FLASH RADIOTHERAPY & PARTICLE THERAPY
VIENNA AND ONLINE
1-3 DECEMBER 2021

Current Status of Dosimetry, QA , Challenges and the Need for Further Developments

Anna Subiel, PhD

Medical Radiation Science, National Physical Laboratory,
Hampton Road, Teddington, Middlesex, TW11 0LW, UK

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

Disclosure

- **Relevant Financial Relationships:**
  i. Research funded by the EMPIR programme co-financed by the Participating States and from the European Union’s Horizon 2020 research and innovation programme (18HLT04 UHDpulse)
  ii. Work supported by the UK’s National Measurement System (NMS) Programme
- **Relevant Nonfinancial Relationships:**
  i. Serves as a Committee Member of the AAPM Task group no. 359: FLASH (ultra-high dose rate) radiation dosimetry
  ii.Serves as reviewer for several peer-reviewed journals

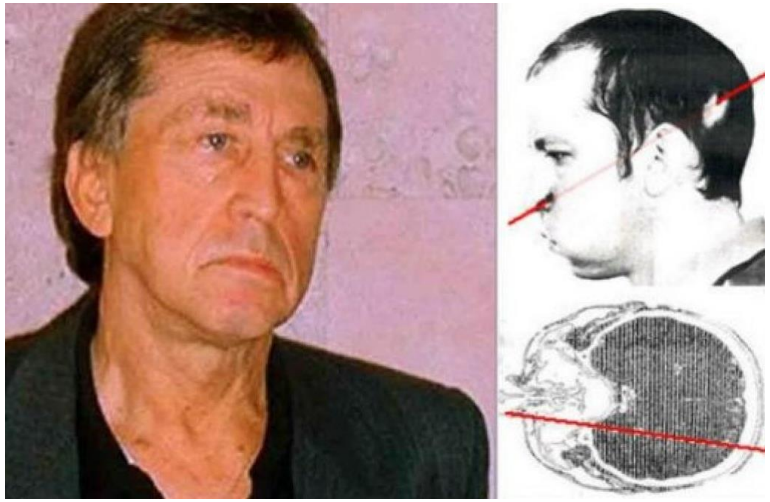
Outline

- FLASH RT
- Radiation sources and temporal beam structure for FLASH RT
- The need for QA in RT
- Clinical implementation of FLASH RT
- Challenges of dosimetry of UHDR beams
- The role of NMI
- The EMPIR UHDpulse project
- Conclusions

“I saw a flash brighter than a thousand suns”

NPL National Physical Laboratory

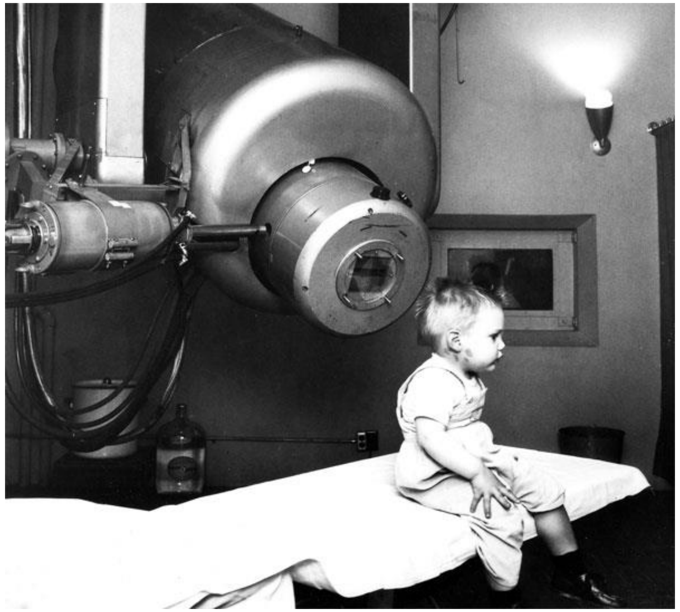
- Researcher at the Institute for High Energy Physics in Protvino, Russia, working the U-70 synchrotron.
- In July 1978, checking a malfunctioning piece of equipment when the safety mechanisms failed
- He stuck his head in the path of the 76 GeV pencil proton beam delivering a dose of approx. 2-3 kGy!!
- The beam passed through the back of his head, temporal lobes of his brain, the left middle ear, and out through the left-hand side of his nose.
- suffered some radiation side effects, such as mental fatigue and loss of hearing in his left ear, but ultimately survived the incident and completed his PhD

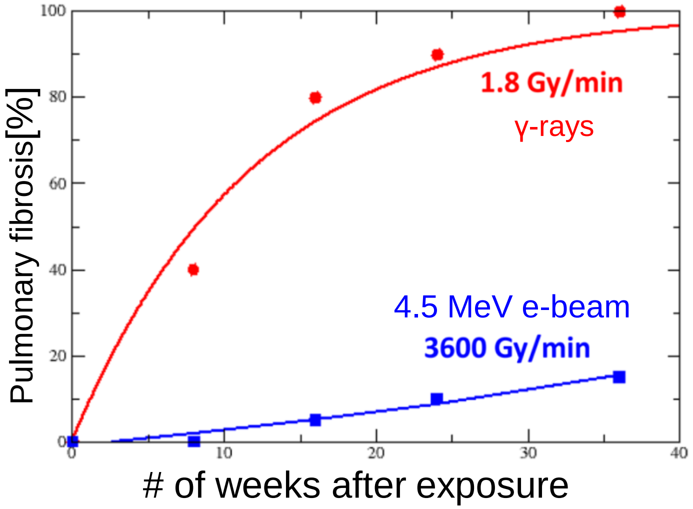


Anatoli Petrovich Bugorski

Modern external beam radiotherapy

- Dating back to 1950s – typically delivered with medical LINACs with dose rate of approx. 6 Gy/min (before FFF implementation)
- Population based TCP and NTCP models have since been derived from extensive clinical outcomes data for patients treated with these machines
- From 2014 – new pre-clinical data came through: exposures to >40 Gy/s beam result in reduction of NTCP while maintaining TCP





Based on Favaudon, *et al.* 2014

Radiation sources used in FLASH RT

- To date, the FLASH effect has been most commonly demonstrated using low energy electron LINACs

- Retrofitted existing technologies (clinical LINACs)

- Synchrotoron source (X-rays)

- Clinical proton beams

Temporal beam structure

Electron LINACs

$DPP = \dot{D}_p \cdot t_p$

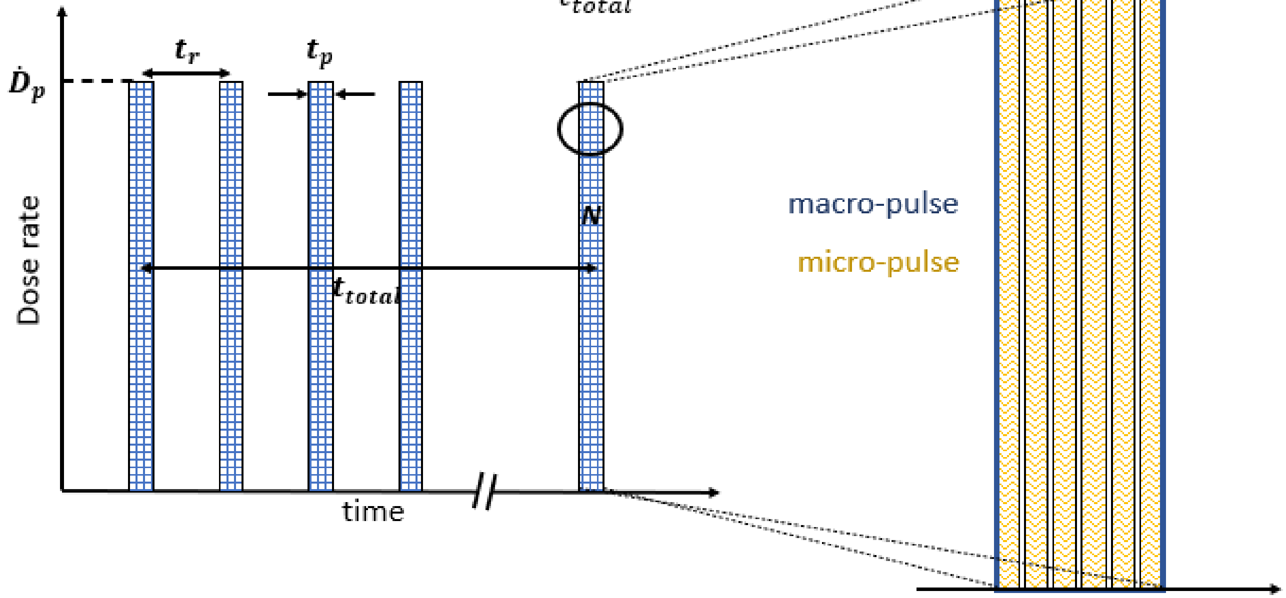
t_p: pulse duration

N: number of pulses

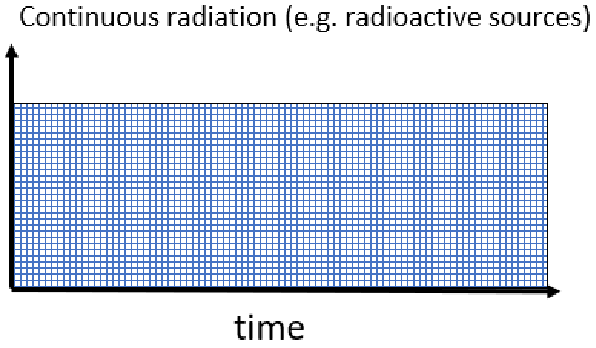
$t_{total} = (N-1) \cdot t_r + t_p$

$\bar{\dot{D}} = \frac{n_p \cdot DPP}{t_{total}}$

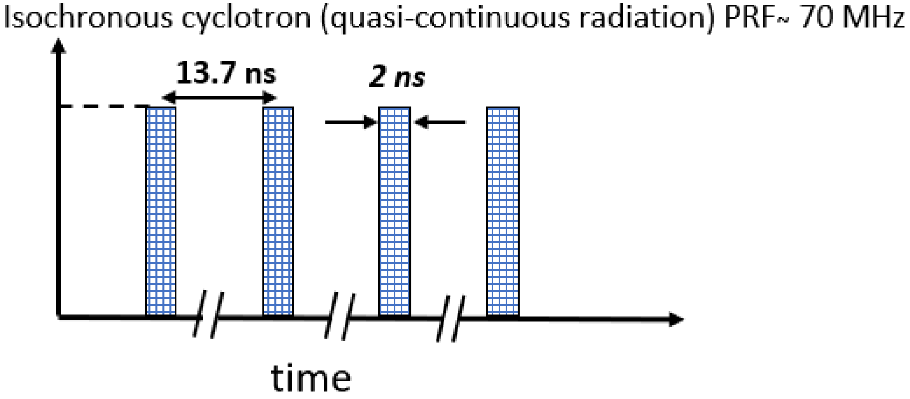
$t_r = \frac{1}{PRF}$ pulse rate

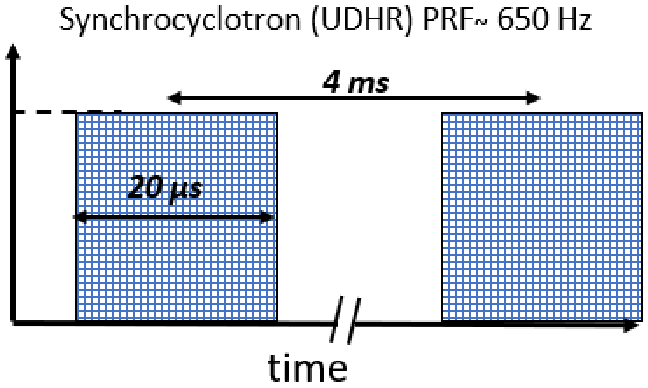


Photons



Protons



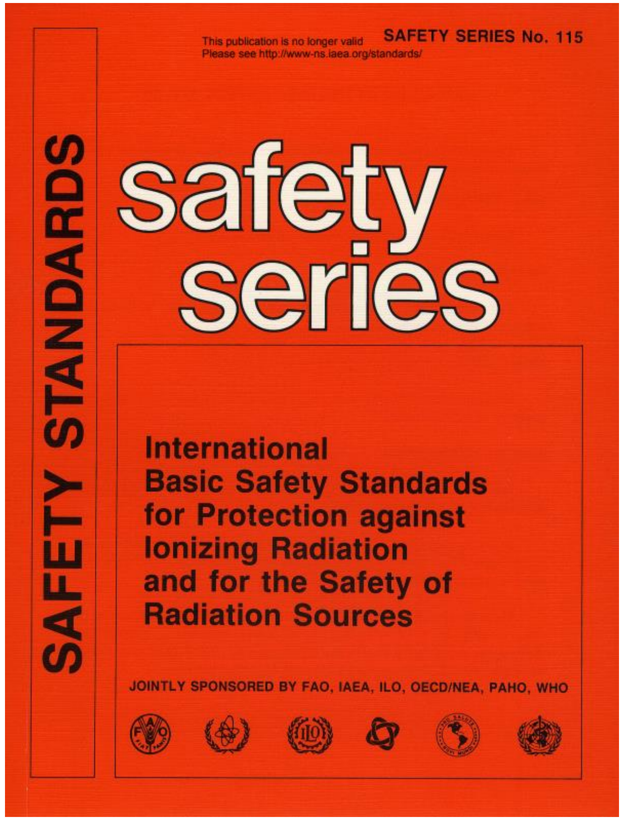


It's not clear what are the necessary delivery parameters to achieve the FLASH effect

- UHDR: >40Gy/s?
- total treatment time <500 ms?
- DPP?

The need for Quality Assurance (QA) in RT

- QA include all procedures that ensure consistency of the medical prescription, and safe fulfilment of RT-related prescription
- Examples of prescription
  - The dose to the tumour (to the target volume)
  - Minimal dose to normal tissue
  - Adequate patient monitoring aimed at determining the optimum end result of the treatment
  - Minimal exposure of personnel



The need for Quality Assurance (QA) in RT

- QA programs must be established, including: (i) measurement of physical parameters of the radiation generators, imaging devices and irradiation installations at the time of commissioning and periodically thereafter and (ii) verification of the appropriate physical and clinical factors used in patient diagnosis or treatment
- To provide the best treatment to the patient
- To provide measures to approach the following objectives:
  - **Reduction of uncertainties and errors** (in dosimetry, treatment planning, equipment performance, treatment delivery etc.)
  - **Reduction of the likelihood of accidents and errors**
  - **Provide reliable inter-comparison of results** among different centres
  - **Full exploitation of improved technology** and more complex treatments in modern RT

Requirement on Accuracy in RT

- The ICRU Rep.24 (1976) states:

An uncertainty of 5% is tolerable in the delivery of absorbed dose to the target volume

- This is interpreted to represent a confidence level of 1.5-2 times the SD
- Currently, the recommended accuracy of dose delivery is generally **5-7% (k=2)**

Given the size of the error in the biological contribution, it is important that the physical errors are minimized

The need for Quality Assurance (QA) in RT

- Complex treatments in modern RT → requires multidisciplinary speciality

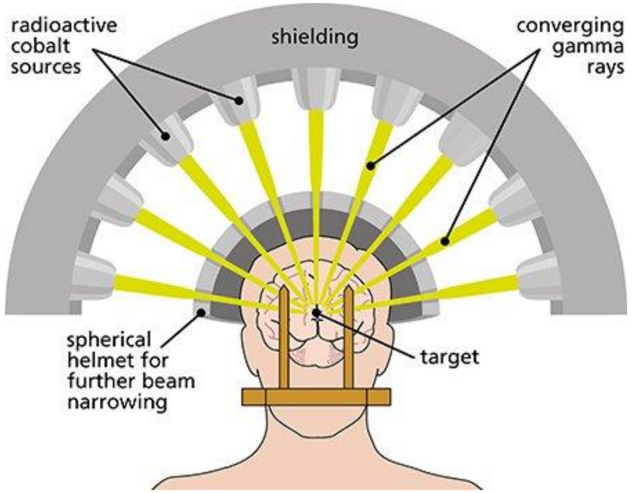

https://www.oncologysystems.com/


https://www.thelondonclinic.co.uk/


https://www.virginiaradiation.com/

https://www.itnonline.com/

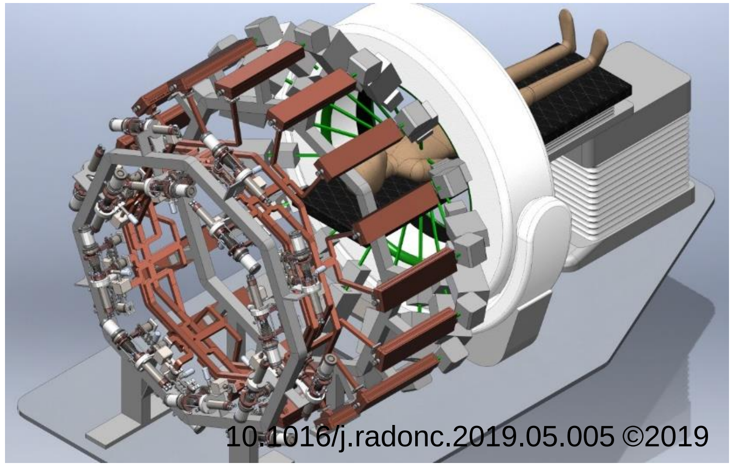
https://www.gosh.nhs.uk/



Machines for UHDR exposures

https://www.soiort.com/

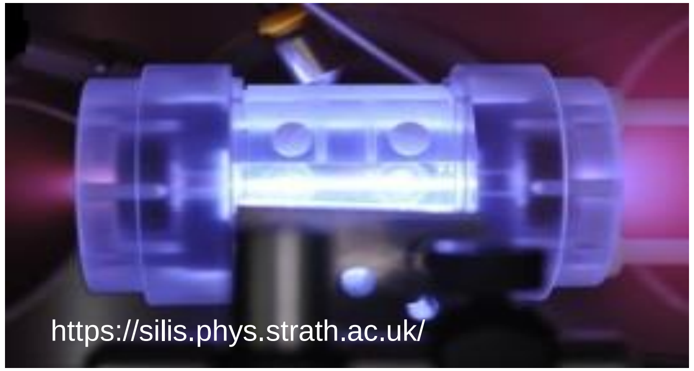
https://www.varian.com/



10.1016/j.radonc.2019.05.005 ©2019

https://www.pmb-alcen.com

https://www.iba-worldwide.com/



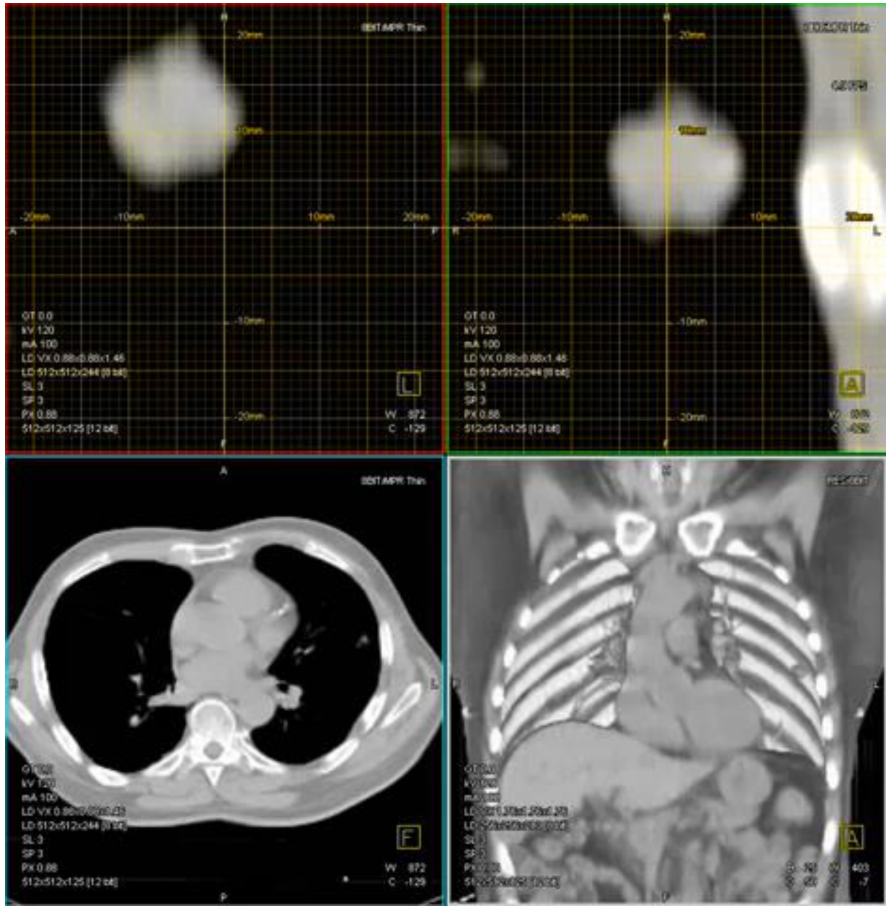
https://silis.phys.strath.ac.uk/

https://intraop.com/

https://www.mevion.com/

Clinical translation of FLASH RT

How to ensure we can **target** the tumour with the **prescribed dose** at **UHDR** ?



Opportunities and challenges for FLASH RT

National Physical Laboratory

- Improved NTCP
- Enables full treatment (or fractions) in <s
- Increased patient throughput
- Better efficacy
- Freezing motion
    - potentially minimize treatment margins (PTV) related to motion (**if we have good motion management**)
    - Less normal tissue exposed to the treatment dose

- Clinical delivery systems
- Beam stability
- **Dosimetry**
- **Real-time beam monitoring**
- Radiation biology (underpinning FLASH effect)
- Radiation protection (e.g. shielding)
- Dose distributions
- Freezing motion

Dosimetry for UHDR beams

Active (online) **detectors**

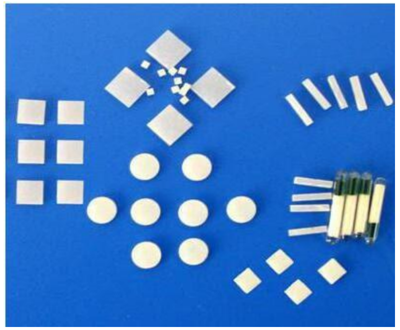
- Ionization chambers
- Transmission chambers
- Diamond detectors
- Calorimeters

Exhibit high dependence as a function of DPP

Passive dosimeters

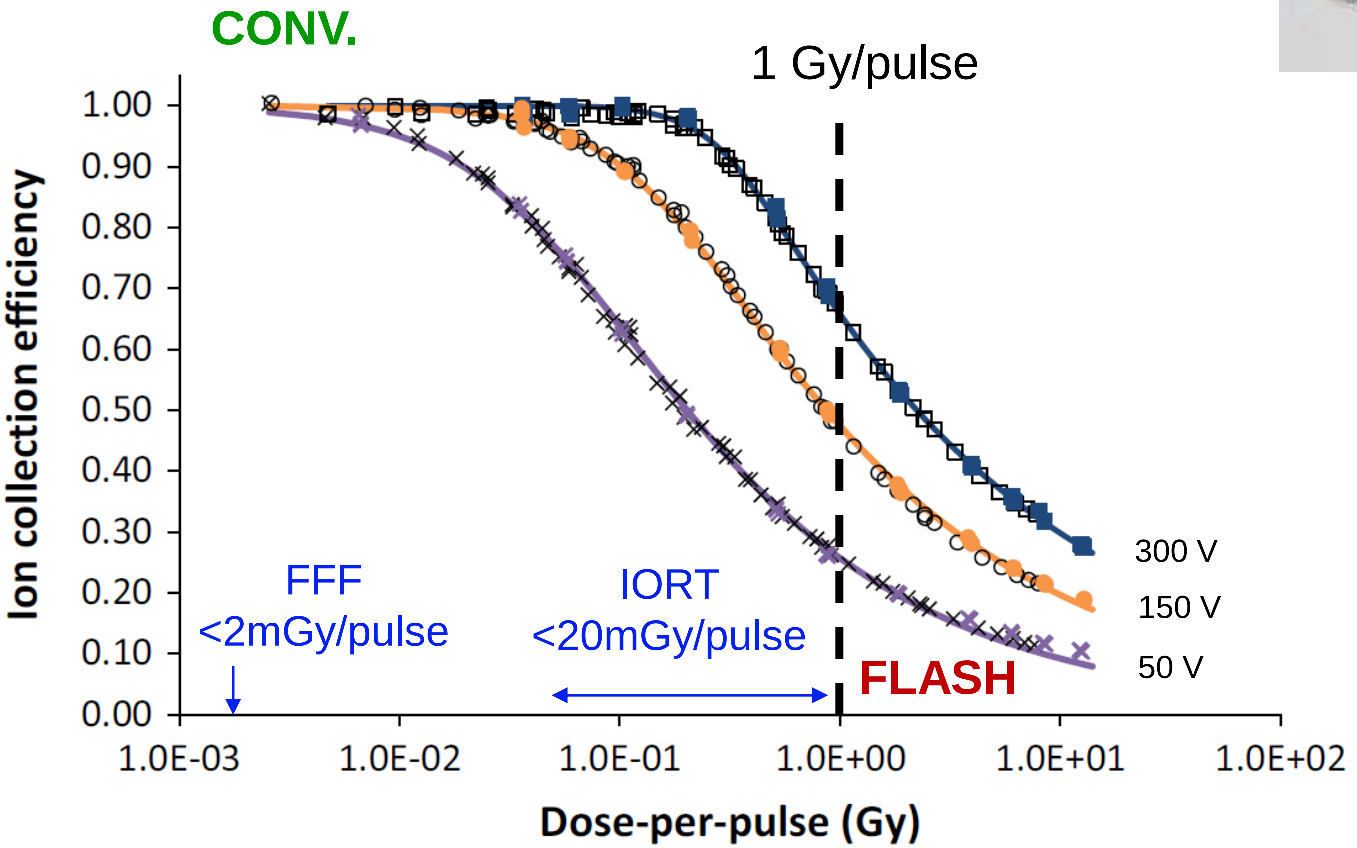
- Alanine
- Radiochromic films
- TLDs
- Methyl viologen

Considered dose rate independent up to 10^7 Gy/s



Challenges of dosimetry of UHPDR beams

Advanced Markus IC
6 MeV electron beam (Oriatron eRT6)



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

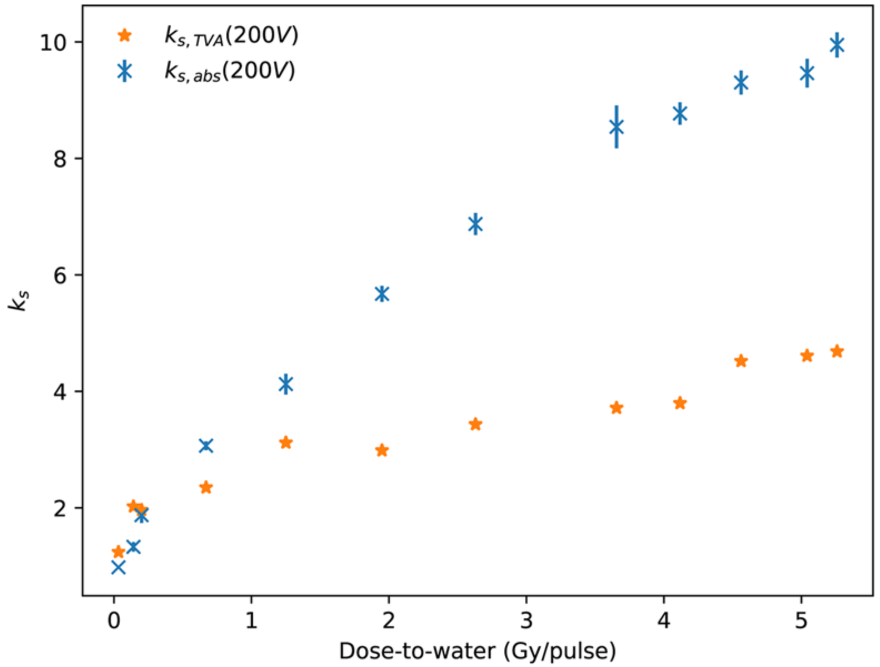
PTW Advanced Markus
(1 mm electrode separation)

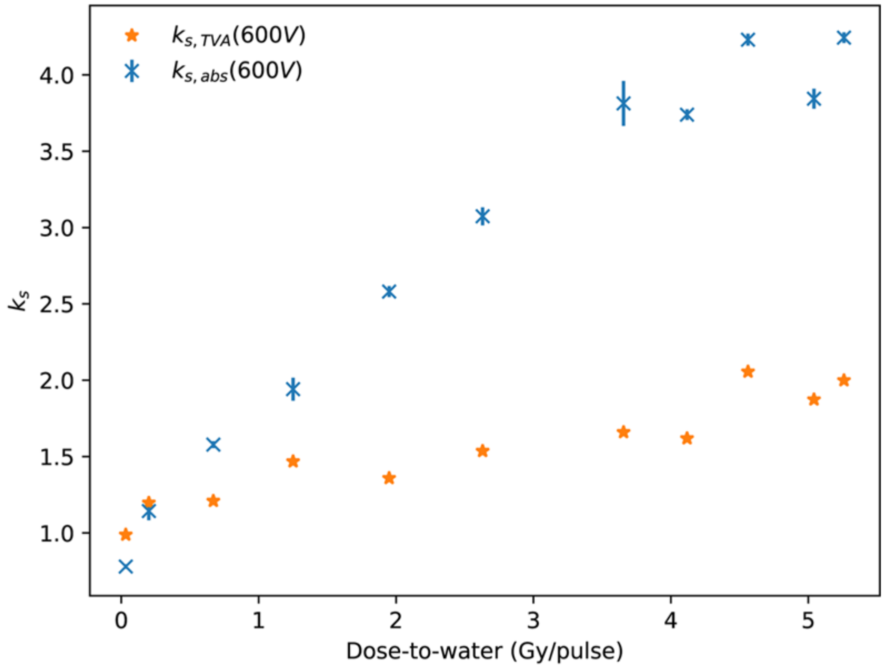
	CONV.		FLASH
Mean dose rate →	0.05 Gy/s	*vs*	40-1000 Gy/s
Dose per pulse →	0.3 mGy	*vs*	1-10 Gy
Dose in a pulse →	10^2 Gy/s	*vs*	10^6 Gy/s
Delivery time →	few min	*vs*	<1s

$$k_s = \left(1 + \left(\frac{DPP[mGy]}{U[V]}\right)^{\alpha}\right)^{\beta}$$

no physical meaning

Challenges of dosimetry of UHPDR beams



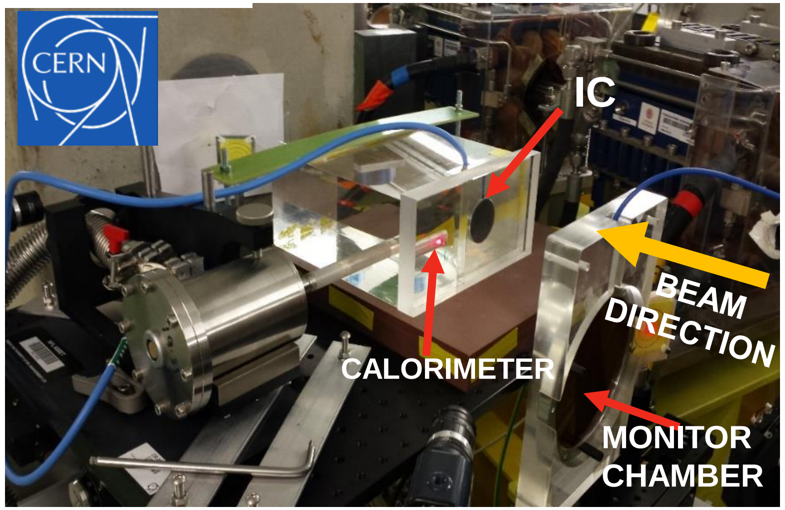


PTW Roos (2 mm electrode separation)

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

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

- 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 do not predict chamber behaviour for such a high DPP



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

Possible solution for UHDR beams

Prototype ionization chambers for ultra-high DPP

Ionization chamber prototype (0.27 mm)

Courtesy of Faustino Gomez

Possible solution for UHDR beams

NPL
National Physical Laboratory

ULTRA THIN PLANE-PARALLEL IONIZATION CHAMBERS: EXPANDING THE RANGE OF AIR IONIZATION CHAMBERS INTO ULTRA-HIGH DOSE RATE.

Type: Abstract Submission FRPT

Topic: A. Radiation modalities / AS02 Quality assurance and real time measurement of FLASH doses: ionisation chambers, film, solid state detectors, scintillators

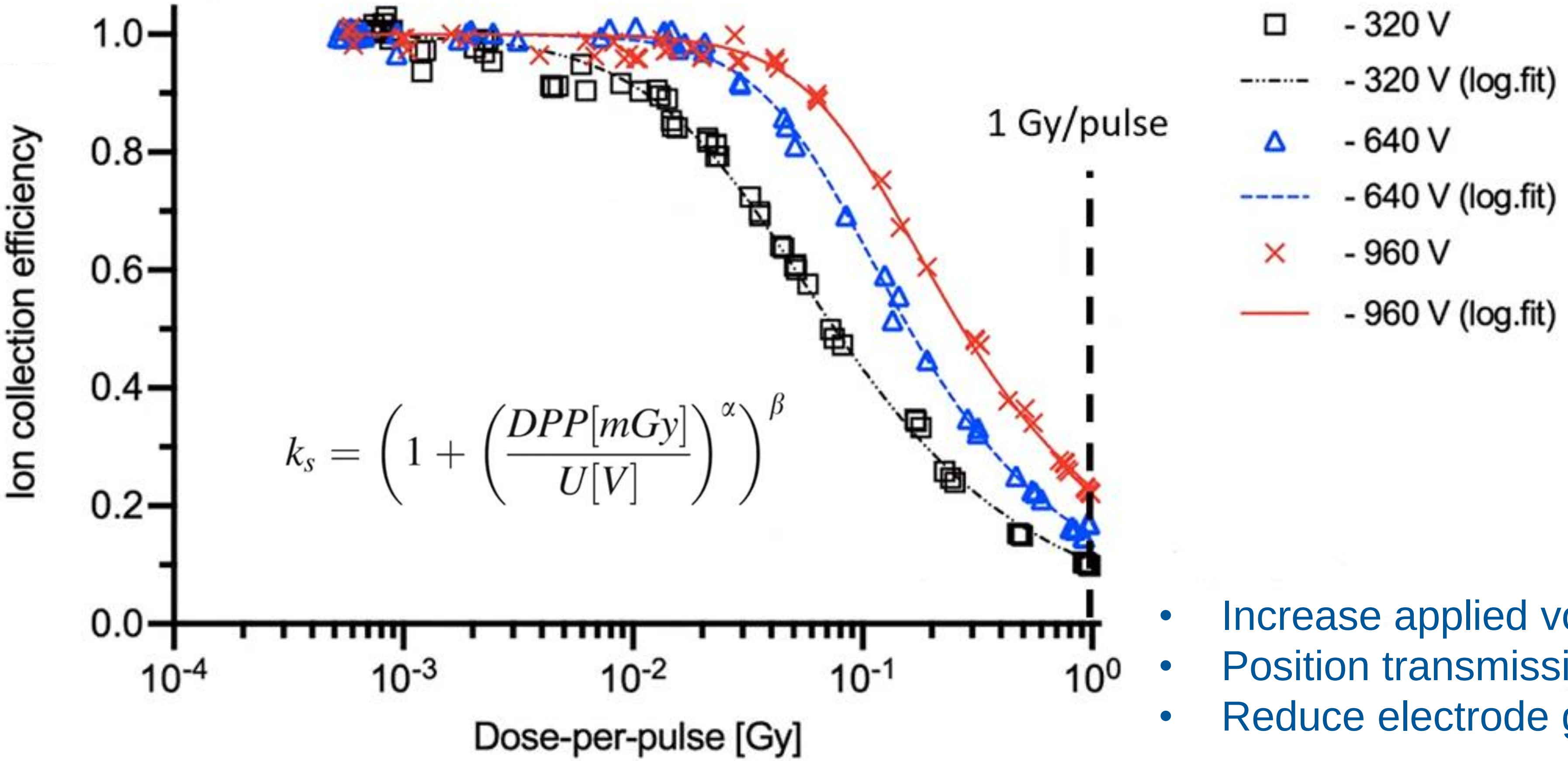
Authors: F. Gomez[1], J. Paz-Martin[1], D. Gonzalez-Castaño[1], N. Gomez-Fernandez[1], A. Gasparini[2], D. Velleren[2], V. Vanreusel[2], R. Kranzer[3], G. Felici[4], A. Schüller[3]; [1]Spain, [2]Belgium, [3]Germany, [4]Italy

VENTED IONIZATION CHAMBERS FOR ULTRA-HIGH DOSE PER PULS CONDITIONS

Rafael Kranzer[1,2], Andreas Schüller[3], Jan Weidner[1], Daniela Poppinga[1], Hui Khee Looe[2], Björn Poppe[2]

[1] PTW-Freiburg (R&D), Freiburg 79115, Germany,
[2] University Clinic for Medical Radiation Physics, Medical Campus Pius Hospital, Carl von Ossietzky University Oldenburg, 26121 Germany
[3] Physikalisch-Technische Bundesanstalt, Braunschweig 38116, Germany

Performance of transmission chambers in UHDR beams



10 MeV e-beam
dose rate ≈ 200 Gy/s
1 Gy/pulse @ 100 cm SSD

- Increase applied voltage further
- Position transmission chamber further downstream
- Reduce electrode gap separation

Konradsson et al., Rad. Res. (2020)

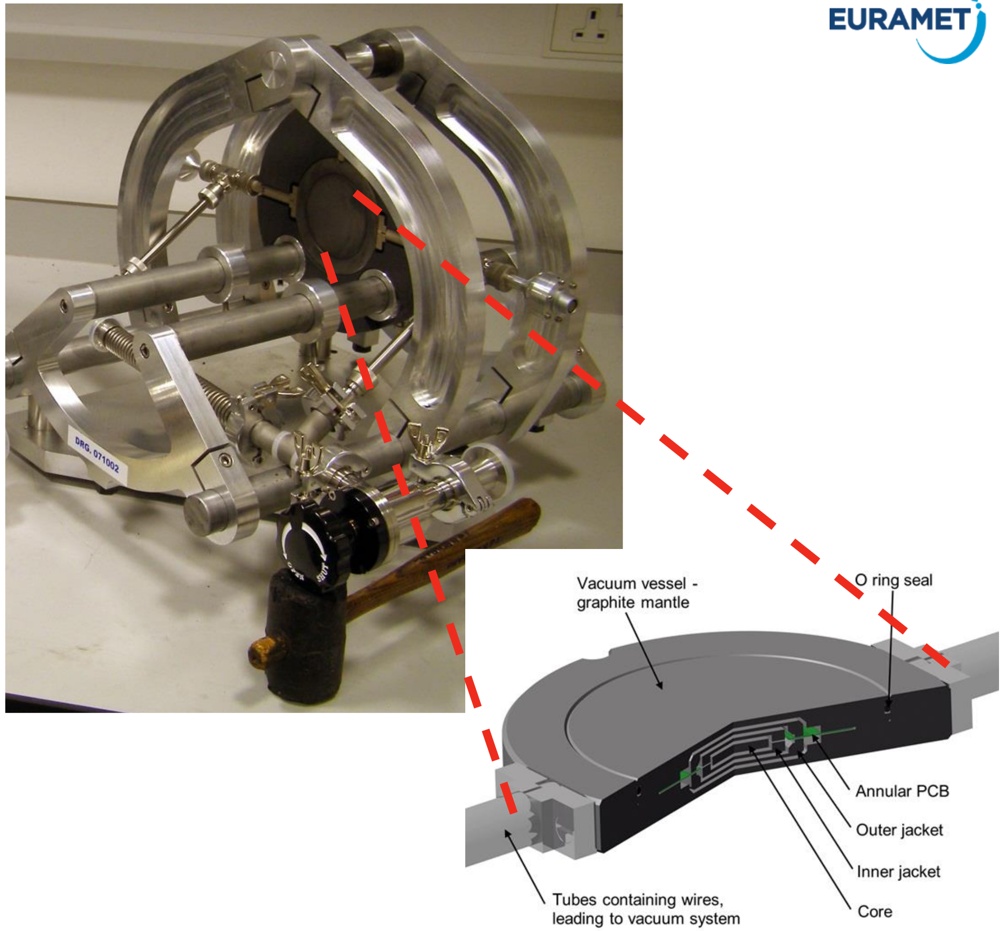
Calorimetry in UHDR beams

NPL National Physical Laboratory

EURAMET

NPL primary standard graphite calorimeter

- developed to facilitate calibration in proton beams primarily for scanned (but also for scattered beam) delivery modes
- Graphite core 2 mm thick and 16 mm diameter
- Surrounded by a graphite inner and outer jacket, and a graphite mantle, arranged in a nested construction
- New UK IPEM code of practice is being developed to deliver an uncertainty on reference dosimetry for protons of approx. 2% (k=2)
  → against 4.6% (k=2) for proton beams currently suggested by IAEA TRS-398 and based on an ionization chamber calibrated in a ^{60}Co beam → ***beam quality correction factor.***



NPL's primary standard graphite calorimeter.

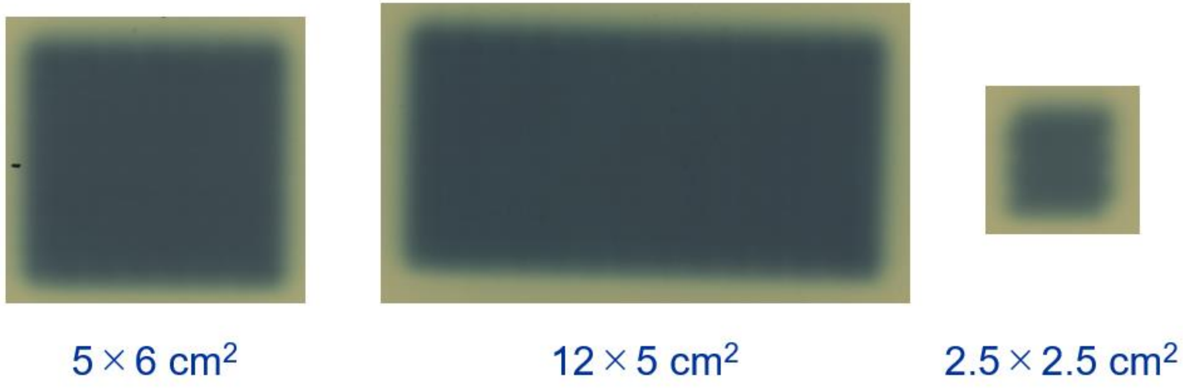
Calorimetry in UHDR proton beam

Calorimetry measurements with NPL primary standard proton calorimeter at Cincinnati Proton Centre with UHDR proton beam:

- 250 MeV (Varian ProBeam® operating in research mode)
- Dose rate ~65 Gy/s (“human” fields) & 0.8-140 Gy/s (“animal” field)
- Absorbed dose measurements performed at 5 cm depth WET for a number of radiation fields:
  - 5×6 cm^2
  - 5×8 cm^2
  - 5×10 cm^2
  - 5×12 cm^2
  - 6×5 cm^2
  - 12×5 cm^2

  $\Big\}$ “human” fields

  - 2.5×2.5 cm^2 “animal” field

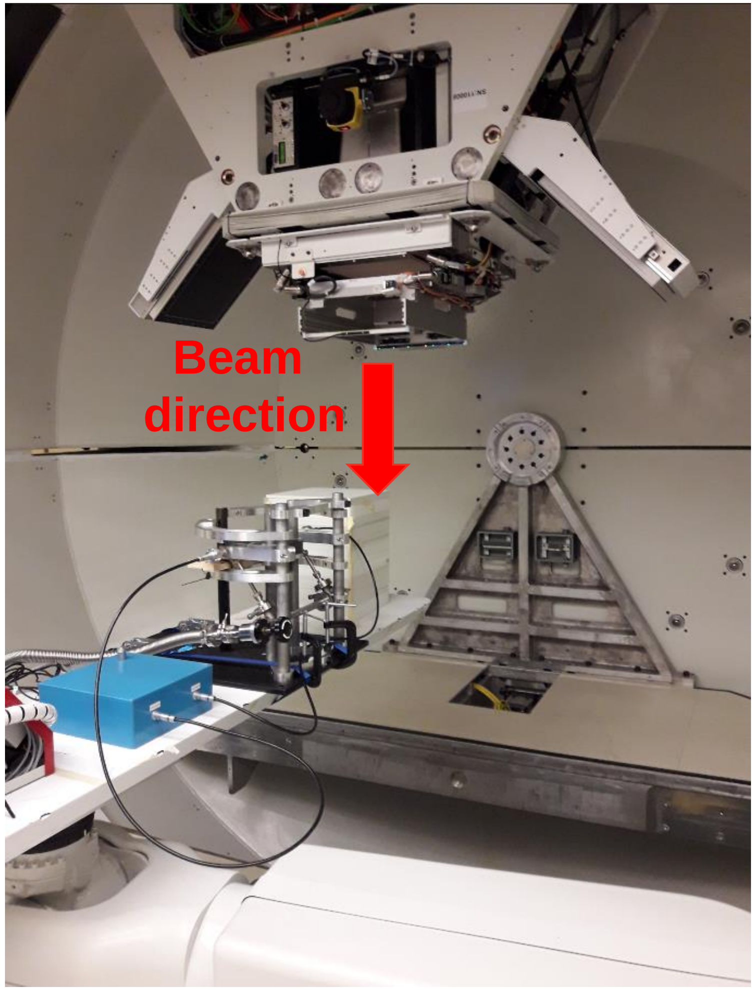


A sample of fields used (captured on the EBT3 films) .

UNPUBLISHED DATA – DO NOT COPY OR DISTRIBUTE

Calorimetry in UHDR proton beam

National Physical Laboratory



Experimental setup of graphite calorimeter in Cincinnati Proton Centre research gantry.

Provisional values of absorbed dose to water measured by the NPL proton calorimeter (MC correction factors are under evaluation).

UNPUBLISHED DATA – DO NOT COPY OR DISTRIBUTE

Measurement is ubiquitous, often unnoticed, but makes everything function

NPL National Physical Laboratory

National Metrology Institute (NMI)

NPL National Physical Laboratory

Metrology is the science of measurement. National Metrology Institute (NMI), provide the measurement capability giving confidence in measurement results and data traceable to SI units.

Important role of NMIs to support translation of FLASH RT to clinics

EMPIR project UHDpulse

Type: Joint Research Project
Duration: Sep/2019-Feb/2023
Start: 1. Sept. 2019
Funding: 2.1 M €
Coordinator: Andreas Schüller (PTB)
Topic: tools for traceable dose measurements for:

- **FLASH radiotherapy**
- VHEE radiotherapy
- laser driven medical accelerators

http://uhdpulse-empir.eu/

EMPIR EURAMET

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

The European Metrology Programme for Innovation and Research (EMPIR):

- metrology-focused programme of coordinated R&D
- enables European metrology institutes, industrial and medical organisations, and academia to collaborate

UHDpulse Partners and Collaborators

Metrology Institutes

- PTB – Physikalisch-Technische Bundesanstalt Braunschweig und Berlin
- Central Office of Measures
- NPL – National Physical Laboratory
- Czech Metrology Institute
- METAS
- NRC·CNRC Canada
- sck cen

Irradiation facility provider

- CHUV – Centre hospitalier universitaire vaudois
- Queen's University Belfast
- institut Curie
- HZDR – Helmholtz Zentrum Dresden Rossendorf
- eli beamlines
- Nuclear Physics Institute of the CAS, public research institution
- InspireProject
- fondazione CNAO
- MedAustron
- DESY.
- SIT
- iridium network

Radiation detector developer

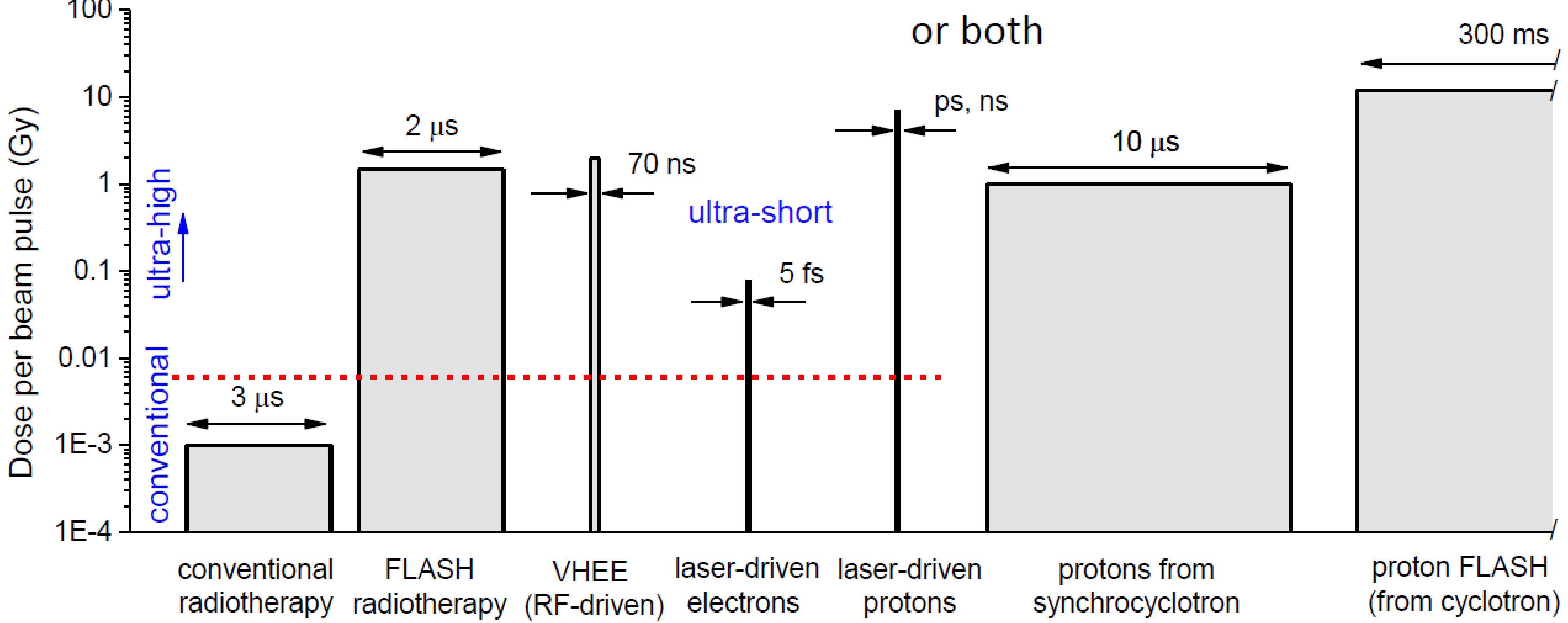
- ADVACAM – Imaging the Unseen
- USC – Universidade de Santiago de Compostela
- CSIC – CNM
- Politecnico Milano 1863
- PTW – The Dosimetry Company
- ECAP – Erlangen Centre for Astroparticle Physics
- Carl von Ossietzky Universität Oldenburg
- LPC Caen – laboratoire de physique corpusculaire
- Sun Nuclear corporation
- iba Dosimetry – Protect, Enhance and Save Lives
- varian
- DETECTOR – Devices and Technologies Torino
- Dartmouth Engineering
- Université Laval

7 Metrology institutes
5 Hospitals
7 Universities
6 Research institutes
7 Companies
+ Proton therapy network

“Metrology for advanced radiotherapy using particle beams with ultra-high pulse dose rates”

electrons, protons
(no photons)

ultra-high dose per pulse,
ultra-short pulse duration
or both



Objectives, WPs

The goal of the project is to provide the metrological tools needed to establish traceability in absorbed dose measurements of ultra-high pulse dose rate beams.

The specific aims of the project are:

- Development of primary and secondary absorbed dose standards and reference dosimetry methods
- Characterization of state-of-the-art detector systems
- Development of methods for relative dosimetry and for the characterization of of stray radiation
- Providing of input data for future Code of Practice

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

Objectives, WPs

UHDpulse

The UHDpulse consortium wrote an overview paper describing the goals of the project, providing details on the state-of-the-art of radiotherapy using particle beams with ultra-high pulse dose rates and introducing promising candidates as suitable FLASH dosimeters to be investigated.

(currently number 7 on the list of most downloaded articles of the last 90 days of this journal)

Figures (15)

ELSEVIER

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]

Show more

+ Add to Mendeley Share Cite

https://doi.org/10.1016/j.ejmp.2020.09.020

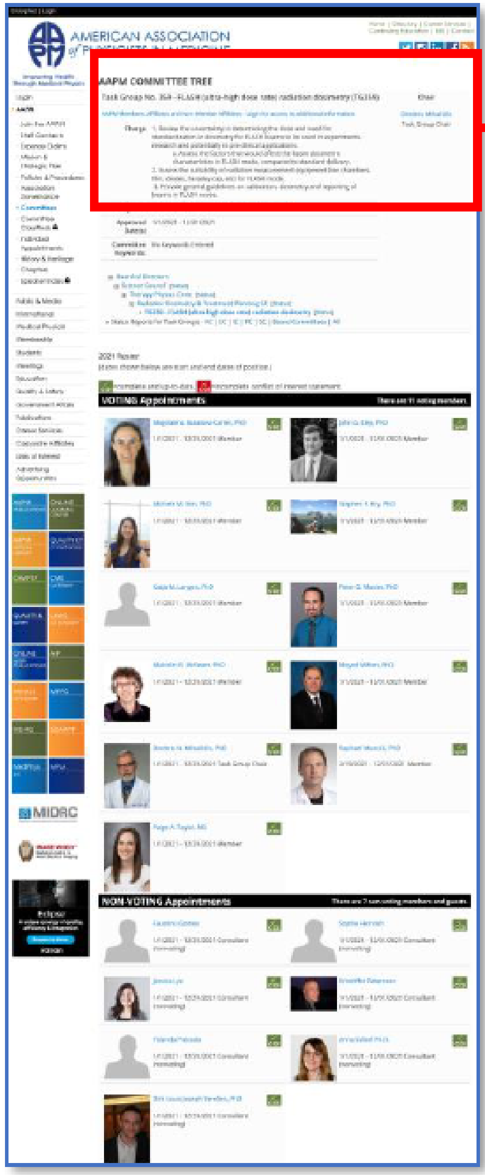
Get rights and content

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.

https://doi.org/10.1016/j.ejmp.2020.09.020

Connection to AAPM Task Group 359



TG359

- 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.
- Assess the suitability of radiation measurement equipment (ion chambers, film, diodes, Faraday cap, etc) for FLASH mode.
- Provide general guidelines on calibration, dosimetry and reporting of beams in FLASH mode.

UHDpulse

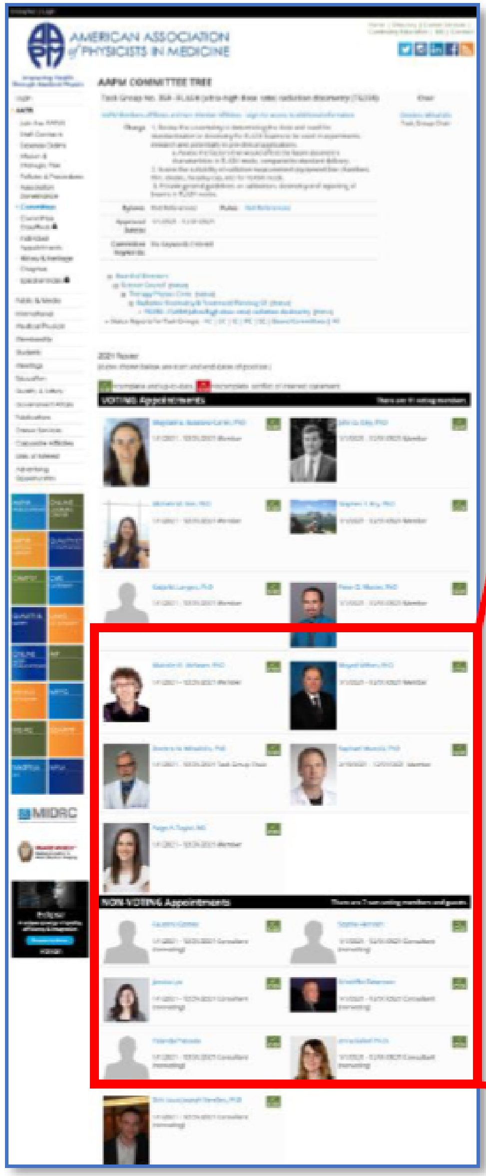
Objective 5:
to facilitate the uptake of the project's achievements by **standards developing organizations** and end users

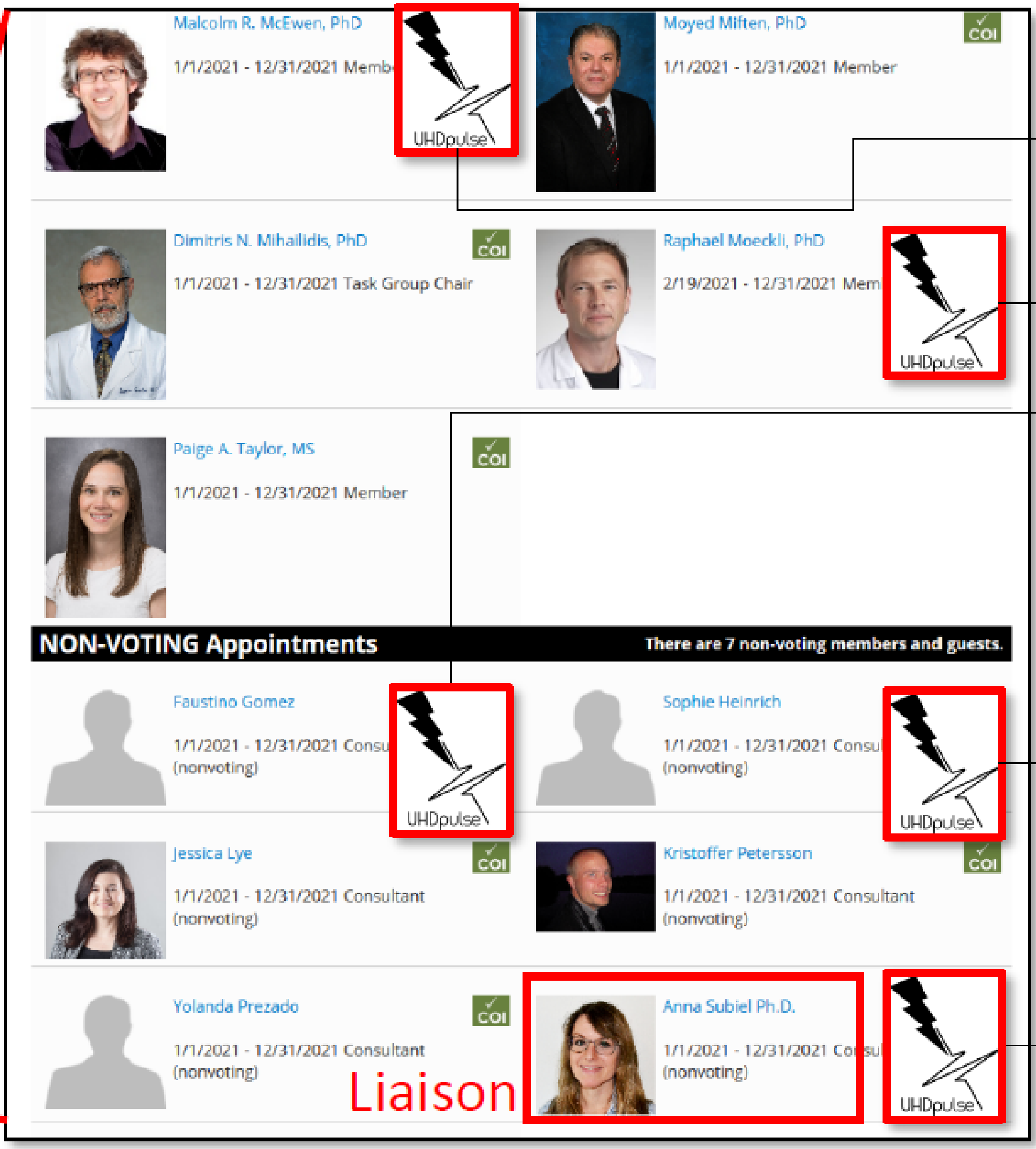
Objective 2:
to characterise the response of available **detector systems**

Objective 4:
provide the input data for **Codes of Practice**

https://www.aapm.org/org/structure/default.asp?committee_code=TG359

Connection to AAPM Task Group 359





https://www.aapm.org/org/structure/default.asp?committee_code=TG359

UHDpulse members:

NRC·CNRC Canada

CHUV Centre hospitalier universitaire vaudois

USC Universidade de Santiago de Compostela

institut Curie

NPL National Physical Laboratory

SIT

iridium network

PTW The Dosimetry Company

Conclusions

National Physical Laboratory

- FLASH RT requires several developments before safe implementation to clinics (including development of comprehensive QA procedures)
- There is no real-time dosimetry system for FLASH RT for electron beams
- Commercially available ionization chambers show large deviations at ultra-high dose per pulse (DPP) due to ion recombination.
- Prototypes of parallel plate ionization chambers with very small electrode gap separation are promising candidates for future secondary standard devices for UHDR beams
- Calorimetry-based detectors could become potential dosimetry devices in UHDR beams, but their operation need to be simplified to allow clinical implementation
- Initiatives such as EMPIR UHDpulse project and AAPM TG-359 will provide further dosimetry input and guidelines for FLASH RT community

National Physical Laboratory

Thank you

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

This project (18HLT04) has received funding from the EMPIR programme co-financed by the Participating States and from the European Union's Horizon 2020 research and innovation programme.

UHDpulse

Q&A: **Russell Thomas**

or email **anna.subiel@npl.co.uk**

http://uhdpulse-empir.eu/