



Development of Improved Dosimetry Standards for FLASH Radiotherapy: The UHDpulse Project

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Outline

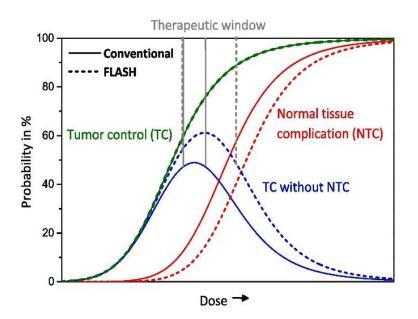
- Flash Radiotherapy
- Metrological Challenges in Flash-RT
- The UHDpulse Project
 - Objectives
 - Work Packages
 - Recent Highlights
 - Impact
- Conclusions



Flash Radiotherapy

FLASH radiotherapy (FLASH-RT) is a modern and promising cancer treatment modality still in its early stages of development and application.

- dose is delivered in few radiation pulses of ultra-high dose rate
- has been proven to significantly reduce adverse side effects to healthy tissues while being as effective for tumor control as conventional radiotherapy
- sparing effectiveness of FLASH-RT is observed using photons, protons, and electron beams
- very high energy electron (VHEE) are require for deep seeded tumor treatment (> 50 MeV)].



Laser-driven accelerators are seen as a compact and cost-effective accelerators for radiotherapy

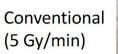
• ultra-short radiation pulses of extremely high dose rate (up to $10^9 - 10^{12}$ Gy/s).



Flash-RT

FLASH irradiation of the skin of a pig

34 Gy



36 weeks post-RT

31 Gy 28 Gy

FLASH (300 Gy/s) 3 Gy/pulse



normal appearance of skin

Vozenin et al., *Clin Cancer Res* **25** (2019) 35 http://dx.doi.org/10.1158/1078-0432.CCR-17-3375

<u>FLASH treatment of a human patient</u> (lymphoma on skin)

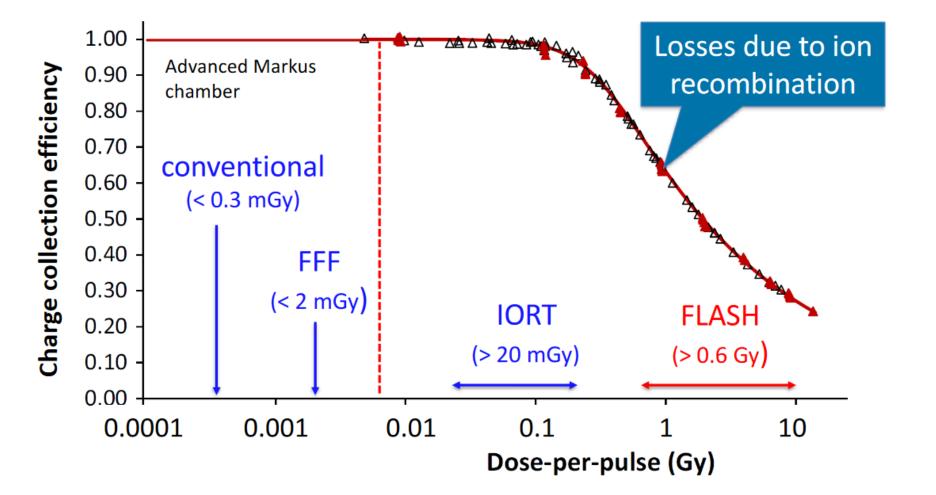




- Total dose 15 Gy
- 10 pulses (1us)
- Treatment time: 90 ms
 - Dose /pulse: 1.5 Gy

Bourhis et al., *Radiother. Oncol.* (2019) http://dx.doi.org/10.1016/j.radonc.2019.06.019

Metrological Challenges in Flash-RT



beamlines

Petersson *et al.*, Med Phys 44 (2017) 1157 https://doi.org/10.1002/mp.12111



UHDPulse

"Metrology for advanced radiotherapy using particle beams with ultra-high pulse dose rates" (UHDpulse)

- Joint Research Project in the framework of the European Metrology Program for Innovation and Research (EMPIR), supported by the European Association of National Metrology Institutes (EURAMET).
- Duration: Sep/2019-Feb/2023
- Coordinator: Andreas Schüller (PTB, Germany)
- Topic: dosimetry for
 - FLASH radiotherapy
 - VHEE radiotherapy
 - laser driven beams

Website: <u>http://uhdpulse-empir.eu</u>



Original paper

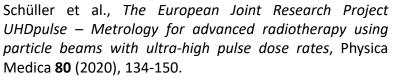
The European Joint Research Project UHDpulse – Metrology for advanced radiotherapy using particle beams with ultra-high pulse dose rates

Andreas Schüller^{1,5}, Sophie Heinrich¹, Charles Foullade¹, Anna Subiel¹, Ludovic De Marzi^{1,64}, Francesco Romano^{1,64}, Peter Peter¹, Maria Trachel¹, Celente Pleta¹, Rafael Kranzer^{1,64}, Marco Caresana, Samuel Salvador¹, Simon Buold¹, Andreas Schönfeld⁻¹, Malcolm McEwen¹, Paustino Gomez¹, Jaroidav Sole², Claude Bailat¹, Vladimi Linhar¹, Jan Jakubek¹, Jög Pavelke^{1,64}, Marco Borghesir, SialF-peter Kapseh¹, Adrian Rovizak¹, Alerta Boso¹, Veronika Olsovcova¹⁰, Christian Kottler¹, Daniela Poppinga¹, Iva Ambrozova¹, Claus-Stefan Schmitzer¹, Severine Rossonme¹, Marine-Catherine Voeznin¹⁶

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						* National Physical Laboratory (NPL), Teddington,	
						* Institut Curie, Centre de Recherche, Inserm U 102	
						* Physikalisch-Technische Bundesanstalt (PTE), Bre	

	URDpulse – Matrology for advanced radiotherapy using particle beams with ultra-bigh pulse does rates is a recently tratef European Joint Research Troject with the aim to develop and improve dosinstry: tradeable for FLASR radiotherapy, very high energy electron (VHEE) radiotherapy and laser-driven medical accelerators. This research roles a door overwise about the current state of developments of radiotherapy with FLASR electrons and
es trology project	protons, very high energy electrons as well as laser-driven particles and the volated challenges in dominary due to the ultra-high done rase during the short radiation pulses. We summarize the objectives and plans of the UHDpulse project and present the 16 participating partners.





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

UHDpulse



Objectives

- **1. Develop a metrological framework** which comprises SI traceable primary standards, secondary reference standards, and validated reference methods for dosimetry measurements for particle beams with ultra-high pulse dose rates.
- 2. Characterize the response of available detector systems when used in ultra-high dose per pulse or with ultra-short pulse duration particle beams.
- **3.** Develop traceable and validated methods for relative dosimetry, as well as for the characterization of stray radiation outside the primary pulsed beams.
- **4. Provide input data for future Codes of Practice** for absolute dose measurements in particle beams with ultra-high pulse dose rates.



Work Packages

NPL O

WP1: Primary standards

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

OMETAS

WP2: Secondary standards, relative dosimetry

- Transfer from primary standards
- Characterizing established detector systems
- Formalism for reference dosimetry CZECH 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





Consortium

Metrology Institutes





- 7 Metrology institutes6 Hospitals
- 9 Universities
- 7 Research institutes
- 12 Companies
- 1 Proton therapy network

Irradiation facilit	ies / providers
Centre hospitalier universitaire vaudois	QUEEN'S UNIVERSITY BELFAST
institut Curie	HZDR HELMHOLTZ ZENTRUM DRESDEN ROSSENDORF
eti Deamlines	Nuclear Physics Institute of the CAS
InspireProject	fondazione CNAO
MedAustron	DESY.
SIT	iridium
PAUL SCHERRER INSTITUT	IntraOp [•]
	CPFR

Irradiation facilitian / providers





Collaborators





Impact

http://uhdpulse-empir.eu/?page_id=734

- 25 Peer-reviewed publications
- 62 Oral presentations
- 15 Poster
- 6 Other publications



Ultra-high Dose Rate Laser-Driven Protons: Methodology and State-of-the-Art

Pankaj Chaudhary¹*, Giuliana Milluzzo², Hamad Ahmed^{2,3}, Boris Odlozilik Aaron McMurray², Kevin M. Prise¹* and Marco Borghesi²*

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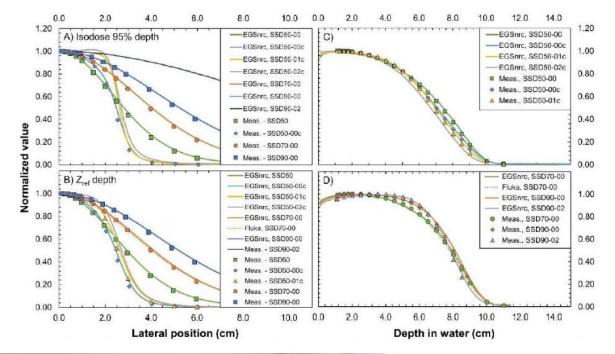
ility [6] while depositing maximal dose within humours [4, 7]. Due to this highe

UHDPulse --- ICRS14



Recent Highlights

Ultra-high Pulse Dose rate reference field at PTB



E = 0.5 - 50 MeV $t_{\text{pulse}} = 0.1 - 3 \text{ us}$

up to **7 Gy per pulse** (SSD 0.7 m, 20 MeV) up to 15 Gy per pulse (SSD 0.5 m, 20 MeV) in preparation



A. Bourgouin et al. *Characterization of the PTB ultra-high pulse dose rate reference electron beam*, Physics in Medicine & Biology, accepted 8 April 2022. https://doi.org/10.1088/1361-6560/ac5de8



Recent Highlights

Development of an ultra-thin parallel plate ionization chamber



4.5 Charge per pulse (nC) 4.0 **PTB** Calibration 3.5 Simulation **Experimental Data** 3.0 2.5 2.0 1.5 1.0 0.5 └ 1.0 2.5 1.5 2.0 3.0 5.0 3.5 4.0 4.5 5.5 Dose per pulse (Gy) Residuals (%) . -0.0 0 0 -0.2 0 -0.4 -0.6 0 -0.8 PTB Calibration -1.0 Simulation -1.2 -1.4 2.5 1.0 1.5 2.0 3.5 4.5 5.0 5.5 3.0 4.0 Dose per pulse (Gy) Medical Physics, Volume: 49, Issue: 7, Pages: 4705-4714, First published: 13 April 2022, DOI: (10.1002/mp.15668)

F. Gómez et al. *Development of an ultra-thin parallel plate ionization chamber for dosimetry in FLASH radiotherapy*, Medical Physics, 13 April 2022. <u>https://doi.org/10.1002/mp.15668</u>



Recent Highlights

Diamond detector for ultra-high dose per pulse (DPP)



Linearity of the prototype detector signal as function of the reference dose per pulse 1.0 1 nC/Gy 2 nC/Gy 3 nC/Gv 0.8 Detector signal per pulse [nC] BBAAAAAAAAAAA 0.6 B1 0.4 \$7051 #7047 #7041 #7052 0.1 nC/G 0.2 000-000-000-000 0.0 0.0 0.2 0.8 1.0 1.2 1.6 1.4 1.8 0.40.6 Dose per pulse reference D_{w,pulse} [Gy]

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

Verona Rinati *et al. Application of a novel diamond detector for commissioning of FLASH radiotherapy electron beams.* Med Phys. 2022; **49**: 5513- 5522. <u>https://doi.org/10.1002/mp.15782</u>

Kranzer et al., Response of diamond detectors in ultra-high dose-per-pulse electron beams for dosimetry at FLASH radiotherapy, 2022 Phys. Med. Biol. **67** 075002. <u>https://doi.org/10.1088/1361-6560/ac594e</u>



Conclusions

- UHDpulse is a European Joint Research Project aimed at developing and improving dosimetry standards for FLASH-RT, VHEE radiotherapy and laser-driven medical accelerators.
- The project was briefly presented in order to raise awareness of its objectives, structure, and results.



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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http://uhdpulse-empir.eu/





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Thank you for your attention!

