Proton imaging for small animals: status and perspectives

K. Parodi

Chair of the Department of Medical Physics,
Ludwig-Maximilians-Universität München, Garching b. München, Germany

Motivation

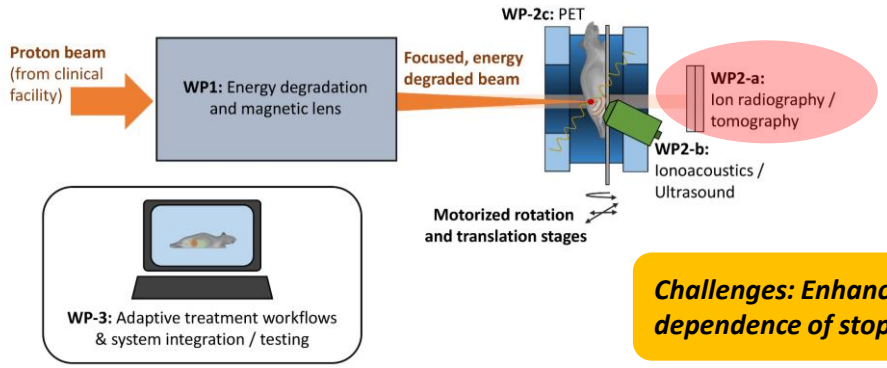
Emerging small animal radiotherapy research platforms for protons and heavier ions

However limited to morphological image guidance typically with X-ray CBCT

The SIRMIO project

Small animal proton irradiator for research in molecular image-guided radiation-oncology

Prototype system for precision, image-guided small animal proton irradiation



Challenges: Enhanced scattering and energy dependence of stopping power ratio (SPR)

Parodi et al, Acta Oncol 2019

WP2a: Proton radiography (pRAD)/tomography (pCT)

Pre-treatment radiographic & tomographic imaging

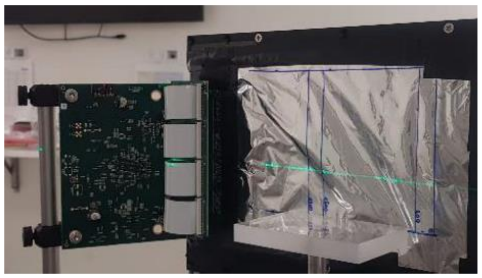
- Vertical irradiation position for imaging & treatment
- In-house holder accommodating sterility, anaesthetization and temperature stabilization, with minimal material budget and possibility of acoustic coupling
- Proton radiography for alignment and recovery of water equivalent thickness (WET)
- Proton tomography for assessment of tissue stopping power relative to water, SPR)

3 solutions being developed for conventional & synchrocyclotron-based facilities

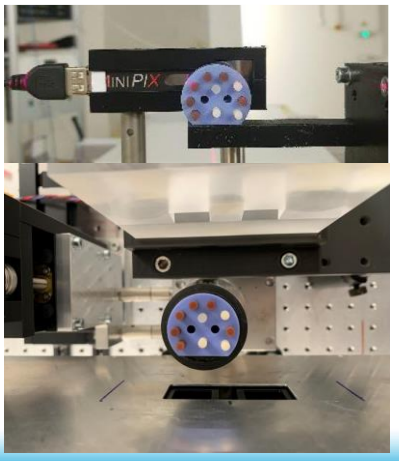
J. Bortfeldt et al, to be published

WP2a: Proton radiography (pRAD)/tomography (pCT)

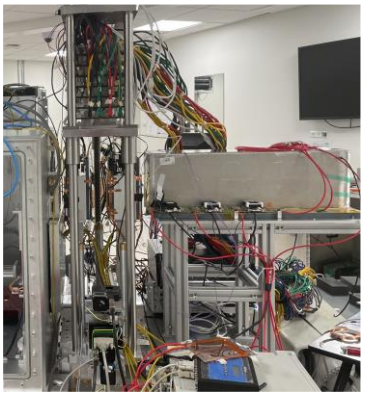
Integrated dE-measurement



Single particle dE-measurement



Single particle tracking and residual range measurement

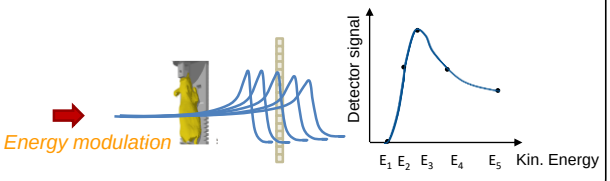


Proton radiography/tomography with pixelated detectors

1. Integrated dE-measurement with commercial CMOS detectors

Commercial pixel-detectors

- High dose (> 1 mGy per radiography)
- Do not account for Coulomb scattering
- Relatively **simple detectors**
- Integrated particle detection

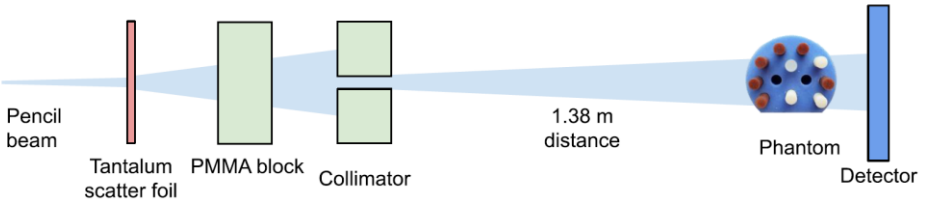


Large area CMOS detectors with linear signal decomposition method to determine WET

Schnürle PhD project, Schnürle et al, submitted to Front Phys

Proton radiography/tomography with pixelated detectors

Example for facility: Danish Centre for Particle Therapy



Beam

1) **Adapt energy to small animals / phantoms:** degrade to 5 – 60 MeV
2) **Energy variation:** treatment plan or degrader wheel
3) **Low beam current,** additional scattering and collimation

Drift space

Achieve homogeneous and low fluence illumination of the object

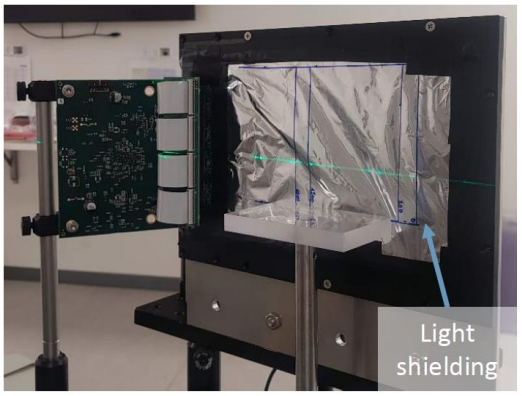
Phantom

µCT calibration phantom*

- Solid water baseplate (ø 30 mm, 10 mm thick)
- 10 tissue-equivalent inserts (ø 3.5 mm, 16 mm length)

Schnürle PhD project, Schnürle et al, submitted to Front Phys

Proton radiography/tomography with pixelated detectors



Lassena Detector (Nordson, Ohio) *

- CMOS sensor
- 50 µm pixel pitch
- 120 x 140 mm² pixel area
- developed for medical **X-ray** applications
- data transfer via optic fibre cable
- thin sensitive layer: 5.5µm
- Linearity of detector signal to proton energy deposition
- Practically no deadtime
- Up to 35 Hz frame rate (full frame)
- Stable acquisition and reliable file transfer

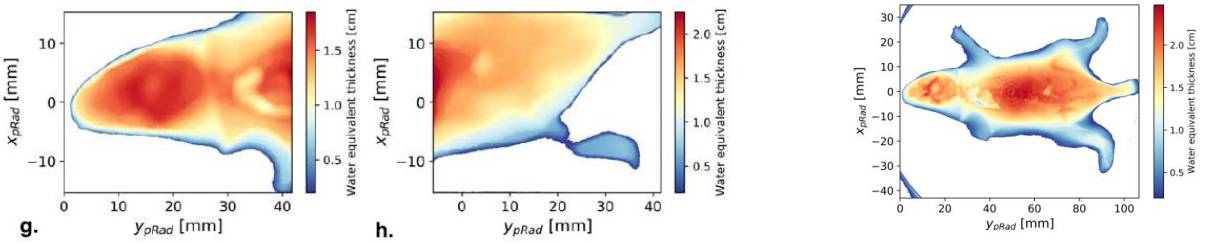
- **Rel. simple commercially available detectors**
- **large area**

* Sedgwick, I. et al. (2013). "LASSENA: A 6.7 Megapixel, 3-sides buttable, Wafer-Scale CMOS Sensor using a novel grid- addressing architecture"

Schnürle PhD project, Schnürle et al, submitted to Front Phys

Proton radiography/tomography with pixelated detectors

Experimental WET | **WET-DRR**



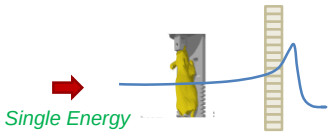
Lascaud, Dash, Schnürle…Parodi, PMB 2022

Proton radiography/tomography with pixelated detectors

2. Single particle dE-measurement with commercial CMOS detectors

Commercial pixel-detectors

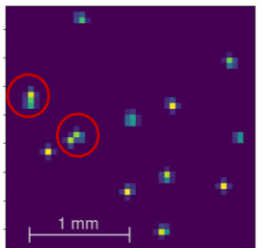
- High dose (> 1 mGy per radiography)
- Do not account for Coulomb scattering
- Relatively **simple detectors**
- Single particle detection

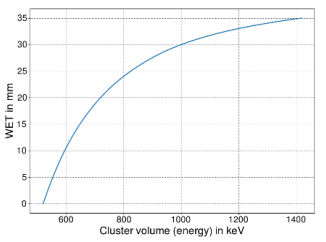


Detect energy deposition of individual particles

Minipix/Timepix, able of single particle detection

(collaboration with Advacam Radiation imaging Solutions)

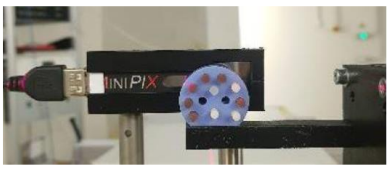


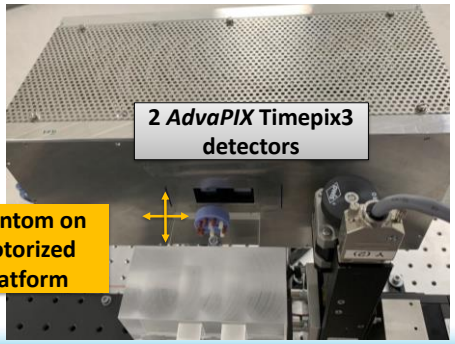


Würl et al, IEEE MIC Conference Records 2020

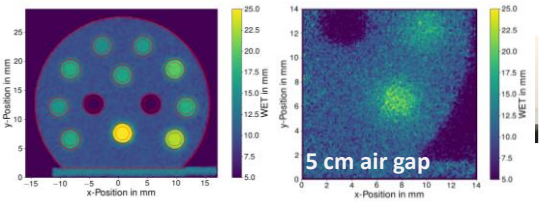
WP2a: pRAD & pCT
Commercial planar pixelated systems

Single particle detection
(i.e., position and dE)





pRad with predecessor *MiniPIX* (Trento 2020)
- Sub-mm spatial resolution
- WET accuracy better than 3%
- Long acquisition time (15 – 20 min)



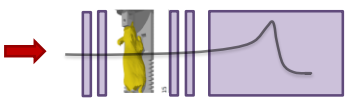
pRad & pCT with Timepix3 (Aarhus 2021)
- Comparable image quality for pRad
- Detailed data analysis in progress
- **Few seconds acquisition time (per radiography)**

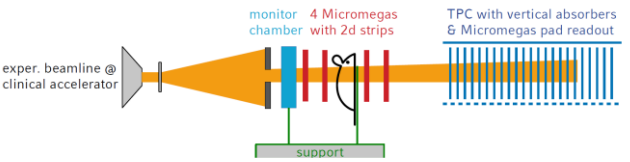
M. Würl et al, IEEE MIC 2020; manuscript in preparation

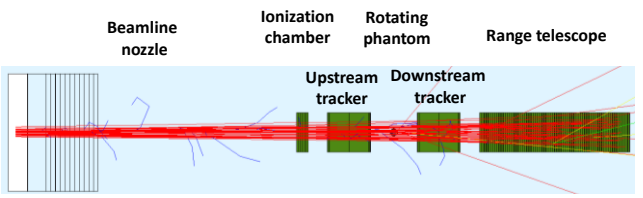
WP2a: Proton radiography (pRAD)/tomography (pCT)

3. Single particle tracking with in-house developed gas detectors

Single particle tracking
- Low dose (< 1 mGy per radiography)
- Accounts for Coulomb scattering
- **Complex detectors**







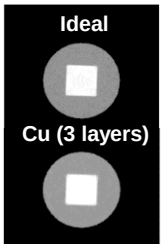
Detailed Monte Carlo modeling including all components and realistic beam

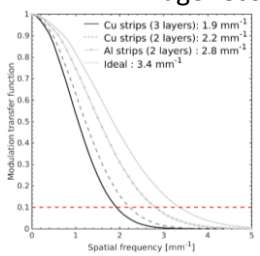
S. Meyer et al, PMB 2020; J. Bortfeldt et al, to be published

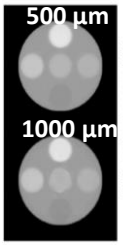
Proton radiography/tomography with in-house gas-based detectors

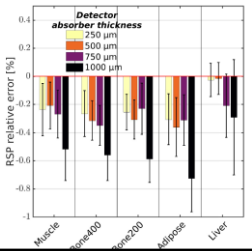
Optimization of single particle tracker and range telescope for best image quality

Image reconstruction using a **TVS OS-SART** algorithm



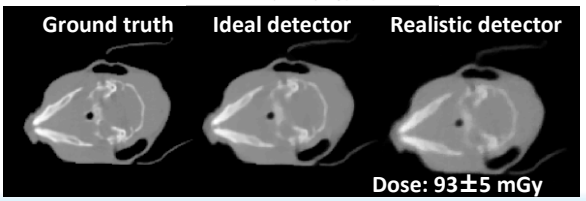


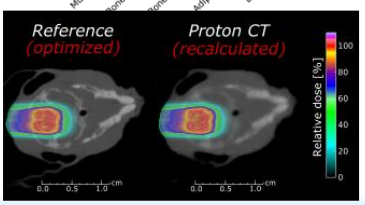


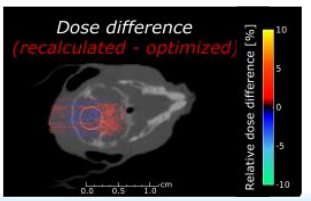


Final choice of tracker with Al strips and range telescope with 600 µm mylar plates

Average range error (0.87±0.98)%





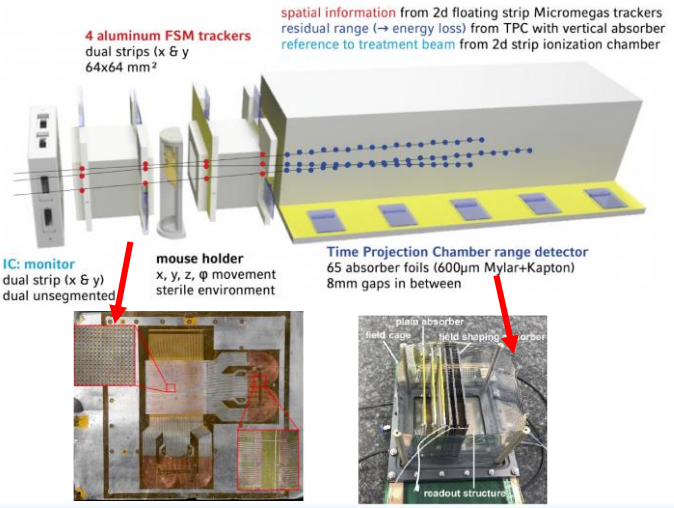


Bortfeldt et al, MPGD 2019; Meyer PhD thesis LMU; Meyer et al PMB 2020

Proton radiography/tomography with in-house gas-based detectors

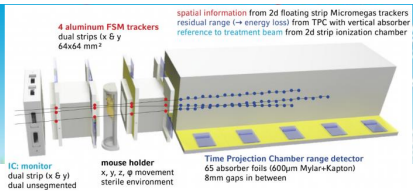
Extensive R&D program

- Since 2018: production methods
- 2019: successful tests of prototypes
- 2020: successful aging tests (MM)
- 2021: commissioning of full-size detectors with new CERN VMM DAQ supporting <1s / pRad



Bortfeldt et al, MPGD 2019 & Small animal conference 2022; Meyer et al PMB 2020; Holthoff et al, DGMP 2022

pRad/pCT with in-house gas-based detectors

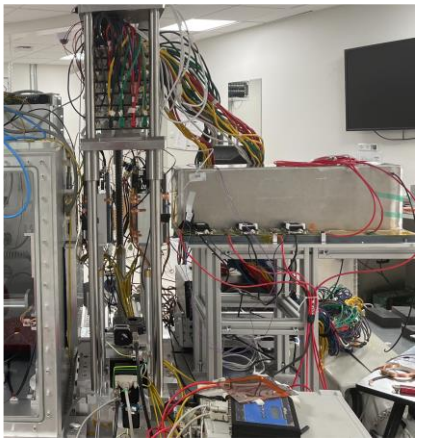


Ongoing work to

- Commission full prototype system

Just concluded beamtime at DPTC in Aarhus and data analysis in progress

- Interface exp. data to iterative image reconstruction framework



Bortfeldt et al, MPGD 2019 & Small animal conference 2022; ongong PhD project G. Hu; Holthoff et al, DGMP 2022 & ongoing MSc project

Future workflows & further developments

- pRAD (all systems) for alignment of imaging system to SIRMIO beamline for transfer to TPS
- pRAD (all systems) combined with xCT to compensate for anatomical changes and refine HU-RSP calibration


Poster panel: 417 — **Model-based and Data-driven Calibration of the X-ray CT Image based on Proton Radiographies** (#2257)
Poster Number: MIC-17-417
C. Gianoli[1], M. Zlatic[1], M. Würl[1], K. Schnürle[1], S. Meyer[1, 2], J. Bortfeldt[1], F. S. Englbrecht[1], P. Palaniappan[1], M. Riboldi[1], K. Parodi[1]
[1] Ludwig-Maximilians-Universität München, Department of Medical Physics - Experimental Physics, Munich, Bavaria, Germany
[2] Memorial Sloan Kettering Cancer Center, Department of Medical Physics, New York, New York, United States of America

To be presented at IEEE MIC, ongoing research in DFG Project HIGH-ART

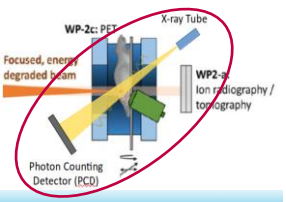

Multi-stage 2D-3D image registration based on proton radiographies for small animal proton irradiation: a simulation study
Prasannakumar Palaniappan[1], Yana Hryhorchyk[1], Sebastian Meyer[1§], Chiara Gianoli[1], Katrin Schnürle[1], Matthias Würl[1], Jonathan Bortfeldt[1], Katia Parodi[1+], Marco Riboldi[1+]
1. Department of Medical Physics – Experimental Physics, Ludwig-Maximilians-Universität München, Munich, Germany
§ Now at: Department of Medical Physics, Memorial Sloan Kettering Cancer Center, New York, NY, USA
+These authors contributed equally to this work

Submitted to ZMP

- pCT (systems 2-3) for online planning

Collaboration with RaySearch Laboratories

M. Pinto et al, to be published

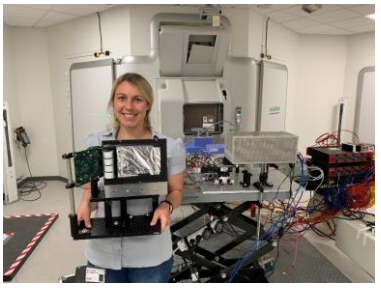


- Assembling small scale setup for combined spectral X-ray/proton imaging

PhD Project M. Chen

Conclusion & Outlook

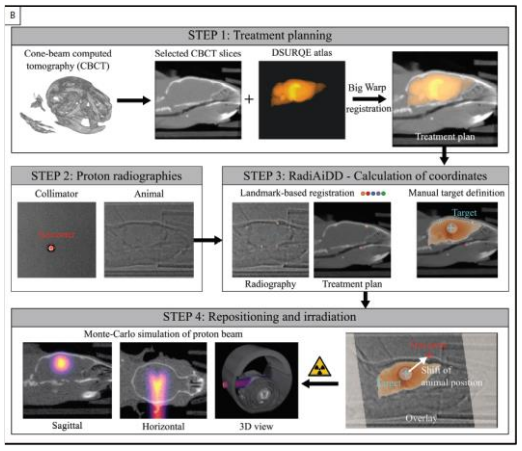
- Developed several small animal pRad/pCT systems, from integrating to single-particle tracking detectors
- Promising performance in terms of WET/SPR accuracy and sub-mm spatial resolution for realistic setups
- Ongoing data analysis of recent experimental campaigns will enable more in-depth assessment for final workflow in SIRMIO platform



Experimental campaigns at Danish Centre for Proton Therapy, Sept 2021 & 2022

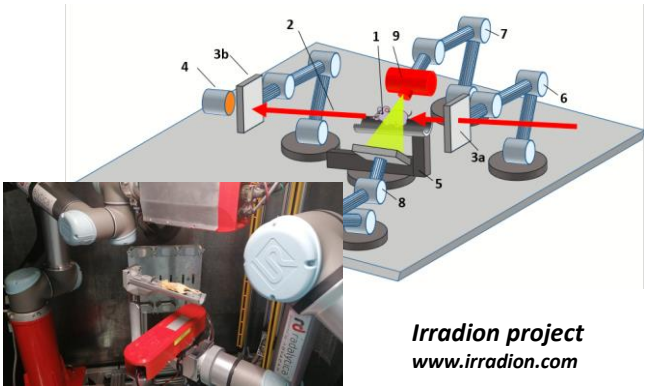
Additional systems under development worldwide

Proton radiography with flat panel



Schneider et al, Front Oncol 2022

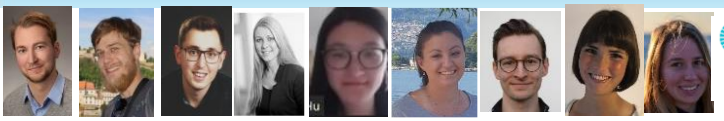
Proton & X-ray imaging with robotic system



Irradion project
www.irradion.com

Verhaegen et al, submitted to PMB

Acknowledgement



J. Bortfeldt M. Würl S. Meyer K. Schnürle G. Hu B. Foglia G. Holthoff P. Lämmer A. Noto

and many more HiWi/BSc students…

Martin Hillbrand
Indra Yohannes
Daniel Köpl

M. Schwarz
E. Verroi
F. Tommasino

M. Vidal
P. Hofverberg
J. Hérault

LMU Department of Experimental Medical Physics

E. Traneus,
R. Nilsson

M. Sitarz
P. Poulsen
C. Søndergaard
C. Grau

C. Granja
C. Oancea

RD51 collaboration

Thank you for your attention