Proton CT
A novel diagnostic tool in cancer therapy

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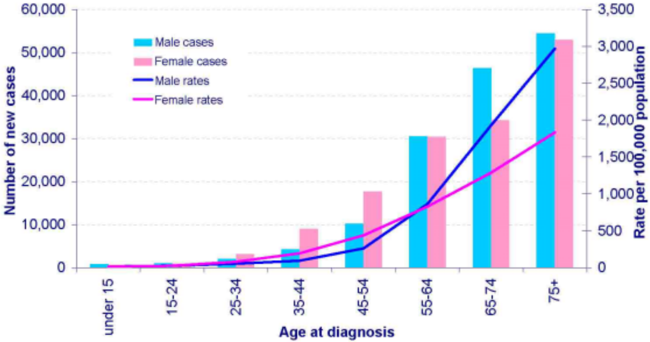
on behalf of the pCT Collaboration

7th December 2018

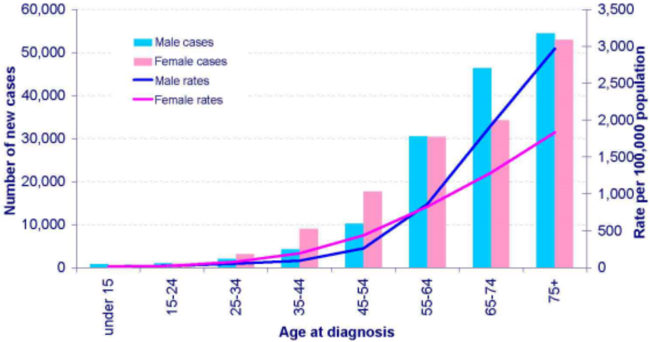
Zimányi School

This work has been supported by the Hungarian NKFIH/OTKA K 120660 grant.

Cancer statistics and therapies



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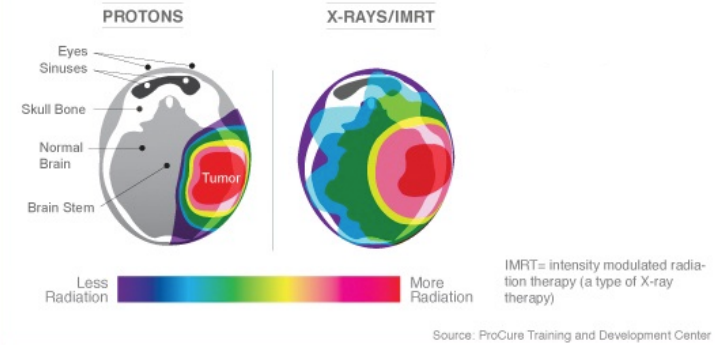
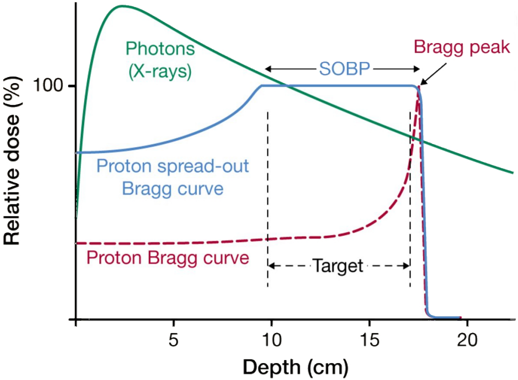
- Treatment with photons or charged particles (e.g. protons)
- Photons: mostly indirect ionization through forming free radicals
- Protons: mostly direct ionization
- Need to minimize the damage to healthy tissue

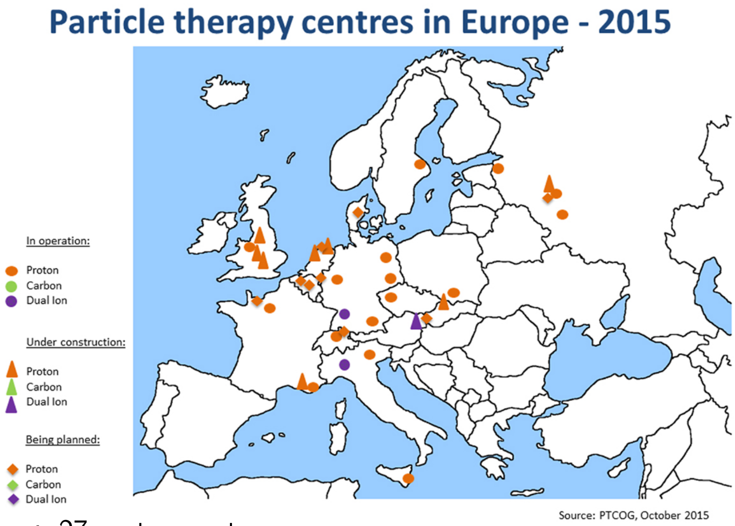




R. Mohan, A. Mahajan and B. D. Minsky,
Clin Cancer Res December 1 2013 (19) (23)
6338-6343
DOI: 10.1158/1078-0432.CCR-13-0614

- **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)

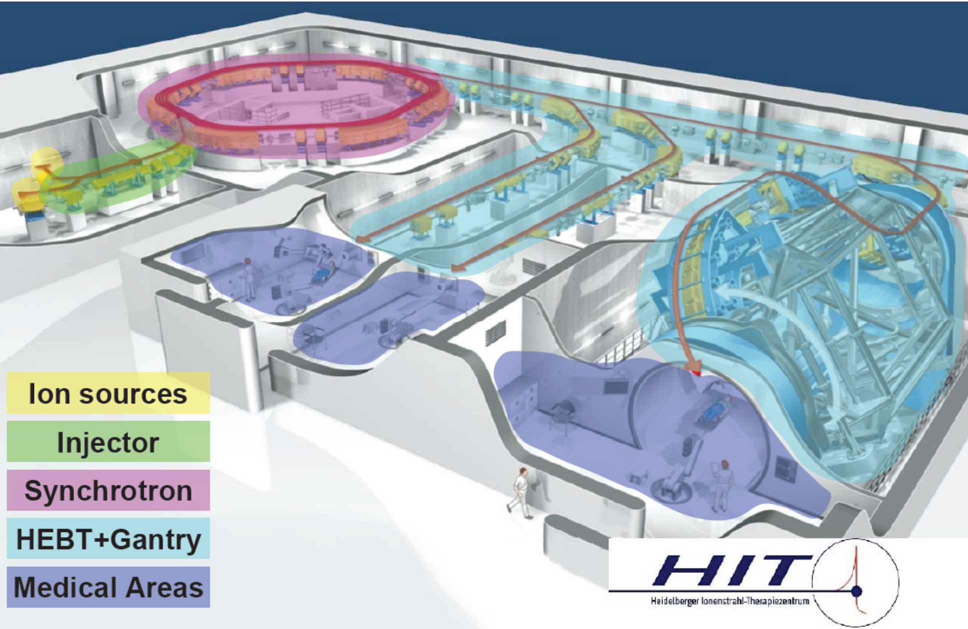
Hadron therapy centers in Europe



- 27 proton centers
- Three C-ion centers

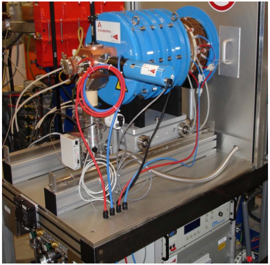
M. Dosanjh, M. Cirilli, S. Myers, S. Navin (2016). Medical applications at CERN and the ENLIGHT network. Frontiers in Oncology. 6. 10.3389/fonc.2016.00009.

Treatment facilities

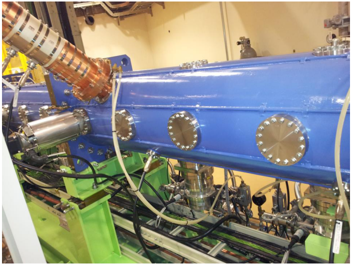


Treatment facilities

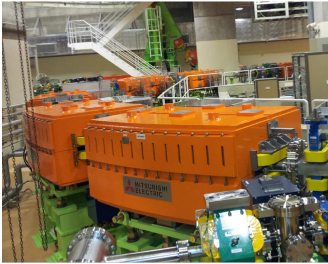
Ion source



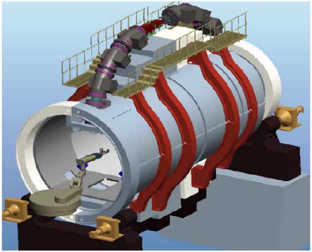
LINAC



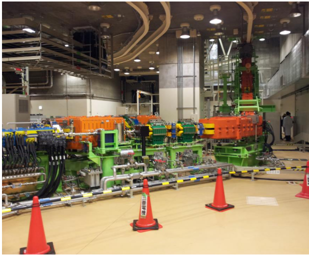
Synchrotron



Treatment room



Superconducting gantry



Extraction and beam transport

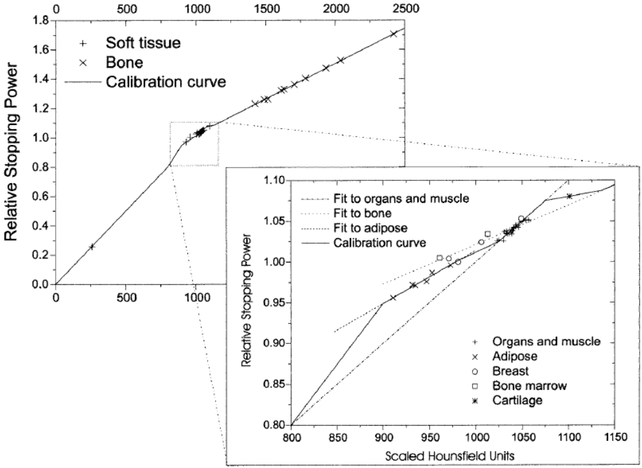
Proton therapy – missing information

- 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 7.4% uncertainty
- Target volume is increased by up to 1 cm in beam direction
- Avoid beam directions with a critical organ behind the tumor
- 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
D. C. Hansen, J. Seco, T. S. Sorensenn, J. B. B. Petersen, J. E. Wildberger, F. Verhaegen and G. Landry

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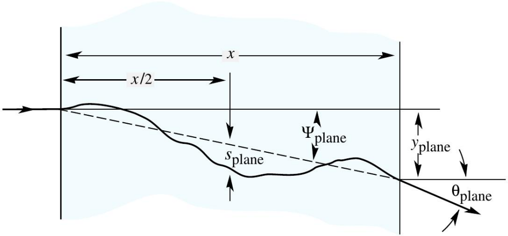
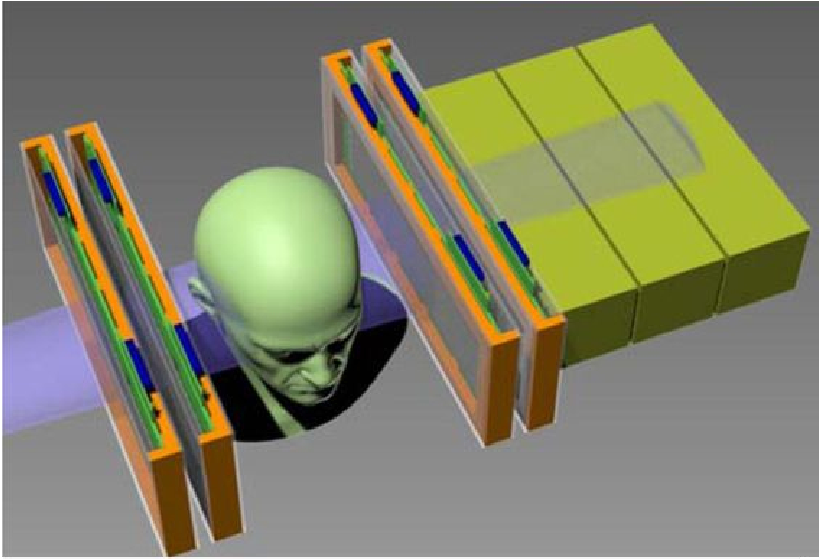


M. Tanabashi et al. (Particle Data Group), Phys. Rev. D 98, 030001 (2018)

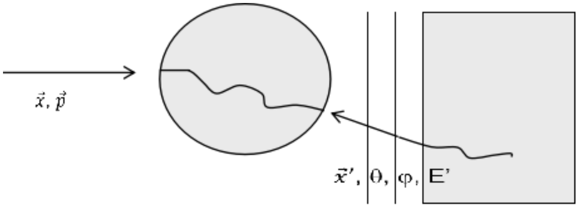
- Multiple Coulomb scattering in the material
- Measurement before and after the patient needed

Proton CT – concept



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

Proton CT – concept



- $\overrightarrow{x}$ and $\overrightarrow{p}$ from beam optics and scanning system
- $\overrightarrow{x'}$, θ, φ and E' to be measured
- Reconstruction of trajectories in 3D $\longrightarrow$ place of irradiation
- Measurement of range in external absorber $\longrightarrow$ lost energy

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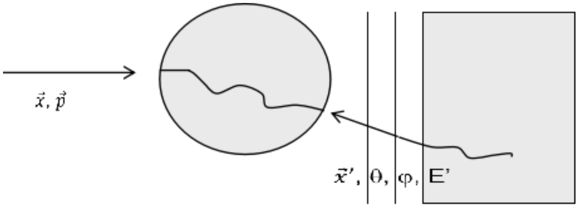

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- Before the treatment $\longrightarrow$ 3D map of electron density in target
- Quasi-simultaneously with therapeutic beam
  - Patient alignment
  - Online verification of dose
  - Dose optimization

Requirements of the detector

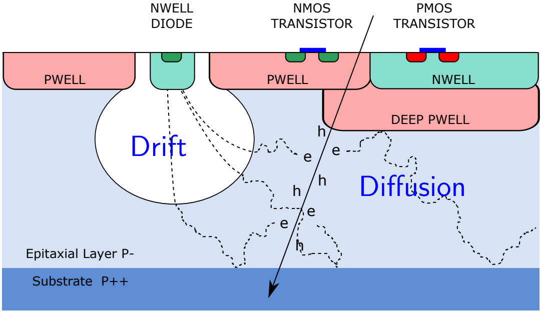
- High position resolution (tens of µm)
- Simultaneous tracking of large particle multiplicities ($10^7 - 10^9$ protons/s)
- Fast readout
- Radiation hardness
- Front detector: low mass, thin sensors ($50 - 100$ µm)
- Back detector: good range resolution

$$\Downarrow$$

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

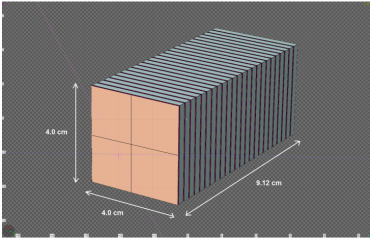
Monolithic Active Pixel Sensors (MAPS)

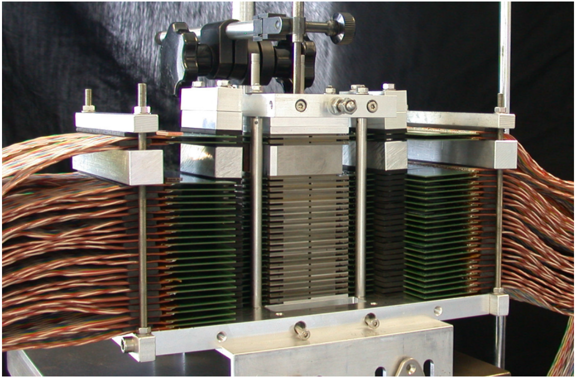
- Silicon sensors
- Using TowerJazz 0.18 μm CMOS imaging process
- High-resistivity ($> 1\text{k}\Omega$ cm) epitaxial layer on p-type substrate
- Deep PWELL shields NWELL of PMOS transistors
    - Allows full CMOS circuitry in active area
- Moderate reverse substrate biasing possible
    - Larger depletion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



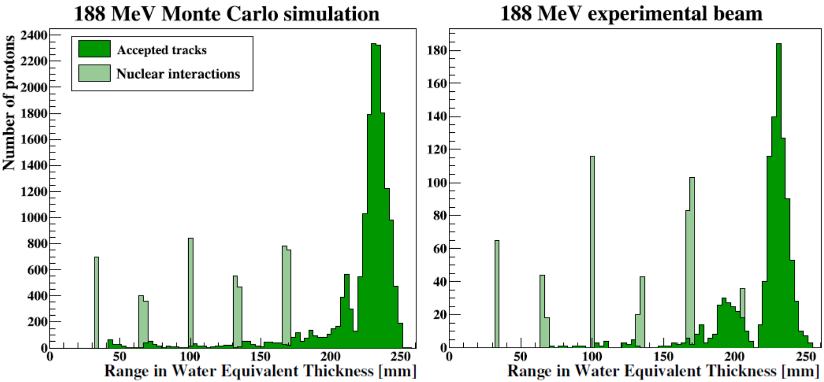
Digital calorimeter prototypes

- 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





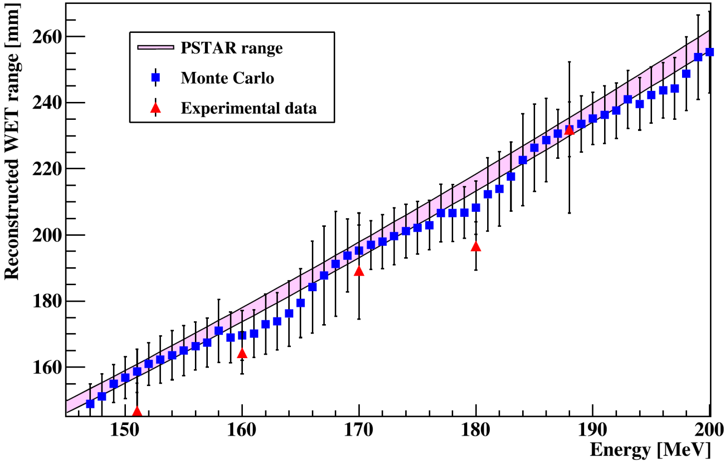
NIMA 860, 51-61, 2017,
https://arxiv.org/abs/1611.02031
Jinst 13, P01014, 2018,
https://arxiv.org/abs/1708.05164



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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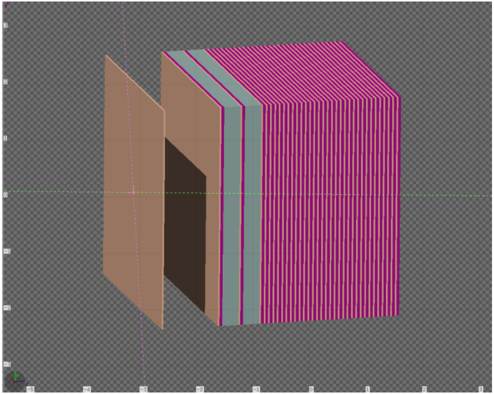
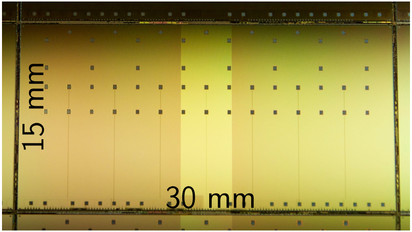
Optimization of the design

- 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



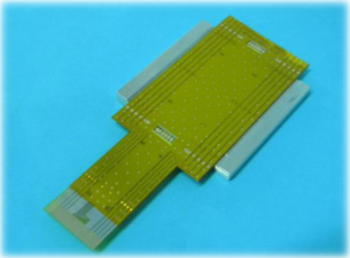
ALPIDE

- ALPIDE – **ALI**CE **PI**xel **DE**tector
- Developed for the upgrade of the ALICE Inner Tacker System
- Large silicon sensor (15 mm × 30 mm)
- 512 × 1024 pixels
- Pixels are 27 µm × 29 µm
- Digital readout with priority encoder
- Thin sensor (50 µm or 100 µm)
- Efficiency > 99%
- Resolution ∼ 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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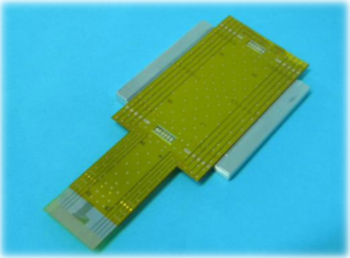
- Final system
  - Flexible carrier board modules with 2×3 strings with 9 chips



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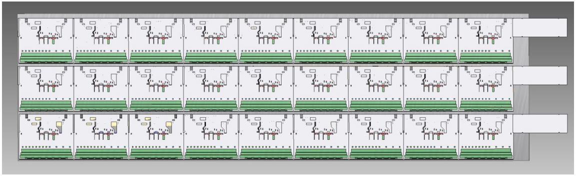
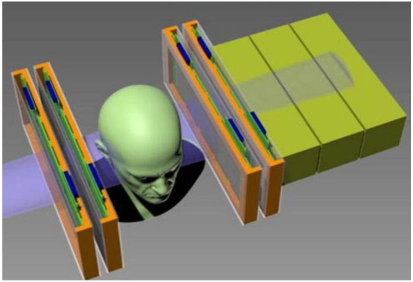


Picture from Utrecht University

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 sensor module by the end of the year



Collaboration:

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

Thank you for your attention!

BACKUP