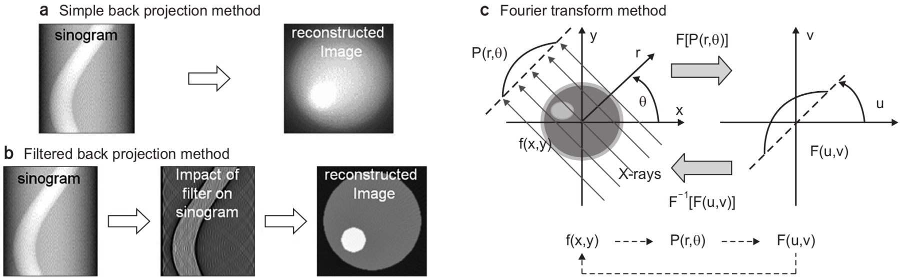
Bringing Proton Computed Tomography into the Treatment Room

Matthias Richter
for the Bergen pCT collaboration and the SIVERT research project

Computed Tomography (CT) scan

- Computed tomography (CT) is one of the most widely used medical imaging modalities
- Measure attenuation of X-ray radiation → 2D projection of attenuation properties
- First clinical CT image in 1971 (Hounsfield and Ambrose)
- 3D images are reconstructed from many 2D projections

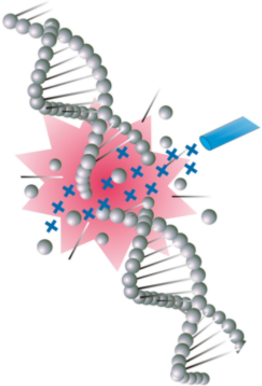


Jung 2021 doi: 10.14316/pmp.2021.32.1.1

Radiotherapy (RT)

- Dose of ionizing radiation is applied to tissue
- Cancer cells killed by damaging cellular DNA
- Conventional RT performed using high energetic x-ray beams

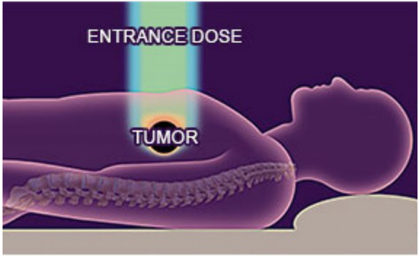
- Ideal radiotherapy:
  - 100% of the dose deposited within planned target volume (PVT)
  - 0% deposited outside PVT, especially to organs at risk



Radiotherapy with charged particles

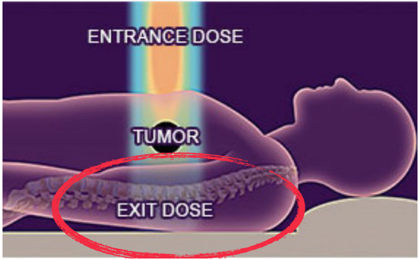
Charged particles undergo different interaction with medium than photons (x-ray)

Charged particle therapy



- low entrance dose
- maximum dose in target volume
- no exit dose

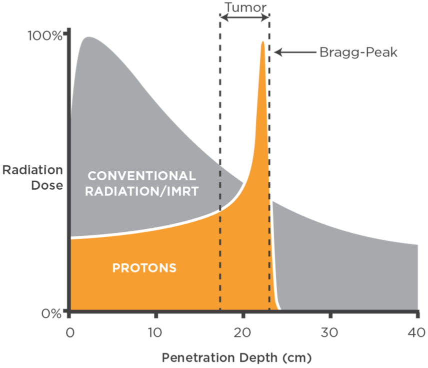
X-ray (photon) radiotherapy

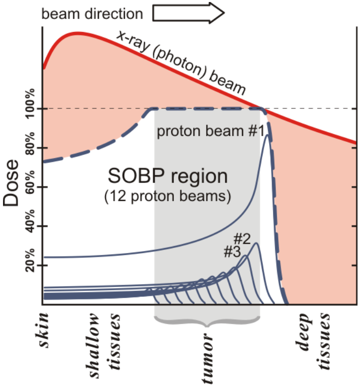


- maximum dose level at entrance
- reduced dose in target volume
- significant exit dose

Physics of charged particle therapy

- Energy deposition focused at a specific depth (particle range)
- range depends on initial protons energy and properties of traversed tissue
- The beam stops in the tumor, no exit dose

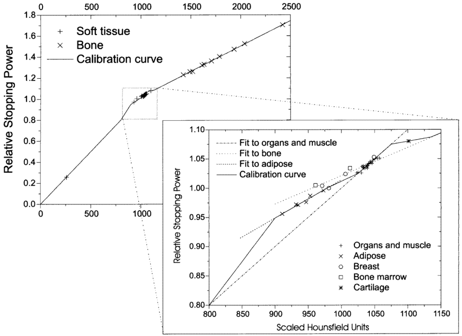




Larger volume can be irradiated by using spread-out proton beam (SOPB)

Treatment planning for proton therapy

- Challenge: the initial energy needs to be chosen such that target volume is irradiated
  - Stopping power of tissue in front of the tumor influences the range
  - Depending on electron density and ionization potential
  - Stopping power is described by Bethe-Bloch formula
  - Crucial input into the dose plan for the treatment
- Current clinical 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
- Range uncertainties need to be accounted for in advanced dose planning
  - single energy CT: up to 7.4% uncertainty
  - Dual energy CT: up to 1.7% uncertainty
  - Proton CT: up to 0.3% uncertainty



B Schaffner and E Pedroni 1998 Phys. Med. Biol. 43 1579

Proton Computed Tomography

- protons with higher initial energy will pass the object
- Measure deviation and attenuation of energy for protons passing through volume to be imaged
  - position, trajectory
  - energy/range
- direct measurement of stopping power
- first setups consist of position detectors on both sides and a residual energy detector

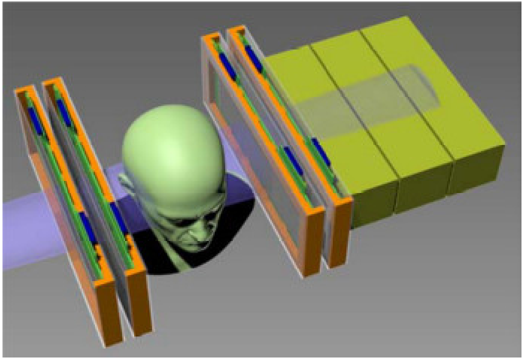
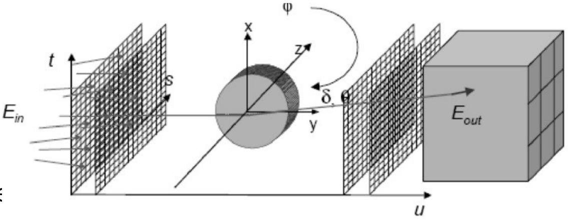


Illustration: Sandrozinski, Nucl. Instruments and Methods in Physics Research A 732 (2013) 34-39

First ideas of Proton CT are from the 1960s alongside conventional CT scan
But: Proton CT is a challenge. Still no clinical system.

Proton CT - concept

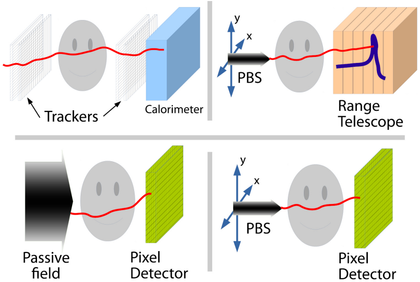
- measurement of entrance and exit position of protons
- reconstruction of trajectories in 3D and range in external absorber
- trajectory, path-length and range depe

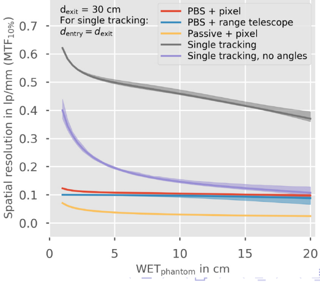


  - nuclear interactions (inelastic collisions)
  - multiple Coulomb scattering (elastic collisions)
  - energy loss dE/dx (inelastic collisions with atomic electrons)
- Multiple scattering (MS) theory and Bethe-Bloch formula of average energy loss in turn depend on electron density in the target (and ionization potentials)
- adjusted reconstruction algorithms: most-likely path method
  $\Rightarrow$ 3D map of stopping power

Proton CT setups

- pCT imaging requires energy and position of protons before and after the phantom/patient
- different setups have been studied
- beam source is dependent on the capabilities of the treatment machine
- it has been shown, that single-sided imaging setups with Pencil Beam Scanning (PBS) can provide comparable spatial resolution



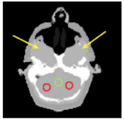


Krah, N., et.al., (2018). A comprehensive theoretical comparison of proton imaging set-ups in terms of spatial resolution, Physics in Medicine & Biology 63 (13): 135013.

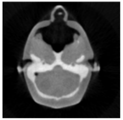
Proton CT images

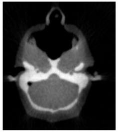
- Traversing proton beam creates three different 2D maps
  $\Rightarrow$ three imaging modalities

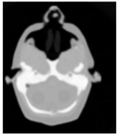
- Transmission map
  - records loss of protons due to nuclear reactions
- Scattering map
  - records scattering of protons off Coulomb potential
- Energy loss map
  - records energy loss of protons (Bethe-Bloch)



Phantom

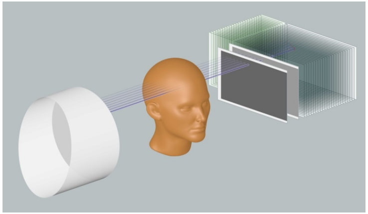






Cecile Bopp. PhD thesis, Strasbourg, 2013

Requirements for a clinical pCT prototype



Operate with clinical beam settings

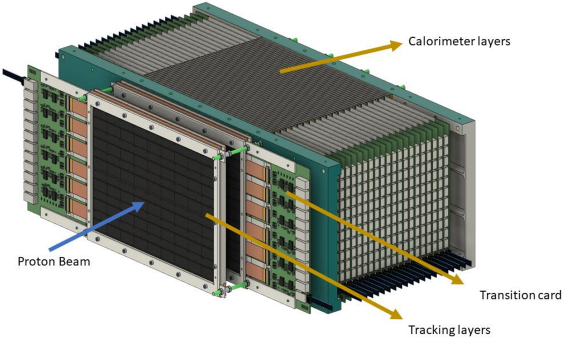
- Pencil beam scanning mode
  - Beam spot size, scanning speed, intensity
- Scanning time
  - Seconds . . . minutes
- Detector
  - Efficient simultaneous tracking of large particle multiplicities
  - Large area (30 x 30 cm2)
  - Radiation hardness
  - High position resolution ($\sim 10\mu$m)
  - Tracking detector (first 2-3 layers): very low mass, thin sensors ($\sim 100\mu$m)
  - Back detector: range resolution $<1\%$ of path-length
- System
  - Compact
  - No gas, no HV
  - Simple air/water cooling

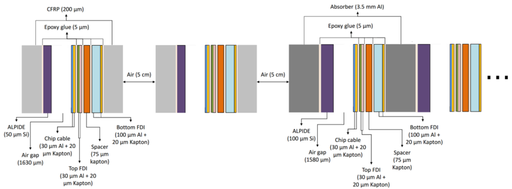
Bergen Proton CT

Introducing novel residual energy detector:
Digital Tracking Calorimeter (DTC)

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

J Alme, et al. A High-Granularity Digital Tracking Calorimeter Optimized for Proton CT, Frontiers in Physics 8, 2020, doi: 10.3389/fphy.2020.568243

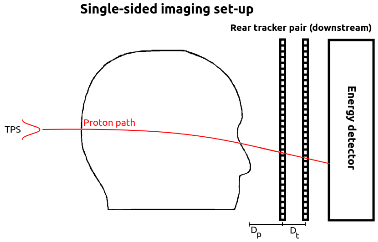




Bergen Proton CT - a single sided setup

Most Likely Path estimate

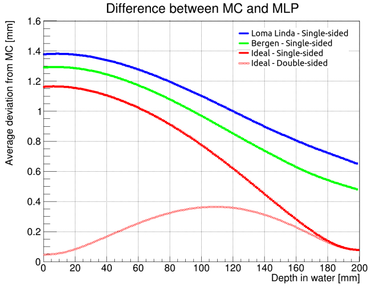
- Entrance – beam optics
- Exit – pCT front trackers



Feasibility study for single sided setup

Difference between MC truth and estimated proton path for beam spot size 7 mm

$\Rightarrow$ deviations $\leq$ 1.2 mm

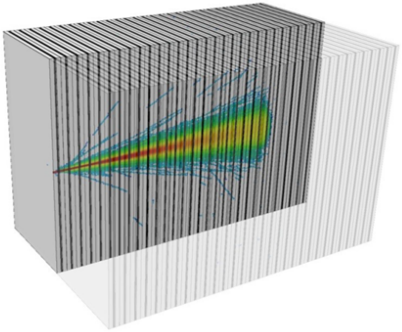


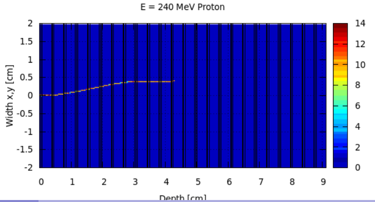
JR Sølie et al 2020 Phys. Med. Biol. 65 135012

Digital Tracking Calorimeter (DTC)

A novel, high-granularity sampling calorimeter

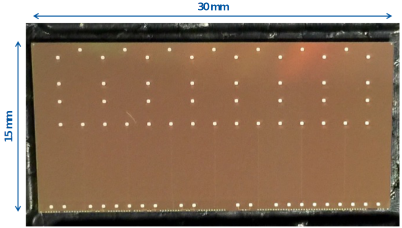
- Digital: each layer has a sensitive pixel area recording yes/no hit data for each pixel
- Tracking of individual protons
- Calorimeter: range and energy loss measurement
- Sensitive pixel matrix 9216 x 6144
- Protons are fully stopped in the calorimeter
- Technical design
  - Planes of CMOS sensors – Monolithic Active Pixel Sensors (MAPS)
  - digital readout

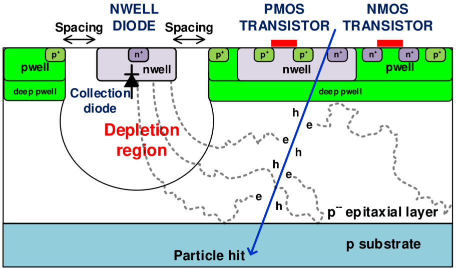




Sensor layers – Monolithic Active Pixel Sensors (MAPS)

- ALPIDE chip
  - sensor for the upgrade of the inner tracking system of the ALICE experiment at CERN
  - chip size 3x1.5 cm^2
  - pixel size 30 μm x 27 μm
  - integration time 4 μs
  - on-chip data reduction
    priority encoding per double column

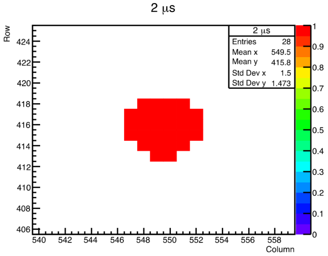


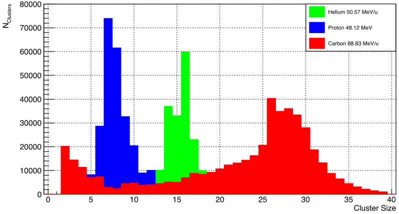


Kim D, et al. J Inst Met (2016) 11(02):C02042. doi:10.1088/1748-0221/11/02/c02042

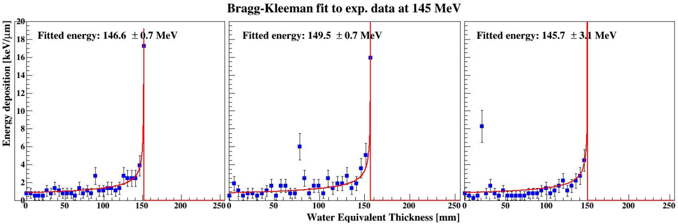
Energy and range measurement

- Operating ALPIDE in *charge-collection-by-diffusion* mode
- Cluster size is a measure of energy loss
- Bragg-Kleeman fit allows precise energy determination





doi: 10.3389/fphy.2020.568243

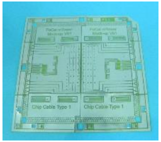


Chip mounting

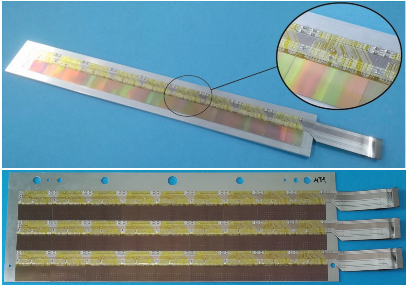
- ALPIDE mounted on thin flex cables (aluminum-polymide dielectrics: 30 μm Al, 20 μm plastic)

ALPIDE

Chip cable



Design and production: LTU, Kharkiv, Ukraine

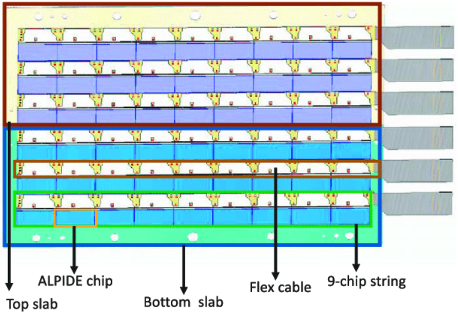


- 9 ALPIDE chips mounted on flex cable
  $\rightarrow$ *String*
- 3 strings with 9 chips mounted on aluminum carrier
  $\rightarrow$ *Slab*

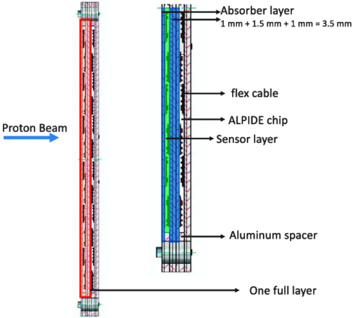
Layer mounting

- Two slabs (top and bottom) form a half-layer
- Two half-layers are assembled to a full layer, the chips facing each other

half-layer



layer side view

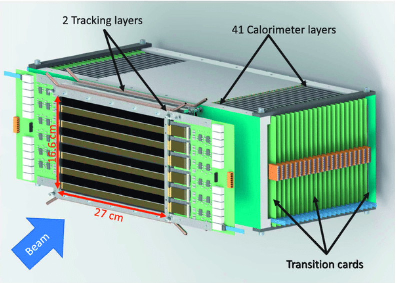


108 chips per layer $\Rightarrow$ 9216 x 6144 pixels $\Rightarrow \sim 56 * 10^6$ pixels

Ultra-thin tracking layers

Tracking layers require special design to reduce material budget to a minimum

- thinned ALPIDEs 50 μm
- mounted on thin flex
- glued to a large sandwiched carbon fiber sheet (pyrolitic graphite paper + carbon fleece + epoxy resin)
- Sandwiched carbon fiber sheet, fabricated at St Petersburg State University

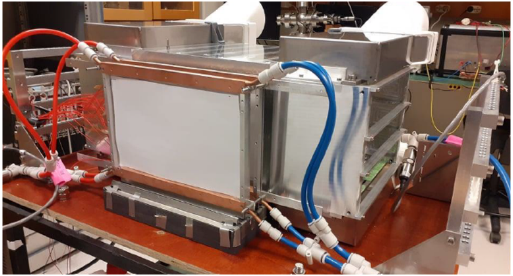


Prototype tracking layers designed and fabricated by Utrecht University, tested at University of Bergen

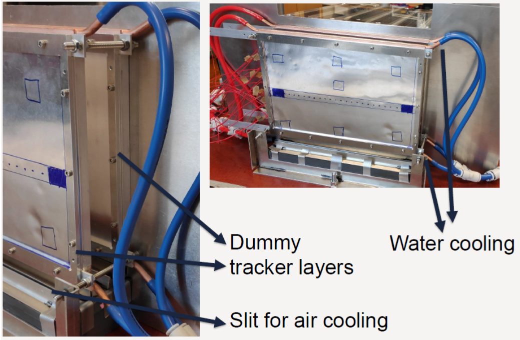
Assembly at IFT - University of Bergen

- All prototype work finished
- We should have entered the production phase ...

Setup in the lab



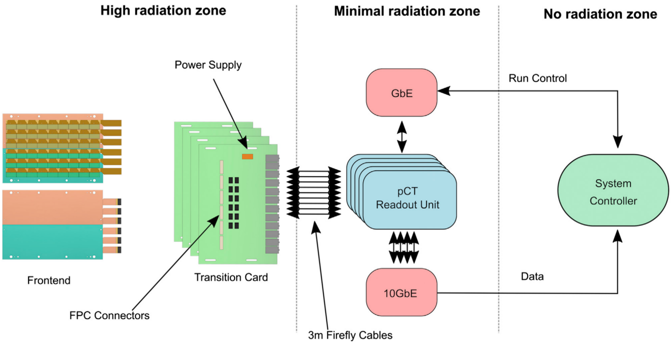
mechanical integration and cooling



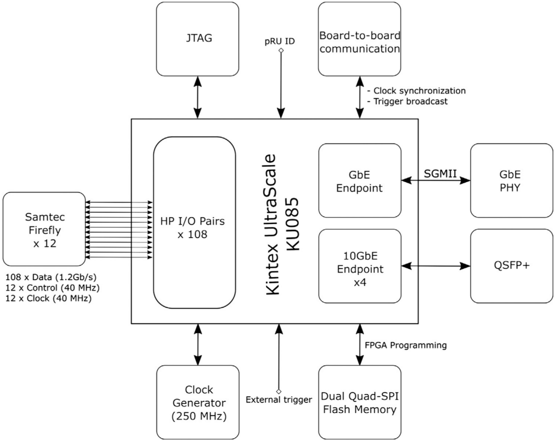
Waiting to get the chips mounted on the sensor layers (LTU Kharkiv)

Bergen proton CT Readout

- The setup is exposed to high level of radiation, beam intensity of $10^7\ s^{-1}$
- Different parts of the readout are placed in distinct radiation level zones to avoid/reduce damage from radiation
- FPGA based design of the pCT Readout Unit (pRU)
- trigger-less readout architecture readout frame duration 5-10 μs



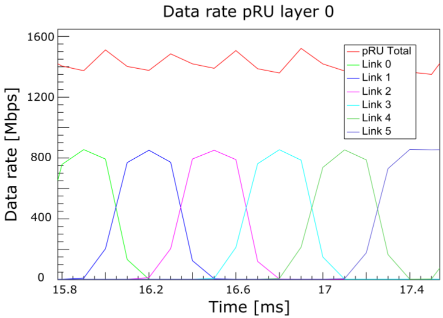
pCT Readout Unit (pRU)

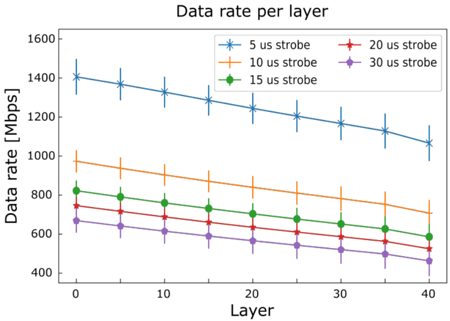


- Based on Xilinx Kintex Ultrascale FPGA
- Tested with the Xilinx VCU118 Evaluation Kit
- 108 data links to Frontend
- up to four separate 10 Gbit Ethernet links for data offload
- custom protocol is implemented to obtain a safe high-speed data transmission over user datagram protocol (UDP)
- Gigabit Ethernet for run control over IPBus protocol

pCT readout data rates

- proton beam intensity of at least 10^7 s^{-1}
- minimal integration time 5 μs
- data rates studied in System C simulations
- 1.4 Gbit/s maximum rate reached for first tracking layer





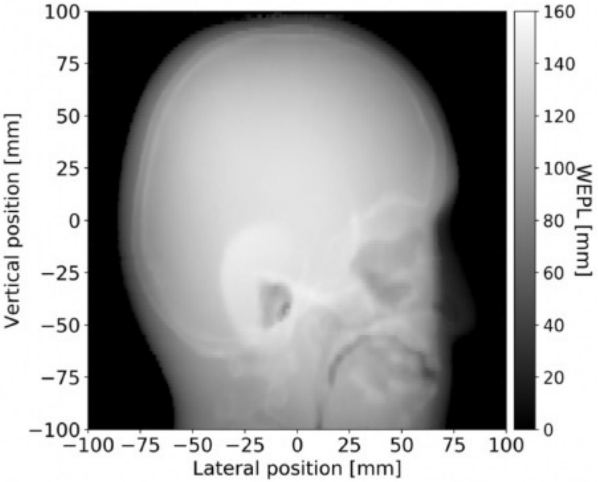
Grøttvik O, TWEPP 2019, doi: 10.22323/1.370.0090

Radiographic image reconstruction - pRAD

Example radiograph of head phantom (simulated)

- proton beam 230 MeV
- $\sim 10^7$ protons per projection
- 15 μS dose deposition

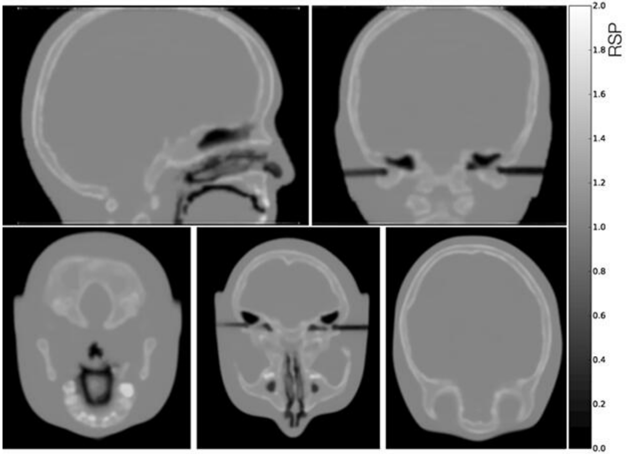
$\Rightarrow$ Many radiographs from different directions are the basis for 3D image reconstruction



Simulation of 3D head phantom reconstruction

- proton beam 230 MeV
- 360 projections,
- 3.5 x 10^6 protons per projection
- 7.9 x 10^8 protons for full 3D reconstruction

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



The treatment room ...

Varian Medical Systems, Inc. is providing the treatment facility for two new proton therapy centers in Norway

HELSE BERGEN
Haukeland universitetssjukehus

Oslo universitetssykehus

The treatment room ...

Varian Medical Systems, Inc. is providing the treatment facility for two new proton therapy centers in Norway

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Our goal is to characterize and demonstrate our detector at a treatment facility

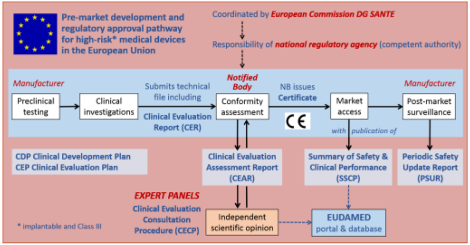
Haukeland Proton Therapy Center

HELSE BERGEN
Haukeland universitetssjukehus

- New proton therapy center currently under construction
- Planned to be operational in 2024
- Dedicated room for research will allow to test the pCT Digital Tracking Calorimeter

Medical regulations

Bergen pCT fulfills requirements of a clinical prototype in order to be tested with the proton beam facility in the treatment room, ... but there is more

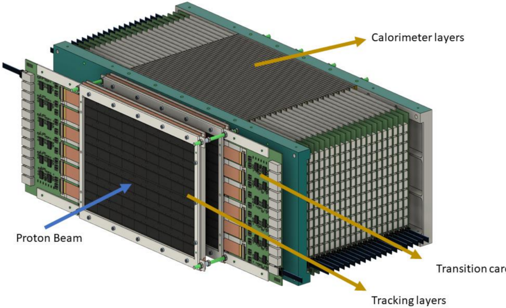


- Classification of medical devices and respective regulations
- Classification of software as a medical device
- No regulations yet how ML or AI being used in the software has to be classified

⇒ to continue with that we will need experienced partners

Summary

- Radiotherapy using charged particles is an established treatment method for cancer
- Increasing number of therapy centers around the world
- Challenge remains to obtain and verify RSP of tissue in front of target volume
- Still a long way to go to use proton CT in clinical diagnosis and treatment planning
- Bergen pCT collaboration has accomplished all R&D work to build clinical prototype of a high-granularity Digital Tracking Calorimeter for pCT
- Production of prototype has started
- New Proton Therapy Center at Haukeland University Hospital will provide research facility to test prototype in a clinical environment



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