Prompt-gamma radiation in proton therapy – activities of the SiFi-CC collaboration

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

20th GGSB Aniversary, Tbilisi/Kutaisi, 11.09.2024

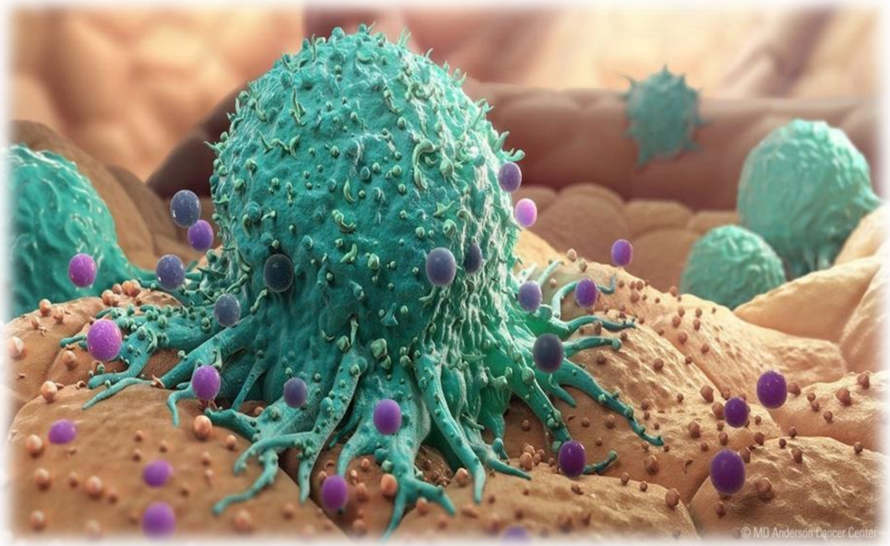
Cancer – a scare and a challenge

Statistics

- 1 in 4 deaths caused by cancer in the EU
- (Poland close to this average)
- 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...

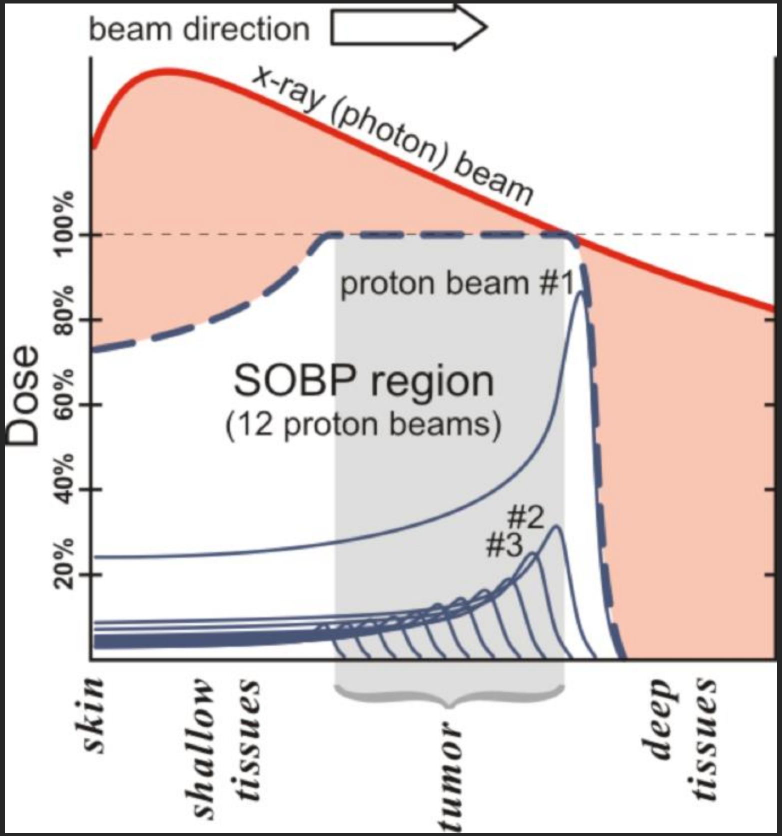
Treatment methods

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

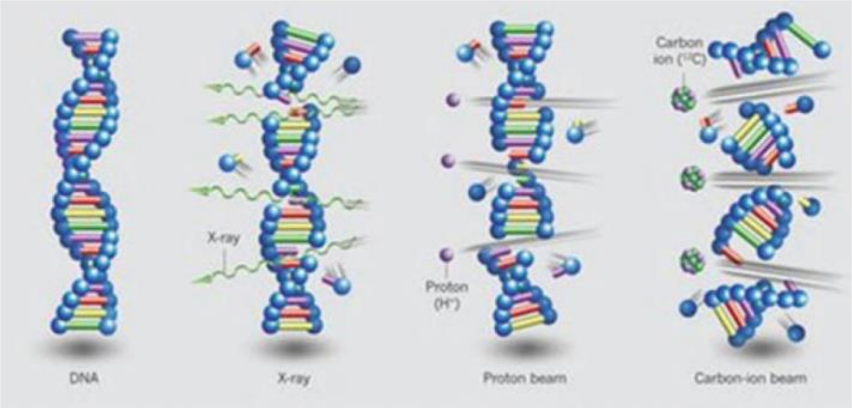


X-ray *versus* hadron therapy

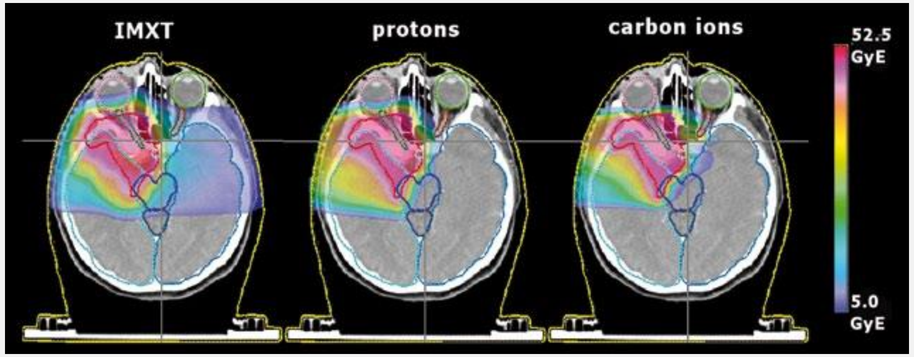
- Tumour irradiation – important way of treatment
- Advantages of hadron therapy compared to X-rays:
  - Conformal dose distribution
  - Biological effectiveness



Levin et al.., British J of Cancer 2005



Marcos dAvila Nunes, Springer 2015



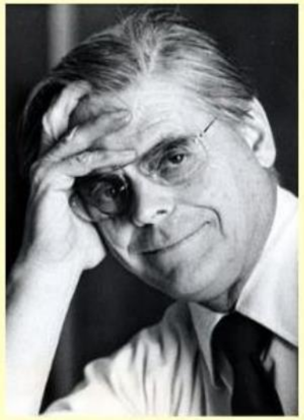
NuPECC, Nuclear Physics for Medicine 2014

Proton therapy - history

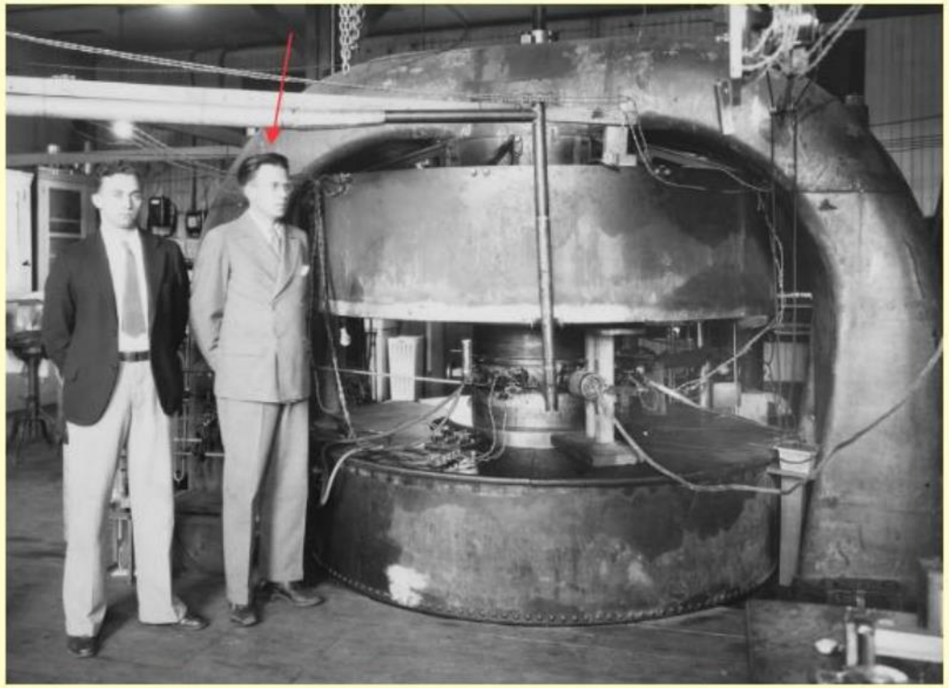
Hans Bethe 1930:
interaction of
hadrons with matter

$$-\left\langle \frac{dE}{dx} \right\rangle = \frac{4\pi}{m_e c^2} \cdot \frac{nz^2}{\beta^2} \cdot \left(\frac{e^2}{4\pi\varepsilon_0} \right)^2 \cdot \left[\ln\left(\frac{2 m_e c^2 \beta^2}{I \cdot (1-\beta^2)} \right) - \beta^2 \right]$$

Robert Wilson 1946:
use of proton beams
for cancer therapy



Ernest O. Lawrence 1932:
construction of cyclotron

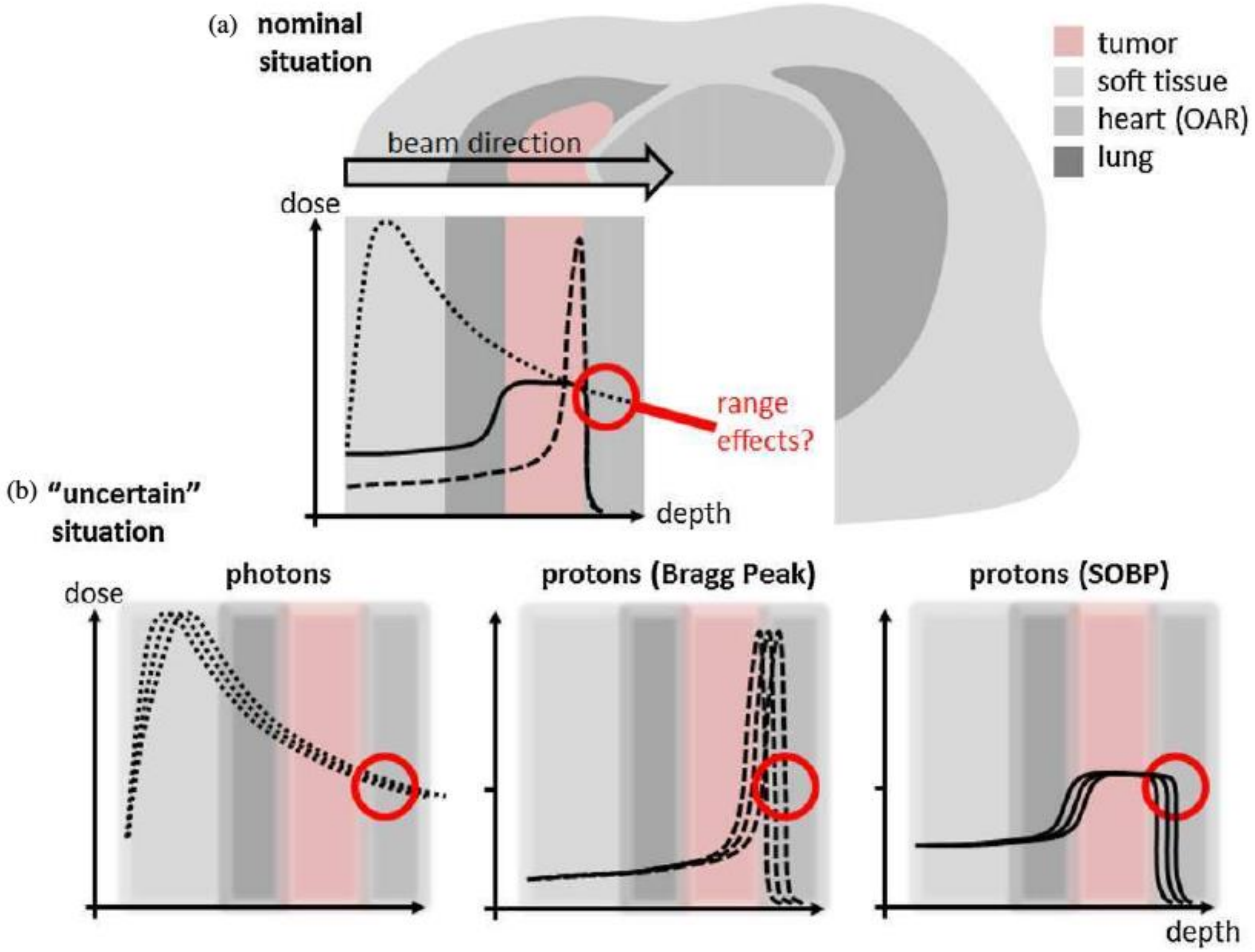


Kraków proton therapy centre: Cyclotron Centre Bronowice

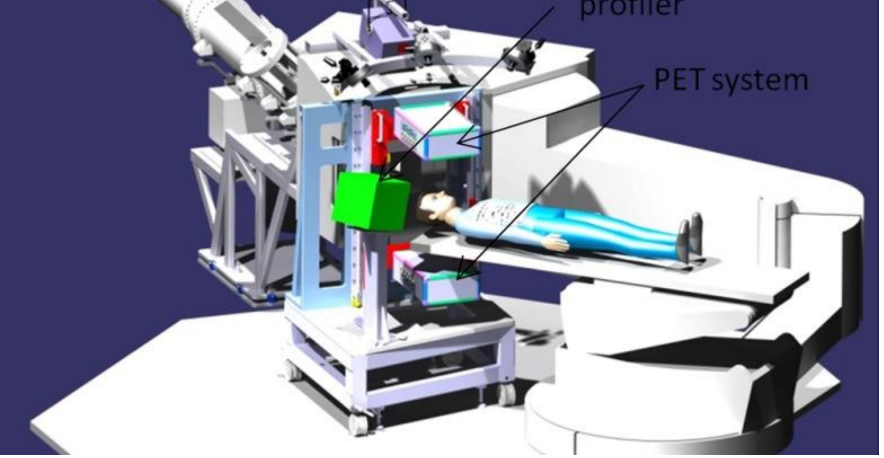
- Modern equipment, iba Proteus C235 cyclotron, 2 gantries + eye
- 2013 – first beam
- 2016 – first patient
- Experienced team
- Today: ~40 patients / day, including children

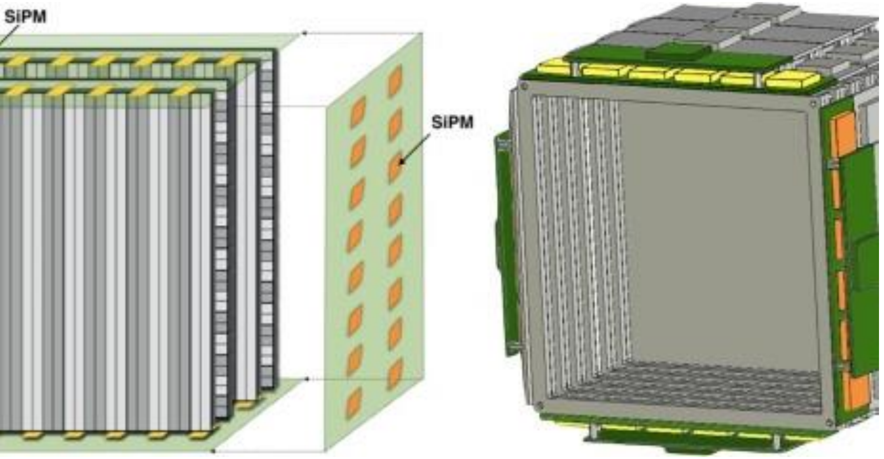
Can we do better in proton therapy?

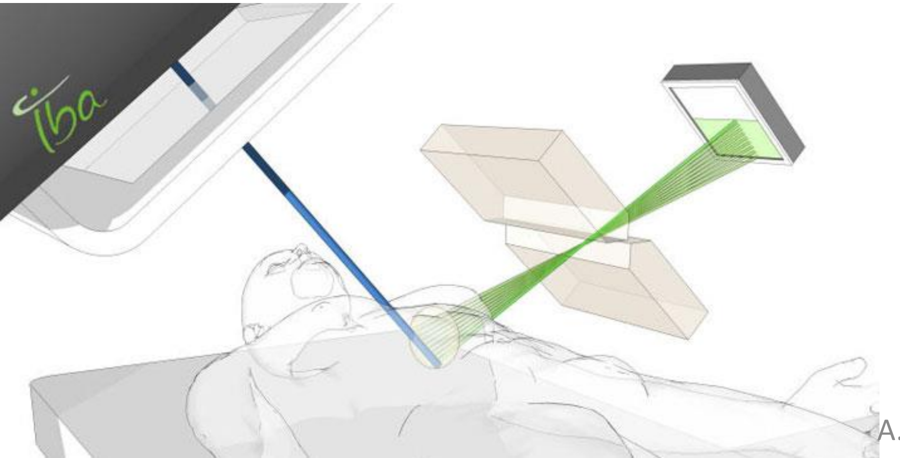
- Safety margins: from a few mm up to > 1 cm
  - Patient positioning
  - Anatomical changes
  - Infections
  - Uncertainties of treatment planning
- Reduction of margins?
- Online monitoring of therapy
  - Determination of Bragg peak position in real time, spot-by-spot
  - Maybe even spatial dose distribution...?



Knopf, Lomax, PMB 2013



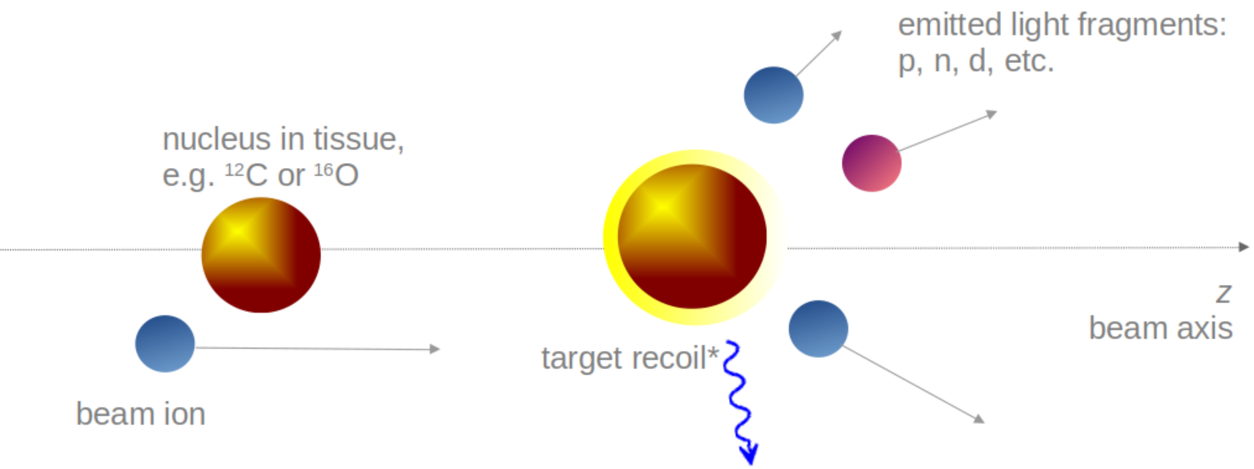


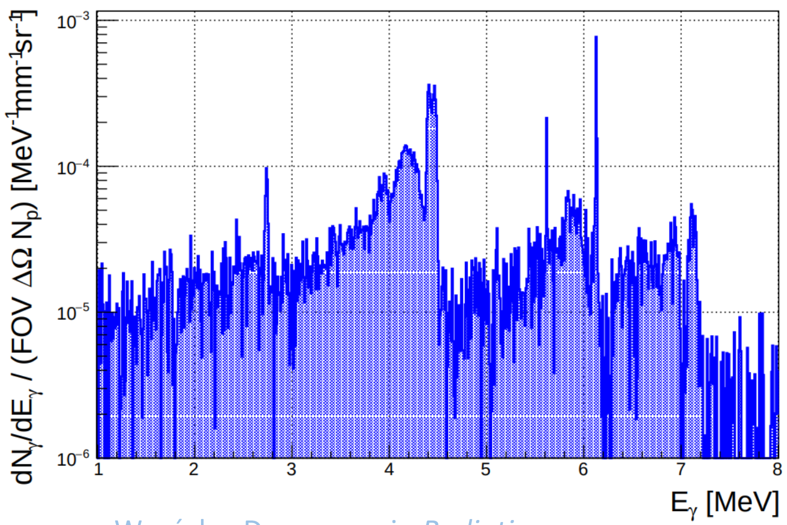


How to monitor PT?

Secondary radiation correlated with dose distribution

- Protons, neutrons - useful in C-ion therapy:
  - Dose Profiler (CNAO) Traini *et al.*, Physica Medica 65, 2019
  - MONDO (CNAO) Mirabelli *et al.*, *IEEE Trans. Nucl. Sci.* 65, 2018
- β+ emitters (PET):
  - INSIDE (CNAO) Bisogni *et al.*, J. Med. Imaging 4, 2017
  - J-PET (UJ) 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





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

Prompt gamma – working conditions

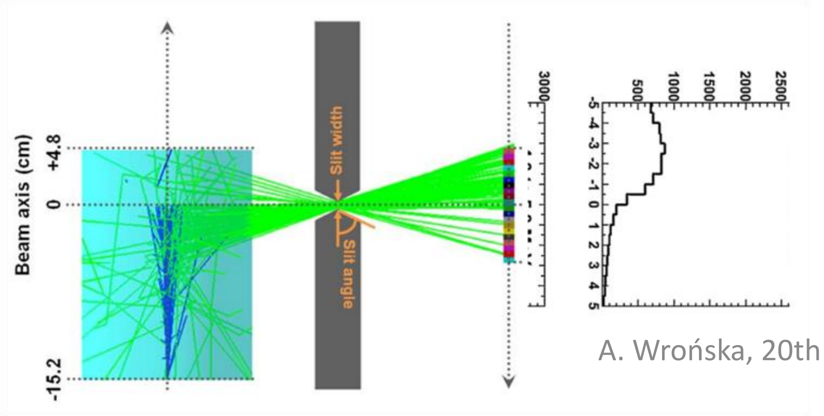
- Large count rates ($n \times 10^5$ s^{-1})
- Typical spot: t=10 ms, N_p~10^8
- Background from other secondaries (neutrons)
- N_γ/N_p~0.15
- Energy range 1-7 MeV (continuum + discrete transitions)
- Detection system of large efficiency, rate capability and fast DAQ needed

Prompt-gamma radiation (PG)

Status

- Beam range monitoring under tests in clinical conditions (PG spectroscopy, slit camera)
  Richter et al., Radiotherapy and Oncology 1 118 , 2016
  Xie et al., Int. J. Rad. Oncol. Biol. Phys 99 210, 2019
  Hueso-Gonzalez et al., PMB 63, 2018
- 1d information

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



Dream

- Registeration of PG vertex distribution (Compton cameras)
- "Translation" of this distribution to the spatial distribution of deposited dose
  Liu, Huang Physica Medica 69, 2020
- Full 3d information

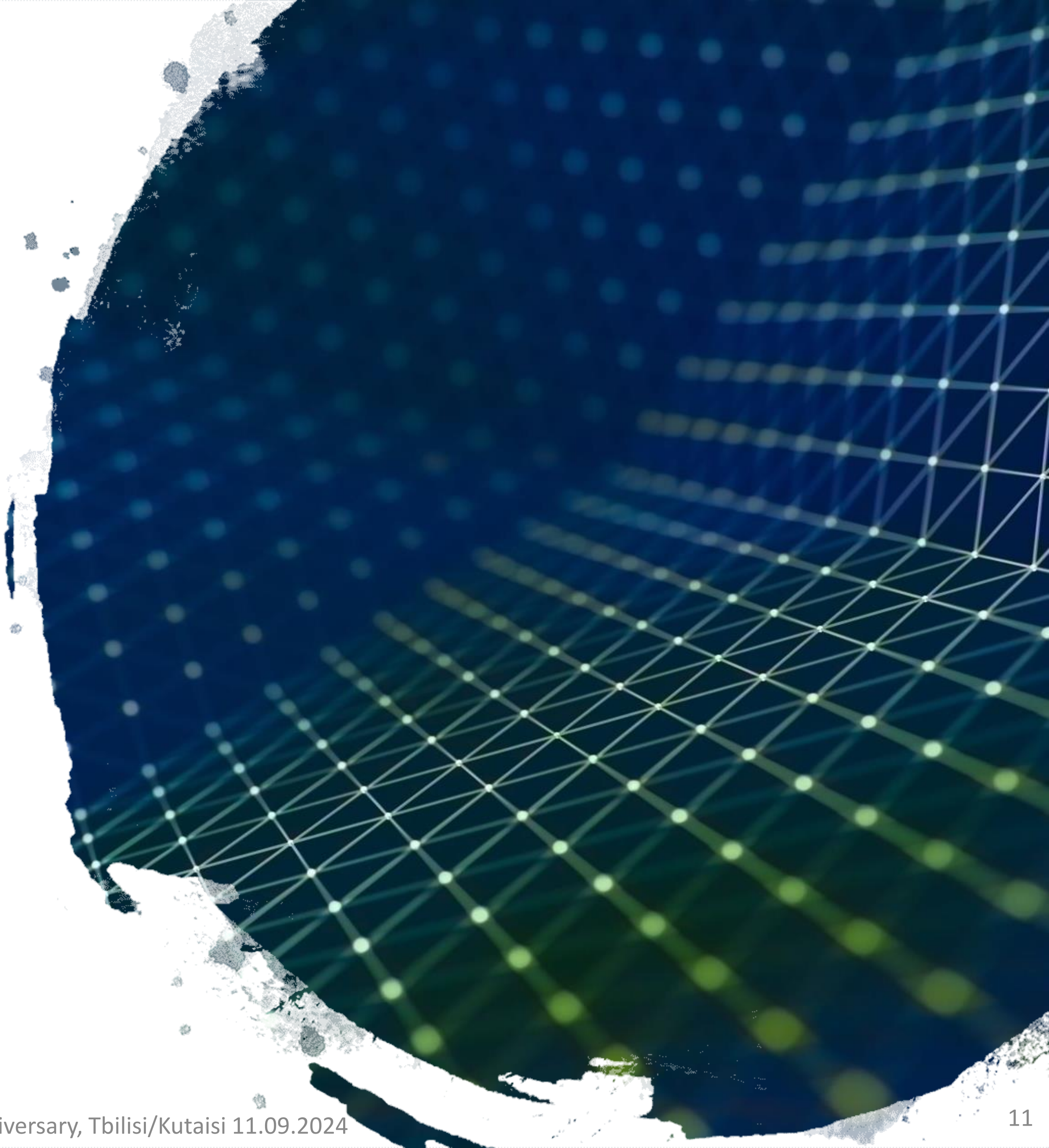
PG – our activities

γCCB: characterization of **PG – experiments**

Monte-Carlo simulations + validation

SiFi-CC setup for beam range monitoring

Beam-activated tumour tracers



The group

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SiFi-CC

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NAWA Narodowa Agencja Wymiany Akademickiej
DAAD Deutscher Akademischer Austauschdienst German Academic Exchange Service
HITRI plus Heavy Ion Therapy Research Integration

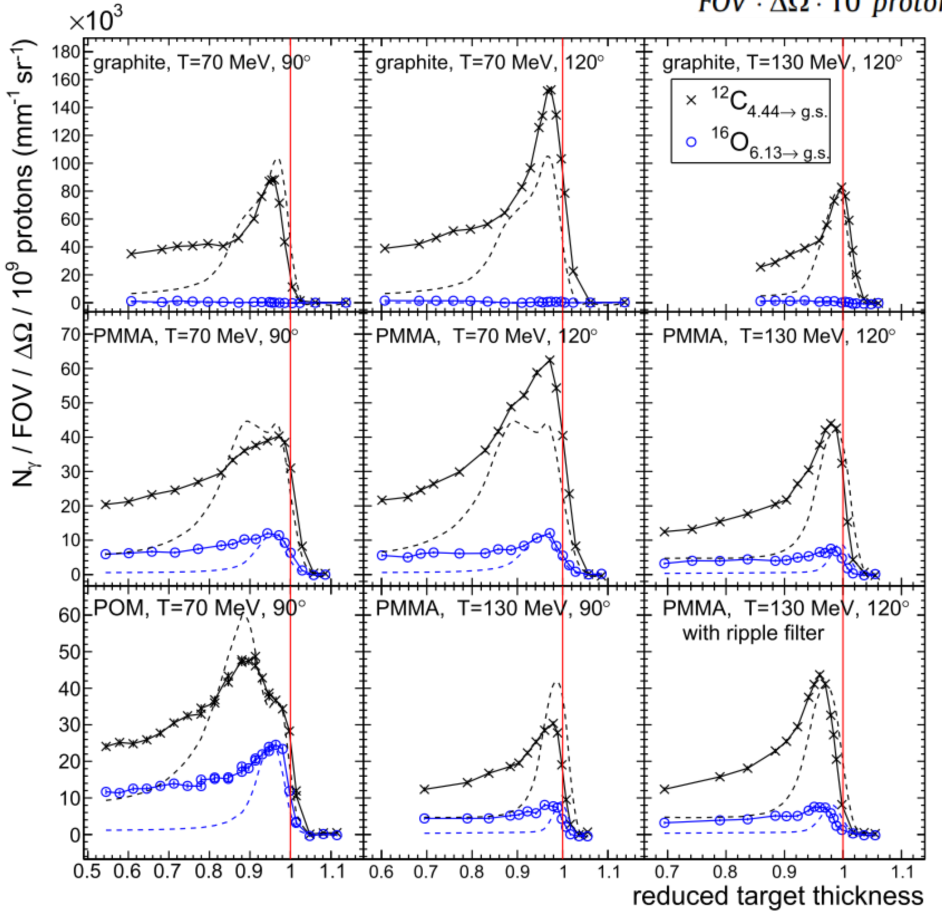
γCCB – experimental characterization of PG

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

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•

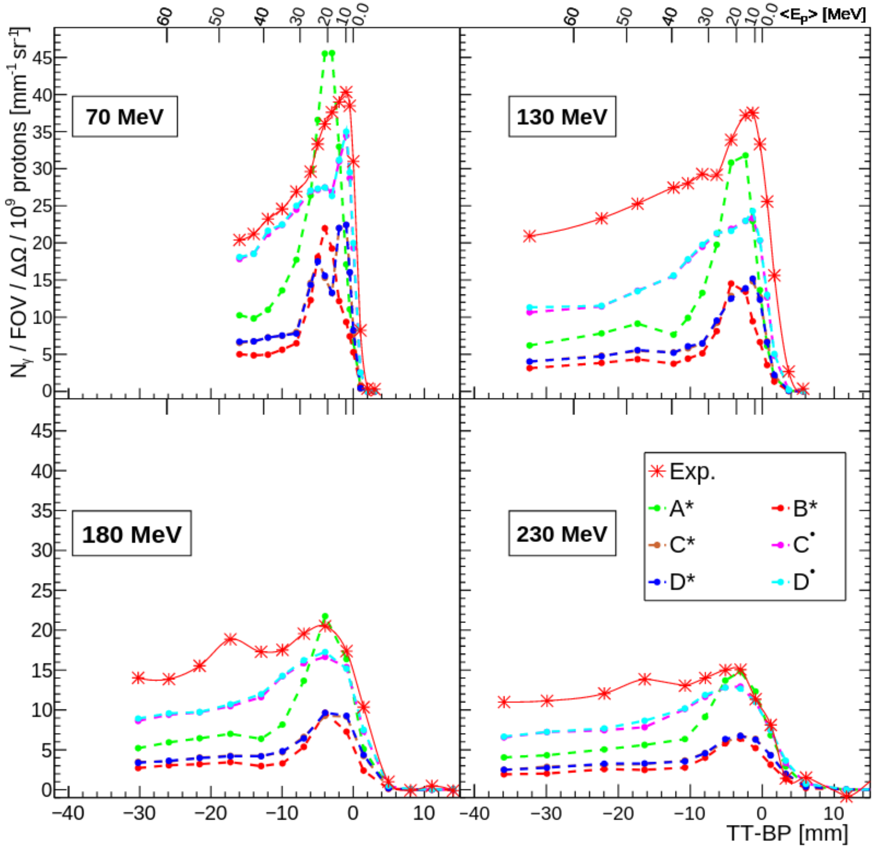
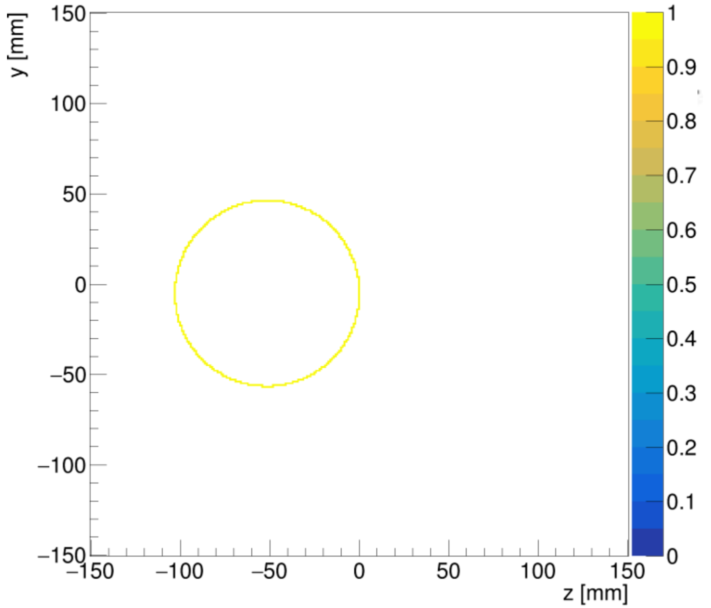


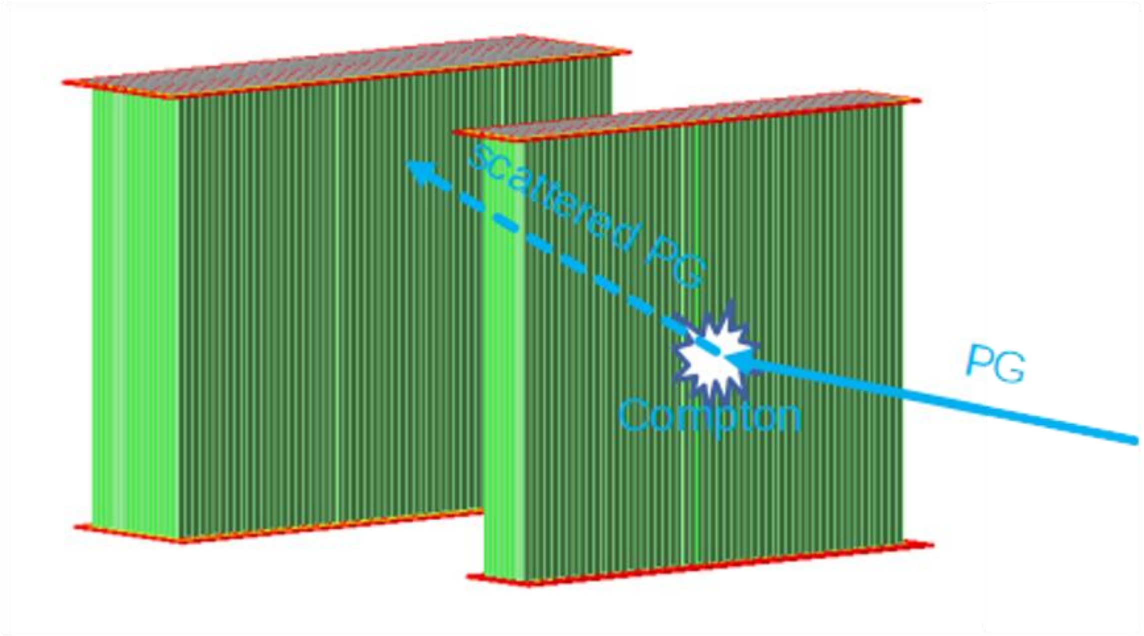
Figure 7: Comparison of gamma emission depth profiles for the 4.44 MeV line obtained from the simulations and the experiments for the beam energies 70 MeV, 130 MeV, 180 MeV and 230 MeV.

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



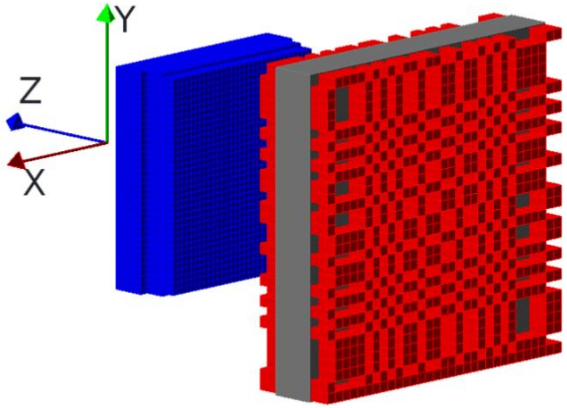
SiFi-CC: Compton camera for PGI

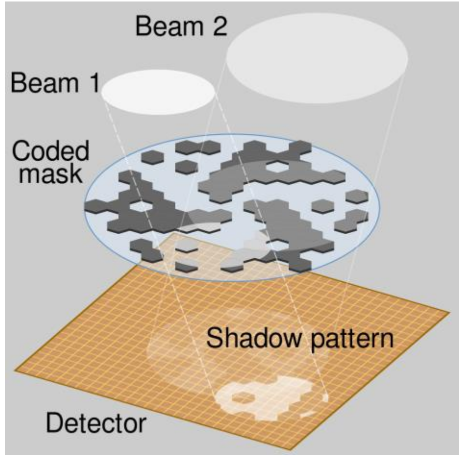
- **Si**PM and scintillating **Fi**bers based **C**ompton **C**amera
- Arrays of LYSO fibres => large efficiency
- 1mm x 1mm x 100 mm (small prototype)
  2mm x 2mm x 100 mm (full-scale)
- Dual readout via SiPMs:
  - 1:1 coupling (small)
  - 4:1 coupling (full-scale)
- Granularity => ~~pile-up~~ !
- DAQ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



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

By-product: coded-mask setup (CM)





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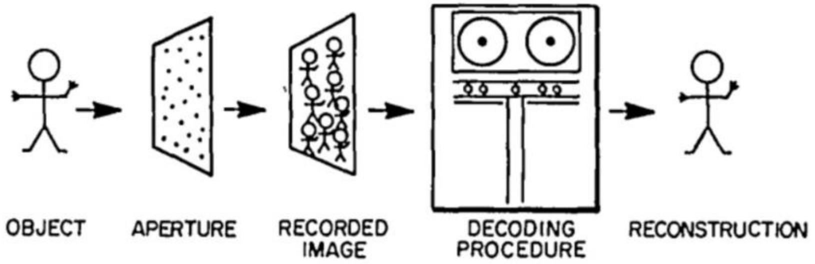


E. E. Fenimore and T. M. Cannon, Coded aperture imaging with uniformly redundant arrays, Appl. Opt. 17, 337-347 (1978)

- 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)?

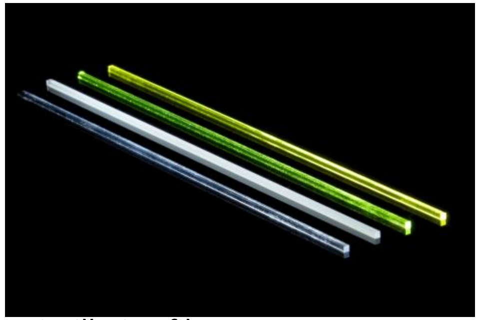
  Rusiecka *et al.*, ISMART2018 (Springer)
  Rusiecka et al., JINST 16, 2021
- Construction of a small module prototype
  - 4 layers
  - 64 fibres
  - re-arrangable

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

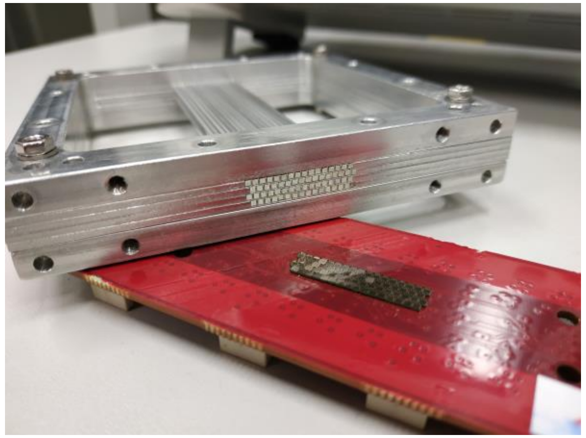
  J. Kasper, PhD thesis, RWTH Aachen 2022
- Image reconstruction software

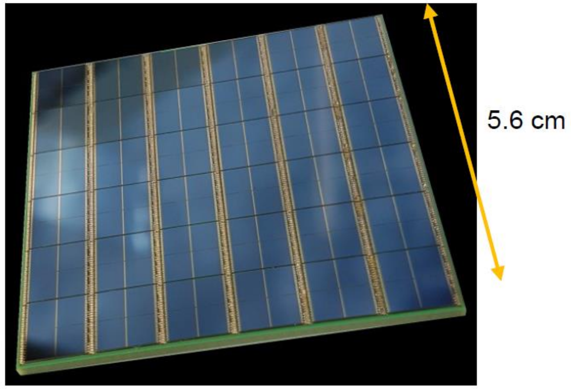
  Kohlhase *et al.*, IEEE Trans. Rad. Plas. Med. Sci. 4, 2020
- FEE+DAQ – classical/digital SiPMs

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

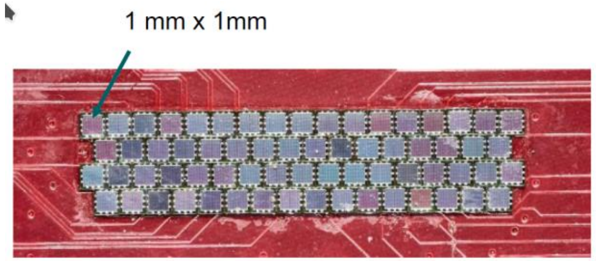


Scintillating fibres

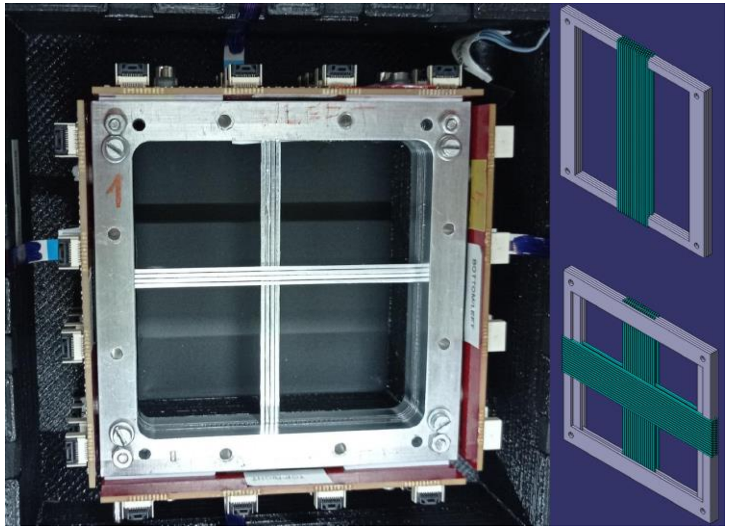




PMI Power Tile Phillips, digital SiPMs

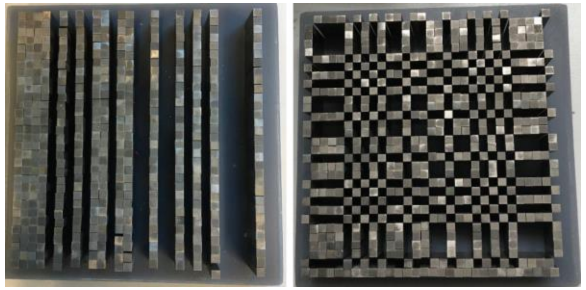


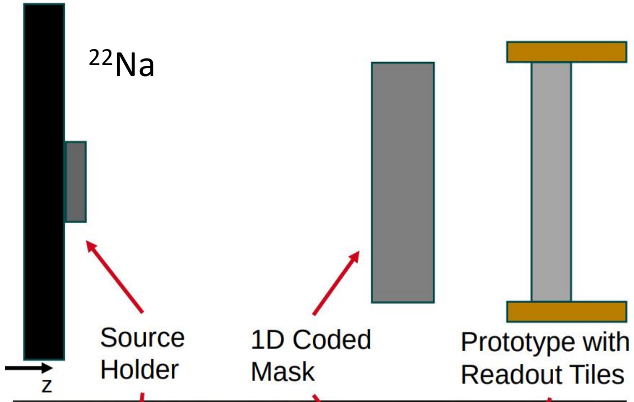
Classical SiPMs custom array

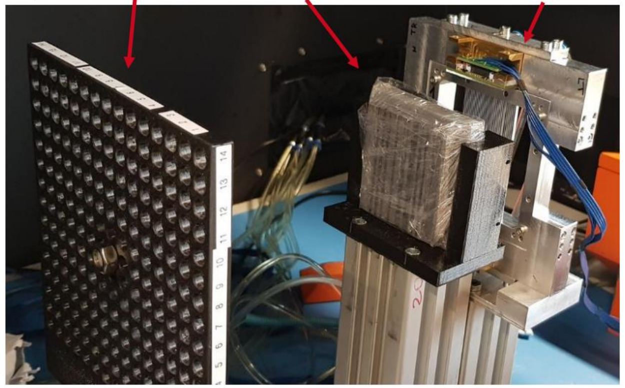


SiFi-CC – setup lab tests

- 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

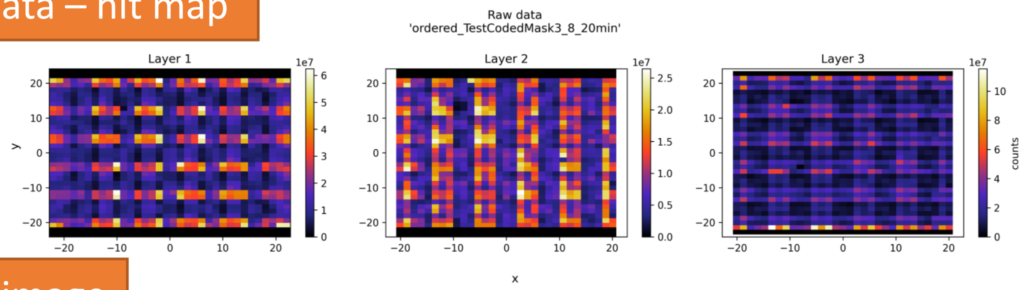




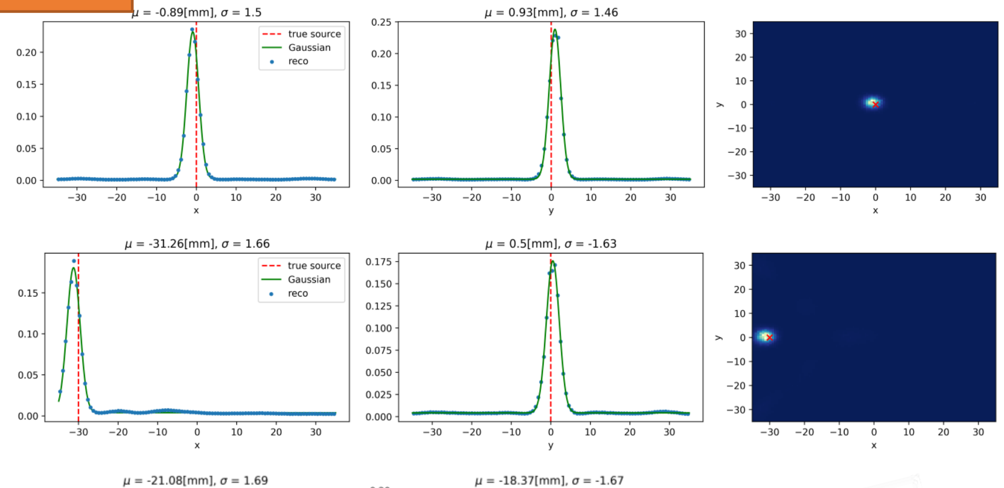


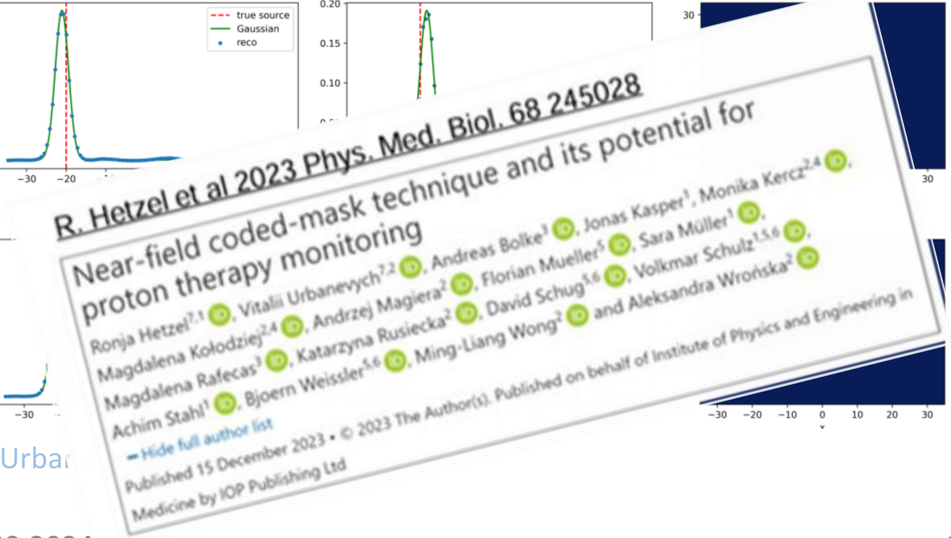
S. Müller, DPG SM 2022

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

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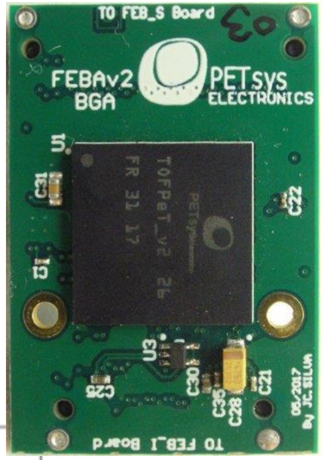
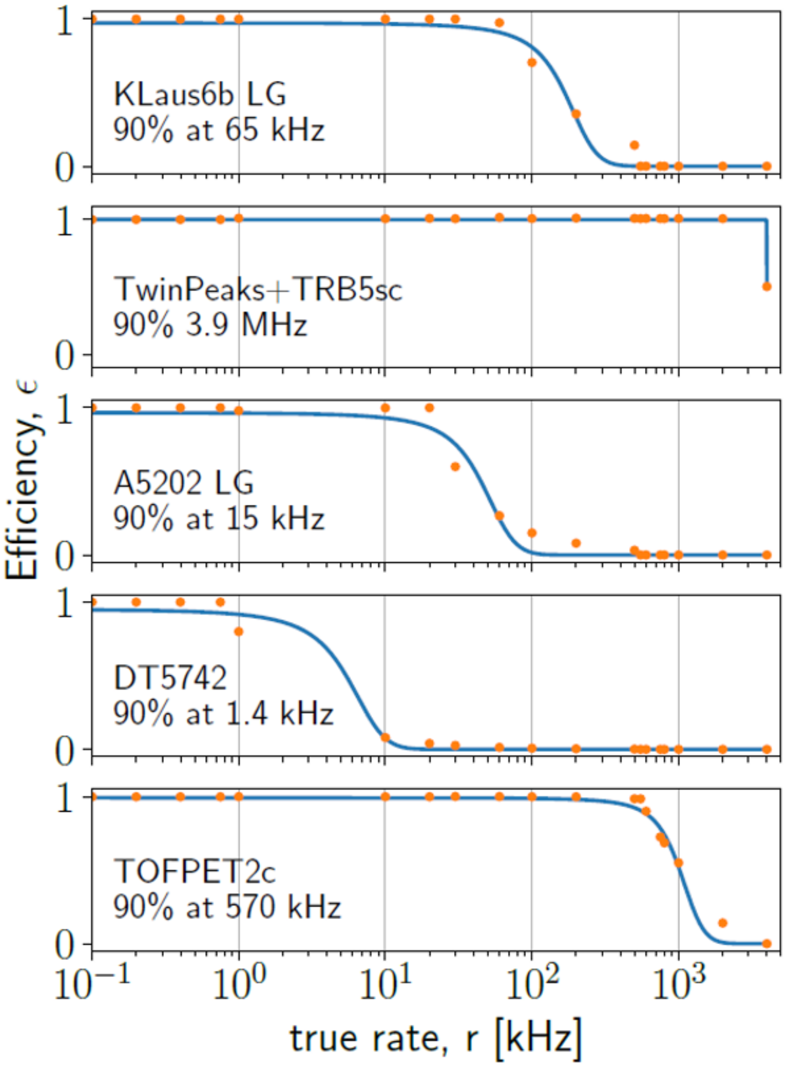
V. Urbar

FEE+DAQ – comparative studies

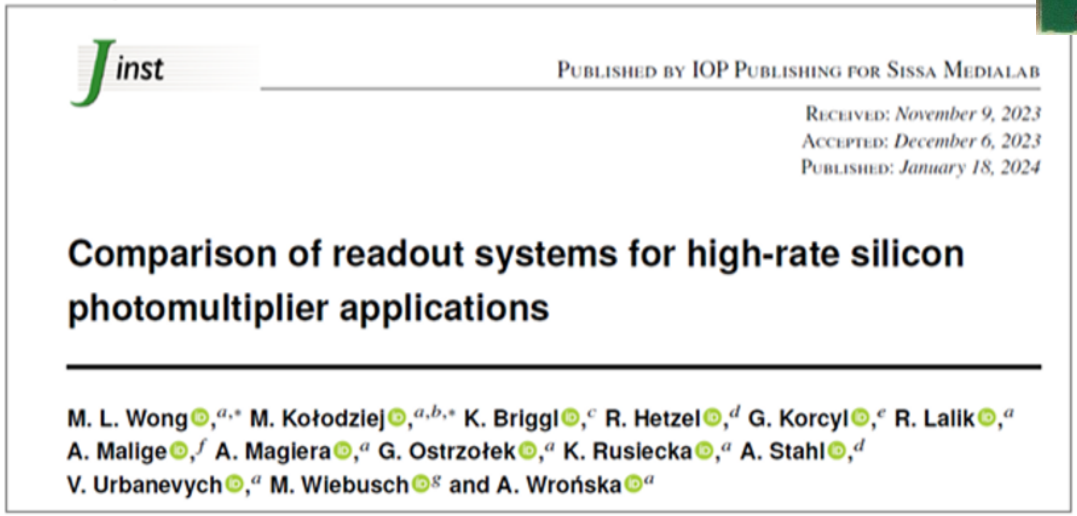
SiFi-CC

- 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

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Comparison of readout systems for high-rate silicon photomultiplier applications

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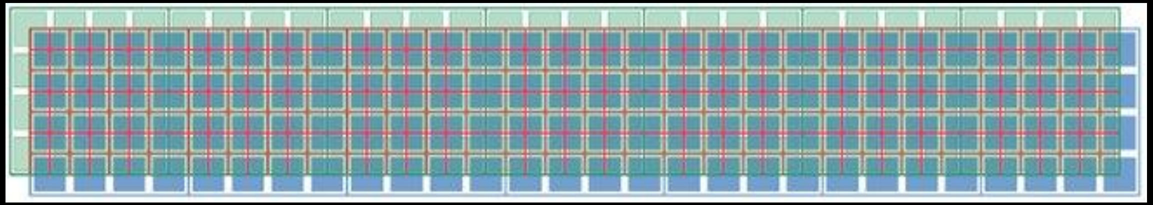
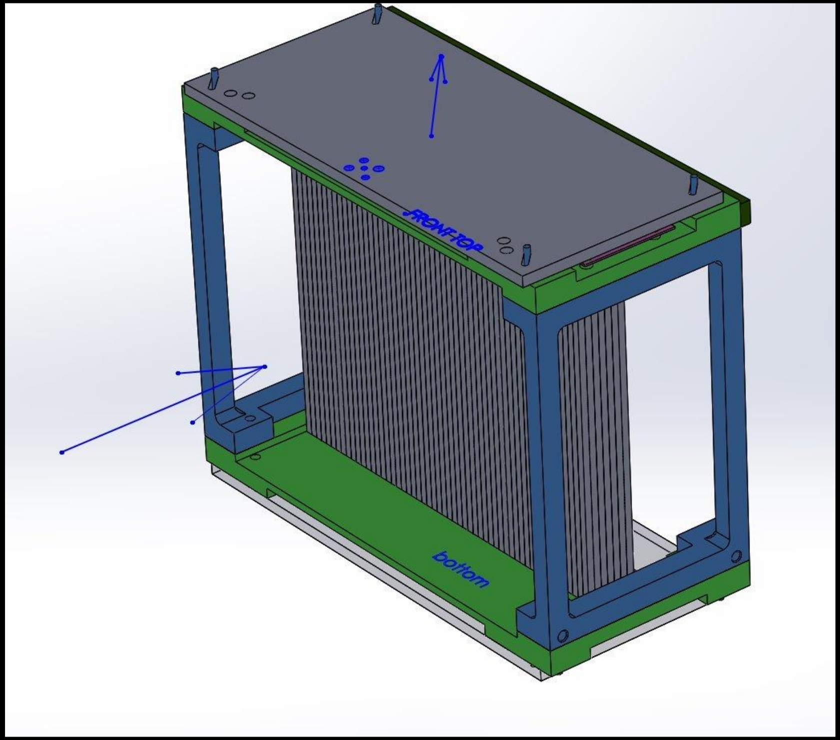
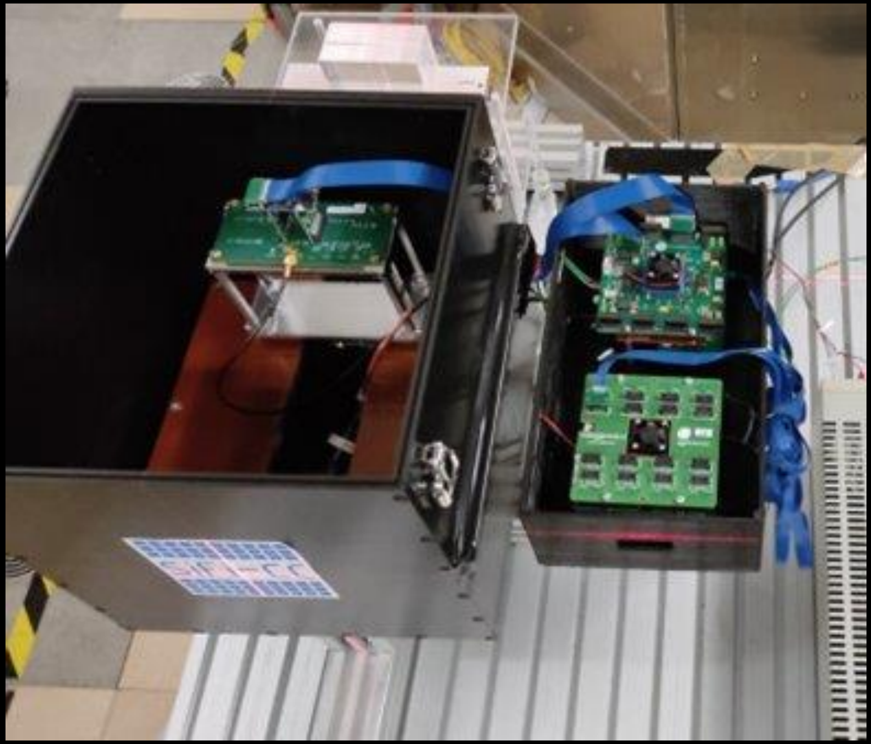
First detector module

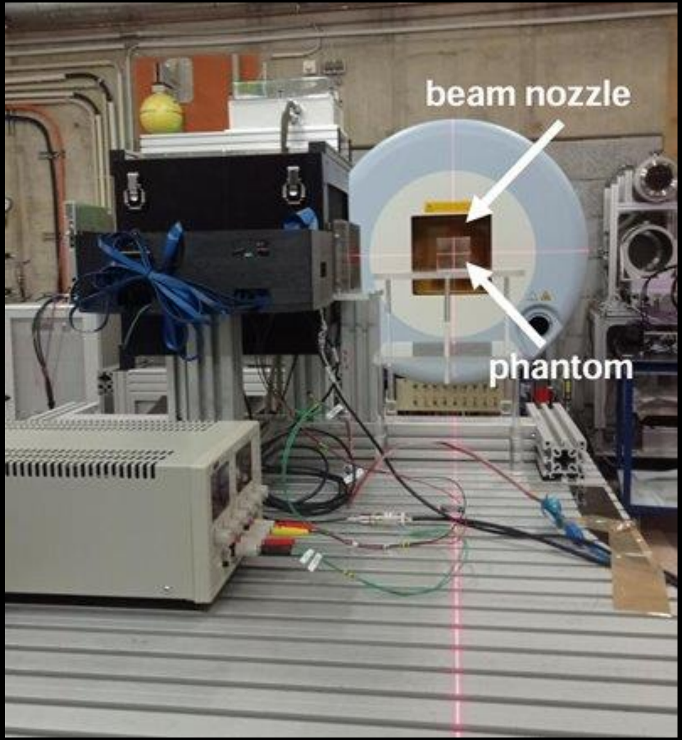


Top and bottom SiPM boards shifted diagonally by half pitch

- 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)

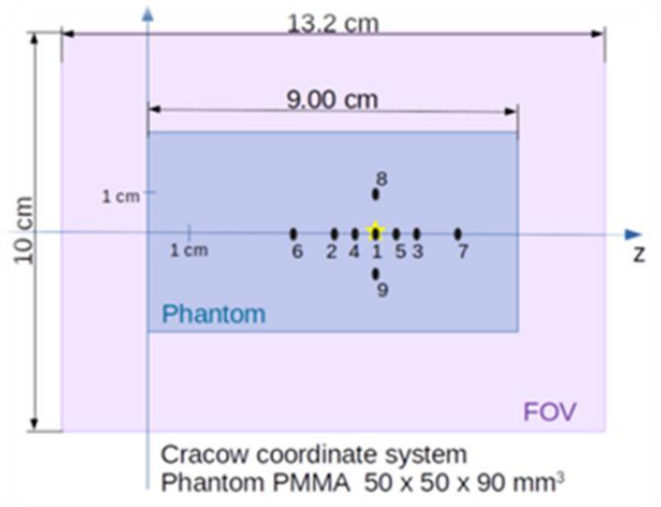


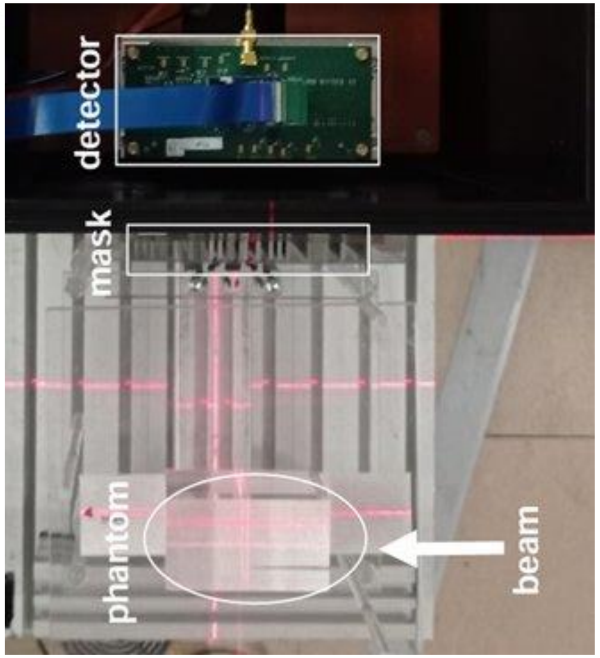




First tests with a proton beam at HIT

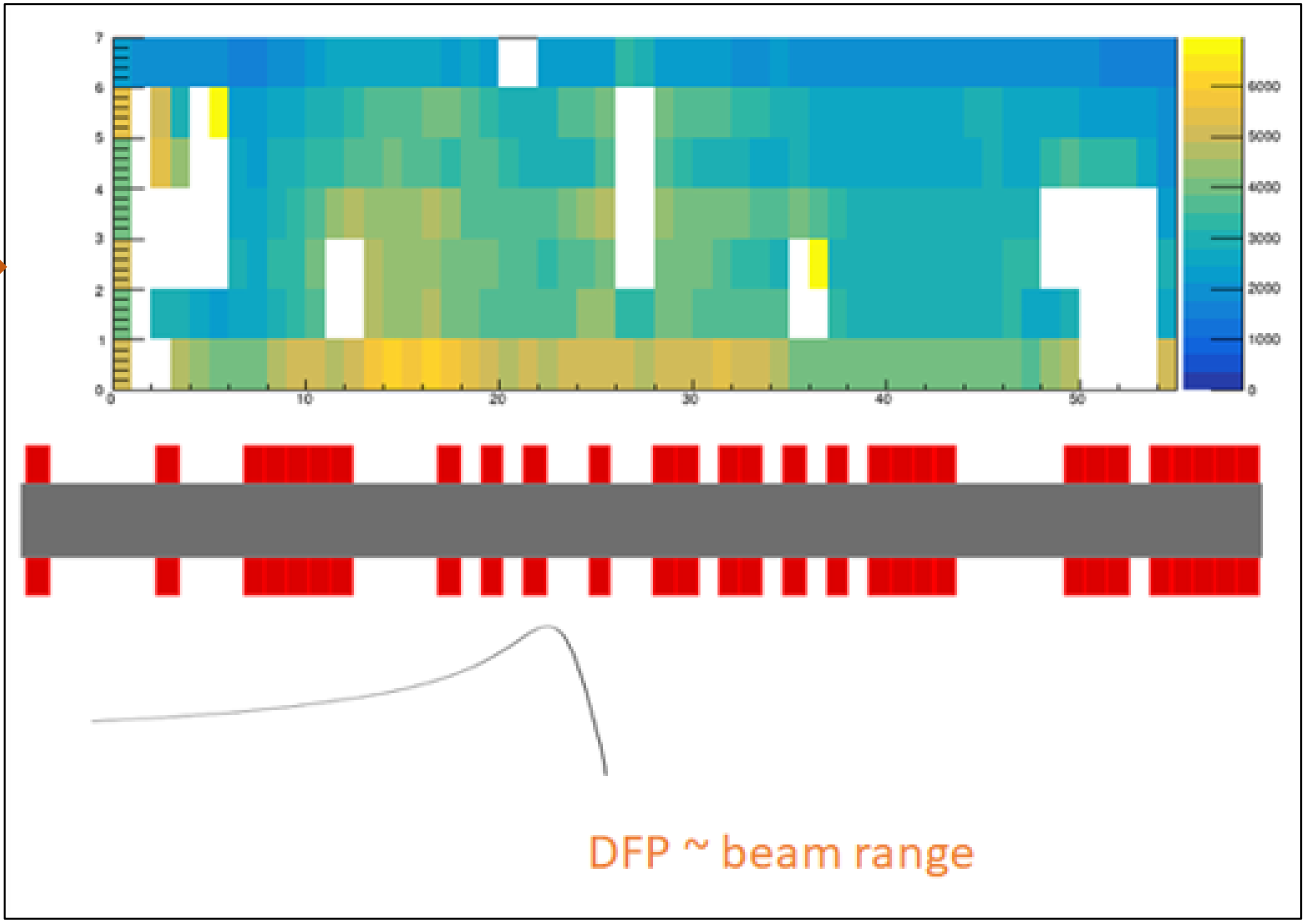
Irradiation plan:





measurement

Hit map - input for MLEM algorithm



First tests with a proton beam at HIT

PRELIMINARY DATA

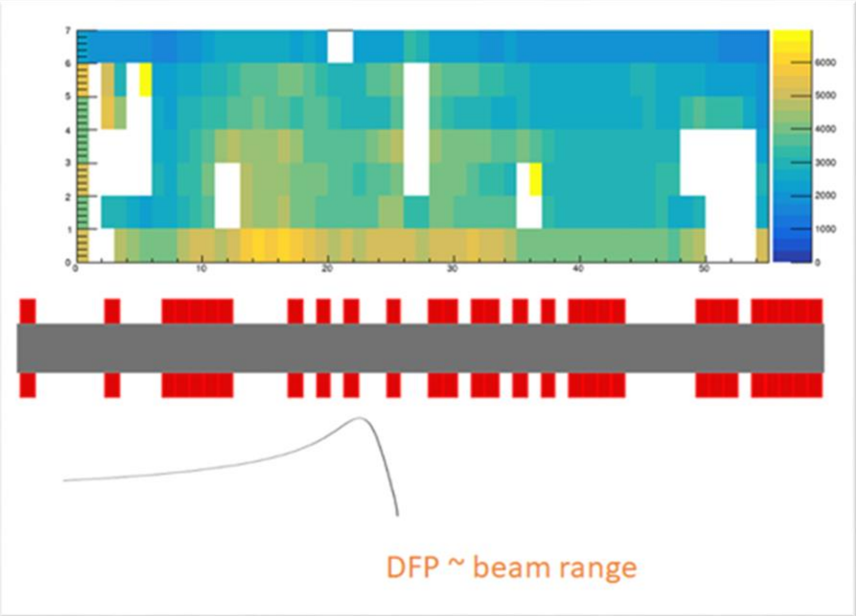
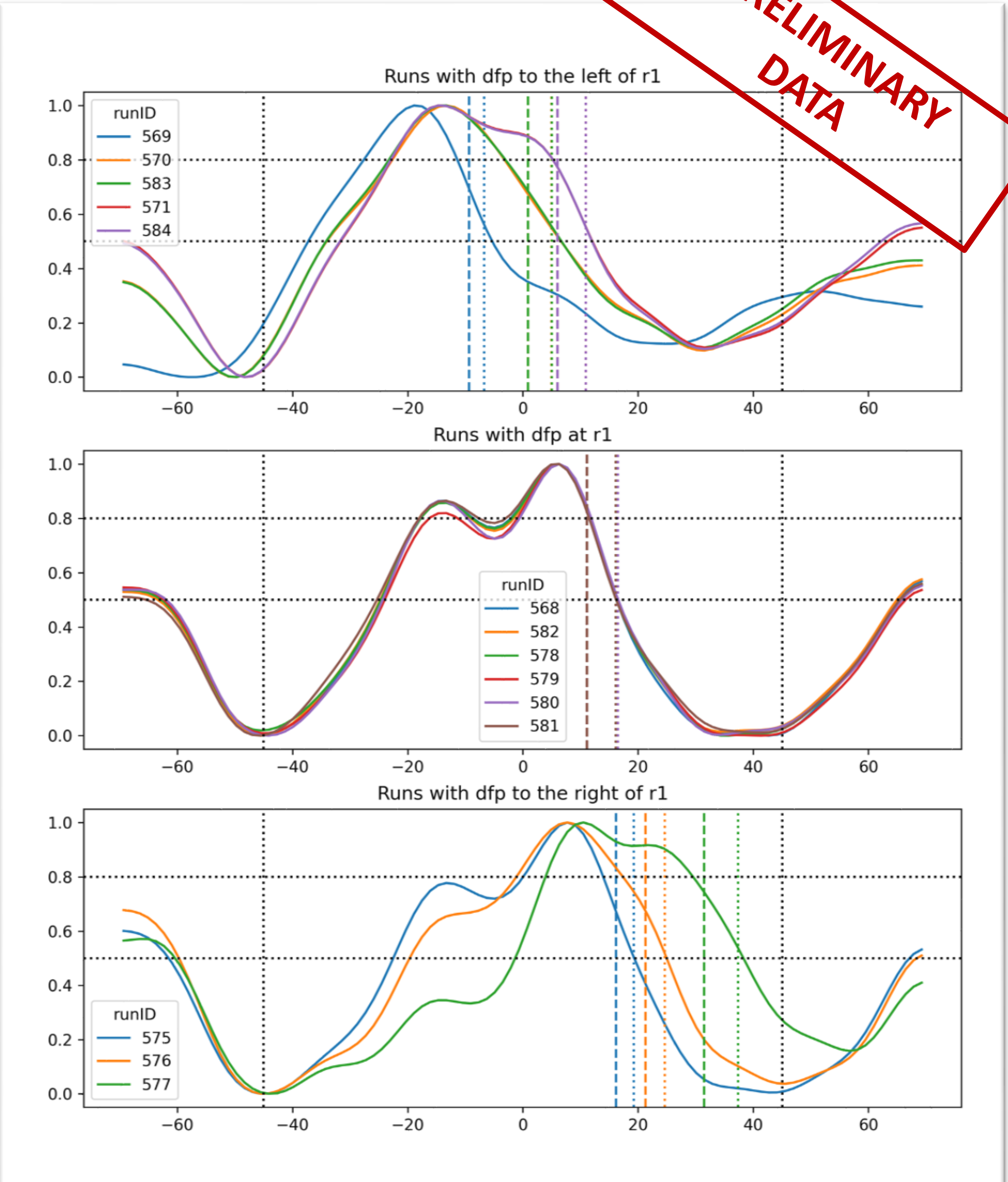
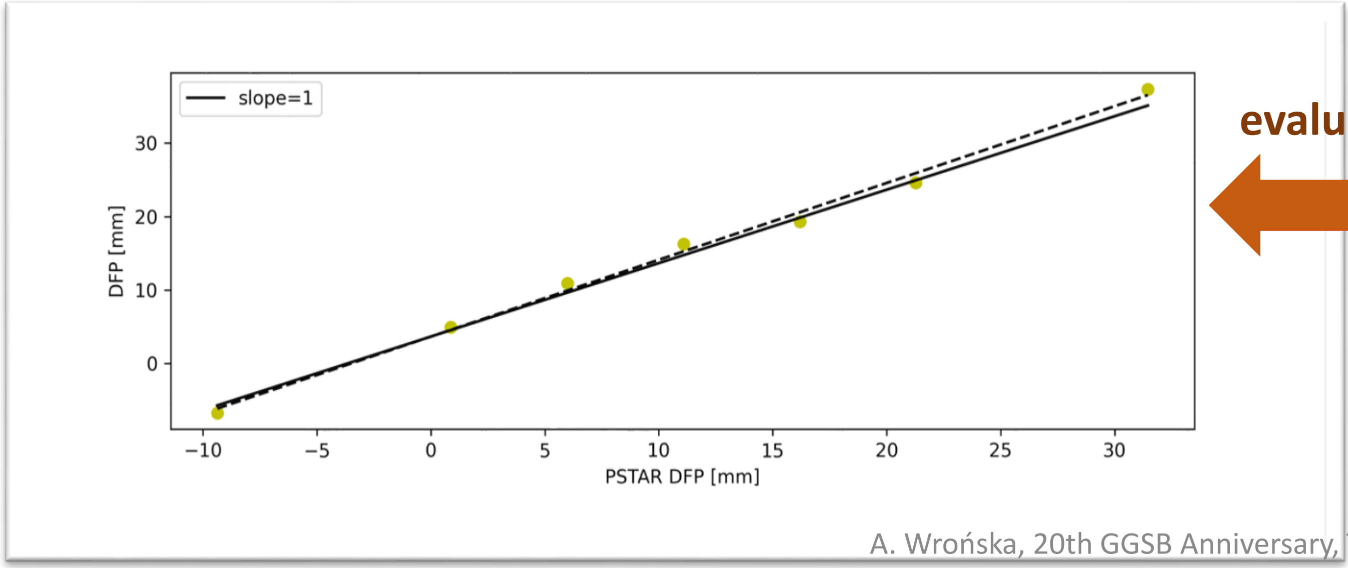


image reconstruction

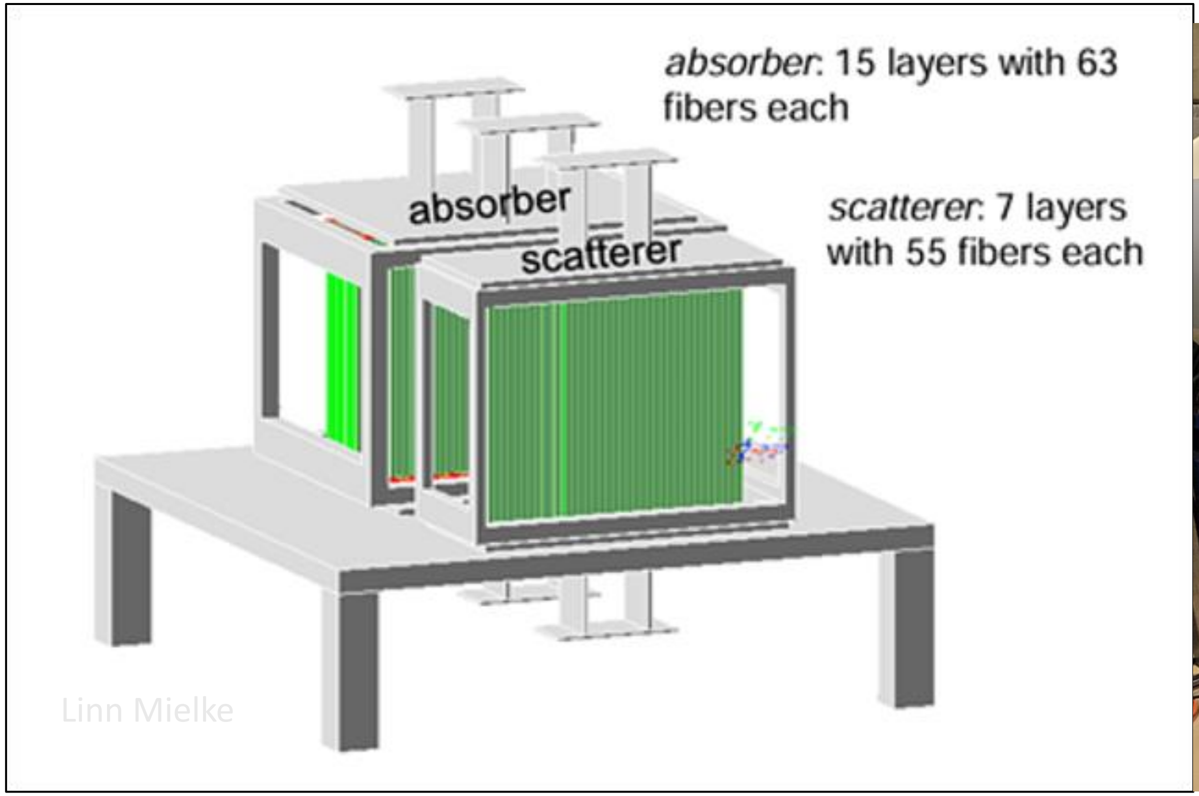


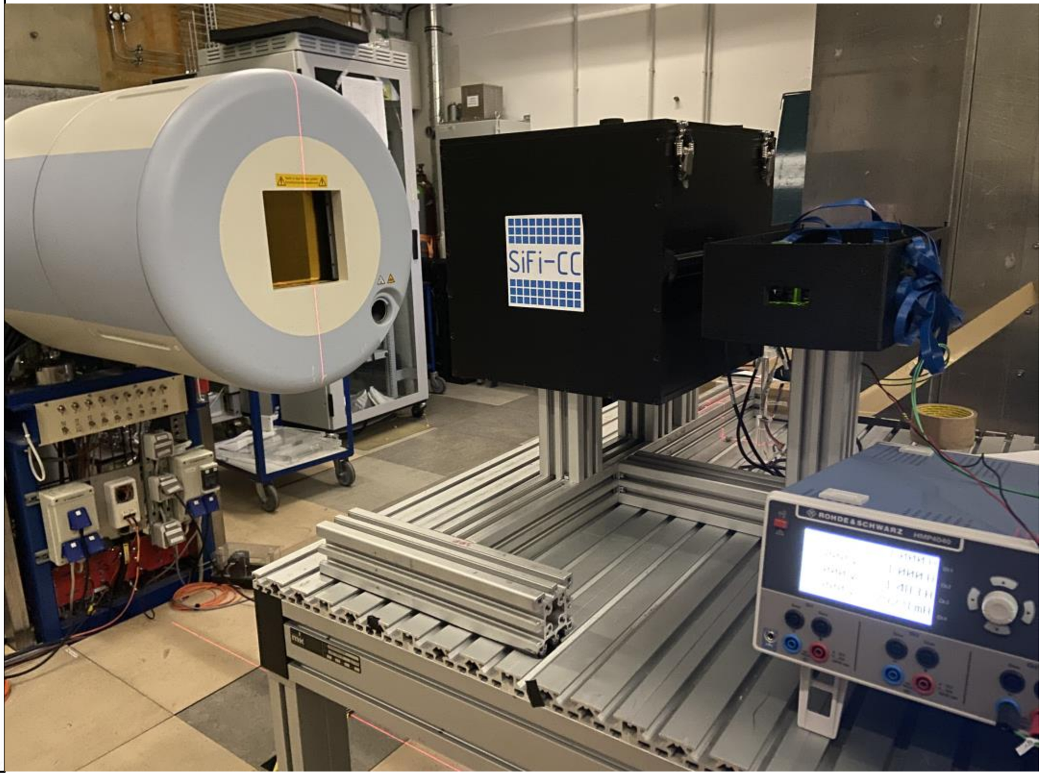
evaluation



What's next with SiFi-CC?

Scatterer reassembly → Tests with a proton beam in the coded mask mode → Construct absorber, full detector ready → Tests with a proton beam in the CC mode





Beam-activated tumour tracers

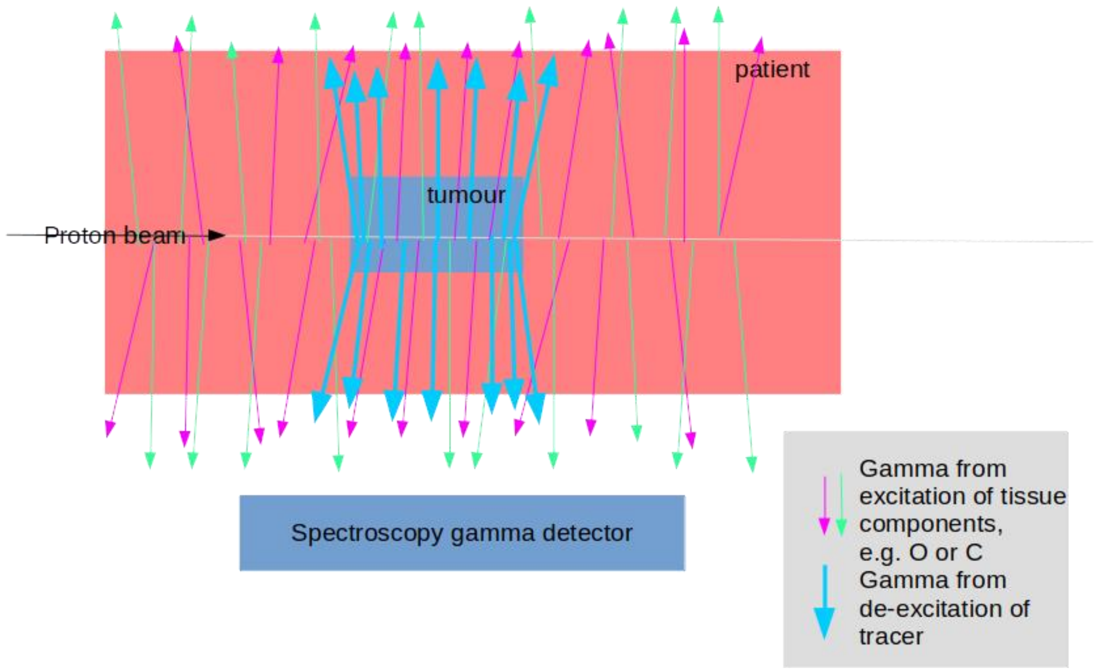
- PG = a footprint of elemental composition
- Are cancerous tissues significantly different from the healthy ones? NOT ALL

  Cai et al., Molecules 25, 2020
  Maughan et al., Med. Phys. 24, 1997

- Can we selectively deliver a selected element to tumour?? YES (PET, BNCT)
- Limitations:
  - Lack of toxicity
  - Absent in body
  - Selective delivery feasible
  - Stable, emits gamma only when excited by proton beam
  - Unique energy of discrete transitions, preferably 1.5-3 MeV
  - Short deexcitation time
  - Large cross section at Bragg peak, i.e. for small proton energies
- Similar in concept (though inversed logic) to
  Magalhaes Martins, Sci. Rep. 11, 2021
- Method proposed by several people about the same time (A. Stahl, G. Gazdowicz from SiFi-CC, also G. Cartechini from Trento Uni.)

https://agenda.infn.it/event/23656/contributions/120652/

Idea in a cartoon

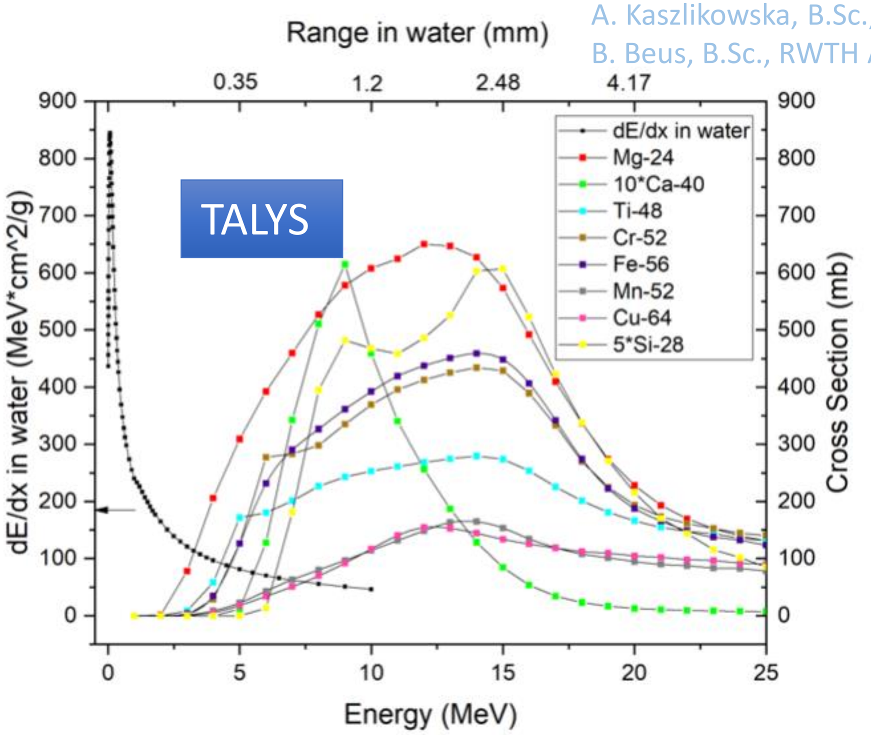


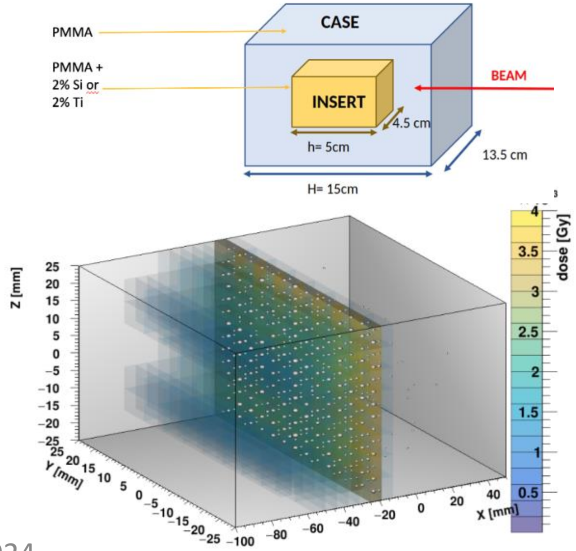
Search for tracers

- Promising $\sigma(E)$ dependence: Mg, Ca, Si
- Simulations to assess signal significance
- How to selectively deliver to tumour? Nanoparticles!
  Biology: a group of M. Parlińska from INP PAS in Kraków
- Initial results:
  - 2% mass concentration feasible for Si and Ti (MTS tests)
  - Signal appears for a proximal layer when BP contained in the tumour
  - Signal drops when BP moves downstream of tumour
  - Results of cell-culture studies encouraging

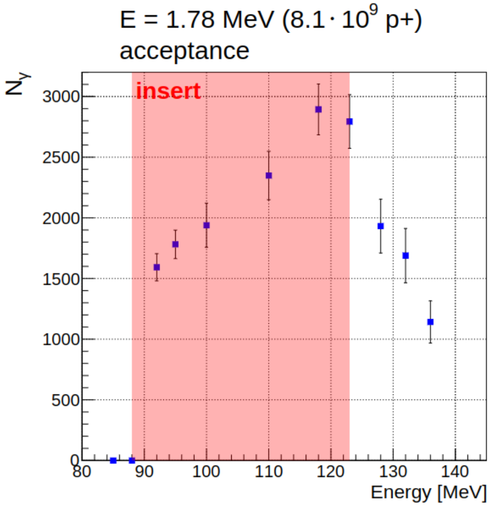
Paper under review in
Int. J. Radiat. Oncol. Biol. Phys.

A. Kaszlikowska, B.Sc., Jag Uni, 2021
B. Beus, B.Sc., RWTH Aachen, 2021





B. Kołodziej, M.Sc., Jag Uni, 2022



Summary

PG radiation is a hot topic in medical physics

Within the γCCB and SiFi-CC projects:

- We characterized in detail the PG emission in PT
- We validated the simulation tools (GEANT4, TALYS)
- We are building a dual-modality SiFi-CC setup for beam range monitoring in PT
- We are testing a method of tumour tracers activated by a proton beam

Educational aspects: work done mainly by students and PhD students.

Example of an intenese (though informal) Polish-German collaboration, with a Georgian support.

About bridges...