Proton tomography imaging for cancer treatment

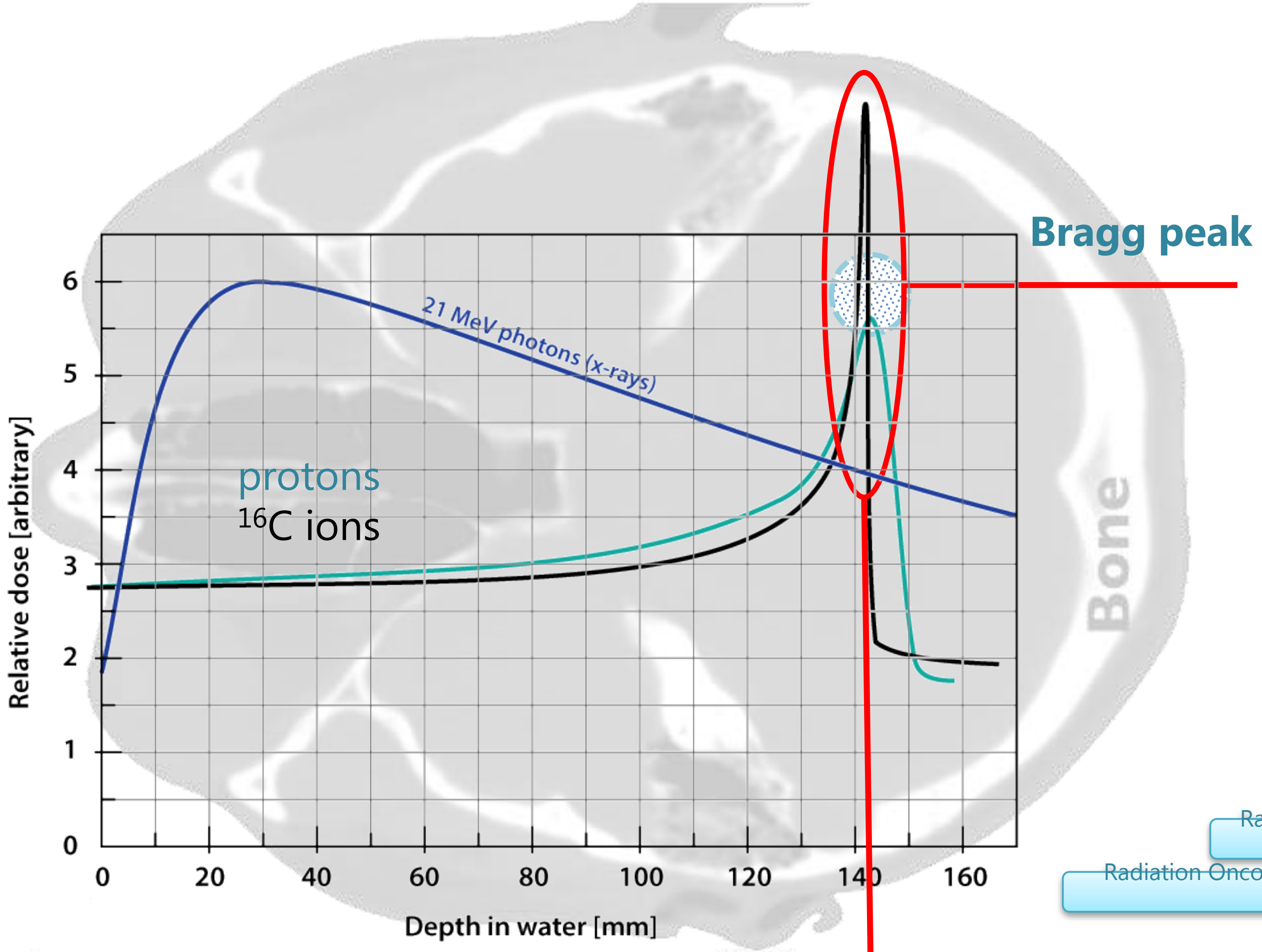
Piero Giubilato – Padova University & INFN – ICHEP 2020

Hadron therapy growth

Hadron therapy – physics rationale

Proton (ion) energy transfer is highly localized (Bragg peak): greater effectiveness and much lower collateral damage respect to traditional x-rays therapy.

ionizing radiation



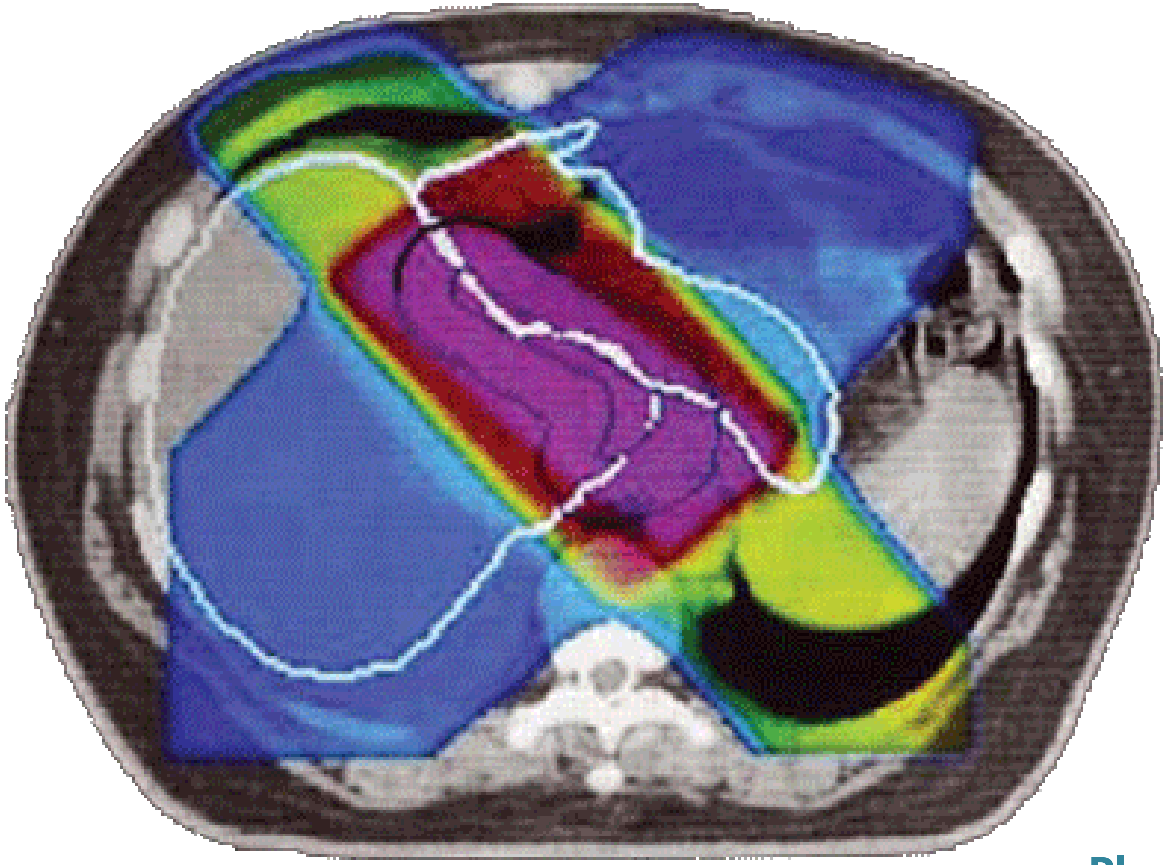
Radiotherapy and Oncology **95** (2010) 3–22

Radiation Oncology*Biology*Physics **83** (2012) 1549–1557

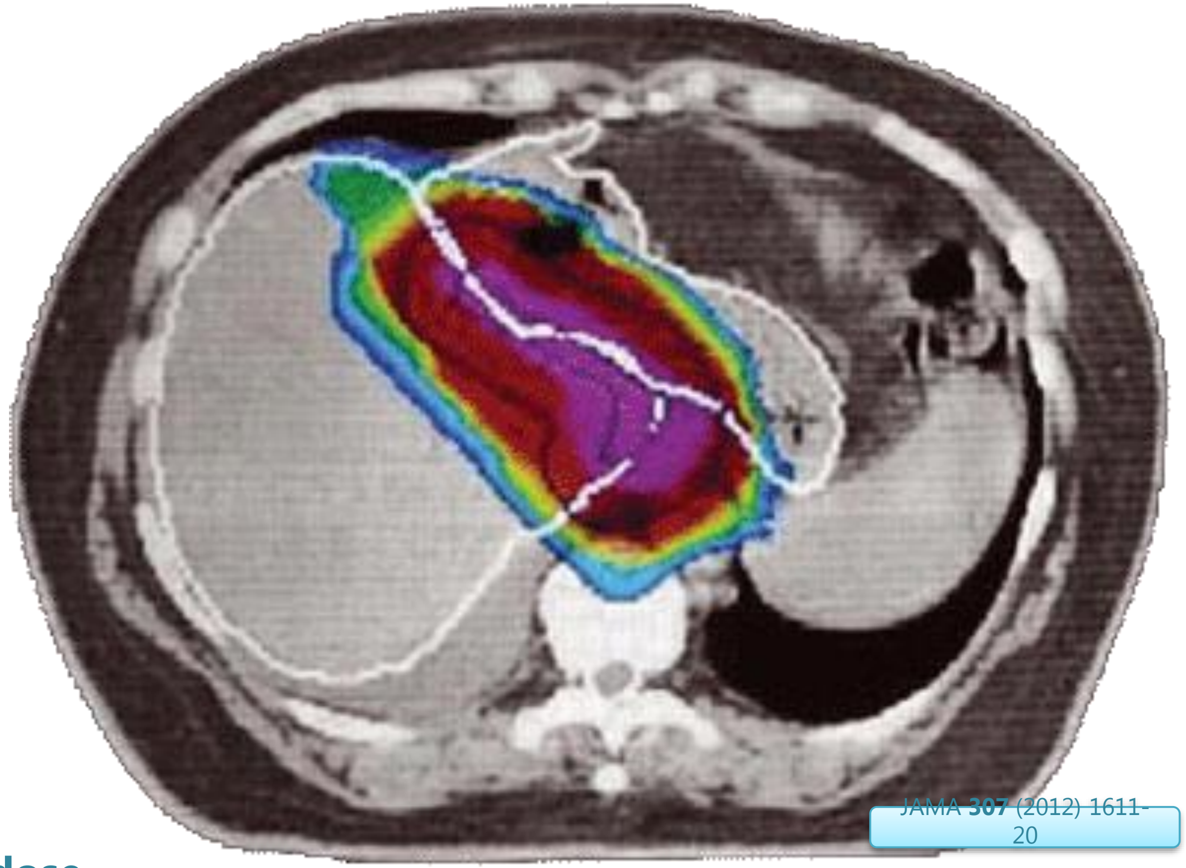
The Bragg peak position (depth) in the body depends on the ion energy and the tissue density it traverses. Changing energy determines the aiming depth.

Hadron therapy – reduced collateral damage

Much lower collateral damage respect to photons due to the focused energy deposition: less damage to surrounding tissues, less chance of secondary tumors.



X-Rays treatment



Protons treatment

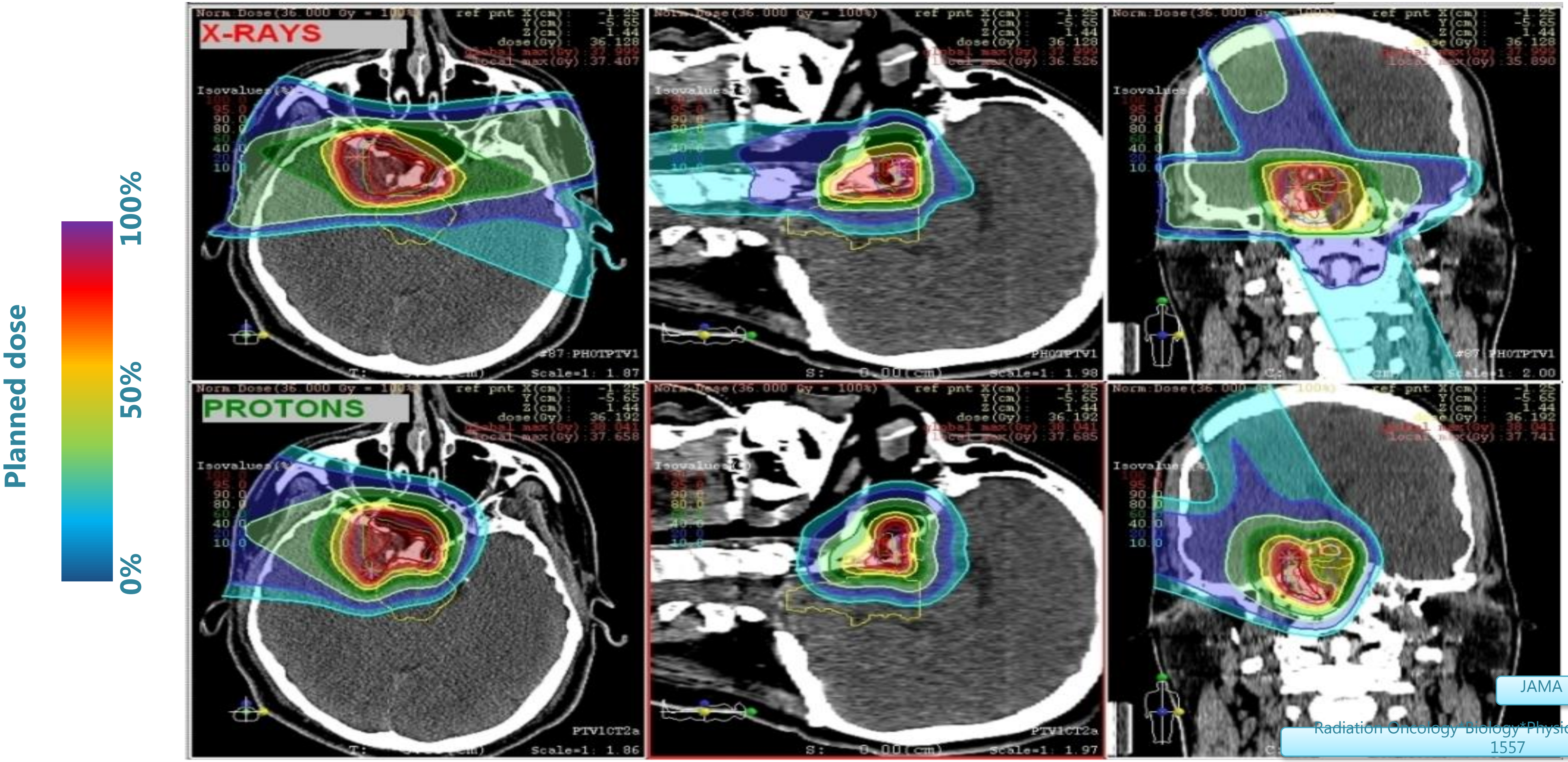
JAMA **307** (2012) 1611-20

Radiation Oncology*Biology*Physics **83** (2012) 1549–1557

Planned dose

Hadron therapy – reduced collateral damage

Much lower collateral damage respect to photons due to the focused energy deposition: less damage to surrounding tissues, less chance of secondary tumors.

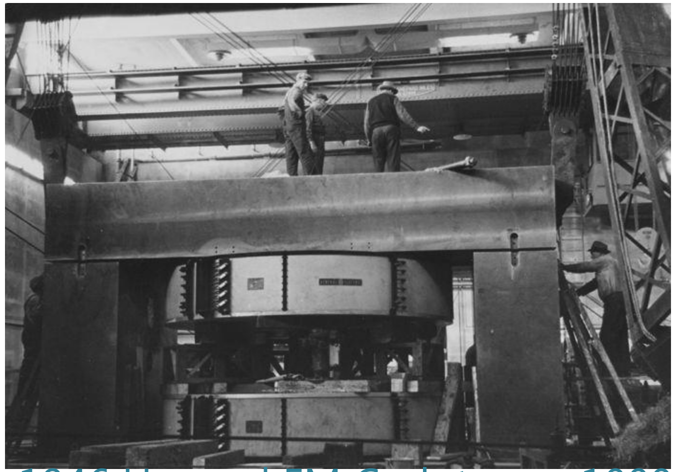


JAMA **307** (2012) 1611-20

Radiation Oncology*Biology*Physics **83** (2012) 1549–1557

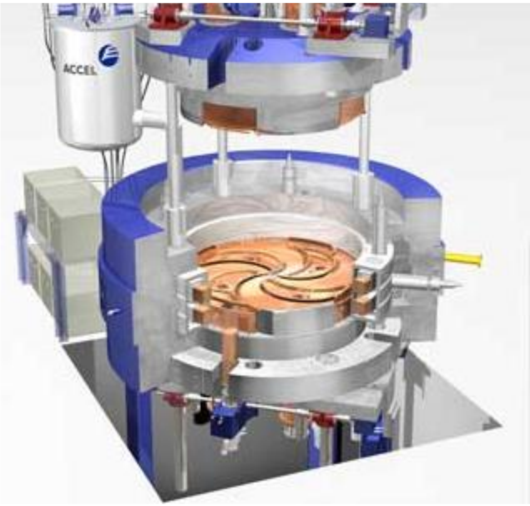
Hadron therapy – accelerator compactification key to applications

Nor exhaustive nor complete, simply to highlight technology progress



1946 Harvard FM Cyclotron ≈ 1000 tons.

1996 - IBA Isochronous Cyclotron ≈ 200 tons.

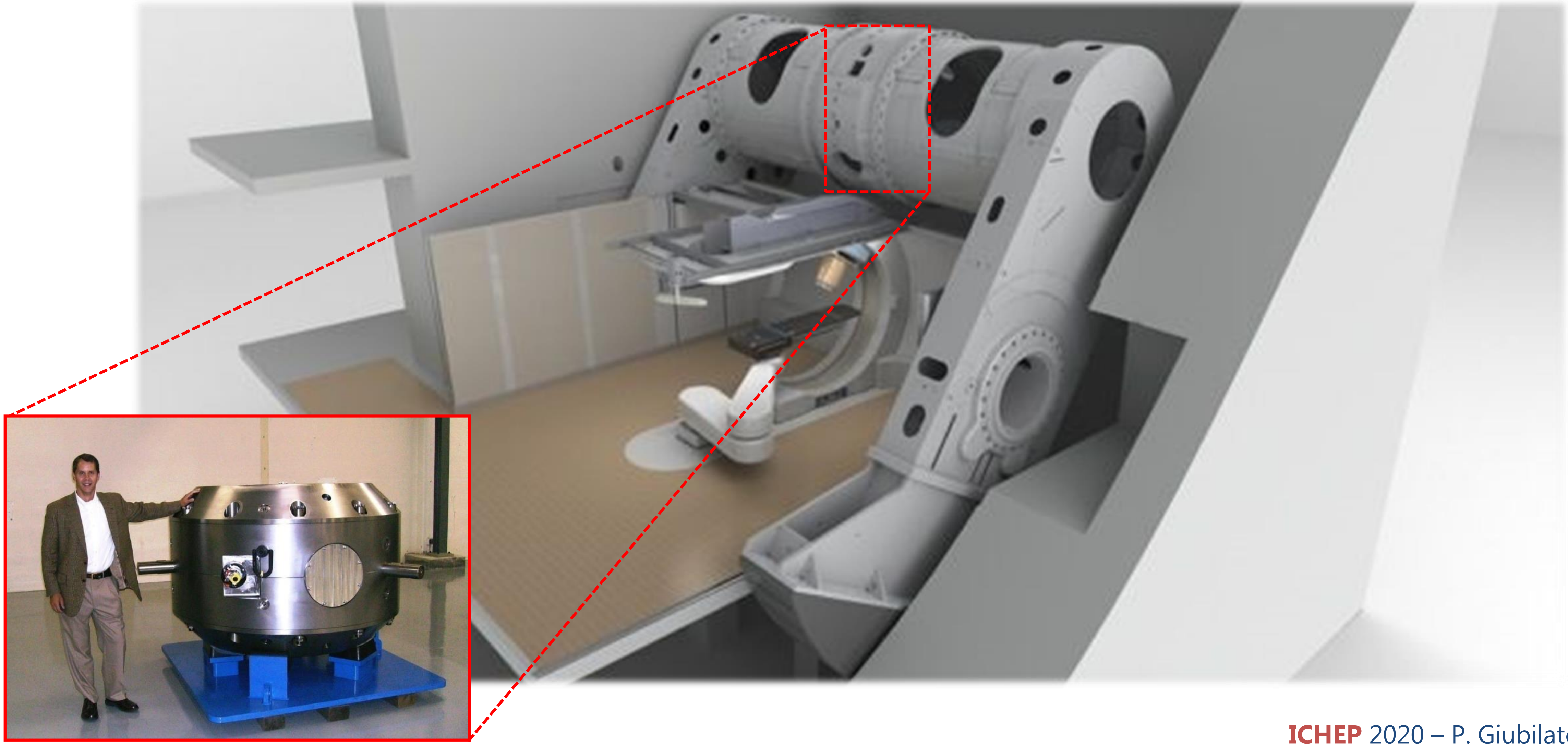


2000 - Accel Superconducting Isochronous ≈ 90 tons.

2008 - Still River Superconducting FM ≈ 15 tons.

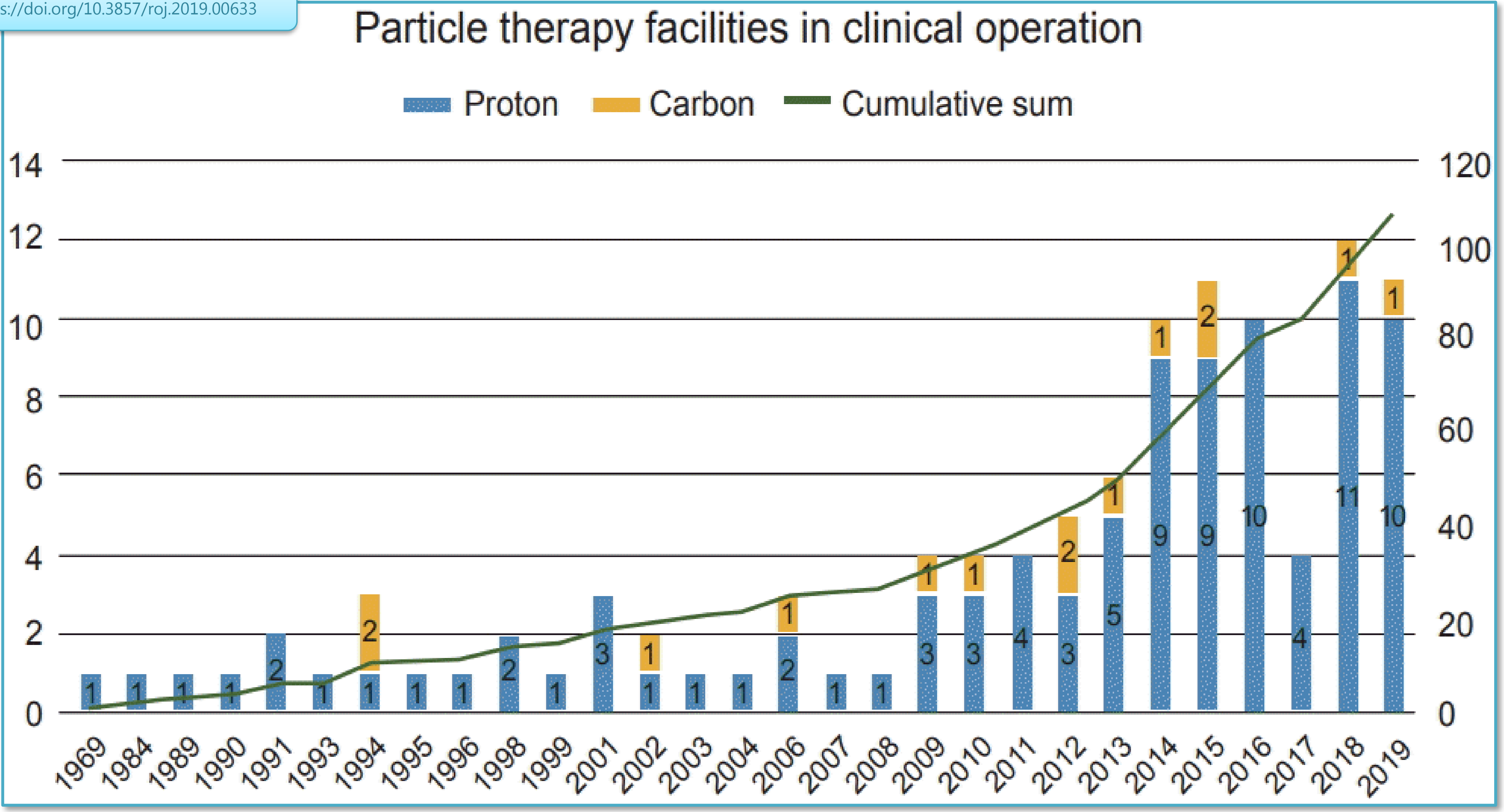
Hadron therapy – accelerator compactification key to applications

- MEVION 250 series accelerator/gantry system fit into as single room
- Superconducting 9 T synchrocyclotron mounted directly on the patient gantry.
- No beam transport line, 98% uptime (www.mevion.com)



Hadron therapy – growth

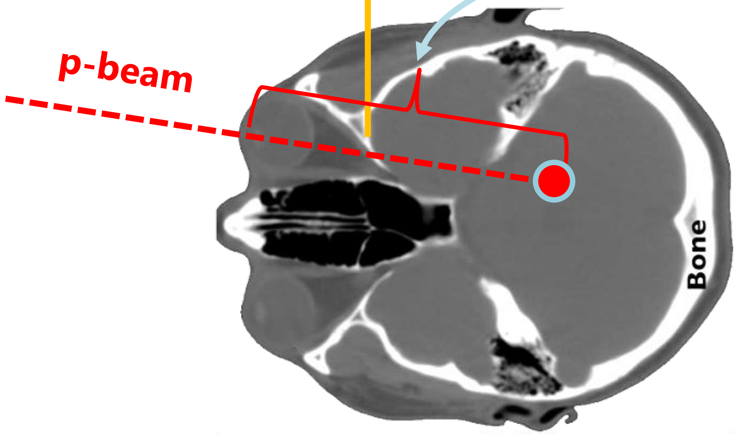
Radiation Oncology Journal 2019; 37(4):232-248.
DOI: https://doi.org/10.3857/roj.2019.00633

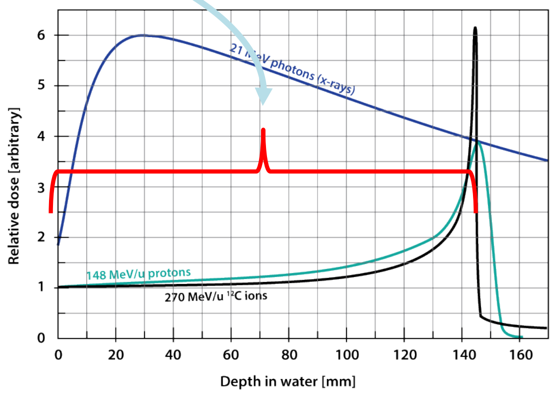


Hadron therapy: pCT necessity

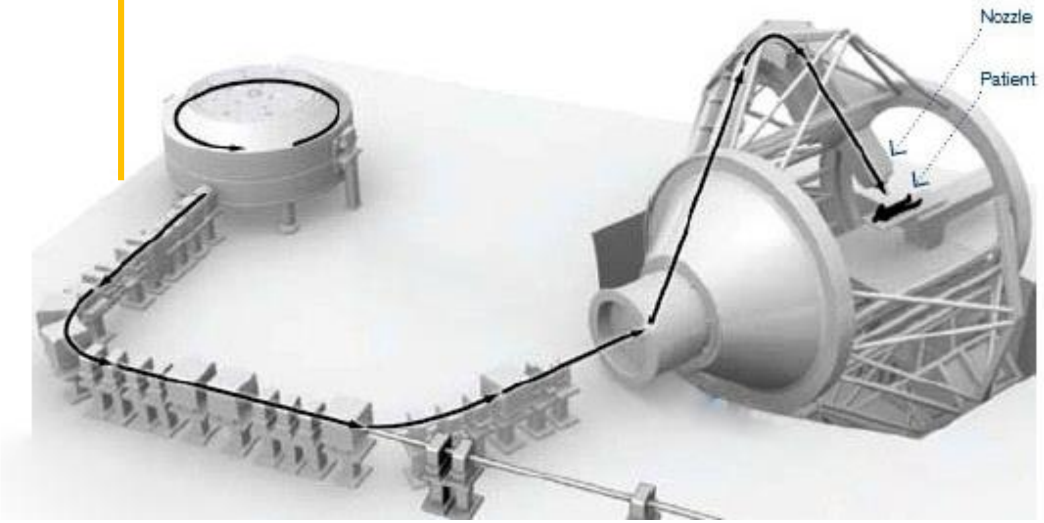
Hadron therapy – the aiming limit **problem**

Aiming the Bragg peak requires fine tuning of the proton energy to account for the tissue densities they have to traverse to reach the tumor.





Poor tissue density resolution from X-Rays CT

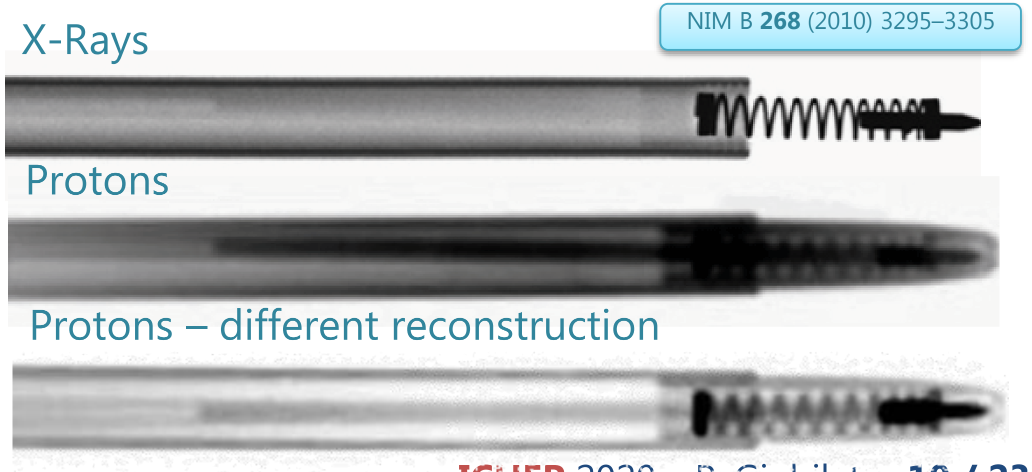


Fine energy tuning better than 0.5%

Eur. Phys. J. Plus (2011) **126**: 78

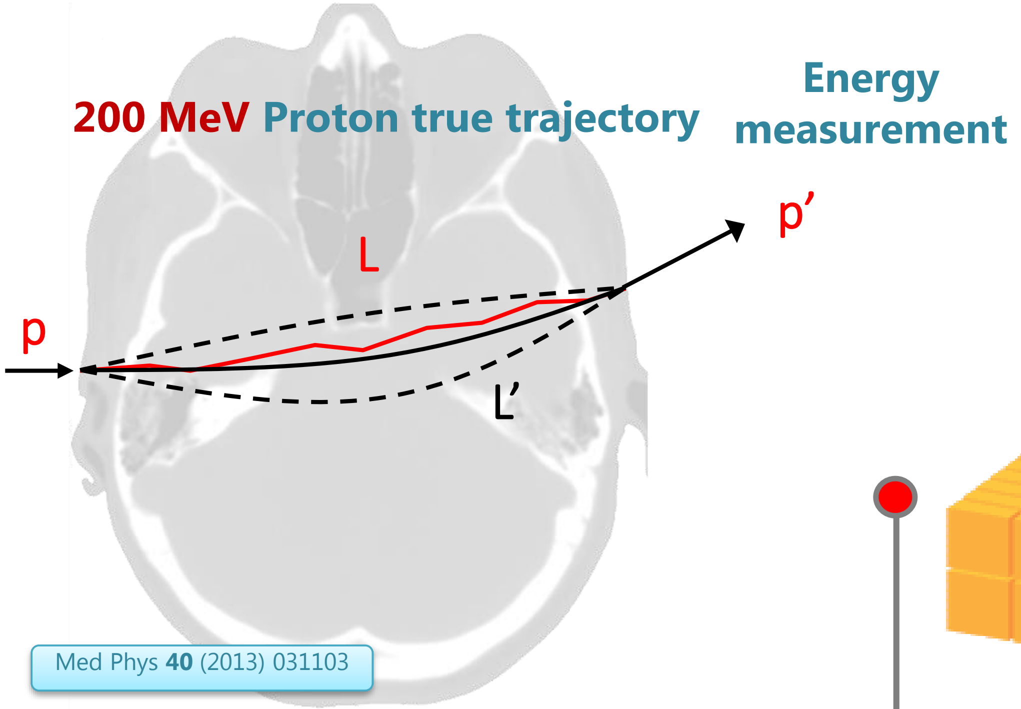
NIM B **268** (2010) 3295–3305

- X-ray 3D CT has low resolution on tissue densities with the required precision: proton therapy limit today (bigger systematic error, up to 5%).
- But protons actually can (and with much less dose, ≈ 1.5 mGy vs. 10-100 mGy).

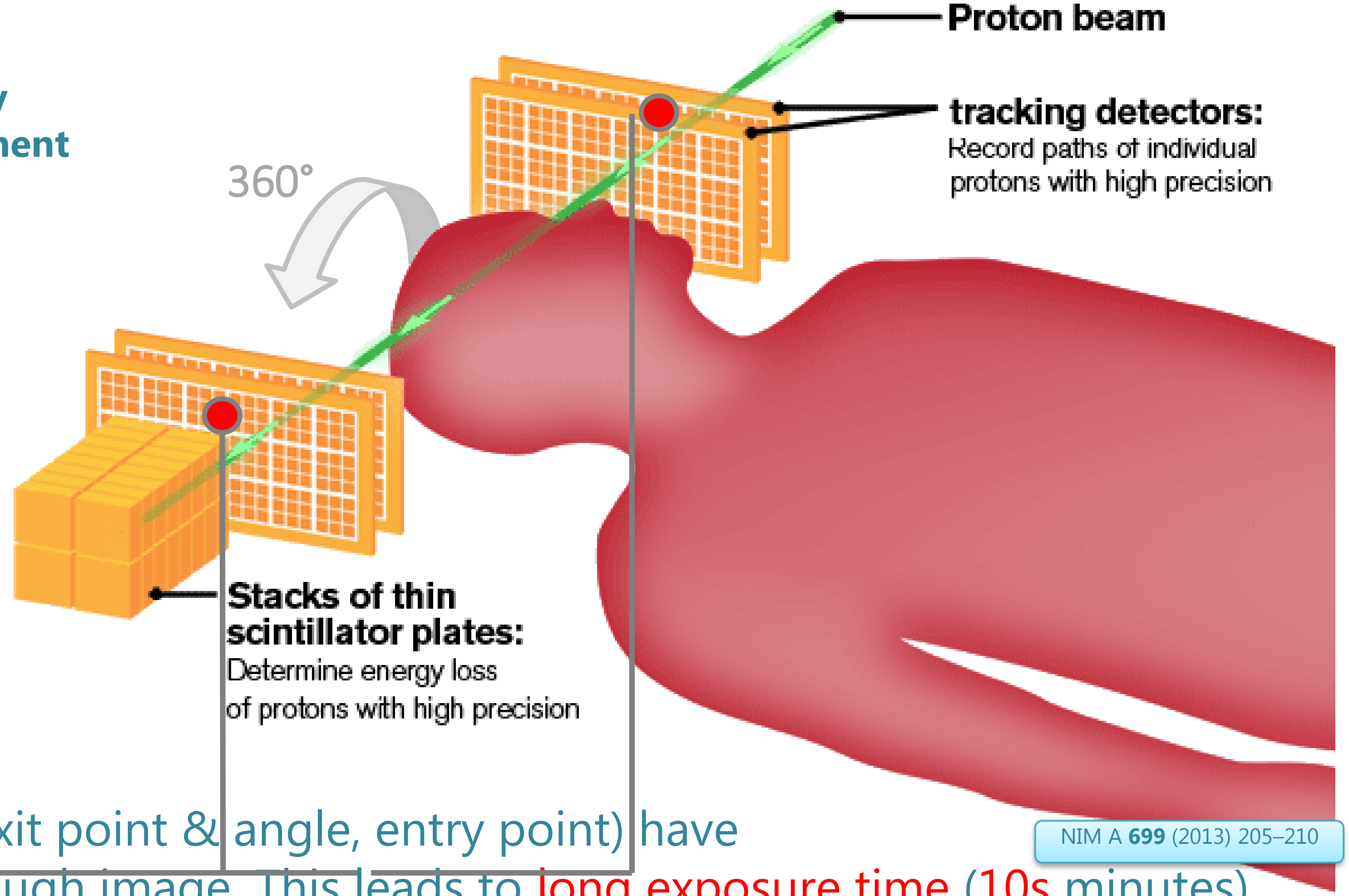


Hadron therapy – the proton Computed Tomography (pCT) scanner

The pCT works on the same principle as a "standard" x-rays CT: recording particles passing through the target from different angles to reconstruct a 3D image. Main difference is that, while photons are simply absorbed, protons also scatters.



Entry and exit points + angle
Most Likely Path calculation



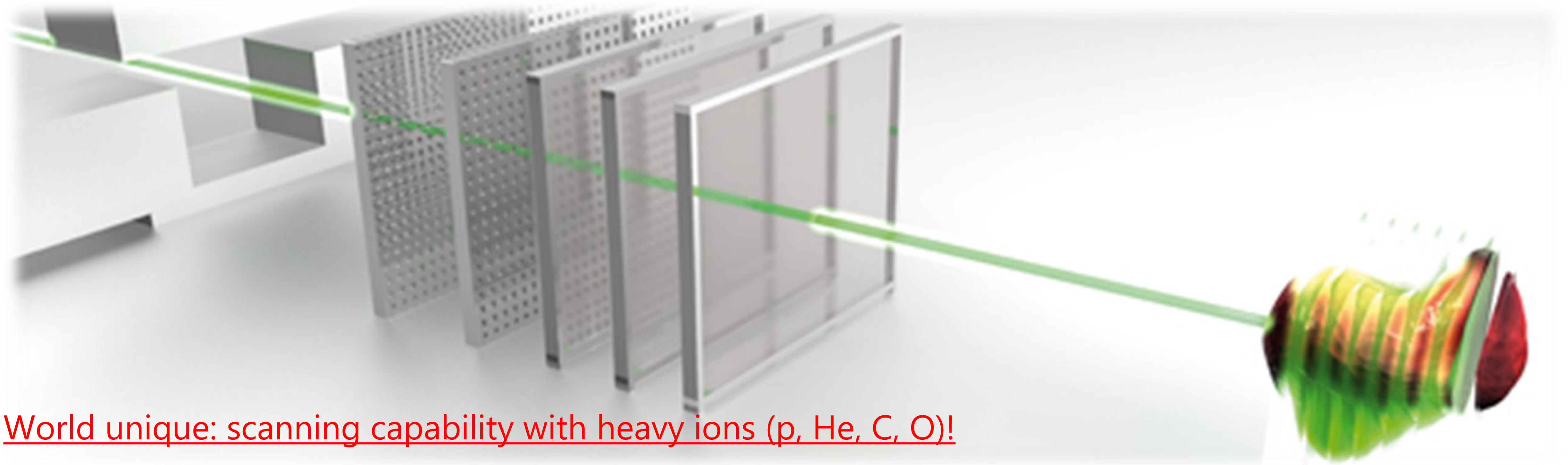
At least 10^9 proton tracks (energy loss, exit point & angle, entry point) have to be recorded to provide a detailed enough image. This leads to long exposure time (10s minutes) with current state of the art: limited to R&D only.

pCT scanner

impact

pCT scanner – Medical (modern) beams are usually scanned (painting)

- Beam energy range from 50 to 430 MeV/u.
- intensity-controlled rasterscan technique: ions pencil beam.
- 255 energy levels per ions – millimeter precision increments in beam's range.
- Penetration depth of the beam: from 20 mm to 300 mm.
- 10 selectable levels of beam intensity. Beam size from 4 mm to 10 mm.
- Online position, shape and intensity monitoring with 100 kHz refresh.
- Ultra-fast 1/2000 s beam stop.
- Facilities, ambulatories, hospital directly connected to the hospital.



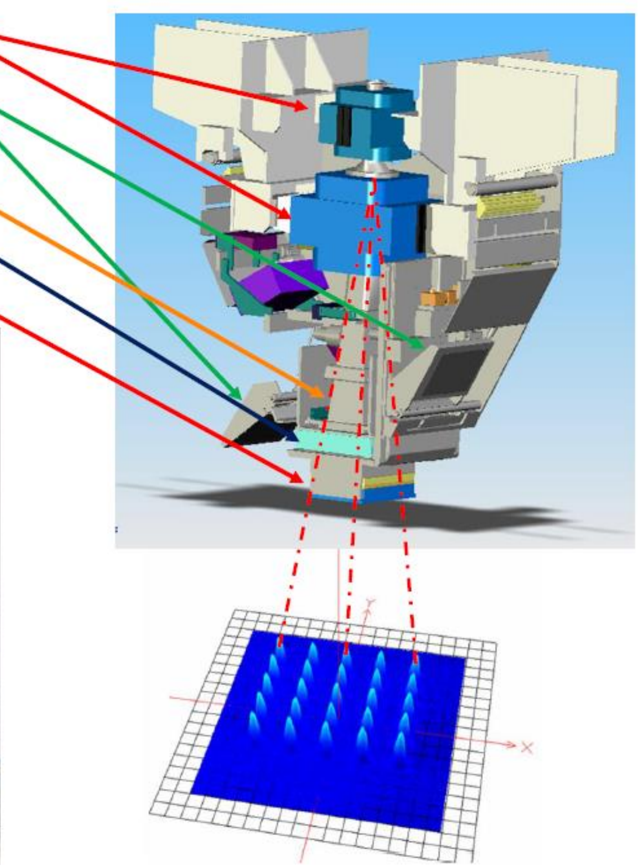
World unique: scanning capability with heavy ions (p, He, C, O)!

Large sensors – scanning beam quick overview

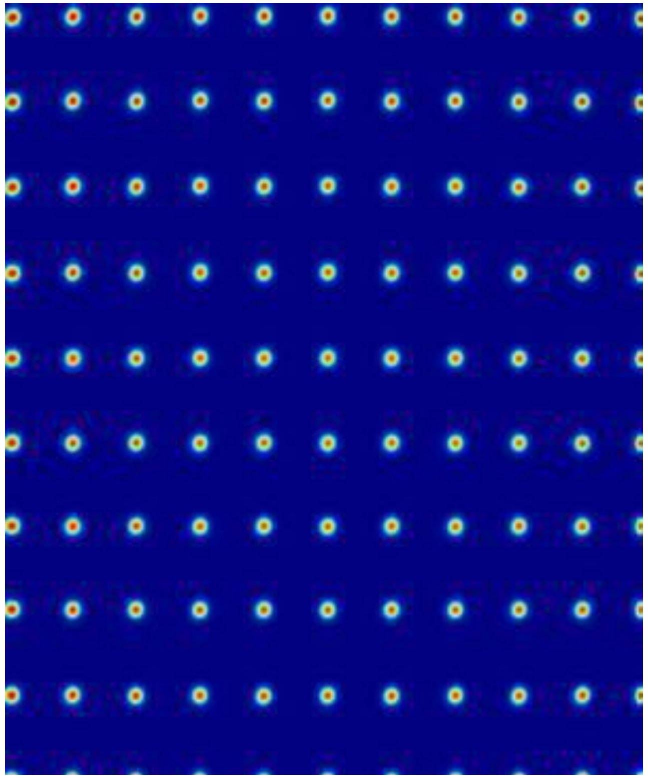
Scanning beam characteristics

Ulrich W. Langner - 6 March 2017
DOI: 10.1002/acm2.12078

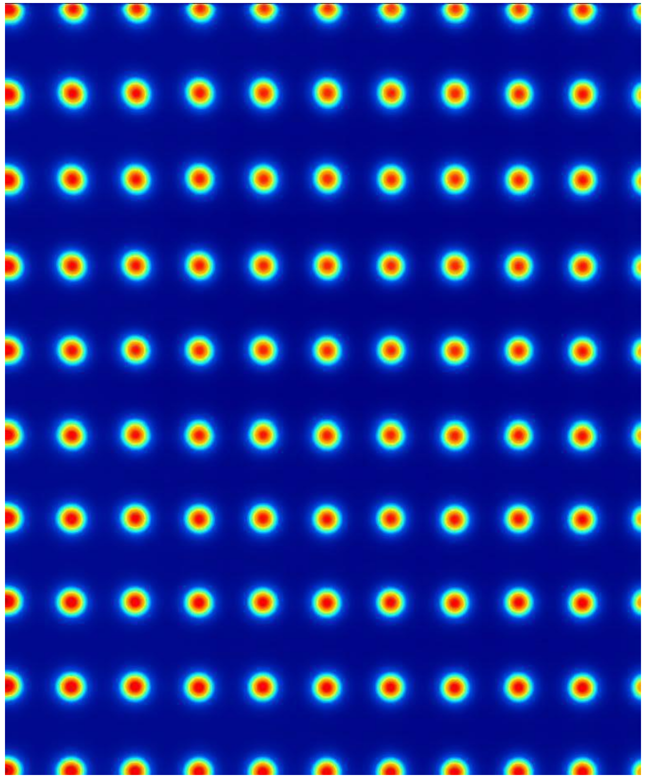
- Clinical protons energy range: 70 MeV to 230 MeV.
- Total area to be covered (with tiling!): from $10 \times 20\ \text{cm}^2$ to $30 \times 30\ \text{cm}^2$.
- Scanning beam spot: $\sigma \approx 4.3$ mm in air at isocentre (energy $\geq$ 200 MeV).
- Continuous current up to 10 nA (1 nA typical) = 6×10^9 p/s (6×10^8 p/s typ).
  - Spot area of about 1 cm^2 $\rightarrow$ 6×10^9 p cm^{-2} s^{-2} (6×10^8 p cm^{-2} s^{-2} typ).



244 MeV



69 MeV

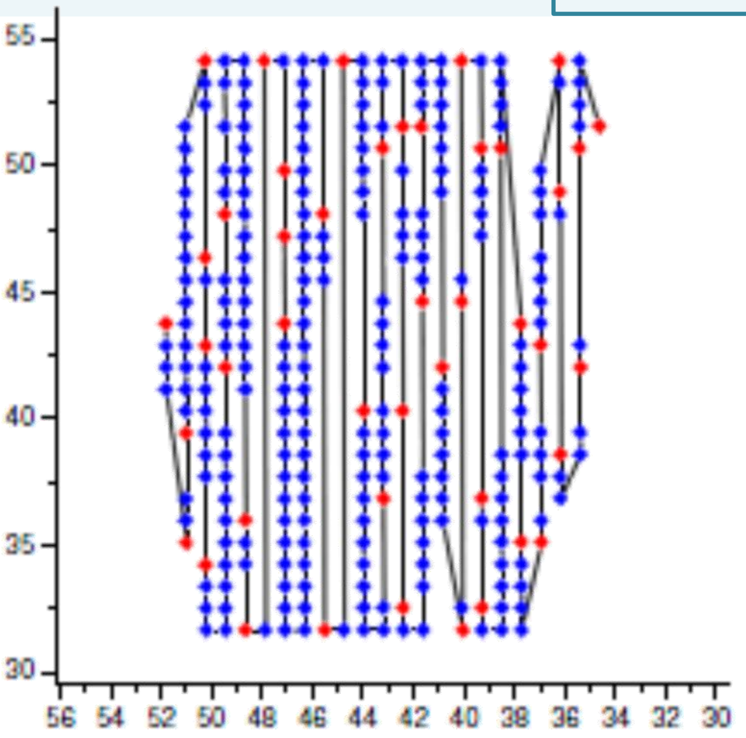


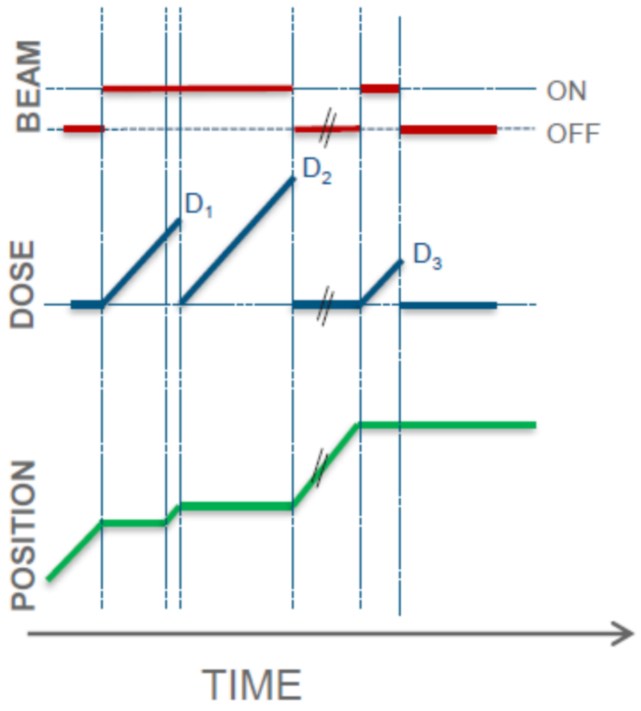
pCT scanner – scanning beam requirements

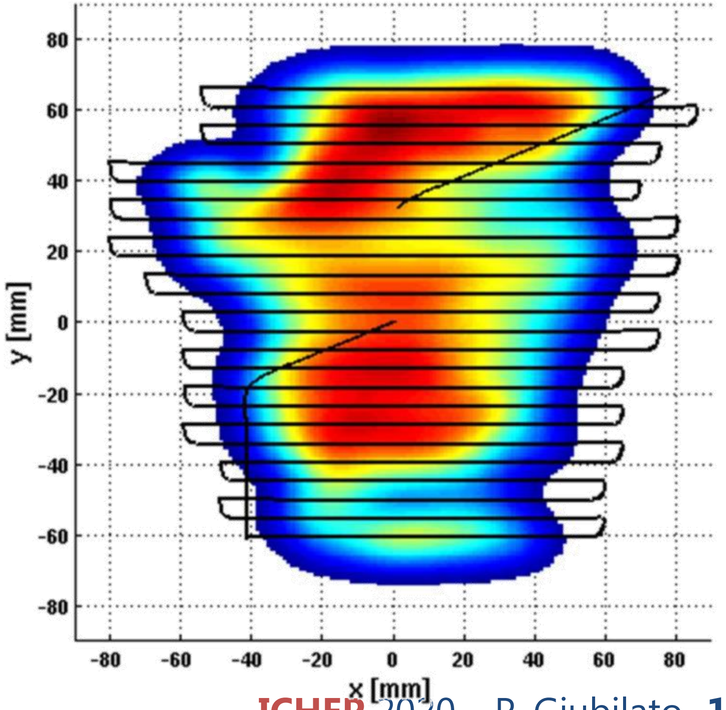
Scanning beam timing

- Variation of energy layer: < 0.9 ms (not needed for pCT).
- Deflection in *x* and *y*: 0.5 ms (spot to spot).
- Typical spot duration: 3 ÷ 50 ms (1.8 ÷ 30 × 10^6 p cm^{-2} at typical current).
- To cover a 20 × 20 cm^2 area with 10^9 p: ≈ 1000 spots necessary, each with 10^6 p.
- (9 ms spot (1 × 10^6 p cm^{-2}) + 1 ms repositioning) × 1000 ≈ 10 s total exposure.

≈ 100 MHz cm^{-2} → **After passing the target (scattering)** → **≈ 10 MHz cm^{-2}**

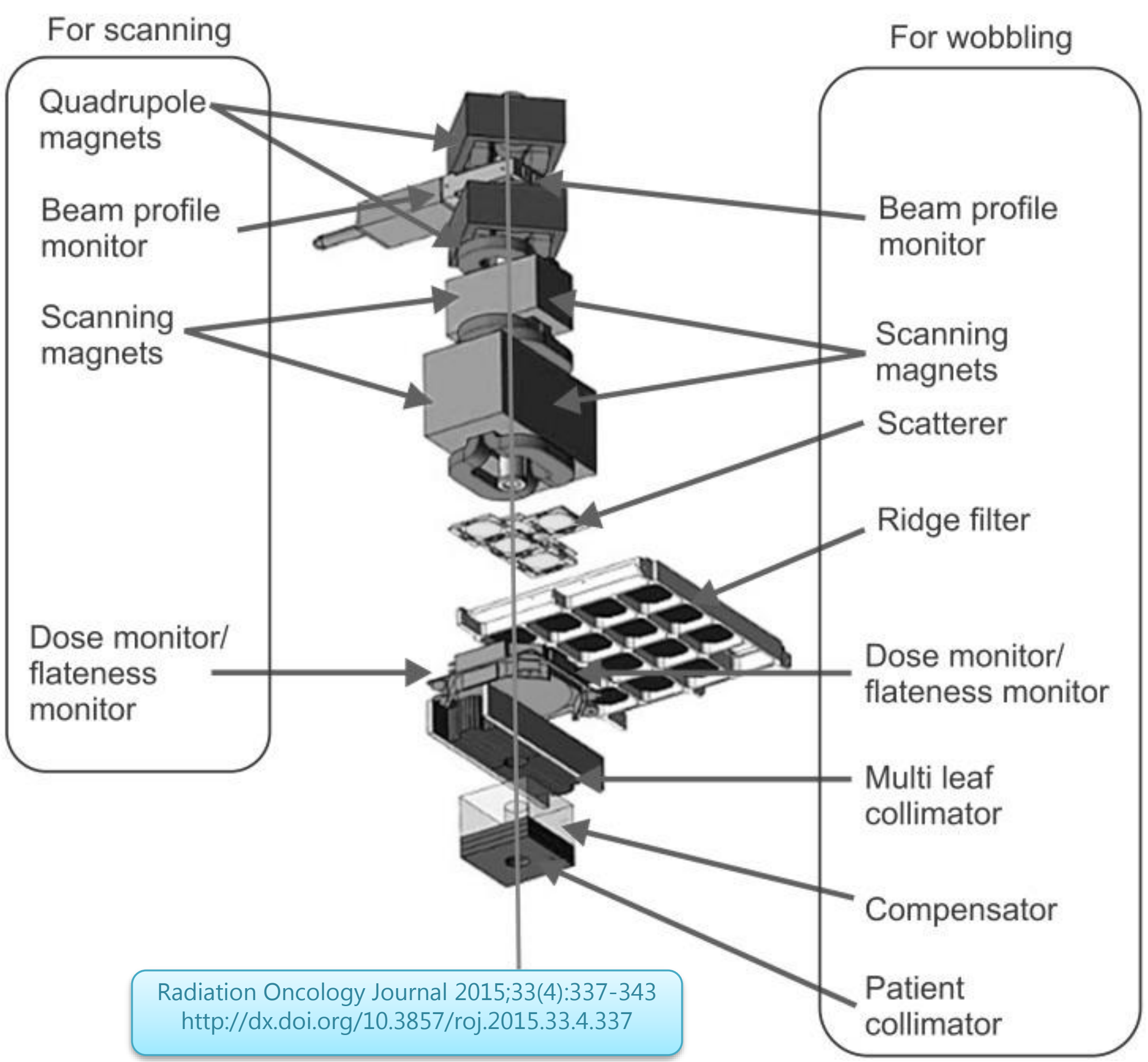






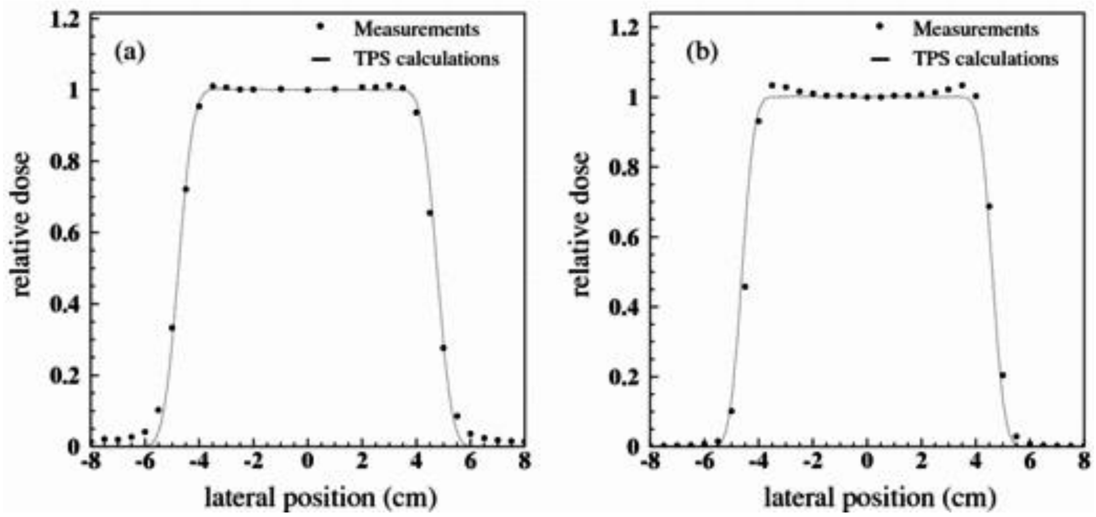
pCT scanner – broad beam also present (but rare)

Broad beam over the entire target area put lesser requirements on the tracking and calorimeter system. Mix of fast (MHz) wobbling magnets and scatterer(s) generates an almost uniform illumination profile (typical example reported in plot).



Radiation Oncology Journal 2015;33(4):337-343
http://dx.doi.org/10.3857/roj.2015.33.4.337

- Mitsubishi multi-purpose nozzle system.
- Broad beam area: 25 × 25 cm^2.
- Scanning beam area: 24 × 24 cm^2.
- For a <u>20 × 20 cm^2 imaging area, 10^9 protons in 10 s exposure</u> → 250 kHz cm^2
- Even considering non uniformity, time fluctuations, etc... → **≈ 1 MHz cm^{-2}**



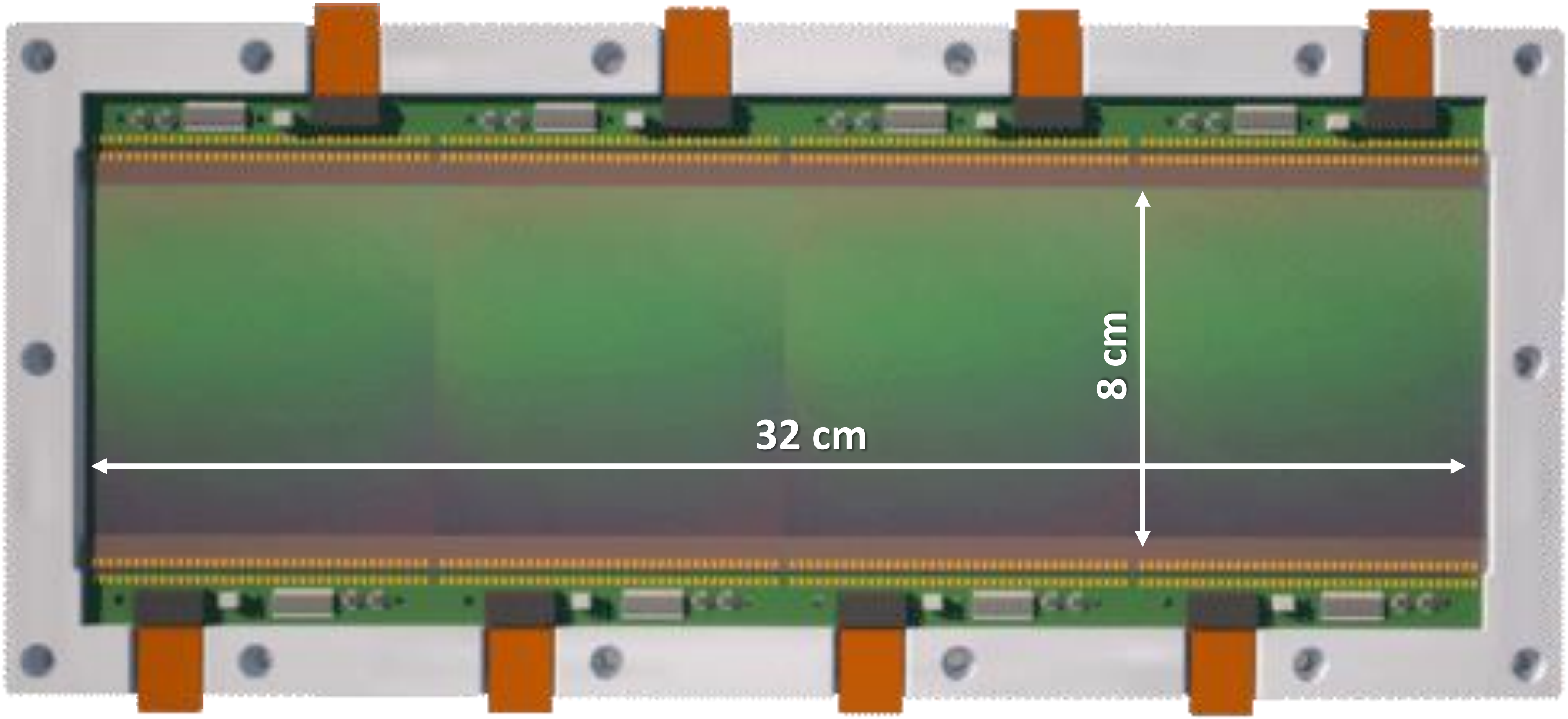
T Akagi et al 2006 Phys. Med. Biol. 51 1919
https://doi.org/10.1088/0031-9155/51/7/020

pCT scanner – the need for very large sensors

Fast (≈ 100 MHz cm^{-2}) proton tracking at low power in silicon (**50 mW cm^{-2}**).

Monolithic, thinned (≤ 50 μm) and large area (≥ **16 cm^2**) device to minimize proton scattering. **No support structure** possible (desirable) behind the silicon.

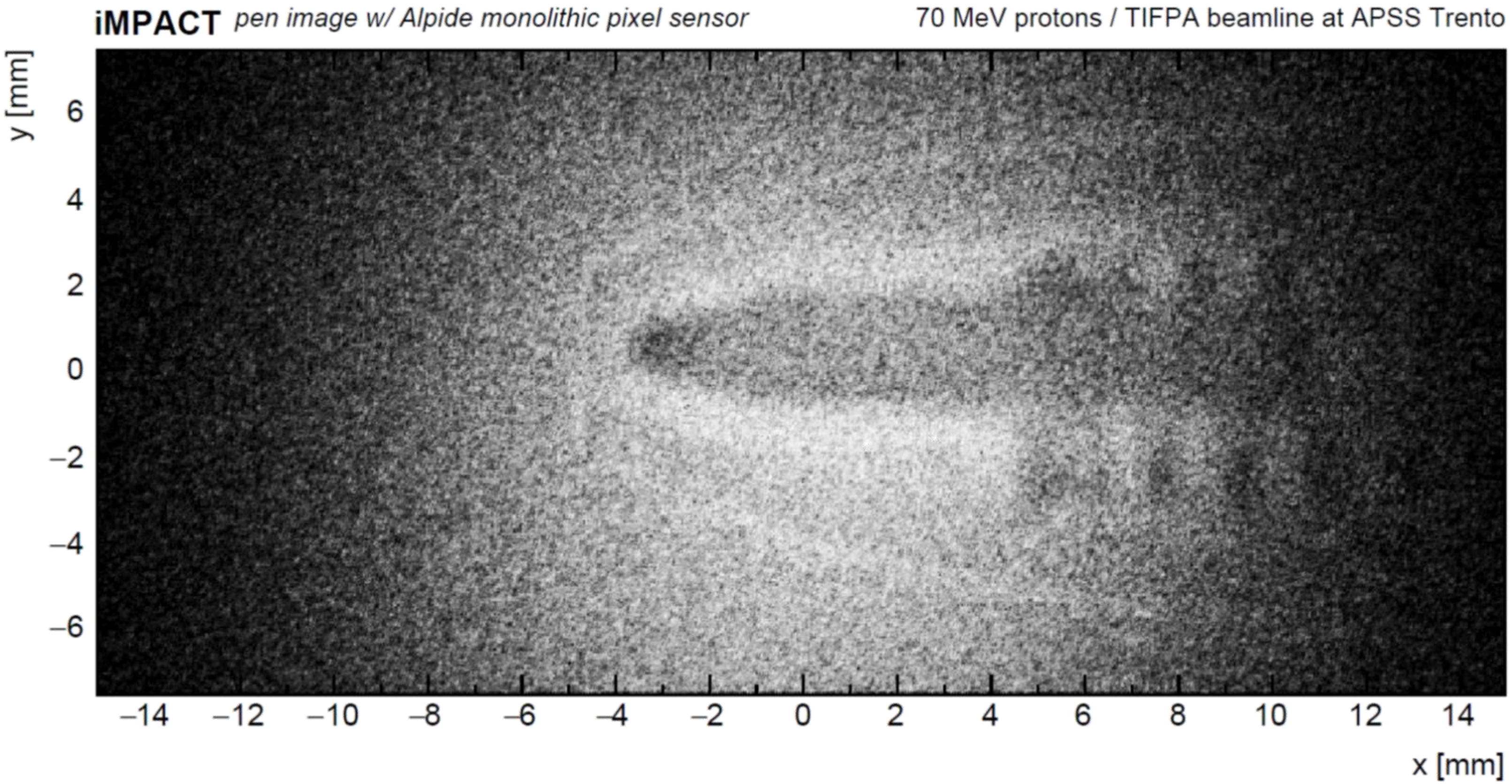
Cost effective, reliable, simplified commissioning & operations, commercial process (for large production), **low voltage** for real clinical usage.



pCT scanner – ALPIDE first “proton” light

ALICE ITS ALPIDE chosen for first pCT prototype (while developing more advanced sensor within the INFN ARCADIA project). Demonstrative proton radiography of a pen: metal, different plastic densities, air distinguishable.

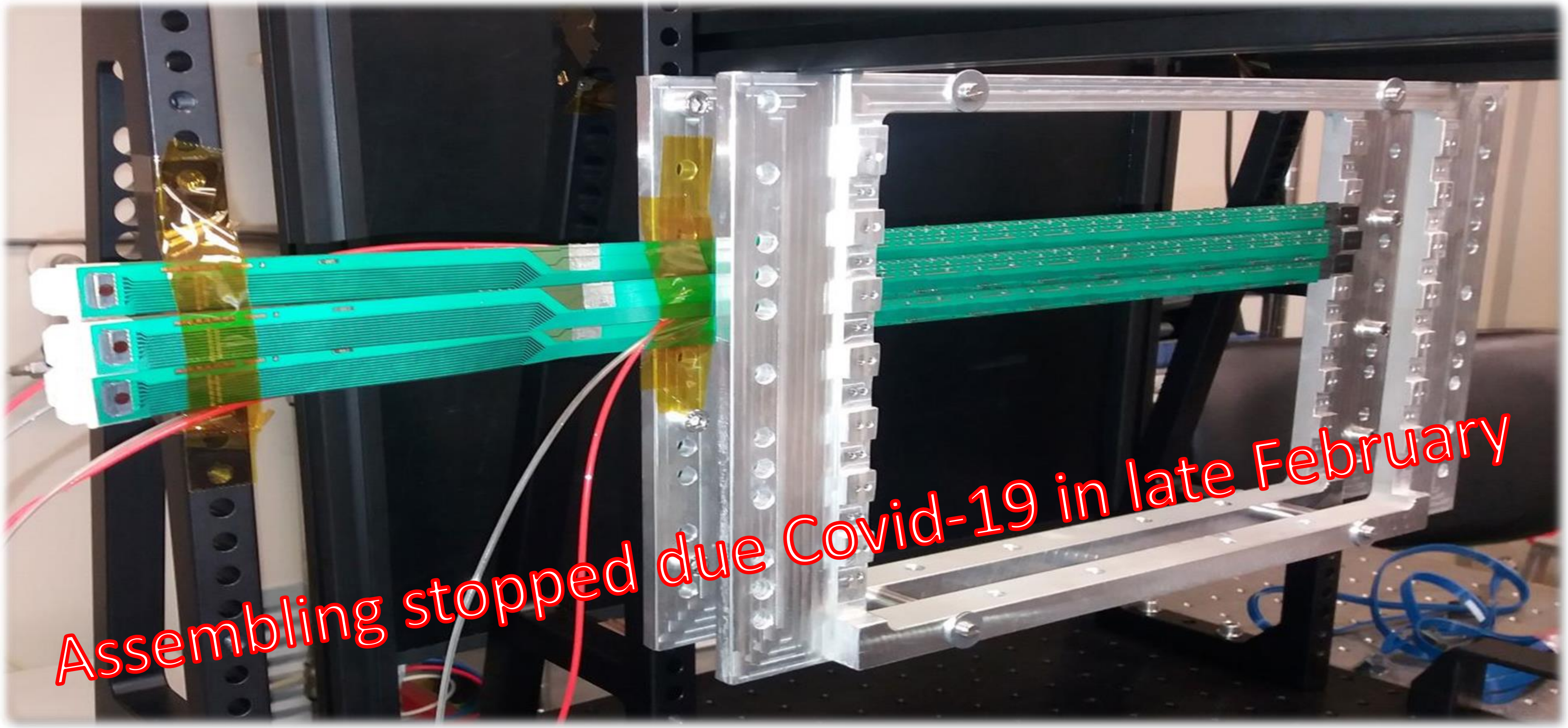
ALPIDE sensor (from ALICE collaboration) 30 × 15 mm^2



pCT scanner – ALPIDE sensors arranged for tracking layers

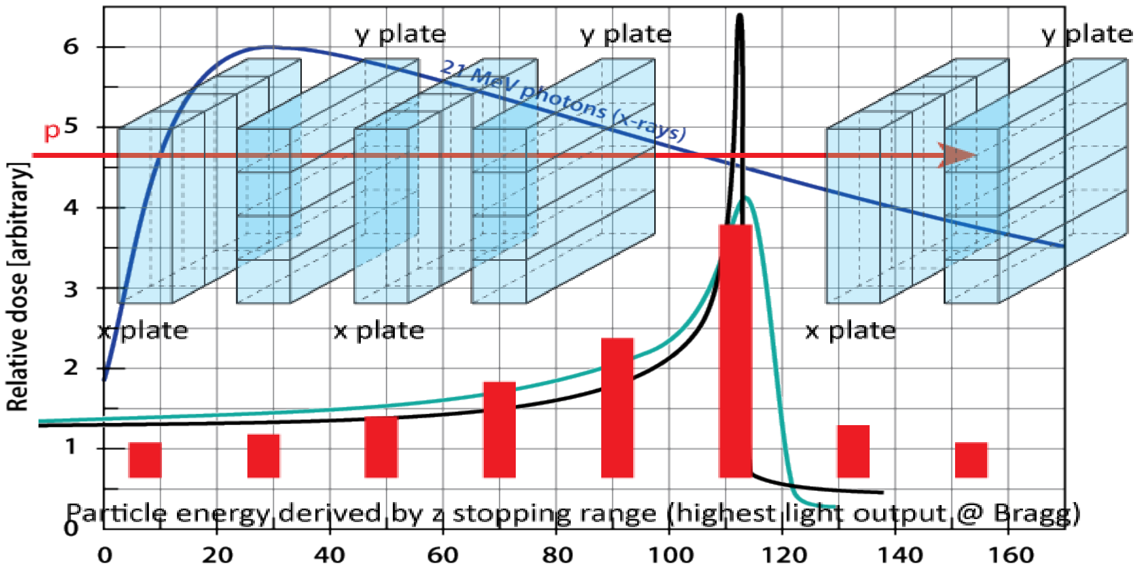
The ALPIDE sensor (15 × 30 mm^2) has been selected for a first tracker prototype:

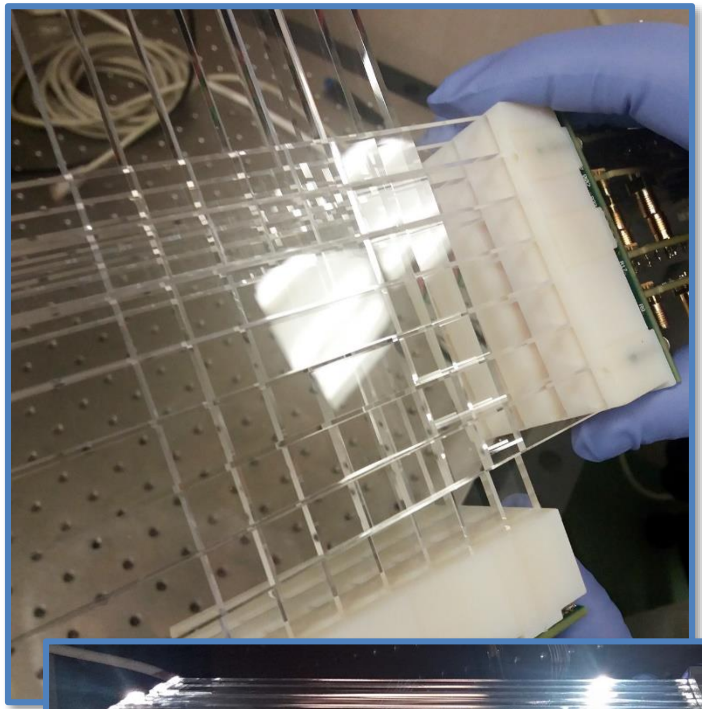
- 5 staves with 6 sensors per plane: 18 x 7.5 cm^2 active area
- 3 planes (4th plane possible for non-orthogonal beams)

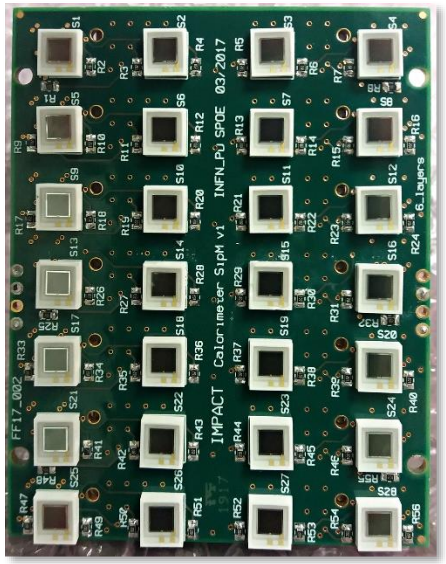


pCT scanner – Energy measurement with range calorimeter

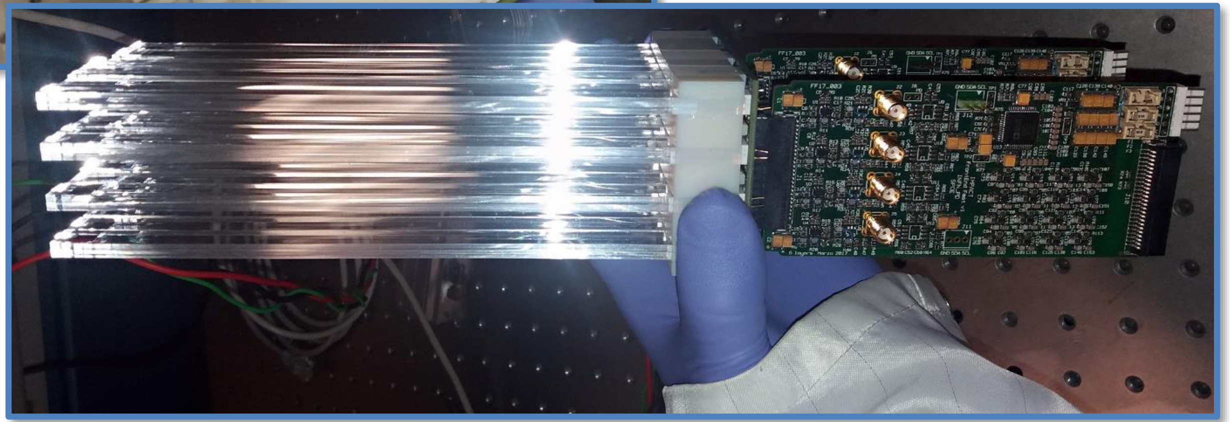
Together with the position, the energy of the proton after it exits the target must be measured. No present solution can achieve the particle rate necessary to keep-up with the foreseen tracker. Most advanced R&D are looking for tracking-calorimeter, using MAPS in the calorimeter.



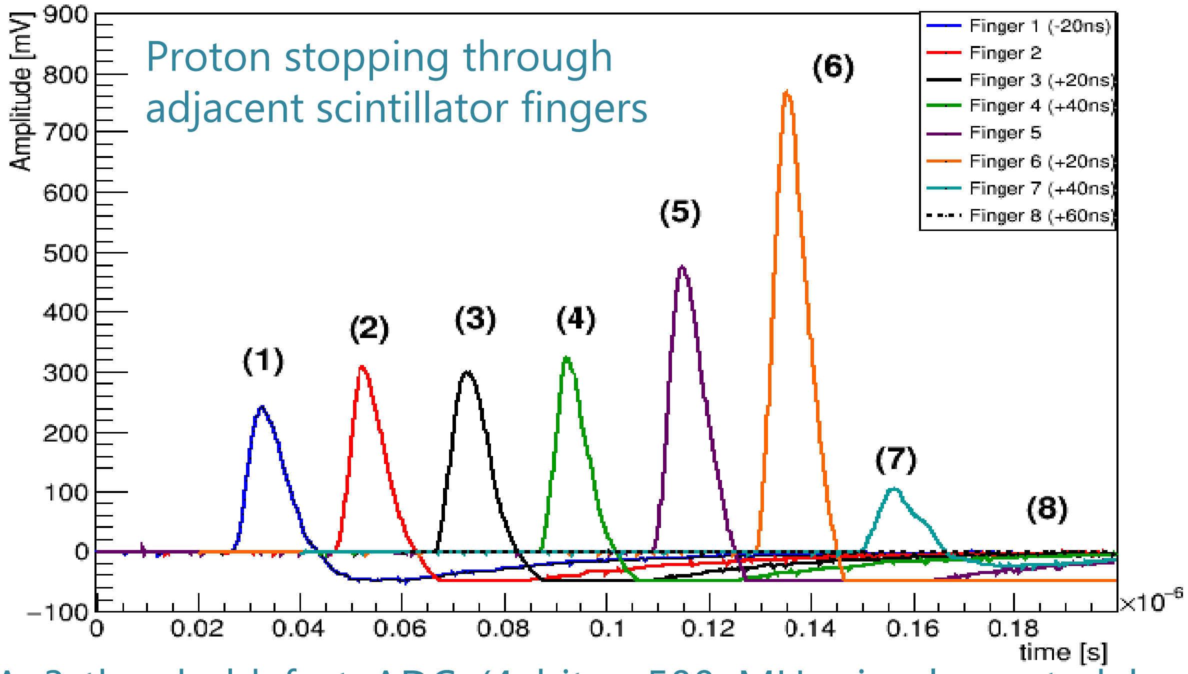




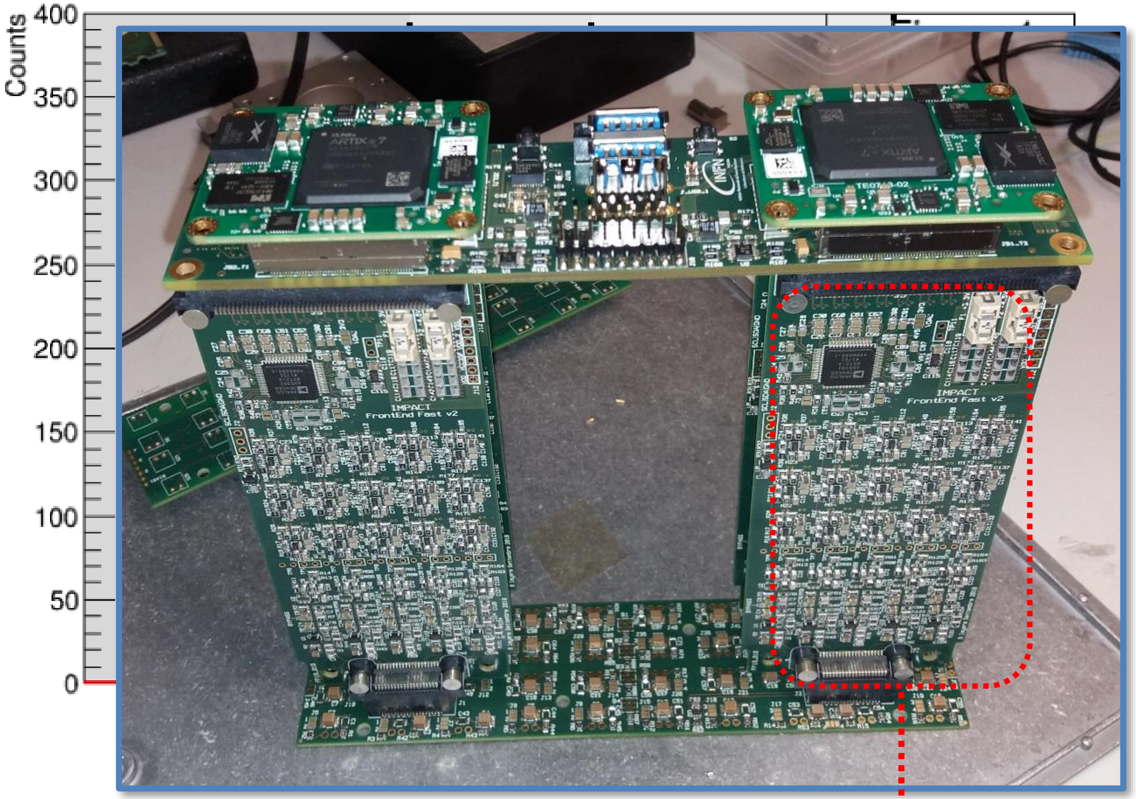
We did chose a simpler approach: a **range proton calorimeter** which exploits the very same Bragg peak characteristic of protons to measure their residual energy. It is based on orthogonal layers of segmented scintillating fingers read out by SiPM and dedicated FPGAs electronic.



pCT scanner – Energy measurement with range calorimeter

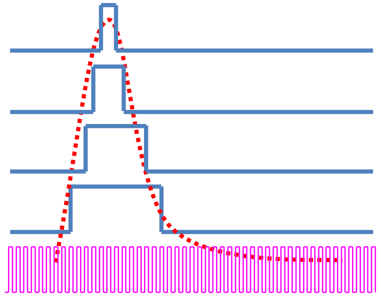


A 3-threshold fast ADC (4 bit - 500 MHz, implemented by discrete comparators) demonstrated effective in discerning the Bragg peak with the required precision.



Fast (<1 ns) comparator, with tunable (separate supply pin) digital output levels.

time



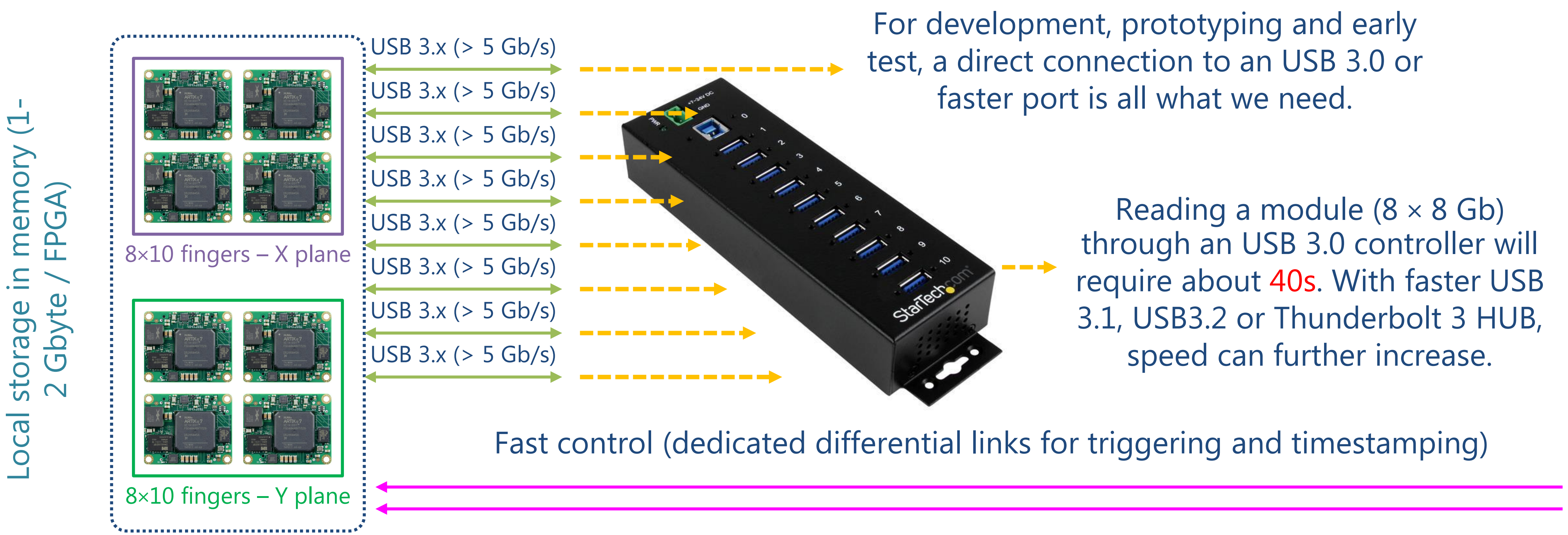
FPGA IO clock up to 500 MHz
Sampling DDR 1 Gb/s (1 ns resolution)

time

Final calorimeter module, managing 40 scintillators, with two FPGA on top. 12 such modules compose the final calorimeter. It is planned to <u>replace</u> the readout boards with custom-made ASIC, likely an adaptation from PET designs.

pCT scanner – Readout through USB based solution

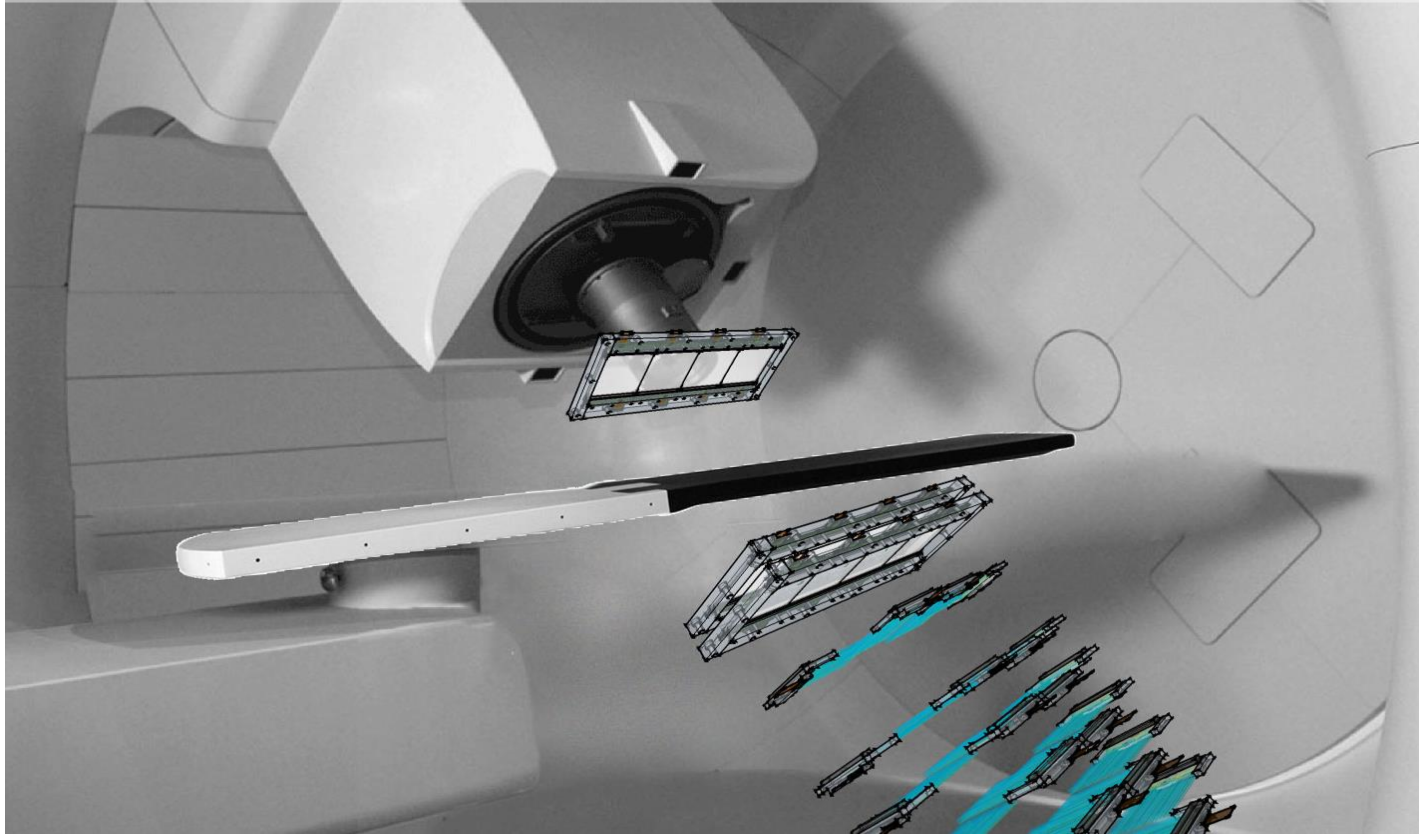
- The calorimeter and the tracker require about **112 high-speed links (> 1 Gb/s)** to stream the data within the 10s time of irradiation. Plus, readout electronic should be moderately radiation tolerant.
- We opted for local storage (DDR memory controlled by the FPGA) and “slow” USB readout.



An USB-based system offers several key advantages:
- Possible to address multiple devices independently on a single bus (up to 127). Easily scalable by adding further endpoints.
- The protocol is transparent and hardware/drivers are commercially available, as well hubs to create complex topologies.
- Multiple “older and slower” lines (e.g. USB 3.0) can be put together into faster standard (e.g. USB 3.2, thunderbolt) through commercially available HUBs by simply connecting the cables. The system can therefore grow without changing our hardware side (the FPGA), but simply upgrading to the best commercially available technology.

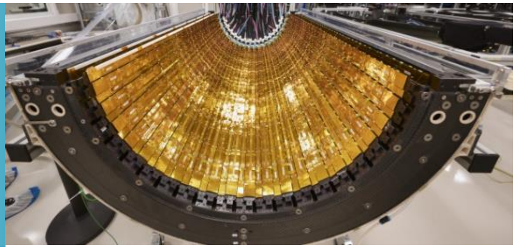
Outlook – Large Sensors from HEP to medical and back to physics

Medical design (low voltage, no gas, lightweight, ultra-fast) will allow on the fly imaging, targeting and patient treatment on the same station.

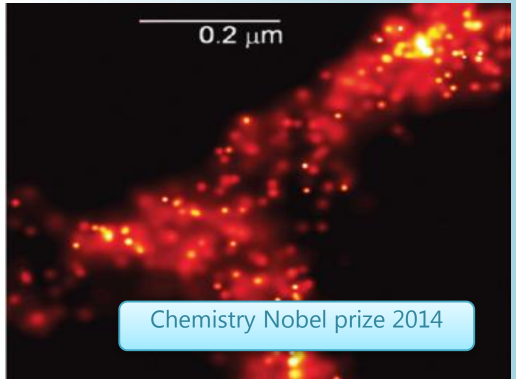


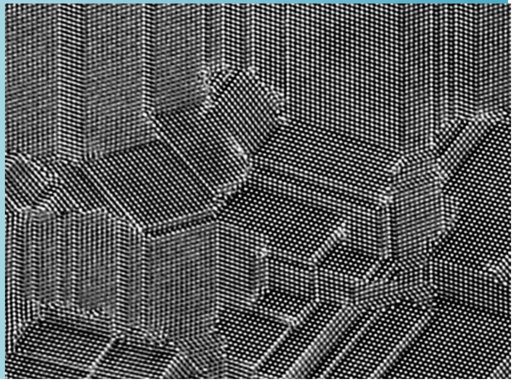
Large area sensor advancements (high speed @ ultra low power & high resolution with reliable, cost-effective sensors) will be an enabling technology for the next generation physics instruments and experiments.

Next generation HEP trackers, calorimeters: large surface, low material, low power.

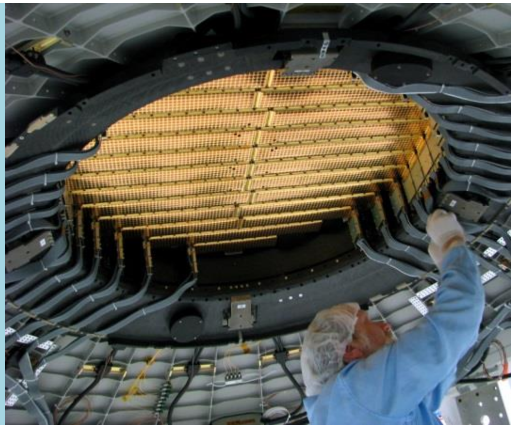


e⁻ and γ microscopy super-resolution requires maximum speed (in-matrix data compression) and small pixel pitch (10 μm).





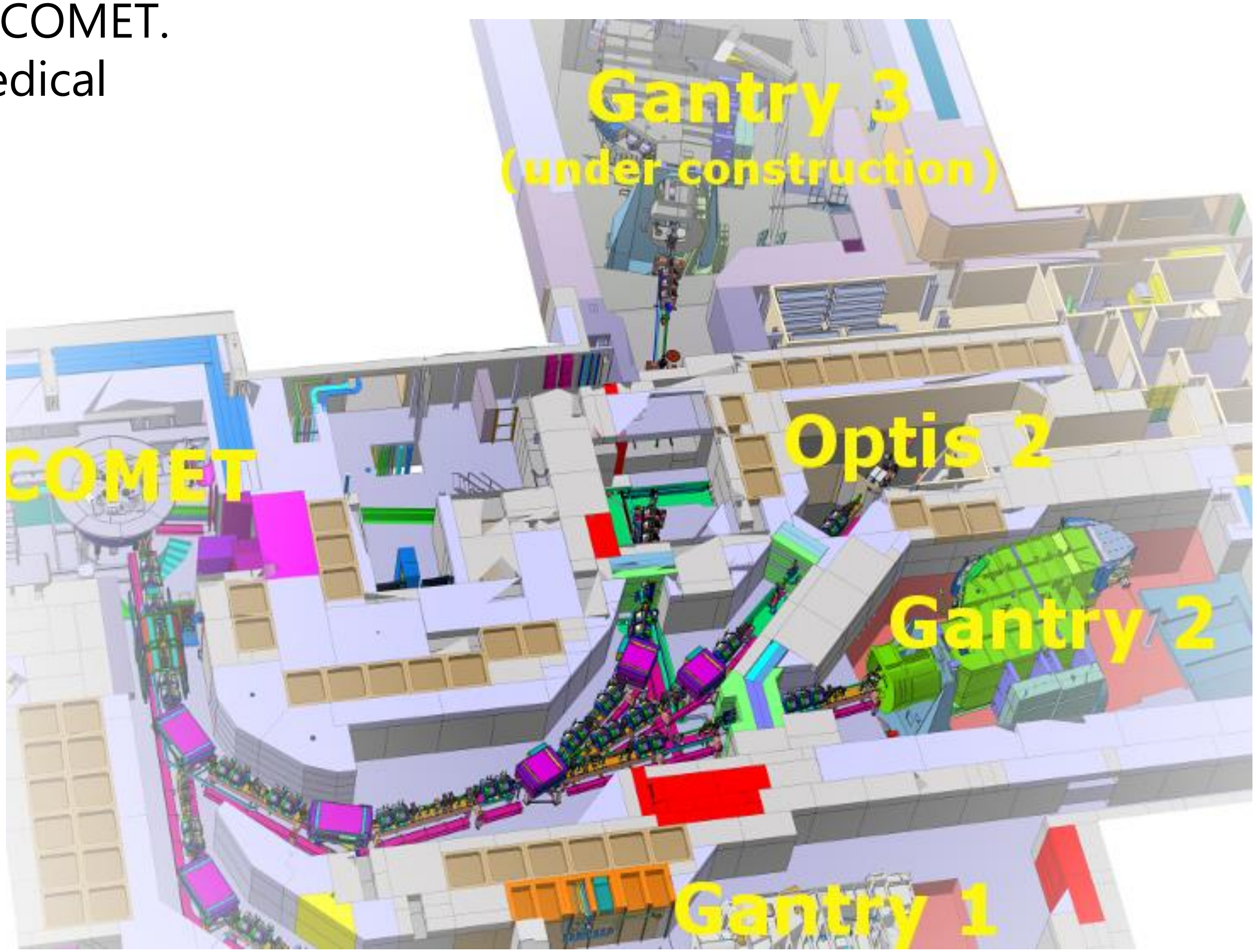
Space-born trackers and telescopes needs ultra low power, ultra high resolution (weak magnets there), extremely reliable (space spec) detectors.



Backup

Hadron-therapy – PSI proton therapy (reference example)

- Cyclotron-based facility, 3 gantry treatment rooms + 1 fixed beam for eye tumor.
- Limited medical annexes (ambulatories).
- In-house built super-conductiong cyclotron COMET. Developed by ACCEL (now part of Varian Medical Systems). Beam energy of 250 MeV.
- Kicker magnet switching time about 200 μs.
- Carbon wedge degrader as energy setting.0



Hadron-therapy – PSI proton therapy – Gantry 2

- Two fast magnets with speeds of 1 to 2 cm / msec in the left-to-right and head-to-feet axes respectively to scan through the tumour.
- In the third dimension, the depth of penetration of the protons, the design allows a change from one tumor layer to the next in about 100 msec (5 mm difference in proton range).

- Small spot size at all energies (for 100-230 MeV, the width is < 3-4 mm).
- X-ray system mounted on the gantry itself, which takes images in the direction of the proton beam.
- In-room sliding CT is for treatment planning and the daily verification of the patient position.

Hadron-therapy – PSI proton therapy – Optis 2

- Clinically open since 2010, 800 patients treated, fixed horizontal beam line.
- More than 99 % protons lost due to energy degradation (230 MeV to 70 MeV).
- Double-scattering process to ensure high transport efficiency of 70 MeV proton.
- Range shifter set the range and ensures pre-scattering of proton pencil beam.
- Homogeneous circular field of maximal 35 mm diameter.

- Two x-rays units provide orthogonal imaging of patient's eye.
- Chair mounted on a hexapod robot allowing a 6-degrees-of-freedom.
- Position of an eye (gazing angle) is defined through the fixation light (small LED).
- Intrafractional motion of patient eye is monitored using compact surveillance cameras.

Hadron-therapy – RINEKER proton therapy center (Munich)

- Clinically open since 2009, more than 1800 patients treated
- Four gantries room. 360° within 1 minute rotation and proton beam delivery with accuracy better than 0.5 mm.
- A fixed-beam room for dedicated precision irradiation of tumors involving the eye, brain, and face.

Hadron-therapy – Heidelberg Ion-Beam Therapy Center (HIT)

World first heavy ions gantry (600 tons movable with sub-mm precision).

Brute force approach necessary to perform effective research. Can be a model for viable practical therapy?

HIT gantry (Heidelberg)

HIT gantry (Heidelberg)