Proton CT
A novel imaging tool in cancer therapy

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MTA Wigner RCP

on behalf of the Bergen pCT Collaboration

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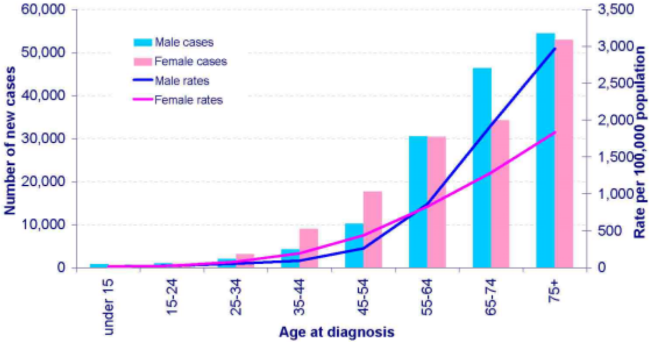
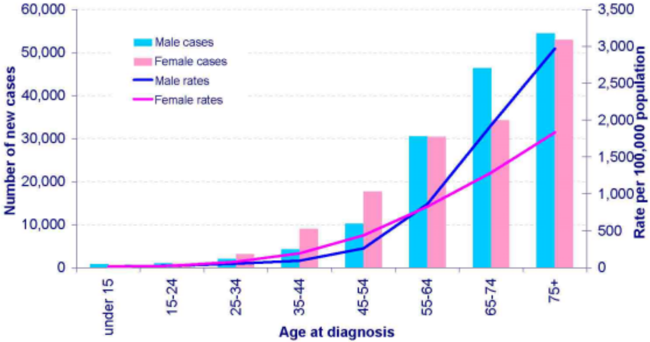
Cancer statistics and therapies





- Contributions to successful treatment of cancer
  - 45-50% surgery
  - 40-50% radiotherapy
  - 10-15% chemotherapy
- Radiotherapy is an important weapon in the battle against cancer

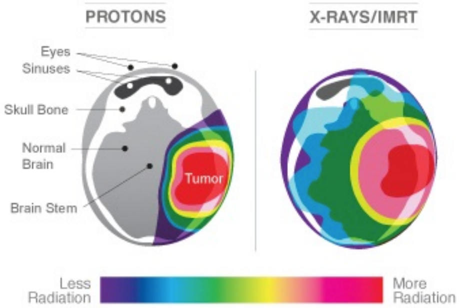
K. Peach, Heavy Ions in Science and Health workshop, Bergen, 2012

Radiotherapy and its problems

- Goal: damage the DNA of cancer cells
- Direct or indirect ionization
- Treatment with photons or charged particles (e.g. protons)
- Photons: mostly indirect ionization through forming free radicals
- Protons: mostly direct ionization

Radiotherapy and its problems

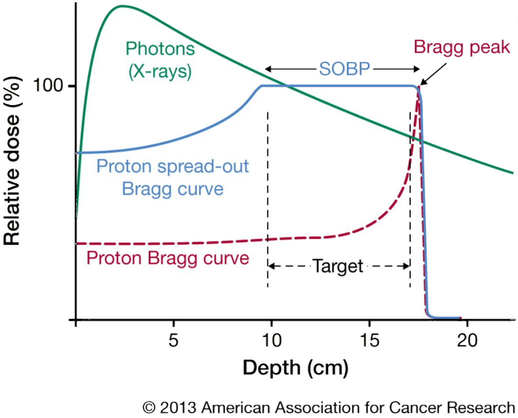
- Goal: damage the DNA of cancer cells
- Direct or indirect ionization
- Treatment with photons or charged particles (e.g. protons)
- Photons: mostly indirect ionization through forming free radicals
- Protons: mostly direct ionization
- Need to minimize the damage to healthy tissue



IMRT= intensity modulated radiation therapy (a type of X-ray therapy)

Source: ProCure Training and Development Center

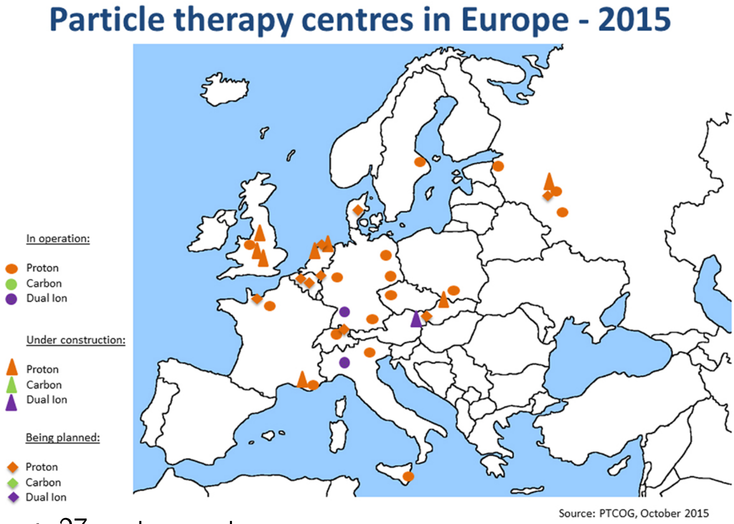
Hadron therapy – advantages



R. Mohan, A. Mahajan and B. D. Minsky, Clin Cancer Res December 1 2013 (19) (23) 6338-6343
DOI: 10.1158/1078-0432.CCR-13-0614

- **Photons** are absorbed mostly at the entrance
- **Charged particles**
  - lose most of their energy in the Bragg peak
  - Relatively low dose in front of the tumor
  - Sharp fall-off of dose deposition ($<$mm)

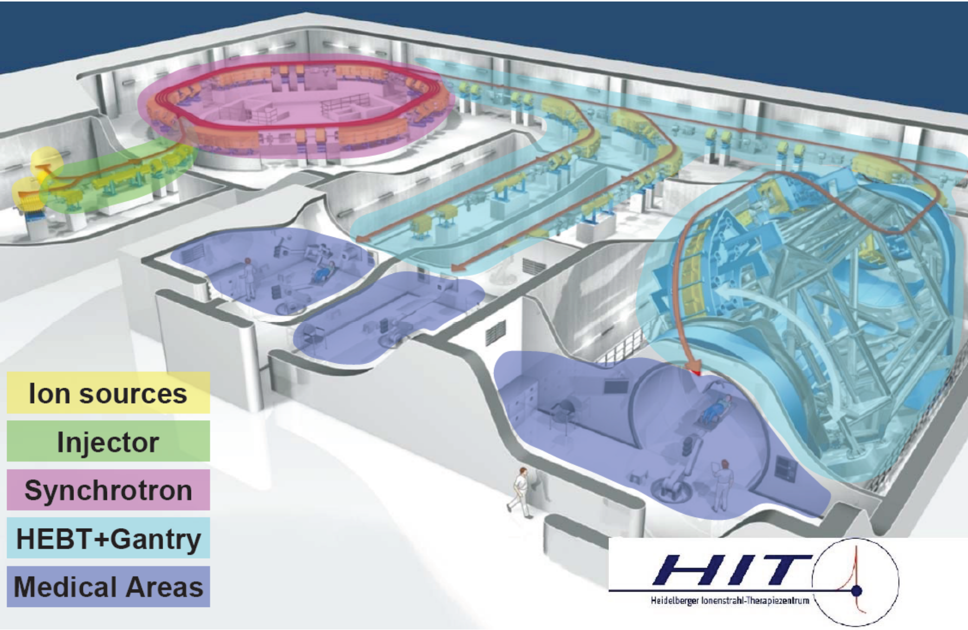
Hadron therapy centers in Europe



- 27 proton centers
- Three C-ion centers

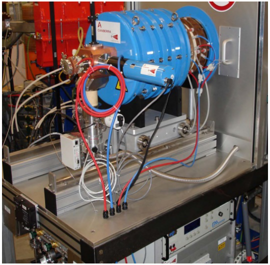
M. Dosanjh, M. Cirilli, S. Myers, S. Navin (2016). Medical applications at CERN and the ENLIGHT network. Frontiers in Oncology. 6. 10.3389/fonc.2016.00009.

Treatment facilities

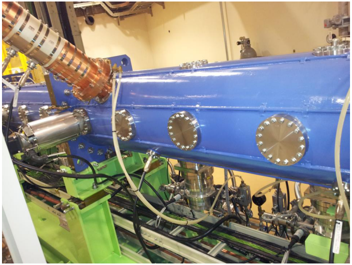


Treatment facilities

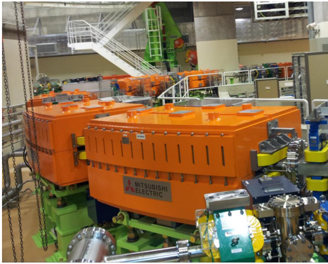
Ion source



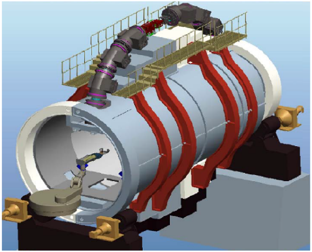
LINAC



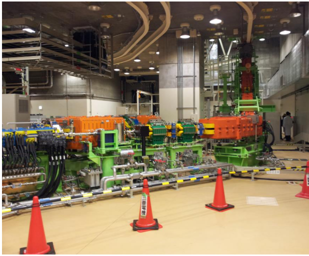
Synchrotron



Treatment room



Superconducting gantry



Extraction and beam transport

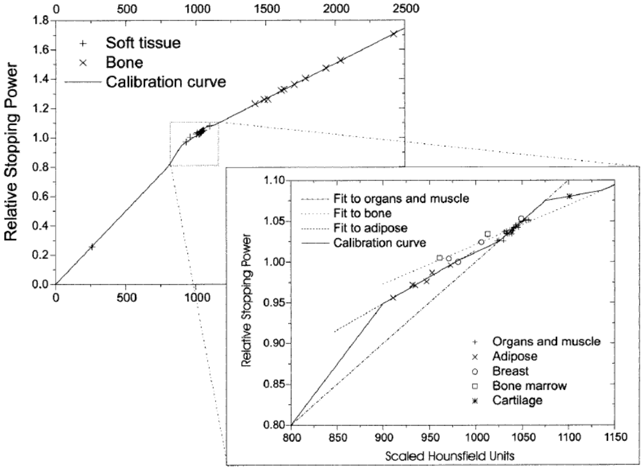
Proton therapy – missing information

- Stopping power in front of the tumor to be known precisely
- Stopping power is described by Bethe-Bloch formula:

$$dE/dx \sim \text{electron density} \times \ln \frac{\text{max. energy transfer in single collision}}{\text{effective ionization potential}^2}$$

- Derive stopping power from X-ray CT
- X-ray attenuation in tissue depends also strongly on Z (Z^5 for photoelectric effect)

Proton therapy – missing information



- Scaled Hounsfield Units (scanner specific) $\sim$ attenuation coefficient
- Not a clear relation with the stopping power

Schaffner, B. and E. Pedroni, Phys Med Biol, 1998. 43(6): p. 1579-92.

Range uncertainties and scattering

- Single energy CT: up to 3–4% uncertainty
- Target volume is increased by up to 1 cm in beam direction
- Avoid beam directions with a critical organ behind the tumor
- Proton CT: up to 0.3% uncertainty

Paganetti, H. Range uncertainties in proton therapy and the role of Monte Carlo simulations. Phys. Med. Biol. 2012, 57, R99–R117.

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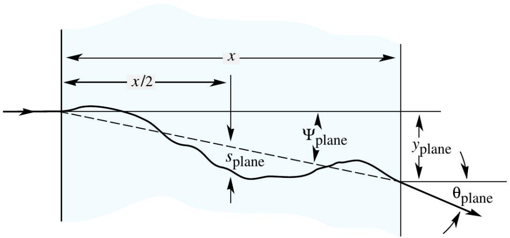
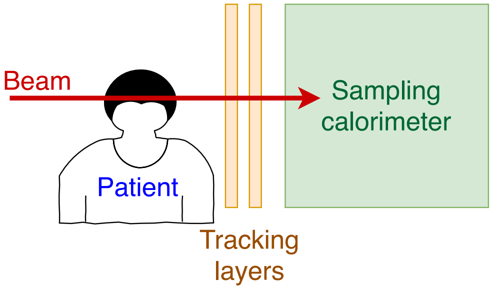


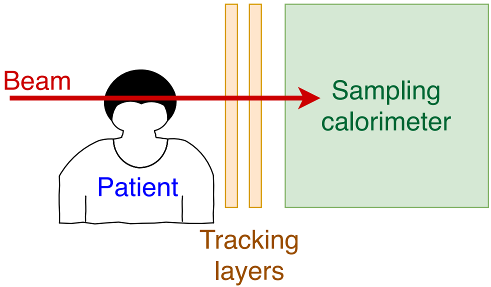
M. Tanabashi et al. (Particle Data Group), Phys. Rev. D 98, 030001 (2018)

- Multiple Coulomb scattering in the material



- Reconstruction of trajectories in 3D $\longrightarrow$ place of irradiation
- Measurement of range in external absorber $\longrightarrow$ lost energy

Proton CT – concept



- Reconstruction of trajectories in 3D $\longrightarrow$ place of irradiation
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- Before the treatment $\longrightarrow$ 3D map of electron density in target
- Quasi-simultaneously with therapeutic beam
  - Patient alignment
  - Online verification of dose
  - Dose optimization

Requirements of the detector

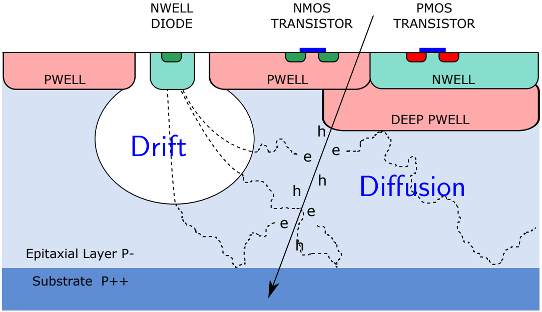
- High position resolution (tens of μm)
- Simultaneous tracking of large particle multiplicities ($10^7 - 10^9$ protons/s)
- Fast readout
- Radiation hardness
- Calorimeter: good range resolution

$$\Downarrow$$

- High granularity digital sampling calorimeter
- Monolithic Active Pixel Sensors (MAPS) as active layers

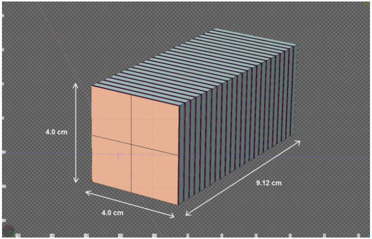
Monolithic Active Pixel Sensors (MAPS)

- Silicon sensors
- Using TowerJazz 0.18 μm CMOS imaging process
- High-resistivity ($> 1k\Omega$ cm) epitaxial layer on p-type substrate
- Deep PWELL shields NWELL of PMOS transistors
  - Allows full CMOS circuitry in active area
- Moderate reverse substrate biasing possible
  - Enlarges the depletion volume

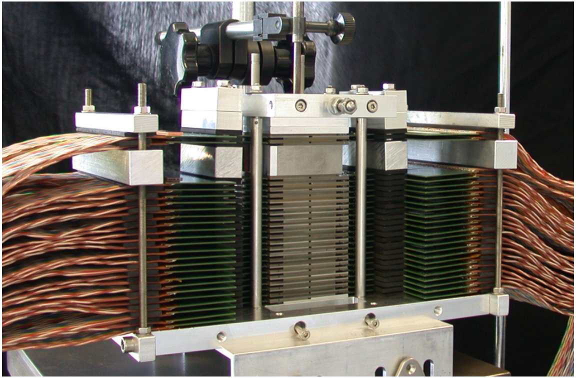


Digital calorimeter prototypes

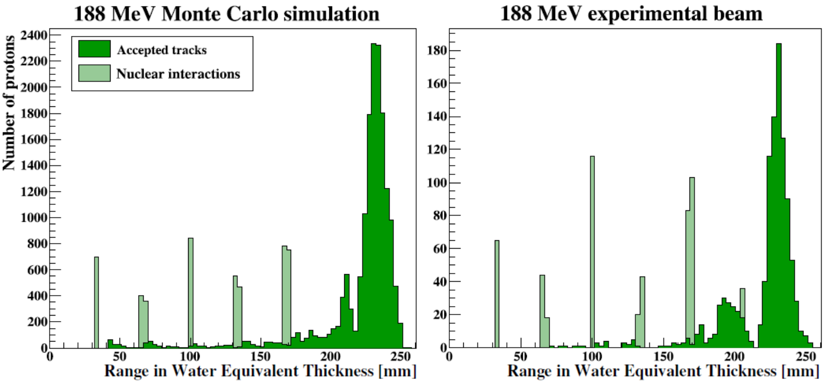
- Silicon-tungsten sampling calorimeter (constructed at Utrecht University)
- Optimized for electromagnetic showers
- Active layers: MAPS (MIMOSA 23 – IPHC Strasbourg)
- Compact design 4 $\times$ 4 $\times$ 11.6 cm^3
- 24 layers
- Absorbers: 3.5 mm of W



NIMA 860, 51-61, 2017,
https://arxiv.org/abs/1611.02031
Jinst 13, P01014, 2018,
https://arxiv.org/abs/1708.05164



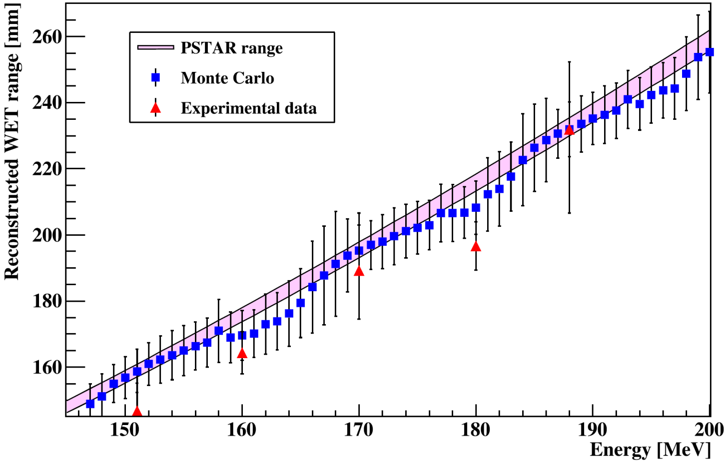
Results from the prototype



H. Pettersen, PhD thesis, UiB, 2018

- Data was taken at KVI in Groningen with 188 MeV protons
- Good agreement between data and simulations

Results from the prototype



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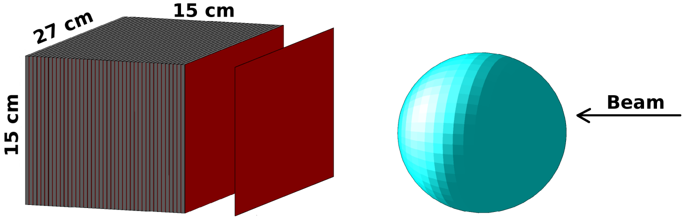
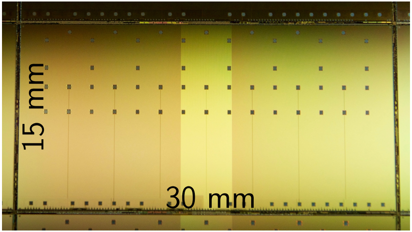
Optimization of the design

- Absorber
  - Energy degrader, mechanical carrier, cooling medium
  - Material choice: Al
  - Thickness: 3.5 mm
- Longitudinal segmentation
  - Number of sensitive and absorber layers: 41
- Geometry
  - Front area: 27 cm x 15 cm



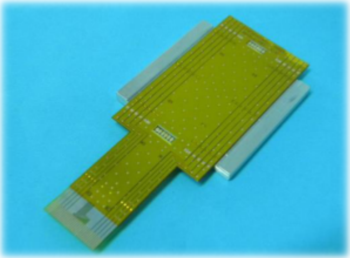
ALPIDE

- ALPIDE – **ALI**CE **PI**xel **DE**tector
- Developed for the upgrade of the ALICE Inner Tacker System
- Large silicon sensor (15 mm $\times$ 30 mm)
- 512 $\times$ 1024 pixels
- Pixels are 27 µm $\times$ 29 µm
- Digital readout with priority encoder
- Thin sensor (50 µm or 100 µm)
- Efficiency $> 99\%$
- Resolution $\sim$ 5 µm



Mounting

- ALPIDE mounted on thin flex cables
  - Aluminum-polyamide dielectrics: 30 µm Al, 20 µm plastic
  - Design and production:
    Utrecht University, Netherlands and LTU, Kharkiv, Ukraine
- Intermediate prototype
  - Chip cable with two ALPIDE sensors



Picture from LTU

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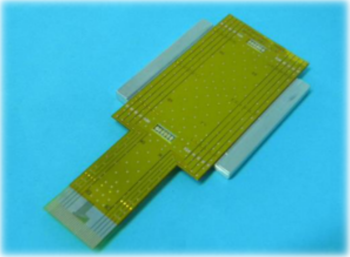
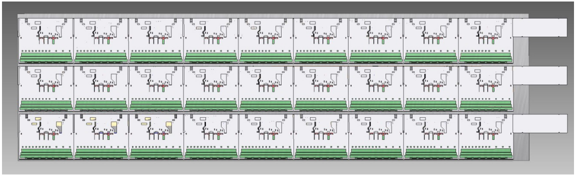
  - Chip cable with two ALPIDE sensors
- Final system
  - Flexible carrier board modules with 2 $\times$ 3 strings with 9 chips

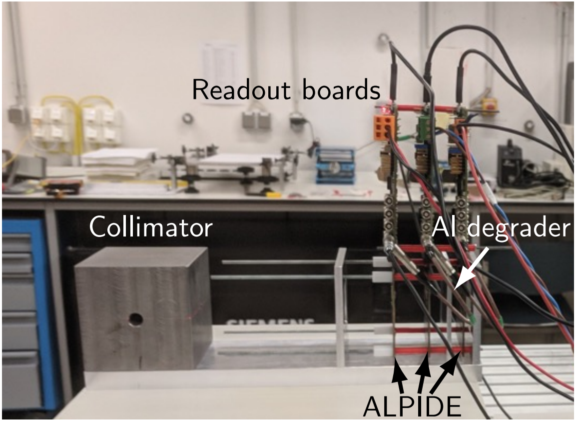




Picture from Utrecht University

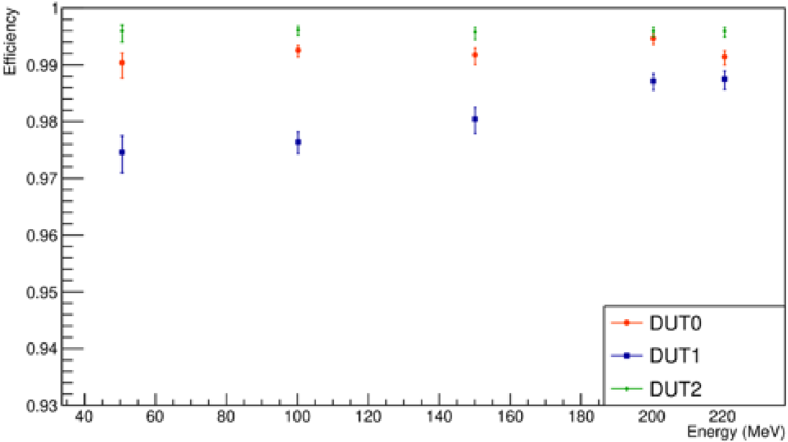
Picture from LTU

Test of the ALPIDE at low energy



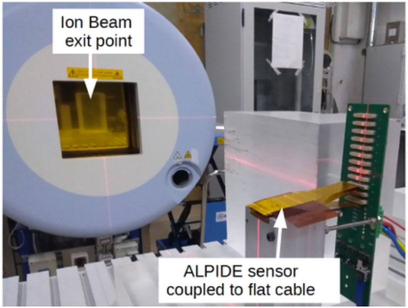
- Three ALPIDE chips with or without Al degrader
- Protons and He ions
- Energy 50 MeV/u – 220 MeV/u
- At the Heidelberger Ionenstrahl-Therapiezentrum (HIT)

Results of the test at low energy



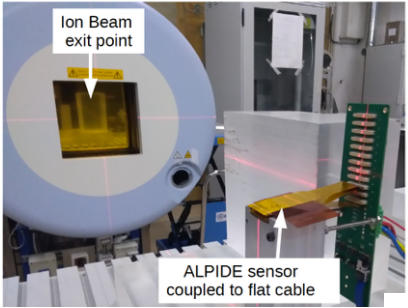
- Tracking efficency measured in all three layers
- Above 97% for all energies and layers

Test of a rotated ALPIDE

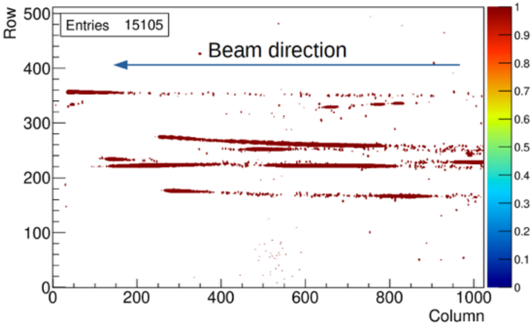


- ALPIDE irradiated from the side along its longer dimension

Test of a rotated ALPIDE



- ALPIDE irradiated from the side along its longer dimension
- Single tracks can be measured in one ALPIDE



Conclusions

- Hadron therapy $\longrightarrow$ lower unnecessary dose for the patient
- Uncertainty in energy loss from extrapolation from CT
- pCT: powerful imaging tool to reduce the uncertainty
- Digital sampling calorimeter made of ALPIDE sensors
- First tests of the prototypes look promising

Thank you for your attention!

Collaboration:

- University of Bergen
- Helse Bergen
- Utrecht University
- DKFZ Heidelberg
- Wigner Budapest
- Western Norway University of Applied Sciences

BACKUP