Medical applications

Outline

What I will cover

- Radiotherapy (the area most closely aligned to physics)
  - Background and timeline of key innovations
  - External vs internal radiotherapy
  - Radiation interactions with matter: photons or protons?
  - Beam delivery
  - Imaging and range uncertainties
  - Monitoring and dosimetry

What I won't cover

- Topics unrelated to radiotherapy: lasers, ultrasound imaging, prosthetics, drugs
- Radioisotope production and PET (maybe next year)
- Monte carlo modelling (maybe next year)
- Radiobiology (maybe next year)

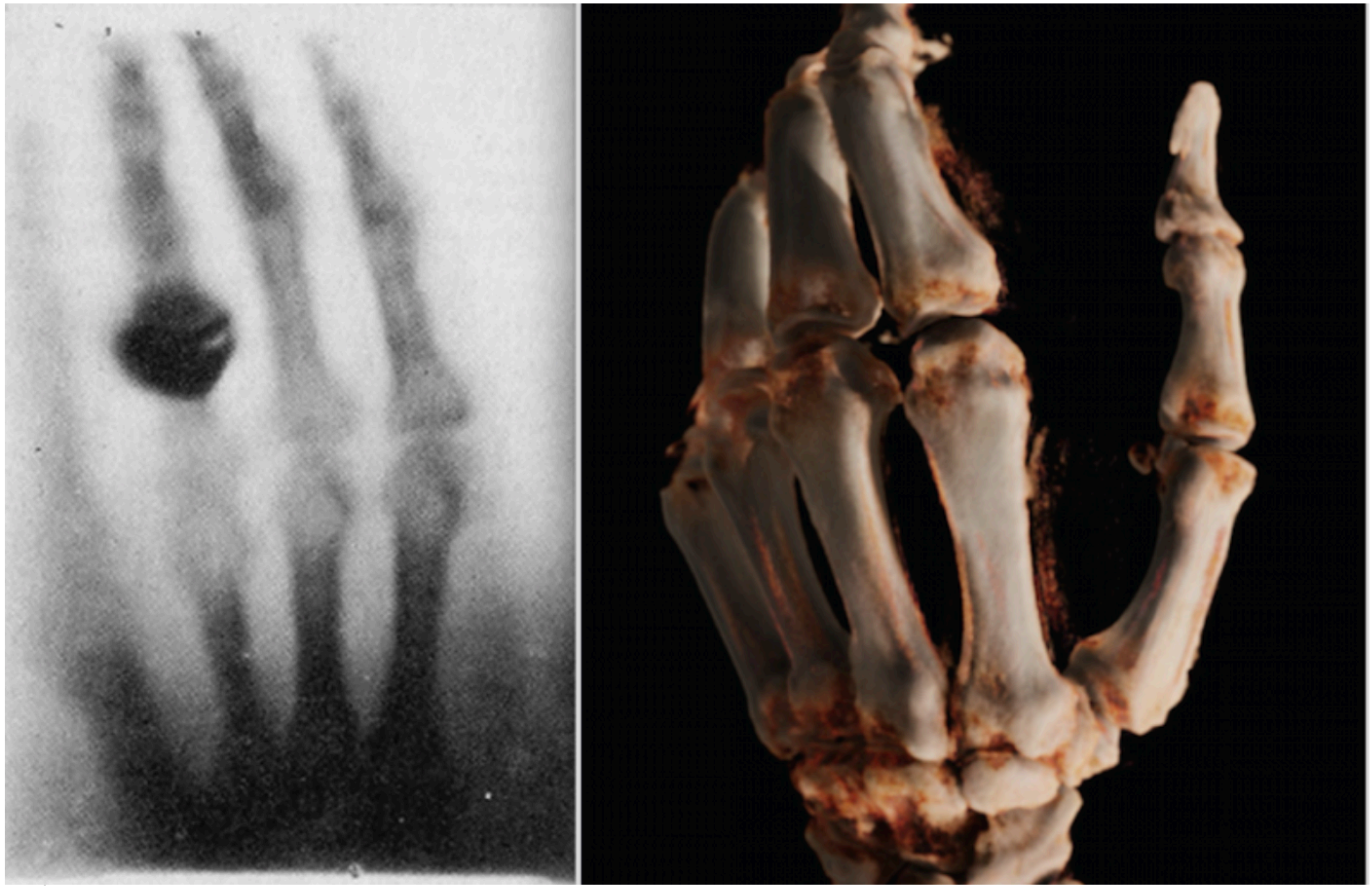
Who cares?

You should!

- Medical applications sometimes seen as very peripheral to e.g. HEP instrumentation but it actually contains interesting physics too (cf Phil Allport's slides on radiation interactions with matter)
- Many (usually non-physicists) often ask what the point of your research is, pointing to applications of your research into imaging and treatment of cancer helps with science communication / outreach
- Many physics students (some after PhD) will complete the NHS medical physics STP course to become medical physics -> one of the primary career paths for physics graduates - at least in the UK

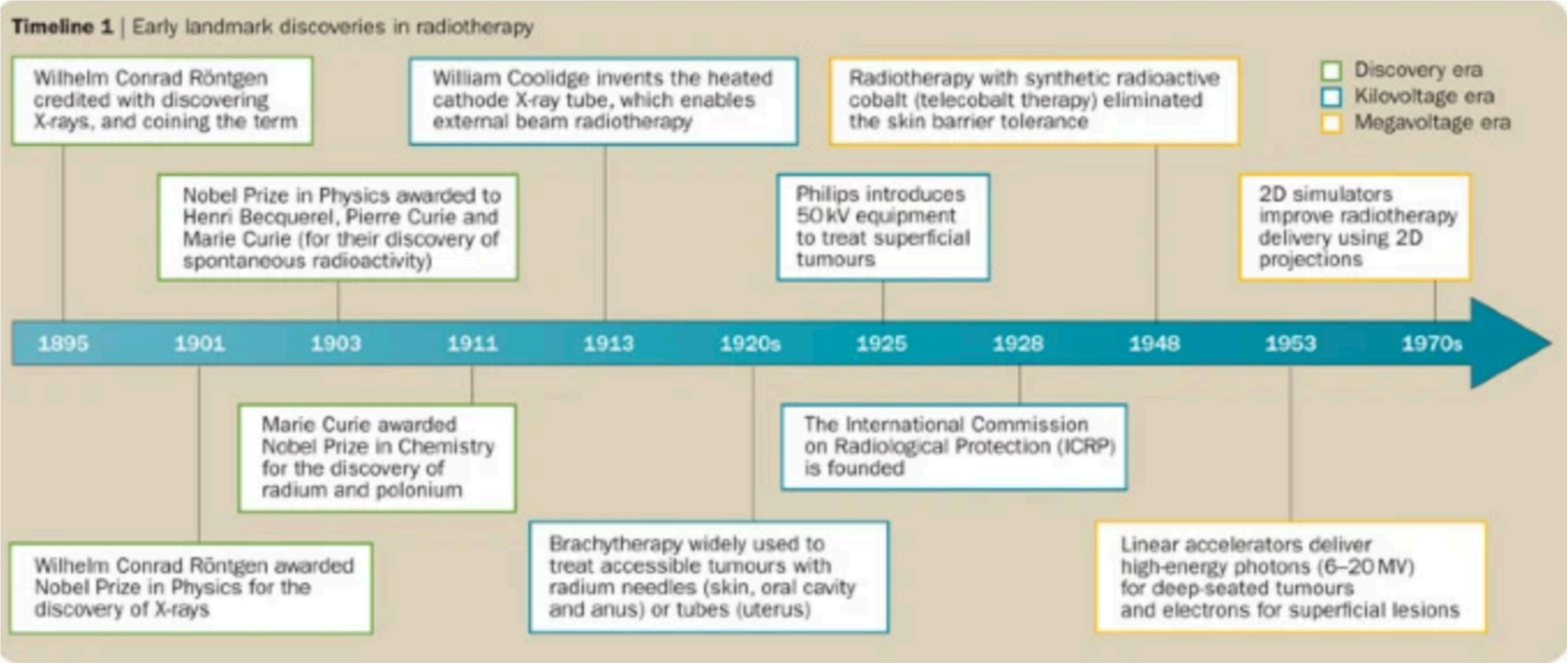
Physics and medicine

X-ray Has Come a Long Way in 100 Years



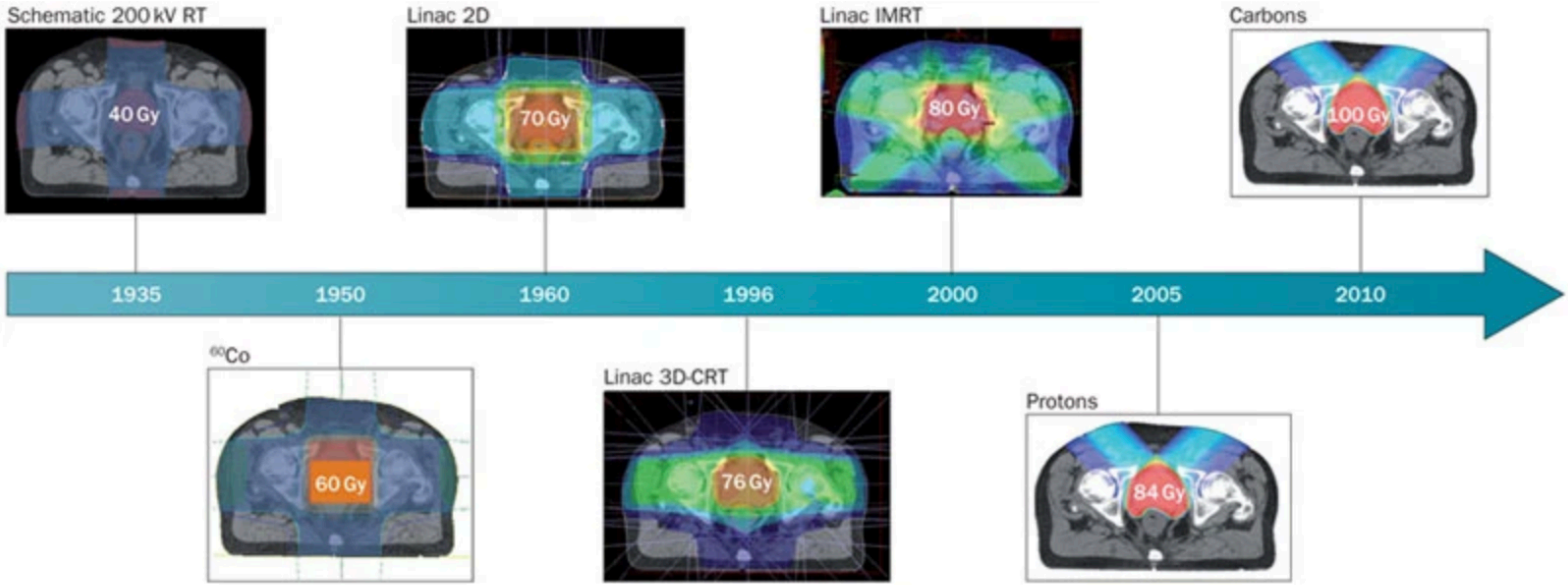
Left, the first X-ray ever made of Roentgen's wife's hand in 1895. Right, a cone-beam CT 3-D reconstruction of a hand in 2015 using a new robotic digital radiography (DR) X-ray system. https://www.itnonline.com/content/blogs/dave-fornell-itn-editor/x-ray-has-come-long-way-100-years

Timeline of radiotherapy with x-rays



Timeline of innovations in x-ray radiotherapy (sorry it's blurry)

Comparison of radiotherapy modalities with time

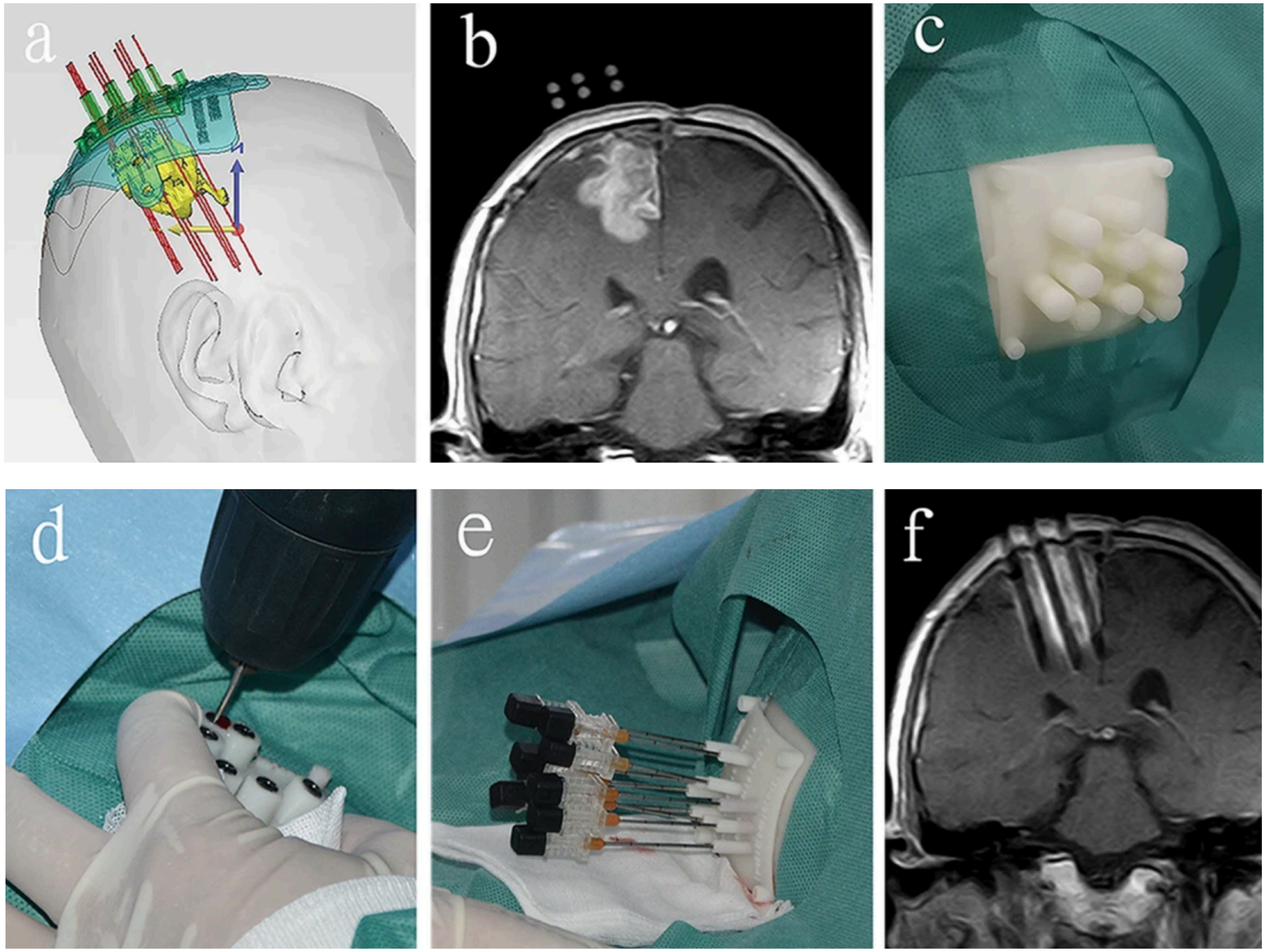


Prostate cancer irradiation is a good example of the improvement of radiotherapy technology over the past decades. By increasing the beam energy and the precision of the targeting, it was possible to escalate the dose to the prostate without exceeding the tolerance dose of healthy tissues; allowing the move from palliative irradiation to curative treatment. https://doi.org/10.1038/nrclinonc.2012.203

External vs internal radiotherapy

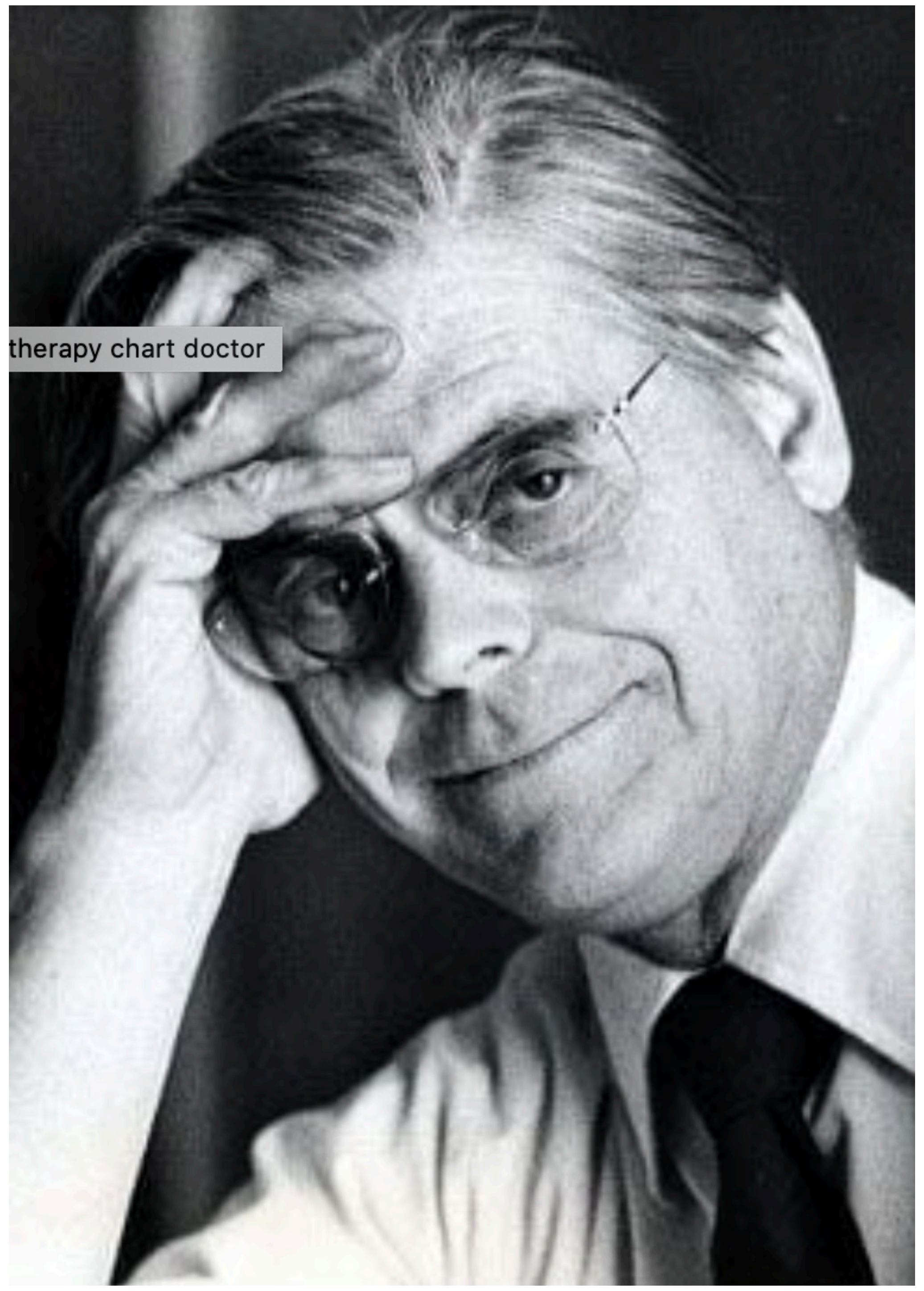
Radiotherapy with an external beam of x-rays

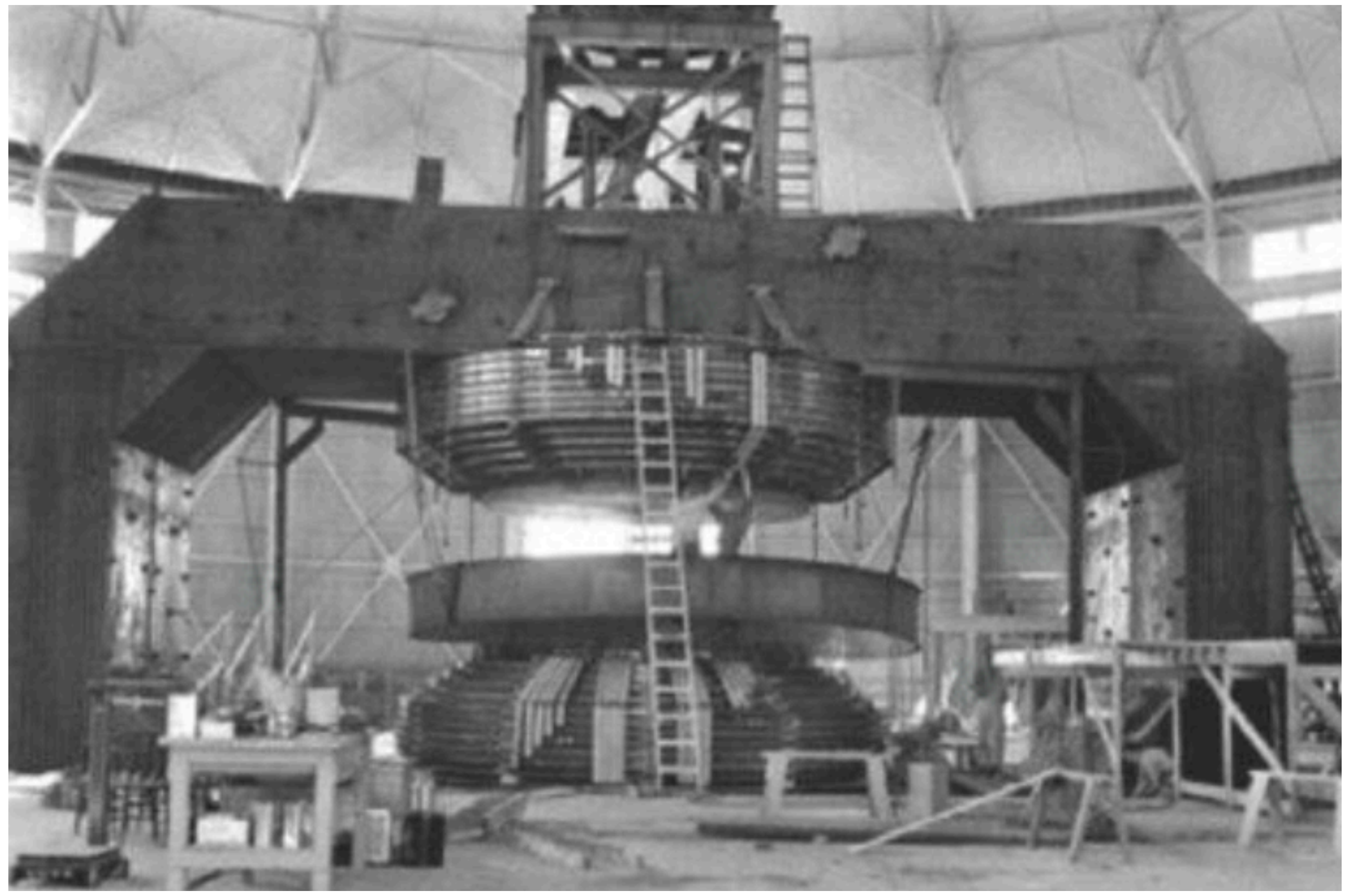
Brachtherapy with ^{125}I wires

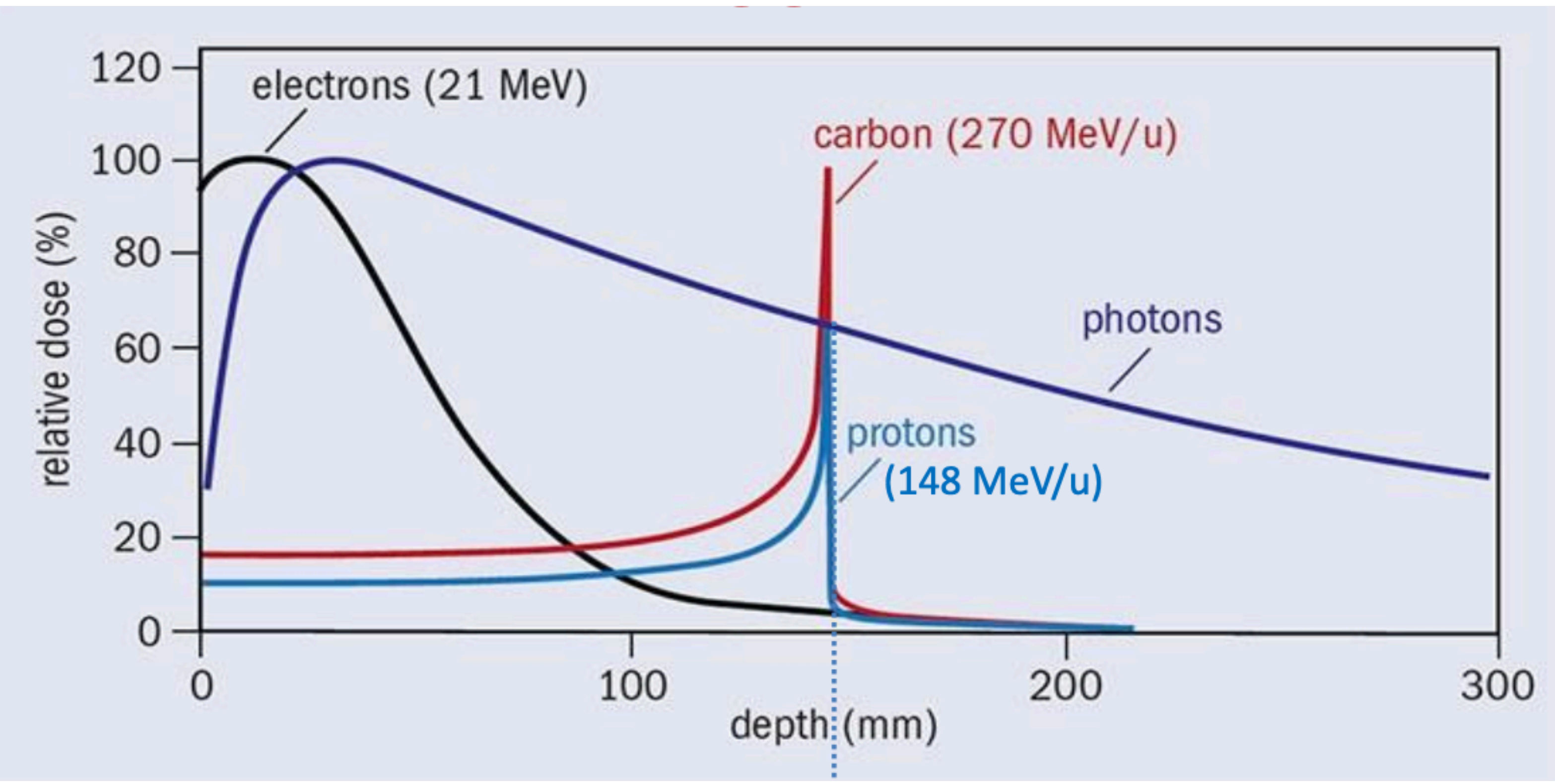


The procedure of 3DNPT combined with MR-guided ^{125}I brachytherapy for recurrent glioblastoma. https://ro-journal.biomedcentral.com/articles/10.1186/s13014-020-01586-4

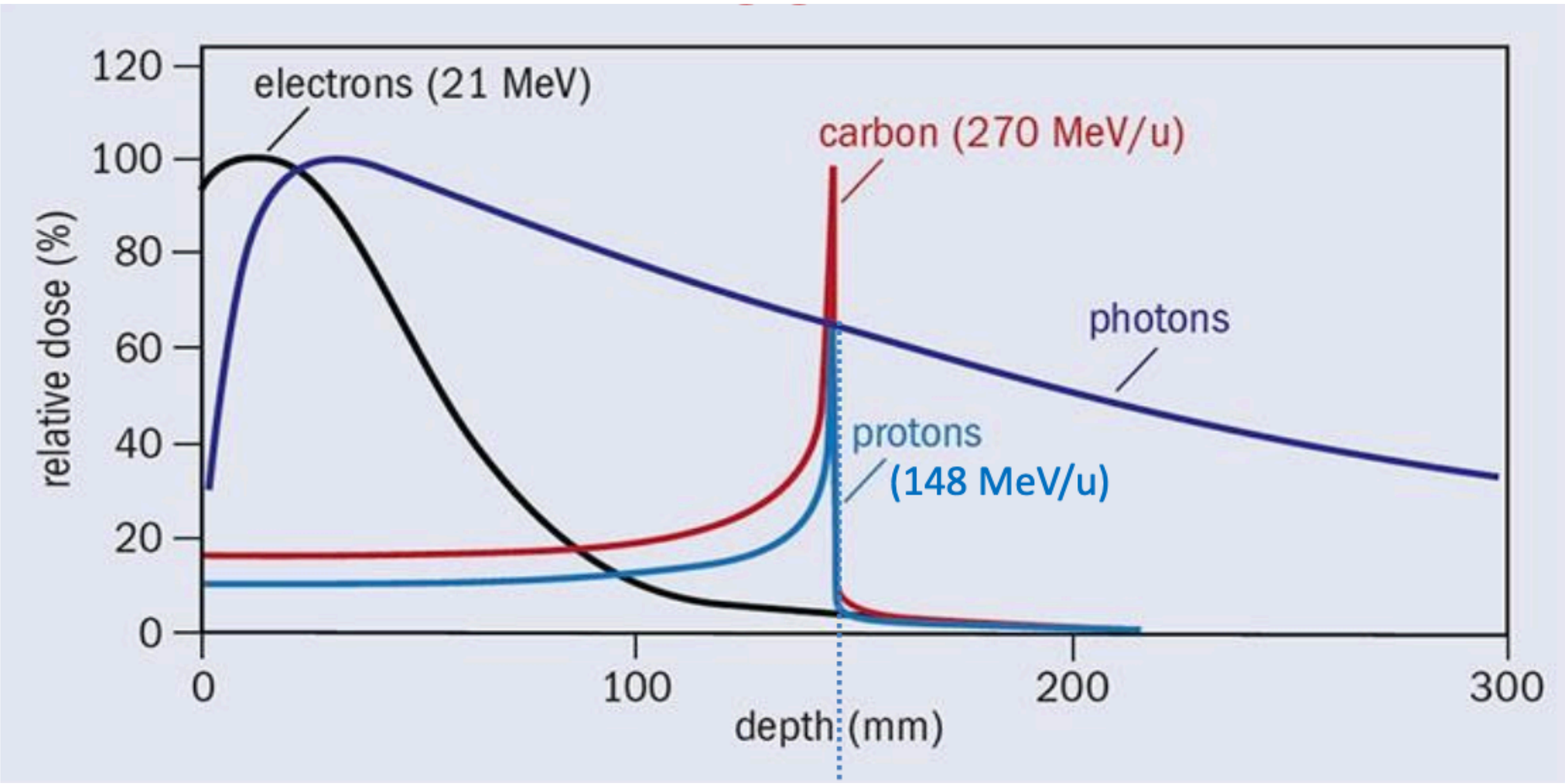
Charged particle radiotherapy

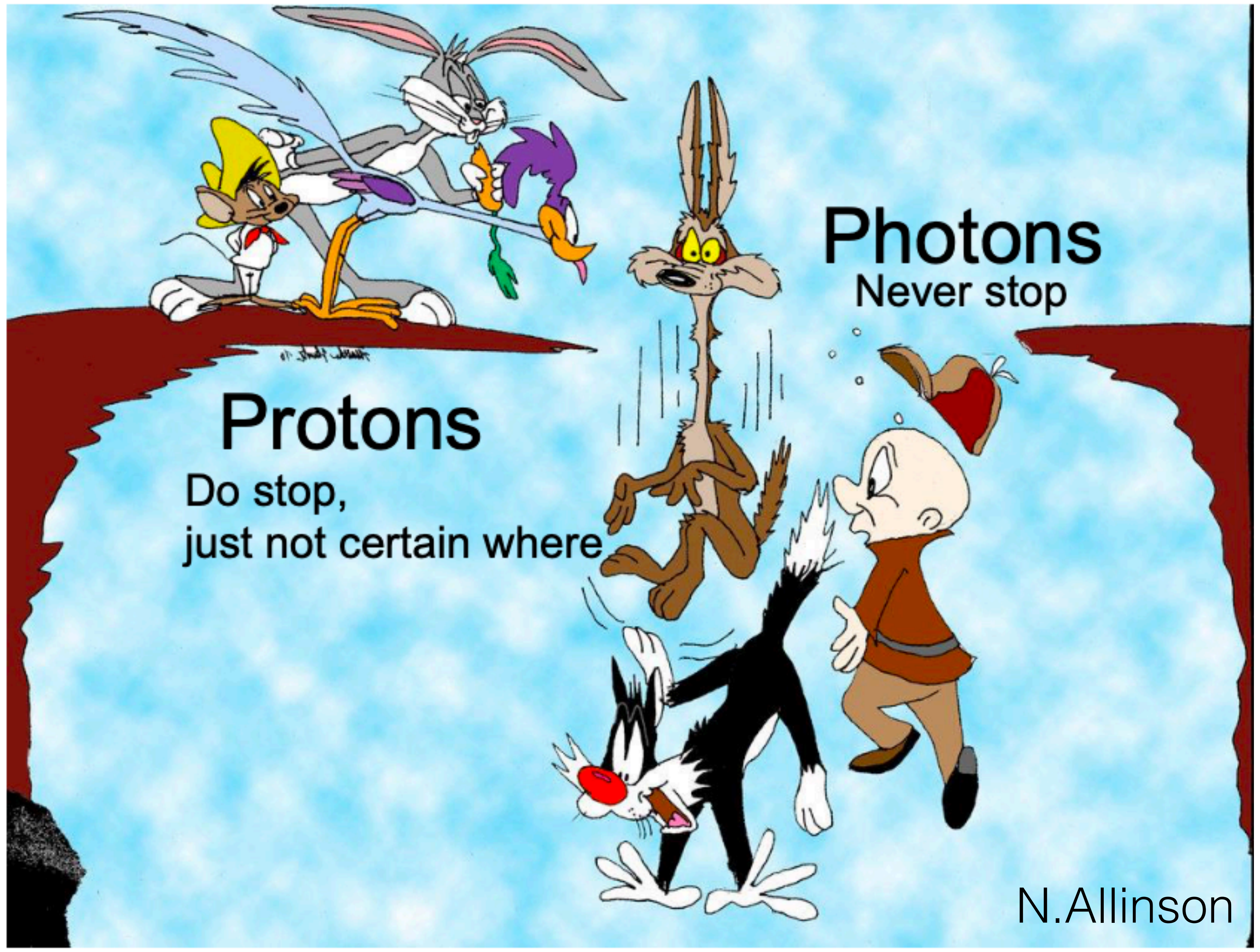






Photons vs protons

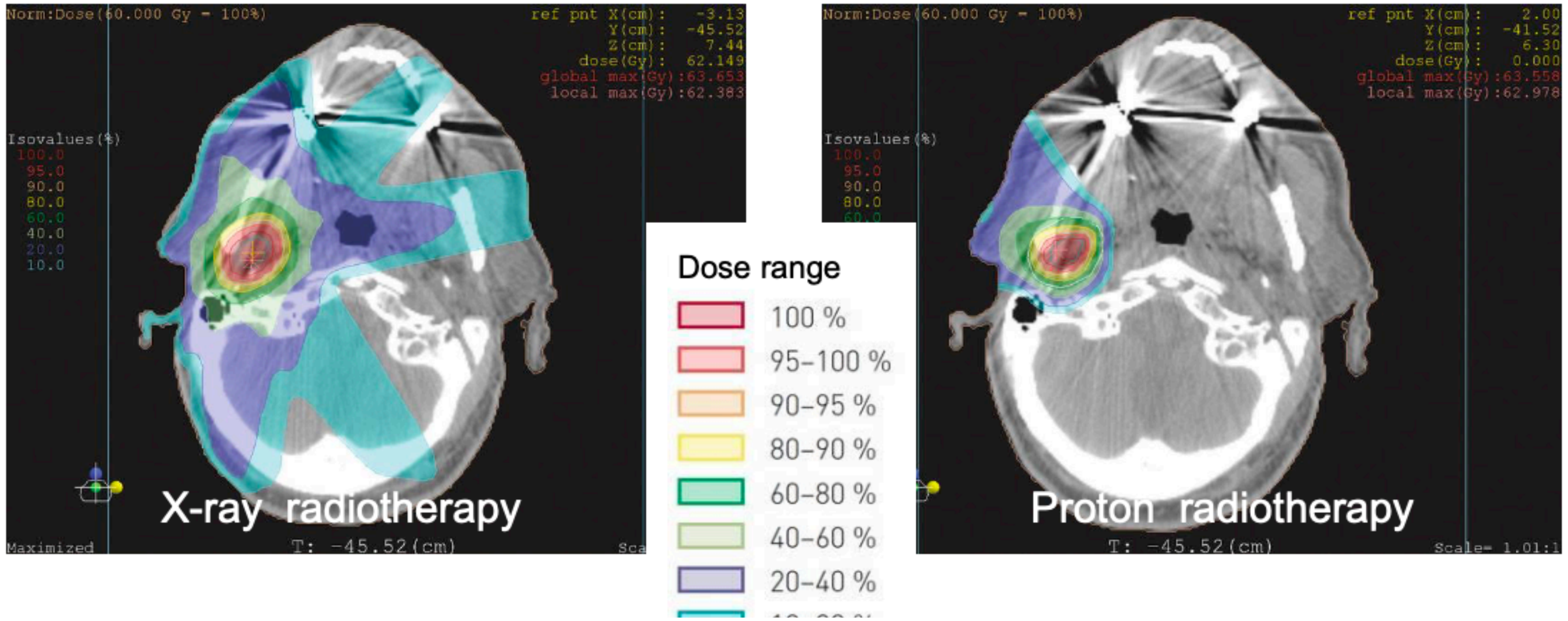


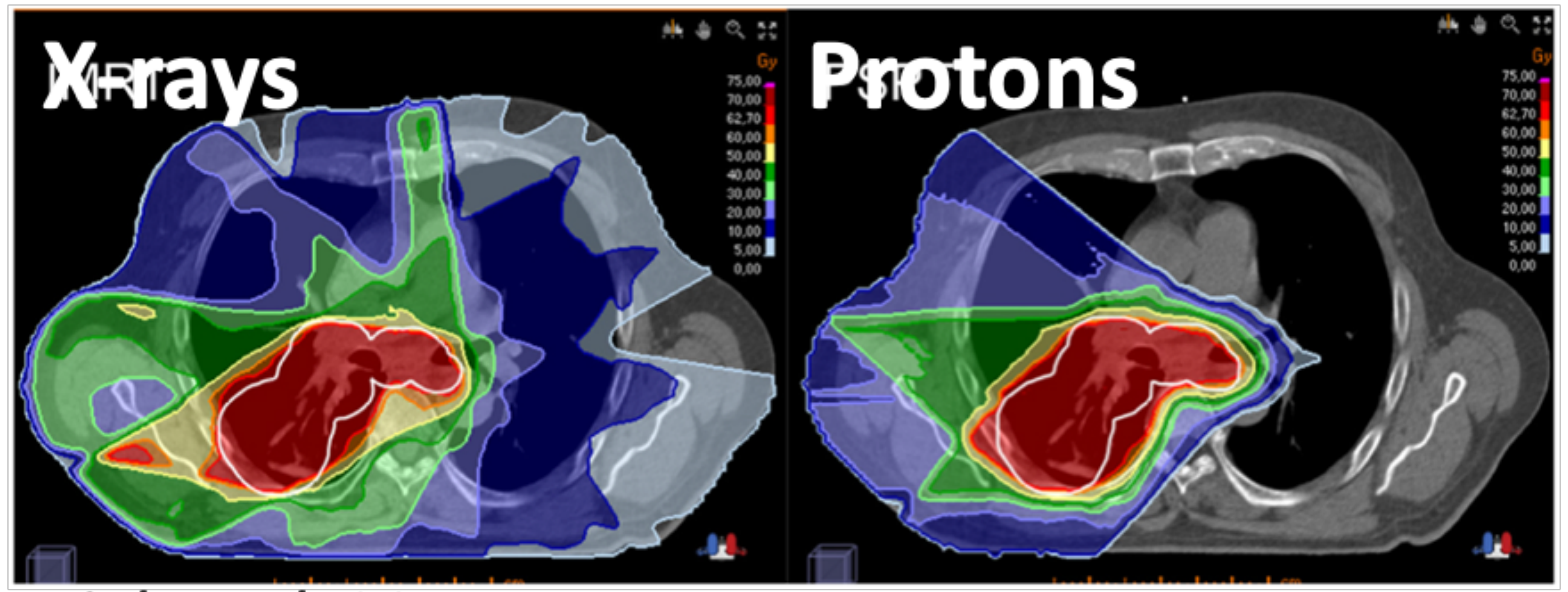


The advantage is the disadvantage

UNIVERSITY OF LIVERPOOL

Photons vs protons





Wink et al. 2014

Advantages of Proton beam therapy (PBT)…..

- Better targeting of tumour, reduced dose to healthy tissue
- Tumours in the head and neck region
- Tumours near the spine or other critical organs
- Some types of brain tumours
- Most childhood cancers

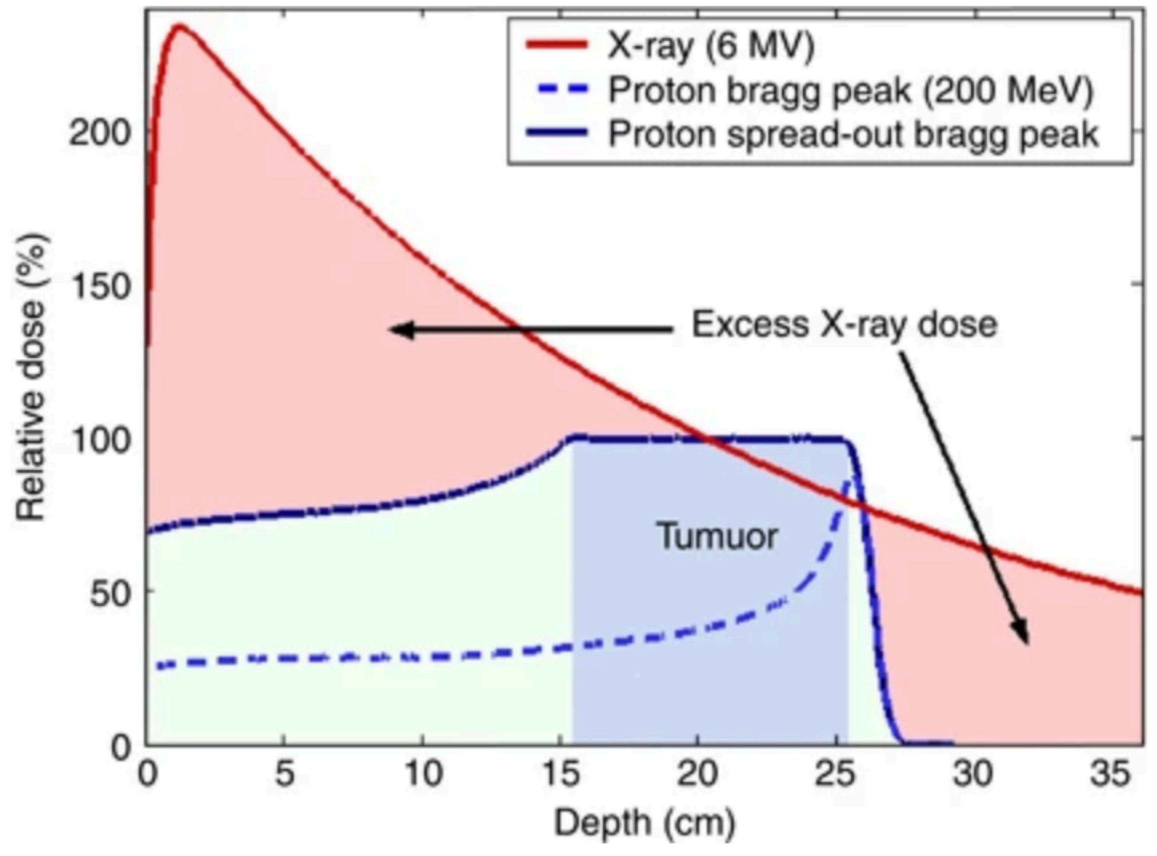
Treatment sites:

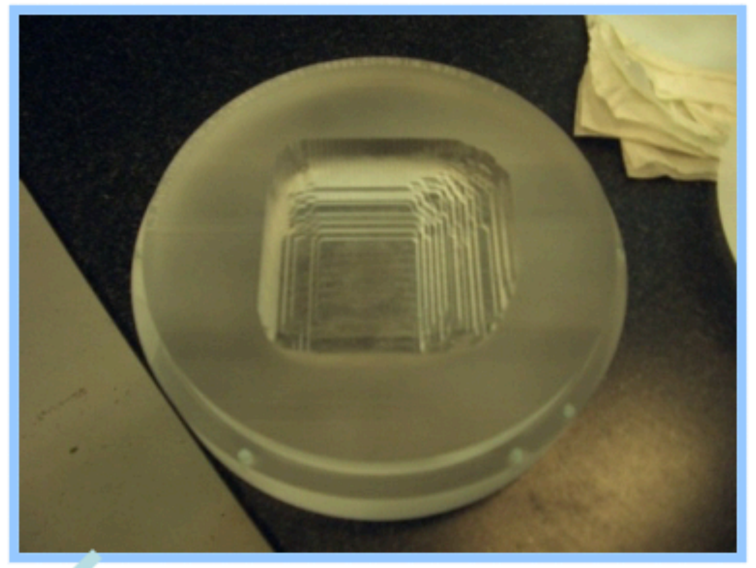
- **Paediatrics – reduced occurrence of secondary cancers**
- **Tumours near critical organs**

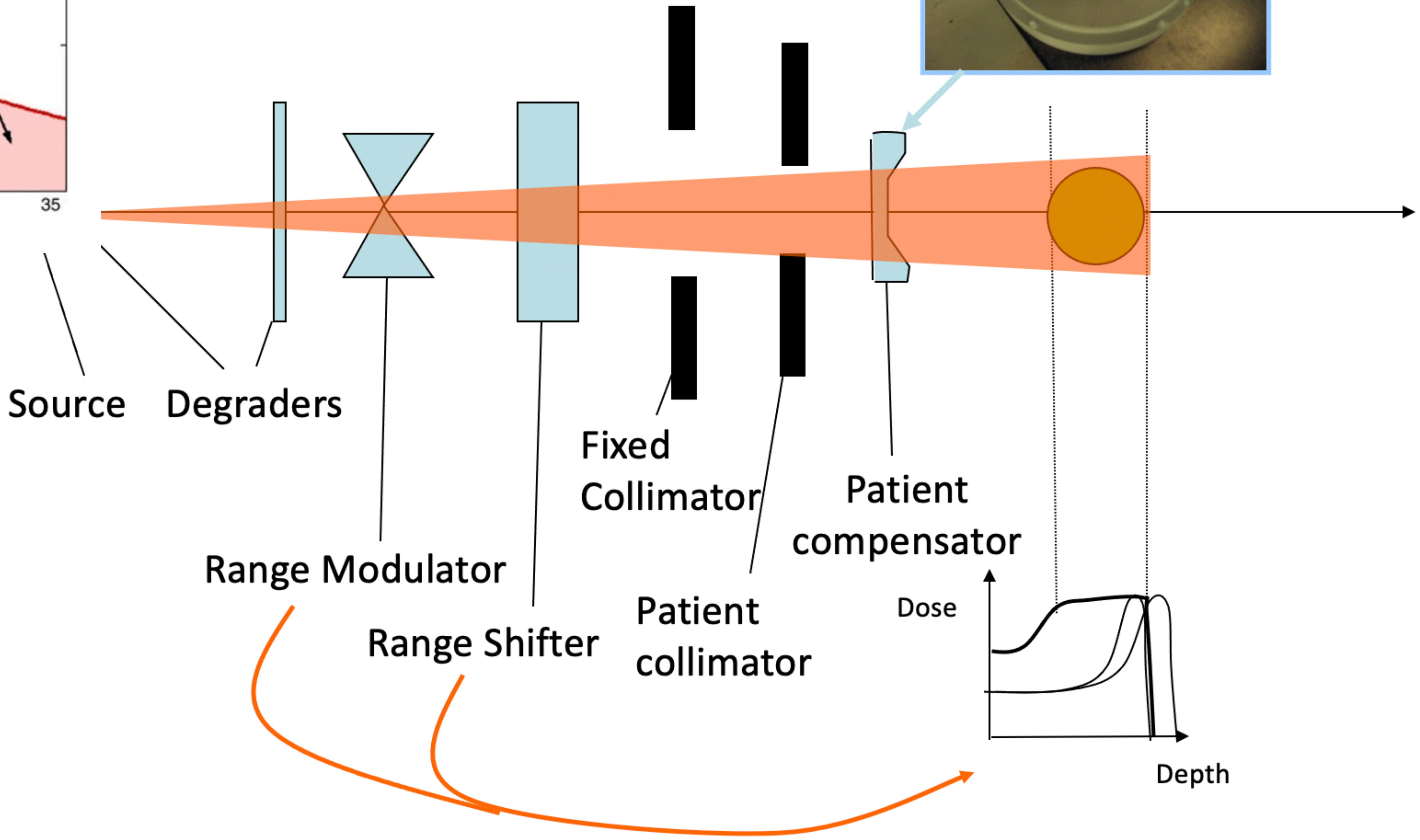
Particle therapy advantages:

- **Potential for much improved dose targeting**
- **Much reduced entrance and exit dose**

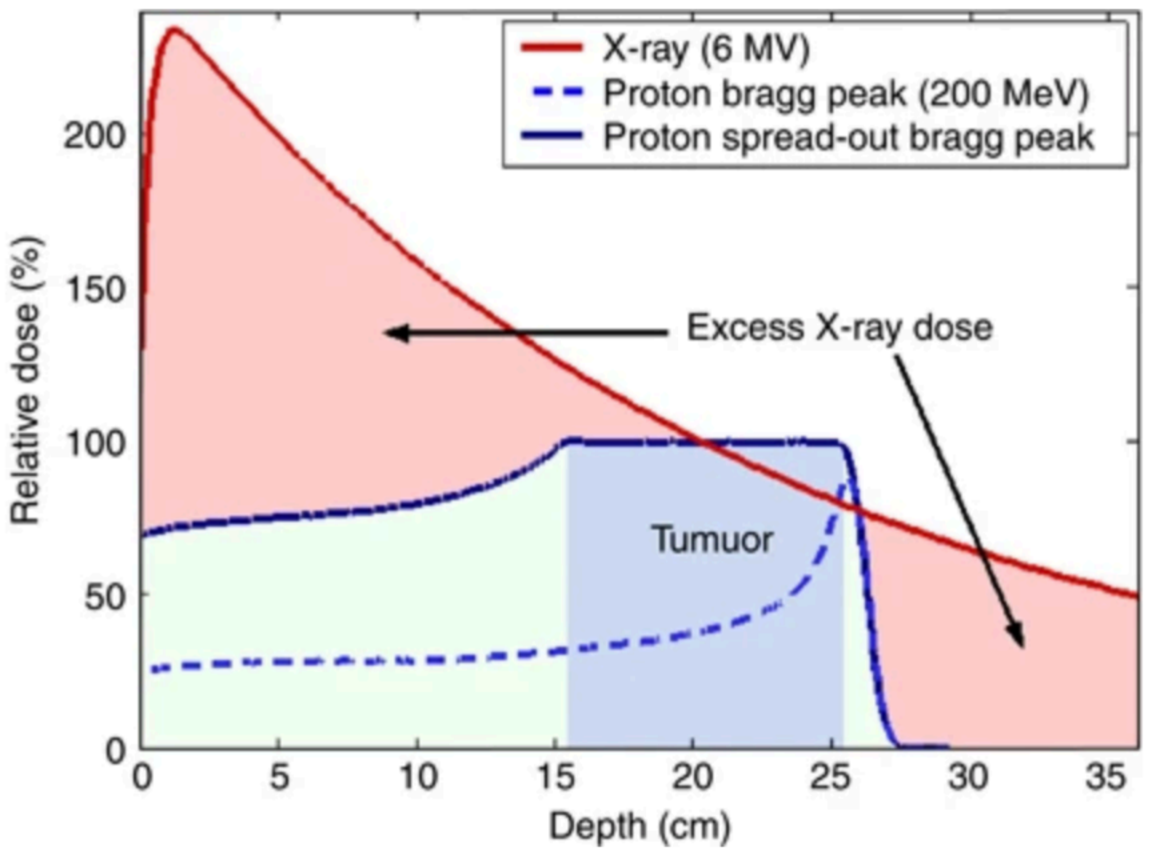
PBT: Passive scattering

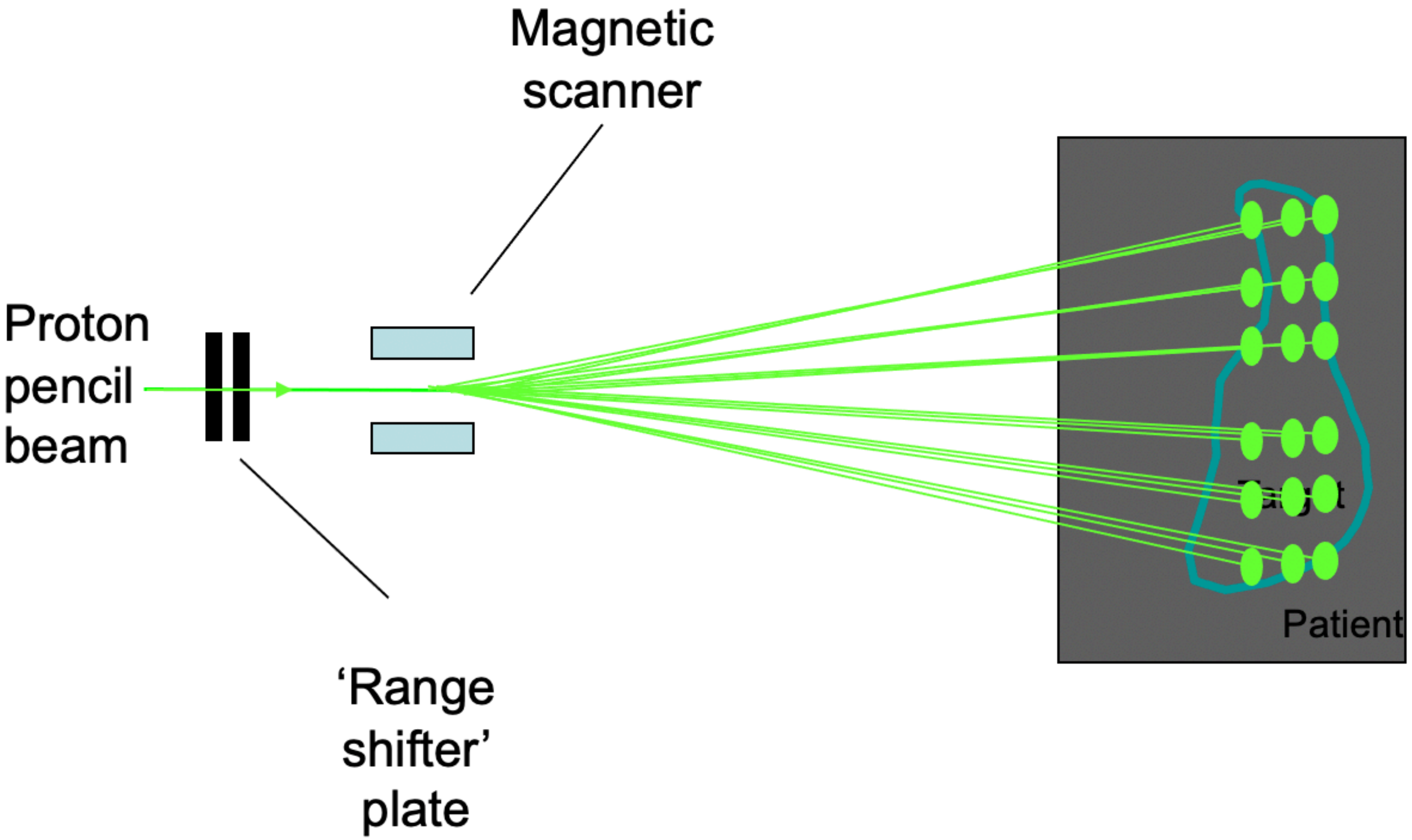




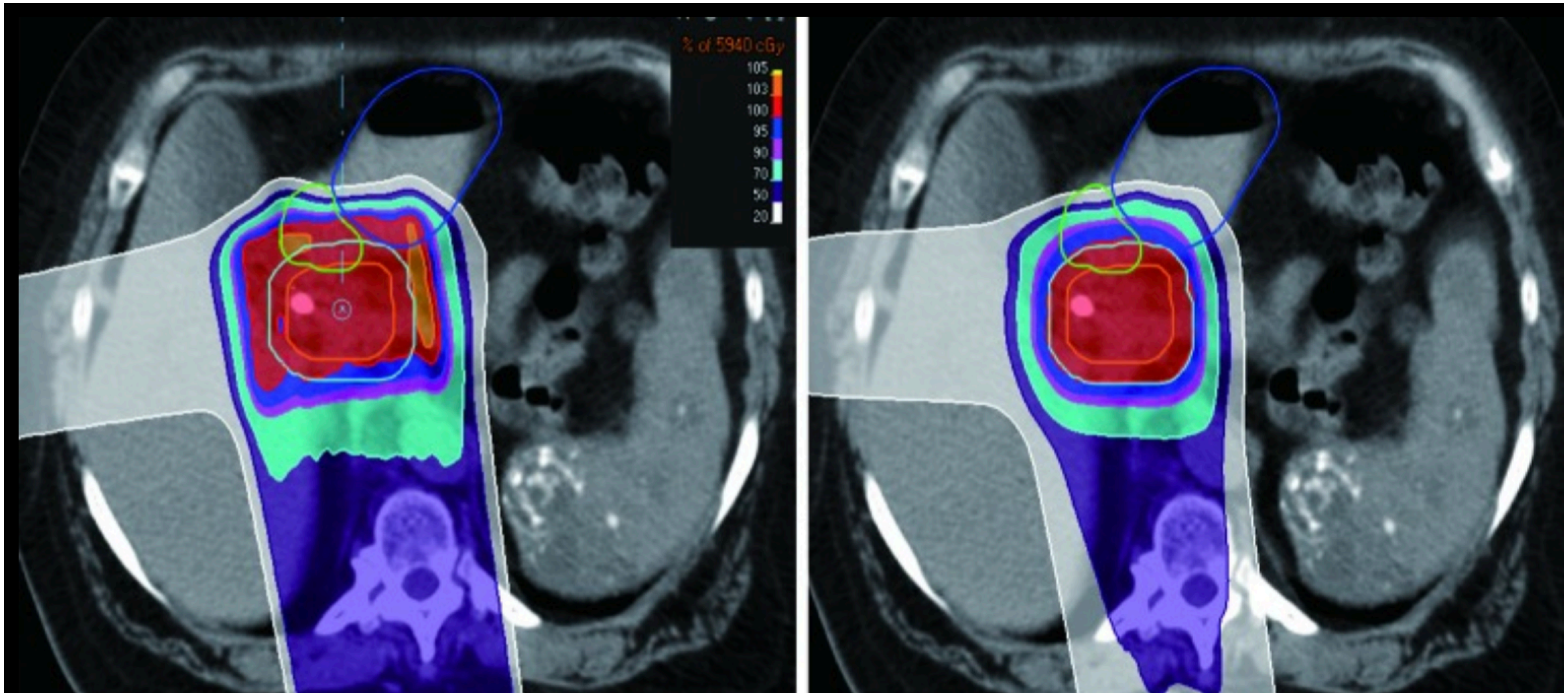


PBT: Spot scanning

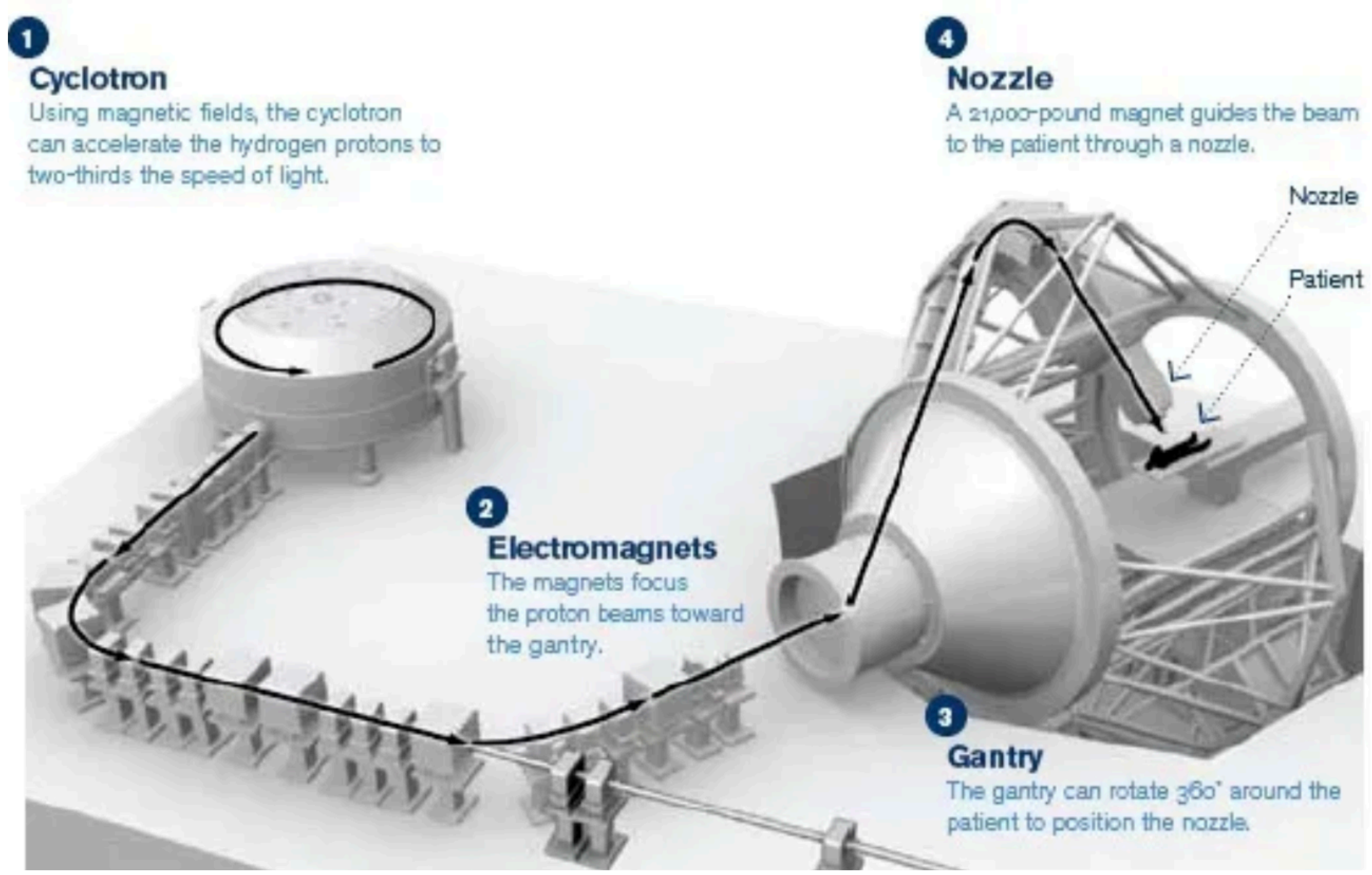




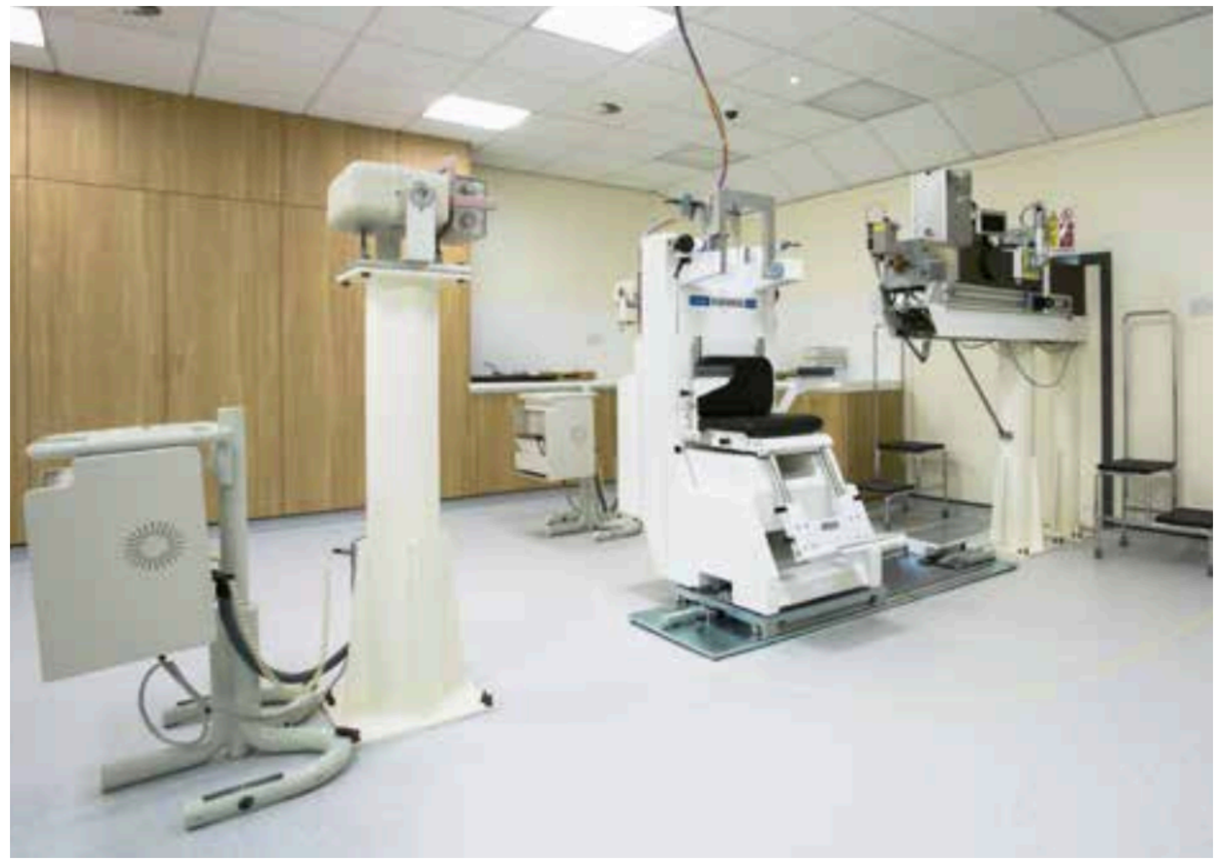
Passive scattering vs pencil beam scanning



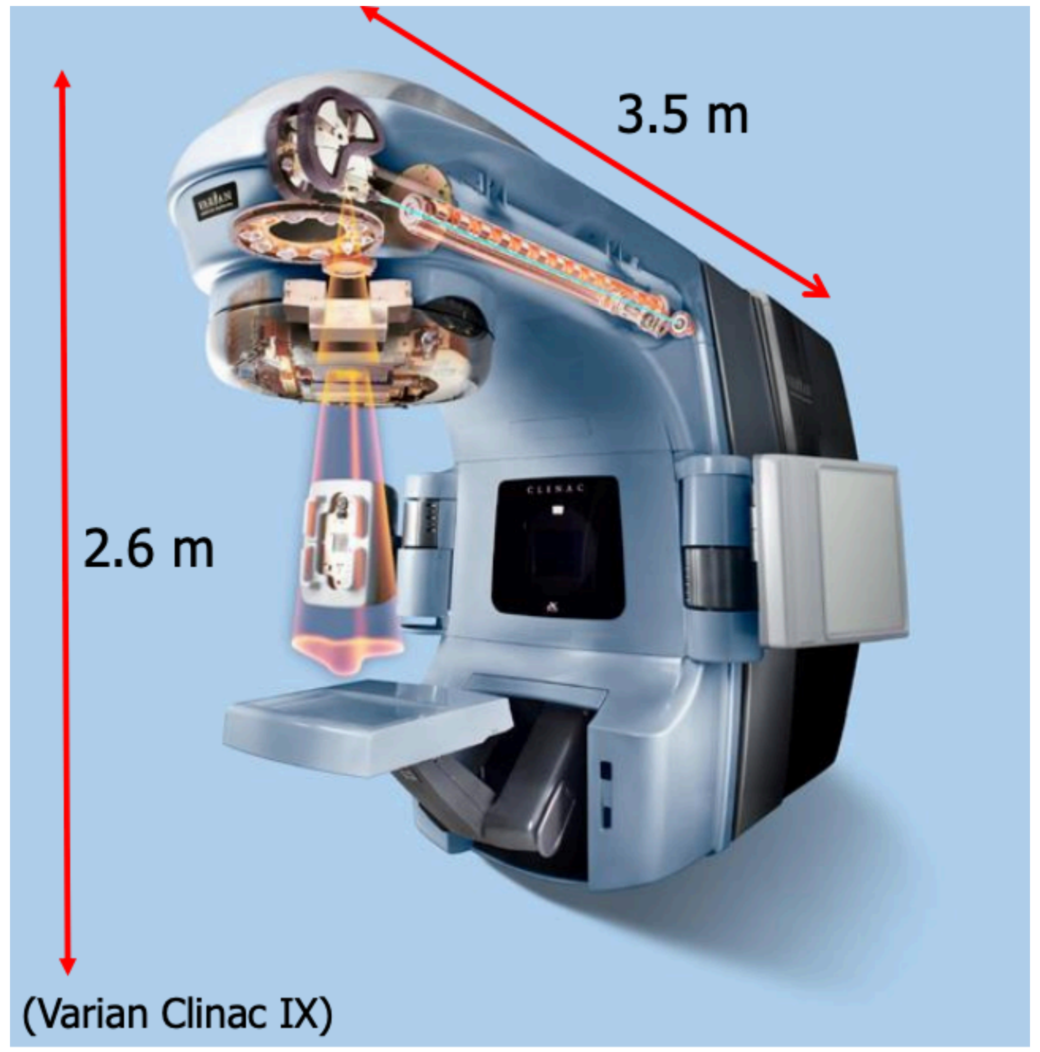
Gantry vs fixed target



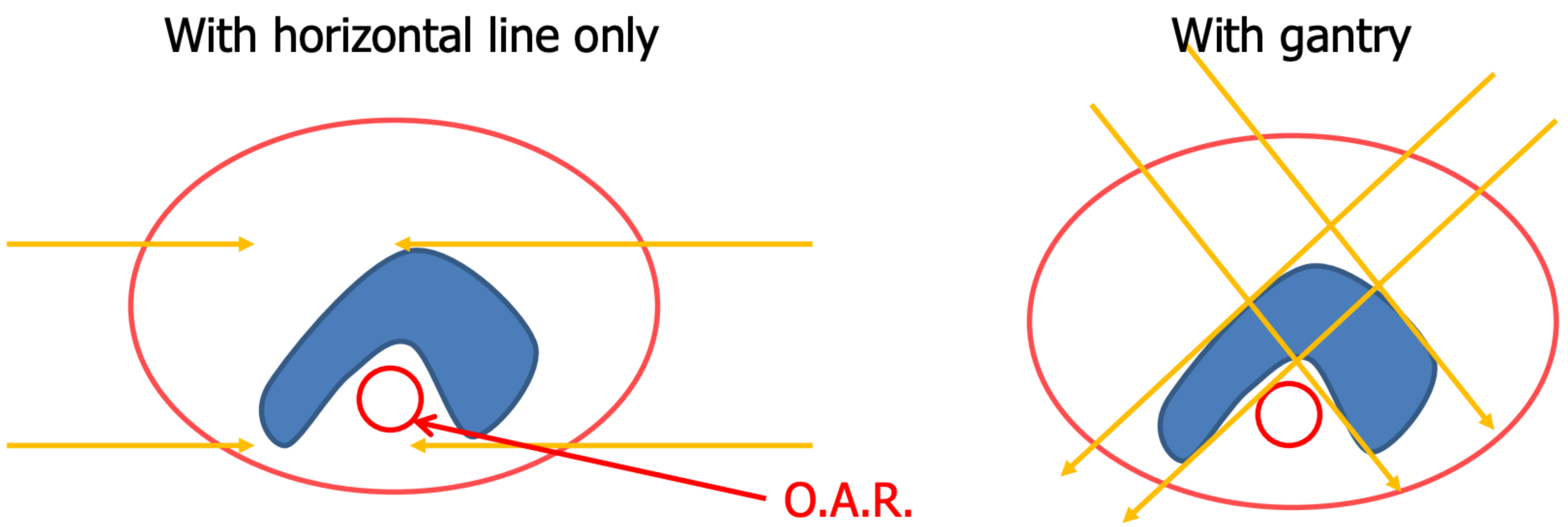
Fixed target proton therapy (Clatterbridge, UK)



- For x-ray machine whole linac is inside the gantry
- For protons or ions the whole beam line including magnets has to rotate around the patient
- Huge additional cost for particle therapy centres



Gantry vs fixed target



- To treat patients in in the same position in which CT, PET and MRI were acquired.
- Patient rotation only around gravity to preserve internal organs and soft tissue geometry
- To provide the maximum flexibility in selecting the irradiation direction when optimising the dose delivery
- To allow a "robust" treatment planning. Exploiting the sharp distal fall off can be risky in some cases and a gantry helps in avoiding fields directed towards an Organ At Risk (OAR)
- Avoid density heterogeneities
- Minimize SOBP extension (less energies required and better peak to plateau ratio)
- For x-ray machine whole linac is inside the gantry
- For protons or ions the whole beam line including magnets has to rotate around the patient

Carbon gantry vs proton gantry!

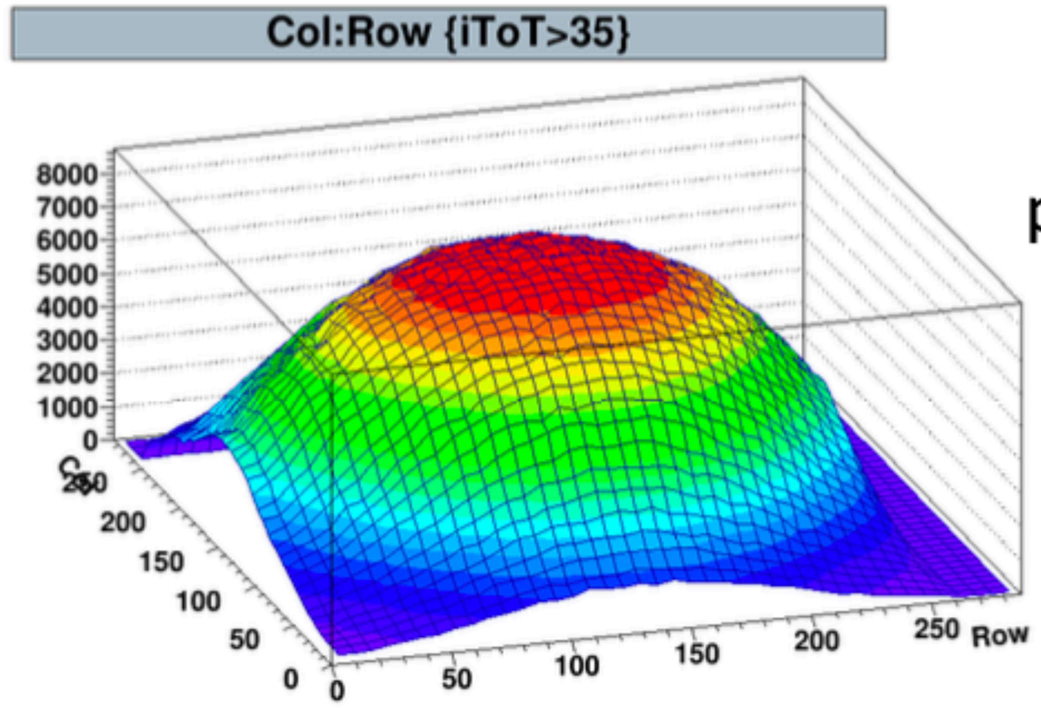
Carbon Gantry

- The HIT Gantry: the only clinical C Gantry
- L = 25 m x f = 13 m, 600 t rotating mass

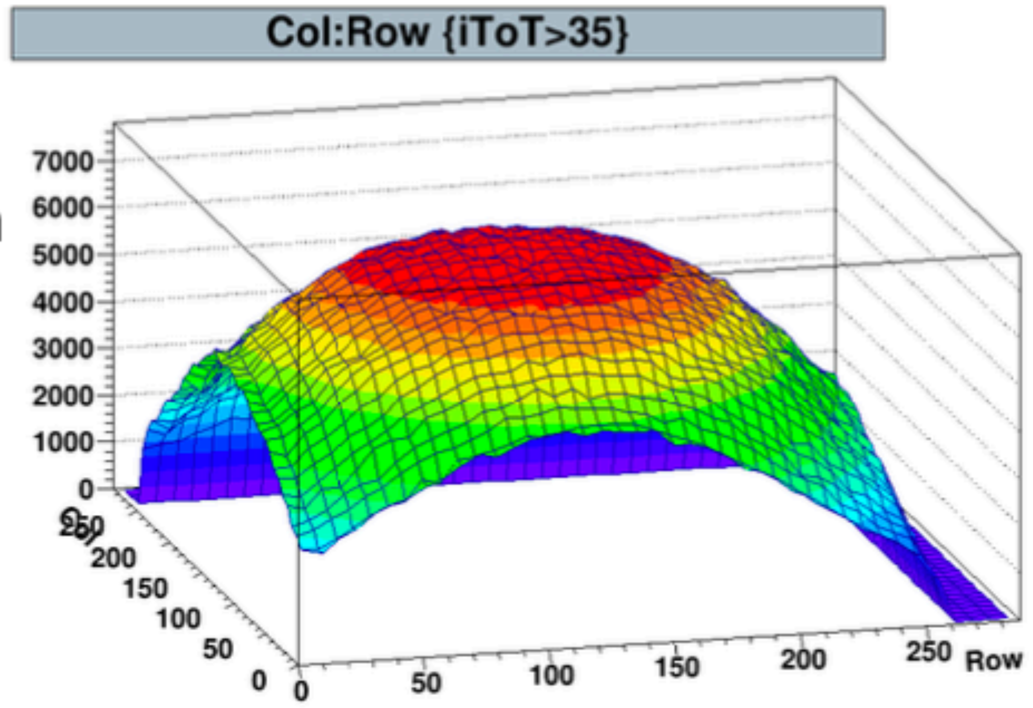
Beam monitoring and dosimetry

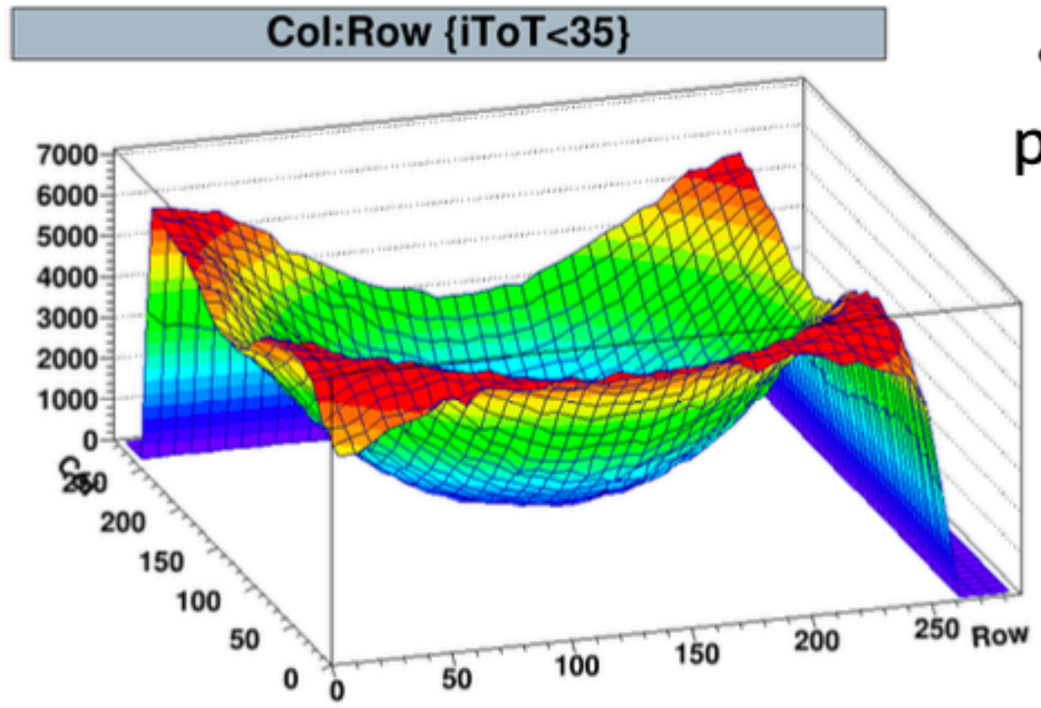
ProteusOne beam profile and Energy measurements with Timepix3 chip

- 25mm water depth
- 120 MeV Protons
- 107mm water depth

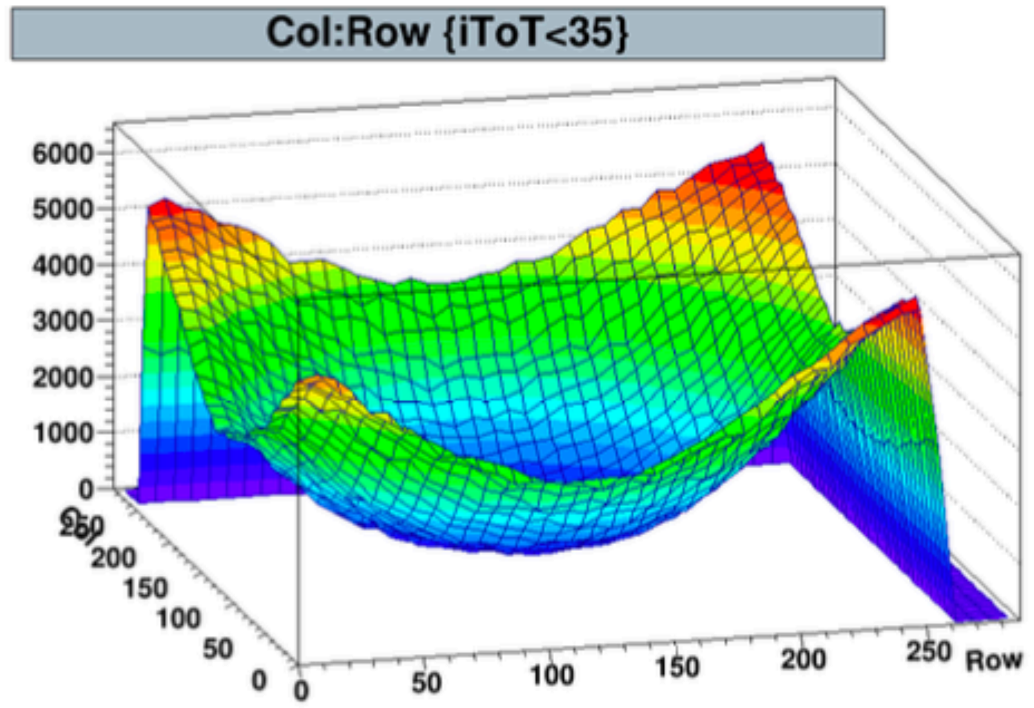


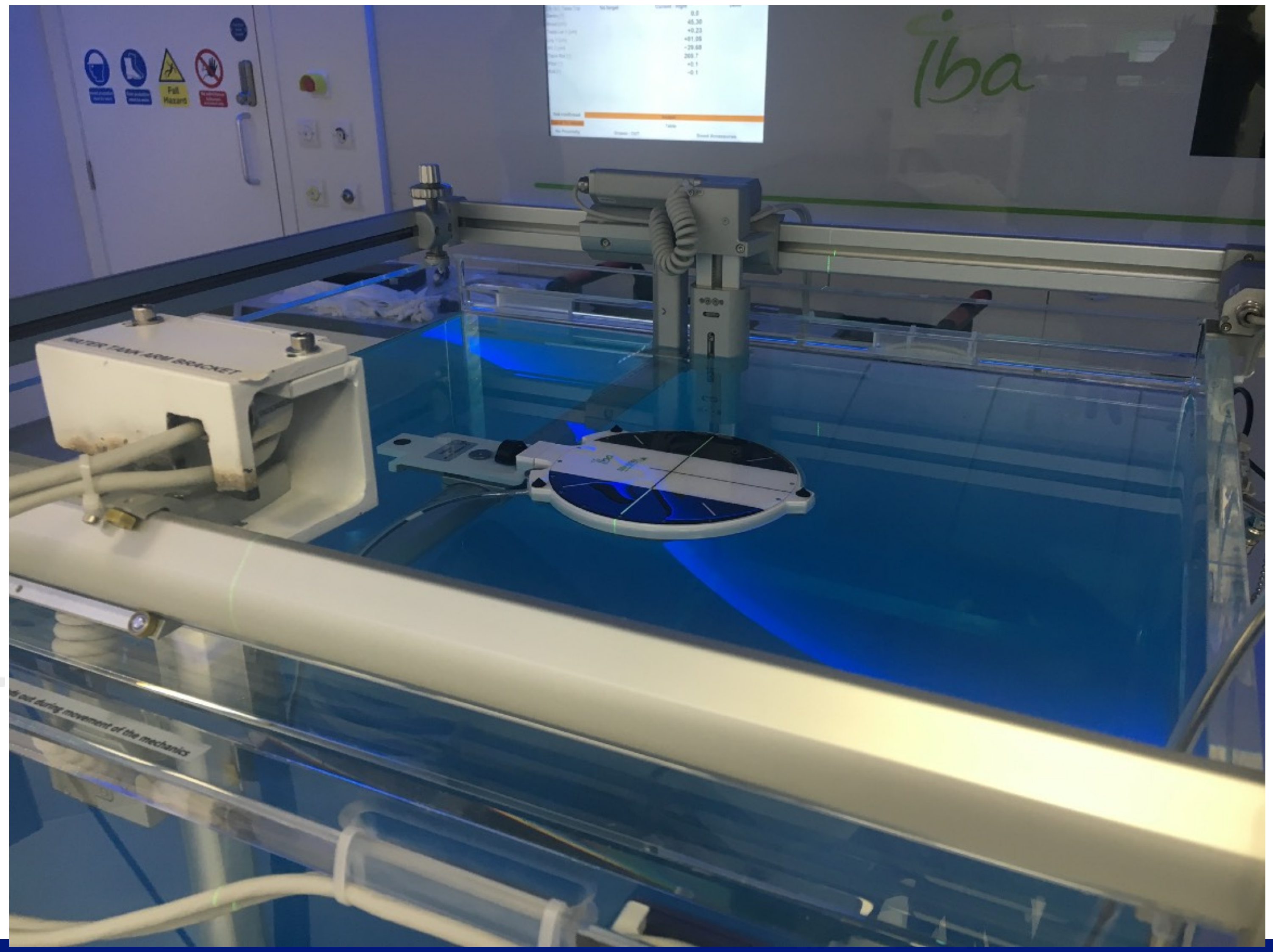
- Most energetic protons in the beam



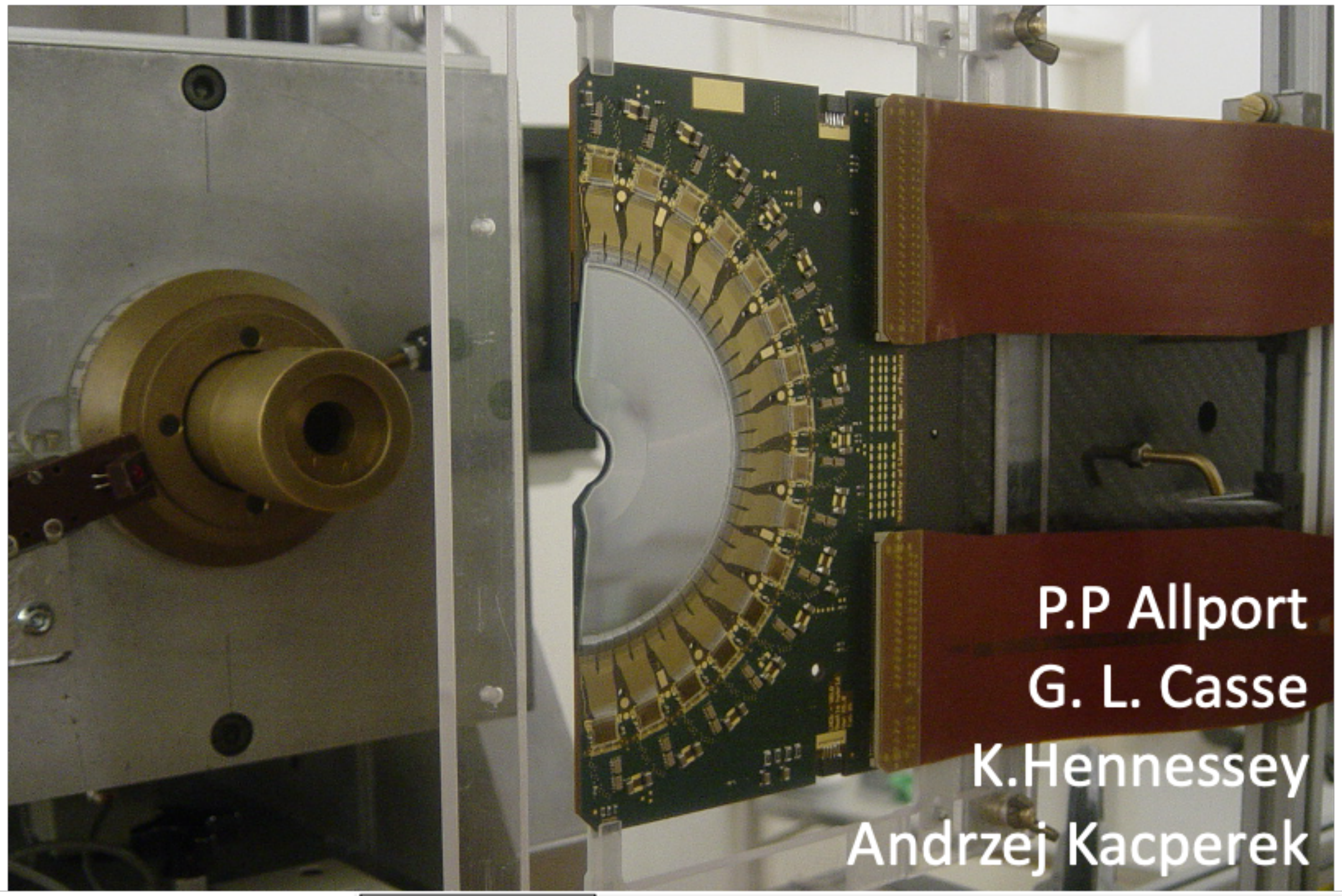


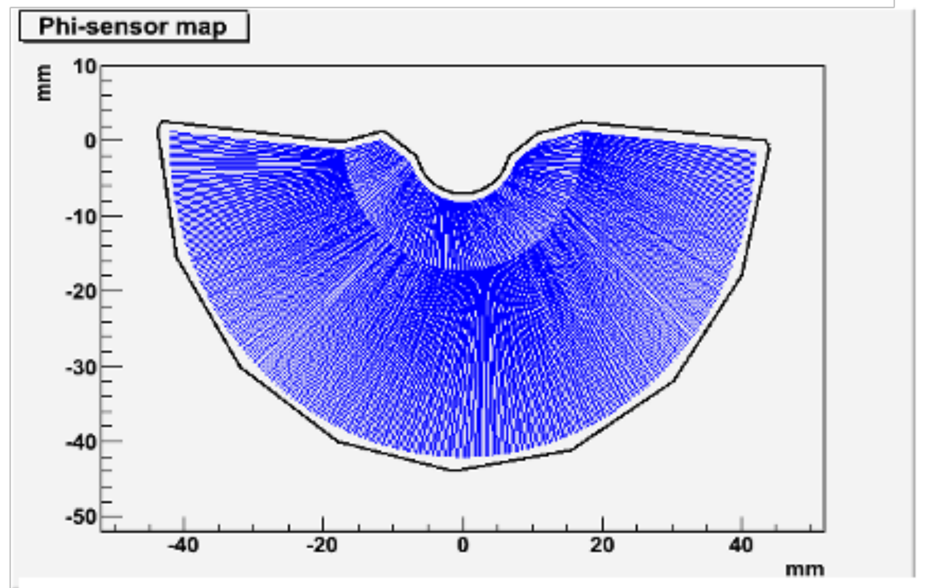
- Least energetic protons in the beam



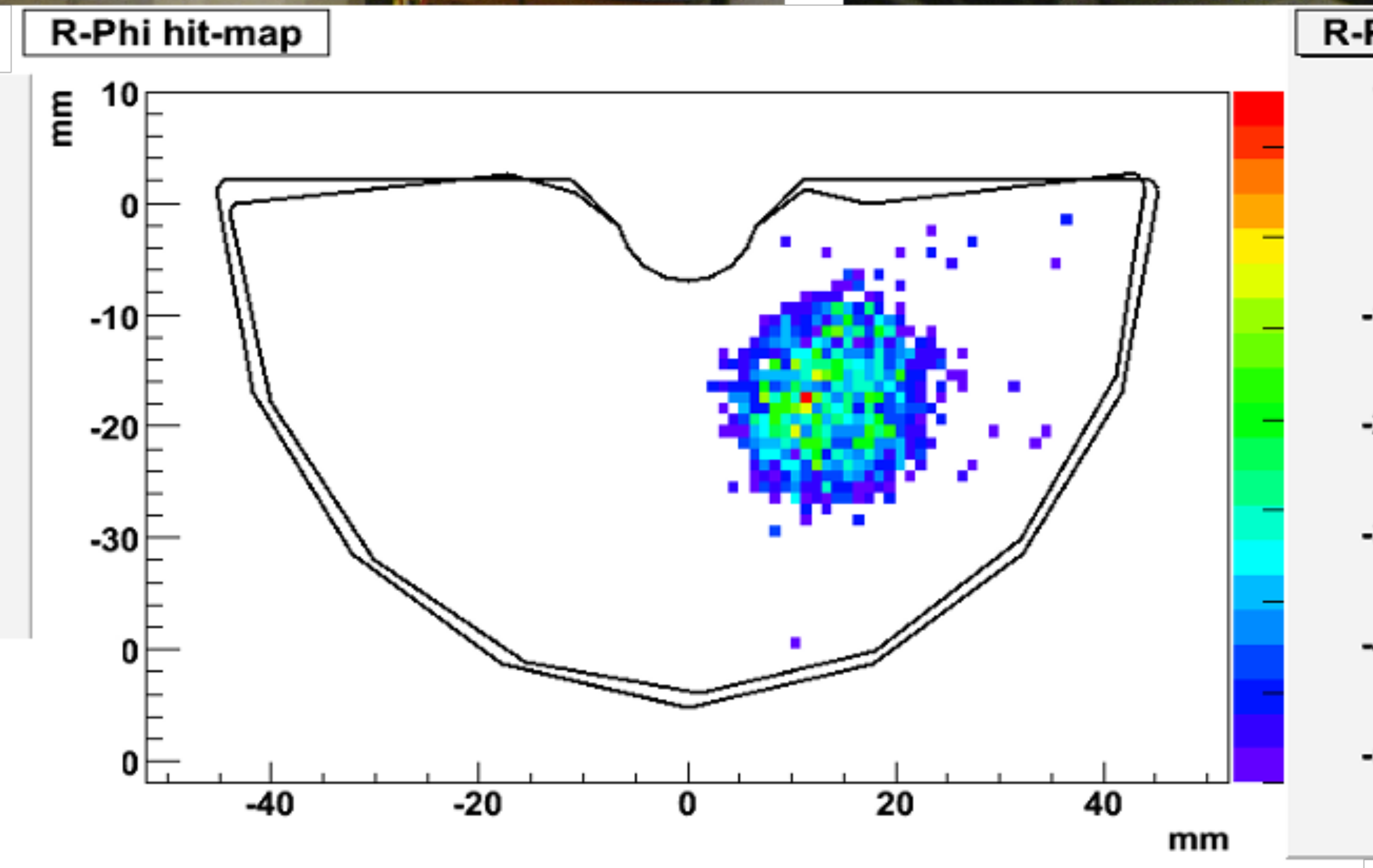


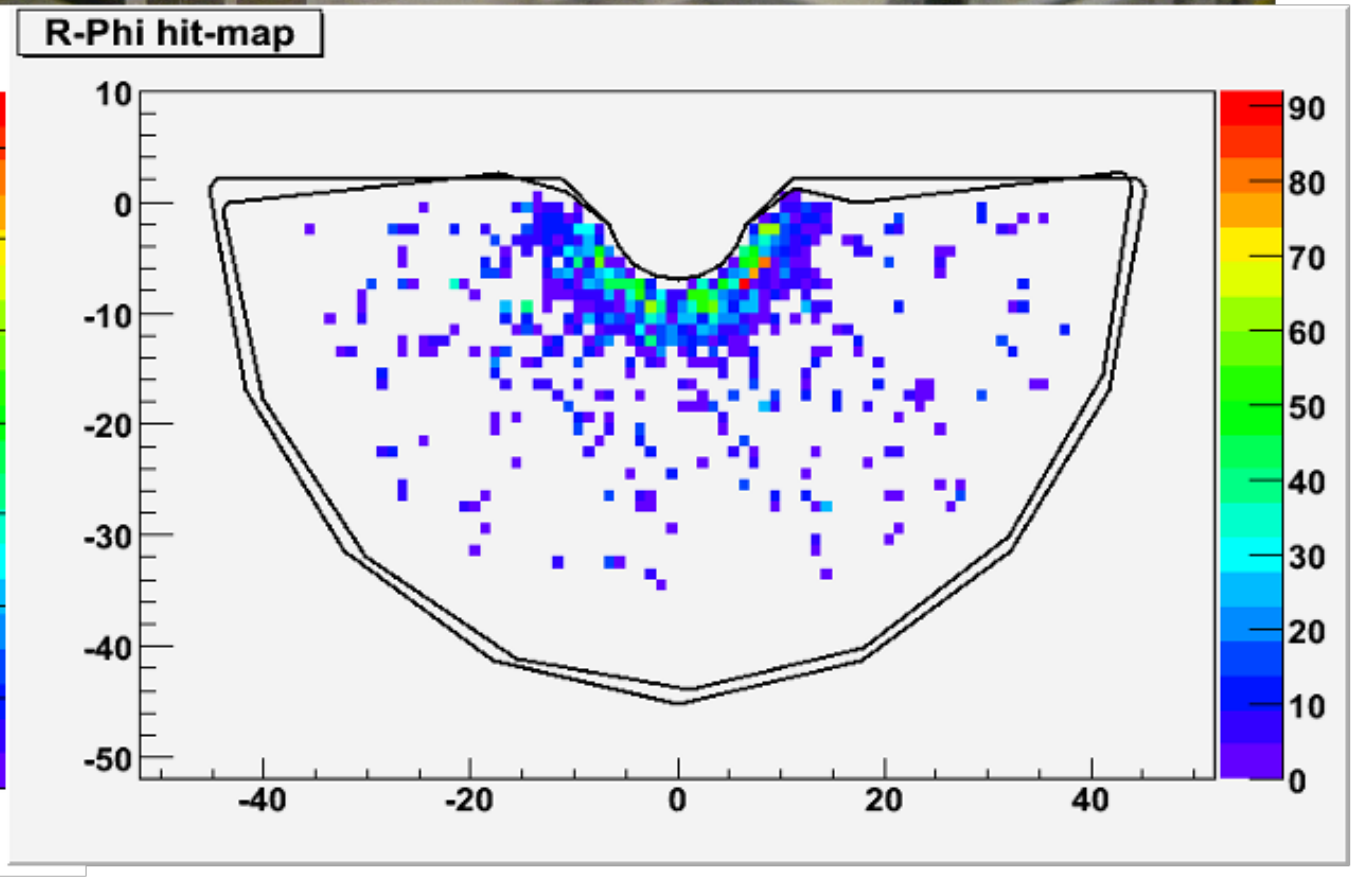
Imaging and planning



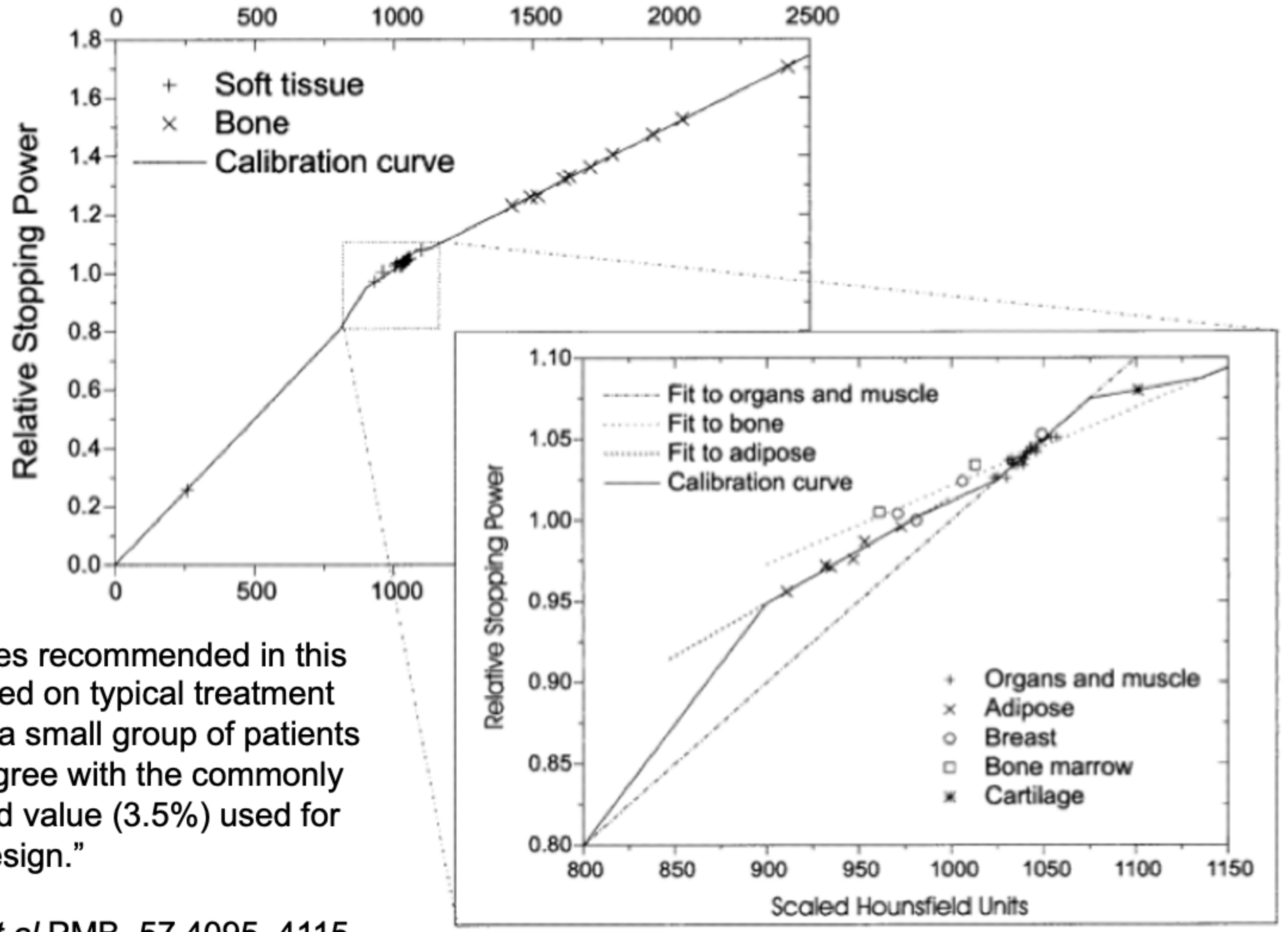


LHCb Back-to-Back Sensor Module



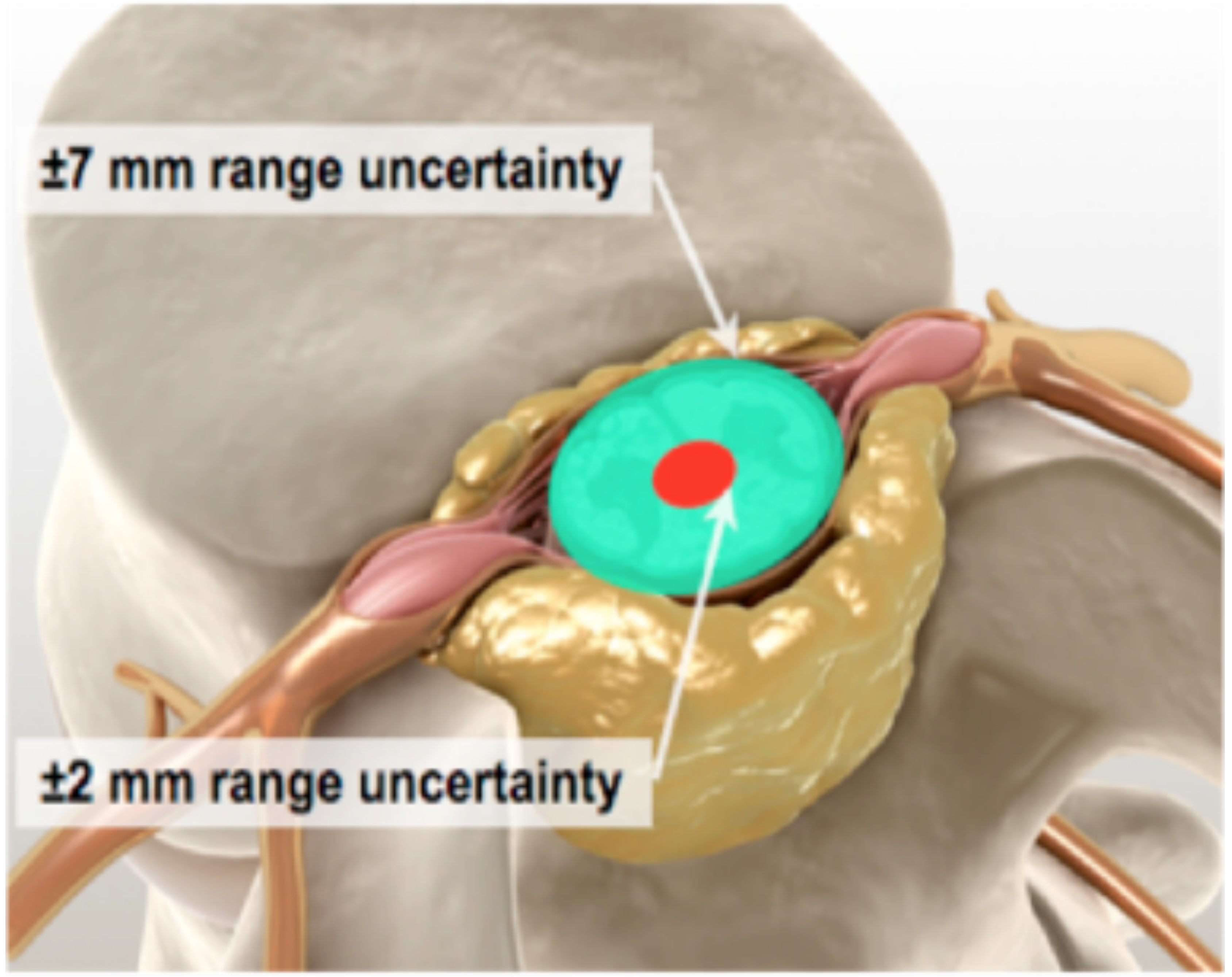


Imaging and planning



"The values recommended in this study based on typical treatment sites and a small group of patients roughly agree with the commonly referenced value (3.5%) used for margin design."

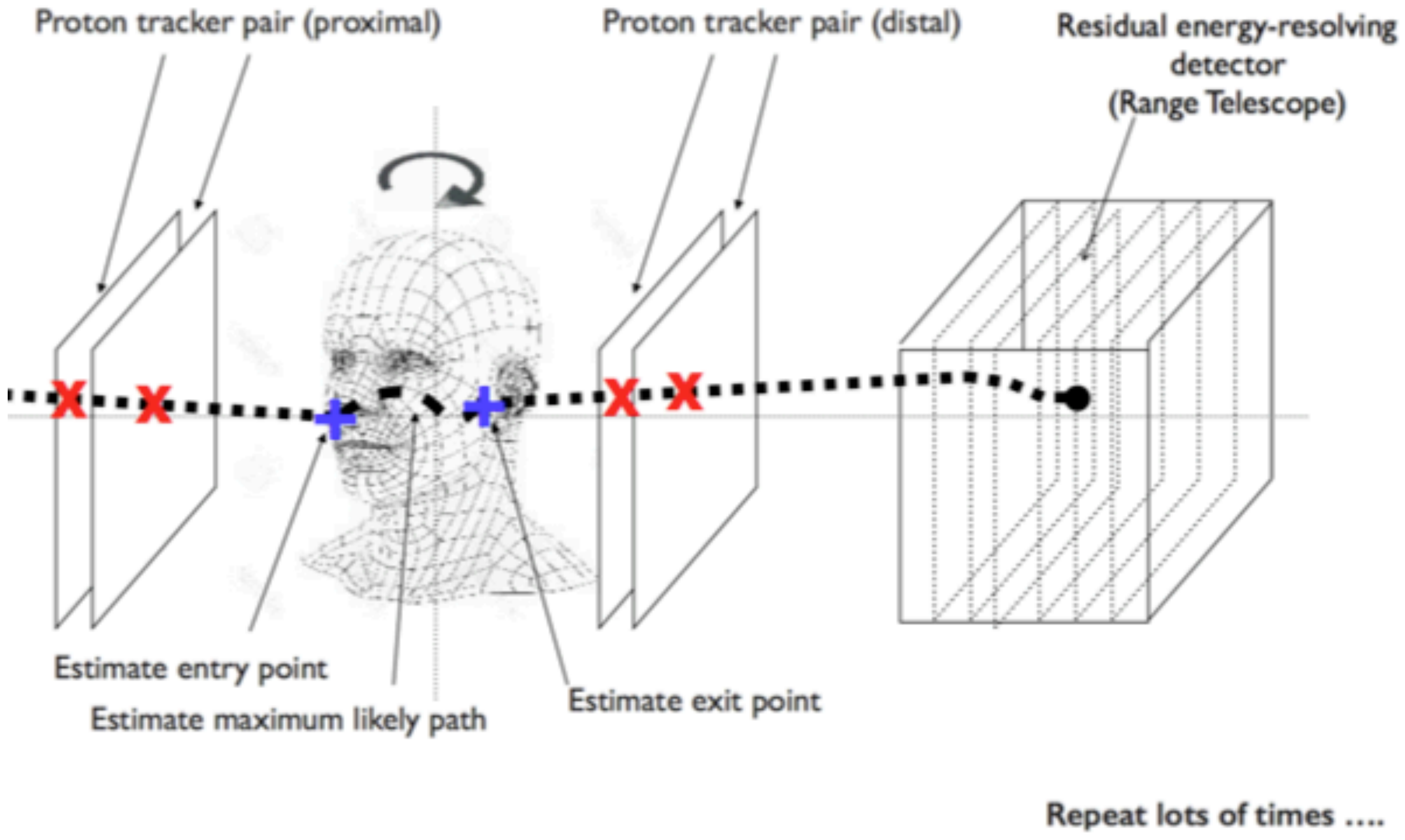
M Yang *et al* PMB. 57 4095–4115 (2012)

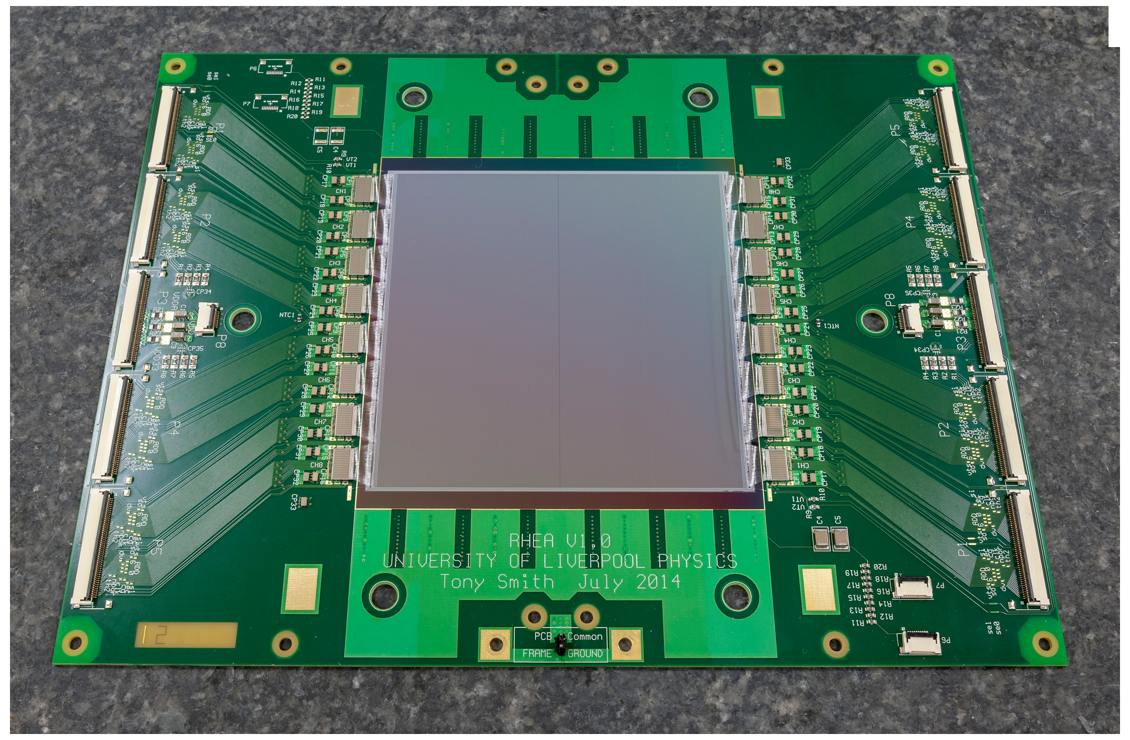


- Imaging with protons could offer benefits to patients

CT and radiography with protons and ions

- Proton CT offers the potential of removing inaccuracies generated by proton treatment plans based upon X-ray CT data
- Experience of proton CT with the PRaVDA project that developed world's first solid state proton CT machine at iThemba LABS, Cape Town
- Proton CT demonstrators also been demonstrated by groups in US, Italy & Japan
- Requires low flux, highest available energy, measurements of 10^5 individual proton histories for each of the 180 projections
- Even if full proton CT is problematic for centres to implement probably safe to say that proton radiography will be used at some point
- Would require Spot scanning accelerators to work in a low current mode -> R&D needed here
- Potential to utilise machine learning techniques developed at FBK for analysis of non-linear proton paths

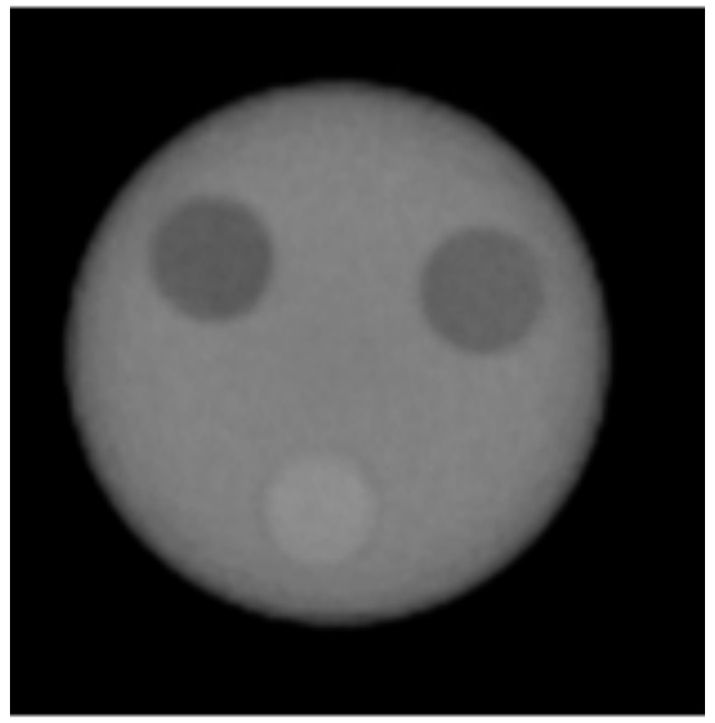




Silicon strip module developed for proton CT

Scattering and energy

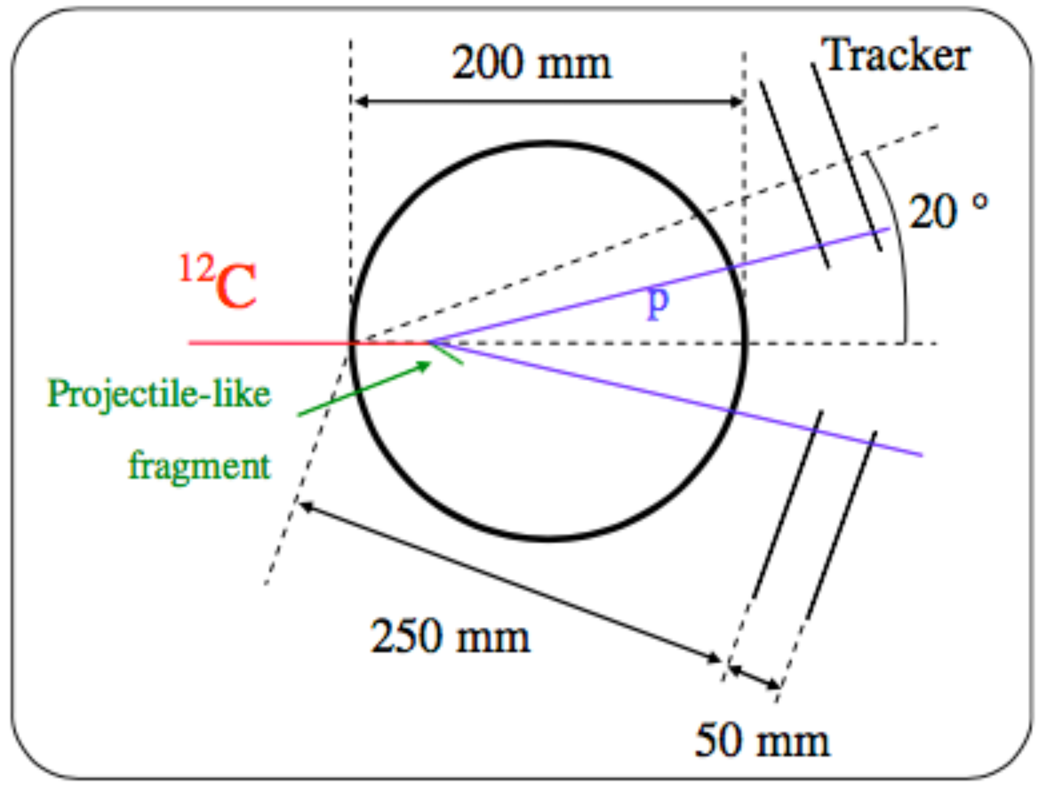
Scattering only

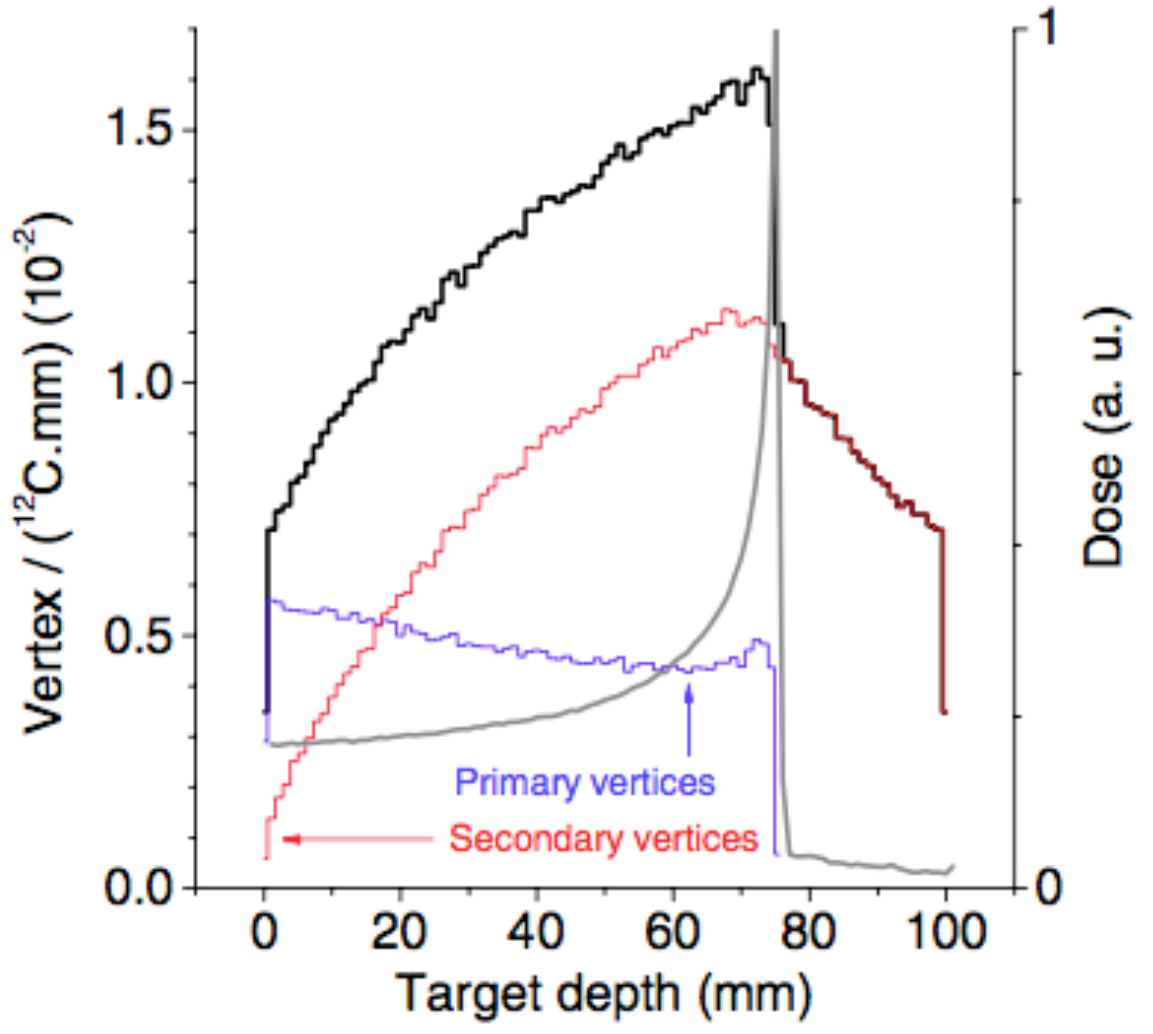


Resulting proton CT images with tissue equivalent inserts visible

Secondary vertex imaging

- Reconstruction of the trajectory of secondary particles allows a non-invasive way of imaging the beam path, range and dose in a patient
- This is typically proposed using so called 'prompt' gamma rays emitted by nuclei excited by the primary beam decaying back to their ground state
- Difficult to track gamma rays, most systems utilise heavily collimation or a Compton camera which result in loss of position/energy resolution and require large statistics
- Secondary protons have also been discussed as a way of range finding for proton therapy (https://doi.org/10.1038/s41598-019-38611-w)
- Ion therapy e.g. with 12C presents an opportunity here -> projectiles have much greater momentum and mass therefore secondary particles will be both more numerous and energetic, so called 'Interaction Vertex Imaging' (IVI)
- **Work beginning later this year with Timepix3 and CNAO in Pavia using their Carbon ion clinical beam**





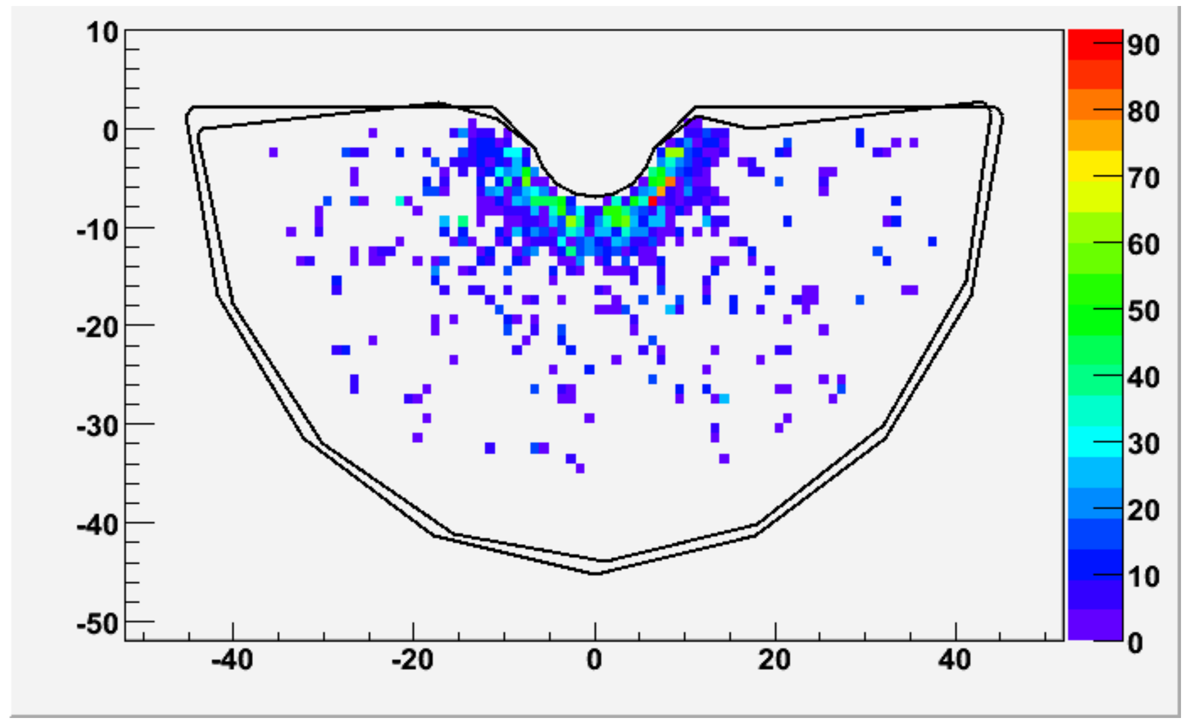
P Henriquet et al 2012 Phys. Med. Biol. **57** 4655

Flash therapy

- Flash therapy uses doses rates in excess of 30 Gy/s generating a more effective treatment in a way nobody seems to fully understand yet (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6979639/)
- Challenges for existing accelerators installed
- Challenges for instrumentation that is used to operating at lower fluences
  - Radiation damage (detector and electronics)
  - Saturation of electronics
  - Single event effects / upsets
  - Larger backgrounds in which to measure
- Presents a greater need for in-situ range monitoring (more can go wrong)
- Potential developments….

•Charge integrator -> doesn’t measure single particles and is low cost and rad hard
•CMOS pixel detectors -> 2x positioned in beam halo, reconstruction of central beam spot

Beam halo measurement at CCC



Radiobiology with elephants?

science & innovation
Department: Science and Innovation
REPUBLIC OF SOUTH AFRICA

Research on tumor-suppressor gene:
"What can we learn from African elephants?"

NRF National Research Foundation 20 1999-2019 iThemba LABS Laboratory for Accelerator Based Sciences

Why do elephants develop less cancer than humans?

Evolution has fine-tuned elephants to make them cancer resistant

Elephants: *20* copies of tumor-suppressor gene

Humans: Only *1* copy of tumor-suppressor gene

Blood samples of African elephants are exposed to radiation at iThemba LABS and the effects are compared to samples from humans

In collaboration with: GSI GSI Helmholtzzentrum für Schwerionenforschung GmbH EVE LR CO

Elephant blood samples in the biology laboratory @iThemba LABS

Ultimate goal: Design a drug that duplicates the effect of the tumor-suppressor gene to prevent and treat human cancer

Summary

- X-ray radiotherapy has come along way since it's conception and has enjoyed considerable improvements thanks to the collaboration of physicists and engineers with clinicians
- Despite a larger cost, particle therapy is on the rise around the world due to the superior dose distribution and additional treatment modalities
- Developments of the sort made for x-ray radiotherapy ie IMRT need to be developed for particle therapy to ensure the benefit to patients is maximised
- Lots of interesting instrumentation challenges ahead!