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

Selected Research Topic number: **SRT-h09**
Version: 1.0

Title: Metrology for multi-modality imaging of impaired tissue perfusion

Abstract

Cardiovascular Disease (CVD) is the leading cause of death in the EU. Accurate and non-invasive measurement of the tissue's blood support (perfusion) using different imaging techniques is important for selecting optimal therapy for the patient. Although significant work has been done to develop quantitative perfusion, its broad clinical application is lacking. Proposals in response to this SRT should aim to develop and establish a metrological framework for accurate, reproducible and comparable perfusion measurements to establish quantitative perfusion imaging for various disease areas.

Keywords

Perfusion, ischemic heart disease, multi-centre studies, multi-modality imaging, quantification

Background to the Metrological Challenges

Physiologically, perfusion describes the process of delivering blood to an organ's microcirculation, allowing exchange of gases and nutrients. Impaired or enhanced perfusion plays a key role in many diseases. Ischemia (low perfusion) often results in an insufficient delivery of oxygen to the tissue, which has significant impact on energy metabolism, and increased perfusion is often seen in cancer and inflammatory diseases.

Quantitative assessment of perfusion is required in many CVDs, such as stroke or ischemic heart disease, which are based on low blood support. Perfusion imaging is well-established for assessing the extent of ischemia and all medical imaging modalities are used to assess coronary artery disease (X-ray angiography, single photon emission computed tomographic (SPECT) imaging, positron emission tomography (PET), ultrasound, computed tomography and cardiovascular magnetic resonance (CMR) perfusion). All perfusion imaging techniques require the injection of contrast agents, but a comparison of different protocols within one imaging modality and cross-modality validation is challenging and in most cases assessment of the acquired imaging data is performed qualitatively by visual inspection of images, making the comparison between imaging modalities difficult.

Over the last decade, significant work has been performed on developing reliable quantification techniques, but so far this has not been adopted into clinical routine. One main reason is the lack of standardisation of analysis methods. Reproducibility studies and cross-modality comparisons of imaging techniques in patients are challenging, requiring the need for standard phantoms to be used for assessing reproducibility of perfusion imaging techniques. For all imaging techniques, the availability of a direct comparison between imaging data and reference values of flow and perfusion is key for quality assurance in clinical practice.

One perfusion phantom does allow reliable, reproducible and efficient simulation of myocardial perfusion using MRI and is capable of simulating the process of first-pass perfusion in a highly reproducible way between different sessions and operators to provide a true physical validation of quantitative perfusion methodologies. This has also been used in assessing perfusion with computed tomography and is of great importance for the development of new acquisition protocols to minimise contrast agent dose while maintaining image data quality for quantification. However, distribution dynamics of the contrast agent in the myocardial compartments of the phantom only simulate the physiological appearance of the signal intensity curves and do not involve diffusion of the contrast agent from vascular to interstitial space, as would occur *in vivo*. There is also a need to develop a phantom that can be used to measure perfusion with ultrasound, SPECT and PET. The development of such a phantom will allow cross-modality validation of measurements, validation of existing and novel quantification methods and will provide an international standard in perfusion imaging as part of quality assurance in clinical imaging centres.

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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 the traceable measurement and characterisation of multi-modality perfusion imaging to and provide accurate, reproducible and comparable perfusion measurements of impaired tissues.

The specific objectives are

1. To develop a standard phantom for multi-modality perfusion imaging and measurements of flow-rates. This should consist of a two-compartment hardware model to simulate realistic perfusion situations.
2. To develop a methodology to quantitatively analyse perfusion data. This should include methods for accurate calibration measurements and advanced corrections (such as attenuation and scatter correction) with corresponding uncertainty assessment.
3. To evaluate a perfusion imaging comparison of different medical imaging modalities using a two compartment standard phantom. This should include evaluating different measurement and quantification techniques and comparing their accuracies and uncertainties.
4. To develop methodology for personalised dosimetry in medical imaging with ionising radiation. This should focus on limiting the high radiation dose to the patient.
5. To facilitate the take up of the perfusion imaging standard phantom and methodologies developed by the project by clinicians and industry in order to promote their use in clinical multicentre trials and improve patient treatment options.

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 1.8 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 multi-modality imaging 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.