Dosimetry for proton beam cancer therapy at NPL

Ana Lourenço

University of Cambridge, February 2023

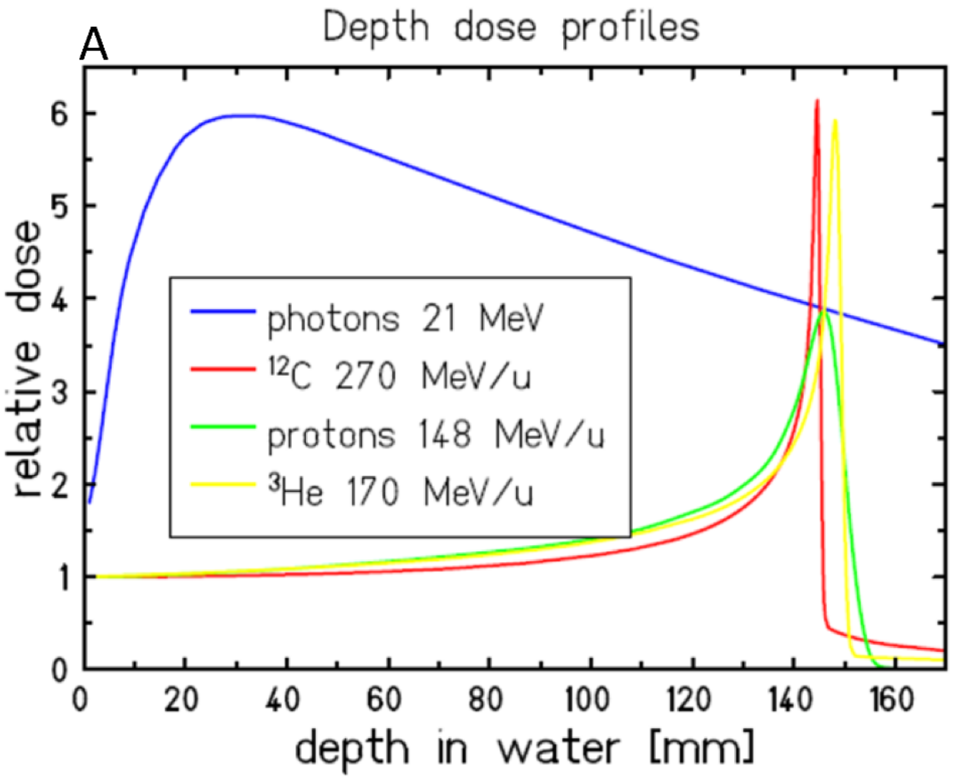
NPL – National Physical Laboratory

- UK's National Measurement Institute (equivalent to NIST in the USA)
- Develop and apply the most accurate measurement standards
- **Primary standard - sufficiently accurate – used to calibrate secondary measurement standards**
- Define standard quantities
- Radiotherapy – absorbed radiation dose
- Dedicated programs on the development of standards and protocols for radiotherapy

Teddington, South London

Rationale for radiotherapy

- About 350000 new cancer cases are diagnosed every year in the UK
- Radiotherapy is the most cost-effective treatment for cancer and 50% of people diagnosed have radiotherapy
- It can be delivered in various modalities
  - Photons
  - Electrons
  - Protons
  - Carbon-ion
  - Helium
  - …



Tinganelli and Durante 2020 Cancers 12

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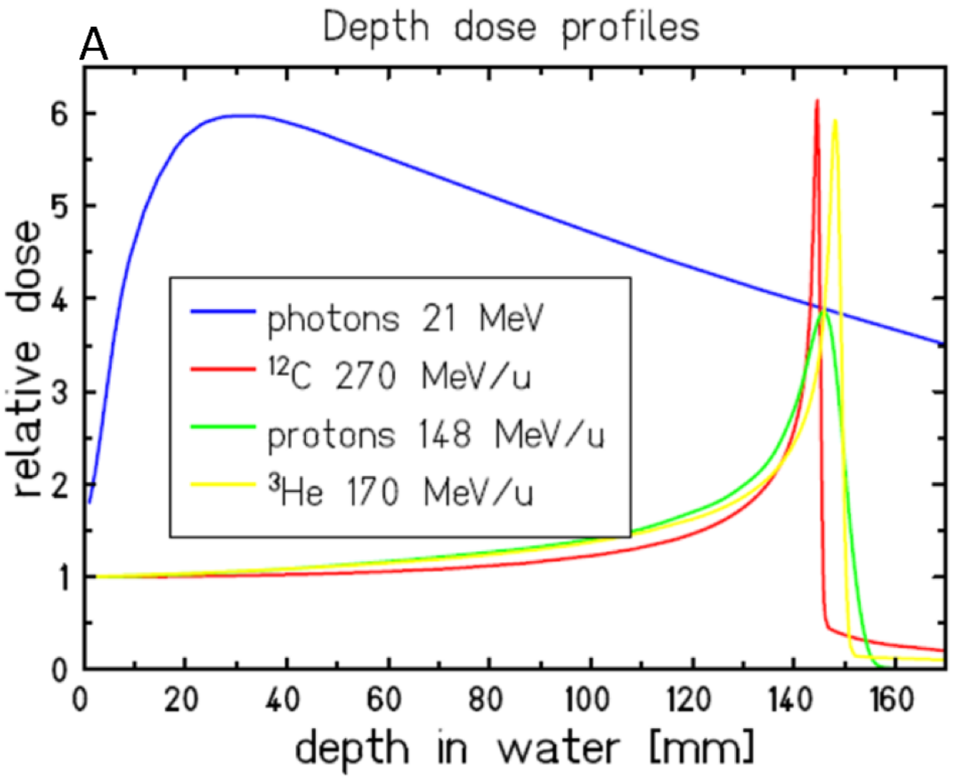

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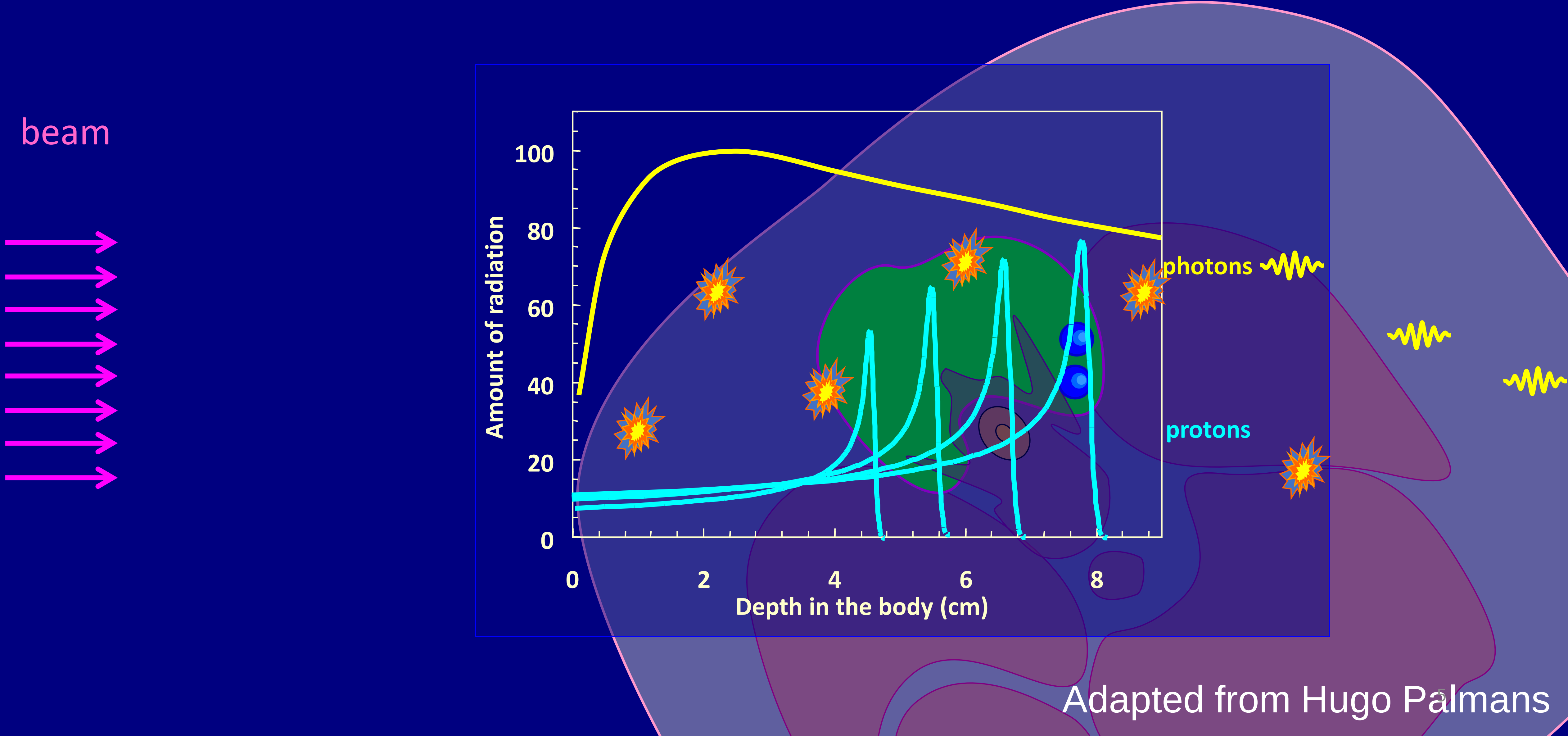
Radiotherapy: photons vs protons

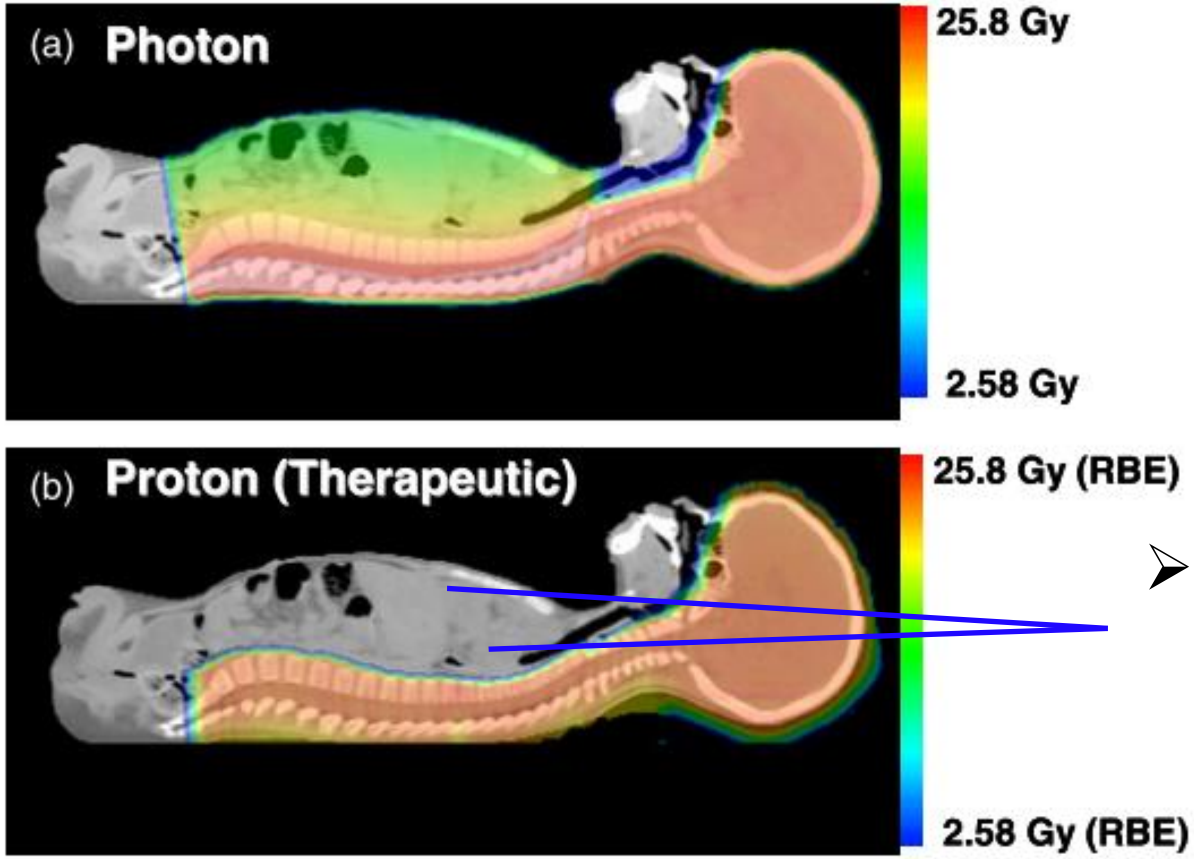


Adapted from Hugo Palmans

A clinical example

Craniospinal radiation dose distribution for a pediatric medulloblastoma patient

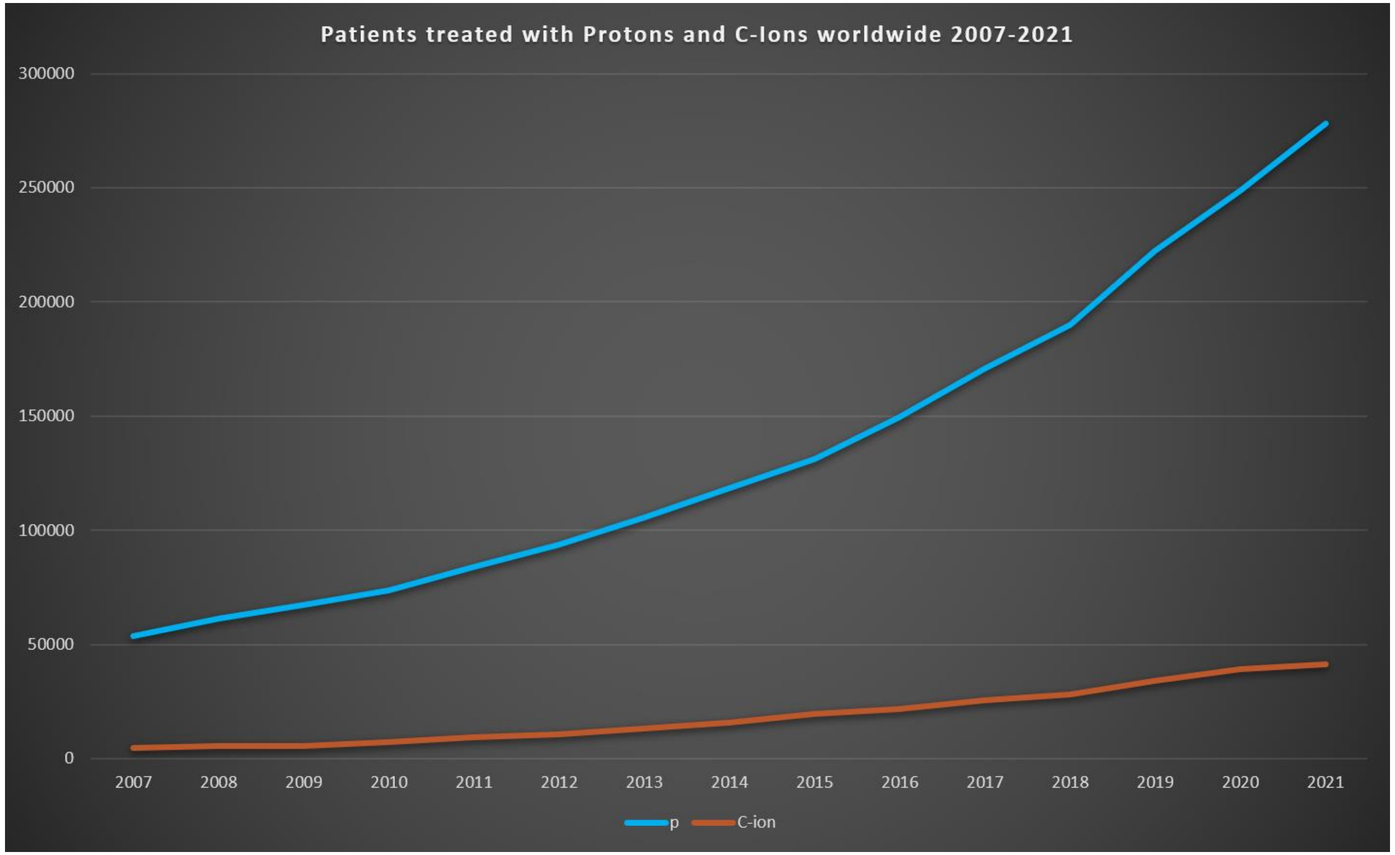
- Colour shows the radiation dose maps, where radiation dose is deposited



- No radiation dose delivered to lungs, heart, etc with protons

Zhang et al 2013 Phys. Med. Biol. 58

Rationale for Proton Beam Therapy



- Per end of 2021 **280000 patients** have been treated worldwide with proton therapy
- UK government invested £250M in 2 NHS state-of-the-art proton therapy clinics

Worldwide:

- 122 facilities in operation
- 88 facilities under construction
- 65 facilities in planning stage

Why consistency and accurate knowledge of radiation dose are important?

The success of radiotherapy depends on delivering the correct radiation dose to the patient

If radiation dose delivered is too low – recurrence of the cancer

If radiation dose delivered is too high – damage healthy tissues

Accurate dosimetry is essential!

science by which radiation dose is determined

- ICRU Report 24, IAEA TRS-398: Radiation dose delivered to the patient should be within 5% of the prescribed radiation dose value (k=1)
  - **Reference dosimetry uncertainty: 1% (k=1)**

Dosimetry chain

- **Aim of NPL Radiotherapy Programme: to support the safe and optimised application of radiotherapy modalities**
- **Primary standard - sufficiently accurate – used to calibrate secondary measurement standards**
- Radiotherapy – absorbed radiation dose

Primary standard
(standard conditions, absolute reference)

→

Reference standard

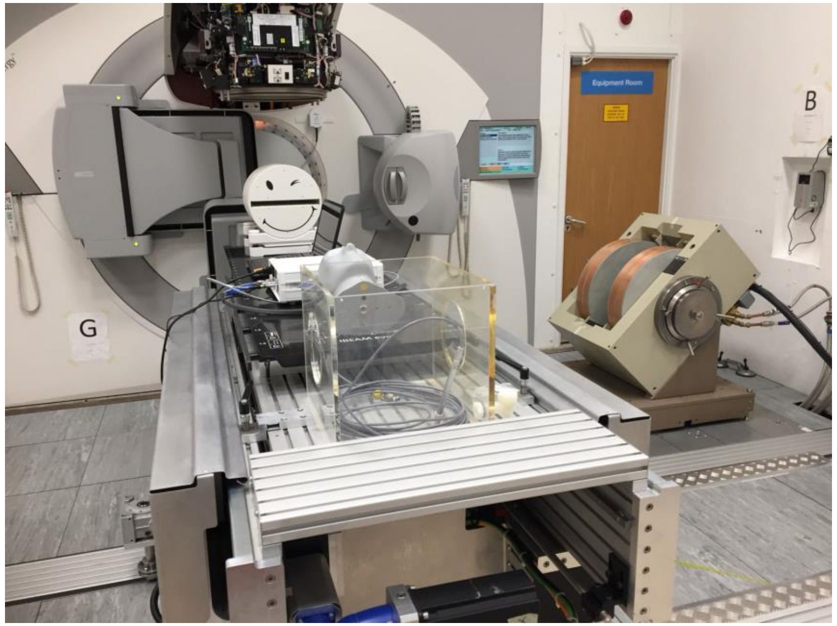
Calorimeter
- complex
- not commercially available
- not portable
- slow to operate

Ionisation chamber
- simple and portable
- calibrated against the primary standard

- ➢ There is no dedicated primary standard for dosimetry directly in proton therapy beams
- ➢ Uncertainty in radiation dose at least 2 times larger than the recommended uncertainty

Developing a primary standard calorimeter for protons at NPL

- No proton beam at NPL
  - Calorimeters are complex and difficult to operate
  - On-site LINACs (medical linear accelerator)
  - Controlled environment



NPL National Physical Laboratory

Developing a primary standard calorimeter for protons at NPL

- No proton beam at NPL
- Established research collaboration with Clatterbridge Cancer Centre

Aim of the original project was to explore the variation of the current recommendations of dosimetry protocols and the feasibility of building a primary standard to routinely operate in the clinical department

Visit and meeting at Clatterbridge 6/11/02

Present: Andrzej Kacperek (AK), Russel Thomas (RAST), Frank Verhaegen (FV), Hugo Palmans (HP)

13:30 Delicious lunch at 400 years old pub

14:30 Visit to workshop and proton treatment room

Inventory of equipment available at Clatterbridge:

- Milling-machine: accuracy 0.005mm, working area 400 mm x 280 mm
  - Plastics, graphite, aluminium, brass,…
  - We could have phantom inserts, etc. made there at no cost for NPL. For parts that need construction, provide drawing + parts that have to be inserted such as ion chamber.
- Computer dedicated to research (we could install MCNPX here!)

ACTION: FV will send AK procedure to obtain MCNPX from NEA database

Developing a primary standard calorimeter for protons at NPL

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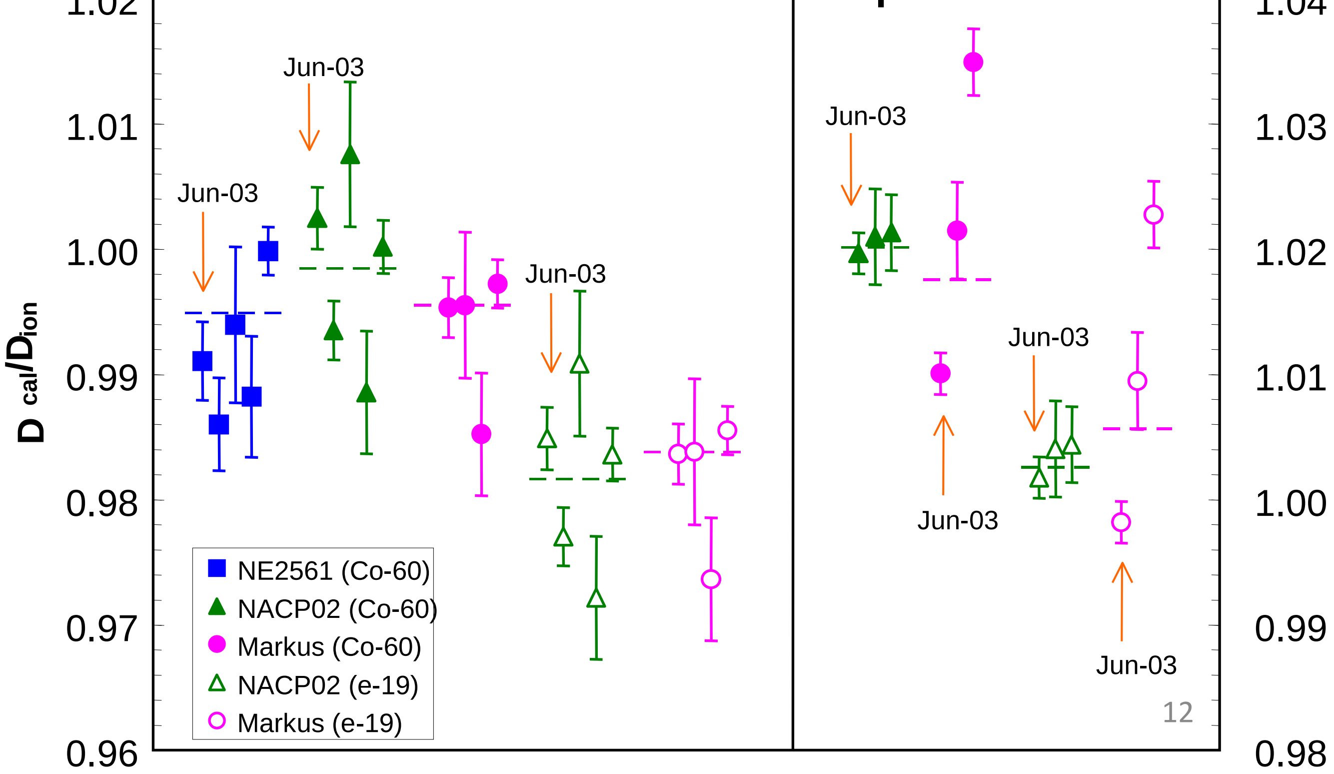
- Built a small-body portable graphite calorimeter for clinical proton beams
- Built the 1st calorimeter as a primary-standard of radiation dose for proton beams

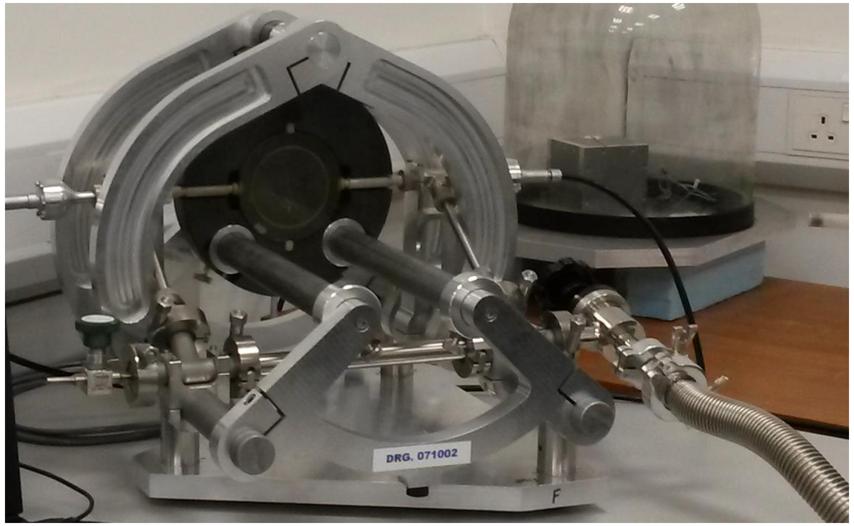


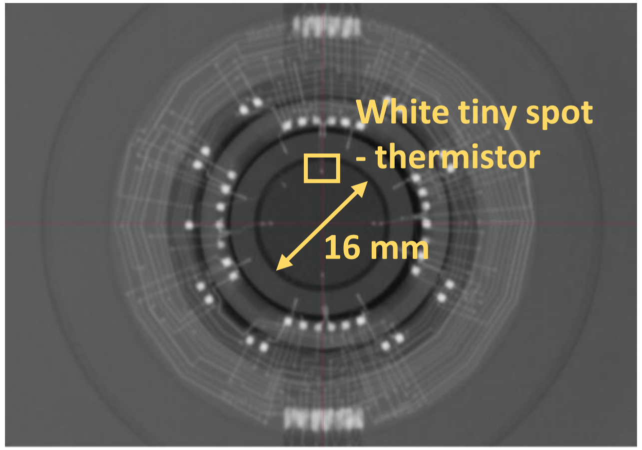
Palmans et al 2004 Phys. Med. Biol. 49

World’s 1st primary-standard calorimeter for protons

$$D = c.\Delta T$$

- Graphite calorimeter
- 4 thermistors – 0.4 mm diameter → typical fraction of treatment - 2 Gy, 0.002 Kelvin
- To deliver an uncertainty on reference dosimetry for protons of less than 1% (k=1)





$$D_{\mathrm{w}} = \left[\left(\mathrm{m}_{\mathrm{core,eff}} \mathrm{c}_{\mathrm{g}} k_{\mathrm{c}} \Delta T_{\mathrm{core}} - \int \Delta P_{\mathrm{core}} dt - \sum_{i} \int h_{\mathrm{core},i} (T_i - T_{\mathrm{core}}) - a_j P_j dt \right) \Big/ m_{\mathrm{core,\ eff}} \right] . k_{\mathrm{imp}} k_{\mathrm{gap}} k_{\mathrm{z,cal}} k_{\mathrm{d,cal}} k_{\mathrm{an,cal}} s_{\mathrm{w,g}} k_{\mathrm{fl}}$$

Developing a primary standard calorimeter for protons at NPL

- No proton beam at NPL
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- Built the 1st calorimeter as a primary-standard of radiation dose for proton beams
- Established the necessary correction/conversion factors

Graphite calorimeter
Absorbed radiation dose-to-graphite

↓

Quantity of interest
Absorbed radiation dose-to-water

Conversion factors

$$D = c.\Delta T$$

	c ($J \cdot kg^{-1} \cdot K^{-1}$)	$\Delta T / D$ ($mK \cdot Gy^{-1}$)
water	4180	0.24
graphite	710	1.41

Developing a primary standard calorimeter for protons at NPL

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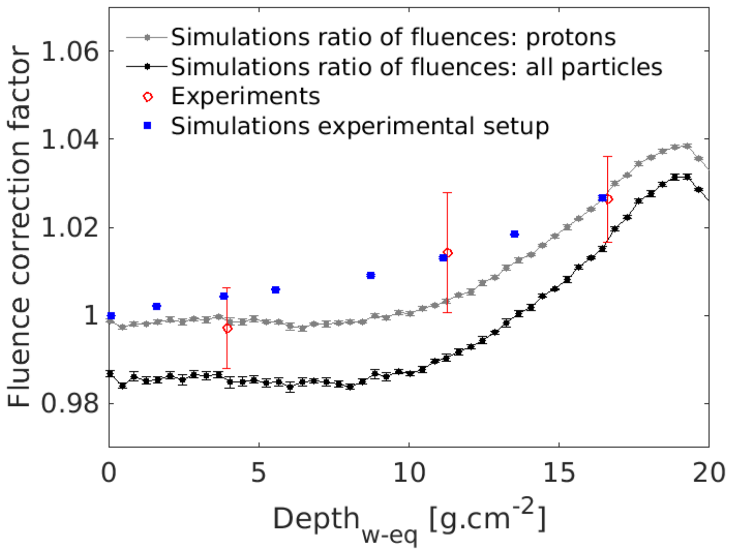
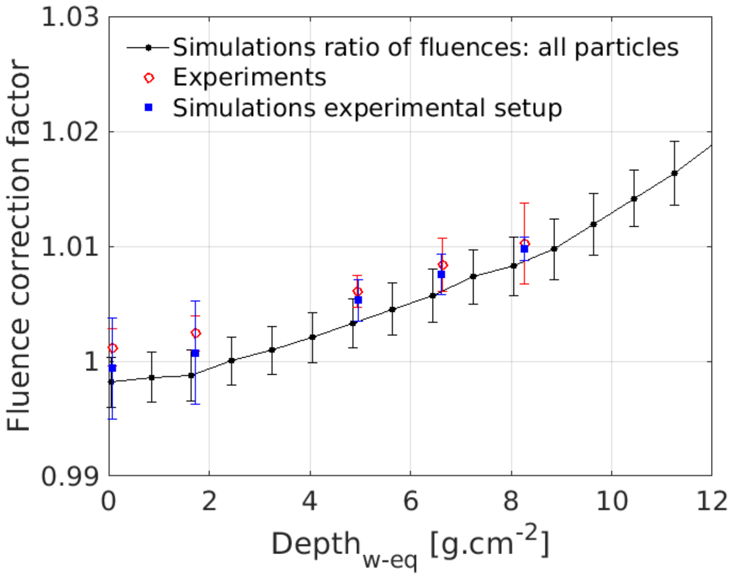
Nuclear interactions dependent of the medium

Different production rates of secondary particles

Fluence correction factor



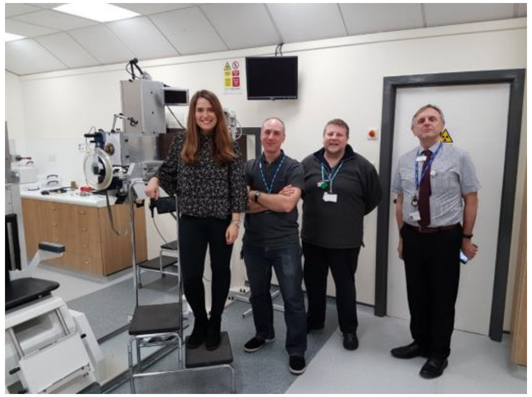


Lourenço et al 2016 Med. Phys. 43
Lourenço et al 2016 Phys. Med. Biol. 61

Developing a primary standard calorimeter for protons at NPL

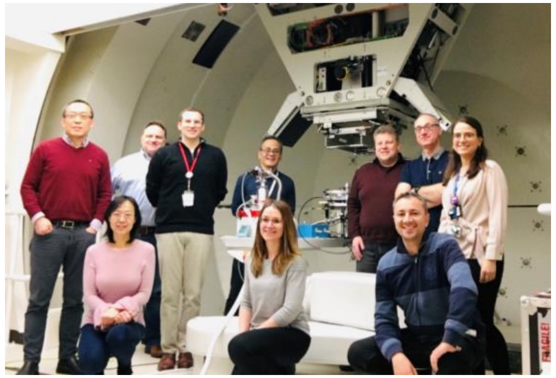
Manchester, UK

Newport, UK

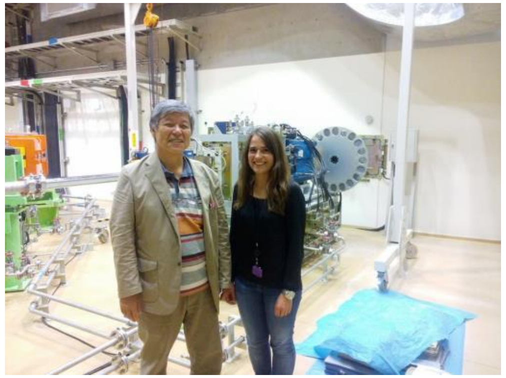


Clatterbridge, UK

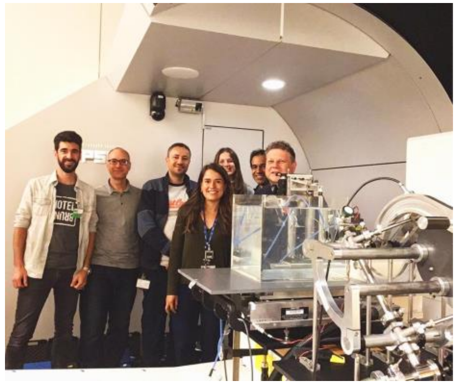
Trento, Italy



Cincinnati, USA



Gunma, Japan



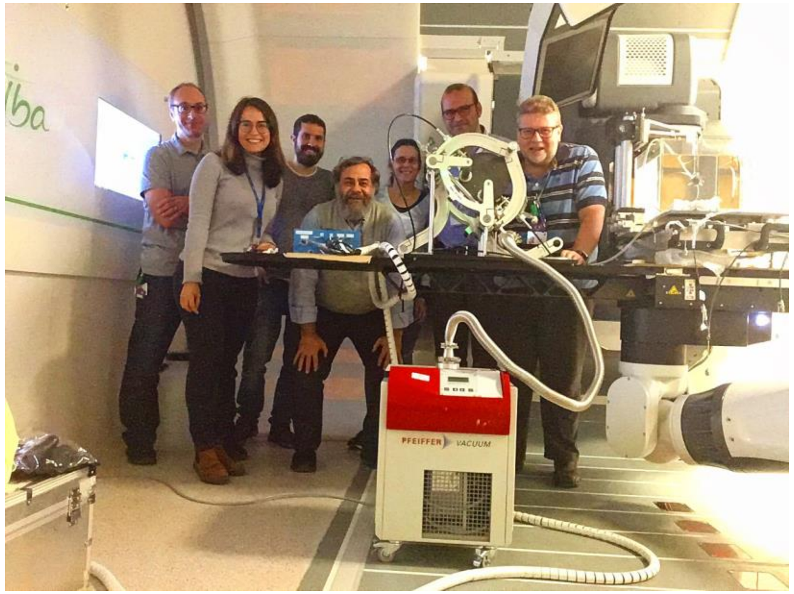
Villigen, Switzerland

Orsay, France

- The new procedure based on the NPL calorimeter **provides a reduction in uncertainty by a factor of two** on the radiation dose for the population - 1st ever Code of Practice for proton beams based directly on a primary standard
- Ensuring optimal tumour control and improved accuracy, and **establish consistent standards** that underpin the development of clinical trials

Dosimetry Audits – existing guidelines based on Ionisation Chambers

- Evaluate the quality of the practice of radiotherapy at a cancer centre
- **Reference dosimetry audit service for proton therapy beams**
- Requirement for quality assurance of proton therapy centres to start treatments



NPL and clinical scientists in the 1st proton therapy centre in Denmark and in Spain

Lourenço et al, PTCOG 2020

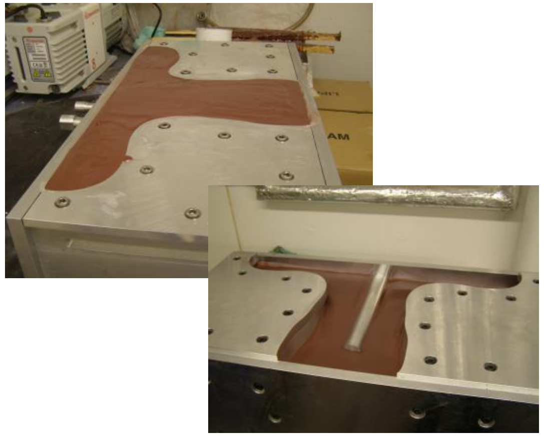
Development of end-to-end dosimetry audits

- Evaluate the quality of practice of the full treatment
- Phantoms are plastic materials that simulate the patient geometry and composition
- **New phantom: PRuDeNCE - PRoton heaD and NeCk Evaluation**

- Clinical facilities treat the phantom in a similar manner as they would treat a real patient. The phantom includes internal detectors, such as ionisation chambers, alanine pellets and radiochromic film, for the measurement of radiation dose and its distribution within the phantom

- Pilot audit performed at the two NHS high-energy proton facilities

- These measurements provide validation of the patient workflow methods and are a requirement for clinical trials



Cook et al (in review)

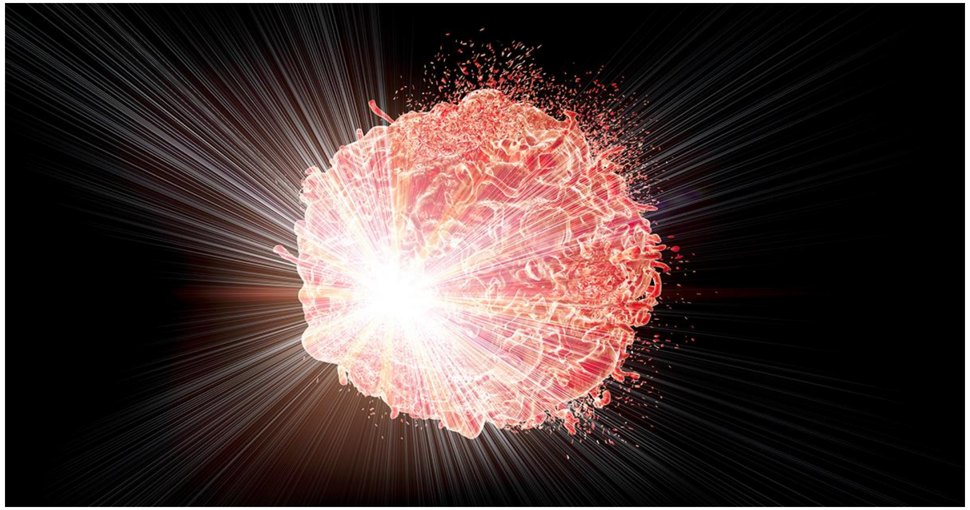
NPL supports the clinical translation of new radiotherapy modalities

- Short pulses of ultra-high radiation dose rate radiation (>40 Gy/s), known as **FLASH radiotherapy (RT)**, can significantly spare normal tissues during radiotherapy treatment

- Paradigm shift in radiotherapy:
  - Conventional radiation dose rate: 6 weeks
  - FLASH radiation dose rate: less than a week

- Considerable reduction in post-treatment complications and reduce the cost of proton beam radiotherapy

- Pioneering measurements at the Cincinnati Children's Hospital (one of the top paediatric hospitals in the United States)



www.nature.com/scientificreports

scientific reports

Check for updates

OPEN **Absolute dosimetry for FLASH proton pencil beam scanning radiotherapy**

Ana Lourenço[1,2], Anna Subiel[1], Nigel Lee[1], Sam Flynn[1,3], John Cotterill[1], David Shipley[1], Francesco Romano[4], Joe Speth[5,6], Eunsin Lee[5,6], Yongbin Zhang[5,6], Zhiyan Xiao[5,6], Anthony Mascia[5,6], Richard A. Amos[2], Hugo Palmans[1,7] & Russell Thomas[1,8]

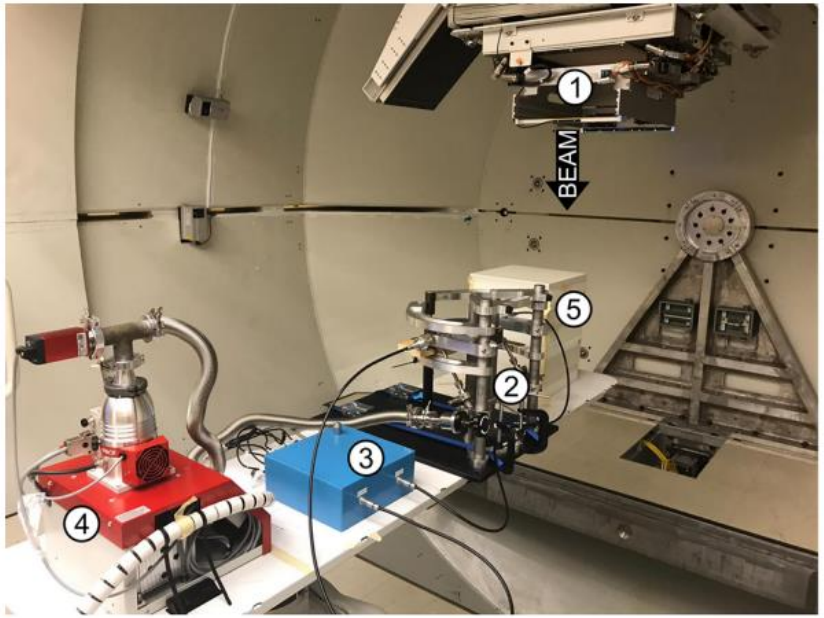
A paradigm shift is occurring in clinical oncology exploiting the recent discovery that short pulses

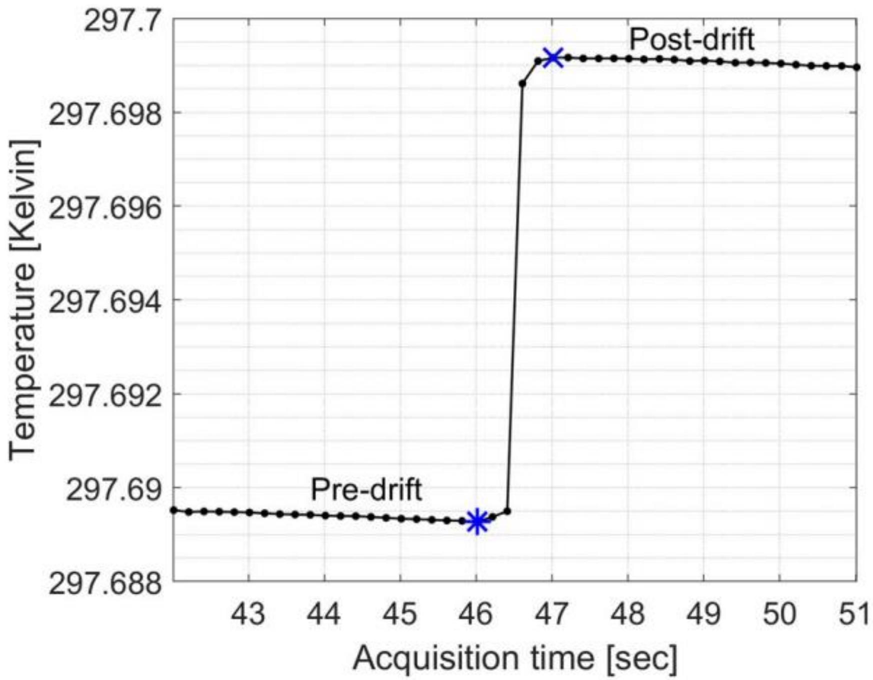
NPL supports the clinical translation of new radiotherapy modalities

- First ever calorimetry measurements

- Established the correction factors required for absolute dosimetry of FLASH proton beam radiotherapy

- **Underpinned the FDA approval and provided the hospital with confidence to commence clinical implementation of this novel technology**
- **Ongoing collaboration with Institut Curie – proton mini-beams**





Lourenço et al 2023 Nature Sci. Rep. 13 2054

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