

# MEASUREMENT OF THE ENERGY LOSS DURING PROTON THERAPY: A NEW TREATMENT VERIFICATION TECHNIQUE

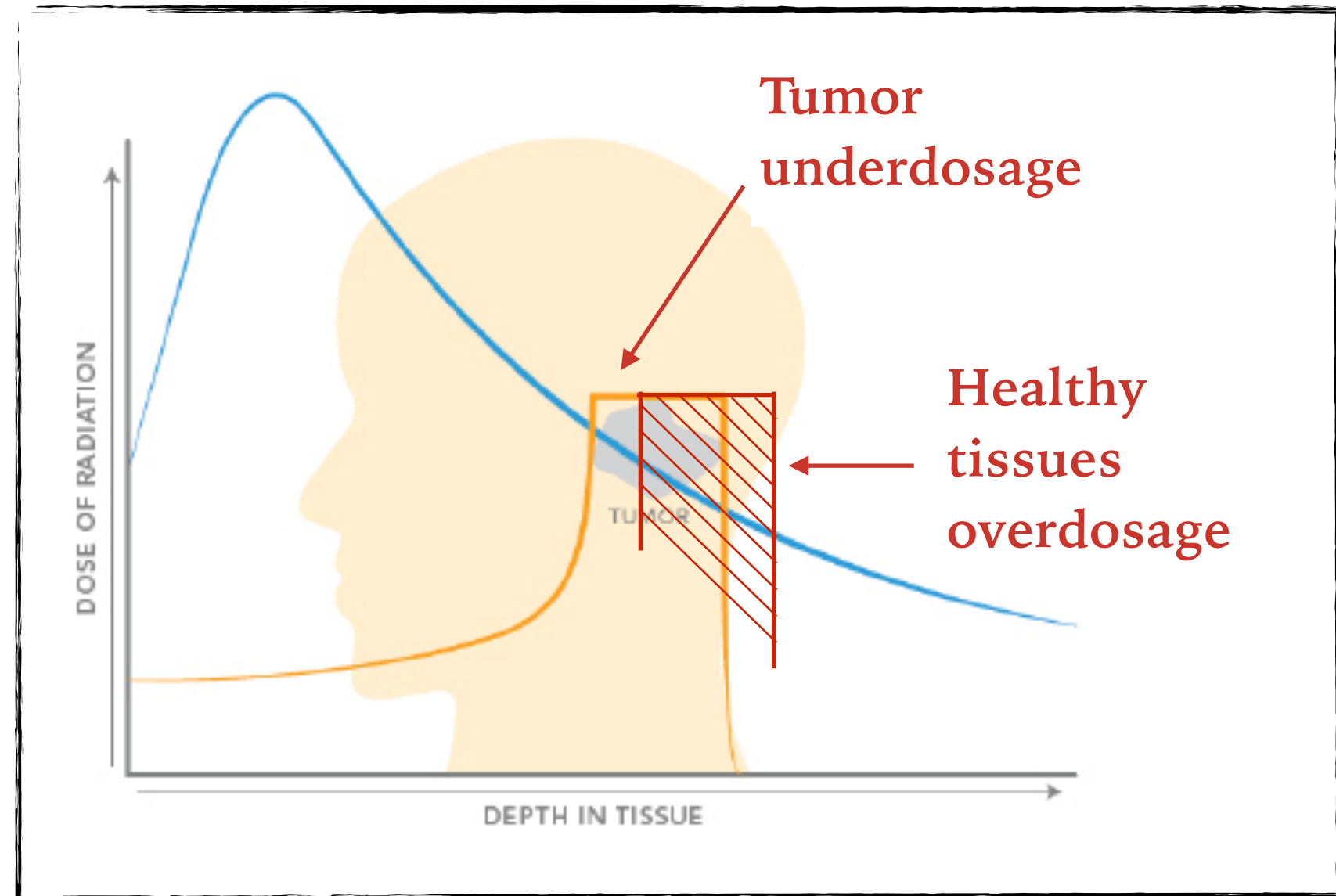
---

*V. Ferrero, M. Aglietta, P. Cerello, E. Fiorina, M.  
Rafecas, A. Vignati, J. Werner and F. Pennazio*



26-30 June 2022, Riva del Garda

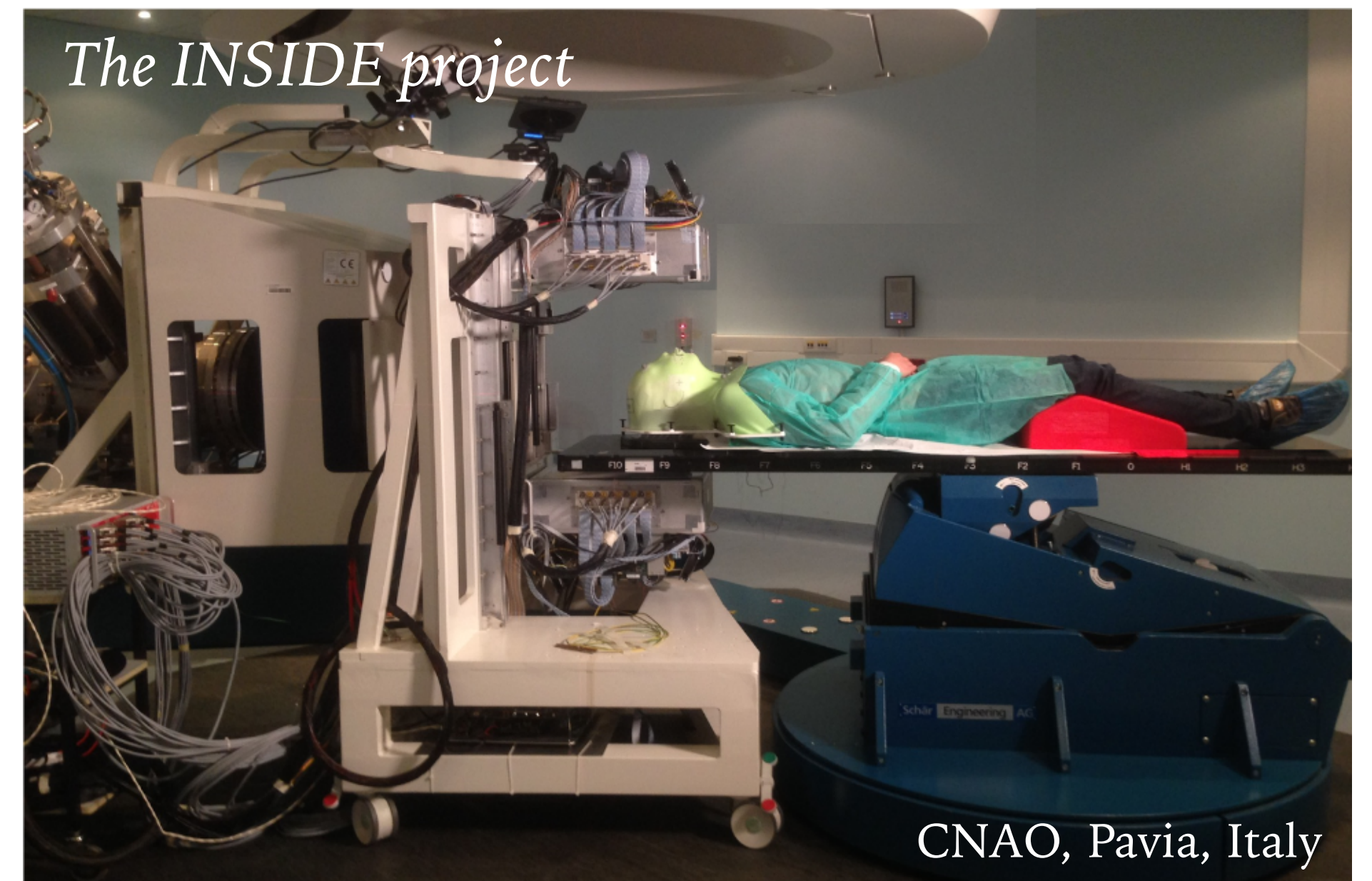
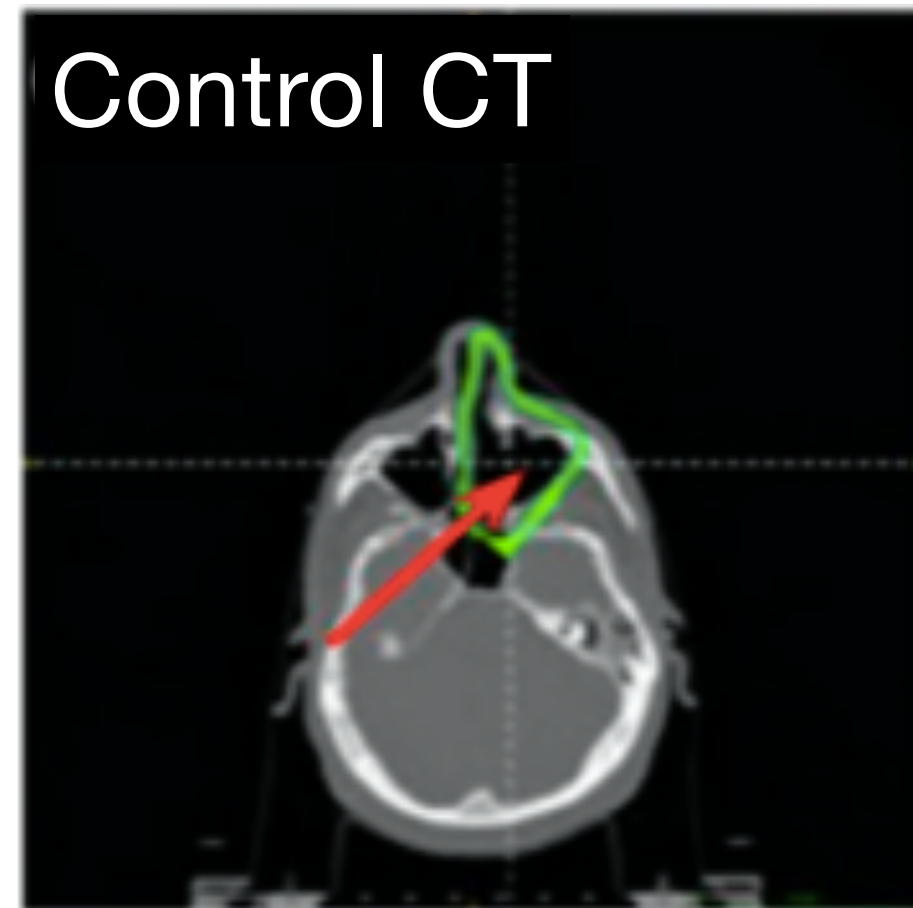
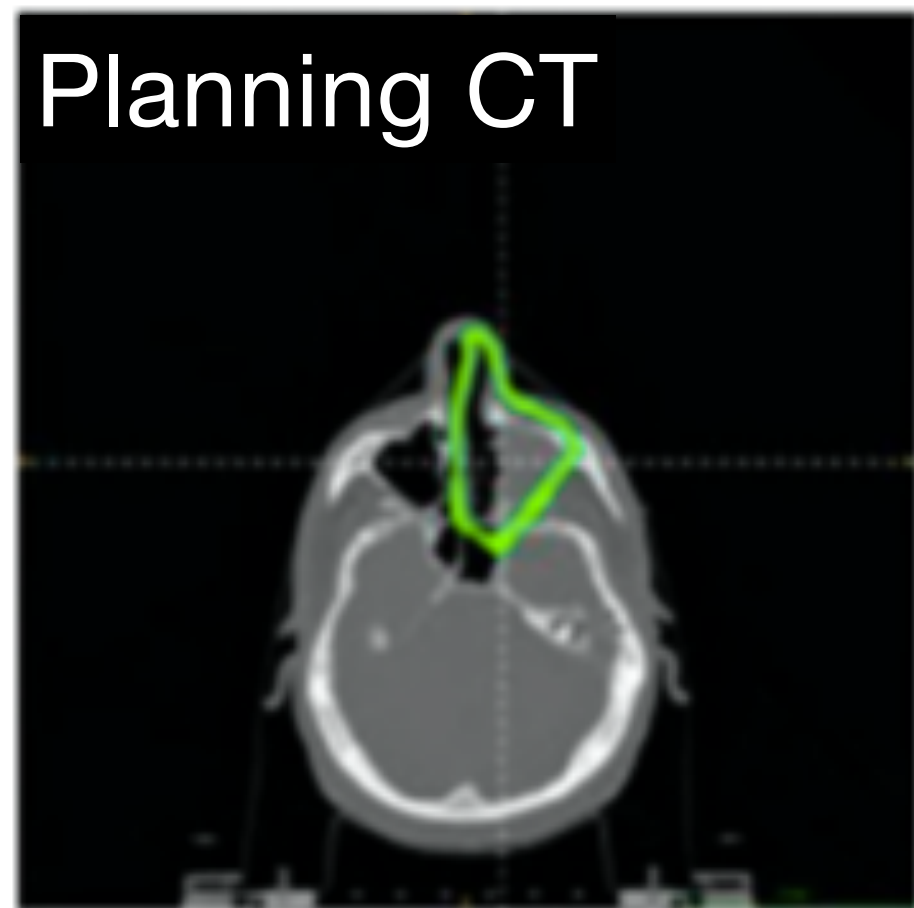
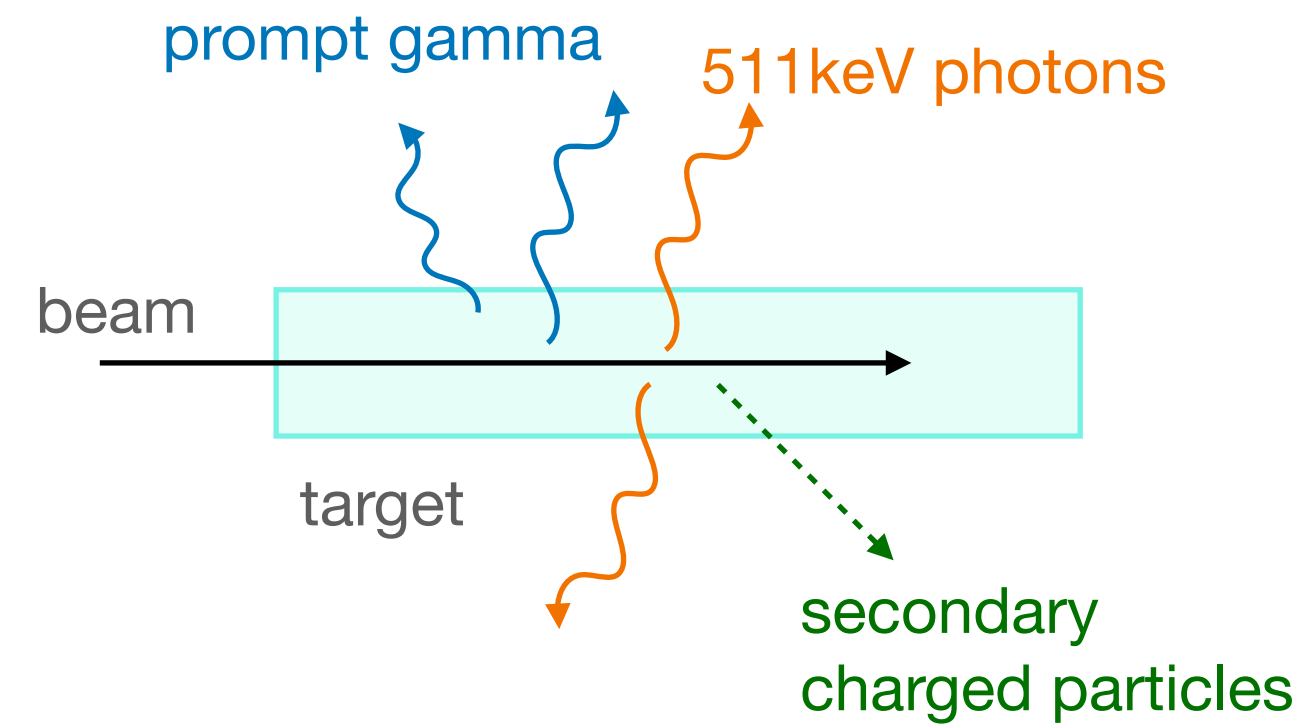
# TREATMENT VERIFICATION



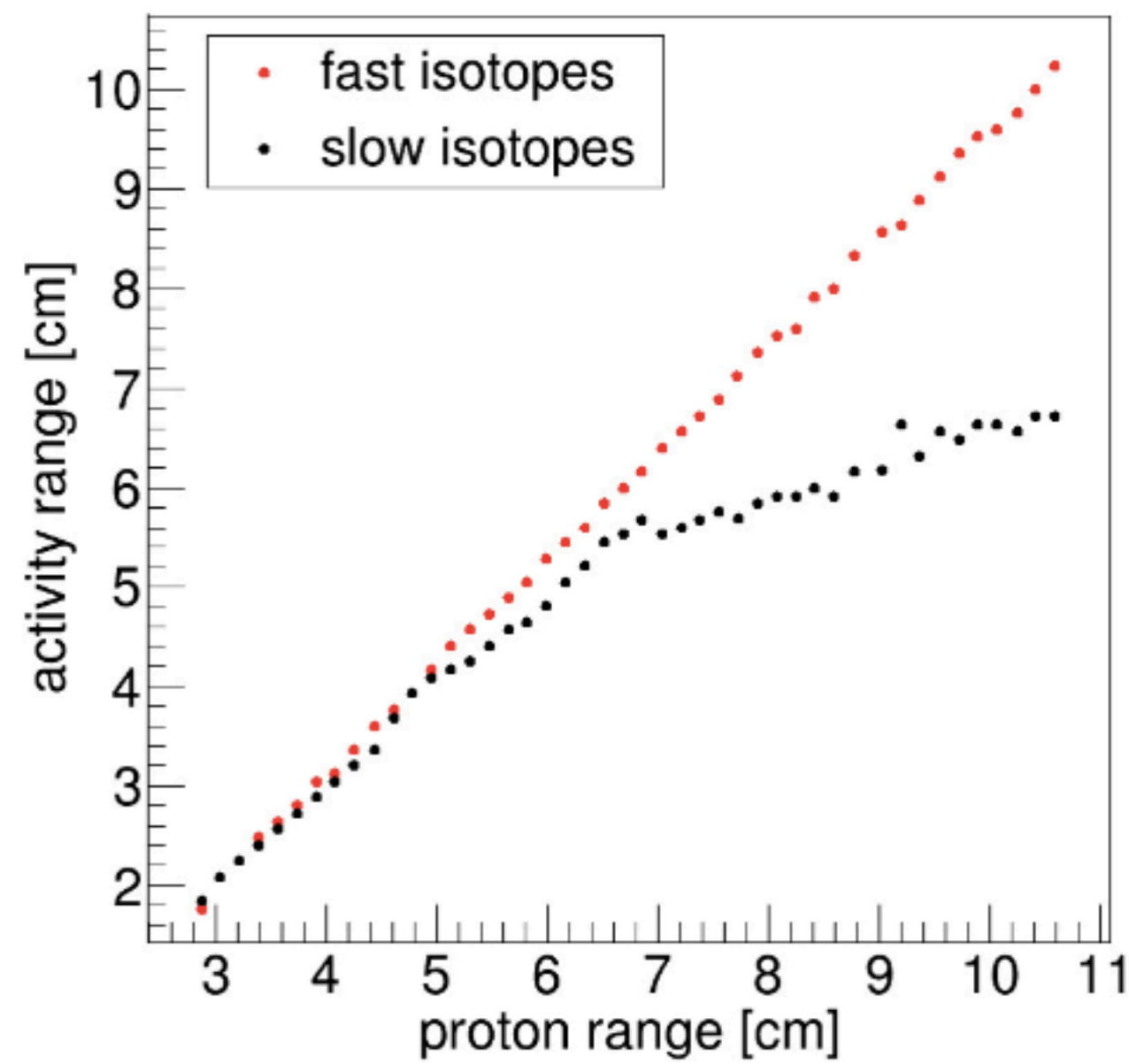
## Dose uncertainties:

- ➔ Patient setup
- ➔ Dose calculation
- ➔ Anatomical changes

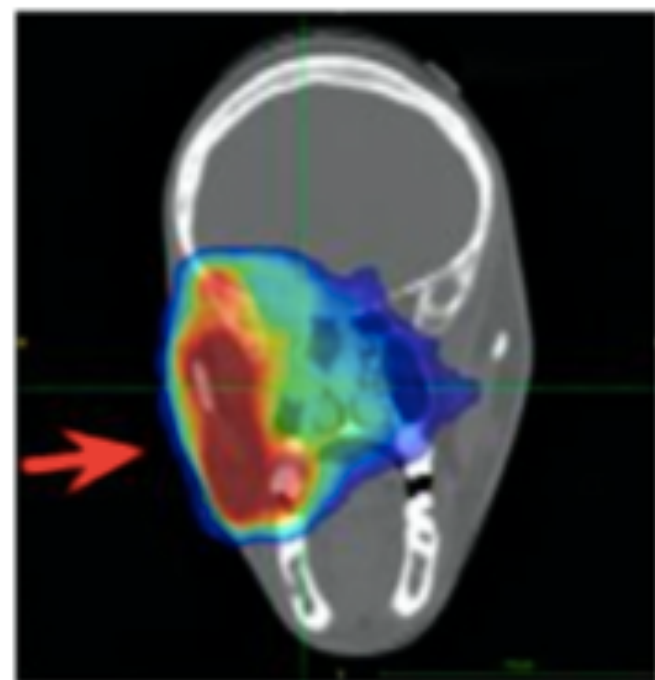
~ 100 proton therapy facilities all over the world (PTCOG)



# SECONDARY PARTICLES FOR RANGE MONITORING



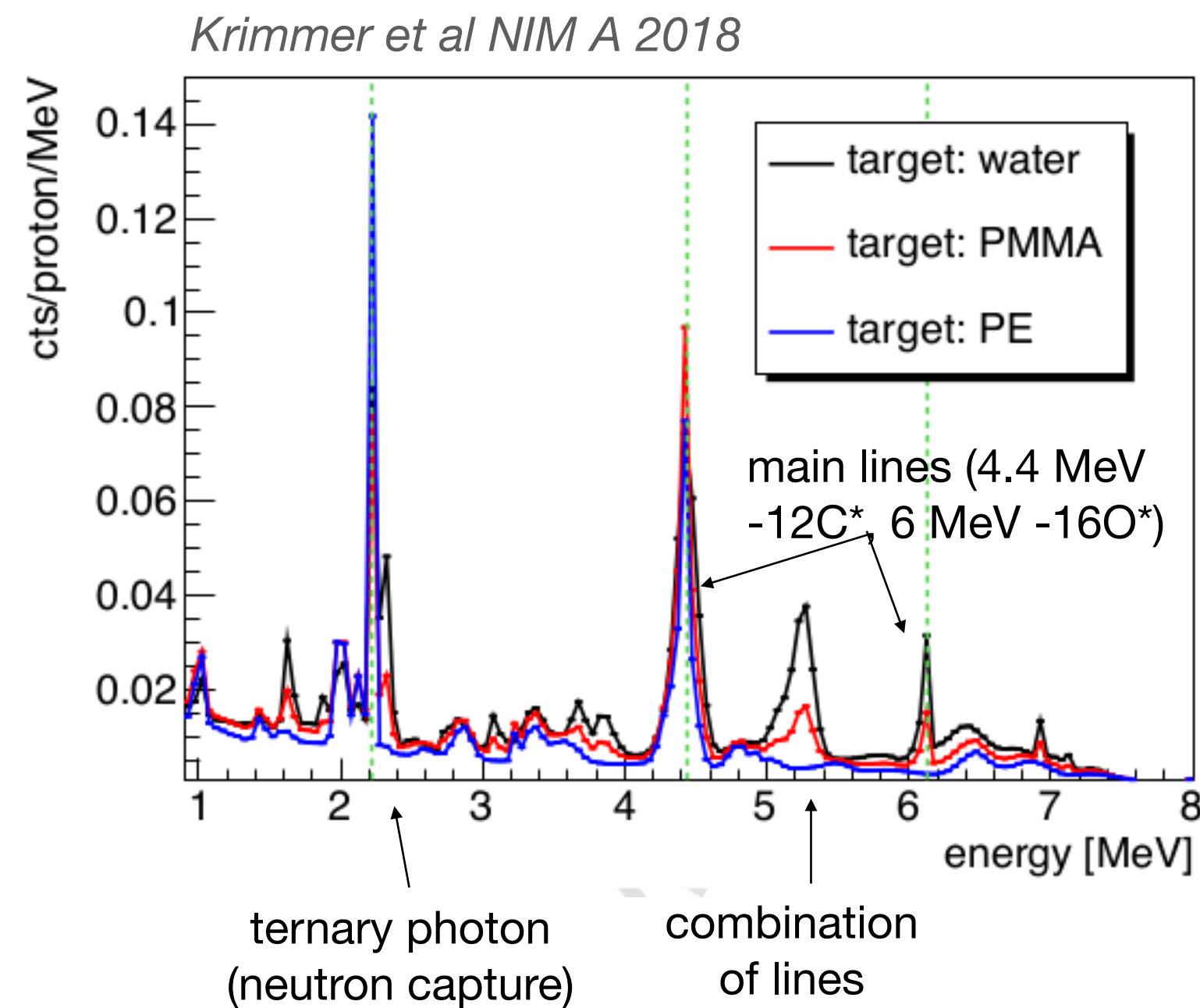
Ferrero V et al. NIM A 2019



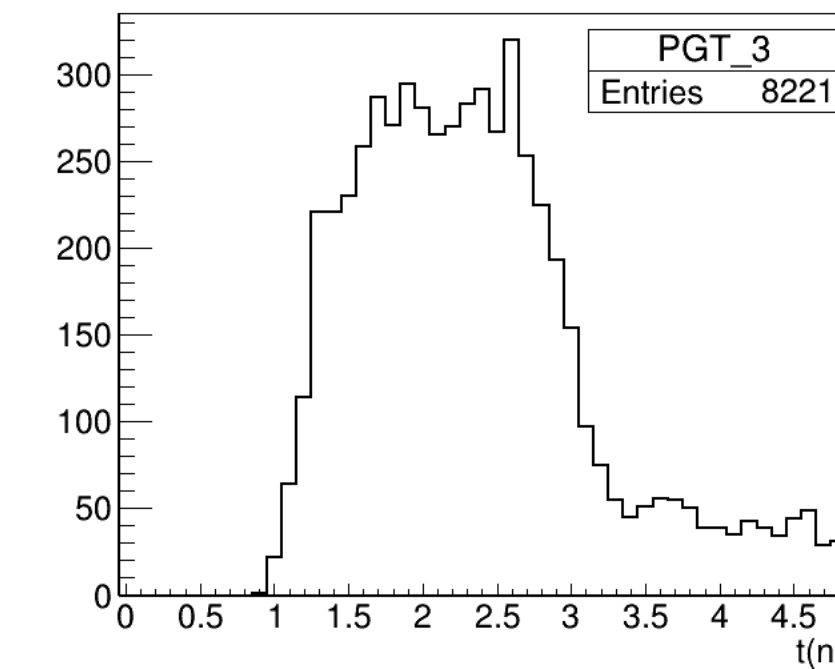
PET signal (MLEM)

Prompt gamma: commercial interest

IBA Knife-Edge Slit Camera (collimator):  
Head-and-neck, brain tumors (range shifts 1-2mm)

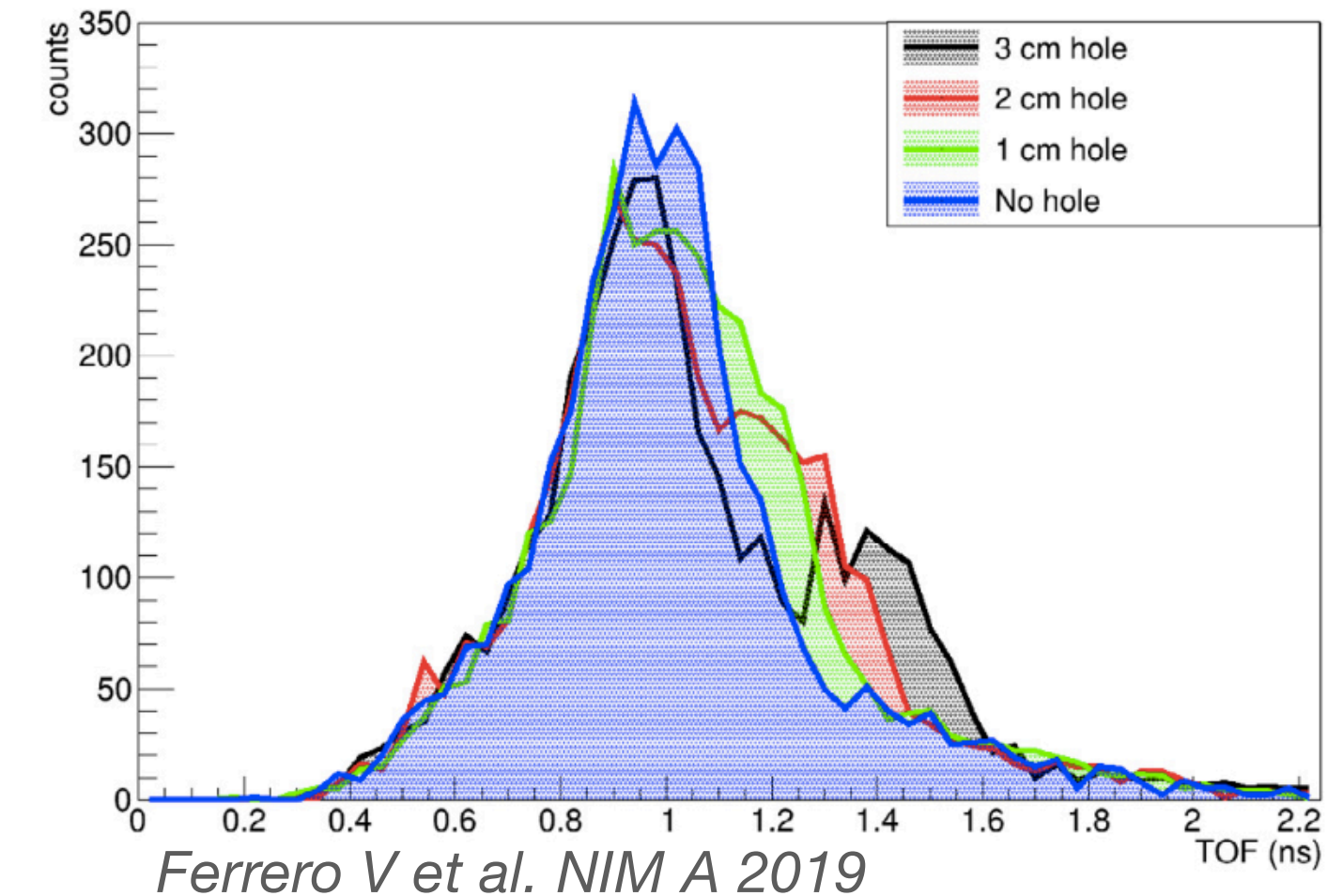


Prompt gamma timing (PGT)

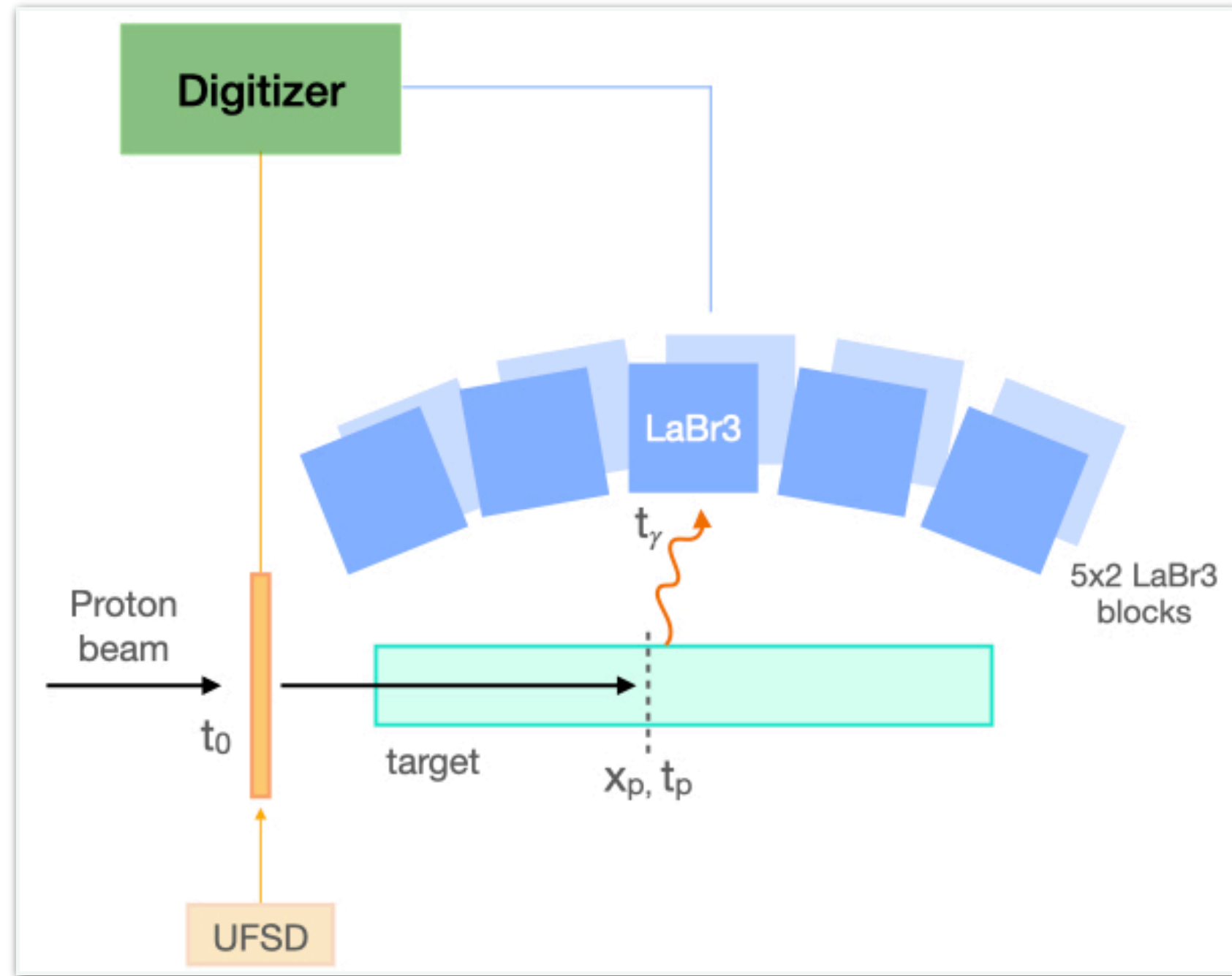


$$\text{TOF} = t_\gamma(z_p) - t_0$$

PGT for range monitoring



# SPATIO-TEMPORAL EMISSION RECONSTRUCTION



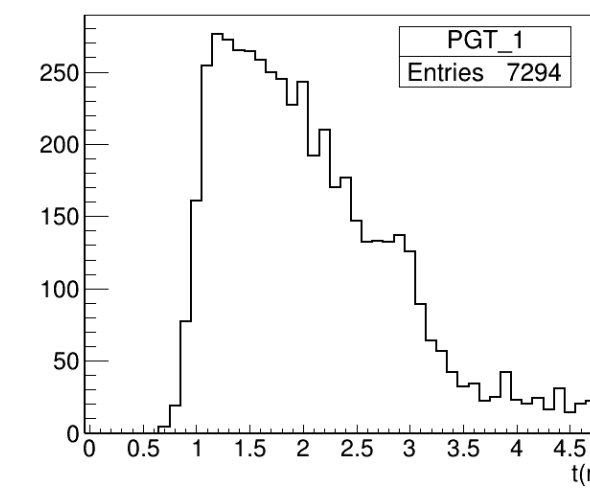
## PGT MULTI-DETECTOR SYSTEM

Setup with N detectors

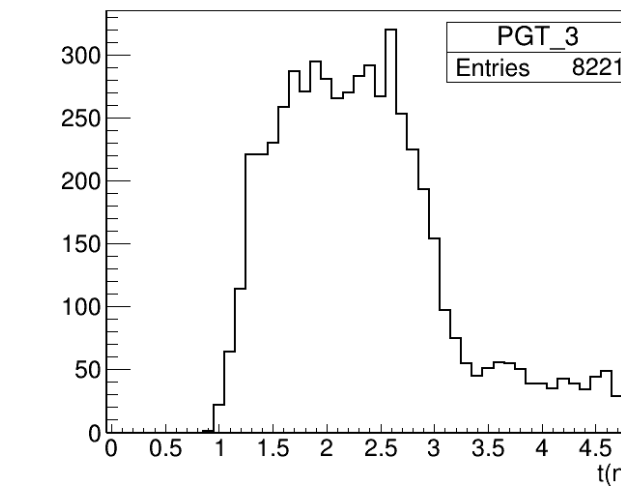
*LaBr3:Ce* for the prompt gamma detection ( $t_\gamma$ )

*UFSD* for the primary proton detection ( $t_0$ )

$$\text{TOF} = t_\gamma - t_0$$



det 1



det 3

... det N

*Pennazio F. et al PMB 2022*

$$m_{jp}^{k+1} = \frac{m_{jp}^k}{S_{jp}} \sum_i \sum_d \frac{n_{id}}{\sum_l \sum_t f_{idlt} m_{lt}^k} f_{idjp}$$

prompt photon

sensitivity

p: time bin (emission)

j: space bin (emission)

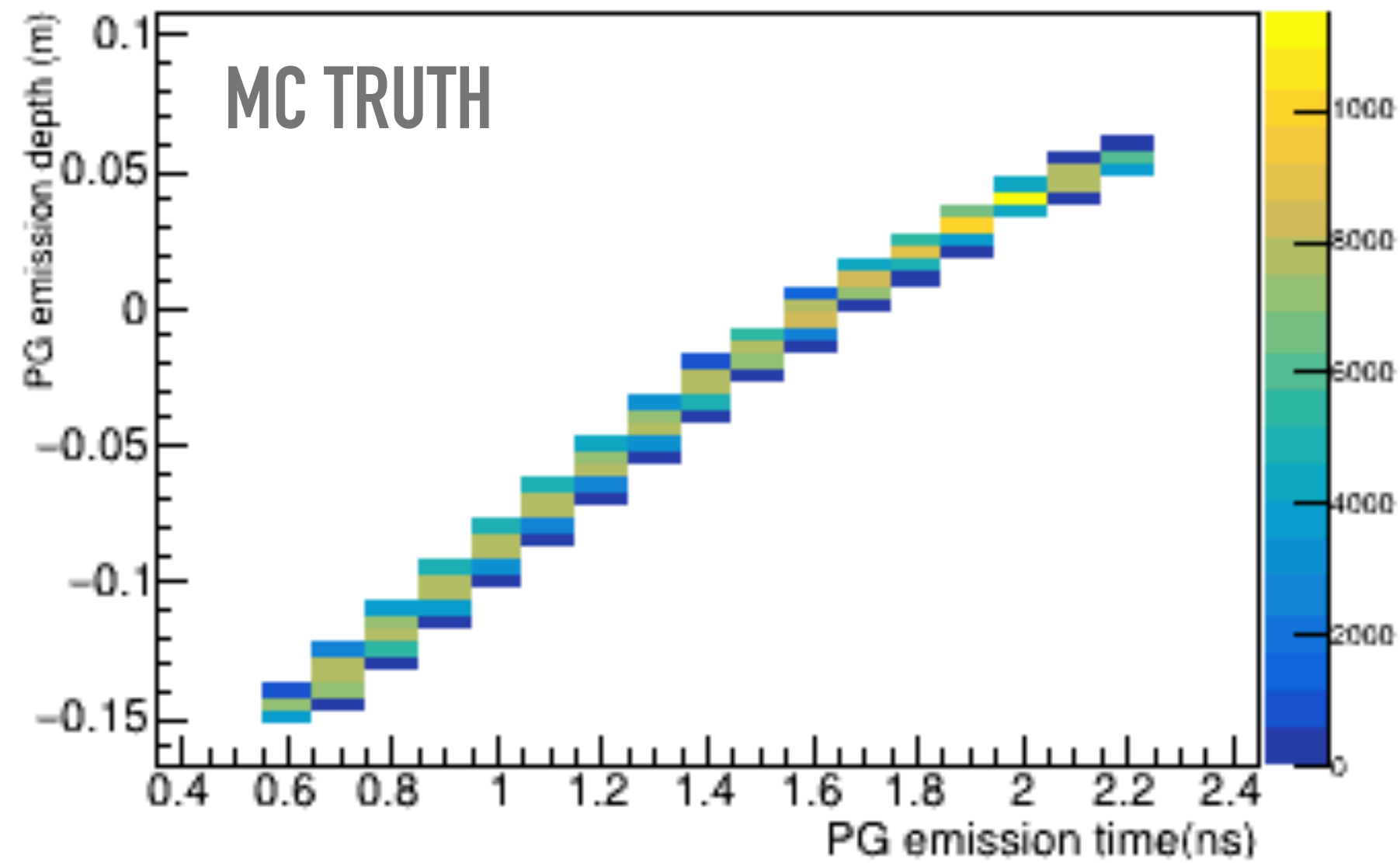
i: time bin (detection)

d: detector

SM

MLEM disentangles the directional information comprised in the multiple TOF to reconstruct the position and time of emission of prompt gammas

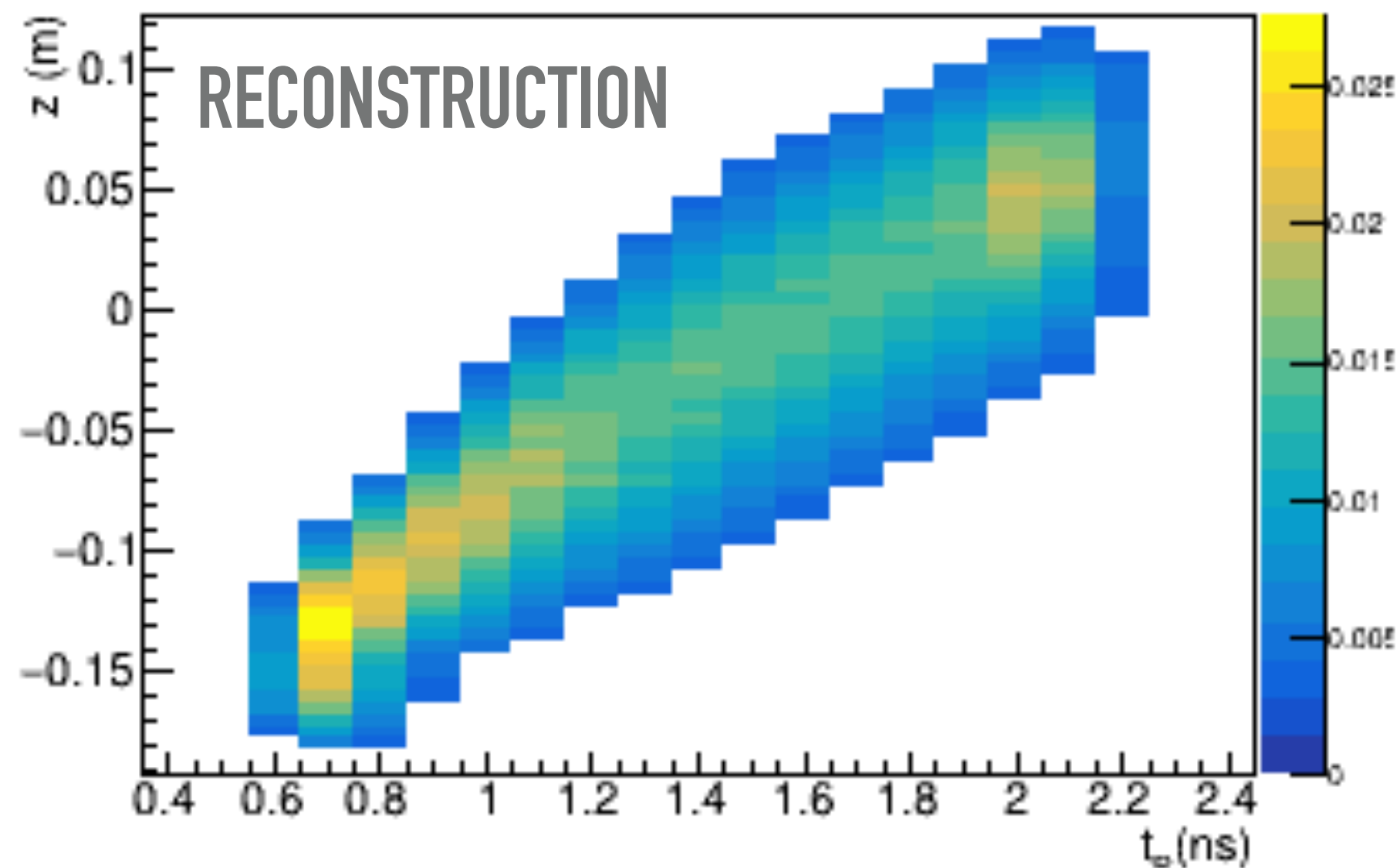
# SPATIO-TEMPORAL EMISSION RECONSTRUCTION



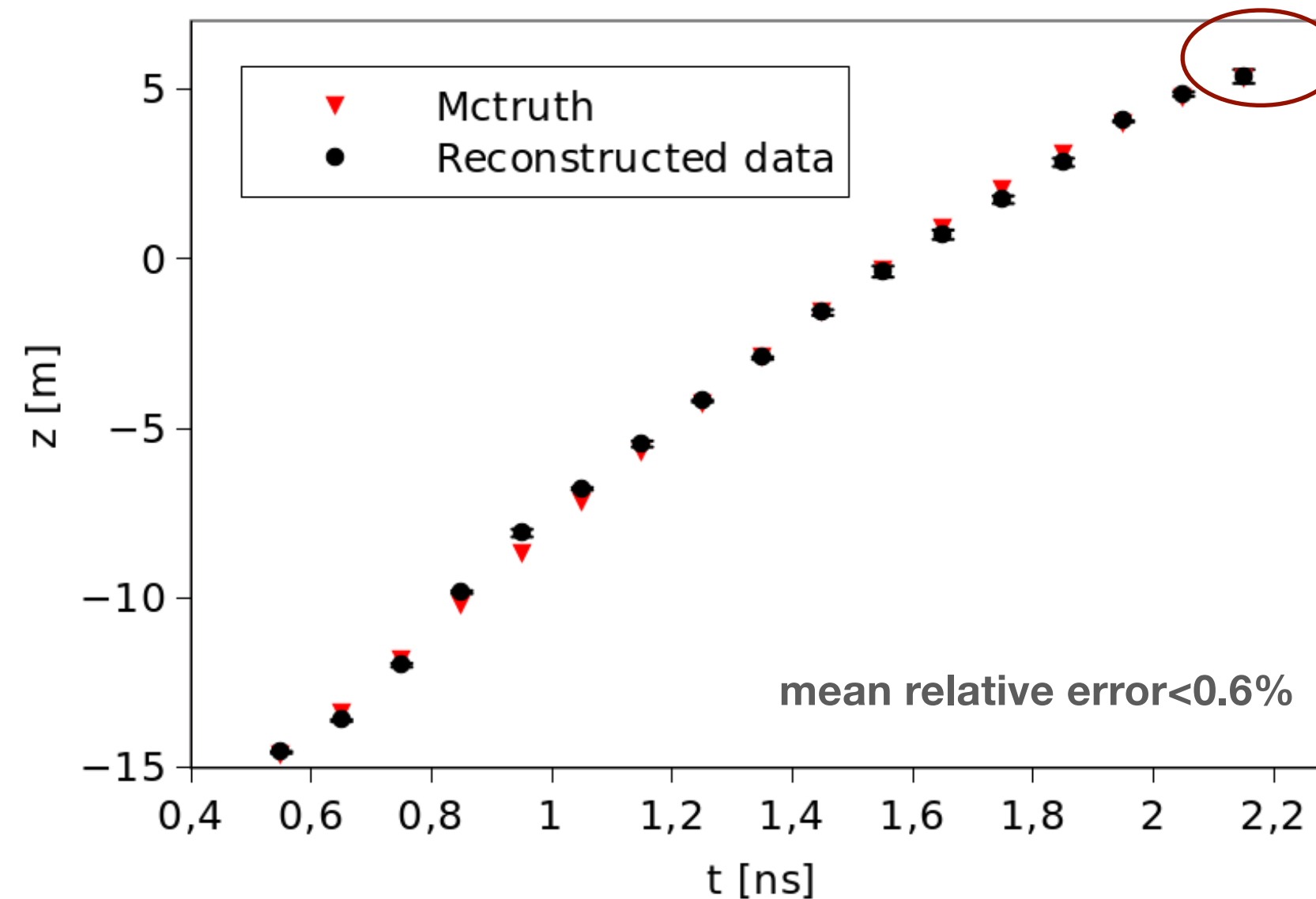
**10<sup>8</sup> protons, 189MeV**  
 10<sup>7</sup> produced photons in 4π  
 Time resolution=100 ps σ  
 Energy cut 1MeV-7MeV  
 ~10<sup>4</sup> events per detector  
 110 detectors (clinical scenario)  
 5 simulation runs  
 FLUKA MC tool

$$m_{jp}^{k+1} = \frac{m_{jp}^k}{S_{jp}} \sum_i \sum_d \frac{n_{id} \cdot f_{idjp}}{\sum_l \sum_t f_{idlt} m_{lt}^k} f_{idjp}$$

data:  $n_{id}$   
 prompt photon:  $m_{jp}^k$   
 sensitivity:  $S_{jp}$   
 SM:  $f_{idjp}$   
 p: time bin (emission)  
 j: space bin (emission)  
 i: time bin (detection)  
 d: detector



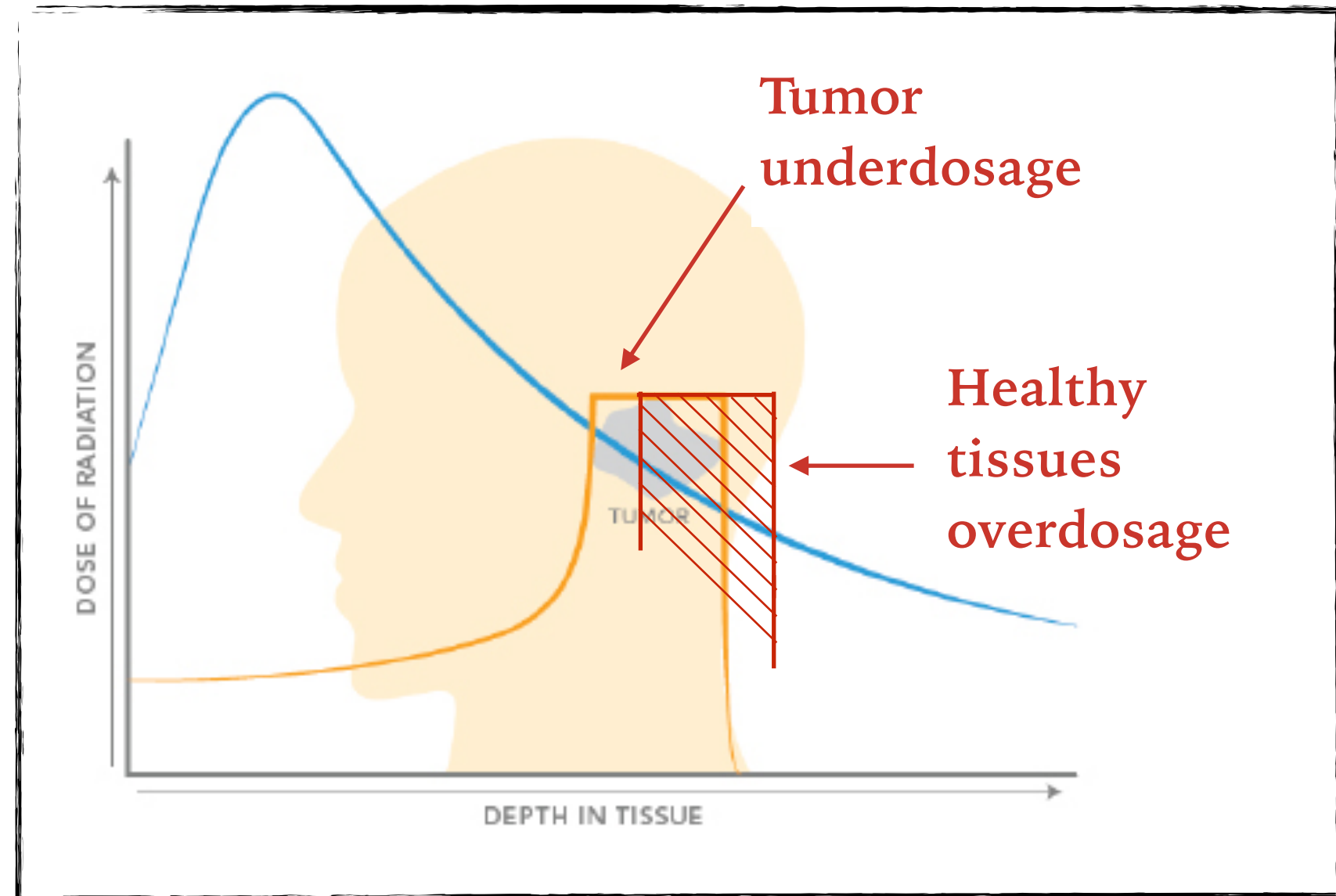
mean z at fixed t



**... but we have the whole (z,t) distribution: proton motion study**

**stopping power evaluation**

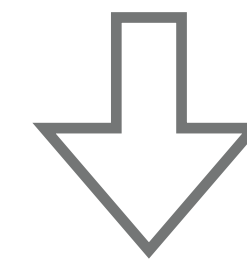
# STOPPING POWER AS TREATMENT VERIFICATION METHOD



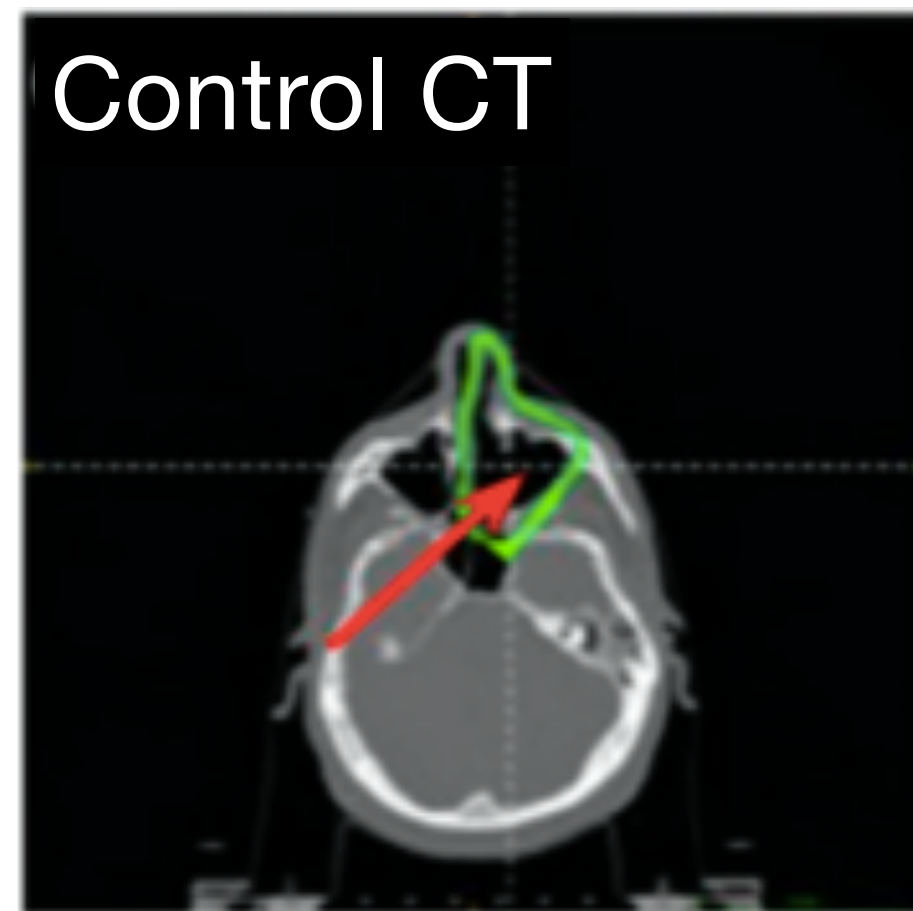
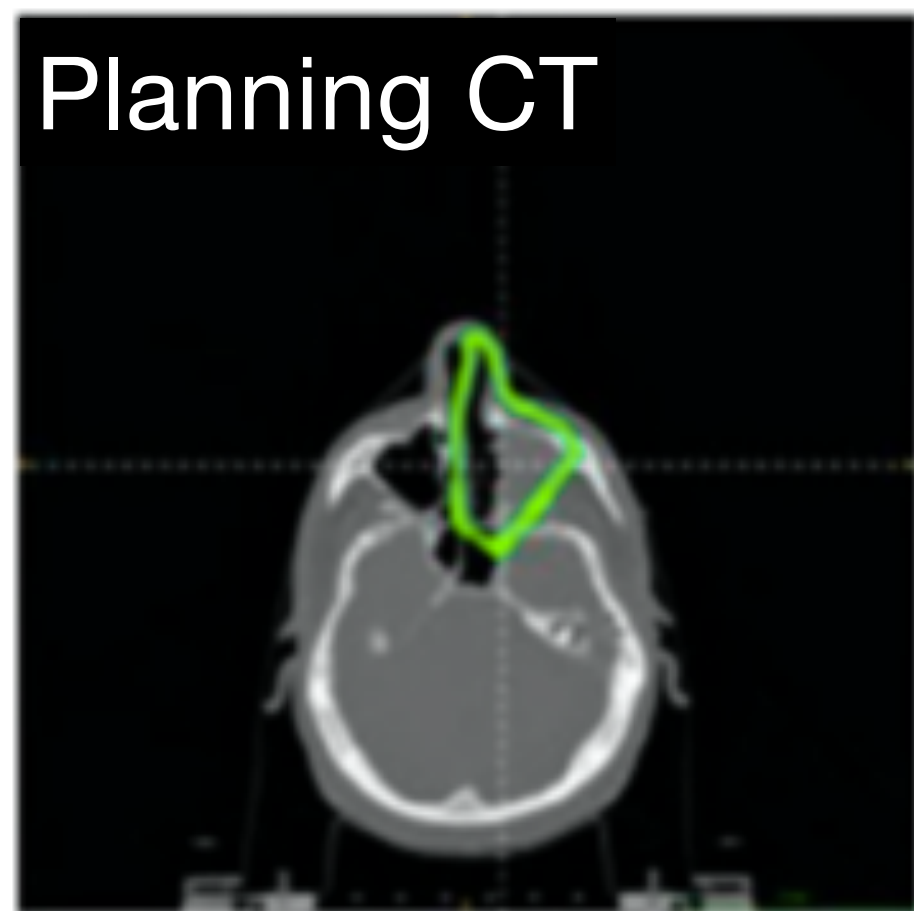
Strong clinical motivations:

- Model approximations
- HU to Stopping Power ratio conversion uncertainties
- Change of morphology

## STOPPING POWER INFORMATION



1. TREATMENT VERIFICATION AND OPTIMIZATION
2. STOICHIOMETRIC APPROACH VERIFICATION (TPS)

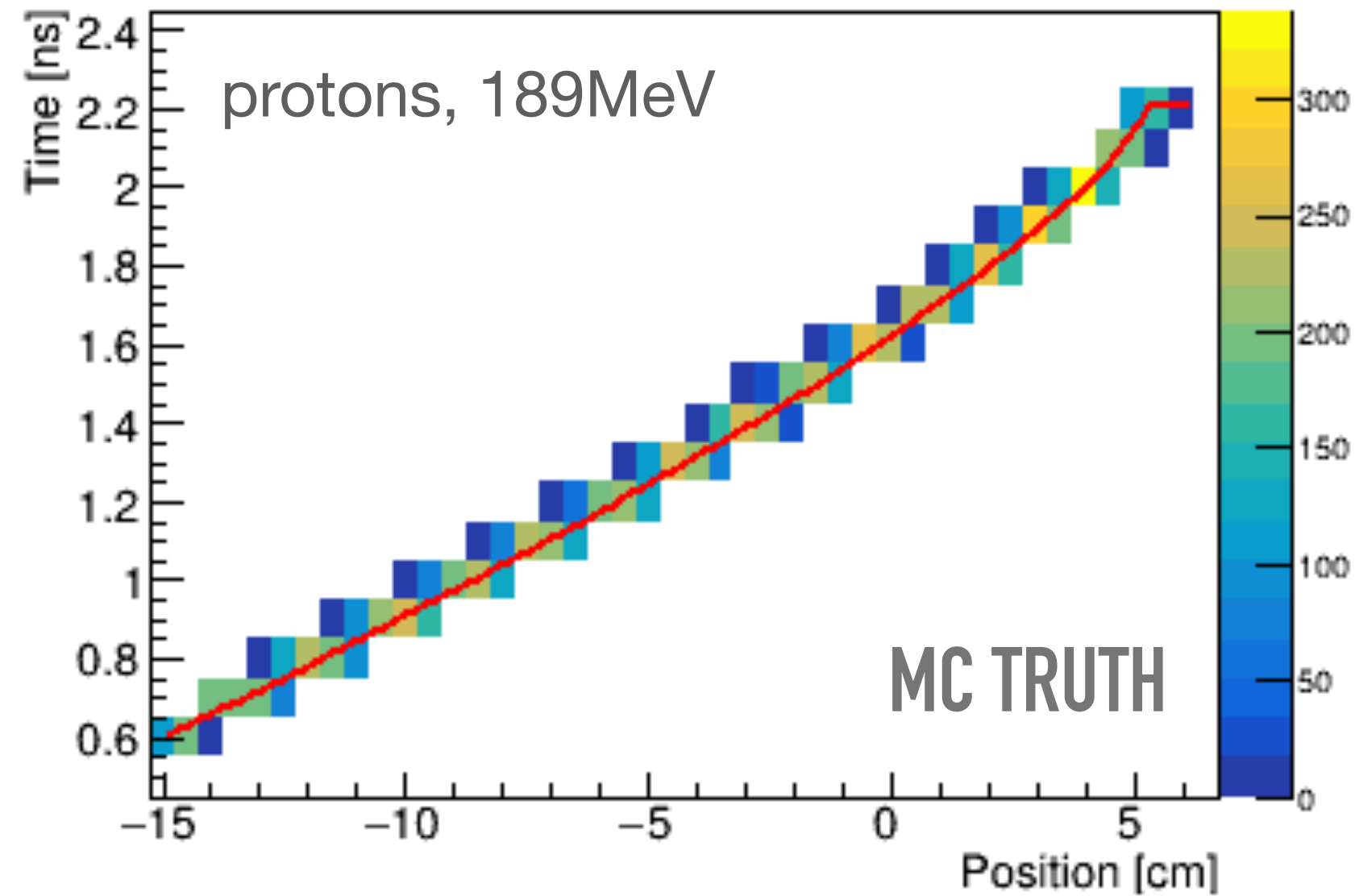


Measurement of the Energy Loss for IN-vivo Optimization in particle therapy (MERLINO)



From the measurement of prompt gamma... to the beam stopping power

# FORMULATION OF THE PROBLEM



**PHYSICAL DESCRIPTION  $t(z)$**   
(based on Bortfeld formulation)

$$R_0 = \alpha E_0^p, \quad E(\hat{z}) = \sqrt[p]{\frac{R_0 - \hat{z}}{\alpha}}$$

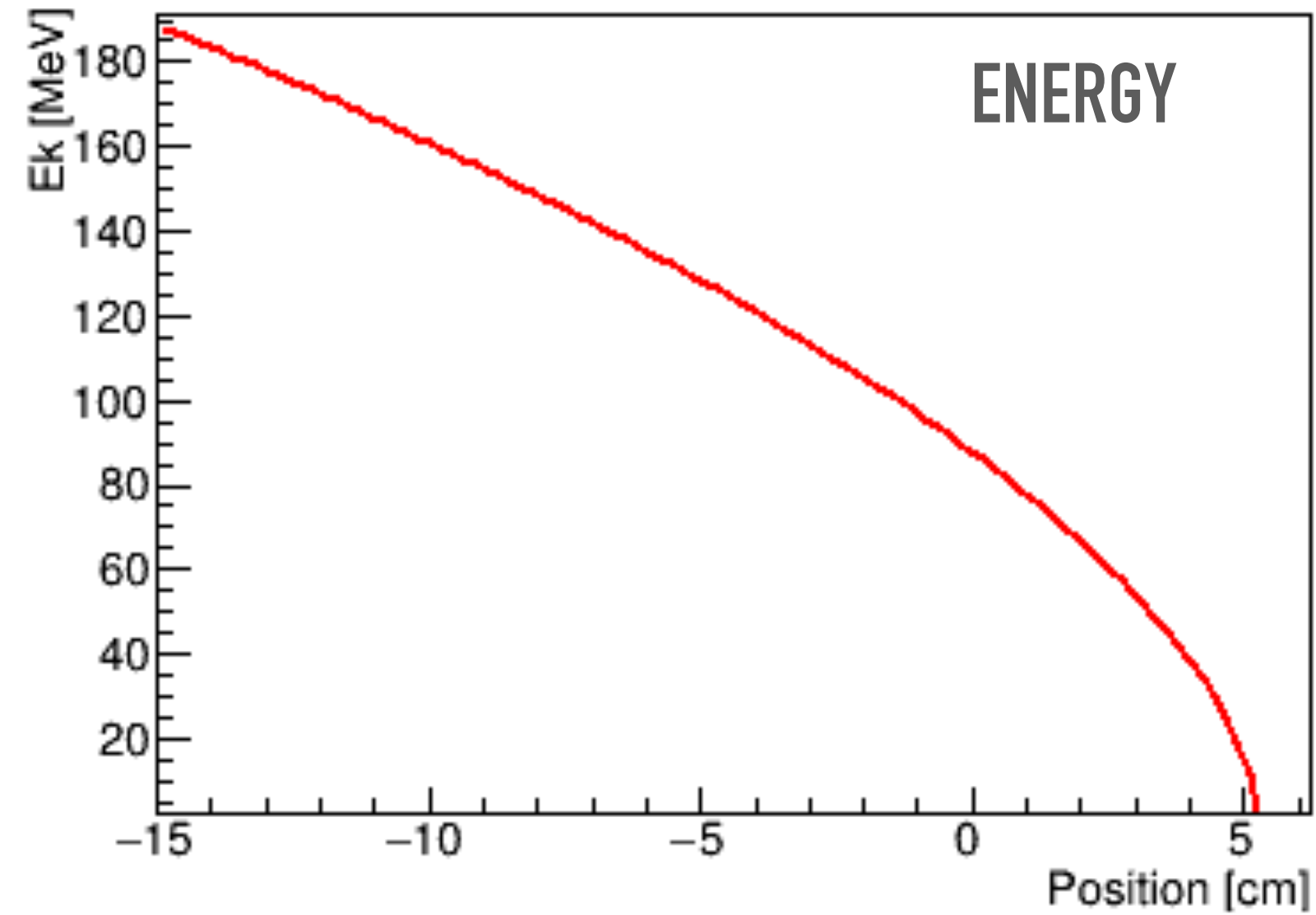
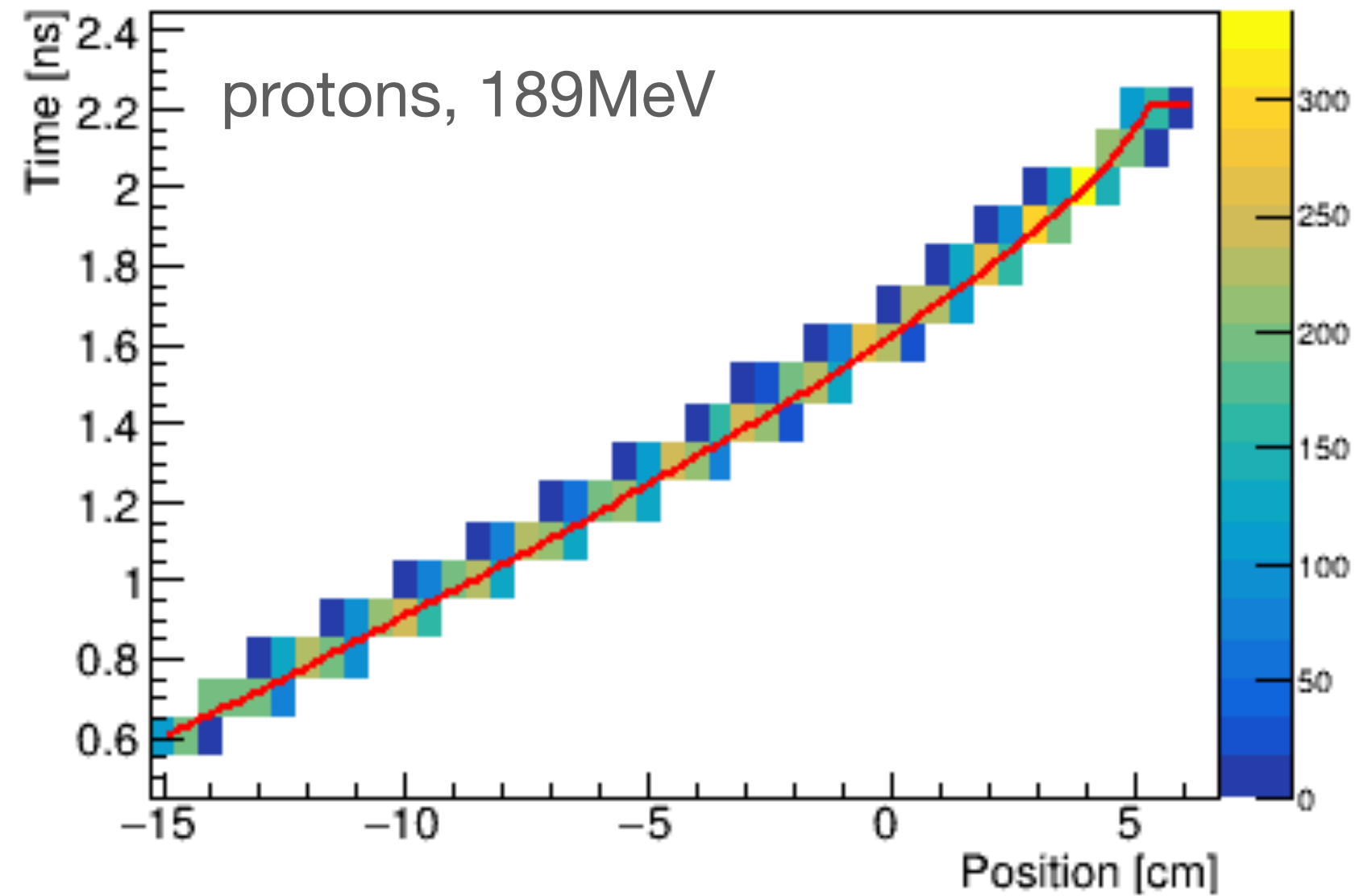
$$S(\hat{z}) = -\frac{dE}{dz} = \frac{1}{p\sqrt[p]{\alpha}} (R_0 - \hat{z})^{1/p-1}$$

$$v(E(\hat{z})) = c \sqrt{1 - \left( \frac{m_0 c^2}{E(\hat{z}) + m_0 c^2} \right)^2} = c \sqrt{1 - \left( \frac{m_0 c^2}{\sqrt[p]{\frac{R_0 - \hat{z}}{\alpha}} + m_0 c^2} \right)^2}$$

$$t(z) = \int_{z_0}^z \frac{dz'}{v(E(z' - z_0))} + t_0 = \int_0^{z-z_0} \frac{d\hat{z}'}{v(E(\hat{z}'))} + t_0.$$

$$\int \frac{d\hat{z}}{v(E(\hat{z}))} = \frac{-p(R_0 - \hat{z})}{c(4p^2 - 1) \sqrt{\frac{2m_0 c^2}{E(\hat{z})} + 1}} \left[ (p-1) \sqrt{\frac{2E(\hat{z})}{m_0 c^2} + 4} {}_2F_1 \left( \frac{1}{2}, p + \frac{1}{2}; p + \frac{3}{2}; -\frac{E(\hat{z})}{2m_0 c^2} \right) + \left( \frac{2m_0 c^2}{E(\hat{z})} + 1 \right) (2p+1) \right]$$

# PRELIMINARY WORK: MC TRUTH

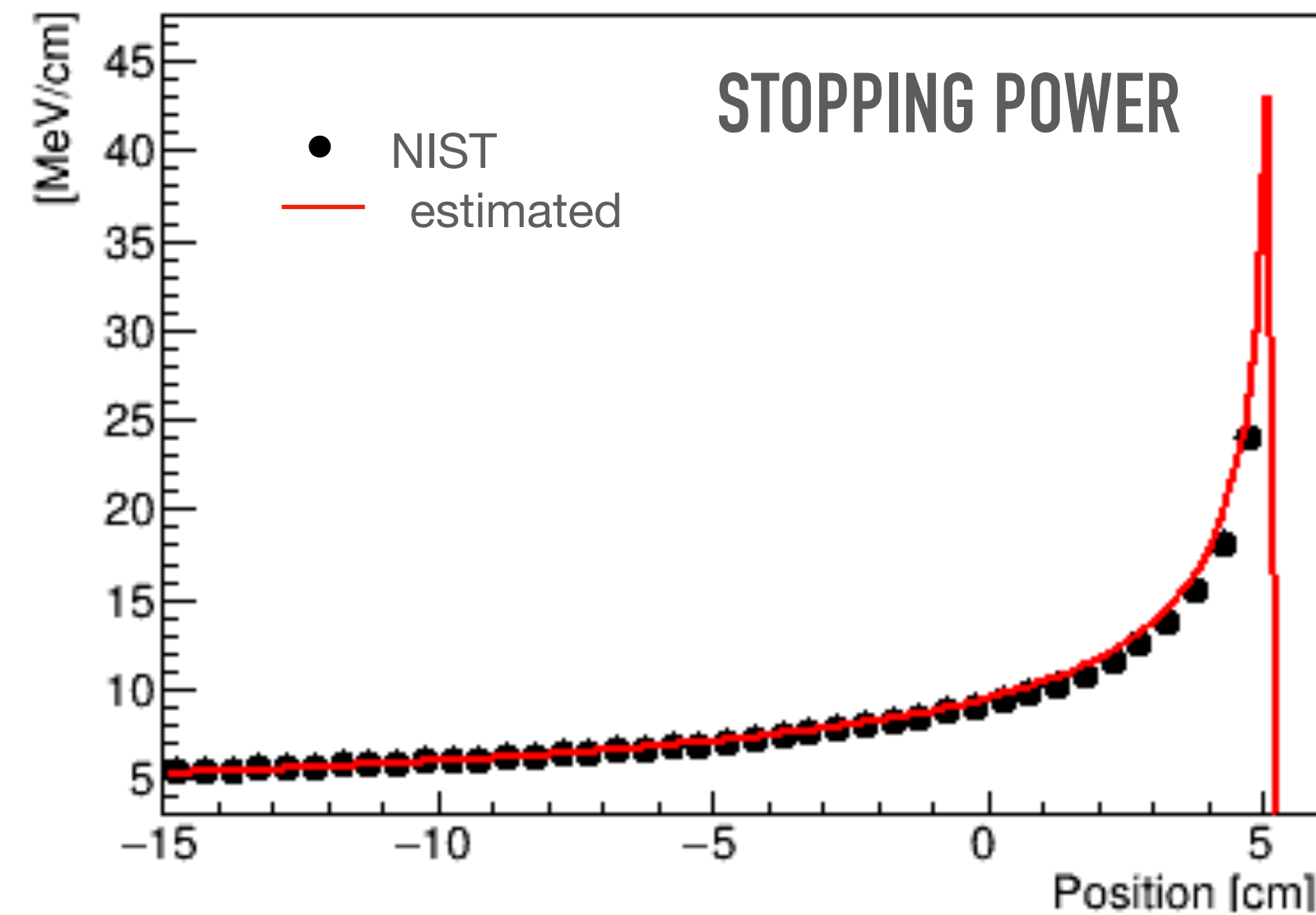


PHYSICAL DESCRIPTION  $t(z)$   
(based on Bortfeld formulation)

$$R_0 = \alpha E_0^p, \quad E(\hat{z}) = \sqrt[p]{\frac{R_0 - \hat{z}}{\alpha}}$$

$$S(\hat{z}) = -\frac{dE}{dz} = \frac{1}{p\sqrt[p]{\alpha}} (R_0 - \hat{z})^{1/p-1}$$

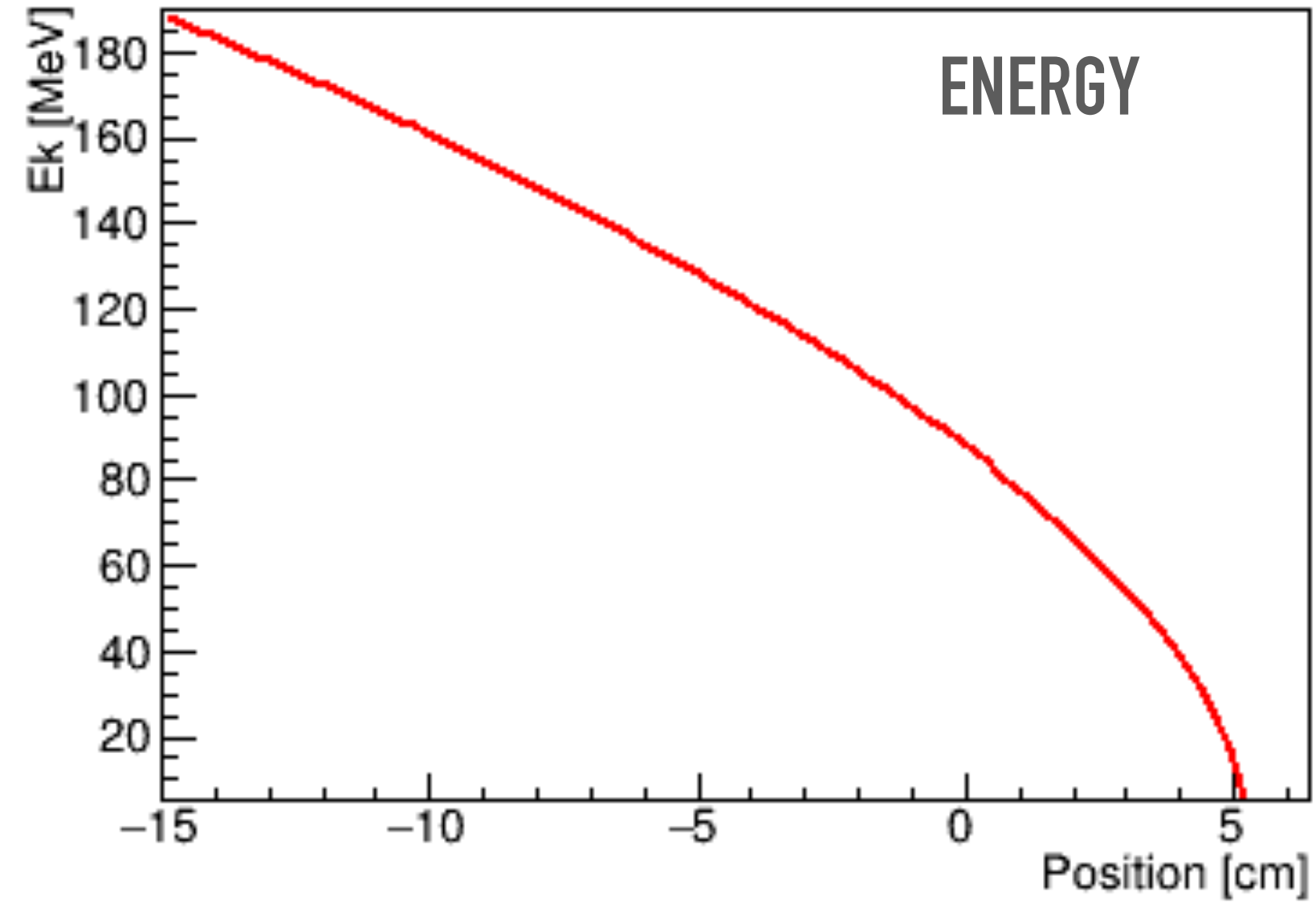
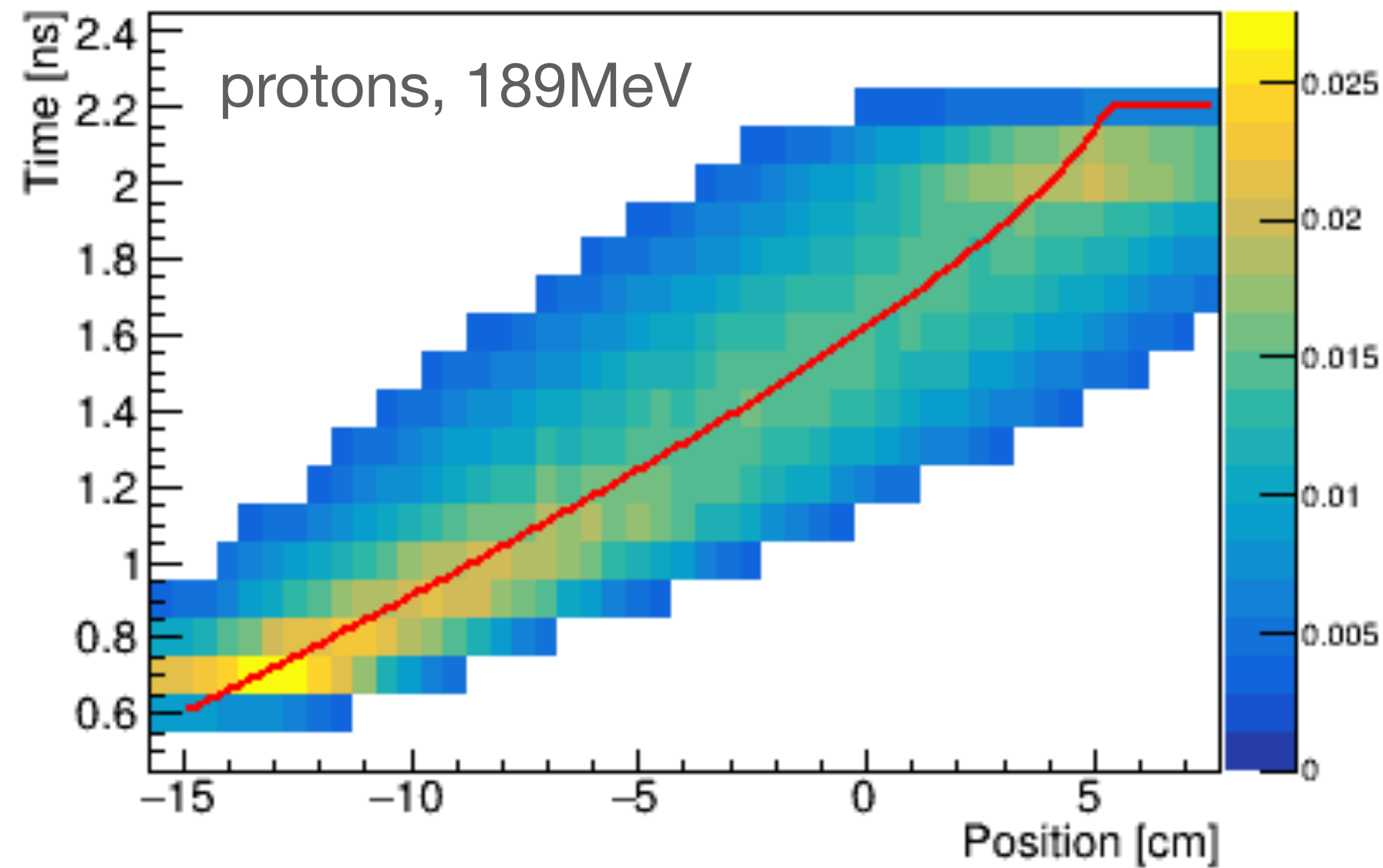
Bortfeld Med Phys 1997



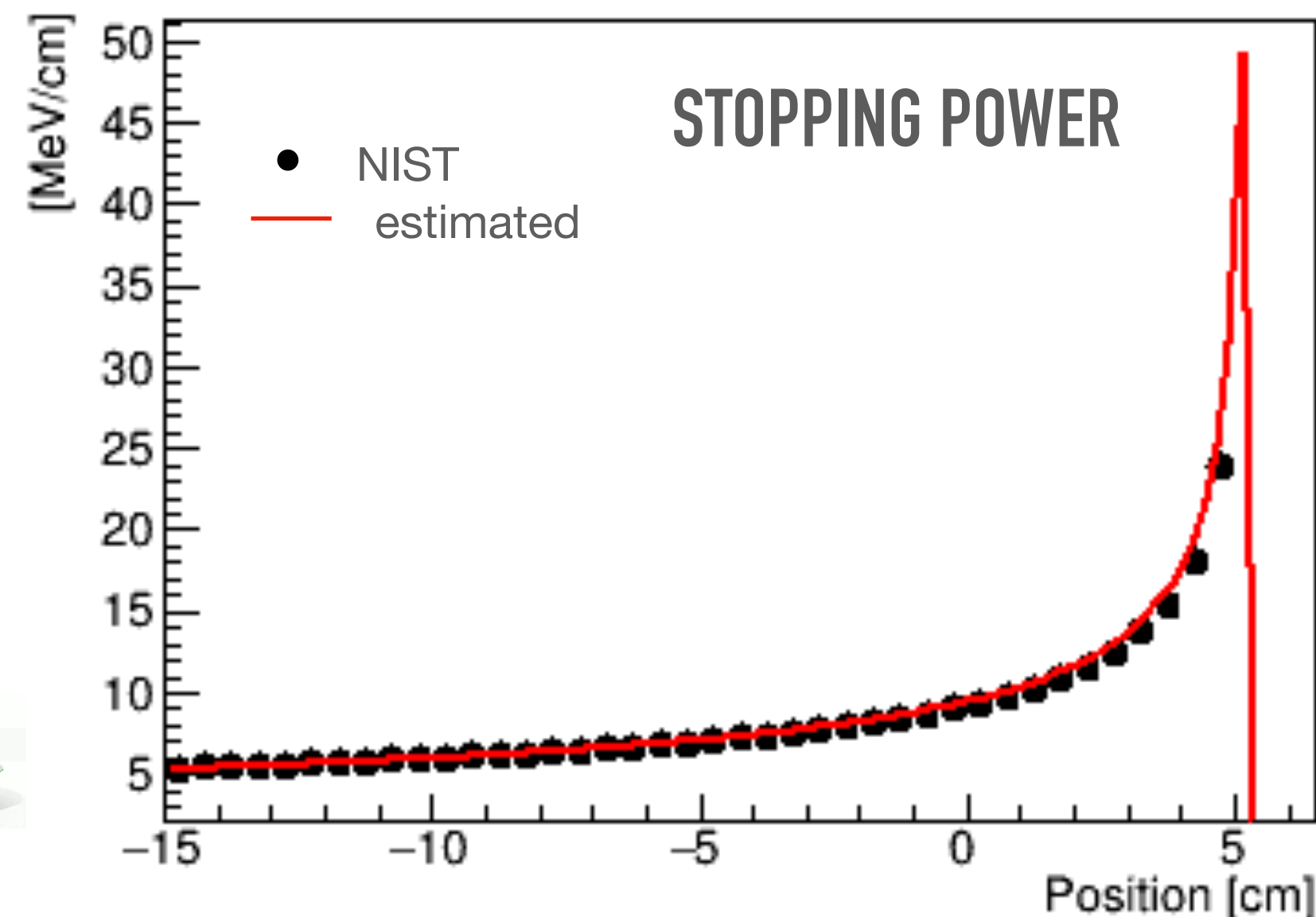
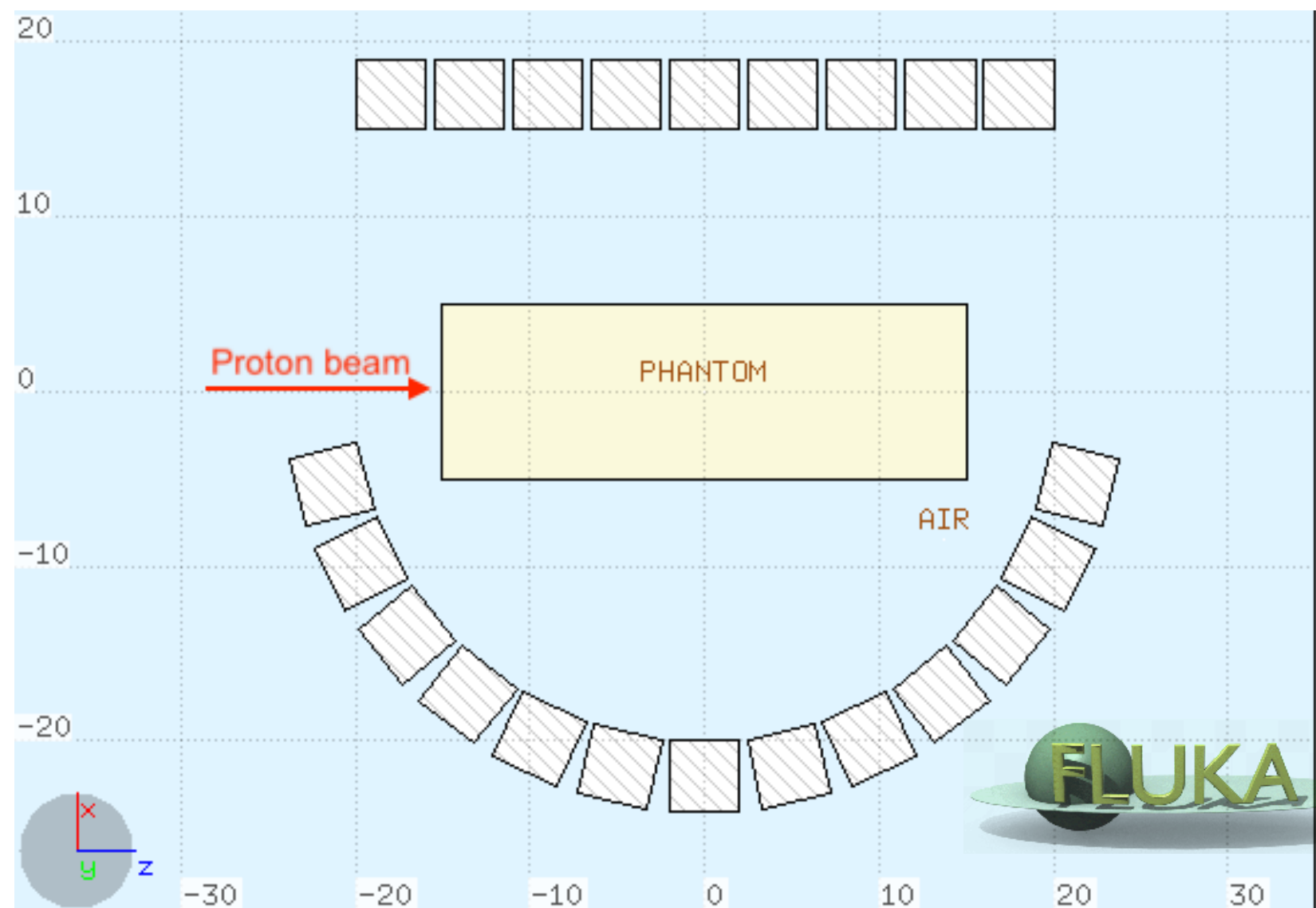
**Mean relative error: 0.4 [MeV/cm]**  
**⇒ 2.8%**  
**PCC=0.9**



# PRELIMINARY WORK: RECONSTRUCTION

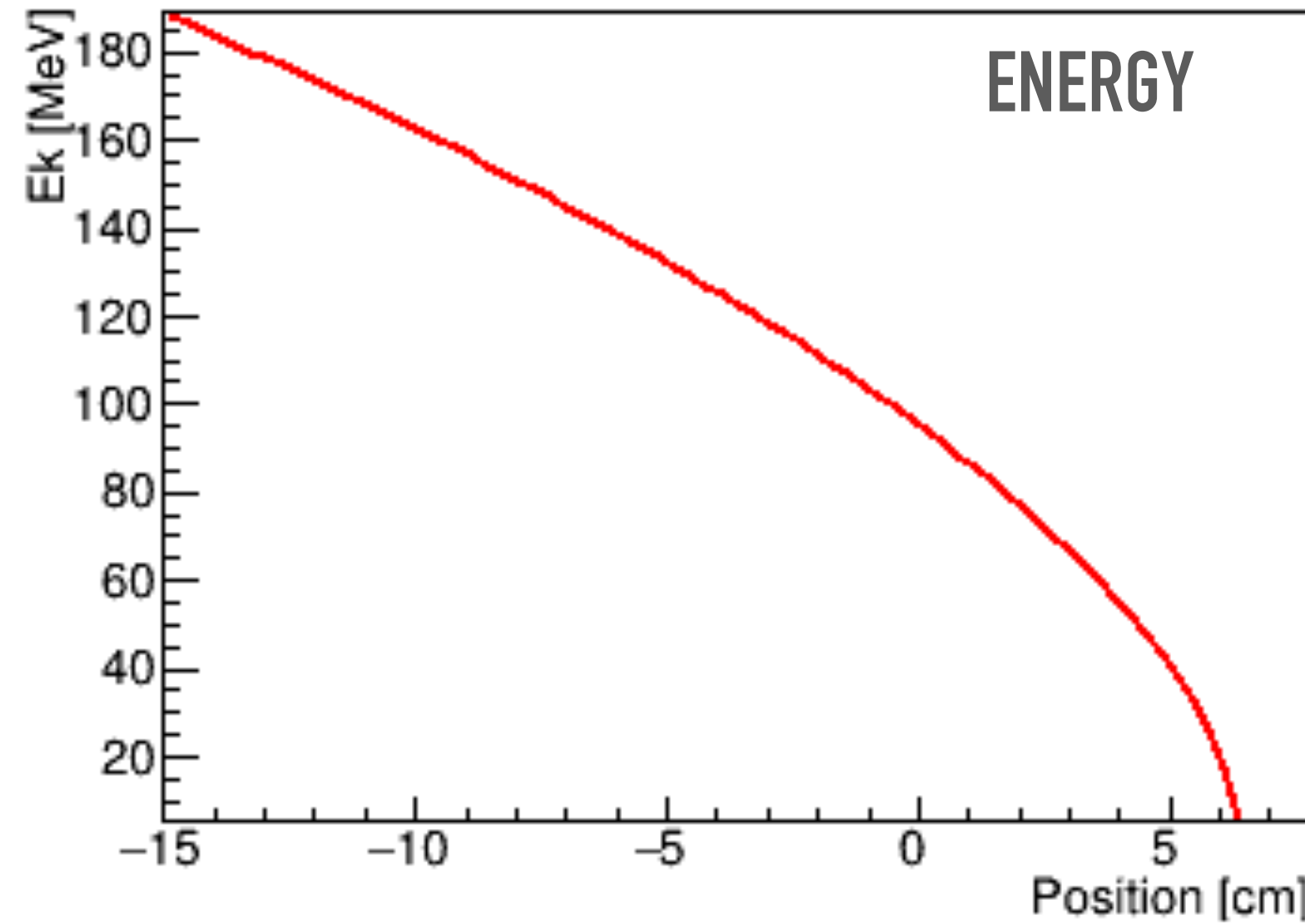
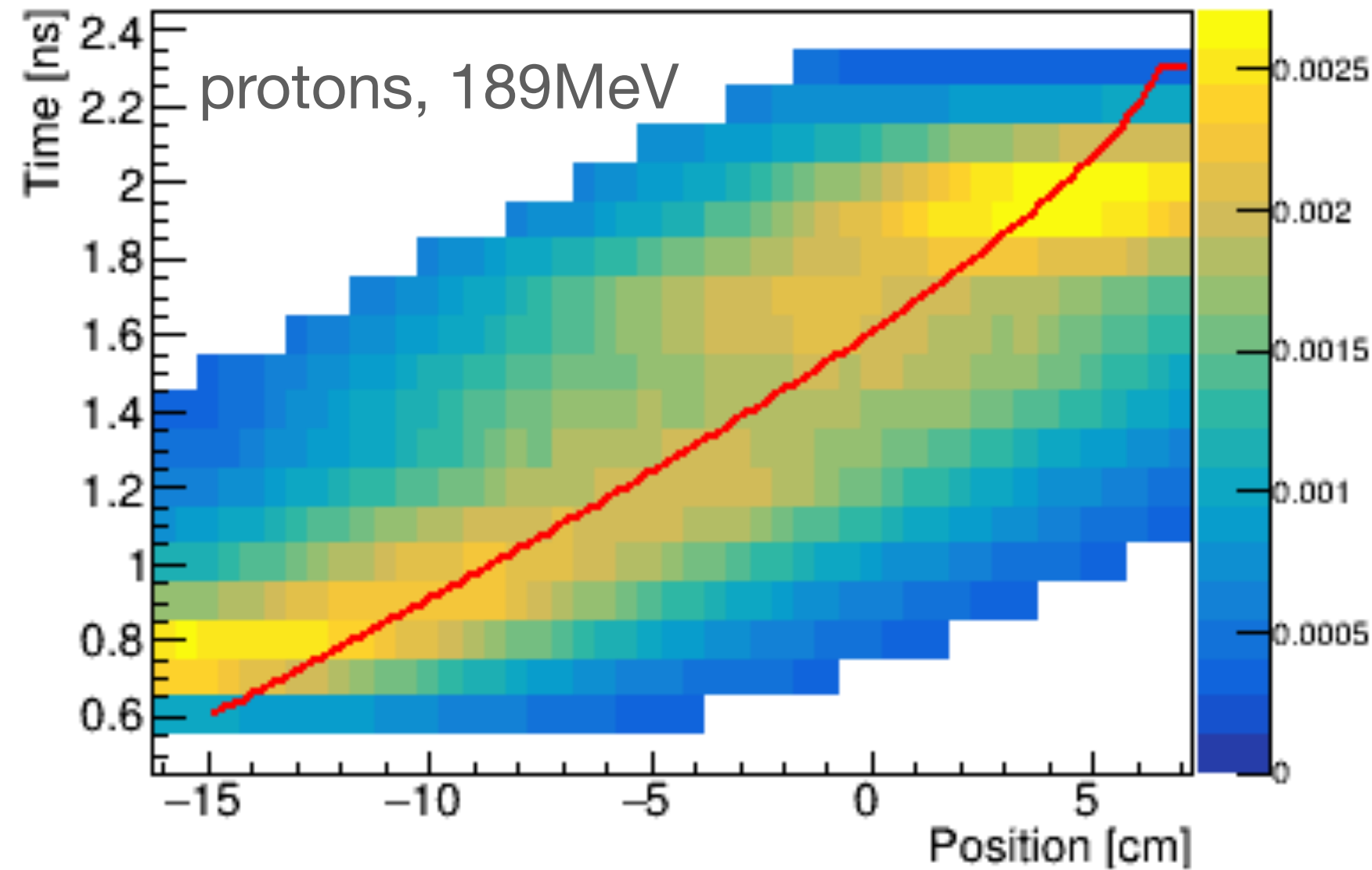


$10^8$  protons, 189MeV  
 $10^7$  produced photons in  $4\pi$   
 $\sim 10^4$  events per detector  
 Energy cut 1MeV-7MeV  
 Time resolution=100 ps  $\sigma$   
**110 detectors** (clinical scenario)

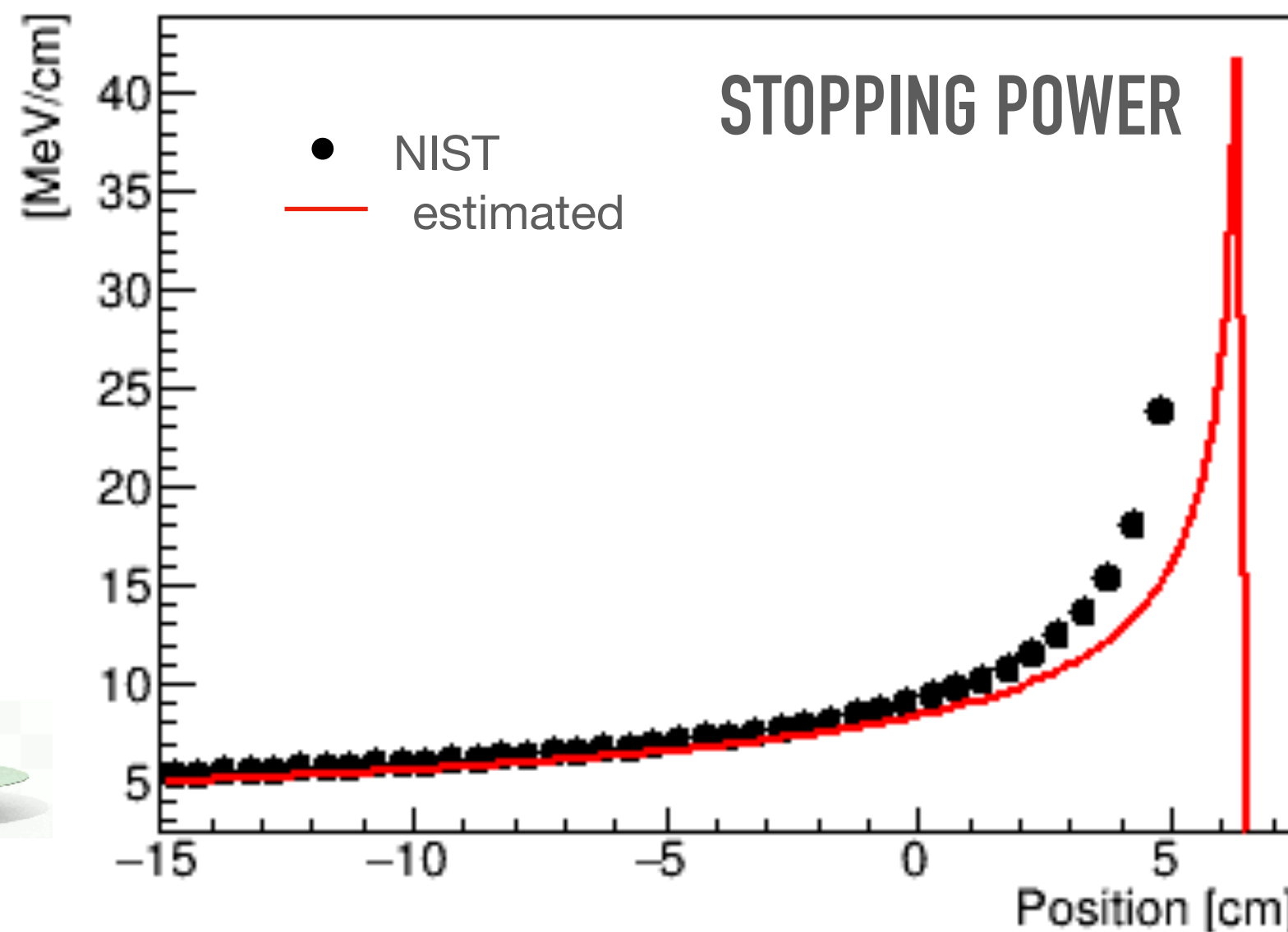
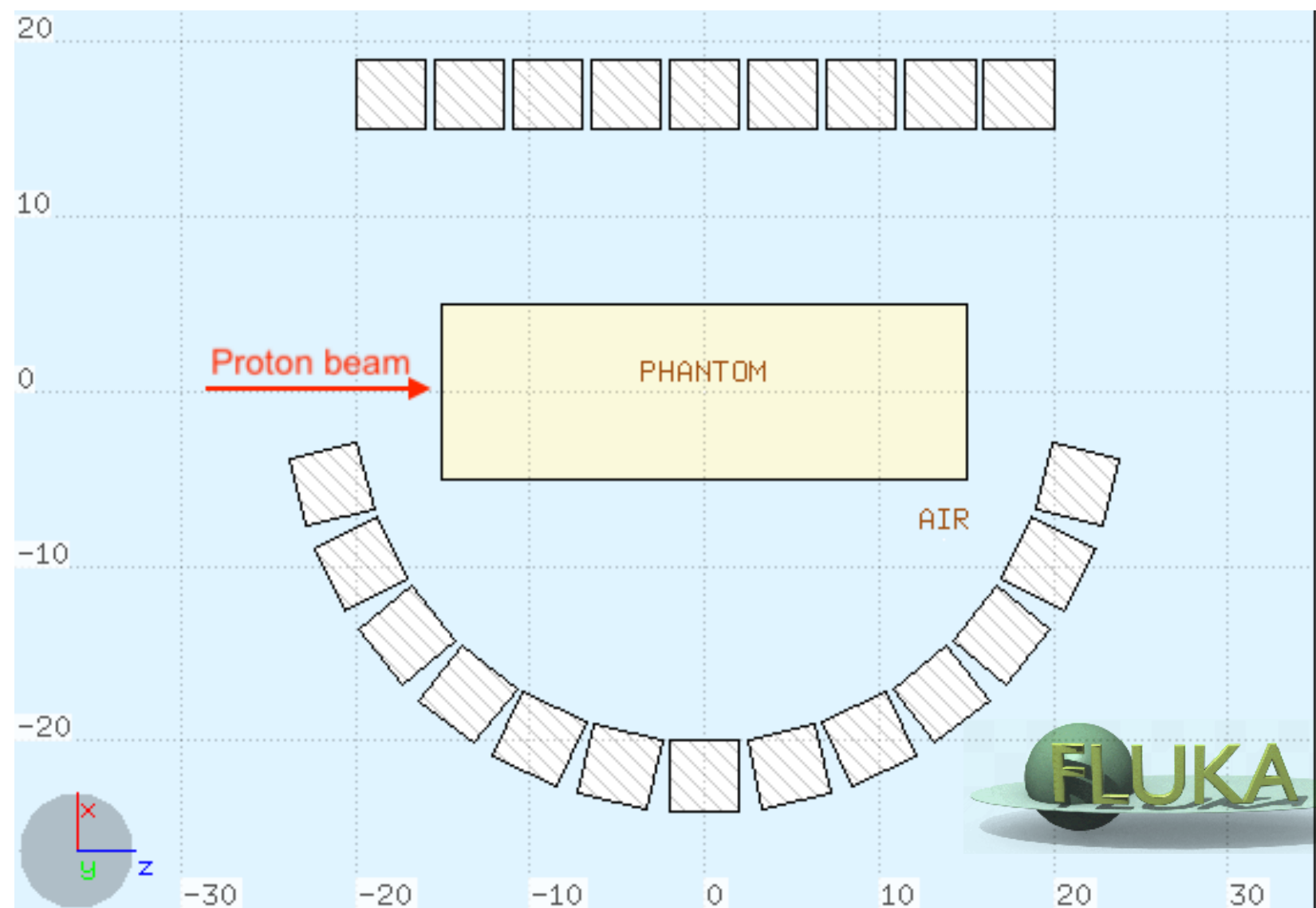


**Mean relative error: 0.4 [MeV/cm]**  
 $\Rightarrow 2.8\%$   
**PCC=0.9**

# PRELIMINARY WORK: RECONSTRUCTION

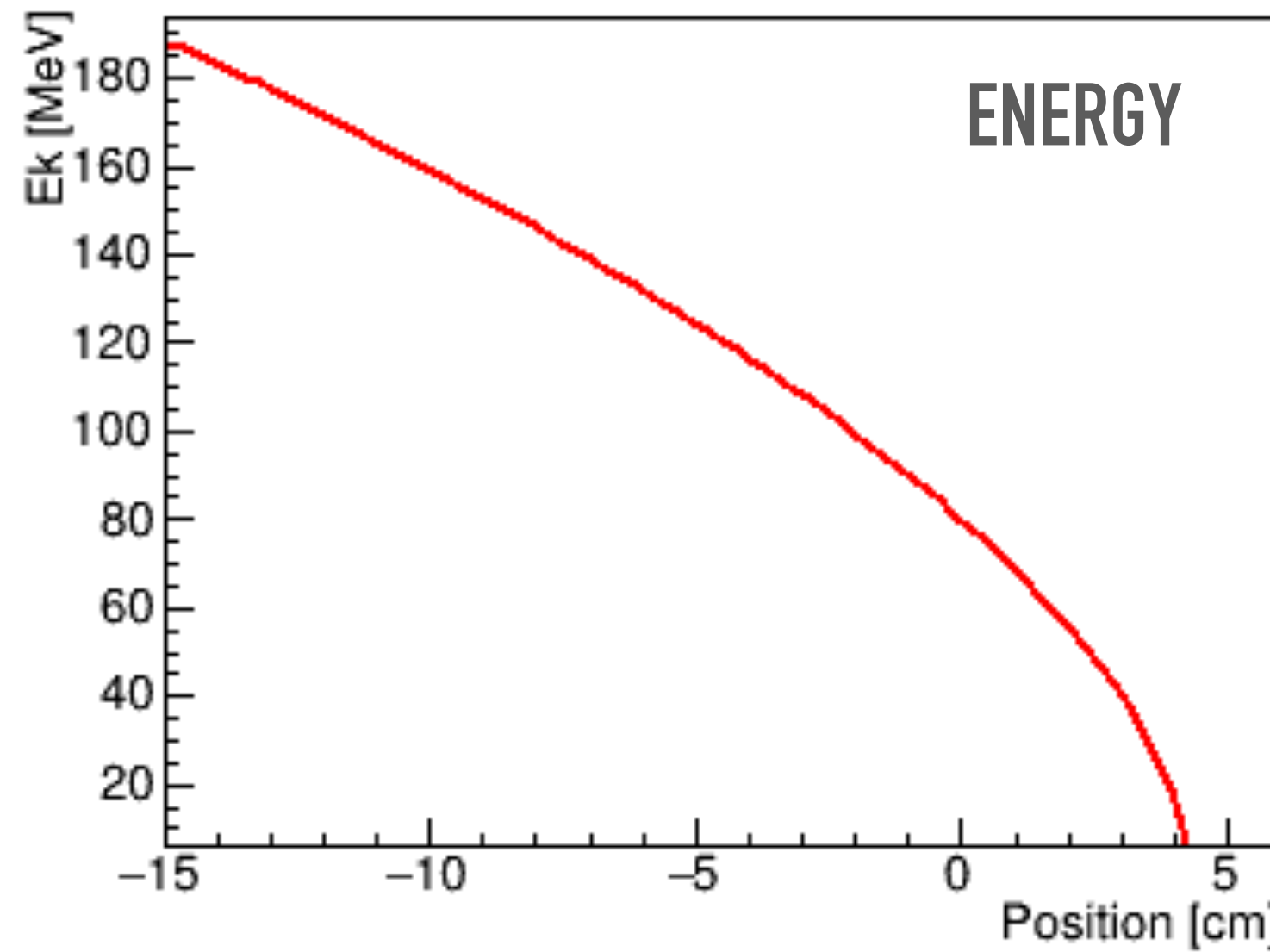
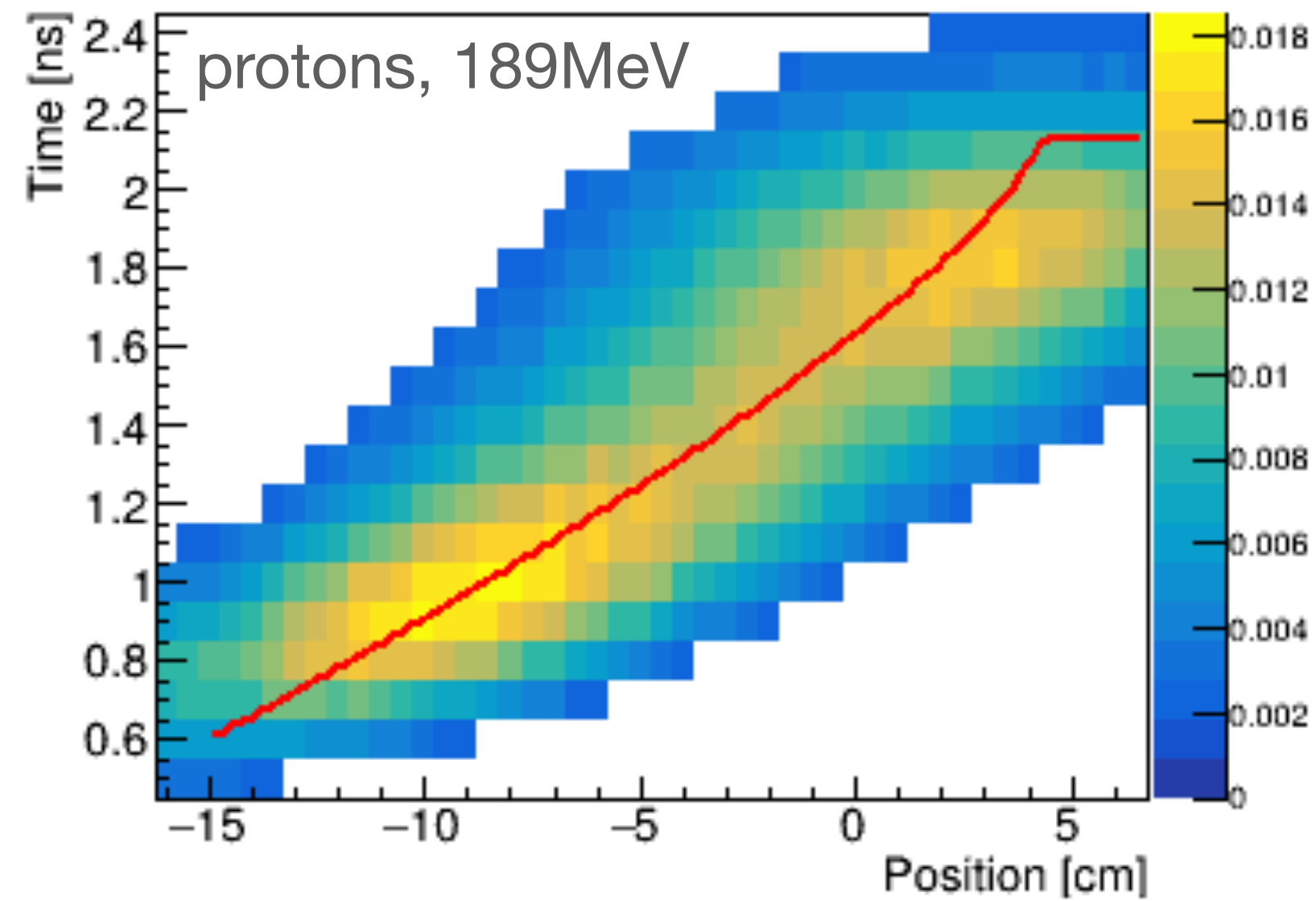


$10^8$  protons, 189MeV  
 $10^7$  produced photons in  $4\pi$   
 $\sim 10^4$  events per detector  
 Energy cut 1MeV-7MeV  
 Time resolution= $100 \text{ ps } \sigma$   
**110 detectors** (clinical scenario)  
 UFSD  $\epsilon=0.2$   
 $10^8$  pps, RF=2.13MHz  
**Random events inclusion**  
**10% true coinc, 90% random evts**

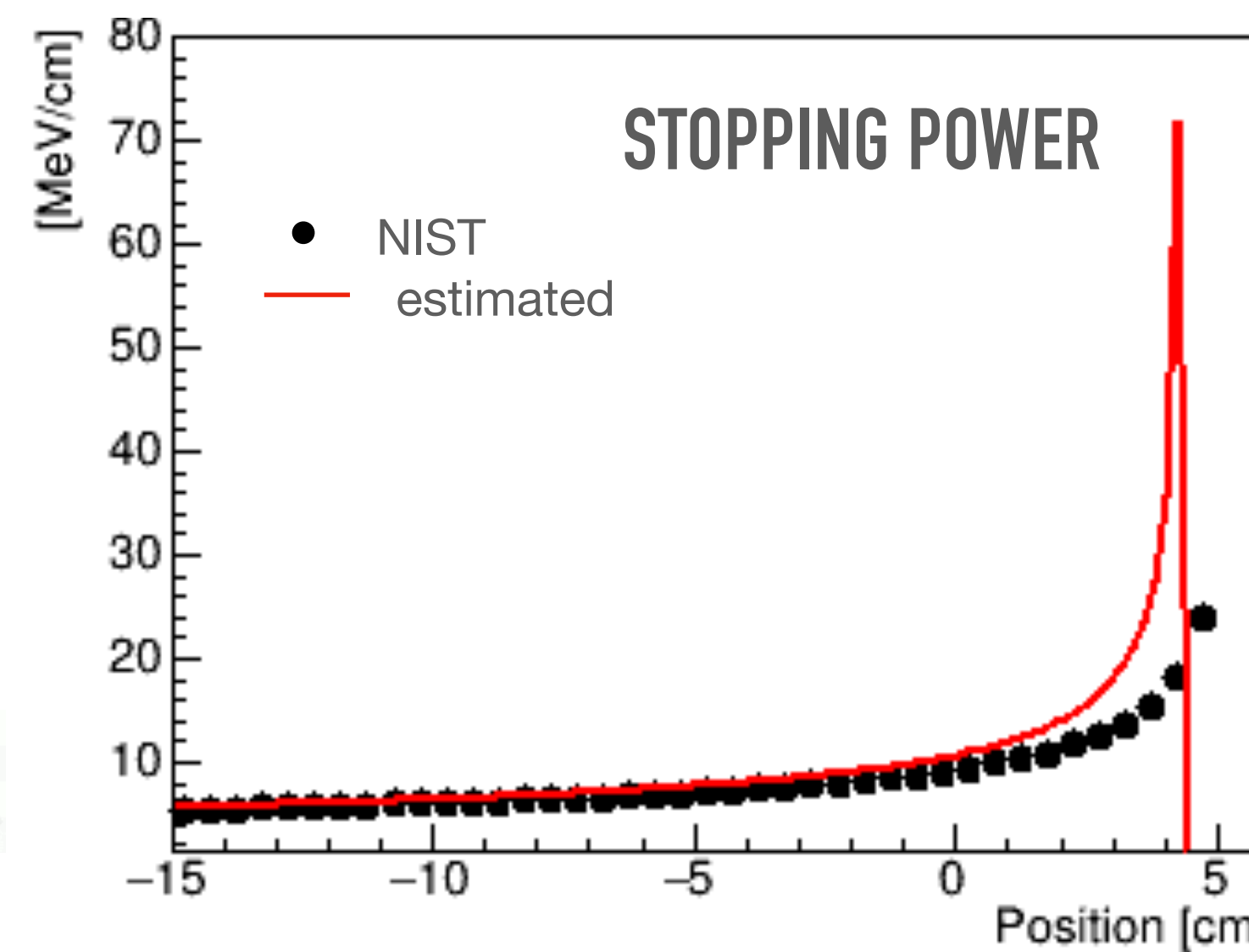
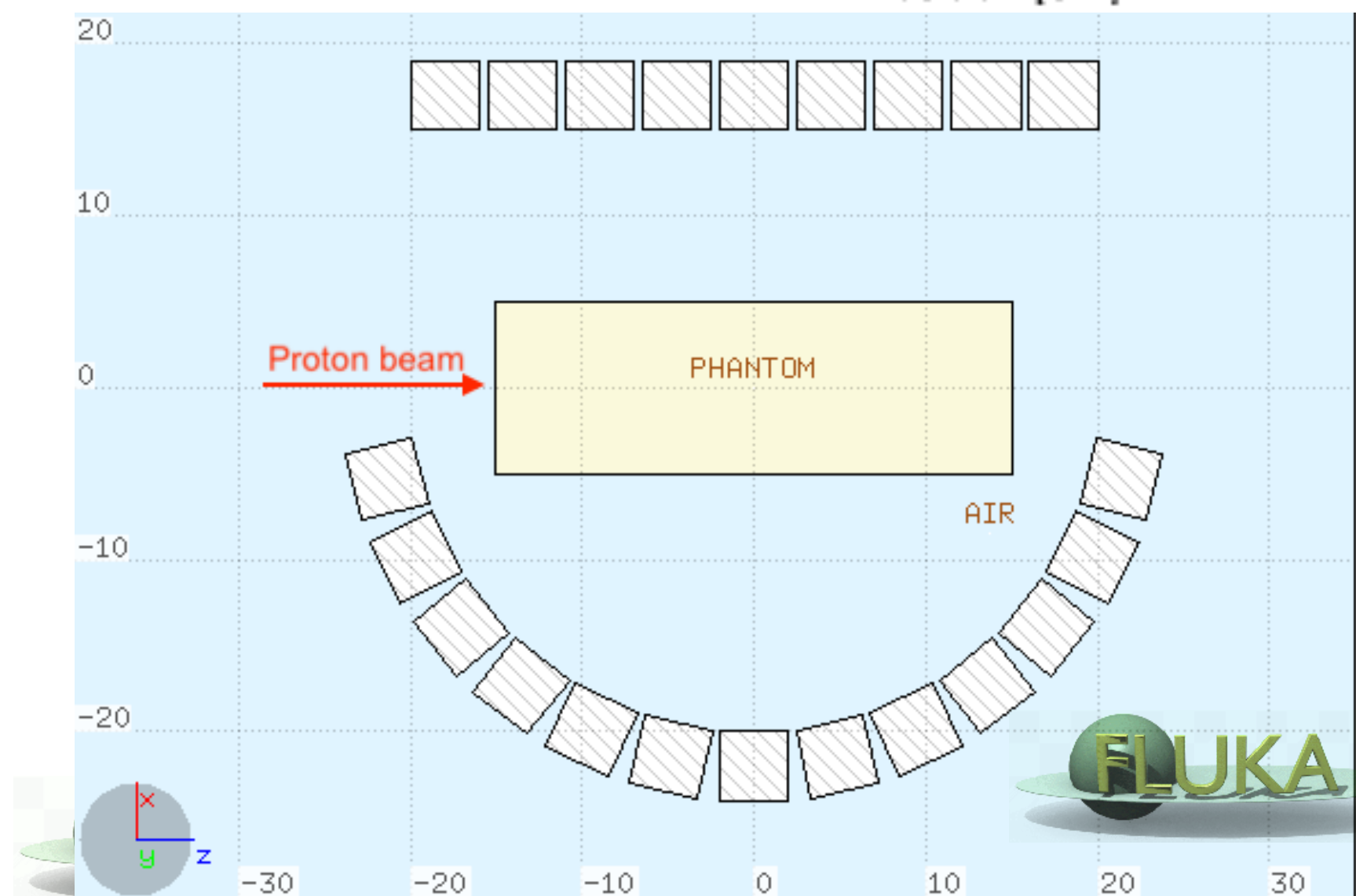


**Mean relative error: 1.08 [MeV/cm]**  
 $\Rightarrow 9.23\%$   
**PCC=0.87**

# PRELIMINARY WORK: RECONSTRUCTION

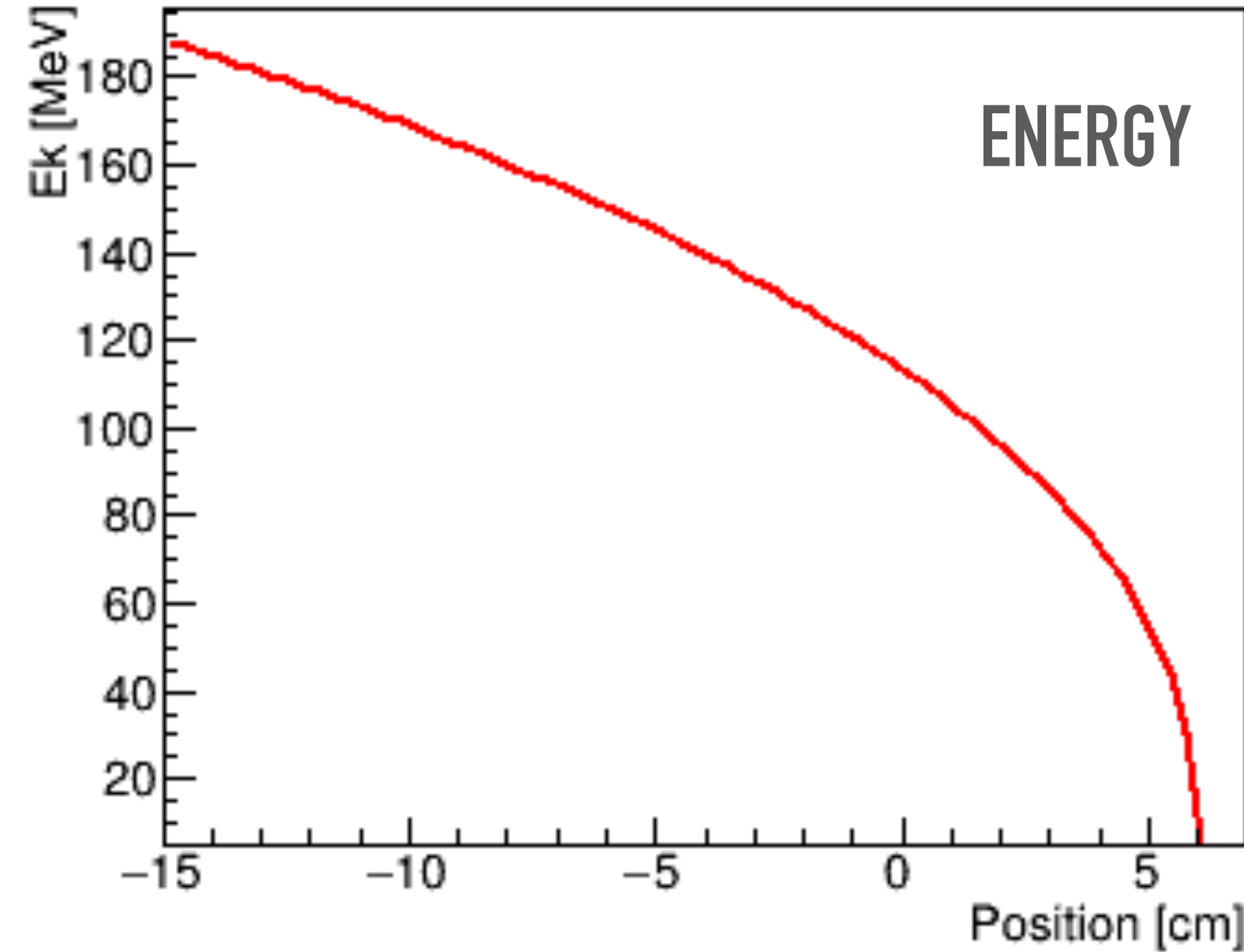
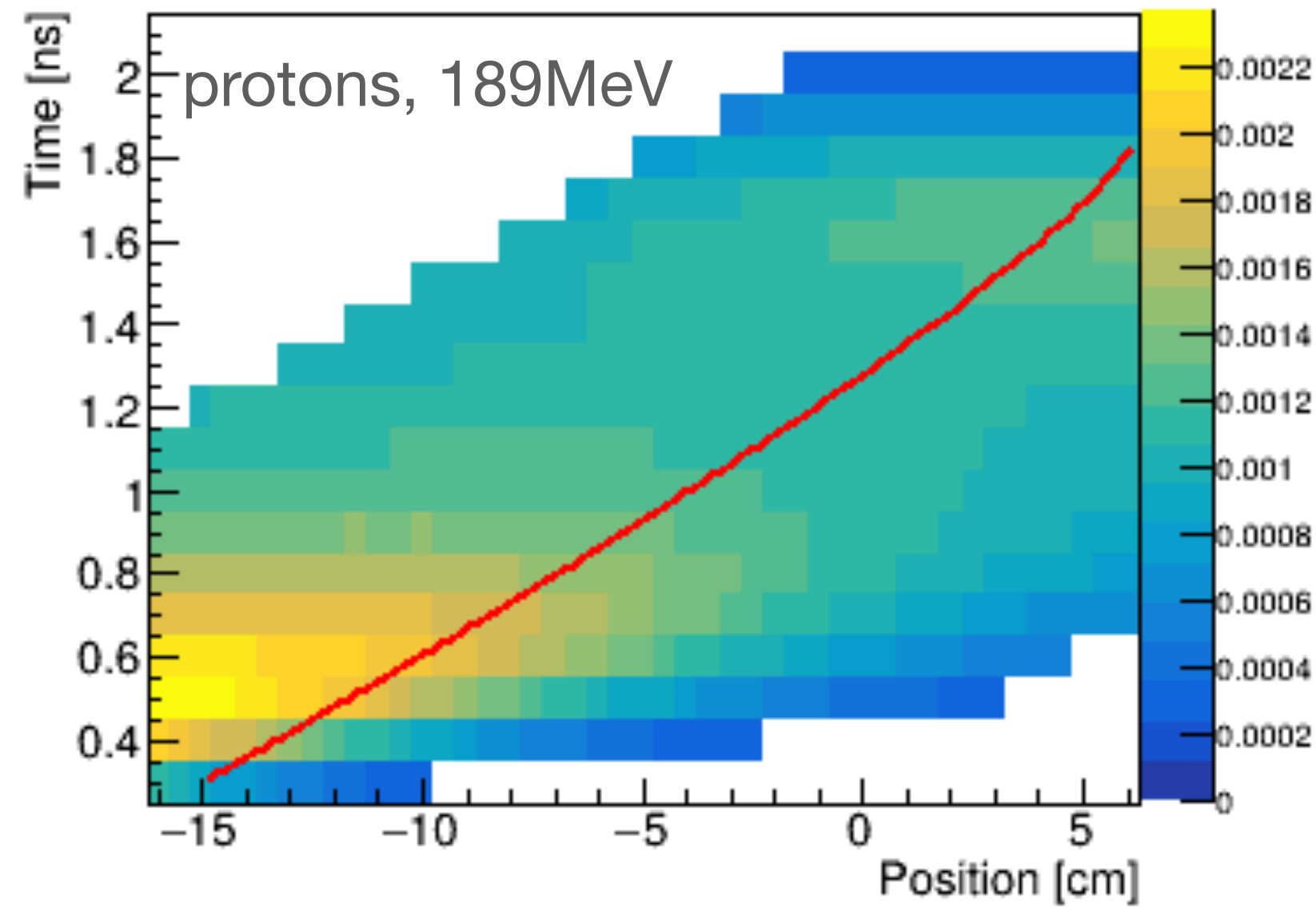


$10^8$  protons, 189MeV  
 $10^7$  produced photons in  $4\pi$   
 $\sim 10^4$  events per detector  
 Energy cut 1MeV-7MeV  
 Time resolution=300 ps  $\sigma$   
**110 detectors** (clinical scenario)

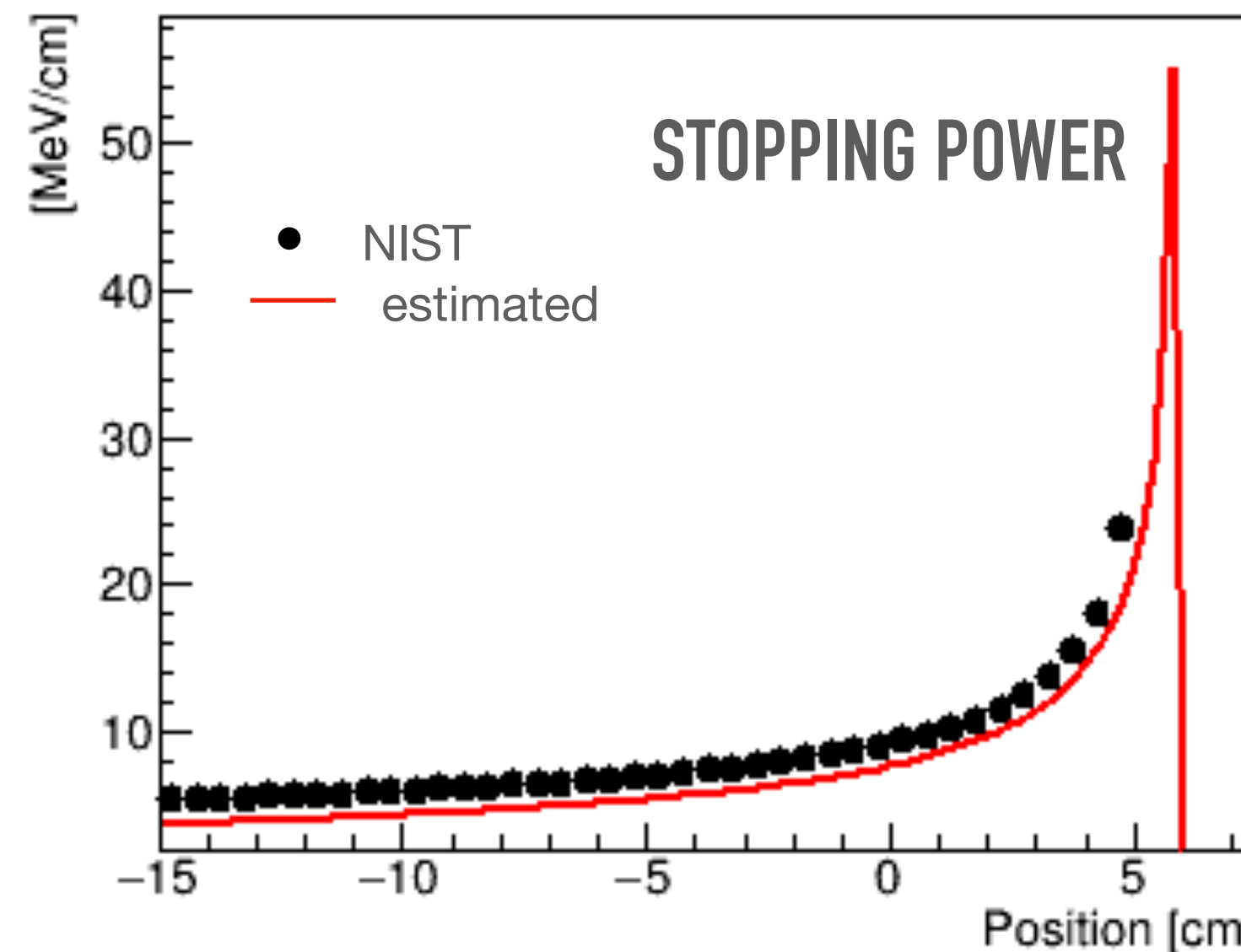


**Mean relative error: 2.5 [MeV/cm]**  
 $\Rightarrow 18.2\%$   
**PCC=0.58**

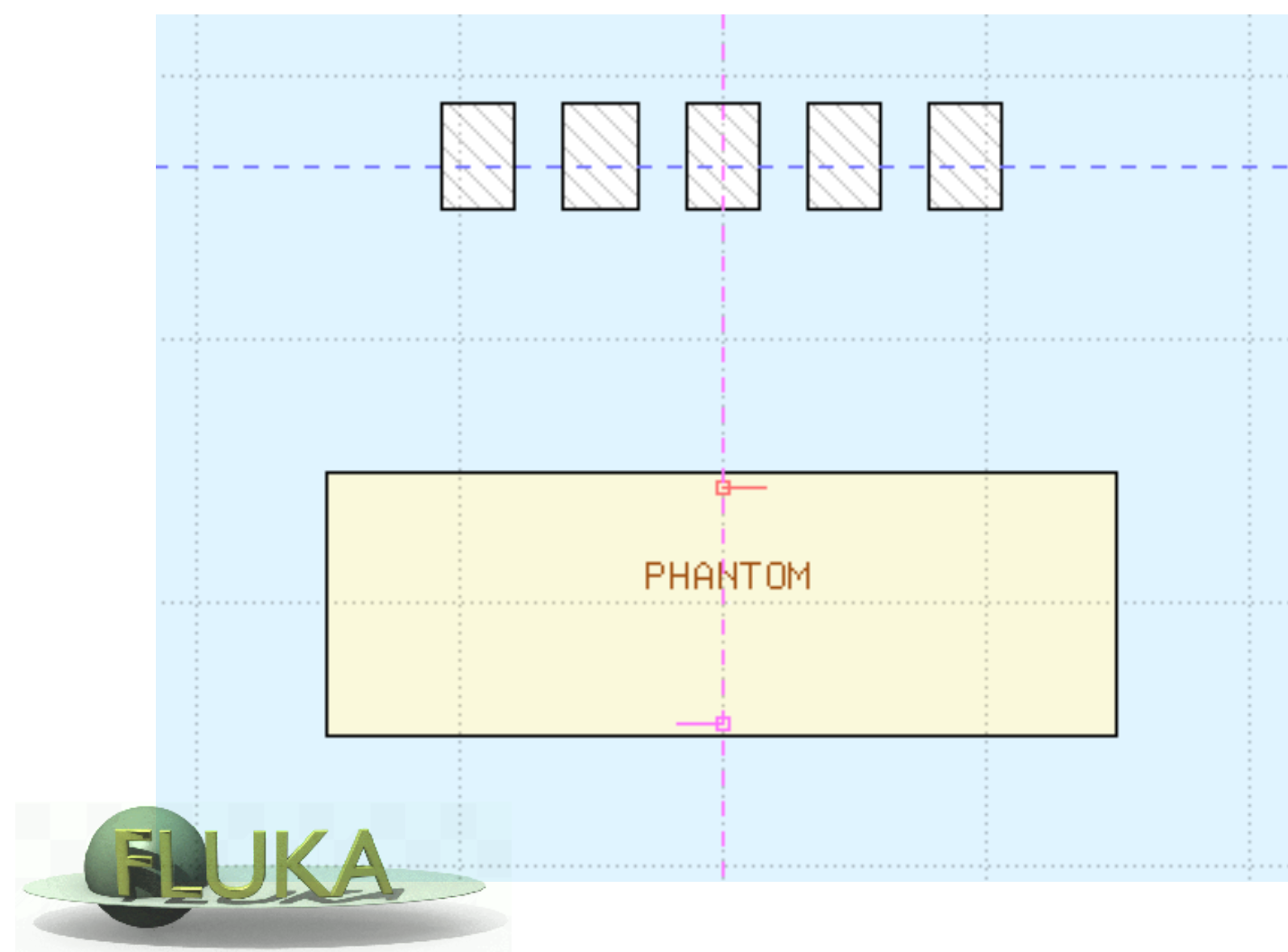
# PRELIMINARY WORK: RECONSTRUCTION



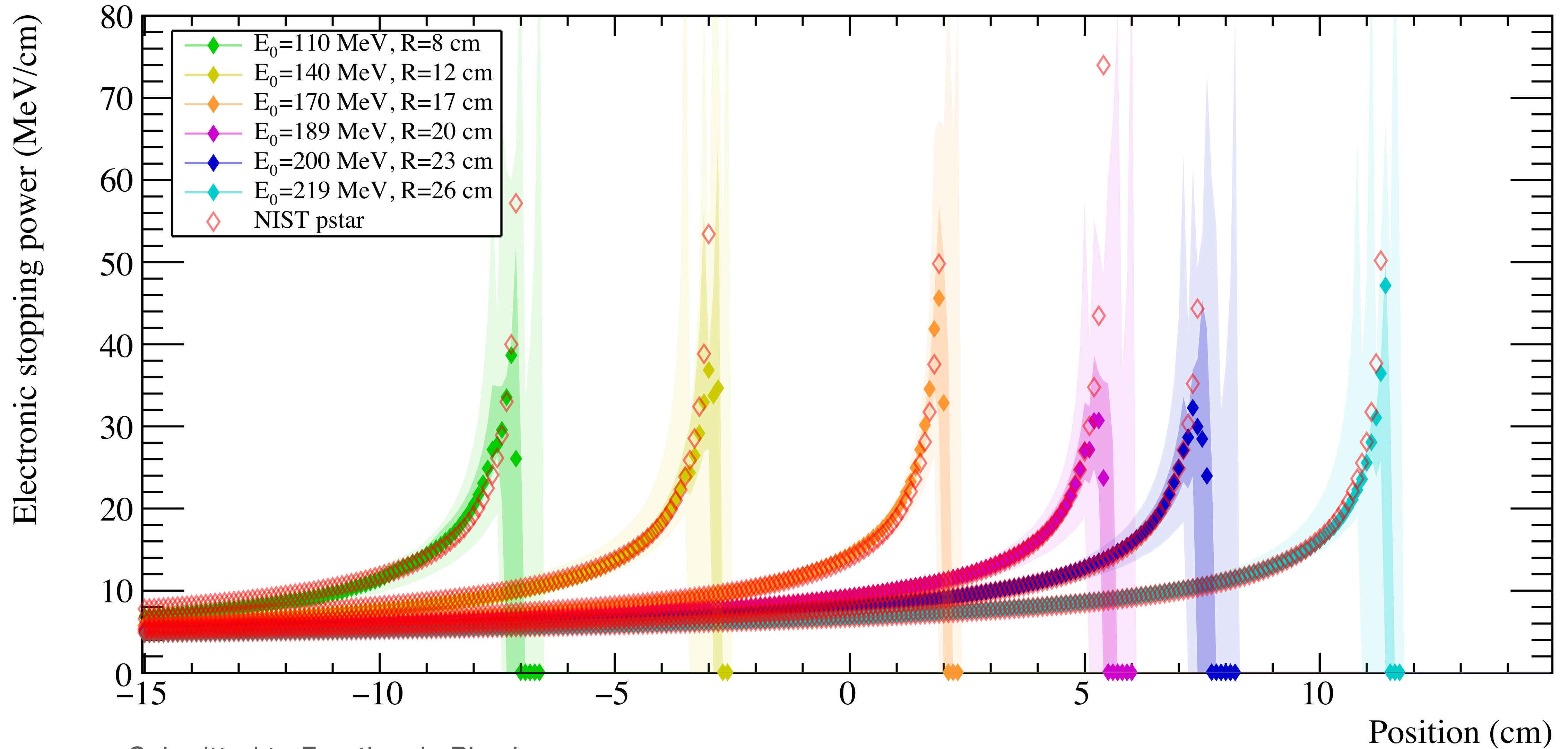
$10^8$  protons, 189MeV  
 $10^7$  produced photons in  $4\pi$   
 $\sim 10^4$  events per detector  
Energy cut 1MeV-7MeV  
Time resolution= $100 \text{ ps } \sigma$   
**10 detectors** (proof of concept)



**Mean relative error: 1.7 [MeV/cm]**  
 **$\Rightarrow 22\%$**   
**PCC=0.95**

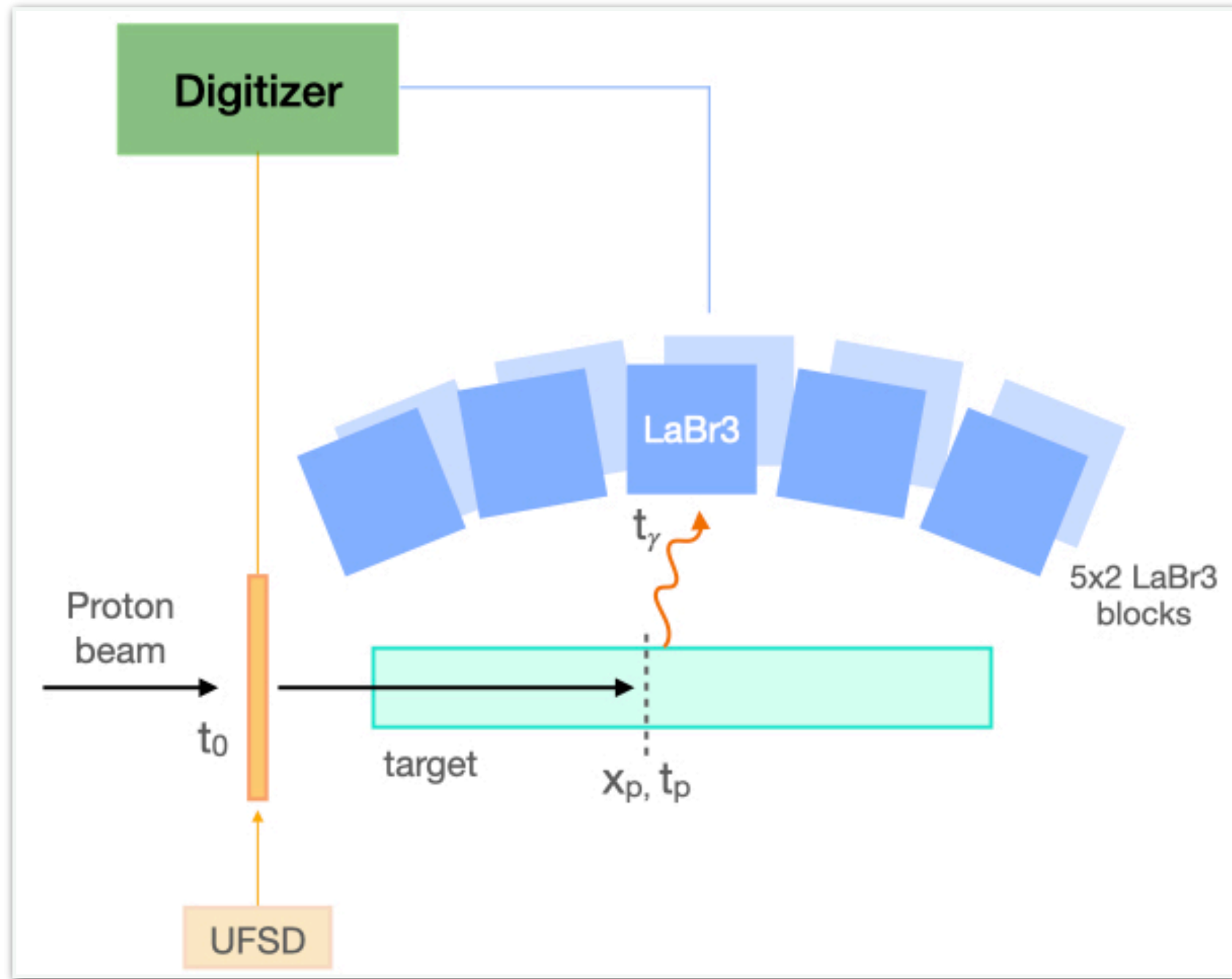


# PRELIMINARY WORK: RECONSTRUCTION



Submitted to Frontiers in Physics

# DETECTOR R&D



## PGT MULTI-DETECTOR SYSTEM

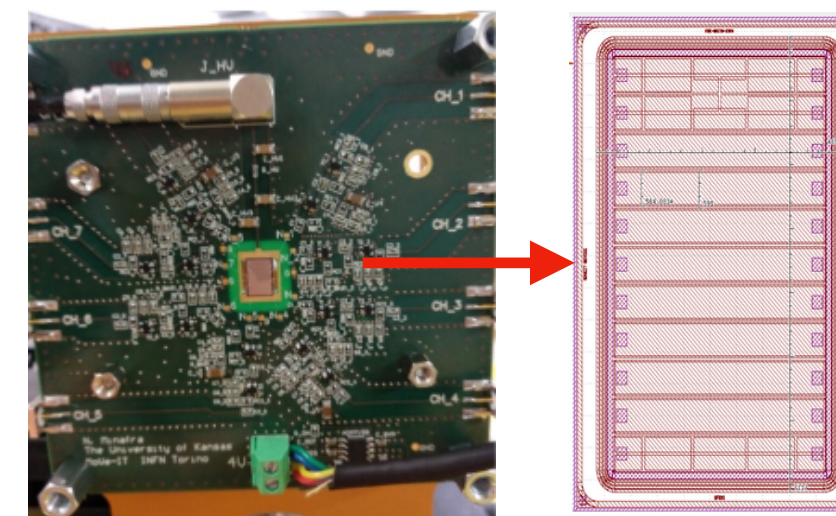
Setup with N detectors

*LaBr3:Ce* for the prompt gamma detection ( $t_\gamma$ )

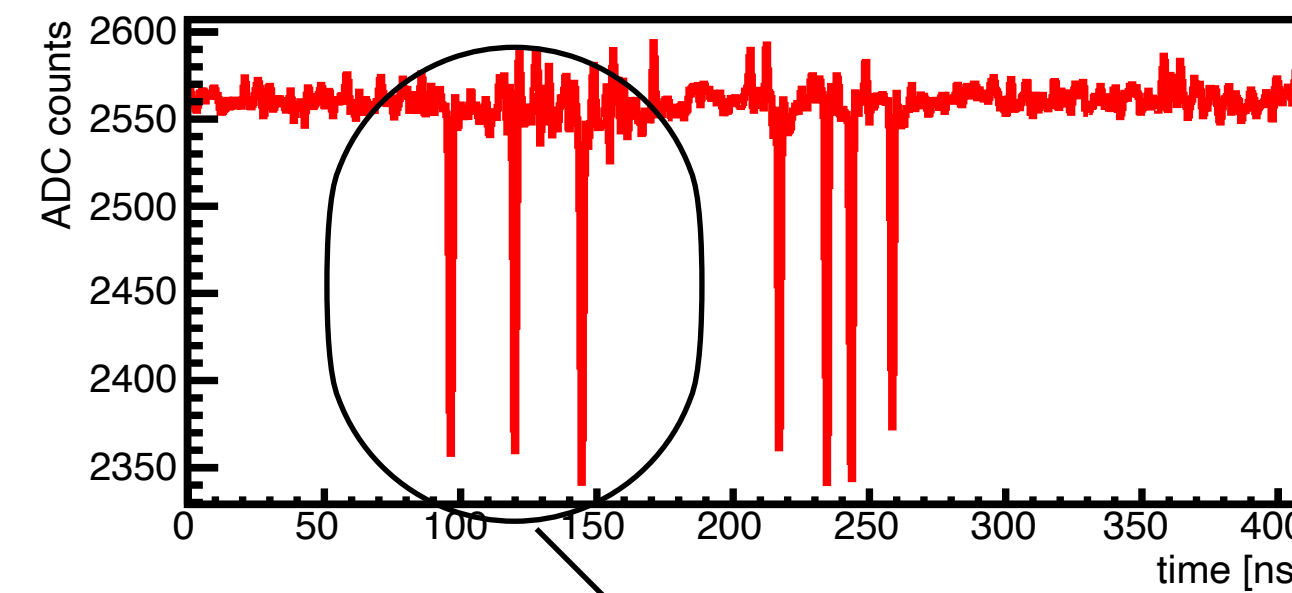
*UFSD* for the primary proton detection ( $t_0$ )

**UFSD:** measure the delivery time of each primary proton

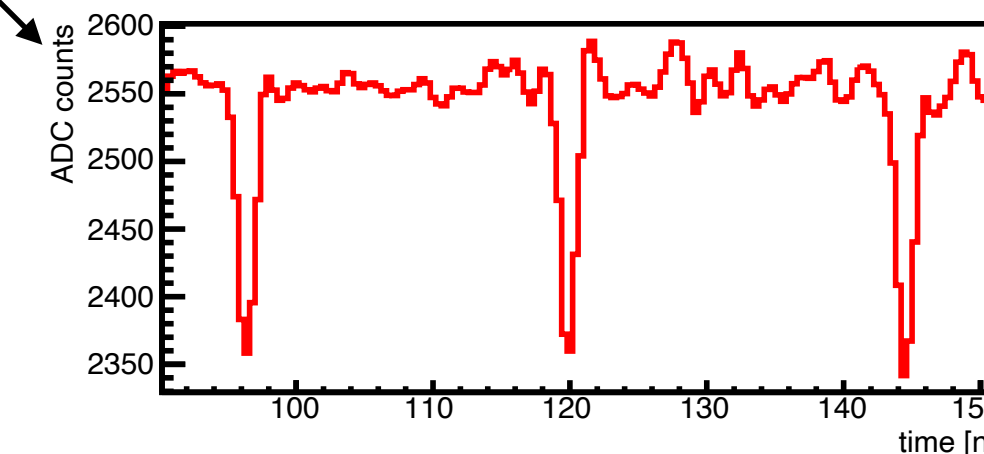
*Developed by MoVeIT collaboration*



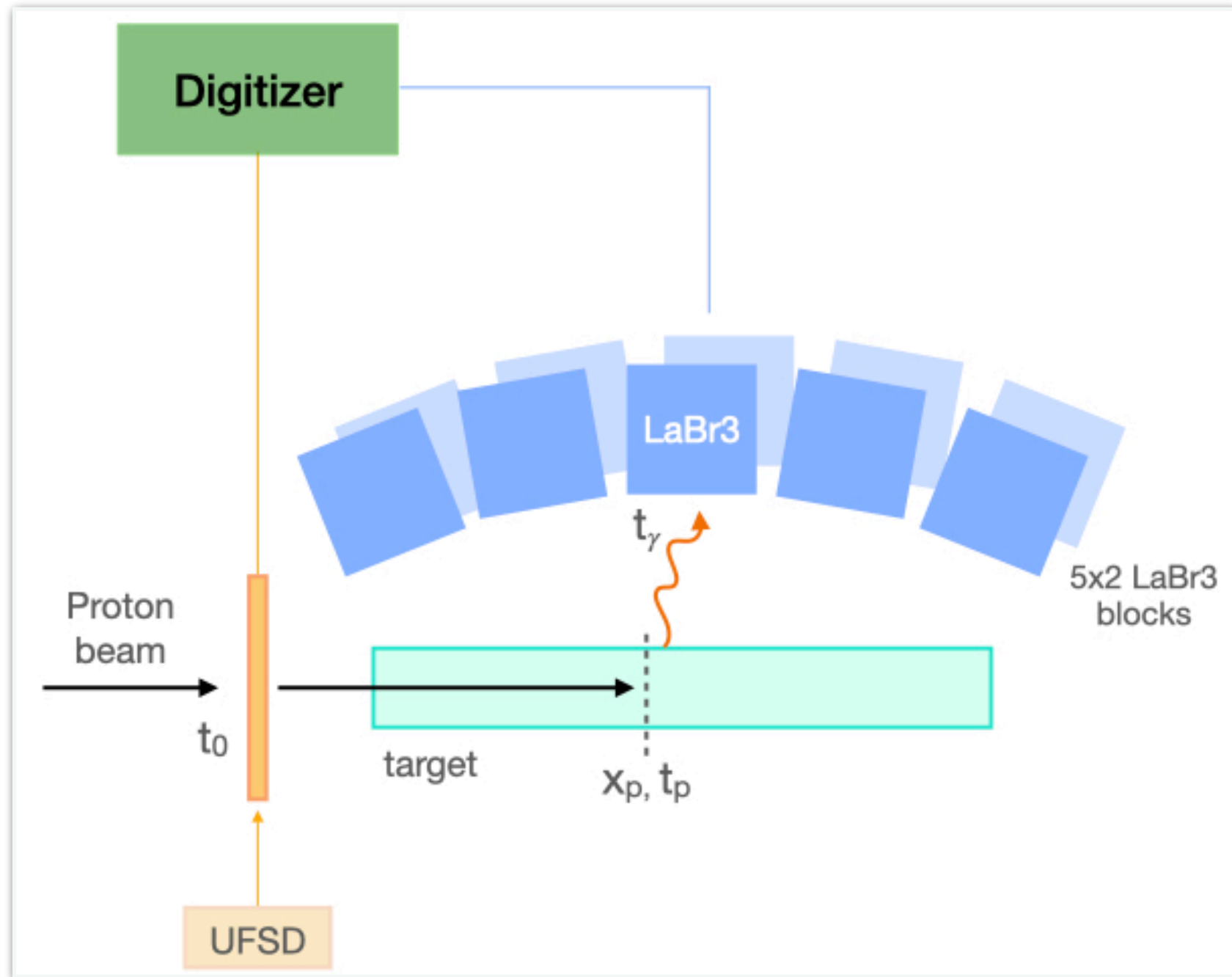
8 ch (2.2 mm<sup>2</sup>)  
Time resolution ~ 10 ps  
Read by digitizer



Beam Test @  
CNAO, Jun 2021  
Protons, 227MeV,  
~10<sup>5</sup> pps



# DETECTOR R&D



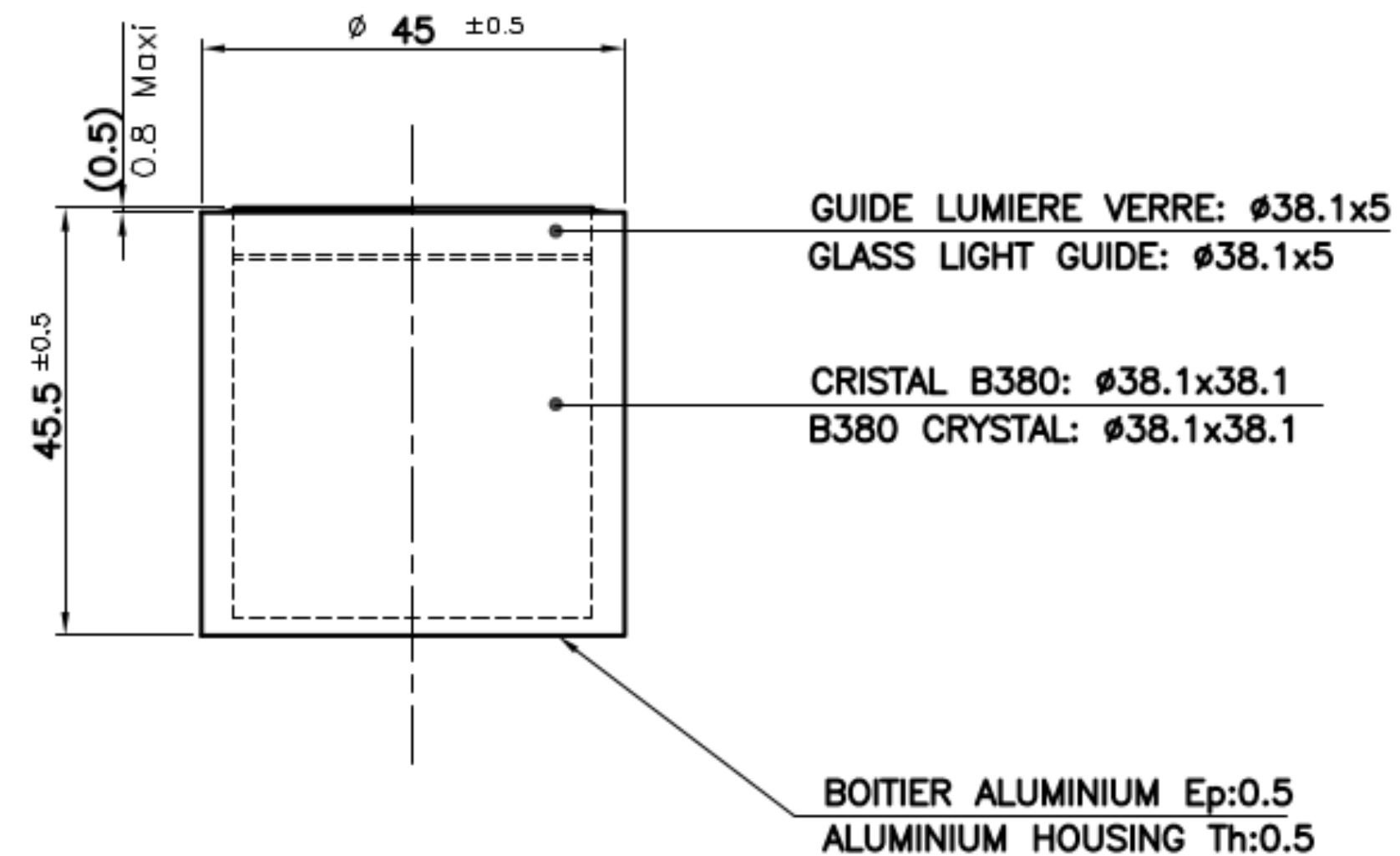
## PGT MULTI-DETECTOR SYSTEM

Setup with N detectors

*LaBr3:Ce* for the prompt gamma detection ( $t_\gamma$ )

*UFSD* for the primary proton detection ( $t_0$ )

**LaBr<sub>3</sub>(Ce):** measure the arrival time of the secondary prompt photons

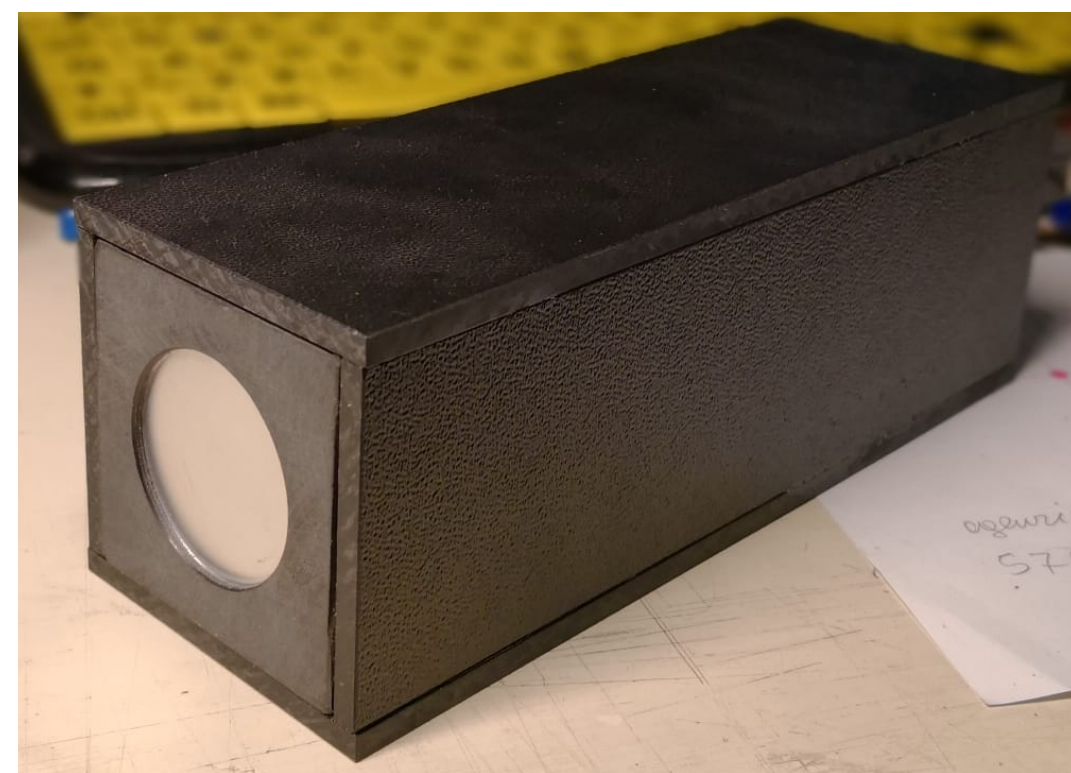
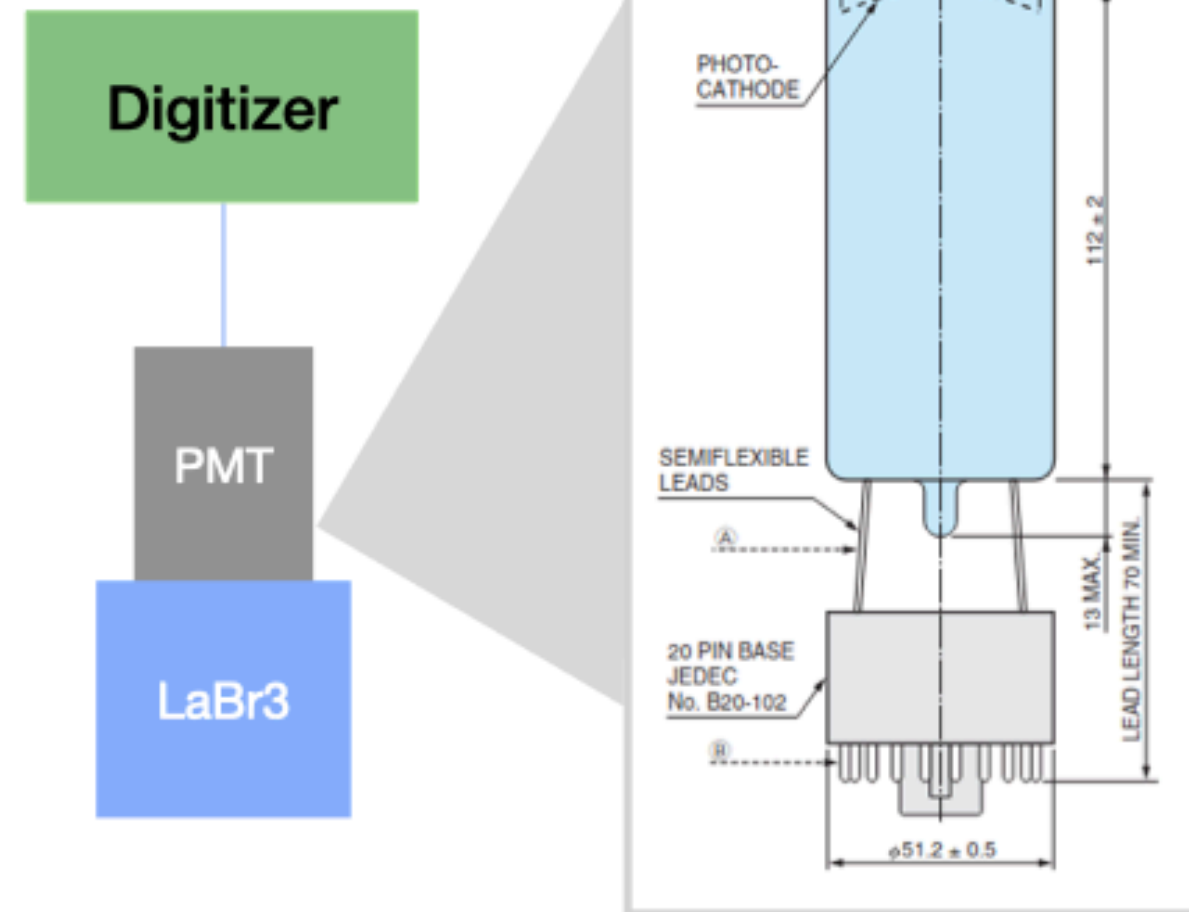


Scintillating crystals, 16 ns decay  
 Dimension: ø38.1 mm, h38.1 mm  
 Energy resolution 1.3% @ 6.1 MeV  
 Expected time resolution: **100 ps  $\sigma$**

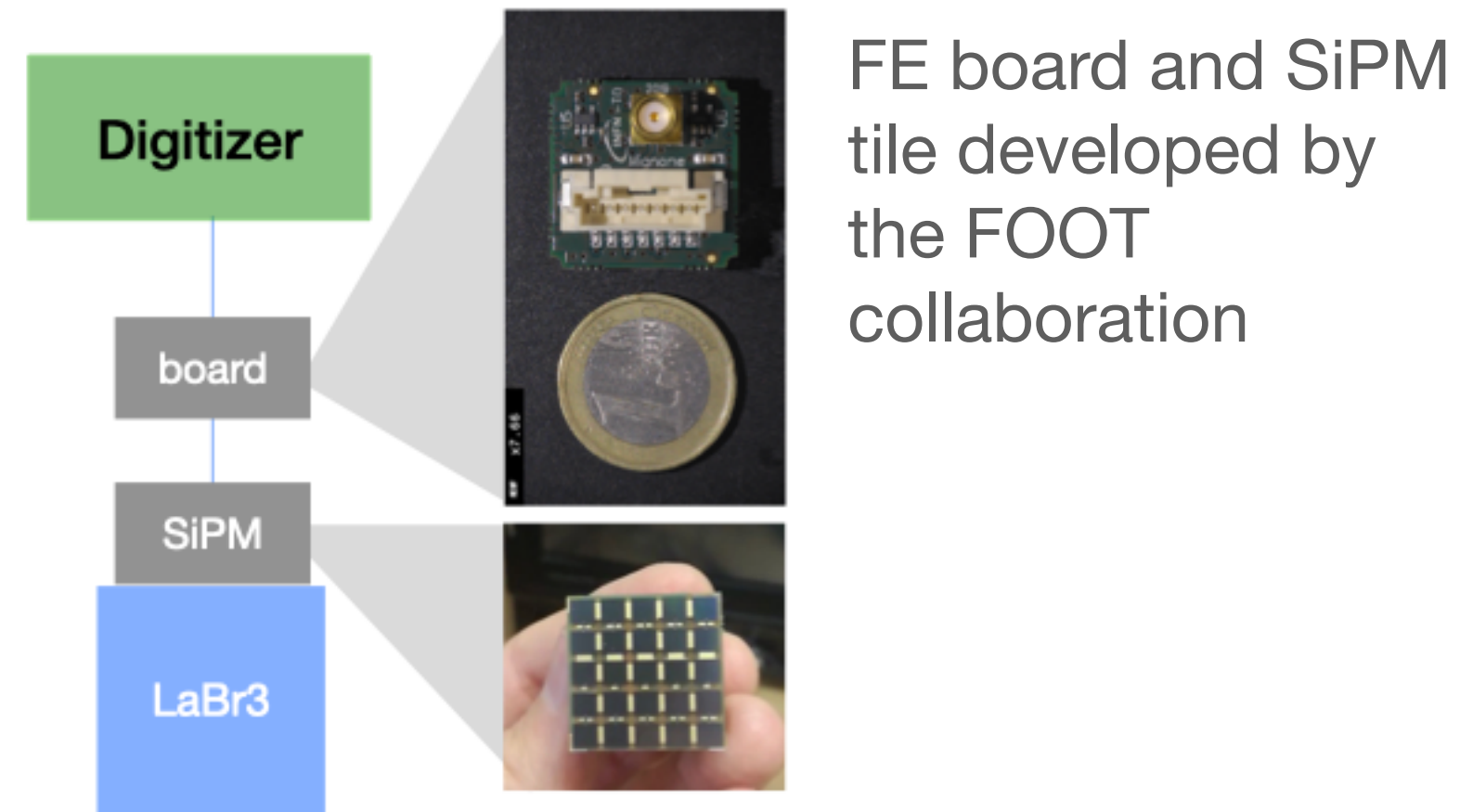
10 crystals, 10 ch  
 Read by digitizer

# DETECTOR R&D

## 1) PMT



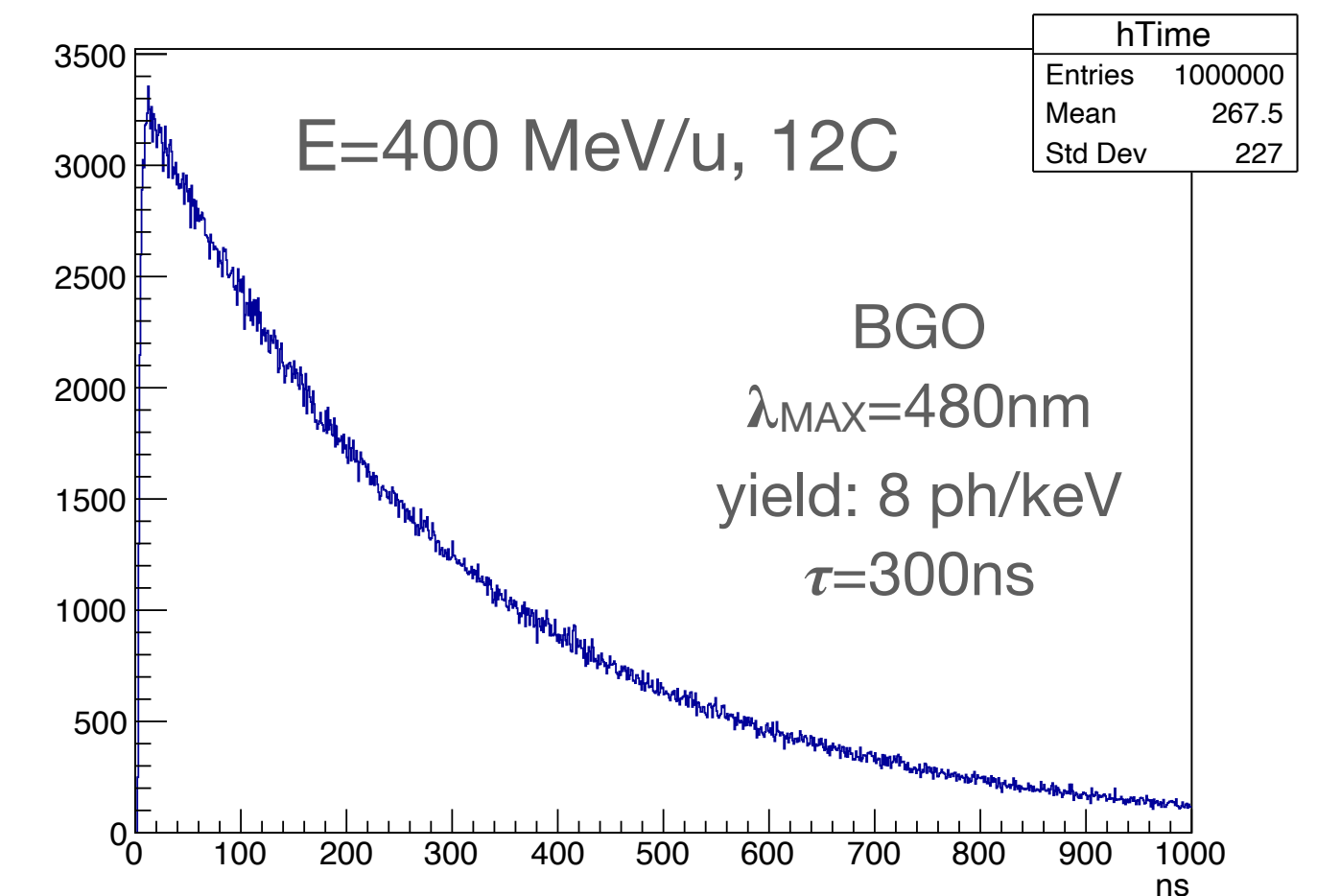
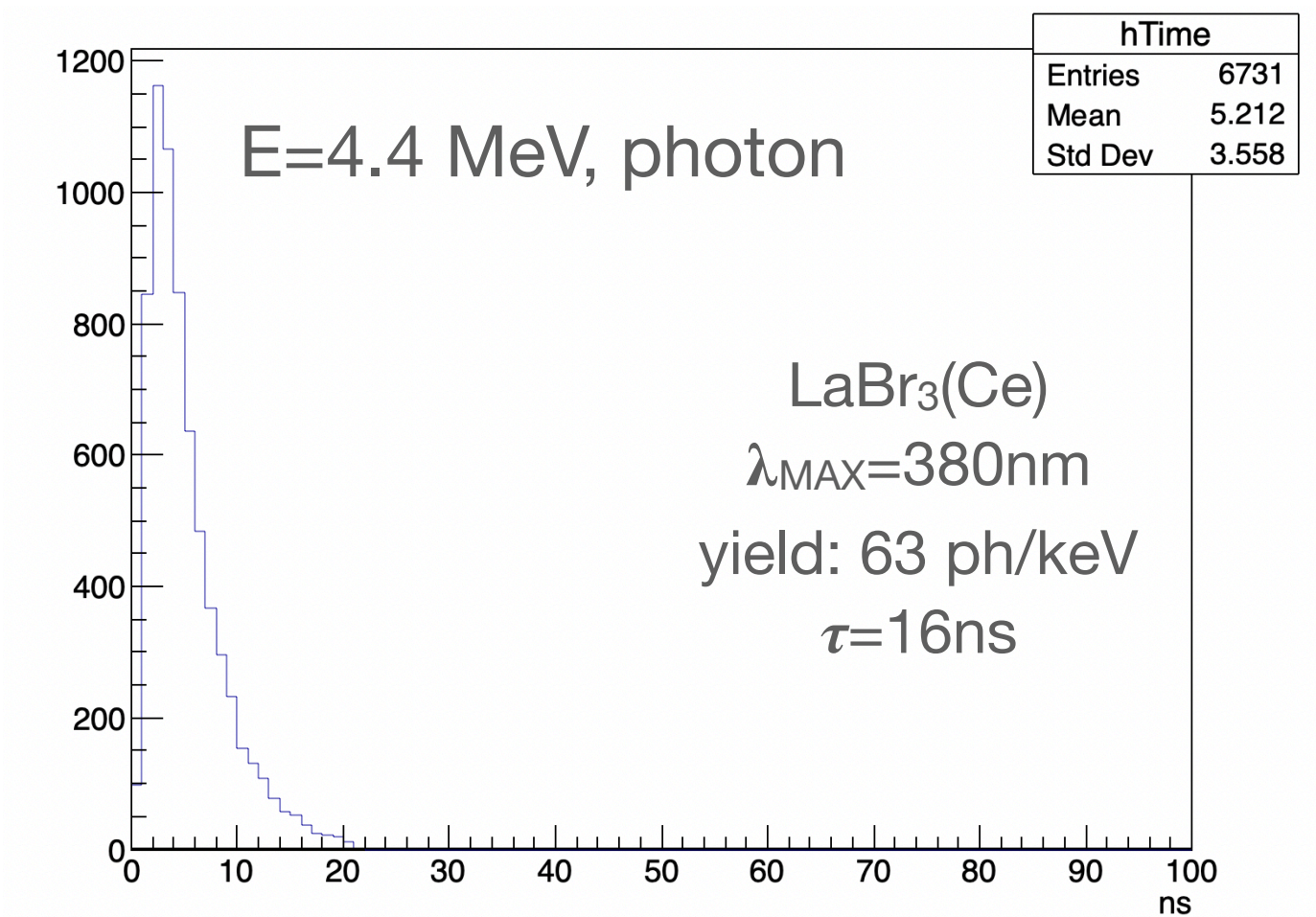
## 2) SiPM



SiPM by FBK  
5x5 tile  
→  $10^6$  microcells per SiPM

FE board and SiPM tile developed by the FOOT collaboration

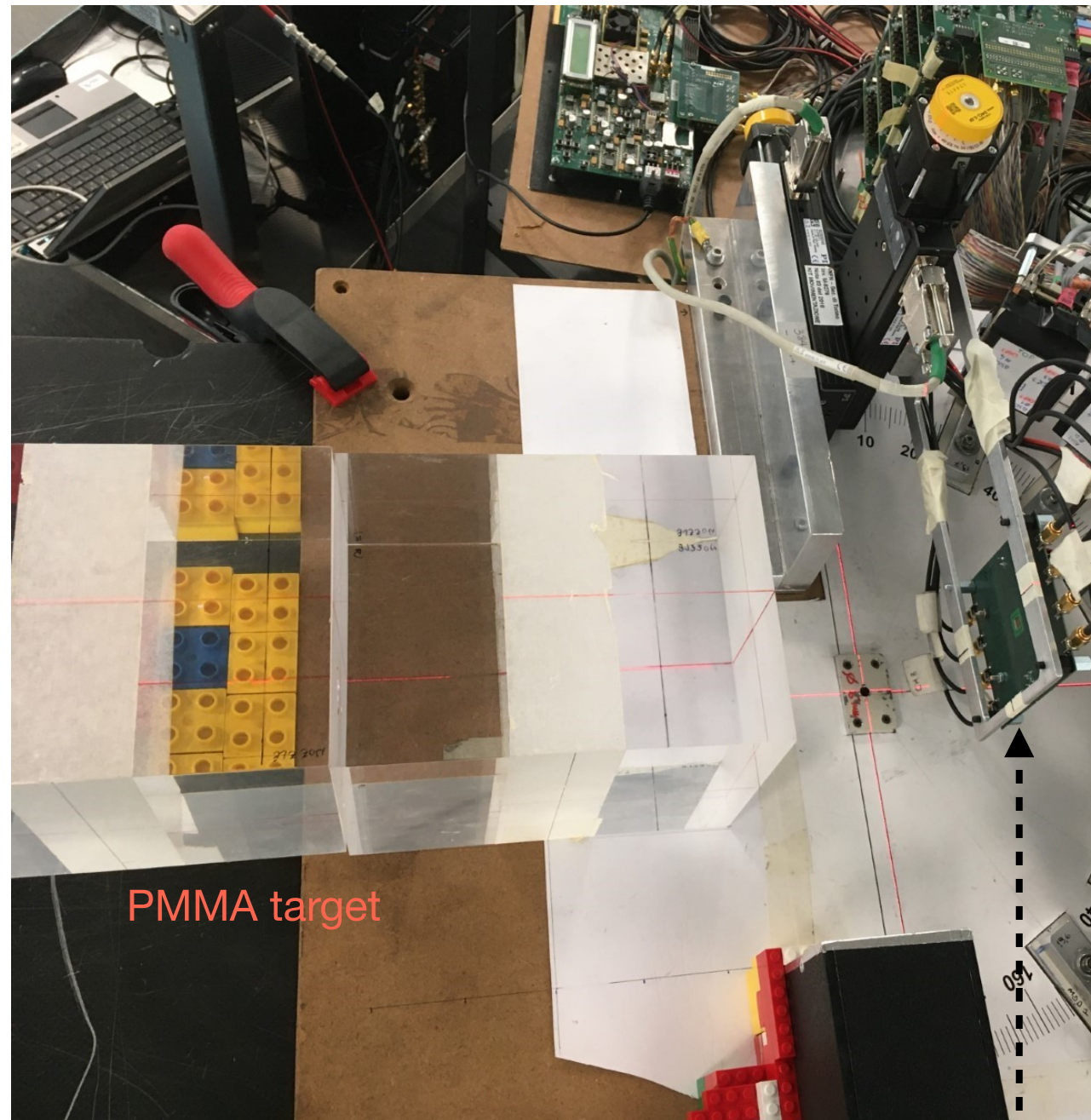
## MC simulatons (FLUKA tool)



→ experimentally validated

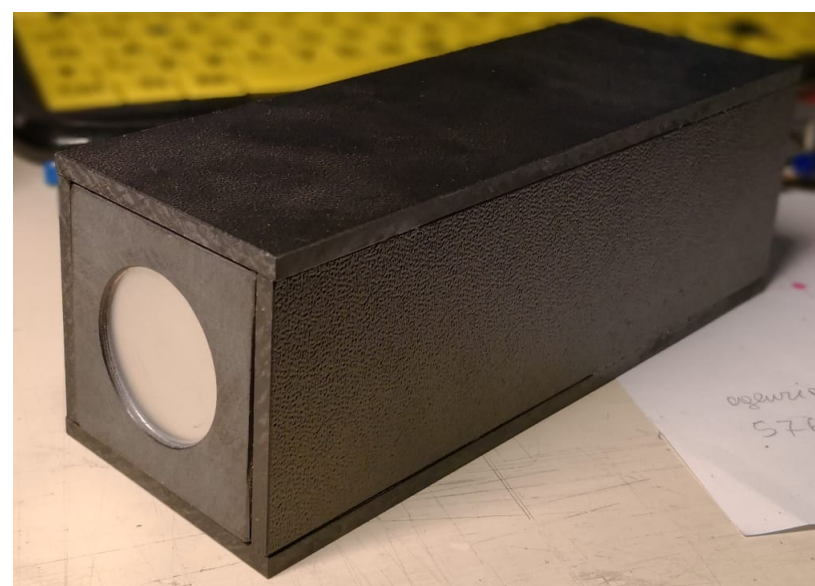


# PRELIMINARY TESTS



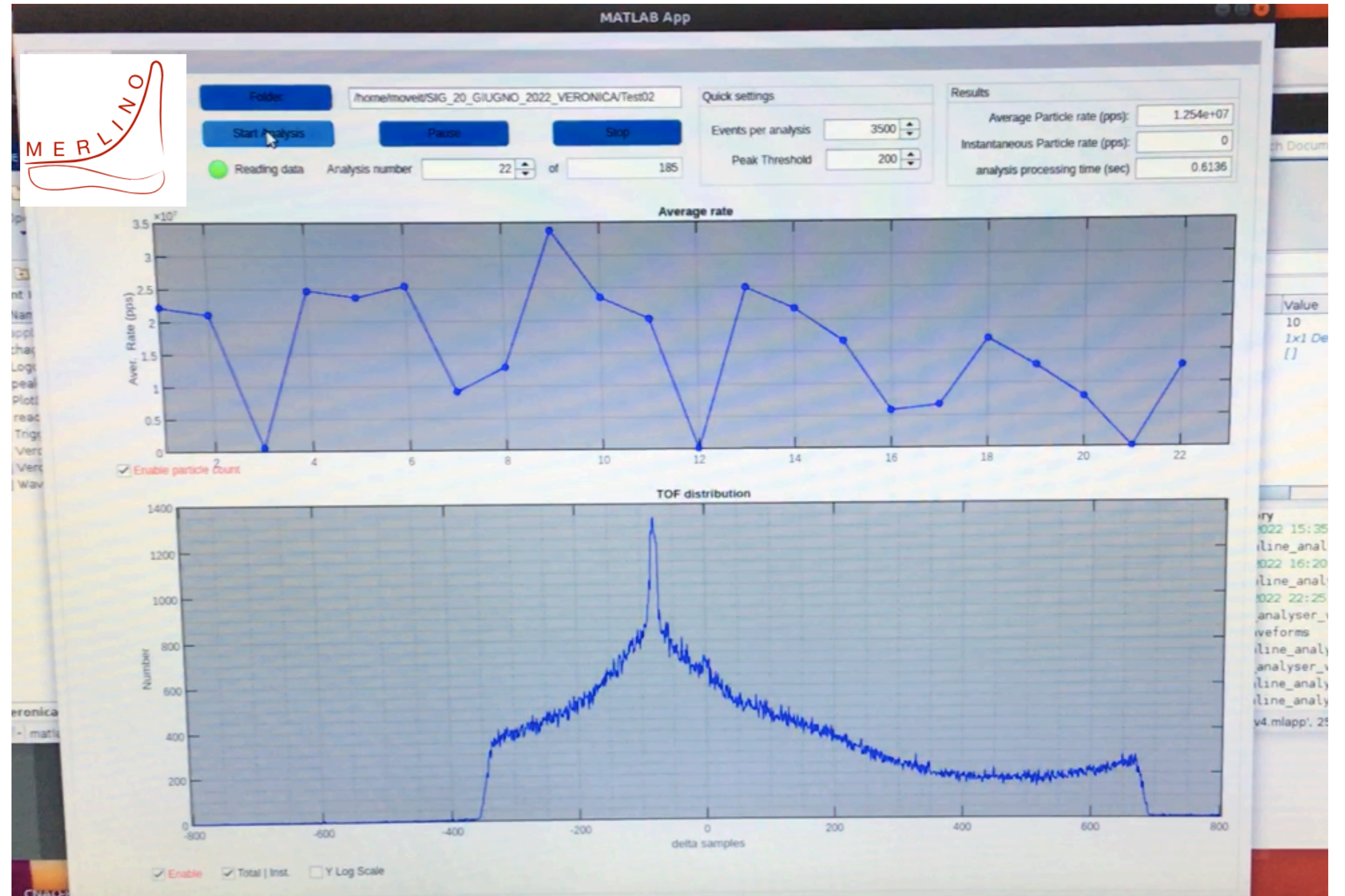
beam

LaBr3+PMT



UFSD  
8 strips (2.2 mm<sup>2</sup>  
active area, 590 um  
pitch)

## ONLINE PGT INTERFACE

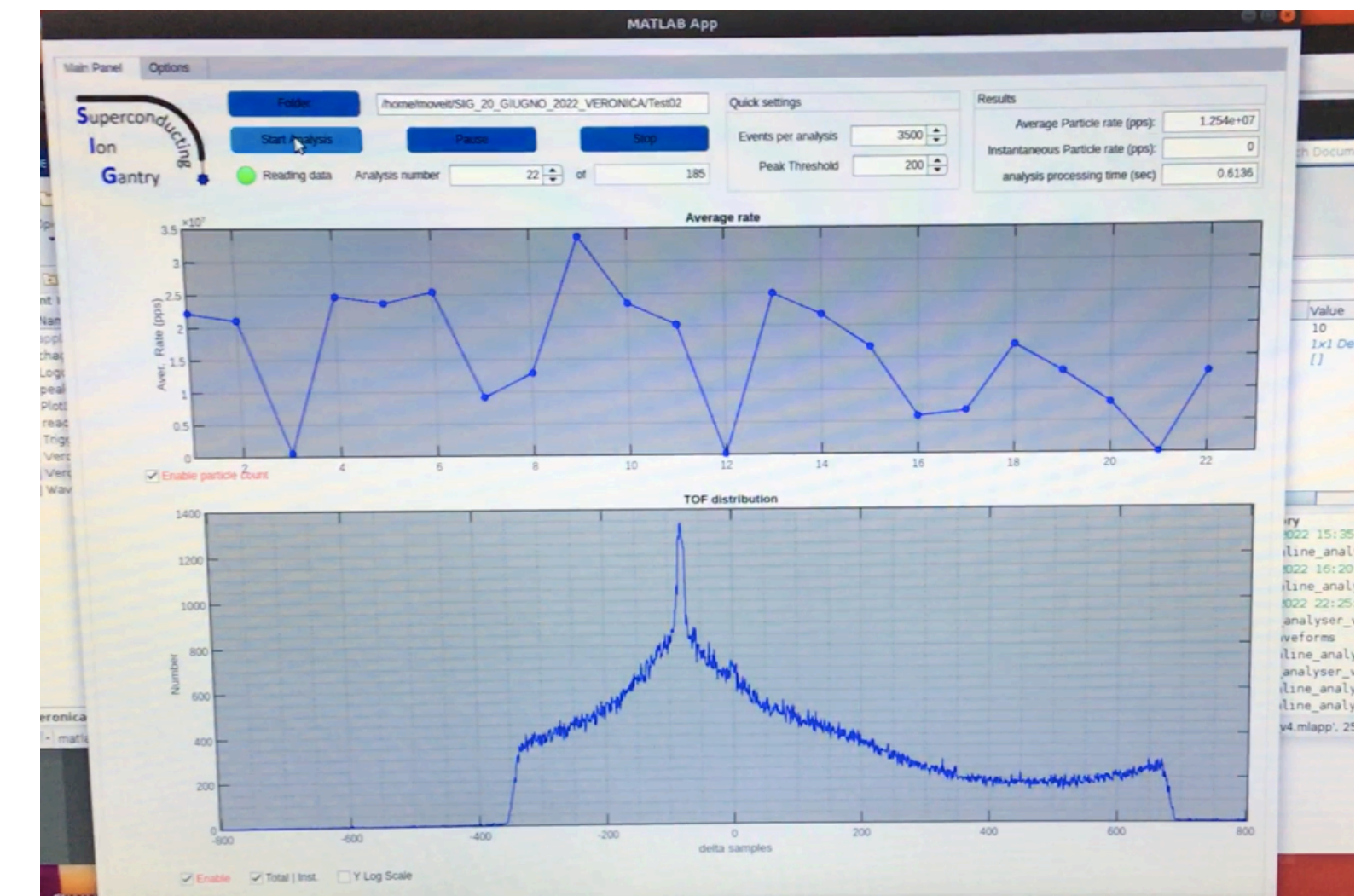
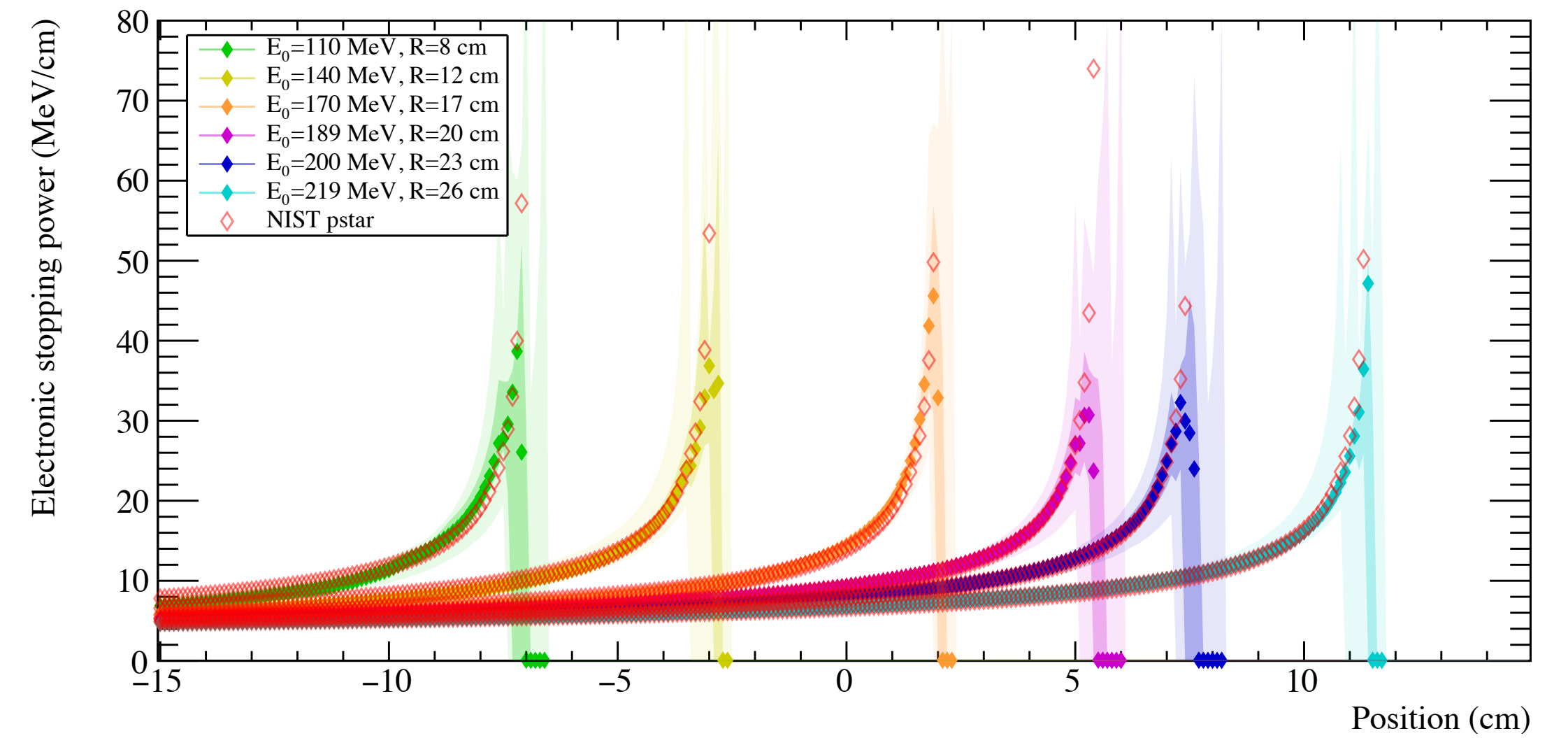
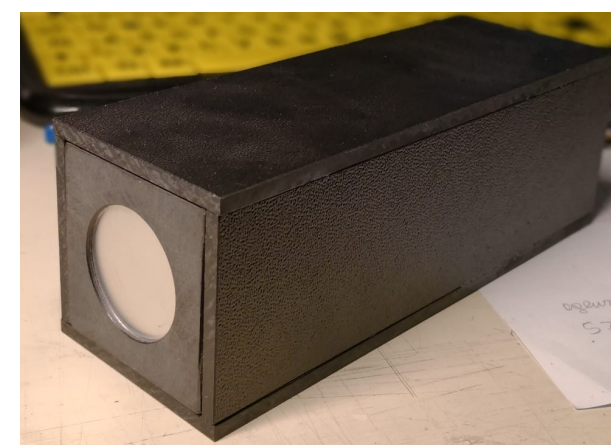
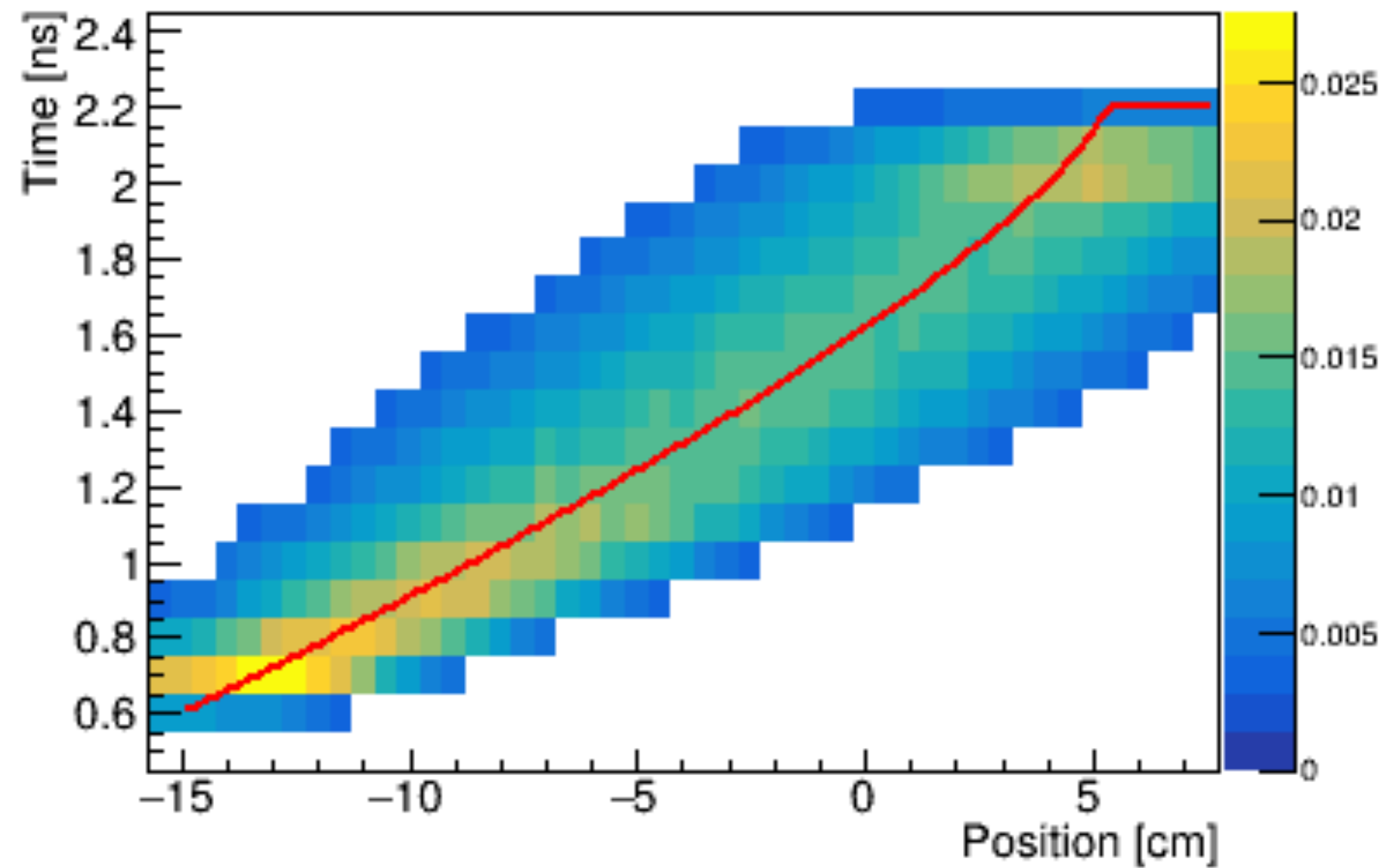


Beam test @ CNAO, 21/06/2022

# CONCLUSIONS

$$m_{jp}^{k+1} = \frac{m_{jp}^k}{S_{jp}} \sum_i \sum_d \frac{n_{id}}{\sum_l \sum_t f_{idlt} m_{lt}^k} f_{idjp}$$

prompt photon  $\rightarrow m_{jp}^{k+1}$   
 sensitivity  $\rightarrow S_{jp}$   
 data  $\rightarrow n_{id}$   
 SM  $\rightarrow f_{idjp}$   
 p: time bin (emission)  
 j: space bin (emission)  
 i: time bin (detection)  
 d: detector

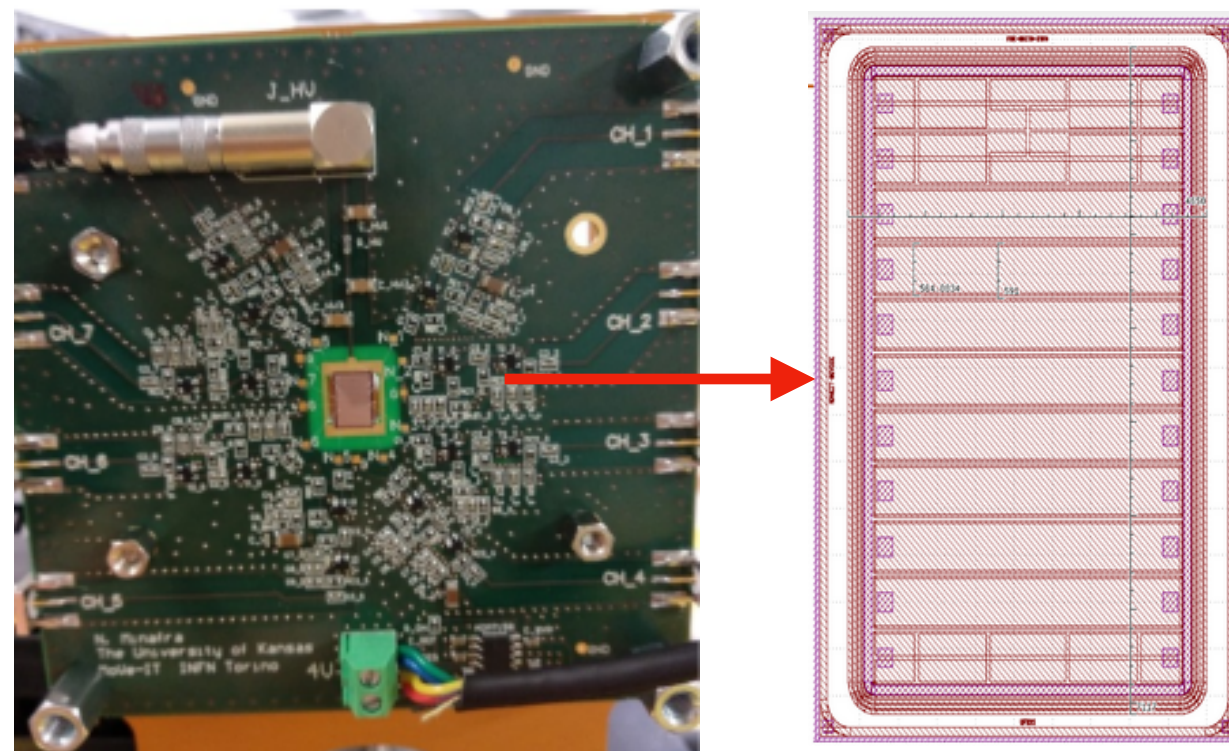


**BACKUP SLIDES**

# ULTRA-FAST SILICON DETECTORS

**UFSD** for beam monitoring: measure the delivery time of each primary particle

*Developed by MoVeIT collaboration (CSN5)*



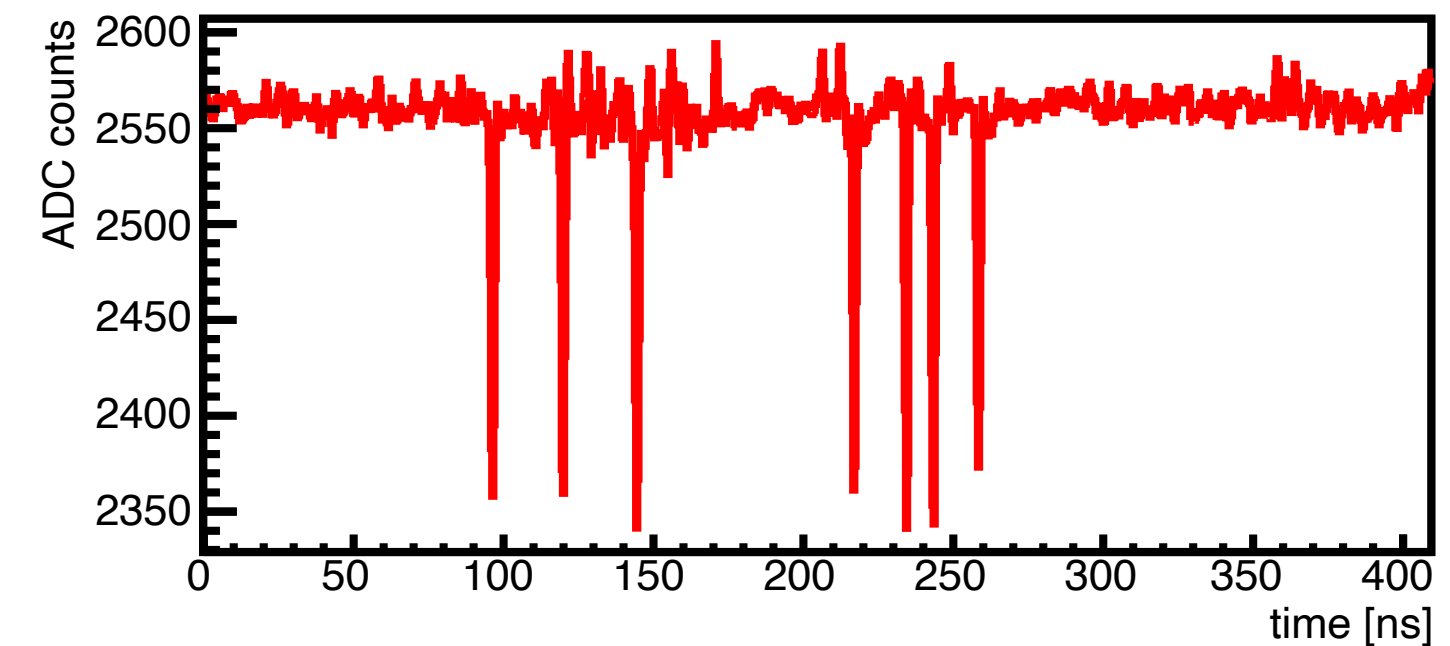
*FE board:* 8ch, 2 amplification stages (fast analog amplifier)

Optimized for timing measurements at high rates

*Dynamic range:* 3-150 fC → 60-250MeV protons

Fast signals ( $\sim 2$ ns), single discrimination up to  $10^9$  ps<sup>-1</sup>cm<sup>-2</sup> ( $> 10$  MHz/ch)

*Ch specifications:* noise  $< 3$  mV, SNR  $> 25$ , jitter  $< 30$  ps



8 strips + 3 test strips, 2.2 mm<sup>2</sup> (3393  $\mu$ m x 550  $\mu$ m, pitch 590  $\mu$ m)

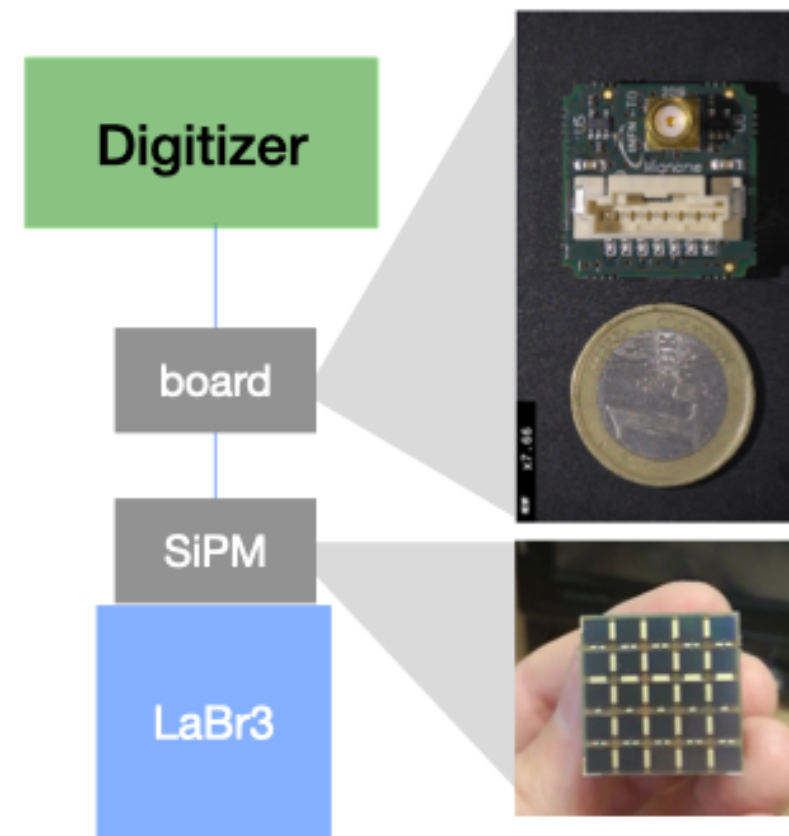
Read by a digitizer (16ch, CAEN DT5742)

Time resolution  $\sim 10$  ps

Detection efficiency up to  $\sim 27\%$  with clinical beams

# FOOT SIPM TILE

Readout 2: SiPMs

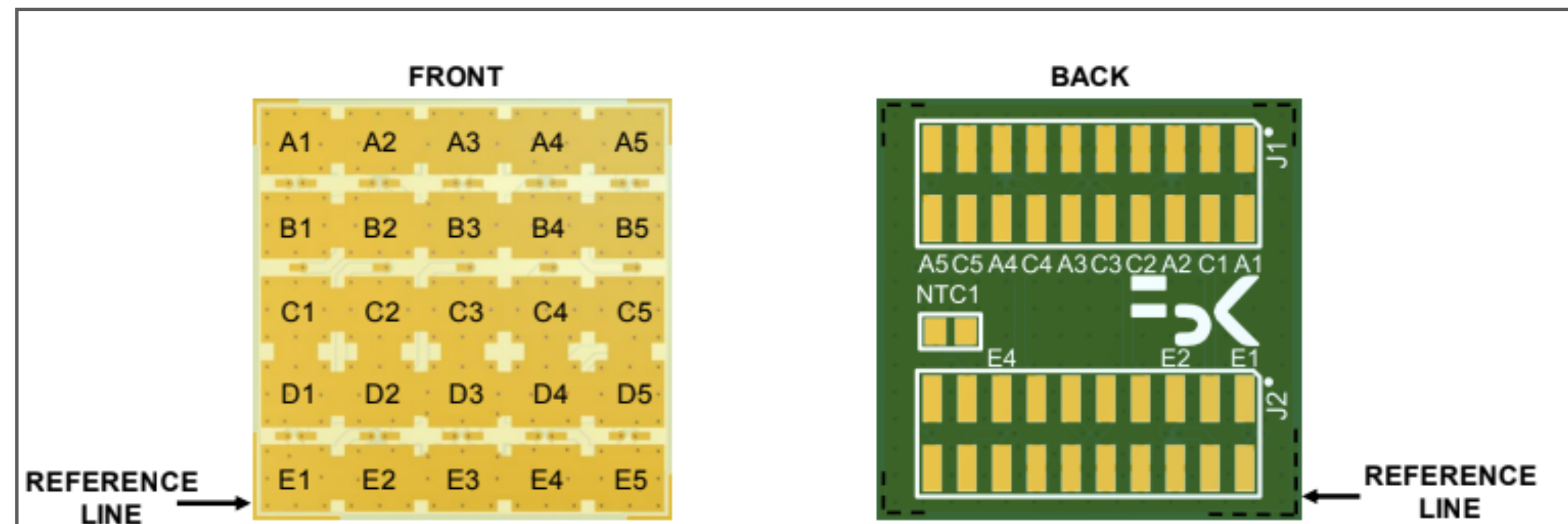


FOOT (CSN3 INFN) FE board and SiPM tile

Pausch et al. "Detection systems for range monitoring in proton therapy: needs and challenges" NIM A 2020

## 5.6. Challenge and potential approach

It seems an obvious approach to rely on the construction scheme and the SiPM light sensors of recent PET-MR detectors but to replace the LSO or LYSO crystals by  $\text{CeBr}_3$  or  $\text{LaBr}_3:\text{Ce}$ . The high light yield



SiPM by FBK:

SiPM Type			Tile		
Technology	Cell size ( $\mu\text{m}$ )	SiPM size ( $\text{mm}^2$ )	Tile size ( $\text{mm}^2$ )	# SiPMs	Resin
RGB-HD	15	16	24x24	25	Epoxy

→  $10^6$  microcells per SiPM

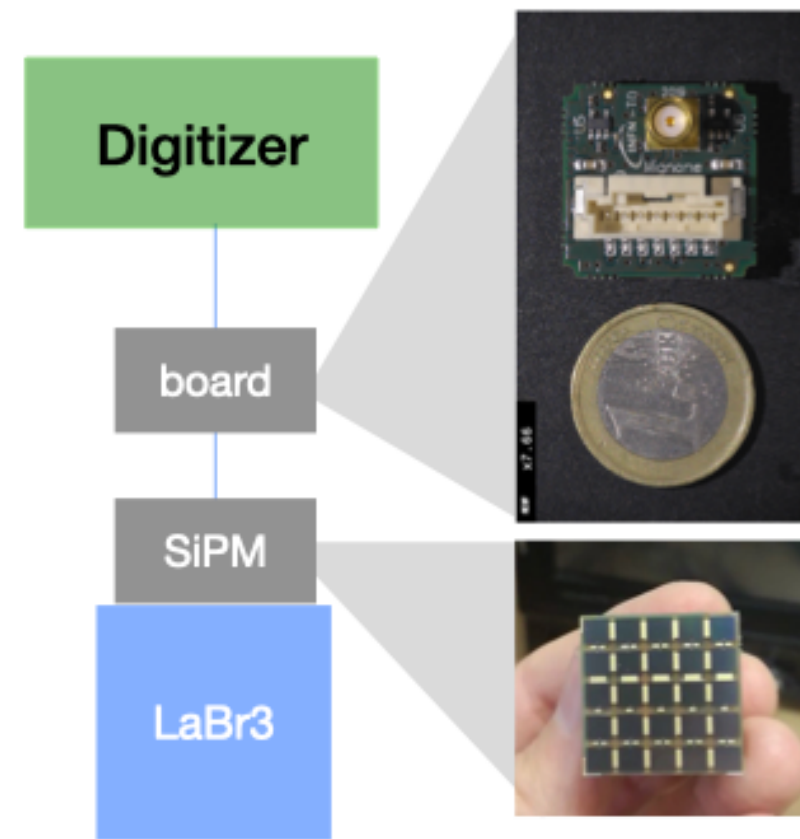
BGO time resolution  $\sim 600$  ps  $\sigma$  (cosmic rays),  $\tau=300$  ns

Digitizer 2.5 Gs/s

→ better time res might be achieved with  $\text{LaBr}_3(\text{Ce})$

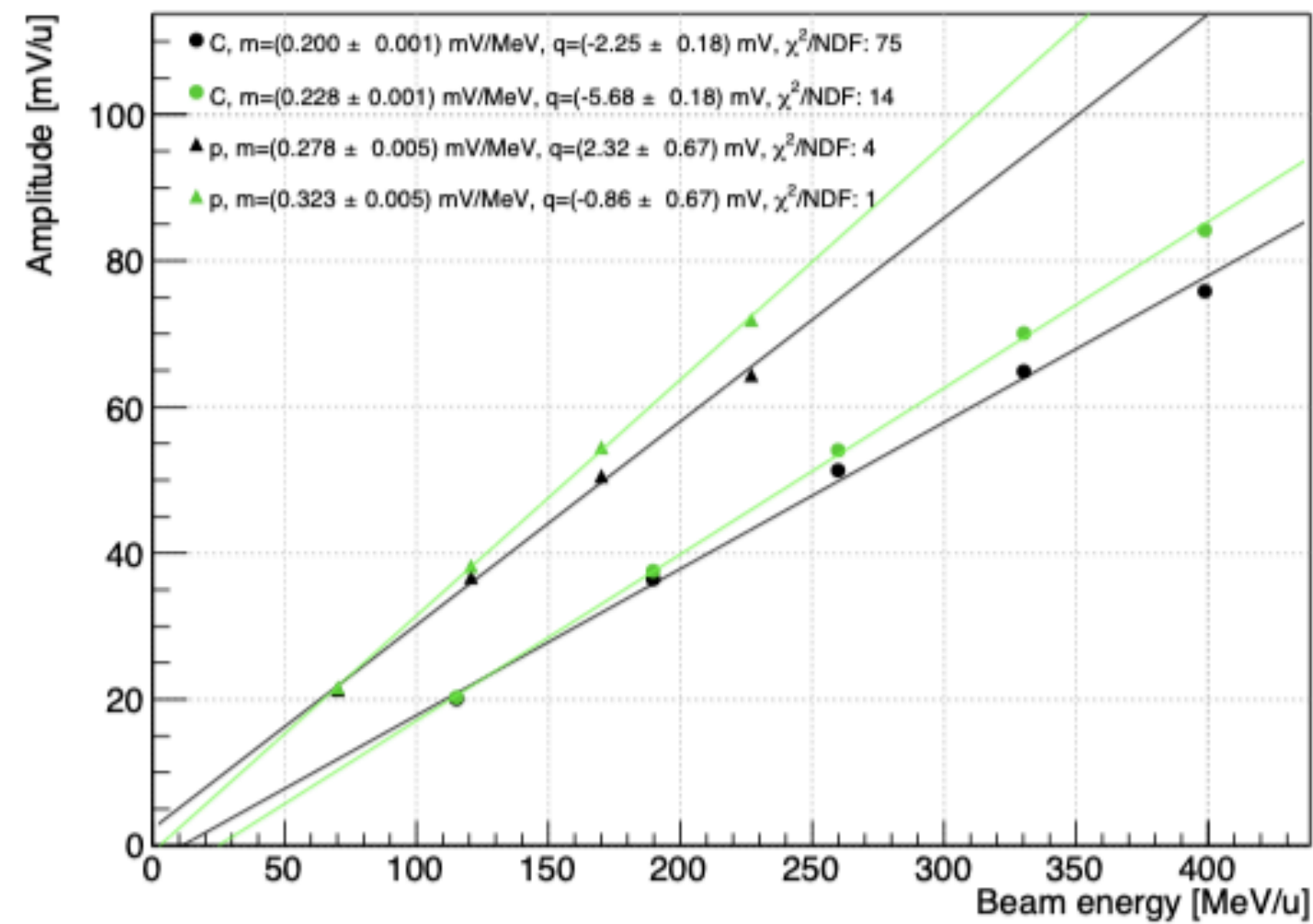
# FOOT SIPM TILE

## Readout 2: SiPMs

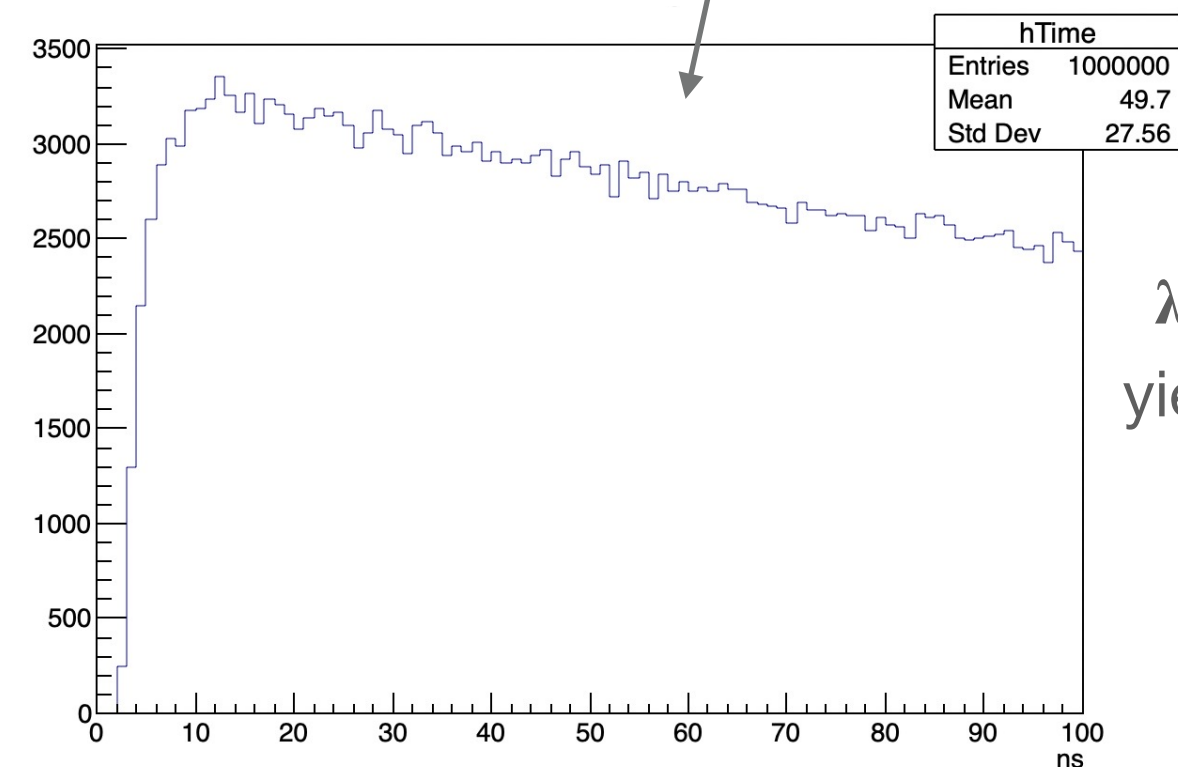
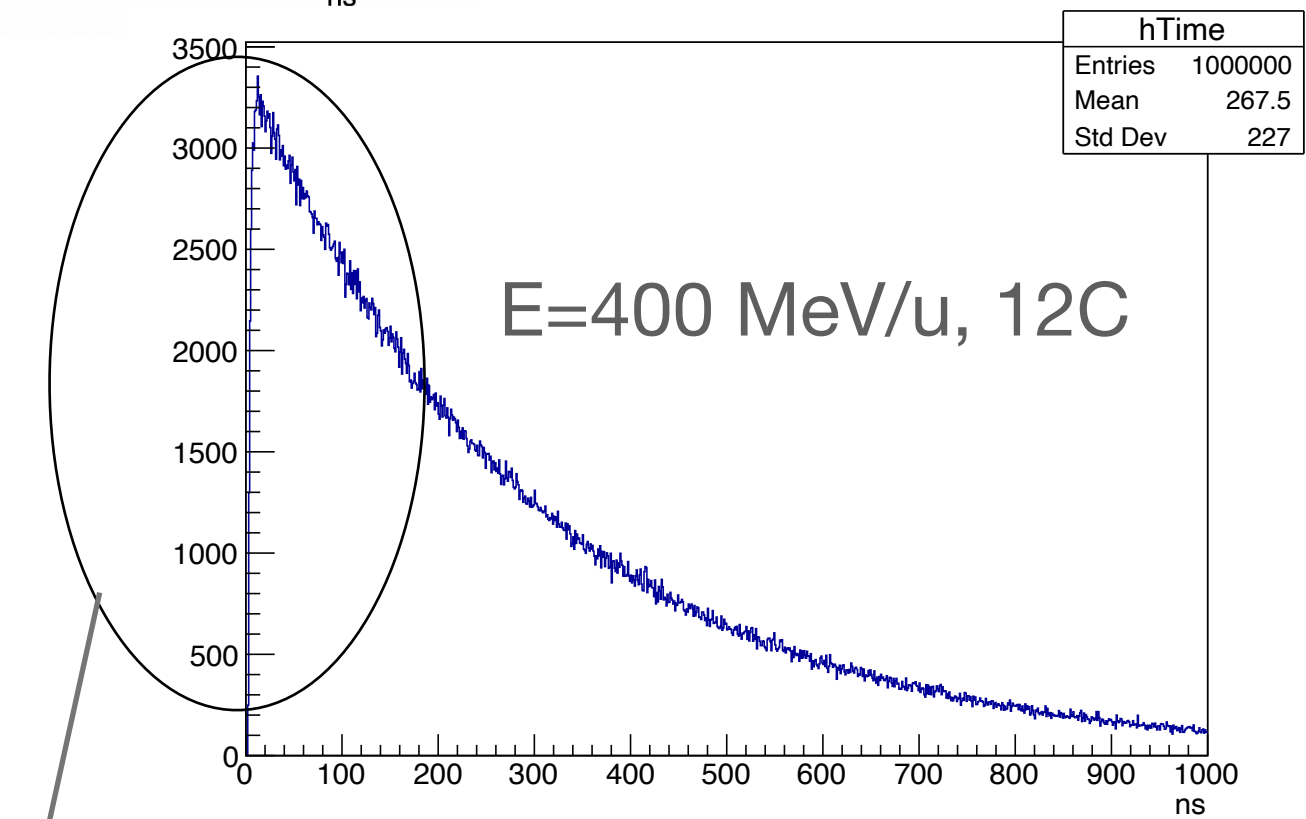
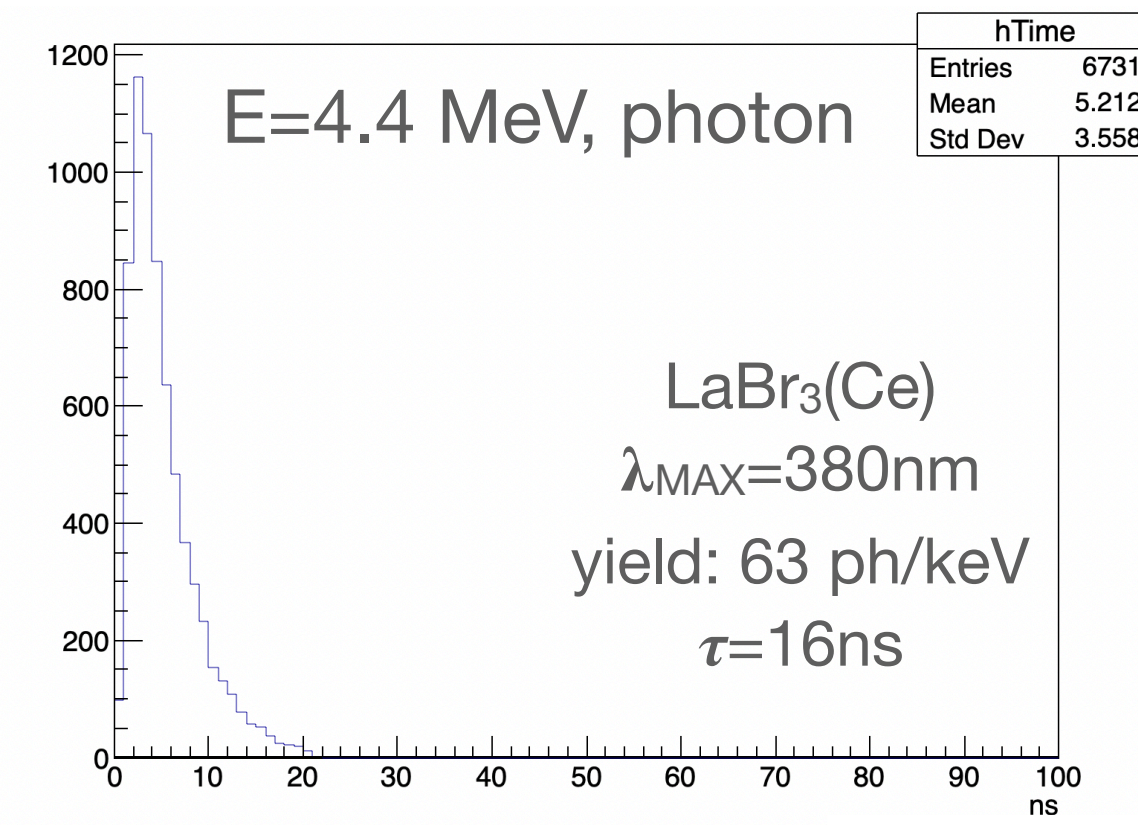


FOOT (CSN3  
INFN) FE board  
and SiPM tile

## SiPM response linearity vs beam energy



## MC simulations



# PROTON CT, DUAL ENERGY CT

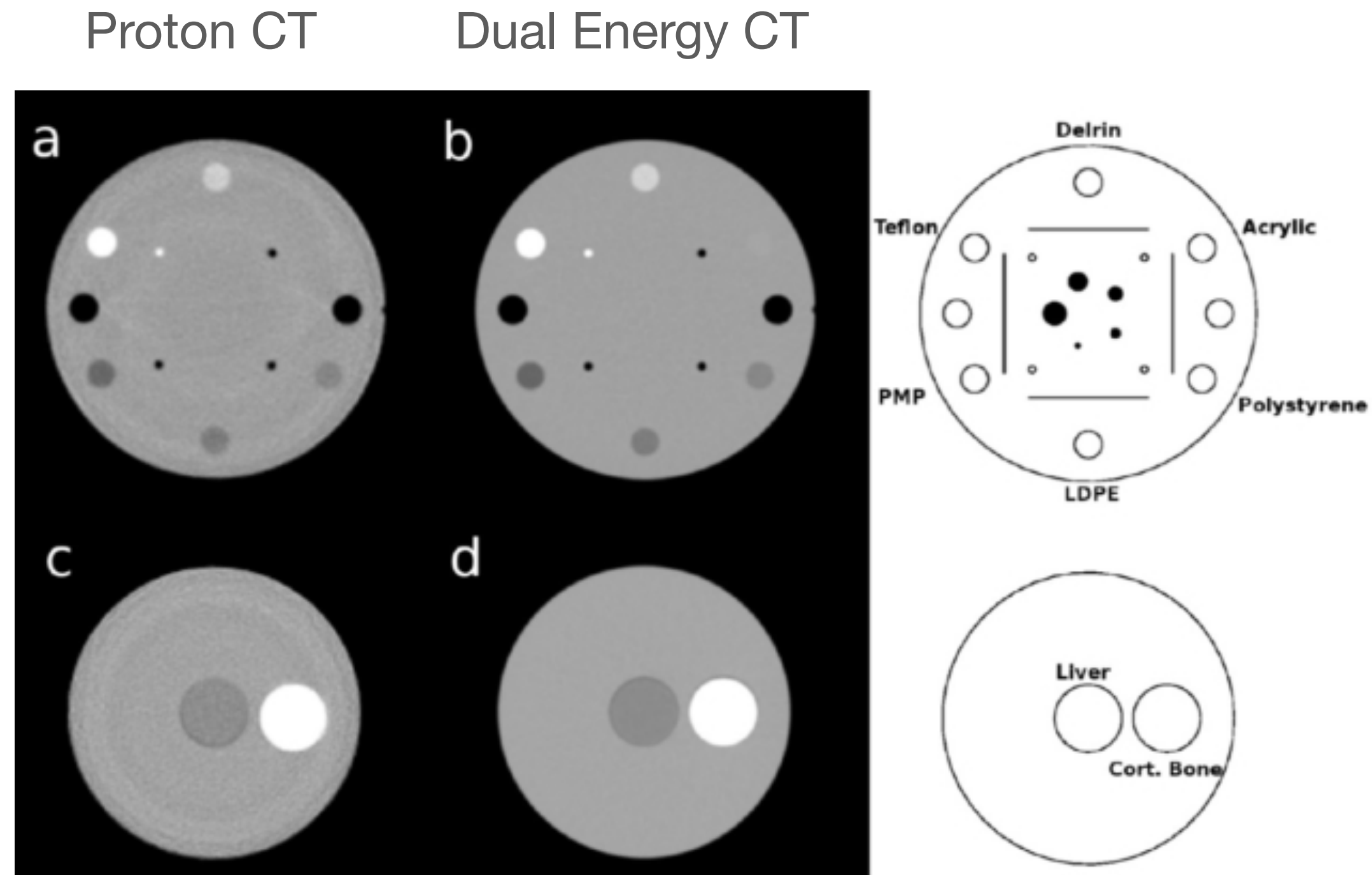
---

→HU to Stopping Power ratio conversion uncertainties

**PCT:** lower doses than DECT

Multiple Coulomb scattering → spatial resolution degradation

**Neither PCT nor DECT can be used for treatment verification**



PCT: <1.31% measured SP accuracy, 0.55% mean absolute error

DECT: <2.38% measured SP accuracy, 0.67% mean absolute error