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

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Department 6.2 “Dosimetry for Radiation Therapy and Diagnostic Radiology”

International Conference on Medical Accelerators and Particle Therapy
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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)

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

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 therapeutic window and FLASH effect](image)

- Tumor control (TC)
- Normal tissue complication (NTC)
- TC without NTC
FLASH radiotherapy

Cat cancer patient trial

before FLASH

7 month after FLASH

nasal carcinoma not eligible for surgery

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)

36 weeks post-RT

necrotic lesions

FLASH (300 Gy/s)

normal appearance of skin

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

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DOI: 10.1016/j.radonc.2019.06.019
metrological challenges

<table>
<thead>
<tr>
<th></th>
<th>FLASH</th>
<th>conventional</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>
</tr>
</tbody>
</table>

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

WP1
WP2
WP5 (impact)

Irradiation facility provider

WP6 (coordin.)
CHUV Centre hospitalier universitaire vaudois

Radiation detector developer

WP3
ADVACAM Imaging the Unseen

WP4
CSIC
CNM

USC

POLITECNICO MILANO 1863

PTW THE DOSIMETRY COMPANY
Contributions of the partners

PTB - Physikalisch-Technische Bundesanstalt (Braunschweig, DE)

contact: Andreas Schüller, Ralf-Peter Kapsch

- 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

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)

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

Contact: Christian Kottler

- Scanditronix 22 MeV microtron
- microtron electron accelerator beam line
Contributions of the partners

CMI - Czech metrology institute (Prague, CZ)

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

contact: Jaroslav Solc

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) 09

- 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

FLASH electron accelerator

setup for FLASH irradiation of mice
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)

- 15 µm diameter x 5.5 µm thick contact:
  - Celeste Fleta,
  - Giulio Pellegrini

**skills**

- production of Si radiation detectors
- leads the development of radiation hardened Si detectors for CERN

**tasks**

- prototype detectors for dosimetry for FLASH proton and electron beams

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

- expert in R&D on dosimetry techniques
- provide a prototype active dosimeter for FLASH-RT
- characterization of detectors in proton and electron FLASH beams

Contact: Prof. Faustino Gómez

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 Olsovcoa, Roberto Versaci
Contributions of the partners

Queen's University Belfast (Belfast, UK)

contact: Prof. Marco Borghesi

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

**skills**

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

**tasks**

- 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

ELBE Center for High Power Radiation Sources
(Electron Linac for beams with high Brilliance and low Emittance, Petawatt laser)

contact: Jörg Pawelke
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

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.)
  - WP1
  - WP2
  - WP5 (impact)

- **Irradiation facility provider**
  - CHUV Centre hospitalier universitaire vaudois
  - institut Curie
  - enerbeams
  - Nuclear Physics Institute of the CAS
  - Queen’s University Belfast
  - HZDR

- **Radiation detector developer**
  - ADVACAM
  - CSIC
  - CNM
  - USC
  - POLITECNICO MILANO 1863
  - PTW THE DOSIMETRY COMPANY
This project 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.