MERLINO

Measurement of the EneRgy Loss for IN-vivo Optimization in particle therapy

Veronica Ferrero - INFN Torino

INFN Young Researchers Grant, CSN5, 01/12/2021

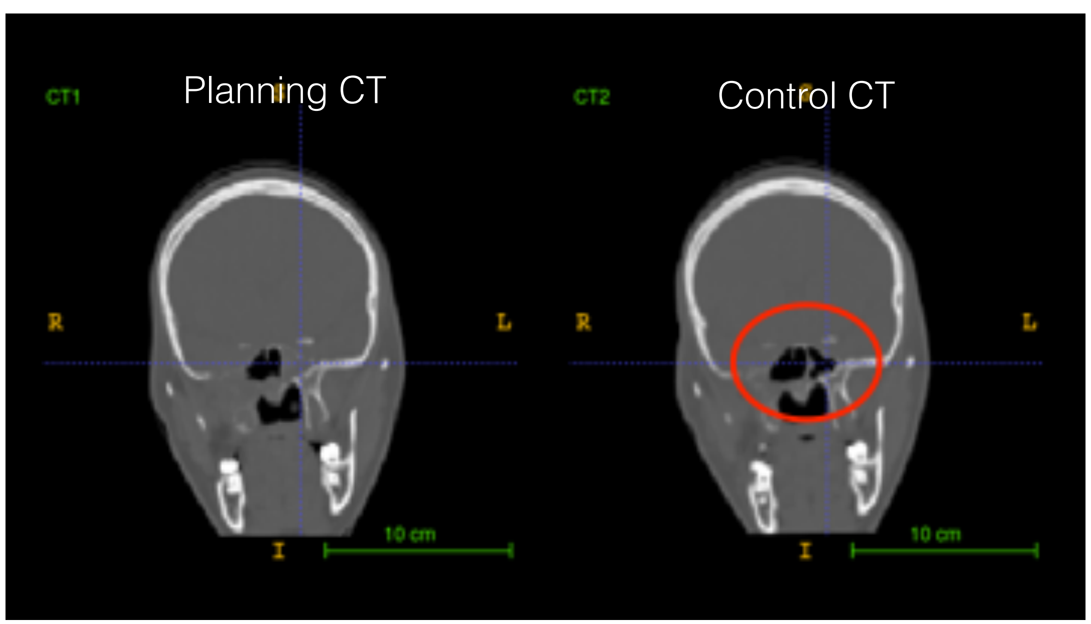
PROJECT MOTIVATION

WHY?

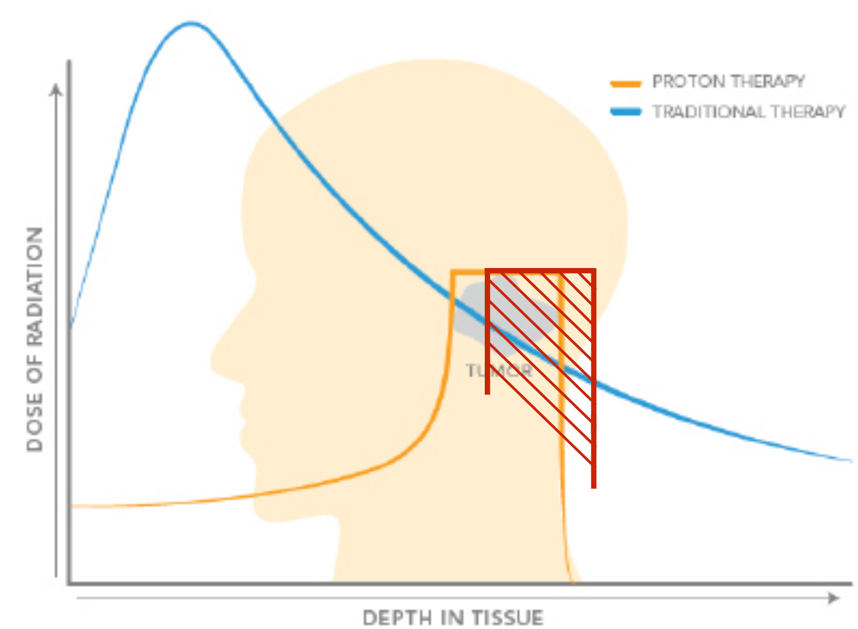
NEED OF A PATIENT-TAILORED TREATMENT OPTIMIZATION

Strong clinical motivations:

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



V. Ferrero, ECMP 2021



PROJECT MOTIVATION

HOW?

Proof-of-concept:

- Detector R&D
- Innovative reconstruction algorithm
- Optimization with proton beams

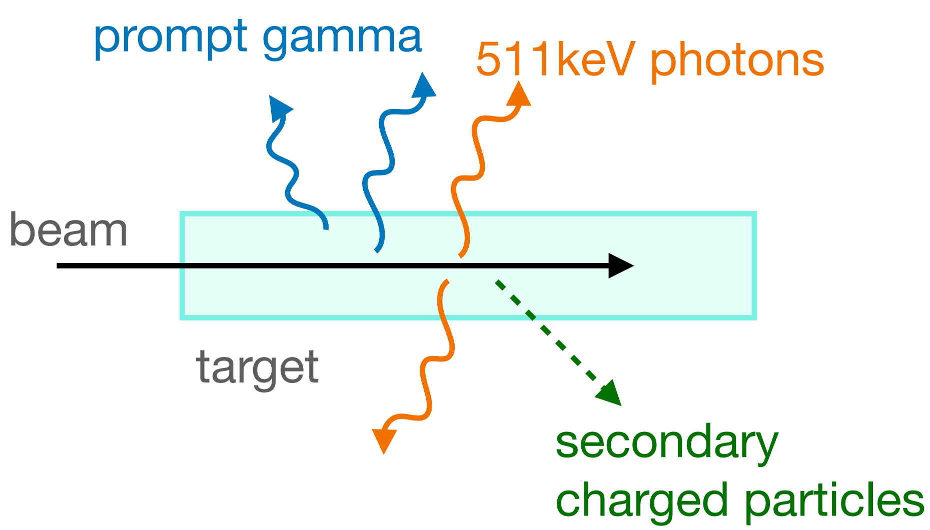
NEED OF A PATIENT-TAILORED TREATMENT OPTIMIZATION

STOPPING POWER INFORMATION: →

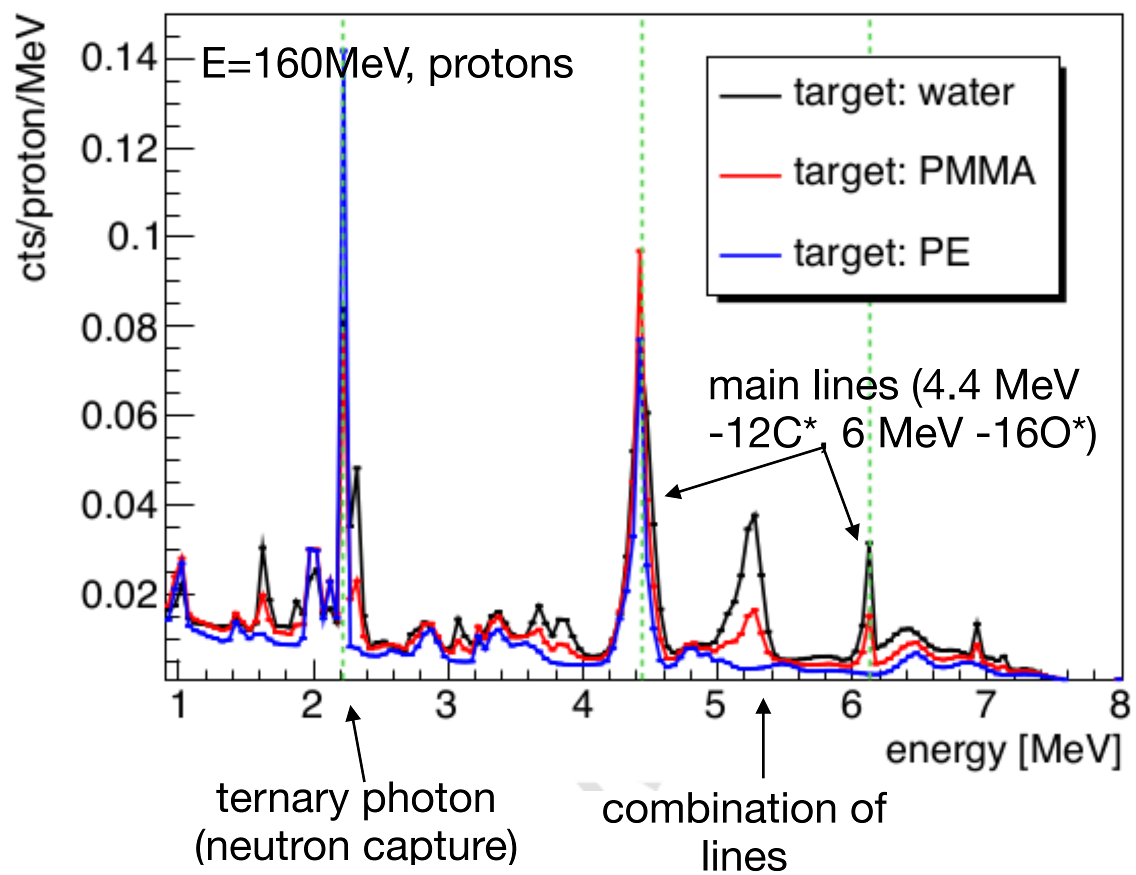
1. TREATMENT VERIFICATION AND OPTIMIZATION
2. STOICHIOMETRIC APPROACH VERIFICATION (TPS)

Never done before: from the measurement of **prompt gamma**… to the **beam stopping power**

RANGE VERIFICATION

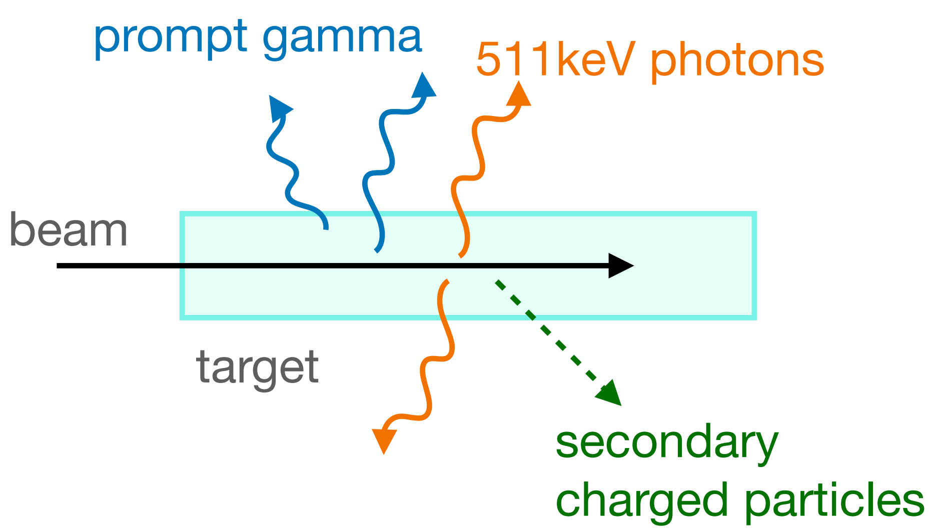


Krimmer et al NIM A 2018



Prompt gamma production yield per proton: ~10% in 4π (Smeets et al. Phys. Med. Bi. 2012)

RANGE VERIFICATION



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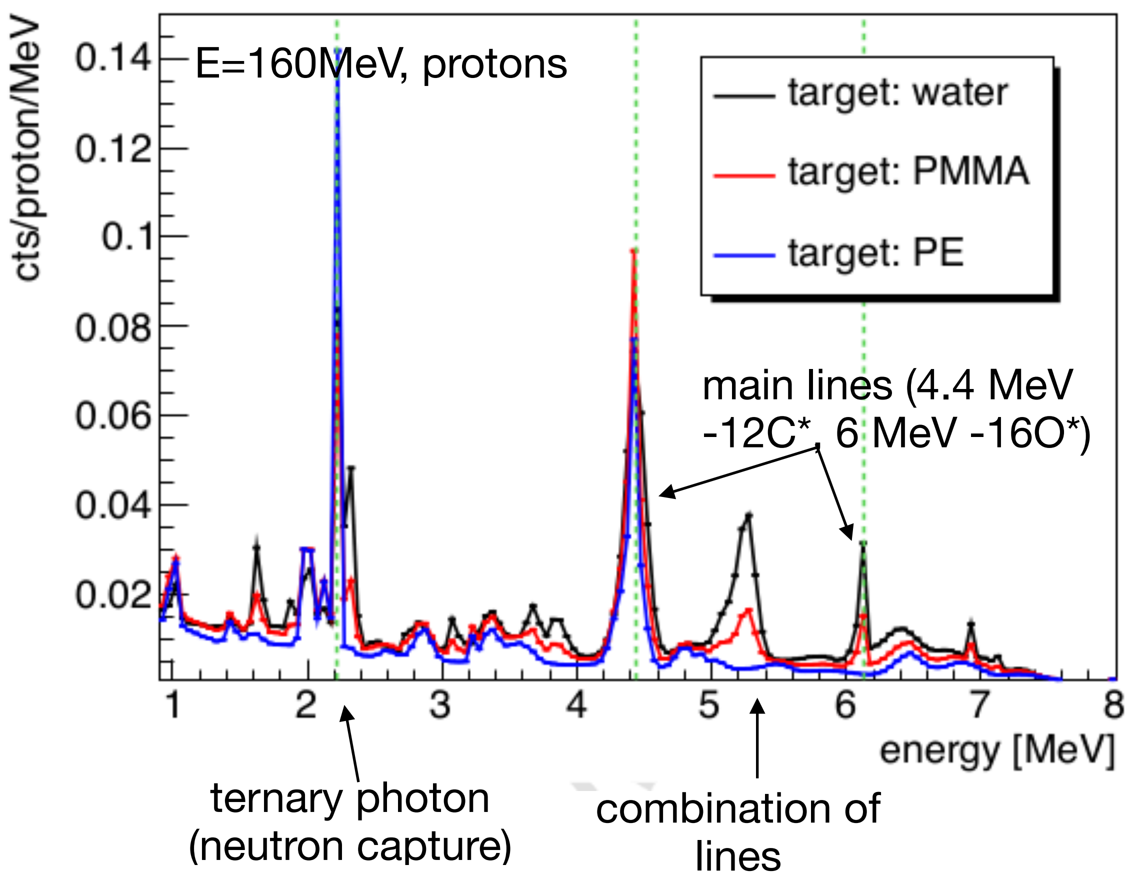


PREVIOUS PROJECT EXPERTISE:

Range monitoring systems

INSIDE

511 keV photons ⇒ PET (Ferrero V et al. Sci Rep 2018)

Secondary particles ⇒ Particle Tracker (Fischetti M et al. Sci Rep 2020)

Clinical trial @ CNAO (ClinicalTrials.gov ID: NCT03662373)

I3PET

511 keV photons + prompt gamma ⇒ PET (Ferrero V et al. TRPMS 2020)

MERLINO

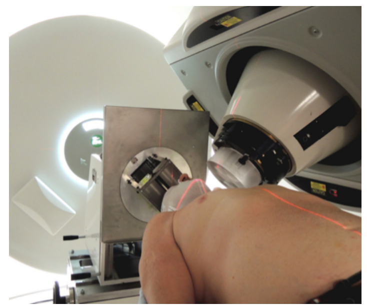
Proof-of-concept: Stopping Power (prompt gamma)

Prompt gamma production yield per proton: ～10% in 4π (Smeets et al. Phys. Med. Bi. 2012)

PROMPT GAMMA: RESEARCH PROSPECTS

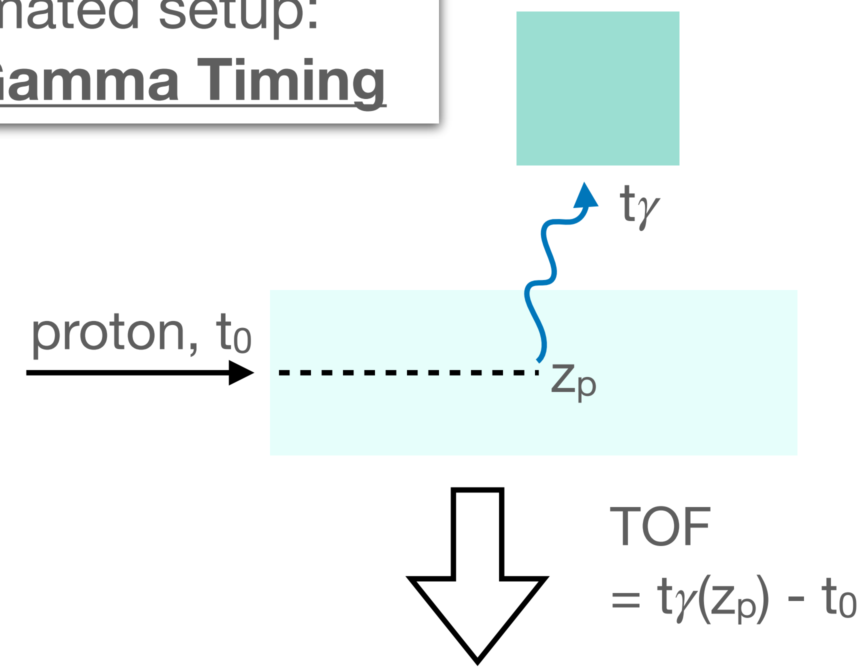
~100 PT facilities all over the word (PTCOG)

Commercial interest:
IBA Knife-Edge Slit Camera
Collimator
Range shifts 1-2mm
Head-and-neck, brain tumors

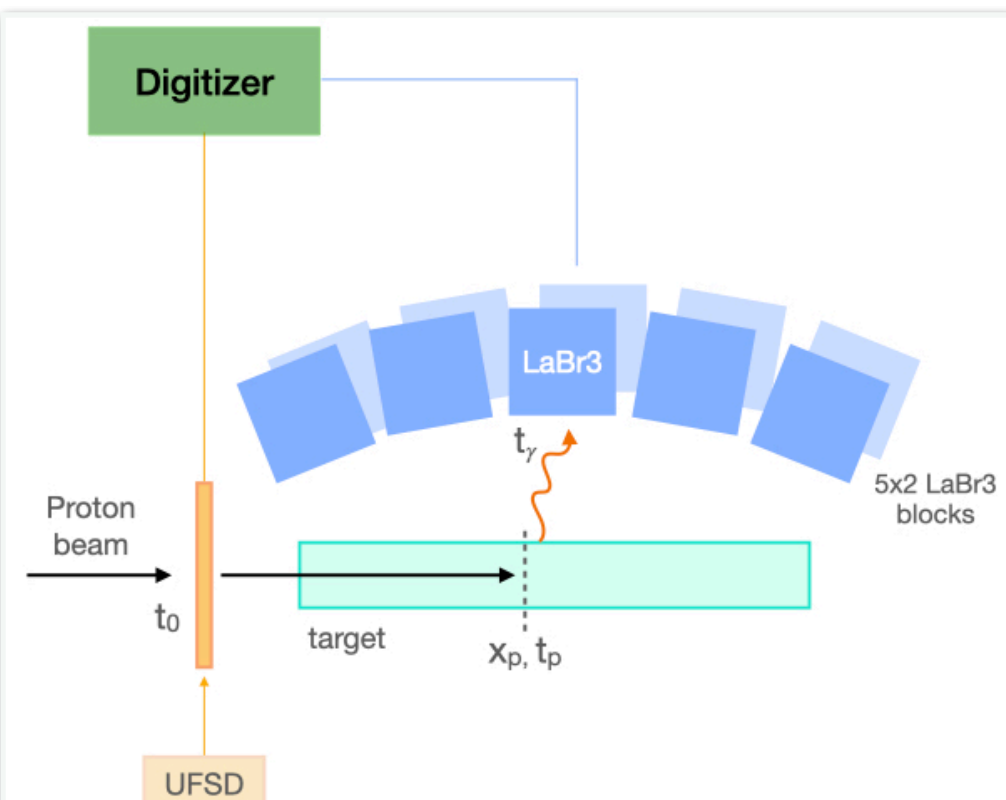


Richter et al. 2016

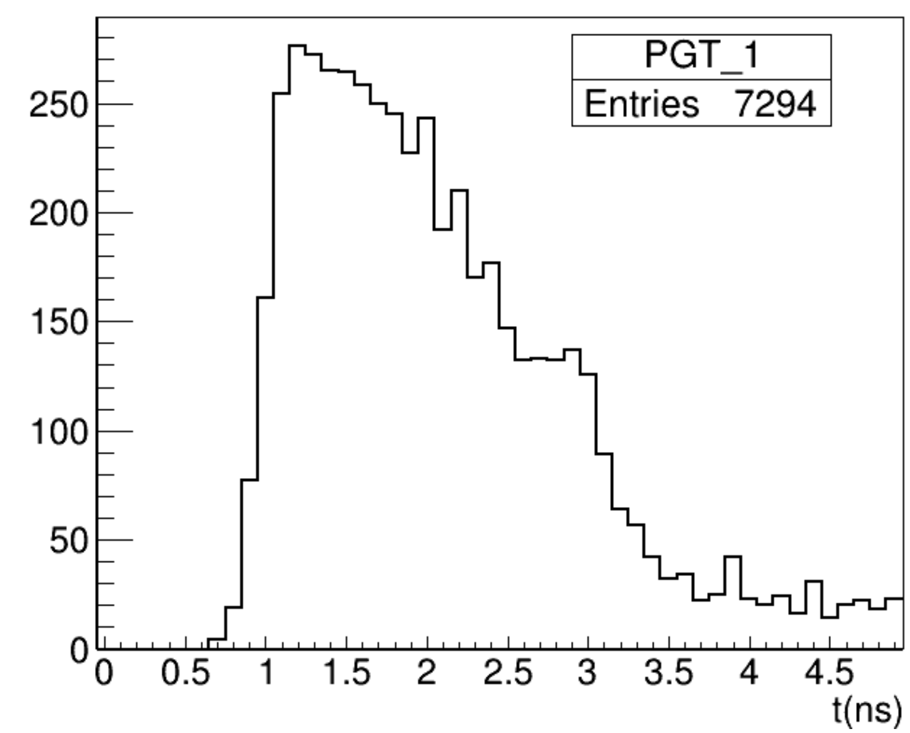
Non-collimated setup:
Prompt Gamma Timing



MERLINO PGT MULTI-DETECTOR SYSTEM



MERLINO PGT simulation



PROMPT GAMMA: RESEARCH PROSPECTS

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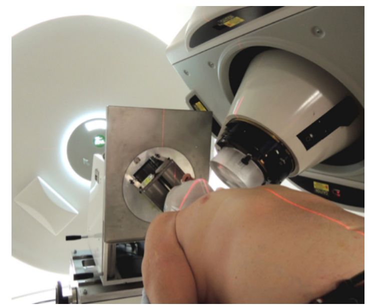
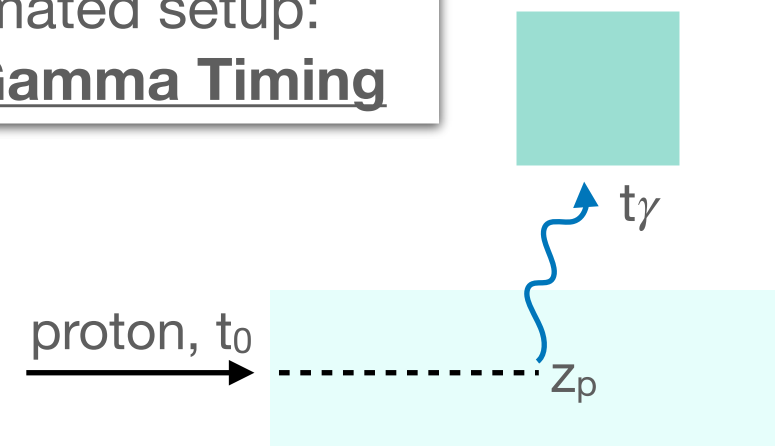


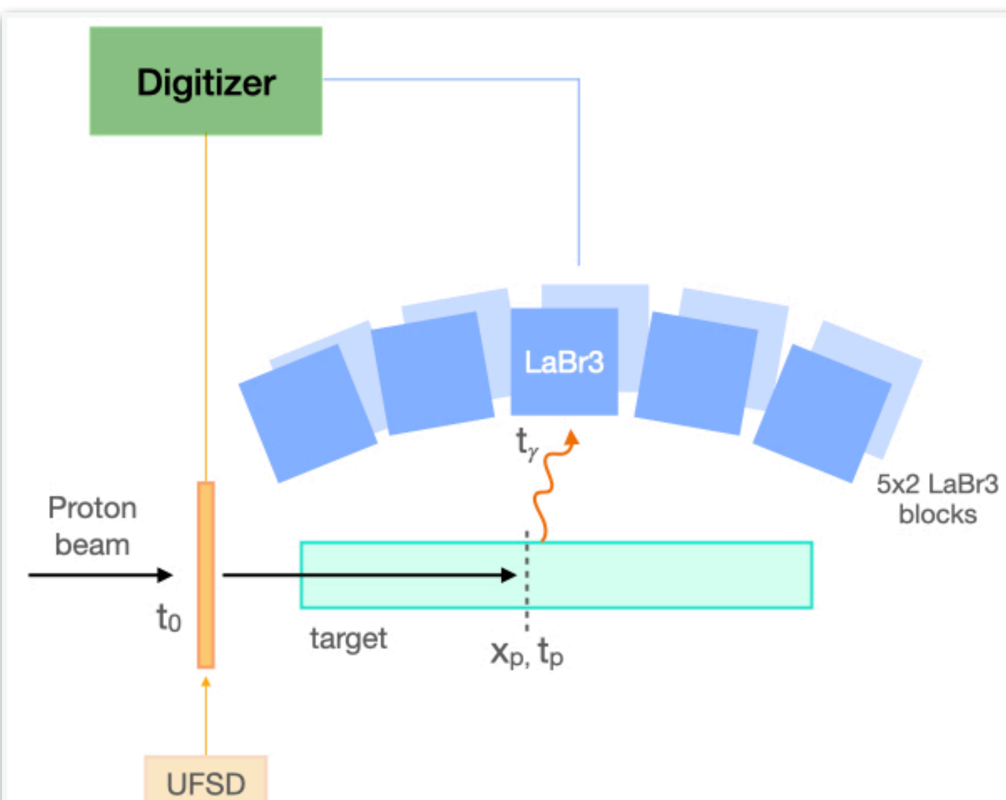
Richter et al. 2016

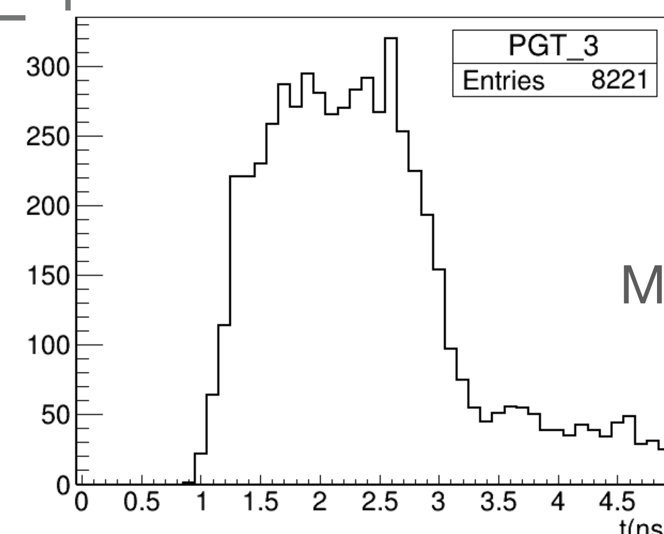
Non-collimated setup:
<u>Prompt Gamma Timing</u>



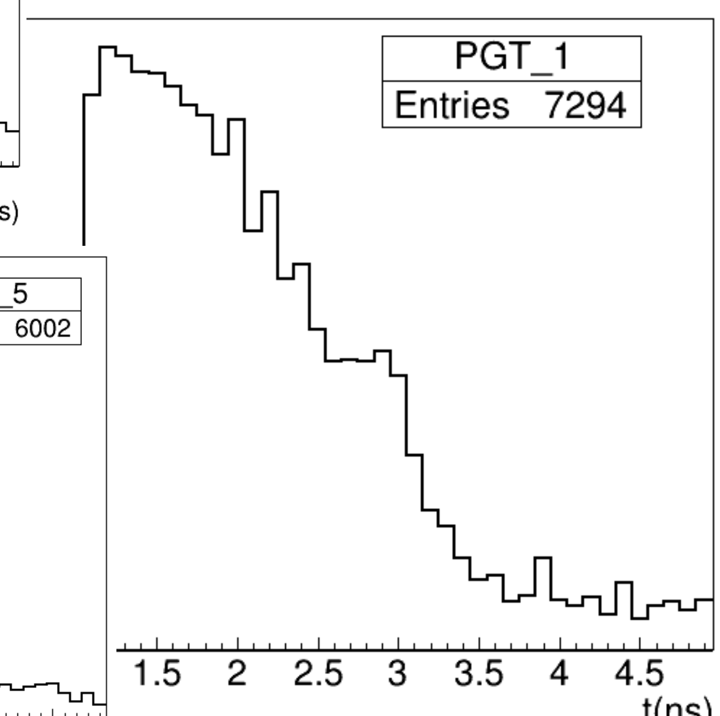
TOF
$= t_\gamma(z_p) - t_0$

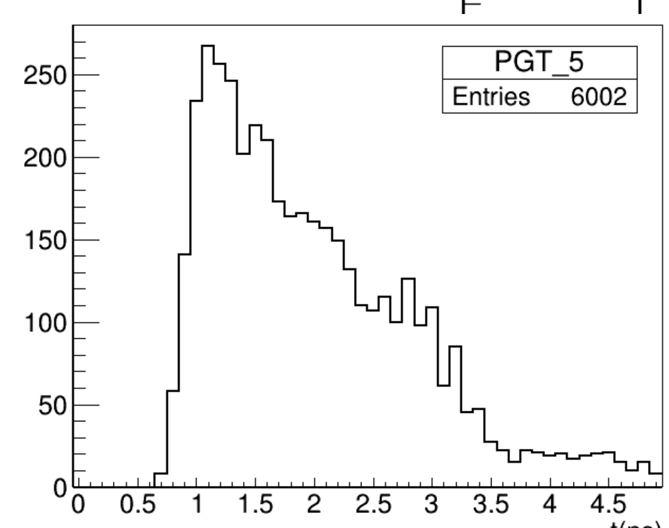
MERLINO PGT MULTI-DETECTOR SYSTEM





MERLINO PGT simulation

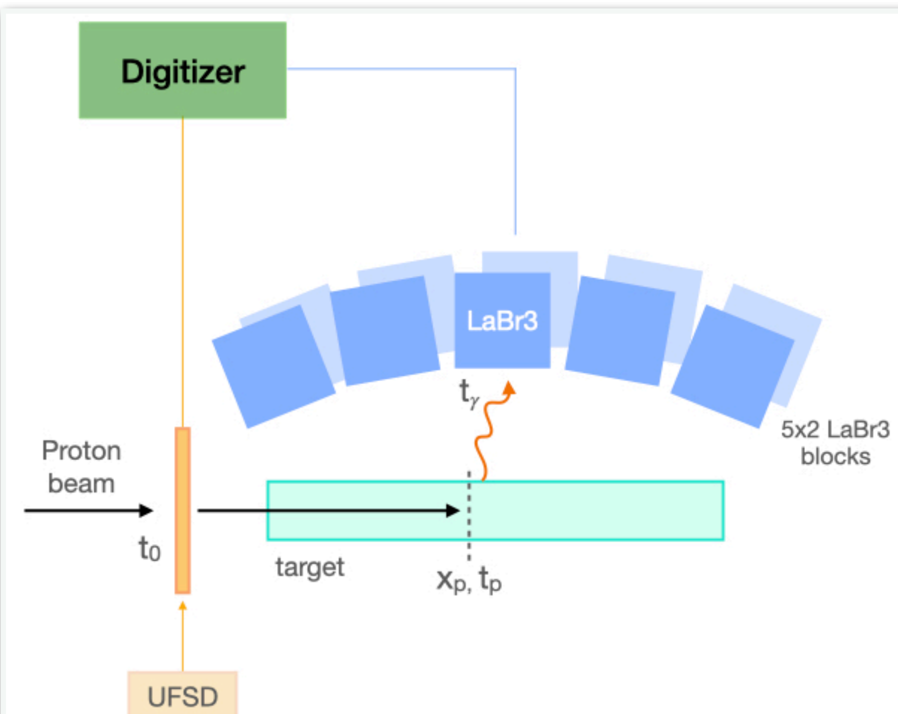




PROJECT GOAL

THE MEASUREMENT OF THE PRIMARY PARTICLE STOPPING POWER

PGT MULTI-DETECTOR SYSTEM



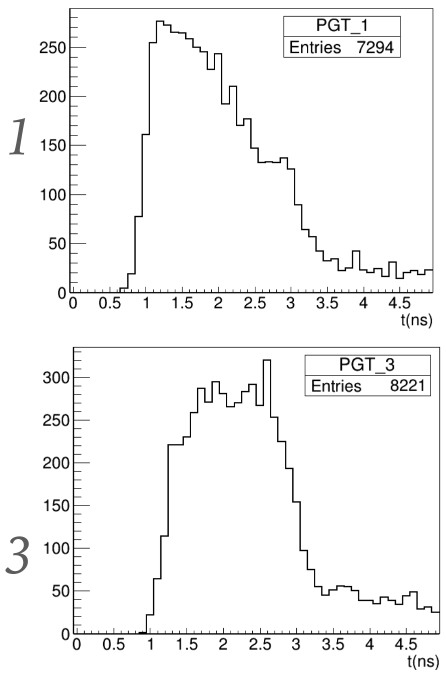
TOF SPECTRA

det 1

det 3

⋮

det N

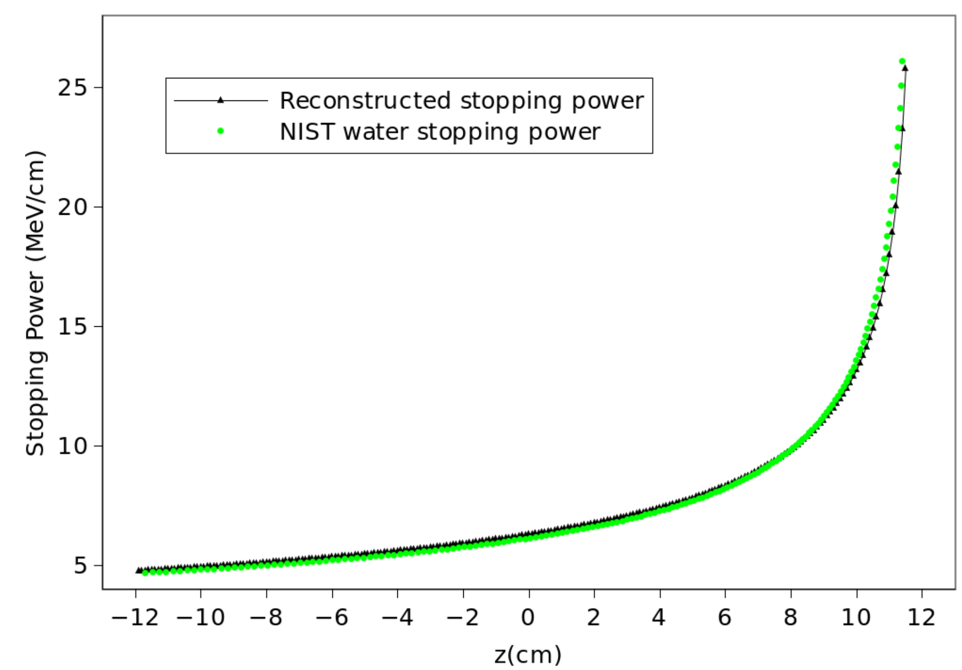


TOF $= t_\gamma(z_p) - t_0$

MINIMIZATION ALGORITHM (MLEM)

$$m_{jp}^{k+1} = \frac{m_{jp}^{k}}{S_{jp}} \sum_{i} \sum_{d} \frac{n*_{id}}{\sum_l \sum_t f_{idlt} m_{lt}^{k}} f_{idjp}$$

$z_p, t_\gamma \Rightarrow$ STOPPING POWER



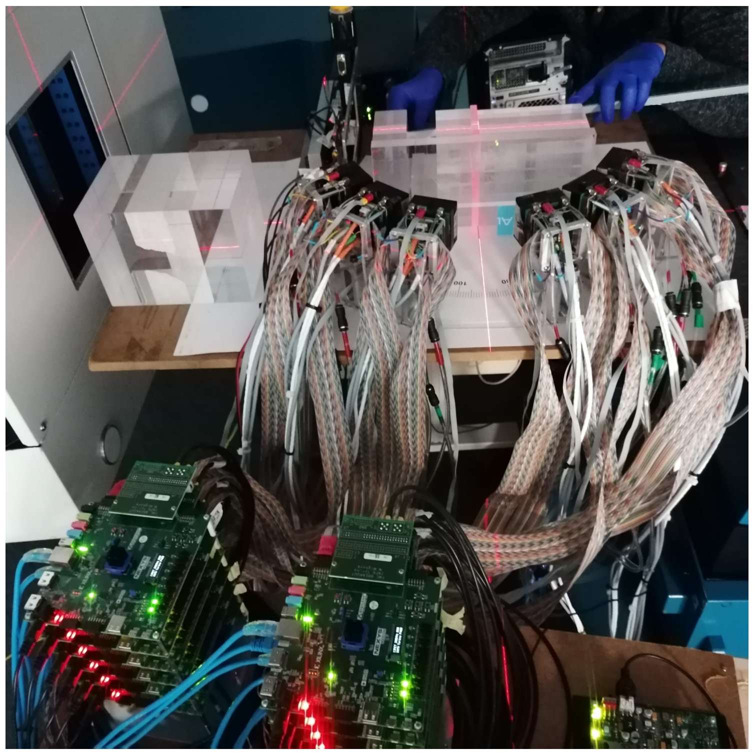
HOW?

<u>Proof-of-concept:</u>

- Detector R&D
- Innovative reconstruction algorithm (stopping power)
- Optimization with proton beams

PREVIOUS PROJECT EXPERTISE: I3PET

I3PET



The I3PET detector @ CNAO

LFS (511 keV)

Segmented detector: > 1500 ch

TOFPET2 ASIC

Xilinx Virtex FPGA

UFSD: digitizer

Asynchronous acquisition

Non-triggered acquisition + non-optimal detector = **low probability to acquire correlated events**

⇒ **Range verification**

MERLINO

$LaBr_3(Ce)$ (up to 10MeV)

Monolithic: 1 ch (10 det→10ch)

Digitizer

UFSD: digitizer

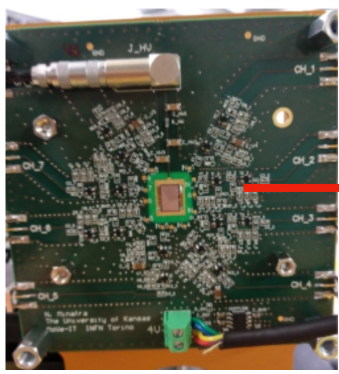
Synchronous acquisition

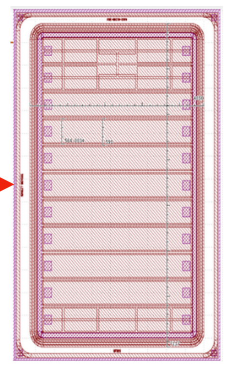
Triggered acquisition on correlated events

⇒Stopping Power

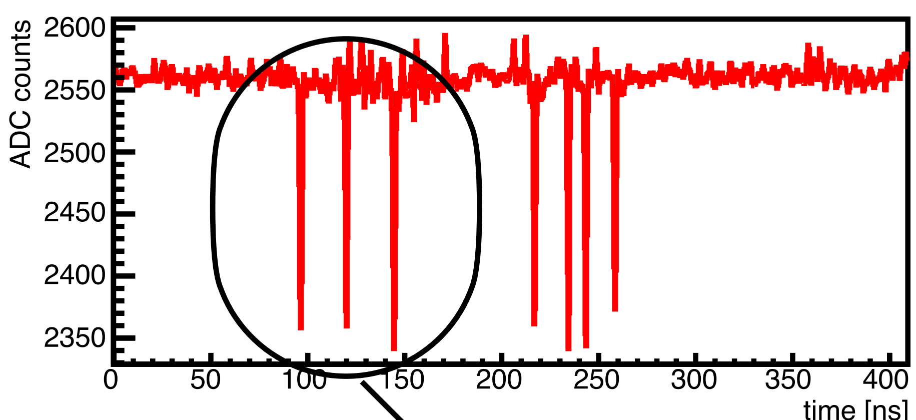
PGT MULTI-DETECTOR SYSTEM

UFSD: measure the delivery time of each primary proton
Developed by MoVeIT collaboration (CSN5)

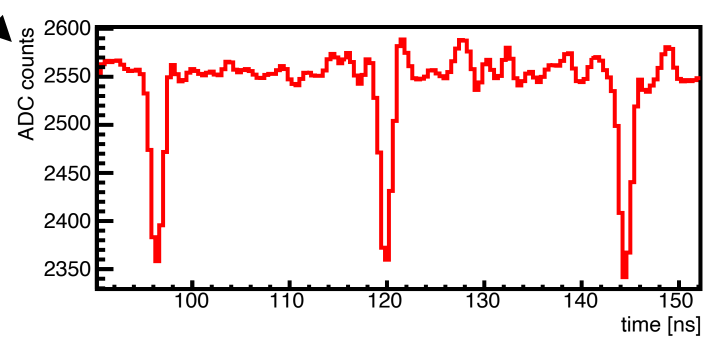




8 ch (2.2 mm²)
Time resolution ~ **10 ps**
Read by digitizer

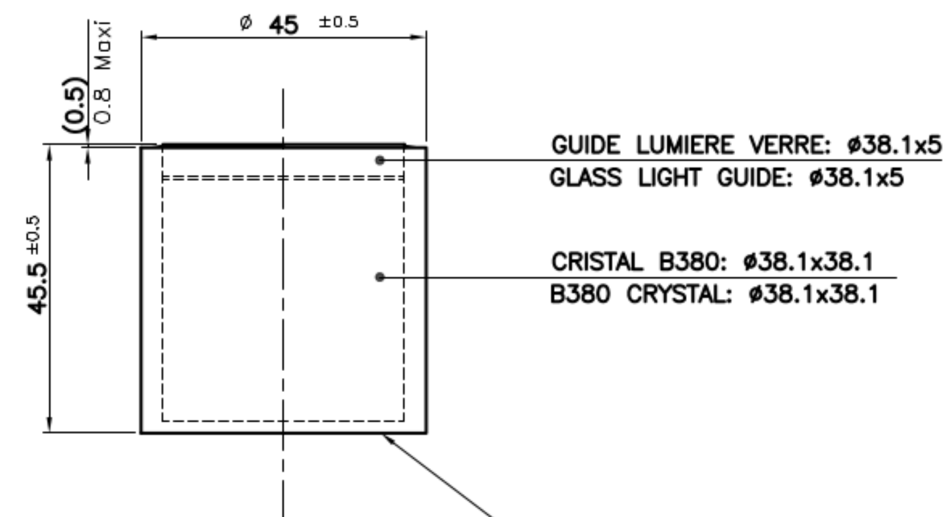


Detection efficiency up to ~27%



Beam Test @ CNAO, Jun 2021
Protons, 227MeV, ~10^5 pps

$LaBr_3(Ce)$: measure the arrival time of the secondary prompt photons



Scintillating crystals, 16 ns decay
Dimension: ⌀38.1 mm, h38.1 mm
Energy resolution 1.3% @ 6.1 MeV
Expected time resolution: **100 ps σ**

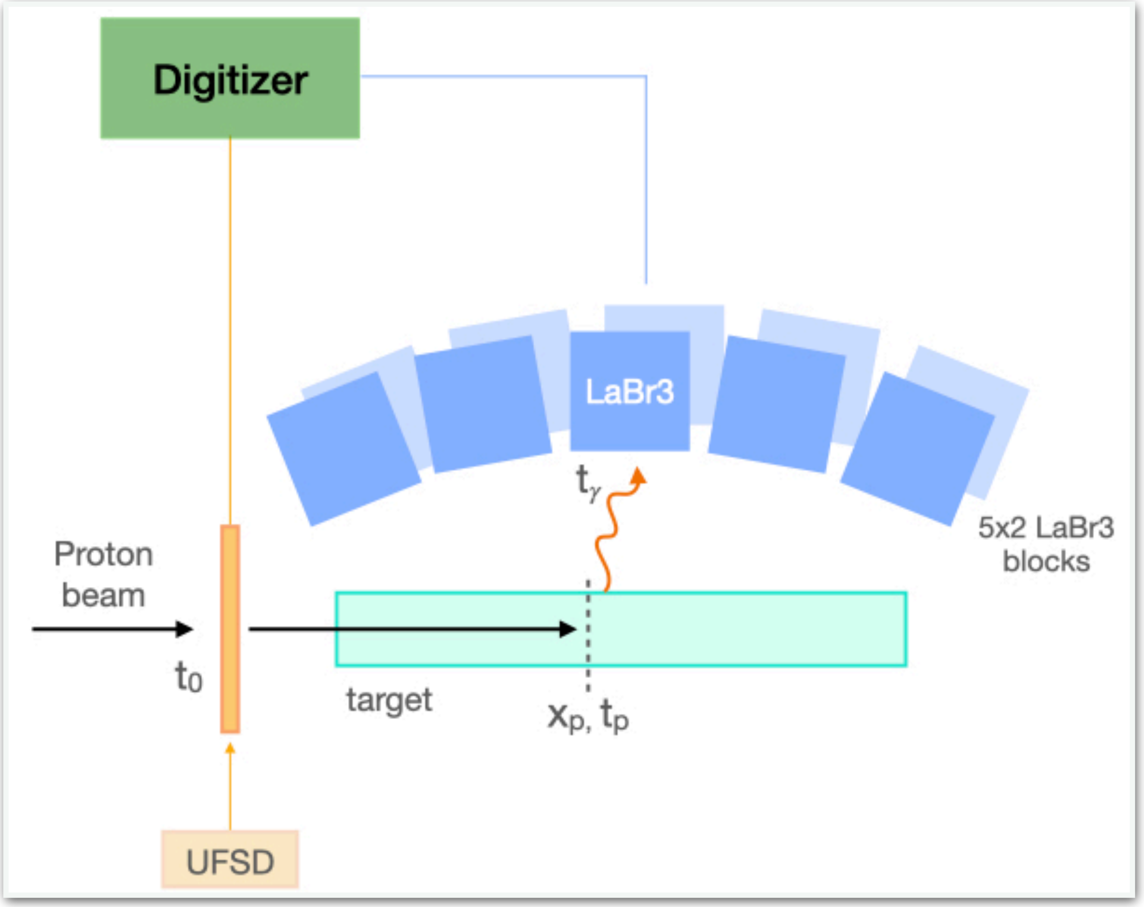
10 crystals, 10 ch
Read by digitizer

10x10x20 cm³ FOV

HOW TO?

Low fraction of valid events	Optimized trigger
PGT measurement optimization	Detector R&D ($LaBr_3(Ce)$)
Full exploitation of the PGT information	Dedicated Reconstruction Algorithm

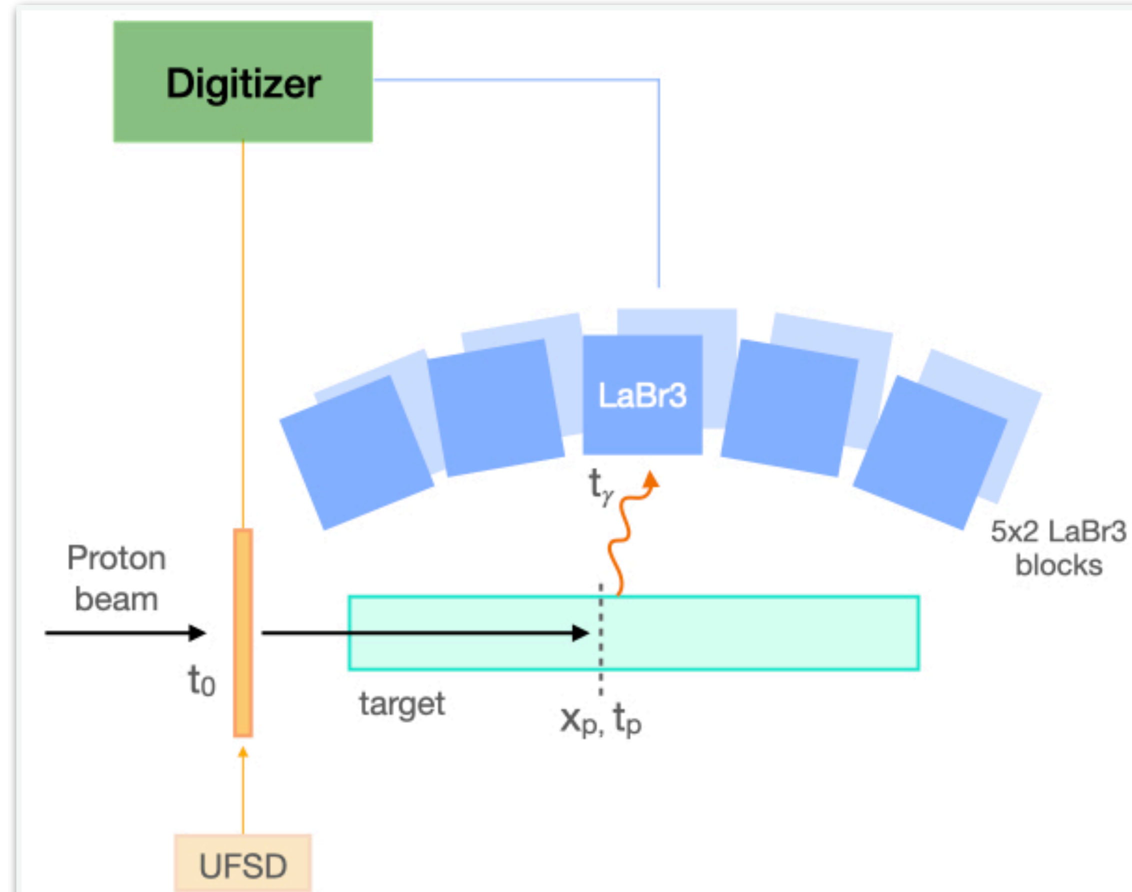
CAEN V1742 32ch Digitizer



$LaBr_3(Ce)$ and UFSD connected to the same digitizer
Triggered acquisition ($LaBr_3(Ce)$ start acquisition)

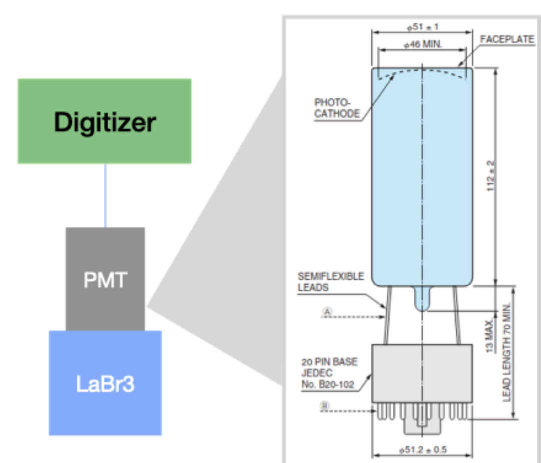
HOW TO?

Low fraction of valid events	Optimized trigger
PGT measurement optimization	Detector R&D ($LaBr_3(Ce)$)
Full exploitation of the PGT information	Dedicated Reconstruction Algorithm

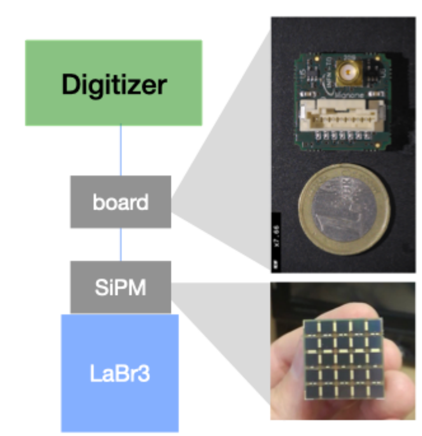


R&D to reach clinical rates

Readout 1: PMT

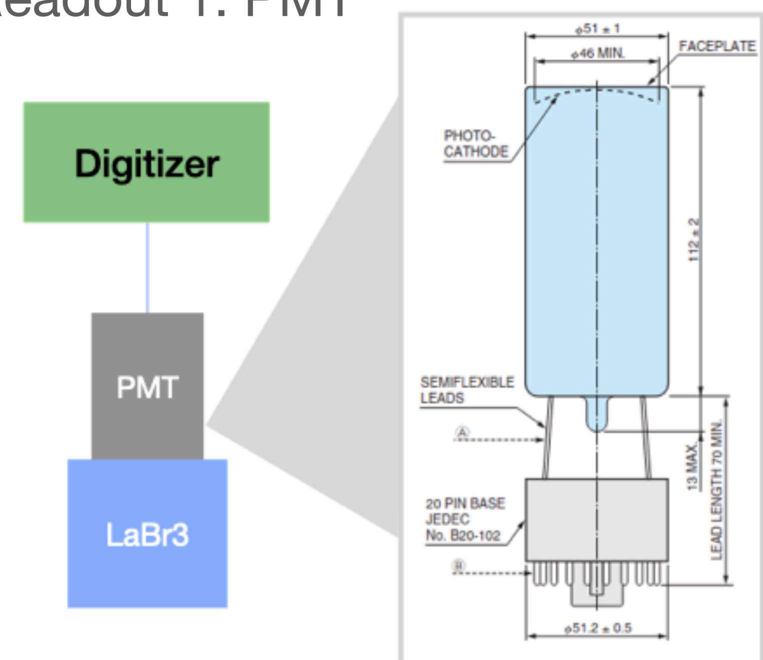


Readout 2: SiPMs



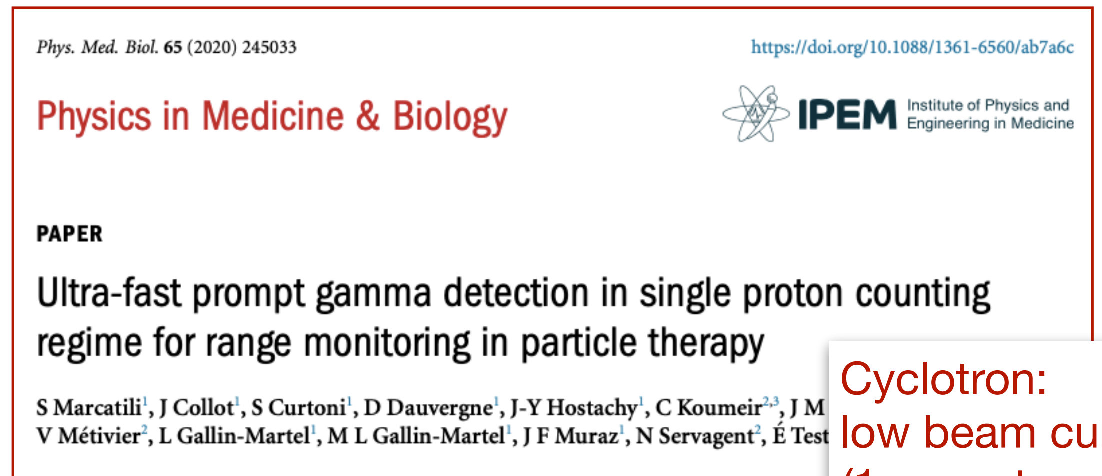
DETECTOR R&D

Readout 1: PMT



Hamamatsu R13089-11 PMT

Challenges: detector load leaps (beam RF) can affect PMT gain, electronic transit time (timing)



Phys. Med. Biol. **65** (2020) 245033 https://doi.org/10.1088/1361-6560/ab7a6c

Physics in Medicine & Biology

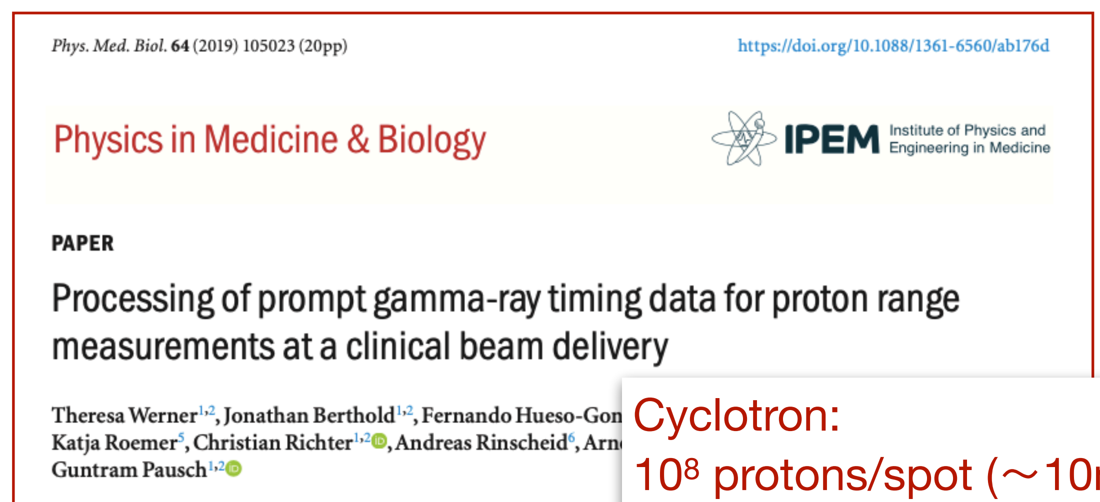
IPEM Institute of Physics and Engineering in Medicine

PAPER

Ultra-fast prompt gamma detection in single proton counting regime for range monitoring in particle therapy

S Marcatili[1], J Collot[1], S Curtoni[1], D Dauvergne[1], J-Y Hostachy[1], C Koumeir[2,3], J M
V Métivier[2], L Gallin-Martel[1], M L Gallin-Martel[1], J F Muraz[1], N Servagent[2], É Test

Cyclotron:
low beam current, 100 ps σ
(1 ns σ at nominal beam intensities)



Phys. Med. Biol. **64** (2019) 105023 (20pp) https://doi.org/10.1088/1361-6560/ab176d

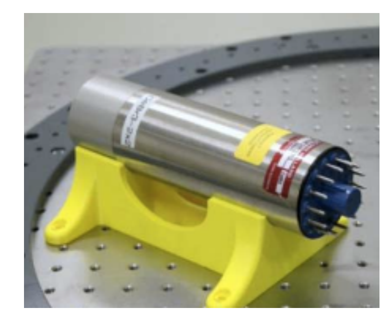
Physics in Medicine & Biology

IPEM Institute of Physics and Engineering in Medicine

PAPER

Processing of prompt gamma-ray timing data for proton range measurements at a clinical beam delivery

Theresa Werner[1,2], Jonathan Berthold[1,2], Fernando Hueso-Gon
Katja Roemer[5], Christian Richter[1,2], Andreas Rinscheid[6], Arn
Guntram Pausch[1,2]



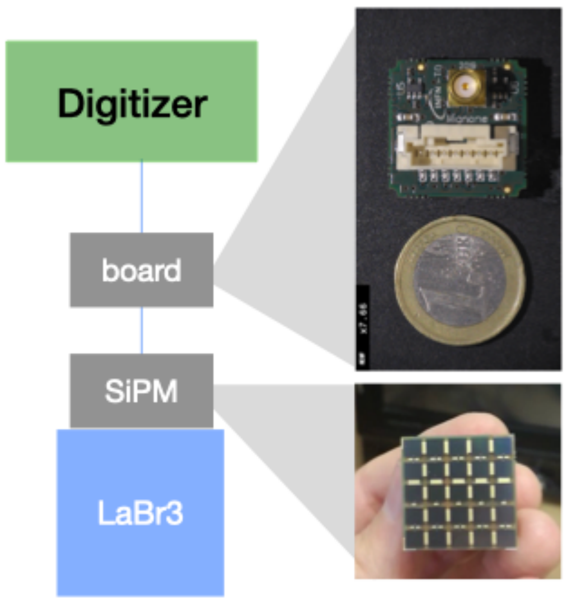
Pausch et al TNS 2016

Cyclotron:
10^8 protons/spot (∼10ms)
Short irradiation times (70ms)
250 ps σ

Clinical rates: $10^8/10^9$ pps (CNAO: synchrotron; TIFPA: cyclotron)

DETECTOR R&D

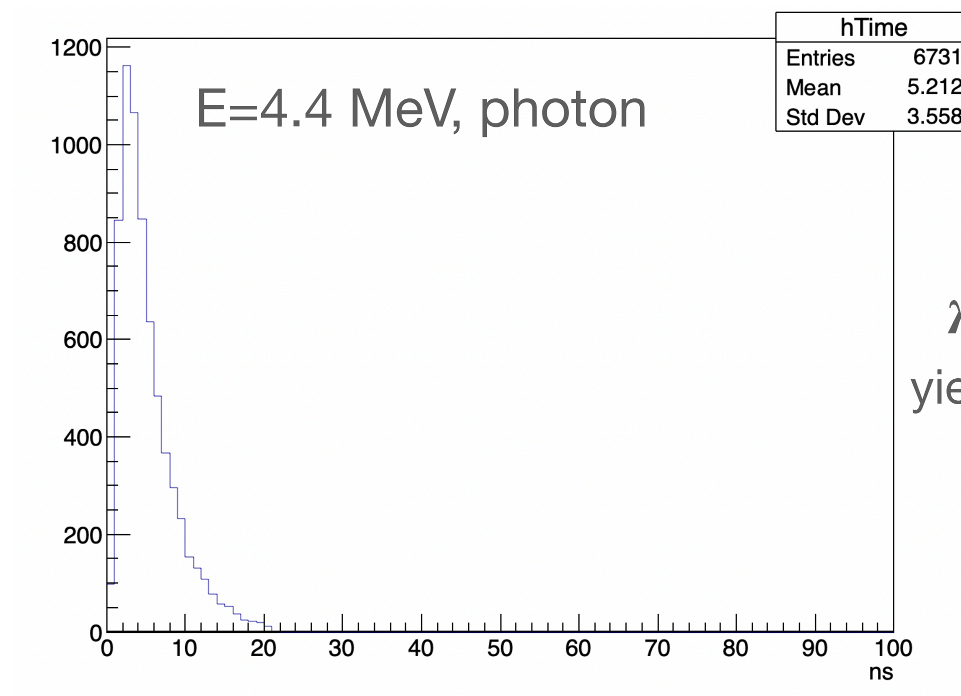
Readout 2: SiPMs



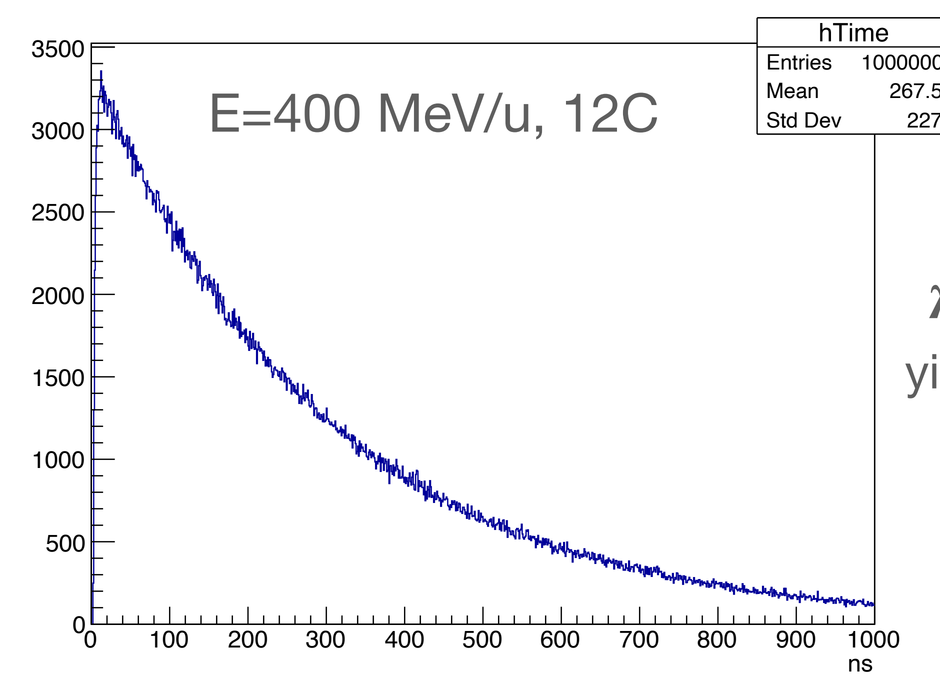
FOOT (CSN3)
FE board and
SiPM tile

SiPM by FBK
→10^6 microcells per SiPM

MC simulatons (FLUKA tool)



LaBr$_3$(Ce)
λ_{MAX}=380nm
yield: 63 ph/keV
τ=16ns



BGO
λ_{MAX}=480nm
yield: 8 ph/keV
τ=300ns

→ experimentally validated

Hasn't been done yet

Challenges:
- saturation (1keV → 63 opt photons), energy resolution deterioration
- sensitivity to temperature

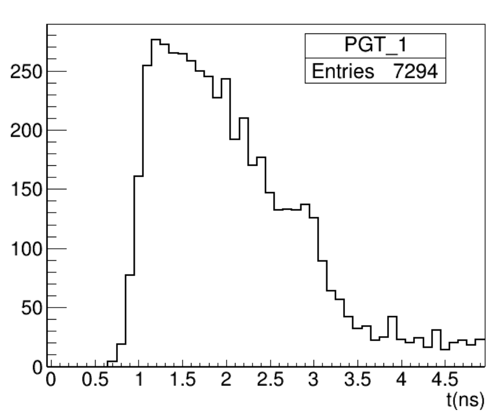
Time resolution?
BGO: ~600 ps σ (cosmic rays)

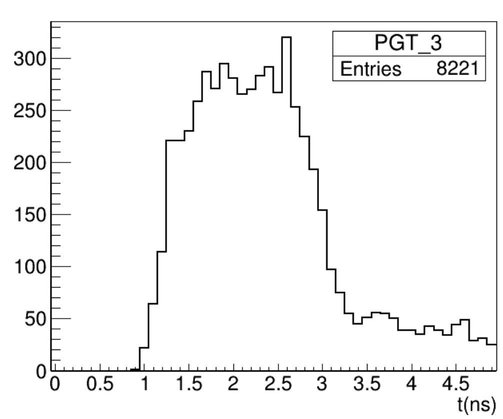
HOW TO?

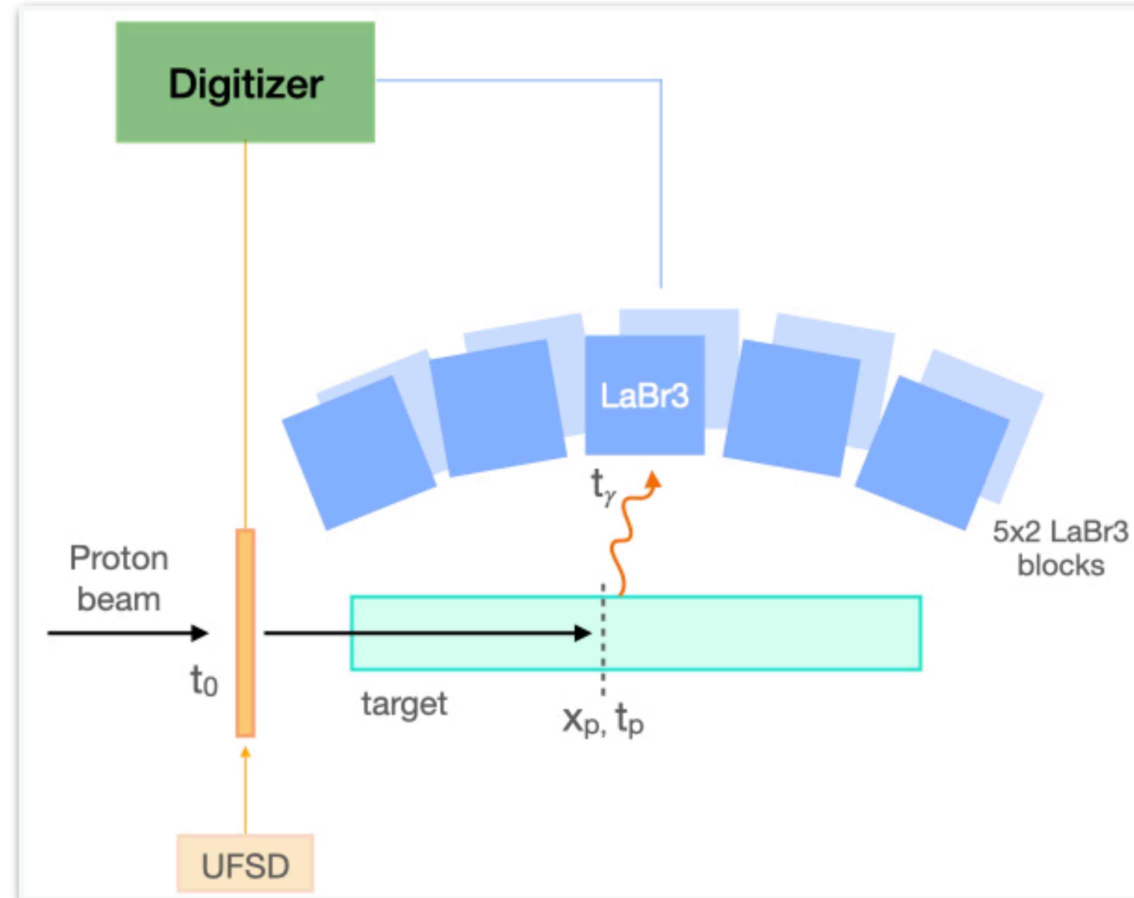
Low fraction of valid events	Optimized trigger
PGT measurement optimization	Detector R&D ($LaBr_3(Ce)$)
Full exploitation of the PGT information	Dedicated Reconstruction Algorithm

10 crystals

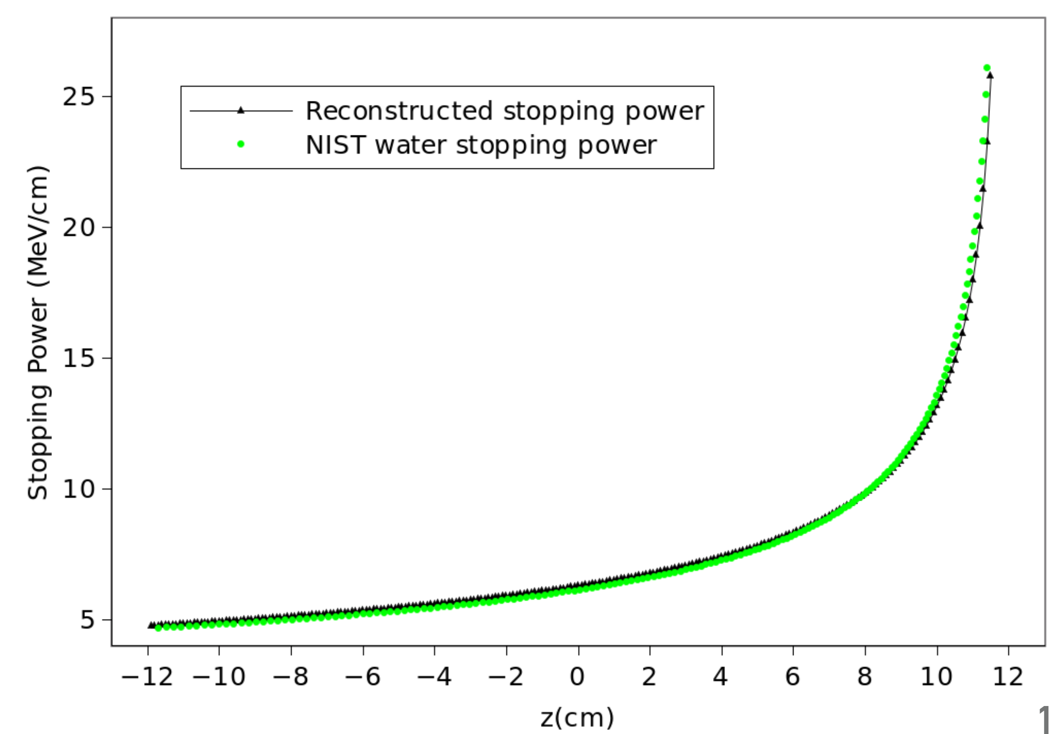
Higher statistics but also diverse information







Innovation: use of the PGT information to reconstruct the stopping power

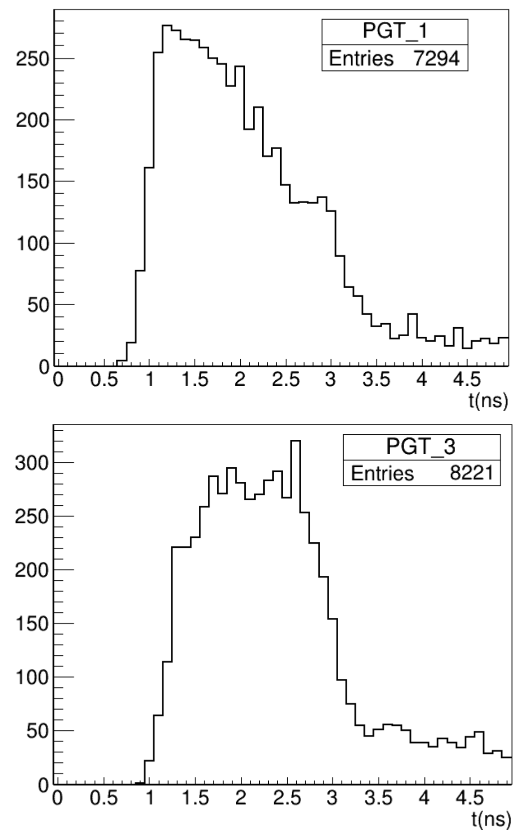


PRELIMINARY WORK: RECONSTRUCTION FORMULATION

TOF SPECTRA

det 1

det 3



⋮

det N

MINIMIZATION ALGORITHM (MLEM)

$$m_{jp}^{k+1} = \frac{m_{jp}^{k}}{S_{jp}} \sum_{i} \sum_{d} \frac{n*_{id}}{\sum_l \sum_t f_{idlt} m_{lt}^{k}} f_{idjp}$$

data

prompt photon

sensitivity

SM

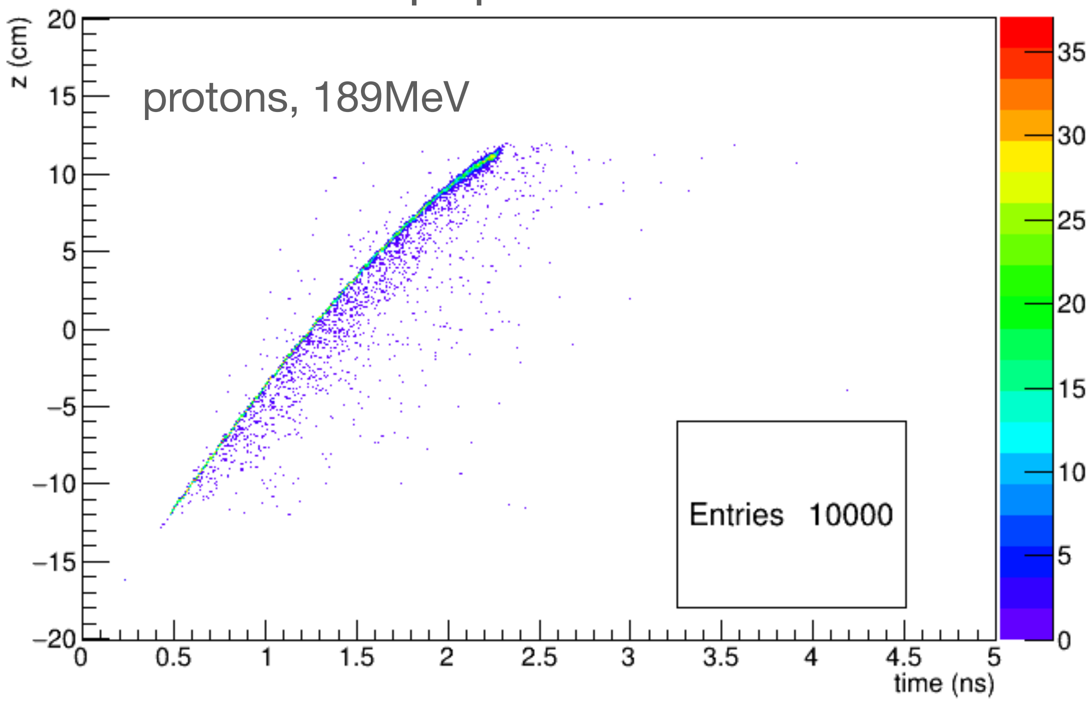
p: time bin (emission)
j: space bin (emission)
i: time bin (detection)
d: detector

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

STOPPING POWER

PRELIMINARY WORK: MC TRUTH

Prompt photon emission

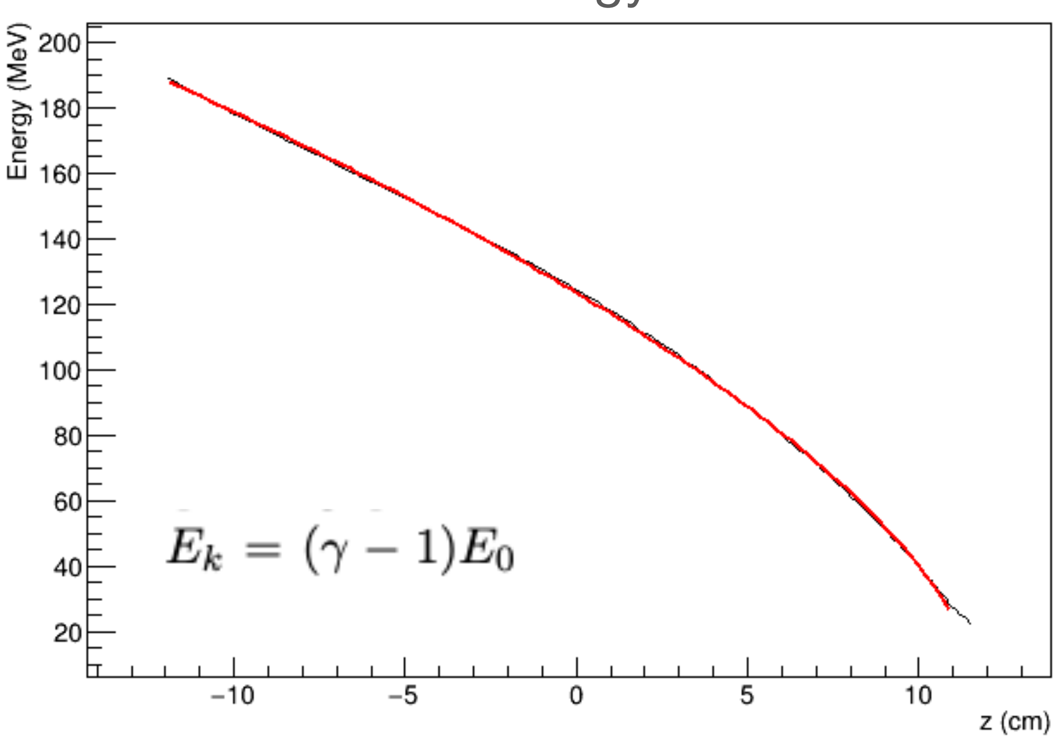


Proposal submitted to CSN5
Non-physical description:
polynomial fit
z,t → v(z) → $E_k(z)$ → $dE_k(z)/dz$

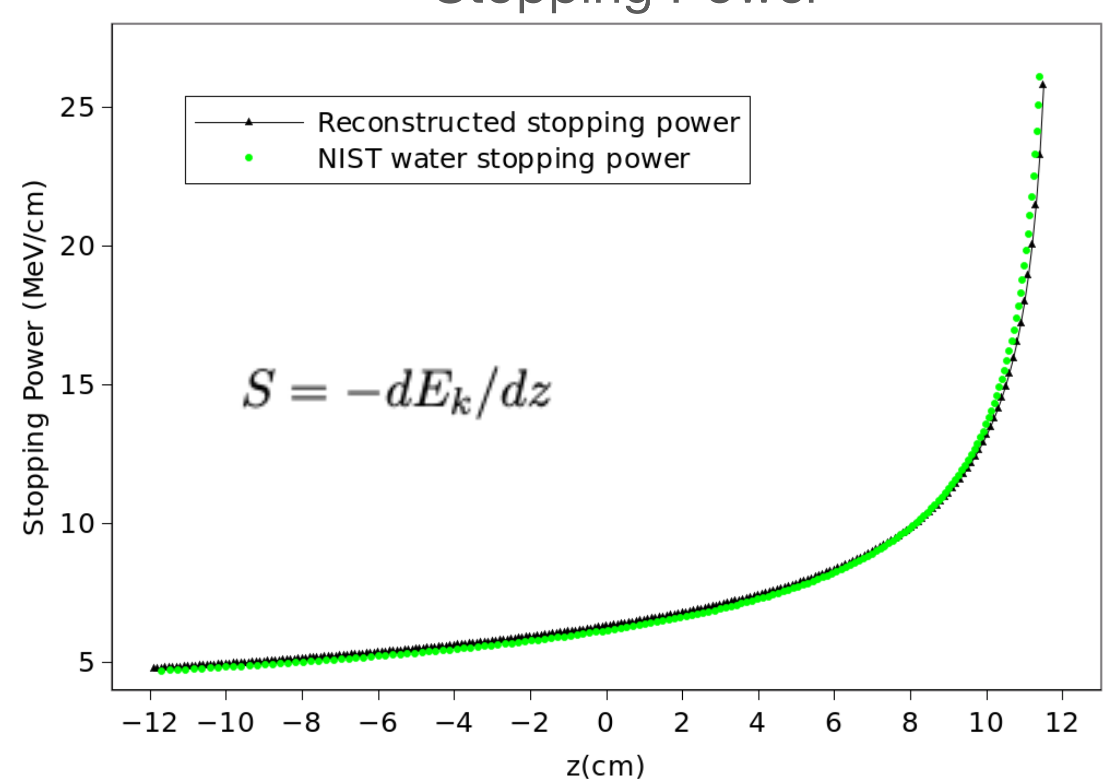
Mean absolute difference: 0.05 [MeV/cm] ⇒0.4%

PCC=0.99

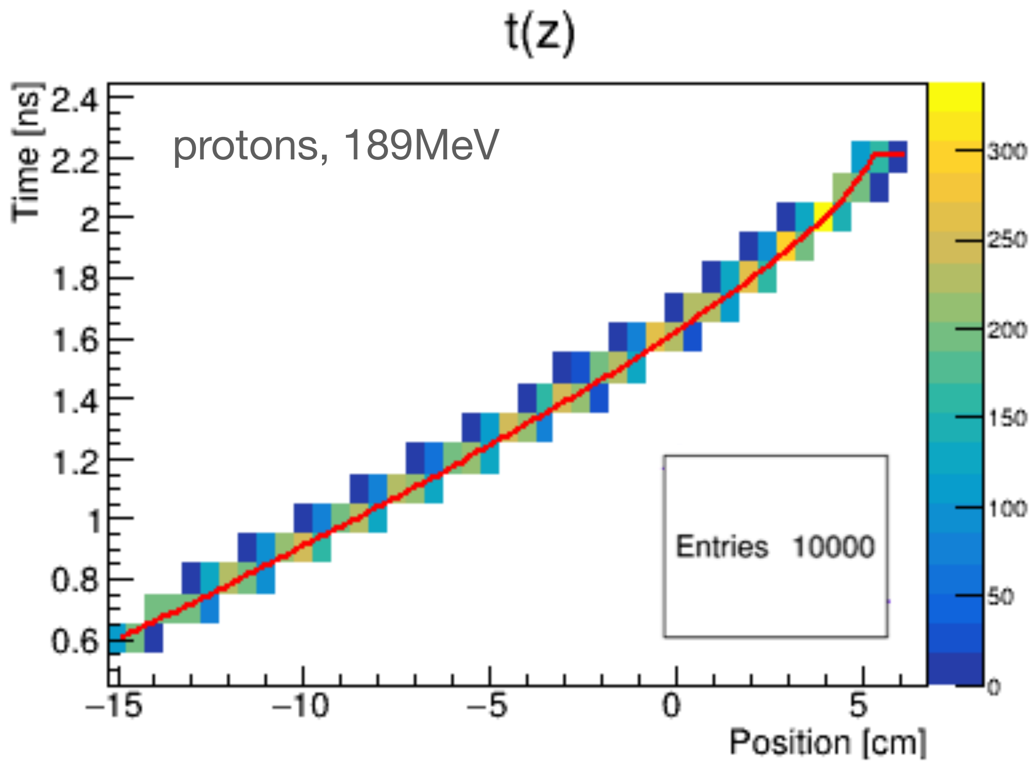
Energy



Stopping Power



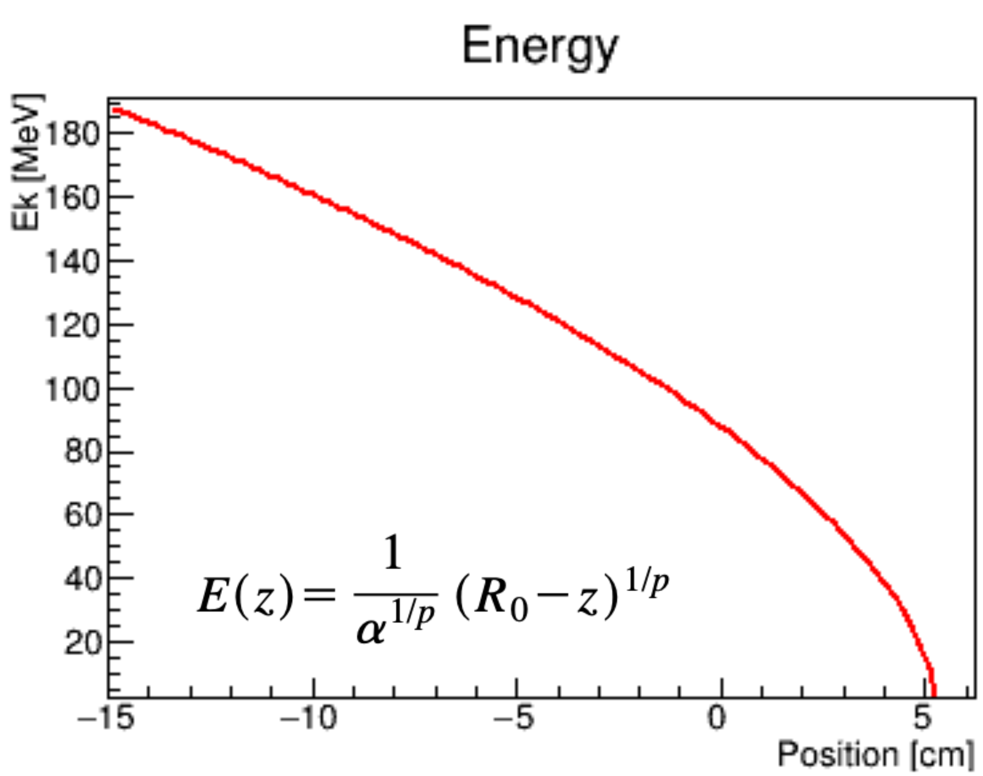
PRELIMINARY WORK: MC TRUTH

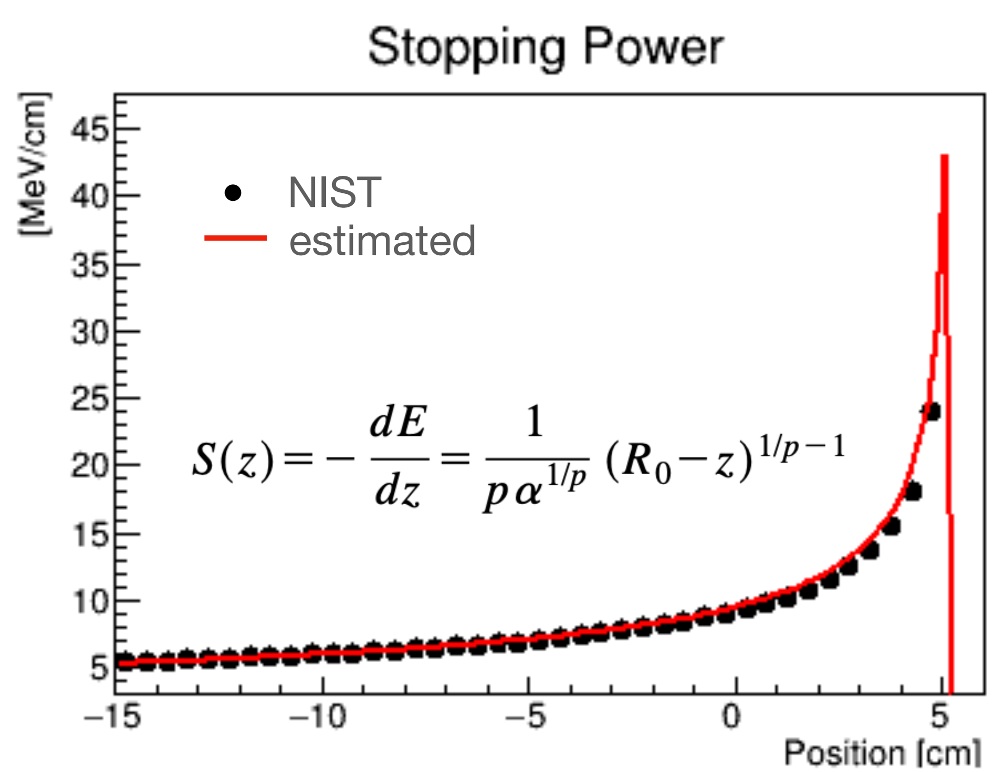


$$v(E)=\frac{dz}{dt}=c\sqrt{1-\left(\frac{m_0c^2}{E+m_0c^2}\right)^2}\ , \qquad t_B(z)=\int_0^{z-z_0}\frac{dz'}{v(E(z'))}$$

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

PHYSICAL DESCRIPTION
Based on Bortfeld formulation

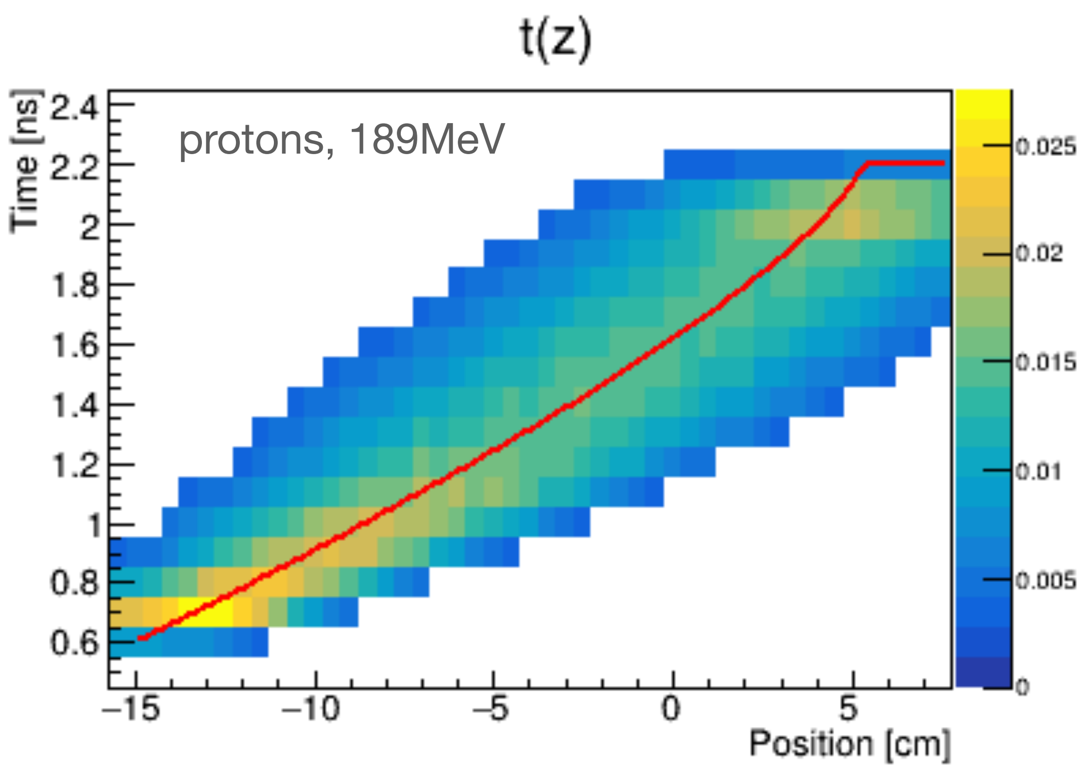


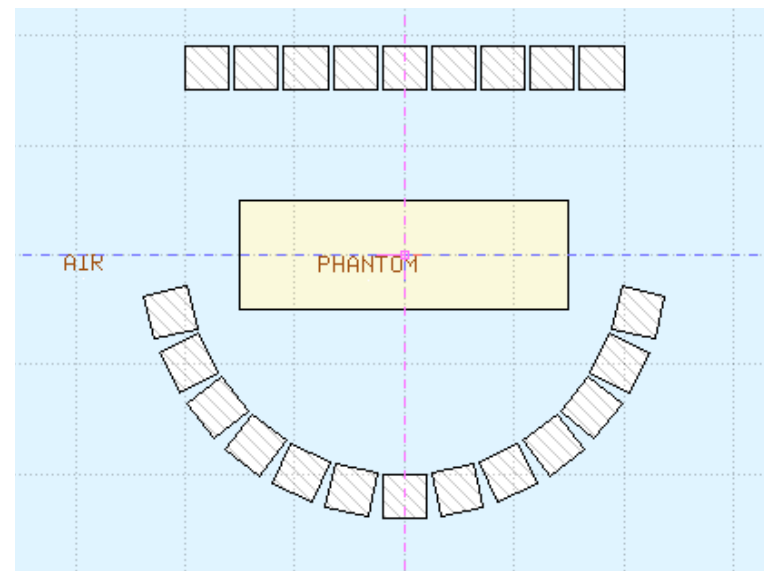


Mean absolute difference: 0.4 [MeV/cm] ⇒2.8%

PCC=0.96

PRELIMINARY WORK: RECONSTRUCTION





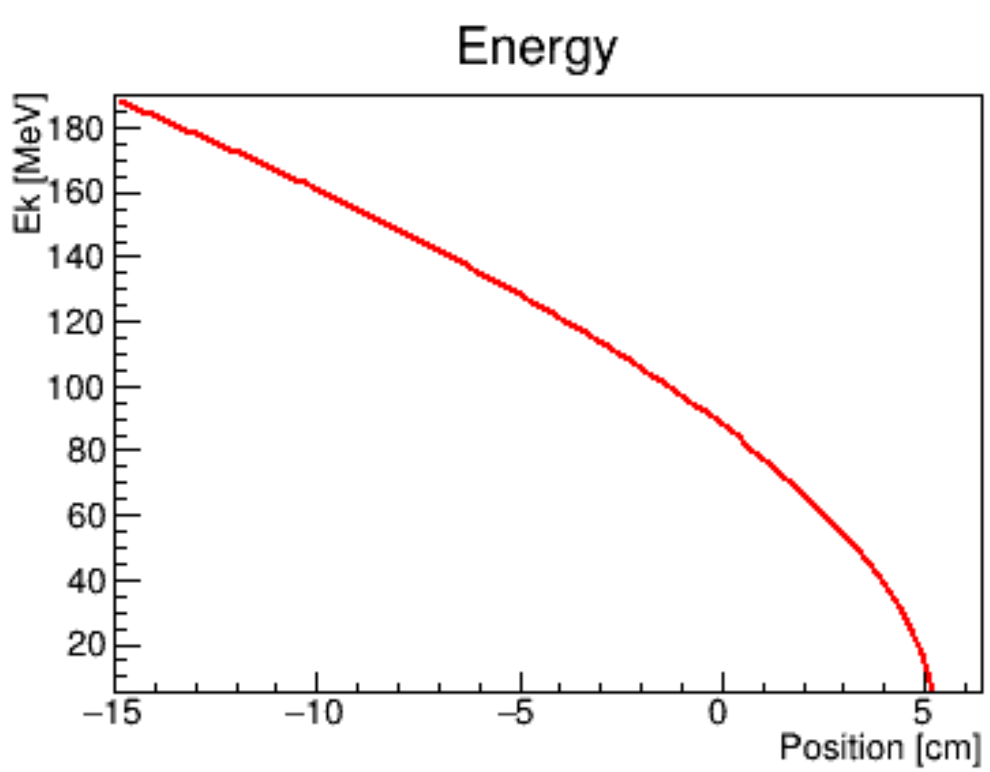
10^8 primary particles

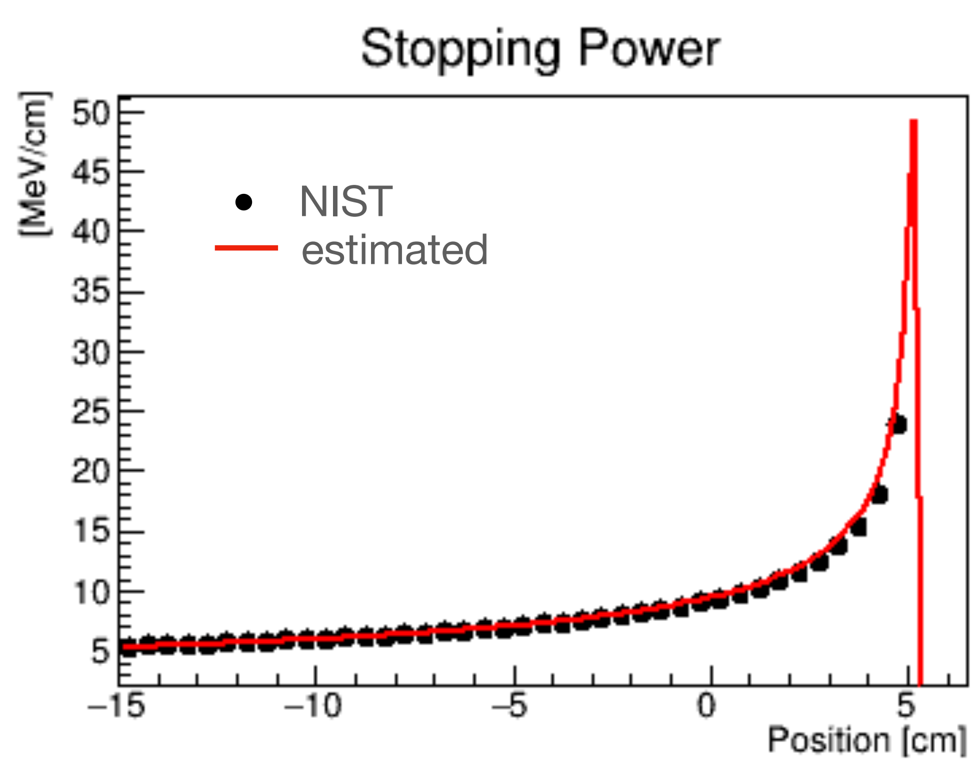
10^7 produced photons in 4π

$\sim 10^4$ events per detector

Time resolution=100 ps σ

110 detectors (<u>clinical scenario</u>)

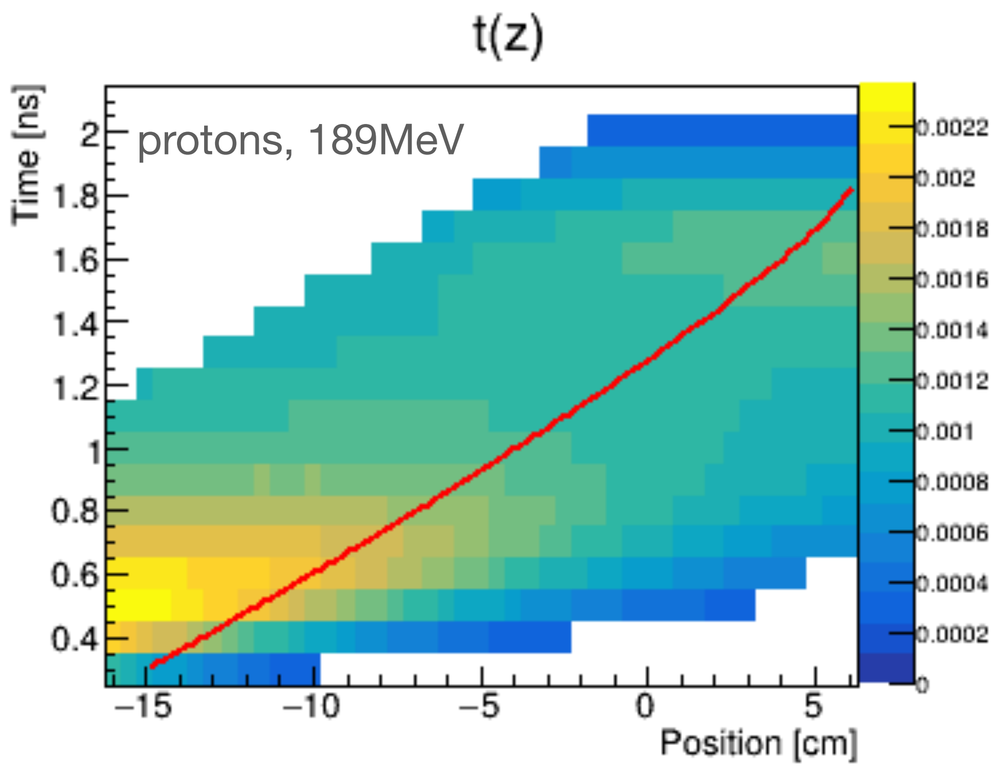


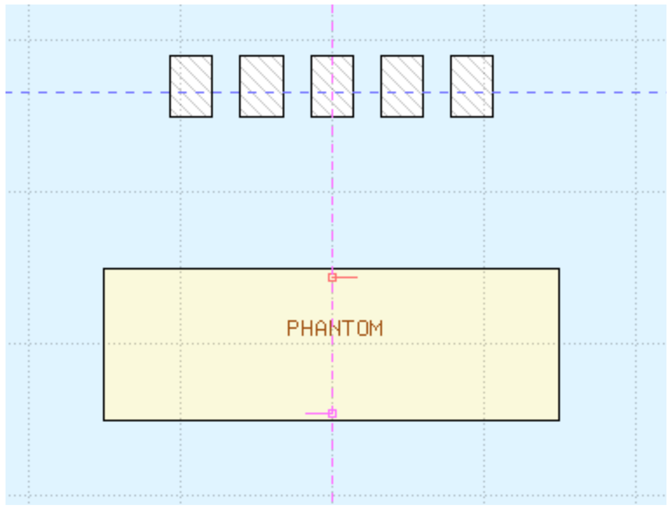


Mean absolute difference: 0.4 [MeV/cm] ⇒2.8%

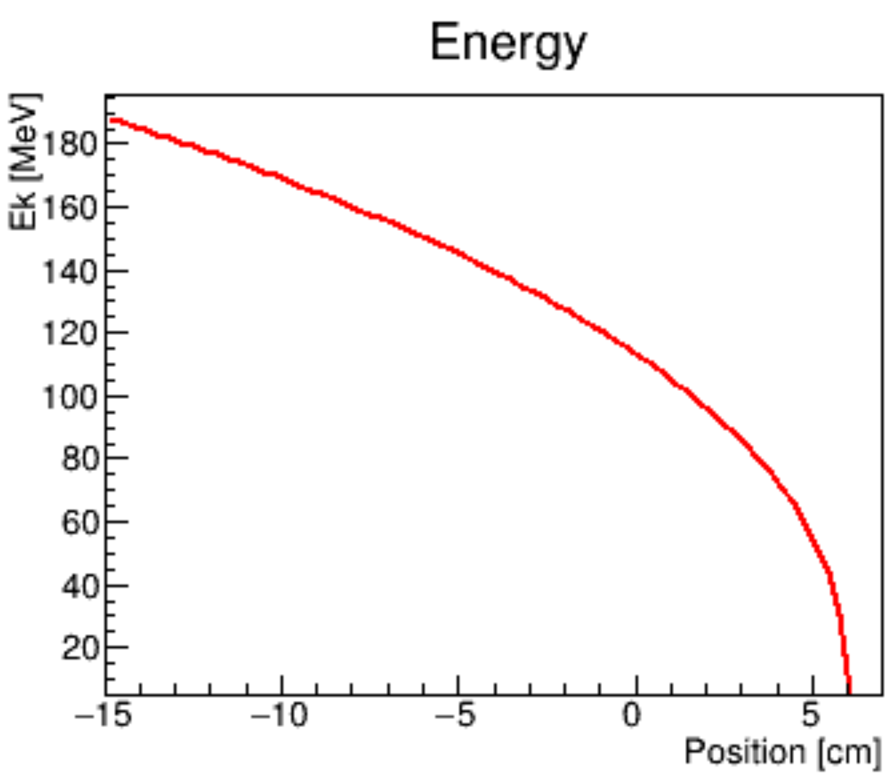
PCC=0.96

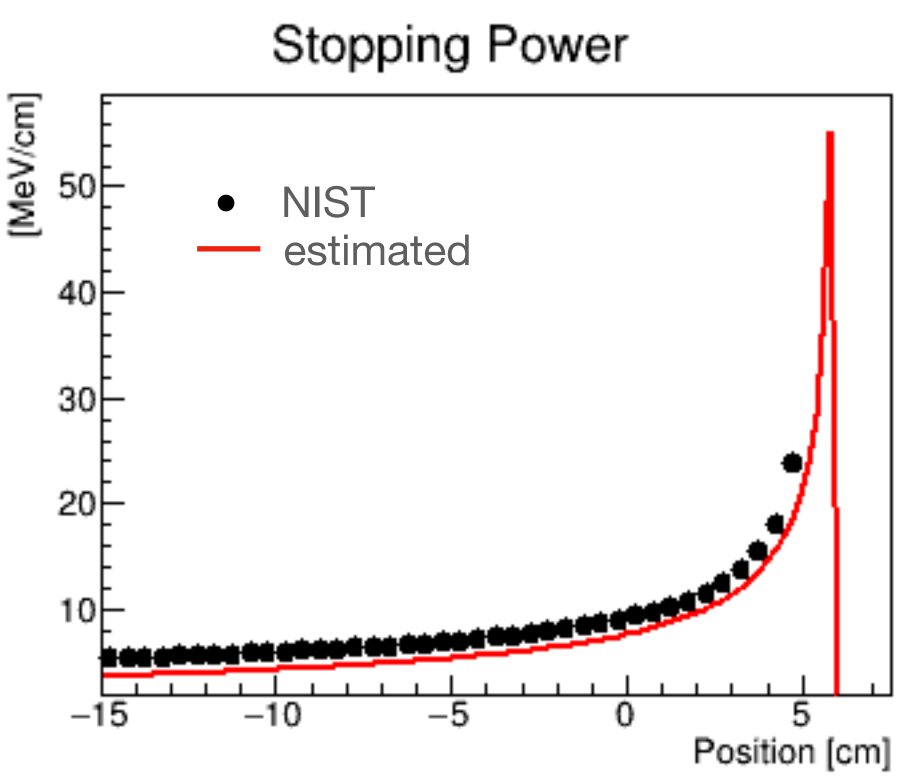
PRELIMINARY WORK: RECONSTRUCTION





10^8 primary particles
10^7 produced photons in 4π
$\sim 10^4$ events per detector
Time resolution=100 ps σ
10 detectors (proof of concept)

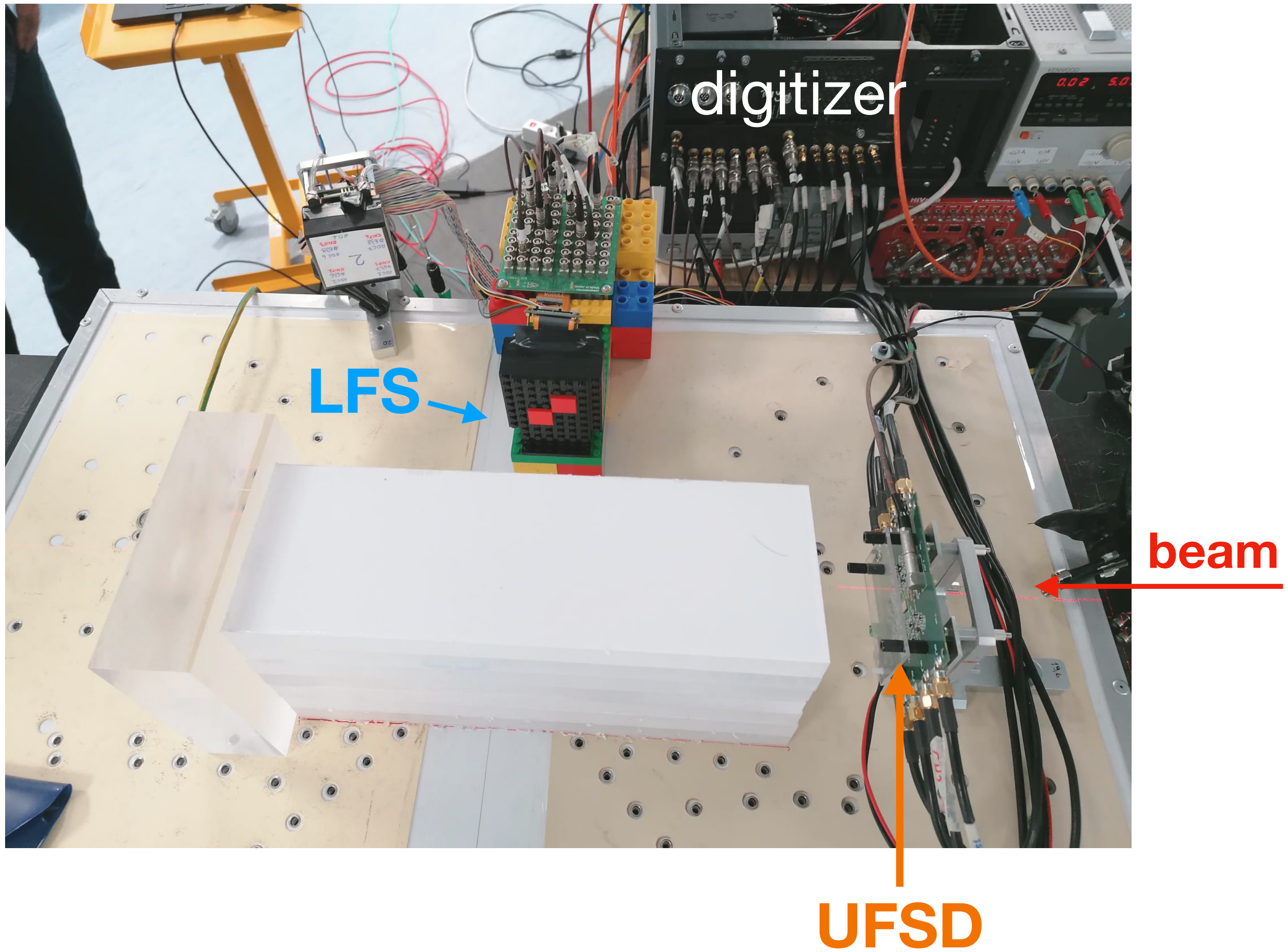




Mean absolute difference: 1.7 [MeV/cm] ⇒22%

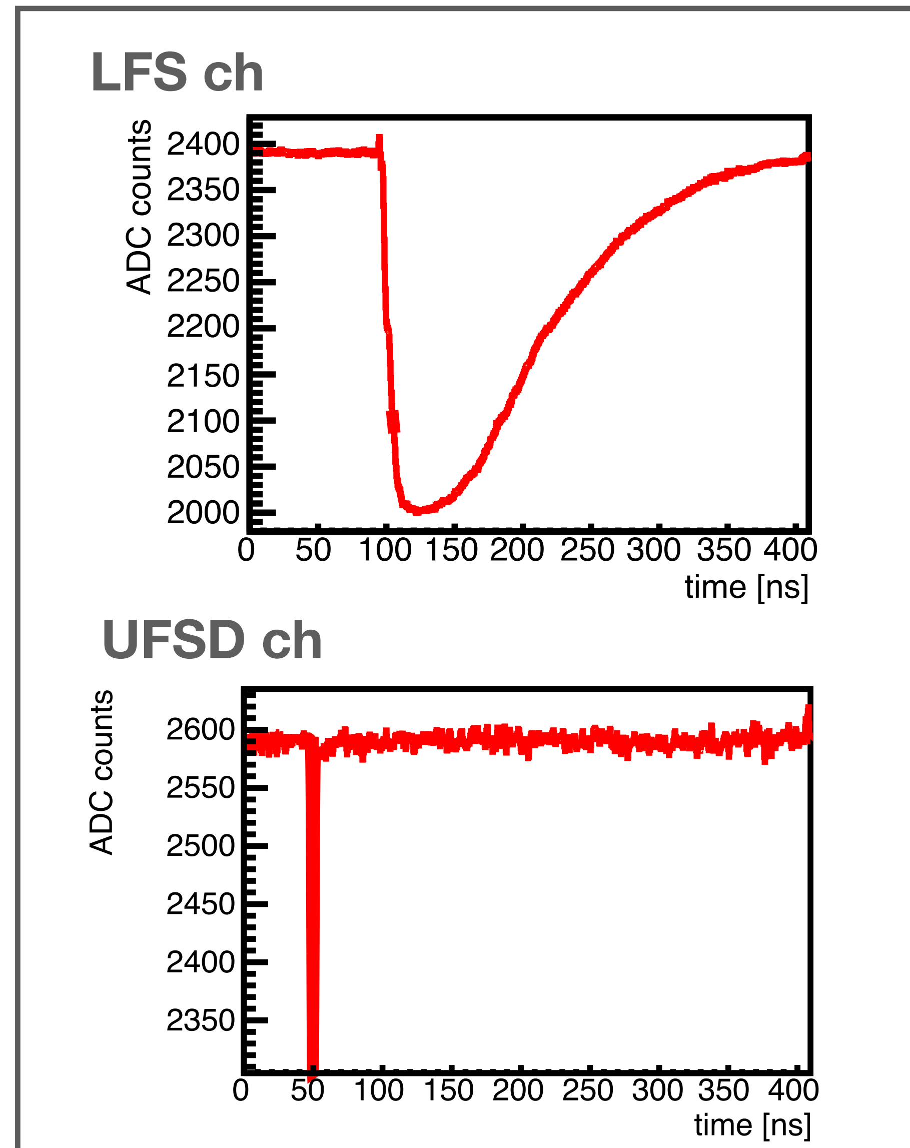
PCC=0.95

PRELIMINARY WORK: PGT EXPERIMENTAL DATA

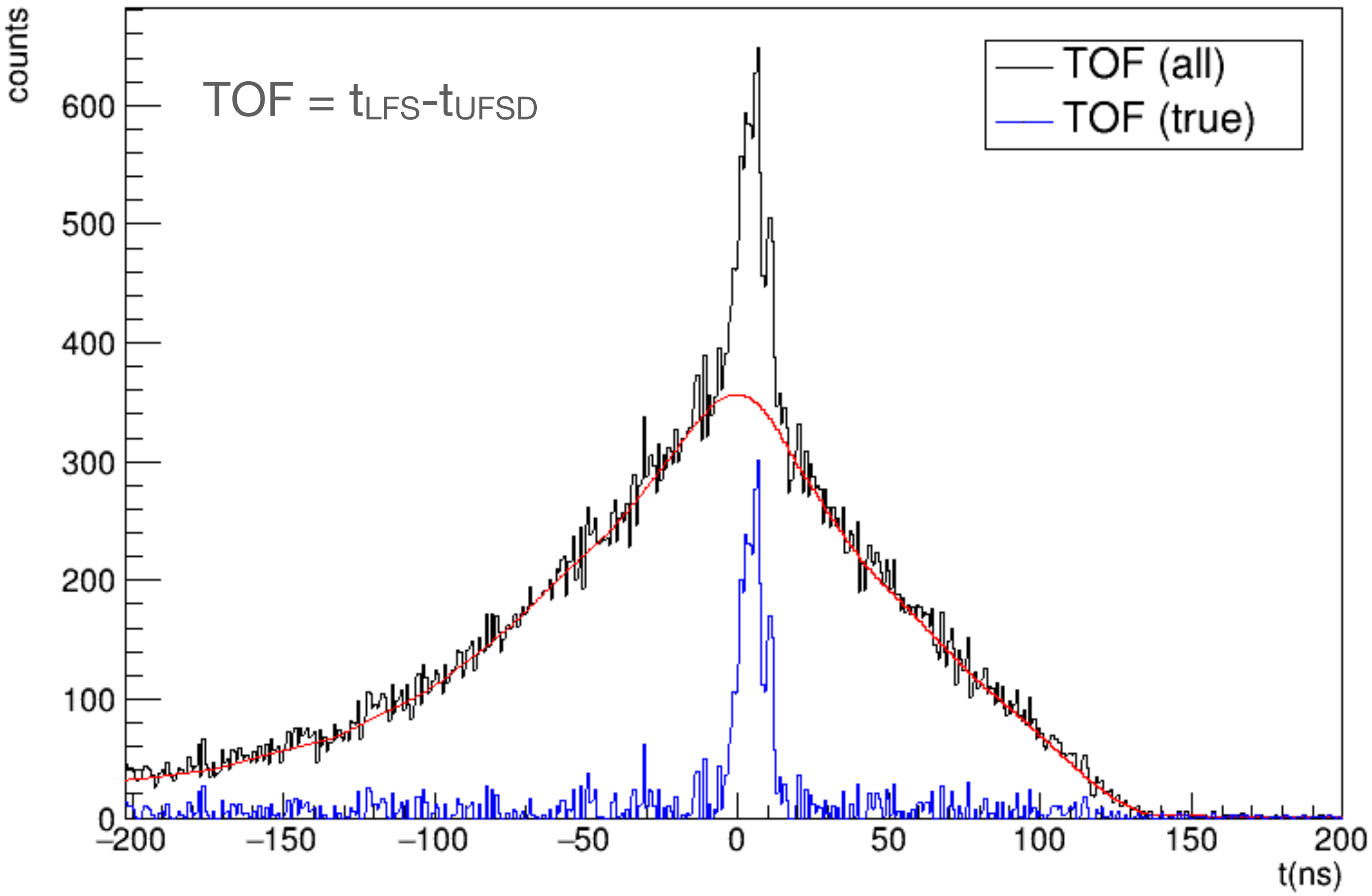


PET LFS crystals (8x8 matrix, 3.1x3.1x20 mm^2) coupled to SiPMs → 8 ch, acquisition trigger
UFSD → 8 ch (8x2.2 mm^2)
16 ch digitizer (2.5 Gs/s)

Beam Test @ CNAO, Jun 2021
Homogeneous PMMA phantom
Protons, E= 227 MeV
UFSD ε=0.266 @ 227MeV
Rate ∼10^5 pps (estimated)

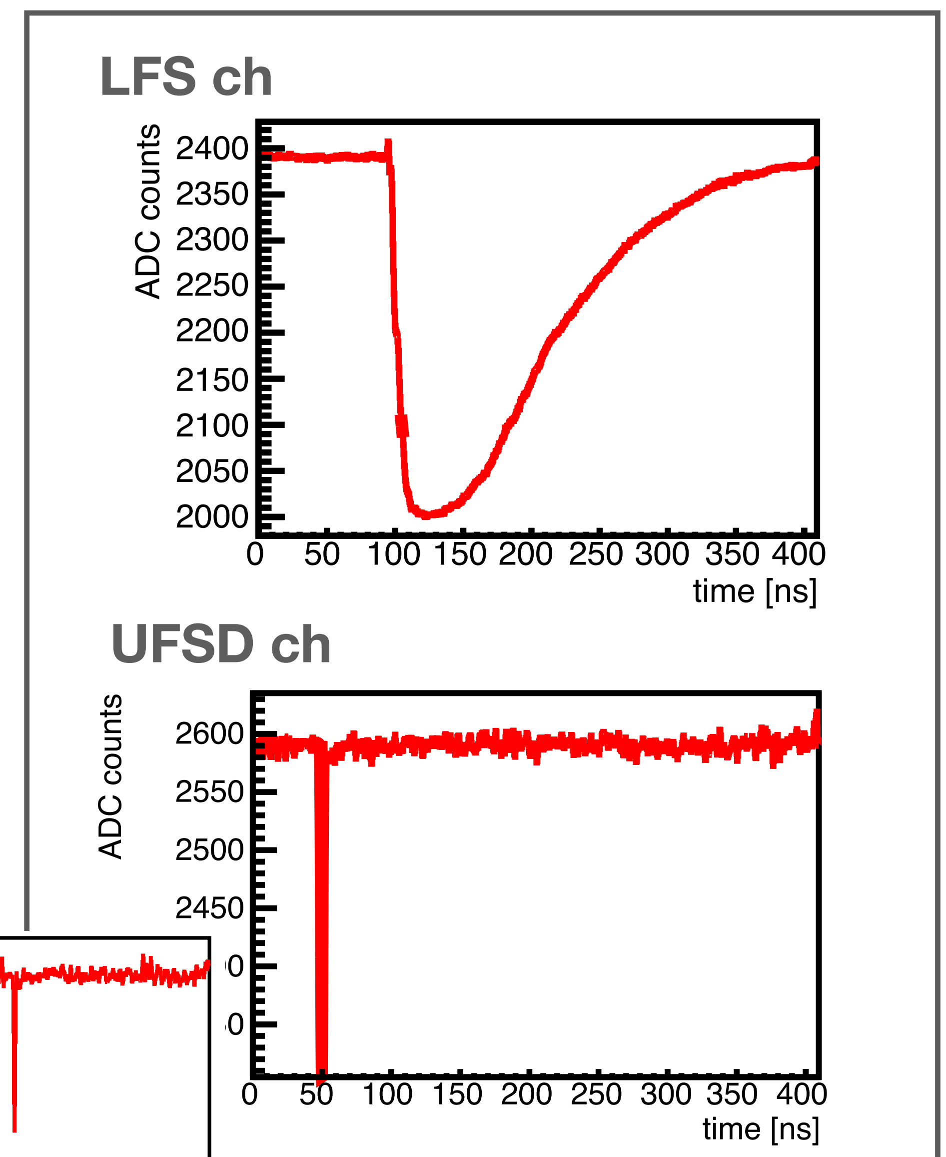


PRELIMINARY WORK: PGT EXPERIMENTAL DATA

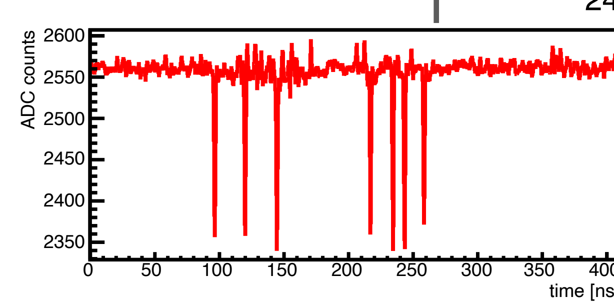


Combinatorial background subtraction (ROOT, TSpectrum)

Beam Test @ CNAO, Jun 2021
Homogeneous PMMA phantom
Protons, E= 227 MeV
UFSD ε=0.266 @ 227MeV
Rate ∼10^5 pps (estimated)



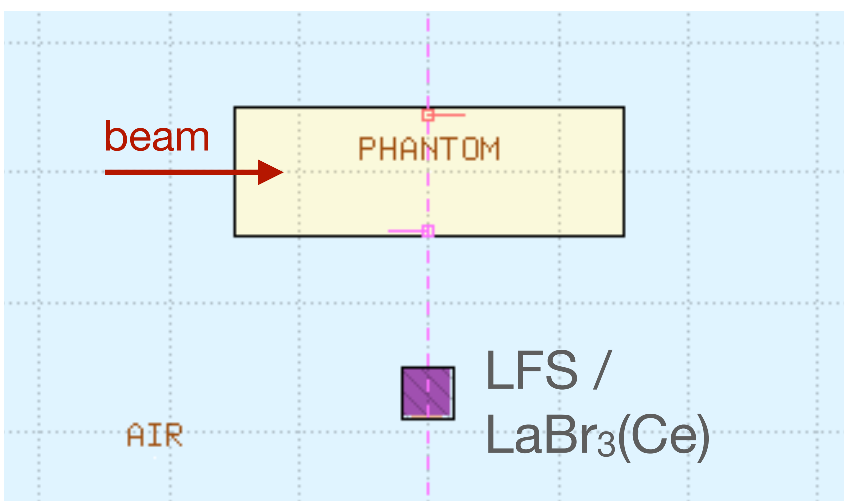
Acquisition time: 20 min
Triggered events (digitizer): 1.3 10^4
True coincidence estimation: 6 10^3 → 10%



PRELIMINARY WORK: PGT EXPERIMENTAL DATA

FLUKA MC simulations

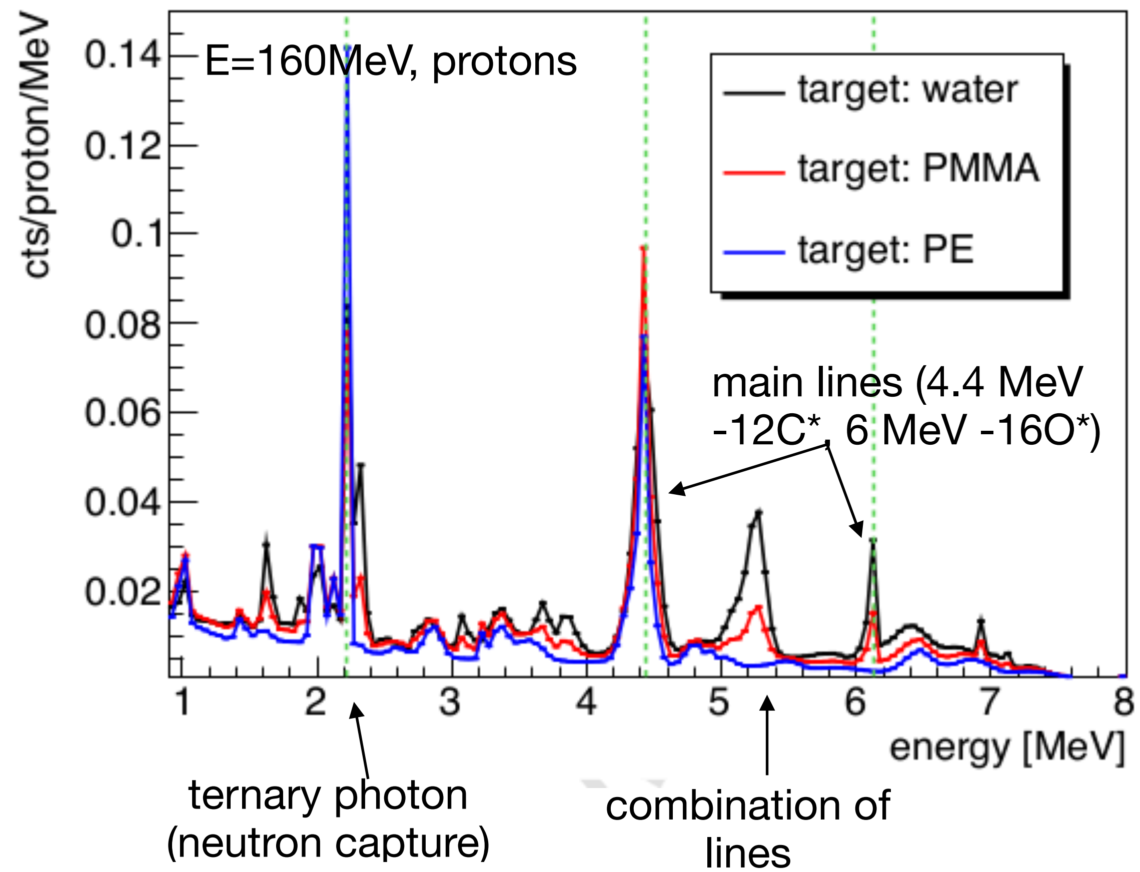
5 10^7 protons (UFSD, ε=0.266)
→ ~10^8 protons



target/detector distance = 15 cm

LFS: 25.5x25.5x20 mm^3
$LaBr_3(Ce)$: ⌀38.1 mm, h38.1 mm

Krimmer et al NIM A 2018



	Concidences	
Energy window	100keV-7MeV	2.2MeV-7MeV
LFS	9 10^3	**34**
$LaBr_3(Ce)$	1.7 10^4	**4.7 10^3**

MEASUREMENTS AND DATA ANALYSIS

A. TOF measurement performance

1. MC simulations
2. Monoenergetic proton beam

B. Particle kinematics reconstruction performance

1. MC simulations
2. Homogeneous and anthropomorphic phantom

C. Clinical Validation

1. Treatment plan (protons)
2. Verification of the stoichiometric approach (TPS, RaySearch)

D. Radiobiological Evaluation

1. Cell cultures

INFN Istituto Nazionale di Fisica Nucleare

fondazione CNAO Centro Nazionale di Adroterapia Oncologica

MoVe IT

SIGILLUM · UNIVERSITATIS · LUBECENSIS

PROJECT BUDGET

Costs by year	Year 1 (€)	Year 2 (€)
Detector Instrumentation	41087	56288
Travel costs (Beam test)	1500	6000
Lubeck visiting	3000	
Workstation (INFN price agreement)	902	
FBK silicon run (INFN FBK agreement)	25000	
Phantoms (PMMA, homogeneous)	500	
Phantoms (bone)		1500
Plexiglass phantom for cellular cultures		500
Cellular cultures CNAO		1000
EBT3 gafchromic film		1000
Consumables	3000	2000
Total per year	**74989**	**68288**

UFSD from MoVeIT collaboration

TEAM AND COLLABORATIONS

Partecipant	Institution	FTE
Veronica Ferrero, principal investigator	INFN TO	1
Piergiorgio Cerello	INFN TO	0.2
Elisa Fiorina	INFN TO	0.2
Francesco Pennazio	INFN TO	0.5
Anna Vignati	UniTO	0.2
Total		**2.1**

Collaborations:

SIG (CSN5) ⇒ range verification, ions (He-O)

FOOT (CSN3)
CNAO
University of Lübeck

Vent'anni di Cnao.

Unità di Fisica Medica, Dip. Medico

Pavia, 28/06/2021

To whom it may concern

Endorsement and availability for MERLINO (Measurement of the EneRgy Loss for IN-vivo Optimization in particle therapy) INFN Grant Giovani 2021 project

Considering the aims and the perspectives of the MERLINO project, related to the development of a novel non-invasive methodology for mapping the energy loss of the particle beams inside the patient body, I wish to express our scientific interest to this initiative, on behalf of Fondazione CNAO.

More specifically, we will provide beam time to the project Team, as well as our full support in terms of know-how and tools in the field of dosimetry, treatment planning, radiobiology, quality assurance and patient care, for the successful completion of this project.

Best regards,

Dr. Mario Ciocca, medical physicist
Head, Medical Physics Unit
Fondazione CNAO, Pavia

Strada Campeggi 53, 27100 Pavia
T. +39 0382 078XXX / F. +39 0382 078XXX
P.IVA 03491780965 / C.F. 97301200156
www.cnao.it

UNIVERSITA' DEGLI STUDI DI TORINO
DIPARTIMENTO DI FISICA
Via Pietro Giuria, 1 – 10125 TORINO
C.F. 80088230018 e P.IVA 02099550010

Torino, the 23rd of June 2021

To Dr. Veronica Ferrero,
INFN Torino
P.I. of the MERLINO project

I have read the interesting proposal of the MERLINO project which aims at developing a technique for the online determination of the energy loss distribution in charged particle therapy through PGT measurements.

Within the INFN MoVe-IT project, we have explored the feasibility of single particle tagging for beam monitoring in proton therapy by exploiting thin UFSD silicon sensors and a fast custom readout electronics. Besides the application to direct particle counting, it also allows for the measurement of the crossing time of protons, opening up to a variety of unprecedented timing applications. I'm very excited about the possibility of testing the concept behind the MERLINO project and I will ensure the availability of sensors, front-end and back-end readout developed in MoVe-IT, as well as the technical support for their use, that will be needed for the MERLINO activity.

Yours sincerely,

Roberto Sacchi

Professor of Physics
Dipartimento di Fisica e INFN
Università degli Studi di Torino

Roberto Sacchi
Tel. +39.011.6707318 – Fax +39.011.2367302
roberto.sacchi@unito.it

UNIVERSITÄT ZU LÜBECK
INSTITUT FÜR MEDIZINTECHNIK

imt Institut für Medizintechnik

Univ.Prof. Dr. Magdalena Rafecas
Ratzeburger Allee 160, Geb. 64
23562 Lübeck, Germany
Tel.: +49 451 3101-5403
Fax: +49 451 3101-5404
Email: rafecas@imt.uni-luebeck.de
URL: www.imt.uni-luebeck.de

Lübeck, 22nd of June 2021

Letter of for Research Proposal MERLINO, Applicant: Dr. V. Ferrero

To Whom It Might Concern

Hereby I express my interest in supporting the proposal entitled *Measurement of the EneRgy Loss for IN-vivo Optimization in particle therapy* (MERLINO) as international collaborator. The P.I. of MERLINO is Dr. Veronica Ferrero, from INFN Torino.

I am full professor at the Institute of Medical Engineering of the University of Lübeck, Germany, and head of the research group "Nuclear Imaging". My research mainly focuses on positron emission tomography (PET) and prompt-gamma (PG) imaging, from formal aspects such as image reconstruction to instrumentation and developement of novel imaging concepts for specific applications. In the last years I have been collaborating with Dr. Veronica Ferrero and other researchers of INFN Torino. Our joint research deals with in-beam PET and prompt-gamma timing.

MERLINO proposes a novel and very promising methodology, aimed to reconstruct the stopping power of charged particles in matter by detecting PG photons emitted during proton therapy treatments. The MERLINO concept will thus allow for non-invasive measurement and optimization of treatment plans based on the estimated stopping power. If funded, MERLINO will thus pave the way for a higly innovative and clinically relevant technique for treatment verification. As external collaborator, I will support MERLINO mainly in those tasks related to reconstruction and optimization algorithms and modeling.

If you need further information, please do not hesitate to contact me

Sincerely,

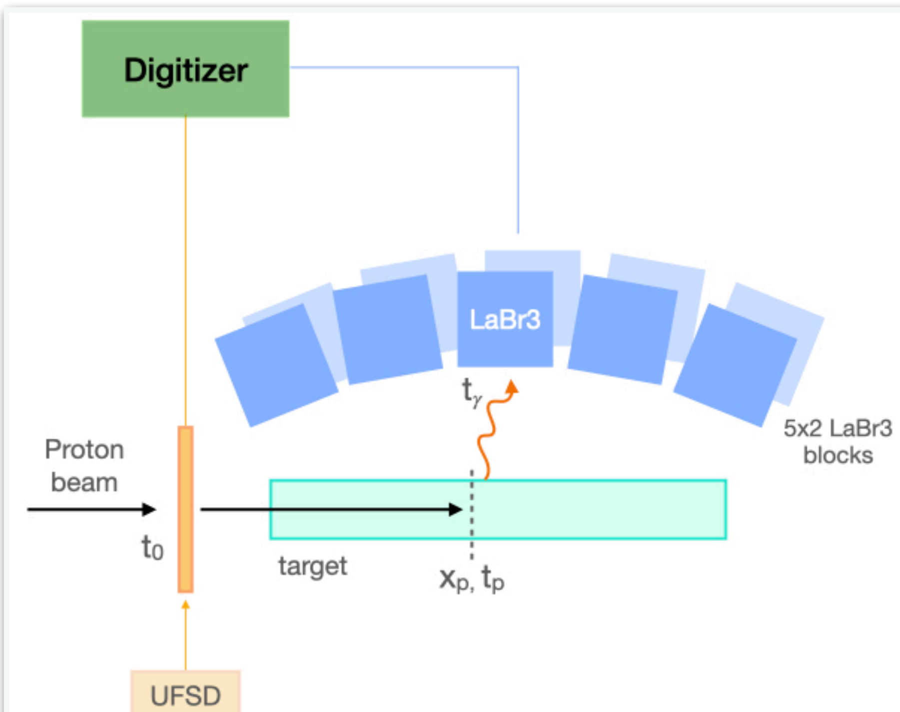
Prof. Dr. Magdalena Rafecas, PhD
Professor for Instrumentation in Medical Imaging

TIMEFRAME

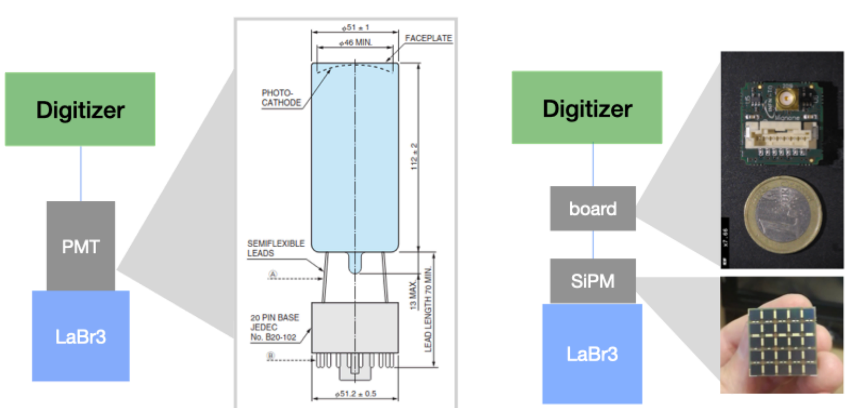
		Months							
Milestone	**Task**	**3**	**6**	**9**	**12**	**15**	**18**	**21**	**24**
M1 - Reconstruction software	T1.1 - Study and development of reconstruction algorithms								
M2 - Detector performance assessment (Readout 1 vs Readout 2)	T2.1 - R&D with PMT								
	T2.2 - R&D with preliminary SiPMs								
	T2.3 - SiPMs scientific run								
M3 - Measurements with complete system	T3.1 - DAQ design and implementation								
	T3.2 - Preliminary measurements								
	T3.3 - Assembly of the complete system								
M4 - Proof-of-concept of the proposed approach	T4.1 - Particle kinematics and energy loss assessment								
	T4.2 - Clinical validation and Radiobiology measurement								

PROJECT OUTCOMES

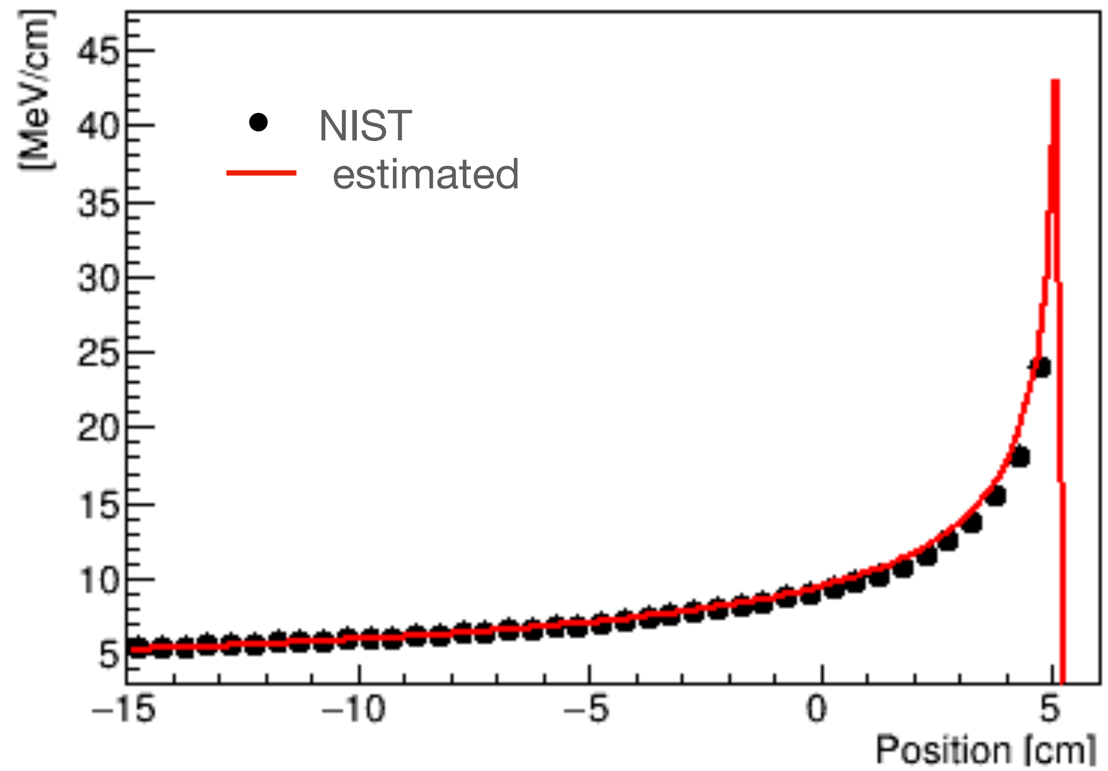
PGT MULTI-DETECTOR SYSTEM



R&D



STOPPING POWER RECONSTRUCTION



2.4% mean difference (MC truth, physical description)

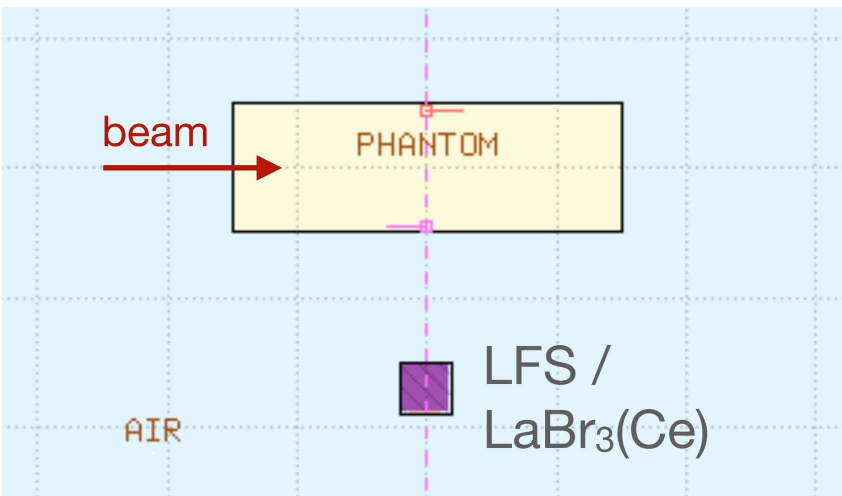
1. TREATMENT VERIFICATION AND OPTIMIZATION
2. STOICHIOMETRIC APPROACH VERIFICATION (TPS)

BACKUP SLIDES

PGT EXPERIMENTAL DATA: PRELIMINARY WORK

FLUKA MC simulations

5 10^7 protons (UFSD, ε=0.266)
→~10^8 protons



target/detector distance = 15 cm

LFS: 25.5x25.5x20 mm^3
$LaBr_3$(Ce): ⌀38.1 mm, h38.1 mm

Δt=5ns coincidence window

	Concidences	
Energy window	100keV-7MeV	2.2MeV-7MeV
LFS	9 10^3	**34**
$LaBr_3$(Ce)	1.7 10^4	**4.7 10^3**

Single events:

LFS ~ 3.2 10^4 evts → 3.5x (100keV-7MeV), 940x (2.2 MeV-7MeV)
$LaBr_3$(Ce) ~ 5.5 10^4 evts → 3.2x (100keV-7MeV), 11x (2.2 MeV-7MeV)

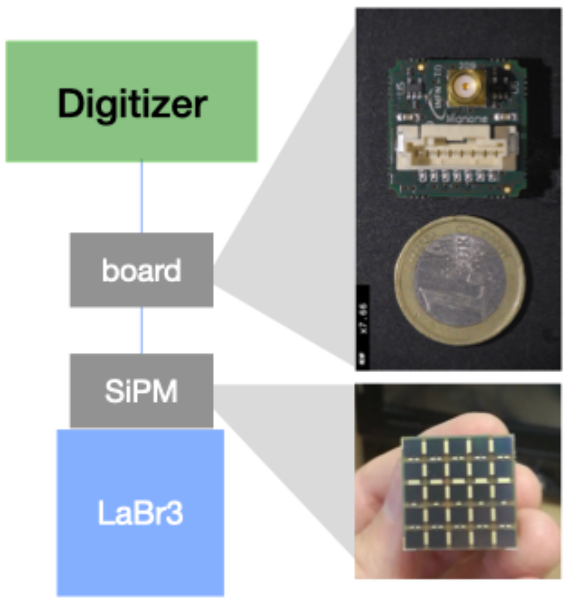
Distance dependence - $LaBr_3$(Ce):
ΔE=2.2MeV-7MeV

target/detector distance = 15 cm
10^8 pps → 4.7 10^3 coincidences/s

target/detector distance = 20 cm
10^8 pps → 2.1 10^3 coincidences/s

FOOT SIPM TILE

Readout 2: SiPMs

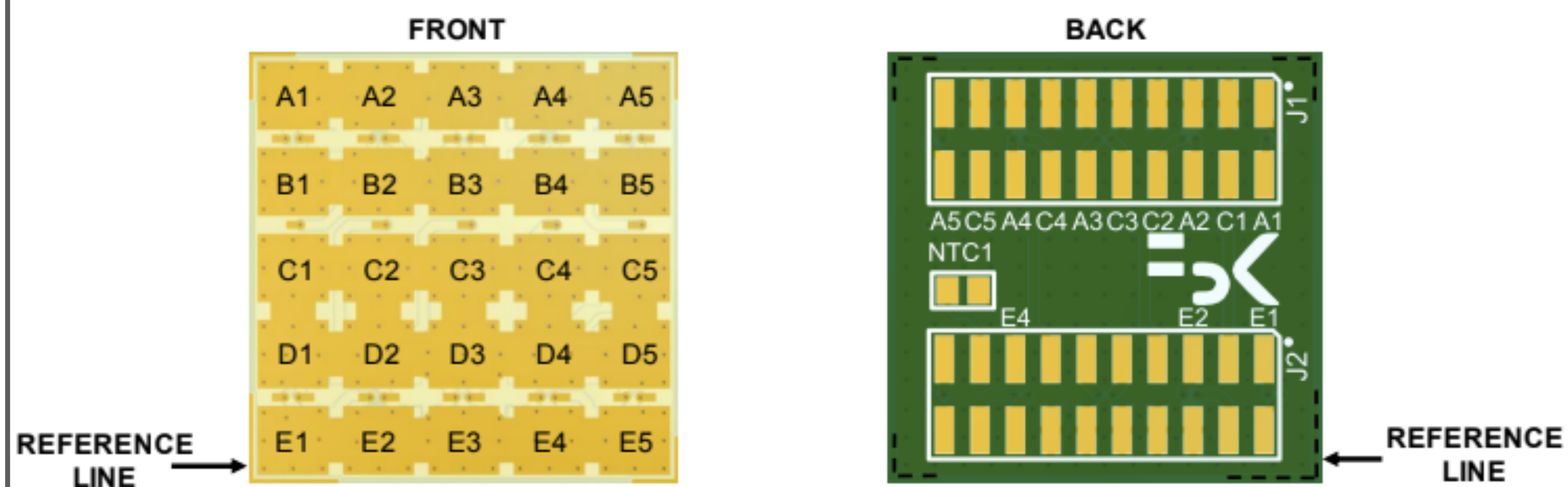


FOOT (CSN3) FE board and SiPM tile

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 $CeBr_3$ or $LaBr_3$:Ce. The high light yield



SiPM by FBK:

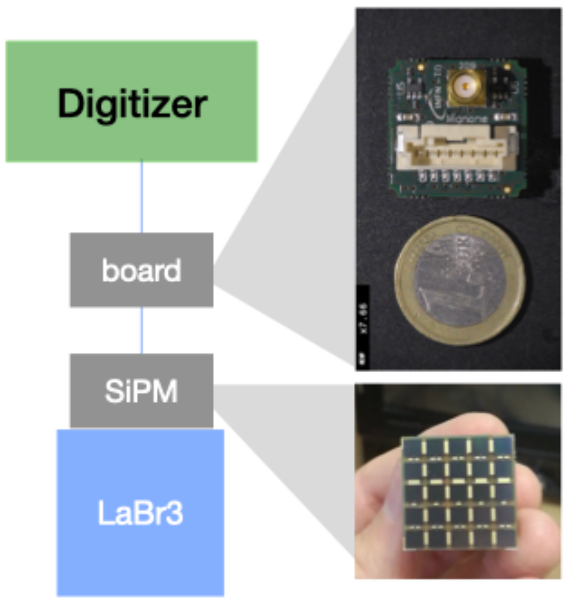
SiPM Type			Tile		
Technology	Cell size (µm)	SiPM size (mm²)	Tile size (mm²)	# SiPMs	Resin
RGB-HD	15	16	24x24	25	Epoxy

→10^6 microcells per SiPM

BGO time resolution ~600 ps σ (cosmic rays), τ=300 ns
Digitizer 2.5 Gs/s
→better time res might be achieved with $LaBr_3$(Ce)

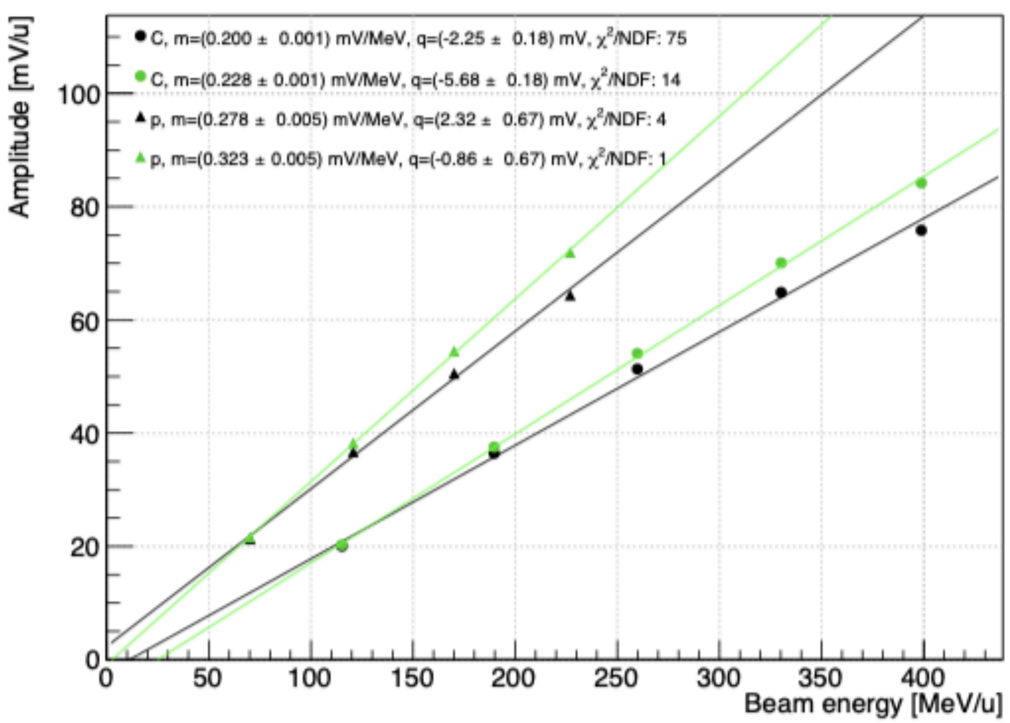
FOOT SIPM TILE

Readout 2: SiPMs

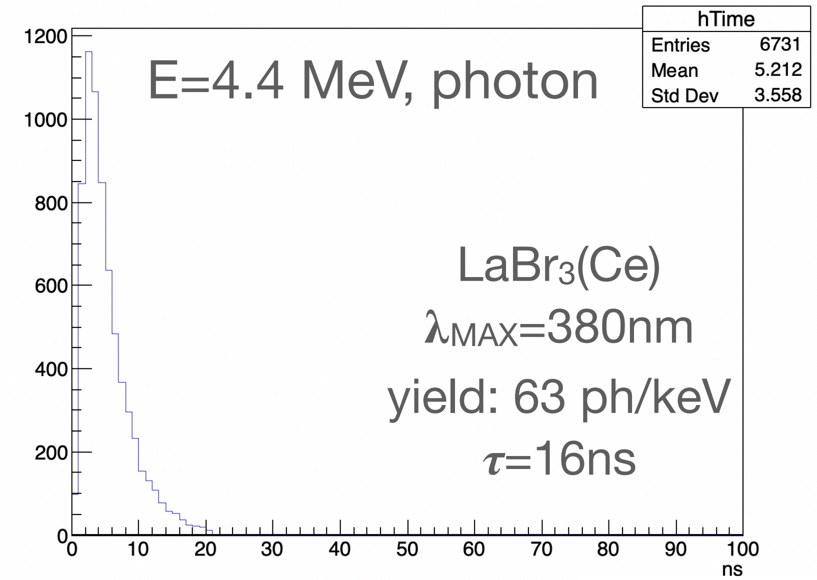


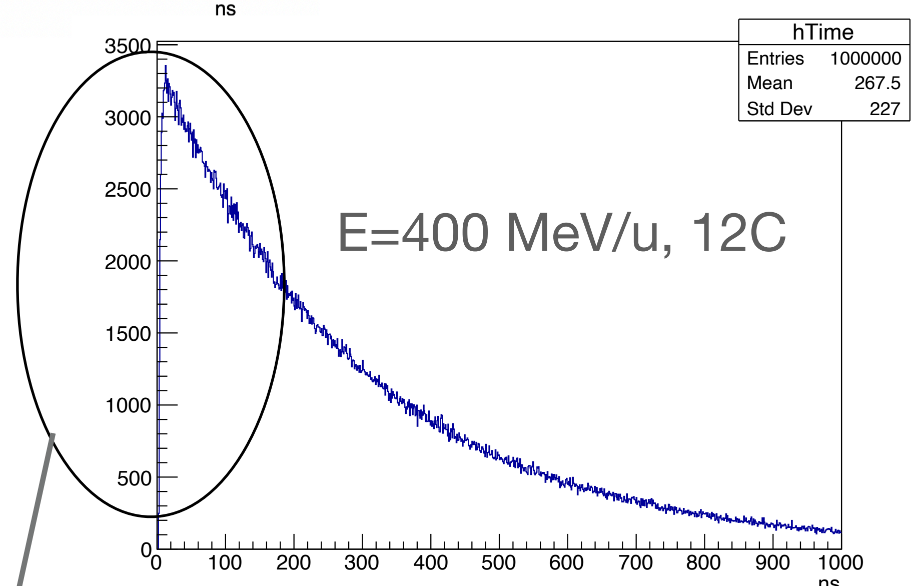
FOOT (CSN3) FE board and SiPM tile

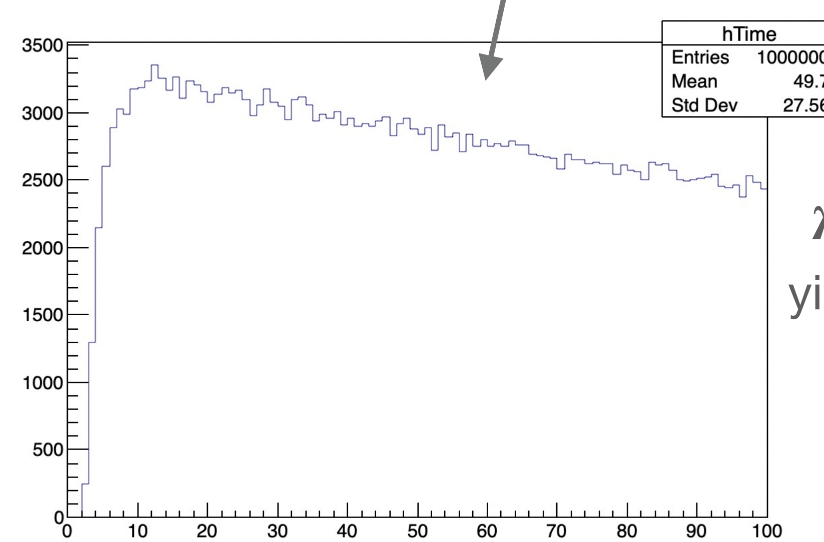
SiPM response linearity vs beam energy



MC simulations







BGO

λ_{MAX}=480nm

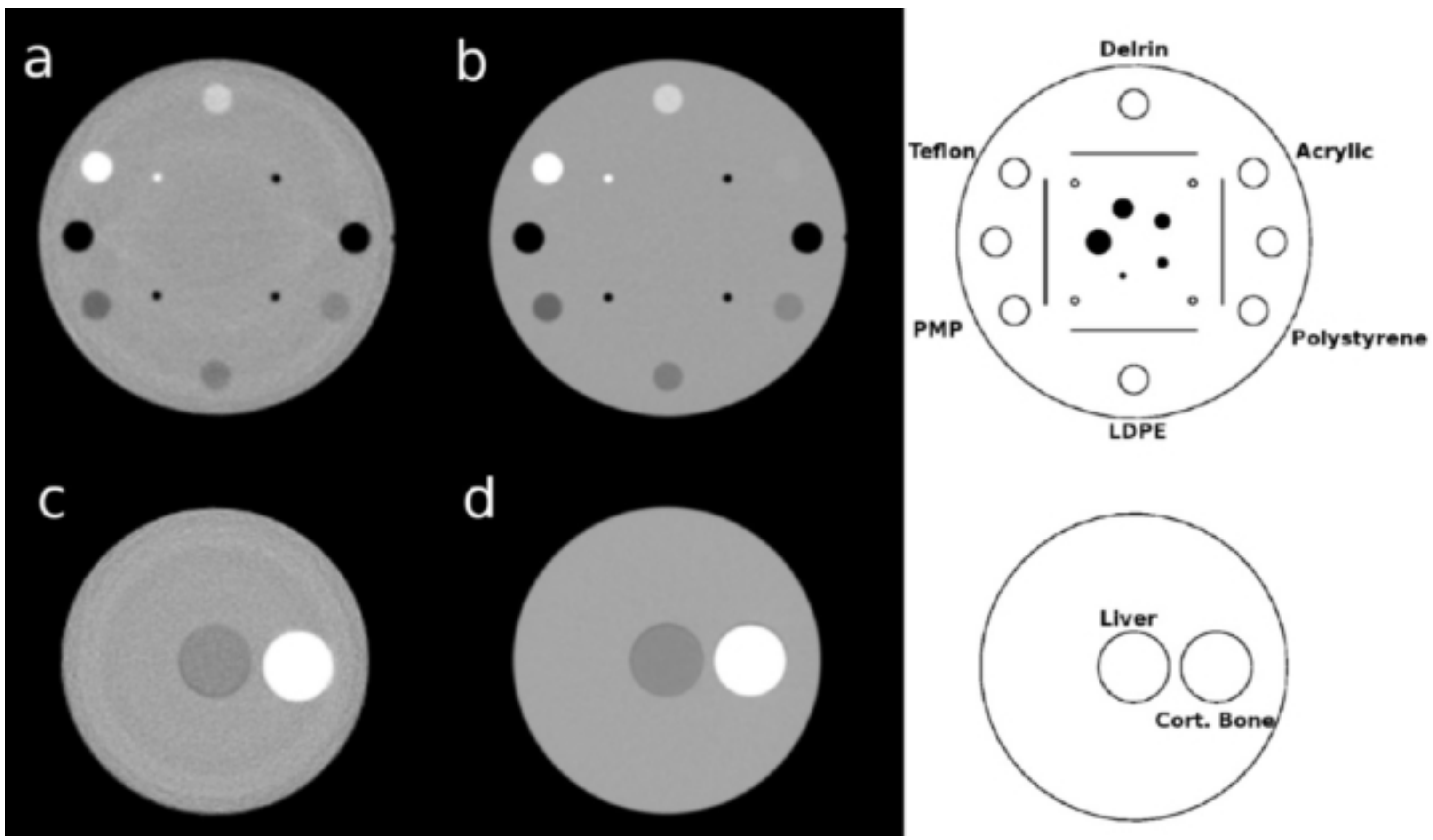
yield: 8 ph/keV

τ=300ns

PROTON CT, DUAL ENERGY CT

→HU to Stopping Power ratio conversion uncertainties

Proton CT   Dual Energy CT



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

BUDGET DETAILS

Detector Instrumentation	Quantity	Unit price (IVA incl)	Year 1 (€)
Saint Gobain LaBr3(Ce) crystals	4	5917	23668
Digitizer V1742 by CAEN	1	8955	8955
VME crate for digitizer power supply - already @ INFN TO			0
PMT with assembly by Hamamatsu	2	1632	3264
CAEN DT5533 for PMT HV	1	3294	3294
SiPM test tiles (FBK)	2	195	390
SiPMs FE board	2	200	400
Power supply MX100TP for SiPM FE boards	1	1115	1115
Total			**41087**

Detector Instrumentation	Quantity	Unit price (IVA incl)	Year 2 (€)
Saint Gobain LaBr3(Ce) crystals	8	5917	47336
Packaging of SiPM tiles (FBK)	10	195	1952
SiPMs FE board	10	200	2000
Custom external trigger board/eMUSIC SCIENTIFICA board	1	2000	2000
Detector mechanics	1	2000	2000
Mechanical support for SiPMs optical coupling	1	1000	1000
Total			**56288**

SUPERCONDUCTING ION GANTRY

INFN: Genova, LNF, Milano, Torino
UniMi, UniTo
CERN, CNAO

Torino tasks:

WP4 - Dose Delivery System (DDS): silicon detector design for single ion counter. **Design, production and test of new silicon sensors for ion therapy.**

WP5 - Range Verification System (RVS): PET signal (fast isotopes), prompt gamma signals (I3PET, LaBr3). **Comparative study of different range monitoring approaches for ion therapy.**

Integration of DDS and RVS inside the ion gantry

⇒Solutions previously applied to proton beams will be investigated on ion beams

Ion beams: from He to O beams → **MERLINO: protons**

Range assessment performance → **New measurement: stopping power**

Risk category	RPN
High	3
Medium	2
Low	1

RISK ASSESSMENT

Risk	RPN	Mitigation
Delay in the $LaBr_3(Ce)$ crystals delivery	1	Reshuffling of the milestones: reconstruction algorithm extensive study, MC simulation for detector optimization
Delay in the SiPMs production or PMTs delivery	1	Tests with spare front-end boards and not optimized SiPMs tile available at INFN Torino to start defining setup and data format
Underperforming of the detector with Readout 1	1	Use of Readout 2
Underperforming of the detector with Readout 2	1	Use of Readout 1
Inability to perform beam tests at the CPT facilities due to external reasons	2	Tests at INFN Torino with a monochromatic laser to assess the multi-detector timing performances. If the inability lasts in the second year of the project, review of the achievable goals, mainly M3 and M4.
Underperforming of the reconstruction algorithm on experimental data and consequent inability to map the stopping power	2	Decreasing of the beam current and proof-of-concept with sub-clinical rates; system performance assessment for standard treatment verification with the PGT method
Underperforming of the detector with both Readout 1 and 2 due to the high clinical rate	3	Decreasing of the beam current and proof-of-concept with sub-clinical rates

RECONSTRUCTION FORMULATION: PRELIMINARY WORK

Maximum Expectation Maximization (MLEM) algorithm

data

$$m_{jp}^{k+1} = \frac{m_{jp}^{k}}{S_{jp}} \sum_{i} \sum_{d} \frac{n*_{id}}{\sum_l \sum_t f_{idlt} m_{lt}^{k}} f_{idjp}$$

prompt photon

sensitivity

p: time bin (emission)
j: space bin (emission)
i: time bin (detection)
d: detector

SM

MLEM disentangles the directional info comprised in the multiple TOF to reconstruct the desired information

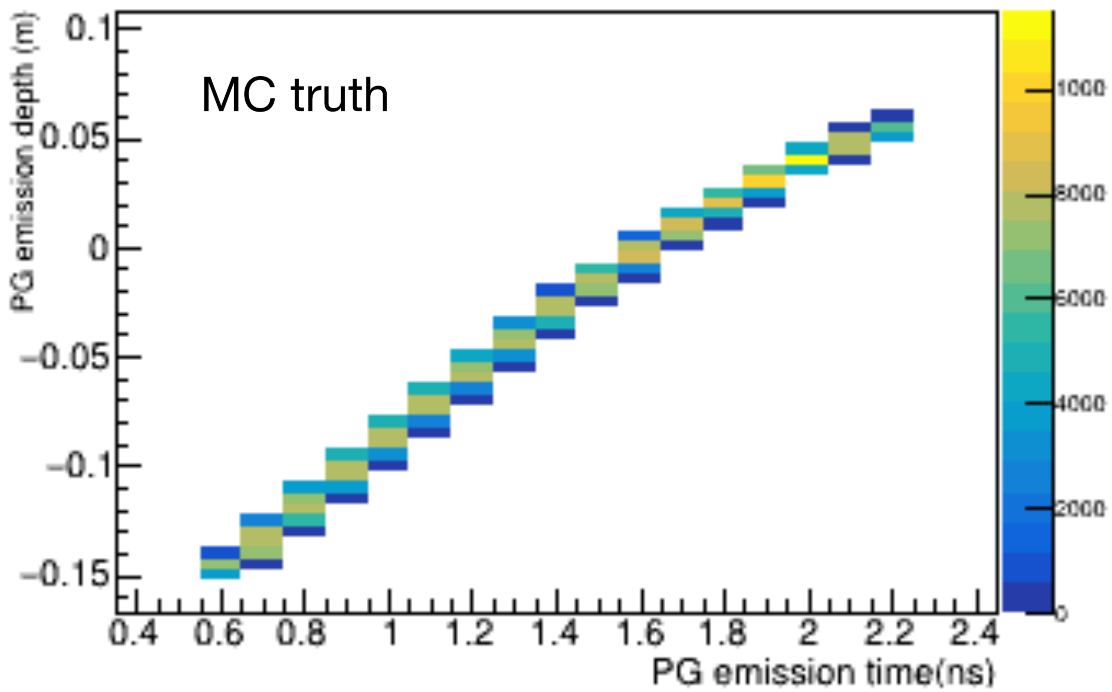
Potential approaches:

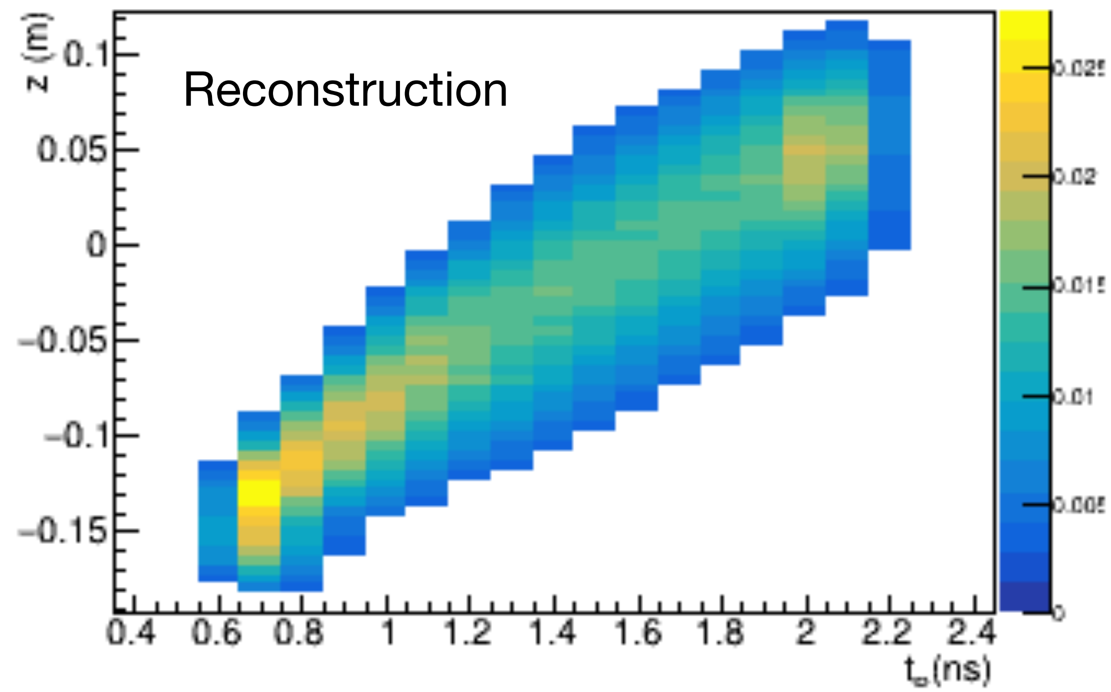
- reconstruction of the prompt gamma **spatiotemporal** distribution, evaluation of SP
- reconstruction of the prompt gamma **energy loss** distribution, evaluation of SP

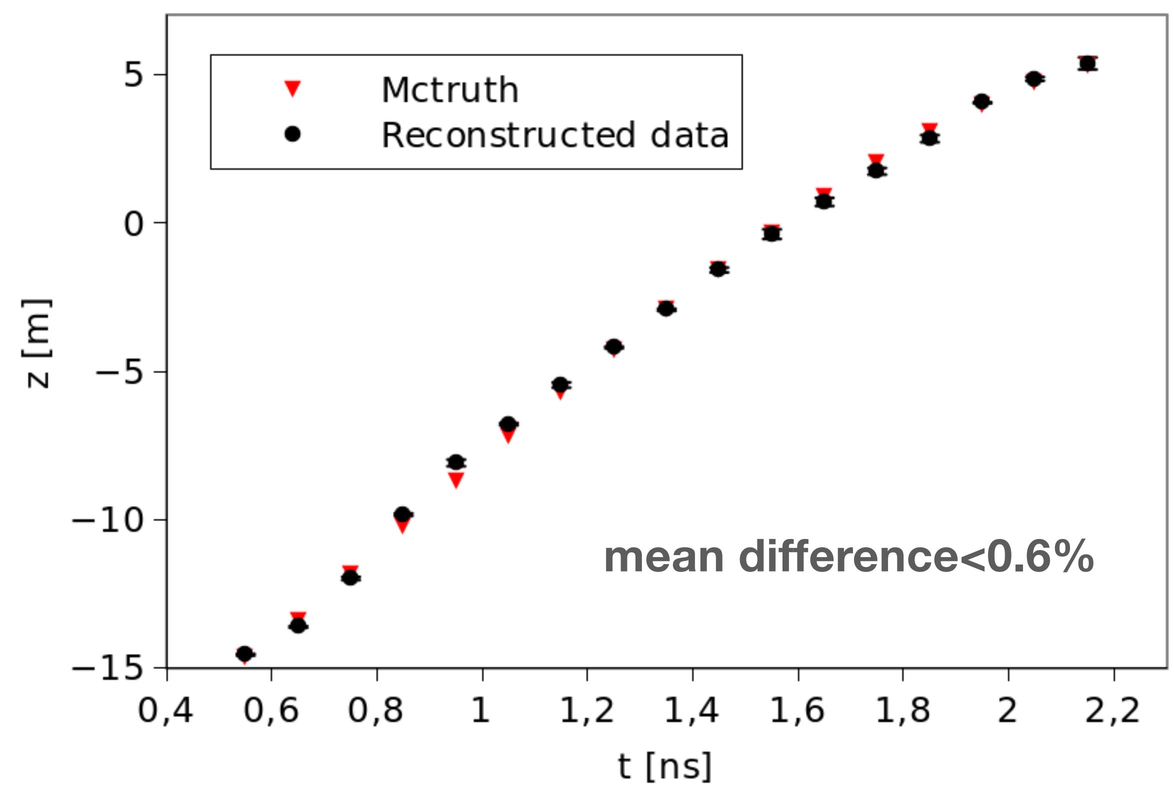
→Paper submitted to PMB, minor revision

Jacquet et al. 2021: Convolution of multiple TOF info: non iterative, vertex distribution reconstruction (1D PG profile)

RECONSTRUCTION FORMULATION: PRELIMINARY WORK







5 simulation runs

10^8 primary particles

10^7 produced photons in 4π

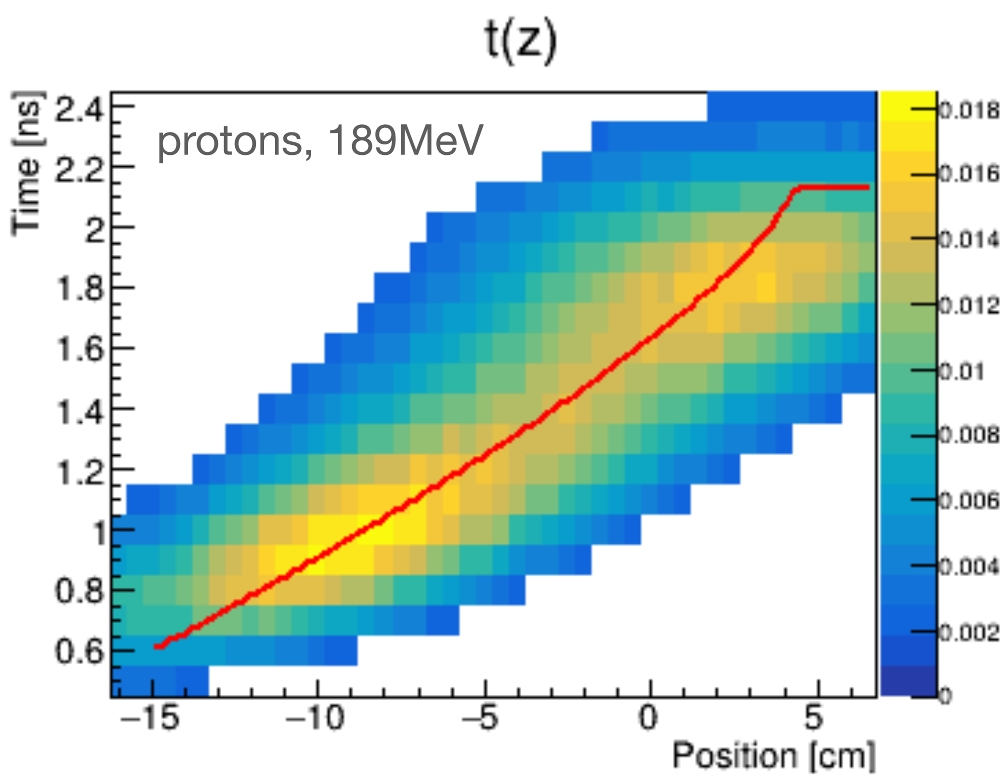
Time resolution=100 ps σ

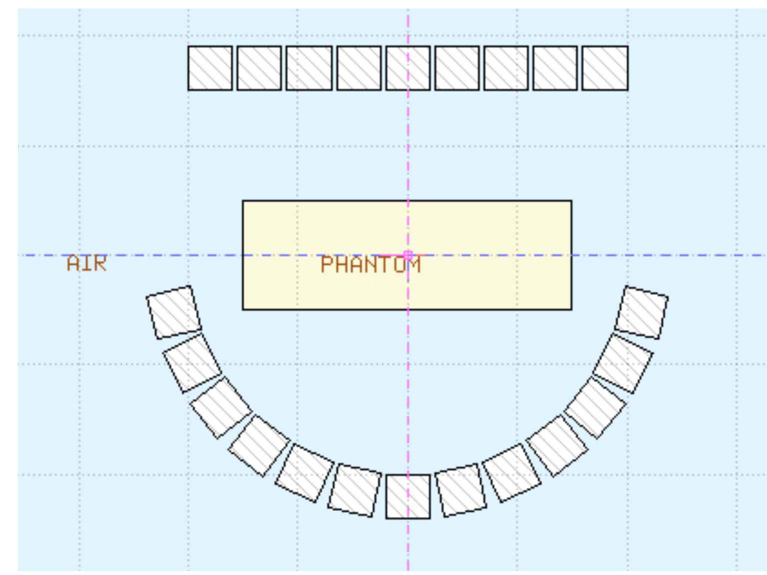
Energy cut 1MeV-7MeV

$\sim 10^4$ events per detector

110 detectors (<u>clinical scenario</u>)

RECONSTRUCTION FORMULATION: PRELIMINARY WORK





10^8 primary particles

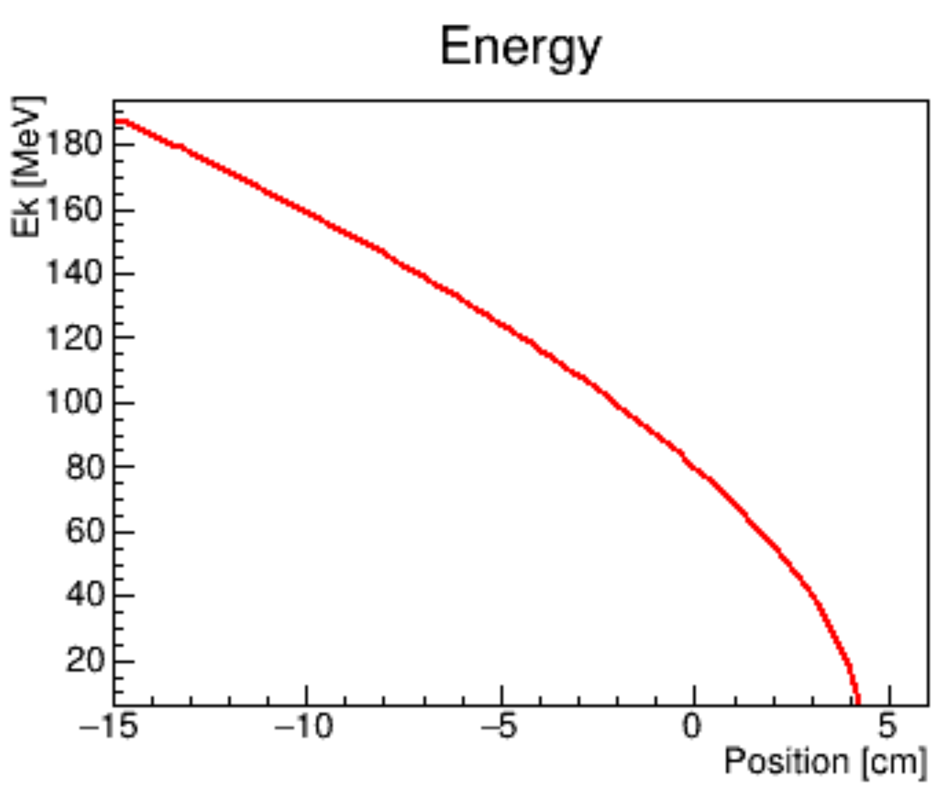
10^7 produced photons in 4π

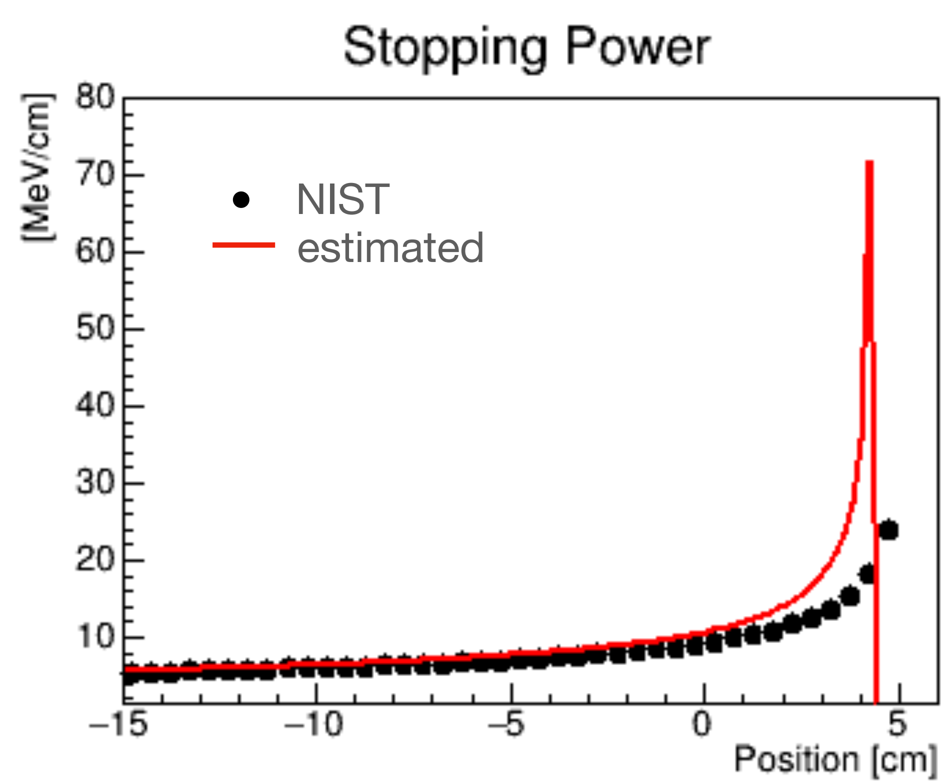
Time resolution=300 ps σ

Energy cut 1MeV-7MeV

$\sim 10^4$ events per detector

110 detectors (<u>clinical scenario</u>)

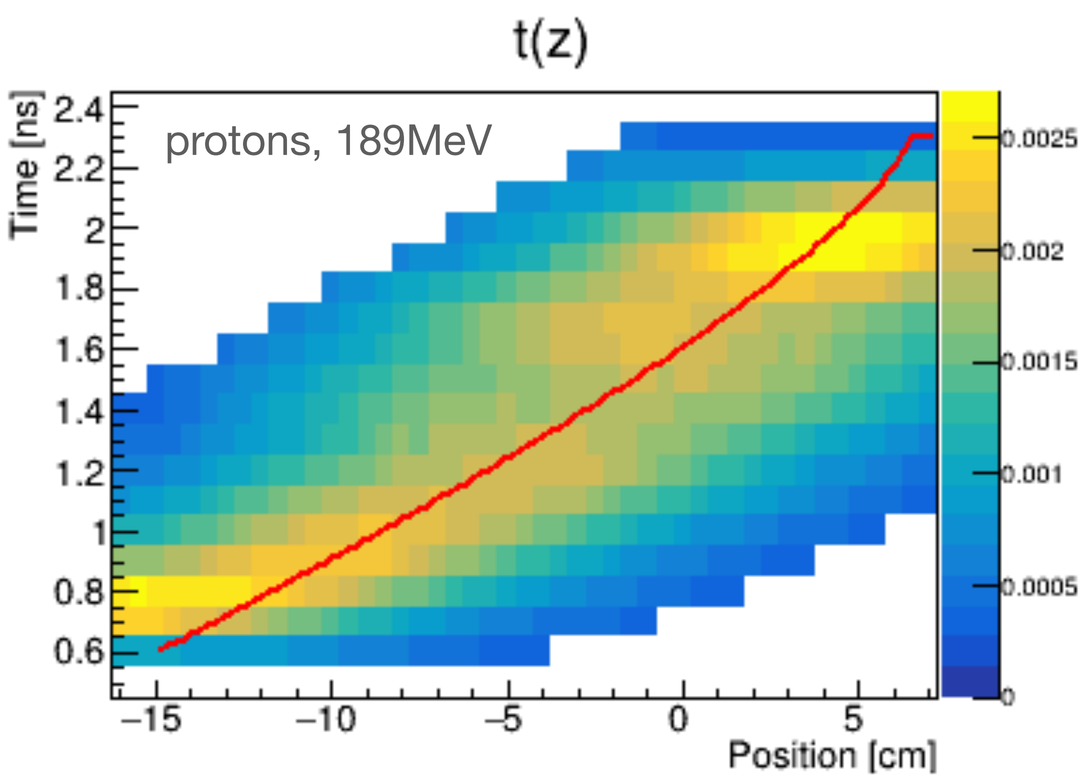


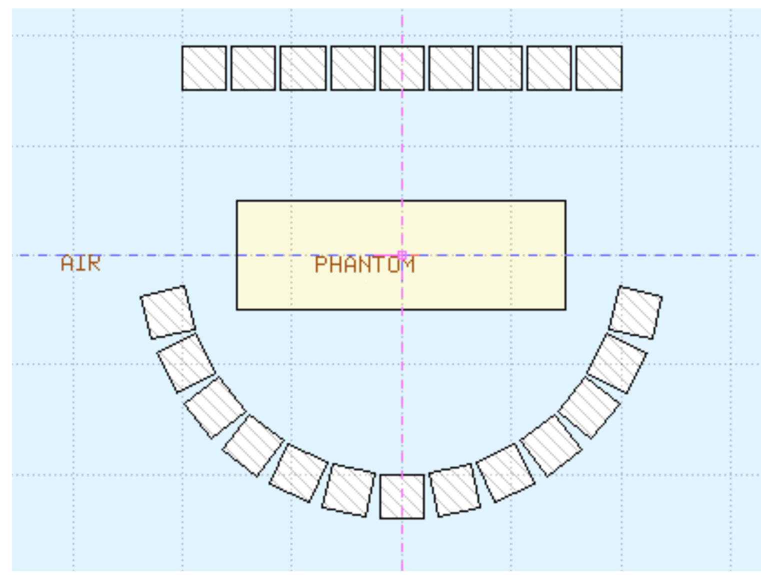


Mean absolute difference: 2.5 [MeV/cm] ⇒18.2%

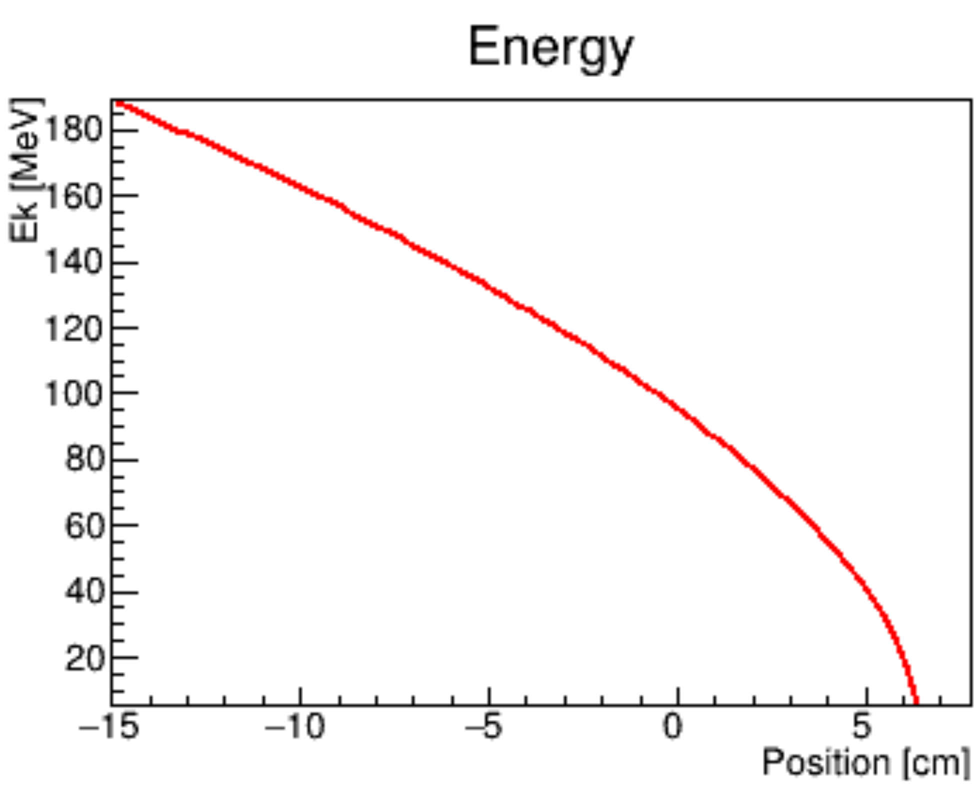
PCC=0.58

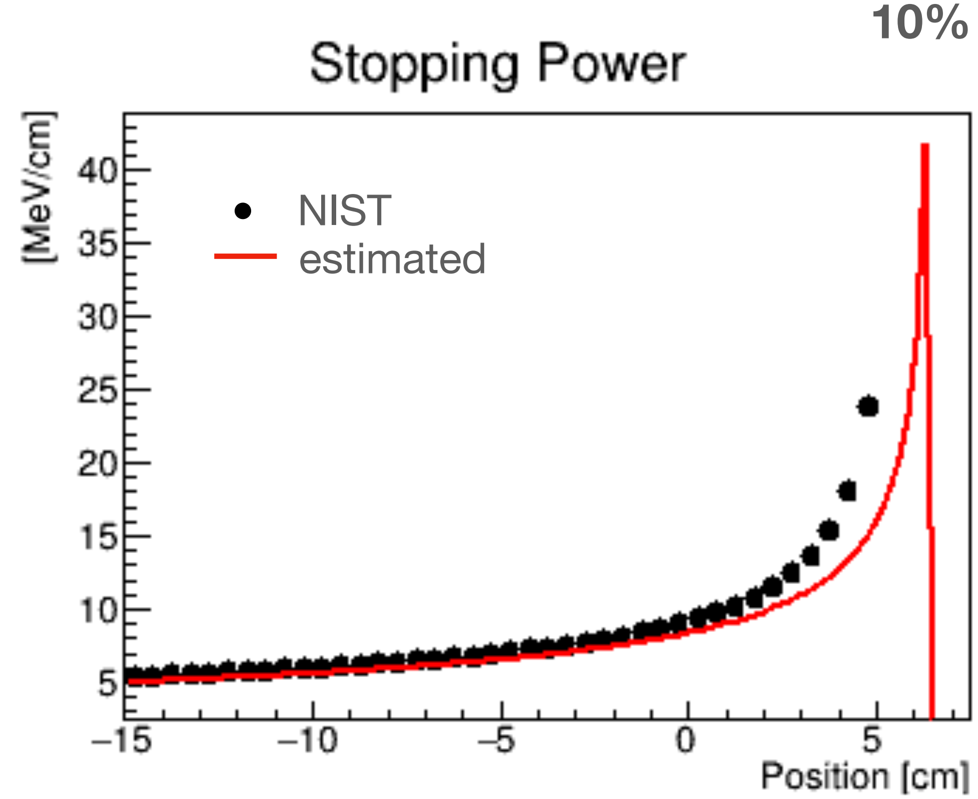
RECONSTRUCTION FORMULATION: PRELIMINARY WORK





10^8 primary particles
10^7 produced photons in 4π
Time resolution=100 ps σ
Energy cut 1MeV-7MeV
~10^4 events per detector
110 detectors (clinical scenario)
UFSD ε=0.266 @ 227MeV
10^8 pps, RF=2.13MHz
Random events inclusion
10% true coinc, 90% random evts





Mean absolute difference: 1.08 [MeV/cm] ⇒9.23%

PCC=0.87

SCINTILLATOR PROPERTIES

Scintillator	Light Yield (photons/ keV)	1/e Decay time t(ns)	F.O.M. $\sqrt{(t/LY)}$	Wavelength of maximum emission λm (nm)	Refractive index at λm	Density (g/cm^3)	Thickness (cm) for 50% attenuation (662keV)
NaI(Tl)	38	250	2.6	415	1.85	3.67	2.5
$LaBr_3$:Ce	63	16	0.5	380	~1.9	5.08	1.8
$LaBr_3$:Ce+Sr	73	25		385	~2.0	5.08	1.8
BaF_2	1.8	0.7	0.6	~210	1.54	4.88	1.9
LYSO	33	36	1.1	420	1.81	7.1	1.1
BGO	9	300	5.8	480	2.15	7.13	1.0

https://www.saint-gobain.com

THE IBA GAMMA CAMERA

The PGI slit camera.

PGI slit camera → projects the prompt-gamma distribution through a knife-edge slit collimator onto a segmented detector

→ **One-dimensional** spatially resolved prompt-gamma distribution

Range shift detection (anthropomorphic phantoms) 1-2 mm, protons

The measured profile is an average over the whole treatment region → The sensitivity depends on the lateral size of the region where the range shift occurs

The measurements is limited to specific target sites and beam directions due to setup geometrical limitation

Developed in collaboration with OncoRay, Dresden

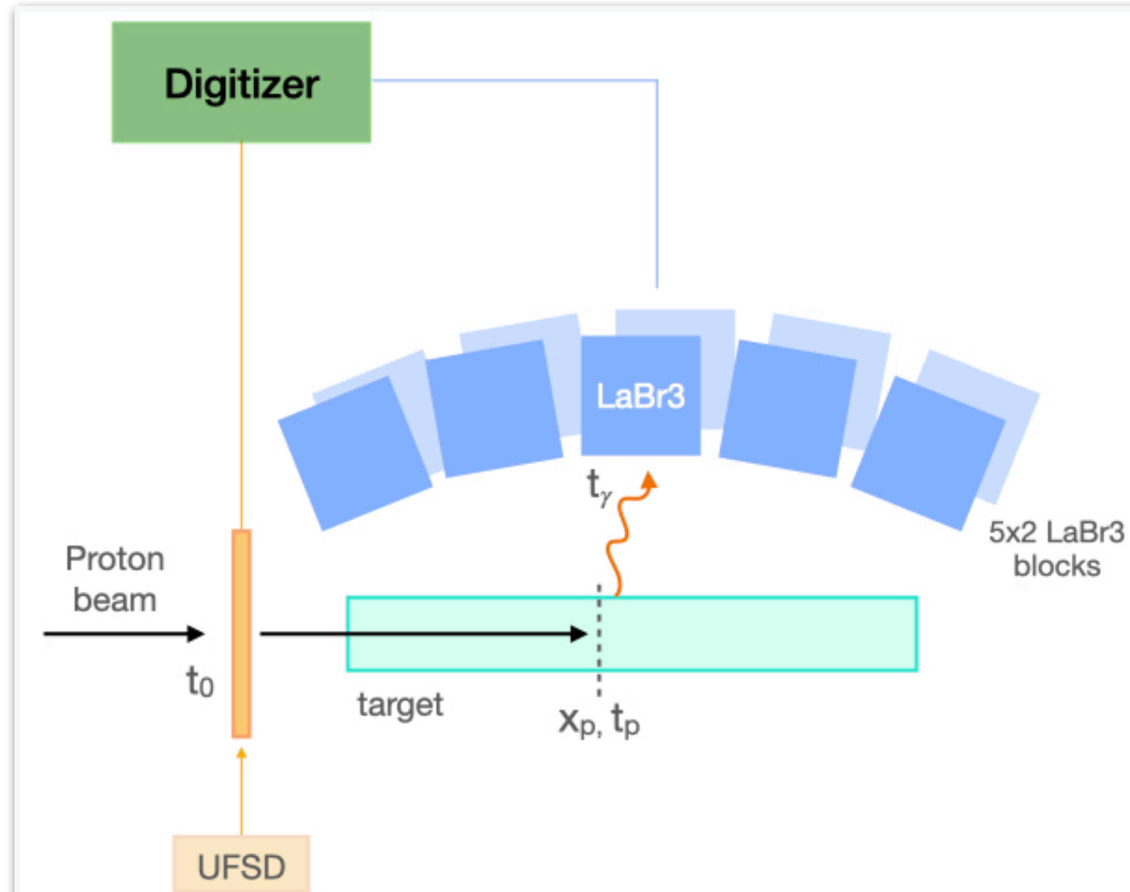
WHY UFSD?

PGT: sensitive to phase mismatch between proton bunch extraction and accelerator RF

→ single proton detector

Cyclotron (constant RF): bunch duration <3 ns

Synchrotron (non constant RF): bunch duration ∼100 ns



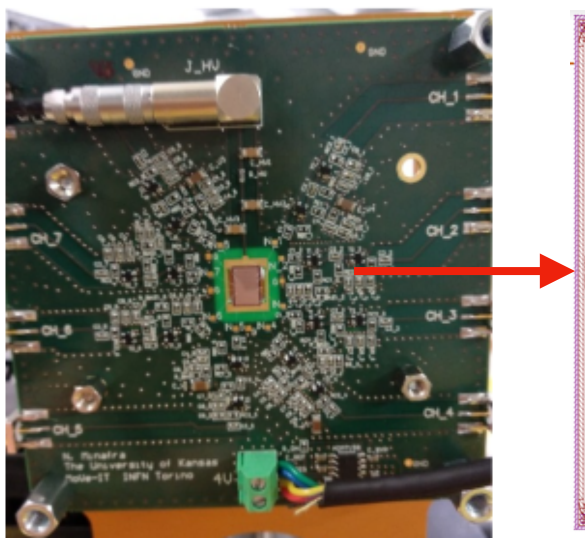
UFSD
Single proton discrimination and timing measurement. Time resolution **∼10 ps σ**

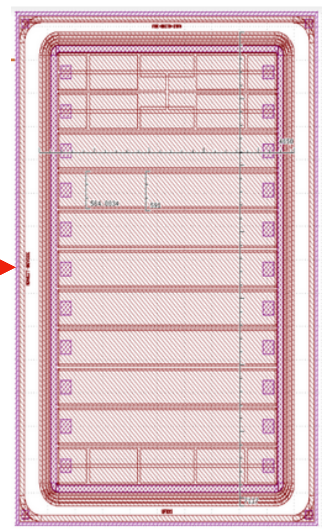
+

LaBr₃(Ce)
Fast scintillating crystals, optimized for prompt gamma energies. Time resolution **∼100 ps σ**

UFSD CHARACTERISTICS

UFSD for beam monitoring: measure the delivery time of each primary particle
Developed by MoVeIT collaboration (CSN5)

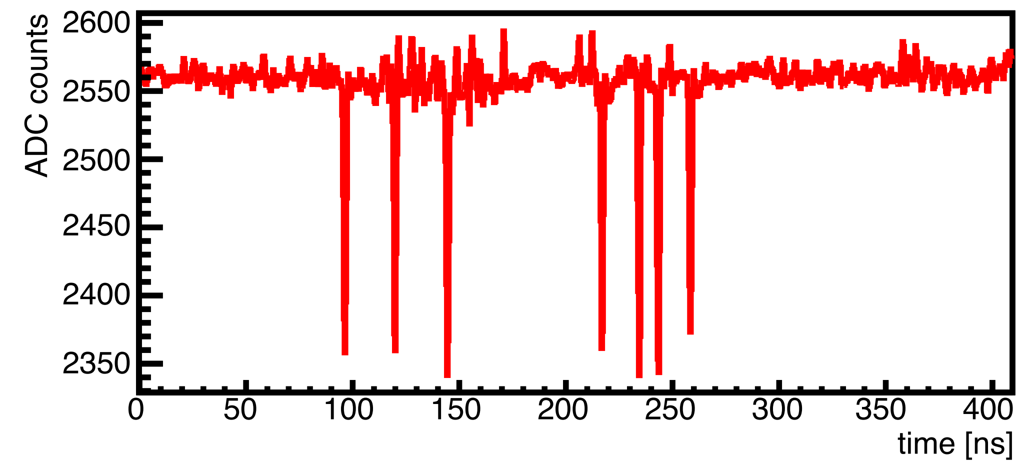




FE board: 8ch, 2 amplification stages (fast analog amplifier)
Optimized for timing measurements at high rates
Dynamic range: 3-150 fC → 60-250MeV protons

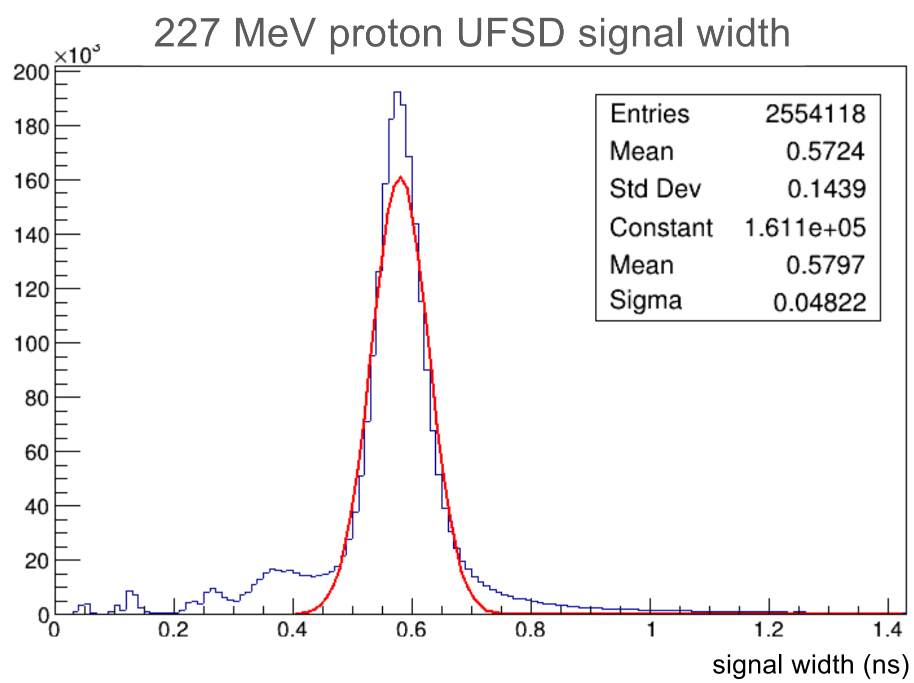
Fast signals (~2ns), single discrimination up to 10^9 $ps^{-1}cm^{-2}$ (> 10 MHz/ch)

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



8 strips + 3 test strips, 2.2 mm^2 (3393 um x 550 um, pitch 590 um)
Read by a digitizer (16ch, CAEN DT5742)
Time resolution ~10 ps
Detection efficiency up to ~27% with clinical beams

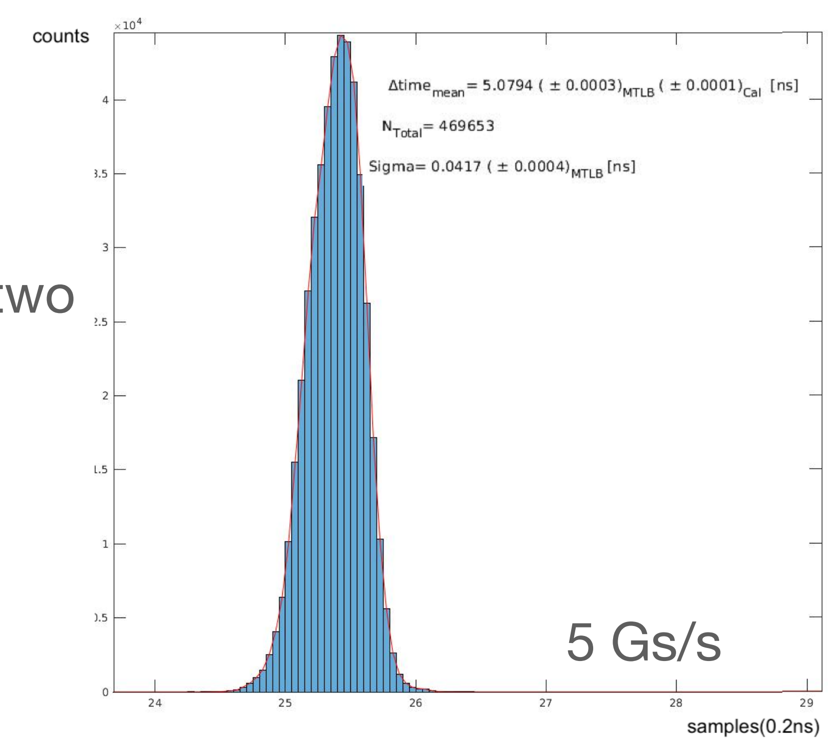
UFSD RESPONSE – PRELIMINARY WORK: EXPERIMENTAL DATA

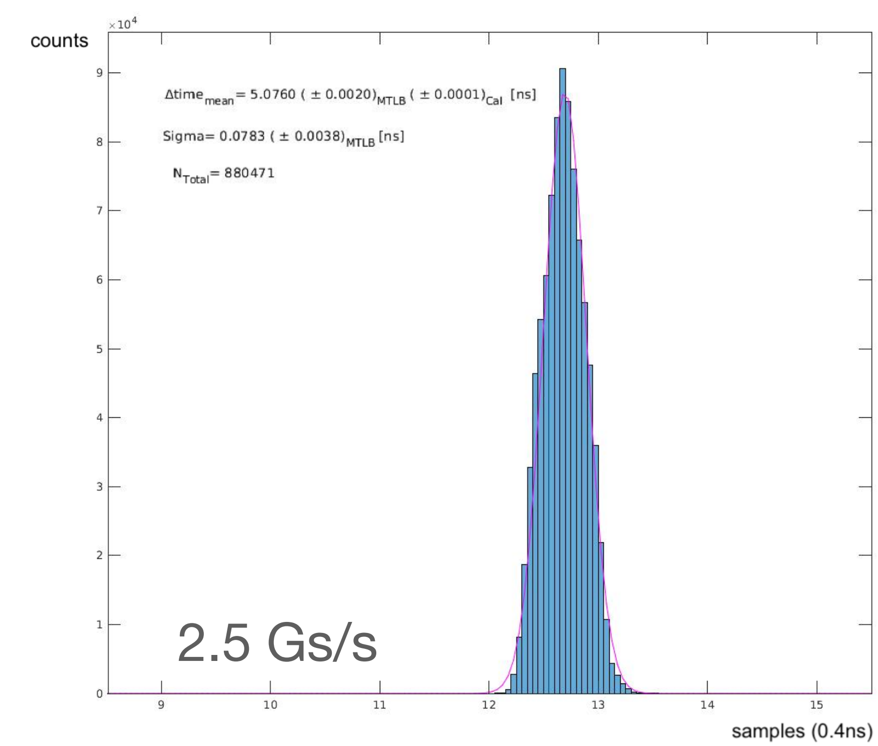


Beam Test @ CNAO, Jun 2021
Homogeneous PMMA phantom
Protons, E= 227 MeV
UFSD ε=0.266 @ 227MeV
Digitizer @ 2.5 Gs/s
Proton signal width ~2 ns

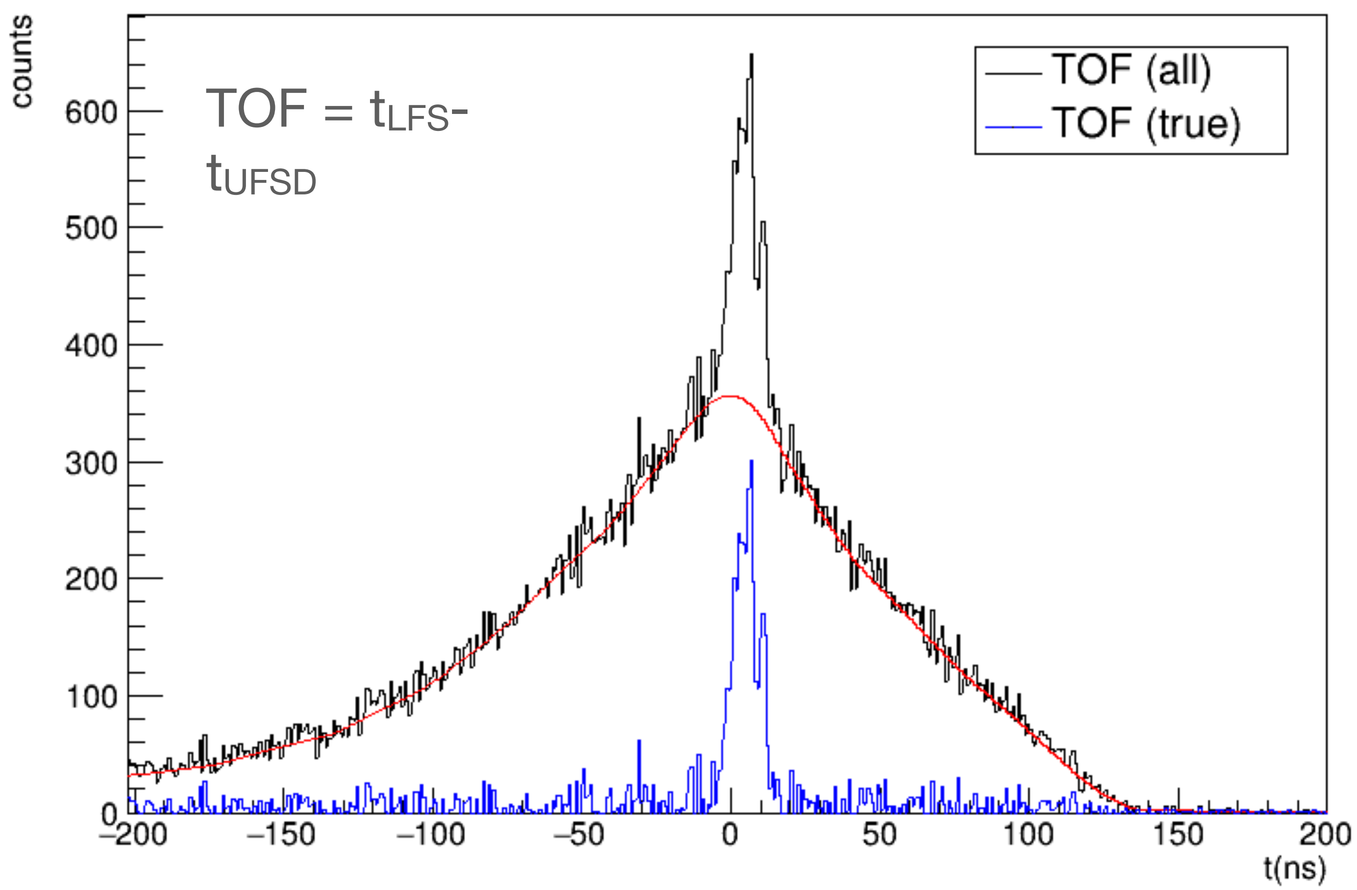
Digitizer (2.5 Gs/s, 400ns snapshot)
trigger freq 3.7kHz
→ 0.0015 data/s
(efficiency 1.5‰)

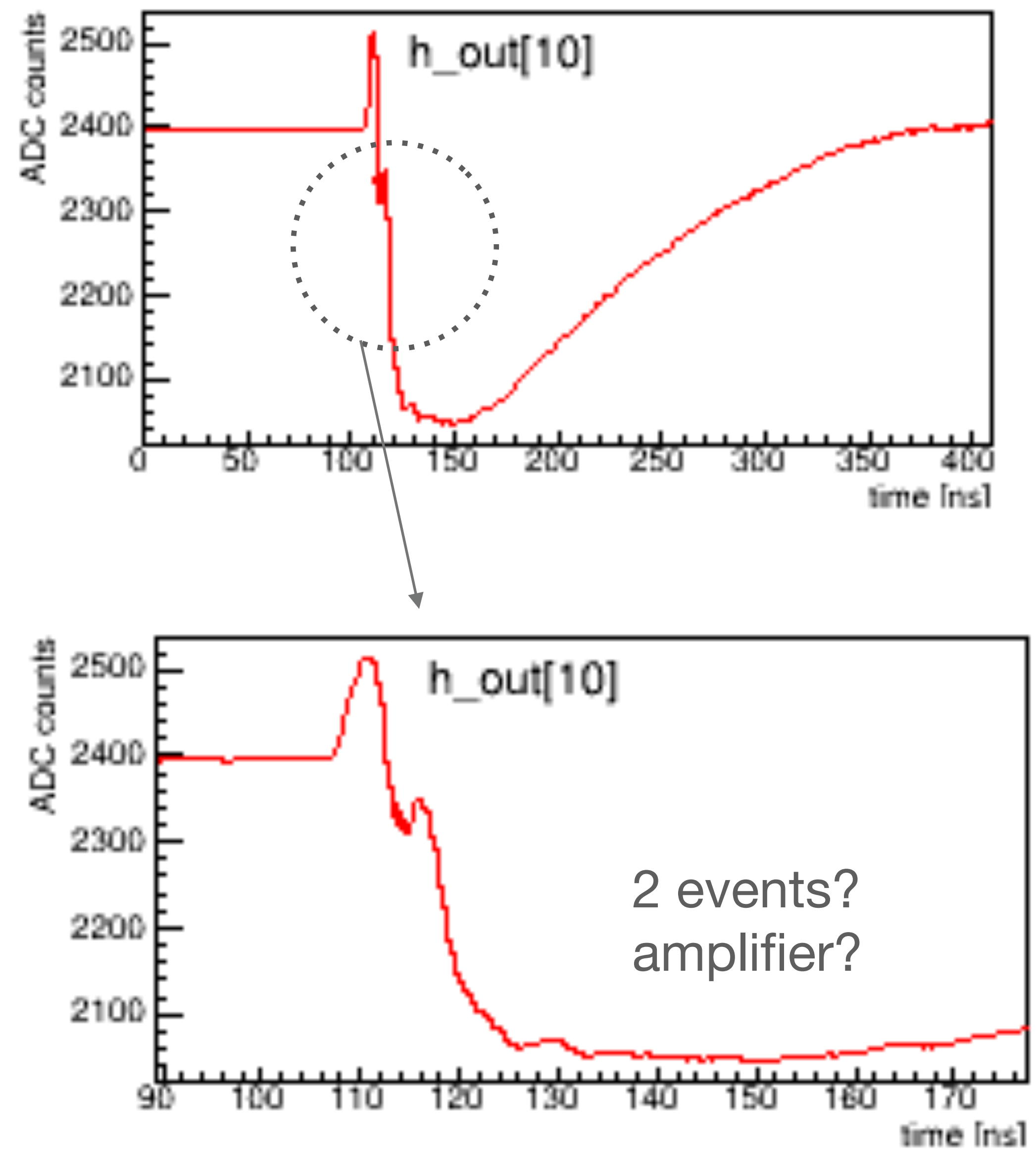
Time resolution (pulse generation-two waveforms with 5ns delay):
Digitizer @ 2.5 Gs/s → 80 ps σ
Digitizer @ 5 Gs/s → 40 ps σ





LFS RESPONSE – PRELIMINARY WORK: EXPERIMENTAL DATA





Beam Test @ CNAO, Jun 2021
Homogeneous PMMA phantom
Protons, E= 227 MeV
UFSD ε=0.266 @ 227MeV
Digitizer @ 2.5 Gs/s
Acquisition time: 20 min
Triggered events (digitizer): 1.3 10^4
True coincidence estimation: 6 10^3 → 10%

MUSIC SCIENTIFICA BOARD

Scientifica MUSIC8R1

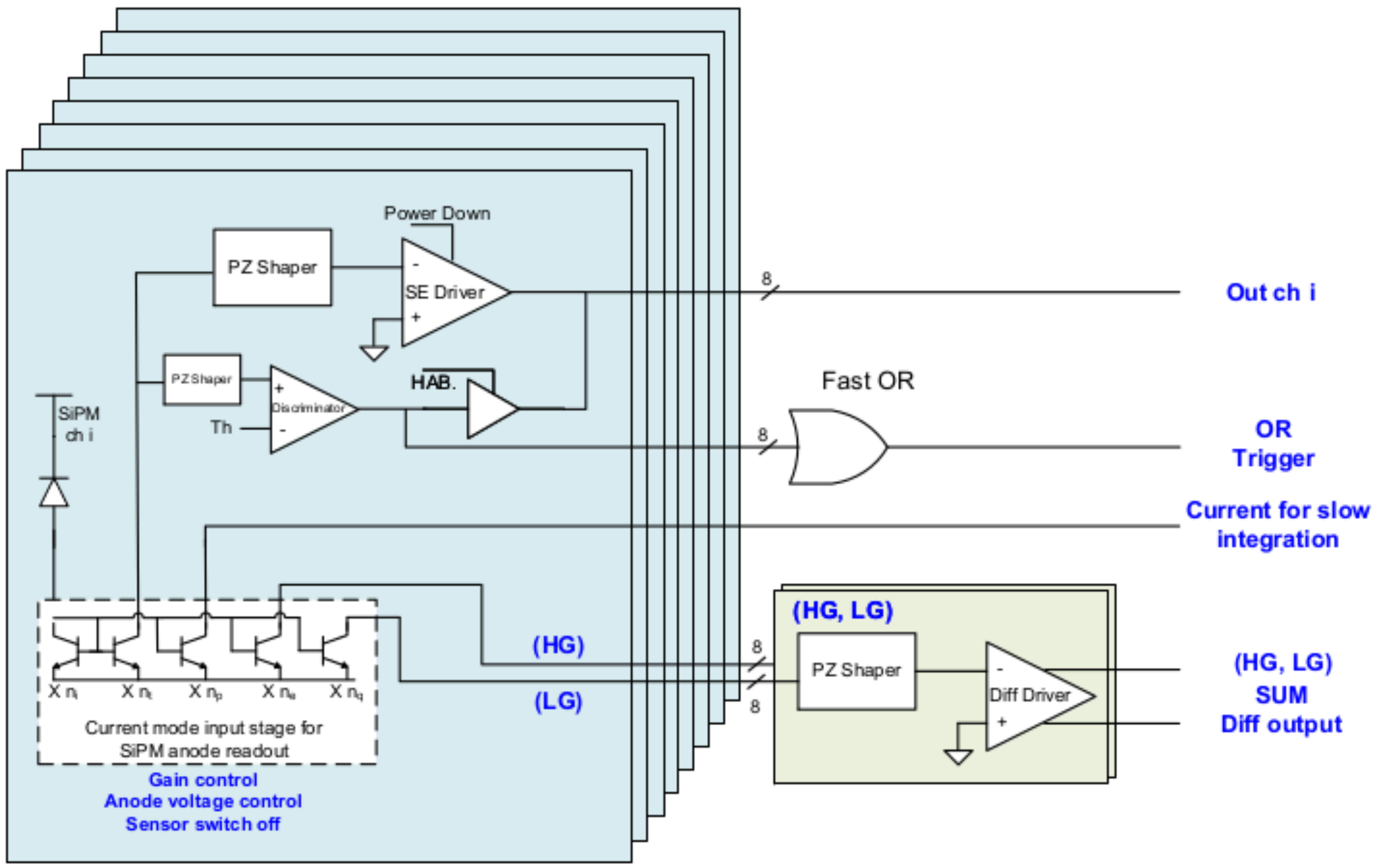


Figure 2: Functional block diagram.

8ch readout for SiPM

AND, OR functions implemented

Output signal:

Sum of the individual input channels + single ch output (signal shaping 5 ns FWHM)

Bandwidth: > 500 MHz for channel sum and 150 MHz for A/D channels

Power consumption: about 30mW per channel.

List of specifications
500MHz bandwidth for channel sum.
150MHz bandwidth for A/D channels.
Low input impedance ($\approx 32\Omega$).
Single photon output pulse width at half maximum (FWHM) between 5 and 10ns.
Power consumption of $\approx$30mW per individual channel.
Power consumption of $\approx$200mW for the 8 channel sum.
Adjustable input node DC voltage per channel.
High dynamic range (15bit) to operate SiPM at high over-voltage.
Zero components interface between sensor and device.
Total die size of 9mm^2 (3274μm x 2748μm).
64-QFN 9x9mm package.

STOPPING POWER

$$-\frac{dE}{dx} = 4\pi N_A r_e^2 m_e c^2 \rho \frac{Z_t}{A_t}\frac{Z_p^2}{\beta^2}\left[ln(\frac{2m_e c^2\beta^2\gamma^2}{I}) - \beta^2 - \frac{\delta}{2} - \frac{C}{Z_t}\right]$$

Bethe-Block equation