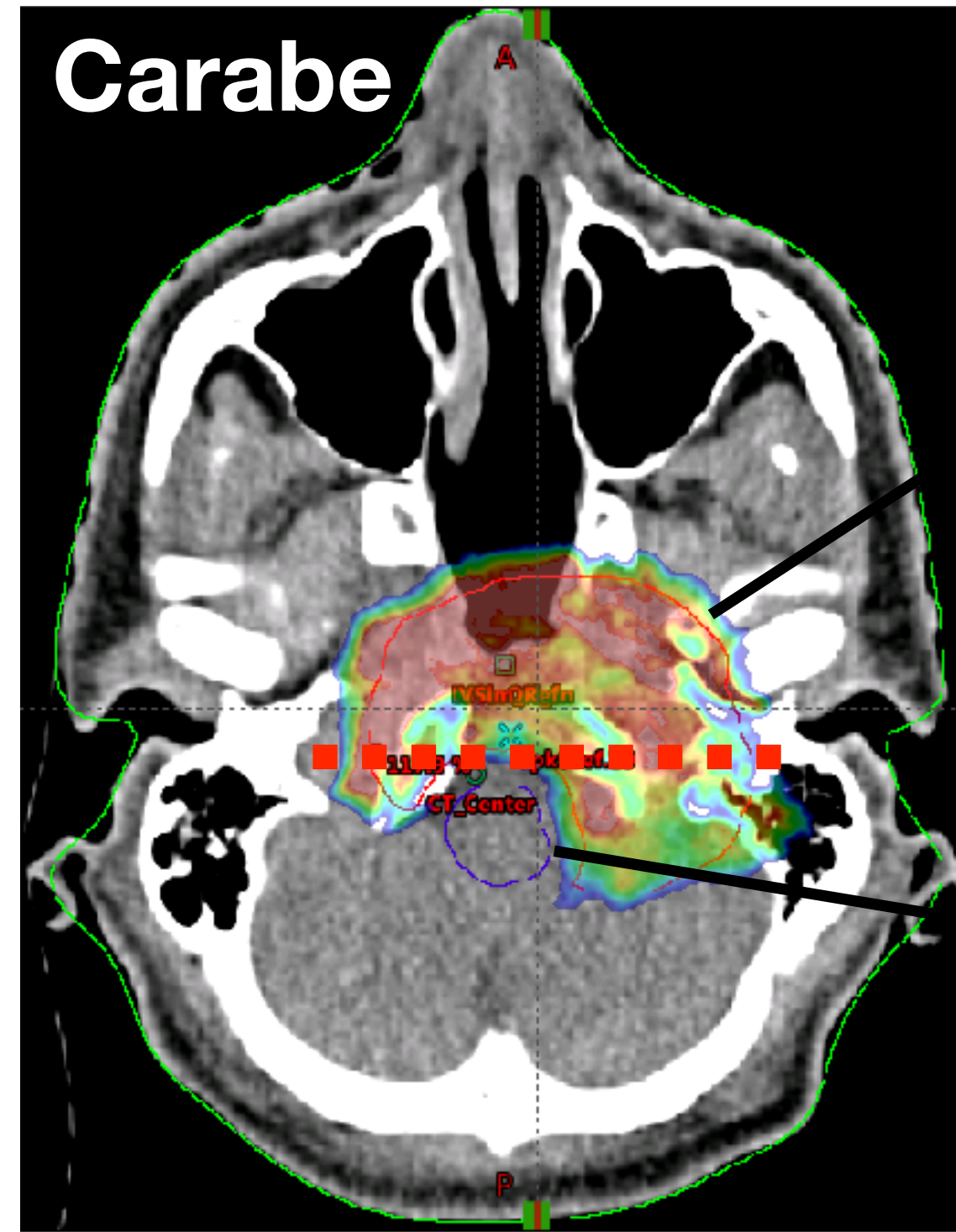


# FRED for independent dose calculation and treatment planning studies

Radiobiological dose  
TPS RBE=1.1



Radiobiological dose  
FRED variable RBE





# Treatment planing studies

10 Head&Neck patients treated in Krakow

PTV	RBE=1.1	Carabe RBE
Dmean	100.1% (0.0%)	107.9% (0.8%)

Brain stem	RBE=1.1 [Gy(RBE)]	Carabe RBE [Gy(RBE)]
D <sub>02</sub>	50.8 (1.8)	55.6 (2.1)

- PTV D<sub>mean</sub> up to ~8% higher that prescribed dose
- OAR (brain stem) D<sub>02</sub> up to ~5 Gy(RBE) higher than calculated in TPS



# Treatment planing studies

10 Head&Neck patients treated in Krakow

PTV	RBE=1.1	Carabe RBE
Dmean	100.1% (0.0%)	107.9% (0.8%)

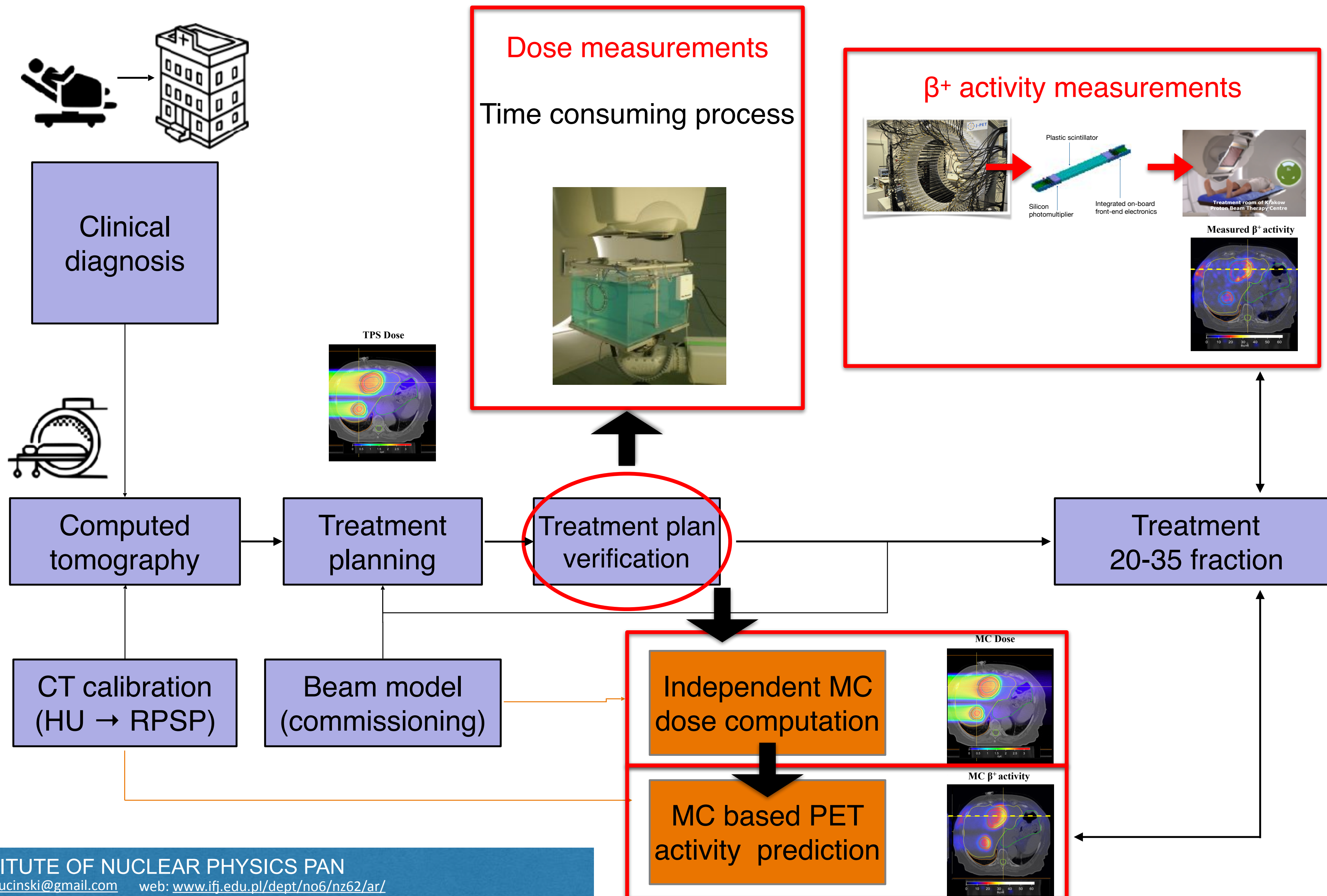
Brain stem	RBE=1.1 [Gy(RBE)]	Carabe RBE [Gy(RBE)]
D <sub>02</sub>	50.8 (1.8)	55.6 (2.1)

- PTV D<sub>mean</sub> up to ~8% higher that prescribed dose
- OAR (brain stem) D<sub>02</sub> up to ~5 Gy(RBE) higher than calculated in TPS

- **The mean time to recalculate a single treatment plan was 3.7 min**
  - 10<sup>5</sup> p/beam
  - 1.2×10<sup>9</sup> p/plan
  - 5.6×10<sup>6</sup> p/s
  - voxel size: 0.7 mm x 0.7 mm x 1.2 mm.



# Proton therapy treatment

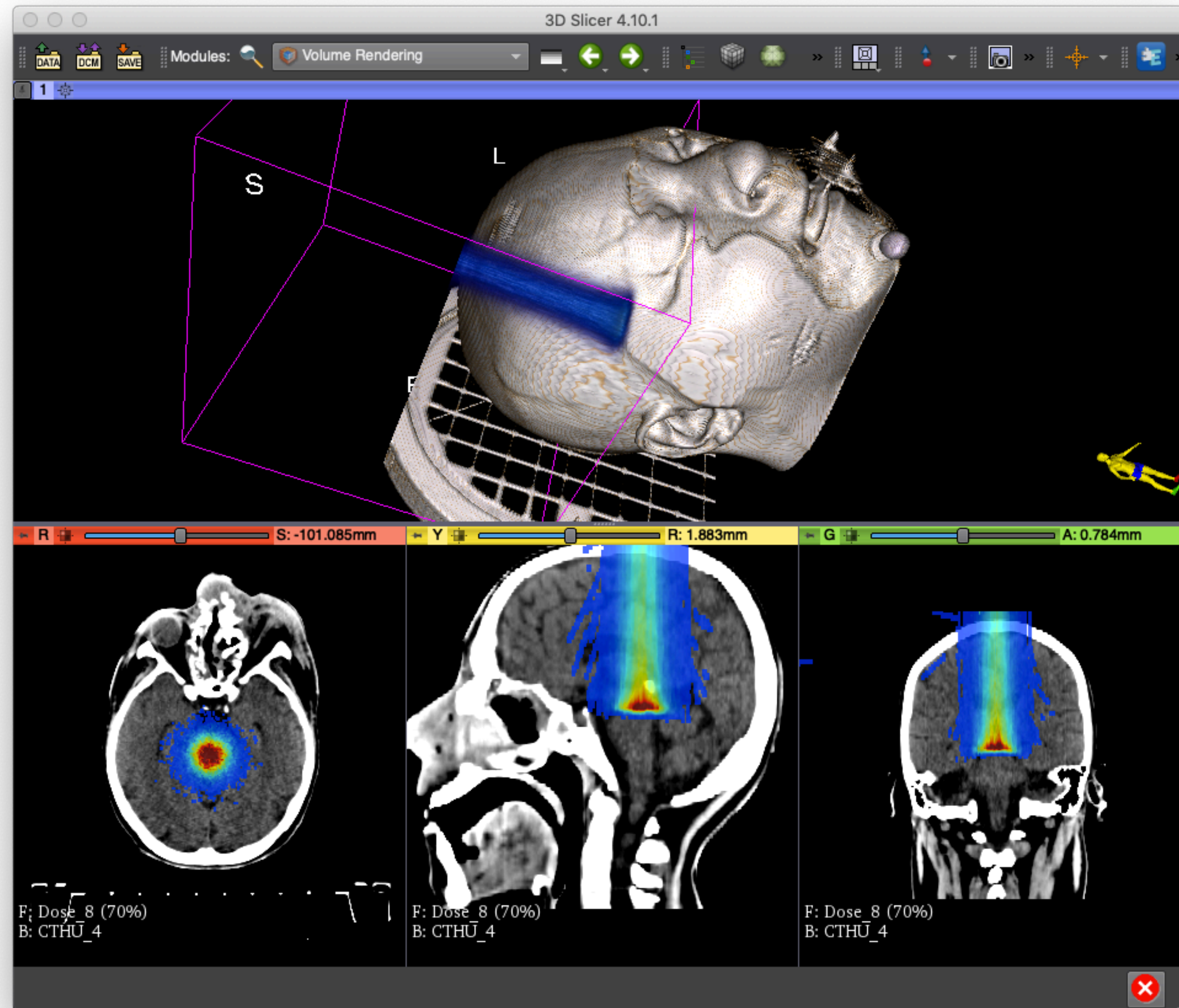


# FRED: New developments and future applications

- Interfacing FRED with Eclipse TPS
- We are currently testing FRED for beam models of **IBA, Varian, and Mevion** facilities
- Scoring in multiple regions to enable application of range shifter, dynamic aperture or detector development for range monitoring
- FRED kernel developments: implementation of photon interactions and nuclear models for light and heavy ions.



# FRED Interface with Slicer3D



# FRED: New developments and future applications

- Potential clinical applications of GPU-accelerated MC code FRED are:
  - independent QA treatment plan recalculation,
  - fast, in-room dose re-calculation based on daily CT images
  - multi-parameter plan optimization (robust, radiobiological, arc optimization).



# Conclusions

- These results confirm excellent performance of the physics models implemented in FRED.
- FRED dosimetric accuracy enables its application in clinical routine and potential improvement of patient treatment with protons.

# Thank you



J. Baran, K. Czerska, J. Gajewski, M. Garbacz,  
L. Grzanka, R. Kopec, A. Krempla, K. Krzempek,  
G. Mierzwińska, N. Mojżeszek, E. Pluta, M. Rydygier



Paweł Moskal  
Monika Pawlik-Niedźwiecka  
& the J-PET collaboration

Nils Krah



Ilaria Rinaldi



Angelo Schiavi, Giuseppe  
Battistoni, Vincenzo Patera

Francesco Tommasino,  
Emanuele Scifoni,  
Marco Durante



Trento Institute for  
Fundamental Physics  
and Applications

Reinhard Schulte



LOMA LINDA UNIVERSITY  
HEALTH