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”

International Conference on Medical Accelerators and Particle Therapy
4-6.9.19, CNA, Seville
EMPIR project UHDpulse
“Metrology for advanced radiotherapy using particle beams with ultra-high pulse dose rates”

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EMPIR project UHDpulse

EMPIR Call: 2018 / Health
Type: Joint Research Project
Duration: 2019-2022
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 on a wide variety of joint research projects

FLASH radiotherapy

FLASH effect

thorax irradiation of mice (17 Gy)

- reduction of the normal tissue complications
- maintains tumour control level

Pulmonary fibrosis in %

1.8 Gy/min

60 Gy/s

Weeks after irradiation

Favaudon et al., Sci Transl Med 6 (2014) 245ra93
DOI: 10.1126/scitranslmed.3008973

(Durante et al., Br J Radiol 91 (2018) 20170628)
DOI: 10.1259/bjr.20170628
FLASH radiotherapy

FLASH effect

- ultra-high dose rate →
  - reduction of the normal tissue complications
  - maintains tumour control level

Graph showing the therapeutic window with conventional and FLASH radiotherapy. The graph illustrates the tumor control (TC), normal tissue complication (NTC), and the therapeutic window.
FLASH radiotherapy

Cat cancer patient trial

nasal carcinoma not eligible for surgery

before FLASH

7 month after FLASH

Vozenin et al., Clin Cancer Res 25 (2019) 35
DOI: 10.1158/1078-0432.CCR-17-3375
FLASH radiotherapy

Reduced pig skin toxicity with FLASH-RT

Conventional (5 Gy/min)

FLASH (300 Gy/s)

36 weeks post-RT

Irradiation with 22 - 34 Gy

Vozenin et al., Clin Cancer Res 25 (2019) 35
DOI: 10.1158/1078-0432.CCR-17-3375
FLASH radiotherapy

Treatment of a first human patient with FLASH-RT

Patient:
lymphoma on skin

History:
110 different conventional irradiations in 10 years
(20 Gy in 6 - 10 fractions)
high grade acute skin reactions
takes >3 months to heal

FLASH-RT:
10 pulses (of 1 us duration) in 90 ms
with 1.5 Gy/pulse

Day 0
3 weeks
(max. of skin reactions)

5 months

DOI: 10.1016/j.radonc.2019.06.019
### metrological challenges

<table>
<thead>
<tr>
<th></th>
<th><strong>FLASH</strong></th>
<th><strong>conventional</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>dose per pulse</td>
<td>1 – 10 Gy</td>
<td>0.3 mGy</td>
</tr>
<tr>
<td>pulse width</td>
<td>1 -2 us</td>
<td>3 us</td>
</tr>
<tr>
<td>dose rate during pulse</td>
<td>$10^6$ Gy/s</td>
<td>$10^2$ Gy/s</td>
</tr>
<tr>
<td>pulse repetition frequency</td>
<td>10 – 100 Hz</td>
<td>200 Hz</td>
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<tr>
<td>mean dose rate</td>
<td>40 – 1000 Gy/s</td>
<td>0.05 Gy/s</td>
</tr>
<tr>
<td>time for dose delivery</td>
<td>100 ms</td>
<td>4 min</td>
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</table>

tools and methods established in dosimetry for conventional RT are not suitable for FLASH-RT

Wrong tool!
metrological challenges

tools and methods established in dosimetry for conventional RT are not suitable for FLASH-RT

typical behavior of ordinary ionization chambers

Petersson et al., Med Phys 44 (2017) 1157
DOI: 10.1002/mp.12111
beams with ultra-high pulse dose rates

ultra-high dose per pulse, ultrashort pulse duration or both
EMPIR project UHDpulse - Consortium

5 National Metrology Institutes
leading in the field of dosimetry

2 academic hospitals
pioneers in FLASH-RT

3 universities
experts in detector development
pioneer in laser-driven beams

3 national research institutes
pioneer in detector development
pioneer in laser-driven beams
dosimetry expert

1 European research institute
laser-driven beam research

2 companies
expert in detector development

NMI’s

Irradiation facility provider

Radiation detector developer

WP6 (coordin.)

WP3

WP1

WP2

WP4

WP5 (impact)
Contributions of the partners

PTB - Physikalisch-Technische Bundesanstalt (Braunschweig, DE)

- accelerator for FLASH electron beams
- ultra-high dose rate proton beam
- water calorimeter primary standard
- alanine dosimetry system
- development and provision of FLASH reference fields
- testing and calibrations of dosimetric equipment for FLASH-RT

contact:
Andreas Schüller,
Ralf-Peter Kapsch

PTB’s research electron accelerator (0.5 – 50 MeV)
Contributions of the partners

NPL - National Physical Laboratory (Teddington, UK)

contact: Anna Subiel, Francesco Romano

- primary standard for proton therapy
- primary standard for neutron radiation
- absolute dosimetry for FLASH proton beams
- dosimetry for laser-driven beams
- dosimetry for VHEE radiotherapy

NPL’s portable graphite calorimeter: primary standard for proton beam
Contributions of the partners

NPL - National Physical Laboratory (Teddington, UK)

- primary standard for proton therapy
- primary standard for neutron radiation
- absolute dosimetry for FLASH proton beams
- dosimetry for laser-driven beams
- dosimetry for VHEE radiotherapy

NPL’s setup for VHEE dosimetry at CERN’s CLEAR (60 - 200 MeV Linac)

contact:
Anna Subiel,
Francesco Romano

6.9.2019
Medical Accelerators and Particle Therapy, 4 – 6 September 2019, Seville, Spain
Contributions of the partners

METAS - Swiss Federal Office of Metrology and Accreditation (Bern, CH)

- chemical dosimetry (Fricke dosimetry)
- accelerator for FLASH electron beams
- Fricke dosimetry as FLASH primary dosimetry technique
- provide reference FLASH electron beams

Microtron electron accelerator beam line

Scanditronix 22 MeV microtron

Contact: Christian Kottler
Contributions of the partners

CMI - Czech metrology institute (Prague, CZ)

contact: Jaroslav Solc

- Monte Carlo simulations
- detector data analysis
- evaluation and interpretation of TimePix-3 data
- characterization of stray radiation

MC Simulation of secondary neutron dose equivalent from 100 MeV proton pencil beam in water phantom
Contributions of the partners

GUM - Central Office of Measures (Warsaw, PL)

- developing primary standards for absorbed dose to water
- Monte Carlo simulation
- measurements of FLASH electron and proton beams with graphite calorimetry
- MC sim. of FLASH beams

contact: Adrian Knyziak

GUM’s portable graphite calorimeter
Contributions of the partners

Institut Curie (Orsay, FR)

- leading center for cancer treatment research
- pioneers of FLASH radiotherapy
- access to a FLASH electron beam
- access to a FLASH proton beam
- new transmission monitor chamber for FLASH proton beam

contact: Charles Fouillade
Contributions of the partners
Orsay Proton Therapy Center (Orsay, FR)

contact: Ludovic De Marzi

- leading center for cancer treatment research
- pioneers of FLASH radiotherapy
- access to a FLASH electron beam
- access to a FLASH proton beam
- new transmission monitor chamber for FLASH proton beam
Contributions of the partners
CHUV - Lausanne university hospital (Lausanne, CH)

- FLASH radiotherapy pioneering work
- clinical dosimetry for FLASH-RT

- access to a FLASH-RT facility as well as dosimetry tools and methods
- establish a code of practice

contact: Claude Bailat

clinical FLASH electron accelerator
Contributions of the partners

Instituto de Microelectrónica de Barcelona (Barcelona, ES)

- Production of Si radiation detectors
- Leads the development of radiation hardened Si detectors for CERN
- Prototype detectors for dosimetry for FLASH proton and electron beams

Contact:
Celeste Fleta, Giulio Pellegrini

Si microsensor with ion collection time < 1 ns
Contributions of the partners
University of Santiago de Compostela (ES)

contact: Prof. Faustino Gómez

skills
- expert in R&D on dosimetry techniques

tasks
- provide a prototype active dosimeter for FLASH-RT
- characterization of detectors in proton and electron FLASH beams

Microdosimeter with electronics assembly from USC

Radiation Physics Laboratory (accredited SSDL)
Contributions of the partners

Nuclear Physics Institute (Prague, CZ)

- electron accelerator for FLASH beams
- expert for dosimetry
- providing access
- will utilize passive detectors (TLD)

contact: Iva Ambrozova

MT25 - The Prague microtron
Contributions of the partners

ADVACAM s.r.o. (Prague, CZ)

Contact
Cristina Oancea,
Jan Jakubek

Skills
- semiconductor sensor manufacturing
- commercialises Timepix technology

Tasks
- Timepix-3 based detectors for FLASH beams and for stray radiation

Timepix-3 Si detector with readout unit
Contributions of the partners

ELI Beamlines (Prague, CZ)

- new laser research facility
- beamline to investigate medical applications of laser-driven beam
- providing access
- Monte Carlo simulation
- will utilize passive detectors

ELIMAIA
(ELI Multidisciplinary Applications of laser-Ion Acceleration)

contact:
Veronika Olsovcova,
Roberto Versaci
Contributions of the partners

Queen's University Belfast (Belfast, UK)

contact: Prof. Marco Borghesi

**skills**

- expertise in laser-driven ion acceleration
- high-power laser facility for ion beam acceleration (TARANIS)

**tasks**

- provision of laser-driven proton beam
- dosimetry for laser-driven beams

TARANIS laser for ion acceleration
Contributions of the partners
Politecnico di Milano (Milano, IT)

contact
Prof. Marco Caresana

- expert for R&D in the field of radiation detection

- adapt a detector system for pulsed neutron stray radiation

LUPIN neutron detector at HIMAC, Osaka
Contributions of the partners

HZDR - Helmholtz-Zentrum Dresden-Rossendorf (Dresden, DE)

- FLASH electron beam (ELBE)
- laser-driven protons and electrons (DRACO)
- pulsed neutron beam (nELBE)
- FLASH protons (medical cyclotron, OncoRay)
- providing access and dosimetry expertise

contact: Jörg Pawelke

ELBE Center for High Power Radiation Sources
( Electron Linac for beams with high Brilliance and low Emittance, Petawatt laser)
Contributions of the partners
PTW The Dosimetry Company (Freiburg, DE)

- designs, develops, manufactures and distributes dosimetry equipment for radiation therapy
- development of a new detector (ionization chamber) for FLASH proton and electron beams

contact:
Daniela Poppinga, Rafael Kranzer

Variety of PTW’s detectors for radiotherapy
UHDpulse - Work Package Structure

WP1: Primary standards
- Definition of reference conditions
- Reference radiation fields
- Adapting primary standards (water calorimeter, Fricke dosimeter)
- Prototype graphite calorimeters for laser-driven beams

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
- Methods with passive detectors
# EMPIR project UHDpulse - Consortium

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## NMI’s

- **WP6 (coordin.)**
  - PTB
  - NPL
  - METAS
  - CMM
  - Central Office of Measures

## Irradiation facility provider

- **WP1**
  - CHUV Centre hospitalier universitaire vaudois
  - institut Curie
  - CEBma
  - Nuclear Physics Institute of the CAS
  - Queen's University Belfast
  - HZDR

## Radiation detector developer

- **WP3**
  - ADVACAM Imaging the Unseen
  - CSIC
  - CNM
  - USC
  - POLITECNICO MILANO 1863
  - PTW The Dosimetry Company
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Braunschweig and Berlin
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