Physikalisch-Technische Bundesanstalt
Braunschweig and Berlin
National Metrology Institute

Overview of the EMPIR project UHDpulse - "Metrology for advanced radiotherapy using particle beams with ultra-high pulse dose rates"

Andreas Schüller

Department 6.2 "Dosimetry for Radiation Therapy and Diagnostic Radiology"

on behalf of the UHDpulse consortium

AAPM-TG359 Meeting, 28.4.21, virtual

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Overview of the EMPIR project UHDpulse - “Metrology for advanced radiotherapy using particle beams with ultra-high pulse dose rates”

UHDpulse

Contents

- EMPIR program, Partners & Collaborators
- Ultra-high dose per pulse, metrological challenges
- Objectives, Work Package structure
- Current progress in FLASH dosimetry

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/

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

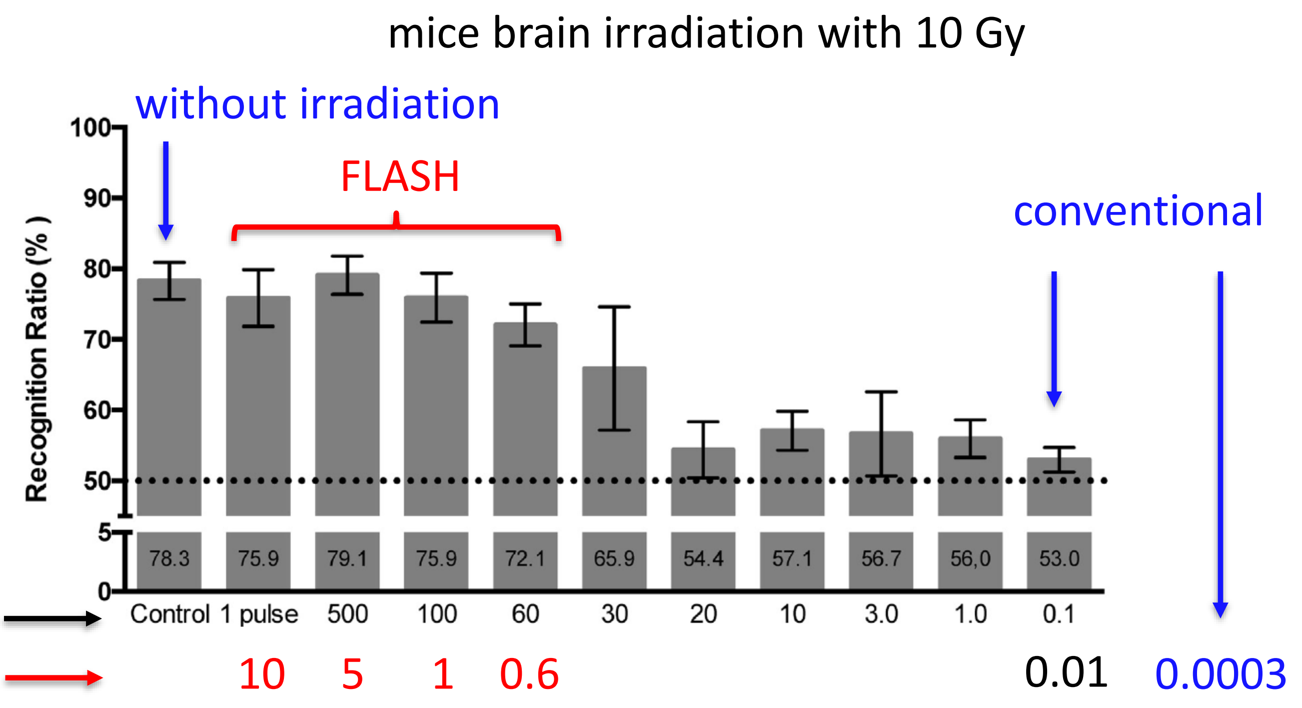
Metrology Institutes

Irradiation facility provider

Radiation detector developer

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

Ultra-high dose per pulse at FLASH radiotherapy



Montay-Gruel *et al.*, Radiotherapy and Oncology 124 (2017) 365

http://dx.doi.org/10.1016/j.radonc.2017.05.003

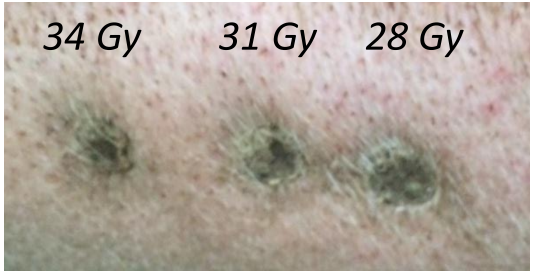
Ultra-high dose per pulse at FLASH radiotherapy

Centre hospitalier universitaire vaudois

Conventional and FLASH Irradiation (with same total dose)

36 weeks post-RT

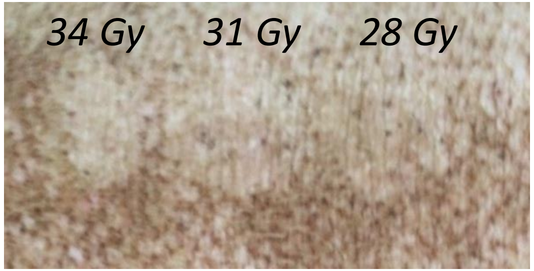
Conventional
(5 Gy/min)



necrotic lesions

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

UHDpulse

Ultra-high dose per pulse at FLASH radiotherapy

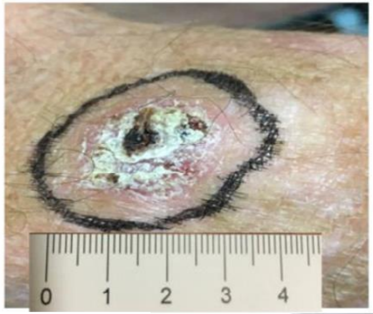
Centre hospitalier universitaire vaudois

human Patient:

lymphoma on skin

FLASH-RT:

10 pulses (of 1 μs duration) in 90 ms
with **1.5 Gy/pulse**



Day 0

3 weeks

(max. of skin reactions)

5 months

Bourhis et al., Radiother. Oncol. (2019)

DOI: 10.1016/j.radonc.2019.06.019

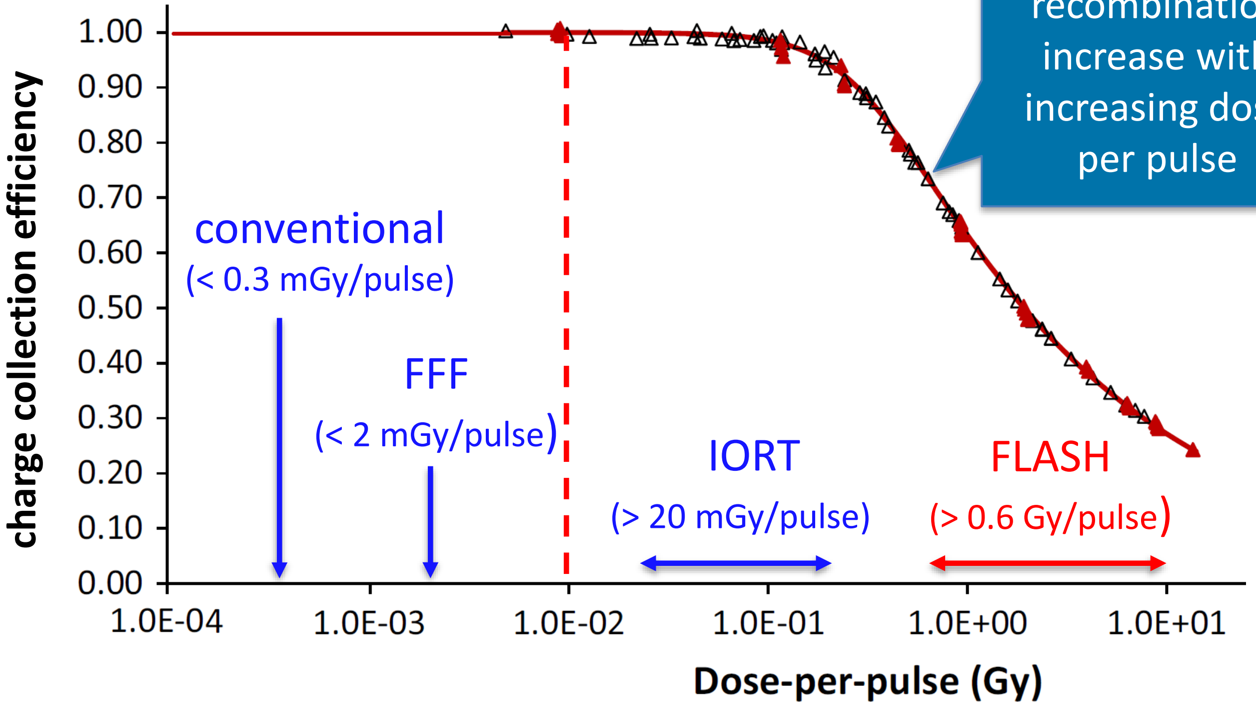
Metrological challenge ultra-high dose per pulse

Due to ultra-high dose rates and pulsed structure of the beams, tools and methods established in dosimetry for conventional radiotherapy are not suitable for FLASH radiotherapy.

There are

- **no** active dosimeters for real-time measurements
- **no** formalism (Codes of Practice) for reference dosimetry
- **no** corresponding primary standards

Typical performance of ionization chambers
(here Advanced Markus chamber)



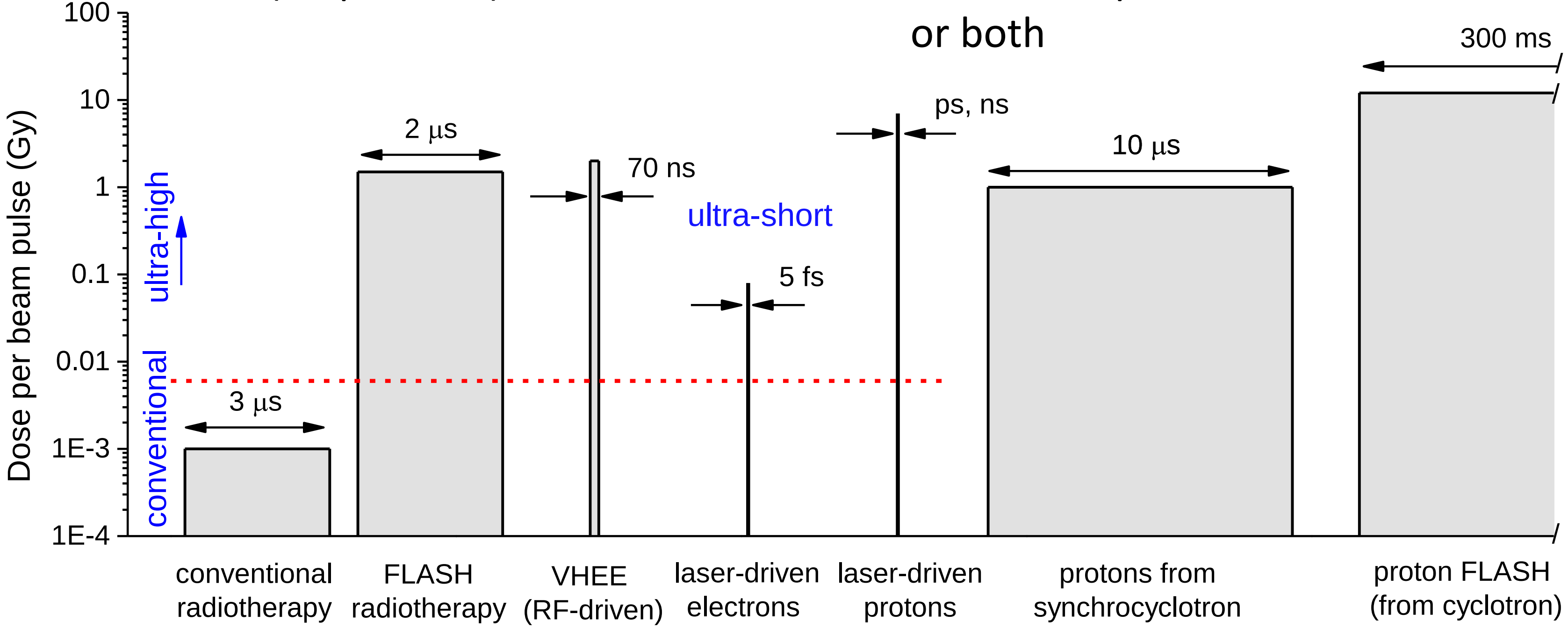
Losses due to ion recombination increase with increasing dose per pulse

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

"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

UHDpulse

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

NPL National Physical Laboratory

WP1: Primary standards

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

METAS

WP2: Secondary standards, relative dosimetry

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

CMI CZECH METROLOGY INSTITUTE

WP5: Impact, WP6: Coordination

PTB Physikalisch-Technische Bundesanstalt Braunschweig und Berlin

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

ADVACAM Imaging the Unseen

CHUV

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)

Outline

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]

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

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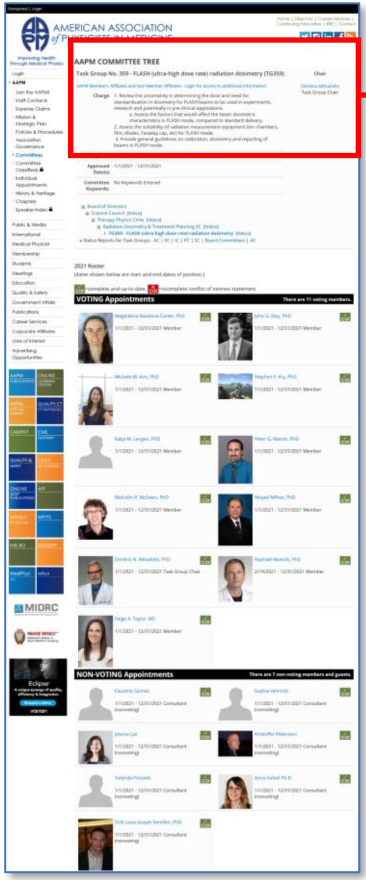
Highlights

- 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.

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

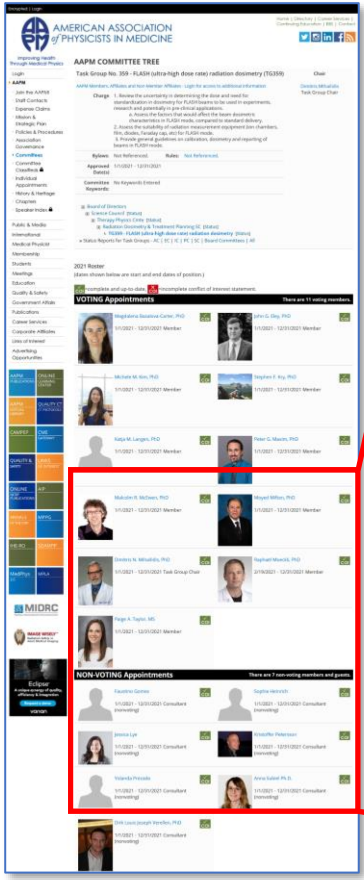
Objective 2:
to characterise the response of available **detector systems**

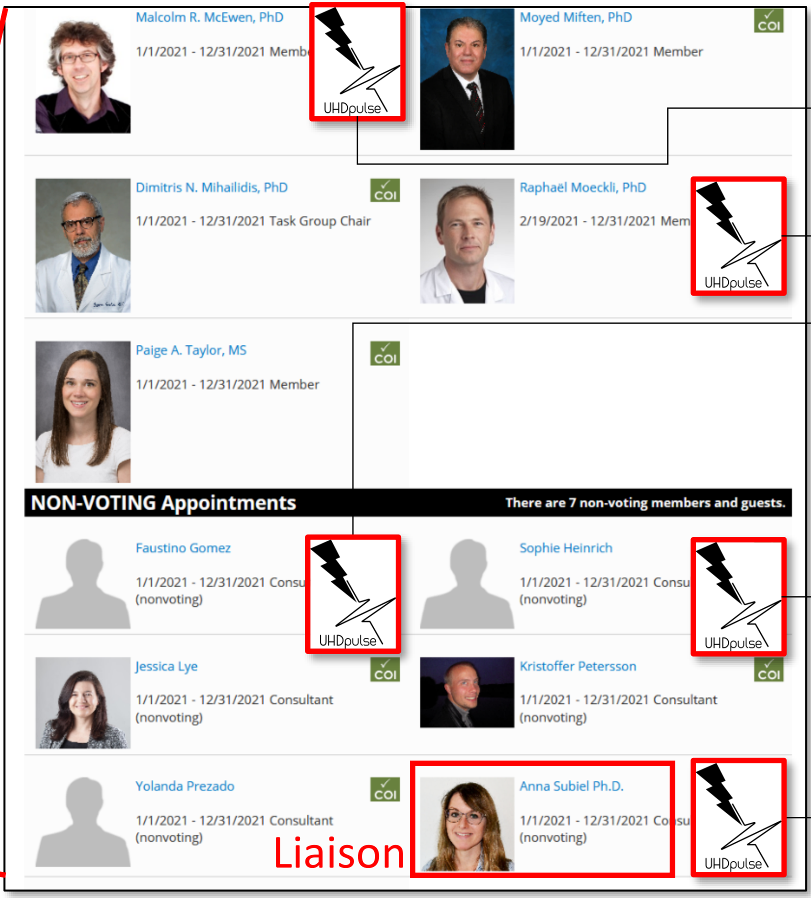
Objective 4:
provide the input data for **Codes of Practice**

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

Connection to AAPM Task Group 359

UHDpulse





Malcolm R. McEwen, PhD
1/1/2021 - 12/31/2021 Memb

Moyed Miften, PhD
1/1/2021 - 12/31/2021 Member

Dimitris N. Mihailidis, PhD
1/1/2021 - 12/31/2021 Task Group Chair

Raphaël Moeckli, PhD
2/19/2021 - 12/31/2021 Mem

Paige A. Taylor, MS
1/1/2021 - 12/31/2021 Member

NON-VOTING Appointments — There are 7 non-voting members and guests.

Faustino Gomez
1/1/2021 - 12/31/2021 Consu
(nonvoting)

Sophie Heinrich
1/1/2021 - 12/31/2021 Consu
(nonvoting)

Jessica Lye
1/1/2021 - 12/31/2021 Consultant
(nonvoting)

Kristoffer Petersson
1/1/2021 - 12/31/2021 Consultant
(nonvoting)

Yolanda Prezado
1/1/2021 - 12/31/2021 Consultant
(nonvoting)

Anna Subiel Ph.D.
1/1/2021 - 12/31/2021 Co su
(nonvoting)

Liaison

UHDpulse members:

NRC·CNRC Canada

CHUV Centre hospitalier universitaire vaudois

USC Universidade de Santiago de Compostela

institut Curie

NPL National Physical Laboratory

SIT

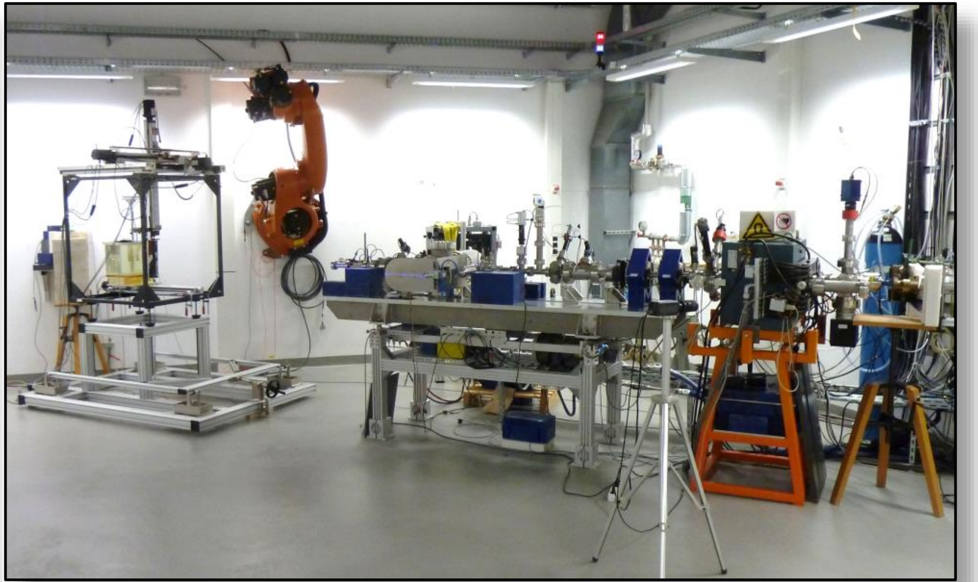
netwerk iridium Topzorg in radiotherapie

PTW The Dosimetry Company

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

PTB's electron reference field for FLASH dosimetry

PTB's Research electron accelerator

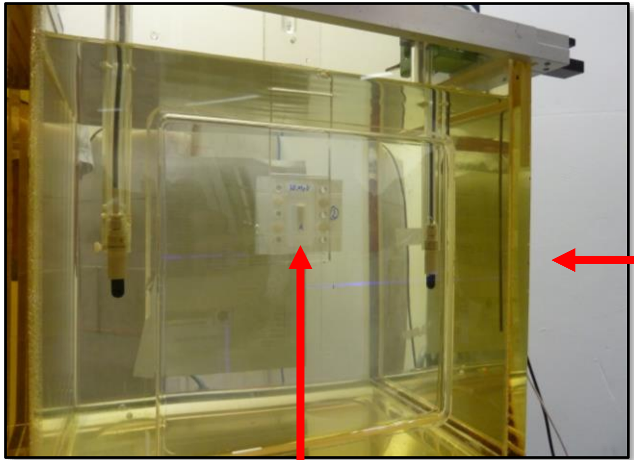


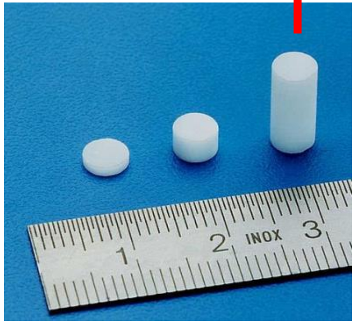
Beam line with water phantom

E = 0.5 – 50 MeV

up to 7 Gy/pulse (SSD 0.7 m, 20 MeV)

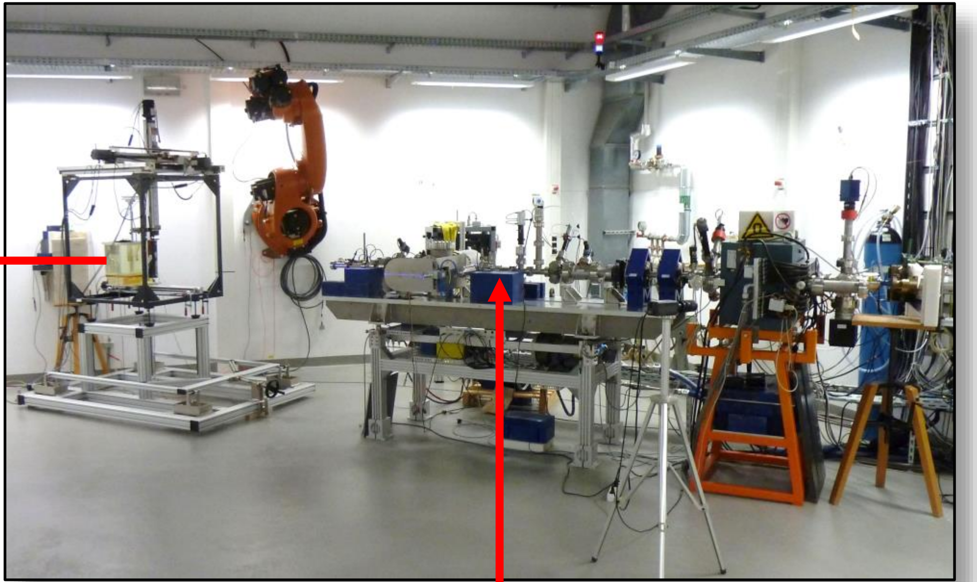
PTB's electron reference field for FLASH dosimetry





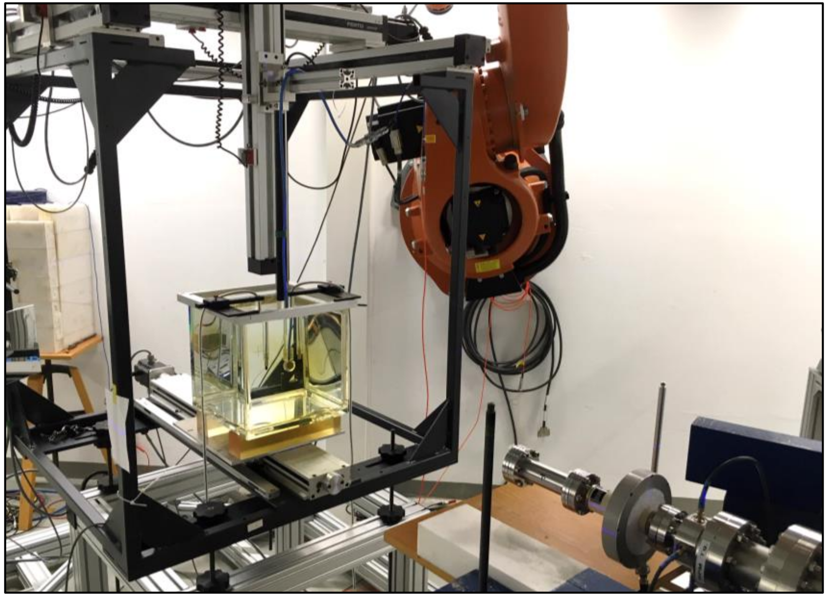
Alanine pellets at reference depth in water phantom

Dose traceable to primary standard

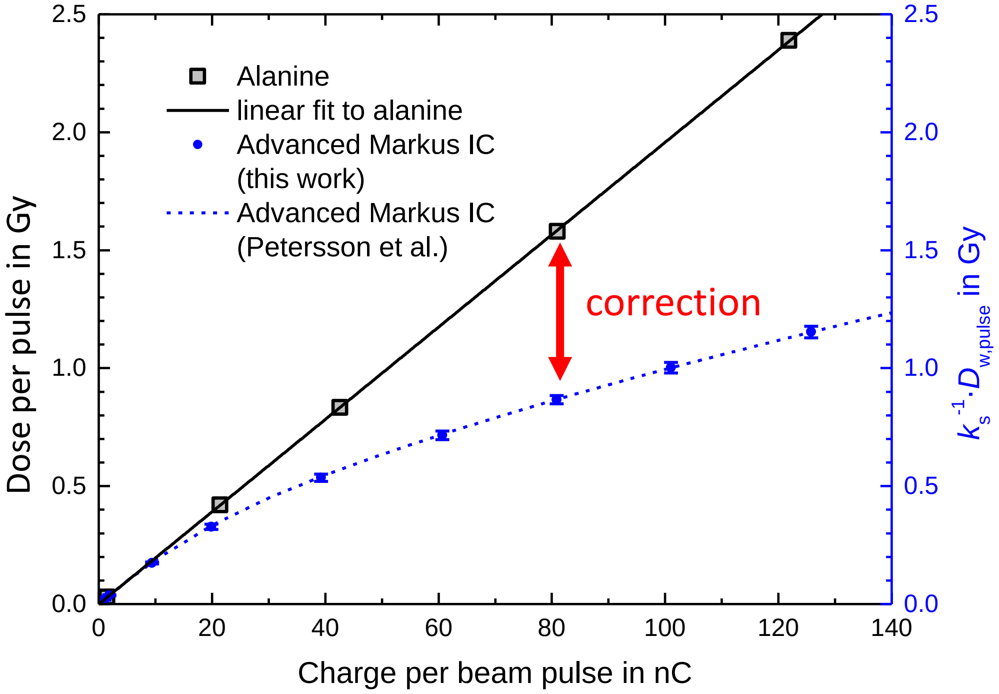


Non-destructive absolute beam pulse charge measurement (uncertainty < 0.1 % @70 nC/pulse)

PTB's electron reference field for FLASH dosimetry

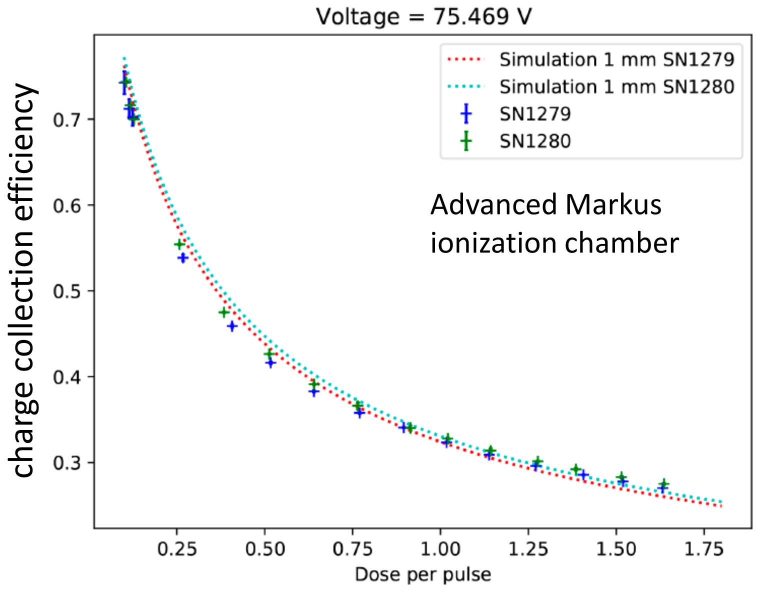


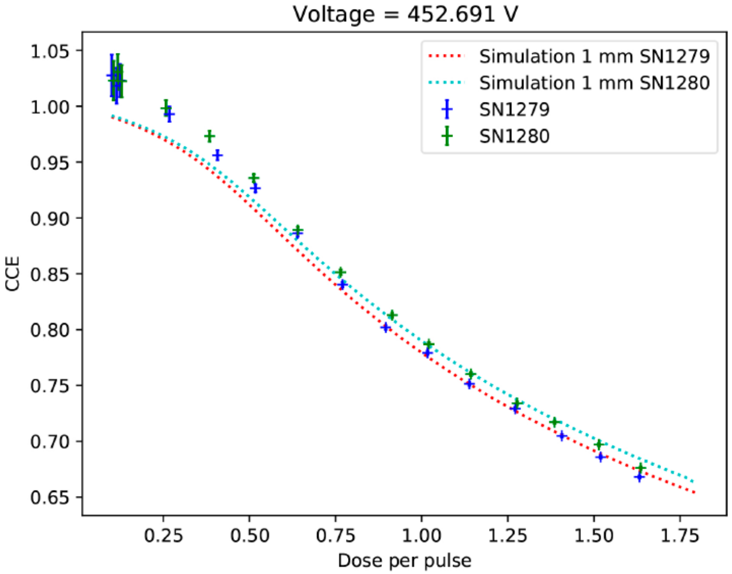
Detector under test at reference depth in water phantom



A Bourgouin et al., Calorimeter for Real-Time Dosimetry of Pulsed Ultra-High Dose Rate Electron Beams
https://doi.org/10.3389/fphy.2020.567340

FLASH dosimetry with ion chambers



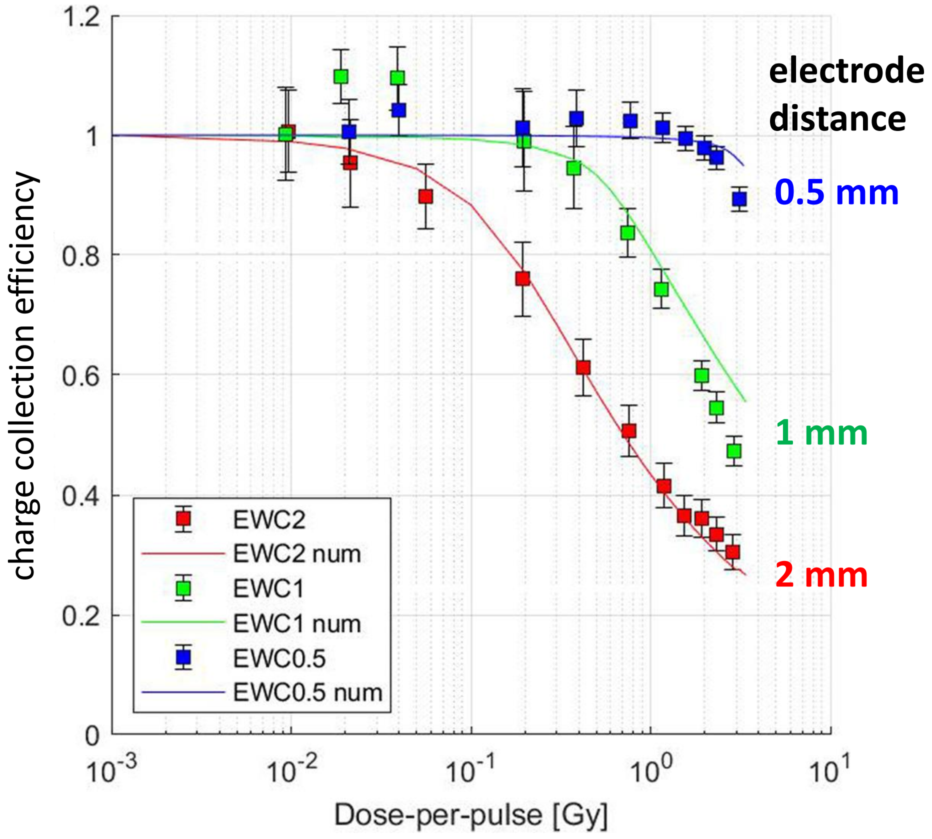


Within the framework of UHDpulse theoretical models for the calculation of the charge collection efficiency of plane parallel ionization chambers at ultra-high dose per pulse are developed, with the aim of to provide an ion recombination correction function.

F. Gomez et al., The Challenge of Dosimetry in Flash Radiotherapy
https://indico.ific.uv.es/event/5983/contributions/13896/

FLASH dosimetry with ion chambers

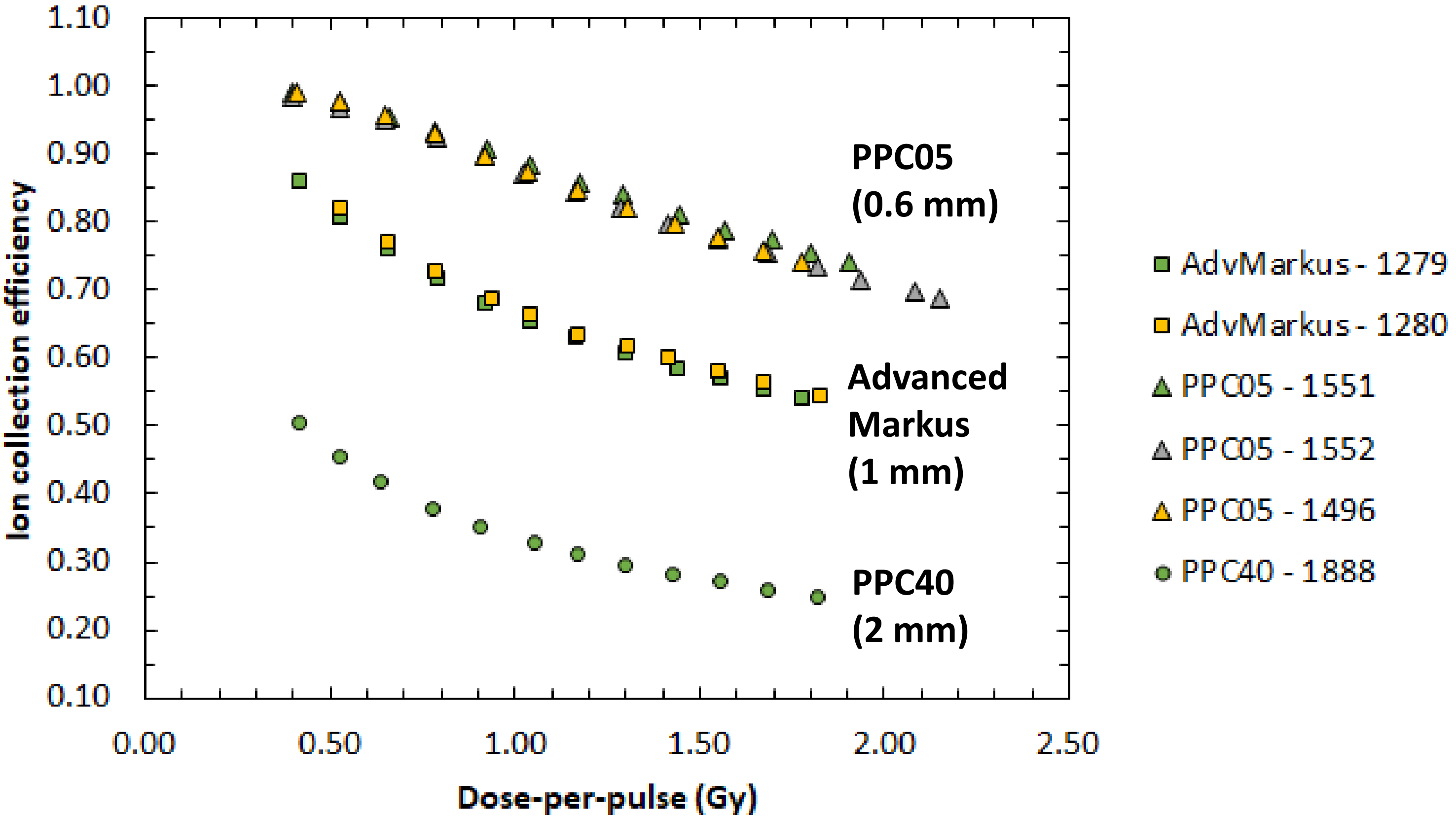
Within the framework of UHDpulse the performance of plane parallel ionization chamber prototypes with different electrode distance at ultra-high dose per pulse are investigated. Reduction of the electrode distance helps to increase the charge collection efficiency.



Rafael Kranzer et al., Medical Physics 2021, https://doi.org/10.1002/mp.14620

FLASH dosimetry with ion chambers

Within UHDpulse the response of different types of commercially available ionization chambers as well as their intra-type variations will be characterized

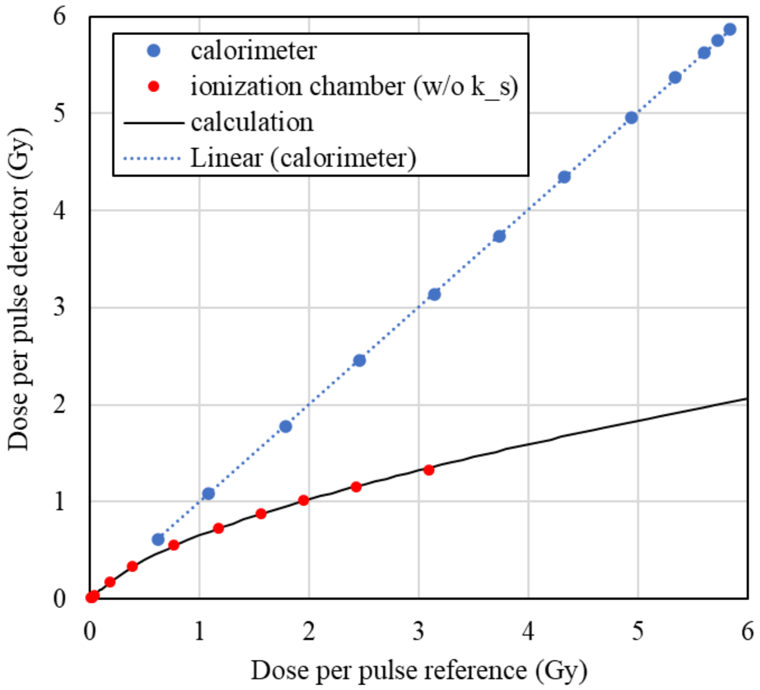


Alexandra Bourgouin et al., still unpublished

FLASH dosimetry with a calorimeter

Within UHDpulse the performance of the Graphite Probe Calorimeter prototype "Aerrow" is investigated. The detector shows linear response in the FLASH range.

Aerrow (and Exradin A12 ionization chamber for size reference). The internal structure of Aerrow is shown as a blended rendering.

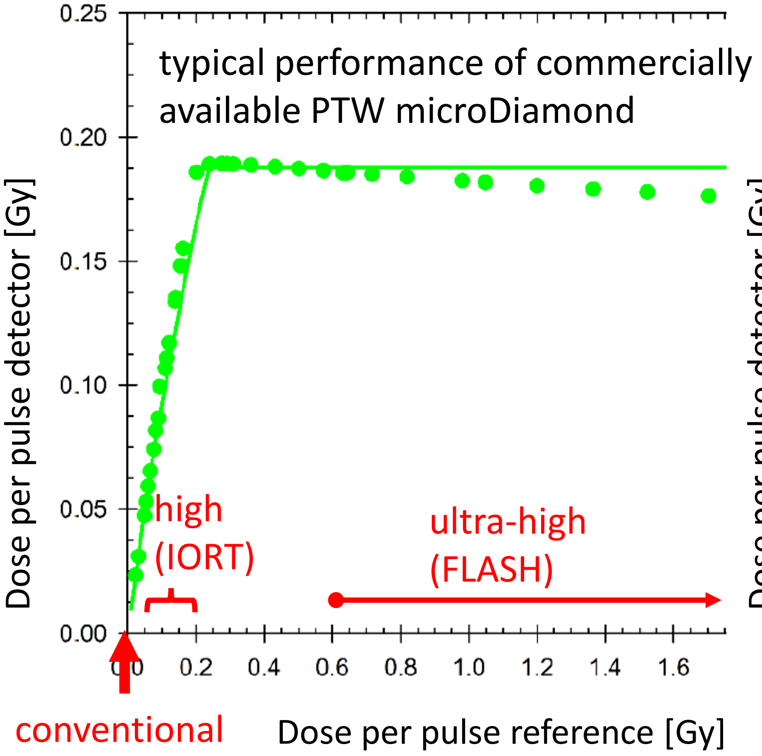


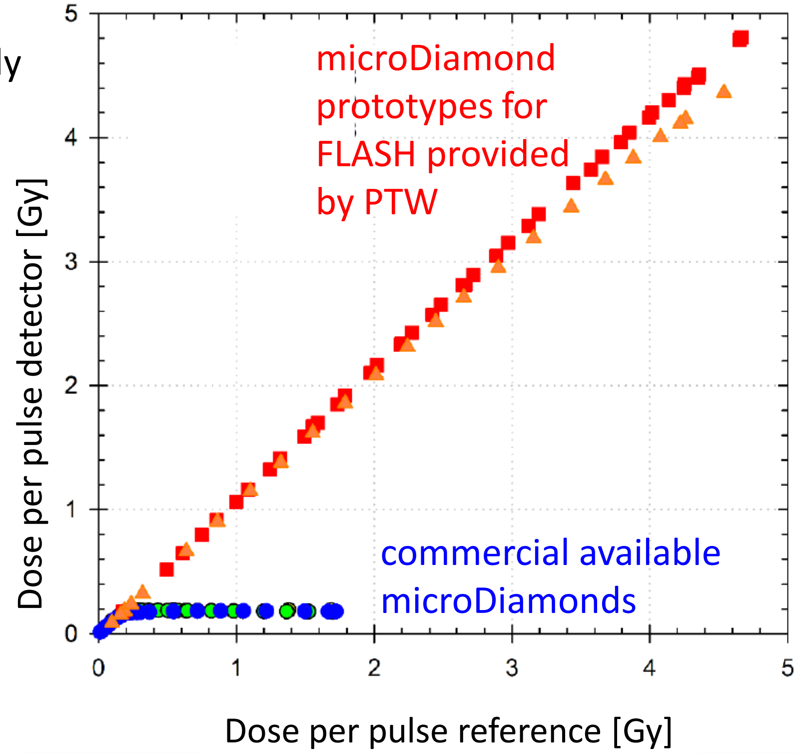
Detector response vs. dose reference from alanine/monitor.

Alexandra Bourgouin et al., still unpublished

FLASH dosimetry with diamond detectors

Within UHDpulse the performance of microDiamond detectors are investigated at ultra-high dose per pulse. Adapted prototypes show linear response in the FLASH range.

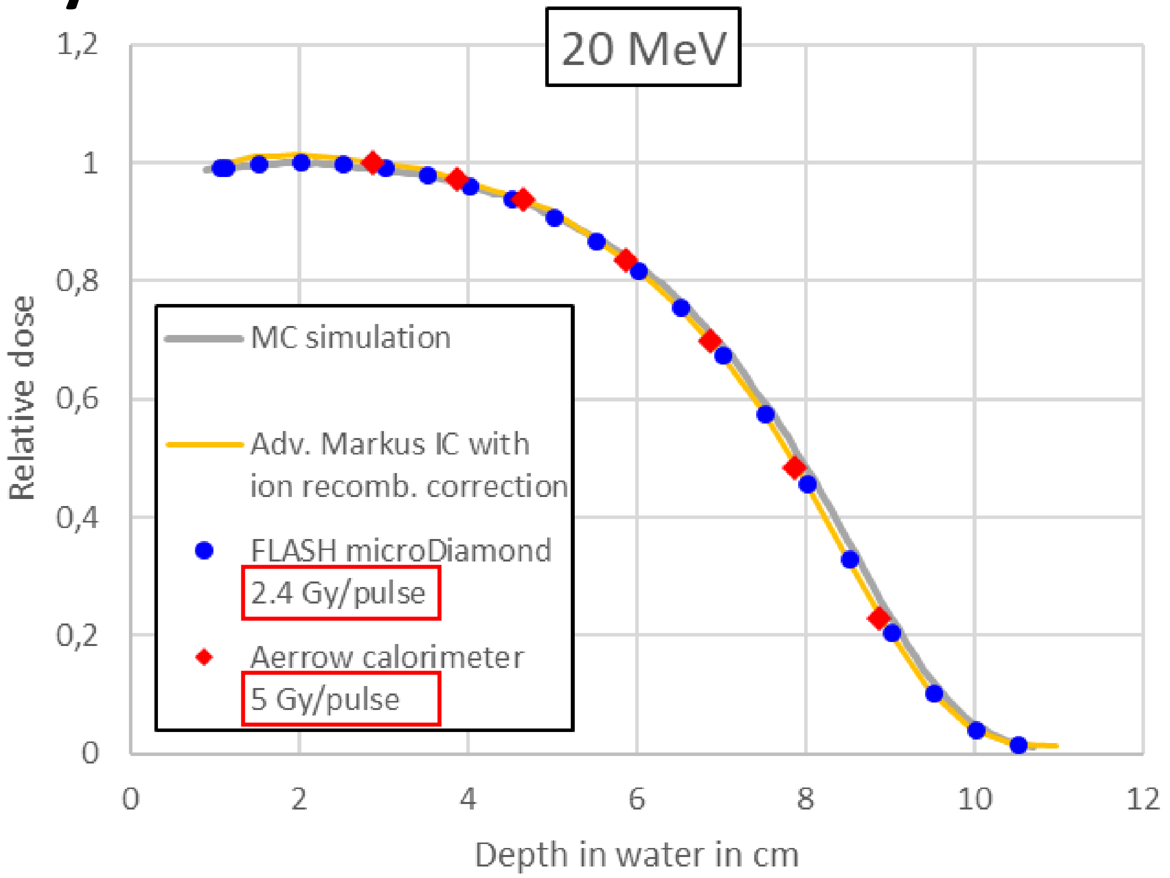




Rafael Kranzer et al., still unpublished

FLASH dosimetry

Conclusion: there are several promising candidates as active detectors for real-time dose measurements for FLASH RT.



Alexandra Bourgouin et al., still unpublished

UHDpulse Activities potentially relevant for TG359

A1.1.1	Review of beam parameters in FLASH radiotherapy (data collection by Sophie Heinrich)
A1.2.2	Primary standard Fricke dosimetry for FLASH electron RT (METAS)
A1.2.4	Water calorimeter as primary standard for FLASH electron RT (PTB)
A1.2.7	Graphite calorimetry of FLASH electron beams (GUM, PTB)
A1.3.3	Graphite calorimetry of FLASH proton beams (NPL)
A2.1.3	Radiochromic dosimetry films (uncertainty budget)
A2.1.5	Ionization chambers as secondary dosimetry standards (incl. novel ultra-thin PP-ICs)
A2.1.6	Solid-state detectors as secondary standard (diamonds, diodes, Si-microsensor, scintillator)
A2.1.7	Recommendation report about detectors as secondary standard and for relative dosimetry
A2.3.1	Reference conditions for FLASH electron beams (draft under preparation based on TRS398)
A2.3.3	Establish a formalism for reference dosimetry in FLASH-RT (extending existing CoP)
A2.3.4	Validation of formalism for reference dosimetry in FLASH (Comparison)
A3.1.1	Monitoring of FLASH beam (aim: repeatability of dose delivery < 0.5 %)
A3.2.3	Custom-built detectors for FLASH proton beams (Si-microsensor, Timepix3, MLFC)

Conference

UHDpulse co-organizes the conference "FLASH Radiotherapy & Particle Therapy" (FRPT2021).

The conference will include the 3rd FLASH Workshop, the workshops of UHDpulse and INSPIRE (integrating activity for European research in proton therapy).

There will be FRPT2021 special issues in "Radiotherapy & Oncology" and in "Physica Medica".

https://frpt-conference.org/

“A wealth of future studies are waiting to be done at all levels of physical, chemical, molecular, biological, and clinical endeavors.”

Jolyon Hendry, Taking Care with FLASH Radiation Therapy
https://doi.org/10.1016/j.ijrobp.2020.01.029

UHDpulse

However, if there is an error in dosimetry, then the difference in tissue response between conventional and ultrahigh-dose rate irradiation at seemingly equal total dose may be due to this error and not due to the FLASH effect.

http://uhdpulse-empir.eu/

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.