European Partnership on Metrology
Call 2023 –Fundamental Metrology, Industry, Normative and Research Potential

Selected Research Topic number: **SRT-n11**
Version: 1.1

Title: Traceable dosimetry for FLASH radiotherapy

Abstract

Radiotherapy with ultra-high dose rates (UHDR) or FLASH radiotherapy (RT), offers the potential of significant reduction in side effects for cancer patients, and associated improvement in quality of life. In the short term, new electron and proton beam facilities for FLASH are currently being installed or being upgraded to FLASH mode. New pre-clinical devices delivering x-rays in UHDR regime also have been introduced. Widespread clinical acceptance of FLASH RT requires Codes of Practice (CoP) for reference dosimetry. However, the development of a CoP for reference dosimetry in FLASH RT is hampered by the lack of suited primary standards, a solid traceability methodology, and definitions of reference conditions.

Keywords

FLASH radiotherapy, ionising radiation, reference dosimetry, absorbed dose, Ultra-High Dose Rate (UHDR), Ultra-high Dose-per-Pulse (UHDPP), Codes of Practice (CoP), primary standards.

Background to the Metrological Challenges

In 2020 2.7 million new cases of cancer were diagnosed in the EU and half of these patients were treated with radiotherapy in which high lethal doses of ionising radiation are delivered to the tumour using treatment modalities based on either high-energy (MeV) photon, electron, proton or hadron beams. In conventional radiotherapy typical delivered dose rates of 0.1 Gy/s are used, whilst in FLASH radiotherapy (radiotherapy at ultra-high dose rates (UHDR)), targeted dose rates in excess of 40 Gy/s spare healthy tissue whilst suppressing tumour growth. Clinical trials for these new therapies are ongoing. In addition, new FLASH facilities based on other particles (photons or carbon ions) are anticipated and these too will need to be incorporated into CoPs and normative standards.

Vendors have already announced FLASH treatment modalities ready for clinical installation based on proton and electron beams that use spot-scanning of continuous and pulsed proton beams for deep-seated tumours or pulsed electron beams for treatment of superficial tumours. To ensure patient safety, medical physicists need to measure the delivered dose under well-defined reference conditions, following procedures described in (inter)-national Codes of Practice (CoP) before clinical acceptance and as part of the regular quality assurance for therapy machines. Due to non-linearities of detectors at these high dose rates, existing secondary standards are not suited for reference dosimetry in FLASH beams, and existing CoPs are inadequate. Several measurement equipment manufacturers have developed detectors (e.g. ultra-thin ionisation chambers and solid state detectors) with improved linearity in electron beams at UHDR and UHDPP conditions, however other characteristics of these detectors still require investigation to enable inclusion of these detectors in CoPs.

Experimental UHDPP electron beams require investments of over 100 M€ per facility putting them beyond the reach of NMIs, therefore, the backbone of a measurement infrastructure for FLASH radiotherapy will be formed by portable primary standards suited for transferring measurement traceability to the user's beam. Several portable primary standards based on either graphite or water calorimeters have been developed and applied to calibrate secondary standards and measure correction factors for CoPs in a range of clinical radiotherapy facilities. However, the measurement infrastructure and standards to support clinics in providing FLASH therapies have yet to be developed. For the clinical introduction upgrades to existing pencil beams scanned (PBS) proton therapy facilities designed for conventional dose rates are envisaged. These upgrades will require the installation of an optimised monitoring chamber and other features so that patient safety[1] during therapy can be assured. An update of TRS-398 CoP on PBS proton beams is being drafted but this does not include either beam modifications required in FLASH proton facilities, or the use of novel detectors dedicated for UHDR dosimetry. This means that current methods for reference dosimetry are inadequate to calibrate beam monitors in FLASH proton therapy beams with uncertainties similar to those reported in modern Codes

of Practice. In addition, new FLASH facilities based on other particles (photons or carbon ions) are anticipated and these too will need to be incorporated into CoPs and normative standards.

Documentary standards and CoPs for dosimetry in radiotherapy are issued by IAEA, AAPM, EFOMP, ESTRO, NCS, IPEM, DIN, AAPM, ISO and IEC. CoPs for reference dosimetry in a specific beam modality or treatment technique are a requirement for widespread clinical introduction of these techniques. The EMN for Radiation Protection orientation has identified a research need for Radiation Protection for Flash RT, integral dose or instantaneous dose rate.

Proposals are invited for the development and validation of traceable measurement methodologies for absorbed dose in support of Codes of Practice for FLASH radiotherapy facilities that are near clinical implementation and FLASH facilities used for pre-clinical in-vivo studies.

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 traceable measurements of absorbed dose to support future Codes of Practice for FLASH radiotherapy facilities near clinical implementation and FLASH facilities used for pre-clinical in-vivo studies.

The specific objectives are

1. To determine and evaluate the characteristics of portable primary standards for absolute dose measurements in clinical UHDR proton beams. This will include the characterisation of existing primary standards for UHDR conditions, a sensitivity analysis of their characteristics on beam parameters and achievement of target uncertainties as specified in international Codes of Practice (e.g. TRS-398) for conventional clinical radiotherapy.
2. To develop a reference dosimetry methodology that transfers traceability from primary UHDR proton beam standards to proton beam standards for clinical UHDR facility use, with targeted uncertainties that meet international Codes of Practice (e.g. TRS-398) for conventional clinical radiotherapy. The methodology is to include beam characterisation for dedicated UHDR beam detectors, the derivation of traceability routes and definitions of reference conditions.
3. To develop a reference dosimetry methodology that transfers traceability from primary UHDPP electron beam standards to standards for clinical UHDPP electron beam facility use with targeted uncertainties that meet international Codes of Practice (e.g. TRS-398) for conventional clinical radiotherapy. The methodology is to include characterisation of (i) novel detectors dedicated for UHDPP beams, (ii) clinical beams and metrological UHDPP facilities and (iii) definition of reference conditions.
4. To adapt existing methods and to develop a methodology for traceable dosimetry in FLASH facilities used for pre-clinical *in-vivo* studies in collaboration with end users. This shall include beam characteristics and the development of validation methods for facilities used for pre-clinical studies based on electron, proton, and x-ray beams.
5. To facilitate the take up of the technology and measurement infrastructure developed in the project into Codes of Practice and reference documents from standards developing organisations (e. g. the proposed AAPM TG-359, IEC/SC 62C/WG 2), the measurement supply chain (accredited laboratories, measurement equipment manufacturers), the EMN Radiation Protection, and end-users (e.g. clinical stakeholders, manufacturers of FLASH facilities).

The proposed research shall be justified by clear reference to the measurement needs within strategic documents published by the relevant Regulatory body or Standards Developing Organisation or by a letter signed by the convenor of the respective TC/WG. EURAMET encourages proposals that include representatives from industry, regulators and standardisation bodies actively participating in the projects. The proposal must name a “Chief Stakeholder”, not a member of the consortium, but a representative of the user community that will benefit from the proposed work. The “Chief Stakeholder” should write a letter of support explaining how their organisation will make use of the outcomes from the research, be consulted regularly by the consortium during the project to ensure that the planned outcomes are still relevant and be prepared to report to EURAMET on the benefits they have gained from the project.

Proposers should establish the current state of the art and explain how their proposed research 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 1.0 M€ and has defined an upper limit of 1.3 M€ for this project.

EURAMET also expects the EU Contribution to the external funded beneficiaries to not exceed 30 % of the total EU Contribution across all selected projects in this TP.

Any industrial beneficiaries that will receive significant benefit from the results of the proposed project are expected to be beneficiaries without receiving funding or associated partners.

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,
- Facilitate improved industrial capability or improved quality of life for European citizens in terms of personal health, protection of the environment and the climate, or energy security,
- 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.