National Physical Laboratory

Ultra-high dose rate (UHDR) dosimetry and the future perspectives

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FFC- QA and Dosimetry Working Group (eFlash)
19th April 2023

The EMPIR initiative is co-funded by the European Union's Horizon 2020 research and innovation programme and the EMPIR Participating States

Outline

- Reminder of the importance of metrology & traceability in RT
- How we calibrate s/s detectors at NMIs?
- Do we need metrology in FLASH RT?
- Initiatives supporting development of metrology & standardization in FLASH RT

UHDpusle project

- Detectors for UHDR beams (focus on active devices)
- Summary

Metrology covers three main tasks:

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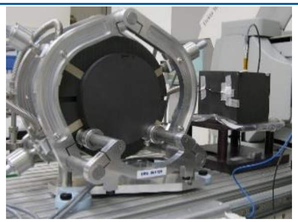
1. The definition of internationally accepted units of measurement

2. The realization of units of measurement by scientific methods

primary standard



secondary standard

working standard

3. The establishment of **traceability** chains

property of a measurement result whereby the result can be related to a reference through a documented unbroken chain of calibrations, each contributing to the measurement uncertainty

Measurement uncertainty

$$\boldsymbol{M = m \pm U \quad (k = 1)}$$

measurand

coverage factor

Traceability chain in Radiotherapy

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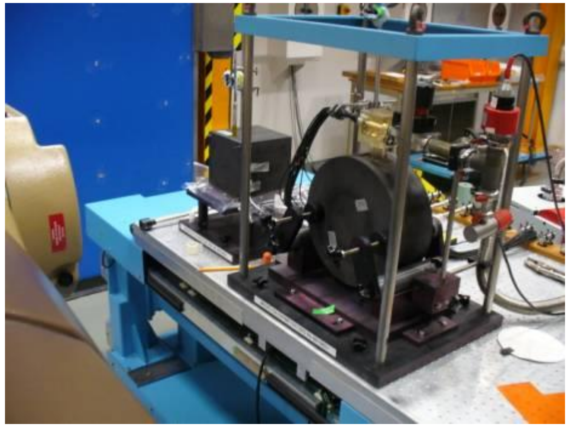
- **MV photon dosimertry under reference conditions**

NPL **primary standard** → calibration → NPL reference chambers → calibration → Hospital **secondary standard** → calibration → Hospital **working standard**

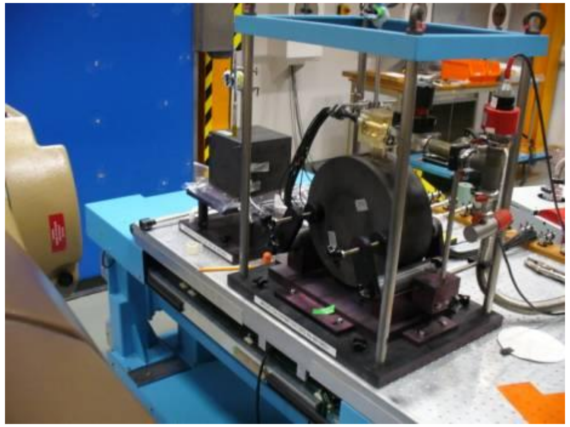


σ: 0.50 % (k=1) | 0.7 % (k=1) | 1.5 % (k=1)

Traceability chain in Radiotherapy

- **MV photon dosimertry under reference conditions**

NPL **primary standard** → **calibration** → NPL reference chambers → **calibration** → Hospital **secondary standard** → **calibration** → Hospital **working standard**



σ:

NPL primary standard	NPL reference chambers	Hospital secondary standard	Hospital working standard
0.50 % (k=1)		0.7 % (k=1)	1.5 % (k=1)

← **TRACEABILITY**

Requirement for accuracy in dosimetry

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- The ICRU Rep.24 (1976) states:

*An uncertainty of **5% (k=1)** is tolerable in the delivery of absorbed dose to the target volume*

This is an **OVERALL UNCERTAINTY**
(incl. dose delivery, dose calculations, patient positioning etc.)

↓

Dose measurement at the reference conditions should to be **less than 1% (k=1)!**

What is recommended by the dosimetry protocols?

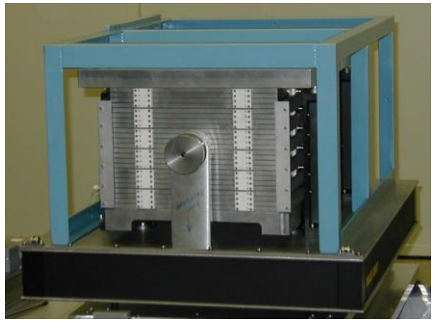
For convectional radiotherapy:

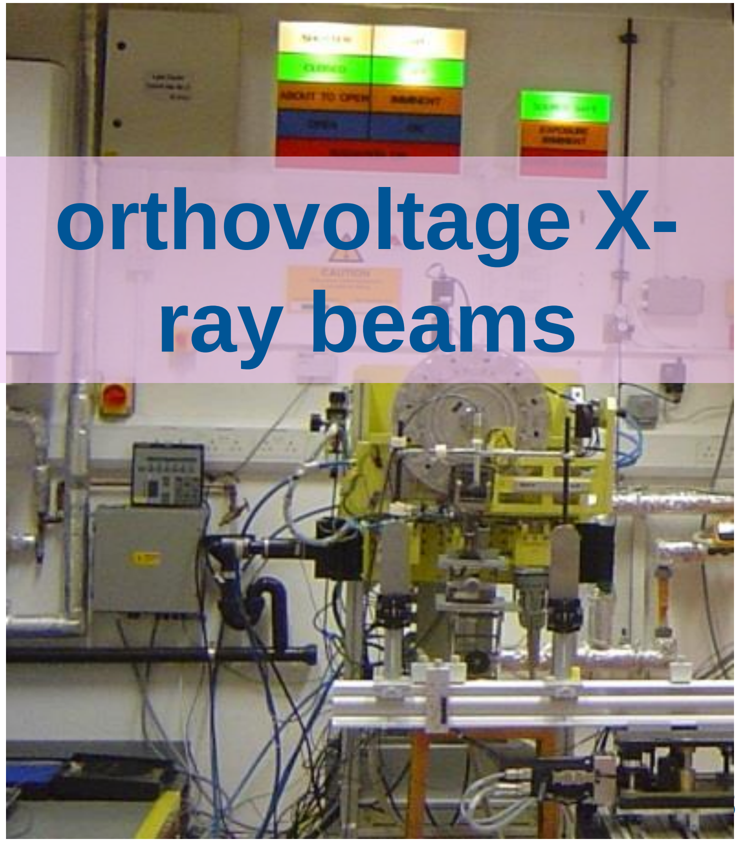
- The IAEA TRS-398 recommends the use of **ionisation chambers with a calibration coefficient** in terms of D_w or N_K in the calibration beam quality. **Ideally, should be the same as the user's beam quality**
- Dissemination of the quantity of interest, K_N, D_w, through a primary standard

primary standard → **secondary standard**

Free Air Chamber
- complex
- not commercially available
- not portable

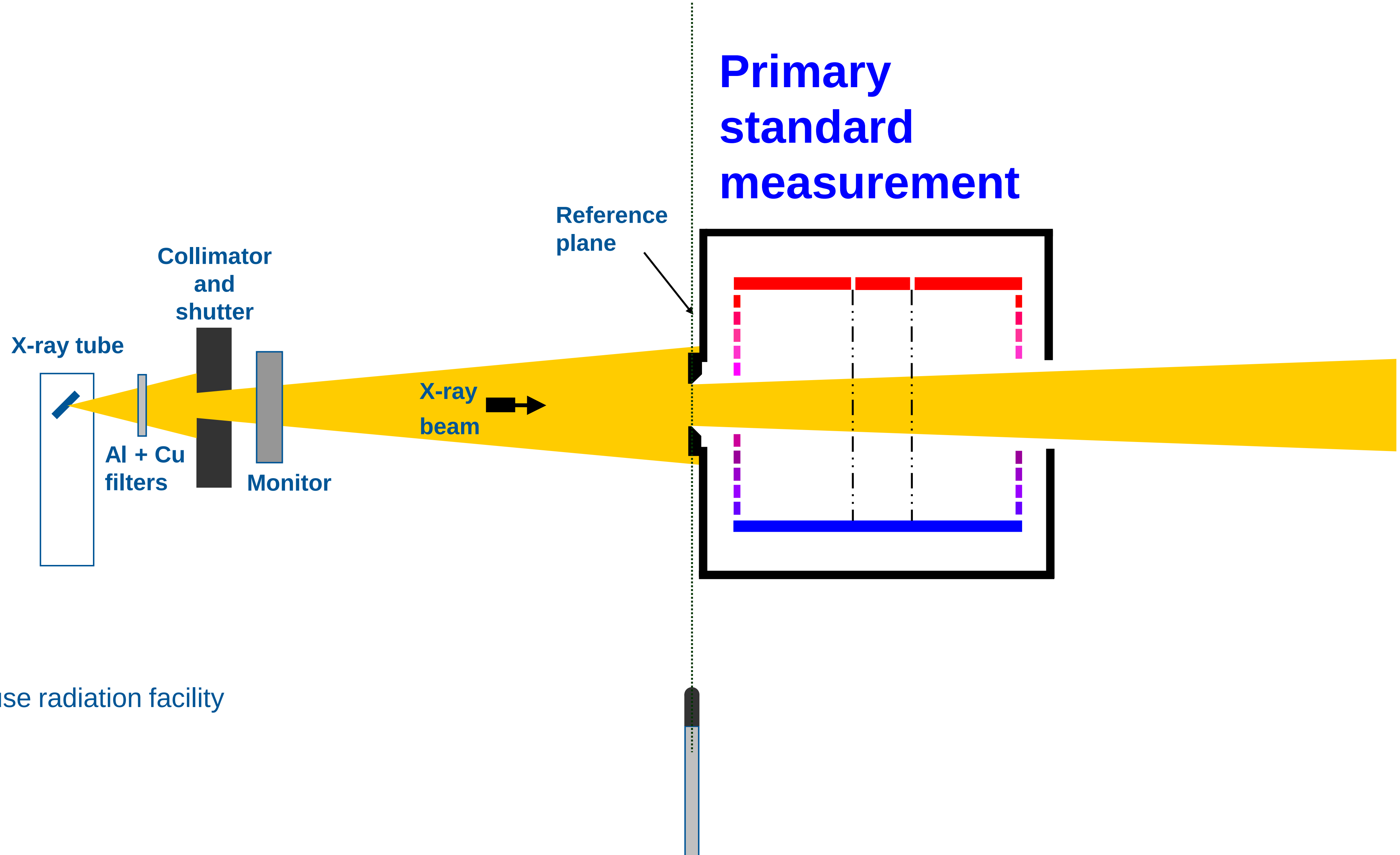
Ionisation chamber
- simple and portable
- calibrated against the primary standard





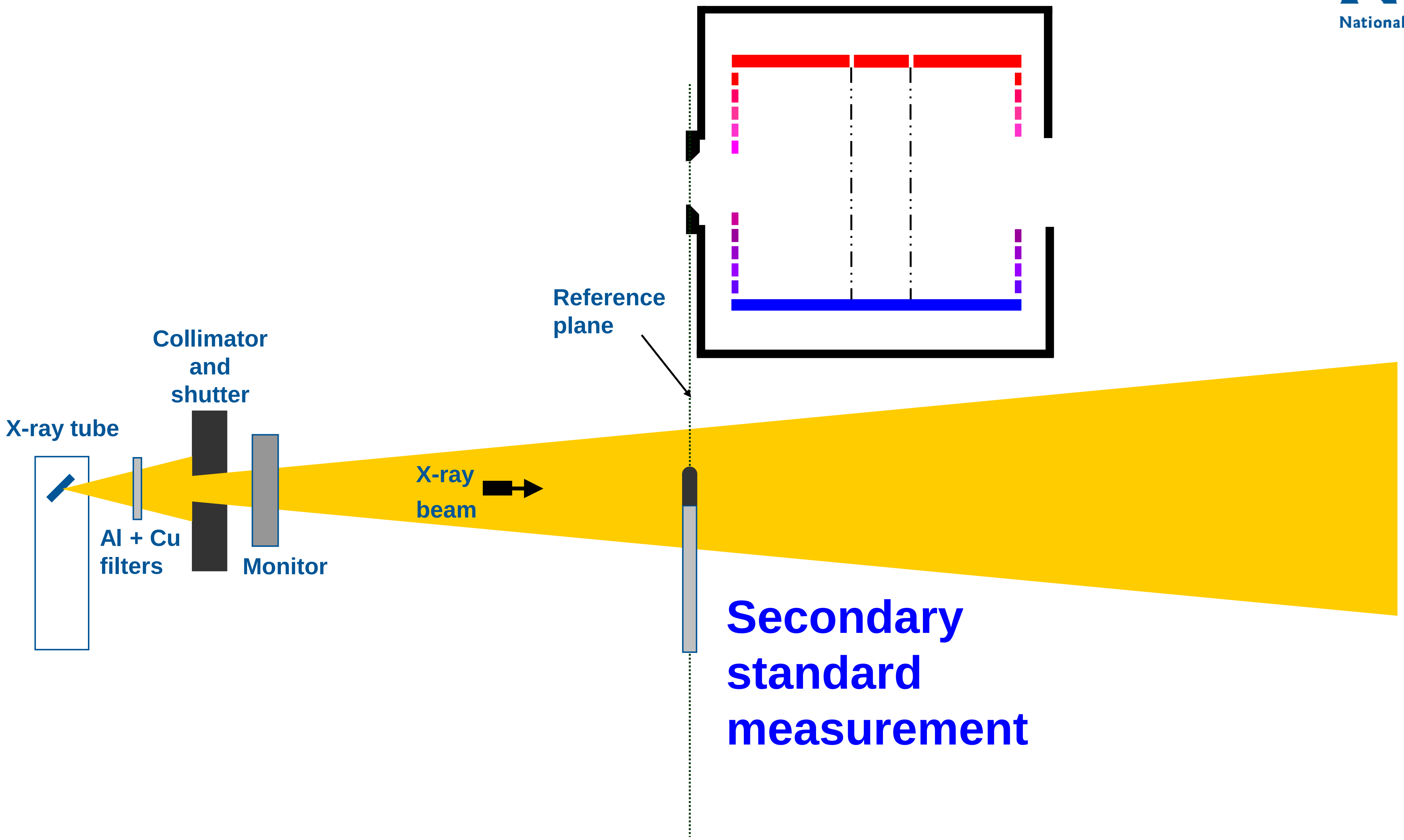
Calibration of secondary standard

Calibration of secondary standard



in-house radiation facility

Calibration of secondary standard



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Teddington Middlesex UK TW11 0LW Telephone +44 20 8977 3222

UKAS CALIBRATION 0478

Certificate of Calibration

OF AN

IONISATION CHAMBER IN TERMS OF AIR KERMA

FOR:	Medical Radiation Physics National Physical Laboratory Hampton Road Teddington Middlesex TW11 0LW
FOR THE ATTENTION OF:	Ileana Silvestre Patallo
DESCRIPTION:	Secondary Standard Ionisation Chamber
DATE OF RECEIPT:	1 January 2022
DATE OF CALIBRATION:	8 February 2022 to 1 March 2022
IDENTIFICATION:	NPL, type 2611, serial number 1007

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Continuation Sheet

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Table 1 – Air kerma calibration coefficients

NPL, type 2611, serial number 1007

Nominal generating potential (kV)	Half Value Layer		Calibration coefficient, N_K (Gy/C)
	mm Al	mm Cu	
50	1.00	0.030	9.24×10^7
70	2.0	0.062	9.07×10^7
100	4.0	0.15	9.04×10^7
105	5.0	0.20	9.05×10^7
135	8.8	0.50	9.12×10^7
180	12.3	1.0	9.12×10^7
220	16.1	2.0	9.13×10^7
280	20.0	4.0	9.17×10^7

Uncertainties

For all beam qualities the uncertainty in the calibration coefficient is 1.4%. The reported expanded uncertainty is based on a standard uncertainty multiplied by a coverage factor $k = 2$, providing a coverage probability of approximately 95%. The uncertainty evaluation has been carried out in accordance with UKAS requirements.

Primary standards for high energy beams

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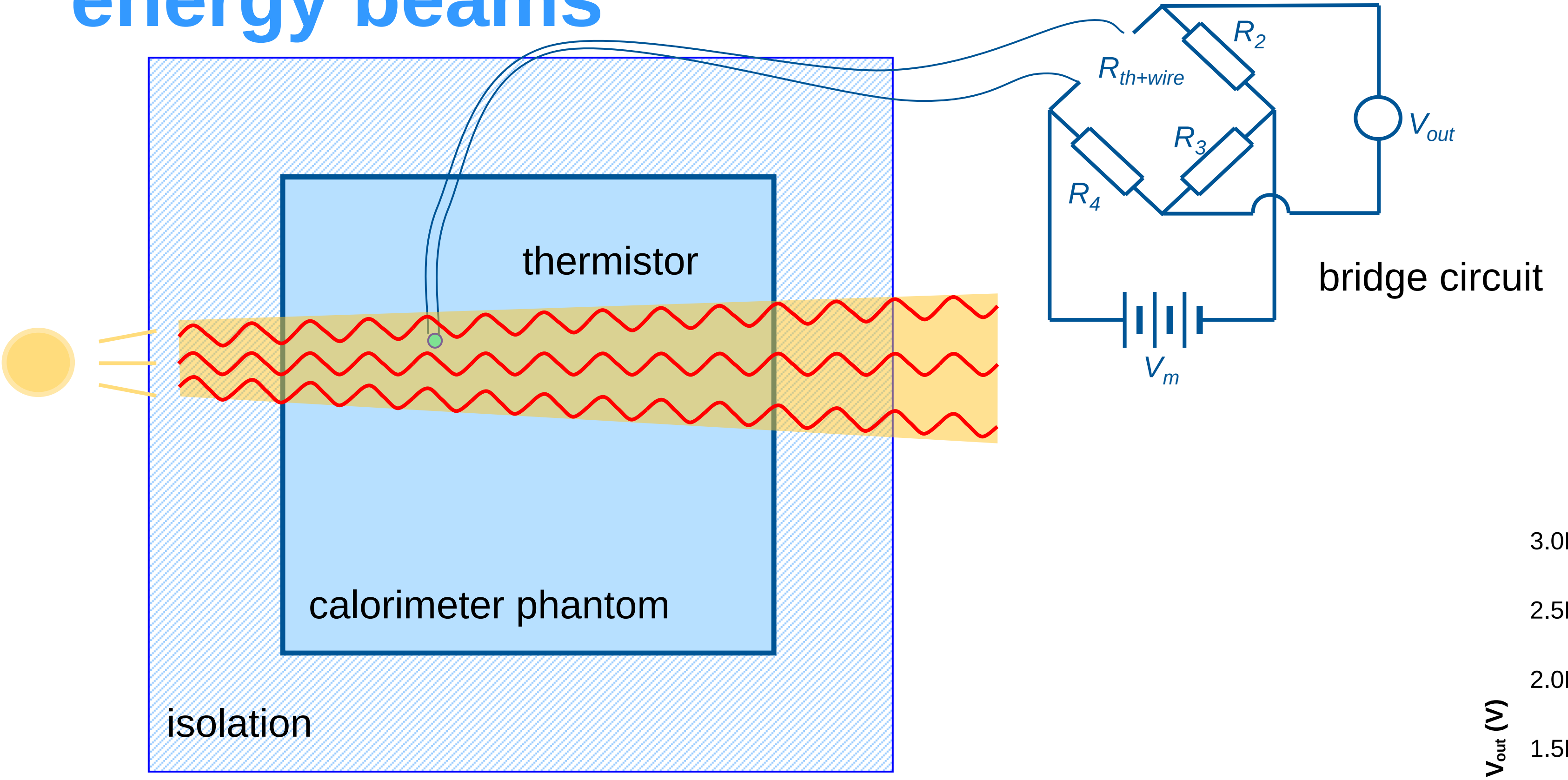
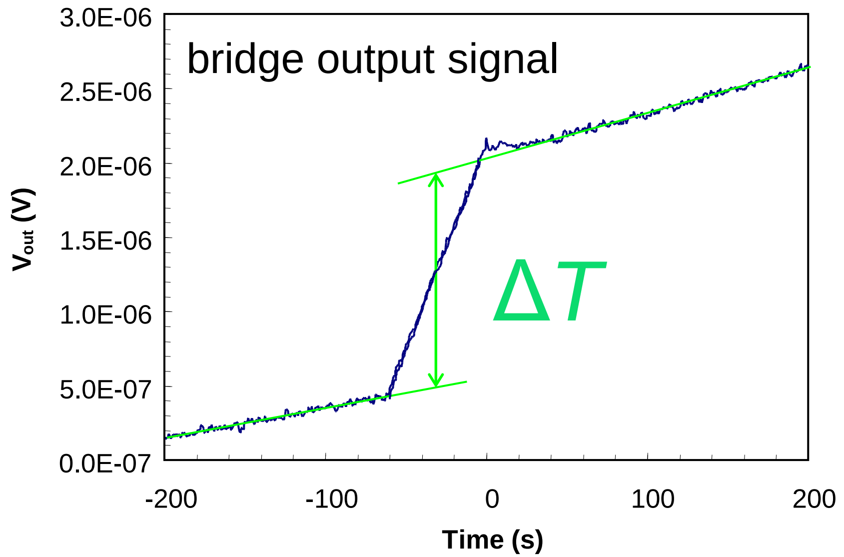
- For MV X-ray, electron and proton beams – calorimeters serve as primary standards (most frequently)
- Quantity of interest - D_w

Calorimeters used as prim. standards in high energy beams



$$D = c \cdot \Delta T$$



Calibrations in high energy beams

- Primary standards - developed to disseminate D_W for each beam modality
- Calibration coefficients for IC determined at the same beam qualities as clinically used

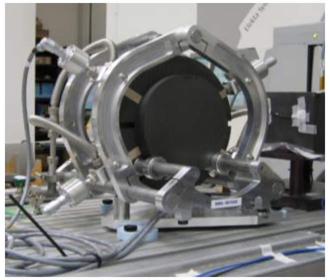
Primary standard
(absolute reference)

→

secondary standard

Clinical linear accelerator

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



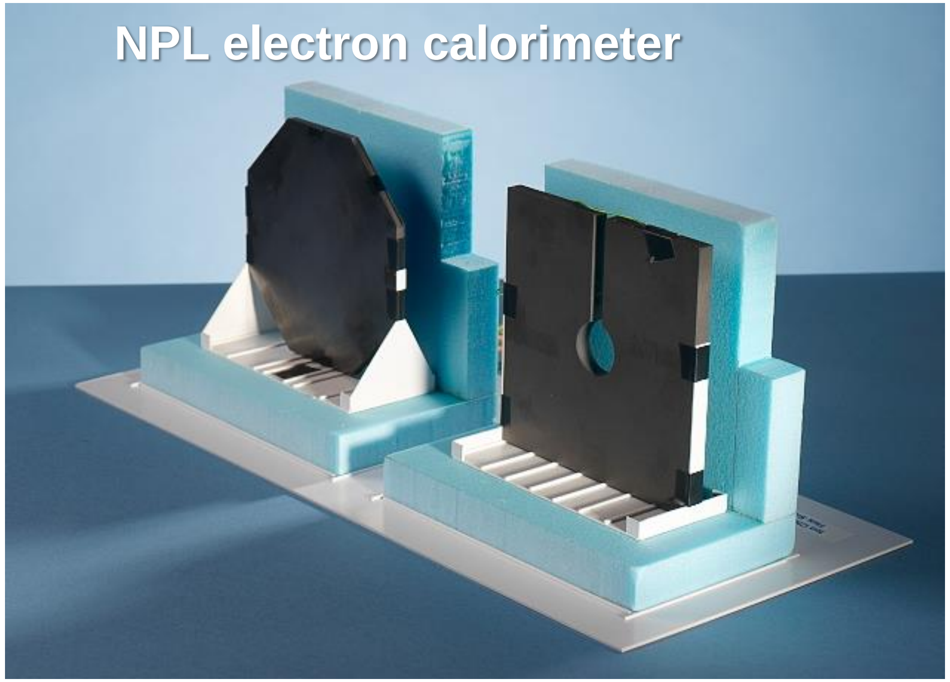
Ionisation chamber
- simple and portable
- calibrated against the primary standard

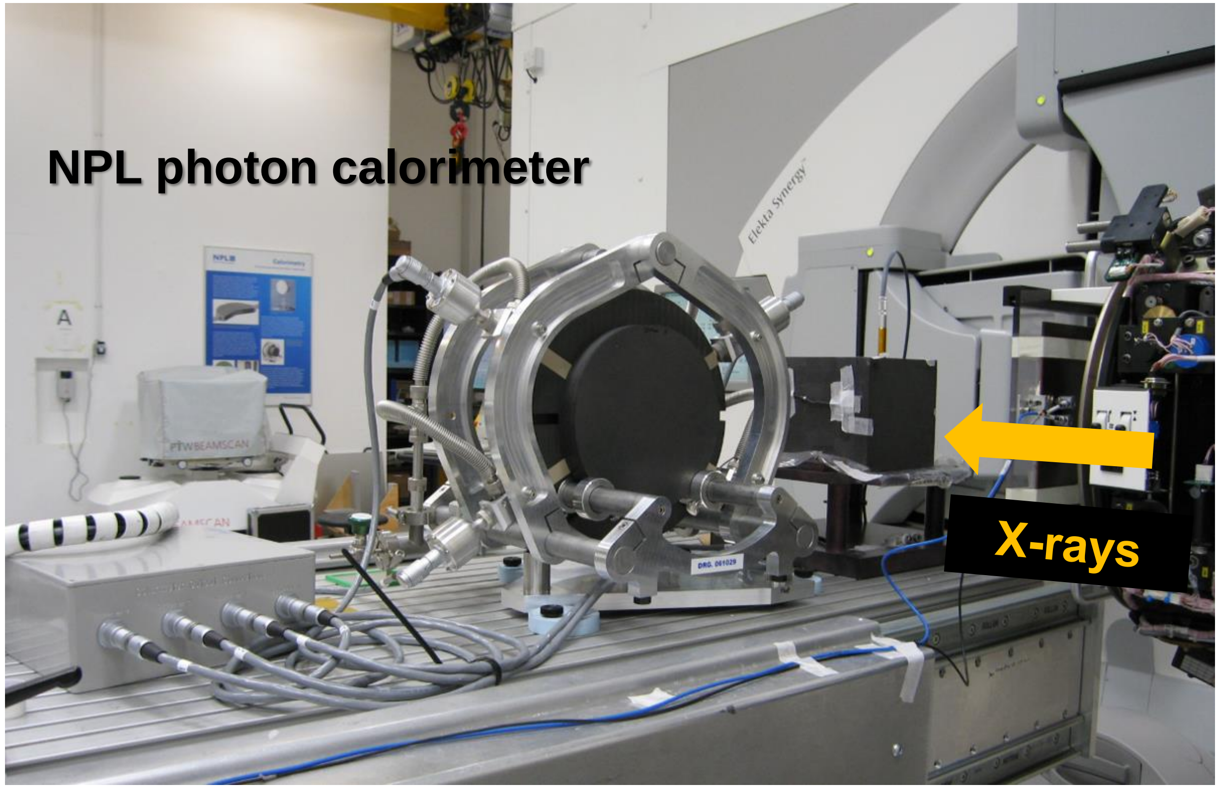
Calibrations in high energy beams

For high-energy photon & electron beams:

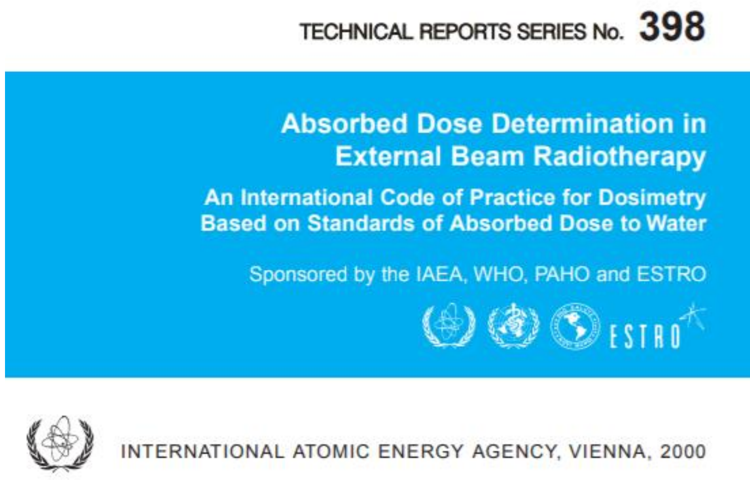
calibrations based on a primary standard calorimeters for the direct determination of absorbed dose to water with uncertainties on reference dosimetry of:

- 0.65% (k=1) for photons
- 0.75% (k=1) for electrons





Proton reference dosimetry



- **2000 – IAEA TRS 398**

  Ionisation chambers

  - Uncertainty on $D_{w,Q}$ for protons: 2.3% (k=1)

Detectors currently used in the proton clinics are calibrated in a Cobalt-60 beam

Uncertainty in dose at least 2 times larger than the recommended uncertainty

Conversion factor, k_{Q,Q_0}

- Analytical

Dose in a proton beam

Courtesy of A. Lourenço

Proton reference dosimetry

Calibrate the detectors directly in the same or similar beam used clinically

Detectors currently used in the proton clinics are calibrated in a Cobalt-60 beam

Conversion factor, k_{Q,Q_0}

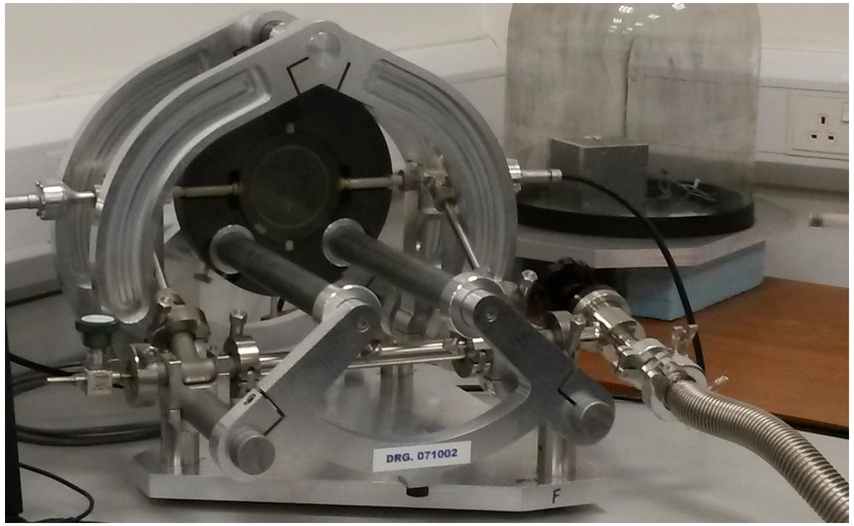
- Analytical

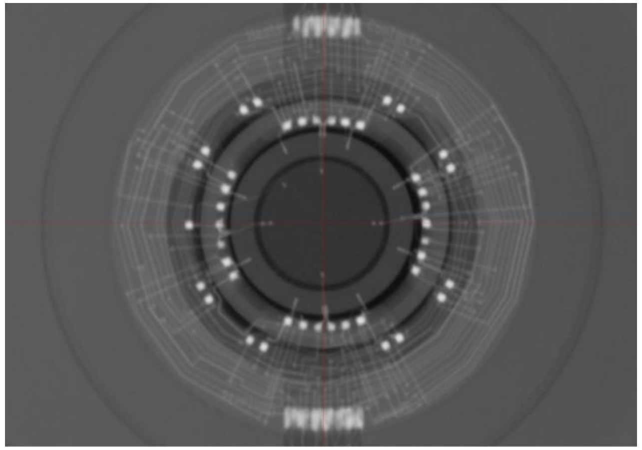
Courtesy of A. Lourenço

Dose in a proton beam

World's 1st Primary-Standard Calorimeter for Protons

Graphite calorimeter
- Originally developed for use with conventional proton beams,





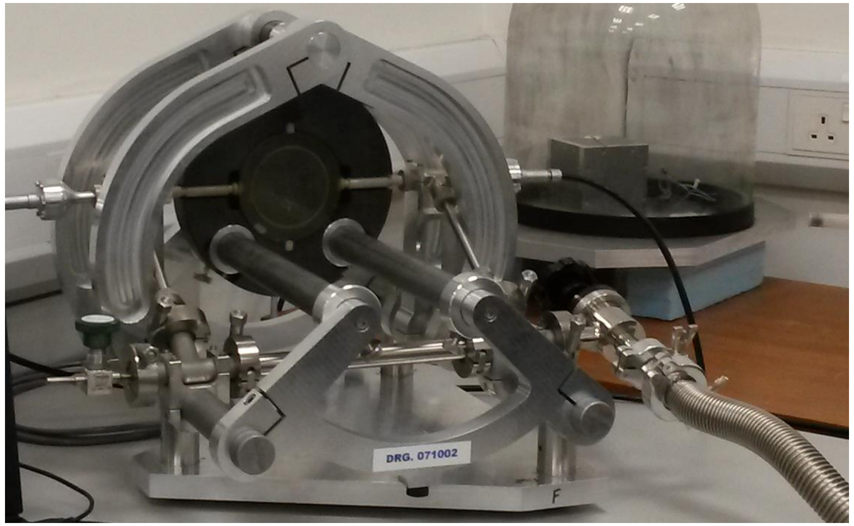
Courtesy of A. Lourenço

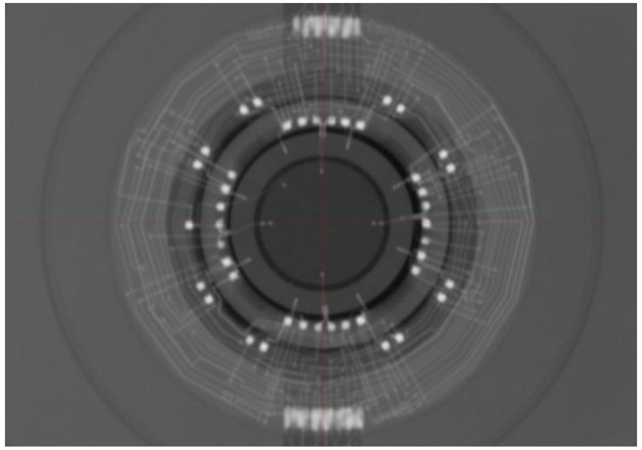
World's 1st Primary-Standard Calorimeter for Protons

$$D = c \cdot \Delta T$$

Graphite calorimeter

- Originally developed for use with conventional proton beams,
- Consists of graphite discs arranged in a nested construction, maintained under vacuum





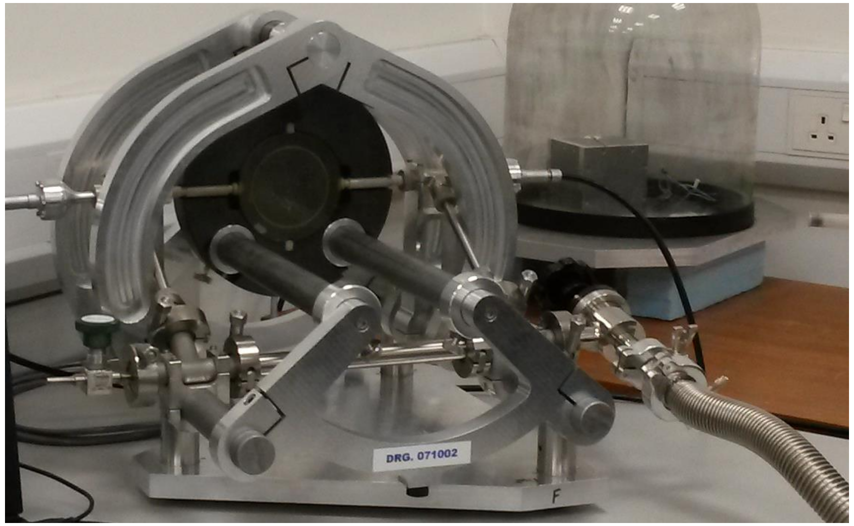
Courtesy of A. Lourenço

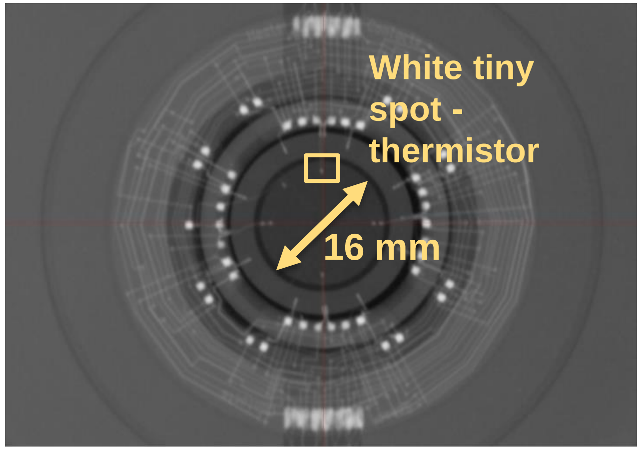
World's 1st Primary-Standard Calorimeter for Protons

$D = c \cdot \Delta T$

Graphite calorimeter

- 4 thermistors – 0.4 mm diameter typical fraction of treatment - 2 Gy, 0.002 degrees
- Delivers an uncertainty on reference dosimetry for protons <1% (k=1)





$$D_w = \left[\left(m_{core,eff} c_g k_c \Delta T_{core} - \int \Delta P_{core} dt - \sum_i \int h_{core,i}(T_i - T_{core}) - a_j P_j dt \right) \Big/ m_{core,\ eff} \right] \cdot k_{imp} k_{gap} k_{z,cal} k_{d,cal} k_{an,cal} s_{w,g} k_{fl}$$

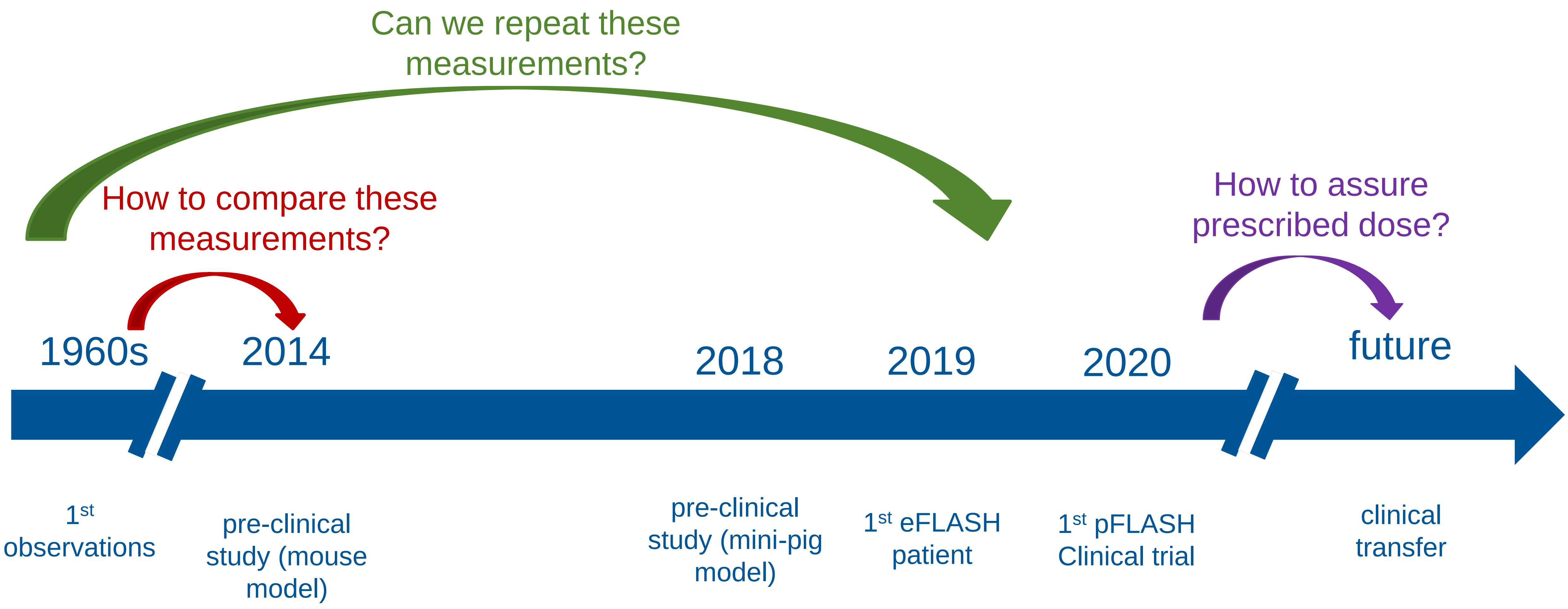
Courtesy of A. Lourenço

Why do we need metrology in FLASH RT?

- To compare different measurements carried out in space and time

Timeline of FLASH RT…

TRACEABILITY IN DOSIMETRY of UHDR beams



Role of National Metrology Institutes

- FLASH community had no support from NMIs with provision of traceability for the UHDR beams
- No standards available
- Developing science and technology that defines the NEED for developments in metrology for UHDR exposures

The support needs to come form NMIs

to provide traceable dissemination of D_w to clinics

Initiatives to support metrology in FLASH RT

- **The EMPIR UHDpulse** project (Sept. 2019 – Feb. 2023) http://uhdpulse-empir.eu/
  Metrology for advanced radiotherapy using particle beams with ultra-high pulse dose rates

- **ESTRO/AAPM TG359** https://www.aapm.org/org/structure/default.asp?committee_code=TG359

Task Group No. 359 - FLASH (ultra-high dose rate) radiation dosimetry (TG359)

- bookmark this page (bookmarks show under "My AAPM" in the menu to left)

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Email You may send email to this group now using gmail or outlook.
- or -
You may save the address *2022.TG359@aapm.org*
to your local address book. This alias updates hourly from the AAPM Directory.

Charge 1. Review the uncertainty in determining the dose and need for standardization in dosimetry for FLASH beams to be used in experiments, research and potentially in pre-clinical applications.
a. Assess the factors that would affect the beam dosimetric characteristics in FLASH mode, compared to standard delivery.
2. Assess the suitability of radiation measurement equipment (ion chambers, film, diodes, Faraday cap, etc) for FLASH mode.
3. Provide general guidelines on calibration, dosimetry and reporting of beams in FLASH mode.

Chair

Dimitris Mihailidis
Task Group Chair

Joint Research Project UHDpulse

Title: Metrology for advanced radiotherapy using particle beams with ultra-high pulse dose rates

Duration: Sep/2019-Feb/2023

Coordinator: Andreas Schüller (PTB)

Topic: **dosimetry for**

FLASH radiotherapy & proton therapy,

VHEE and laser-driven beams

Website: http://uhdpulse-empir.eu

The EMPIR initiative is co-funded by the European Union's Horizon 2020 research and innovation programme and the EMPIR Participating States

enables European metrology institutes to collaborate with industrial and medical organisations, and academia

Joint Research Project UHDpulse

National Physical Laboratory

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EMPIR EURAMET
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Outline
Highlights
Abstract
Keywords
1. Introduction
2. Overview of novel radiotherapy techniques using ultra-...
3. Metrological challenges and possible solutions for dosi...
4. The UHDpulse project
5. Conclusion
Acknowledgements
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Figures (15)

Physica Medica
Volume 80, December 2020, Pages 134-150

Original paper

The European Joint Research Project UHDpulse – Metrology for advanced radiotherapy using particle beams with ultra-high pulse dose rates

Andreas Schüller [a], Sophie Heinrich [b], Charles Fouillade [b], Anna Subiel [c], Ludovic De Marzi [b, d], Francesco Romano [e, c], Peter Peier [f], Maria Trachsel [f], Celeste Fleta [g], Rafael Kranzer [h, i], Marco Caresana [j], Samuel Salvador [k], Simon Busold [l], Andreas Schönfeld [m], Malcolm McEwen [n], Faustino Gomez [o], Jaroslav Solc [p], Claude Bailat [q] ... Marie-Catherine Vozenin [q]

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Highlights

- Ultra-high dose rate reduces adverse side effects in radiotherapy (FLASH effect).
- Studies and implementation in practice requires accurate dose measurements.
- An European joint research project was started to develop a measurement framework.
- Tools for dosimetry of ultra-high pulse dose rate beams will be provided.

Schüller et al., Physica Medica 80 (2020), 134-150
https://doi.org/10.1016/j.ejmp.2020.09.020

UHDpulse Partners and Collaborators

Metrology Institutes

Irradiation facilities / providers

Detector developers

7 Metrology institutes
6 Hospitals
9 Universities
7 Research institutes
12 Companies
+ Inspire proton therapy network

Work package structure

WP1: Primary standards

- Definition of reference conditions
- Reference radiation fields
- Adapting primary standards (water calorimeter, Fricke dosimeter)
- Prototype graphite calorimeters

WP2: Secondary standards, relative dosimetry

- Transfer from primary standards
- Characterizing established detector systems
- Formalism for reference dosimetry for future Code of Practice

WP5: Impact, WP6: Coordination

WP4: Detectors and methods outside primary beam

- Active detection techniques for pulsed mixed radiation fields of stray radiation and pulsed neutrons
- Methods with passive detectors

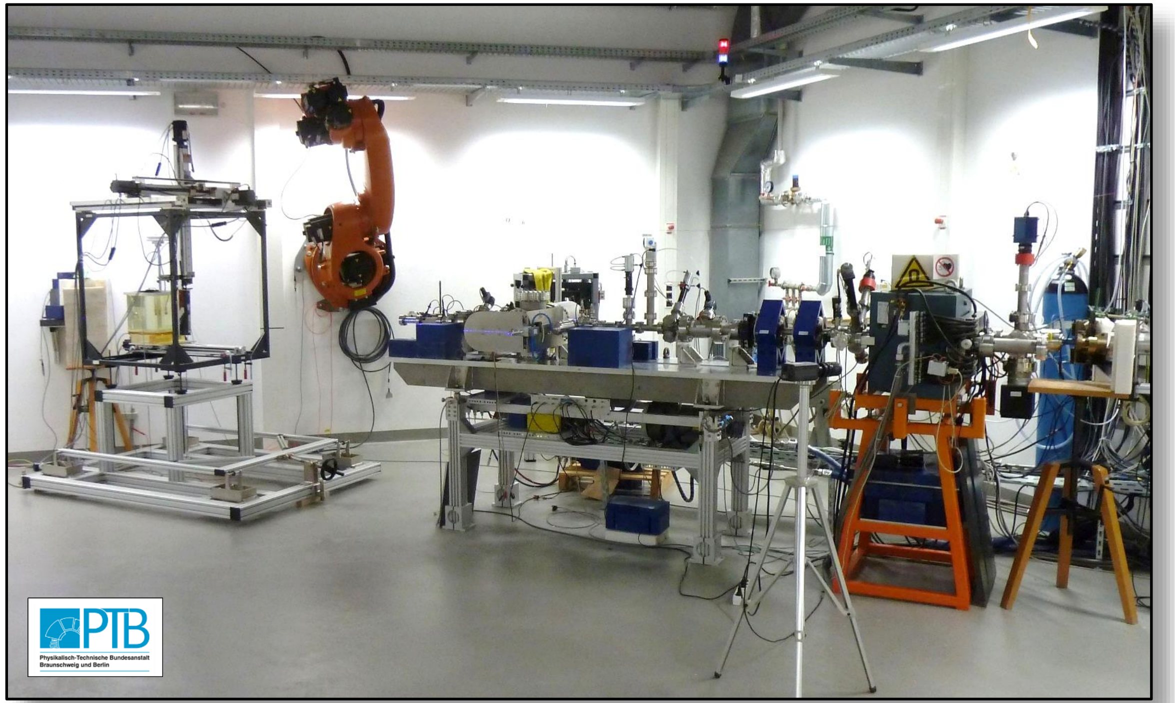
WP3: Detectors for primary beam

- Novel and custom-built active dosimetric systems
- Beam monitoring systems

UHPDR reference electron beam

PTB's Research electron accelerator

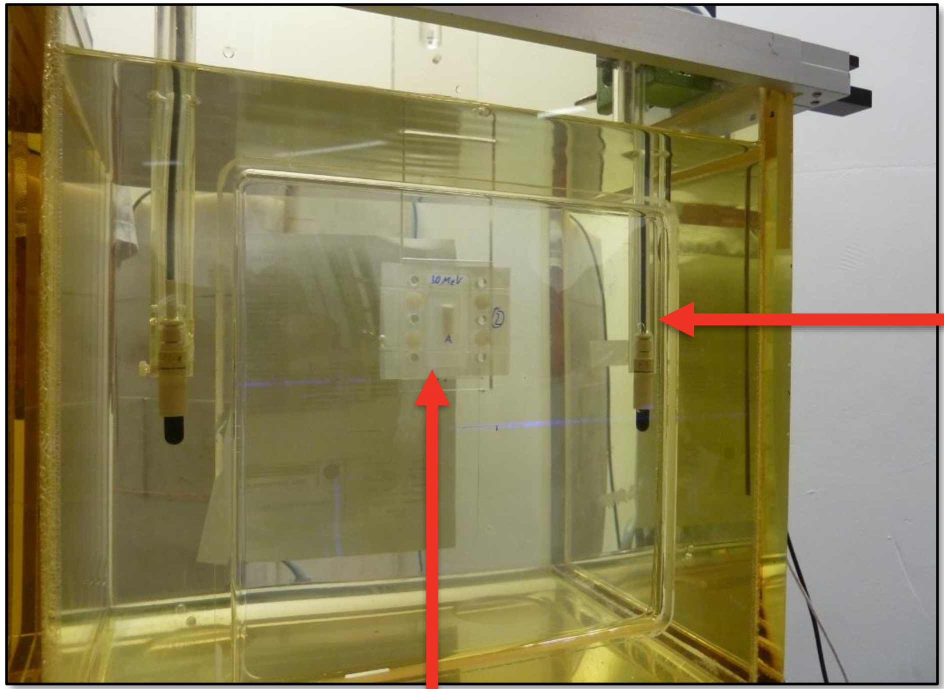
E = 0.5 – 50 MeV, t_{pulse} = 0.1 – 3 us
up to **12 Gy per pulse** (SSD 0.7 m, 20 MeV)

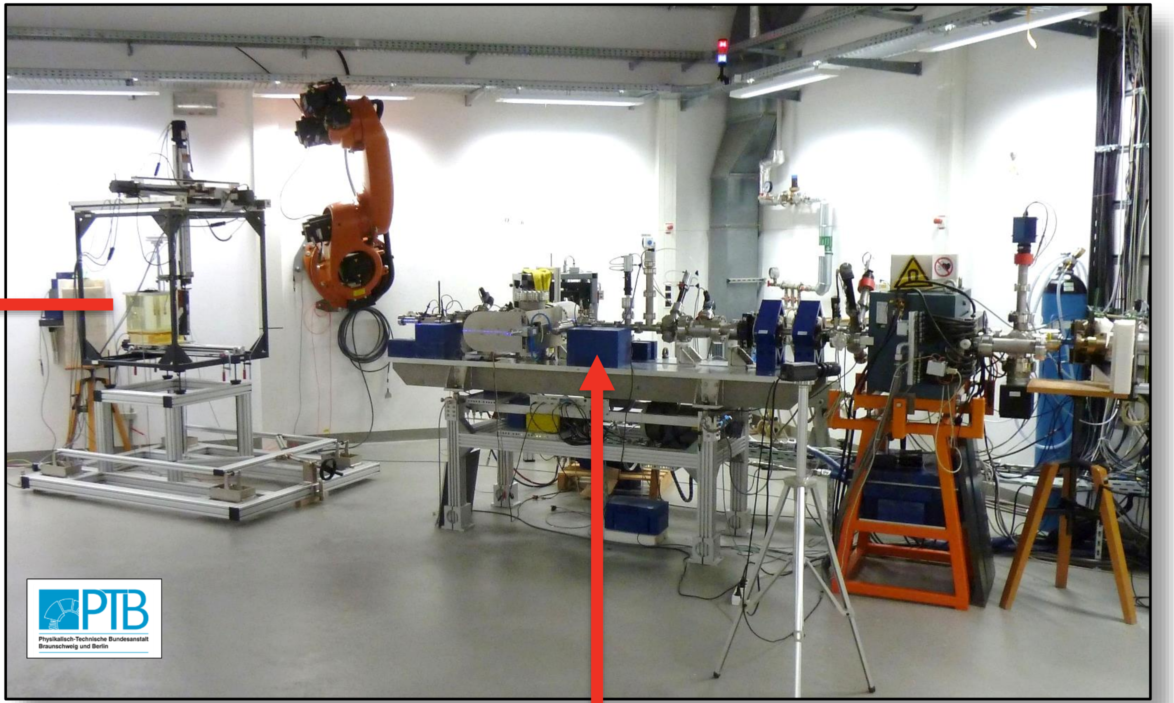


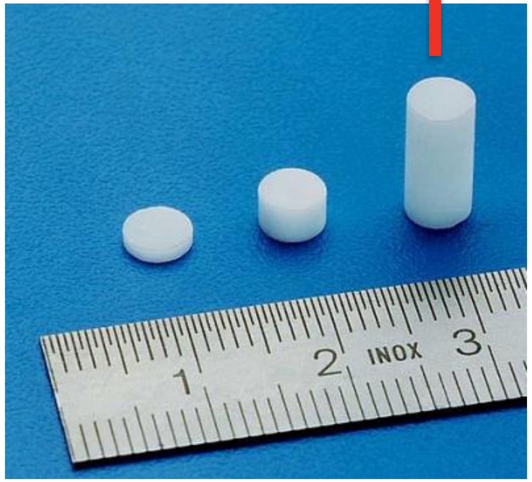
Beam line with water phantom

A. Bourgouin *et al*. "Characterization of the PTB ultra-high …"
Phys. Med. Biol. **67** (2022) 085013.
https://doi.org/10.1088/1361-6560/ac5de8

UHPDR reference electron beam







Alanine pellets at reference depth in water phantom

Dose traceable to PTB's primary standards

Current transformer (Bergoz ICT): Non-destructive absolute beam pulse charge measurement

A. Bourgouin *et al*. "Characterization of the PTB ultra-high …" *Phys. Med. Biol.* **67** (2022) 085013.
https://doi.org/10.1088/1361-6560/ac5de8

UHPDR reference electron beam

Lateral profile of the reference e-beam at PBT (taken from Deliverable 1 of the UHDulse project)

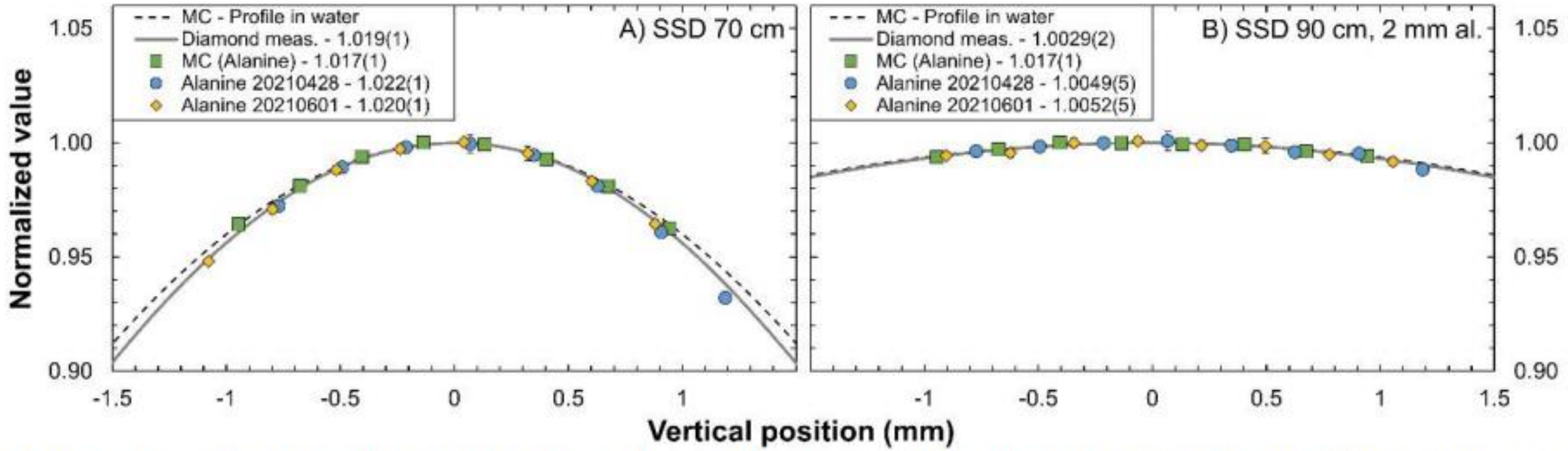


Figure 13: The PTB UHPDR electron beam vertical profile simulated by Monte Carlo on water scoring volume (error bar not shown, ± 0.4%) and in alanine pellets scoring volume, and measured by a diamond detector (error bar not shown, ± 0.2%) and alanine pellets. In A) for the set-up at an SSD70-00 and B) for the set-up at an SSD90-02. The number indicated in the legend is the value estimated for the Y correction factor.

Challenge – the reference UHDR e-beams are NOT widely available for calibrations

- Ideally flat profile for primary standard calibrations
- If not possible, correction factor needs to be applied for field non uniformity
- User beam will require a separate correction factor due to non-uniformity of the beam

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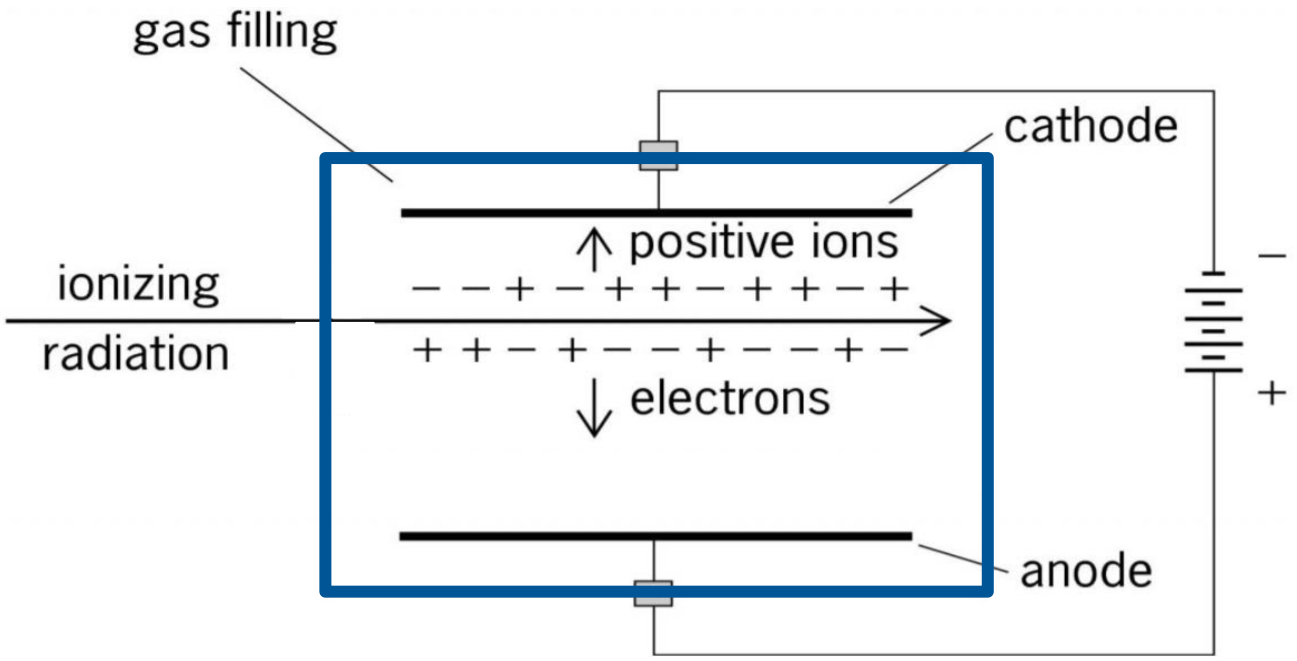
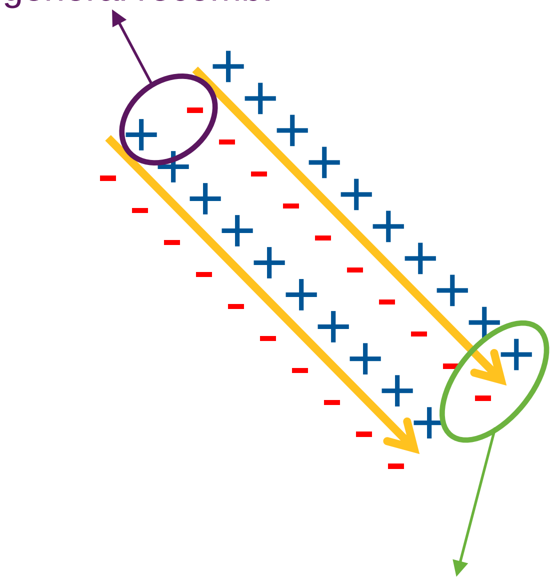
Dosimeters for UHDR

Ionization chambers

Ionization chamber – principle of operation





Initial Recombination

- Recombination along a single charged particle track.
- **Independent of dose and dose-rate.**
- More pronounced in highly ionising particles such as alpha-particles.

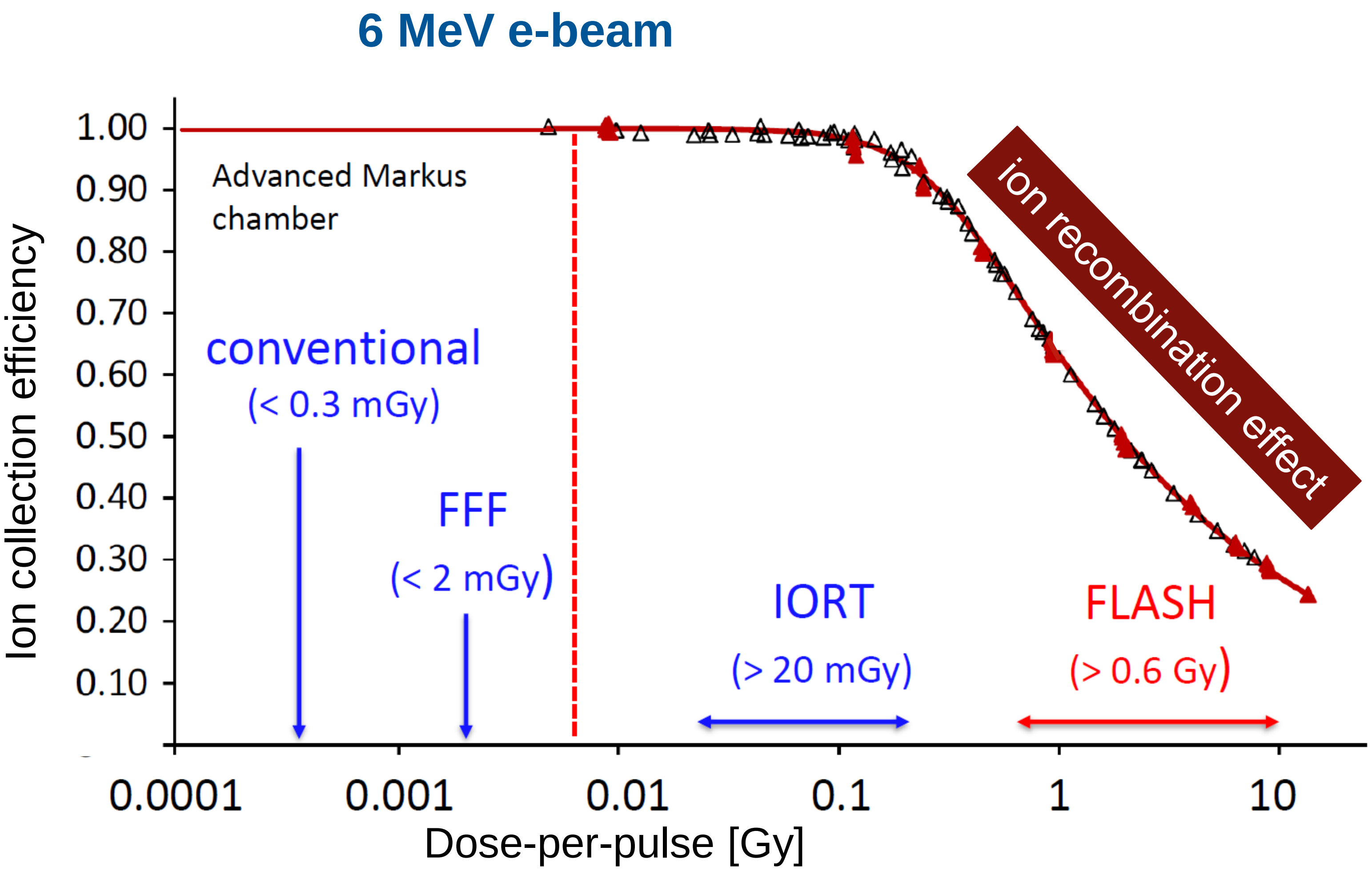
General Recombination

- Recombination between separate charged particle tracks.
- Directly dependent on charge density i.e the number of ions produced per unit volume.
- **Dose-rate dependent.**

General recombination is likely to play a much larger role in recombination effect in UHDR pulsed beams

IC: Metrological challenges of dosimetry at UHDR

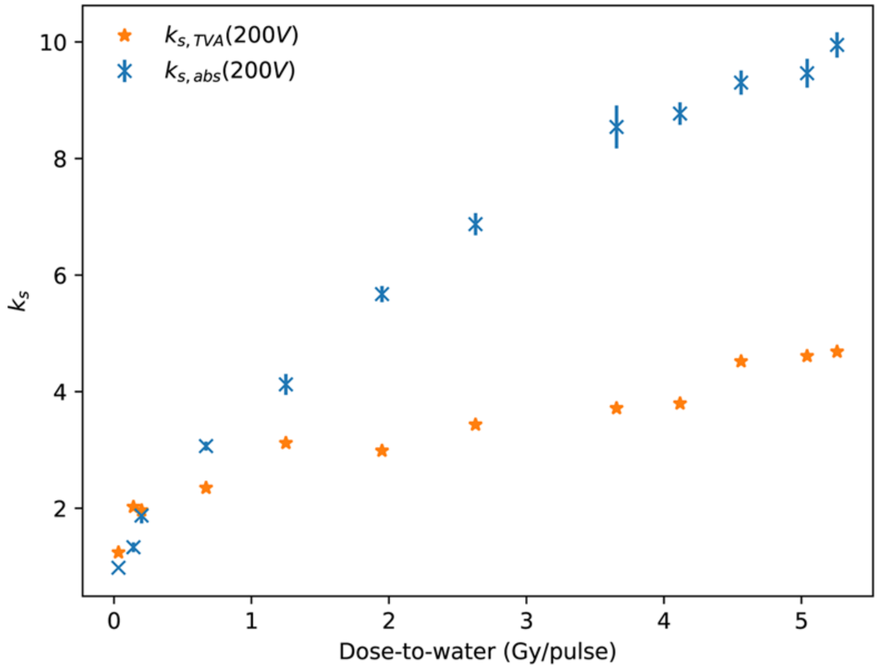
Typical behaviour of an IC at UHDR dose rates for **pulsed electron beams**

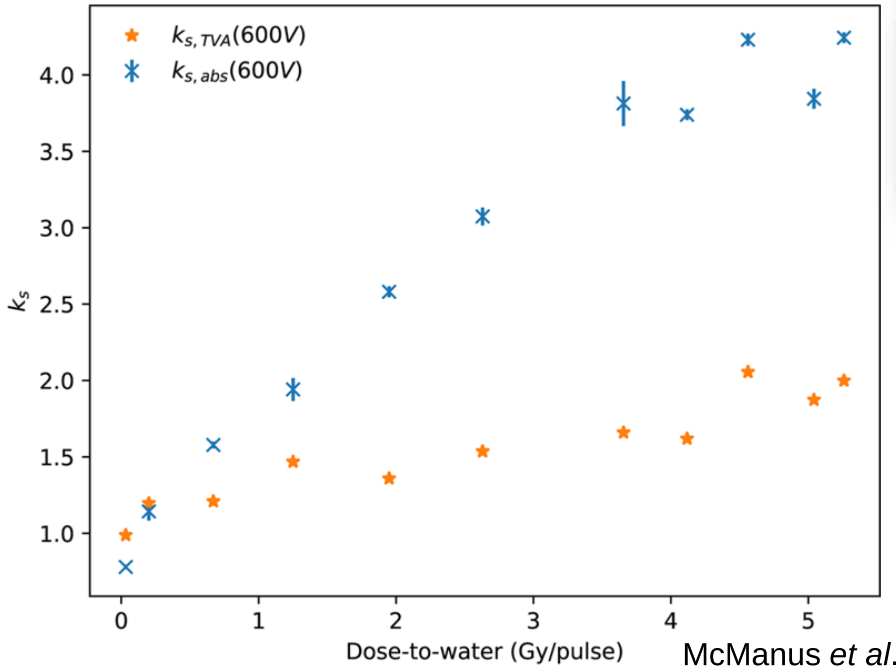


PTW Advanced Markus
(1 mm electrode separation)

Petersson *et al.*, Med Phys 44 (2017) 1157

IC: Metrological challenges of dosimetry at UHDR





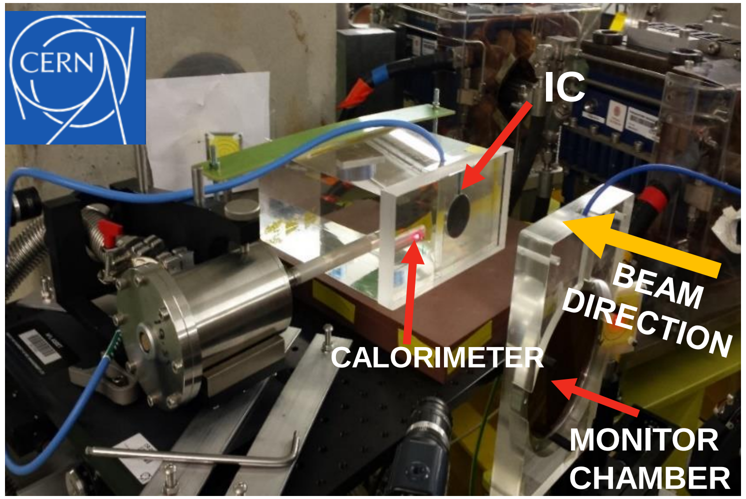
PTW Roos (2 mm electrode separation)

- 200 MeV VHEE beam
- DPP: 0.03 – 5.3 Gy/pulse
- Graphite calorimeter employed as reference detector

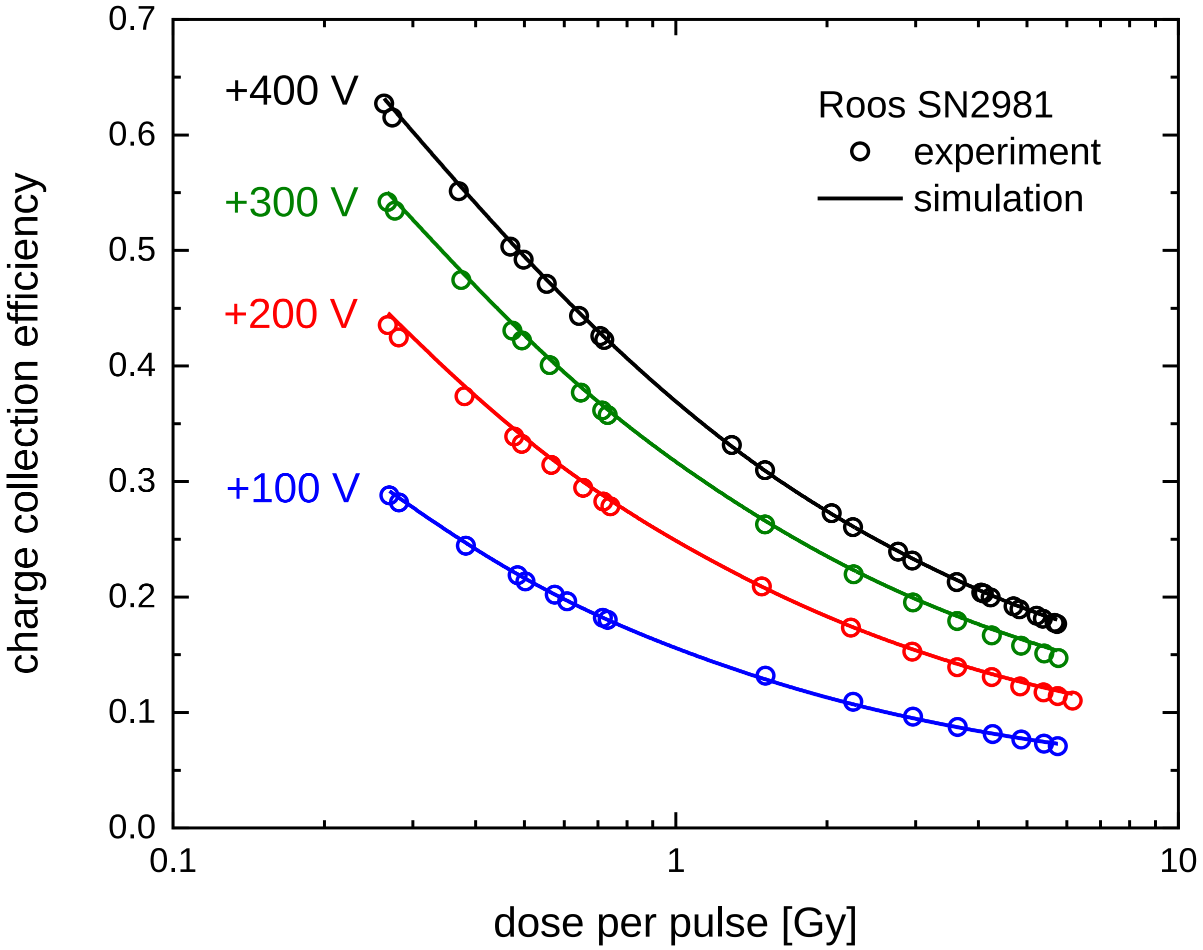
$$k_{s,abs} = \frac{D_{w,cal}}{M k_{pol} k_{TP} k_{Q,Q_0} N_{D,w,Q_0}}$$

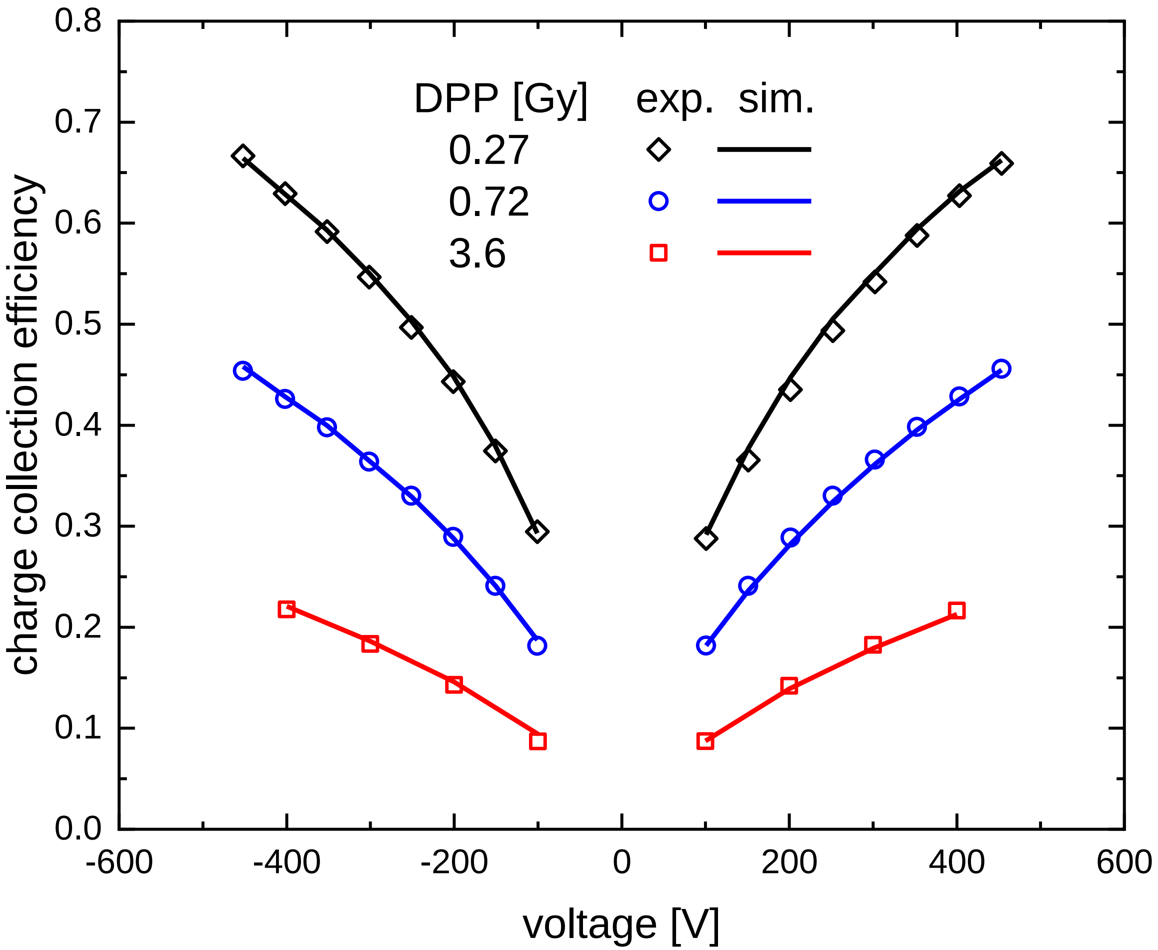
McManus *et al.*, Sci. Rep. (2020)

- k_s up to 10 (V = 200 V) → **collection eff. 10%**
- k_s up to 4 (V = 600 V) → **collection eff. 25%**
- $k_{s,abs}$ compared with $k_{s,TVA}$ (two-voltage method)
- Available **analytical ion recombination models cannot predict chamber behaviour** for such a high DPP



Calculation of charge collection efficiency





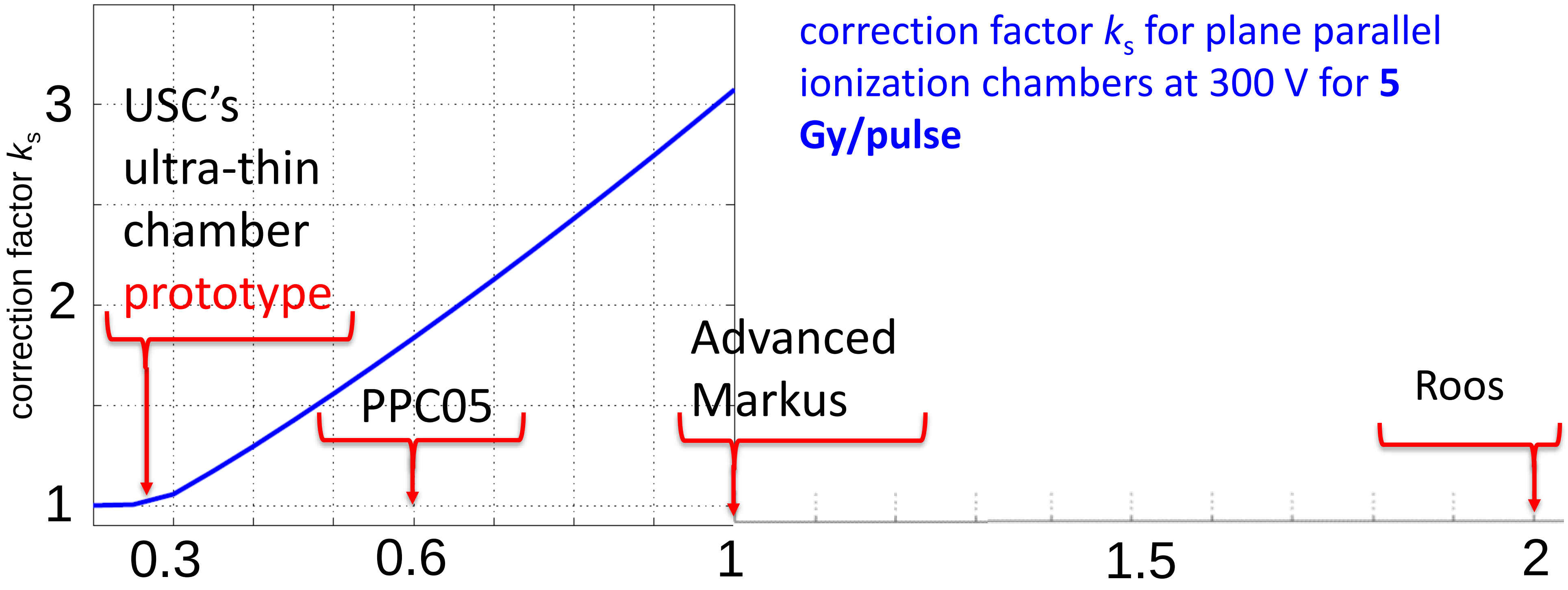
J. Paz-Martín *et al*., "Numerical modelling …" Phys. Med. **103** (2022) 147.
https://doi.org/10.1016/j.ejmp.2022.10.006

Ionization chambers – possible solutions

Possible solution for UHDR beams

USC's prototype ionization chambers for ultra-high DPP

Fig. Ionization chamber prototype (0.27 mm)



Schüller *et al.*, Phys.Med. 80 (2020)

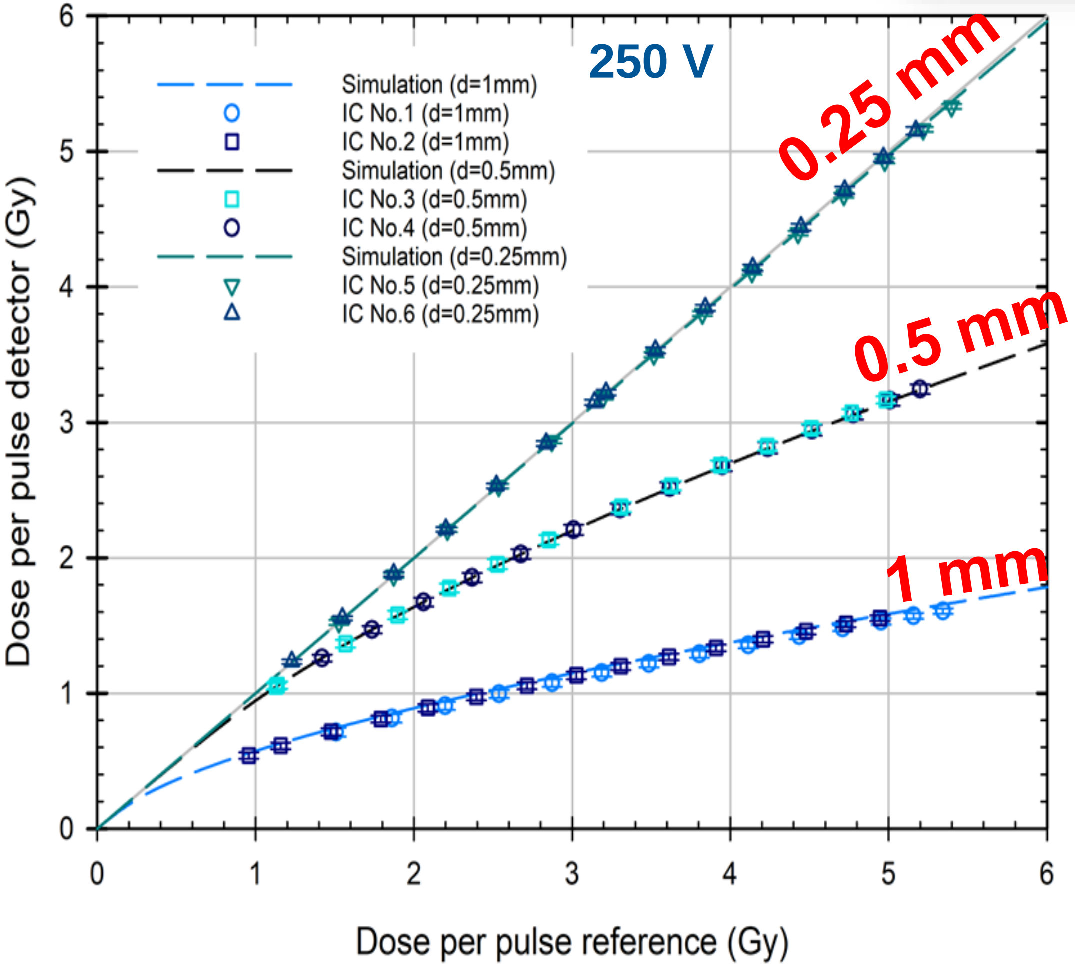
Simulated ion recombination correction factor k_s for plane parallel ionization chambers at 300 V for **5 Gy/pulse**

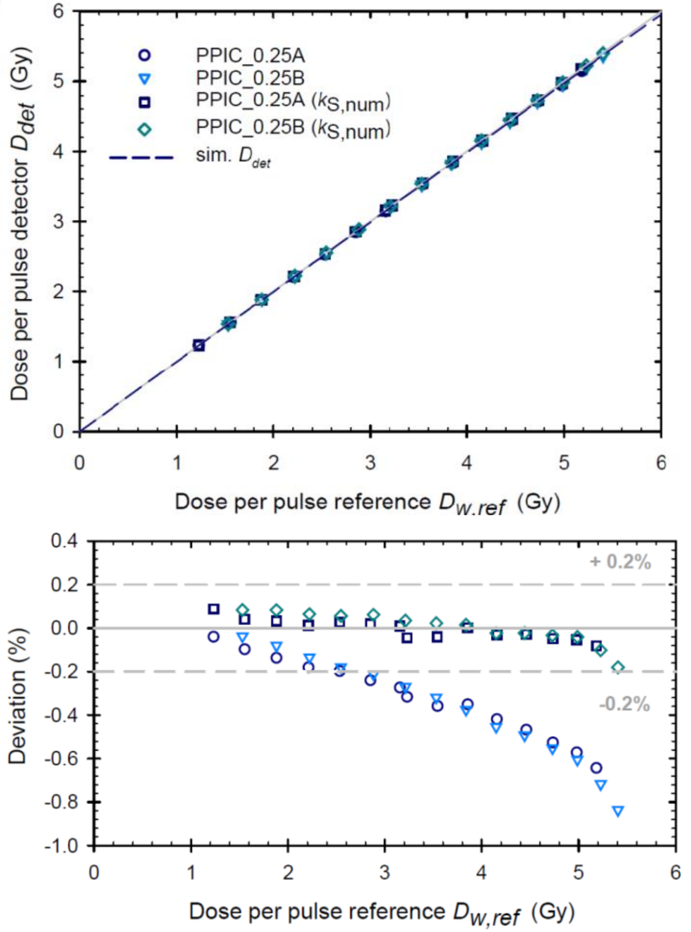
Courtesy of Faustino Gomez

Possible solution for UHDR beams

PTW's prototype ionization chambers for ultra-high DPP

Fig. PTW IC prototype (0.25 mm)





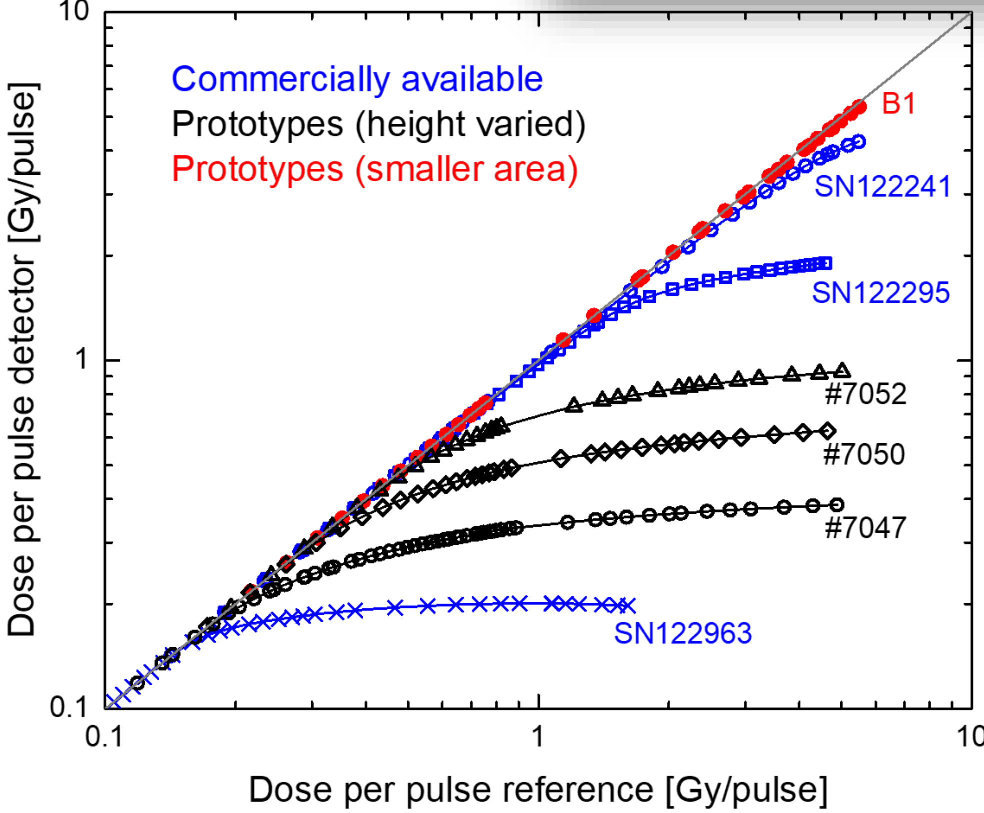
Kranzer *et.al.* Phys.Med. 104, 10-17

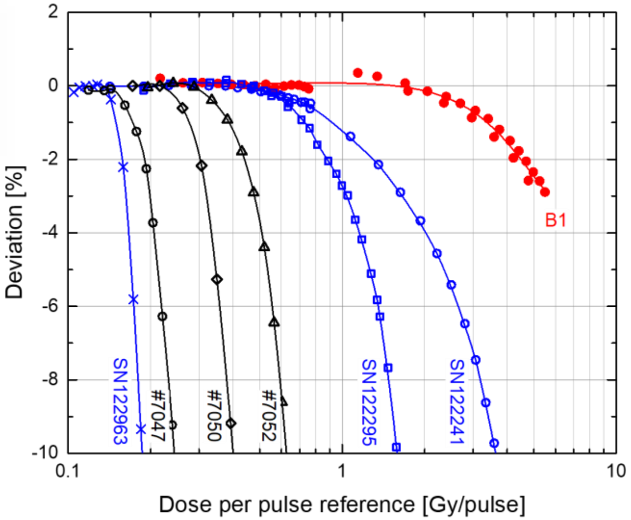
Diamond detectors

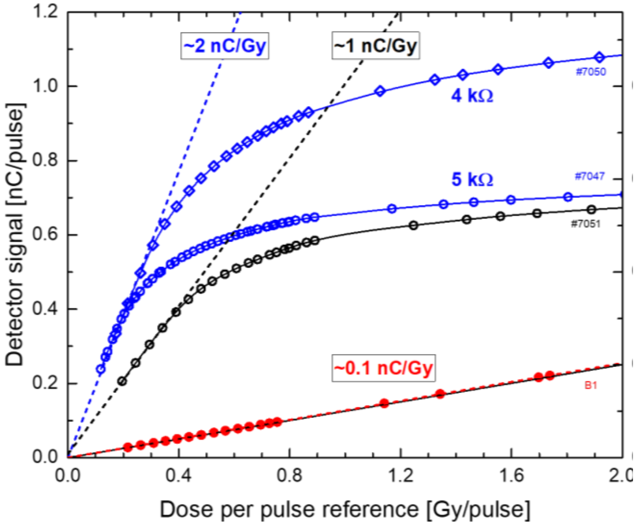
Possible solution for UHDR beams

PTW's microDiamond for ultra-high DPP

Fig. microDiamond







- Commercially available microDiamond detectors show saturation effects at different DPP levels.
- The linear range can be extended to the ultra-high DPP range by reduction of sensitivity and resistance.

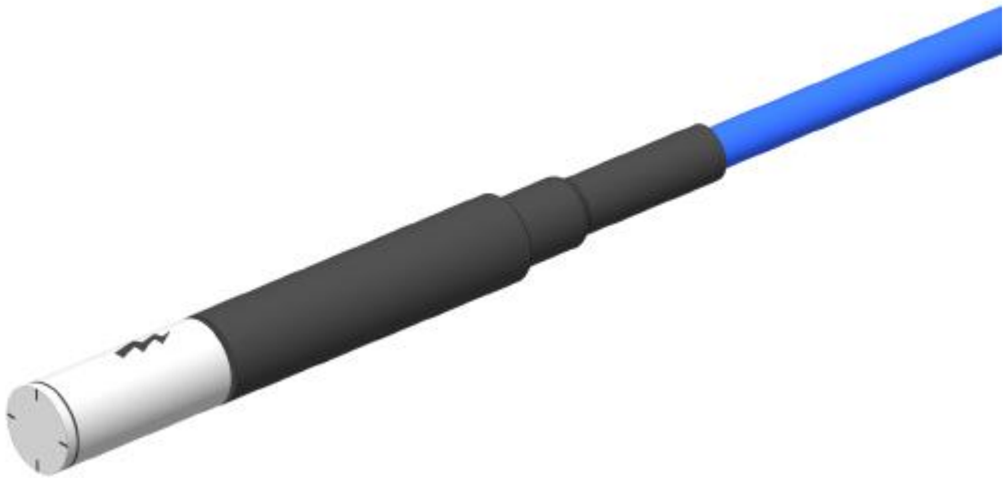
Kranzer *et al., PMB 67 (2022)*

flashDiamond – Fundamental investigations

- The applicability for the commissioning of FLASH RT electron beams was shown in the following work

  G. Verona Rinati et al. 2022 (DOI: 10.1002/mp.15782)

- Successfully tested in terms of:
  - Linearity with ultra-high dose per pulse (UH-DPP)
  - Depth dose curves (PDD)
  - Lateral dose profiles
  - Output factors



PDD measurements with the fDiamond using SIT ElectronFlash accel.

flashDiamond (fD) for ultra-high DPP

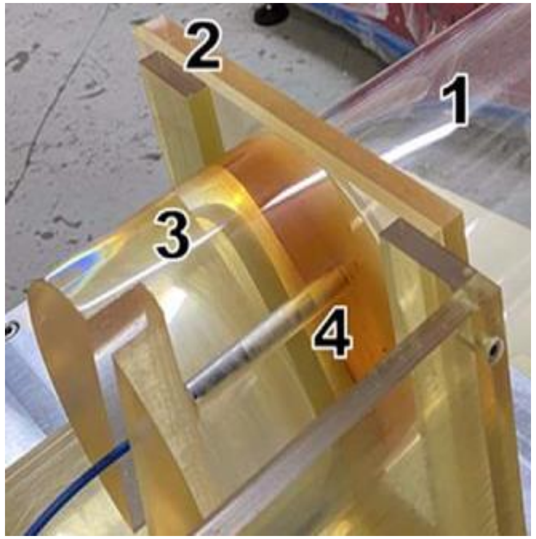
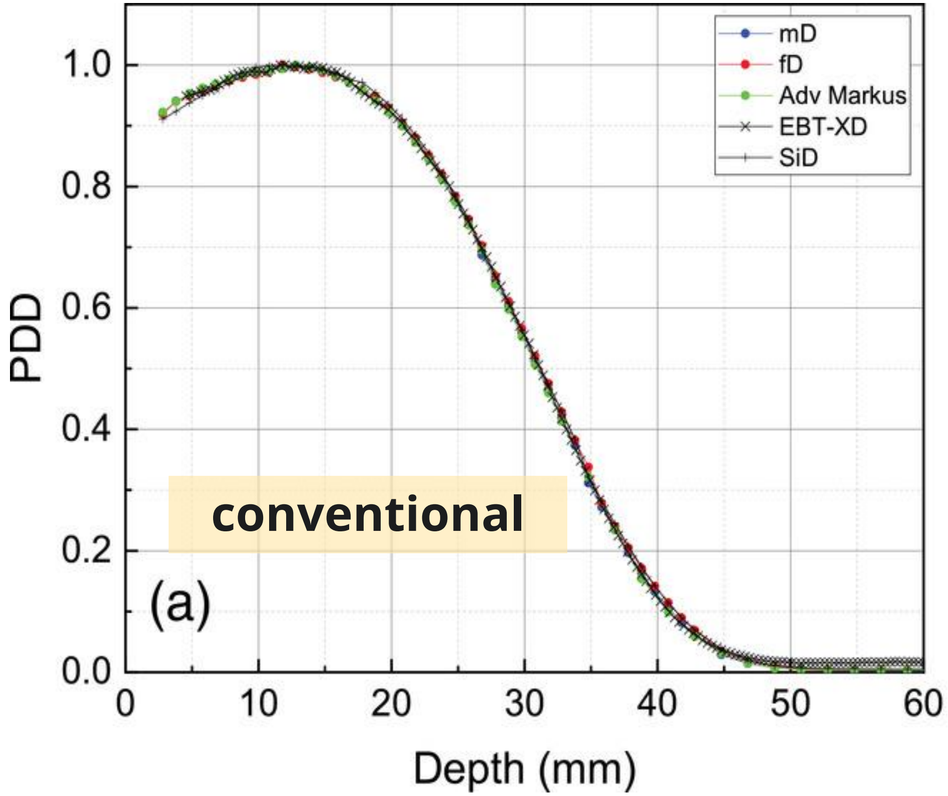
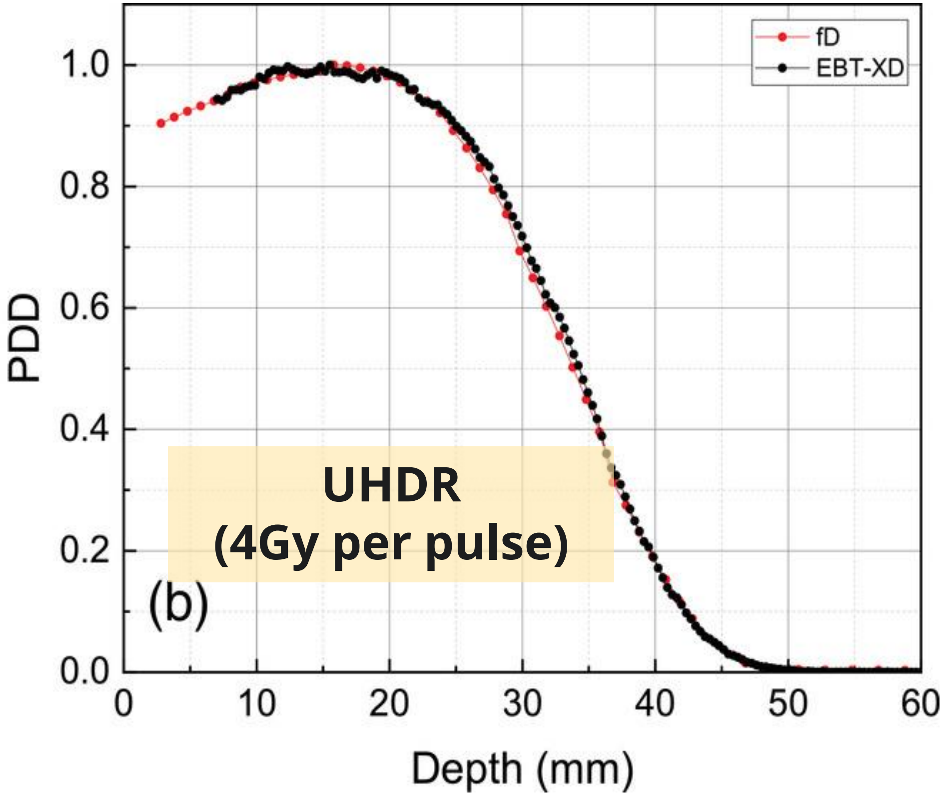


Fig. fD (4) positioned in the experimental setup

Marinelli *et al. Med. Phys*. **49** (2022)





Verona Rinati *et al. Med.Phys.* (2022)

More work done foth eFLASH (Varian) and Mobetron (IntraOp) - upublished

flashDiamond - Applications

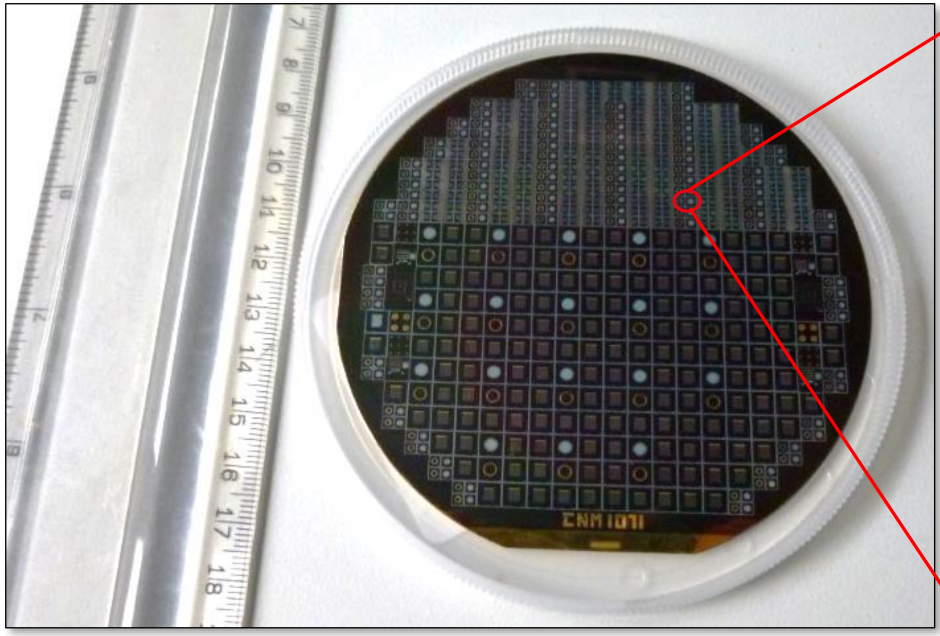
National Physical Laboratory

- Relative Dosimetry
  - Measurement of three-dimensional dose distribution with high spatial resolution
  - Direct measurement of absorbed dose to water, no need to convert depth dose curves
- Consistency check (beam stability)
- Time resolved measurements (Verona Rinati)
- Absolute dose measurements
  - After cross-calibration against a suitable reference
  - A methodology for the determination of absorbed dose to water is still missing
- The **flashDiamond Type 60025 is commercialized** as a laboratory device for research purposes and thus available for further users and a variety of dosimetric applications

PTW THE DOSIMETRY COMPANY

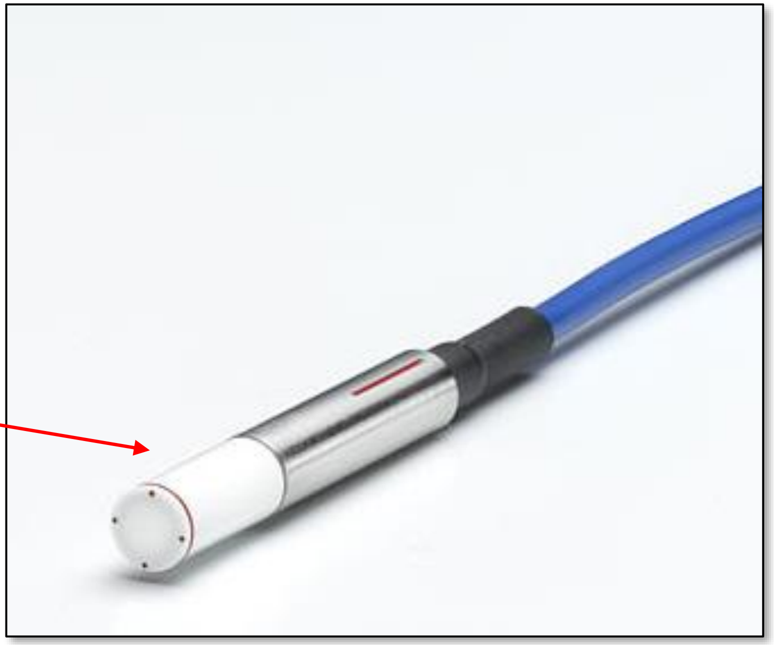
Silicone carbide (SiC)

SiC diodes for FLASH dosimetry



4” SiC wafer

1 mm diode



Encapsulation by PTW (microSilicon housing)

By Institute of microelectronics in Barcelona

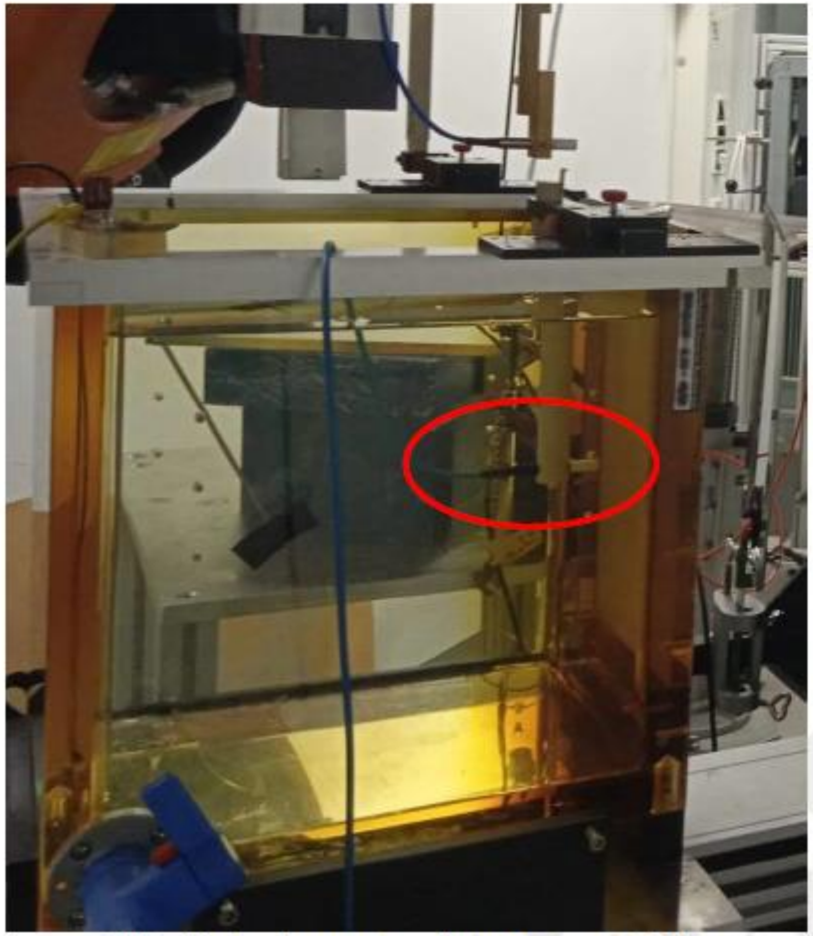
- CNM-CSIC has designed and fabricated a set of SiC diodes for dosimetry
- *EU Patent pending* → Patent EP22383168.6
- Devices tested: circular 1 mm diameter PiN diodes on 3 µm epitaxial 4H-SiC
- Encapsulated by PTW with their microSilicon housing for electrical connectivity

Application for Patent EP22383168.6

Test with e-beam at PTB

- Measurements at PTB UHDPP electron beam
- Electron energy 20 MeV
- Repetition rate 5 Hz, pulse duration 0.6, 1.6 and 2.9 µs
- Measurements in PMMA water tank with a motorized positioning system
- SSDs 90 and 70 cm
- Reference dosimetry provided by Alanine and prototype flashDiamond*
- SiC diode operated without external bias

(*) M. Marinelli et al. “Design, realization and characterization of a novel diamond detector prototype for FLASH radiotherapy dosimetry” Med Phys. 2022;49:1902–1910



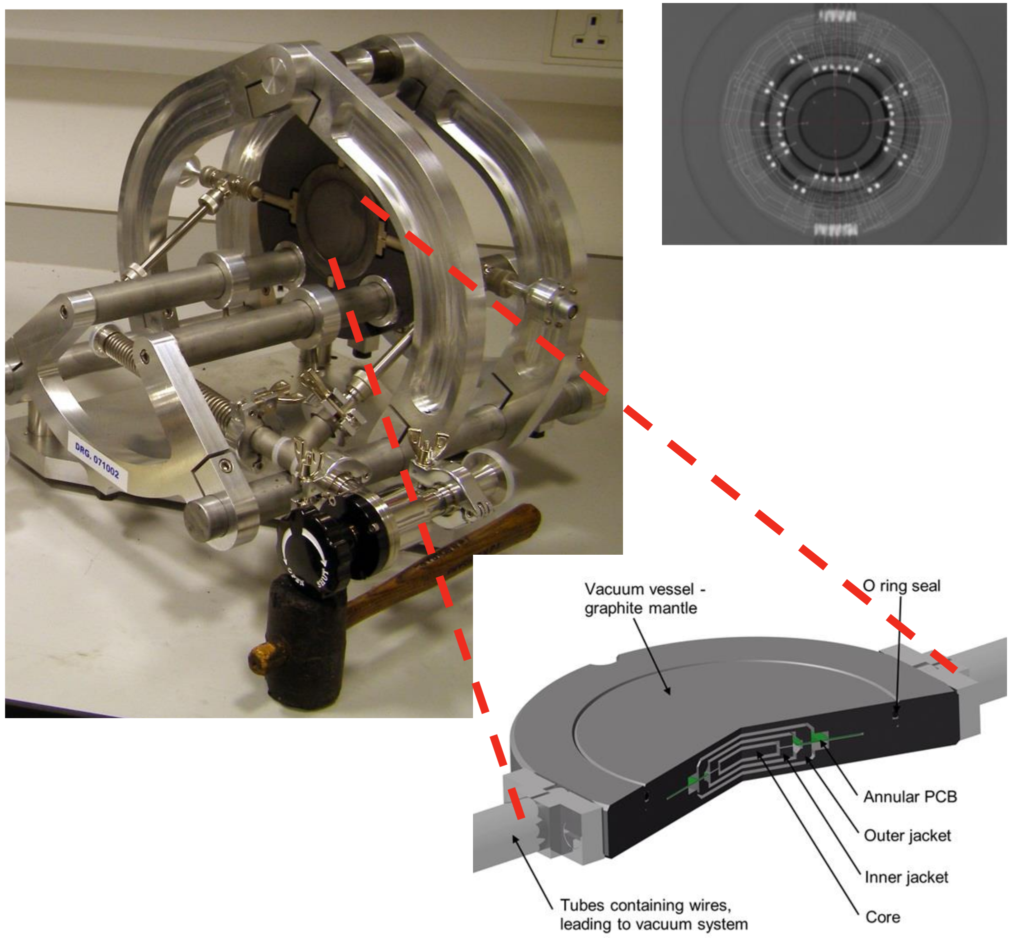
SiC diode in water phantom at PTB

Calorimeters

Calorimetry in UHDR beams

NPL primary standard graphite calorimeter

- the control and analysis software was reconfigured to enable it to be used with UHDR particle beams
- Operated in quasi-adiabatic mode, thermistors detect changes in temperature of the graphite created by energy absorbed from the radiation beam allowing derivation of absorbed dose



NPL's primary standard graphite calorimeter.

Calorimetry in UHDR beams

NPL primary standard graphite calorimeter

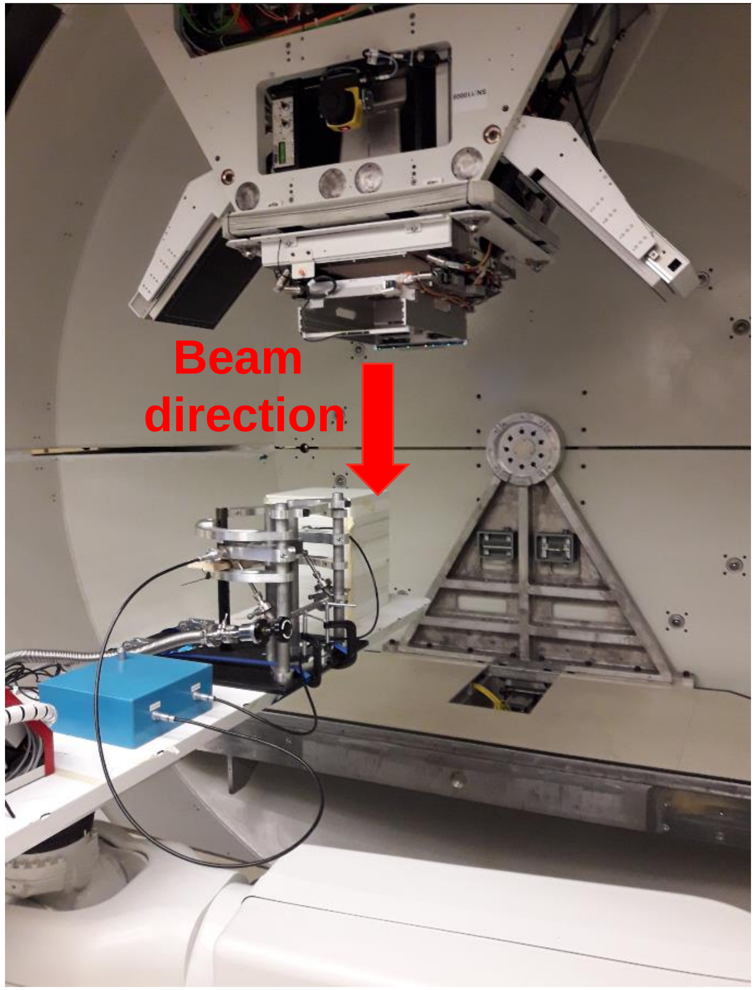
- 250 MeV (Varian ProBeam® operating in research mode) at ~65 Gy/s
- The core of the calorimeter was positioned at the isocentre with graphite plates placed in front to position the core at a WET of 5 gcm^{-2}

	Proton calorimeter				dose to water	
Field size, cm	5 x 6	5 x 8	5 x 10	5 x 12	6 x 5	12 x 5
Mean Dose, Gy	**7.654**	**7.690**	**7.726**	**7.736**	**7.666**	**7.741**
SDOM, %	0.04%	0.04%	0.04%	0.04%	0.04%	0.03%

Parameter	Value
c (J·kg^{-1}·K^{-1})	651.57+2.74· (T-273.15)
k_{imp}	1.0016
k_{gap}	1.0029
$s_{w,g}$	1.1210
k_{fl}	0.9713
$k_{z,cal}$	1.0000

Sources of uncertainties (%)	Type A	Type B
Physical dimensions	<0.01	0.09
Electrical calibrations	0.20	0.06
Specific heat capacity	0.08	0.26
k_{imp}, k_{gap}	0.01	0.11
$s_{w,g}$, k_{fl}	0.07	0.71
$k_{z,cal}$	-	0.10
Positioning on beam axis and reference depth	0.06	0.13
PCB	-	0.25
Calorimeter measurements and analysis	0.04	0.15
Total	0.24	0.84
Overall (1σ)	0.9	

Lourenço *et al. Sci.Rep*. under review



Calorimetry in UHDR proton beams

→ **First ever calorimetry measurements in UHDR proton beam**

- Established the correction factors required for absolute dosimetry of FLASH proton beam radiotherapy (Lourenço et al., 2022 (under review))
- Measurement uncertainty of 0.9% (k=1) – in line with clinical requirement
- **Underpinned the FDA approval and provided the hospital with confidence to commence clinical implementation of this novel technology**

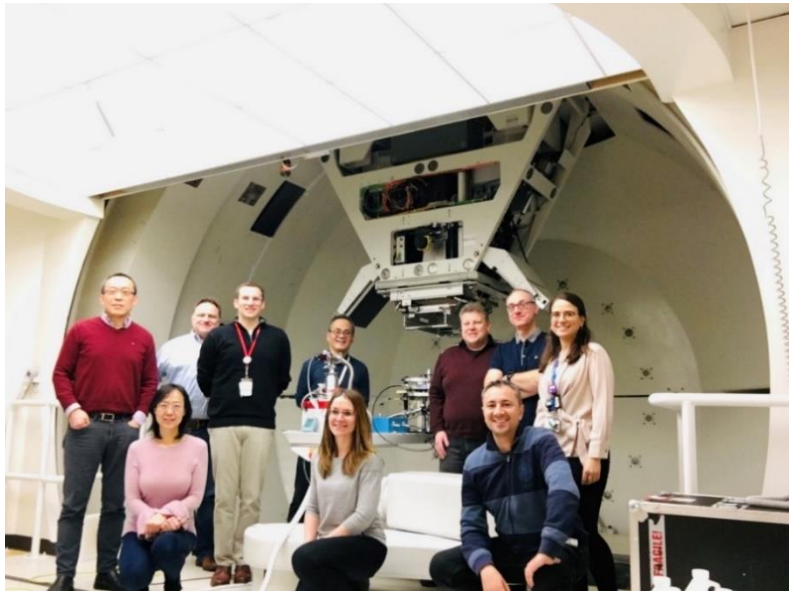
U.S. National Library of Medicine

ClinicalTrials.gov

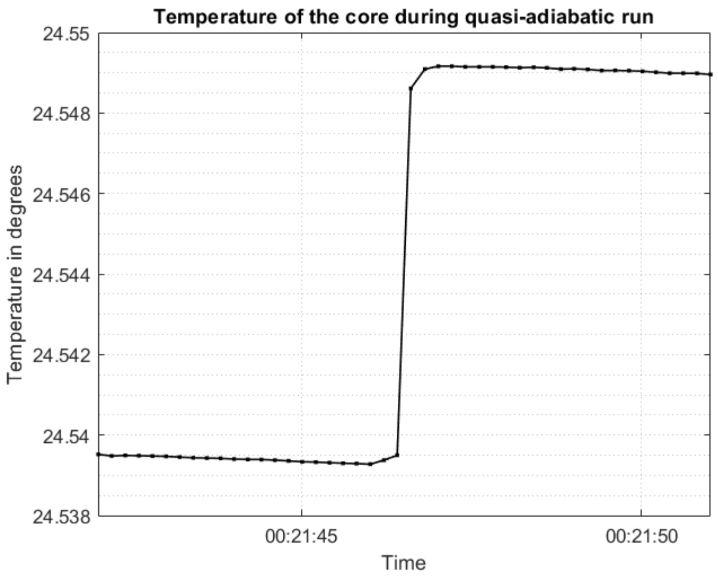
Feasibility Study of FLASH Radiotherapy for the Treatment of Symptomatic Bone Metastases (FAST-01)

ClinicalTrials.gov Identifier: NCT04592887

Recruitment Status : Active, not recruiting
First Posted : October 19, 2020
Last Update Posted : November 1, 2021



NPL and Cincinnati Teams



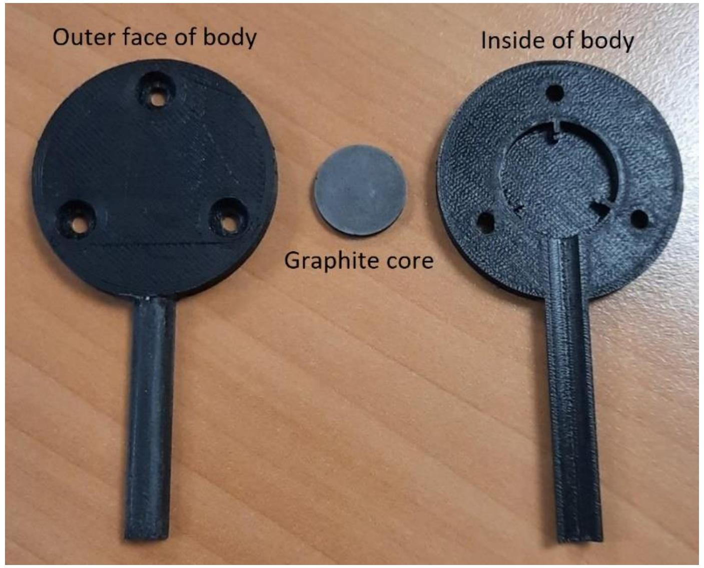
National Physical Laboratory

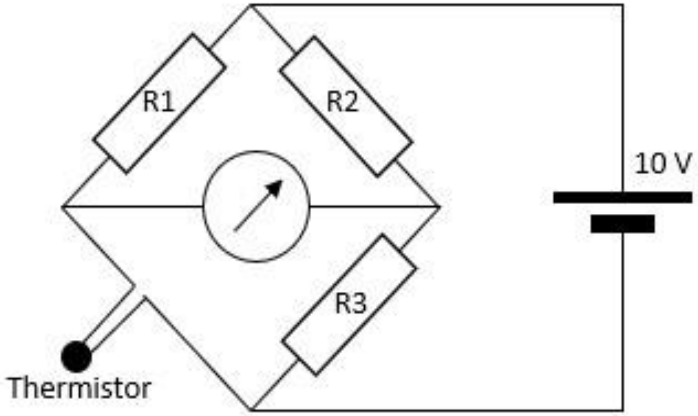
Simple Design Calorimeters as secondary standards for FLASH RT

Secondary standard calorimeter: *basic design & measurement system*

- Shaped like a Roos or PPC05 IC
- Solid graphite or aluminium core 16 mm Ø, 2 mm thick, supported on 3 plinths, surrounded by air gap
- Single thermistor embedded in core, 10 kΩ at 25 °C
- 3D-printed body, in two halves
- Can be lacquered to be waterproof

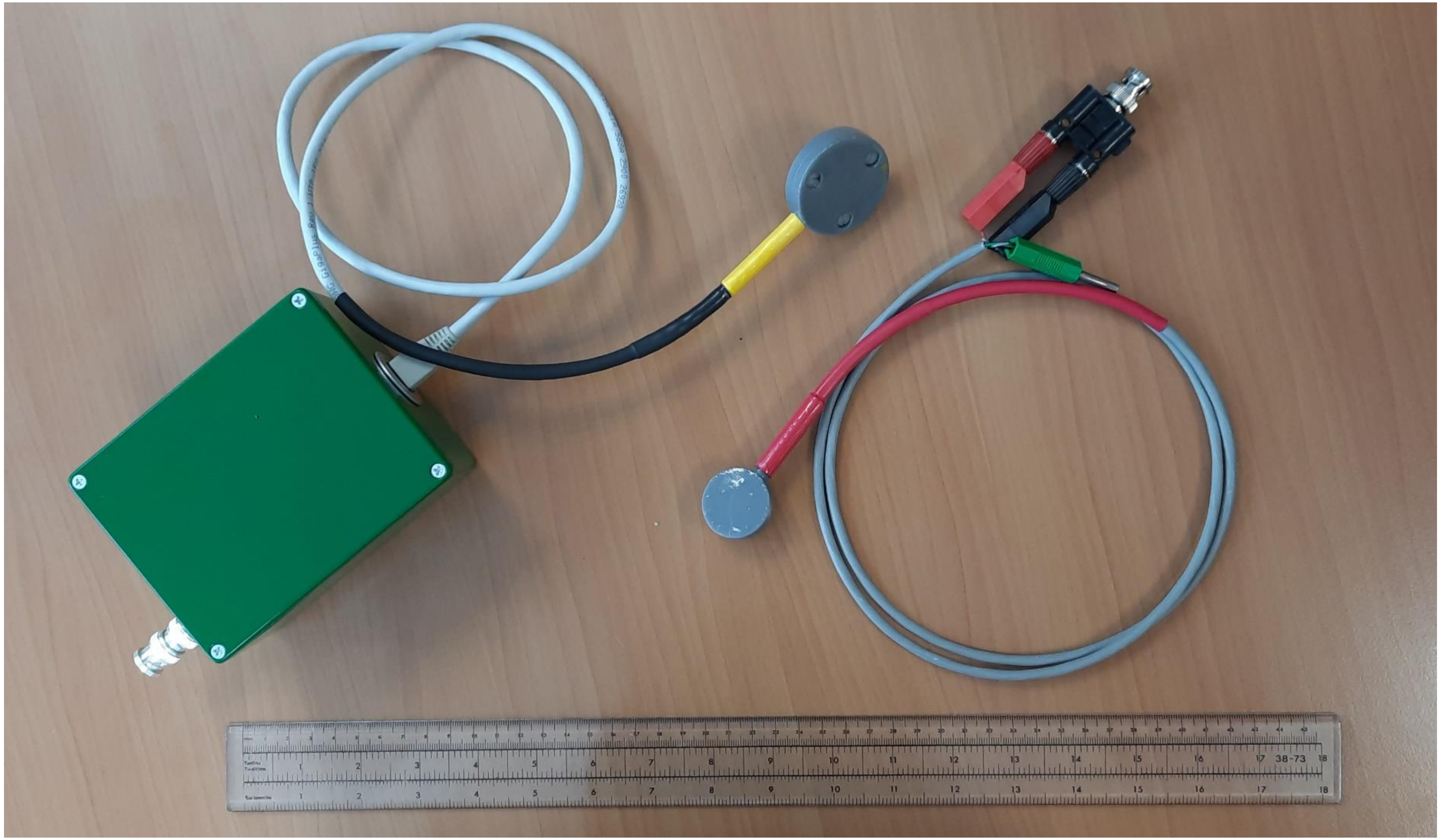
- Simple DC Wheatstone bridge
- Sensing thermistor in one arm
- Resistors 10 kΩ ± 0.01 %, ± 2 ppm/°C
- 10 V supply voltage





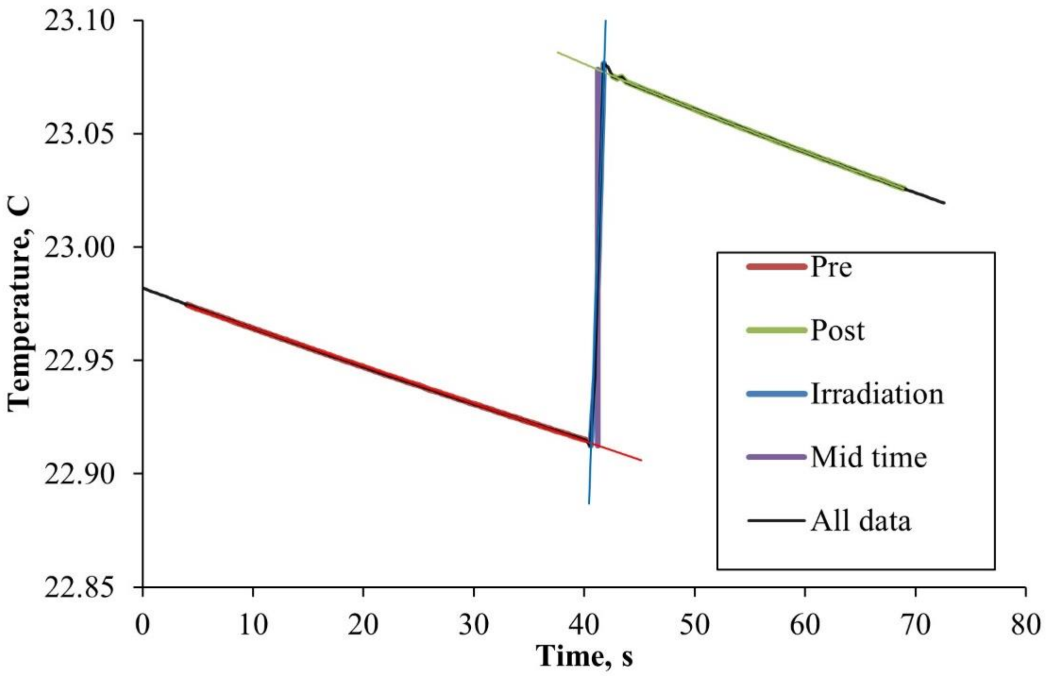
Bass et al., *Br J Radiol* (2022) 10.1259/bjr.20220638.

Secondary standard calorimeter: *built examples*



Secondary standard calorimeter:
UHDR beam response

- test in research 28 MeV proton beam
- ~100 Gy beam delivery in < 0.5s
- Much higher SNR compared to conv. delivery
- Extrapolation of pre- and post-irradiation drifts over much shorter duration → resulting in lower uncertainty



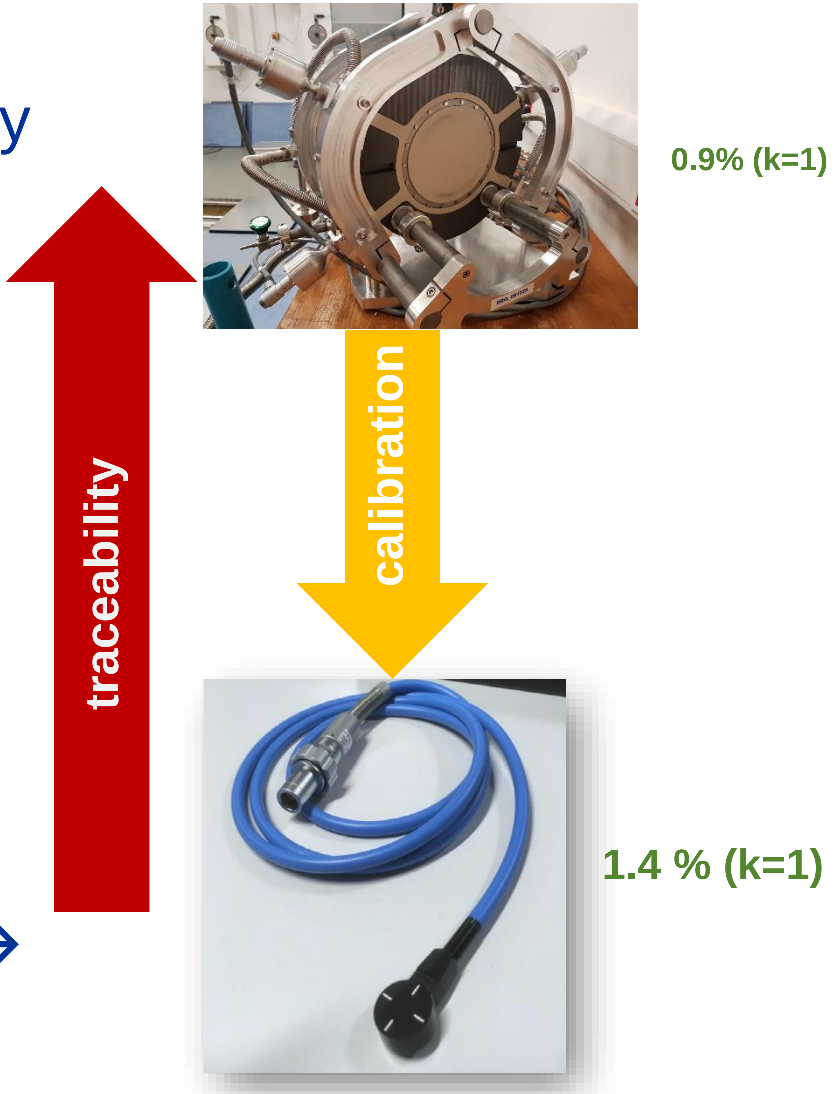
How to ensure traceability in FLSH RT?

NPL National Physical Laboratory

1. Disseminate the D_w in the UHDR beam with a primary standard

2. Use adequate detectors as a s/s and calibrate them against primary standard under the reference conditions

- The reference conditions need to be specified (TBC) → these will depend on the UHDR radiation device



Summary

- Significant developments have been made in metrology for UHDR beams, but the field is still under development
- Commercially available IC are not suitable for dosimetry of UHDR pulsed e-beams
- New detectors become/will become available for accurate dosimetry for FLASH RT:
  - fDiamond
  - ultra-thin IC
  - clinical calorimeters
  - SiC
  - …
- Reference dosimetry for e-FLASH RT still needs to be established (this will be driven by availability of UHDR e-beams)

NPL National Physical Laboratory

The EMPIR initiative is co-funded by the European Union's Horizon 2020 research and innovation programme and the EMPIR Participating States

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Thank you

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http://uhdpulse-empir.eu/