EMPIR Call 2015 – Health, SI, Normative and Research Potential

Selected Research Topic number: **SRT-h18**
Version: 1.0

Title: Metrology for clinical implementation of dosimetry in molecular radiotherapy

Abstract

Molecular radiotherapy (MRT) is prescribed to patients on the basis of the maximum activity of the therapeutic radiopharmaceutical that has been shown in clinical trials to minimise the incidence of damage to critical normal tissues to less than an acceptable fraction of the trial population (typically 5 %). However the radiation doses received by individual patients vary hugely because of differences in uptake and retention of the therapeutic agent. The treatments could be improved dramatically by measurement of absorbed dose to the critical tissues on individual patients.

Keywords

Molecular radiotherapy; radionuclide dosimetry; dose inhomogeneity; absorbed dose uncertainty; traceable calibration, quantitative imaging.

Background to the Metrological Challenges

Molecular radiotherapy (nuclear medicine therapy) is conventionally prescribed to patients on the basis of the maximum activity of the therapeutic radiopharmaceutical that has been shown in clinical trials to minimise the incidence of damage to critical normal tissues to an acceptable fraction of the trial population (typically 5%). This implies that the other 95% potentially could have received a higher activity and therefore a more effective treatment. Treatment planning based on individual patient dosimetry is clearly desperately needed.

A critical element that is lacking is a strong metrology driven standardised dosimetry protocol that can be used in multi-centre clinical trials and accepted as the new standard practice.

The current state-of-the-art of dosimetry for external beam radiotherapy (photons, protons, and heavy ions) and brachytherapy, is to use an internationally agreed dosimetry protocol giving traceability to primary standards of absorbed dose, and agreed standard practice for commissioning and using patient treatment planning systems. No such protocols or standard practice exist for MRT.

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 metrology research necessary to provide a standardised and harmonised European framework for clinical implementation of dose planning in molecular radiotherapy (MRT).

The specific objectives are

1. To develop more accurate and metrologically traceable activity measurements with reduced uncertainties of therapeutic and imaging radionuclides including both beta- and alpha-emitters. Exploit new technologies to develop a suitable transfer instrument for measurements of activity to be used in clinics. Branching ratios and emission probabilities for the chosen radionuclide(s) should be determined for improved quantitative imaging accuracy and dose estimation.
2. To develop methods for more accurate and harmonised quantitative multimodal imaging by

EURAMET MSU, Hampton Road, Teddington, Middlesex, TW11 0LW, UK
Phone: +44 20 8943 6666 Email: msu@npl.co.uk
msu.euramet.org

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(i) development of 3D printings method to generate biologically equivalent phantoms with heterogeneous activity distributions with a range of geometrical complexity for validation of multimodal imaging used for dose planning of MRT treatments

(ii) development of a reference database of images of phantoms that are universally readable and by the development of measurement protocols for in-clinic validation measurements.

3. To improve the accuracy and metrological traceability in the calculation of dose from activity-time distributions: refinement of absorbed dose standards; validation of alternative calculation methods in phantoms and patients by employing novel 3D detection techniques of dose distribution using measurements and Monte Carlo simulations.

4. To determine uncertainties in relation to the full MRT dose measurement chain from activity administration to the patient; image quantification including uncertainties in the selection of volumes of interest and image reconstruction; interpolation/extrapolation and integration of activity-time curves and determination of the overall evaluated uncertainty in the absorbed dose quantification process by application of Bayesian approaches.

5. To facilitate the take up of the technology and measurement infrastructure developed by the project by healthcare professionals (clinical centres) and industry (scanner manufacturers and software developers).

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. In particular, proposers should outline the achievements of the EMRP project HLT11 MetroMRT (Metrology for molecular radiotherapy) and how their proposal will build on those.

EURAMET expects the average EU Contribution for the selected JRPs in this TP to be 1.8 M€, and has defined an upper limit of 2.1 M€ for this project.

EURAMET also expects the EU Contribution to the external funded partners to not exceed 35 % of the total EU Contribution to the project. Any deviation from this must be justified.

Any industrial partners that will receive significant benefit from the results of the proposed project are expected to be unfunded 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,
- Transfer knowledge to the nuclear medicine therapy sector.

You should detail other impacts of your proposed JRP as specified in the document “Guide 4: Writing a Joint Research Projects (JRPs)”.

You should also detail how your approach to realising the objectives will further the aim of EMPIR 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.