The Bergen proton CT project – proton tracking in a high-granularity digital tracking calorimeter

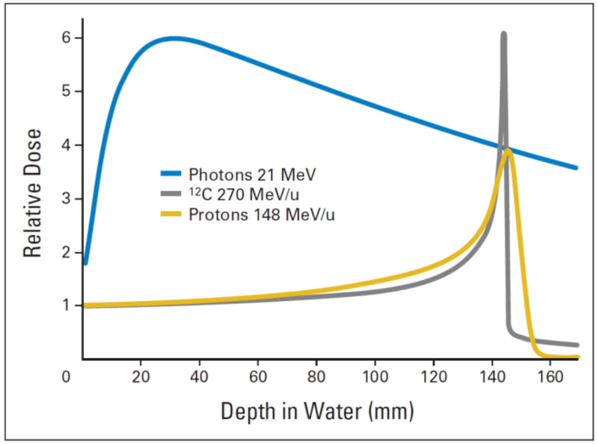
Dieter Roehrich
University of Bergen
for the Bergen pCT collaboration

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

Norway: University of Bergen - Helse Bergen - Western Norway University of App. Sci. –
The Netherlands: Utrecht University - Hungary: Wigner Institute Budapest - Germany: DKFZ Heidelberg

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)!**

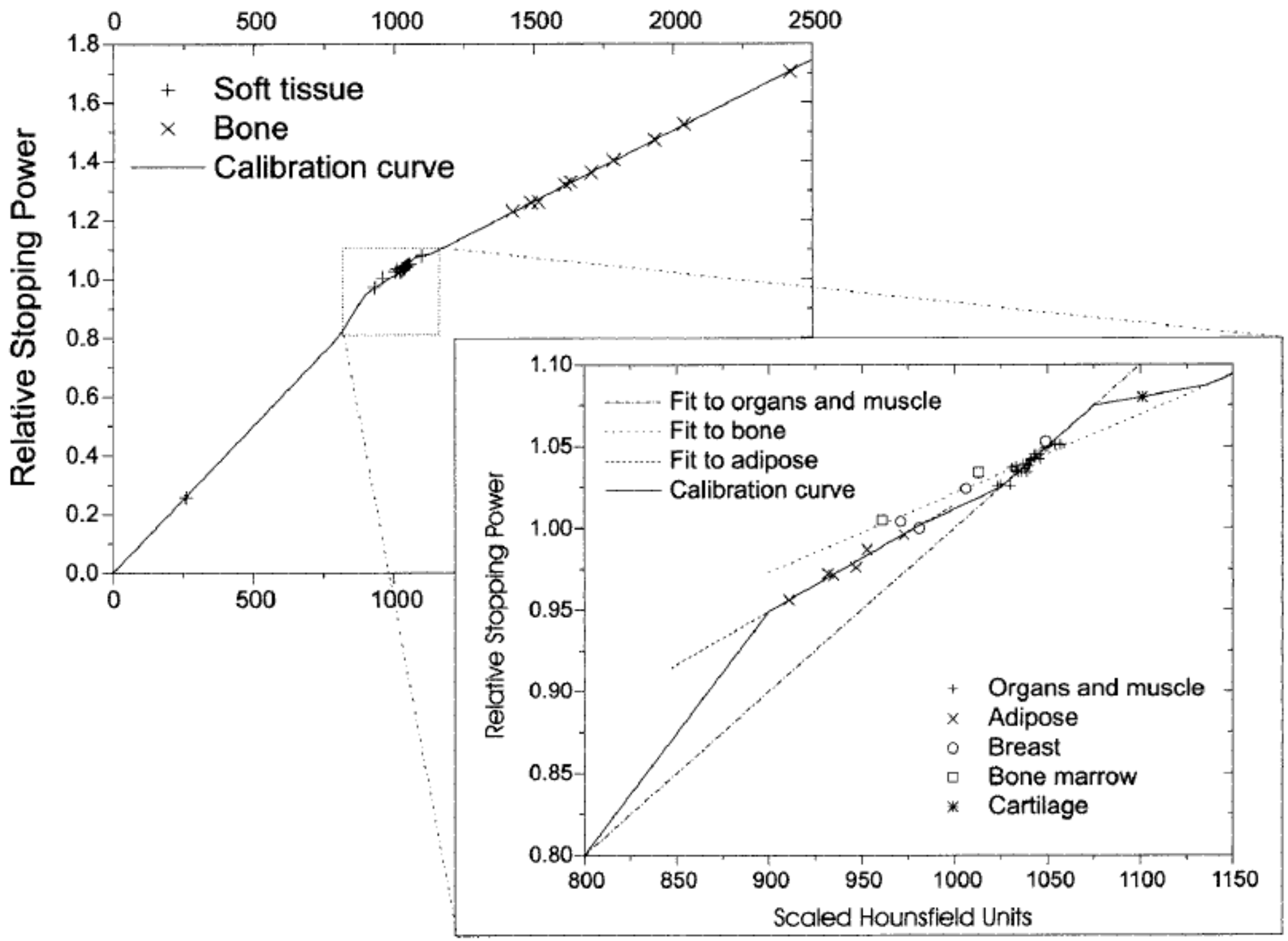


- **Challenge**
  - **Stopping power of tissue in front of the tumor has to be known – crucial input into the dose plan for the treatment**
  - **Stopping power is described by Bethe-Bloch formula:**

    - 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



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.

Range uncertainties

Clinical practice:

- 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 limitiations -> reduce range uncertainties

Estimates for advanced dose planning:

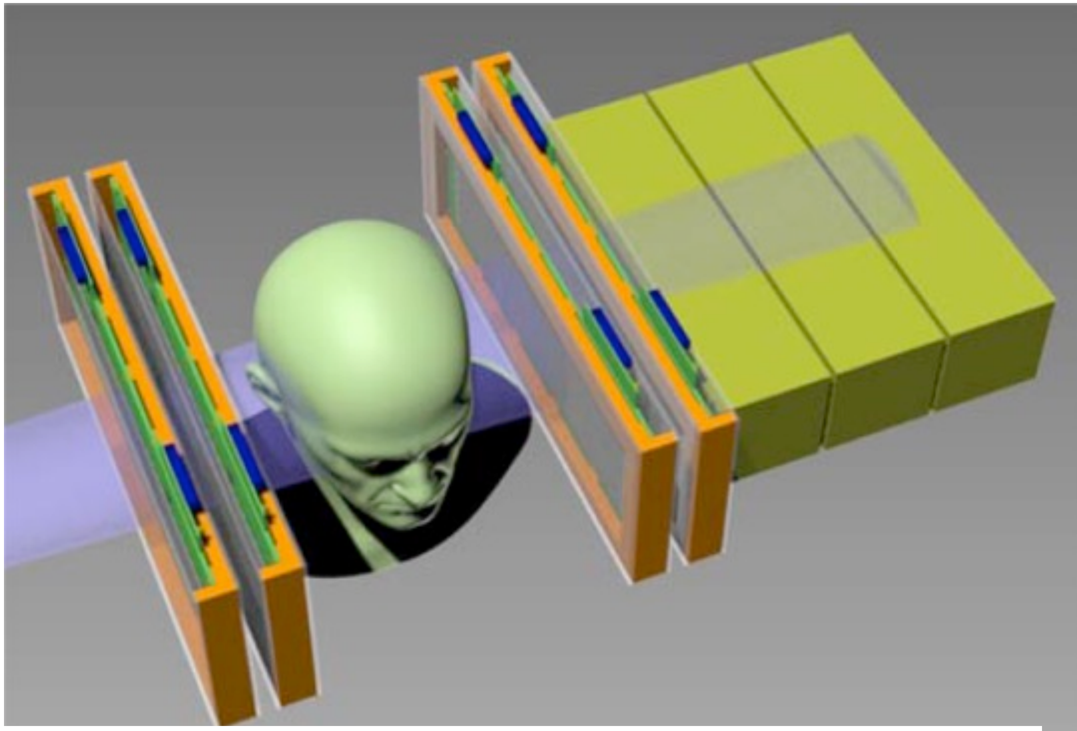
- Dual energy CT: up to 1.7 % uncertainty
- Proton CT: up to 0.3 % uncertainty

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*

Proton CT



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

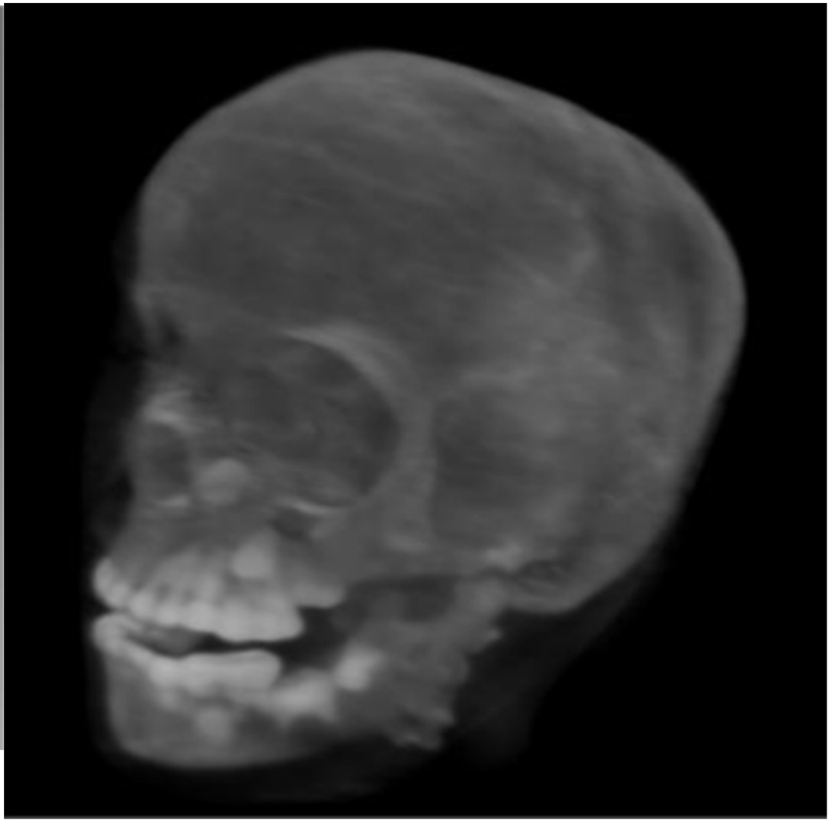


Fig. 14. 3D rendering of the pCT-reconstructed RSP map of a pediatric anthropomorphic head phantom.

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

Imaging with protons – nothing new

- **Proton radiography**

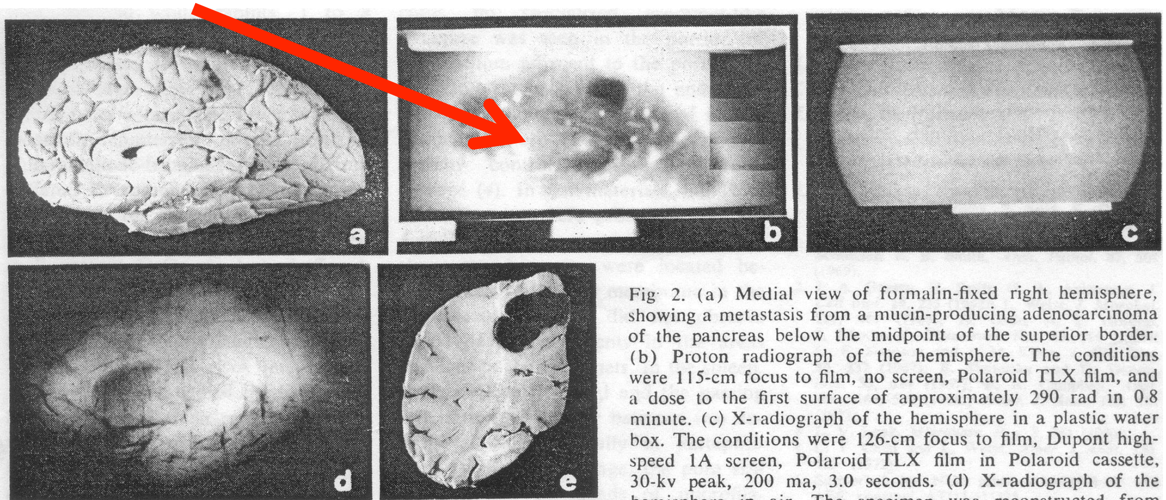
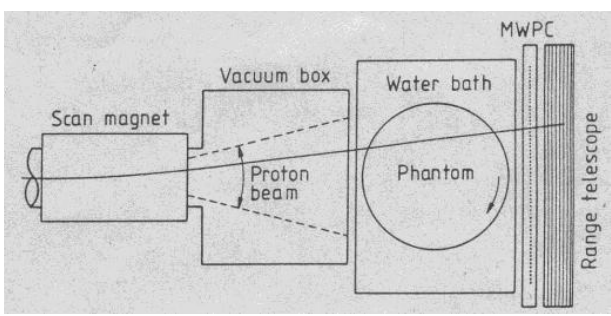


Fig. 2. (a) Medial view of formalin-fixed right hemisphere, showing a metastasis from a mucin-producing adenocarcinoma of the pancreas below the midpoint of the superior border. (b) Proton radiograph of the hemisphere. The conditions were 115-cm focus to film, no screen, Polaroid TLX film, and a dose 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.

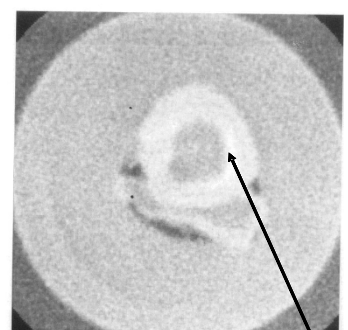
Steward and Kohler (1973)

- **Proton CT**

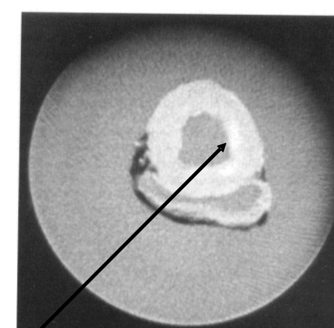


Hanson et al (1982)

Protons (Dose=2.7 mGy)



X-rays (Dose 21 mGy)



Myokardinfarkt

Imaging with protons – many prototypes

… still no clinical system

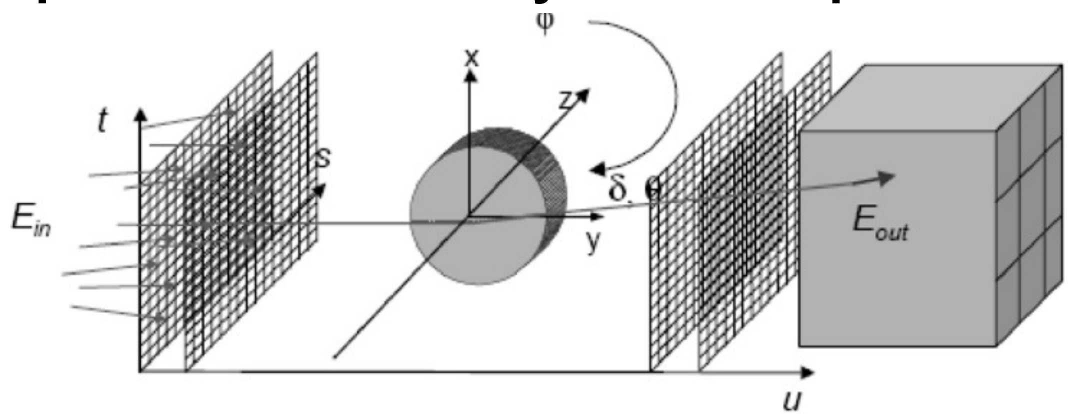
Table 3. A summary of current and recent proton radiography (pRG)/proton CT (pCT) prototypes

Group	Year of reference	Area (cm^2)	Position-sensitive detector technology (number of units)	Residual energy-range detector technology	Proton rate (Hz)	pCT or pRG
Paul Scherrer Institute[43]	2005	22.0 × 3.2	*x-y* Sci-Fi (2)	Plastic scintillator telescope	1 M[a]	pRG
LLU/UCSC/NIU[6]	2013	17.4 × 9.0	*x-y* SiSDs (4)	CsI (Tl) calorimeters	15 k[a]	pCT
LLU/UCSC/CSUSB[55]	2014	36.0 × 9.0	*x-y* SiSDs (4)	Plastic scintillator hybrid telescope	2 M[a]	pCT
AQUA[59]	2013	30.0 × 30.0	*x-y* GEMs (2)	Plastic scintillator telescope	1 M[a]	pRG
PRIMA I[66]	2014	5.1 × 5.1	*x-y* SiSDs (4)	YAG : Ce calorimeters	10 k[a]	pCT
PRIMA II[66]	2014	20.0 × 5.0	*x-y* SiSDs (4)	YAG : Ce calorimeters	1 M	pCT
INFN[69]	2014	30 × 30	*x-y* Sci-Fi (4)	*x-y* Sci-Fi	1 M	pCT
NIU/FNAL[70]	2014	24.0 × 20.0	*x-y* Sci-Fi (4)	Plastic scintillator telescope	2 M	pCT
Niigata University[71]	2014	9.0 × 9.0	*x-y* SiSDs (4)	NaI(Tl) calorimeter	30[a]	pCT
PRaVDA[72]	2015	9.5 × 95	*x-u-v* SiSDs (4)	CMOS APS telescope	1 M	pCT

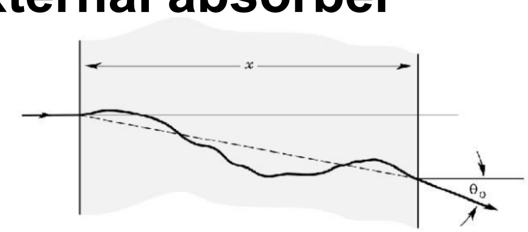
G. Poludniowski, N. M. Allinson, and P. M. Evans, "Proton radiography and tomography with application to proton therapy", *Br. J. Radiol.*, vol. 88, no. 1053, pp. 1–14, 2015

Proton-CT
- quasi-online dose plan verification

- **high energetic proton beam quasi-simultaneously 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)**



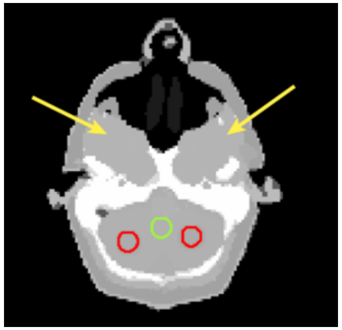
- **MS theory and Bethe-Bloch formula of average energy loss in turn depend on electron density in the target (and ionization potentials)**

-> 3D map of stopping power

-> online verification of dose plan

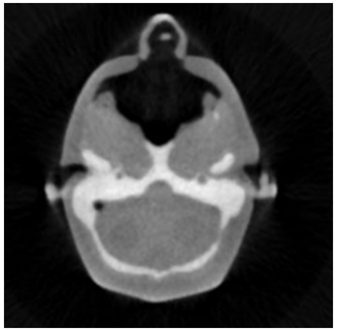
Proton-CT - images

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

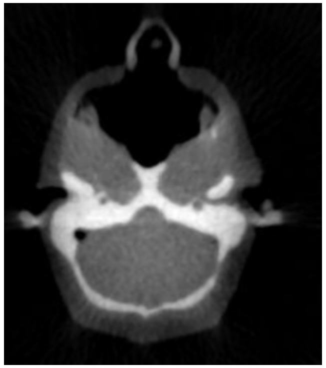


Phantom

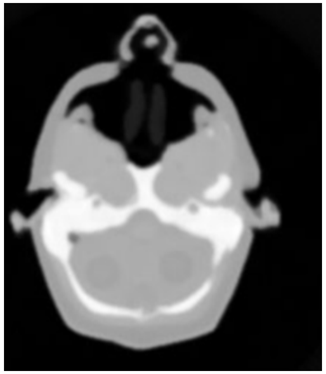
- Transmission map
  – records loss of protons due to nuclear reactions



- Scattering map
  – records scattering of protons off Coulomb potential



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



Cecile Bopp. PhD thesis, Strassbourg, 2013

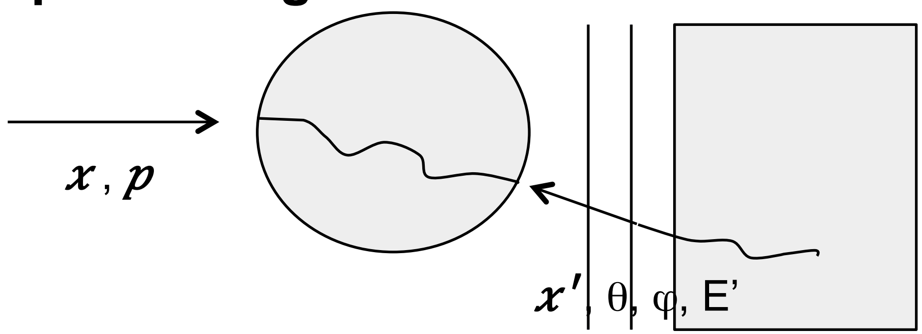
Clinical pCT - requirements

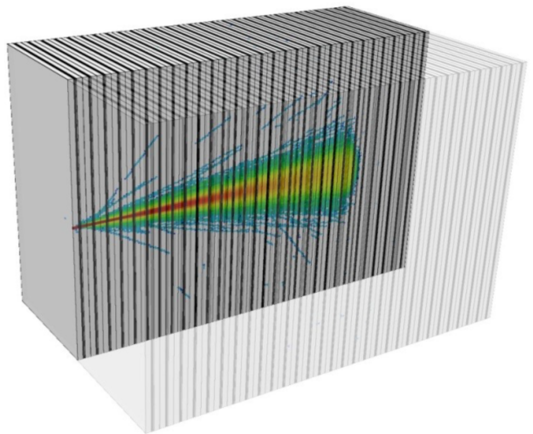
High energetic proton beam traversing the phantom

- **Beam**
  - **Intensity ~ 10^7 – 10^9 protons/sec**
  - **Pencil beam scanning mode**
- **Detector**
  - **High position resolution (~10 μm)**
  - **Simultaneous tracking of large particle multiplicities**
  - **Large area (> 30 x 30 cm^2)**
  - **High reconstruction efficiency**
  - **Fast readout**
  - **Radiation hardness**
  - **Front detector (first 2-3 layers): 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

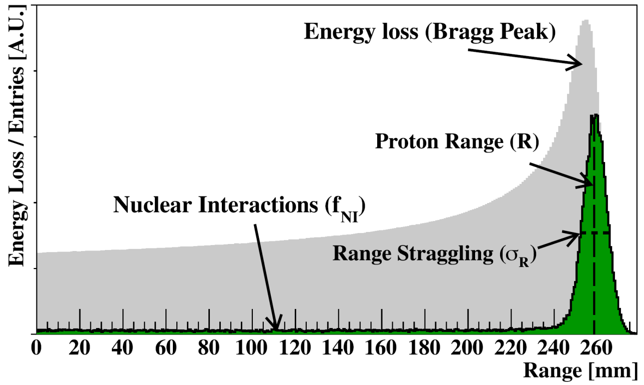




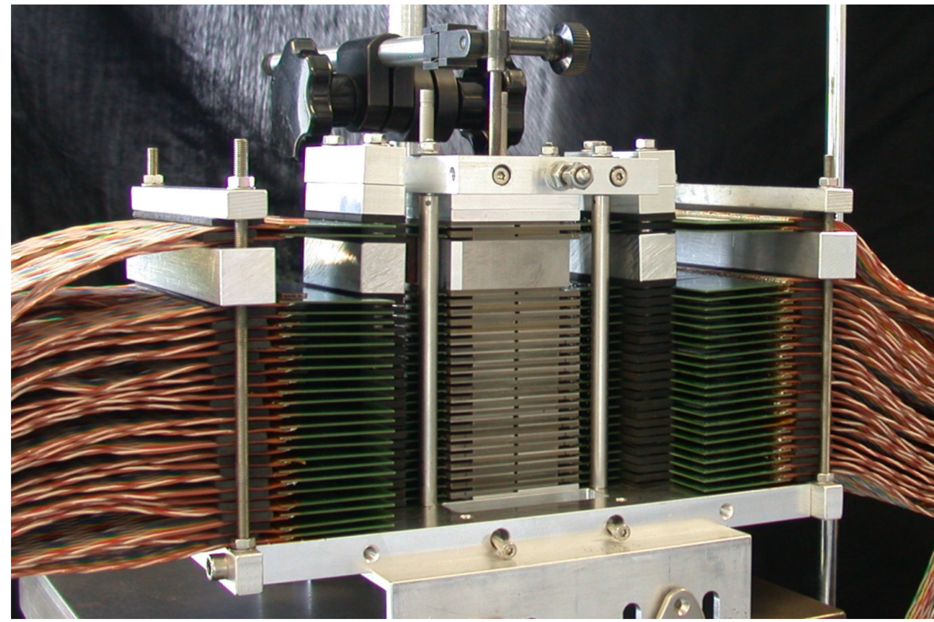
  - x , p given by beam optics and scanning system
  - x', θ, φ have to be measured with high precision
    - position resolution ~5 μm with minimal MS i.e. very thin first two tracking layers

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

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

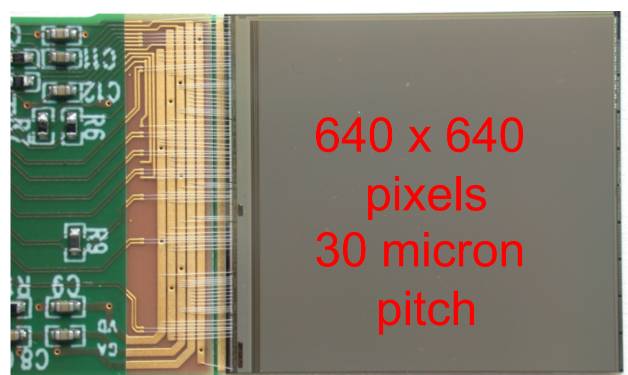


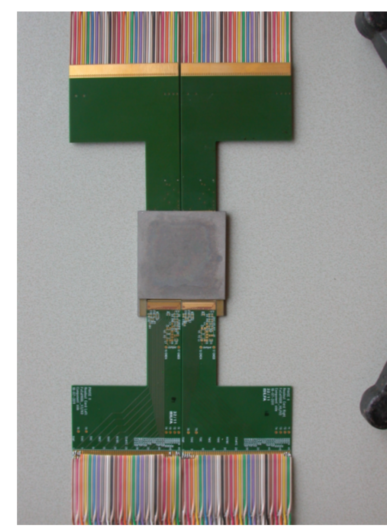
Digital tracking calorimeter prototype (I)



Silicon-tungsten sampling calorimeter

- **optimised for electromagnetic showers**
- **compact design 4x4x11,6 cm^3**
- **24 layers**
  - **absorbers:**
    3.5 mm of W (≈ 1 X_0)
    Molière radius: 11 mm
  - **active layers:**
    MAPS – MIMOSA 23*
    4 chips per layer
    -> 96 chips in total
    - **on-chip digitisation**
    - **chip-level threshold setting**
    - **1 bit per pixel**





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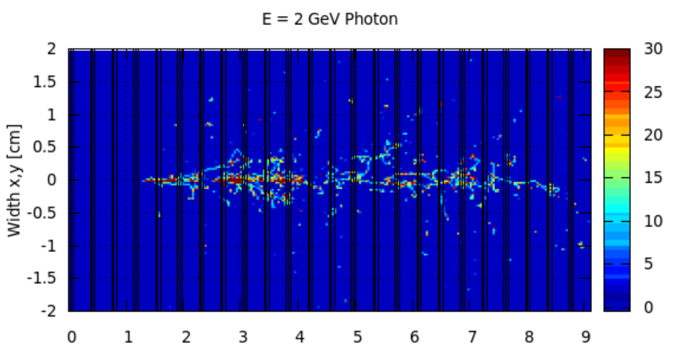
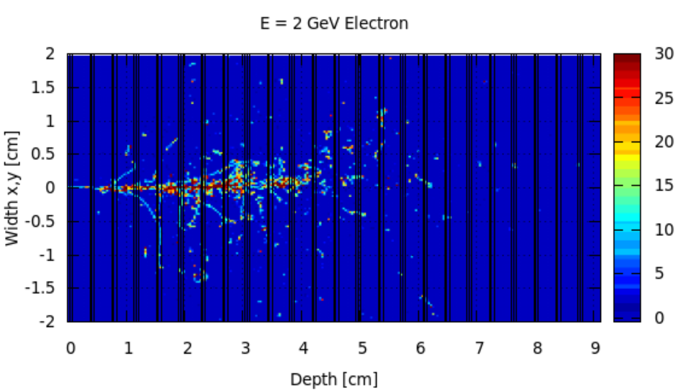
* IPHC Strasbourg

Simulation results

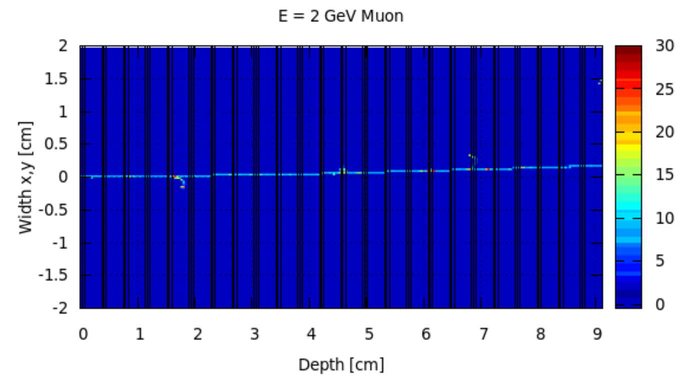
Detector response

Photons and electrons (e.m. shower)

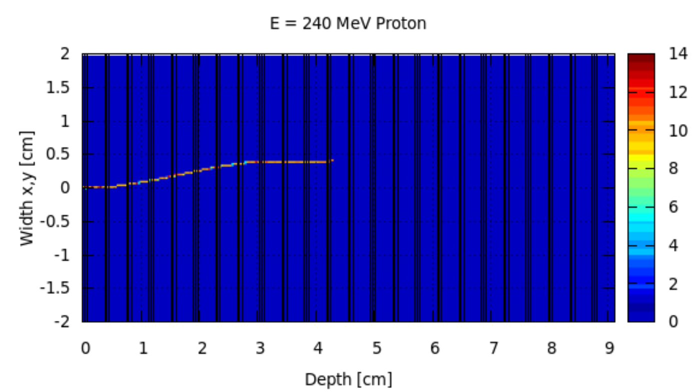




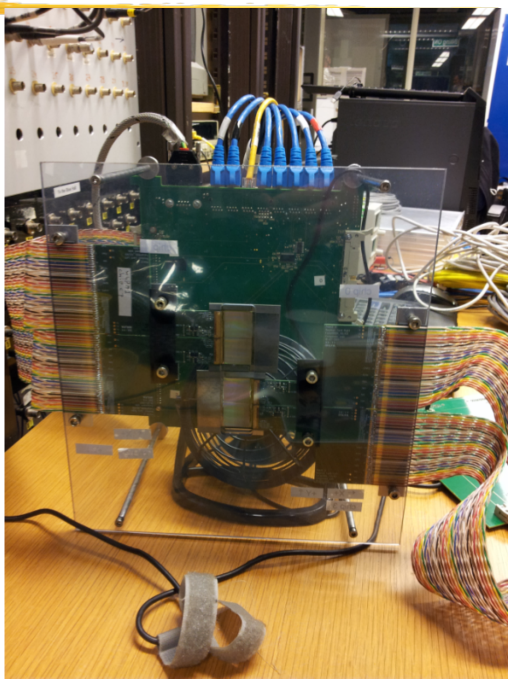
muons (MIP)



protons



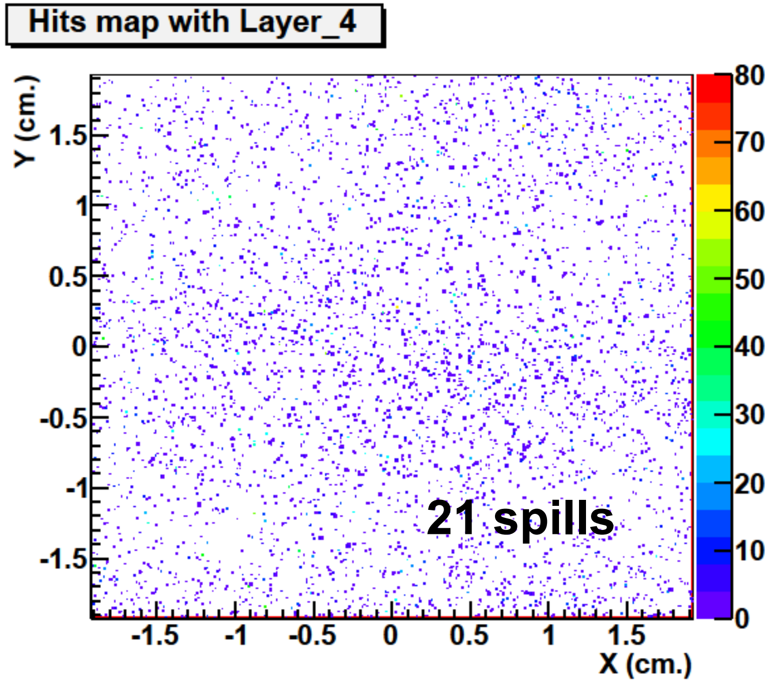
Digital tracking calorimeter – rangemeter (I)

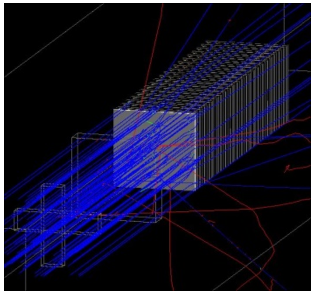


Range measuring resolution

- **Stopping: proton beam tests at KVI (Groningen)**
  - **Full prototype (24 layers, tungsten absorber)**
    -> validation of simulations
  - **Energy: from 122 to 190 MeV**
  - **Intensity:**

    ≈ 1 proton per frame (640 μsec), 800 protons per spill





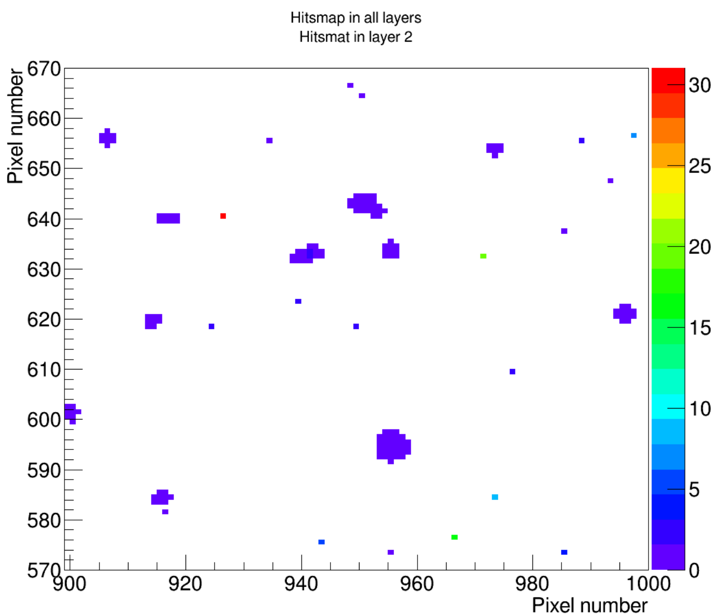
broad beam spot

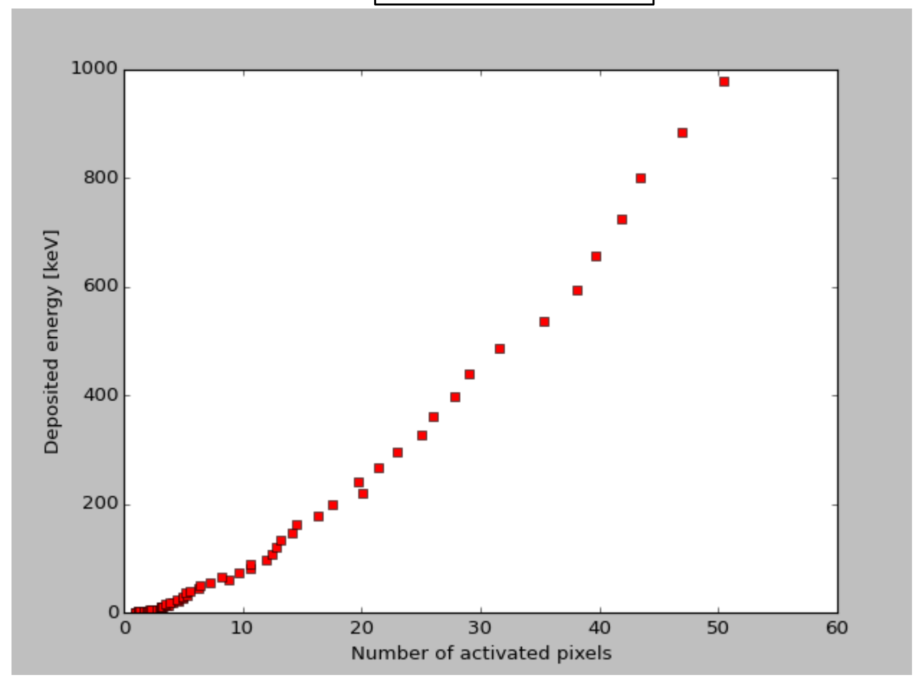
single track in 4 layers

Digital tracking calorimeter – rangemeter (II)

Range measuring resolution

H. Pettersen



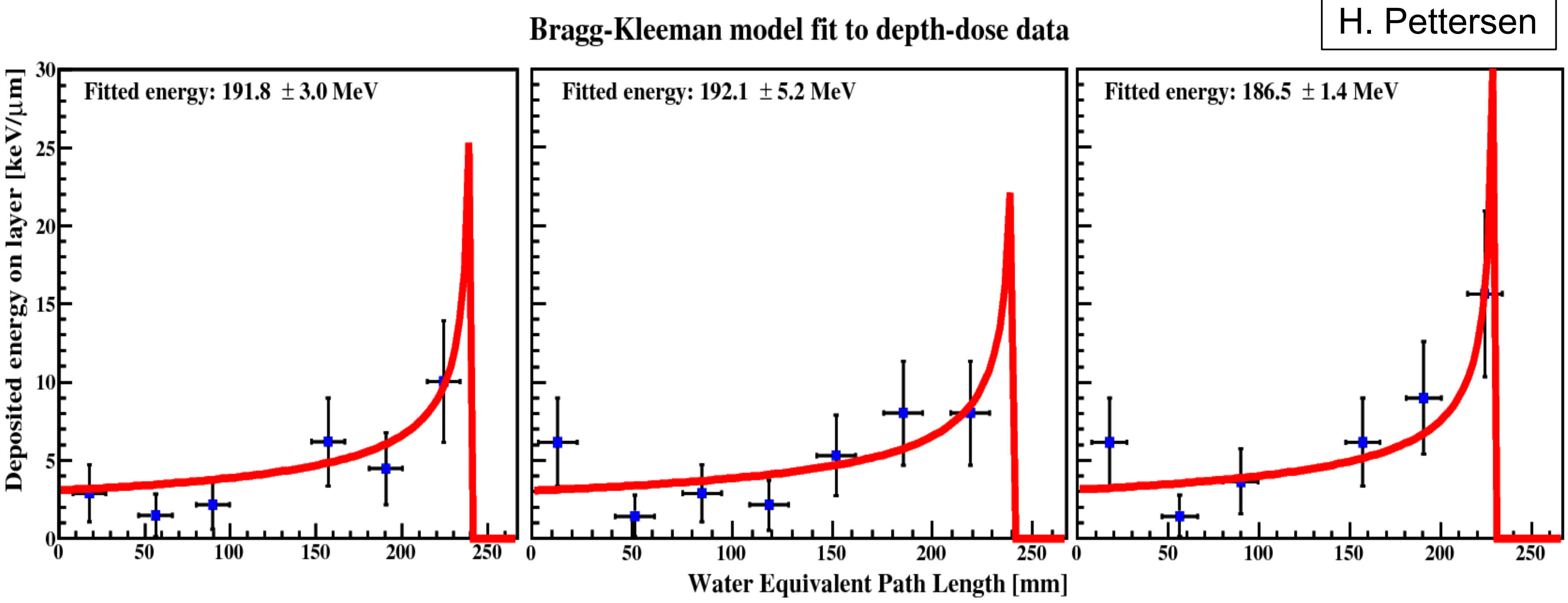


- **Energy loss measurement**
  - **hadron tracks:**
    number of hits in a sensitive layer along the particle trajectory ("cluster size") depends on the energy loss

Digital tracking calorimeter – rangemeter (IV)

- **Tracking of a single proton, collecting clusters along the trajectory and fitting a Bragg curve***

H. Pettersen

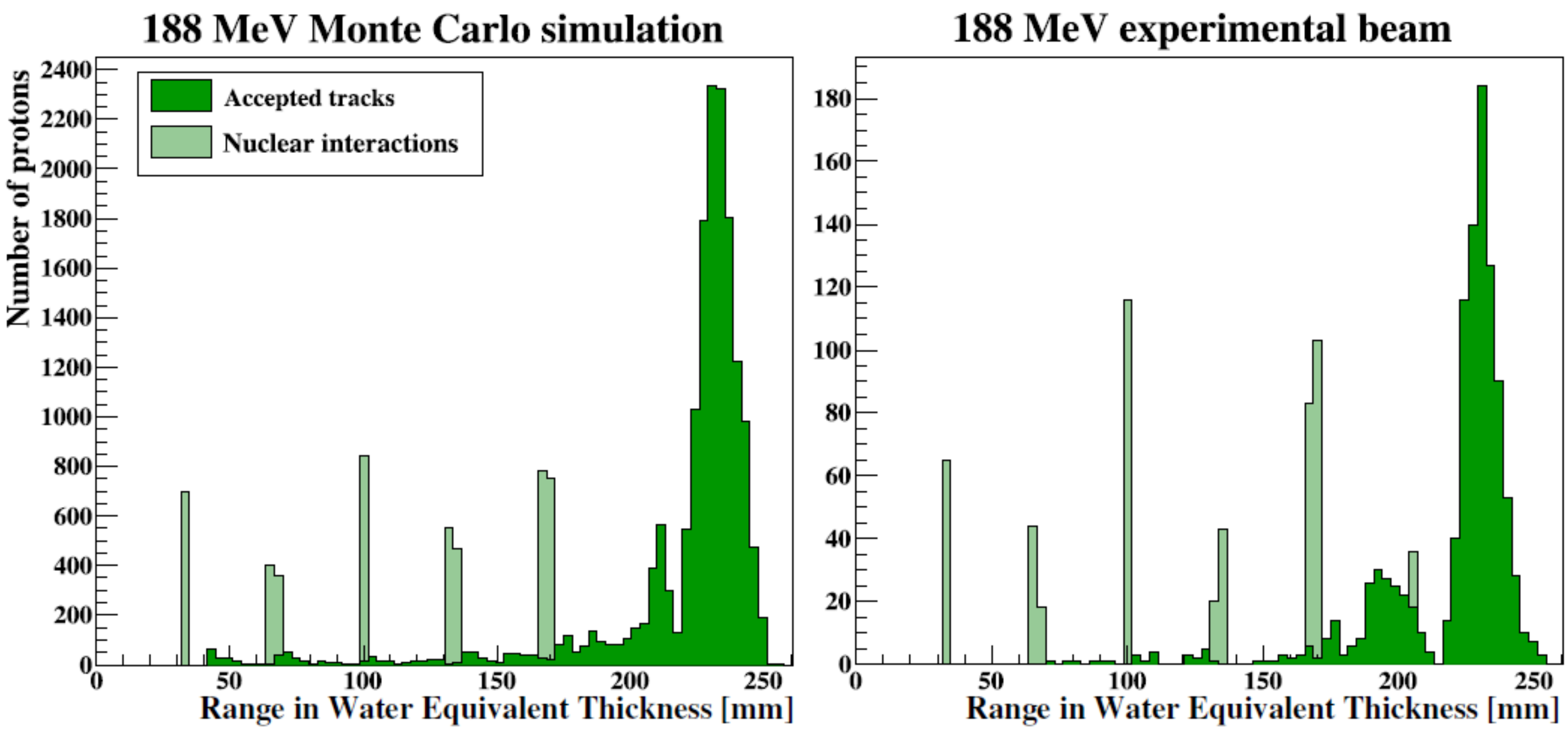


* **Bortfeld, T. *An Analytical approximation to the Bragg curve for therapeutic proton beams.* Med. Phys 24 2024-33 (1997)**

Digital tracking calorimeter – rangemeter (V)

- **Energy/range resolution for 188 MeV protons**

H. Pettersen, PhD thesis, UiB, 2018



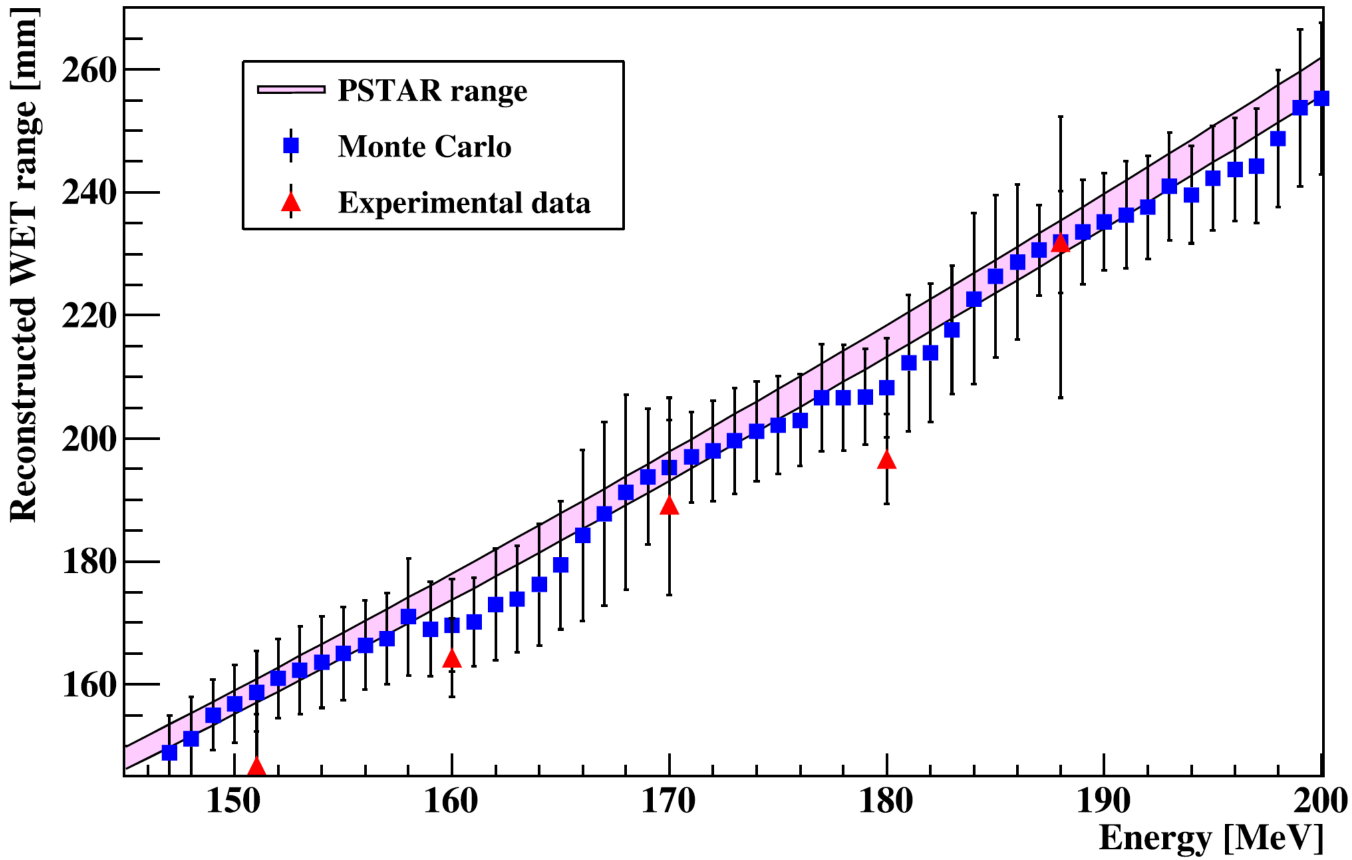
$$\langle \hat{R} \rangle = \frac{\sum_{i=i'}^{\infty} w_i x_i}{\sum_{i=i'}^{\infty} w_i},$$

$$\langle \hat{\sigma}_R \rangle = \sqrt{\frac{\sum_{i=i'}^{\infty} w_i (x_i - \langle \hat{R} \rangle)^2}{\left[\sum_{i=i'}^{\infty} w_i\right] - 1}}$$

Digital tracking calorimeter – rangemeter (VI)

- **Range vs proton beam energy**

H. Pettersen, PhD thesis, UiB, 2018



-> good agreement between data and MC

Towards a clinical prototype – Bergen pCT Collaboration

UNIVERSITY OF BERGEN

HØGSKOLEN I BERGEN
BERGEN UNIVERSITY COLLEGE

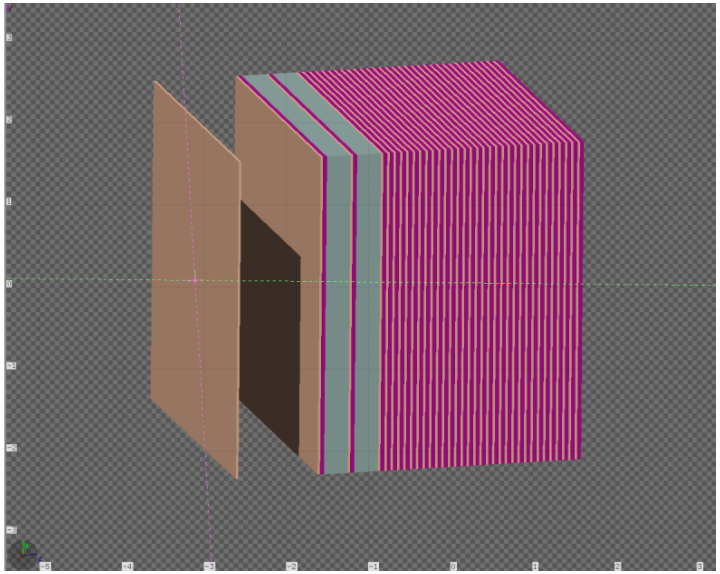
HELSE BERGEN
Haukeland University Hospital

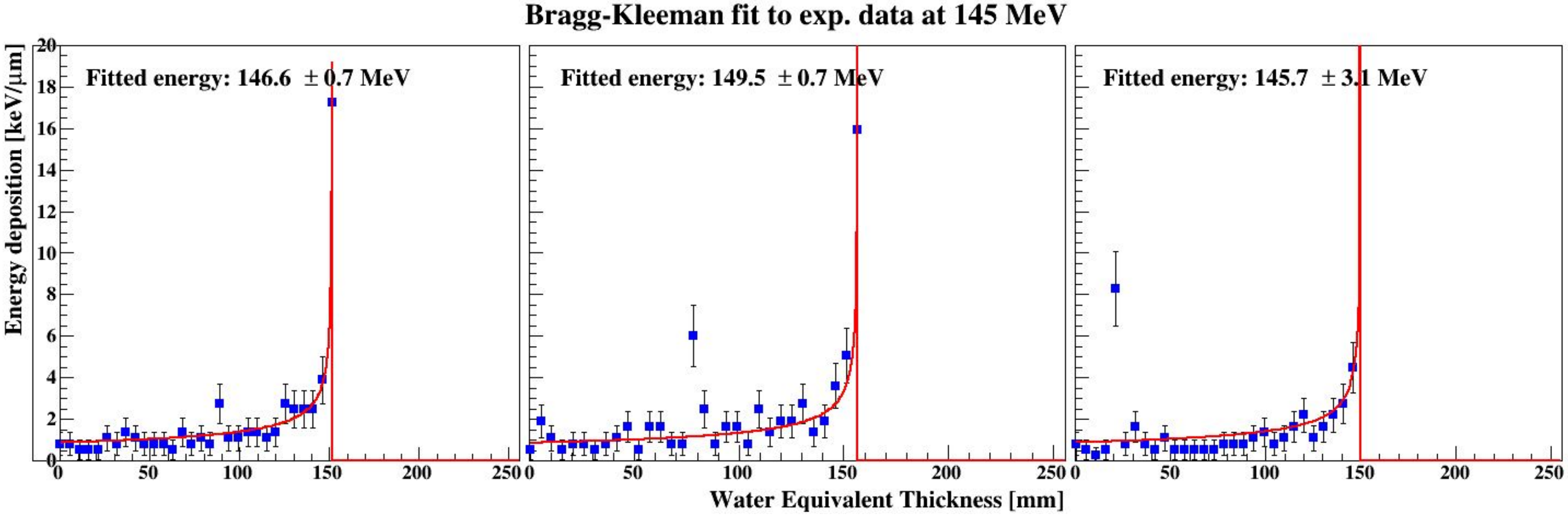
- **Organisation**
  - UiB, HiB, HUS
  - Utrecht University
  - DKFZ Heidelberg
  - Wigner, Budapest
- **Financing**
  - 44 MNOK, 5 years (2017-2021)
- **Status**
  - Finishing the optimisation of the design
  - Sensor characterisation
  - Start massproduction of ALPIDE chips soon

Norwegian government has decided to build two particle therapy facilities (Oslo, Bergen), to be operational by 2022 rep. 2025

Towards a clinical prototype - Optimisation of the design

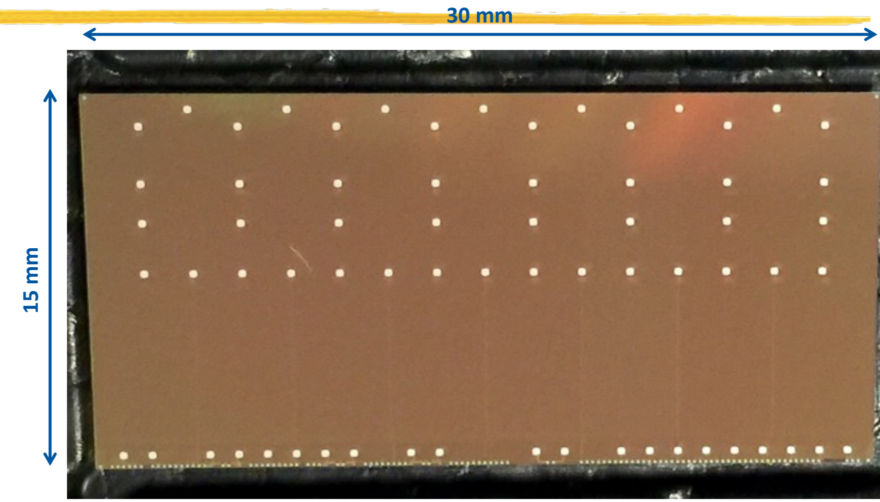
- **geometry**
  - front area: 27 cm x 15(18) cm
- **longitudinal segmentation**
  - number of sensitive resp. absorber layers: 41
- **absorber**
  - energy degrader, mechanical carrier, cooling medium
  - material choice: Al
  - thickness: 3.5 mm

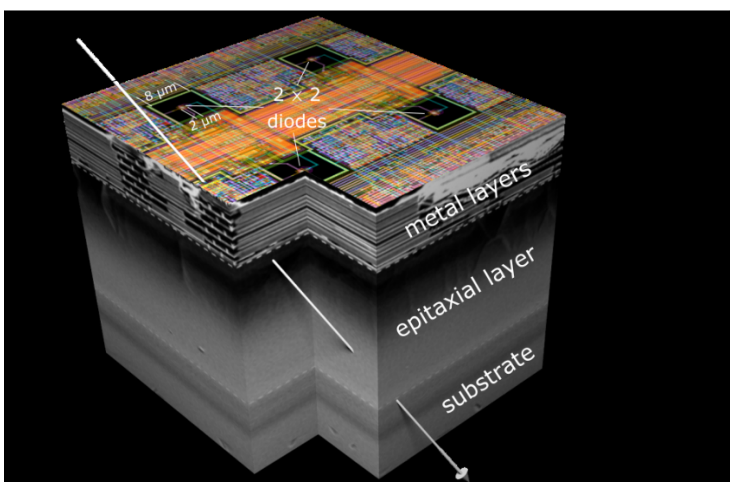




Pixel sensor – MAPS

- **ALPIDE chip**
  - **sensor for the upgrade of the inner tracking system of the ALICE experiment at CERN**
  - **chip size ≈ 3x1.5 cm^2, pixel size ≈ 28 µm, integration time ≈ 4 µs**
  - **on-chip data reduction (priority encoding per double column)**



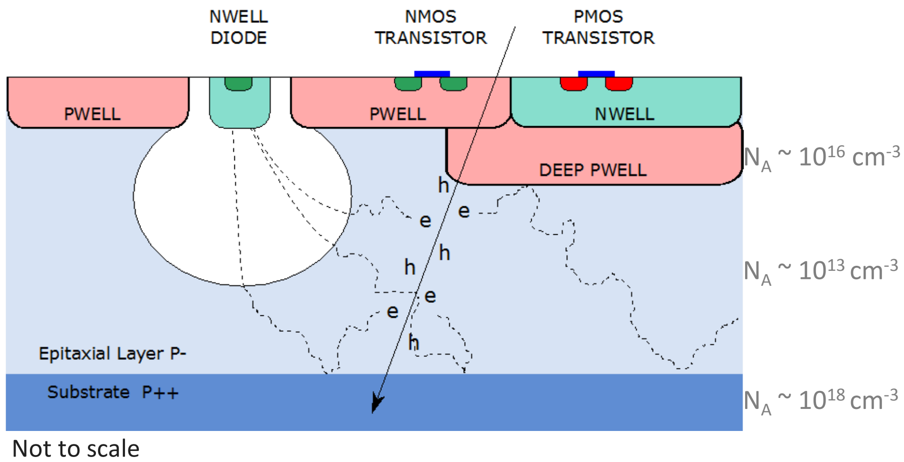


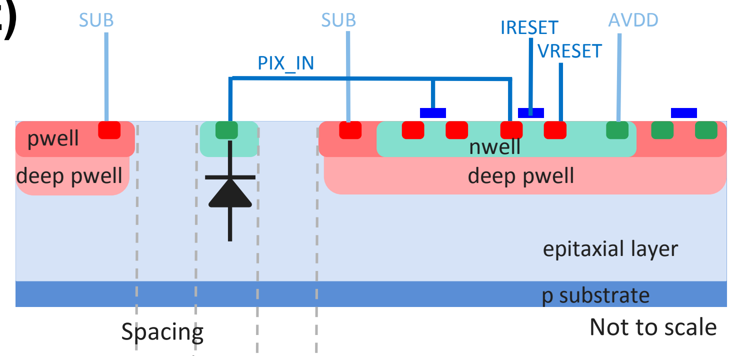
M. Magner, IFEE 2014

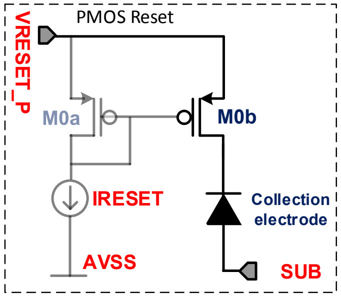
Design team:
CCNU Wuhan, CERN Geneva, YONSEI Seoul, INFN Cagliari, INFN Torino, IPHC Strasbourg, IRFU Saclay, NIKHEF Amsterdam

ALPIDE – pixel cell

- **CMOS 180 nm Imaging Process (TowerJazz)**
  - 3nm thin gate oxide, 6 metal layers



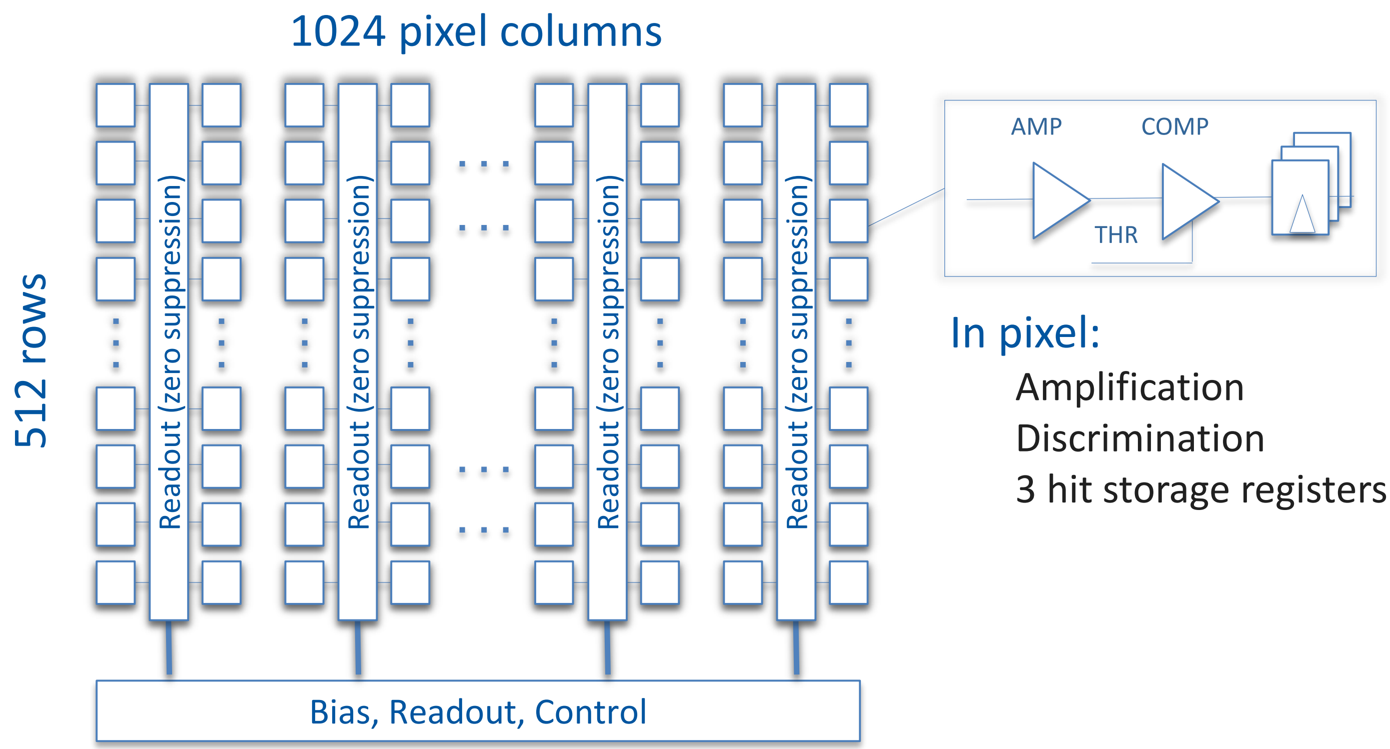




- **29 µm x 27 µm pixel pitch, 25 µm thick epitaxial layer**
- **Substrate thinned to 100 µm or 50 µm**
- **1024 x 512 pixels**
- **Small n-well diode -> low capacitance -> large S/N**
- **Reverse bias to substrate -> increased depletion volume -> charge collection by drift**

ALPIDE – architecture

- **29 µm x 27 µm pixel pitch**
- **Deadtime-free frond end**
- **Zero-suppressed matrix readout**
- **Triggered or continuous readout**

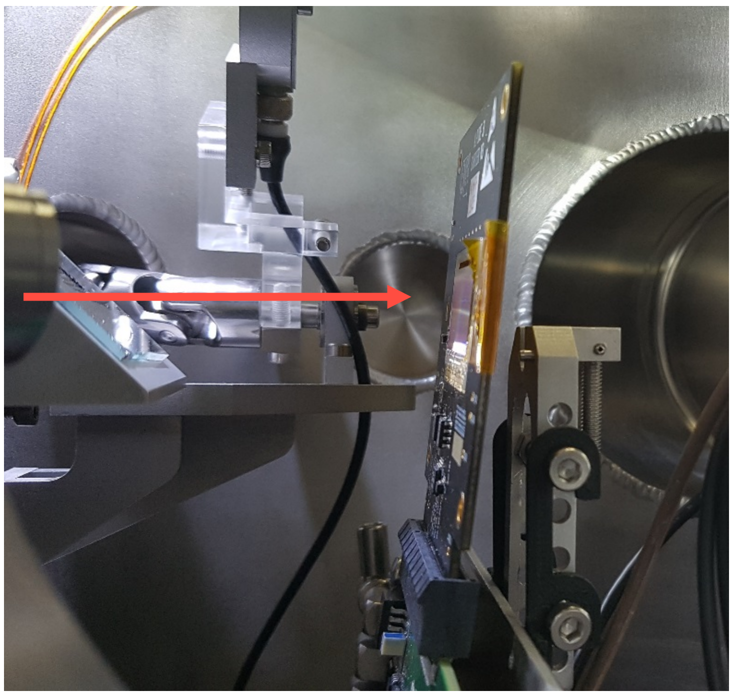


In pixel:
Amplification
Discrimination
3 hit storage registers (MEB)

Helium-4 microbeam test

Aim: Study the effect of beam position on cluster size

Test done at Australia Nuclear Science and Technology Organization (ANSTO) in Australia



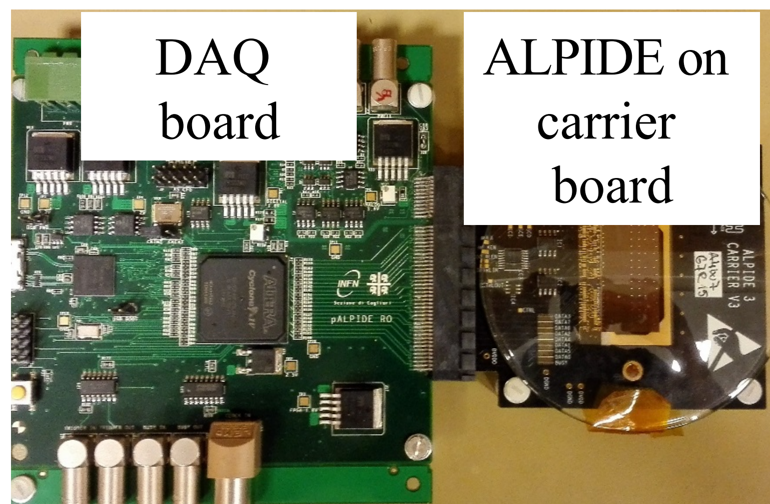
ALPIDE inside the vacuum chamber

ALPIDE tilted by ~ 5^0

Beam direction shown by Red arrow

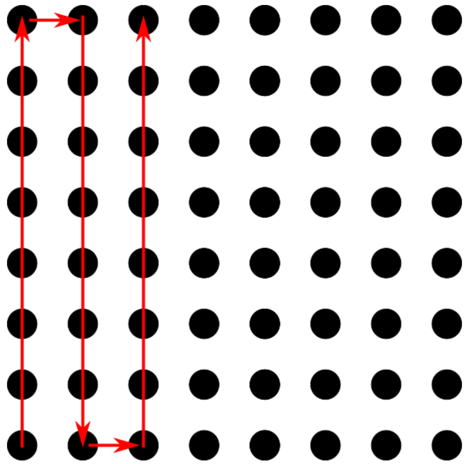
- Test parameters

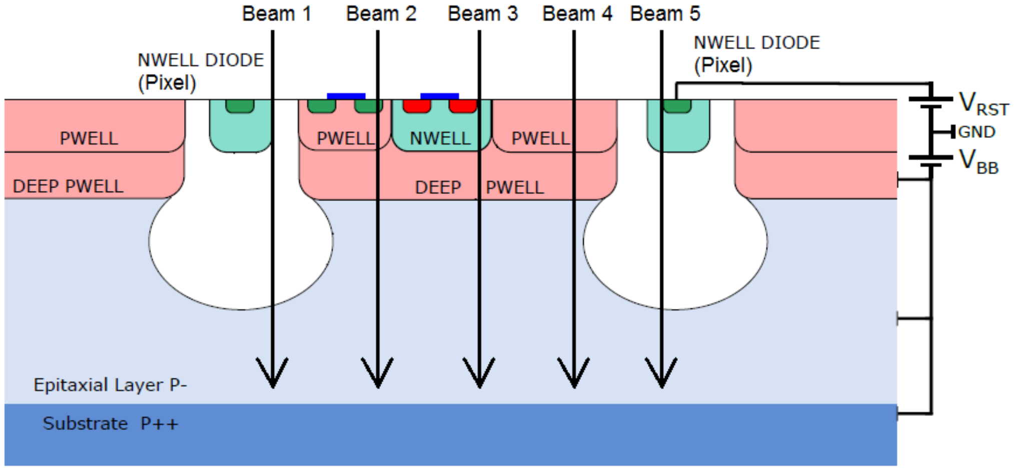
→ Ion beam	Helium-4
→ Energy	10 MeV (± 0.1 MeV)
→ Beam size	1 µm
→ Rate	2 k to 10 k ions/sec
→ Trigger freq.	100 kHz (10 µs)
→ Bias Voltage	0 V and -3 V



Helium-4 microbeam test

- ALPIDE surface was raster scanned
  - Spot size 1 µm
  - Area 128 x 128 µm²
  - Dwell time 200 ms / spot
  - Single pixel size 27 µm x 29 µm

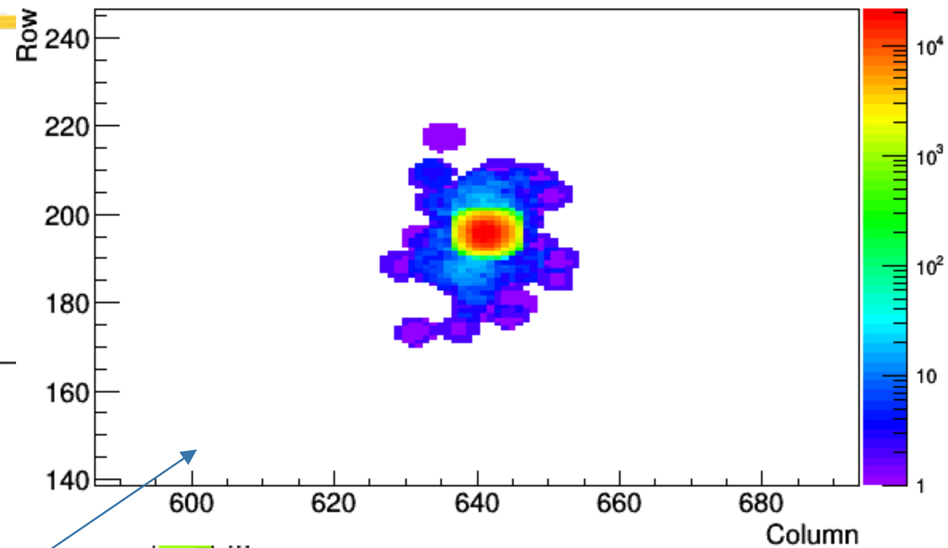


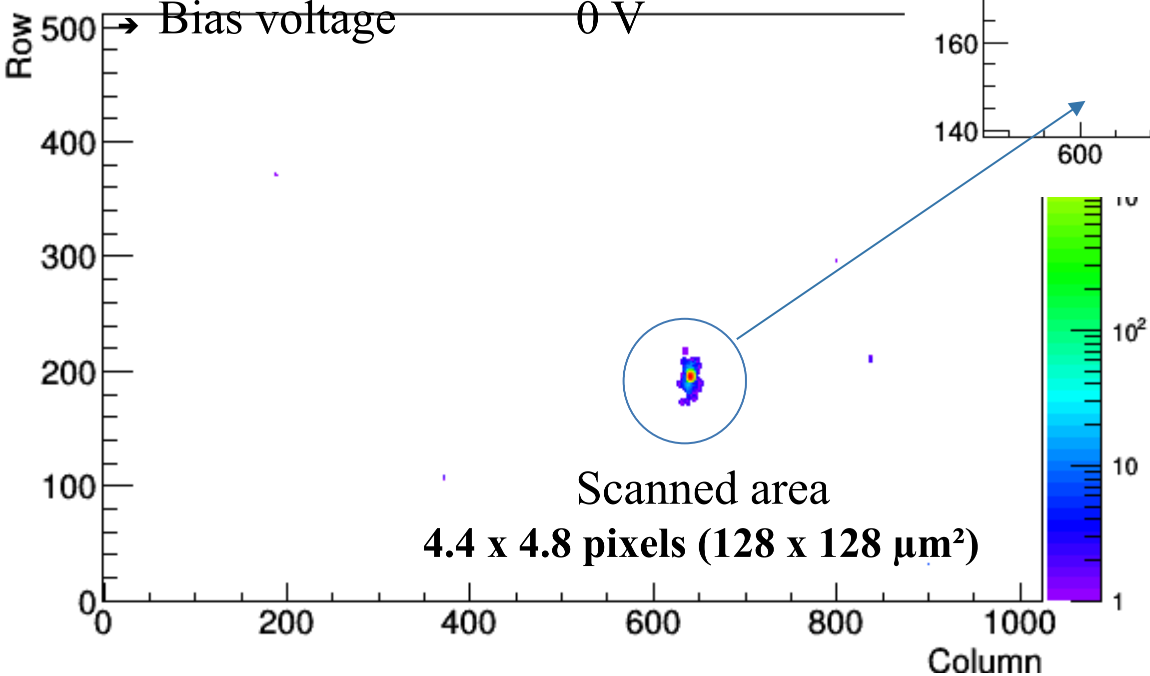


Dot – beam spot
Red arrow – beam spot moving direction
Dwell time – the time spent by beam on a dot

Scanned area

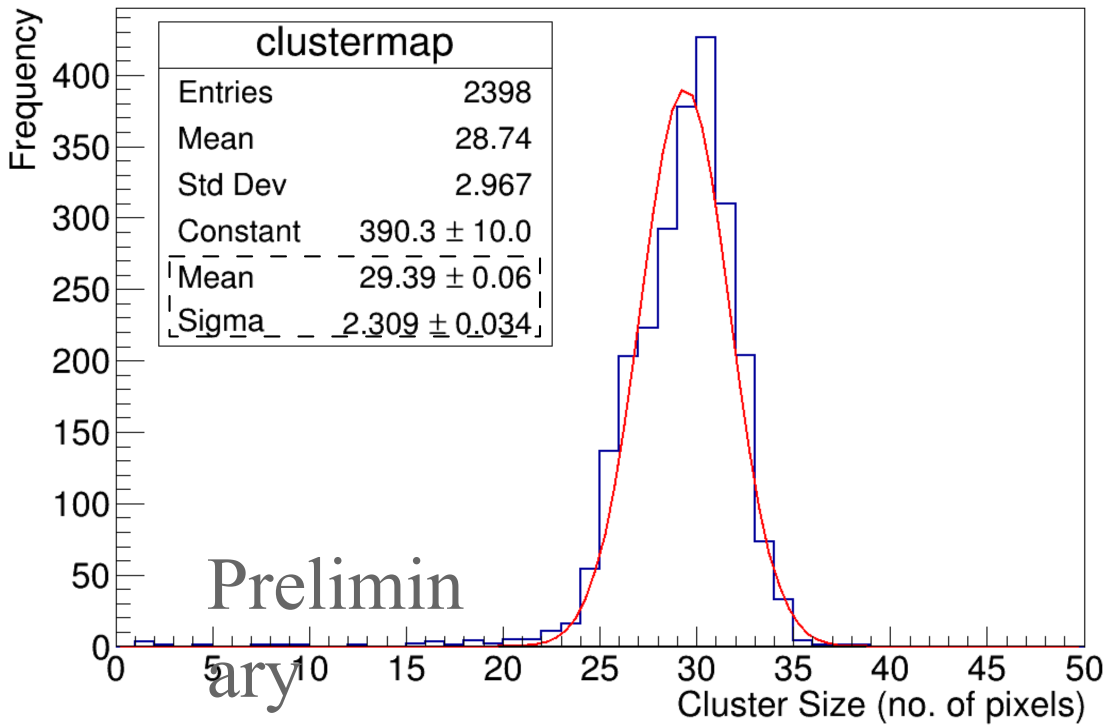
- He4 beam energy 10 MeV
- Beam freq. 10 kHz
- Dwell time 200 ms/spot
- Bias voltage 0 V





Cluster size: High LET microbeam

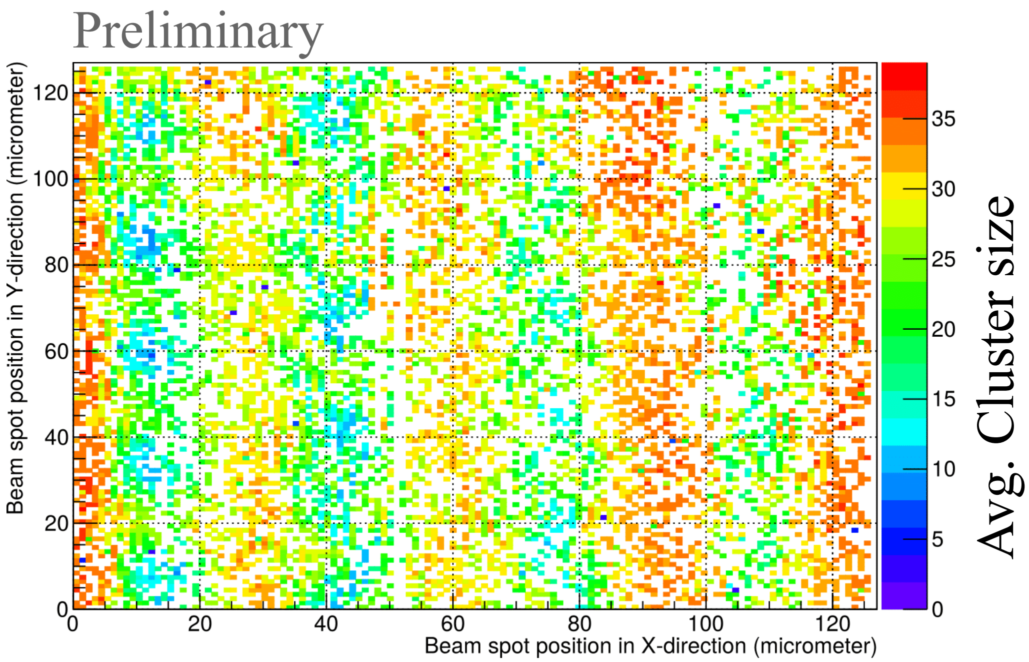
Data set selected for few spots



Possible to record heavy ions with ALPIDE!

LET: Linear Energy Transfer

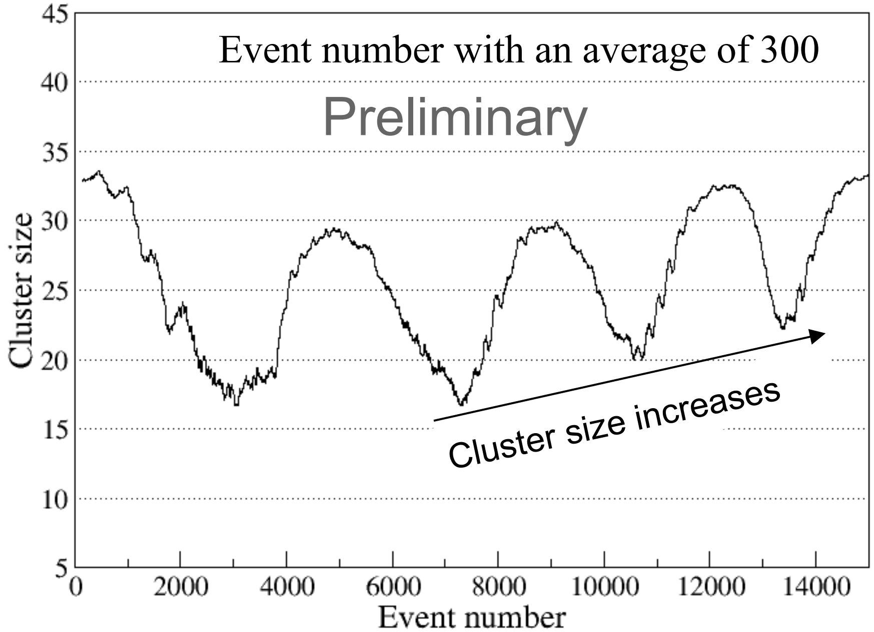
Cluster size map



- Clusters are dependent on the beam position
- Clusters are rather constant in vertical bands visible on various X-values
- Clusters could be smaller when the beam is positioned in the vicinity of collection diode than in its periphery
- No direct impact on particle tracking: cluster center is used for particle tracking

Avg. cluster size vs. Event number

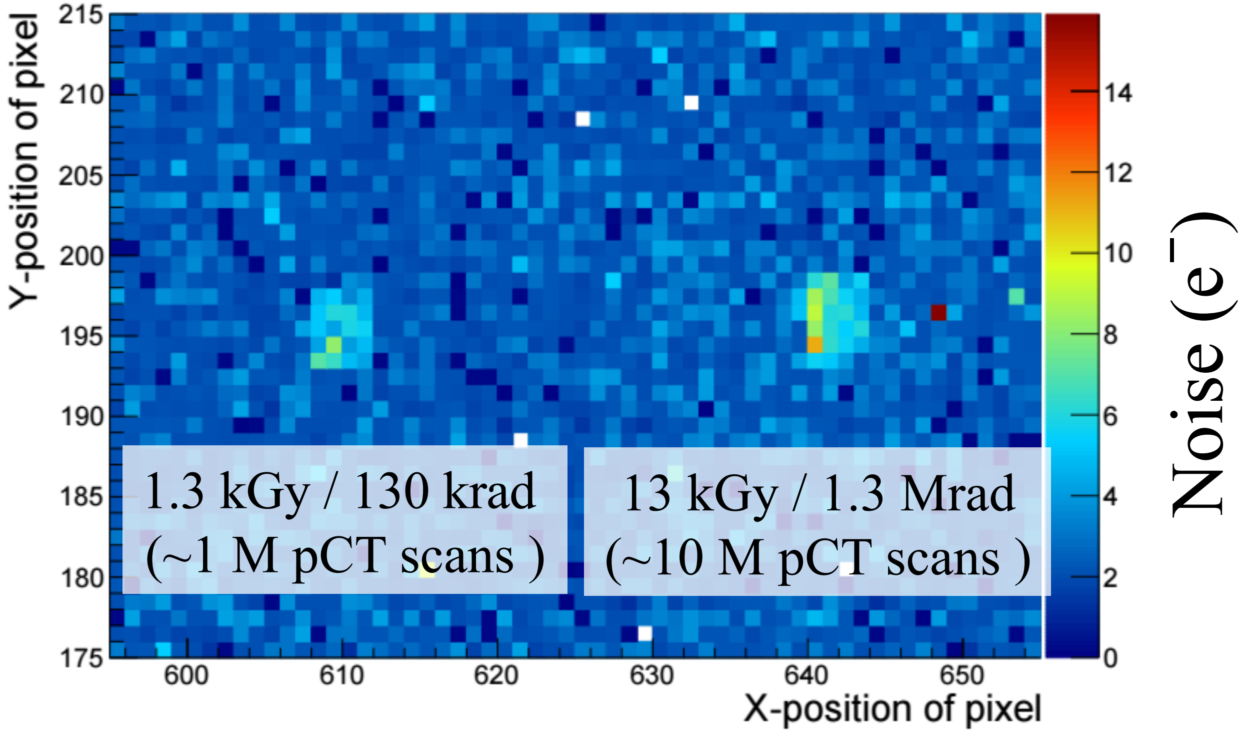
Event number →X - position → Irradiation time



- Beam moving from left to right, across the columns
- Small clusters disappear with time (from event #8000 onwards)
- This could be due to
  - Some areas are slightly more sensitive than others due to process variations
  - Rise in temperature, chip was in vacuum – cooling required (~ 20^0 C)
  - Small increase in noise due to irradiation

Noise Map: Irradiated ALPIDE

- Scanned two places in ALPIDE:
  - → 2 kHz beam freq. (at right) and 10 kHz beam freq. (at left)

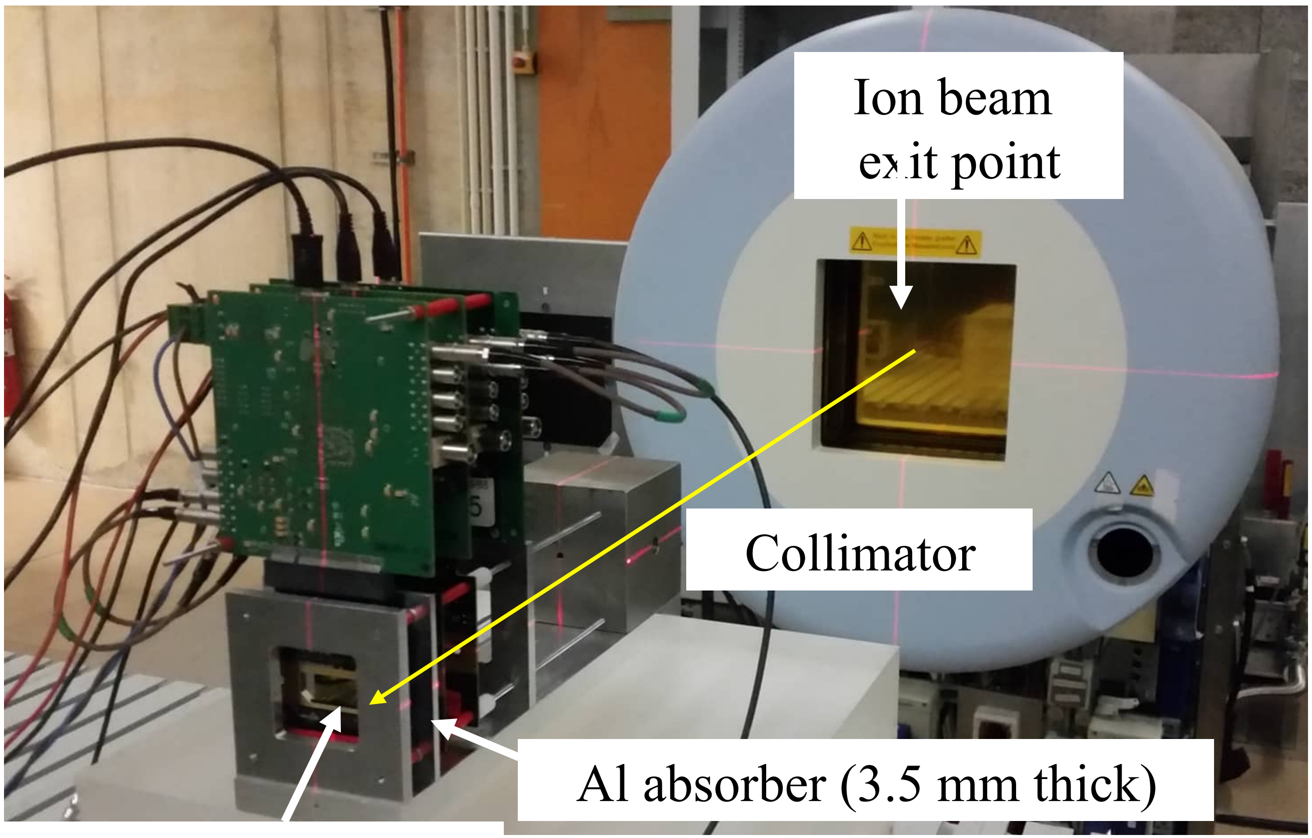


- Increase in noise but ALPIDE was working→No serious issues!!

ALPIDE telescope experiment at HIT, Heidelberg

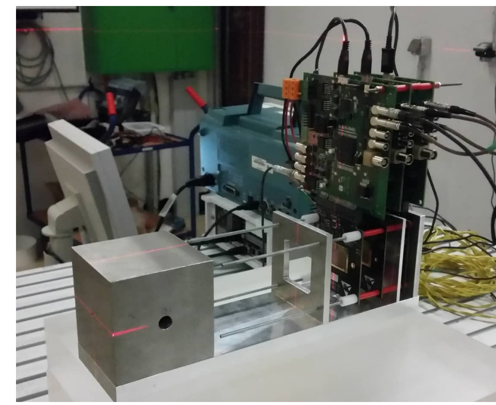
Aim: Ion tracking, clusters vs. ion energy (LET)

Test setup at HIT



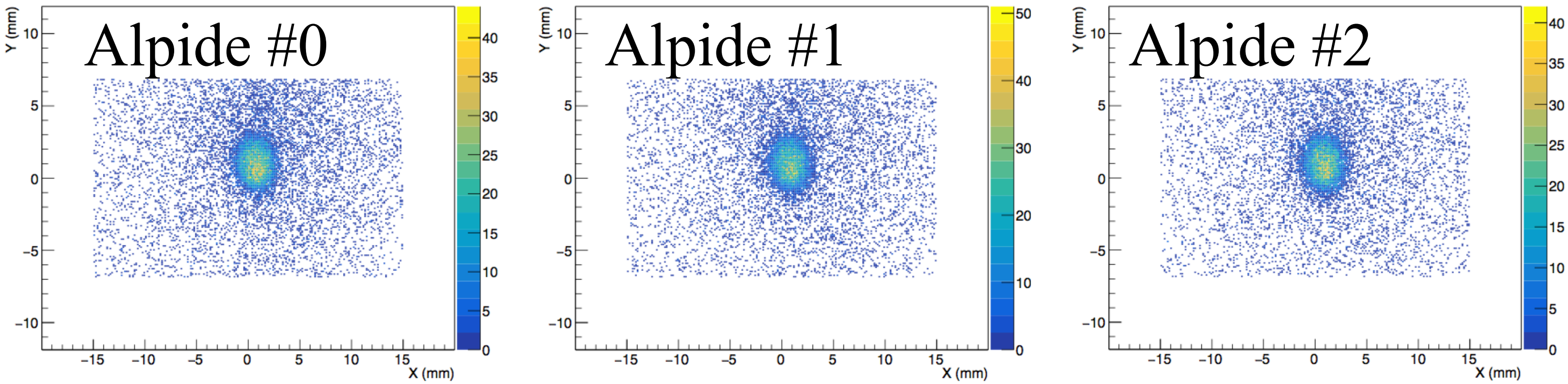
ALPIDE sensor coupled to DAQ board

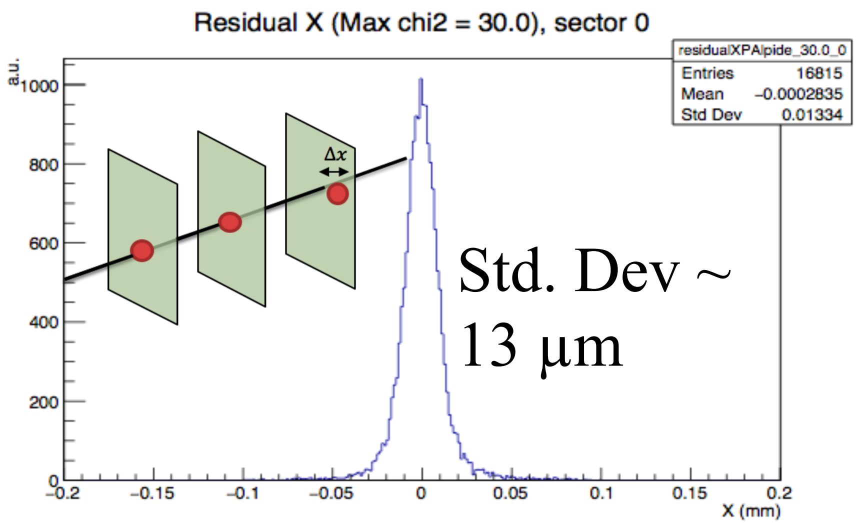
Telescope – 3 ALPIDE



Beam energy (MeV/u)	
Helium	Proton
50.57	48.12
100.19	200.11
150.11	221.06
200.38	
220.5	

Position resolution

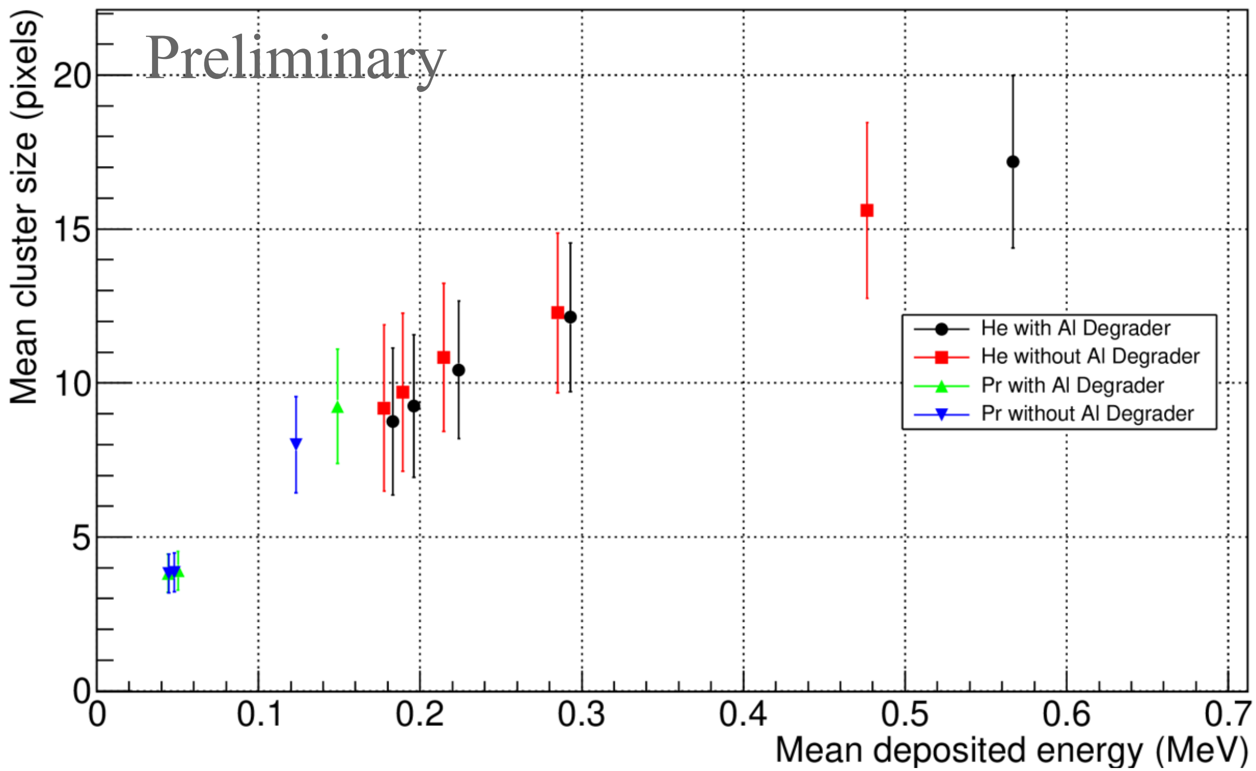




- Energy 220.5 MeV/u (FWHM = 10.1 mm)
- ^{4}He rate ~ 80 kHz
- Time frame 10 µs
- Collimator 3 mm

Cluster size vs. Energy loss in ALPIDE

For proton and helium in layer3

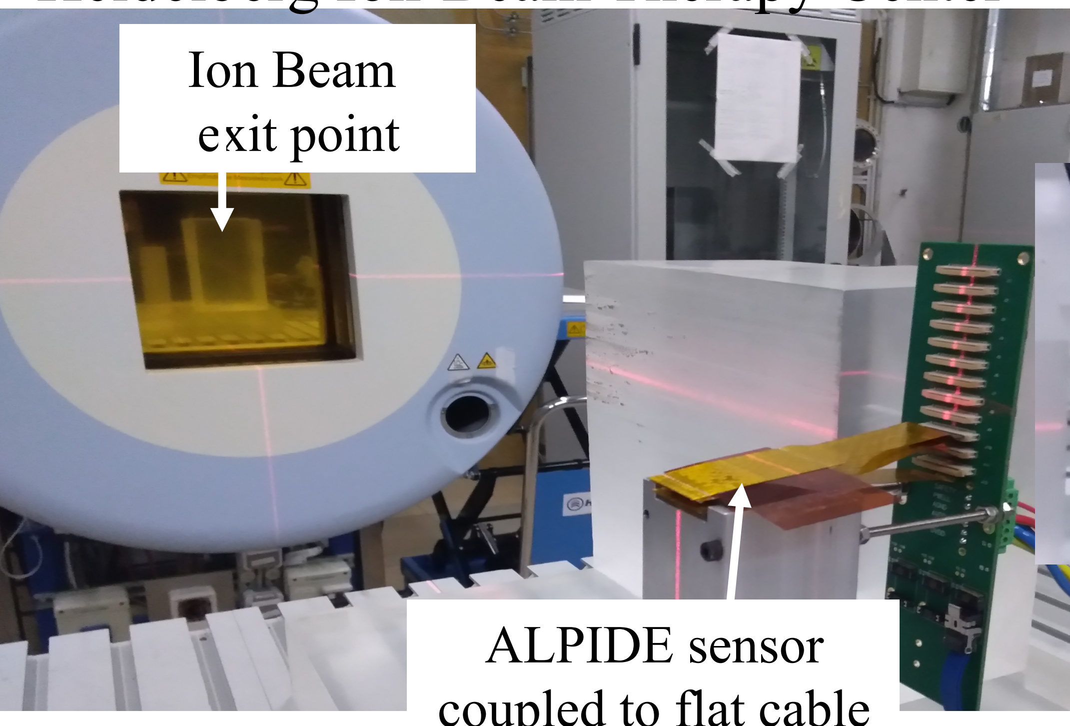


- Ion-energy deposit in ALPIDE obtained using Geant4 simulation
- Tracking of He and p beam is possible down to 50 MeV/c w/o absorber
- Cluster size decreases in proportion with LET
- Proton clusters are smaller than Helium as expected

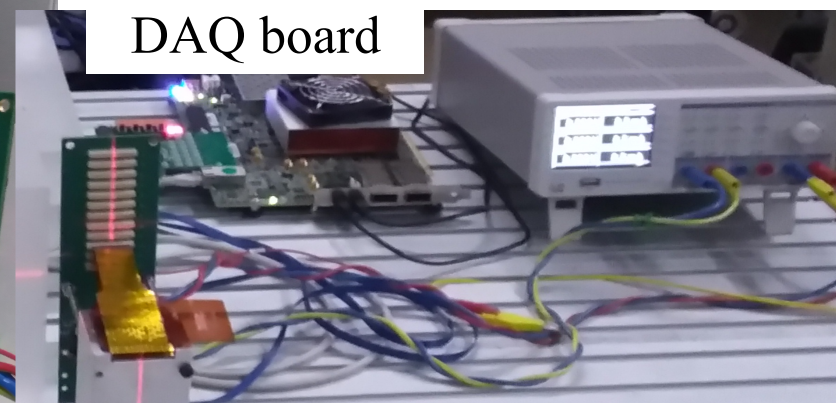
Single ALPIDE experiment at HIT Heidelberg

Aim: Lateral scan of ALPIDE – capture ion tracks for high LET ion beam

Heidelberg Ion-Beam Therapy Center



Carbon beam energy: 140.4 MeV/u

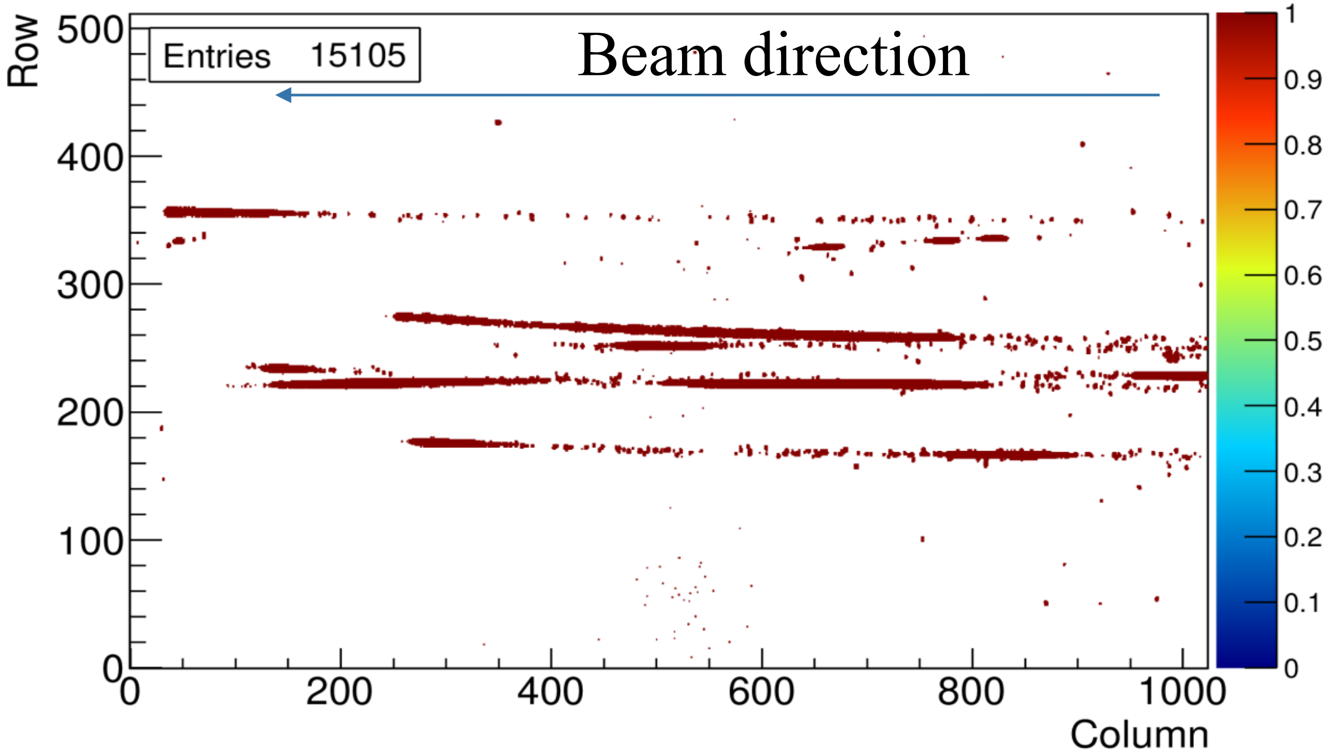


Range of Carbon
in ALPIDE (50 μm thick) ~ 2.5 cm

The ALPIDE chip was kept at few meters away from the beam exit to stop the beam in sensitive volume of the chip – Record high multiplicity events

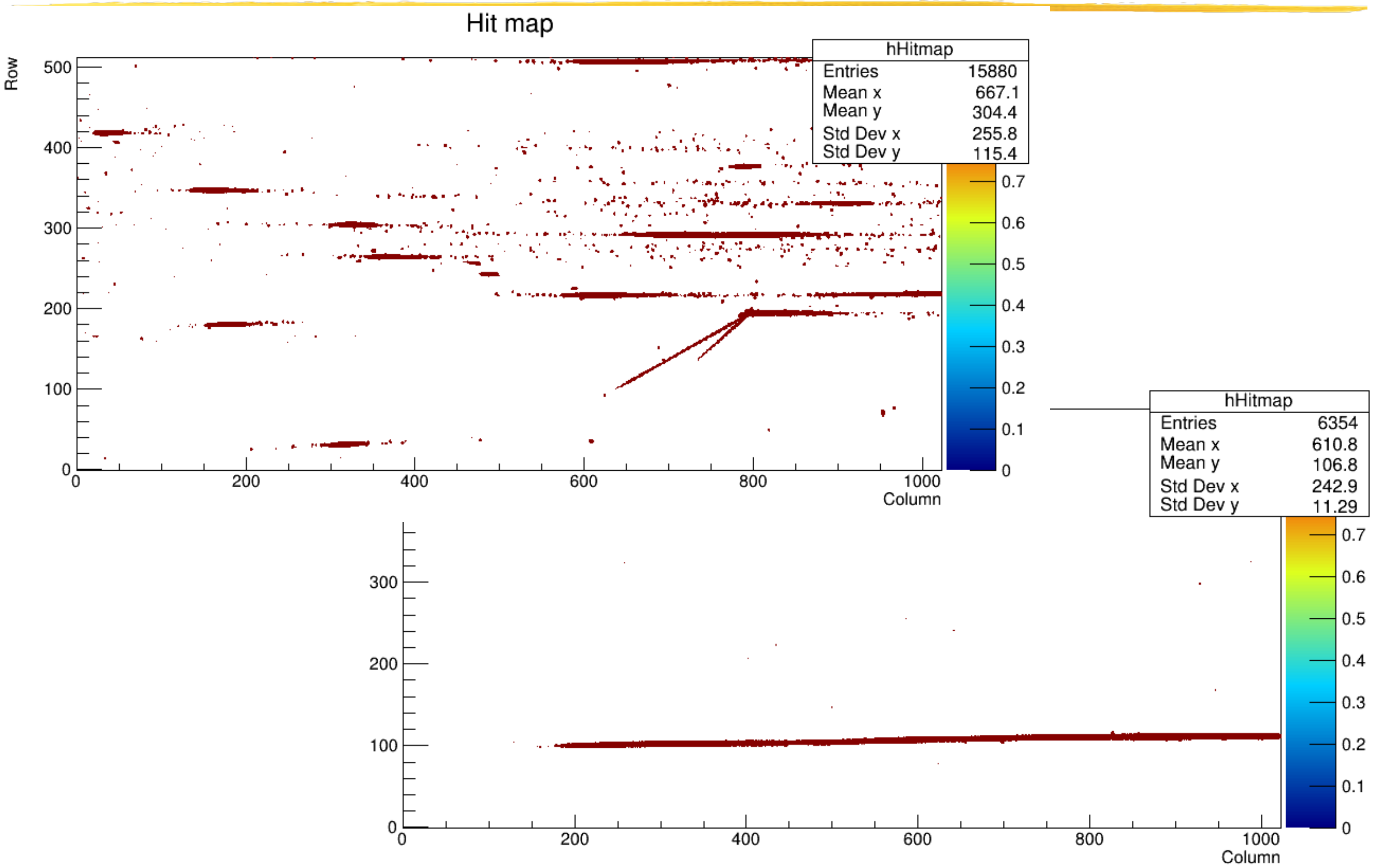
Hitmap: Carbon ions

Hitmap of 1 time frame or 1 event = 485 μs



Possible to record high multiplicity event !

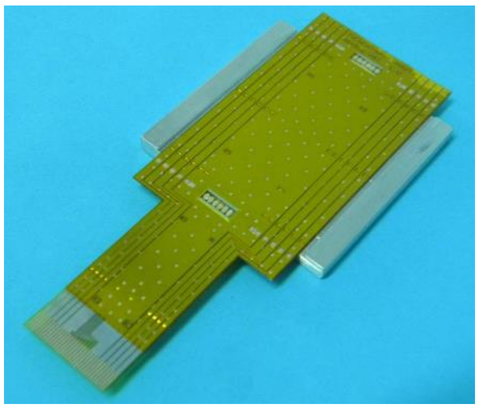
Hitmap: Carbon ions



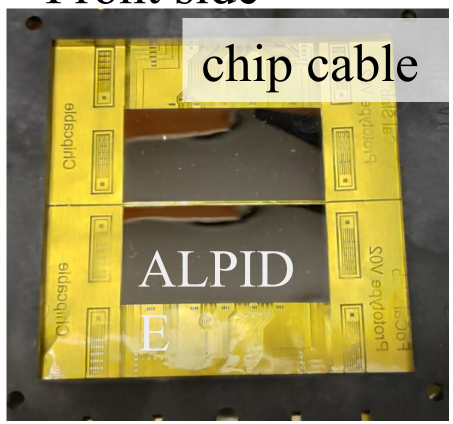
Mounting sensors on flexible cables

Intermediate prototype: chip cable with two ALPIDEs

Back side



Front side

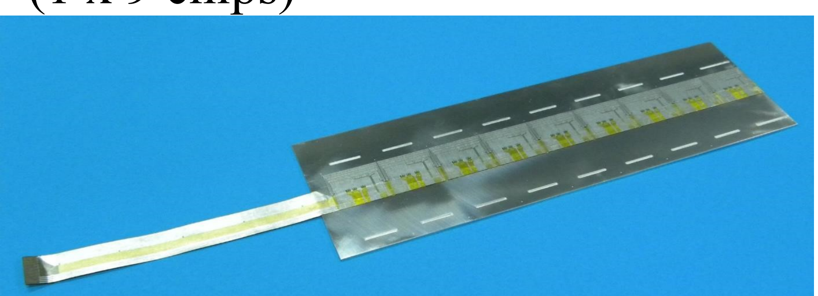


- ALPIDE mounted on thin flex cables:
  Aluminum-polyamide dielectric (30 um Al, 20 um plastic)

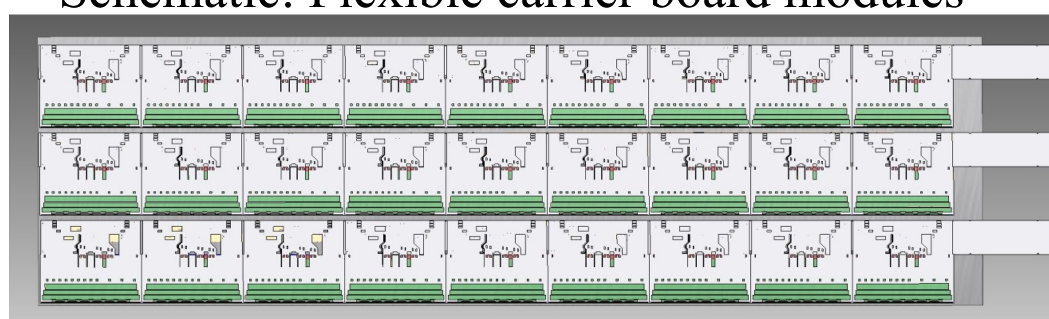
- Design and production:
  Utrecht University,
  The Netherlands and
  LTU, Kharkiv, Ukraine

Final system

Flexible carrier board modules
(1 x 9 chips)



Schematic: Flexible carrier board modules



Towards the clinical prototype

- Challenges
  - Two tracking layers at the front face - total thickness < 0.4 mm, 2 cm apart
    - Sensors: thinned down to 50 μm
    - Flex: ~100 μm
    - Carrier: Al or carbon foam/prepreg ~200 μm

- Readout system and DAQ
  - PCBs with Xilinx Virtex Ultrascale+ FPGAs (one per layer)

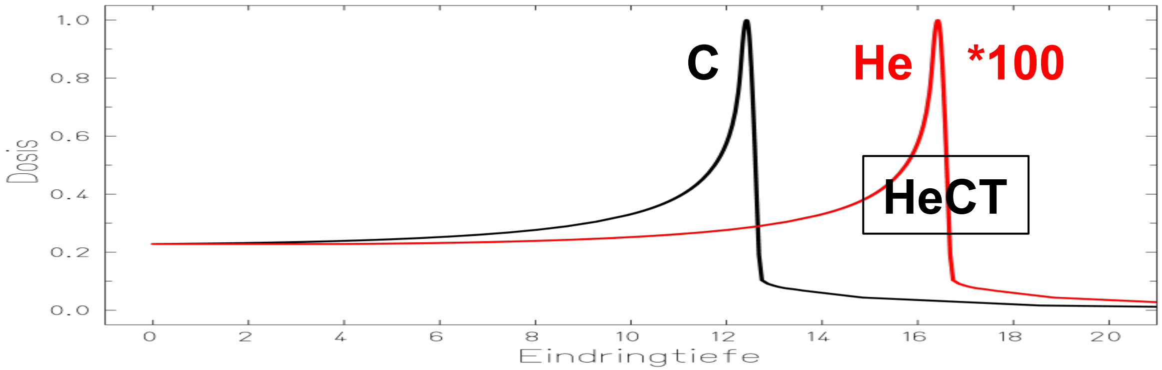
- Expected performance (simulation and beam tests)
  - Range accuracy: < 0.5 mm WET
  - Position resolution: 5 μm
  - Radiation hardness > 5 kGy resp. 1.7×10^{13} 1 MeV neq/cm^2
  - Flux: > 1...8 x 10^6 particles/cm^2/s

Next steps - Outlook

- **Construction of prototype**
  - **First chip cables with mounted chips are being tested**
  - **First sensor modules will be produced soon**

- **Extensive commissioning with proton beams**

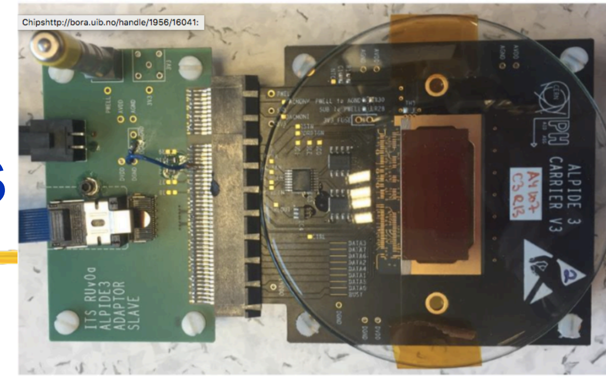
- **Commissioning with He beams**
  - **HeCT – less MS, better resolution***
  - **Carbon beam with 1% Helium (as proposed by GSI/HIT and CNAO):**



* PhD thesis C. Collins Fekete, Univ. Laval, 2017

This is the end

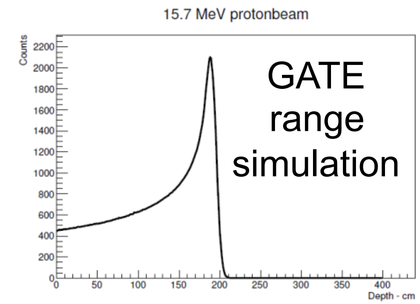
Characterisation of ALPIDE with proton and Helium beams



Cluster size vs dE/dx

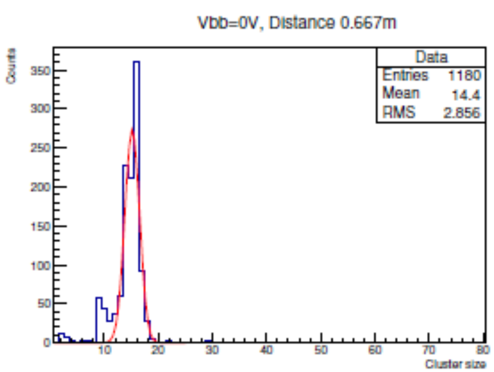
- 16 MeV external proton beam in air @ OCL

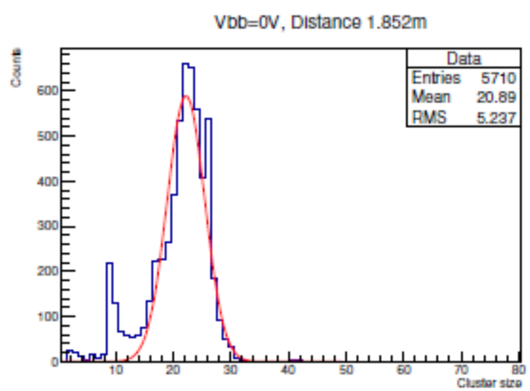
  (cluster size of a MIP: about 4 pixels)



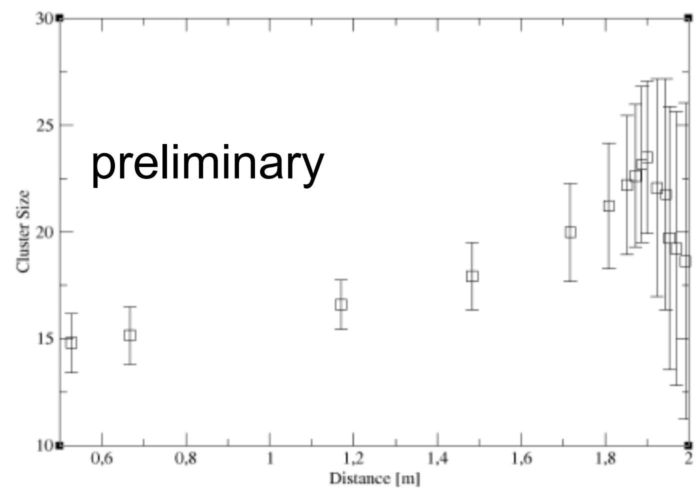
cluster size distribution

LET: 10 keV/μm 15 keV/μm



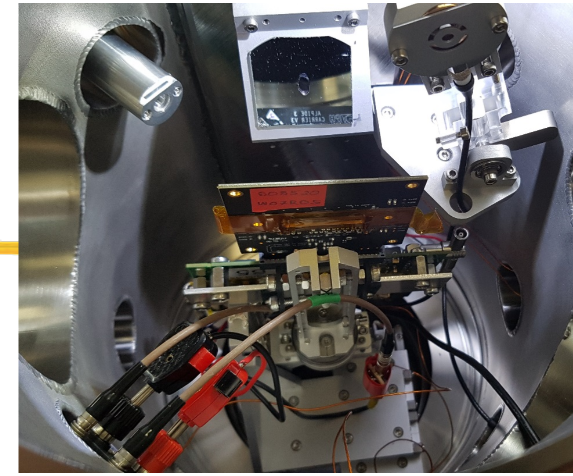


average cluster size vs range



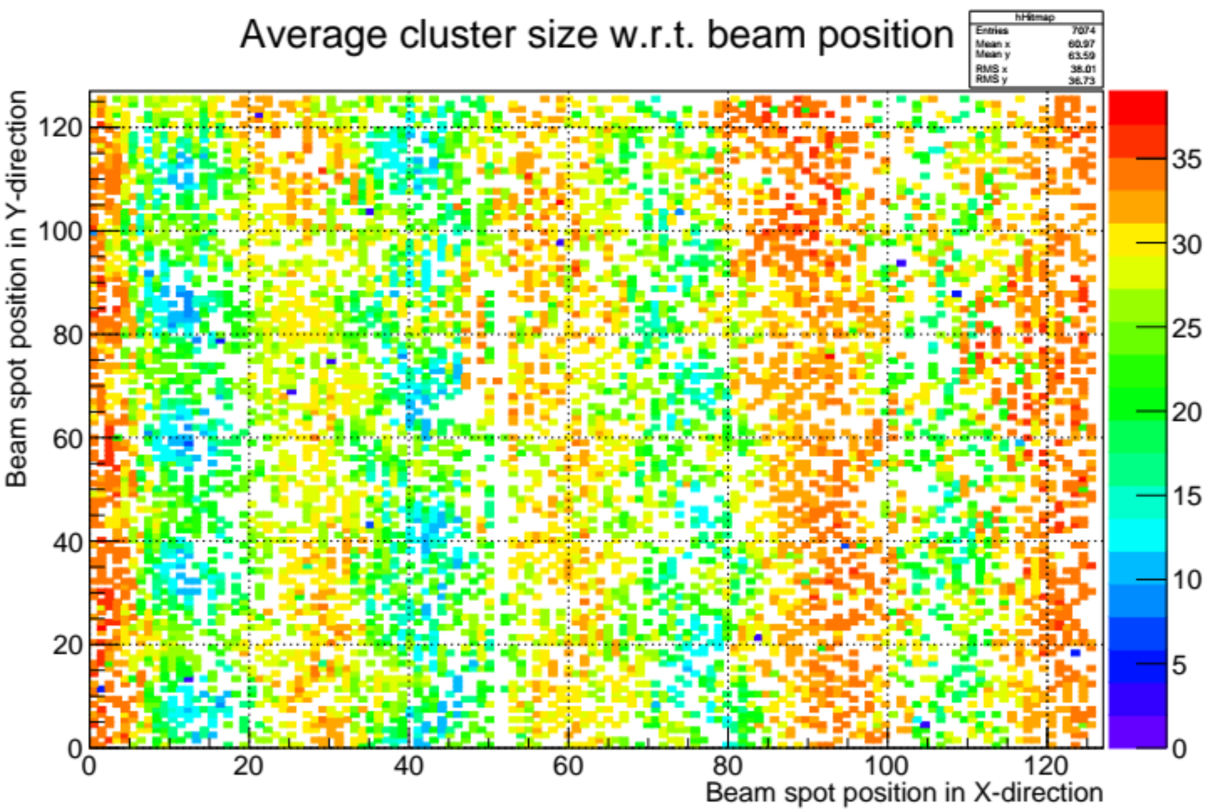
V. Eikeland, Master thesis, UiB, 2018

Characterisation of ALPIDE with proton and Helium beams



Uniformity of cluster size

- He microbeam @ ANSTO
  - Scan area: 4.5 x 4.5 pixels
  - Beam spot: 1 μm
  - Energy: 10 MeV



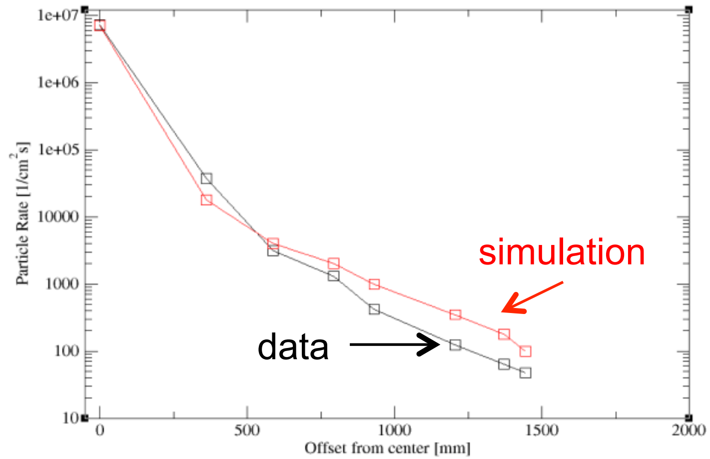
preliminary

S. Huiberts, Master thesis, UiB, 2018

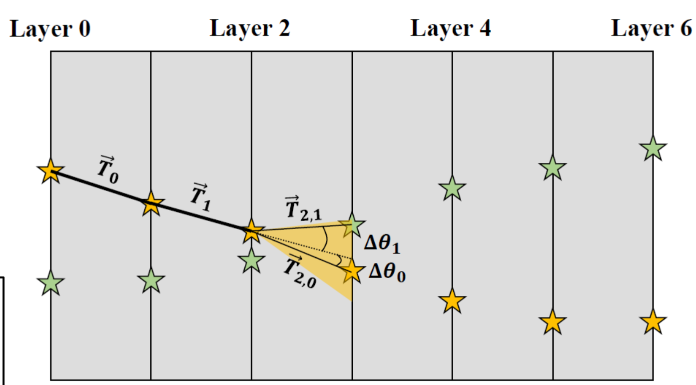
Rate Capability

- **How many hits can a single ALPIDE chip handle?**
  - **ALPIDE readout frame: 10 μs**
  - **Flux: 8×10^6 protons/cm²/s**
    -> 3.6×10^7 protons/chip/s
    -> protons per chip and frame: 360

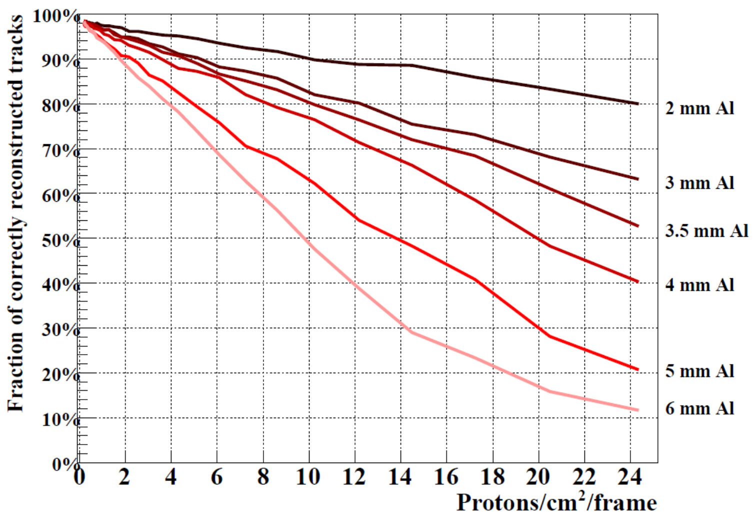
V. Eikeland, Master thesis, UiB, 2018



- **How many tracks can be reconstructed?**
  - **Simulation: 41 layers, 3.5 mm Al**
  - **10 protons/cm²/frame @ 80% efficiency**
    -> 10^6 protons/cm²/s



H. Pettersen, PhD thesis, UiB, 2018

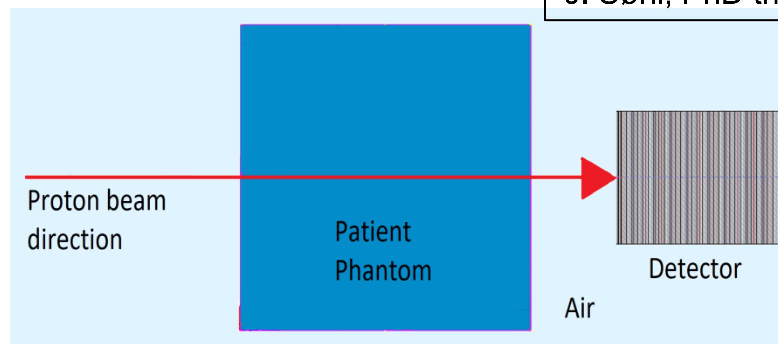


Radiation hardness - simulation

J. Sørli, PhD thesis, UiB

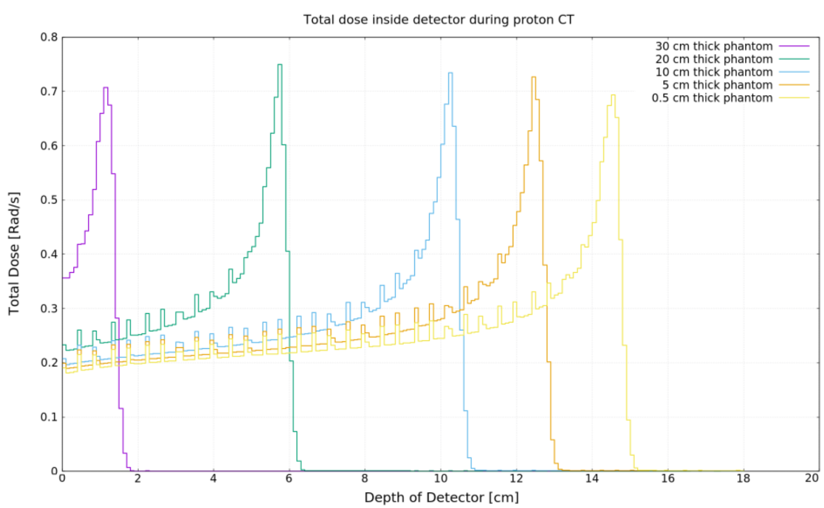
FLUKA simulation

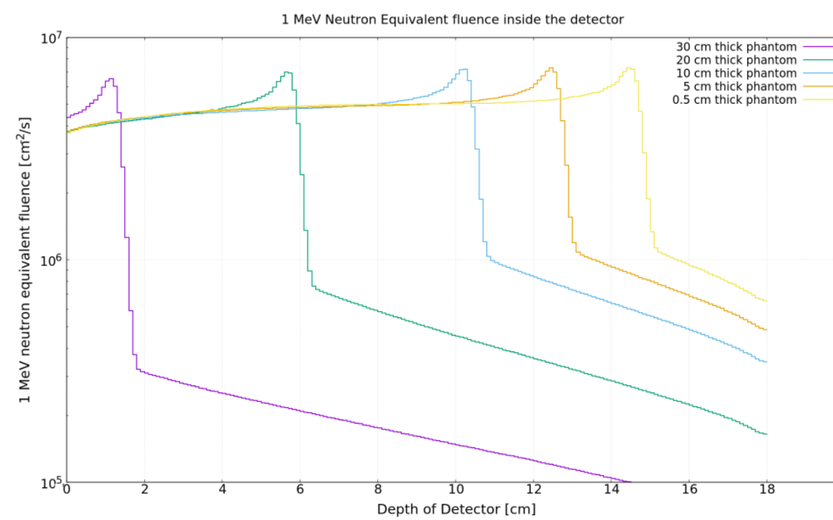
- **proton beam**
  - **energy: 230 MeV**
  - **scan field: 22 x 14 cm^2**
  - **intensity: 10^9 p/sec**



Total dose TID
< $8 \cdot 10^{-3}$ Gy

1 MeV neutron equivalent fluence
< 10^7 cm^{-2}

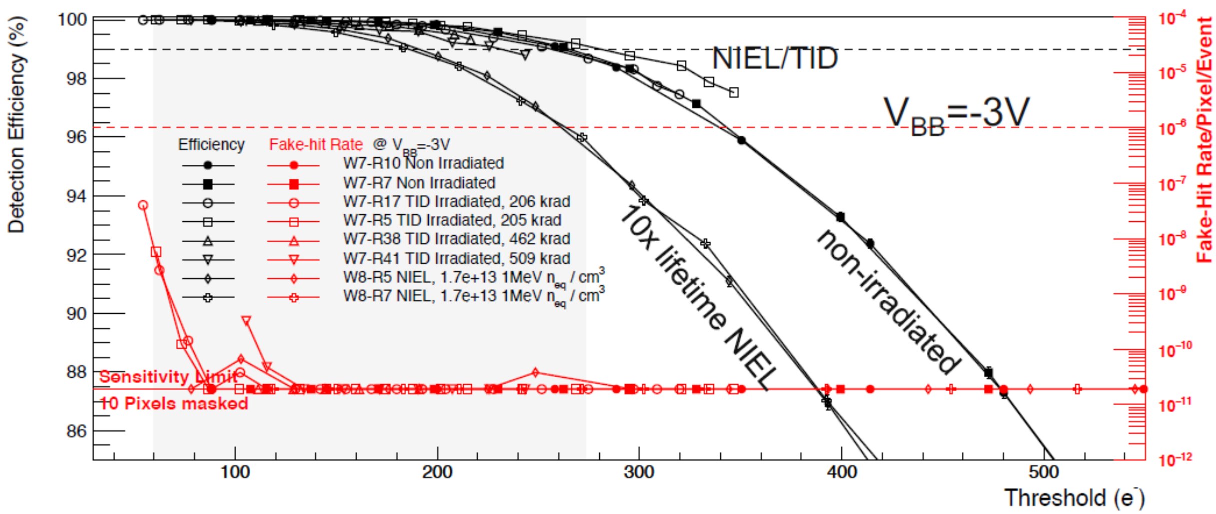




Radiation hardness - ALPIDE

ALPIDE irradiation tests

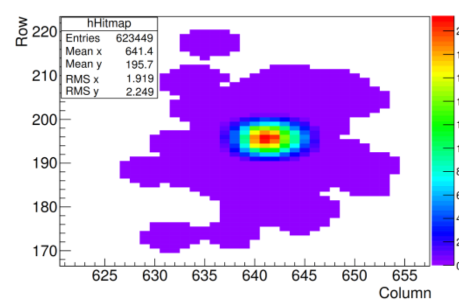
- excellent detector performance in terms detection efficiency and fake hit rate (for minimum ionizing particles) after a TID of 509 krad (5 kGy) and a NIEL irradiation of 1.7×10^{13} 1 MeV neq/cm^2



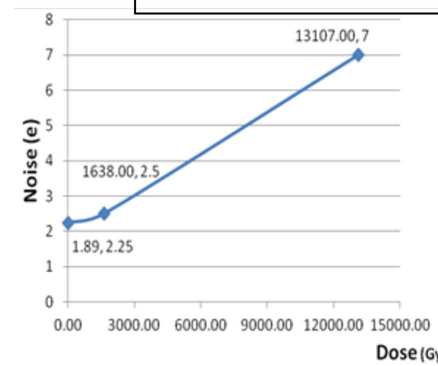
Operational margin overlaid in grey

ALICE | LHC Radiation Effects | April 23, 2018 | Hartmut HILLEMANNS, CERN

- Helium microbeam @ ANSTO
  - Energy: 10 MeV
  - Beam spot < 1 µm
  - ➢ Irradiated pixels are still operational (albeit with higher noise) after 13 kGy



S. Afroz, Master thesis, UiB, 2018

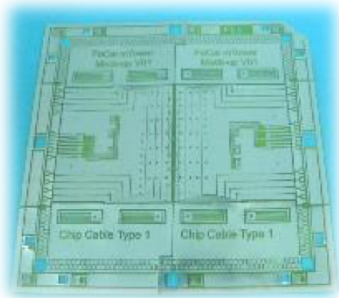


Mounting sensors on flexible cables

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

ALPIDE chip

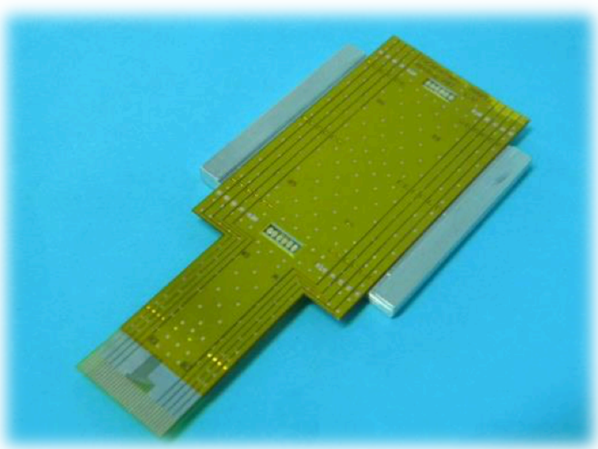
chip cable



design and production: LTU, Kharkiv, Ukraine

- **Intermediate prototype**

  chip cable with two ALPIDEs



- **Final system**

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