European Partnership on Metrology
Call 2024 –Digital Transformation, Green Deal, Normative and Research Potential

Selected Research Topic number: **SRT-n04**
Version: 1.0

Title: Traceable dosimetry for FLASH radiotherapy

Abstract

FLASH radiotherapy (RT) performed with ultra-high dose rates (UHDR) or ultra-high-dose-per-pulse (UHDPP) beams has the potential to significantly reduce the side effects experienced by cancer patients, and to improve their quality of life. At present, new UHDPP electron and UHDR proton beam facilities for FLASH are currently being installed or being upgraded to FLASH mode. Widespread clinical acceptance of FLASH radiotherapy requires reliable quality assurance in dosimetry, i.e. development of Codes of Practice (CoP) for reference dosimetry. However, CoP development for reference dosimetry in FLASH RT is hampered by the lack of suited primary standards, characterised secondary standards, and solid methodology.

Keywords

Health, 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

FLASH radiotherapy could completely revolutionise cancer treatment with its ability to spare normal tissue while still suppressing tumour growth so offering improved health benefits and a better quality of life to the millions of EU cancer patients diagnosed each year. Based on a smaller number of high dose FLASH-RT treatments per patient than conventional therapies, it could halve treatment times whilst increasing the number of patients treated each day saving both time and money. FLASH proton therapy has the potential for treating deep-seated tumours and may become the treatment of choice for a sizable group of patients instead of photon radiotherapy. Extending the number of patients treated with the EU's current €3 Billion radiotherapy funding whilst supporting the major European manufacturers of both proton and electron FLASH facilities would have both healthcare and economic benefits.

Traditionally, cancer patients are treated with a high dose of ionising radiation, typically dose rates of 0.1 Gy/s are delivered to tumours using treatment modalities based on either high-energy (MeV) photon, electron, proton, or ion beams. However, these doses also cause unwanted damage to healthy adjacent tissue. In FLASH radiotherapy, ultra-high dose rates (UHDR, > 40 Gy/s) or ultra-high-dose-per-pulse (UHDPP, > 0.6 Gy/pulse) enable better tumour targeting that minimises damage to healthy tissue. The first FLASH proton and clinical trials have recently been completed and the subsequent clinical trial is underway. Manufacturers have already installed FLASH treatment modalities based on ultra-high-dose-per-pulse (UHDPP) electron beams for treatment of superficial tumours and are planning facilities for deep-seated tumours. In parallel, existing continuous scanning beam proton therapy facilities have been upgraded to ultra-high-dose-rate (UHDR) mode for treatment of deep-seated tumours.

Medical physicists need to calibrate the radiotherapy facility monitor used, either as part of commissioning a new facility and for regular quality assurance purposes. This requires the use of a series of operations based on using firstly portable primary standards to enable absolute dose measurements in UHDR proton beams. Some portable graphite or water calorimeters have been developed and used for dose measurements in a range of clinical radiotherapy facilities, but to date few experiments with a graphite calorimeter in a clinical FLASH proton facility have been reported. Primary standards could then be used to calibrate secondary standards combined with their calibration in Co-60 reference beams, but recombination corrections are needed. However, formulas for these corrections, derived from theoretical descriptions of recombination effects are limited to avoid increased uncertainties which is restricting the use of existing secondary standards. CoPs, such as IAEA TRS-3989, describe how to determine the secondary standard's calibration coefficient, and are based on formulas for recombination corrections. However, these are derived from theoretical descriptions of recombination effects with a maximum value that is limited to avoid increasing uncertainties. This restricts the use of existing secondary standards. To avoid these restrictions and the theoretical approximations, dedicated recombination effect simulation models validated by experiments for both UHDPP electron and scanning UHDR proton beams are needed. In addition, most secondary standards exhibit a strong non-linearity between measurement signal and dose due to enhanced recombination effects at high dose rates and dose per pulse, which is not adequately covered in existing CoPs, leading to higher uncertainties. This lack of suited CoPs is hampering the wide-spread application of 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 proposal shall focus on metrology research necessary to support the development of reference dosimetry Codes of Practice (CoP) required by UHDPP electron and UHDR proton beam facilities.

The specific objectives are:

1. To determine and evaluate the characteristics of portable primary standards for absorbed dose measurements in clinical scanning UHDR proton beams. This will include the characterisation and determination of correction factors of existing primary standards for UHDR conditions, a sensitivity analysis of their characteristics and correction factors on beam parameters, and the achievement of target uncertainties matching those in international Codes of Practice for conventional clinical radiotherapy.
2. To determine secondary standard correction factors for clinical UHDR proton and UHDPP electron beams by the development of dedicated simulation models. This is to include: (i) modelling the radiation fields, (ii) simulations of recombination effects, (iii) simulations of beam quality correction factors (k_Q) for novel detectors, (iii) validation of models and their uncertainties, and (iv) application of the models for sensitivity analysis.
3. To develop a reference dosimetry methodology for scanning UHDR proton beams that transfers traceability from primary standards to secondary standards, with targeted uncertainties that match those in international Codes of Practice (e.g. TRS-3989) for conventional clinical radiotherapy. This is to include (i) measurement of beam characteristics (ii) determination of dose-rate parameters, (iii) calibration of secondary standards against portable primary standards (iv) measurement of recombination and k_Q correction factors for secondary standards, (v) assessment of the suitability of secondary standards, and (vi) the derivation of traceability routes.
4. To develop a reference dosimetry methodology for UHDPP electron beams that transfers traceability from primary standards to secondary standards, with targeted uncertainties that match those in international Codes of Practice (e.g. TRS-398) for conventional clinical radiotherapy. This is to include (i) measurement of beam characteristics, (ii) establishment of clinical-like reference fields (iii) measurement of recombination and k_Q correction factors for secondary standards, (iv) assessment of the suitability of secondary standards, and (v) the derivation of traceability routes.
5. To facilitate the take up of the technology and measurement infrastructure developed in the project by Codes of Practice and the reference documents from standards developing organisations (e.g. AAPM TG-359, IEC/SC 62C/WG 3, DIN NAR AA1), 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 project and how their proposal will build on it.

Proposers should note that the programme funds the activity of researchers to develop the capability, not the required infrastructure and capital equipment, which must be provided from other sources.

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 proposal.

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 proposal's 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 Metrology 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.

Timescale

The project should be of up to 3 years duration.