Proton CT –
quasi-online dose plan verification and online dose delivery monitoring

Dieter Roehrich
University of Bergen
for the Bergen pCT collaboration

- **Bragg peak position – the critical parameter in dose planning**
- **Proton-CT – a diagnostic tool for**
  - **quasi-online dose plan verification**
  - **online dose delivery monitoring**
- **Towards a clinical prototype**
  - **Digital tracking calorimeter**
  - **Results from simulations and beam tests**

The Bergen proton CT collaboration

The Bergen pCT collaboration and the SIVERT research group

Institutions

University of Bergen, Norway

Helse Bergen, Norway

Western Norway University of Applied Science, Bergen, Norway

Wigner Research Center for Physics, Budapest, Hungary

DKFZ, Heidelberg, Germany

Saint Petersburg State University, Saint Petersburg, Russia

Utrecht University, Netherlands

RPE LTU, Kharkiv, Ukraine

Suranaree University of Technology, Nakhon Ratchasima, Thailand

China Three Gorges University, Yichang, China

University of Applied Sciences Worms, Germany

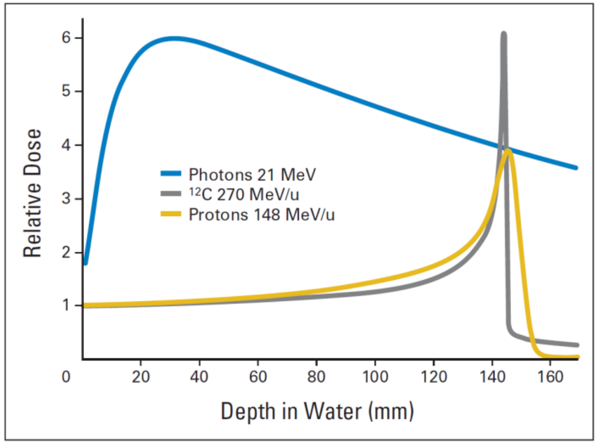
University of Oslo, Norway

Eötvös Loránd University, Budapest, Hungary

Technical University TU Kaiserslautern, Germany

Particle therapy - the Bragg peak position

- **Key advantage of ions: Bragg peak**
  - **Relatively low dose in the entrance channel**
  - **Sharp distal fall-off of dose deposition (<mm)!**



- **Challenge**
  - **Stopping power of tissue in front of the tumor has to be known – crucial input into the dose plan for the treatment**
  - **Stopping power is described by Bethe-Bloch formula:**

    - dE/dx ~ (electron density) x
    ln((max. energy transfer in single collision)/(effective ionization potential)^2)

- **Current practice**
  - **Derive stopping power from X-ray CT**
  - **Problem:**
    X-ray attenuation in tissue depends not only on the density, but also strongly on Z (Z^5 for photoelectric effect) and X-ray energy

Stopping power calculation from X-ray CT – range uncertainties

Clinical practice

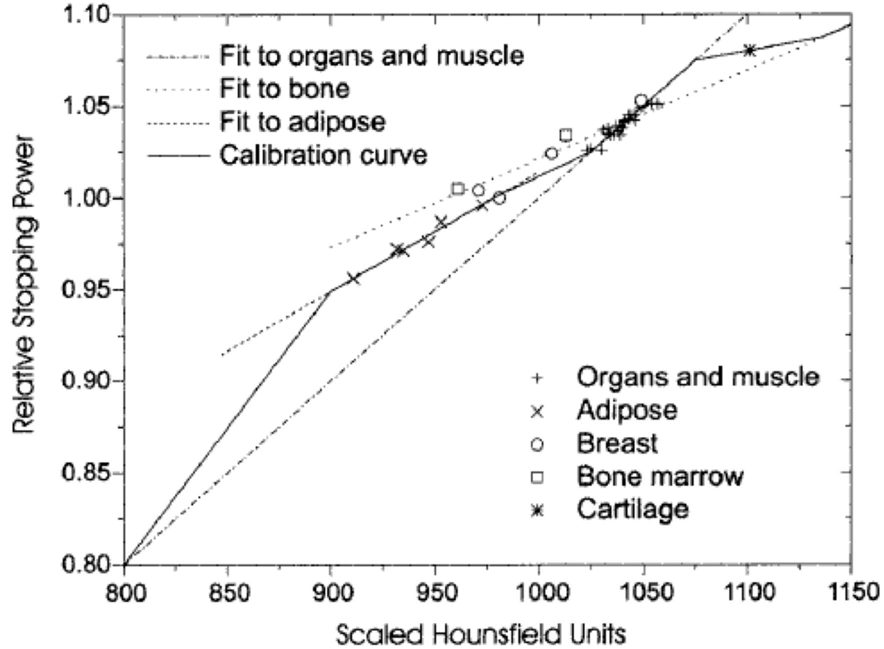
- Stopping power calculation derived from single energy CT:
  up to 7.4 % uncertainty

How to deal with range uncertainties in the clinical routine?

- Increase the target volume by up to 1 cm in the beam direction
- Avoid beam directions with a critical organ behind the tumor

Unnecessary limitations

-> reduce range uncertainties



Schaffner, B. and E. Pedroni, *The precision of proton range calculations in proton radiotherapy treatment planning: experimental verification of the relation between CT-HU and proton stopping power.* Phys Med Biol, 1998. 43(6): p. 1579-92.

Estimates for advanced dose planning:

- Dual energy CT: up to 1.7 % uncertainty
- Proton CT: up to 0.3 % uncertainty

A comparison of dual energy CT and proton CT for stopping power estimation

David C. Hansen,[1, a)] Joao Seco,[2] Thomas Sangild Sørensenn,[3] Jørgen Breede Baltzer Petersen,[4] Joachim E. Wildberger,[5] Frank Verhaegen,[6] and Guillaume Landry[7]

[1)] *Department of Experimental Clinical Oncology, Aarhus University*

Imaging with protons – nothing new

- **Proton radiography**

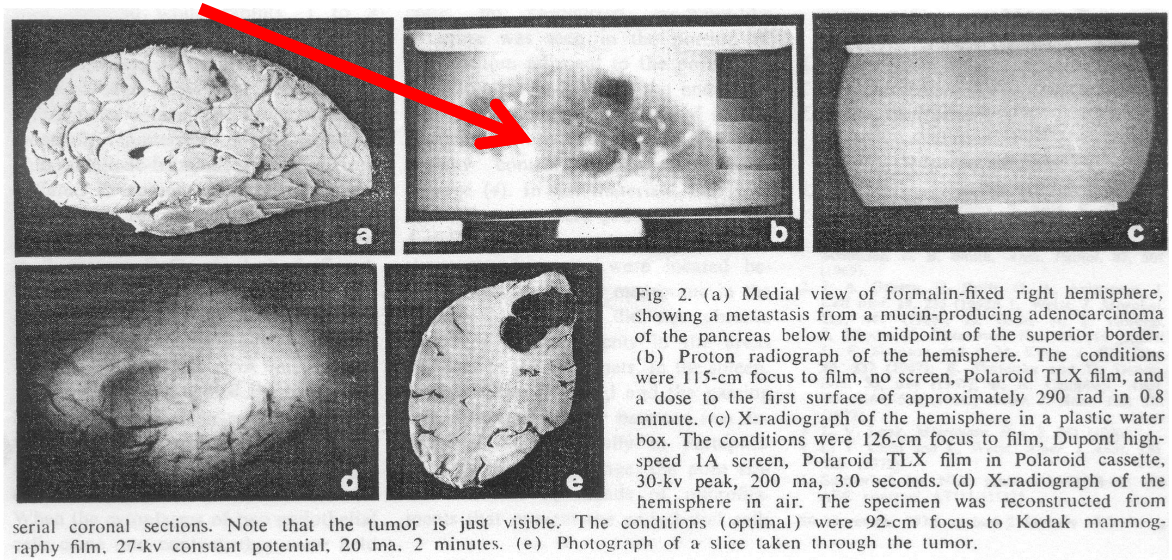
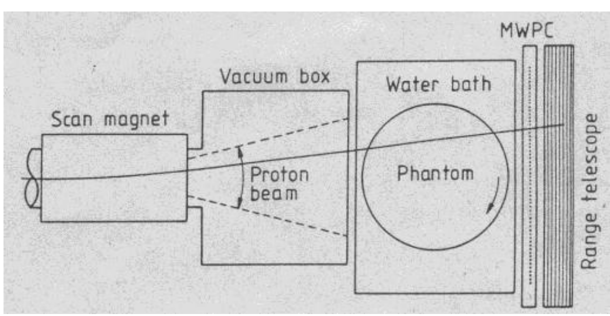


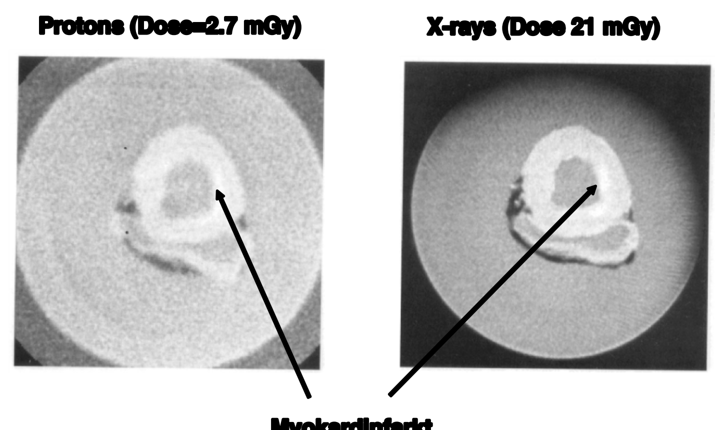
Fig 2. (a) Medial view of formalin-fixed right hemisphere, showing a metastasis from a mucin-producing adenocarcinoma of the pancreas below the midpoint of the superior border. (b) Proton radiograph of the hemisphere. The conditions were 115-cm focus to film, no screen, Polaroid TLX film, and a dose to the first surface of approximately 290 rad in 0.8 minute. (c) X-radiograph of the hemisphere in a plastic water box. The conditions were 126-cm focus to film, Dupont high-speed 1A screen, Polaroid TLX film in Polaroid cassette, 30-kv peak, 200 ma, 3.0 seconds. (d) X-radiograph of the hemisphere in air. The specimen was reconstructed from serial coronal sections. Note that the tumor is just visible. The conditions (optimal) were 92-cm focus to Kodak mammography film, 27-kv constant potential, 20 ma, 2 minutes. (e) Photograph of a slice taken through the tumor.

Steward and Kohler (1973)

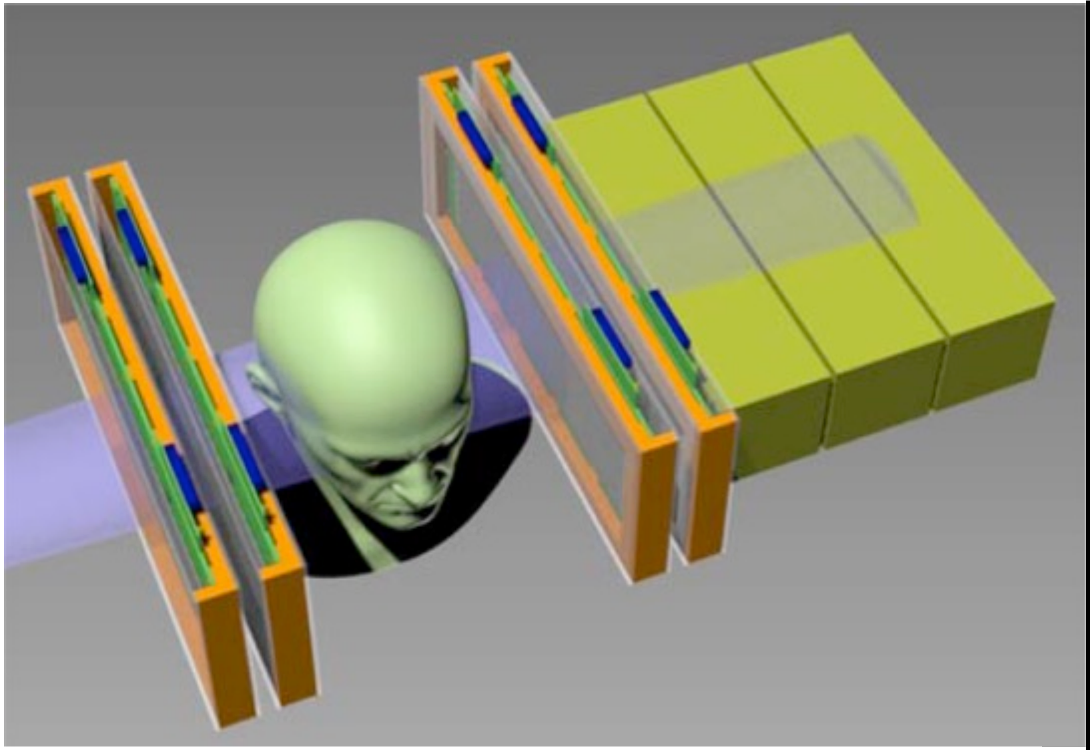
- **Proton CT**



Hanson et al (1982)



Proton CT



H.F.-W. Sadrozinski / Nuclear Instruments and Methods in Physics Research A 732 (2013) 34–39

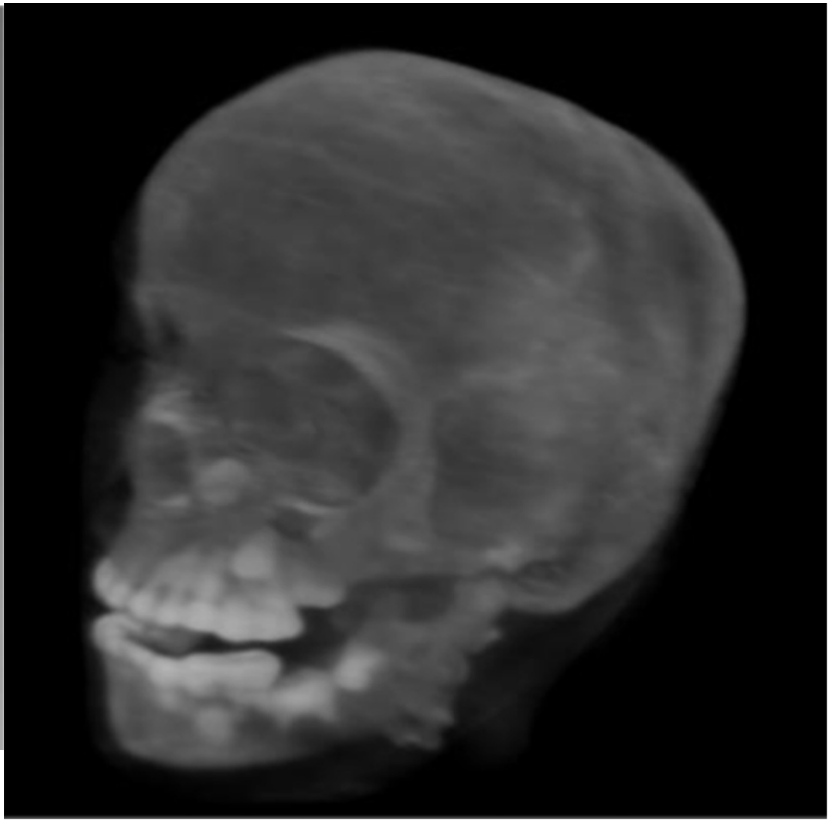
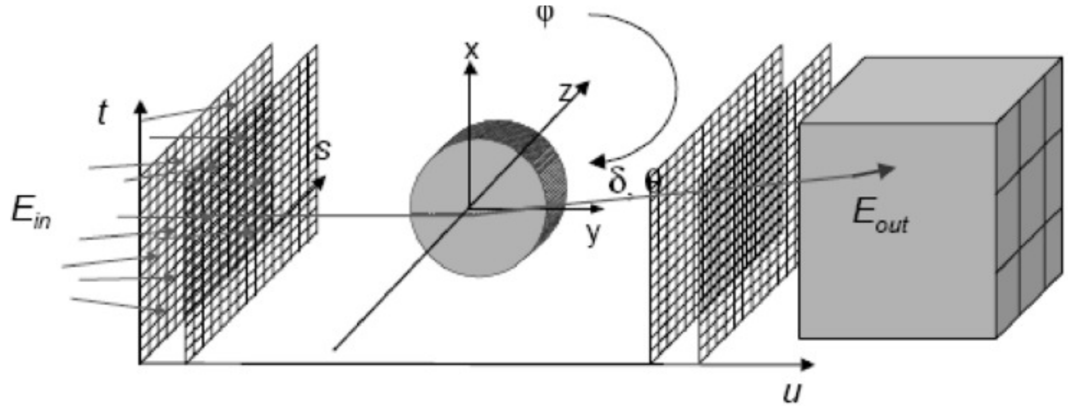


Fig. 14. 3D rendering of the pCT-reconstructed RSP map of a pediatric anthropomorphic head phantom.

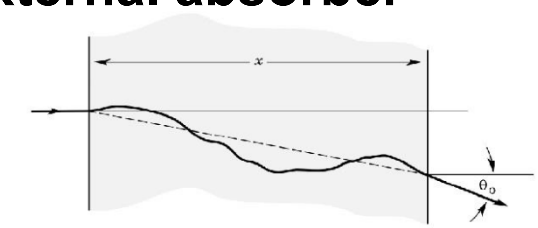
V.A. Bashkirov et al. / Nuclear Instruments and Methods in Physics Research A 809 (2016) 120–129

Proton-CT
- quasi-online dose plan verification

- **high energetic proton beam quasi-simultaneous with therapeutic beam**
- **measurement of scattered protons**
  - **position, trajectory**
  - **energy/range**



- **reconstruction of trajectories in 3D and range in external absorber**
  - **trajectory, path-length and range depend on**
    - **nuclear interactions (inelastic collisions)**
    - **multiple Coulomb scattering (elastic collisions)**
    - **energy loss dE/dx (inelastic collisions with atomic electrons)**



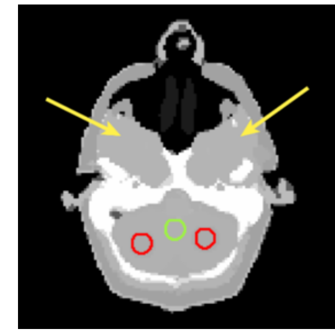
- **MS theory and Bethe-Bloch formula of average energy loss in turn depend on electron density in the target (and ionization potentials)**

-> 3D map of stopping power

-> online verification of dose plan

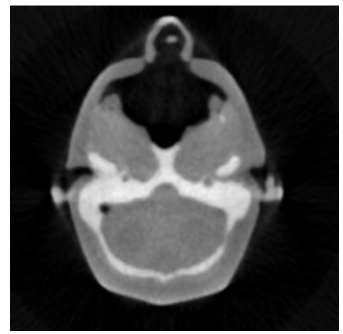
Proton-CT - images

- Traversing proton beam creates three different 2D maps
  → three imaging modalities



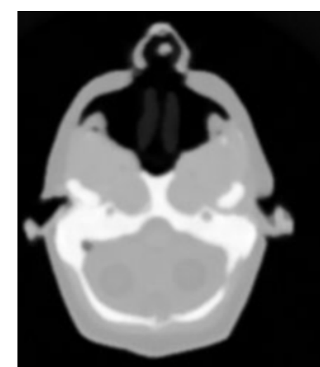
Phantom

  - Transmission map
    – records loss of protons due to nuclear reactions



  - Scattering map
    – records scattering of protons off Coulomb potential

  - Energy loss map
    – records energy loss of protons (Bethe-Bloch)

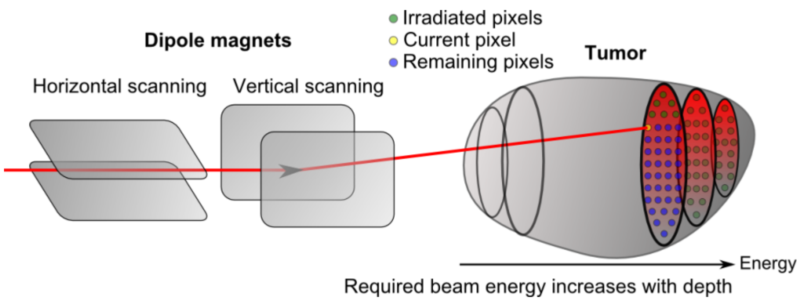


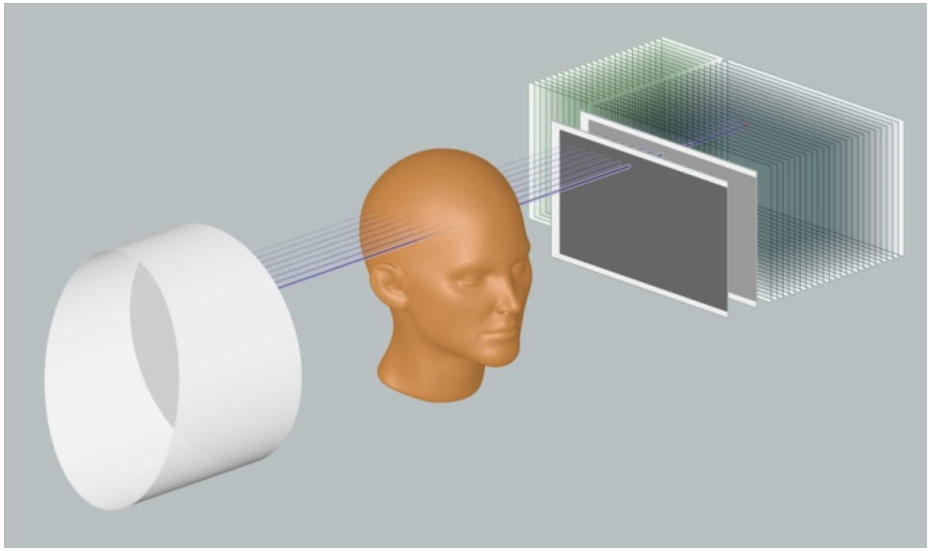
Cecile Bopp. PhD thesis, Strasbourg, 2013

Clinical pCT - requirements

Operate with clinical beam settings

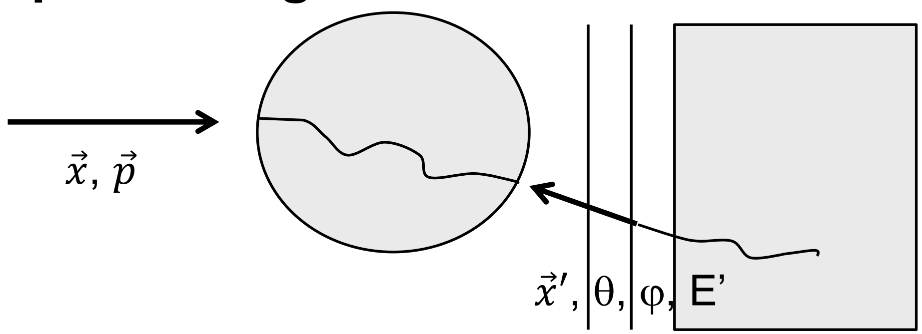
- **Pencil beam scanning mode**
  - **Beam spot size, scanning speed, intensity**
- **Scanning time**
  - **Seconds … minutes**
- **Detector**
  - **Efficient simultaneous tracking of large particle multiplicities**
  - **Large area (~30 x 30 cm^2)**
  - **Radiation hardness**
  - **High position resolution (~10 μm)**
  - **Front detector (first 2-3 layers):**
    very low mass, thin sensors (~100 μm)
  - **Back detector:**
    range resolution <1% of path-length
- **System**
  - **Compact**
  - **No gas, no HV**
  - **Simple air/water cooling**

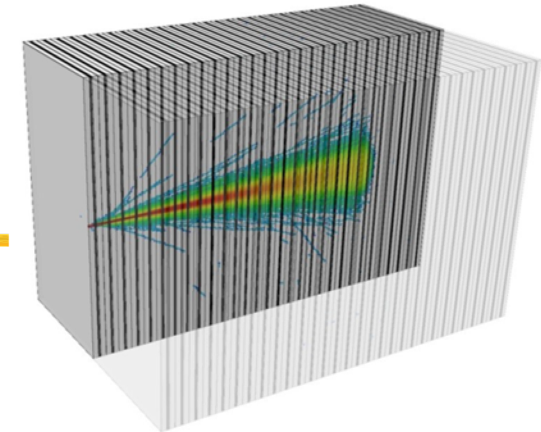


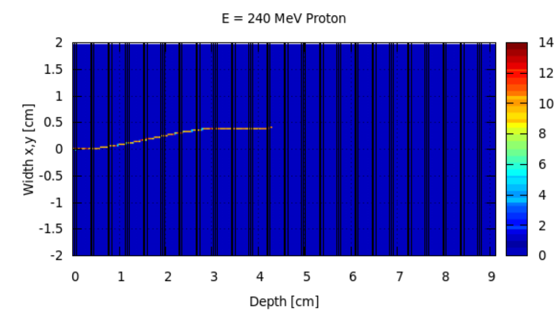


Clinical pCT - design

- Conceptual design



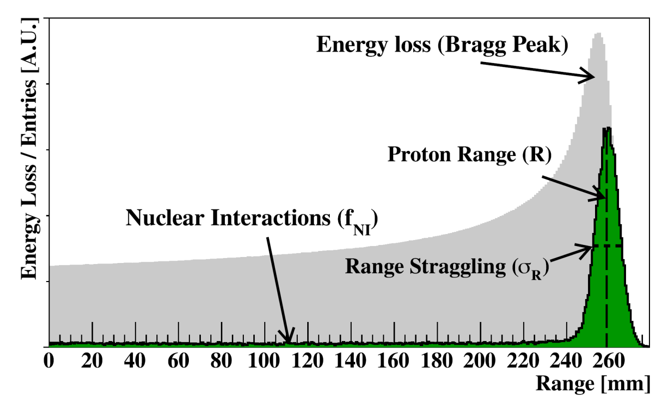




  - ***x,p*** given by beam optics and scanning system
  - ***x'****, θ, φ, E'* **have to be measured with high precision**
    - position resolution ~5 μm with minimal MS, i.e. first two tracking layers very thin

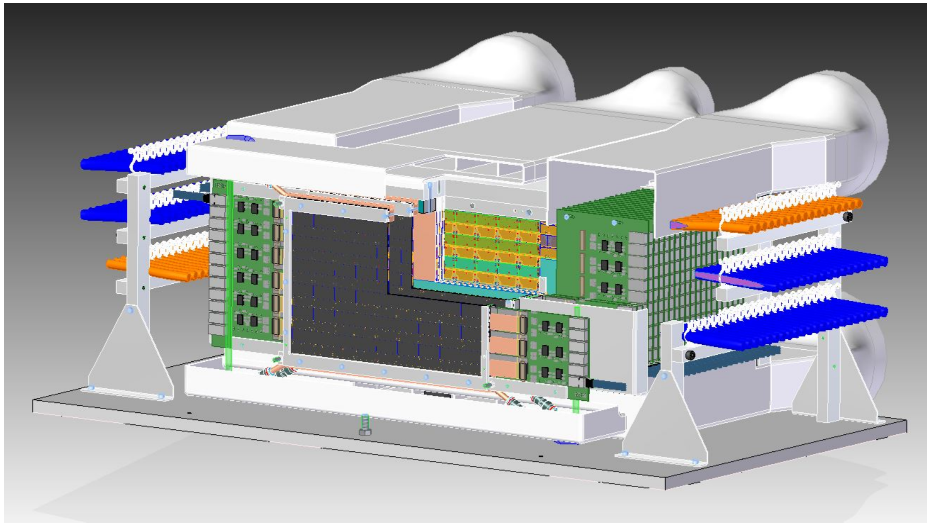
→ Extremely high-granularity digital calorimeter for tracking, range and energy loss measurement

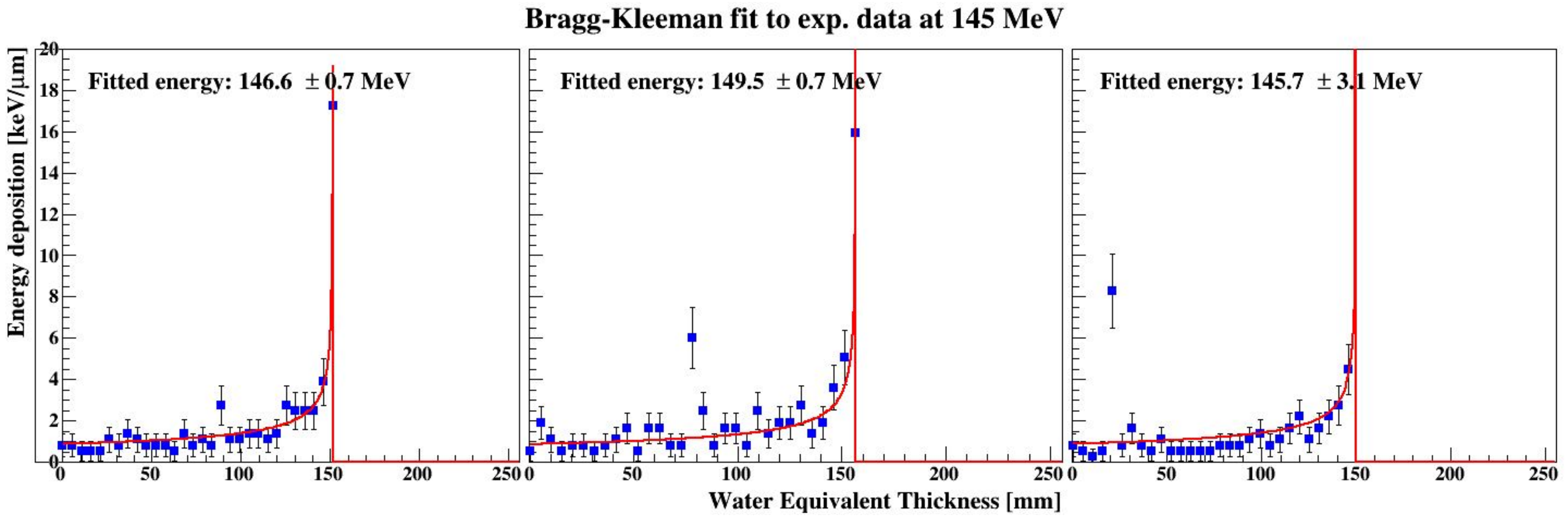
- Technical design
  - Planes of CMOS sensors – Monolithic Active Pixel Sensors (MAPS) with digital readout– as active layers in a sampling calorimeter



The Bergen pCT (clinical) prototype

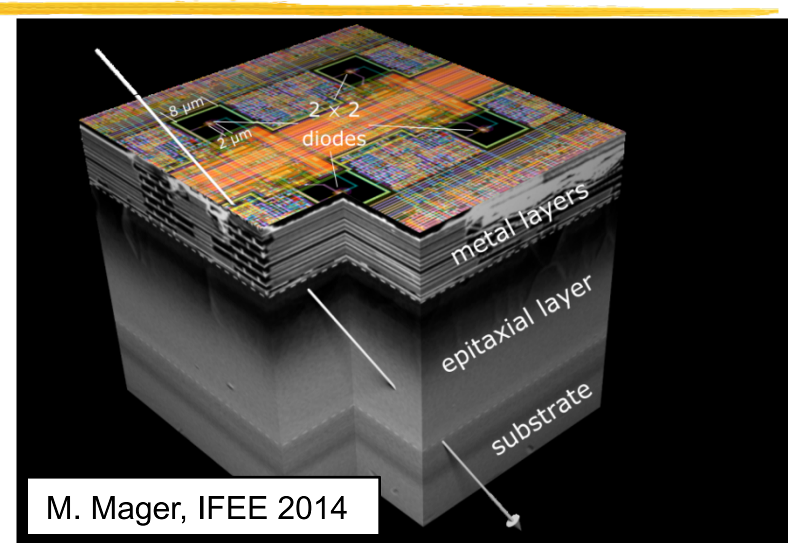
- **geometry**
  - **front area: 27 cm x 18 cm**
- **”sandwich” calorimeter**
  - **alternating layers of absorbers and sensors**
  - **longitudinal segmentation: 41 layers**
- **aluminium absorbers**
  - **energy degrader, mechanical carrier, cooling medium**
  - **thickness: 3.5 mm**



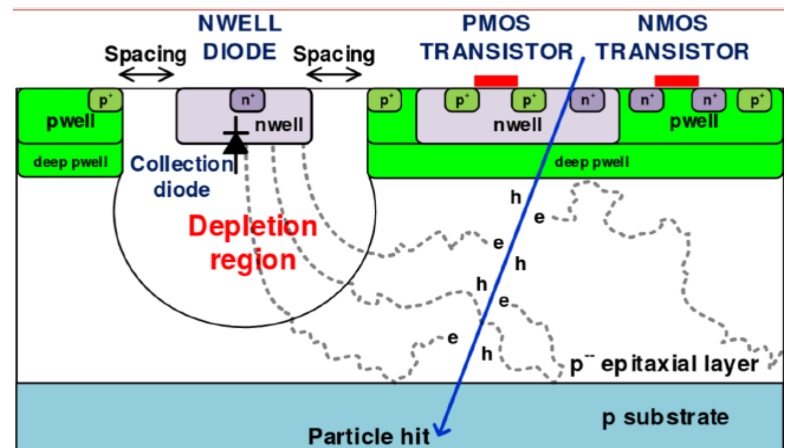


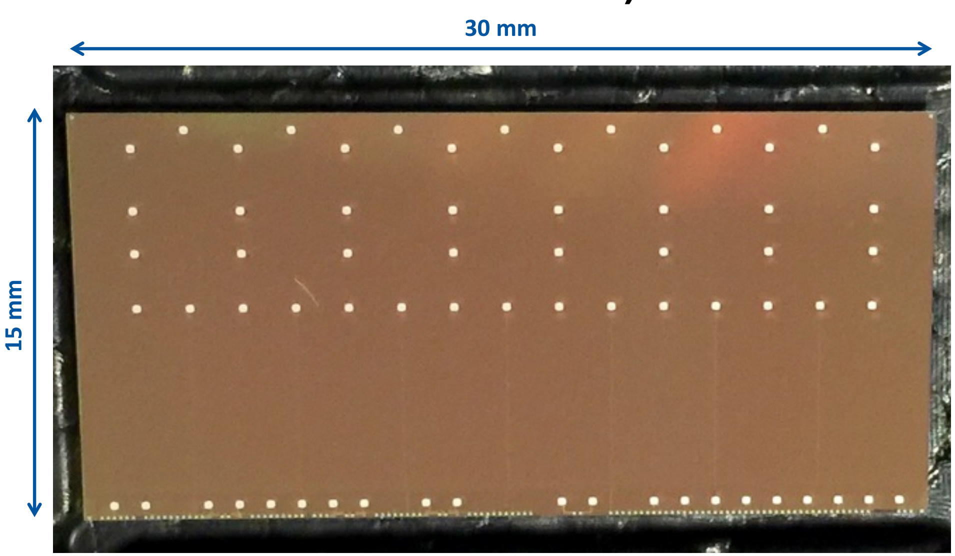
Sensor layers –
Monolithic Active Pixel Sensors (MAPS)

- **ALPIDE chip**
  - **sensor for the upgrade of the inner tracking system of the ALICE experiment at CERN**
  - **chip size ≈ 3x1.5 cm², pixel size ≈ 28 µm, integration time ≈ 4 µs**
  - **on-chip data reduction (priority encoding per double column)**



M. Mager, IFEE 2014





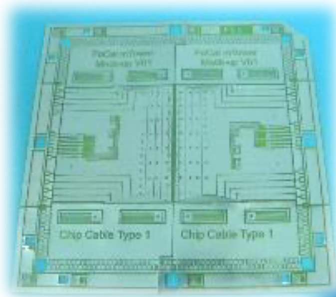
Design team:
CCNU Wuhan, CERN Geneva, YONSEI Seoul, INFN Cagliari, INFN Torino, IPHC Strasbourg, IRFU Saclay, NIKHEF Amsterdam

Mounting sensors on flexible cables

- **ALPIDE mounted on thin flex cables (aluminium-polymide dielectrics: 30 μm Al, 20 μm plastic)**

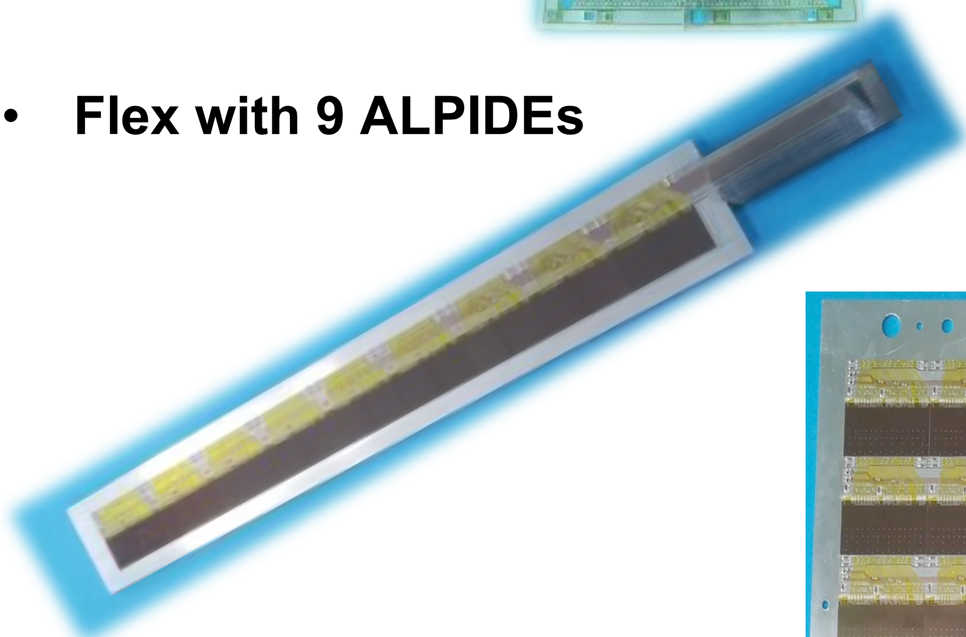
ALPIDE chip

chip cable



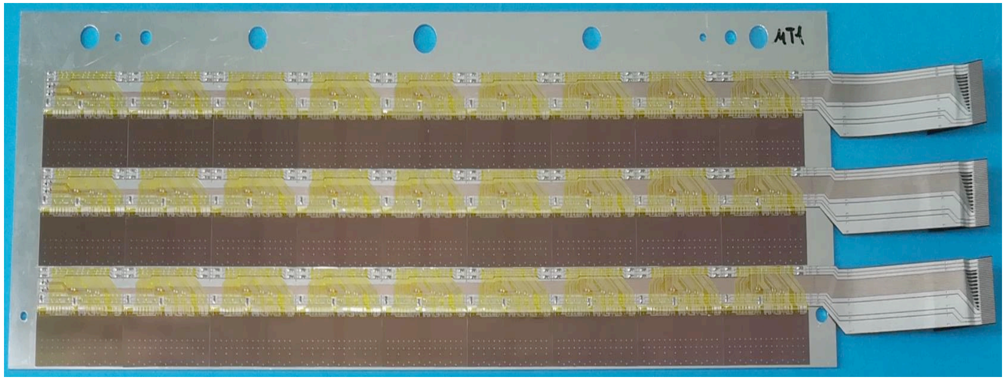
Design and production:
LTU, Kharkiv, Ukraine

- **Flex with 9 ALPIDEs**



- **Module - flex on Al carrier**

flexible carrier board modules with 2x3 strings with 9 chips each

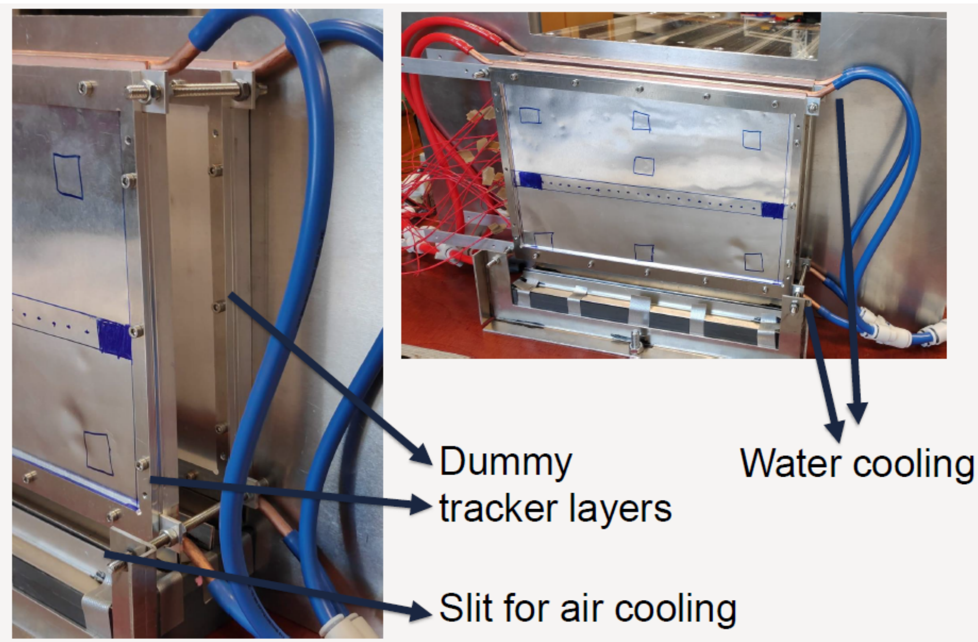


Assembly at IFT/UiB

- **Ultra-thin tracking layers**
  - **thinned ALPIDEs (50 μm) mounted on a thin flex and glued to a large sandwiched carbon fiber sheet (pyrolytic graphite paper + carbon fleece + epoxy resin)**

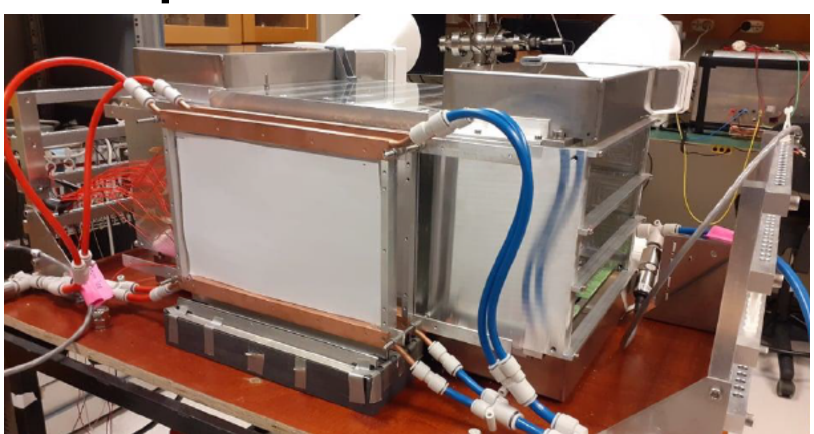
Sandwiched carbon fiber sheet, fabricated at St Petersburg State University

mechanical integration and cooling



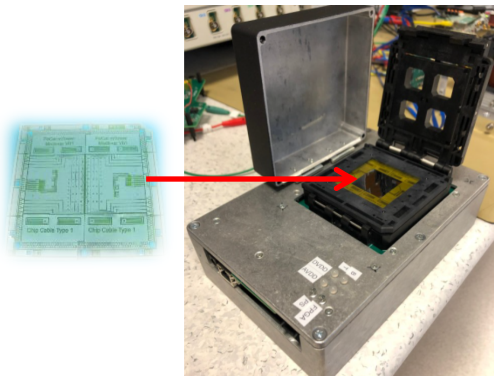
Prototype tracking layers designed fabricated by Utrecht University, tested at University of Bergen

- **Setup in the lab**

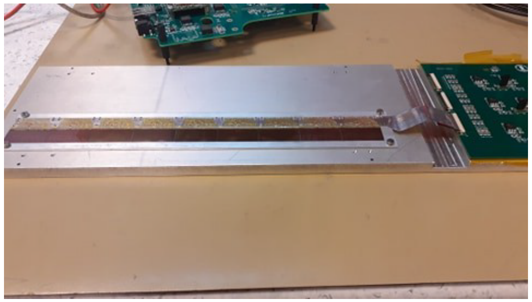


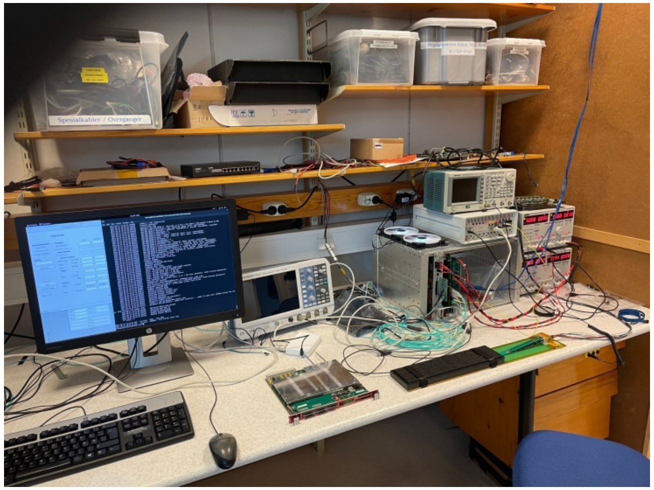
Readout electronics

- Test station for ALPIDE sensor mounted on chip cable

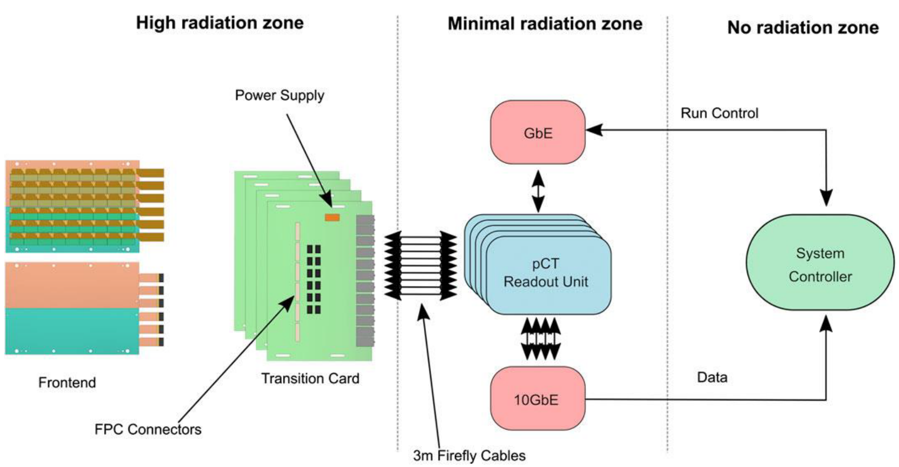


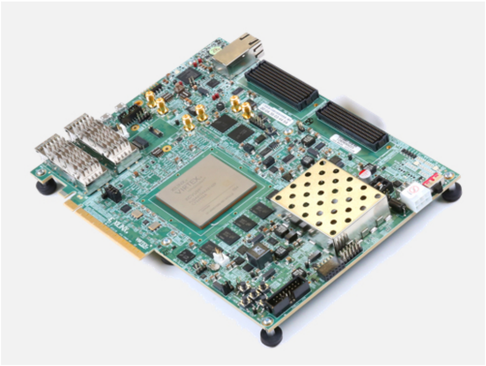
- Test station for full 9-chip string





- pCT readout unit – FPGA based design

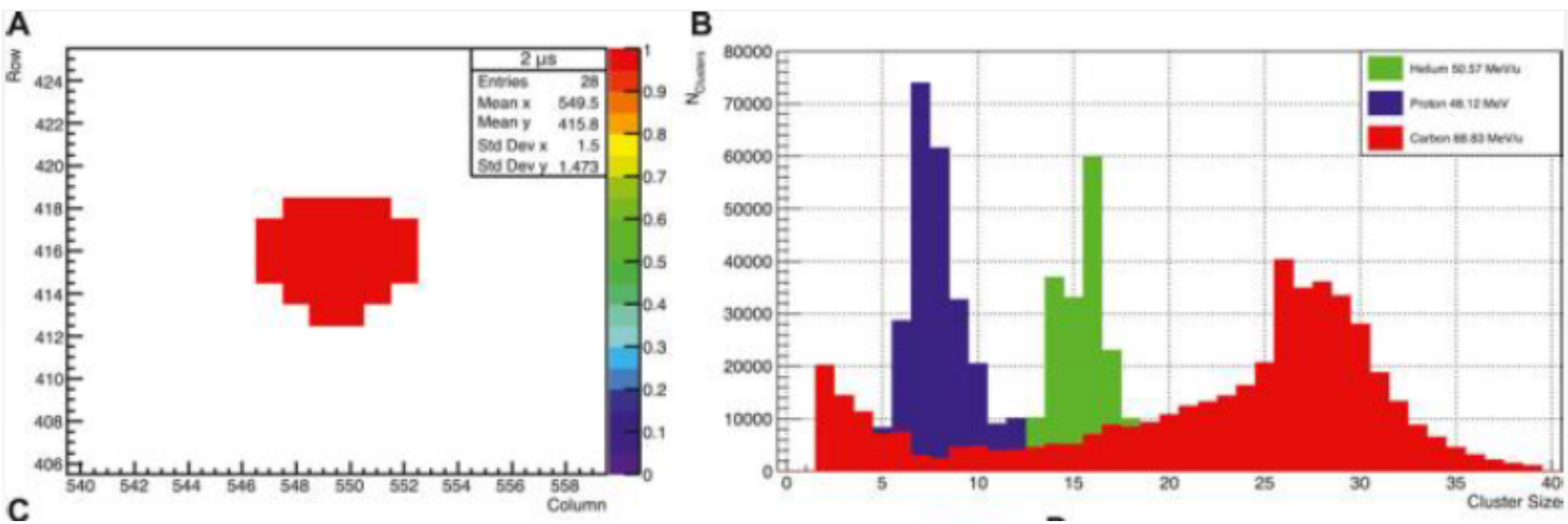




How to measure energy loss with a digital pixel sensor?

- **Operate ALPIDE in ”charge collection by diffusion mode”**
- **Measure size of charge cluster**

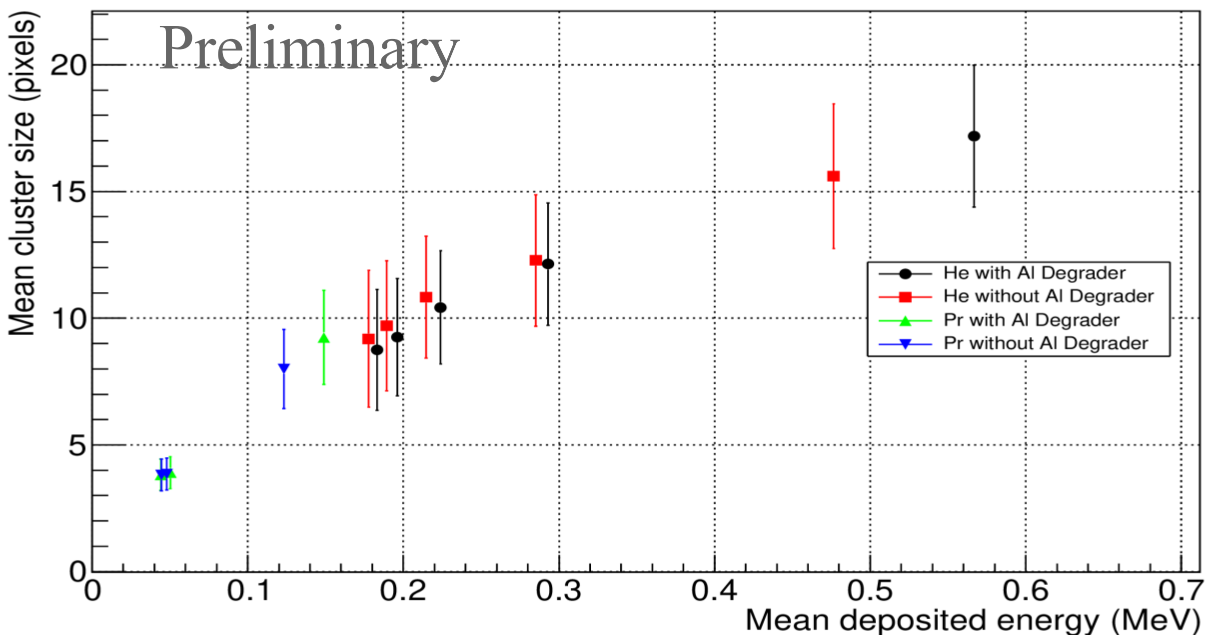
α particle **proton – α – C**



How to measure energy loss with a digital pixel sensor?

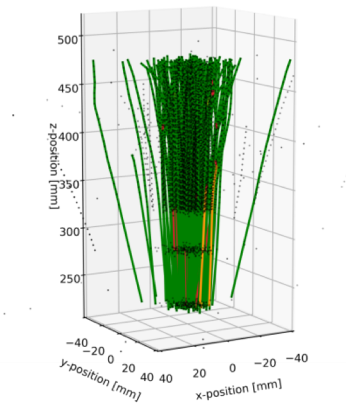
- **Operate ALPIDE in ”charge collection by diffusion mode”**
- **Measure size of charge cluster**

- **Results from proton and He-beams at different energies (HIT)**

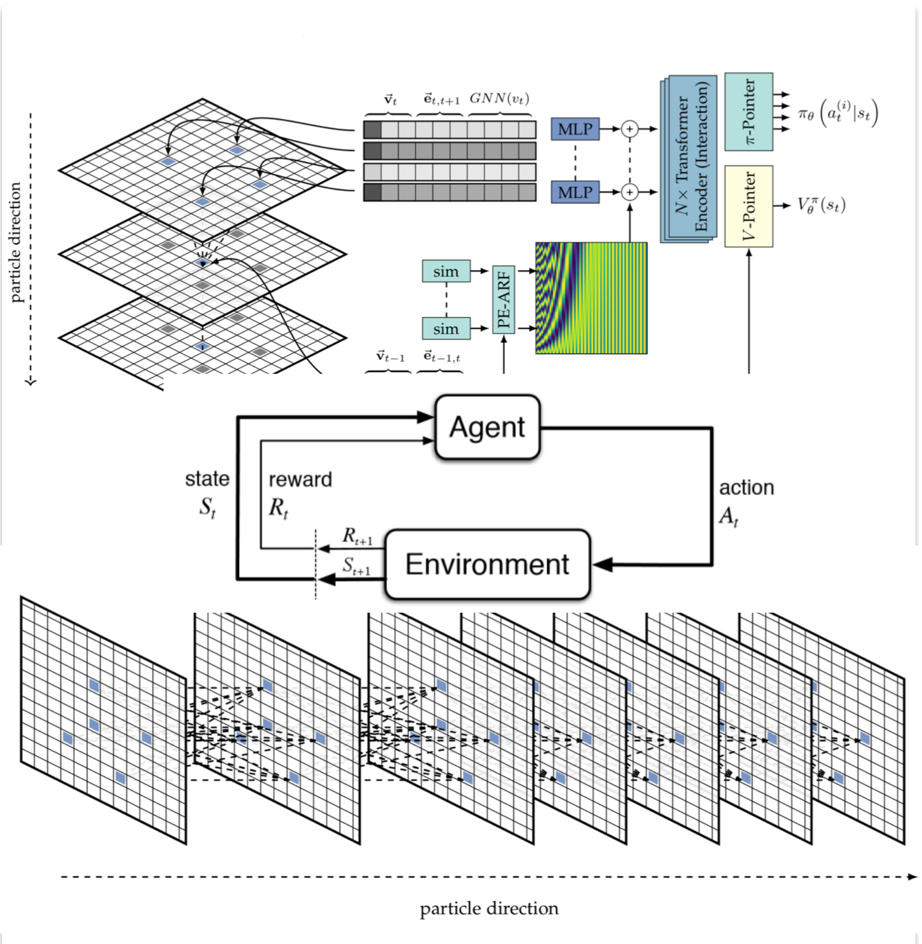


- **Cluster size increases with simulated energy loss**

Track reconstruction

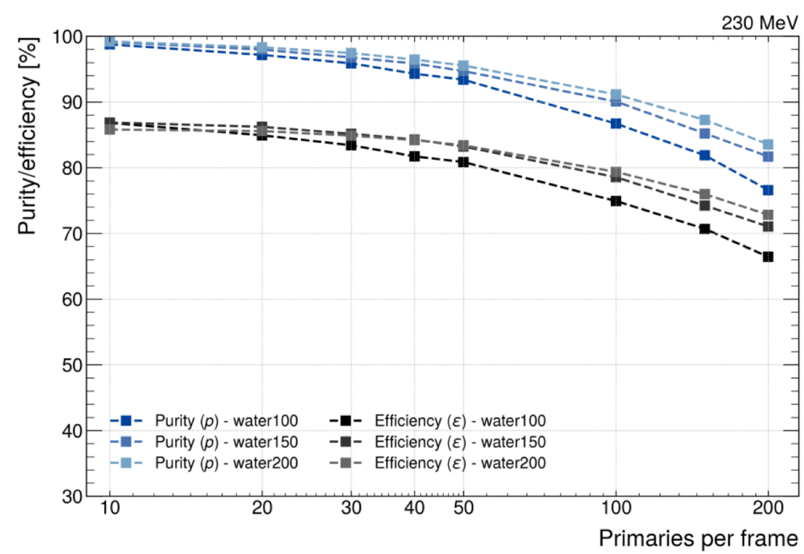


- **Reinforcement Learning for particle tracking**



- **Optimization technique for track reconstruction requiring no manual supervision**
- **Architecture allows for generalization to previously unseen phantom geometries and particle densities**

- **Preliminary results:**

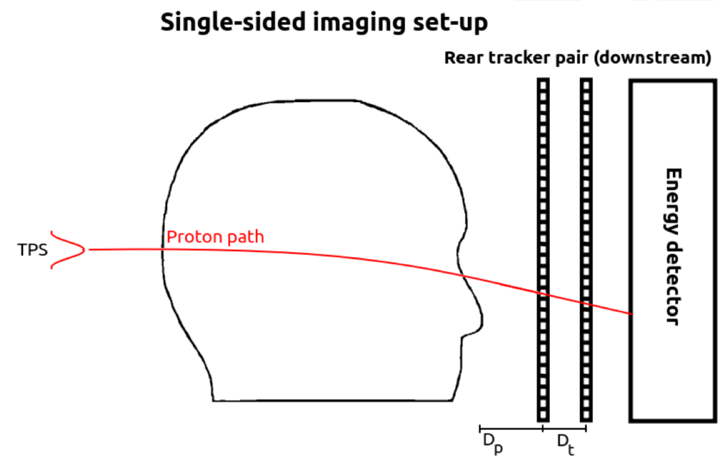


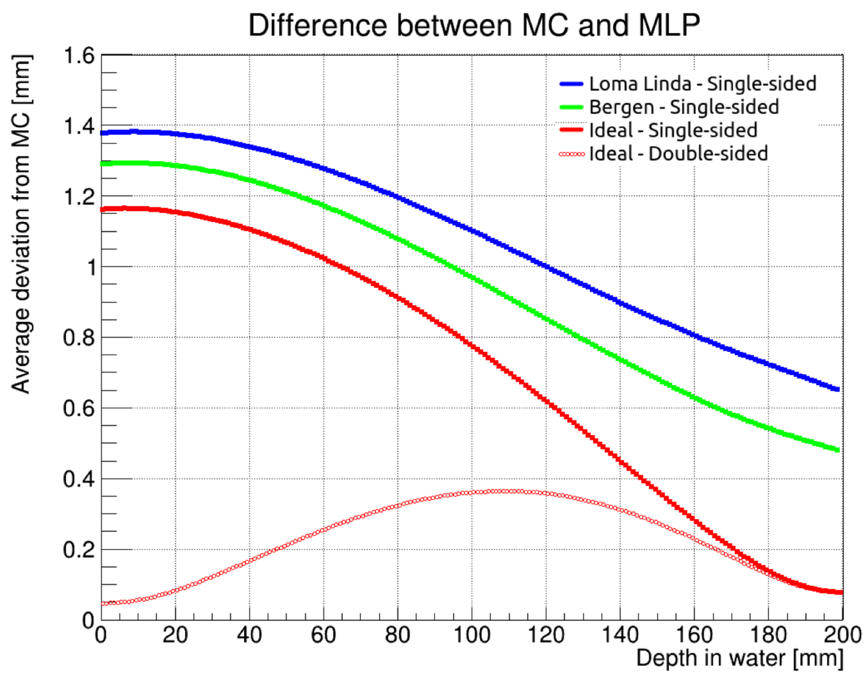
T. Kortus, University of Applied Sciences Worms, PhD thesis (TU Kaiserslautern), in preparation

Does 3D reconstruction work with trackers only behind the phantom?

- **Single-sided imaging**
  - **Most Likely Path estimate**
    - **Entrance – beam optics**
    - **Exit – pCT front trackers**
  - **Difference between MC truth and estimated proton path**
    - **Beam spot size: 7 mm**

-> deviations ≤ 1.2 mm



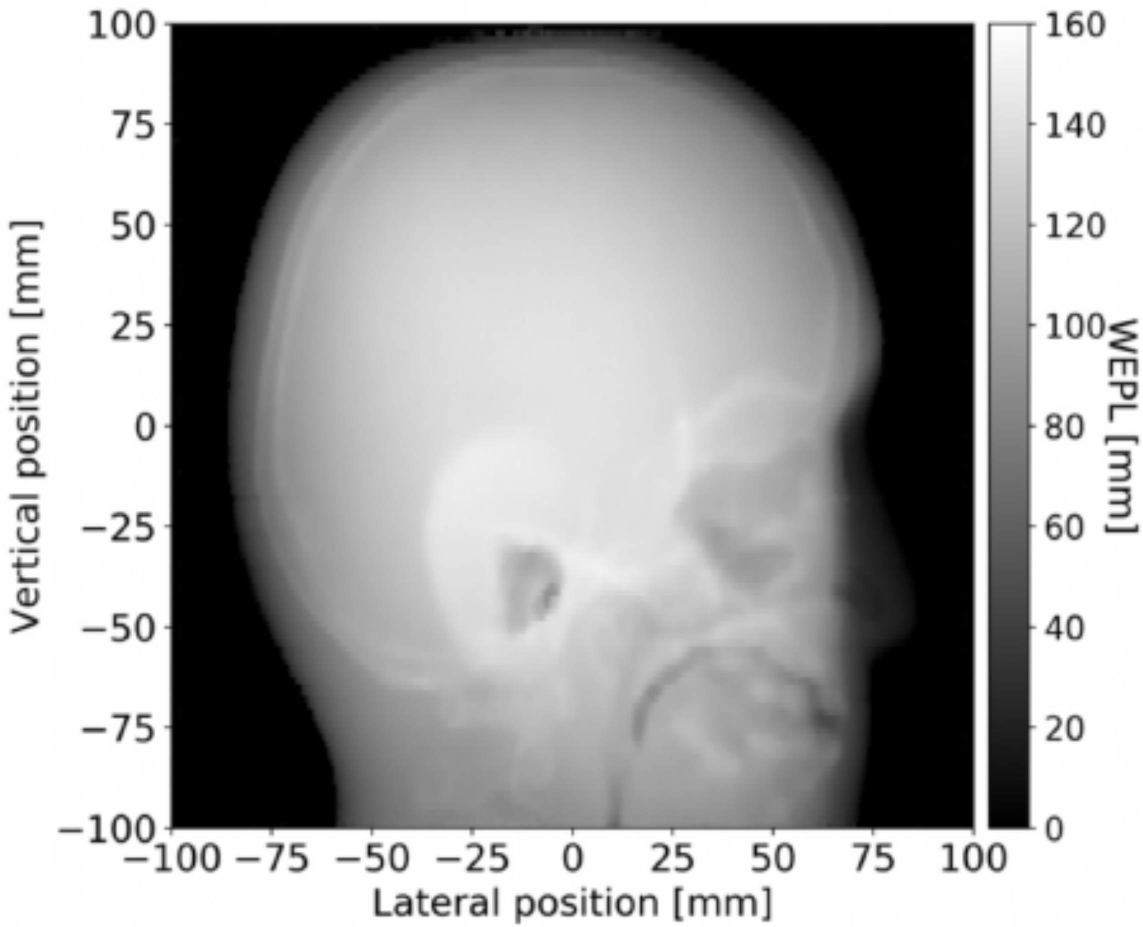


Krah, N., et.al., (2018). A comprehensive theoretical comparison of proton imaging set-ups in terms of spatial resolution, Physics in Medicine & Biology 63 (13): 135013.

Radiographic image reconstruction - pRAD

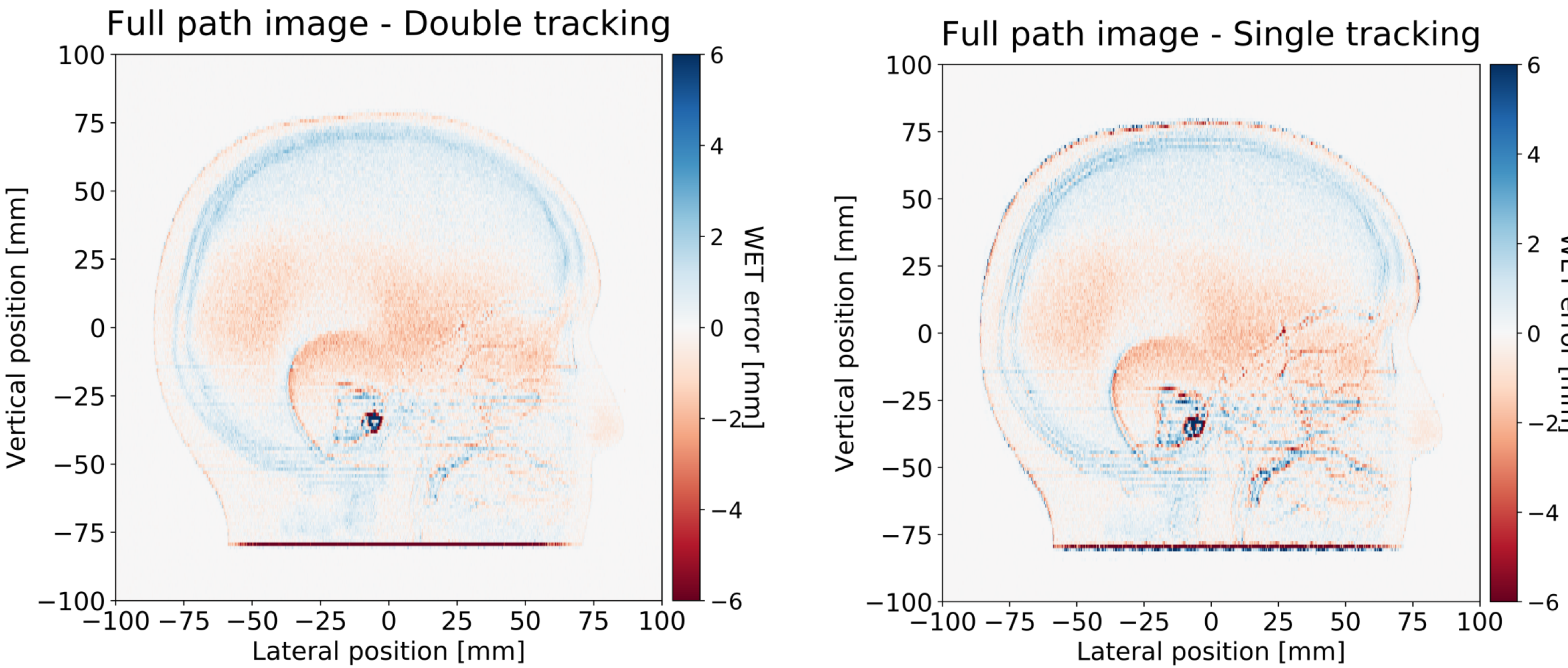
- **Head phantom radiograph (simulation)**

  - **230 MeV**
  - **10^7 protons**
  - **~ 15 μSv deposited dose**



Radiographic image reconstruction - pRAD

- **Quality of head phantom radiographs – WET* errors (simulation)**

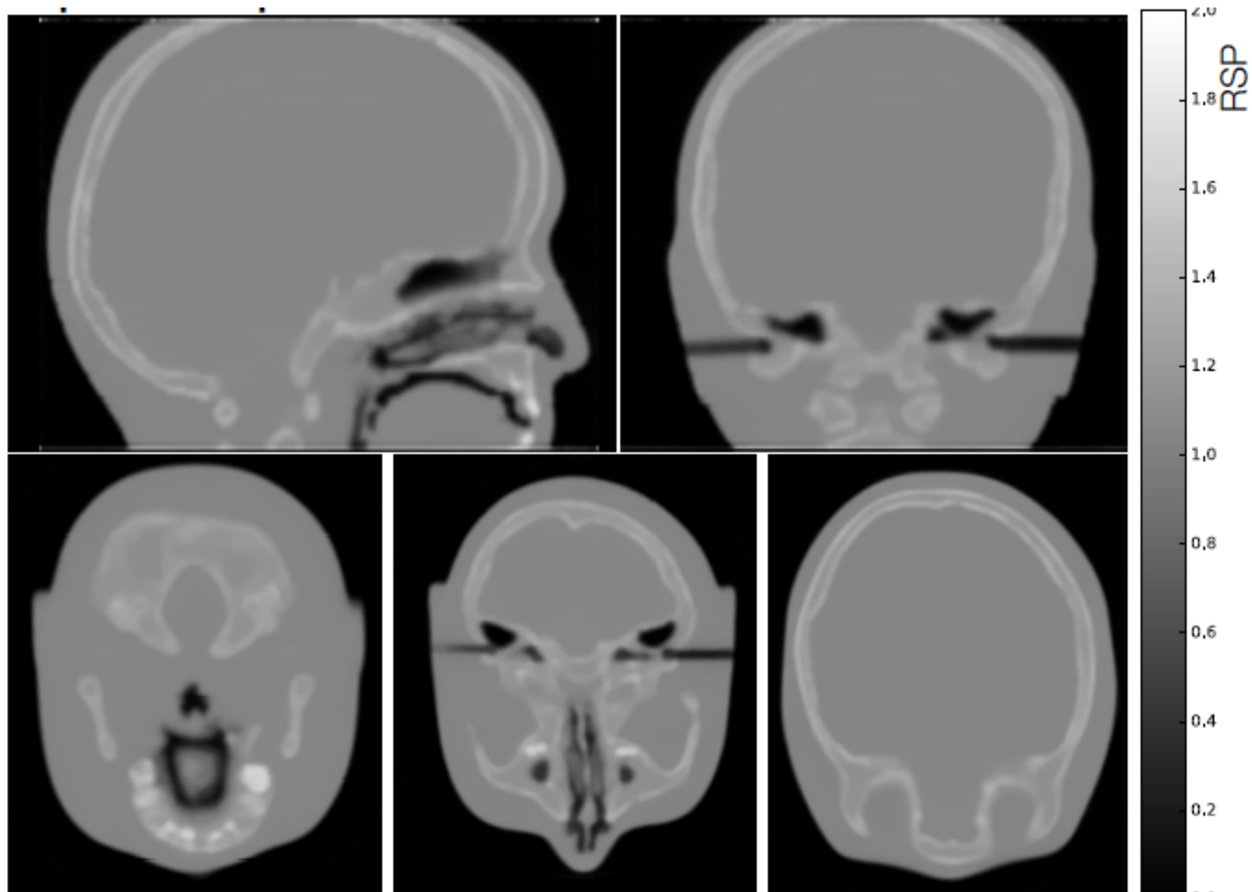


* WET: Water Equivalent Thickness

Collins-Fekete, C.-A., et al., (2016). A maximum likelihood method for high resolution proton radiography/proton CT, Physics in Medicine and Biology 61 (23): 8232.

pCT (3D) reconstruction

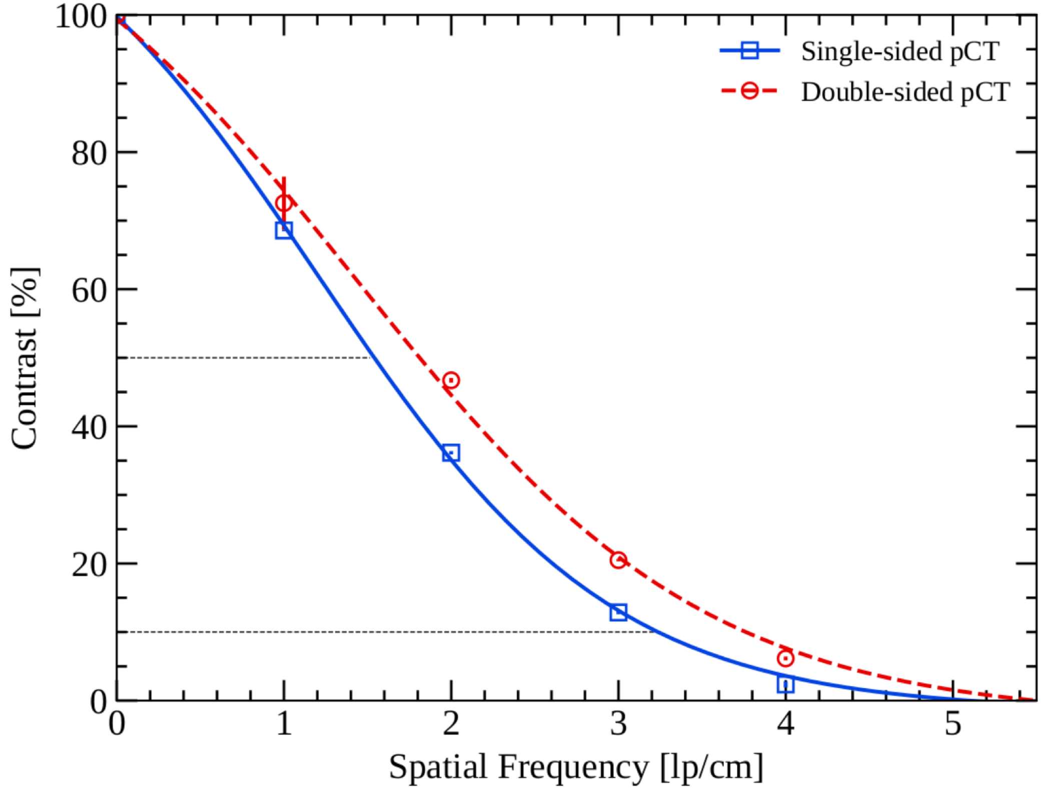
- **Head phantom pCT (simulation)**
  - **230 MeV**
  - **360 projections, 1° steps**
  - **3.5×10^6 protons per projection**
  - **7.9×10^8 protons for 3D reconstruction**

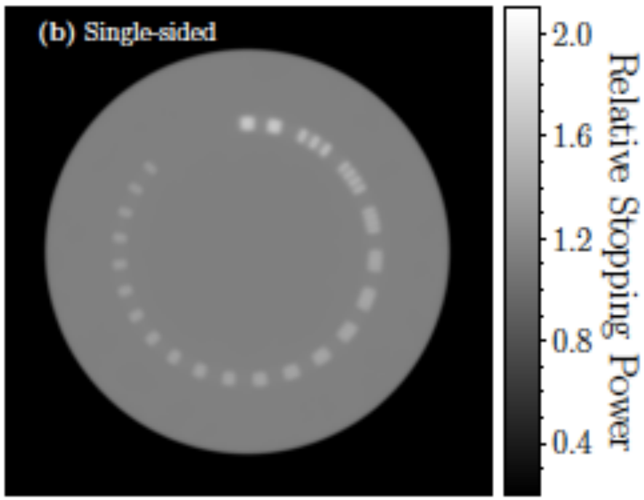


Algorithms:
DROP, TVS, FDK;
Penfold, S. N., et al., (2010). Total variation superiorization schemes in proton computed tomography image reconstruction, Medical Physics 37 (11): 5887–5895.

pCT (3D) reconstruction

- **Reconstruction of the Catphan® CTP528 line pair module (simulation)**



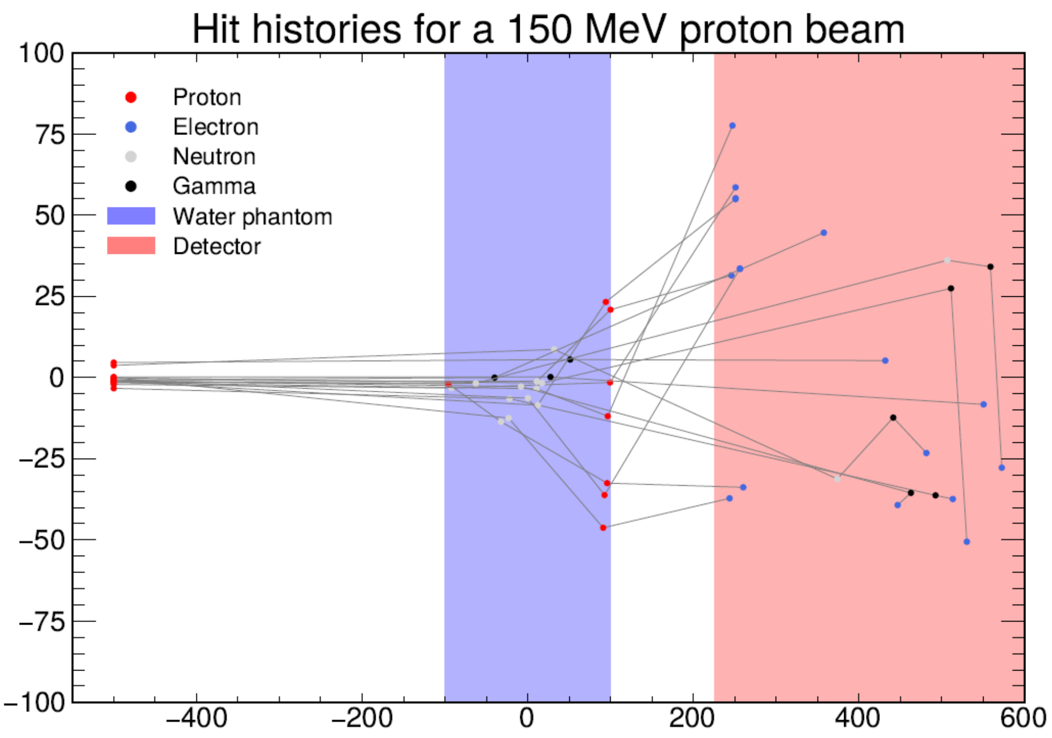


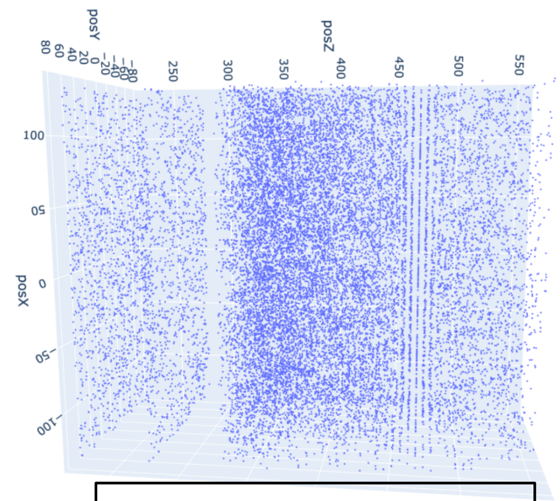
Algorithms:
DROP, TVS, FDK;
Penfold, S. N., et al., (2010). Total variation superiorization schemes in proton computed tomography image reconstruction, Medical Physics 37 (11): 5887–5895.

Online dose delivery monitoring

- **Online Bragg peak monitoring during treatment**
  - **pCT as an imaging calorimeter detects all secondaries – charged particles, photons and neutrons**

-> pCT as particle/energy flow monitor



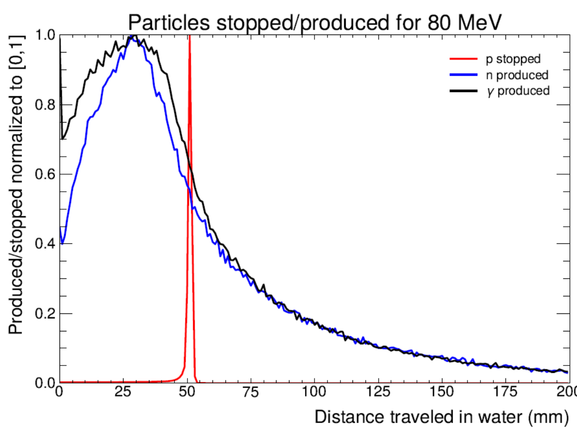


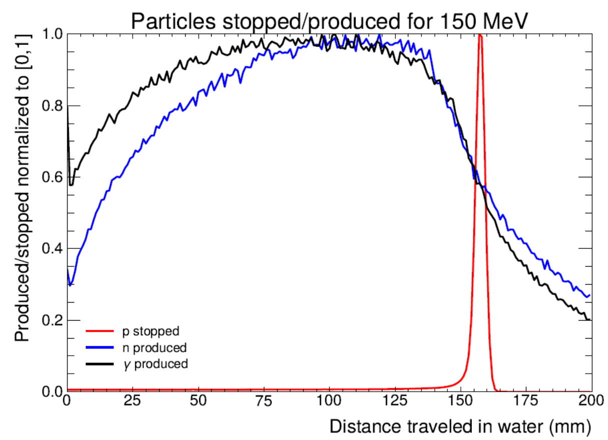
Detected secondaries, produced by $3.11 \cdot 10^7$ primary protons at 69.4 MeV, 160 mm water

A. Schilling, University of Applied Sciences Worms, PhD thesis (TU Kaiserslautern), in preparation

Detection of secondaries

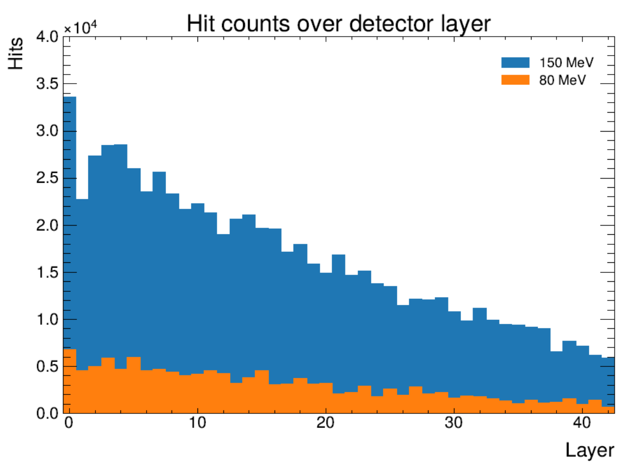
- **Production points of secondaries in a water phantom of 200 mm thickness**

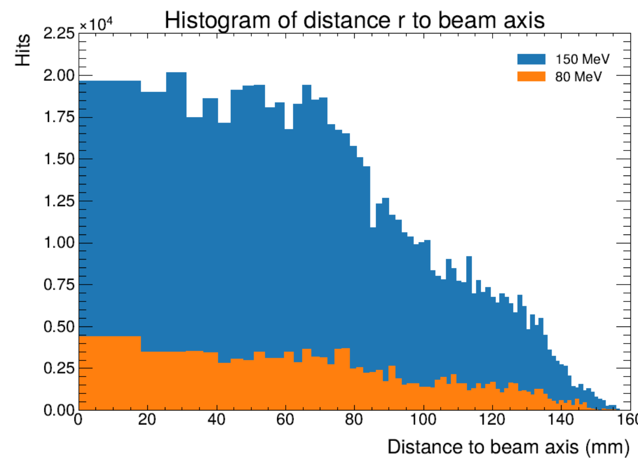




A. Schilling, University of Applied Sciences Worms, PhD thesis (TU Kaiserslautern), in preparation

- **Hit distribution in the pCT detector**

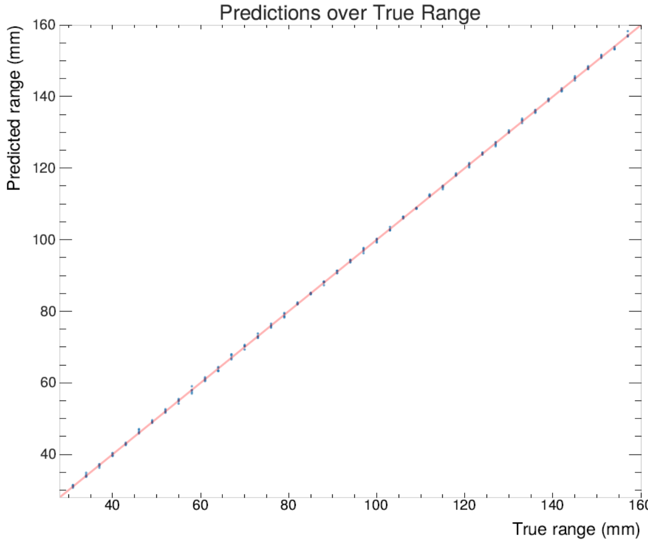


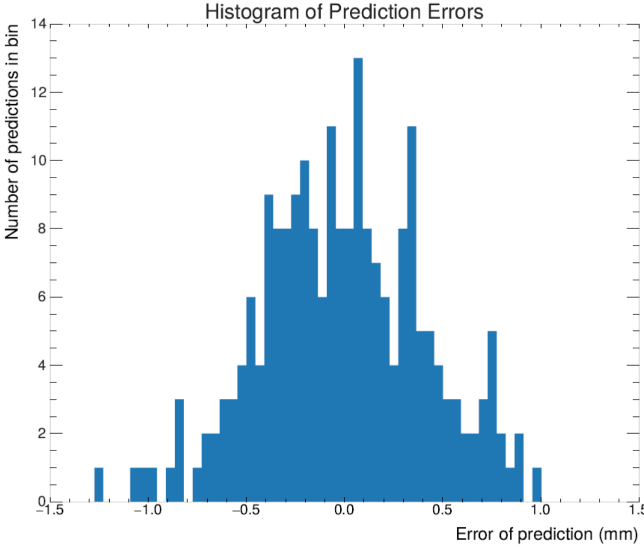


Matching the 3D-position of the Bragg-peak inside the patient to the shower shape of emitted particles

A. Schilling, University of Applied Sciences Worms, PhD thesis (TU Kaiserslautern), in preparation

- **Machine Learning**
  - **Feature Extraction**
    - **29 features: total number of active pixels, cluster size, linear and cubic fit for hits, clusters and energy deposition vs layer, …**
  - **Regression models predict beam range based on extracted features**
    - **Linear Regression, Gaussian Process, Deep Neural Network, ...**





preliminary results

→ Sub-mm position resolution of the Bragg-peak position

What's next?

- **Construction of the pCT system**
  - **Sensors have been produced**
  - **Mounting of sensors to flex cables will start soon**
  - **Assembly and integration into services (power, cooling, readout)**

- **Commissioning with proton beams at the Bergen proton therapy facility in 2024/25 (Varian ProBeam multi-room system)**

This is the end