Publishable Summary for 18HLT04 UHDpulse

Metrology for advanced radiotherapy using particle beams with ultra-high pulse dose rates

Overview

Recently, in vivo radiobiological experiments have shown that irradiation with electron beams, with ultra-high dose per pulse, may dramatically reduce adverse side effects, while being equally efficient for tumour control as conventional irradiation. Extreme dose rates are delivered by laser-based accelerators, which are considered as the next generation of accelerators for radiotherapy. They may allow the development of more efficient therapeutic techniques and healthcare at lower cost. Pulses with dose rates orders of magnitude higher than in conventional radiotherapy presents significant metrological challenges, which need to be addressed to enable the translation of these novel radiotherapy techniques to clinical practice.

Need

According to the WHO the estimated number of new cases of cancer in Europe in 2018 is about 4.2 million. Approximately half of the European cancer patients receive radiotherapy. The therapeutic window, i.e. the range of dose which provides effective cure, is limited by adverse side effects of the radiation on the healthy tissue surrounding the tumour.

Several animal studies demonstrated that delivering the radiation dose in a short time, i.e. with only a few beam pulses of ultra-high dose per pulse, may dramatically reduce adverse side effects, while the anti-tumoral efficacy is preserved. Due to this so-called FLASH effect, the prescribed dose could also be increased resulting in a more effective tumour control. The future application of FLASH radiotherapy requires that its performance, safety and effectiveness are reliably measured and optimised. Accurate dosimetry is vital in delivering successful radiotherapy.

Additionally, laser-driven accelerators are being considered as the next generation of cost-effective accelerators for radiotherapy, which enable further alternative advanced treatment modalities. The pulse duration of laser-driven beams is much shorter than that of conventional clinical accelerators and the dose rate in the pulse can be orders of magnitude higher.

Both, FLASH radiotherapy and laser-driven beams, cause significant metrological challenges related to the ultra-high pulse dose rates, which need to be addressed to enable the translation of these advanced radiotherapy techniques to clinical practice. The complexity and the resources needed for research in advanced radiation therapy using particle beams with requires wide, multidisciplinary scientific approaches that go beyond the capabilities of a single research institute. The project and the consortium are well suited to form a nucleus for a European network for long-term metrological support for modern and emerging forms of radiotherapy.

Objectives

The overall goal of the project is to provide the metrological tools needed to establish traceability in absorbed dose measurements of particle beams with ultra-high pulse dose rates (UHPDR), i.e. with ultra-high dose per pulse or with ultrashort pulse duration.

The specific objectives of the project are:

1. To develop a metrological framework, including **SI-traceable primary and secondary reference standards** and validated reference methods for dosimetry measurements for particle beams with ultra-high pulse dose rates.

2. To characterise the response of available **detector systems** in particle beams with ultra-high dose per pulse or with ultrashort pulse duration.
3. To develop traceable and validated methods for **relative dosimetry** and for the **characterisation of stray radiation** outside the primary pulsed particle beams.
4. Using the results from objectives 1-3, to provide the input data for **Codes of Practice** for absolute dose measurements in particle beams with ultra-high pulse dose rates.
5. To facilitate the uptake of the project's achievements by the measurement supply chain, standards developing organisations (e.g. those associated with International Atomic Energy Agency (IAEA) and International Commission on Radiation Units (ICRU) reports) and end users (clinical and academic laboratories, hospitals and radiotherapy manufacturers).

Progress beyond the state of the art and results

SI-traceable primary and secondary reference standards

In this project for the first time reference radiation fields for electron beams with ultra-high dose per pulse comparable to fields used for FLASH radiotherapy will be developed, optimised, commissioned and compared against each other. As result, it will be possible to determine correction factors needed for Codes of Practice for FLASH radiotherapy as well as to calibrate dosimetry systems for this new treatment modality.

Furthermore, different methods for the realisation of a corresponding primary standard will be adapted, examined and compared against each other. The outputs of this project will provide a calibration chain up to an adequate primary standard for FLASH radiotherapy both for treatment with electrons and with protons. The suitability of different commercially available detector systems as secondary standard for UHPDR electron beams will be investigated.

This project will contribute to the generation of roadmaps for the development of future primary standards suitable for novel laser-driven medical accelerators which allow, for e.g., the cost-effective generation of very high energy electrons (VHEE) which enable a further alternative advanced treatment modality known as VHEE radiotherapy.

Detector systems

The capabilities of different existing and novel active dosimetric detectors for UHPDR particle beams will be investigated. Different types of custom-built detectors will be optimised or redesigned for UHPDR particle beams for primary beam as well as for the stray radiation field. As a result, it will be possible to determine the dose at UHPDR also by means of active instruments in real-time, i.e. in a much more efficient way than up to now with passive dosimeters.

Relative dosimetry and characterisation of stray radiation

The suitability of investigated detector systems for relative dosimetry in UHPDR electron beams will be studied resulting in recommendations for the necessary correction factors. Furthermore, validated methods of relative dosimetry in emerging pre-clinical laser-driven beams will be investigated and published.

Stray radiation causes parasitic doses to healthy tissue and critical organs. It consists on a mix of different types of radiation. Traceable and validated methods for characterisation of stray radiation outside the UHPDR primary particle beam will be developed. Active detection techniques will be development by the optimisation of a custom-built detector type which is able to cope with short radiation pulses and to distinguish and characterise radiation components. A custom-built detector type will be optimised to enable active measurement and precise dose determination of pulsed neutrons, which are an unwanted component at high-energy laser-driven proton beams. A Best Practice Guide for the characterisation of stray radiation outside UHPDR beams will be published.

Codes of Practice

A protocol, i.e. a validated formalism (preferably by extending an existing Code of Practice) for traceable absorbed dose measurement in ultra-high pulse dose rate electron beams under reference conditions will be drafted and published. This protocol will be the basis of a future established Code of Practice for dosimetry at FLASH radiotherapy or for a future update or revision of an existing Code of Practice.

Impact

Impact on industrial and other user communities

The project will provide the metrological tools needed by (medical) physicists and radiobiologists to perform traceable dosimetric measurements in clinical or pre-clinical UHPDR particle beams. This will improve ongoing and future radiobiological, pre-clinical or clinical studies on the effect of UHPDR irradiations by ensuring a better comparability between studies carried out in different facilities as well as with conventional radiotherapy treatment modalities. Ultimately, it will allow to ensure that cancer patients who are treated by UHPDR particle beams receive the prescribed dose.

The definition of reference conditions for dosimetry in UHPDR particle beams together with the availability of well-characterised and optimised irradiation facilities, as results of this project, will allow manufacturers of detector and measurement equipment to characterise and calibrate existing and novel detectors for dosimetry of UHPDR particle beams. The increased knowledge gained in the project related to methods for precise measurement of absorbed dose to water in such beams will enable manufacturers to develop the necessary devices for safe clinical application of UHPDR particle beams in advanced radiotherapy. This will foster the competitiveness of European manufacturers of radiotherapy and dosimetry equipment.

Impact on the metrology and scientific communities

For reference dosimetry in conventional radiation therapy, several types of primary standards for absorbed dose to water are available (mainly water and graphite calorimeters are used), whose equivalency is regularly verified by international key comparisons organised by the BIPM (Bureau International des Poids et Mesures). Within this project the dose-rate limits of application of existing primary standards will be extended and new prototype calorimeters applicable in UHPDR particle beams will be developed. Additional international dosimetry comparisons might become needed and can be undertaken based on the facilities and primary standards adapted for UHPDR beams in this project.

The data and information obtained in this project related to the behaviour of secondary standards as a function of dose rate will support the development and improvement of theoretical models of the response of dosimetric detectors (e.g. charge recombination of ionisation chambers). It will generally lead to a better understanding and adequate theoretical description of the response of dosimetric detectors in UHPDR particle beams.

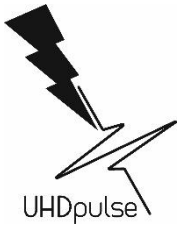
Impact on relevant standards

Dosimetry in conventional radiotherapy is done based on nationally and internationally standardised Codes of Practice (CoP), which are currently not applicable in UHPDR particle beams. In this project a metrological infrastructure and a validated formalism for dosimetry in UHPDR beams will be developed, which will contribute significantly to a future update or revision of the existing CoPs to extend their field of application. It will allow (medical) physicists and radiobiologists to perform dosimetric measurements in clinical or pre-clinical UHPDR particle beams at a level of uncertainty, which is comparable to the uncertainty achievable in conventional radiotherapy. The consortium's existing links with both national (IPEM, DIN) and international standardisation bodies (IAEA) provides an efficient route for the uptake of the results of this project in a future CoP for dosimetry in UHPDR particle beams. Furthermore, the close cooperation between hospitals, manufacturers of dosimetry equipment and national metrology institutes will enhance the uptake of such a CoP by the wider hospital community.

Longer-term economic, social and environmental impacts

Cancer incidence is expected to significantly increase due to the ageing of the European population. Approximately half of the cancer patients in Europe are treated by radiotherapy as it is one of the most cost-effective strategies in oncology. Therefore, innovation and clinical advancement in radiotherapy, such as FLASH radiotherapy, significantly contribute to the quality of life of a large group of European citizens by increasing long-term cancer survival (which is especially important for children) and reducing the occurrence and severity of early and late complications affecting normal tissue.

The research done in this project will contribute to the definitive demonstration of the feasibility of using laser-driven beams for therapeutic purposes, providing a large group of European patients with faster access to



more advanced, more cost effective, and safer radiotherapy treatments. In addition, this project will promote future industrial developments of laser-driven irradiation facilities.

Project start date and duration:	1 September 2019, 36 months	
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