Advancing Proton Therapy with Prompt Gamma-Based Monitoring Methods

Aleksandra Wrońska
Jagiellonian University in Kraków
SiFi-CC group

https://bragg.if.uj.edu.pl/sificc

DeSyT2025 - International Workshop on Detection Systems and Techniques in Nuclear and Particle Physics

Catania, 24-26 February 2025

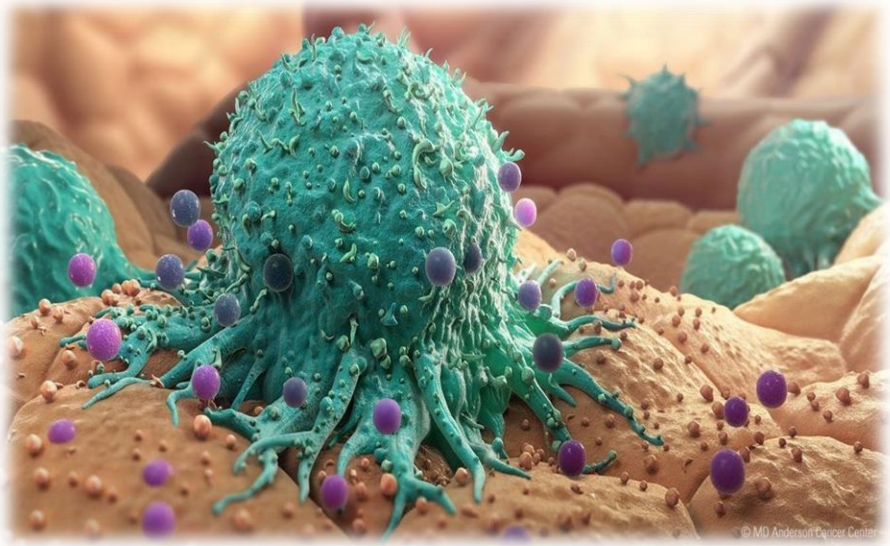
Cancer – a scare and a challenge

Statistics

- 1 in 4 deaths caused by cancer in the EU
- responsible for more than 35% of deaths among those aged less than 65, and under 25% amongst those aged 65 and over
- >3.7 million new cases and ~1.9 million deaths/year make cancer the second most important cause of death and morbidity in Europe
- main causes: tobacco and alcohol consumption, inappropriate diet, obesity and insufficient physical activity, longer life
- trend: increasing...

Treatment methods

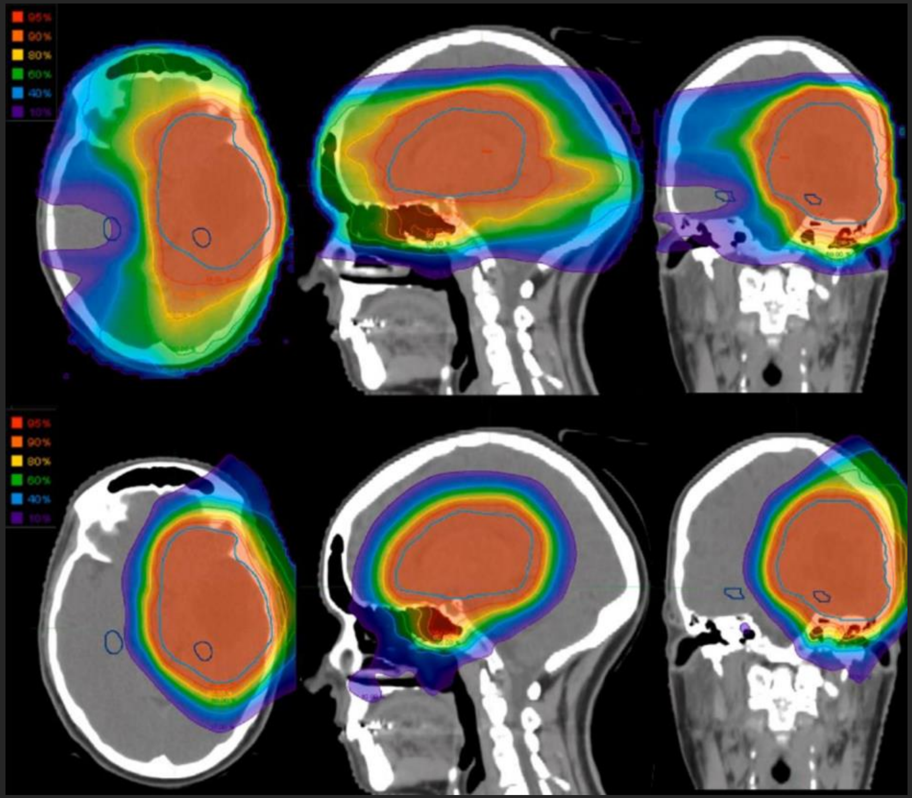
- Surgery
- Chemotherapy
- Radiotherapy
- Immunotherapy (Nobel 2018)



X-ray *versus* hadron therapy

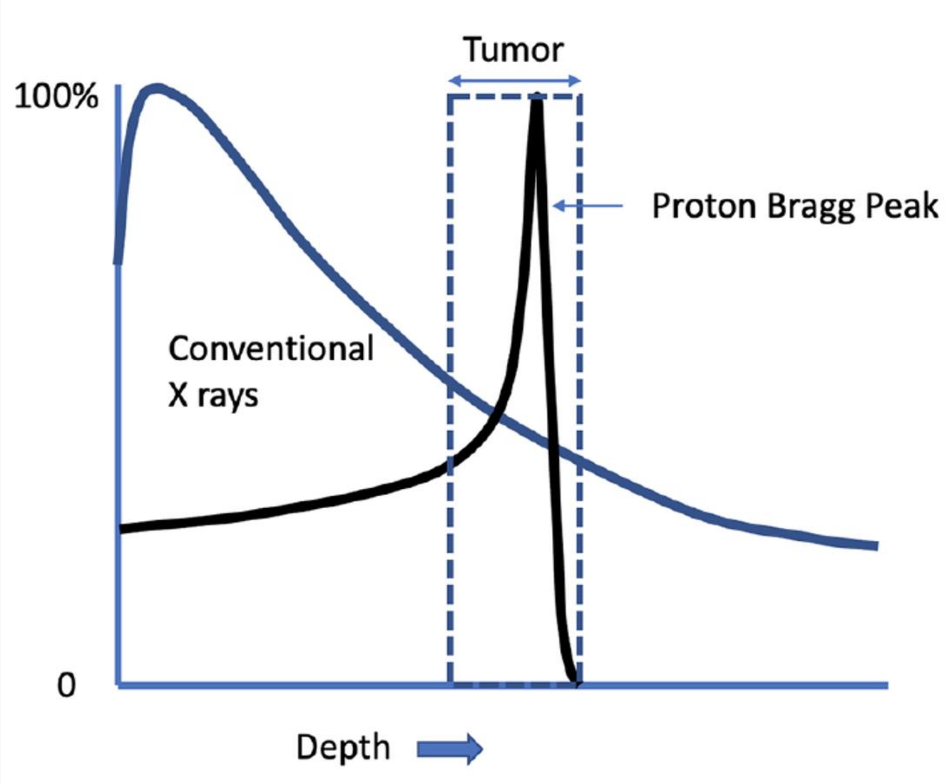
photons

protons



C. Byskov et al., 2021

- Tumour irradiation – important way of treatment
- Advantages of hadron therapy compared to X-rays:
  - Conformal dose distribution
  - Biological effectiveness



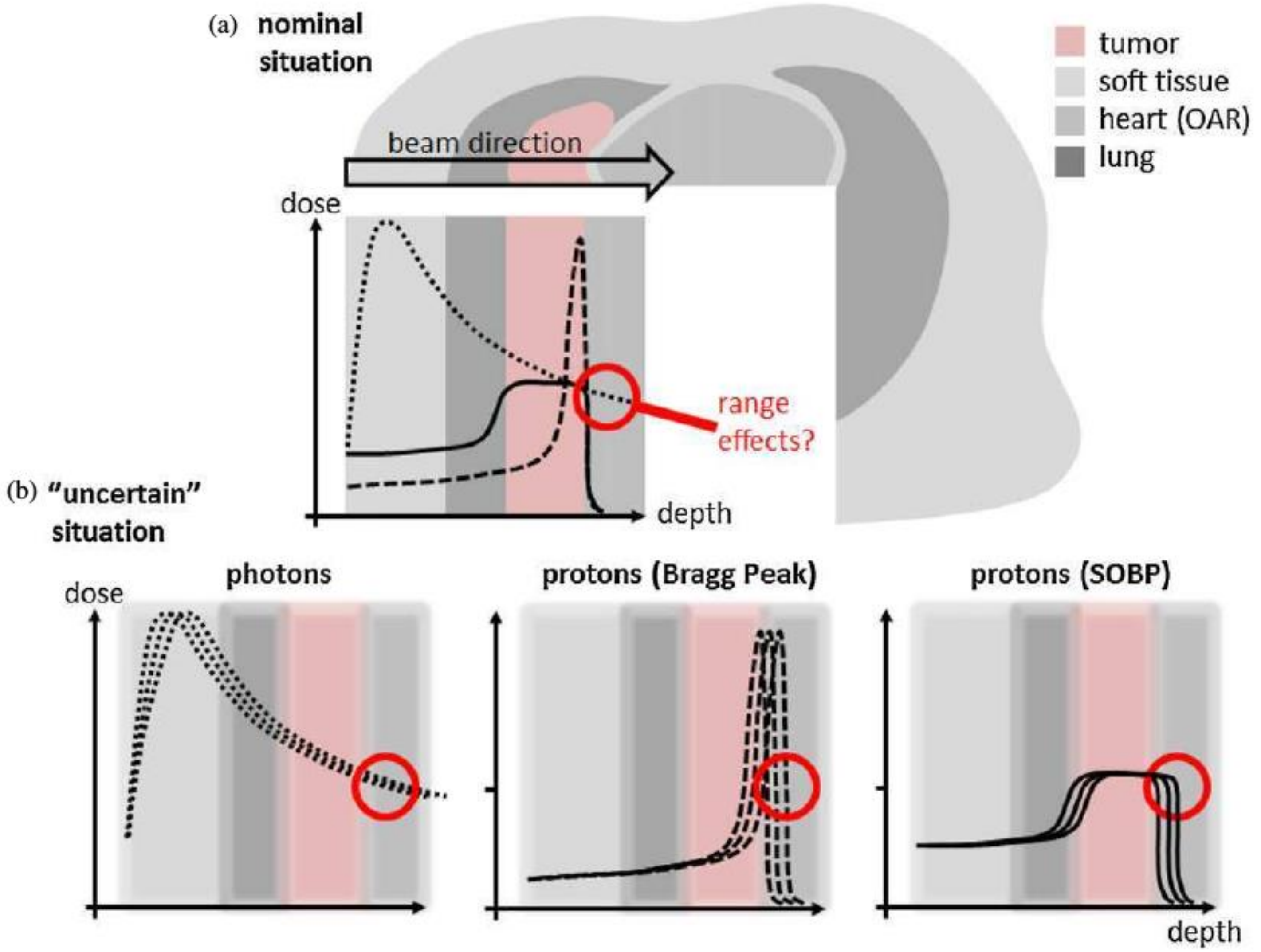
K. Lapen, Y. Yamada (2023)

Kraków proton therapy centre: Cyclotron Centre Bronowice

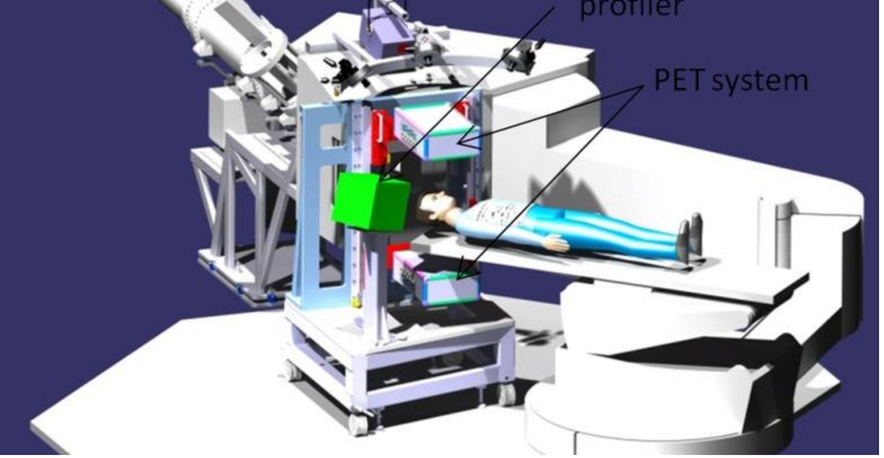
- Modern equipment, iba Proteus C235 cyclotron, 2 gantries + eye
- 2013 – first beam
- 2016 – first patient
- Experienced team
- Today: ~40 patients / day, including children

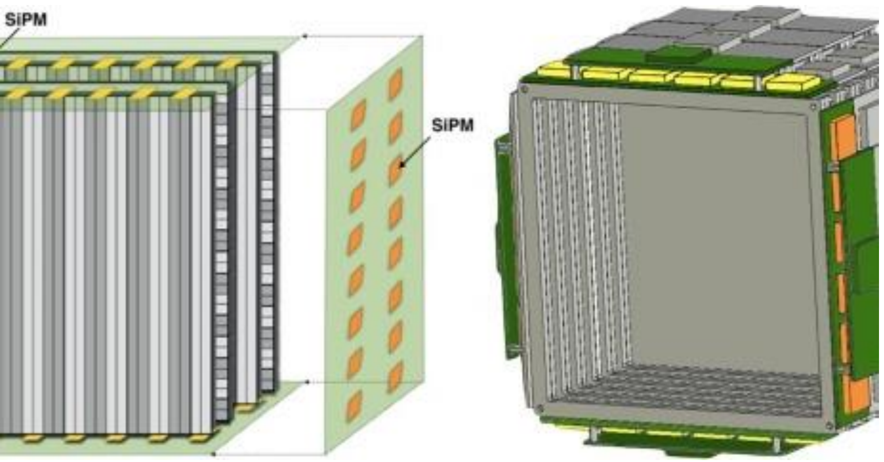
Can we do better in proton therapy?

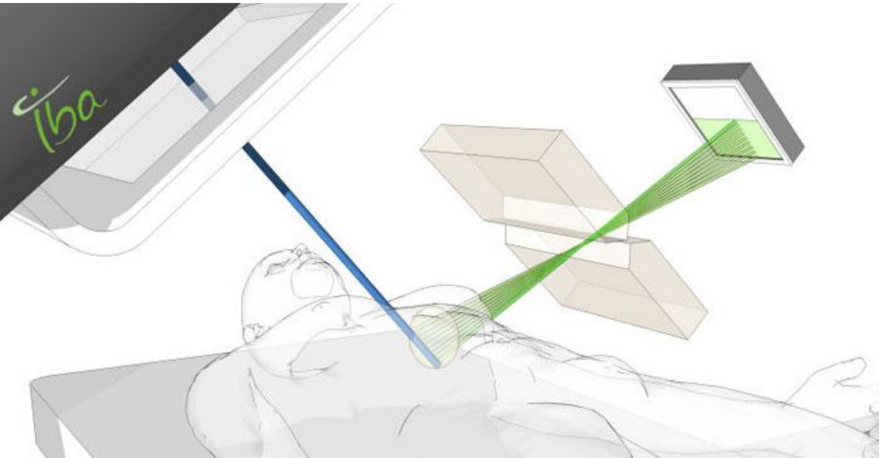
- Safety margins: from a few mm up to > 1 cm
  - Patient positioning
  - Anatomical changes
  - Infections
  - Uncertainties of treatment planning
- Reduction of margins?
- Online monitoring of therapy
  - Determination of Bragg peak position in real time, spot-by-spot
  - Maybe even spatial dose distribution...?
- Adaptive proton therapy



Knopf, Lomax, PMB 2013



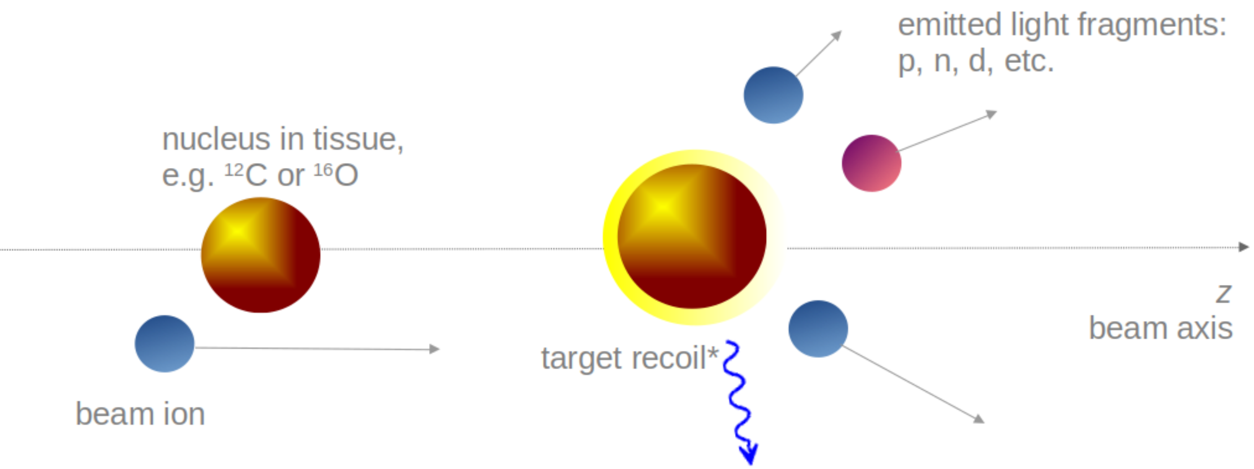




How to monitor PT?

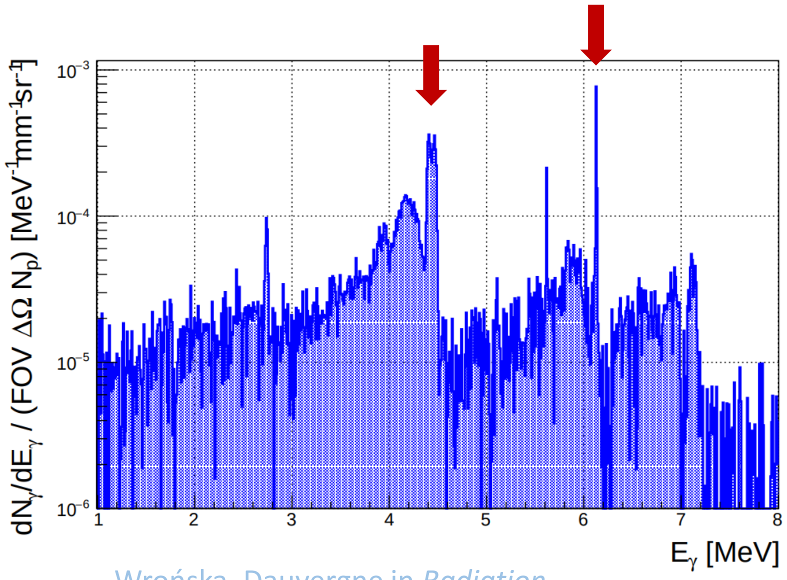
Secondary radiation correlated with dose distribution

- Protons, neutrons - useful in C-ion therapy:
  - Dose Profiler (CNAO, Pavia) Traini *et al.*, Physica Medica 65, 2019
  - MONDO (Frascati & Trento) Mirabelli *et al.*, *IEEE Trans. Nucl. Sci.* 65, 2018
- β+ emitters (PET):
  - INSIDE (CNAO, Pavia) Bisogni *et al.*, J. Med. Imaging 4, 2017
  - J-PET (UJ, Kraków) Baran *et al.*, MSS/MIC 2019
- Prompt-gamma radiation:
  - OncoRay+IBA (Dresden) Richter *et al.*, Radiotherapy and Oncology 1 118, 2016,
  - MGH Boston Hueso-Gonzalez et al., PMB 63, 2018, Xie *et al.* Int. J. of Rad. Oncol. Biol. Phys. 99 210 2017
  - Many others review: Wrońska, Dauvergne in *Radiation Detection Systems*, CRC Press 2021

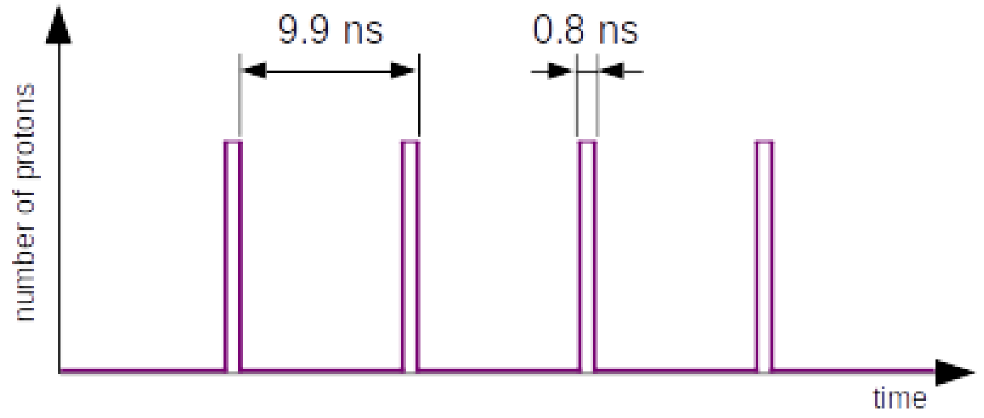


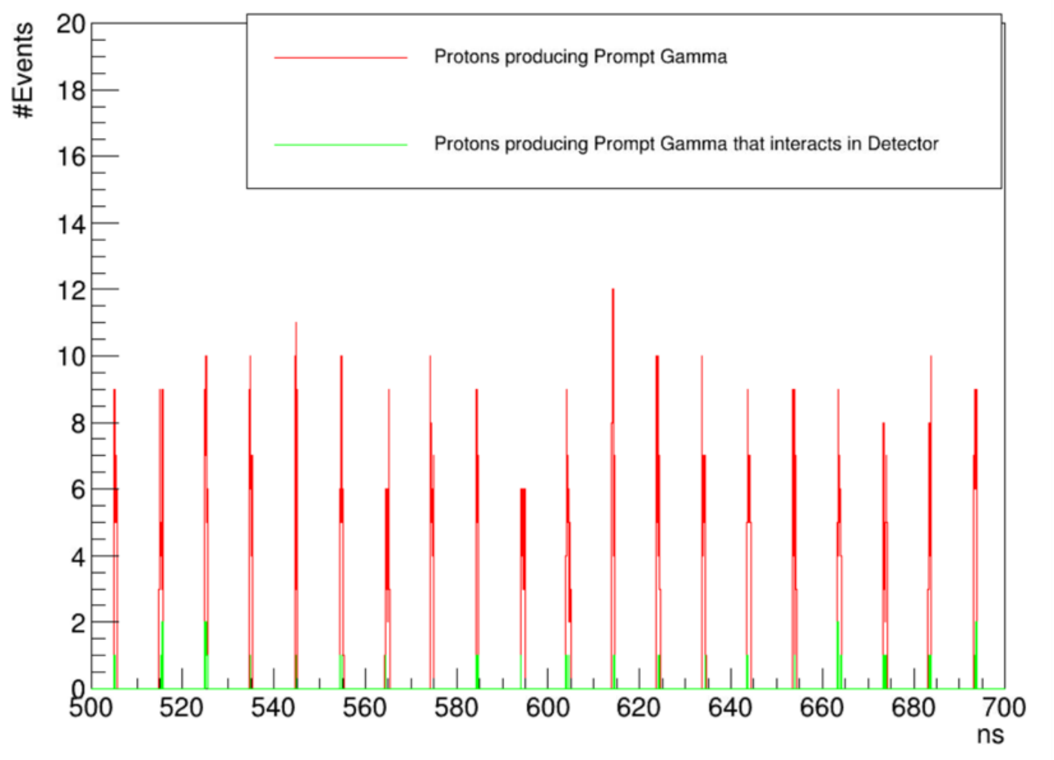
Prompt gamma (PG) – working conditions

- Large count rates ($n \times 10^5$ s^{-1})
- Background from other secondaries (neutrons)
- N_γ/N_p~0.15
- Energy range 1-7 MeV
  (continuum + discrete transitions)
- Typical spot: t=10 ms, N_p~10^8 => limited statistics!
- Detection system of large efficiency, rate capability and fast DAQ needed



Wrońska, Dauvergne in *Radiation Detection Systems*, CRC Press 2021





Prompt gamma (PG) – working conditions

- Large count rates (n×10^5 s^{-1})
- Background from other secondaries (neutrons)
- N_γ/N_p~0.15
- Energy range 1-7 MeV
  (continuum + discrete transitions)
- Typical spot: t=10 ms, N_p~10^8 => limited statistics!
- Detection system of large efficiency, rate capability and fast DAQ needed

PG in proton therapy monitoring

State of the art

- Beam range monitoring using a slit camera
- 1d information
- Tests in clinical conditions (Dresden, Boston)
  Richter et al, PMB, 2016
- Clinical trials

Dream

- Registeration of PG vertex distribution (Compton cameras)
  Draeger et al., PMB 63, 2018
  Barrientos et al.., Phys. Med. 117, 2024
  Koide et al.., Sci. Rep. 8, 2018
- "Translation" of this distribution to the spatial distribution of deposited dose
  Liu, Huang Physica Medica 69, 2020
- Full 3d information
- Difficult!

Trends

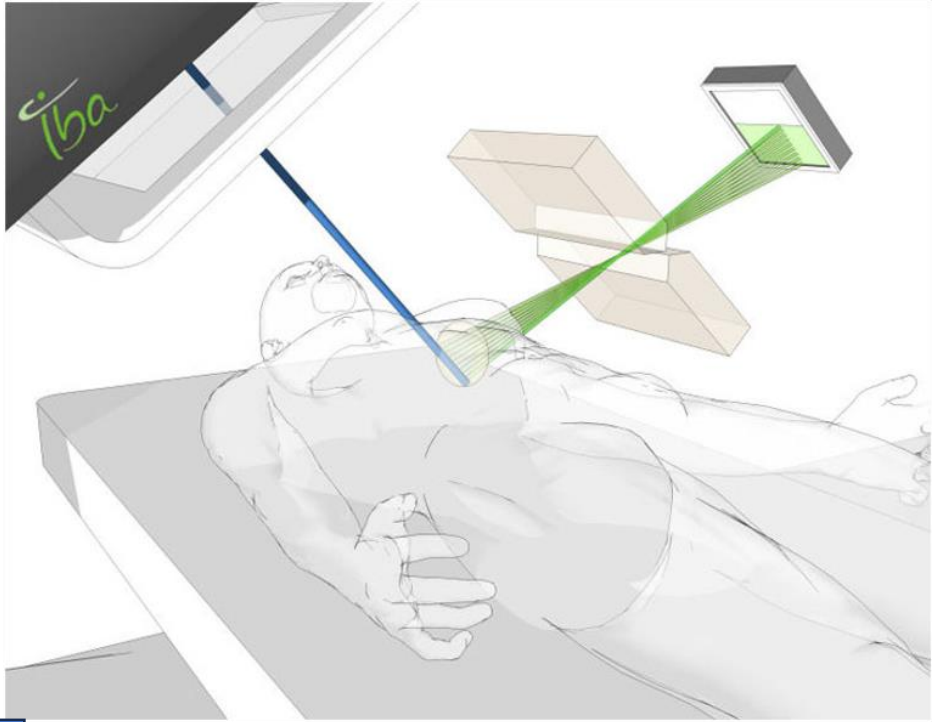
- Use simple, fast detectors
- Stick to simple observables
- Avoid image recon.

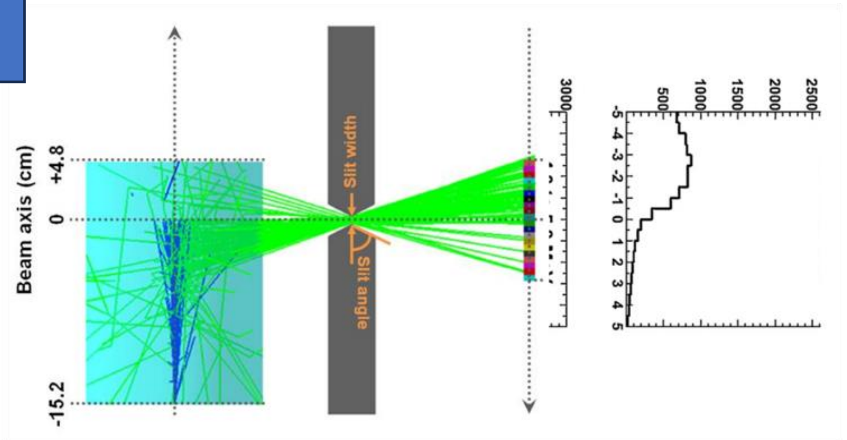
- PG spectroscopy
  Hueso-Gonzalez et al.. PMB 63, 2018
- PG timing
  Werner et al.. PMB 64, 2018
- PG peak integrals
  Krimmer et al.. Appl. Phys. Lett. 110, 2017
- PG energy integrals
  Everaere et al.. Front. Phys. 2024

Leaders – slit camera from Dresden

- Solution developed at Dresden/Rossendorf in collaboration with IBA
- A scintillation gamma camera with a knife-edge-shaped slit, fixed position
- 1d information
- First clinical test: 2016
  Richter et al., Radiotherapy and Oncology 1 118 , 2016
- Now: second setup version
- Overall range prediction validaton uncer 1 mm (2σ) Berthold et al, IJROBP 111 , 2021
- ...but per spot "only" 2 mm (1σ)
- Consequence: reduction of safety margins from 7 to 3 mm in prostate cancer patients
  Bertschi et al, PIRO 26 , 2023
- Ongoing clinical trial

Statistically driven. Could be improved with more PG used!





Smeets et al., Phys Med Biol 57 (2012)

The group

The project SiFi-CC is a joint effort of the group:


Aleksandra Wrońska[1] — PI, professor


Magdalena Rafecas[5] — professor


Jorge Roser[5] — post-doc


Katarzyna Rusiecka[1] — post-doc


Achim Stahl[2] — professor


Mark Wong[1] — post-doc


Vitalii Urbanevych[1] — post-doc

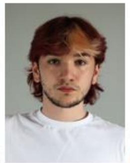

Magdalena Kołodziej[1] — PhD student


Monika Kercz[1] — PhD student


Gabriel Ostrzołek[1] — Master student


Philippe Clement[1,2] — Master student


Mikołaj Dubiel[1] — Master student


Szymon Machura[1] — Bachelor student


Dominik Szubartowski[1] — Bachelor student

Associated researchers:


Ronja Hetzel[6, formerly 2] — post-doc

Former members, also those working on the gCCB project:

Awal Awal[2], Piotr Bednarczyk[3], Anna Bekas[1], Andreas Bolke[5], Daniel Böckenhoff[2], Arshiya Anees Ahmed[1], Arkadiusz Bubak[4], Richard Chomjak[1], Michelle Dombeu[2], George Farah[2] Sabine Feyen[2], Grzegorz Gazdowicz[1], Aleksandra Kaszlikowska[1], Majid Kazemi Kozani[1], Laurent Kelleter[2], Jonas Kasper[2], Nadia Kohlhase[5], Barbara Kołodziej[1], Adam Konefał[4], Wojciech Kozyra[1], Karim Laihem[2], Rafał Lalik[1], Johannes Leidner[2], Andrzej Magiera[1], Sara Müller[2], Grzegorz Obrzud[1], Marek Pałka[1], Mareike Profe[2], Damian Stachura[1], Szymon Świstun[1], Aneta Wiśniewska[1], Anna Władyszewska[1], Mirosław Ziębliński[3] Alexander Fenger[2] Linn Mielke[2]

[1]Institute of Physics, Jagiellonian University, Kraków [2]III. Physikalisches Institut B, RWTH Aachen University, Aachen [3]Institute of Nuclear Physics PAN, Kraków [4]University of Silesia, Katowice [5]Institute of Medical Engineering, University of Lübeck [6]Biophysics Department, GSI Helmholtzzentrum für Schwerionenforschung GmbH, Darmstadt

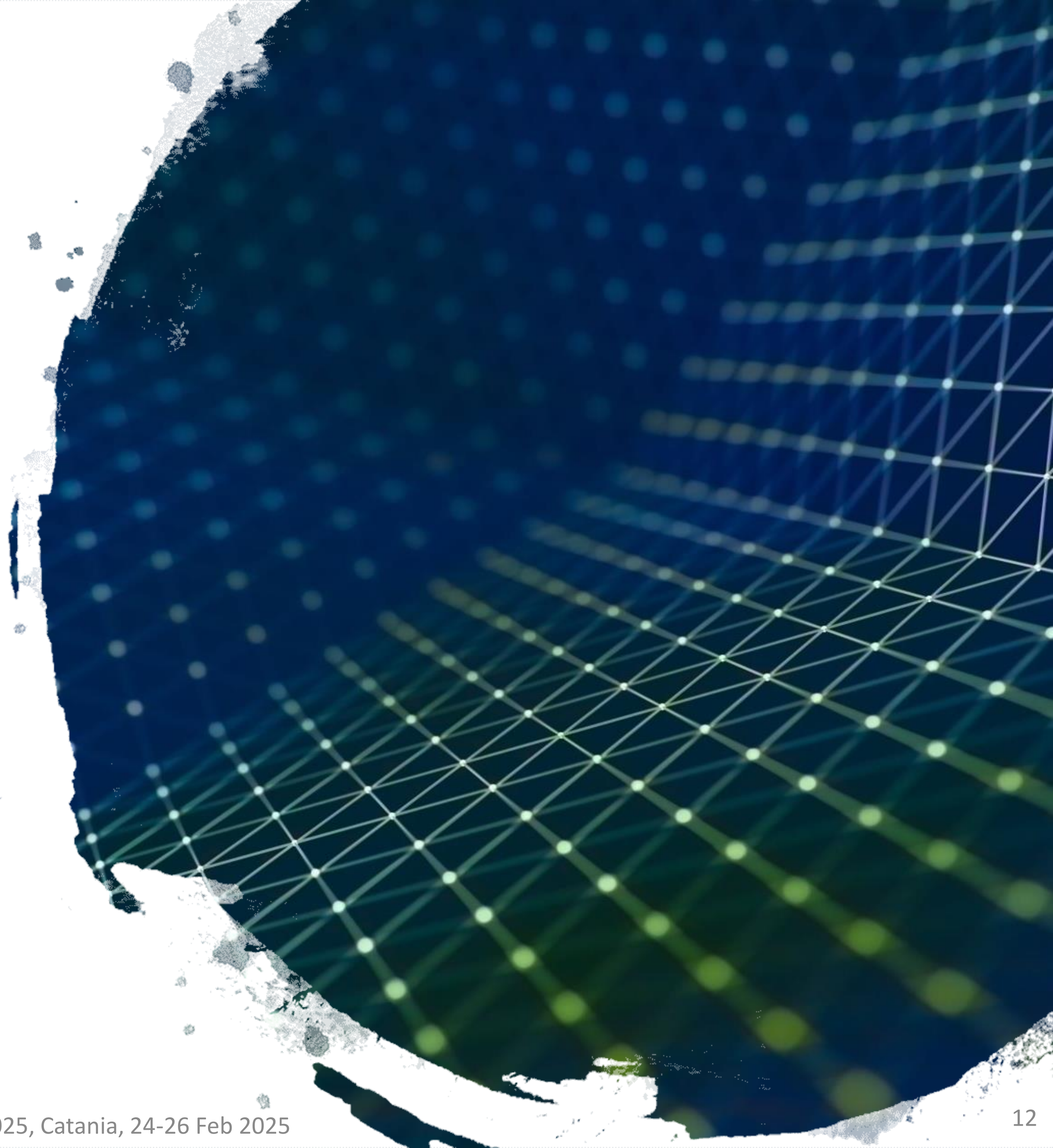
SiFi-CC

PG – our activities

γCCB: characterization of **PG – experiments**

Monte-Carlo simulations + validation

SiFi-CC setup for beam range monitoring



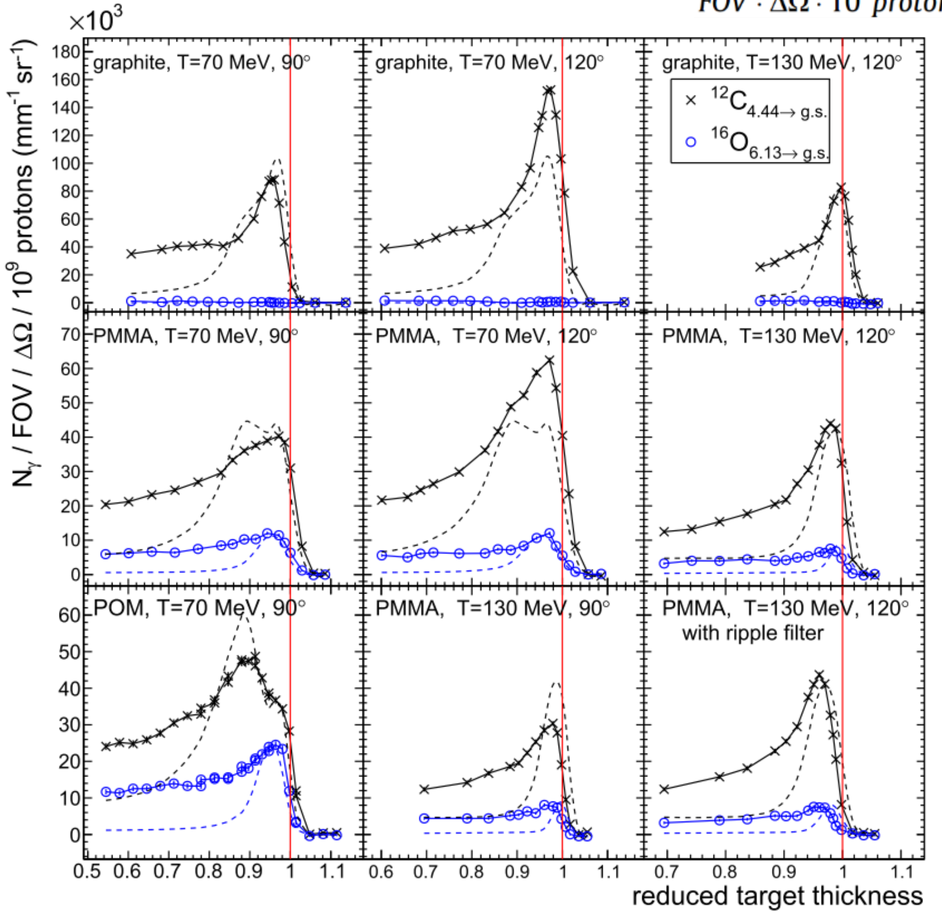
γCCB – experimental characterization of PG

$$\frac{N_\gamma}{FOV \cdot \Delta\Omega \cdot 10^9 protons}(\theta,z) = \frac{g(z) N_t}{FOV} \int \frac{d\sigma}{d\Omega}(\theta,E) f(E) dE$$

Beam attenuation from GEANT

Energy dependent angular distributions **from TALYS**

Proton energy distribution at given depth from GEANT



- Experiments: CCB, HIT, CCB
- Spectroscopy HPGe detector with ACS
- Phantoms with different elemental composition
- T_p=70, ..., 230 MeV
- Different detection angles
- Focus: lines 4.44 MeV and 6.13 MeV
- Results confronted with TALYS and literature data
- Details of correlation PG-dose

Kelleter, Wrońska et al., Physica Medica 34, 2017
Wrońska et al., Acta Phys. Pol. B 48, 2017
Wrońska, Kasper et al., Physica Medica 88, 2021

γCCB – validation of simulations

- Comparison of simulated and measured PG emission from a PMMA phantom irradiated with proton beam
- Various G4 versions and physics lists
- Newest not always means best...
- Best match for G4 v10.4.2, QGSP_BIC_HP
- Theoretically better QGSP_BIC_AllHP does not reproduce line shapes
- ...but best match also has issues (unphysical lines in spectrum)

GEANT4
A SIMULATION TOOLKIT

Beam energy (MeV)	Proton range (mm)	Beam current (nA)	Facility
70.54	35.06	0.5	HIT
130.87	105.46	0.5	HIT
130	104.23	50	CCB
180	184.10	10	CCB
230	280.35	1.5	CCB

Physics list	GEANT4 version	Label
QGSP_BIC_HP	10.4.2	A*
	10.5.1	B*
	10.6.3	C*
	10.7.1	D*
QGSP_BIC_AllHP	10.6.3	C•
	10.7.1	D•

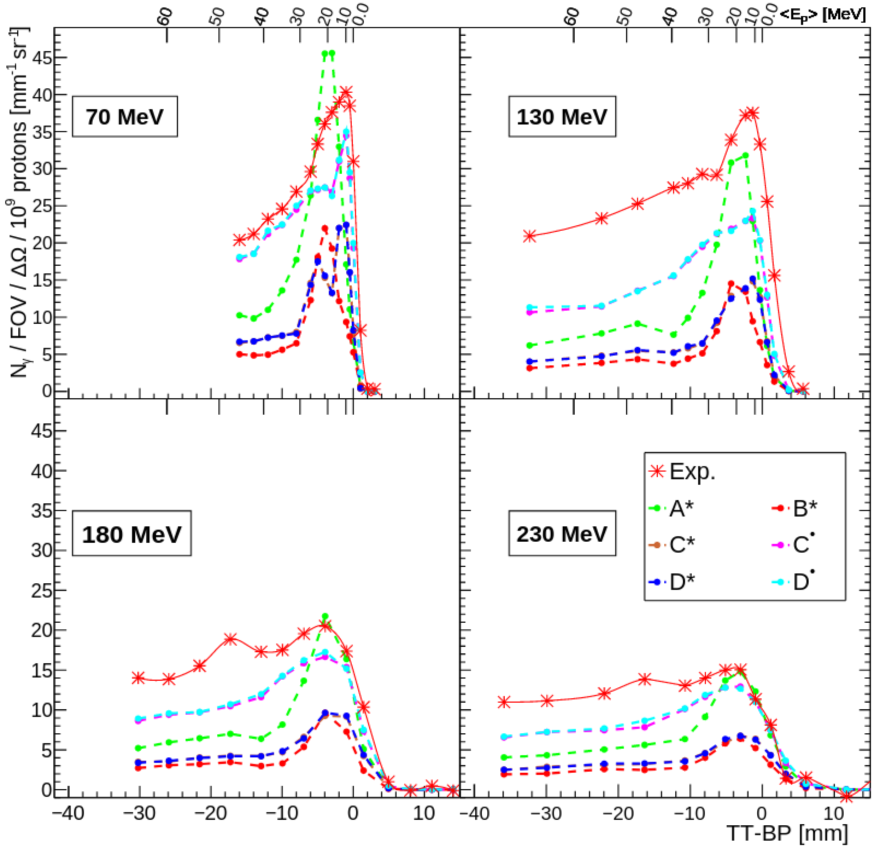
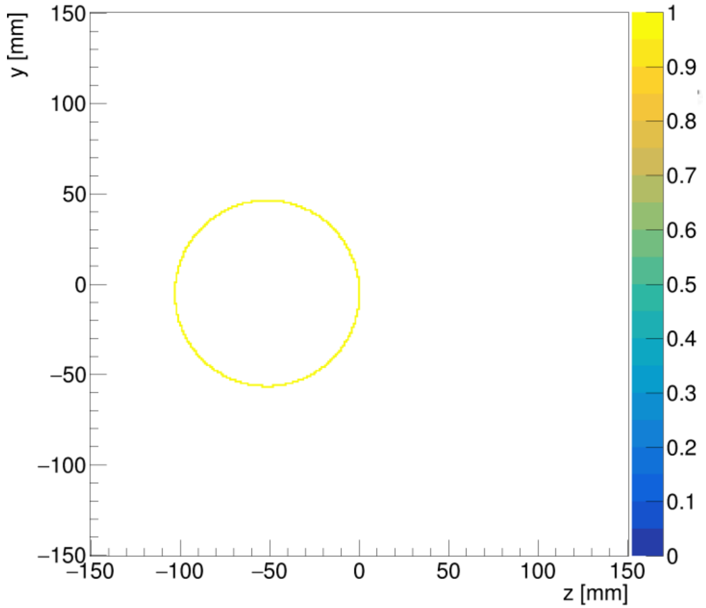


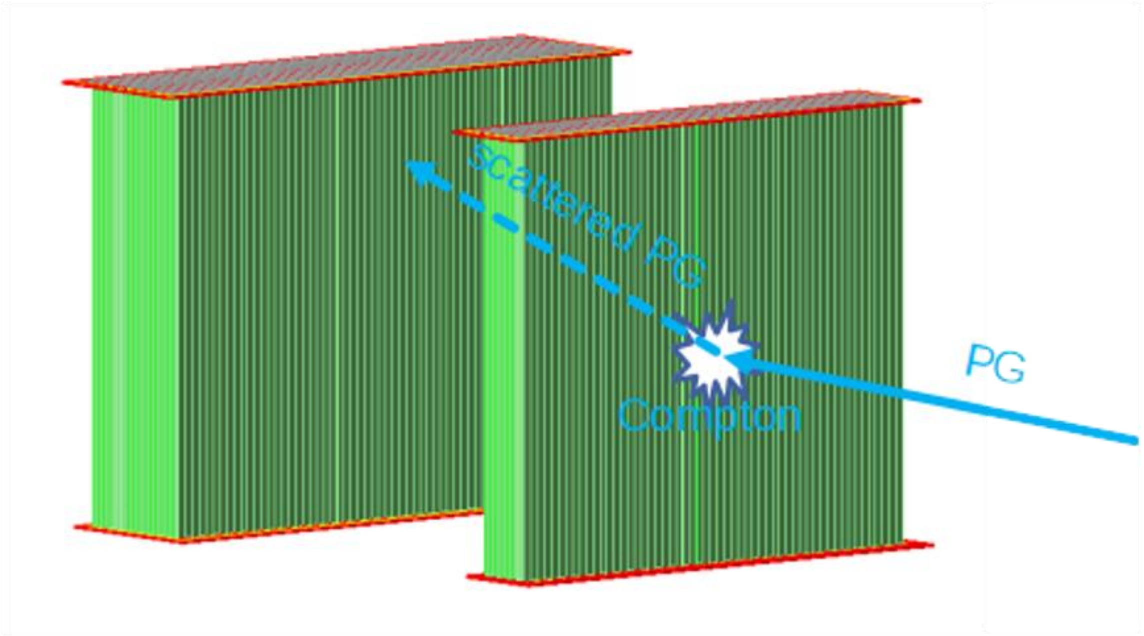
Figure 7: Comparison of gamma emission depth profiles for the 4.44 MeV line obtained from the simulations and the experiments for the beam energies 70 MeV, 130 MeV, 180 MeV and 230 MeV.

Wrońska, Kasper et al., Physica Medica 88, 2021



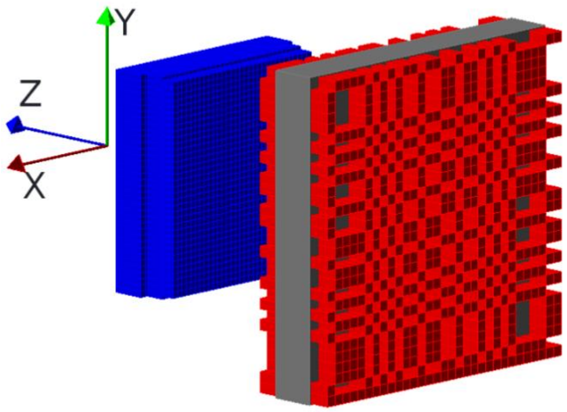
SiFi-CC: Compton camera for PGI

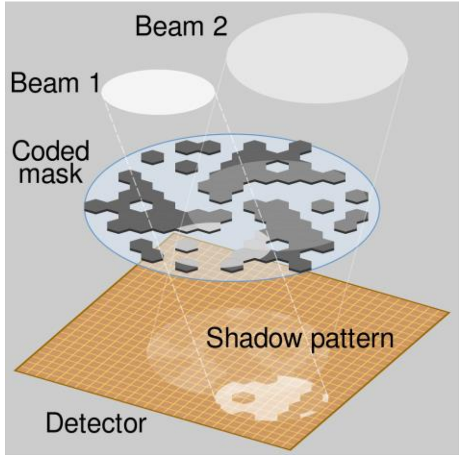
- **Si**PM and scintillating **Fi**bers based **C**ompton **C**amera
- Arrays of LYSO fibres => large efficiency
- 1mm x 1mm x 100 mm (small prototype)
  2mm x 2mm x 100 mm (full-scale)
- Dual readout via SiPMs:
  - 1:1 coupling (small)
  - 4:1 coupling (full-scale)
- Granularity => ~~pile-up~~ !
- DAQ with selective coincidence trigger => large data throughput



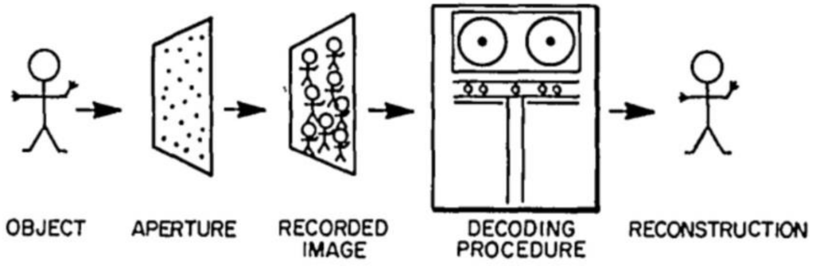
L. Mielke, M.Sc.. thesis, RWTH Aachen, 2024

By-product: coded-mask setup (CM)





By Cmglee - Own work,
https://commons.wikimedia.org/w/index.php?curid=47569900



E. E. Fenimore and T. M. Cannon, Coded aperture imaging with uniformly redundant arrays, Appl. Opt. 17, 337-347 (1978)

- Technique used in astronomy, also for γ sources (far field)
- So far not tested experimentally for PT   Sun *et al.*, Rad. Phys. Chem. 174 (2020)
- 2d image
- Larger statistics than in a single-aperture camera
- **Will this work for the near field?**

SiFi-CC - prototyping

- Investigation of fibre properties
  - Energy resolution?
  - Position resolution (along the fibre)?

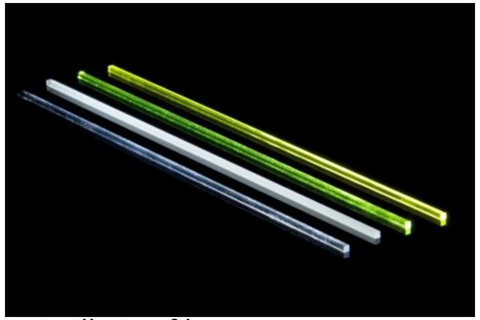
  Rusiecka *et al.*, ISMART2018 (Springer)
  Rusiecka et al., JINST 16, 2021
- Construction of a small module prototype
  - 4 layers
  - 64 fibres
  - re-arrangable

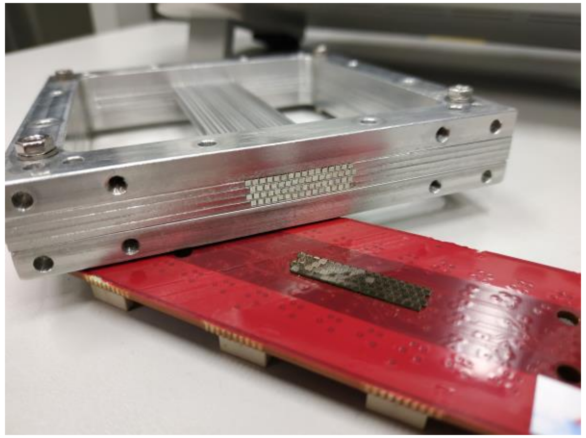
  Rusiecka, PhD thesis in preparation, Jag. Uni. 2022
- Data analysis software

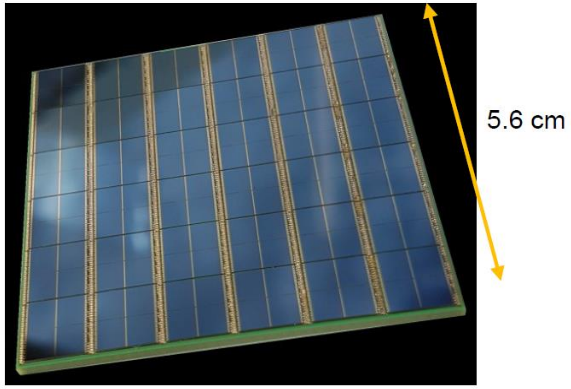
  J. Kasper, PhD thesis, RWTH Aachen 2022
- Image reconstruction software

  Kohlhase *et al.*, IEEE Trans. Rad. Plas. Med. Sci. 4, 2020
- FEE+DAQ – classical/digital SiPMs

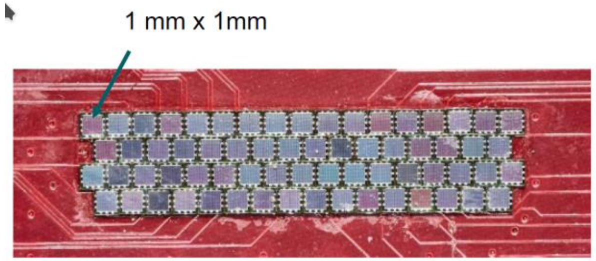
  Schug, Schulz *et al.*, PMB 61, 2016


Scintillating fibres

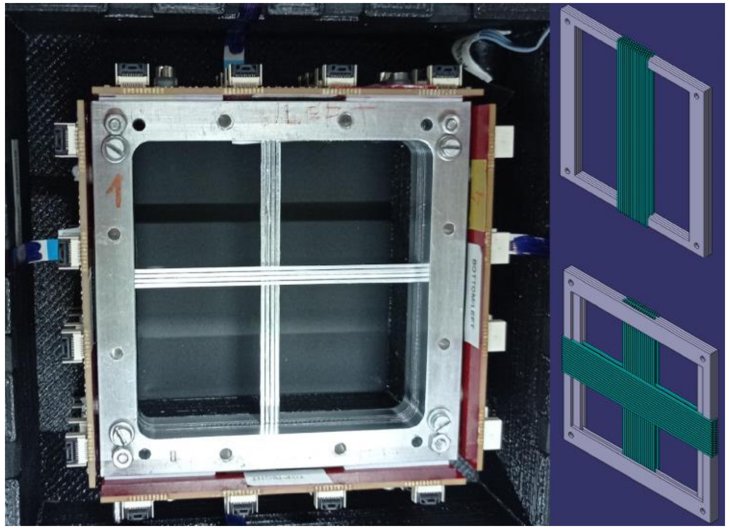




PMI Power Tile Phillips, digital SiPMs

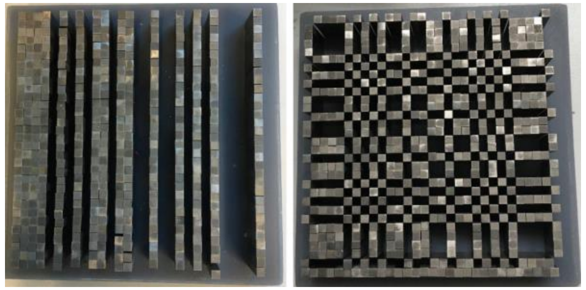


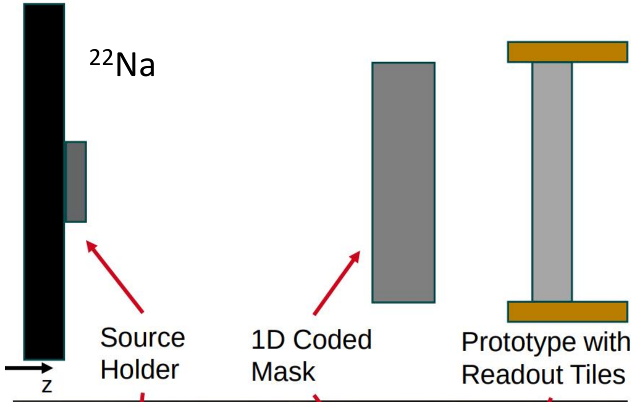
Classical SiPMs custom array

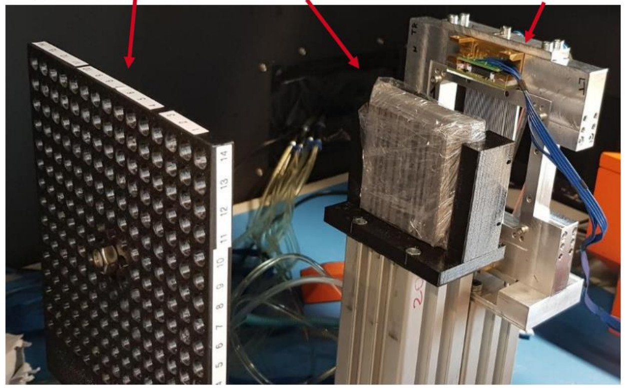


SiFi-CC – setup lab tests

- Calibration
- Collective effects (optical cross-talk)
- Test CM setup
    - **1d** with our prototype + PowerTiles
    - **2d** with PET stack + PowerTiles
    - This works!
    - Next step: continuous source

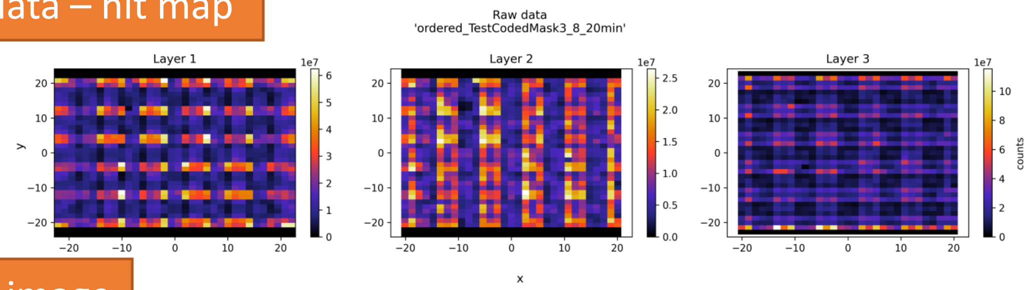




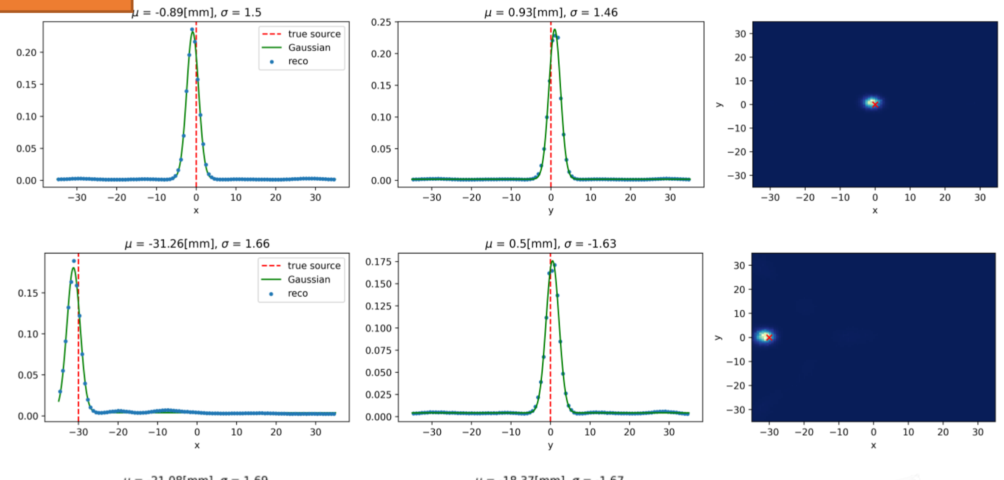


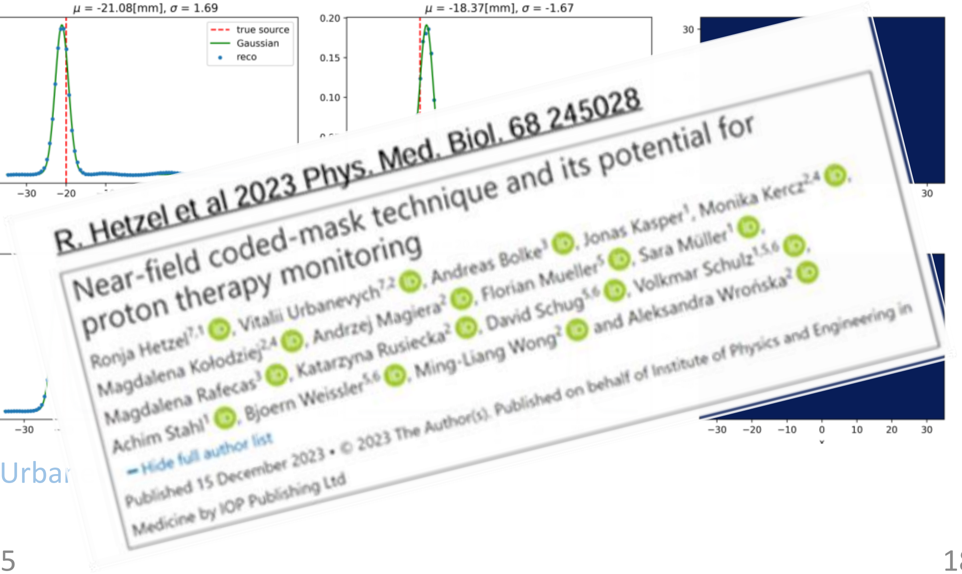
S. Müller, DPG SM 2022

Raw data – hit map



Reco image




R. Hetzel et al 2023 Phys. Med. Biol. 68 245028

Near-field coded-mask technique and its potential for proton therapy monitoring

Ronja Hetzel, Vitalii Urbanevych, Andreas Bolke, Jonas Kasper, Monika Kercz, Magdalena Kołodziej, Andrzej Magiera, Florian Mueller, Sara Müller, Magdalena Rafecas, Katarzyna Rusiecka, David Schug, Volkmar Schulz, Achim Stahl, Bjoern Weissler, Ming-Liang Wong and Aleksandra Wrońska

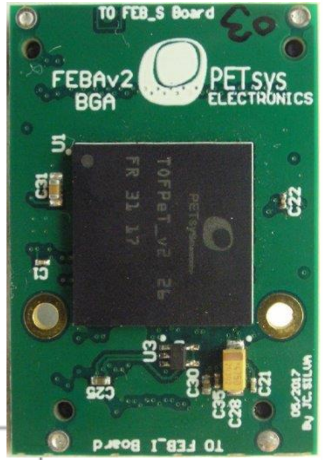
Hide full author list

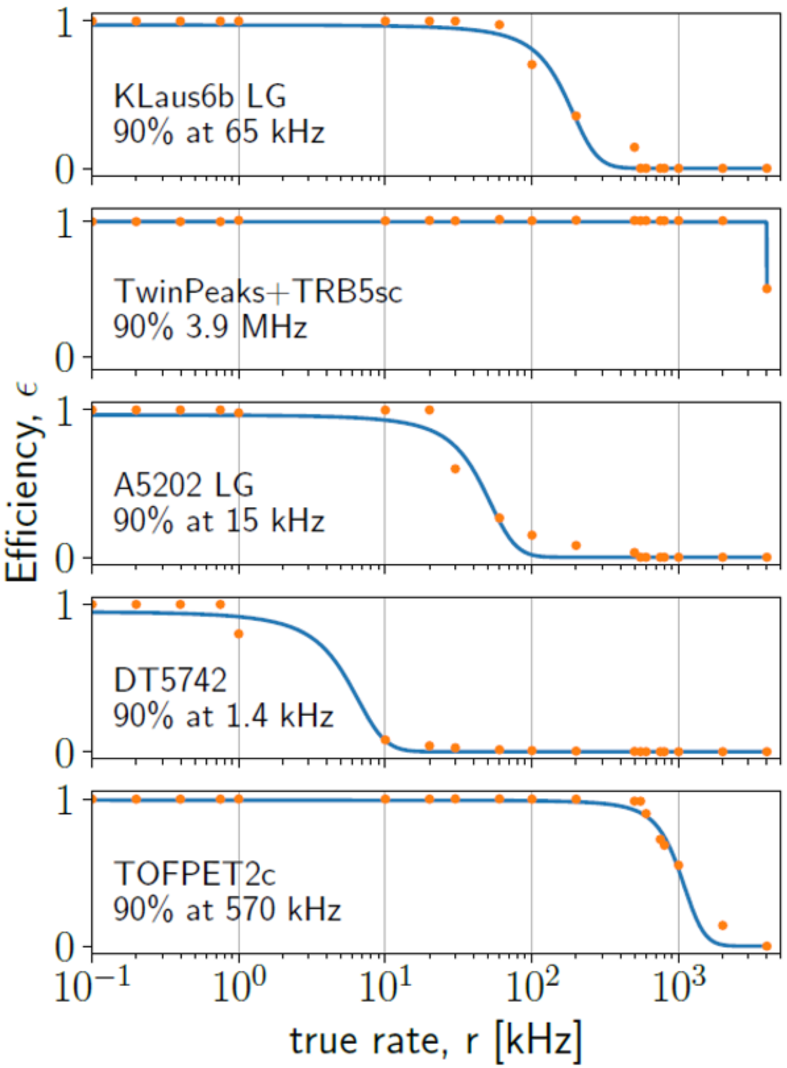
Published 15 December 2023 • © 2023 The Author(s). Published on behalf of Institute of Physics and Engineering in Medicine by IOP Publishing Ltd

V. Urbar

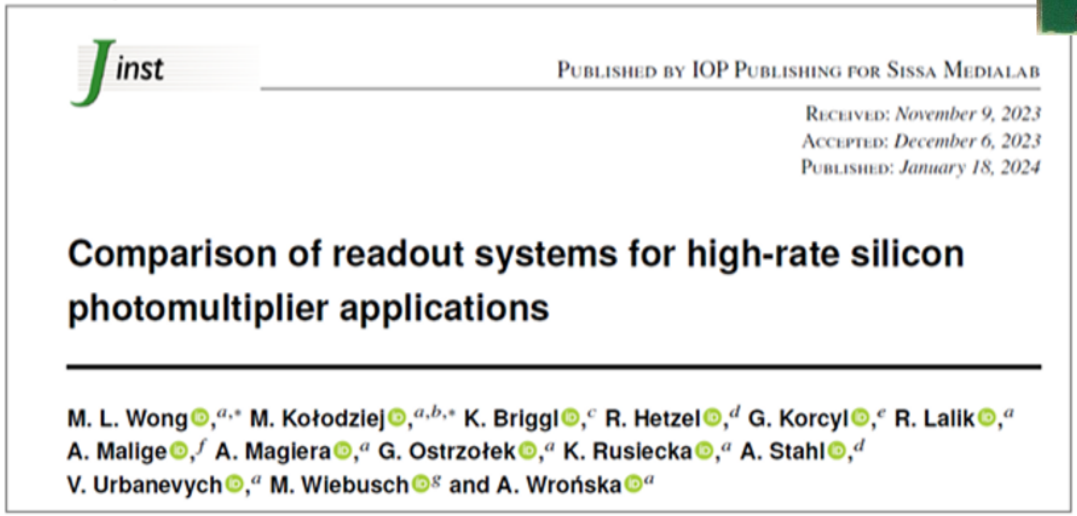
FEE+DAQ – comparative studies

- 5 FEE+DAQ systems: TOFPET2c, A5202, KLauS6b, TwinPeaks+TRB5sc, DT5742
- Compared features:
  - energy & time resolution
  - dead time
  - efficiency
  - dynamic range





Wong, M.-L. et al. (2024). JINST 19 P01019

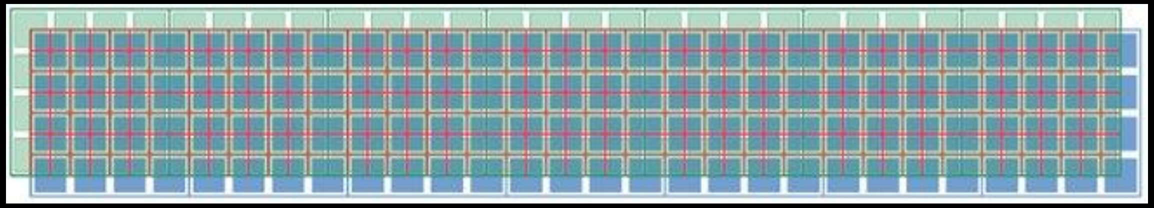


Jinst
PUBLISHED BY IOP PUBLISHING FOR SISSA MEDIALAB
RECEIVED: November 9, 2023
ACCEPTED: December 6, 2023
PUBLISHED: January 18, 2024

Comparison of readout systems for high-rate silicon photomultiplier applications

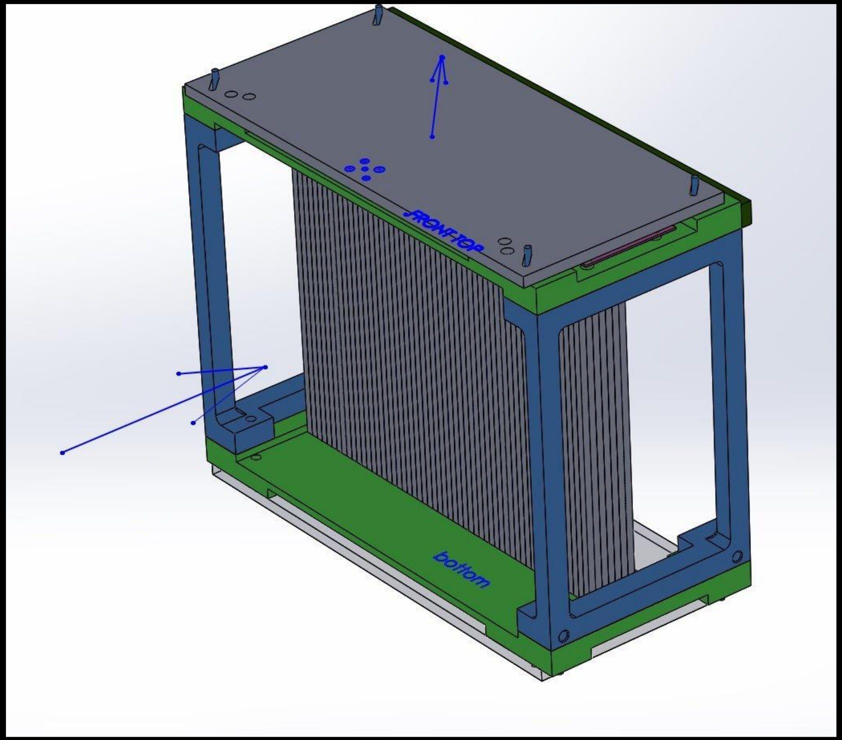
M. L. Wong[a,*] M. Kołodziej[a,b,*] K. Briggl[c] R. Hetzel[d] G. Korcyl[e] R. Lalik[a] A. Malige[f] A. Magiera[a] G. Ostrzołek[a] K. Rusiecka[a] A. Stahl[d] V. Urbanevych[a] M. Wiebusch[g] and A. Wrońska[a]

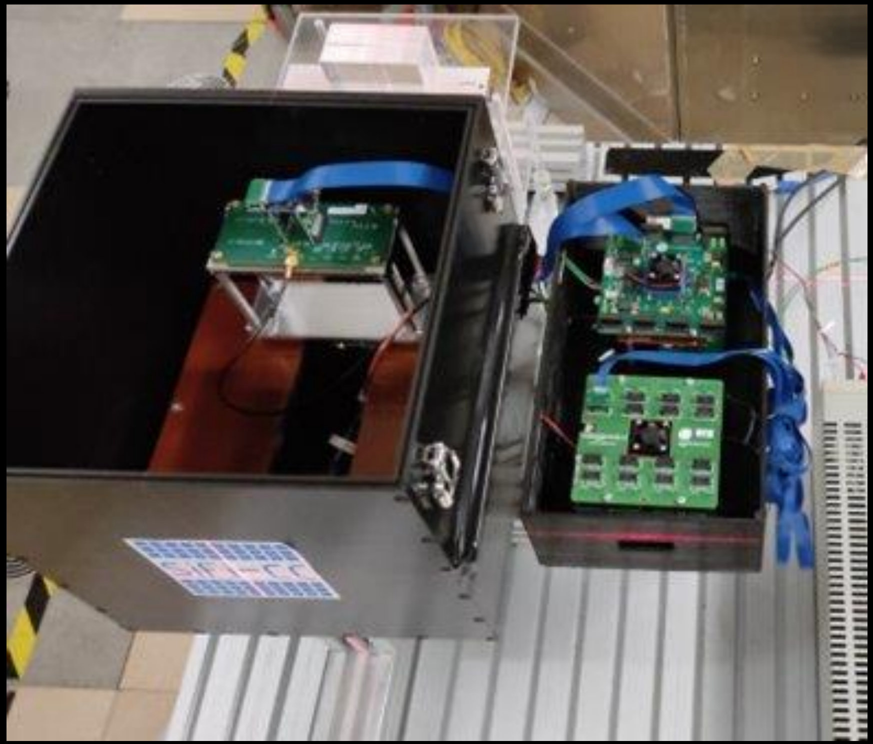
First detector module

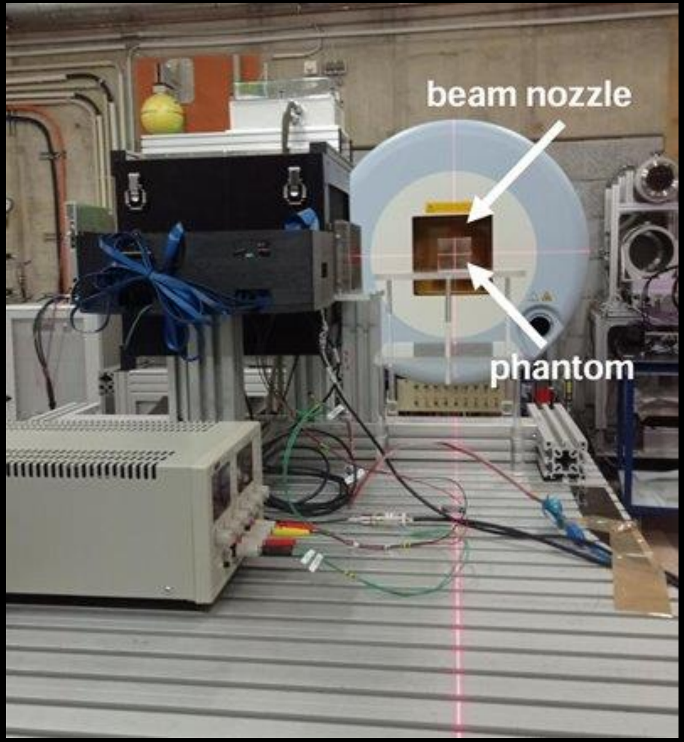


Top and bottom SiPM boards shifted diagonally by half pitch

- First module - scatterer
- 7 layers of LYSO fibers, 55 fibers in each layer + Al wrapping
- Fiber pitch 2 mm
- Broadcom SiPM arrays (4 x 4 pixels, 16 x 16 mm^2) mounted on custom PCBs
- DAQ: TOFPET2 by PETsys
- Tested with the proton beam at HIT in coded mask mode (1D and 2D)

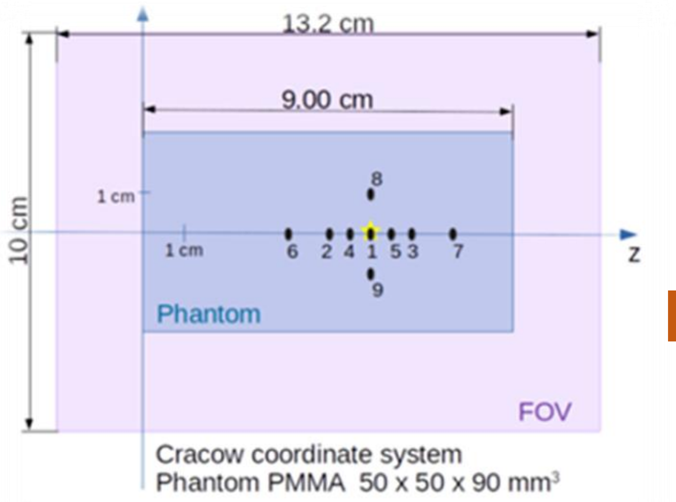


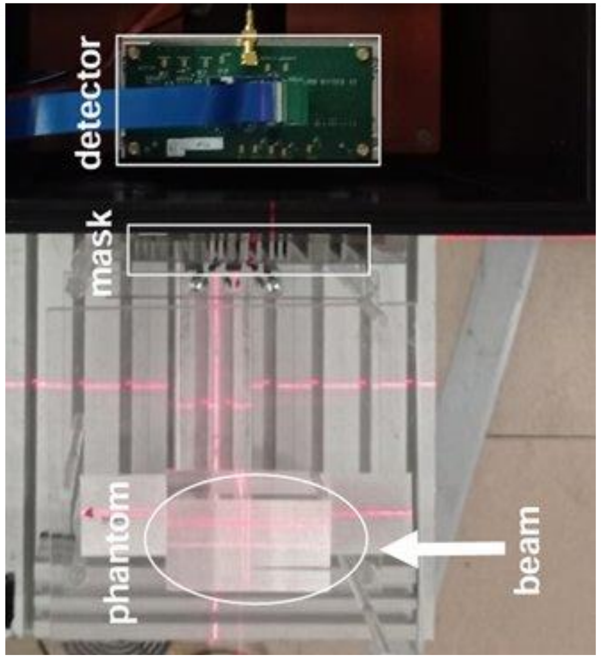




First tests with a proton beam at HIT

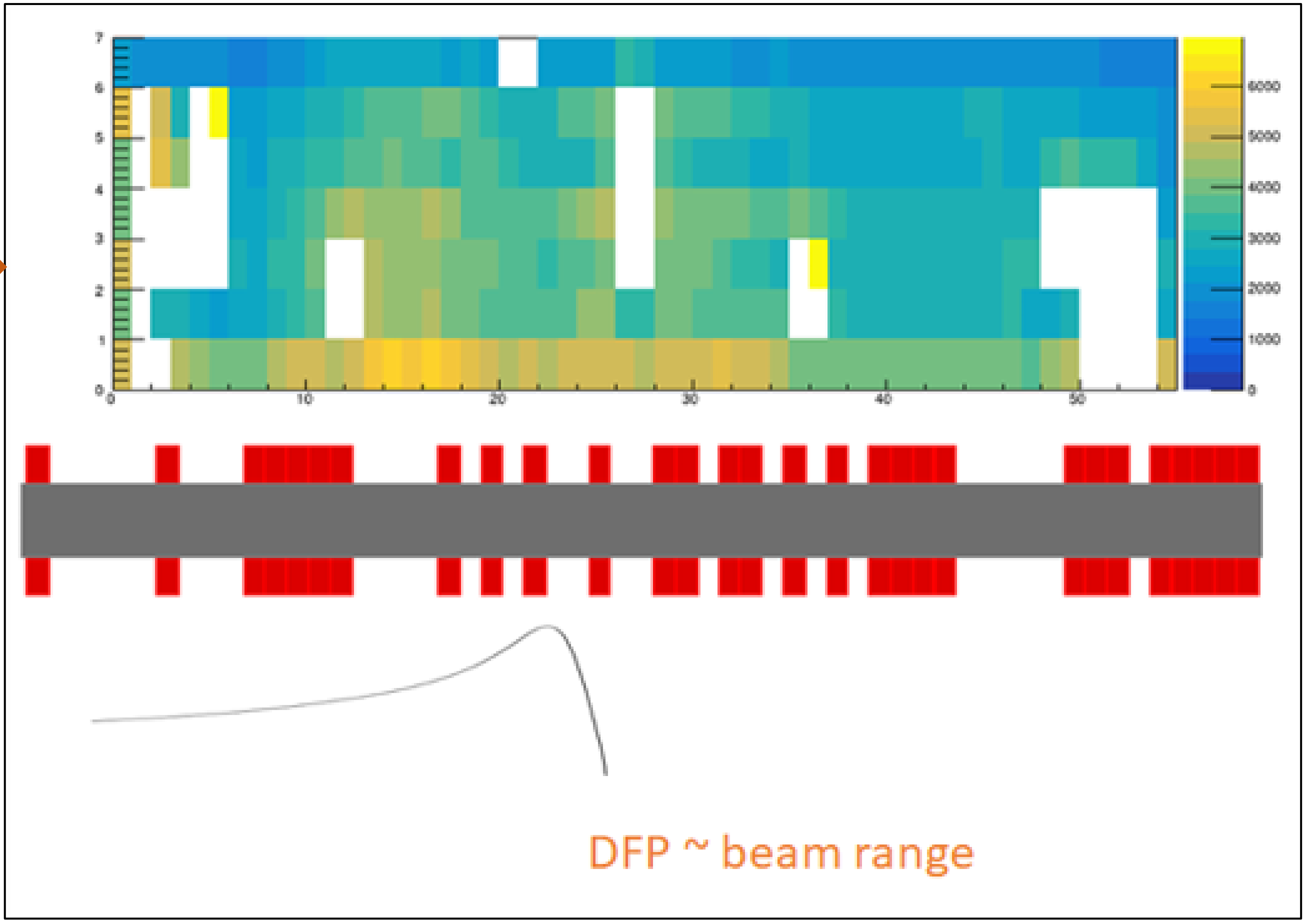
Irradiation plan:





measurement

Hit map - input for MLEM algorithm



First tests with a proton beam at HIT

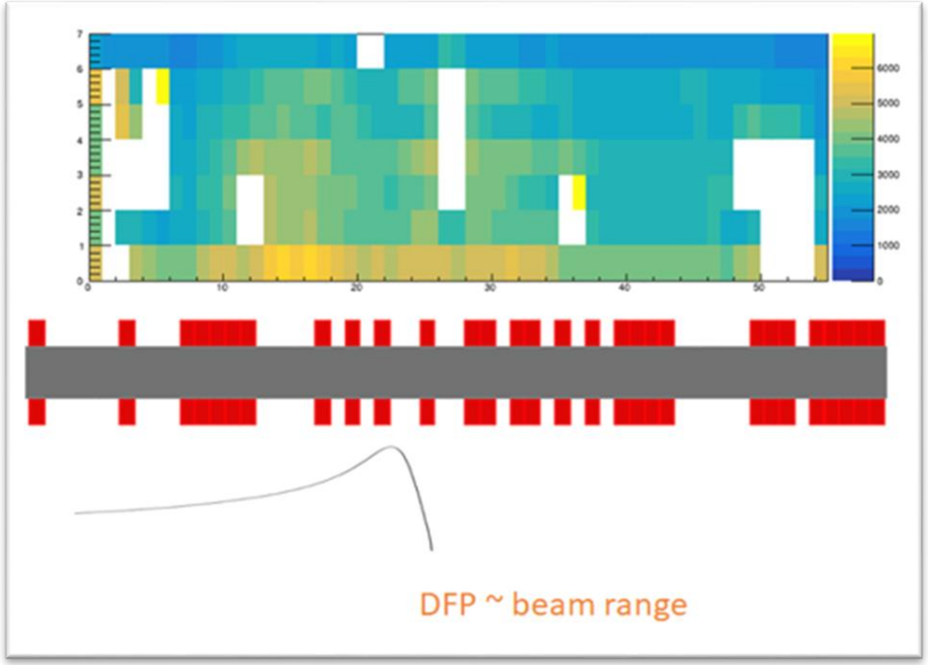
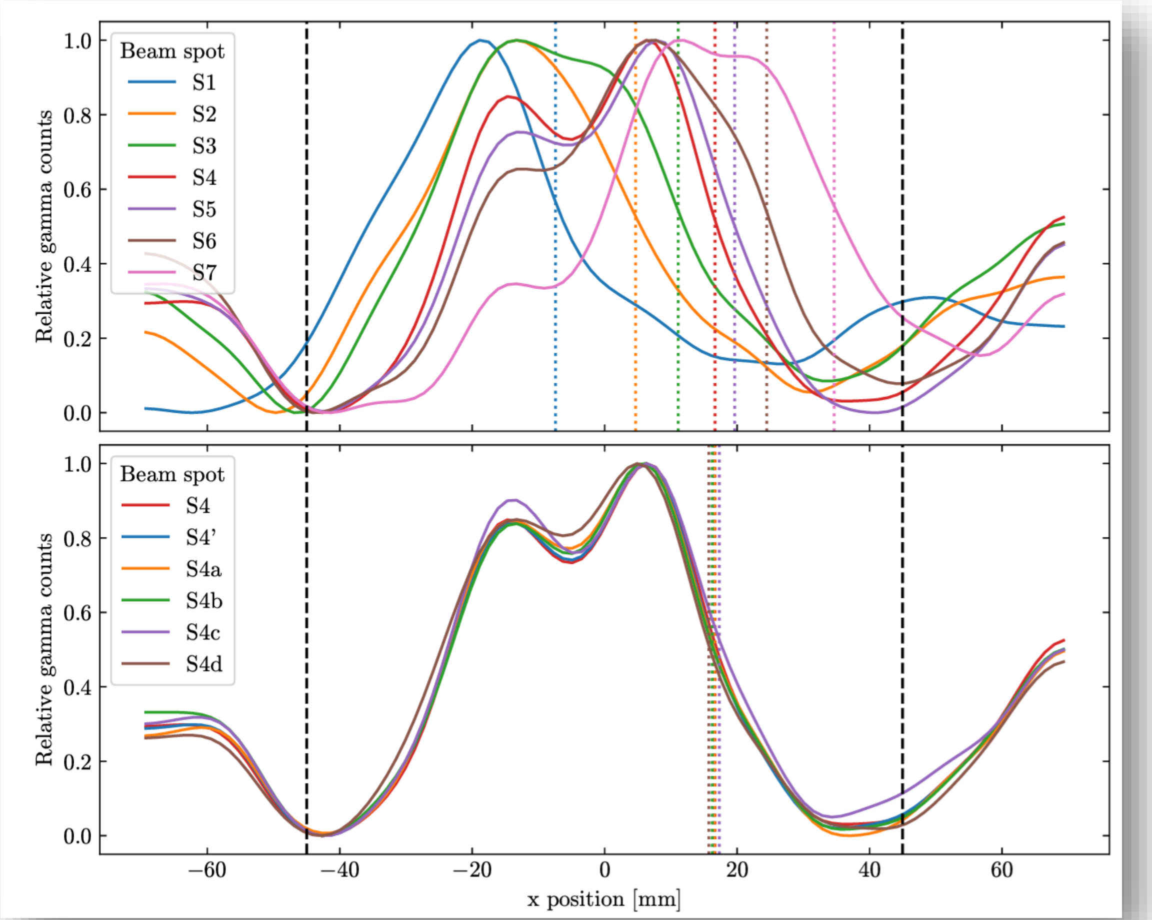
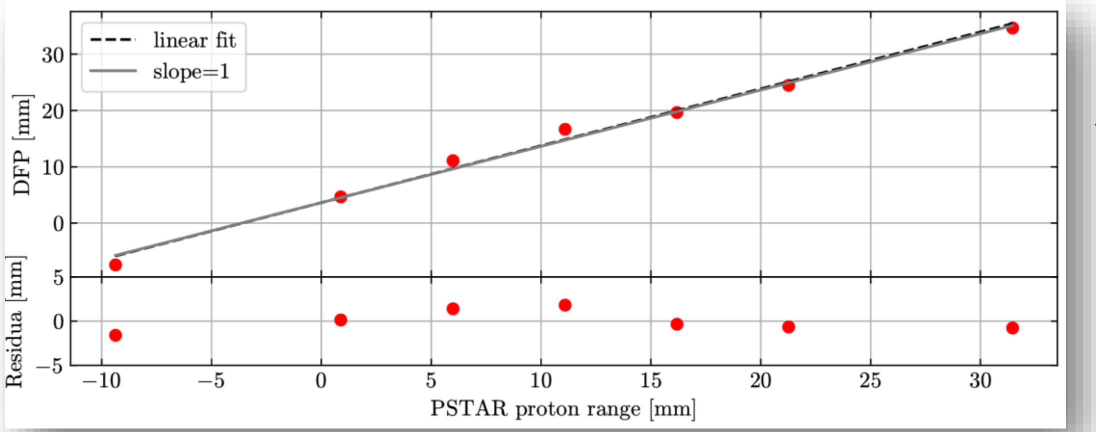


image reconstruction



evaluation



First tests with a proton beam at HIT

arXiv > physics > arXiv:2501.00666

Submitted to PMB

Search...

Help | Adv

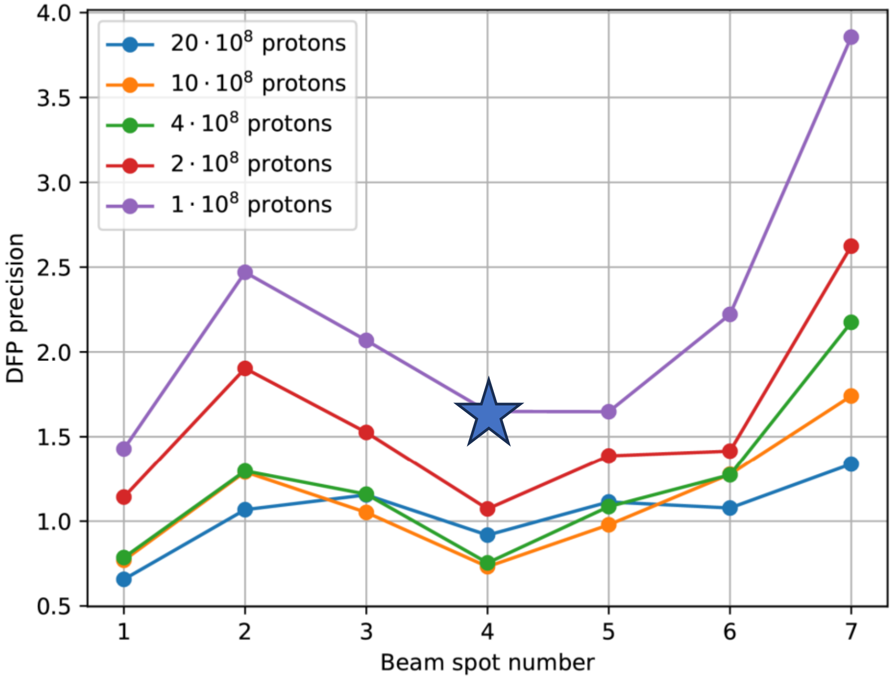
Physics > Medical Physics

[Submitted on 31 Dec 2024]

First experimental test of a coded-mask gamma camera for proton therapy monitoring

Magdalena Kołodziej, Stephan Brons, Mikołaj Dubiel, George N. Farah, Alexander Fenger, Ronja Hetzel, Jonas Kasper, Monika Kercz, Barbara Kołodziej, Linn Mielke, Gabriel Ostrzołek, Magdalena Rafecas, Jorge Roser, Katarzyna Rusiecka, Achim Stahl, Vitalii Urbanevych, Ming-Liang Wong, Aleksandra Wrońska

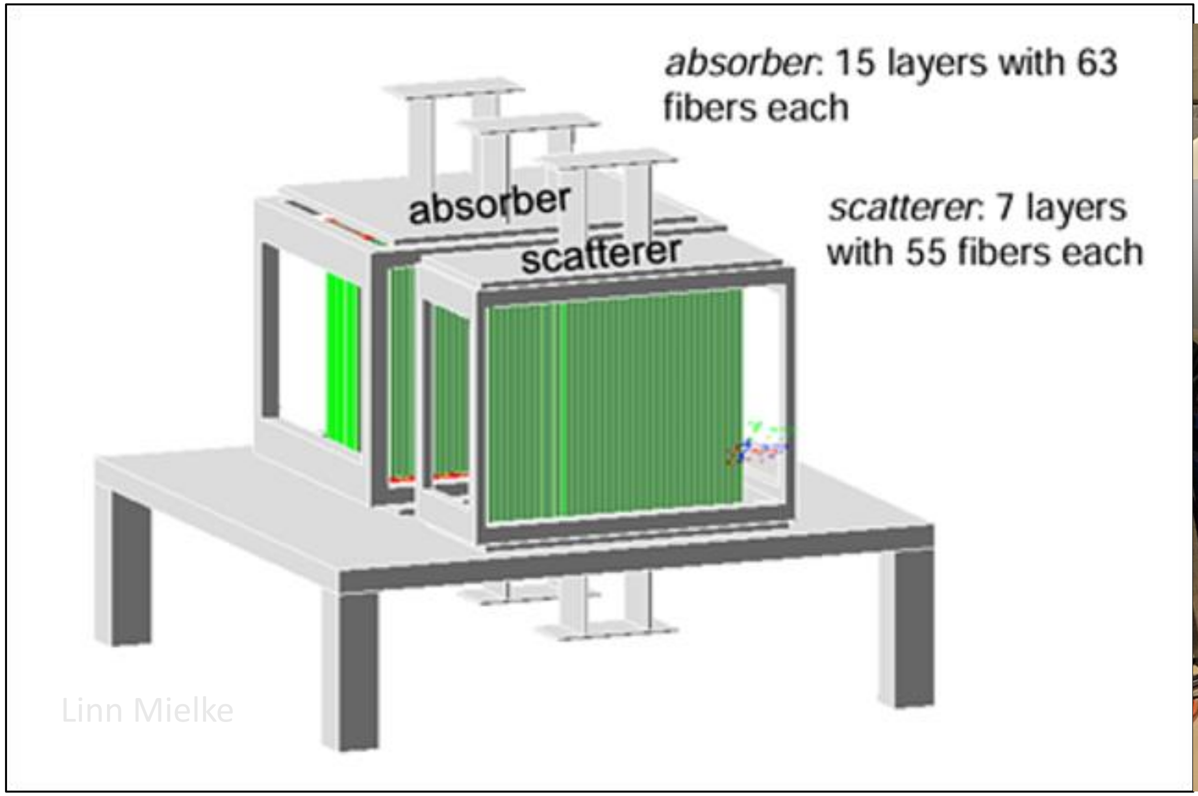
Range precision of **1.7 mm** at 1e8 protons

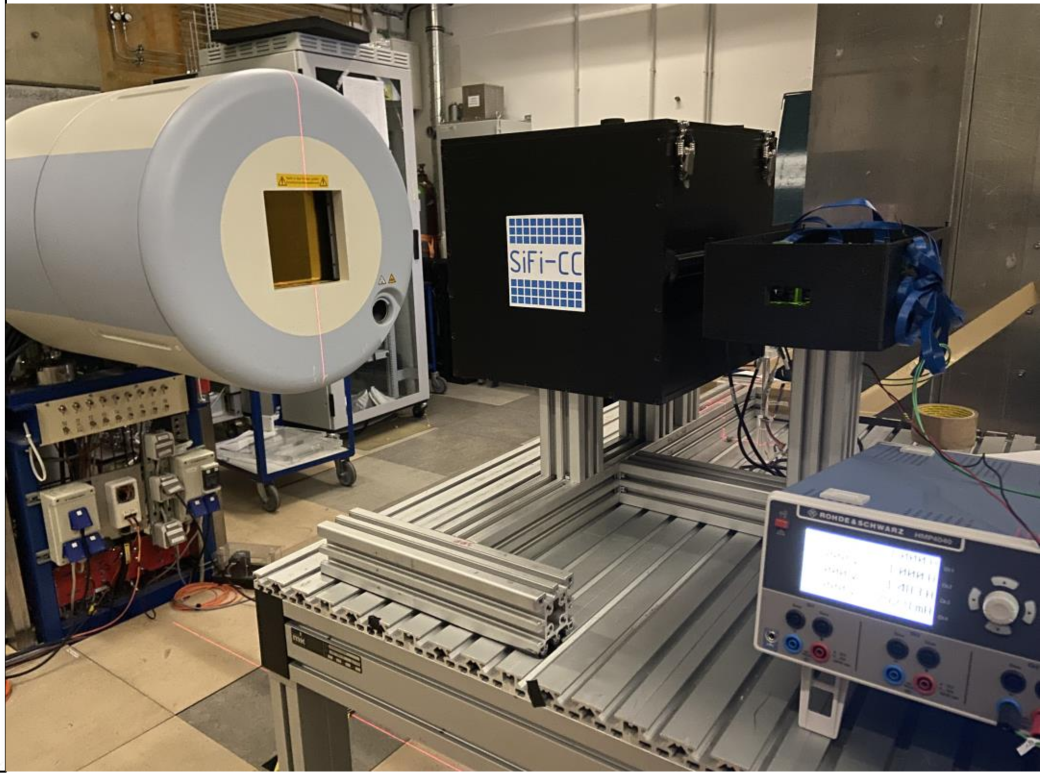


- CM camera operable at clinical conditions
- Rate cabability fully sufficient
- First test delivers per-spot range determination precision comparable to world leaders
- Result reproduced by Monte Carlo simulations => setup well understood
- MC simulations without acceptance gaps => range precision 4 times better!
- Work in progress on second iteration of the module

What's next with SiFi-CC?

- New PCBs in place → **fix for holes in the acceptance** of the 1st module
- Module reassembly → **improved position resolution along Y**
- **Tests with the proton beam in the coded mask mode**
- Construct the absorber, full CC detector **ready**
- **Tests with the proton beam in the CC mode**





Summary

- PG-based methods of proton therapy monitoring still alive
- Various methods still under consideration
- A simplest solution – a single-slit camera – is reaching clinical maturity
- Coded-mask camera with hardware flaws gives comparable results
- Prospect to improve the CM-camera range determination precision ~4 times
- Way to imaging in 2D or 3D still long, but possible