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

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- **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”

- 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)
- Synchrotron source (X-rays)
- Clinical proton beams
Temporal beam structure

Electron LINACs

\[ D_{PP} = \frac{n_p \cdot DPP}{t_{total}} \]

\[ D = \frac{DPP}{t_{total}} = \frac{n_p \cdot DPP}{(N - 1) \cdot t_r + t_p} \]

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
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.soirt.com/

https://www.varian.com/

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

https://intraop.com/

https://www.mevion.com/

https://www.pmbalcen.com

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

- 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

**Passive dosimeters**
- Alanine
- Radiochromic films
- TLDs
- Methyl viologen

Exhibit high dependence as a function of DPP

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)

PTW Advanced Markus
(1 mm electrode separation)

CONV.
FLASH

Mean dose rate $\rightarrow$ 0.05 Gy/s vs 40-1000 Gy/s
Dose per pulse $\rightarrow$ 0.3 mGy vs 1-10 Gy
Dose in a pulse $\rightarrow$ $10^2$ Gy/s vs $10^6$ Gy/s
Delivery time $\rightarrow$ few min vs <1s

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

no physical meaning
Challenges of dosimetry of UHPDR beams

- $k_s$ 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

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

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

Possible solution for UHDR beams

Prototype ionization chambers for ultra-high DPP

Ionization chamber prototype (0.27 mm)

Courtesy of Faustino Gomez

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Possible solution for UHDR beams

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. Gomez¹, J. Paz-Martin¹, D. Gonzalez-Castaño¹, N. Gomez-Fernandez¹, A. Gasparini², D. Velleren², V. Vanreusel², R. Kranzer³, G. Felici⁴, A. Schüller³. ¹Spain, ²Belgium, ³Germany, ⁴Italy

VENTED IONIZATION CHAMBERS FOR ULTRA-HIGH DOSE PER PULS CONDITIONS

Rafael Kranzer¹,², Andreas Schüller³, Jan Weidner¹, Daniela Poppinga¹, Hui Khee Looe², Björn Poppe²

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³ Physikalisch-Technische Bundesanstalt, Braunschweig 38116, Germany
Performance of transmission chambers in UHDR beams

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

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

Konradsson et al., Rad. Res. (2020)
Calorimetry in UHDR beams

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 cm²
  - 5×8 cm²
  - 5×10 cm²
  - 5×12 cm²
  - 6×5 cm²
  - 12×5 cm²
  - 2.5×2.5 cm²

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

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Calorimetry in UHDR proton beam

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

Experimental setup of graphite calorimeter in Cincinnati Proton Centre research gantry.
Measurement is ubiquitous, often unnoticed, but makes everything function
National Metrology Institute (NMI)

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

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

http://uhdpulse-empir.eu/
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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

Graph showing dose per beam pulse for different methods:
- Conventional radiotherapy
- FLASH radiotherapy (RF-driven)
- VHEE
- Laser-driven electrons
- Laser-driven protons
- Protons from synchrocyclotron
- Proton FLASH (from cyclotron)

Dose per beam pulse values:
- Conventional radiotherapy: 3 μs, 10 μs
- FLASH radiotherapy: 2 μs
- VHEE: 70 ns
- Laser-driven electrons: 5 fs
- Laser-driven protons: 10 μs
- Protons from synchrocyclotron: 300 ms
- Proton FLASH (from cyclotron)
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

WP3: Detectors for primary beam
- Novel and custom-built active dosimetric systems
- Beam monitoring systems

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

WP5: Impact, WP6: Coordination
Objectives, WPs

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)
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
Conclusions

- 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.
Thank you

Q&A: Russell Thomas
or email anna.subiel@npl.co.uk

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http://uhdpulse-empir.eu/