EMPIR Call 2018 – Health, SI Broader Scope, Normative and Research Potential

Selected Research Topic number: **SRT-h17**
Version: 1.0

Title: Improved methods for activity measurement and distribution in patient for personalised nuclear medicine

Abstract

Malignant tumour diseases (i.e. cancer) are the cause of death for approximately two million people per year in Europe. Lowering this number is a priority, however the use of radiopharmaceuticals requires a reliable basis for accurate and traceable activity measurements before treatment of a patient in accordance with the European Pharmacopoeia, EU Directive 2013/59/ EURATOM and European Association of Nuclear Medicine (EANM) and International Atomic Energy Agency (IAEA) guidelines. Nuclear medicine is one of the main treatment options for cancer patients, however both emerging radionuclides and even some established radionuclides used in nuclear medicine clinics, lack traceable nuclear data. Further to this improved activity measuring devices that are more suitable for on-site use are needed to enabling traceable on-site activity measurement of radiopharmaceuticals and radionuclide impurities. This will enable more accurate radiopharmaceutical measurements hence treatment of patients.

Keywords

Nuclear medicine, cancer treatment, activity measurement, activity distribution, nuclear data

Background to the Metrological Challenges

Currently in nuclear medicine, activity measurements for a number of established and prospective diagnostic and therapeutic radionuclides are based on calibration factors provided by measuring instrument manufacturers, or calibration factors simply estimated from other factors with similar decay schemes e.g. ^{15}O and ^{13}N. Such measurements are not traceable to primary standards and thus, the requirements of the European Pharmacopoeia or EU legislation are not met.

Radionuclide impurities, including very harmful long-lived pure beta or alpha emitting radionuclides, are currently stated only by radiopharmaceutical producers. These stated values are often not supported by reliable measurements, as the required low limits of 10^{-7} % cannot be reached due to a lack of metrological knowledge and the need for advanced sensitivity measurement techniques. For the same reasons, clinical 'in-house' preparation of novel radiopharmaceuticals suffers from a lack of accurate measurements.

Problems with patient monitoring during or after nuclear medicine treatment are predominantly caused by insufficient on-site measuring systems that cannot cover the wide range of activity measurements (i.e. from kilobecquerels to gigabecquerels (Gbq)) and do not enable sufficiently sensitive measurement of spatial activity distribution. For example, after radionuclide treatment with I^{131} for thyroid gland cancers, current devices cannot measure Gbq activity levels or are available immediately after the injection of the radiopharmaceutical. Therefore, only the later part of the activity curve describing the activity retention in a patient's body as a function of time can be determined and hence the estimated dose calculation suffers from high uncertainty levels. In addition, current methods require patients to be moved/relocated to where the device is for each consecutive activity measurement for several days after treatment, which can be uncomfortable, impractical and stressful for them. To address this, continuous measurement of spatial distribution of respective radionuclide together with improved spatial resolution is needed for the accurate determination of patient dose, particularly in treated organs. This could be done by using a wireless network of integrated detectors, worn by patients, with on- line communication to an evaluation unit. Such a patient worn system would enable more effective and accurate treatment planning as well as supporting personalised nuclear medicine treatment and patient comfort.

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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 traceable activity and distribution measurements in patients, for personalised nuclear medicine.

The specific objectives are

1. To develop SI-traceable and accurate methods for 'true' patient dose for radionuclides used in nuclear medicine. This should include short-lived radioisotopes with half-lives of the order of minutes (e.g. ^{11}C, ^{13}N and ^{15}O), inhaled radiopharmaceuticals (e.g. $^{11}CO_2$ and $^{15}O_2$), and a range of measuring geometries. In addition, to transfer this traceability from primary to secondary instrumentation, such as gas-filled re-entrant ionisation chambers, using validated Monte Carlo calculations.
2. To determine accurate nuclear decay data and to establish new activity standards for existing nuclear medicine radioisotopes (e.g. PET radionuclides, ^{11}C, ^{13}N, ^{15}O, ^{64}Cu, ^{68}Ga, and ^{124}I), emerging radioisotopes (e.g. PET/SPECT and theranostic isotopes/isotope pairs, $^{61}Cu/^{67}Cu$, $^{44}Sc/^{47}Sc$, $^{66}Ga/^{67}Ga$, ^{76}Br, ^{82}Rb, $^{90}Y/^{86}Y$, ^{89}Zr and ^{94m}Tc) and radionuclides used for preclinical research (e.g. palliative medicine, tumours and/or metastases treatment, ^{186}Re, ^{161}Tb and ^{212}Bi). The nuclear decay data should include half-lives and emission probabilities for photons and alpha- or beta- particles. The list of radionuclides must be agreed with nuclear medicine stakeholders.
3. To develop a reliable and accurate measurement system for the monitoring of patients during and after nuclear medicine treatment, for both the time dependency and spatial distribution of activity in a treated organ. The target uncertainty for time dependency is <10 %, for activity levels up to gigabecquerels. For spatial distribution, the resolution should be significantly better than current nuclear medicine systems (e.g. gamma cameras).
4. To evaluate the performance of current nuclear medicine systems based on pixelised detectors. Then using the results of this, objective 3 and input from nuclear medicine stakeholders, to develop an integral nuclear medicine system. This system should be wirelessly connected to the evaluation unit, thereby enabling patient comfort and treatment optimisation (e.g. for thyroid cancer treatment or bone metastases localisation.
5. To facilitate the take up of the technology and measurement infrastructure developed in the project by the measurement supply chain, standards developing organisations (e.g. those associated with EU Directive 2013/59/EURATOM, and guidelines of the European Association of Nuclear Medicine (EANM) and International Atomic Energy Agency (IAEA)) and end users (e.g. clinicians, nuclear medicine clinics, PET centres, radiopharmaceuticals producers and instrumentation manufacturers).

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, 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 1.8 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 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 medical and health 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 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.