Technology Transfer
HEP Detectors in Radiotherapy

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AG Kröninger

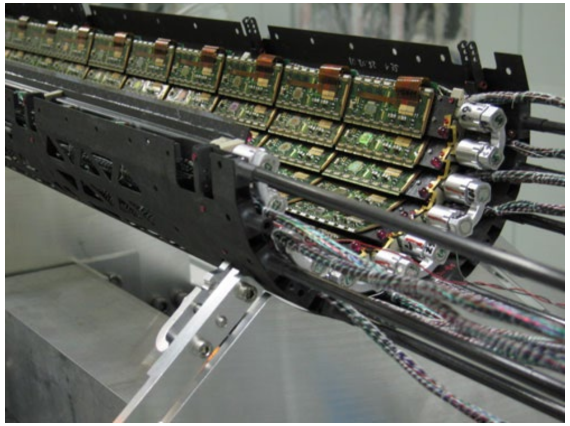
A short introduction

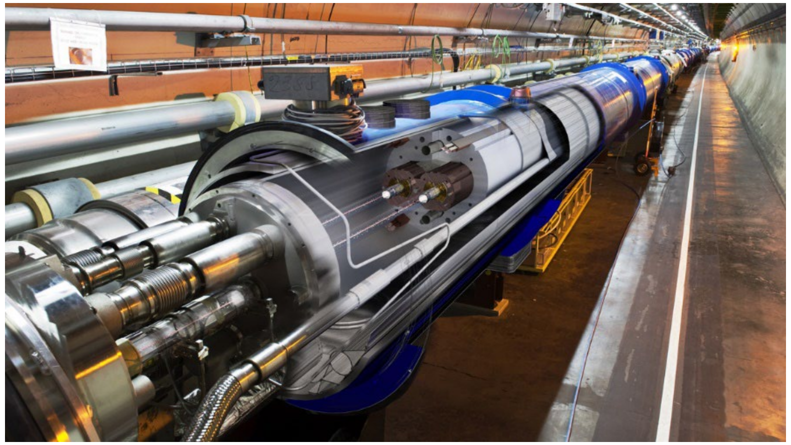
High energy physicist by training, worked mostly on silicon pixel detectors for the ATLAS experiment at the LHC

- Pixel, IBL, and ITk Upgrades

Joined TU Dortmund University in 2018

- Still ATLAS: Pixel and Strip Detectors for HL-LHC Upgrade
- Move to Medical Physics
  → Proton Radiotherapy in collaboration with WPE Essen and OncoRay Dresden





wpe

OncoRay ZIK Radiation Research in Oncology

Universitätsmedizin Essen Westdeutsches Protonentherapiezentrum (WPE)

Universitäts Protonen Therapie Dresden Klinik für Strahlentherapie OncoRay

Content

Radiotherapy

Radiotherapy

One of three types of therapy for cancers: Surgery, Chemotherapy, Radiotherapy
Goal: Deposit enough dose in the tumour tissue to damage cells irreparably

→ accumulate enough DNA damage, so it can't be repaired
➔ cell kills itself in a certain way (no toxic residue)

High-LET radiation is more effective than low-LET radiation

LET: Linear energy transfer
→ Equivalent to stopping power if only secondaries up to a certain range are taken into account
➔ $LET_{\infty} = dE/dx$ = Stopping Power

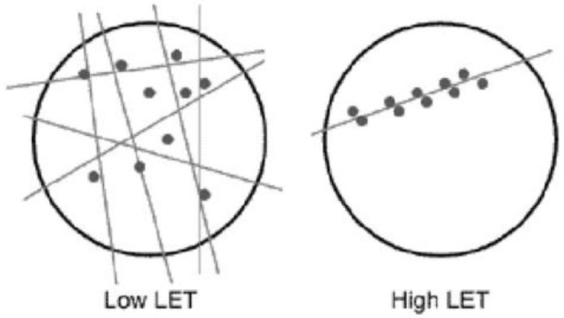


Abbildung: Verteilung der Ionisierung in gleichen Volumina durch niedrige und hohe LET-Strahlung [1]

Strahlungsart	LET keV/µm
Photonen	< 3,5
Elektronen	< 3,5
Protonen	5 - 100 (f(E))
α -Teilchen	100 - 200 (f(E))
Neutronen	50 - 250 (f(E))

Abbildung: LET verschiedener Strahlungsarten

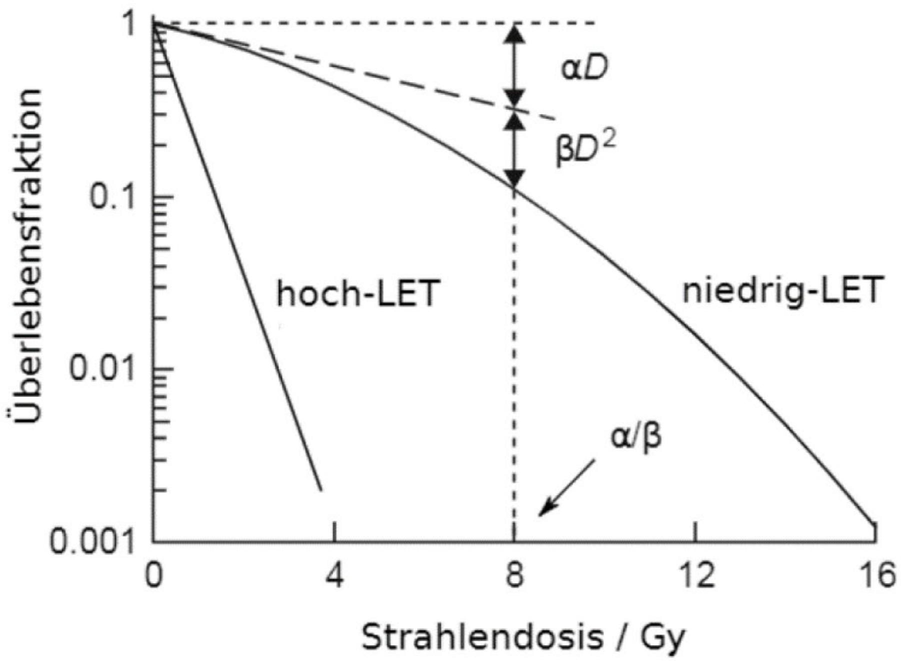


Abbildung: Überleben der Zellen wird über Linear-Quadratisches Modell beschrieben

Radiotherapy

Goal: Deposit enough dose in the tumour tissue to damage cells irreparably

Dose: (Ionizing) Energy dose $D = \frac{\mathrm{d}E_{abs}}{\mathrm{d}m} = \cdots = \Phi \cdot \frac{1}{\rho}\frac{\mathrm{d}E}{\mathrm{d}x} \Rightarrow [D] = \frac{1\,\mathrm{J}}{1\,\mathrm{kg}} =: 1\,\mathrm{Gy}$

Proton Fluence (Φ)

Stopping Power <-> Proton Energy ($\frac{1}{\rho}\frac{\mathrm{d}E}{\mathrm{d}x}$)

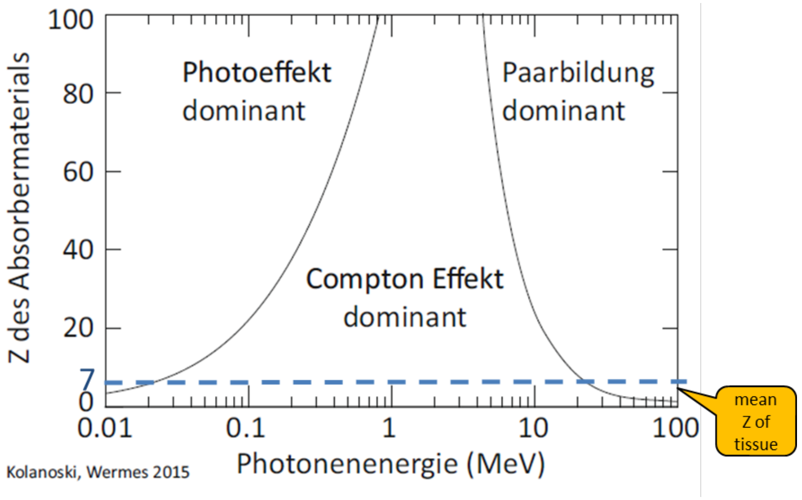
Typical dose values:
About 50-70 Gy deposited in the target volume, spread out over few (~2) or many (~30) sessions: fractions

For comparison:
- 50% lethal whole-body dose is 4 Gy
- Adult (80 kg) radiates about 100 W in body heat → energy deposition of 4 Gy ≙ 3 sec of body heat

Protons vs Photons

(External) radiotherapy uses ionizing radiation to deposit dose in tissue

1. Photons up to about 18MV acceleration of the electron linac
   → (relatively) cheap, available in many hospitals
2. Ions, mostly protons up to 230 MeV (isochronous cyclotrons, less often synchrotrons)
   → very expensive, available in 5 centres in Germany
   (plus one centre for neutron therapy)

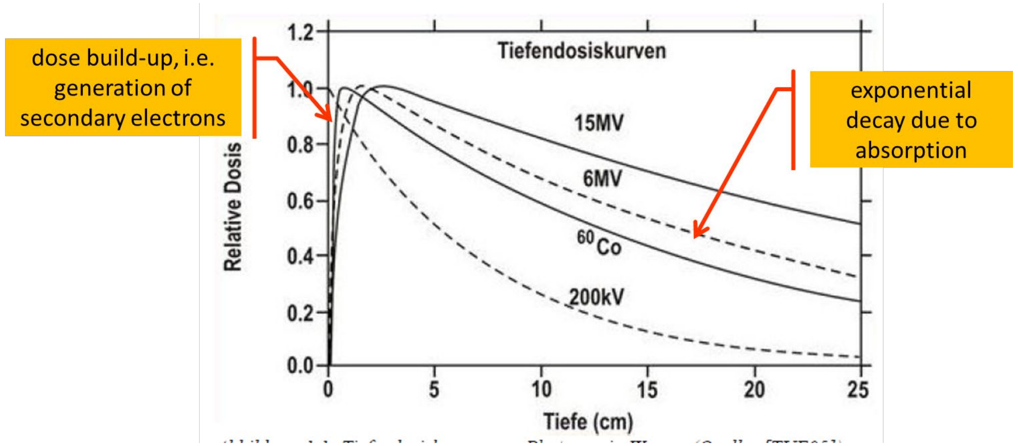


Photons are “indirectly ionizing”:

Mostly Compton effect in clinically relevant energy range

→ Radiation damage mostly from secondary electrons

→ depth dose curve



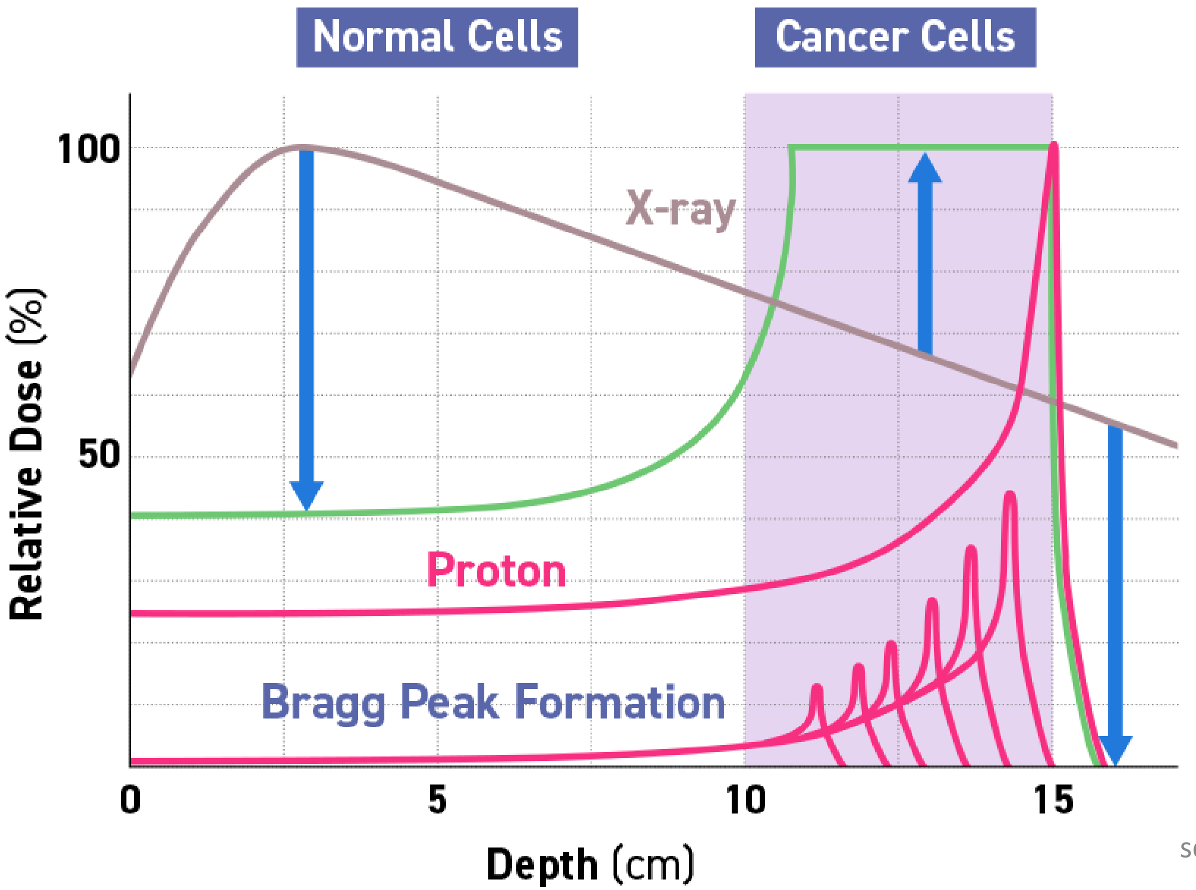
1. Need large dose deposition at shallow depth to reach target dose at tumour depth
2. Photon range unlimited → dose deposition downstream of tumour

➔ Significant damage to healthy tissue

Radiotherapy using Protons

Protons are (directly) ionizing:

Vary proton energy to irradiate the full depth of the tumour → spread-out Bragg-peak SOBP



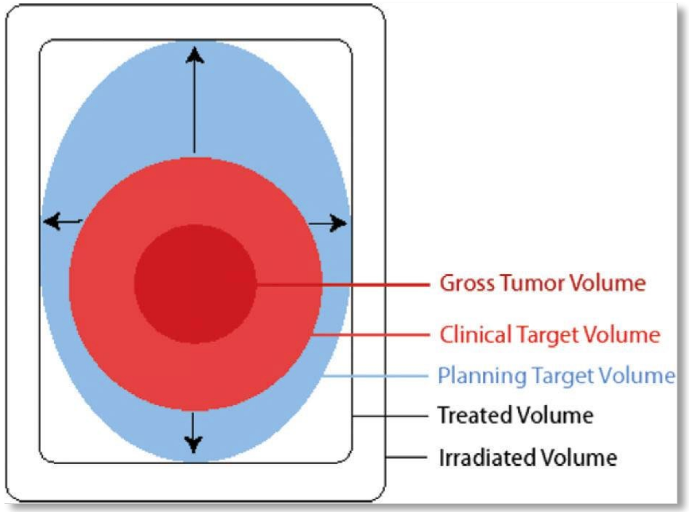
Problem: Proton range not as well-known as one would hope

- range straggling (Landau fluctuations)
- inelastic nuclear scattering → secondary particles
- tissue composition (water-equivalent thickness WET) uncertain (x-ray absorption → stopping power)

➔ range uncertainty 3.5% + 1mm

→ extent target volume

→ damage to healthy tissue



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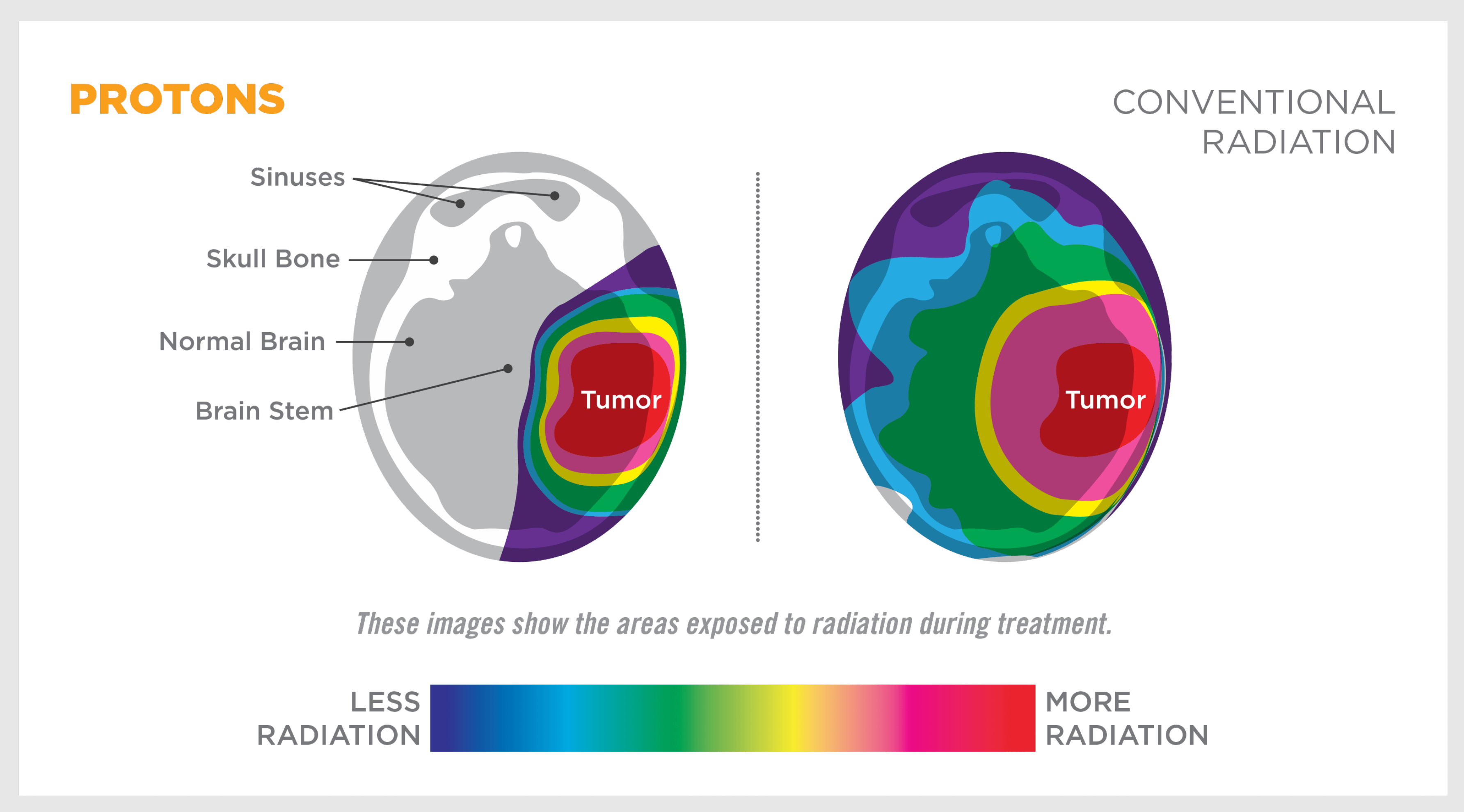
Radiotherapy using Protons



Source: Provision CARES Proton Therapy Center

The treatment process→ Very much simplified!

1. Take x-ray CT of the affected part of the body → Oncologist identifies tumour volume (GTV) and organs-at-risk (OAR), prescribes target dose and fractionation (number of treatments and dose per treatment)
2. Medical physicist takes into account uncertainties in dose delivery, enlarges target volume accordingly (PTV)
3. Treatment Planning System (TPS) optimizes beam directions, energy, and intensity

4. Patient positioning in treatment room: Movement restraints, x-ray for position verification
5. Treatment, i.e. shoot a high intensity proton beam at a person…

Repeat steps 4 and 5 for the number of fractions N with dose per fraction D (typically one fraction per day)

Mostly two cases:

- Few fractions at high dose $N \approx 2,\ D \approx 25\,\mathrm{Gy}$
- Many fractions at low dose $N \approx 30,\ D \approx 2\,\mathrm{Gy}$

Disclaimer: Just orders of magnitude

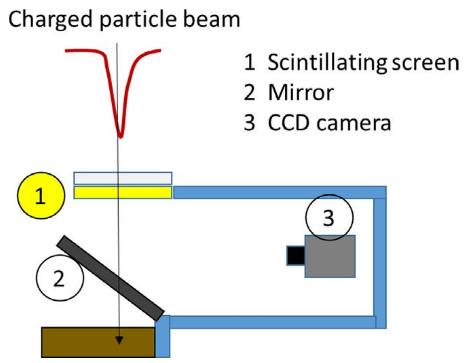
1. Beam Quality (not today)
2. Repeatability: Deposit the same dose in the same volume for each fraction
   → Is the beam the same as last time?
   → Is the target in the same place wrt. accelerator?

Daily Quality Assurance

Commercial solutions

Transversal dose profiles

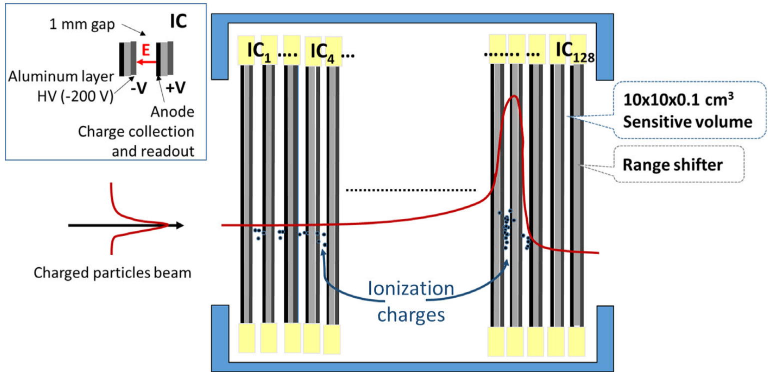
- Radiochromic films: non-linearity with dose/LET, time consuming analysis
- Arrays of ionization chambers: fast but low spatial resolution (5-8 mm pitch)
- Scintillating screens: fast but non-linearity with dose/LET
- Solid-stat detectors: see next slide



Medical Physics, 45 (11), November 2018

Longitudinal dose profiles

- Ionization Chamber: slow but high depth resolution (moved through water phantom)
- Films: positioned parallel to beam axis, measure penetration depth
- 2D scintillator with wedge phantom: range → position on screen
- Multi Layer Ionization Chamber: one-shot consistency check, calibration needed for conversion to depth in water

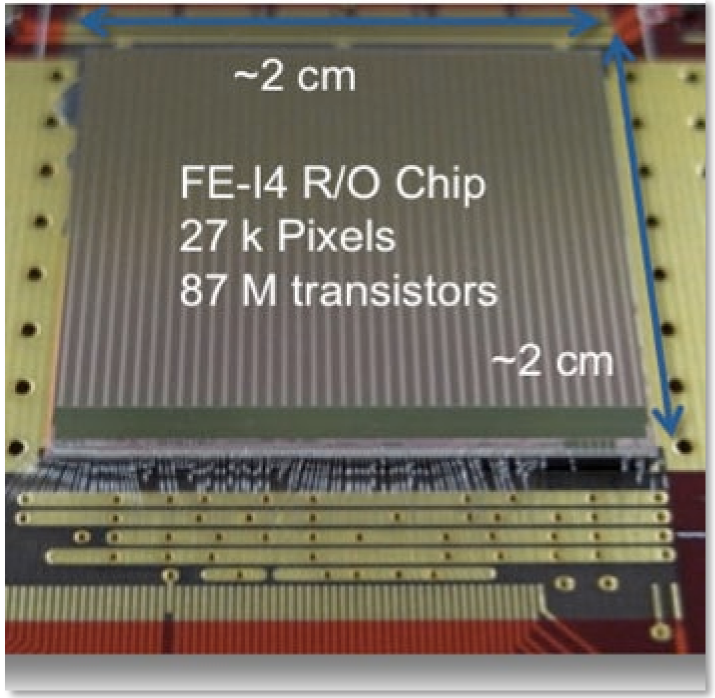


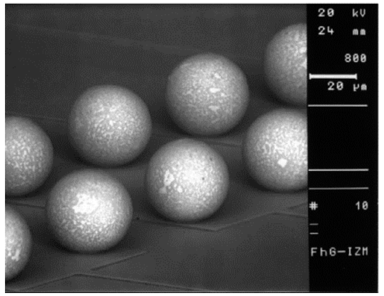
So far, DailyQA mostly uses multiple detector technologies
→ Setup takes time, reduces patient throughput → €, $, £

IBL detectors: Tools for medical physics

These are LHC tracking detectors, which means

- + hit efficiency for single charged particles >98.5% before irradiation
- + pixel size 50x250 µm² → spatial resolution ≈ 14µm
- + 336x80 pixels → active area 16.8 x 20.0 mm² per chip
- + radiation hard: 250 Mrad & $5x10^{15}$ $n_{eq}cm^{-2}$
- + designed for minimum inactive area around edge





- - clock frequency 40 MHz
  → timing resolution 25 ns
- - avg. hit rate with <1% data loss: 400 MHz/cm² ≡ 60kHz/pixel
- - max sustained trigger rate: 200kHz
- - resolution of charge measurement (ToT): 4 bit
- - max charge ~100 ke

They are also hybrid detectors

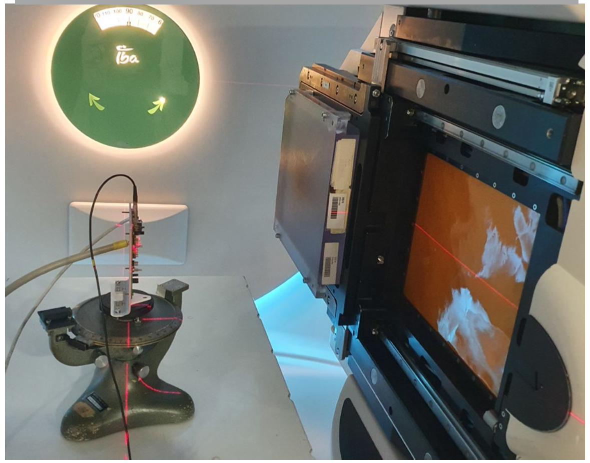
+ can connect to different sensors
  - mostly planar Si
  - looking into diamond

- extra cost and material

Biggest advantage: Easily available still

Daily Quality Assurance

Measurements and photos curtesy of I. Schilling



Monitoring quantities we can address

1. Beam spot position, size, shape → Spatial resolution
2. Dose calibration (i.e. proton flux) → High count rate due to large number of channels
3. Proton range (i.e. proton energy) → Energy resolution of the detectors

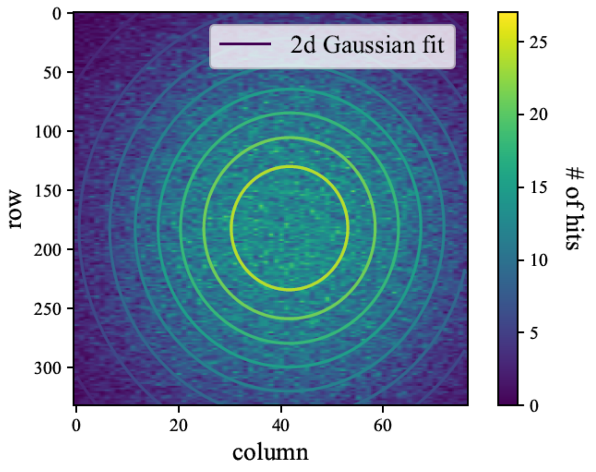


Figure 1. Hitmap of a single pencil beam spot. The intensity profile is fitted with a two-dimensional Gaussian function.

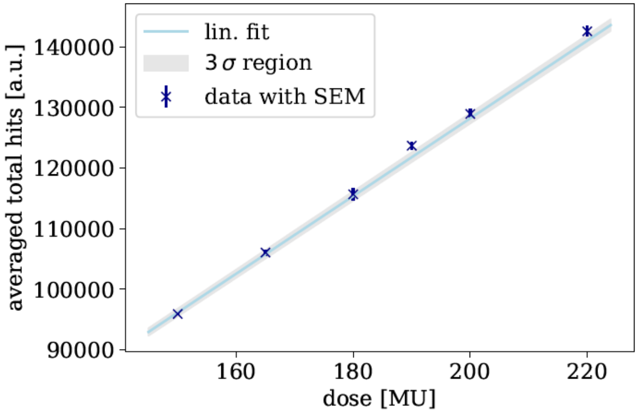
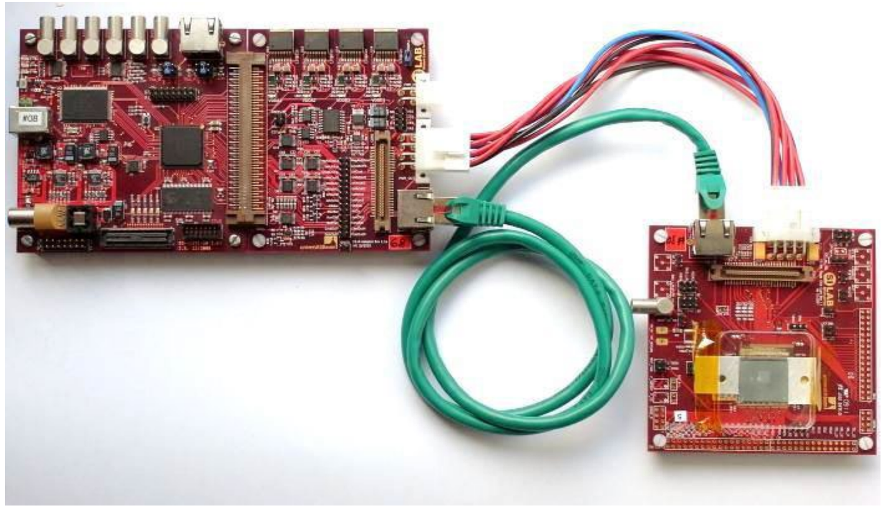


Figure 2. Total hits summed across the sensor as a function of the irradiated dose given in facility specified Monitor Units.

arXiv:2204.02060



Proton Energy/Range

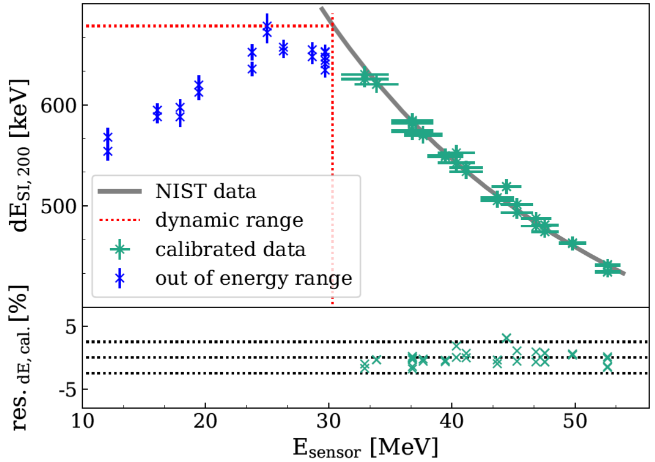
Requirement

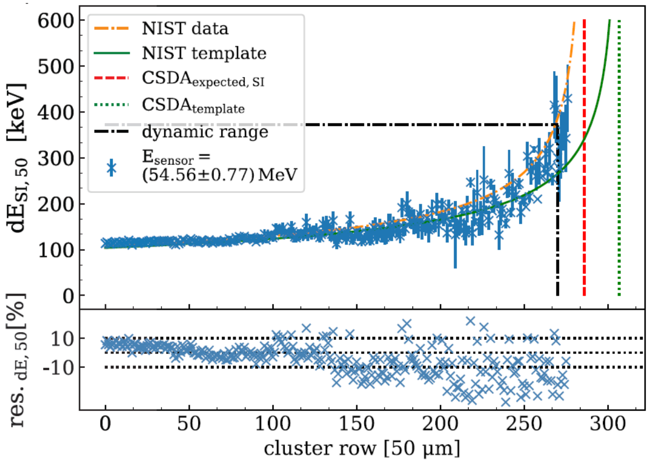
Measure proton range in water with uncertainty < 1mm

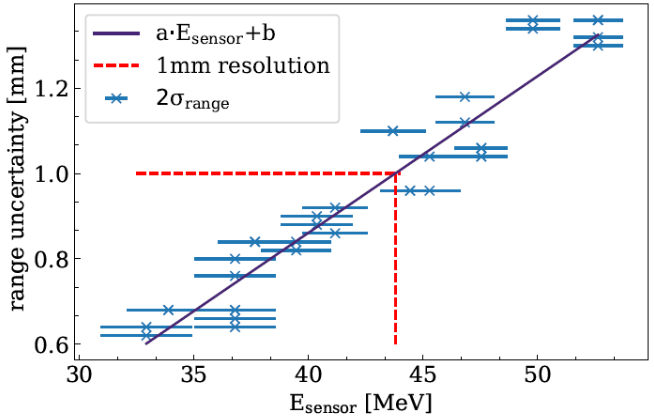
Approach: Energy deposition in silicon sensor ➔ proton energy

- 4 bit ToT information for individual protons
- due to huge statistics we can measure dE with few keV uncertainty

➔ For proton energy below about 4 MeV, we can measure the range well enough for Daily QA purposes







Also looking into track length in silicon

- multiple Coulomb scattering
- sensor thickness/bow
- tuning

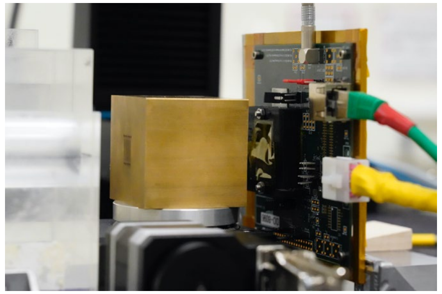
➔no improvement

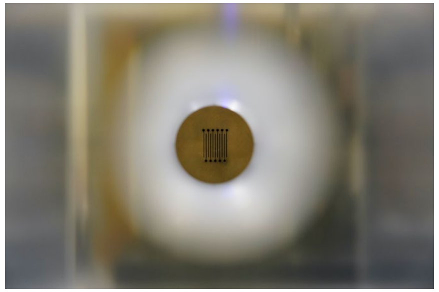
Publication in progress

Nano dosimetry

Proton Minibeams

Pre-clinical studies have shown improved healthy tissue sparing using very narrow photon beams
→ Figure-of-merit: Peak-to-valley dose ratio (PVDR)
→ Microbeam Radiotherapy (MRT)



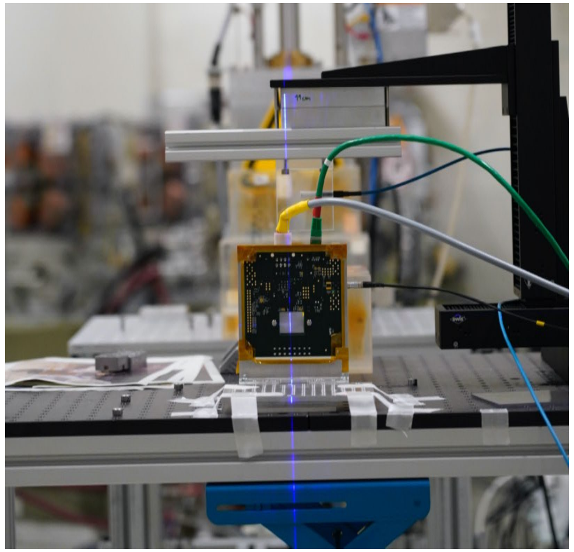


Does that work with protons as well? → Proton Minibeams
→ Cell experiments ongoing at OncoRay

Slit collimator to create 200µm - 1mm wide beams
1. Alignment collimator to beam axis → EBT3 film
2. Determine PVDR → microdiamond (type 60019, PTW, Freiburg, Germany)

→ both measurements slow and labour-intensive

Medical Physics, Volume: 47, Issue: 3, Pages: 1305-1316

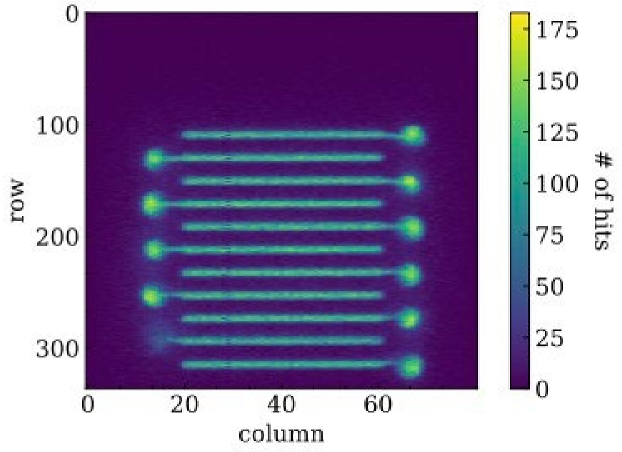


Proton Minibeams

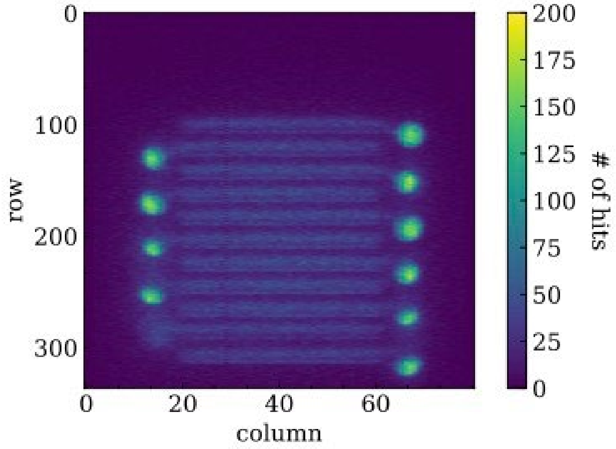
Alignment:
- about 10s per measurement
- rotation stage

→ working on automation of alignment

179.2°



178.9°

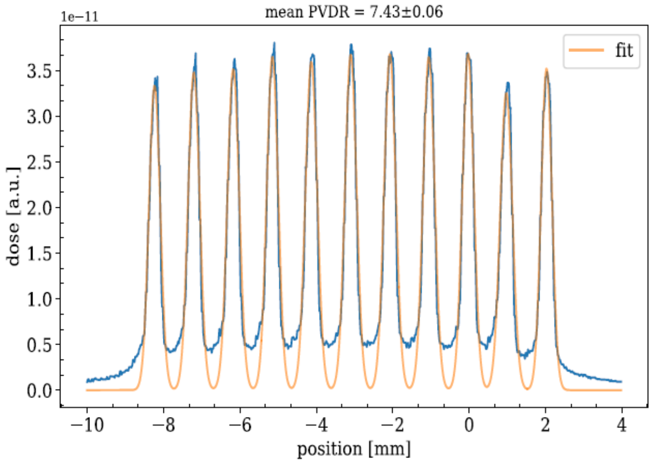


Measurement of PVDR:

one shot measurement

→ significantly faster at comparable spatial resolution

microDiamond



IBL Pixel Detector

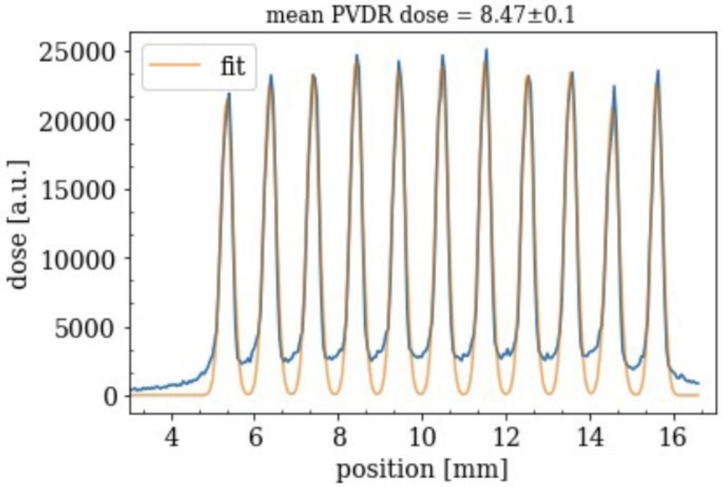


Image Guidance

Targeting in three dimensions

“Alignment” of the patient wrt beam isocenter

→ transversal patient positioning

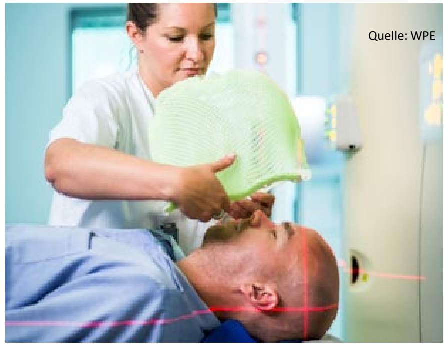
Patient mechanically held in a known position, position checked before treatment using in-room x-ray imager

→ Problem solved, right?

- No real-time position monitoring (movement)
- Not possible in MR-guided PT

→ Use radiation hard, counting detector to take a “proton x-ray”

→ Patient position verification



Add-On: Water-equivalent path length (WEPL) along proton trajectory

→ Measure proton energy to determine stopping power along trajectory

→ proton range verification

- Changes to patient anatomy between fractions

→ <u>Spectral Proton Radiography</u>

Proton Range Uncertainty

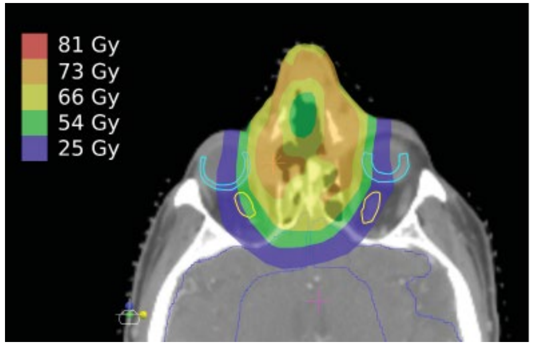
The problem with Proton Range

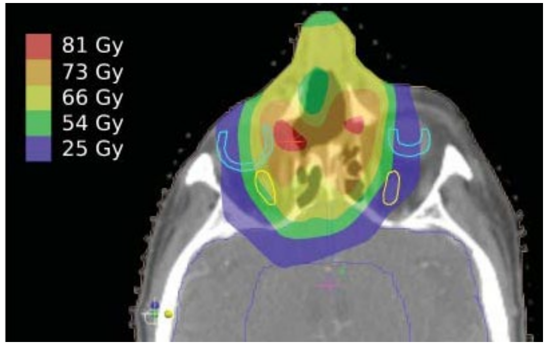
1. Initial proton energy
   - measurement uncertainties during commissioning ($\sigma_E \approx 0.5$ MeV)
2. Proton range depends on stopping power, planning CT measures electron density
   - contributions to uncertainty: grey-scale to HU, HU to SPR, parametrization of I values,
3. Changes to patient anatomy between fractions
   - weight gain/loss, filling of nasal cavities, etc.
   - no CT scans done between fractions

Table 1. Estimated proton range uncertainties and their sources and the potential of Monte Carlo for reducing the uncertainty. Paganetti and Goitein (2000), Robertson *et al* (1975) and Wouters *et al* (1996). The estimations are average numbers based on 1.5 standard deviations. Extreme cases, such as lung treatments, might show bigger uncertainties.

Source of range uncertainty in the patient	Range uncertainty without Monte Carlo	Range uncertainty with Monte Carlo
Independent of dose calculation		
Measurement uncertainty in water for commissioning	±0.3 mm	±0.3 mm
Compensator design	±0.2 mm	±0.2 mm
Beam reproducibility	±0.2 mm	±0.2 mm
Patient setup	±0.7 mm	±0.7 mm
Dose calculation		
Biology (always positive) ˆ	+∼0.8%	+∼0.8%
CT imaging and calibration	±0.5%[a]	±0.5%[a]
CT conversion to tissue (excluding I-values)	±0.5%[b]	±0.2%[g]
CT grid size	±0.3%[c]	±0.3%[c]
Mean excitation energy (I-values) in tissues	±1.5%[d]	±1.5%[d]
Range degradation; complex inhomogeneities	−0.7%[e]	±0.1%
Range degradation; local lateral inhomogeneities *	±2.5%[f]	±0.1%
Total (excluding *, ˆ)	2.7% + 1.2 mm	2.4% + 1.2 mm
Total (excluding ˆ)	4.6% + 1.2 mm	2.4% + 1.2 mm

The number are estimations based on finding by
[a] Chvetsov and Paige (2010).
[b] Schaffner and Pedroni (1998) and Matsufuji *et al* (1998).
[c] Espana and Paganetti (2011).
[d] ICRU (1993), Bichsel and Hiraoka (1992) and Kumazaki *et al* (2007).
[e] Sawakuchi *et al* (2008), Bednarz *et al* (2010) and Urie *et al* (1986).
[f] Bednarz *et al* (2010).
[g] Espana and Paganetti (2010).





https://www.na-mic.org/wiki/DBP:Head_and_Neck_Cancer

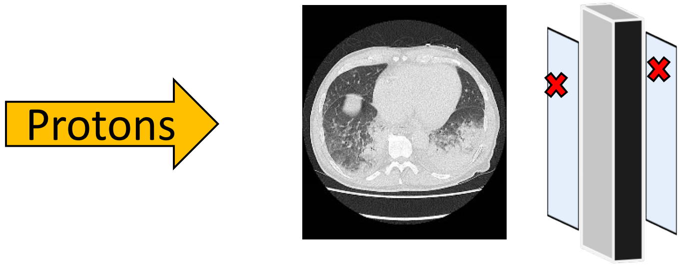
For many years now, this has been taken into account by adding a safety margin of 3.5% + 1mm
→ Improvement needed!

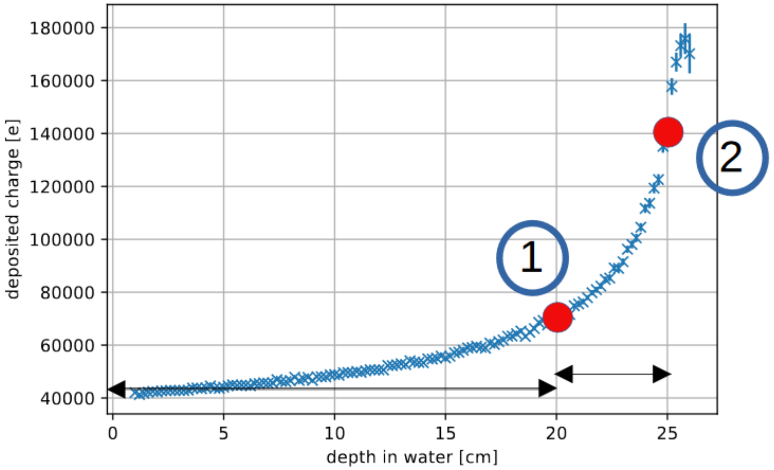
Spectral Proton Radiography

Simple concept:
- Number of protons for image
- Energy of protons to determine RSP

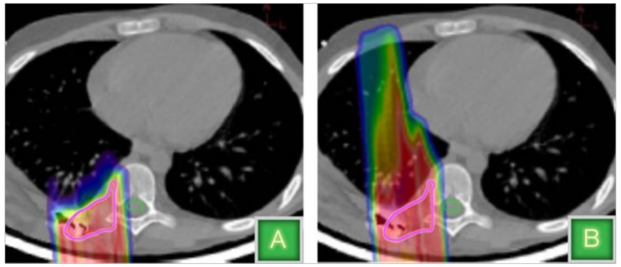
Many groups working on proton CT, but effort doesn't seem worth the gain
- expected range uncertainty ~1%
- can be reached with DECT, already in clinical use

Energy measurement using tracking detectors demonstrated to work
➔ Spectral Proton Radiography
  - Image for position verification
  - Energy for RSP and anomaly detection

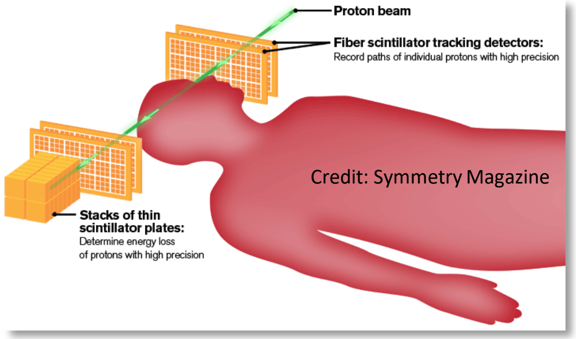




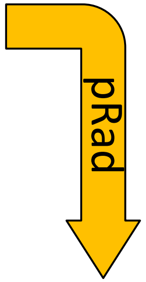
Courtesy of Dr. Reinhard Schulte, Dept. of Radiation Medicine, Loma Linda University Medical Center

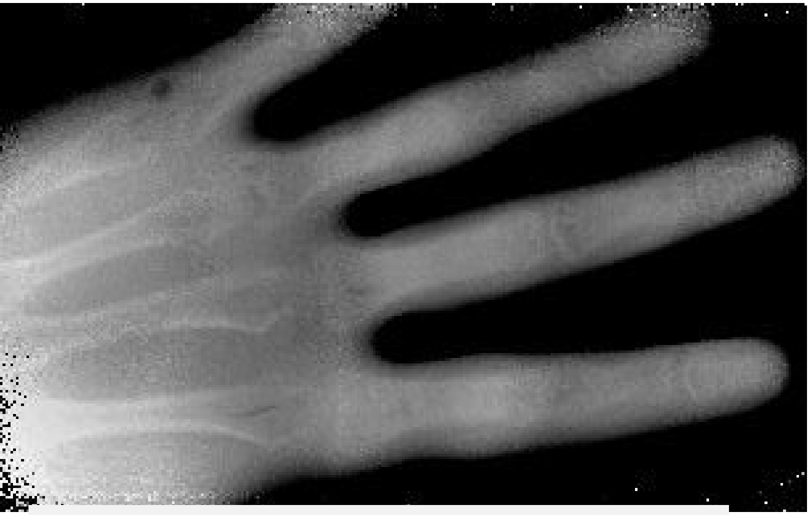


Planned dose deposition | Dose deposition resulting from density error from CT scan



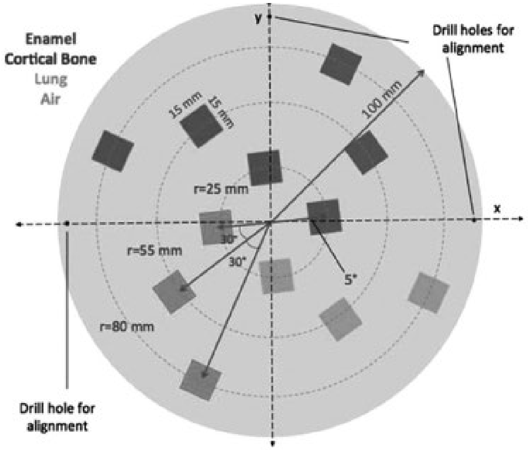
Proton Radiography



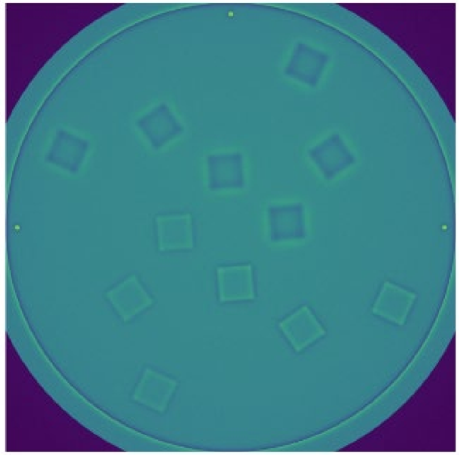


https://news.ucsc.edu/2012/10/proton-radiography.html

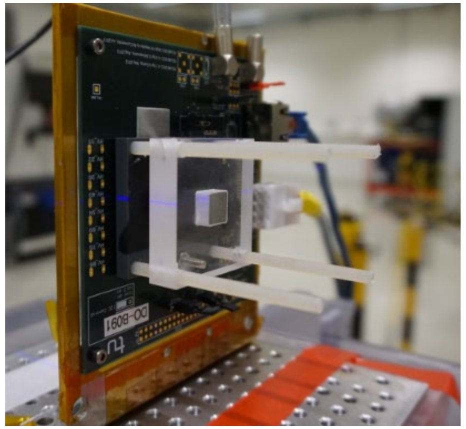
Simulation

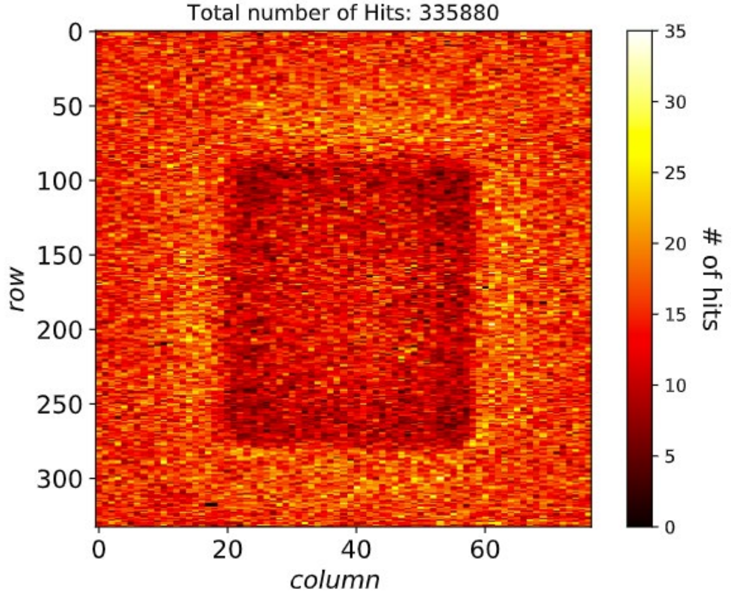


Analysis of characteristics of images acquired with a prototype clinical proton radiography system, **C. Sarosiek. et al**



Messung





Summary

Proton Therapy - Next Steps

Goal: Availability for more patients, i.e. make it cheaper!

- Reduce costs for manufacturing and service of accelerators and beam optics
- Reduce construction costs for a treatment centre → single-room facilities
- Increase patient through-put while maintaining treatment quality
  - Faster daily quality assurance
  - Improve treatment efficiency and accuracy
  - Faster treatment using higher dose rate, i.e. beam current

Lots of (detector) technologies exist to address different requirements, just need to come together

➔ Technology Transfer

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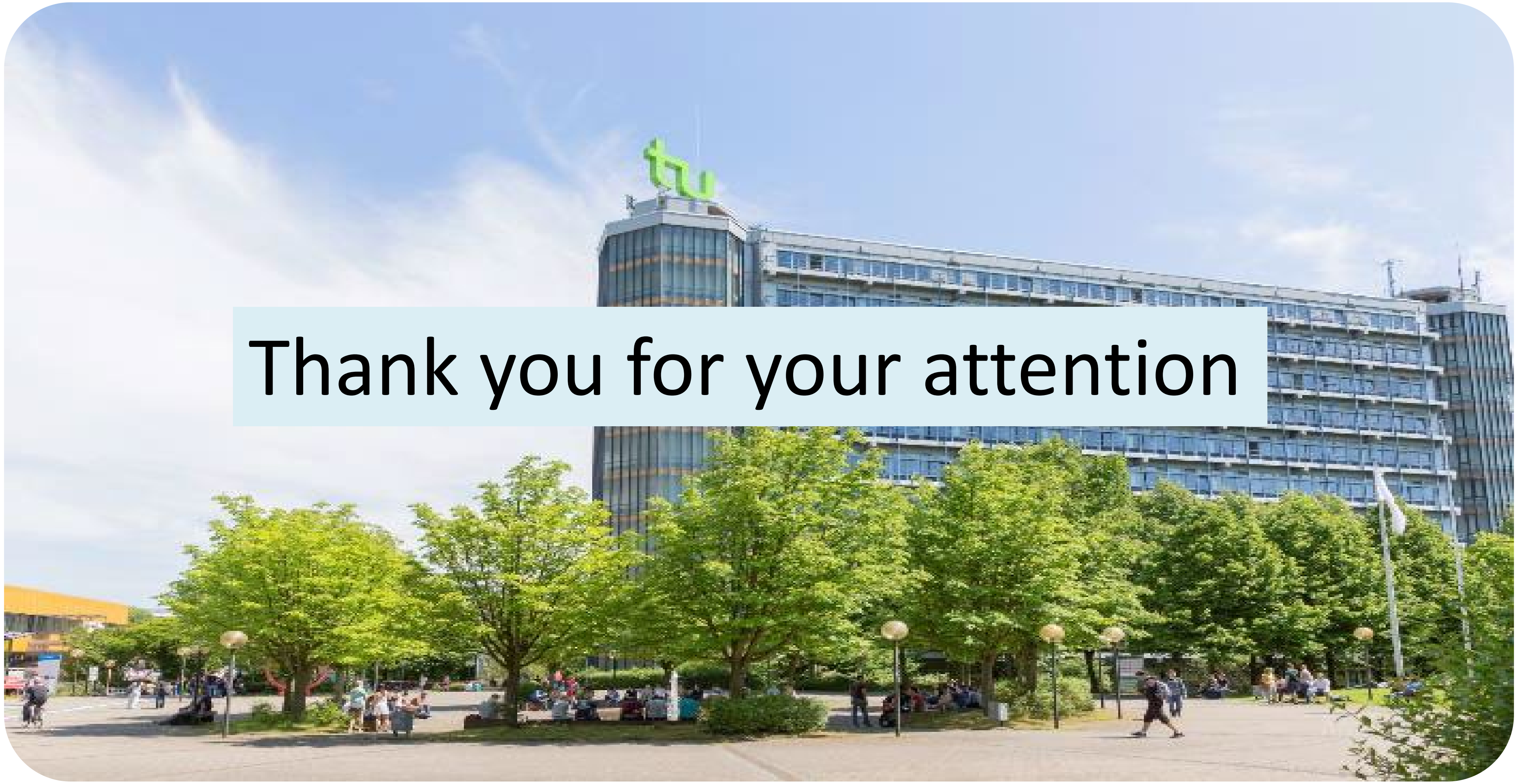

www.tu-dortmund.de