Publishable Summary for 24NRM01 FLASH-DOSE
Traceable dosimetry for FLASH radiotherapy

Overview

FLASH radiotherapy 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 are being installed or being upgraded to prepare for clinical FLASH radiotherapy. However, future widespread clinical introduction of FLASH radiotherapy requires reliable methods for traceable dosimetry under reference conditions (reference dosimetry). Further to this, development of Codes of Practice (CoP) for reference dosimetry in FLASH radiotherapy facilities is hampered by the lack of suited primary standards, characterised secondary standards, and solid methodology. This project will address these issues by developing traceable dosimetry, including upgraded primary and characterised secondary standards, to support the development of reference dosimetry CoPs required by UHDPP electron and UHDR proton beam facilities.

Need

More than 1.0 M cancer patients in the EU are currently treated with radiotherapy per year/annually, which delivers a lethal dose of ionising radiation to the tumour. However, at the same time radiation dose is unavoidably delivered to healthy tissue which may lead to unwanted side effects. In conventional radiotherapy, the dose is delivered with typical dose-rates of 0.1 Gy/s. Pre-clinical *in vivo* investigations have demonstrated the so-called FLASH effect. The FLASH effect is the capability to spare healthy tissue up to 40 %, while still suppressing tumour growth, by delivery of the same dose at UHDR (> 40 Gy/s) or UHDPP (> 0.6 Gy/pulse) conditions.

To prepare for clinical treatments with FLASH radiotherapy, vendors are already installing new FLASH treatment facilities based on static pulsed electron beams delivering an UHDPP or on scanning proton beams delivered at UHDR. But for clinical introduction of these beams, medical physicists need methods for reference dosimetry. These methods, described in CoPs from standards developing organisations (SDOs) such as the International Atomic Energy Agency (IAEA) and the American Association of Physicists in Medicine (AAPM), are used to determine the absorbed -dose -to -water (D_w), which is needed to calibrate the beam monitor. The current international CoP IAEA TRS-398 prescribes the methodology for reference dosimetry in conventional radiotherapy with ionisation chambers as secondary standards traceable to primary standards and data sets of correction factors valid for the end -user's clinical beam.

Because UHDR/UHDPP conditions introduce high recombination effects in commercial ionisation chambers, existing methods to determine the recombination correction, k_s are currently insufficient. This not only makes the IAEA TRS-398 methodology to determine the absorbed -dose inappropriate, but it also affects the determination of other correction factors and calibration coefficients with primary standards valid for the clinical beam. Therefore, existing CoPs urgently require revision at multiple levels for FLASH modalities. This necessitates fundamental investigations on k_s using simulations, validation of primary standards for scanning UHDR proton beams and methodology, and data sets of correction factors for clinical reference dosimetry in scanning UHDR proton and UHDPP electron beams, as well as uptake of the methodology by standards developing organisations.

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The project has received funding from the European Partnership on Metrology, co-financed from the European Union's Horizon Europe Research and Innovation Programme and by the Participating States.

Objectives

The overall objective of the project is to develop traceable dosimetry to support the development of reference dosimetry CoP required by UHDPP electron and UHDR proton beam facilities aimed for FLASH radiotherapy.

The specific objectives of the project 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: (i) the characterisation and determination of correction factors of existing primary standards for UHDR conditions, (ii) a sensitivity analysis of their characteristics and correction factors on beam parameters, and (iii) the achievement of target uncertainties matching those in international CoP 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 (k_s), (iii) simulations of beam quality correction factors (k_Q) for novel detectors, (iv) validation of models and their uncertainties, and (v) 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 CoP (e.g. IAEA TRS-398) 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 (k_s) and beam quality (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 CoP (e.g. IAEA 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 (k_s) and beam quality (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 CoP and the reference documents from standards developing organisations (e.g. AAPM TG-359, IEC/SC62C/WG3, 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).

Progress beyond the state of the art and results

Portable primary standards for scanning UHDR proton beams:
Primary standards, based on water or graphite calorimetry, are currently able to realise D_w with an uncertainty smaller than 0.5 % in reference beams available at NMIs. However, in order to calibrate and determine correction factors of secondary standards, for the development of CoPs such as IAEA TRS-398, measurements with portable primary standards in clinical facilities are essential. So far, the results of only one measurement with a portable graphite calorimeter in a scanning UHDR proton beam with an uncertainty of 0.9 % have been published. Water calorimetry is considered the most direct method to realise D_w. This project will go beyond the current state of the art by characterising two portable graphite calorimeters and one portable water calorimeter as primary standards for scanning UHDR proton beams with a target uncertainty of 0.5–0.9 %. Their uncertainty will be validated in a direct comparison.

Simulation of secondary standard correction factors
The recently updated IAEA TRS-398 provides practical formalisms for experimental determination of k_s which have been derived from theoretical descriptions and based on idealised geometries. But experimental results indicate that measured k_s values for ionisation chambers are significantly higher than these k_s practical formalisms allow for, which results in increased uncertainties for UHDR/UHDPP beams. This project will progress beyond the state of the art by calculating k_s in UHDR/UHDPP conditions using existing numerical simulation models of recombination with a more accurate physical description of recombination effects and more realistic ionisation chamber geometry models. Using this k_s data, the accuracy of more sophisticated

practical formalisms for k_s will be investigated. Moreover, a sensitivity analysis of k_s corrections to beam parameters and environmental conditions will be conducted to evaluate uncertainty budgets for k_s.

Currently IAEA TRS-398 provides tabulated beam quality correction factors, k_Q, to correct for differences in beam quality between the user beam and calibration beam for a set of ionisation chambers. This project will progress beyond this, by using Monte Carlo radiation transport simulations to investigate the impact of potential divergence in reference conditions on k_Q, for scanning UHDR proton and UHDPP electron beams.

Reference dosimetry methodology for scanning UHDR proton beams and UHDPP electron beams:
This project will develop recommendations for how to extend existing CoPs for reference dosimetry to scanning UHDR proton beams and static UHDPP electron beams, as these do not currently exist. As FLASH beam reference conditions potentially diverge from IAEA TRS-398 reference conditions, the project will also investigate the impact of this divergence on correction factors and calibration coefficients and demonstrate the validity of the IAEA TRS-398 methodology for the reference conditions in FLASH beams. For scanning UHDR proton beams, the project will do this by comparing D_w measured with secondary standards according to the IAEA TRS-398 method, using both calculated and measured k_s and k_Q data, with D_w measurements from a primary standard and with D_w measurements from a dose-rate independent passive dosimeter under the same set of reference conditions. For UHDPP electron beams, this project will realise reference conditions in clinical--like reference fields at NMIs which can be used to calibrate secondary standards close to the reference conditions in clinical conditions. Recently, novel secondary standards with reduced recombination corrections have been introduced for which correction factors are lacking, and as part of this project these corrections will be determined.

Outcomes and impact

Key dissemination and communication activities

The FLASH-DOSE project was briefly outlined in a teaching lecture at ESTRO 2025. A poster was presented at the celebration of 150th anniversary of the Metre Convention. A direct link was made by NPL to the ESTRO FLASH Focus Group dealing with dosimetry for FLASH radiotherapy.

Outcomes for industrial and other user communities

This project will impact radiotherapy clinics, and manufacturers of measurement equipment and facilities for FLASH radiotherapy. The project will develop recommendations for traceable reference dosimetry for scanning UHDR proton and static UHDPP electron facilities aimed for FLASH radiotherapy. This will support medical physicists in their commissioning of new UHDR proton and static UHDPP electron radiotherapy facilities as well as the upgrade of existing facilities with FLASH capabilities by manufacturers.

The project will improve the existing measurement infrastructure for dosimetry in FLASH radiotherapy within Europe by extending the operational range of primary standards to high-dose rates and by developing (i) software for the simulation of recombination effects in secondary standards, (ii) data sets of recombination corrections k_s and k_Q correction factors, (iii) reference dosimetry methodology for scanning UHDR proton beams and for UHDPP electron beams, and (iv) characterised clinical--like reference fields for UHDPP electron beams. This will allow manufacturers of detectors for dosimetry in radiotherapy beams to assure the quality of their products for applications in UHDR scanning proton and UHDPP electron beam facilities. Further to this, the involvement of several manufacturers in the project's stakeholder committee will provide much needed end-user feedback and help to ensure that facilities meet their needs to enhance utilisation.

In addition, the project will engage with healthcare sector and other user communities via social media, webinars and stakeholder symposiums. The project will also disseminate its outcomes to them through the scientific councils of AAPM (chief stakeholder for the project), the European Society for Radiotherapy and Oncology (ESTRO) dissemination network and via the Varian Flash Forward Consortium (FFC). The Varian FFC includes a range of institutions and has the goal to establish preclinical study designs, develop technical solutions, and share research protocols to advance clinical translation of FLASH therapy. The project's inputs to AAPM, ESTRO and the Varian FFC will help to transfer of the project's developments to the wider European radiotherapy community.

Outcomes for the metrology and scientific communities
This project will improve capabilities of European NMIs active in the field of dosimetry for advanced radiotherapy. The project will develop primary standards to ensure traceability of dosimetry in FLASH beams to the SI. Primary standards for conventional radiotherapy are subject to regular verifications through

international key comparisons, and this project will establish primary standards for scanning UHDR proton beams. The comparisons of these standards in these beams by NMIs participating in this project will be the first ever attempt to ensure international traceability of dosimetry for FLASH radiotherapy.

This project will enable NMIs to extend their existing electron accelerators to clinical--like reference fields similar to those in clinical UHDPP electron accelerators. In addition, the project will enable NMI's to demonstrate the validity of their existing portable primary standards for UHDR proton beam standards for UHDR proton beams.

The simulation of recombination effects in ionisation chambers is a relatively new research topic. Therefore, the project will extend existing models to more realistic situations and compare the results with experimental results. This will lead to a better understanding of recombination effects in ionisation chambers which could lead to improved methods for determination of k_s by simulations. The project will develop model software for the simulation of recombination effects, which will be shared publicly as opensource software in order to allow stakeholders from other scientific communities to benefit from it.

Finally, the project will disseminate its outcomes to the metrology and scientific communities through peer-reviewed journal, presentations at conferences and via the EURAMET EMN for Radiation Protection and European Particle Therapy Network.

Outcomes for relevant standards

Documentary standards and CoPs for reference dosimetry in radiotherapy have been issued by the IAEA, IEC, DIN, AAPM, the Institute of Physics and Engineering in Medicine (IPEM) and the Netherlands Commission on Radiation Dosimetry (NCS). The IAEA TRS-398 is used globally for dosimetry for conventional radiotherapy. Additionally, DIN, IPEM, NCS, AAPM have issued CoPs with slightly different approaches, that are extensively used by medical physicists. However, these CoPs are not applicable in FLASH radiotherapy and specific CoPs for reference dosimetry for FLASH radiotherapy do not currently exist.

AAPM TG 359 is working on recommendations for FLASH radiotherapy, and IEC 62C WG3 is in the process of updating the standard IEC 60731 "Medical electrical equipment - Dosimeters with ionisation chambers as used in radiotherapy". DIN has also recently started a working group with the aim to develop a CoP on reference dosimetry for FLASH radiotherapy facilities. Therefore, these committees and working groups are highly relevant for this project and the consortium will use its existing contacts with them to disseminate recommendations for reference dosimetry for scanning UHDR proton and UHDPP electron beams.

Longer-term economic, social and environmental impacts

More than 1 M cancer patients are treated with radiotherapy annually in the EU. FLASH radiotherapy offers future, huge potential benefits to patients by significantly reducing side -effects (e.g. a 40 % reduction in normal -tissue toxicity) while still suppressing tumour growth. This perfectly fits with the long -term 2030 vision of ESTRO: 'Radiation oncology. Optimal health for all, together'. However, to support the longer -term roll out and clinical implementation of FLASH radiotherapy it is vital to have reference dosimetry based on CoPs. The outcomes of this project will provide this reference dosimetry for scanning UHDR proton beams and UHDPP electron beams and hence facilitate patient care across the EU with significantly improved oncology care and quality of life.

As FLASH radiotherapy produces significantly less normal tissue damage, it should be possible to use a smaller number of high dose FLASH radiotherapy treatments for patients in the future, thus saving both time and money and enhancing patient care and reducing side effects. This should reduce the cost of treatment for each patient and more fully offset Europe's € 3bn investment in proton therapy. The clinical use of FLASH radiotherapy requires novel secondary standards for which their suitability for application remains to be investigated. The standardisation of accurate radiation dosimetry for FLASH beams is a prerequisite for successful clinical application of these beams in cancer therapy. Therefore, the uptake of the project's results in new CoPs for FLASH radiotherapy should support and stimulate scientific advances and economic growth in both FLASH radiotherapy and associated secondary standards.

List of publications

This list is also available here: https://www.euramet.org/repository/research-publications-repository-link/

Project start date and duration:		1st June 2025, 36 months
Coordinator: Jacco de Pooter, VSL E-mail: jdpooter@vsl.nl Project website address: https://flash-dose.eu/		
Chief Stakeholder Organisation: AAPM (The American Association of Physicists in Medicine)		Chief Stakeholder Contact: Dimitris Mihailidis
Internal Beneficiaries: 1. VSL, Netherlands 2. CEA, France 3. CMI, Czechia 4. DTU, Denmark 5. ENEA, Italy 6. GUM, Poland 7. NPL, United Kingdom 8. PTB, Germany	External Beneficiaries: 9. AU, Denmark 10. HPTC, Netherlands 11. USC, Spain	
Associated Partners: 12. METAS, Switzerland 13. PSI, Switzerland		