European Partnership on Metrology
Call 2022 – Digital Transformation, Health, Integrated European Metrology, Normative and Research Potential

Selected Research Topic number: **SRT-h14**
Version: 1.0

Title: Dosimetry for FLASH radiotherapy

Abstract

Radiotherapy (RT) using FLASH (ultra-high dose rate) proton beams will soon become commercially available. These beams can reach deep-seated tumours with full control of time and position of the dose delivery. Metrology required for pre-clinical research and the clinical introduction of FLASH RT, for example, in the Bragg peak mode is non-existent or in an early phase of development. Urgent needs also exist for electron FLASH systems planned for installation at several centres. This research therefore needs to develop dose and dose-rate metrology required to bring FLASH RT safely into the clinic. FLASH RT offers the potential of a significant reduction in side effects and treatment times for cancer patients, leading to a significant improvement in quality of life.

Keywords

Ionizing radiation dosimetry, FLASH radiotherapy, preclinical and clinical use, time-resolved measurements, absorbed dose rate, absorbed dose, ultra-high dose rate.

Background to the Metrological Challenges

FLASH radiotherapy in which ultrahigh radiation doses are delivered in fractions of a second has the potential to revolutionise radiotherapy and is on the verge of commercialisation. It has huge potential to spare healthy tissue (e.g. 40 % reduction in normal-tissue toxicity) while still suppressing tumour growth. This means larger doses can be administrated in each patient treatment session, therefore fewer radiotherapy sessions will be needed leading to greater cancer treatment efficiencies and cost savings to European health services. FLASH therapy doses are delivered very rapidly (a treatment session may take less than 1 s) and therefore accurate metrology of beam parameters responsible for the FLASH effect, such as dose and dose rate, are essential to enable this new technology to make a smooth and safe transition into clinics.

Currently, the most viable treatment modalities nearing clinical use are based on proton and electron beams for which metrology to underpin preclinical studies, treatment plan validation, and safety aspects, and for comprehensive FLASH dosimetry for user and patient safety all need to be developed. For protons, no methods are available for time-resolved measurements in the spread-out Bragg-peak at FLASH conditions. Here, the scanned pencil proton beams present a significant metrological challenge given the combined effect of patterns of small geometrical beam spots (< 10 mm diameter), high dose rates of short duration (< 3 ms) at different energies and with a significant increase in linear energy transfer (LET). For electrons, some methods are available at the fundamental level, but these need to be adapted to support pre-clinical and clinical studies. Online detector systems with high time resolution for dose and dose rate quantification able to operate at the high transitory radiation levels envisaged, and detector systems that can be used in zoomorphic and anthropomorphic phantoms to validate the ability of FLASH systems to deliver prescribed full treatment plans accurately are urgently needed.

To maximize the benefit of FLASH dose delivery, all physical aspects of the treatment workflow (e.g., beam calibration, imaging, treatment planning and quality assurance) need evaluation and optimization. The target uncertainty in dose delivery for FLASH radiotherapy would be equivalent to the 3 %/3 mm limits normally required in conventional radiotherapy. FLASH radiotherapy would also be subject to requirements regarding dose rate. Also, there is a need for a framework that can harmonize dose and dose-rate measurements for the entire field of FLASH radiotherapy, including continuous and pulsed beams of protons and electrons from spot scanning and static broad beam delivery systems.

Research proposals into FLASH-RT will strengthen the position of European industry within the field of treatment technology (e.g. electron intraoperative equipment) and measurement equipment (e.g. detector systems tailored for FLASH radiotherapy).

Objectives

Proposers should address the objectives stated below, which are based on the PRT submissions. Proposers may identify amendments to the objectives or choose to address a subset of them in order to maximise the overall impact, or address budgetary or scientific / technical constraints, but the reasons for this should be clearly stated in the protocol.

The JRP shall focus on the development of dose and dose-rate metrology for proton and electron beams used in FLASH radiotherapy to support pre-clinical and clinical studies. The specific objectives are:

1. To develop the measurement methods required for traceable dose and dose rate measurements from primary standards to clinical users for FLASH-RT beams (continuous or pulsed) for (i) protons and (ii) electrons using detectors with different time and spatial resolution to provide a traceability chain. Target uncertainty in dose delivery for FLASH radiotherapy is the 3 %/3 mm limits required in conventional radiotherapy. In addition, for protons, to develop a time-resolved measurement procedure for determining the spread-out Bragg-peak at FLASH conditions.
2. To develop and validate methods for determining relevant dosimetric quantities (e.g. energy, fluence, penetration depth of Bragg peak) and their associated uncertainties during pre-clinical *in-vivo* studies based on using measurement techniques with high spatial and temporal resolution that provide detailed information about beam parameters for individual irradiations.
3. To develop and validate methodologies that support FLASH-RT clinical treatment planning based on tools for treatment plan validation and auditing methods (e.g. spatial maps or point measurements of dose and dose rate in anthropomorphic phantoms).
4. To develop and validate methodologies for the demonstration of compliance with safety regulations for FLASH-RT dose delivery based on the measurements required to demonstrate that beams can be terminated within regulatory requirements in case of system failures.
5. To facilitate the take up of the technology and measurement infrastructure developed in the project by the measurement supply chain (accredited laboratories, measurement equipment manufacturers), organisations developing standards and reference documents (ESTRO, IAEA, AAPM), and end users (e.g. clinical stakeholders, manufacturers of FLASH-RT machines).

These objectives will require large-scale approaches that are beyond the capabilities of single National Metrology Institutes and Designated Institutes, and it is expected that multidisciplinary teams will be required. To enhance the impact of the research, the involvement of the appropriate user community such as medical practitioners, medical (academic) hospitals and industry is strongly recommended, both prior to and during methodology development.

Proposers should establish the current state of the art and explain how their proposed project goes beyond this. In particular, proposers should outline the achievements of the EMPIR project 18HLT04 UHDpulse and how their proposal will build on those.

EURAMET expects the average EU Contribution for the selected JRPs in this TP to be 1.9 M€ and has defined an upper limit of 2.6 M€ for this project.

EURAMET also expects the EU Contribution to the external funded beneficiaries to not exceed 35 % of the total EU Contribution across all selected projects in this TP.

Potential Impact

Proposals must demonstrate adequate and appropriate participation/links to the ‘end user’ community, describing how the project partners will engage with relevant communities during the project to facilitate knowledge transfer and accelerate the uptake of project outputs. Evidence of support from the ‘end user’ community (e.g., letters of support) is also encouraged.

You should detail how your JRP results are going to:

- Address the SRT objectives and deliver solutions to the documented needs,
- Feed into the development of urgent documentary standards through appropriate standards bodies,
- Transfer knowledge to the healthcare sector.

You should detail other impacts of your proposed JRP as specified in the document “Guide 4: Writing Joint Research Projects (JRPs)”

You should also detail how your approach to realising the objectives will further the aim of the Partnership to develop a coherent approach at the European level in the field of metrology and include the best available contributions from across the metrology community. Specifically, the opportunities for:

- improvement of the efficiency of use of available resources to better meet metrological needs and to assure the traceability of national standards
- the metrology capacity of EURAMET Member States whose metrology programmes are at an early stage of development to be increased
- organisations other than NMIs and DIs to be involved in the work.

Time-scale

The project should be of up to 3 years duration.