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

Selected Research Topic number: **SRT-h12**
Version: 1.0

Title: Quality Assurance for online and real-time Adaptive Radiotherapy

Abstract

The advancement of image-guided radiotherapy (IGRT), especially the consolidation of diagnostic magnetic resonance (MR) scanners with linear accelerators (linac), has made real-time anatomical (and functional) imaging during the entire treatment possible. In online and real-time adaptive radiotherapy (ART) the patient's treatment plan is updated using feedback on patient-specific anatomic variations and previously delivered dose to provide an individual and optimised therapy regime. However, many quality assurance procedures established for conventional radiotherapy are no longer applicable to ART therapies, therefore new quality assurance procedures based on metrology methods are now needed to enable the greater adoption of adaptive radiotherapy.

Keywords

Quality assurance, adaptive radiotherapy, treatment planning, dose calculation, artificial intelligence, real-time imaging, image-guided radiotherapy, in-vivo dosimetry

Background to the Metrological Challenges

Approximately 2.7 million EU27 citizens had cancer in 2020, mainly due to the aging of the population, and roughly half of these underwent radiotherapy. Adaptive radiotherapy (ART) enables less invasive and more effective cancer treatments to be delivered compared to conventional radiotherapy and offers the potential for greater tailored radiotherapy and improved personal dose management. Considering the different timescales of changes to the patient's anatomy, ART can be implemented broadly over three timescales: offline between different treatment fractions, online immediately prior to a fraction, and in real-time during a fraction. While in offline ART the treatment plan is often modified by repeating, the same workflow as in conventional radiotherapy, online and real-time ART protocols modify the treatment plan while the patient remains on the couch. Because time is a very important limiting factor for online and real-time ART, a high level of automation (with no or very limited user interaction) is needed. Many guidelines and publications recommend machine- and patient-specific QA methods for conventional radiotherapy and these can be directly adopted for offline ART, but for online or real-time ART these are not usable mainly due to time restrictions for all QA measures. Furthermore, with the patient present on the treatment couch, it is impractical to perform measurement-based pre-treatment QA, for plan evaluation, and physics QA.

Adaptive radiotherapy workflows are highly complex and require thorough end-to-end tests in anthropomorphic phantoms before use in regular treatments. As imaging of deformed or moving anatomical structures is an essential part of adaptive radiotherapy, phantoms require anthropomorphic imaging contrast (e.g. in CT or MRI) as well as deformable or movable structures with integrated detectors. Furthermore, an accurate dose assessment of fractionated radiotherapy requires a dose accumulation for deformable targets or organs. For real-time ART, in which a time-resolved analysis is desired, additional challenges such as speed and latency come into play and require further evaluation using dedicated end-to-end testing, within which an adaptive workflow is fully integrated and system dependencies such as those relating to the image guidance and treatment planning systems as well as the QA system. The impact of the uncertainty in each step needs evaluation to identify the essential aspects of end-to-end testing in real-time ART.

Currently, the verification of conventional radiotherapy and offline ART treatment chains consists mainly of equipment checks and pre-treatment dosimetry measurements in phantoms. However, these cannot detect errors that may occur during individual patient treatment delivery. Therefore, *in vivo* dosimetry (IVD) methods that can detect treatment errors, assist in treatment adaptation, and record the actual dose delivered to the

patient are needed. Many types of point detector systems are available for IVD, but the usefulness of these measurements is limited for modalities delivering highly conformal dose distributions to the patient and these detectors have the potential to disturb the dose, are intrusive to the patient, and lack automation. Electronic portal imaging devices (EPID) are increasingly used for IVD in conventional and especially adaptive radiotherapy. Currently, commercial EPID dosimetry software products are available with vendor specific guidelines and system support. Independent guidelines are needed so users can verify the potential, limitations, and correct utilisation of EPID for IVD, and for the evaluation and performance comparison of such systems. Better uncertainty quantification and reduction of in vivo EPID dose measurements and investigations into alternative measurement techniques are needed to verify that EPID based IVD systems for assessing delivered patient dose lie within tolerance limits and that these limits have been robustly set.

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 traceable measurement and characterisation of patient doses delivered by adaptive radiotherapy and the development of quality assurance procedures to enable its greater uptake into clinical practice.

The specific objectives are

1. To develop recommendations on quality assurance equipment and procedure requirements for radiotherapies used in current clinical practice and to extend their applicability to dynamic real-time ART based on the investigation and development of metrological measurements for the comparison of equipment and procedures.
2. To evaluate and validate algorithms for the fast calculation and optimization of three-dimensional dose distributions in patients including the analysis of uncertainties based on methods of artificial intelligence (e.g., deep neural networks). This is to include a systematic verification of the algorithms for dose distributions of different complexity by measurements or Monte-Carlo simulations and the determination of their limits of applicability.
3. To develop a methodology for dynamic end-to-end tests in ART using at least one patient treatment regime by:
    a. the determination of the relevant aspects in the clinical workflow to be tested,
    b. the development and characterization of appropriate phantoms with movable and deformable inserts,
    c. the development of recommendations for 3D, planar and point dosimetry systems,
    d. the validation of dose accumulation methods in moving, deforming, and density changing volumes and
    e. the analysis of timing issues related to the ART workflow (e.g., frame rate of imaging, delays, time lags).
4. To prepare generally applicable quality assurance recommendations based on the methodology for dynamic end-to-end tests in ART developed in Objective 3 and the development of metrologically validated traceable *in-vivo* dosimetry (IVD) methods applicable in online and real-time adaptive radiotherapy, inclusive of measurement uncertainty determinations.
5. To facilitate the take up of the technology and measurement infrastructure developed in the project by the measurement supply chain (e.g., manufacturers of linacs, imaging systems, detectors, treatment planning software,), organisations developing standards and reference documents (e.g. ISO, IAEA), and end users (e.g. clinical stakeholders, manufacturers of medical and healthcare products).

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.

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.