Medical applications and dosimetry

Outline

What I will cover

- Radiotherapy (the area most often contributed to by physicists)
  - Background and timeline of key innovations
  - External vs internal radiotherapy
  - Radiation interactions with matter: photons or protons?
  - Beam delivery technology
  - Imaging and range uncertainties*
  - Monitoring and dosimetry instrumentation*

*including examples of measurements made with HEP detectors I have been involved with

What I won't cover

- Topics unrelated to radiotherapy: lasers, ultrasound imaging, prosthetics, drugs
- Radioisotope production and PET (maybe next year)
- Monte Carlo modelling and machine learning techniques (maybe next year)
- (Much) radiobiology (a little this year, maybe more next year)

Who cares?

You should!

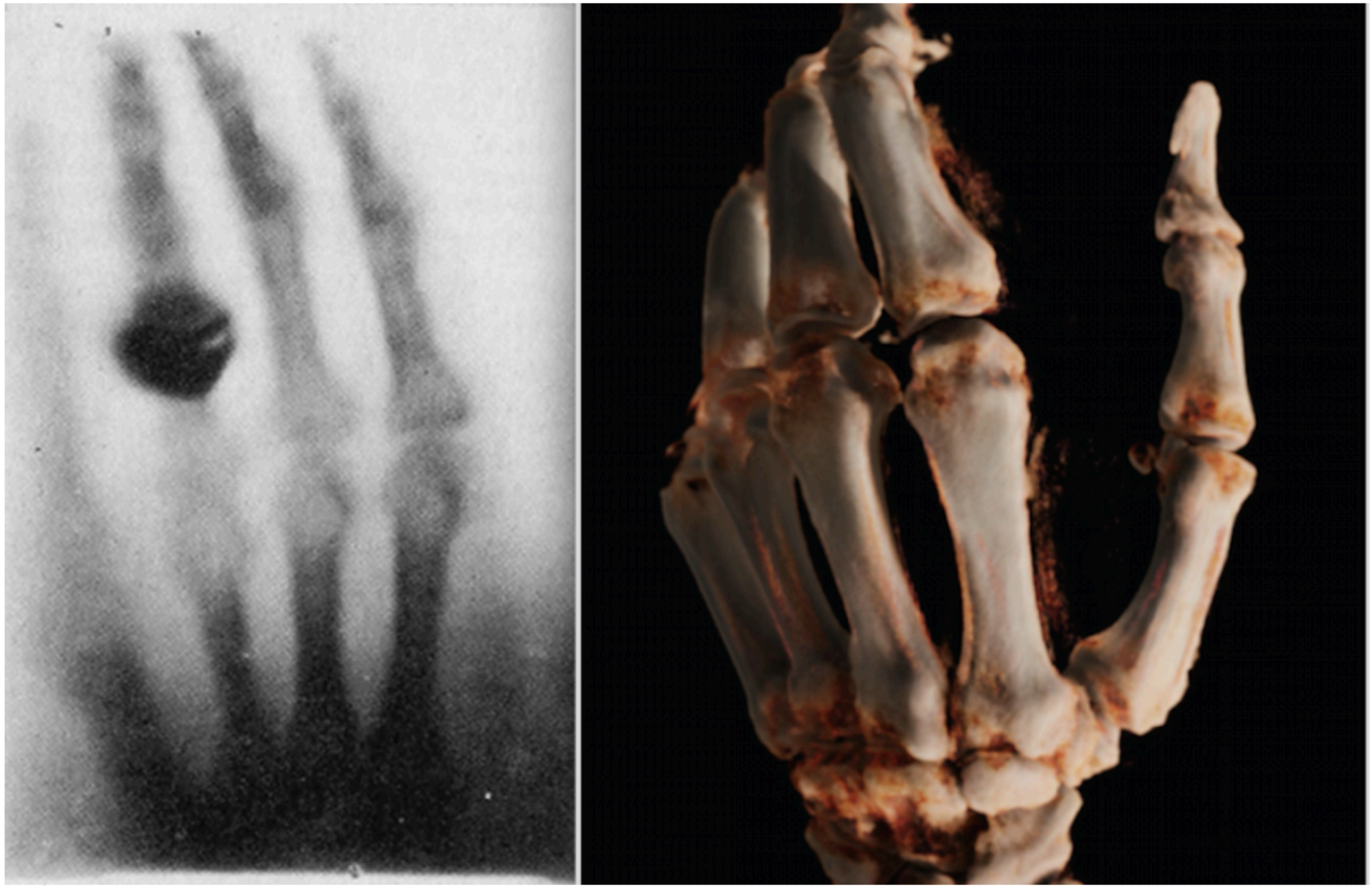
- Medical applications might seem peripheral to HEP instrumentation but it actually contains interesting physics too (cf lecture on radiation interactions with matter in this series: https://indico.cern.ch/event/1401451/timetable/#13-interaction-of-particles-wi

- ‘Normal’ people (read: non-physicists) may ask what the point of your research is. At least one answer to this question is to point out applications of your research to things widely regarded as societal problems. So application of detectors to imaging and radiotherapy can become a science communication tool as well

- Many physics students (even some after PhD) will complete the NHS medical physics STP course to become medical physicists -> seems to be a popular career path for physics graduates - at least in the UK

Physics and medicine

X-ray Has Come a Long Way in 100 Years

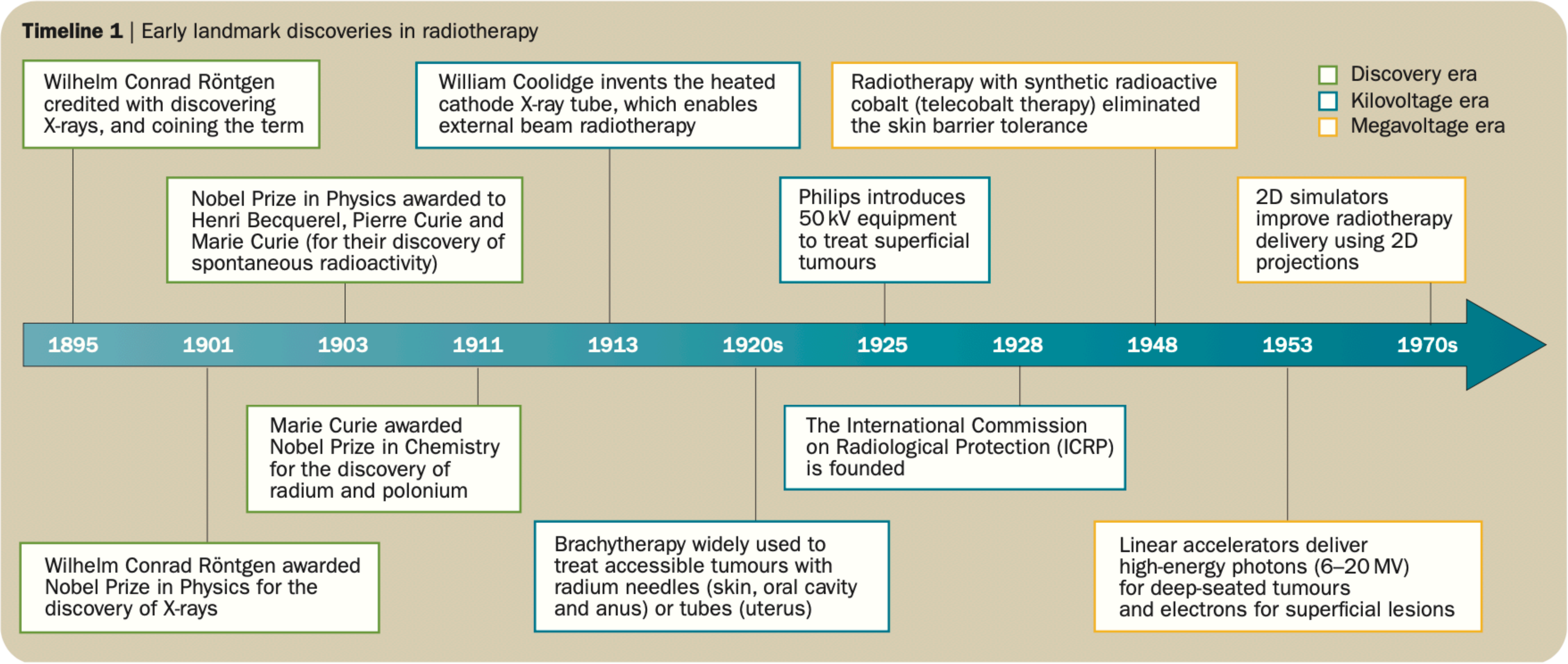


https://www.itnonline.com/content/blogs/dave-fornell-itn-editor/x-ray-has-come-long-way-100-years

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.

Timeline of radiotherapy with x-rays



Timeline 1 | Early landmark discoveries in radiotherapy

🟩 Discovery era
🟦 Kilovoltage era
🟨 Megavoltage era

1895: Wilhelm Conrad Röntgen credited with discovering X-rays, and coining the term

1901: Wilhelm Conrad Röntgen awarded Nobel Prize in Physics for the discovery of X-rays

1903: Nobel Prize in Physics awarded to Henri Becquerel, Pierre Curie and Marie Curie (for their discovery of spontaneous radioactivity)

1911: Marie Curie awarded Nobel Prize in Chemistry for the discovery of radium and polonium

1913: William Coolidge invents the heated cathode X-ray tube, which enables external beam radiotherapy

1920s: Brachytherapy widely used to treat accessible tumours with radium needles (skin, oral cavity and anus) or tubes (uterus)

1925: Philips introduces 50 kV equipment to treat superficial tumours

1928: The International Commission on Radiological Protection (ICRP) is founded

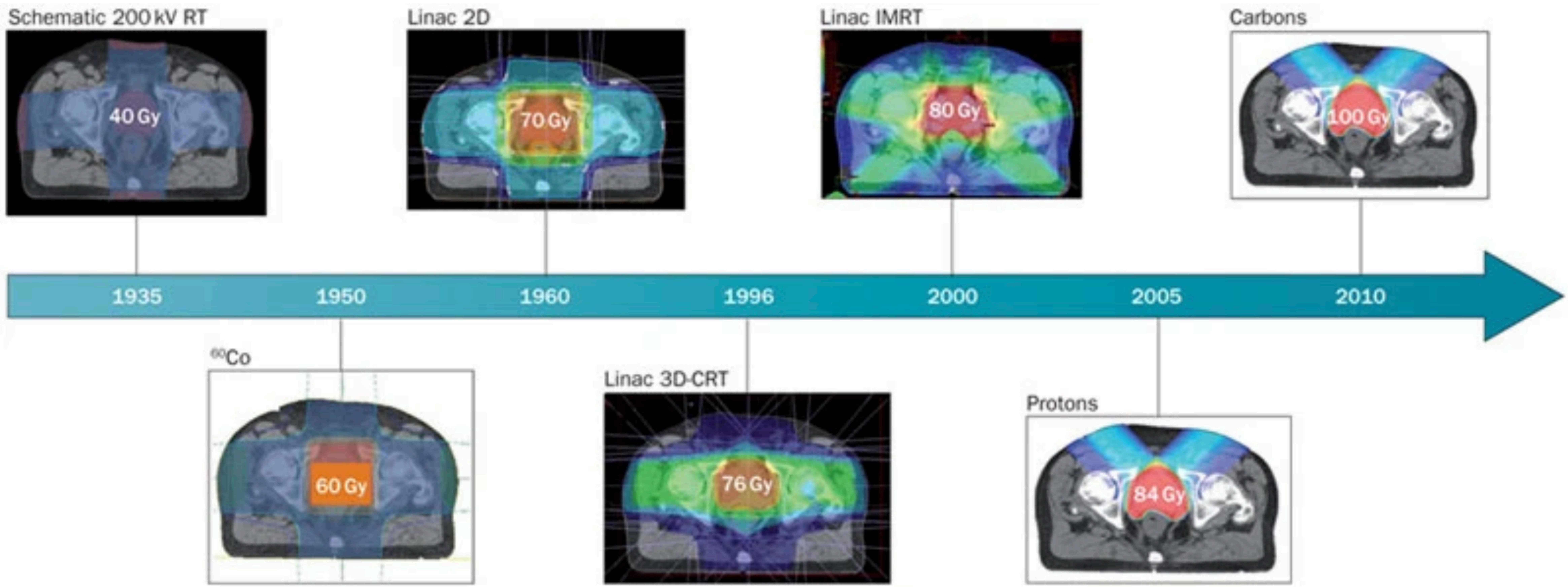
1948: Radiotherapy with synthetic radioactive cobalt (telecobalt therapy) eliminated the skin barrier tolerance

1953: Linear accelerators deliver high-energy photons (6–20 MV) for deep-seated tumours and electrons for superficial lesions

1970s: 2D simulators improve radiotherapy delivery using 2D projections

Timeline of innovations in x-ray radiotherapy: https://doi.org/10.1038/nrclinonc.2012.203

Comparison of radiotherapy modalities with time



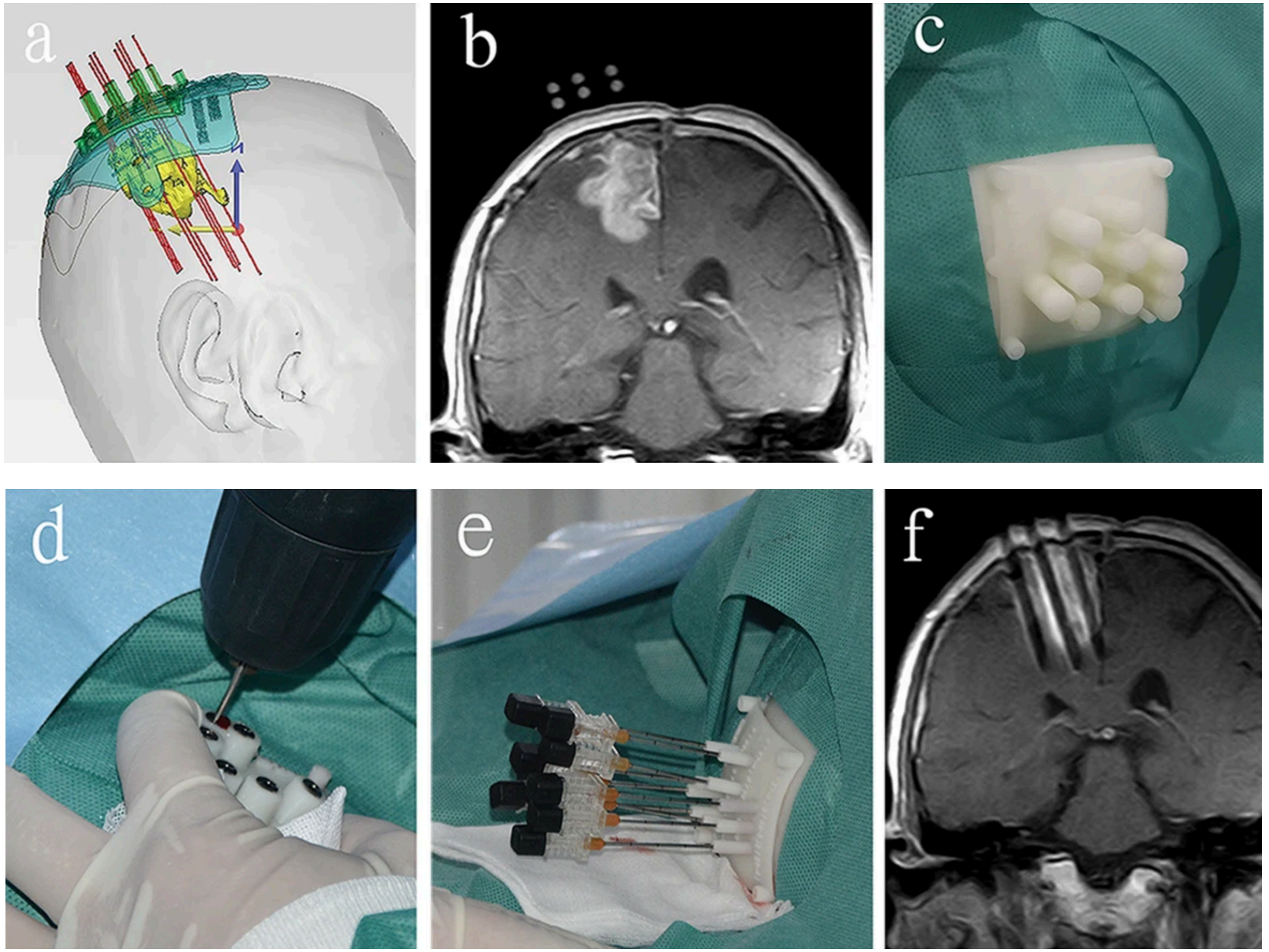
"Prostate cancer irradiation is a good example of the improvement of radiotherapy technology over the past decades. By increasing the beam energy and the precision of the targeting, it was possible to escalate the dose to the prostate without exceeding the tolerance dose of healthy tissues; allowing 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 from a rotating linac. Typical patient throughput can be ~100 / week

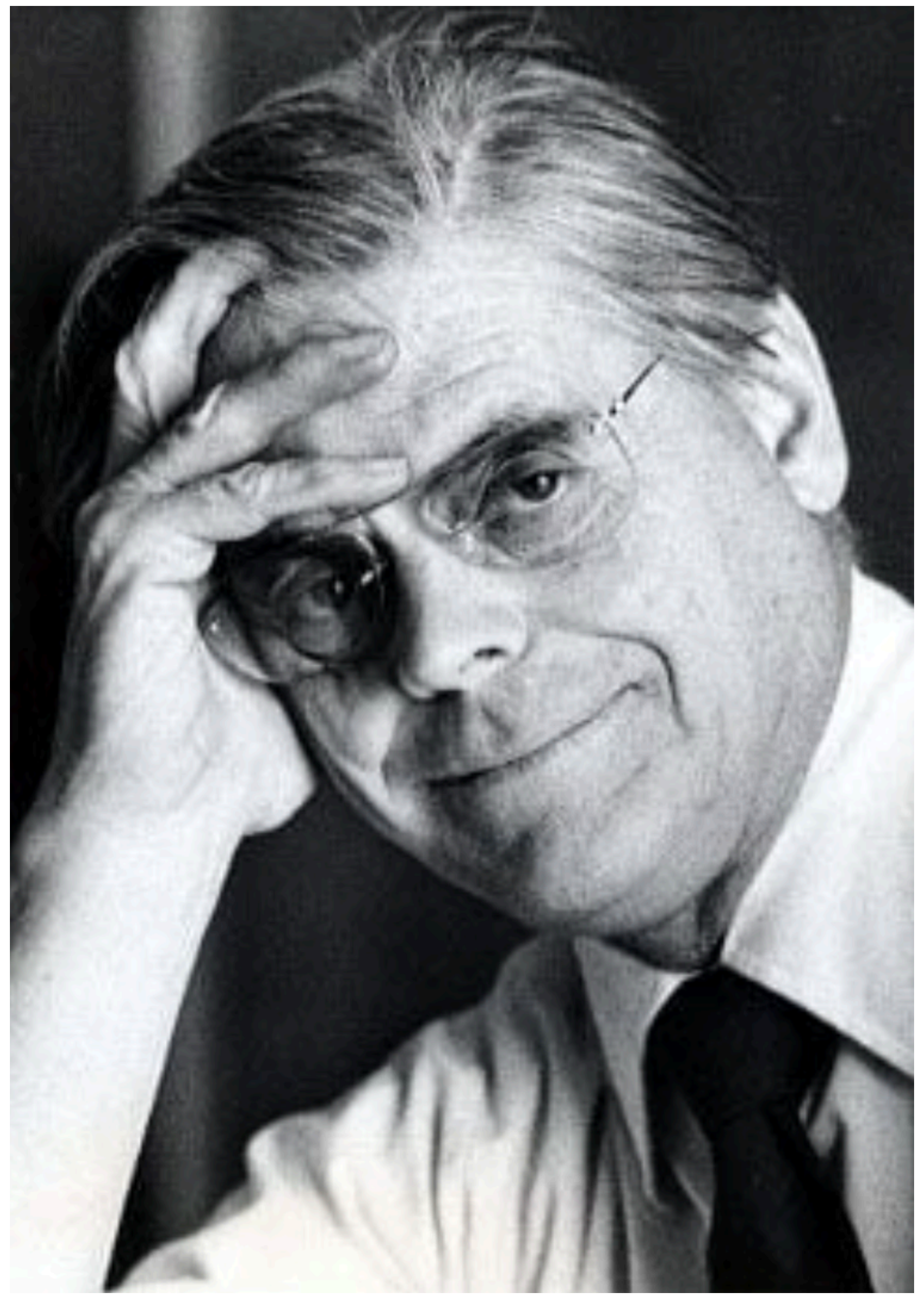
Rutherford Cancer Centre Liverpool

Brachtherapy with ^{125}I wires, low energy gamma / x-rays that only damage nearby (cancerous) cells



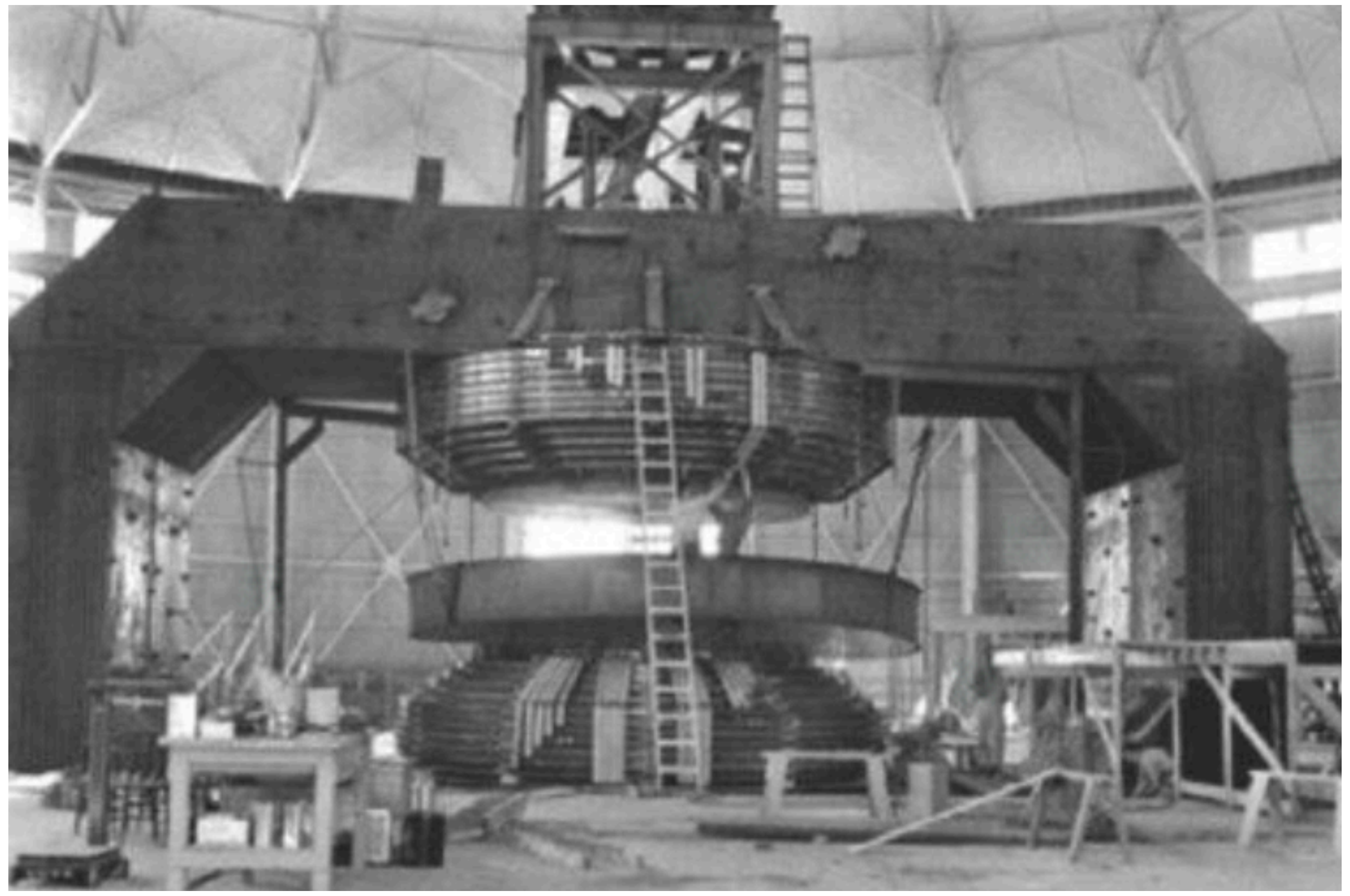
The procedure of 3DNPT combined with MR-guided ^{125}I brachytherapy for recurrent glioblastoma. https://ro-journal.biomedcentral.com/articles/10.1186/s13014-020-01586-4

Charged particle radiotherapy



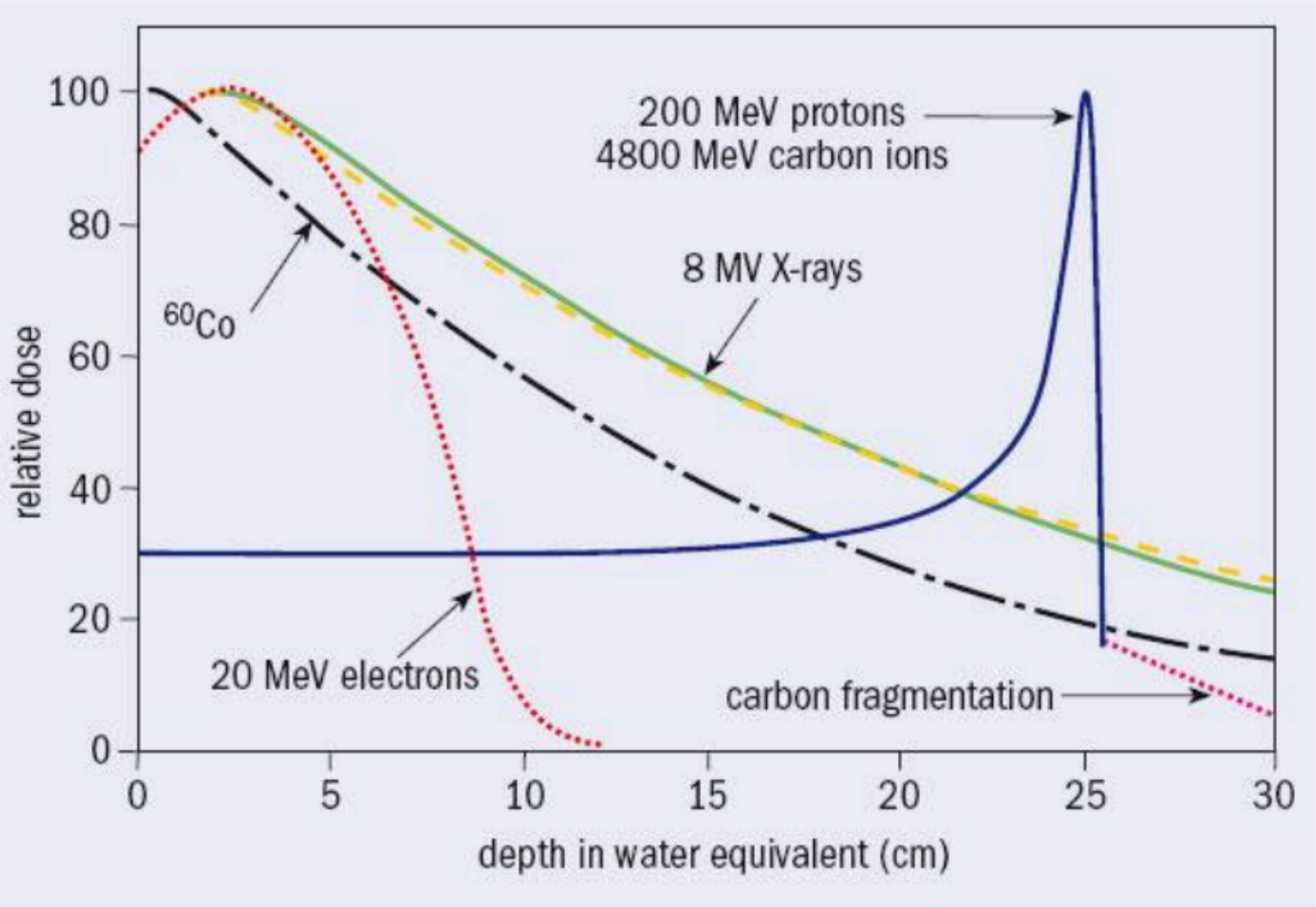
Robert R Wilson, the father of proton therapy c.1950

Construction of the 184-inch synchrocyclotron at the Radiation Laboratory at the University of California, Berkeley, USA 1942. This cyclotron was developed by the laboratory's director Ernest Orlando Lawrence.

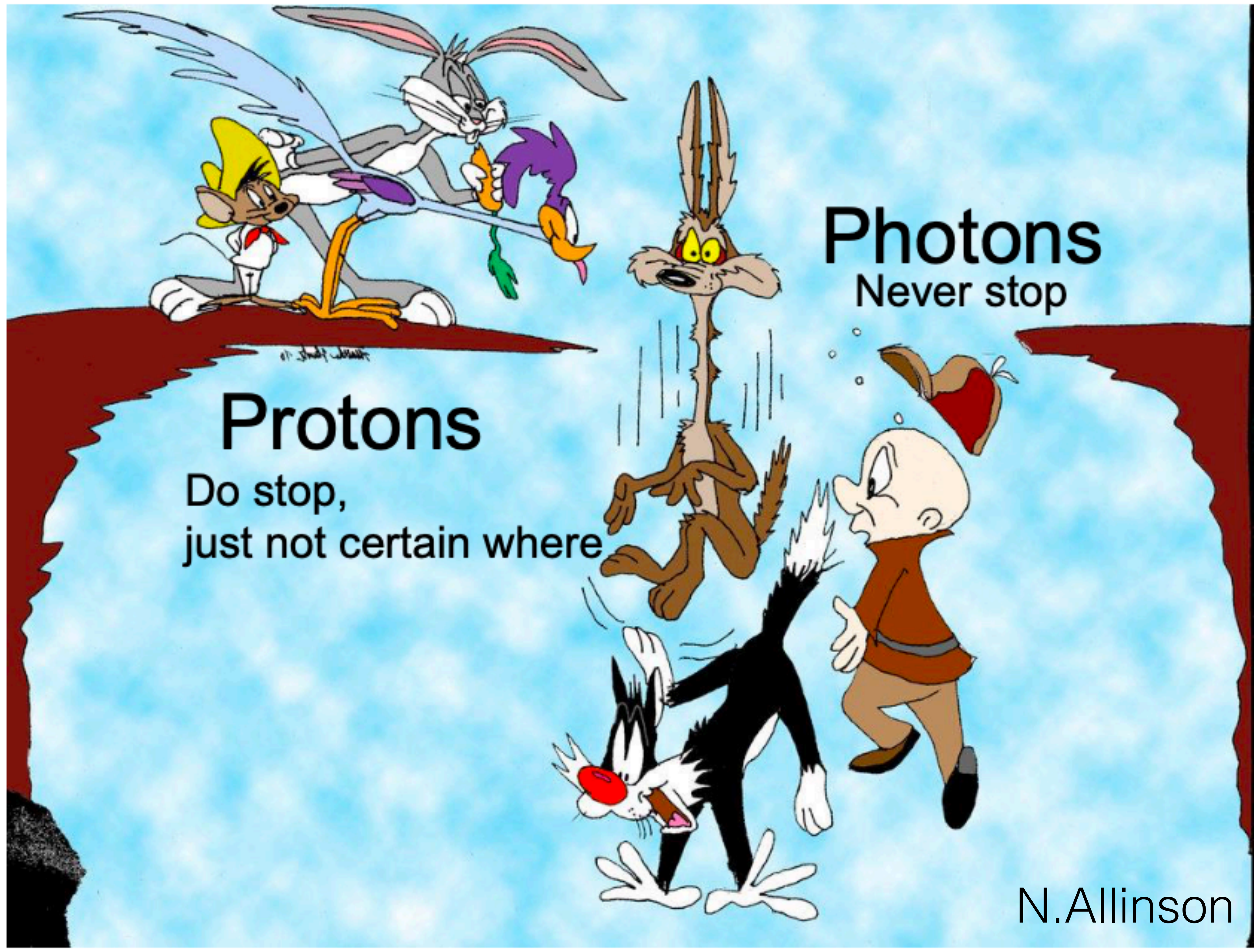


Ernest O. Lawrence and his associates were the first to invent the cyclotron in 1929 & developed it as a particle accelerator during the 1930s, winning the 1939 Nobel Prize for physics for this work. In 1931, he founded the Radiation Laboratory, later named the Lawrence Berkeley Laboratory. A decade later, his advanced version of the synchrocyclotron, which is 184 inches in diameter, is capable of producing 340 MeV protons

Photons vs protons

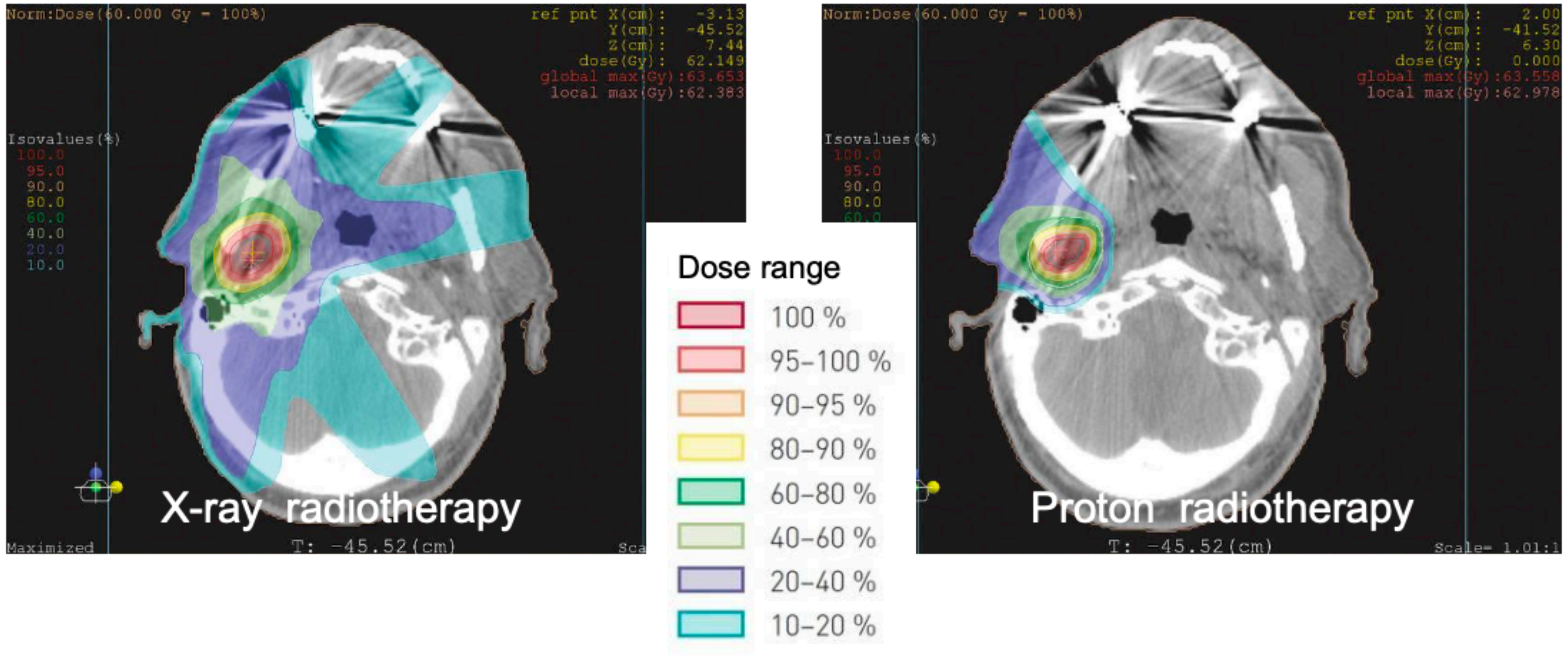


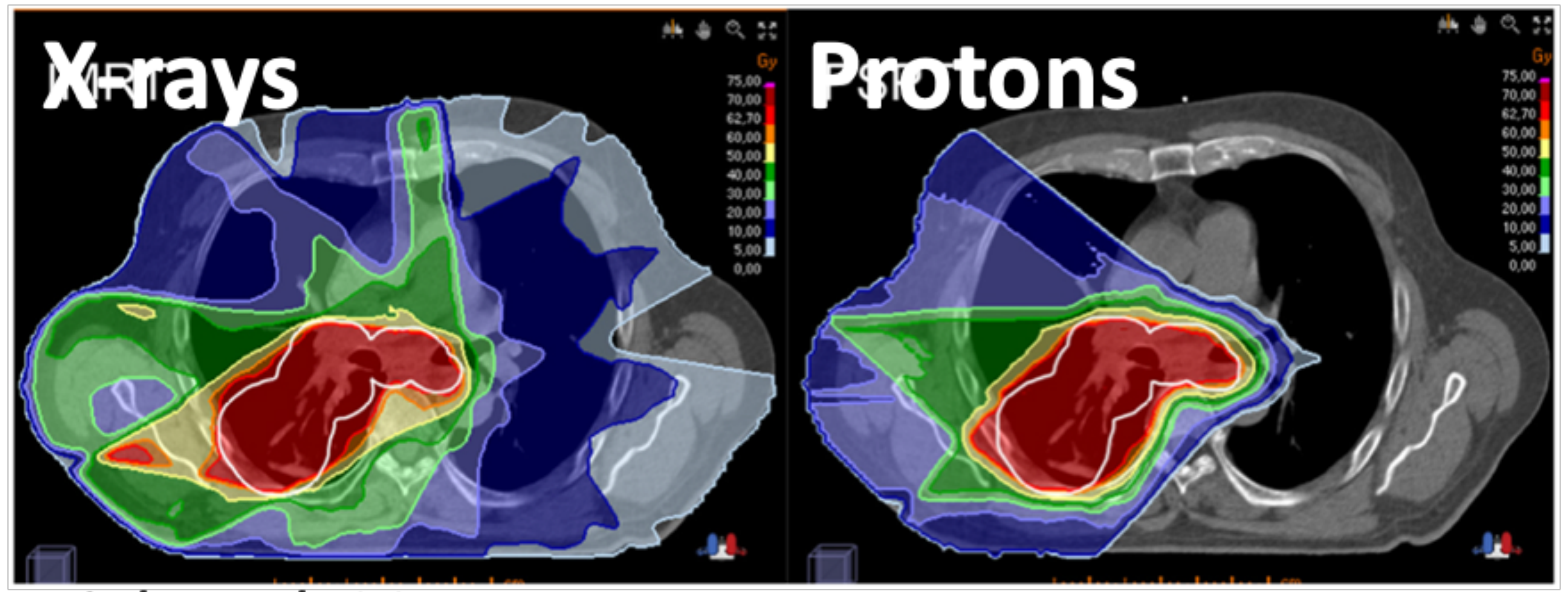
$$-\frac{dE}{dx} = \frac{4\pi}{m_e c^2} \cdot \frac{nz^2}{\beta^2} \cdot \left(\frac{e^2}{4\pi\varepsilon_0}\right)^2 \cdot \left[\ln\left(\frac{2m_e c^2\beta^2}{I\cdot(1-\beta^2)}\right) - \beta^2\right]$$



The advantage is the disadvantage

Photons vs protons





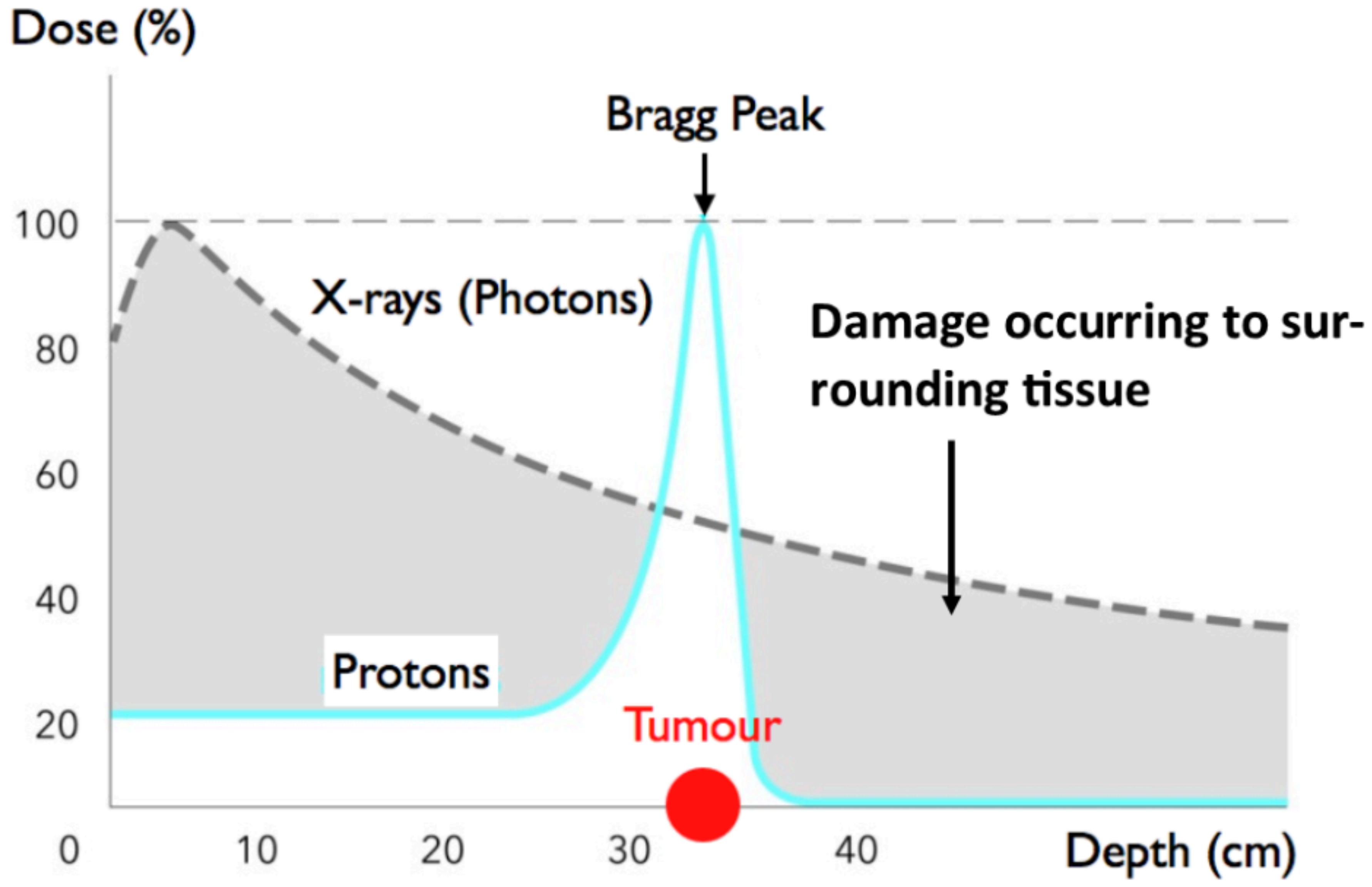
Wink et al. 2014

Treatment sites:

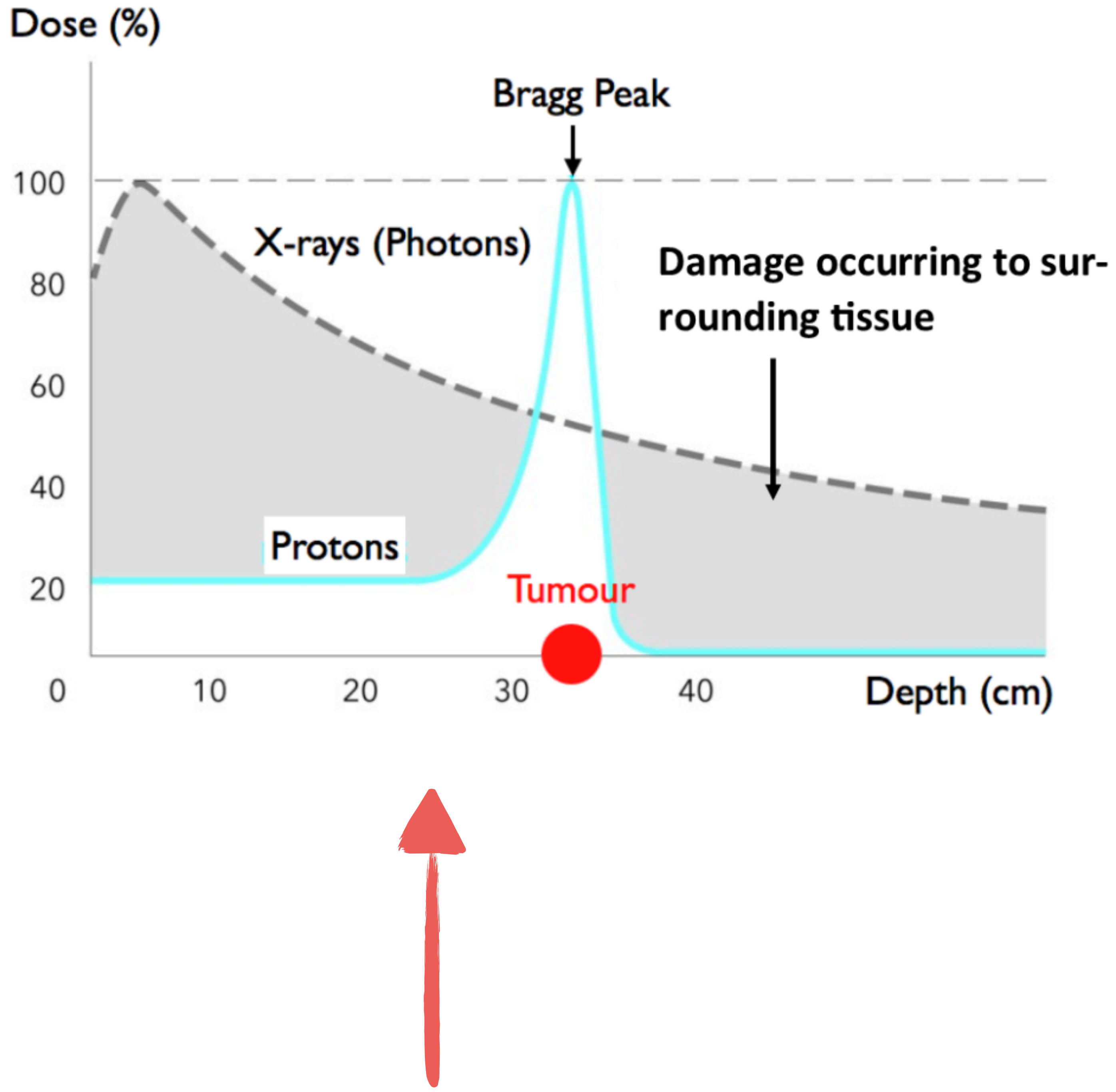
- **Paediatrics – reduced occurrence of secondary cancers**
- **Tumours near critical organs**

Particle therapy advantages:

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



Spread out bragg beak (SOBP)



An unhelpful caricature…

https://www.mdpi.com/2072-6694/11/7/946

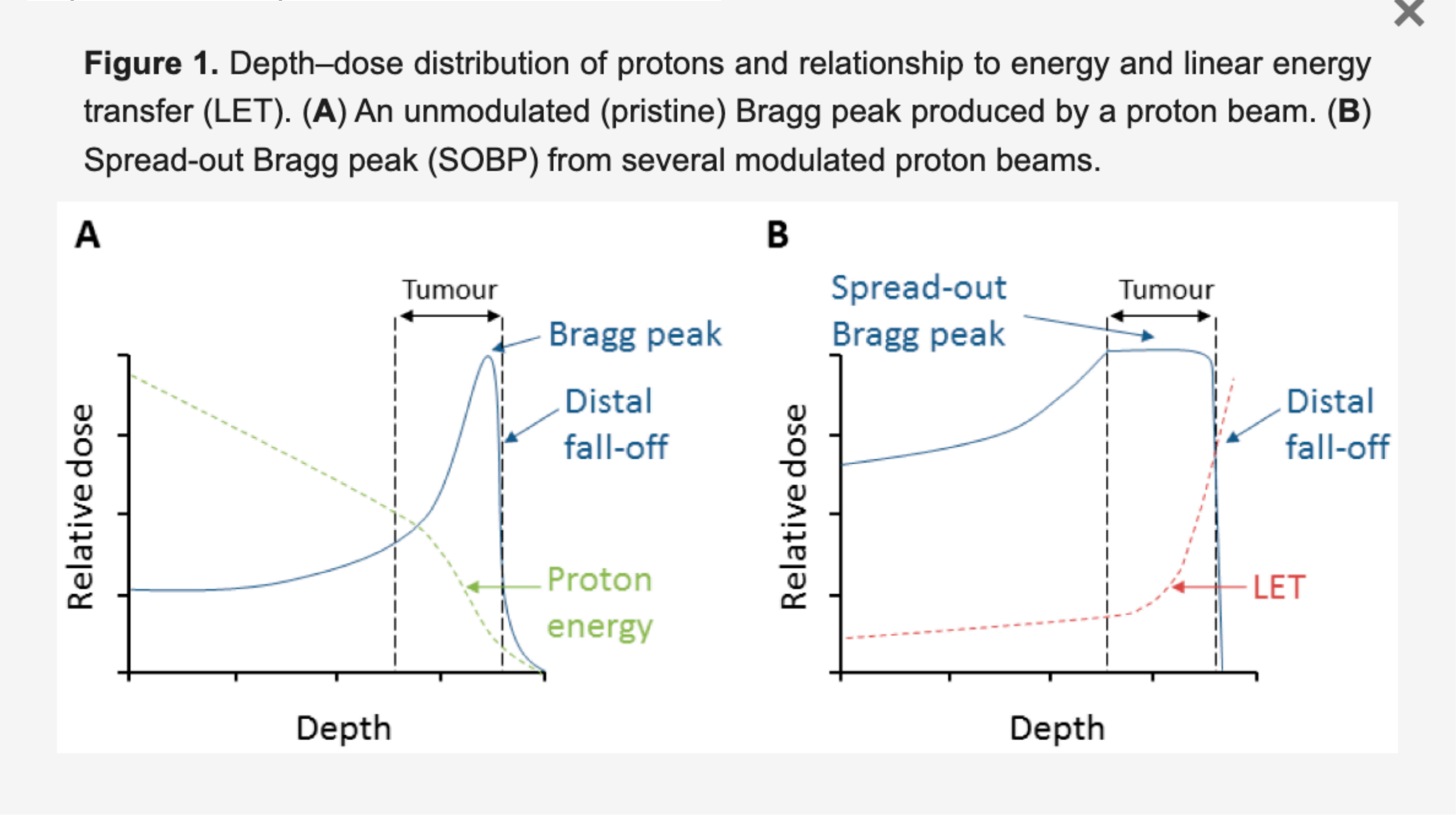
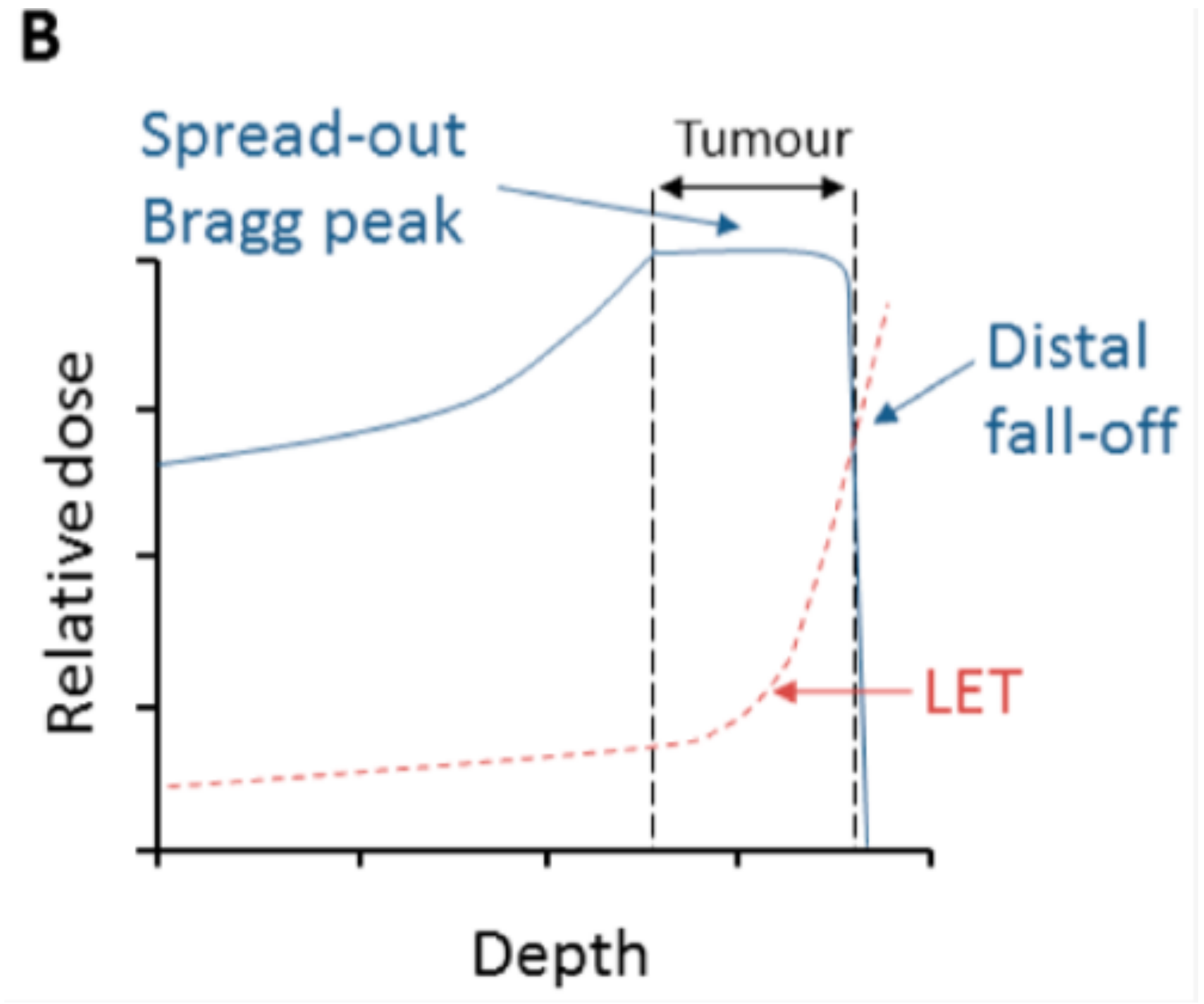


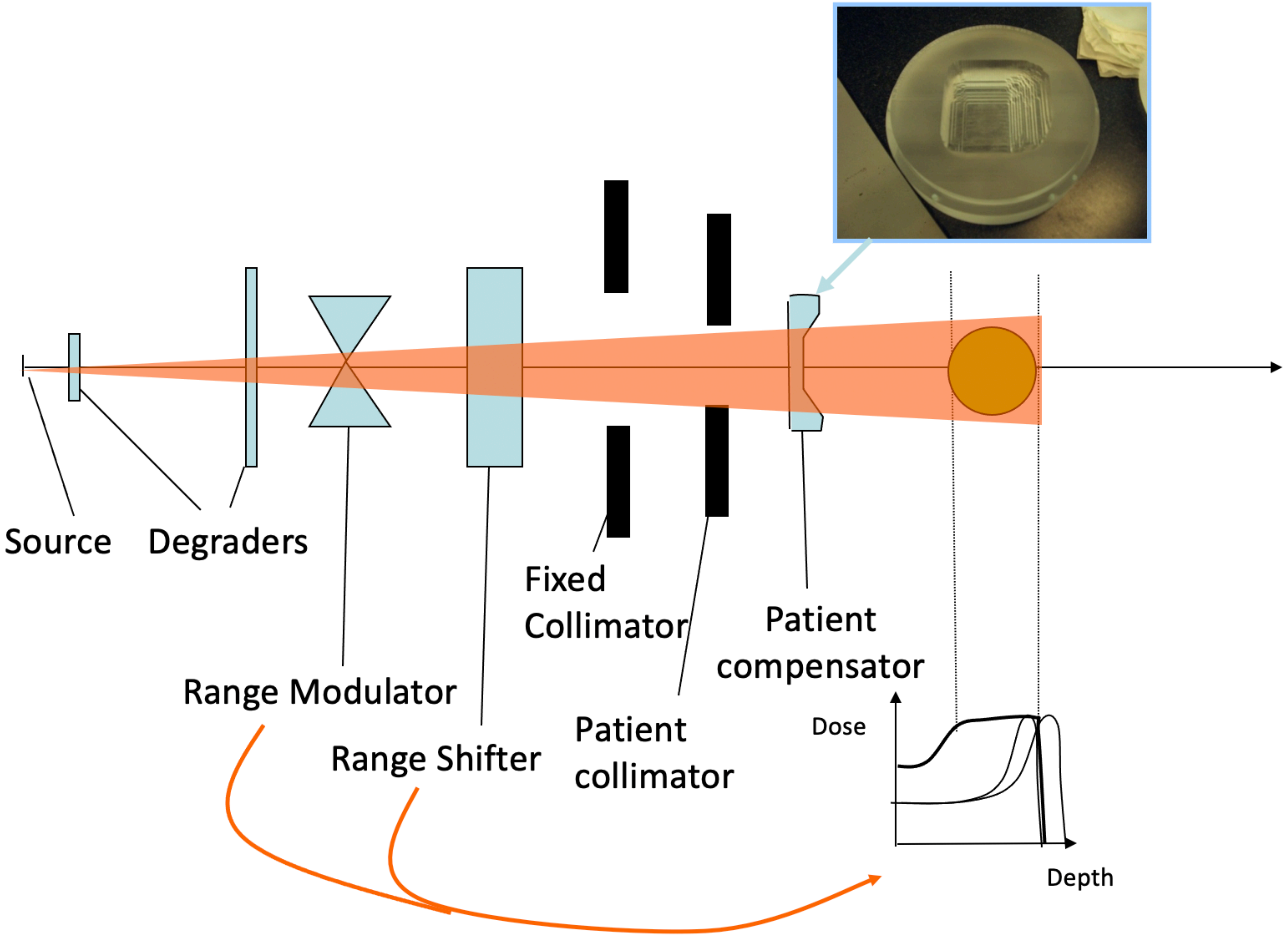
Figure 1. Depth–dose distribution of protons and relationship to energy and linear energy transfer (LET). (**A**) An unmodulated (pristine) Bragg peak produced by a proton beam. (**B**) Spread-out Bragg peak (SOBP) from several modulated proton beams.

$$-\frac{dE}{dx} = \frac{4\pi}{m_e c^2} \cdot \frac{nz^2}{\beta^2} \cdot \left(\frac{e^2}{4\pi\varepsilon_0}\right)^2 \cdot \left[\ln\left(\frac{2m_e c^2\beta^2}{I\cdot(1-\beta^2)}\right) - \beta^2\right]$$

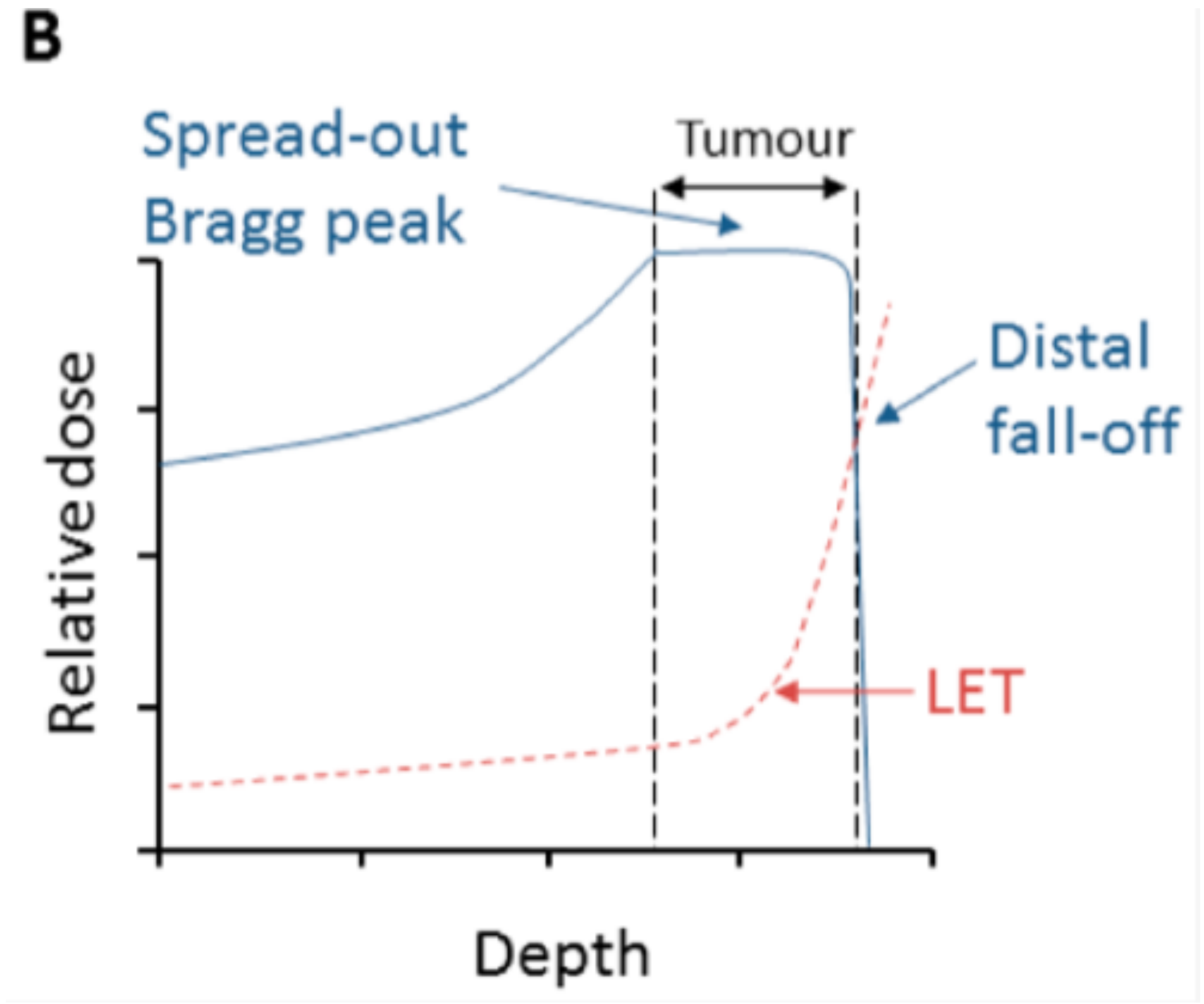
Passive scattering

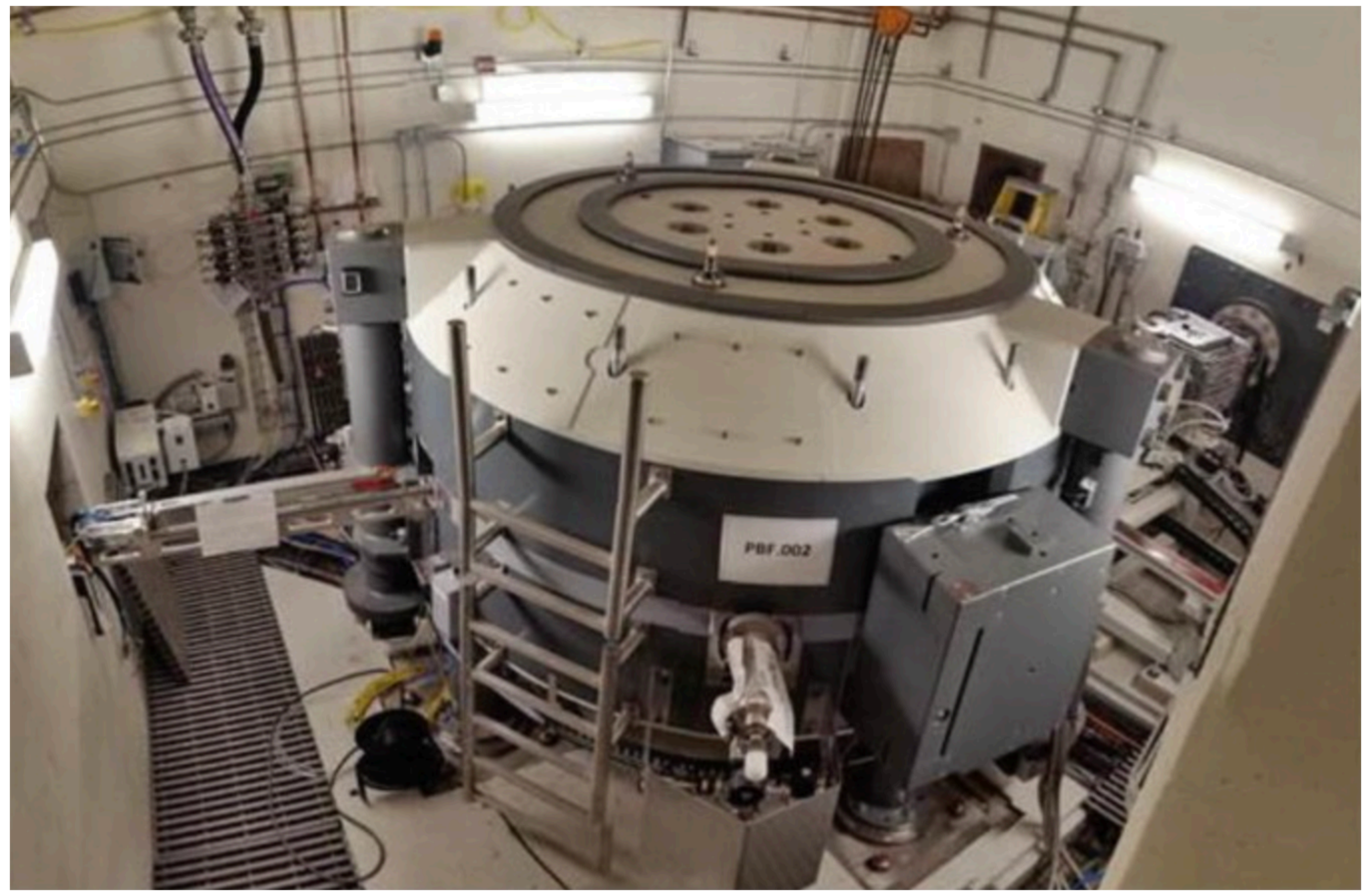


Clatterbridge – 62 MeV Scanditronix cyclotron
Basis for much UK technology and clinical-related research

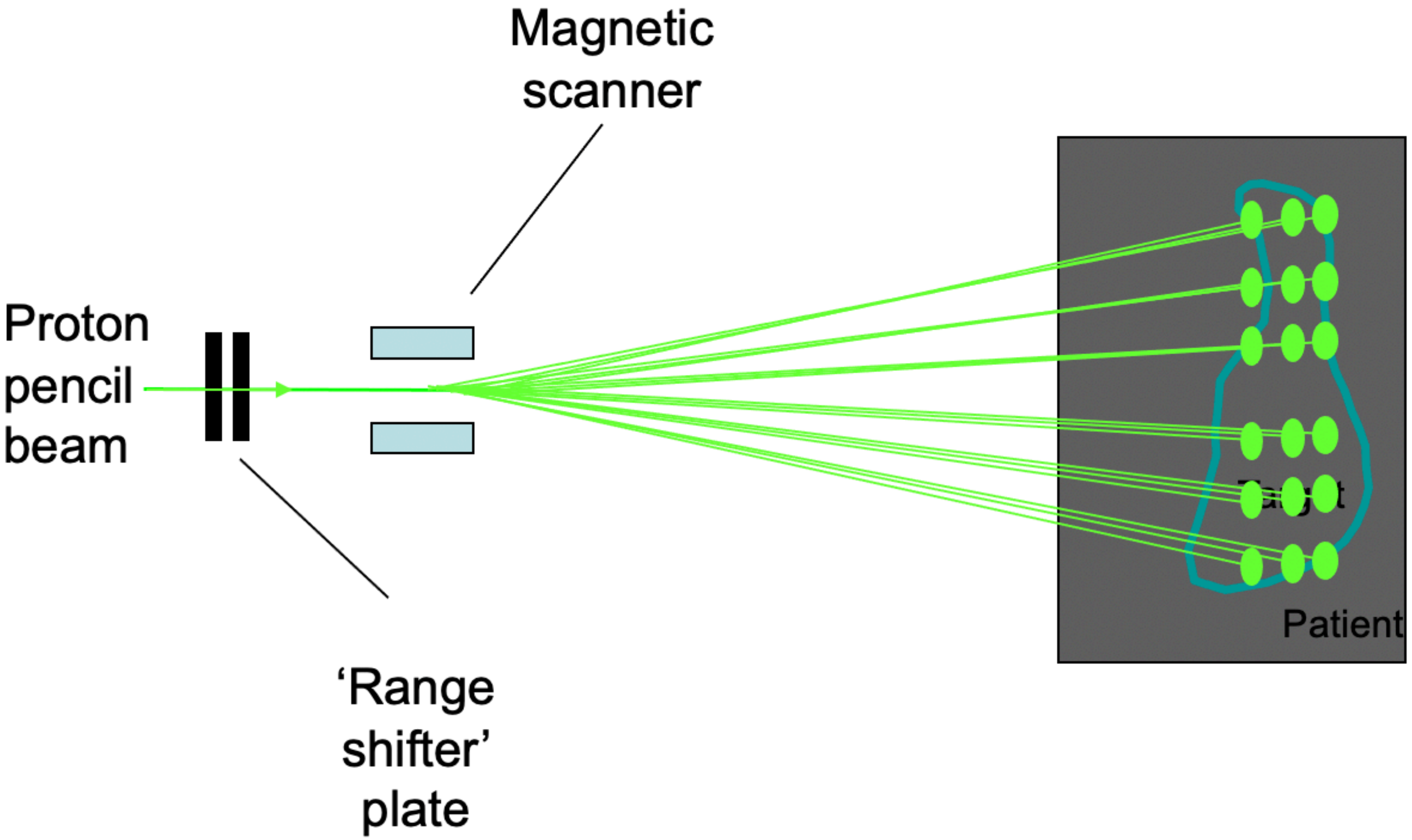


Spot scanning

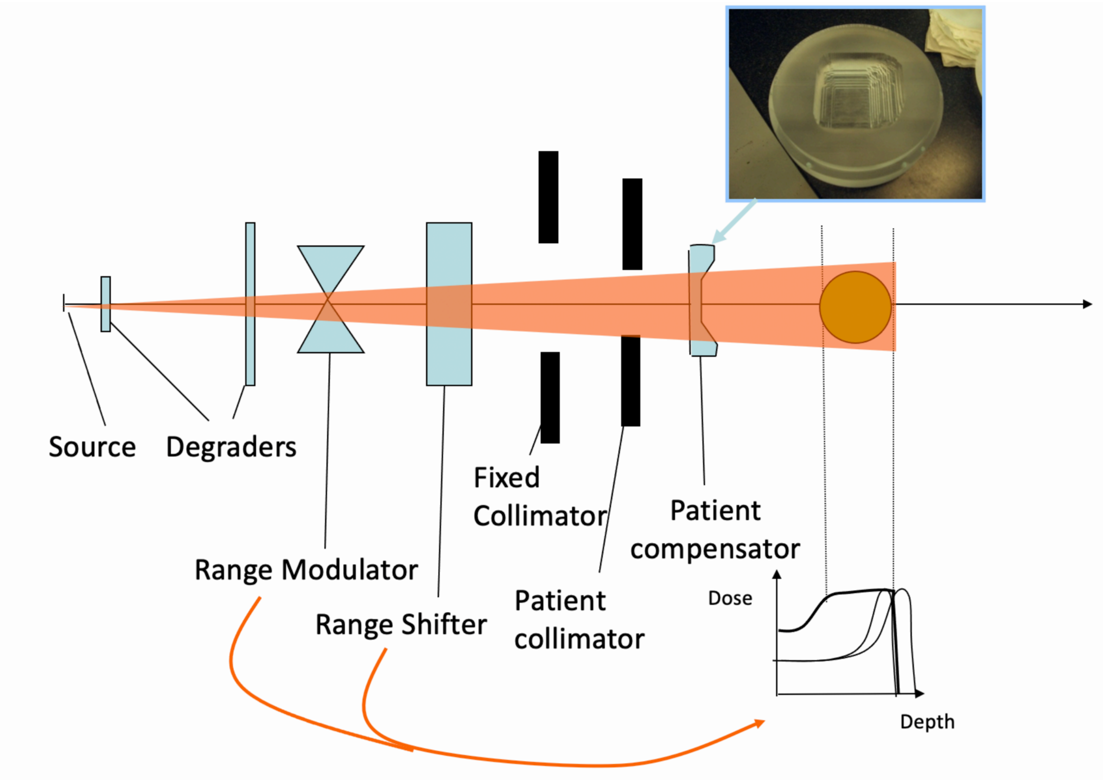


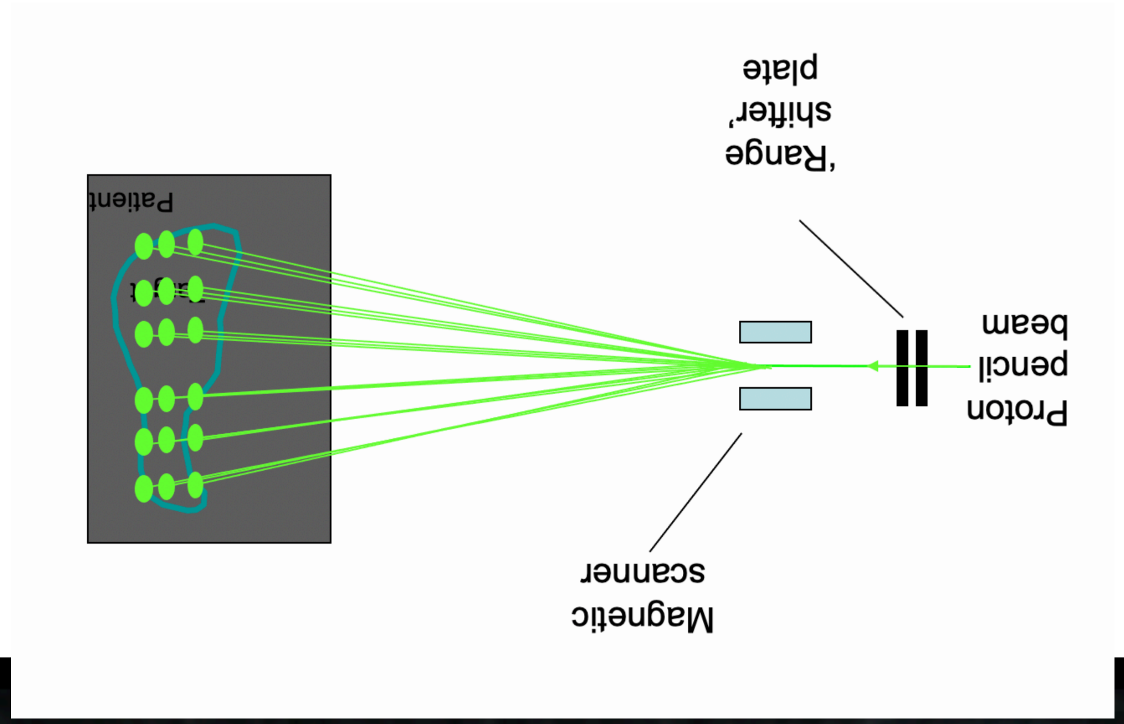


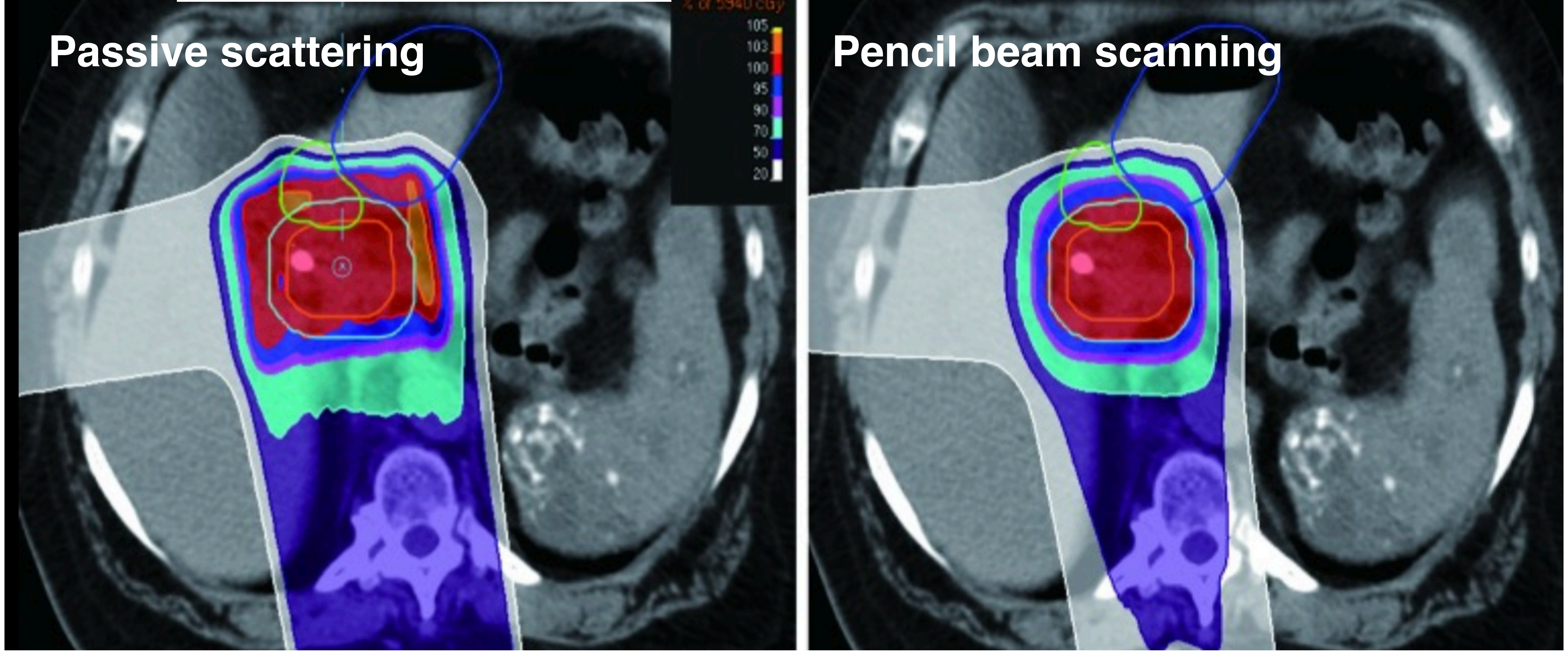
IBA Proteus one superconducting cyclotron
(230 MeV protons)



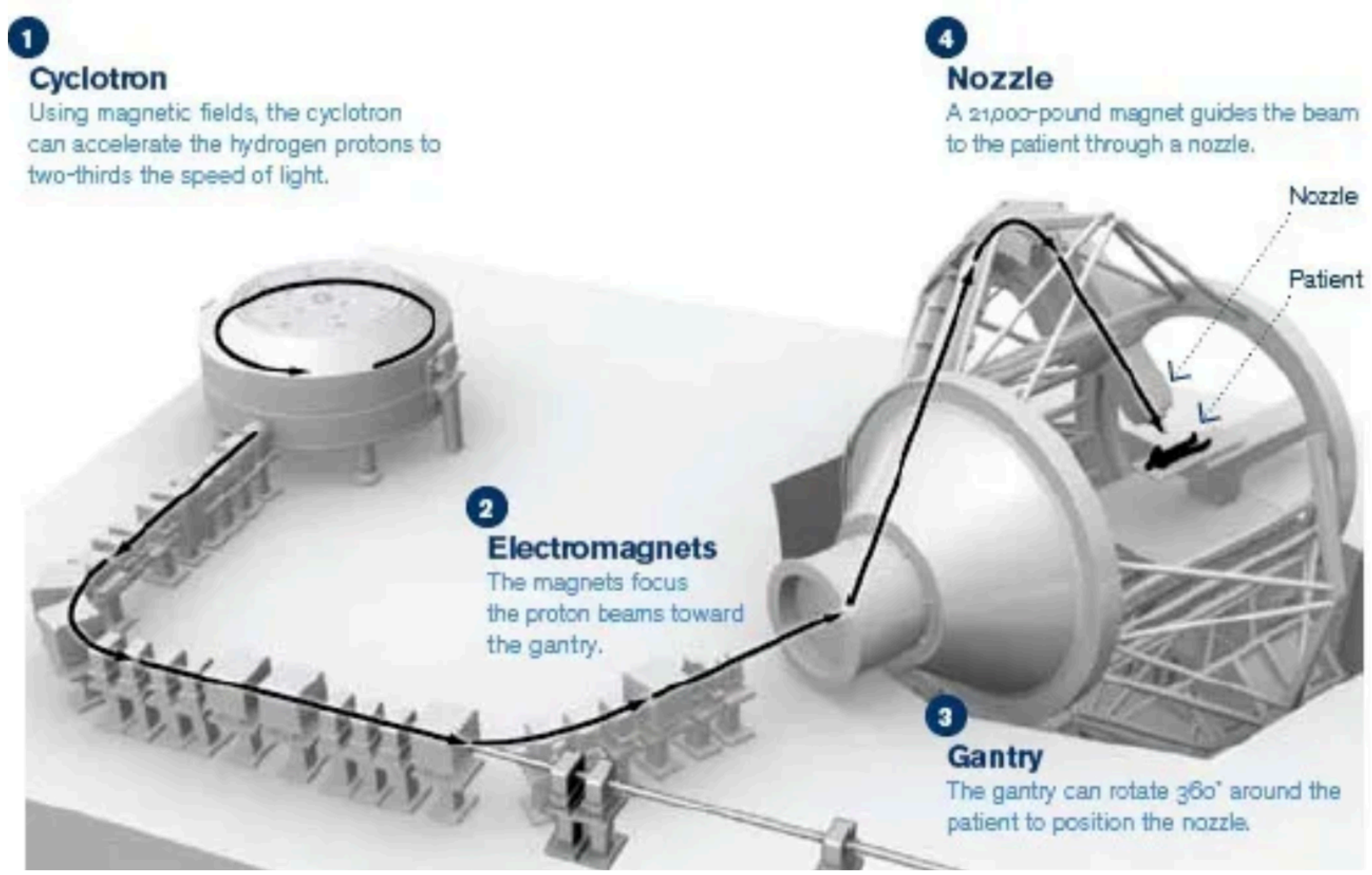
Passive scattering vs pencil beam scanning





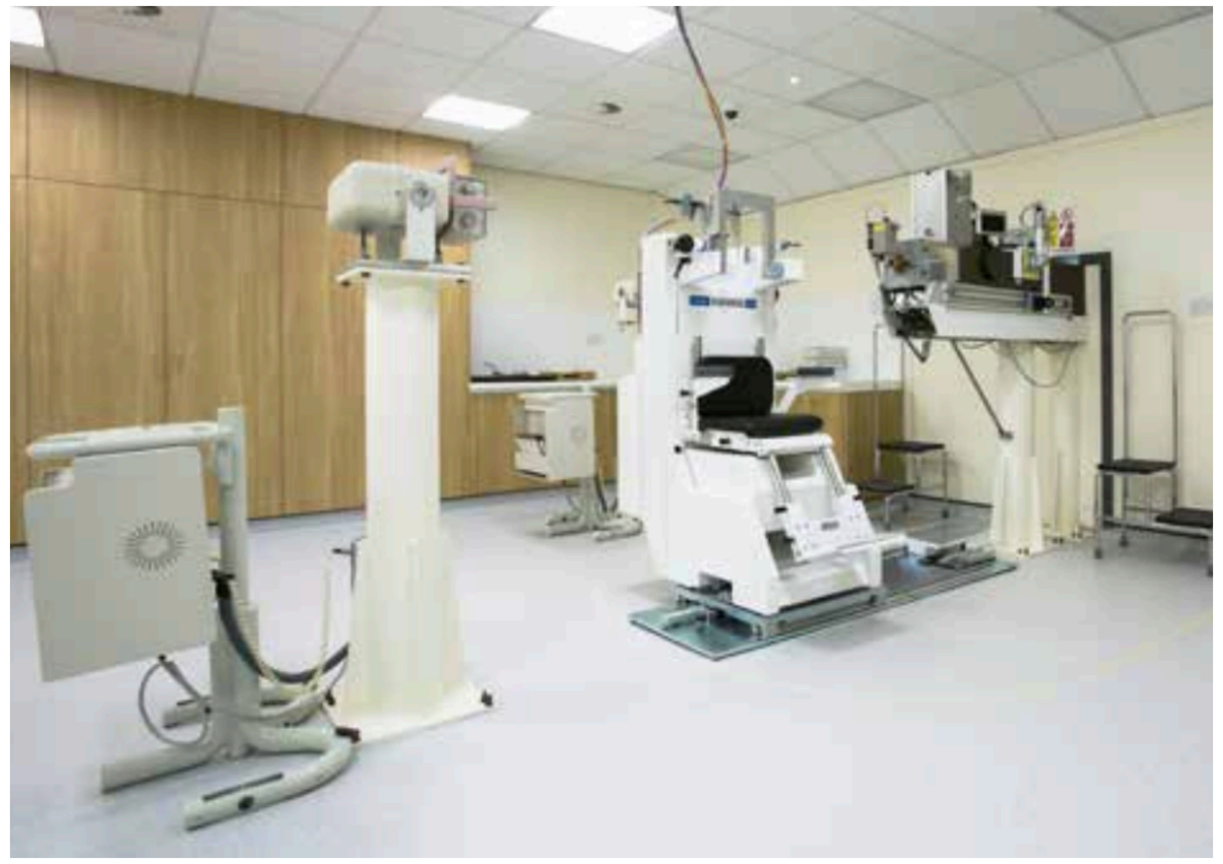


Gantry vs fixed target

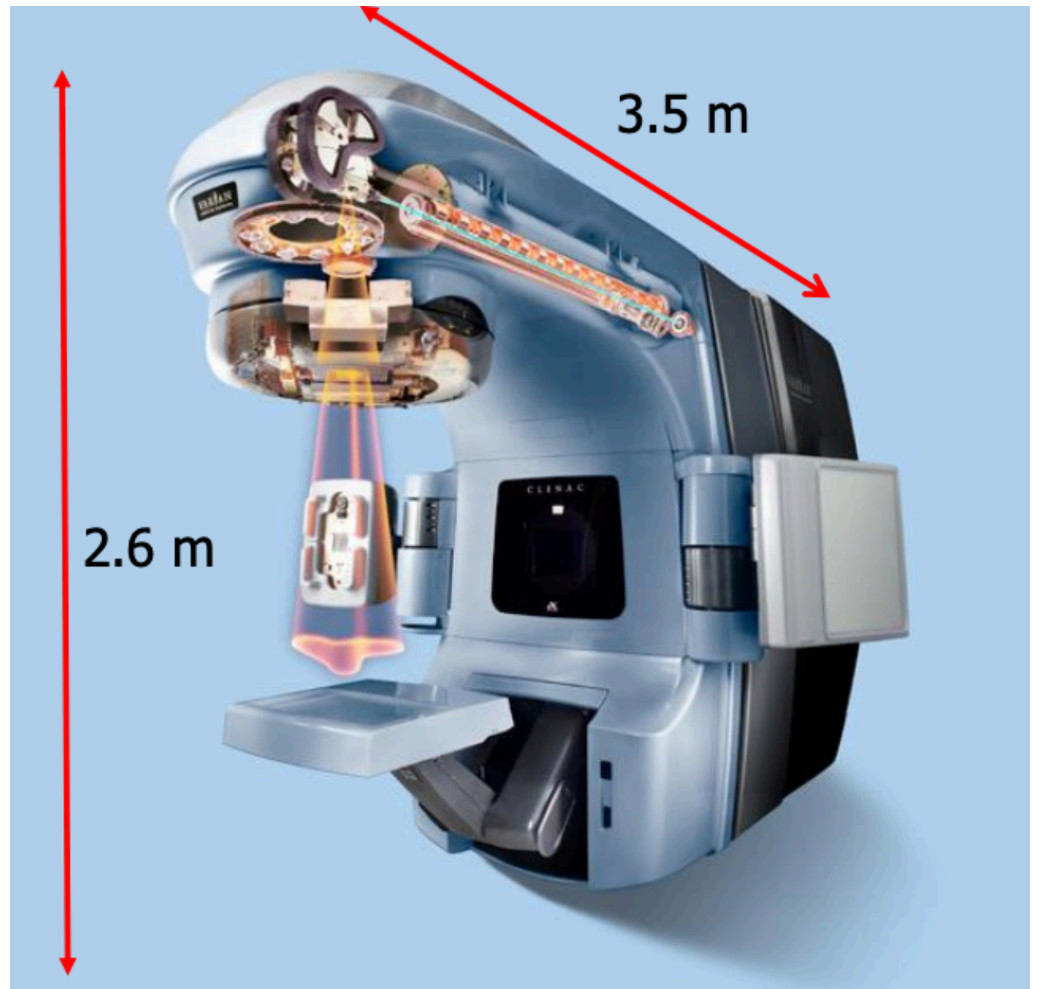



Proton gantry treatment room

Fixed target proton therapy (Clatterbridge, UK)



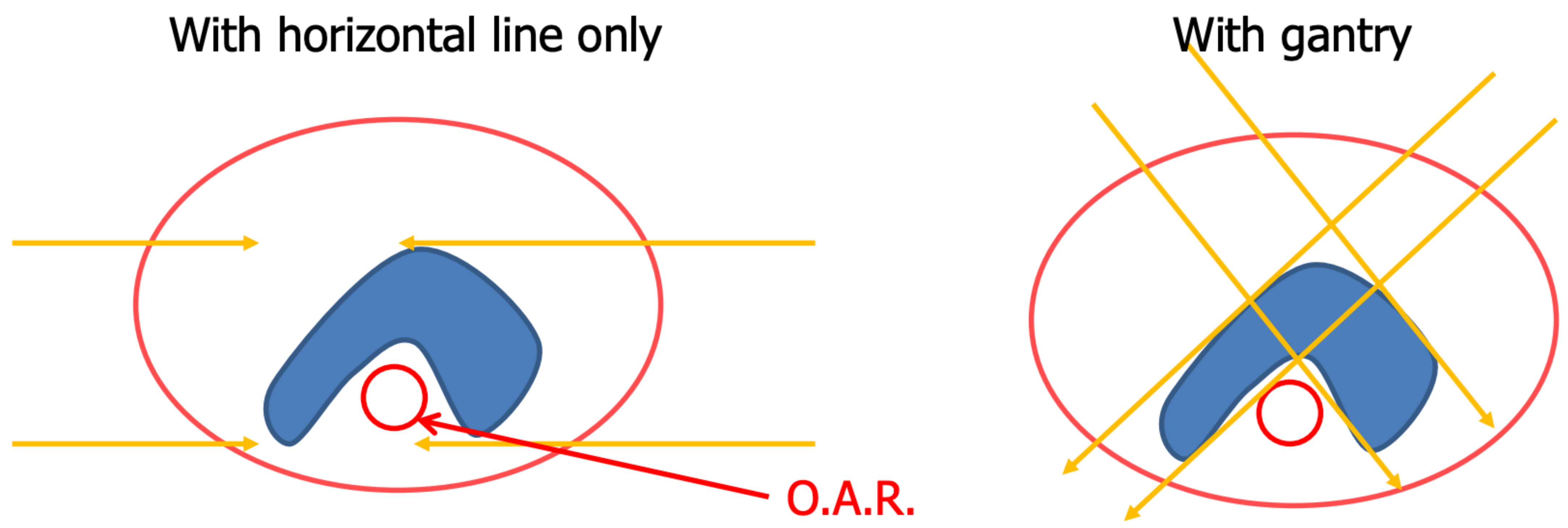
- For x-ray machine whole linac is inside the gantry
- For protons or ions the whole beam line including magnets has to rotate around the patient
- Huge additional cost for particle therapy centres



(Varian Clinac IX)


X-ray gantry

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 beam line including magnets (!) has to rotate around the patient

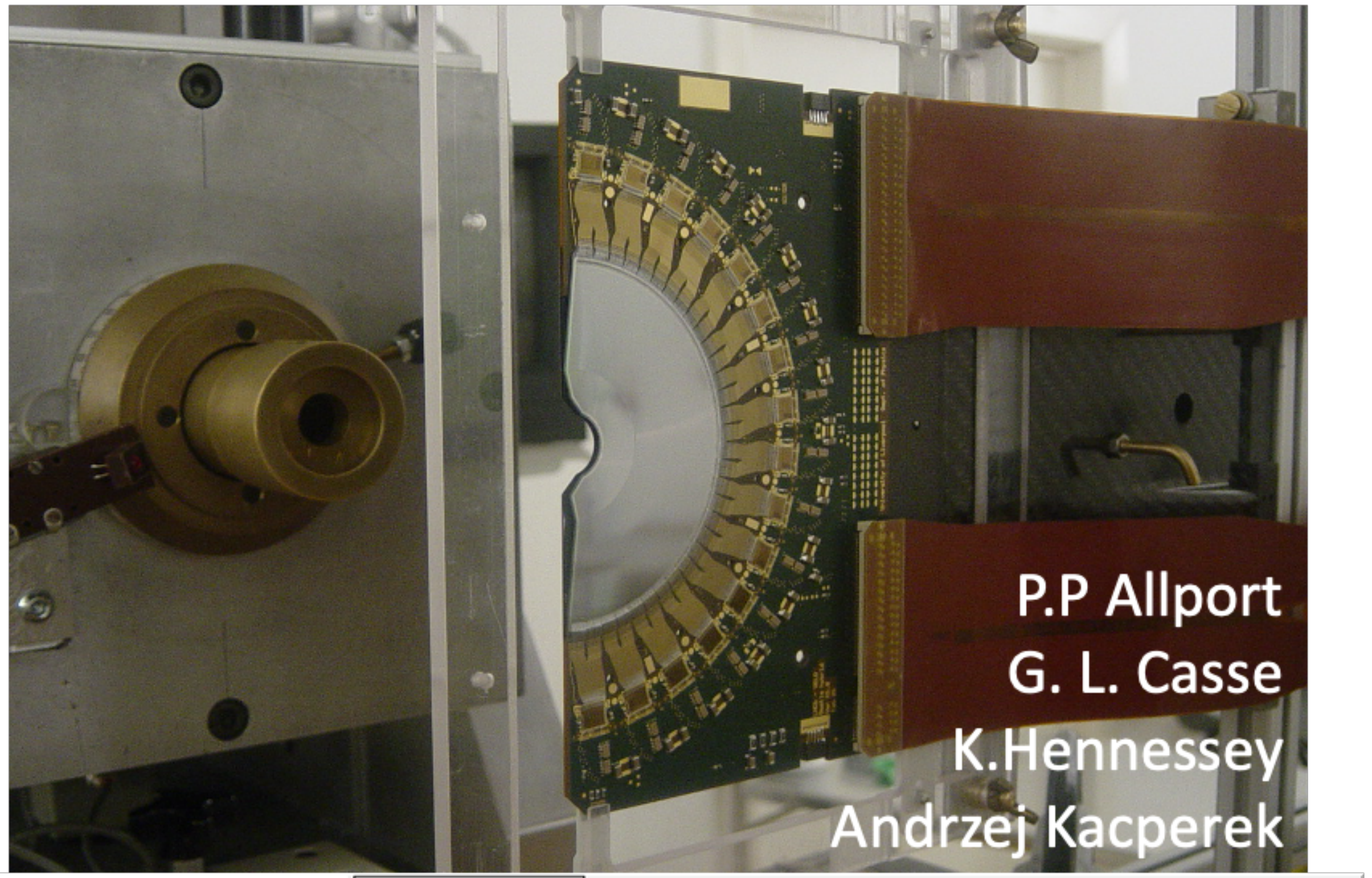
Carbon gantry vs proton gantry!

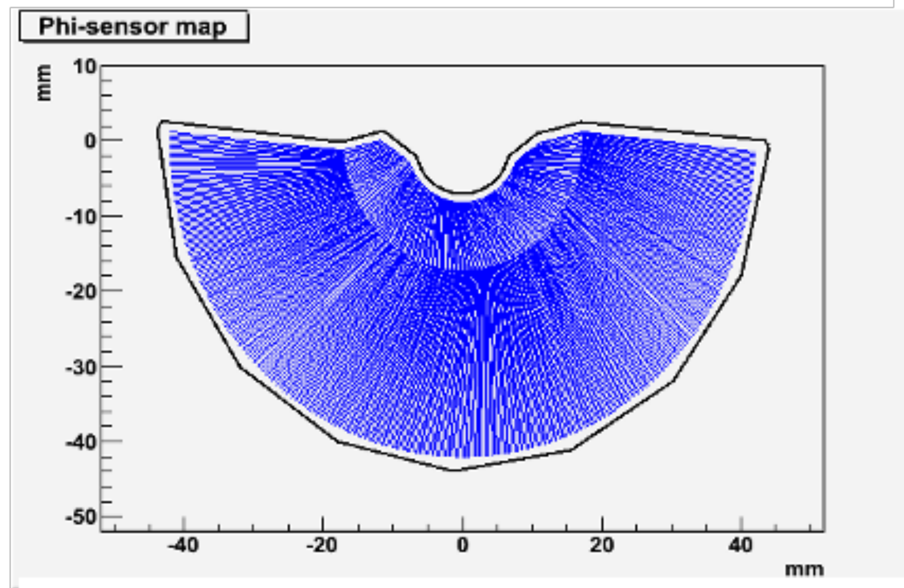
Carbon Gantry

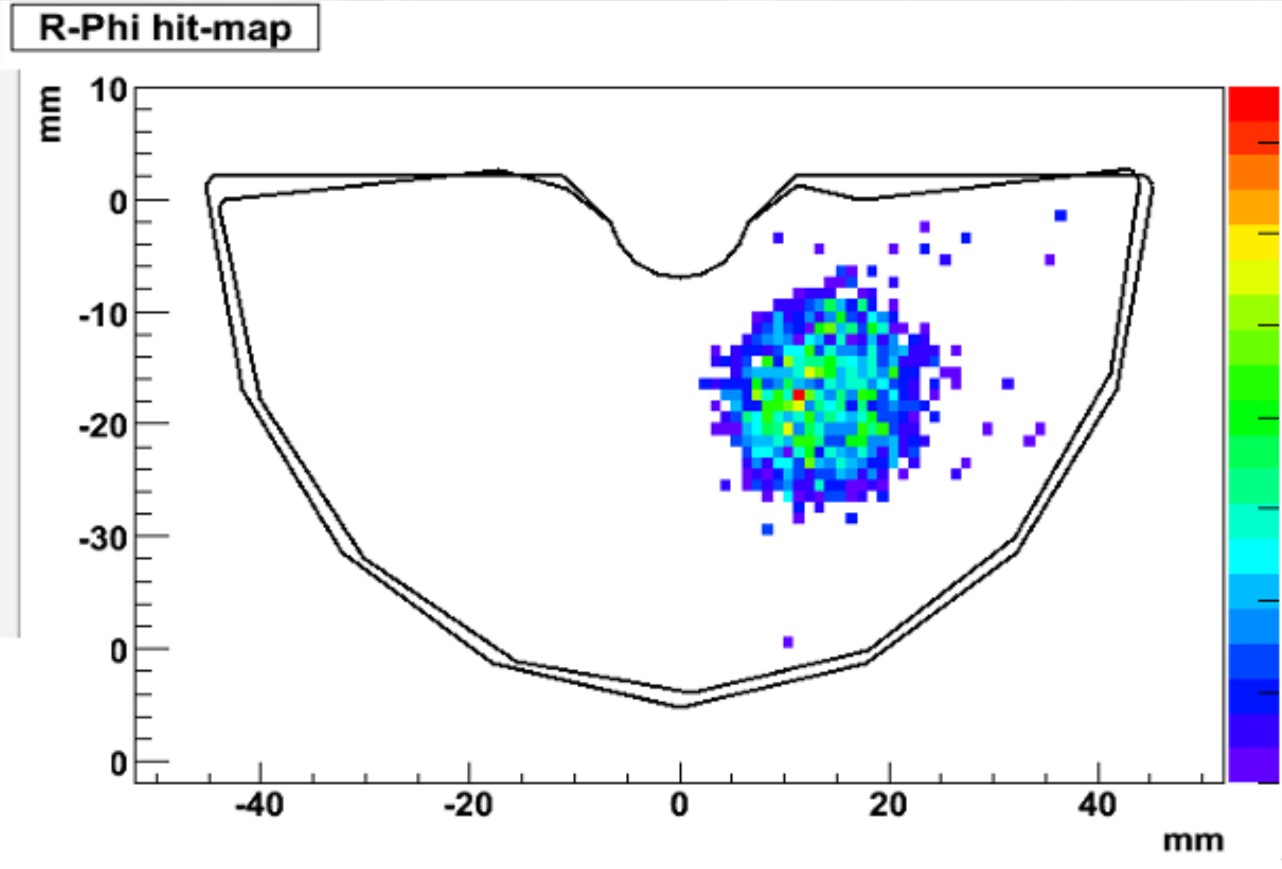
- The HIT Gantry: the only clinical C Gantry
- L = 25 m x f = 13 m, 600 t rotating mass

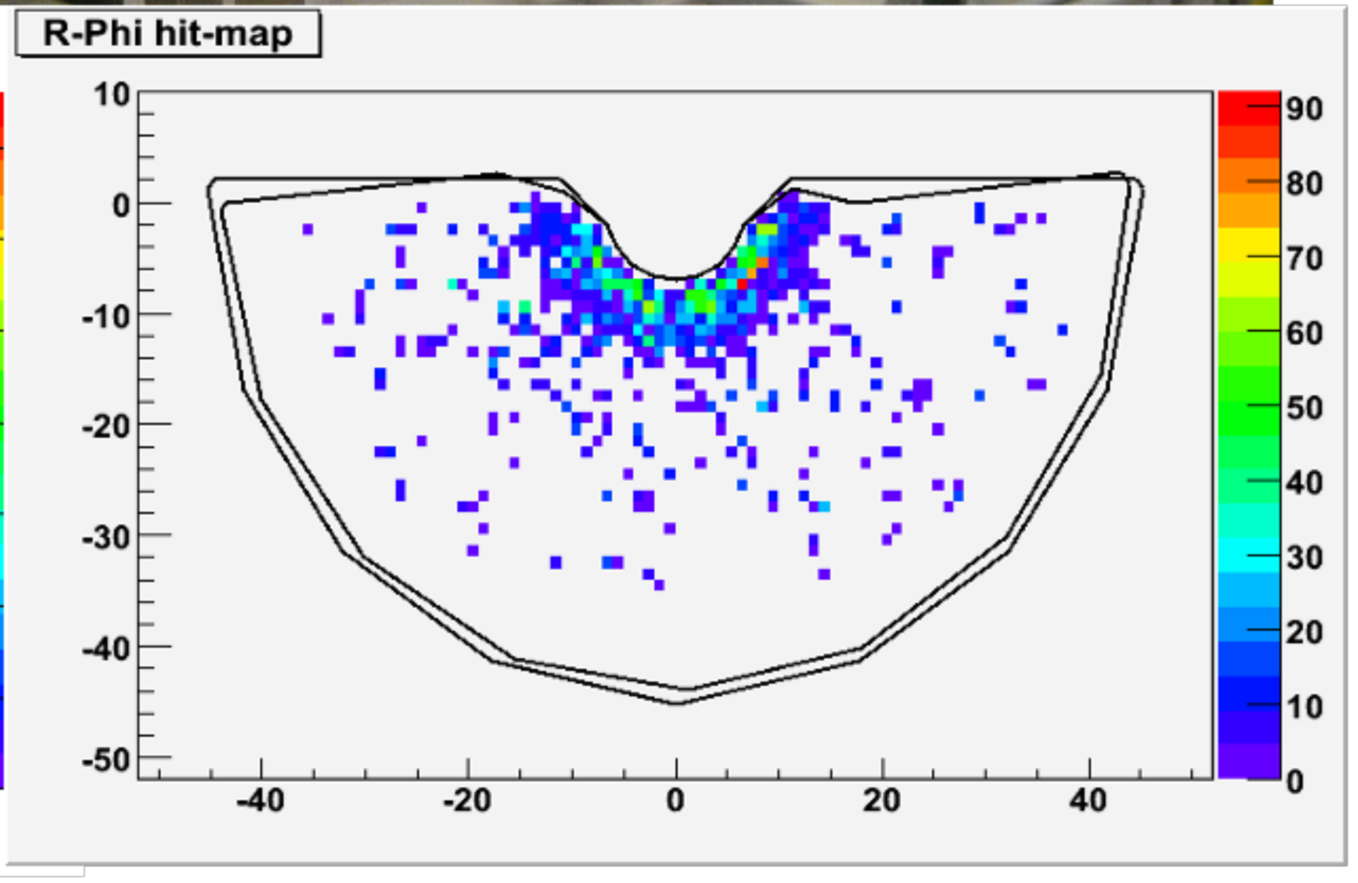
Beam monitoring and dosimetry


Clatterbridge Centre for Oncology
Proton Therapy Facility


P.P Allport
G. L. Casse
K.Hennessey
Andrzej Kacperek





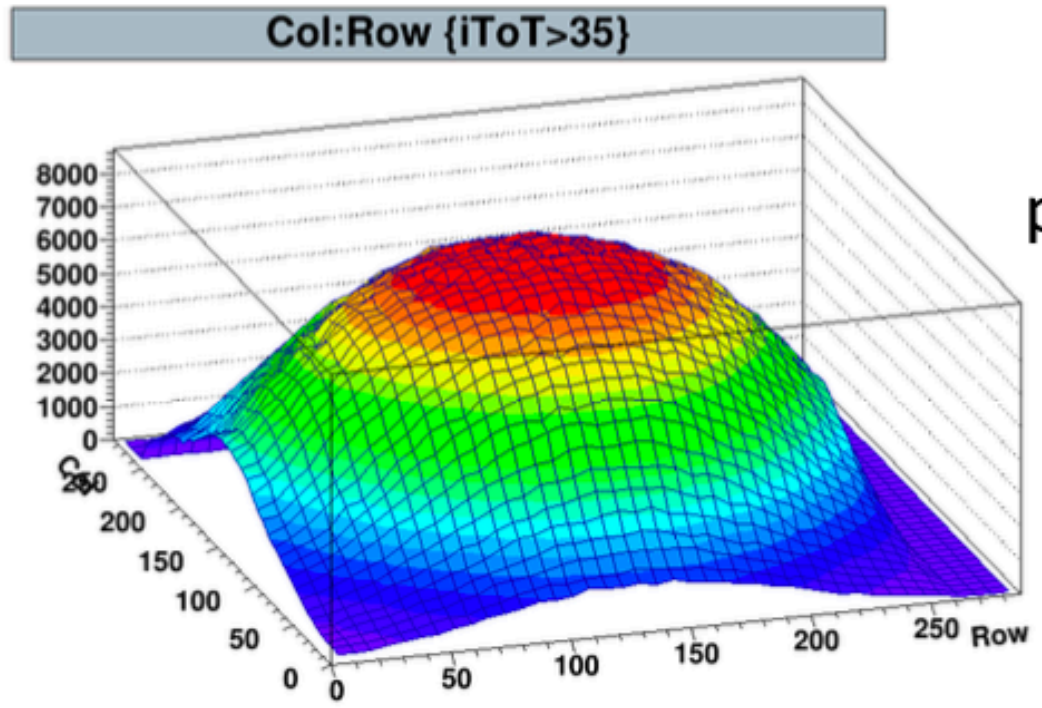


LHCb Back-to-Back Sensor Module

Beam monitoring and dosimetry

ProteusOne beam profile and Energy measurements with Timepix3 chip

- 25mm water depth
- 120 MeV Protons
- 107mm water depth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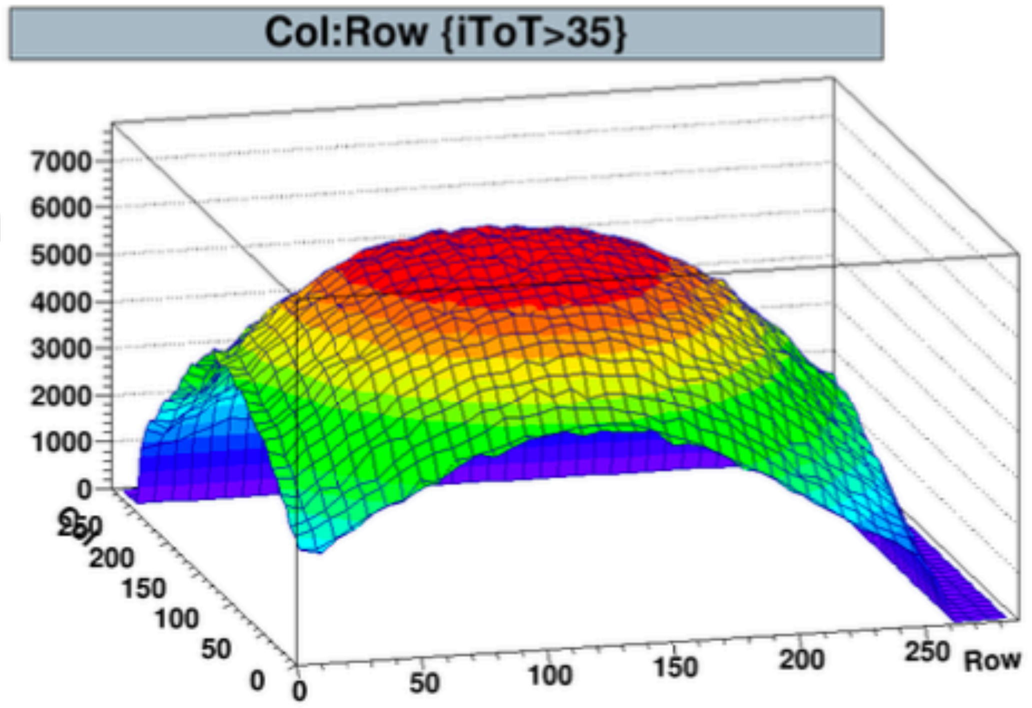
- Most energetic protons in the beam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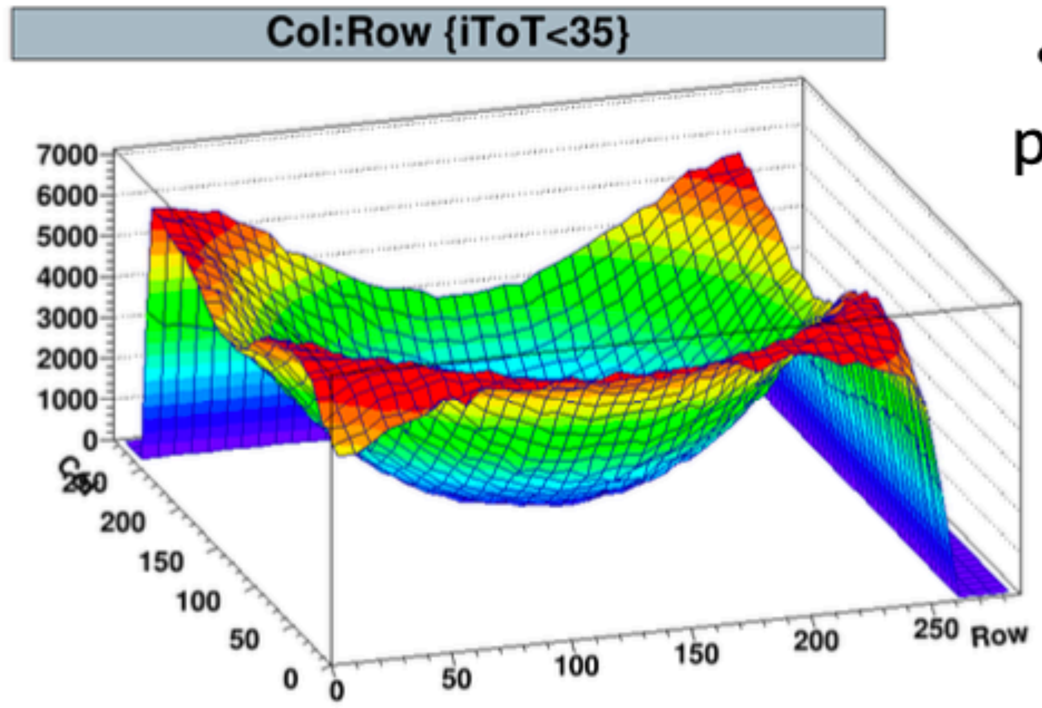
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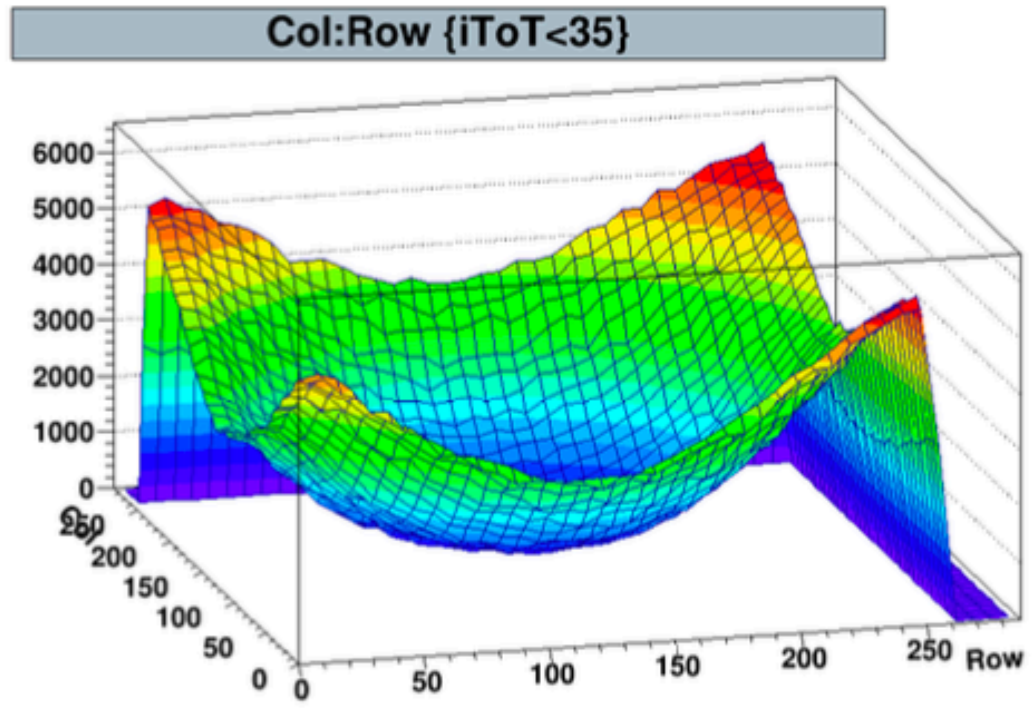
- Least energetic protons in the beam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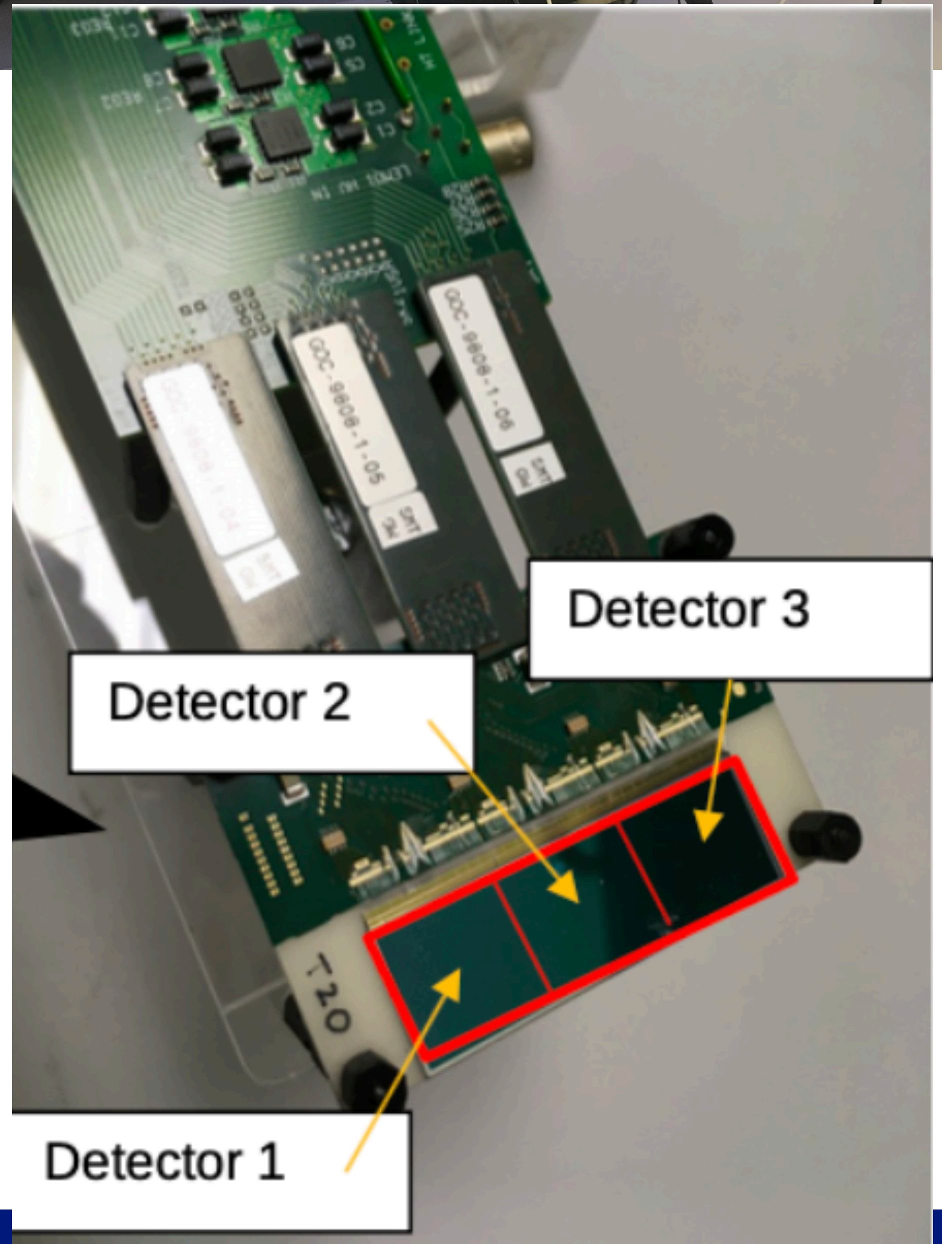
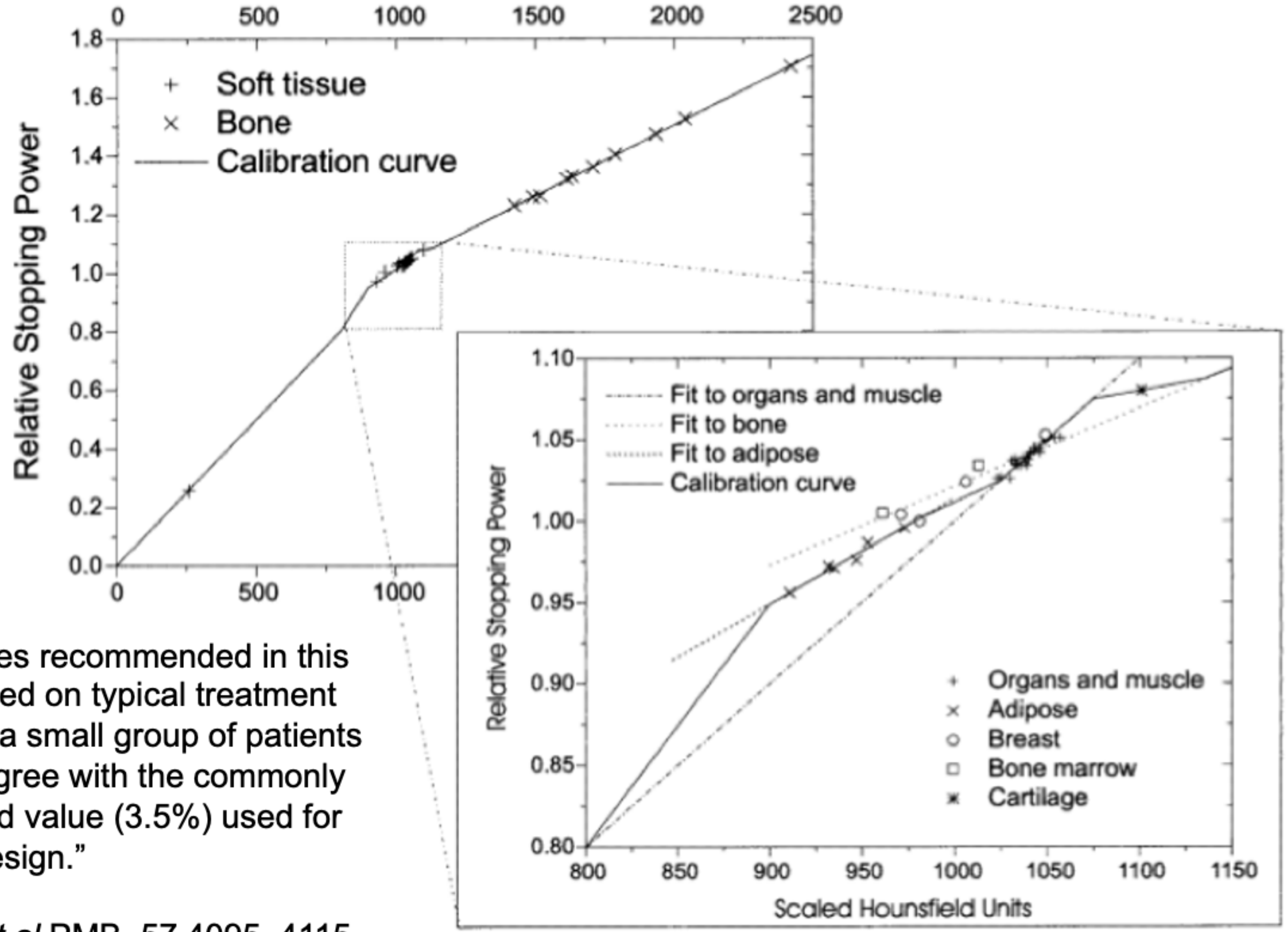
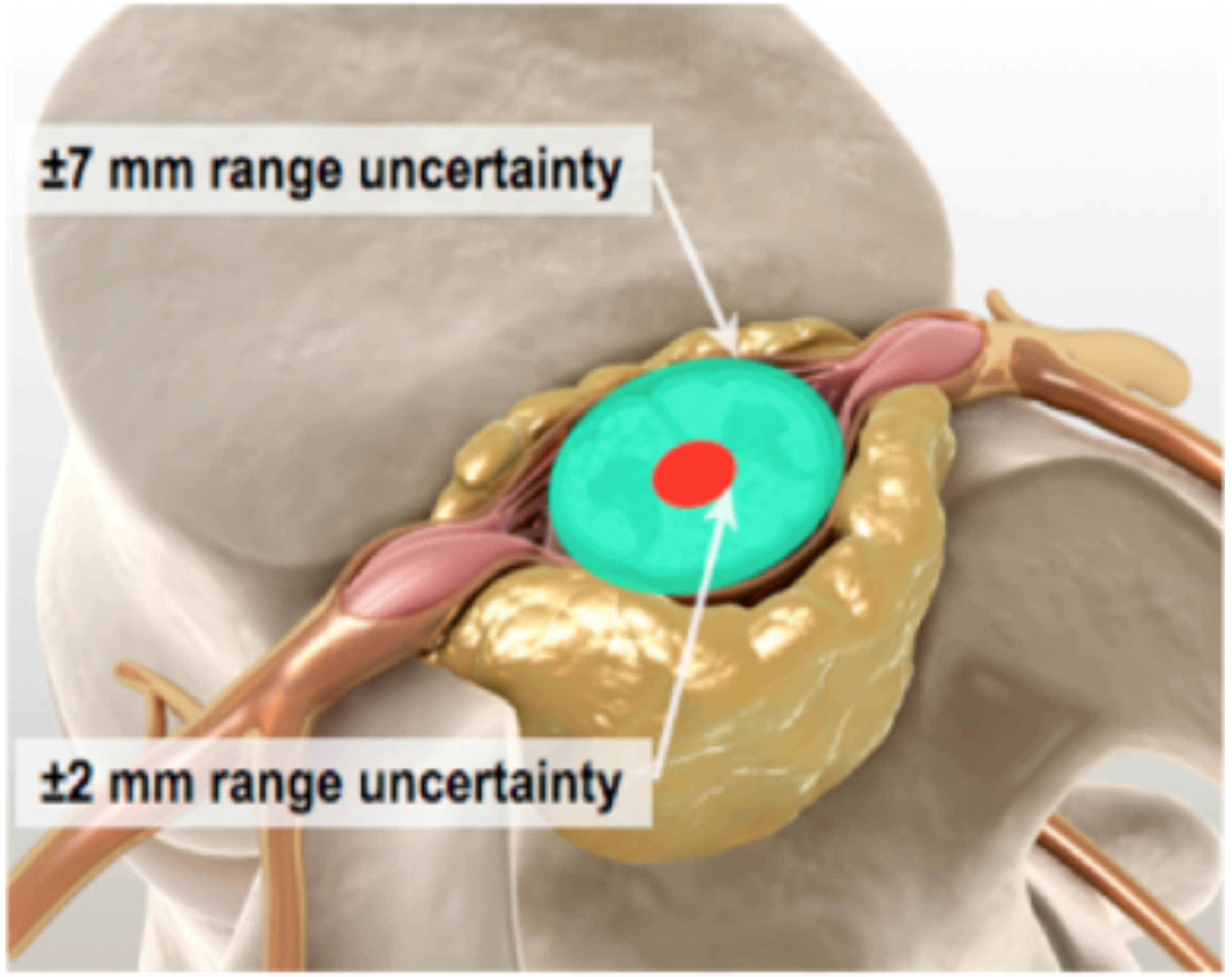


Imaging and planning



"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."

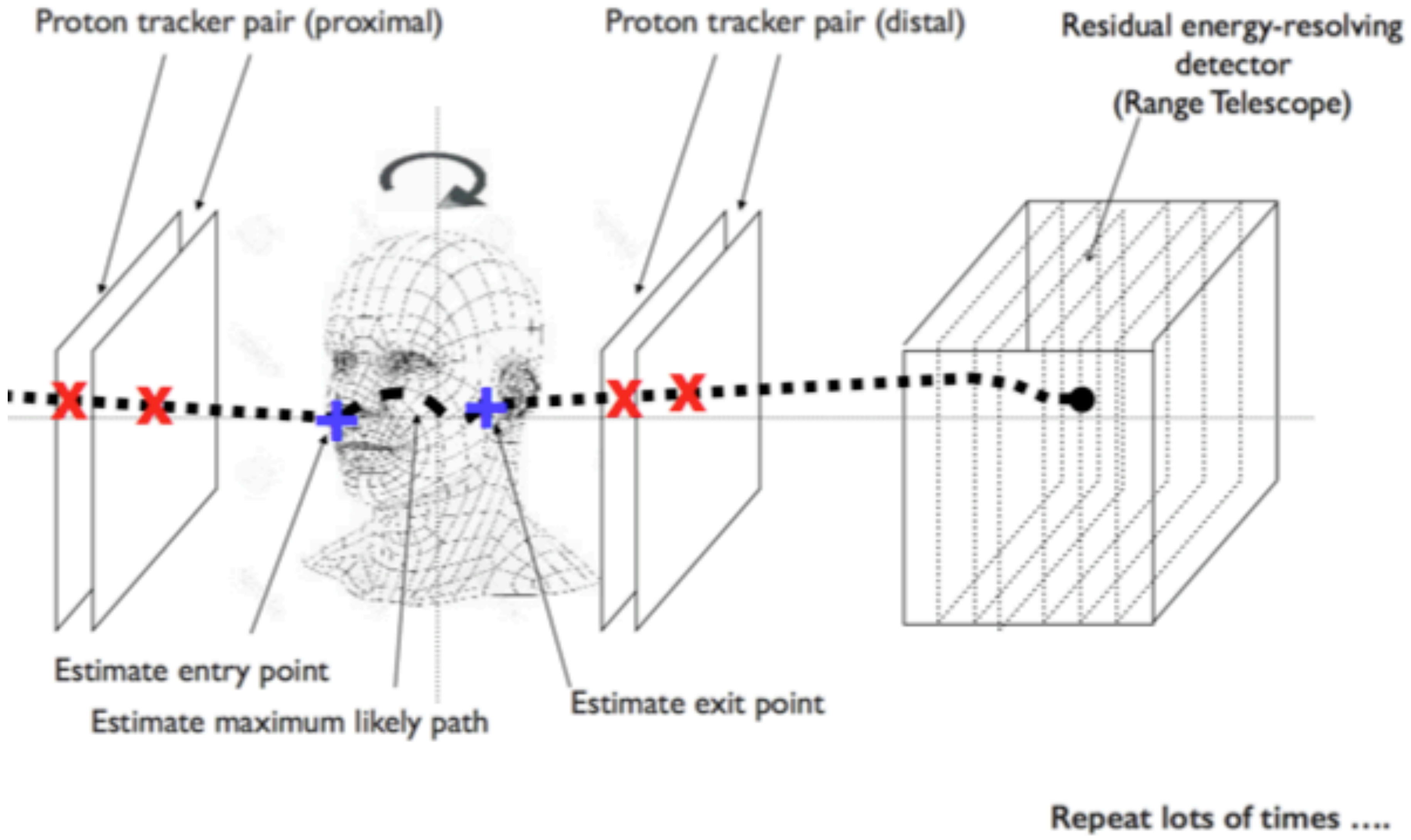
M Yang *et al* PMB. 57 4095–4115 (2012)

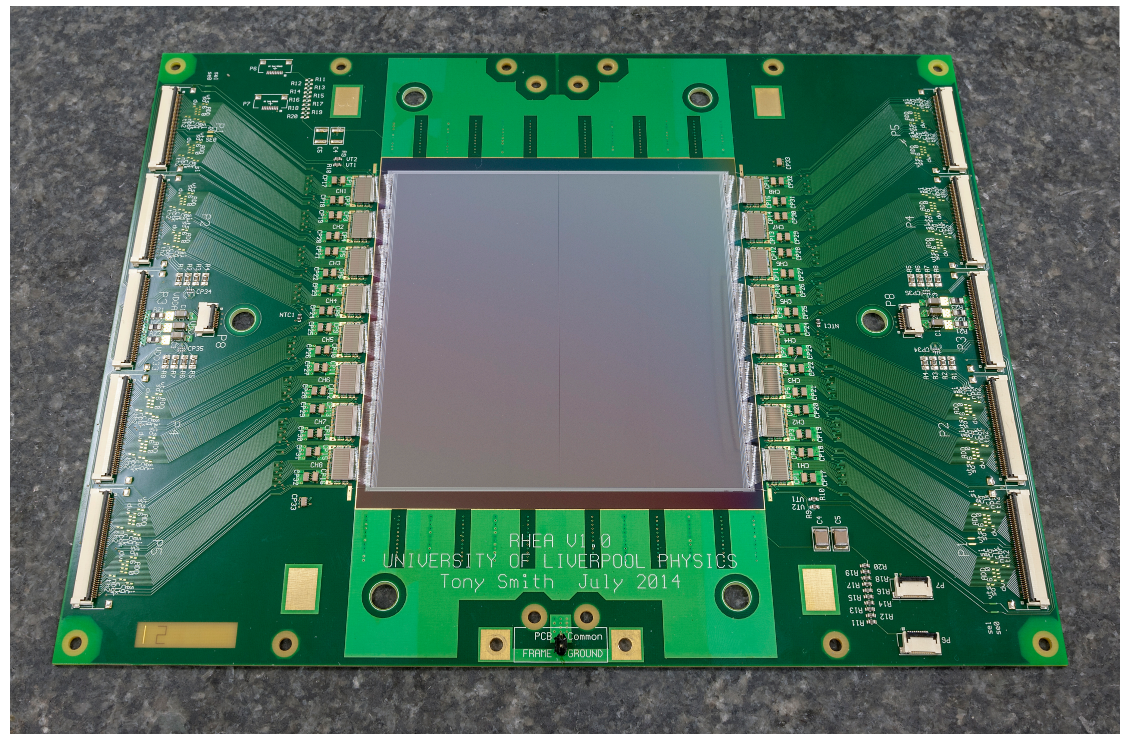


Imaging **and** treating with ions rather than imaging with x-rays and treating with ions offers benefits to patients

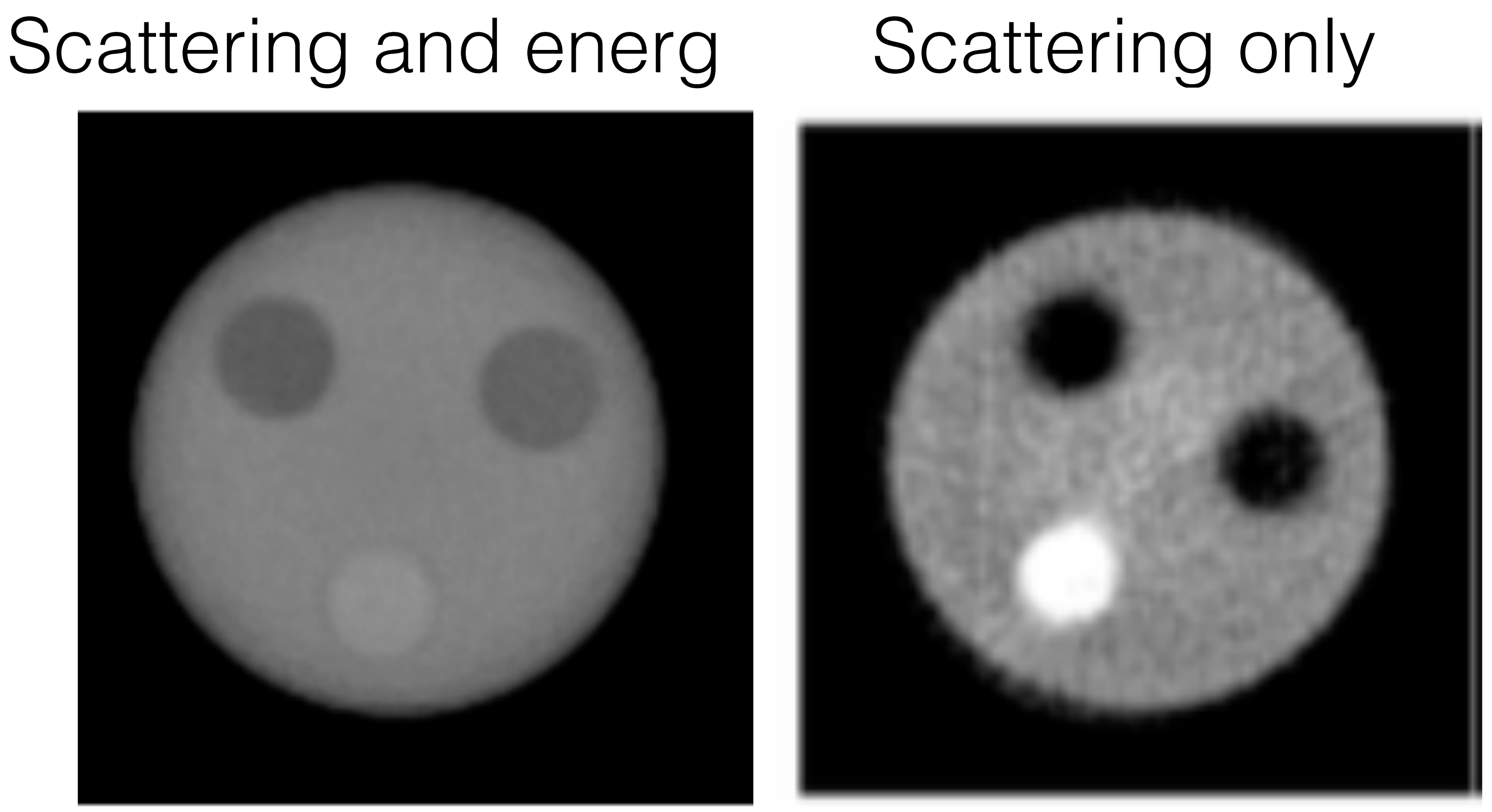
Imaging and planning: CT / radiography with ions

- Proton CT offers the potential of removing inaccuracies generated by proton treatment plans based upon X-ray CT data
- Silicon based proton CT (PRaVDA project) scanner developed within the UK and tested 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 proton radiography could still be used for patient monitoring
- 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

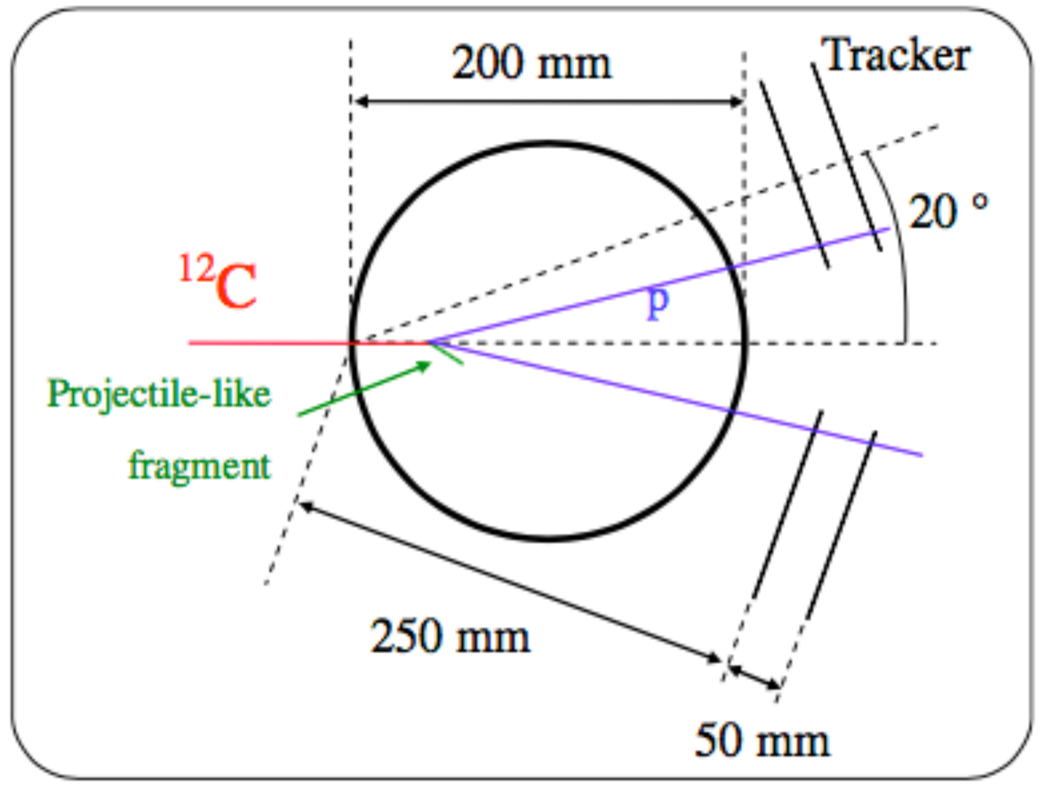

Scattering and energ

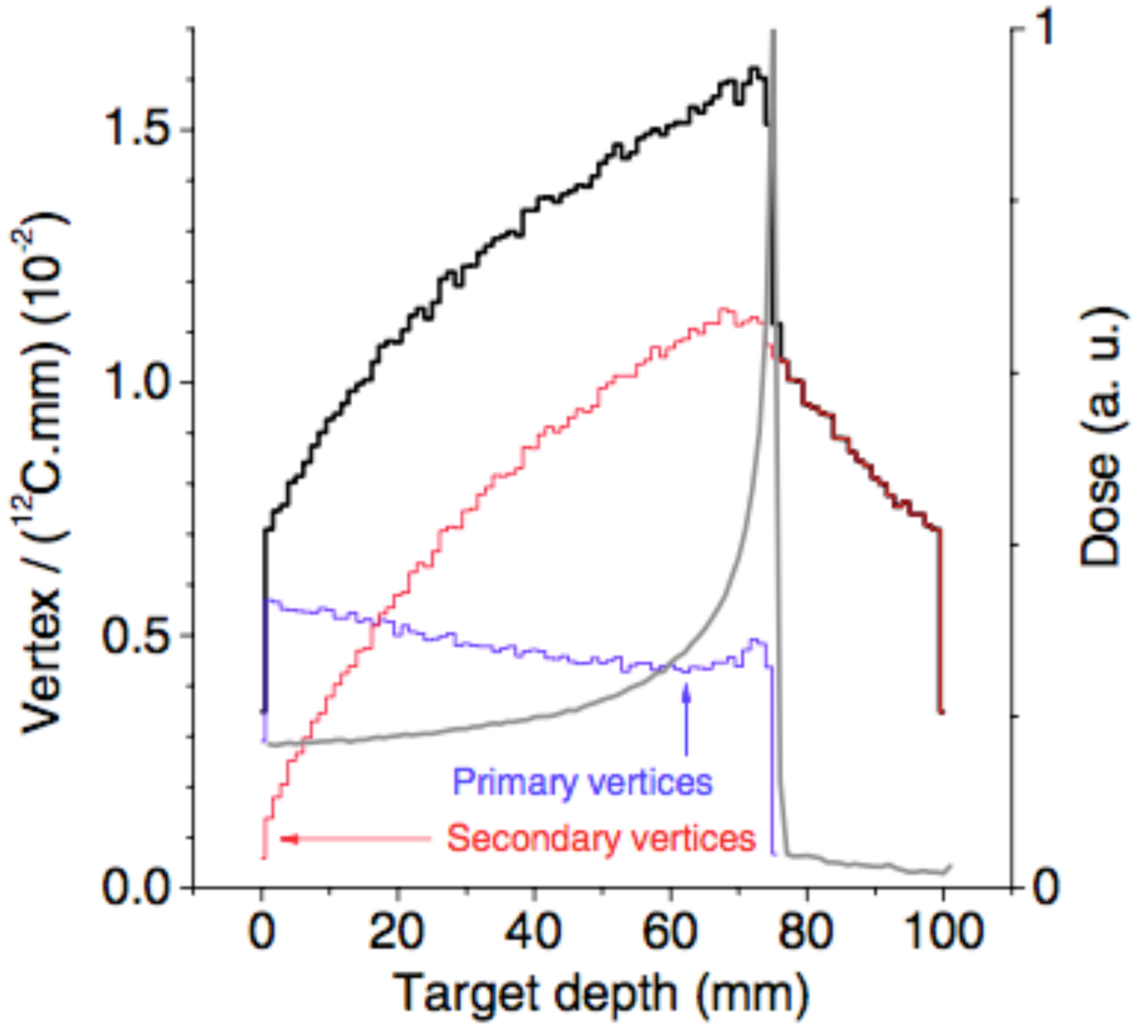
Scattering only

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)
- **Silicon tracking detectors have the potential to be used for this application**



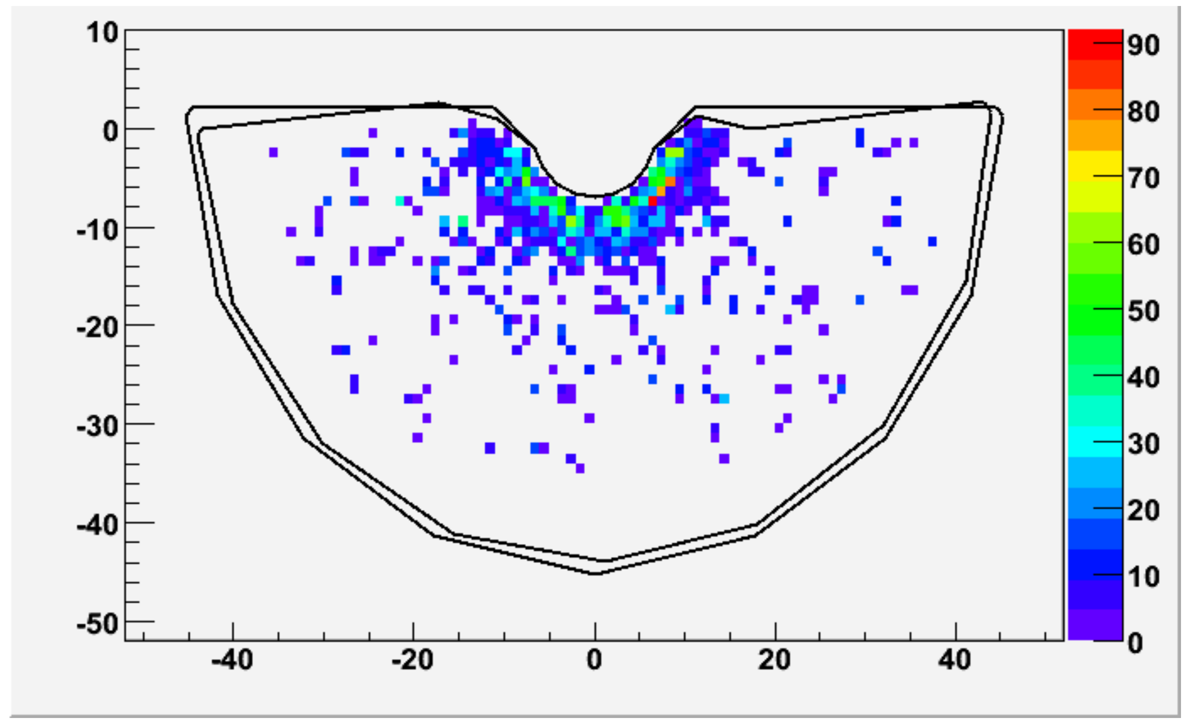


P Henriquet et al 2012 Phys. Med. Biol. **57** 4655

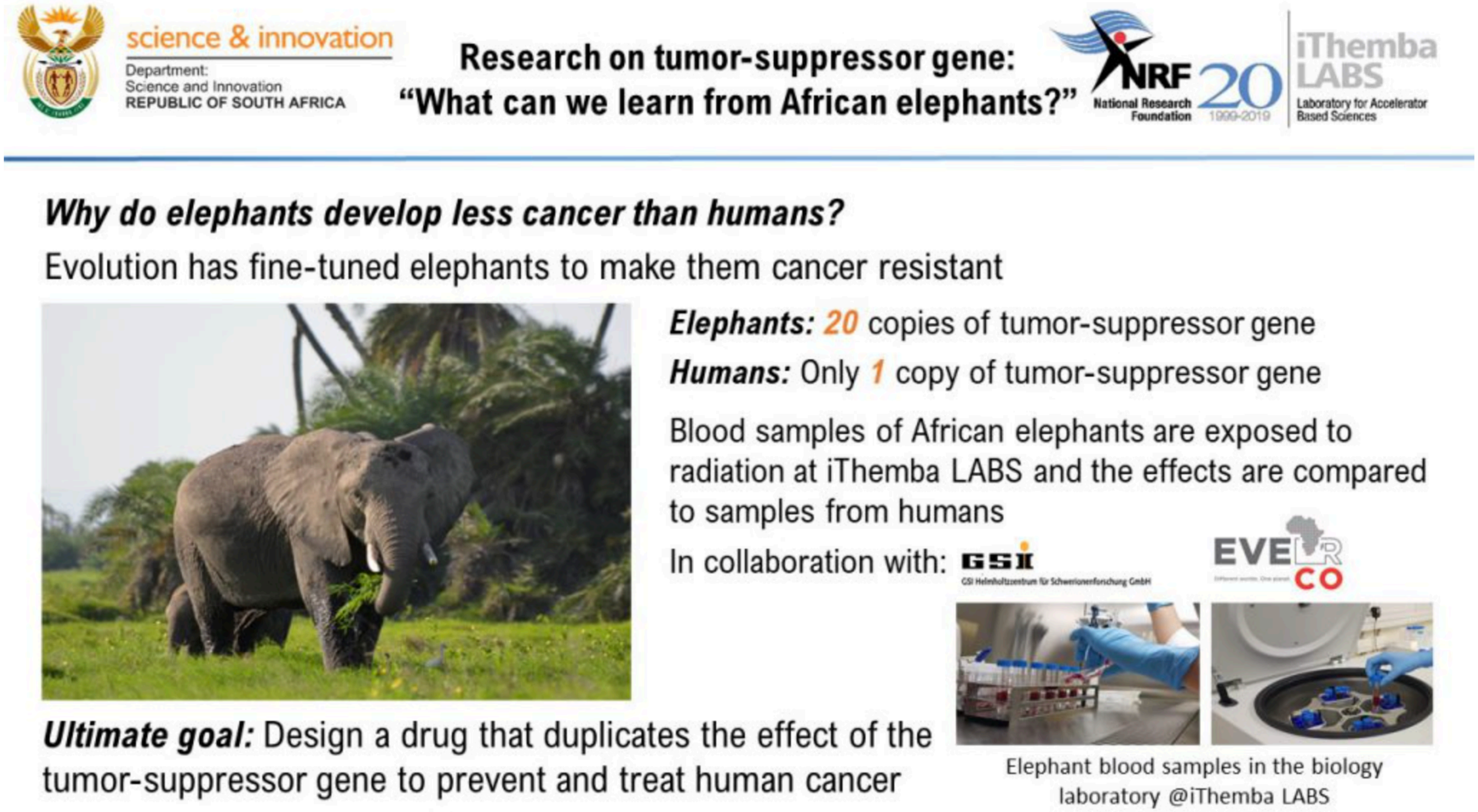
Flash therapy

- 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
  - HV-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?"**

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

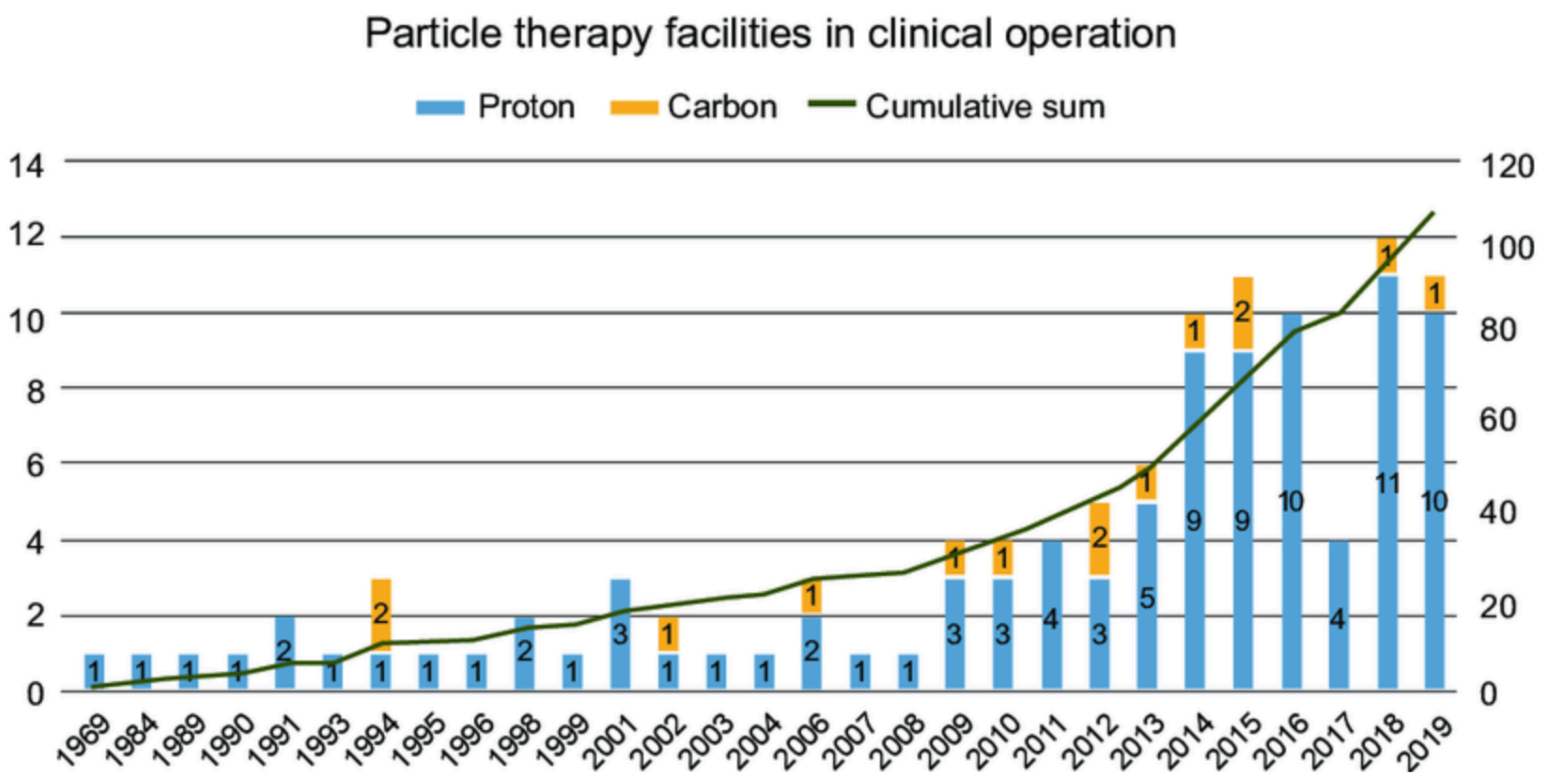
Blood samples of African elephants are exposed to radiation at iThemba LABS and the effects are compared to samples from humans

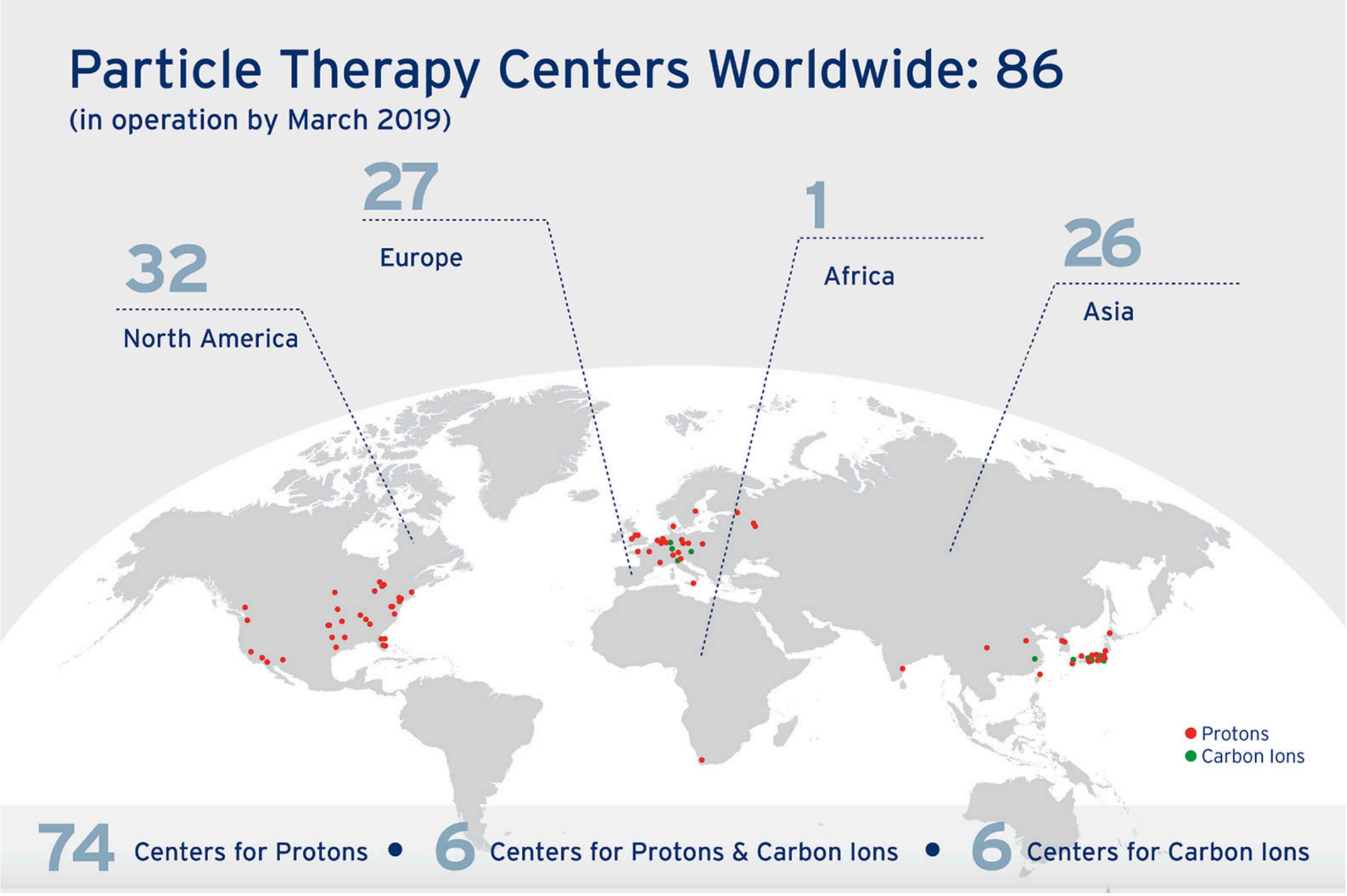
In collaboration with: GSI
GSI Helmholtzzentrum für Schwerionenforschung GmbH

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

The Future..





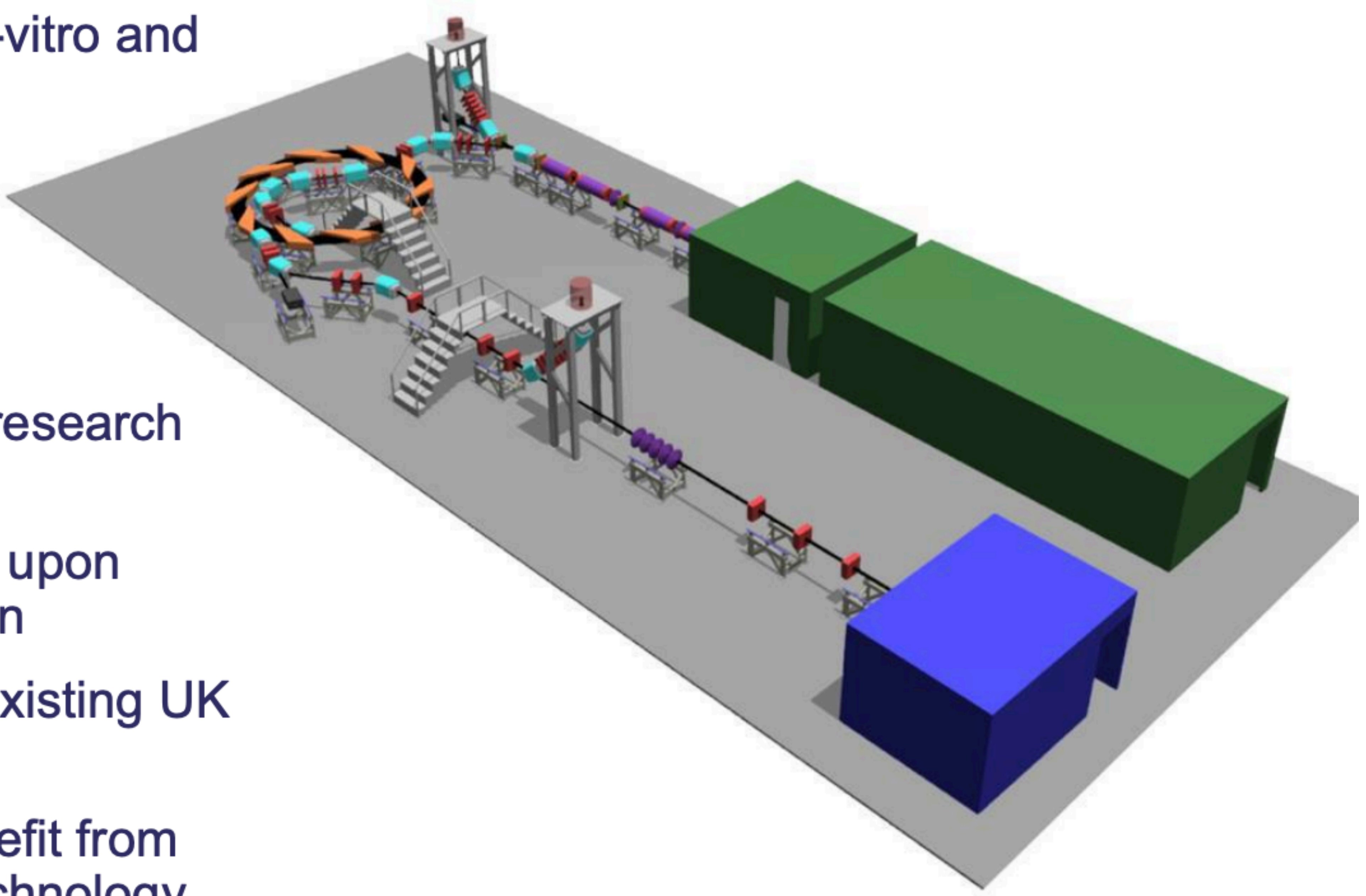
- Many centres under construction worldwide but still dominated by Northern hemisphere
- Increase in carbon ion facilities an also facilities that have multiple ion species available

The Future..

Ion Therapy Research Facility – the ambition

HOW

- A compact, single-site national research infrastructure delivering very high dose rates
- Protons and beyond, at energies sufficient for both in-vitro and in-vivo studies
- Consider technical options, with different risk profiles



PROPOSED PLAN

- Conceptual design of layout, cost and operation of a research facility
- Develop innovative laser-plasma technology, building upon world-leading expertise within the LhARA collaboration
- Develop innovative end-station designs, building on existing UK expertise in proton radiobiology research
- Collaborative agreement with CERN allows us to benefit from enormous experience and expertise in accelerator technology and successful projects

Closer to home in the UK….

https://indico.stfc.ac.uk/event/668/contributions/4320/attachments/1494/2626/1272-pa1-pm-prs-0016-v0.1%20EndStationMtg1%20ITRF%20Owen.pdf

Summary

- The link between physics and medical technology is as strong today as it has ever been, maybe more so given the increased use of particle accelerators for radiotherapy
- 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 physics of the superior dose distribution allowing better treatment and additional treatment modalities
- Physicists and engineers need to lead developments for particle therapy to ensure the maximum potential benefit from the physics is transferred to maximum beneficial outcomes for patients. This was already done for x-ray radiotherapy with great success (ie IMRT)
- Many new centres for proton and ion therapy are under construction worldwide and with them lots of interesting instrumentation challenges ahead! Well worth considering research projects / further study in this area