

Title: Towards the quantification of medical images in terms of physical quantities

Abstract

Clinical imaging is a hugely powerful tool in medicine. Despite this, image assessment is normally restricted to a qualitative operator-dependent assessment of tissue structures through visualisation of image contrast, which greatly reduces diagnostic accuracy. A theoretical and experimental underpinning to support imaging based on absolute, traceable tissue properties, would result in a paradigm shift in imaging capability to support the comparison of images with time, across patients and different types of instrumentation, leading to advances in the sensitivity and specificity of clinical diagnosis.

Keywords

Physical quantity imaging, quantitative medical imaging, Maxwell-Bloch simulations, magnetic resonance fingerprinting, tissue properties, ultrasound attenuation

Background to the Metrological Challenges

Imaging techniques (such as x-ray, magnetic resonance imaging (MRI), positron emission tomography (PET) and ultrasound) are a major weapon in the fight against disease, but are often limited to detecting structural changes and quantitative measures of tissue characteristics and are often difficult to interpret. Subtle differences in tissue properties (defining tissue pathologies) are often masked by unknown details of the imaging processing, equipment type or settings and lead to errors in diagnosis.

Physical quantitative imaging (PQI) works on any imaging modality and generates images based on the physical quantities of tissues (e.g. viscoelasticity), making each image pixel a measurement with its own value, unit and uncertainty and delivering images independent of operator, method or instrument employed. Transforming imaging into a measurement introduces established metrological standards and PQI can extend the scope of metrology into biomedicine.

FDA-approved ultrasound scanners generate 3D maps of sound, speed and attenuation, but are subject to artefacts. There has been rapid growth in the development of ultrasound-applied elastography to determine and image tissue stiffness. However, observed system dependent variations in elastographic measurements limit the clinical utility of these measurements and introduce uncertainties.

State-of-the-art clinical MRI is through non-quantitative “weighted” measurements and although PQI methods do yield quantitative maps of tissue, electrical properties of the tissues and/or equipment are often incompletely assessed. Validated numerical techniques quantitatively simulate the human body’s electromagnetic field distribution based on the conductor geometry of an MRI scanner’s radio-frequency (RF) coil; and MR images based on sequence parameters, like gradient and RF pulses, can also be calculated, but attempts to combine both have not yet been reported.

The ‘fingerprinting’ concept works by retrieving tissue properties with high signal-to-noise ratio (SNR) from a prefabricated database and accelerates measurements by orders of magnitude without SNR penalty. The sparse information of measurement outcome is amended by information from a pre-calculated dictionary. Initially fingerprinting was invented for MRI, but strategies are now needed to extend it to other modalities.

A reference phantom for MRI relaxation times has been developed, but the value of phantoms with relatively large compartments of homogeneous material for *in-vivo* determinations of the same quantities remains limited and validated reference methods for this purpose are required. Across all imaging modalities, efforts to state the uncertainties of existing PQI techniques are currently under-developed or do not yet exist. Proposals in response to this SRT should aim to advance and metrologically underpin PQI.

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 fast PQI to allow machine independent quantitative measurement of biological images based on the specific physical quantities of the tissues.

The specific objectives are

1. To develop and validate mathematical models to quantitatively describe MRI generation. These should be based on tissue properties and known hardware geometry, independent of the sequence or scanner type.
2. To develop fast PQI techniques with a high signal-to-noise ratio. This should be based on advanced statistical techniques and include detailed implementation of the novel magnetic resonance fingerprinting concept to general quantitative medical imaging.
3. To develop and validate standard ultrasound phantoms based on tissue-like materials and develop and validate ultrasound measurement techniques for key physical properties, such as ultrasound speed of sound, attenuation and viscoelasticity (of tissues and tissue-like materials). The phantoms should be simple, anthropomorphic and span a range of observations for different tissue pathologies; and the ultrasound measurement techniques should be applicable to *in-vivo* and *in-vitro* applications and validated by cross-centre comparisons.
4. To develop an uncertainty budget for ultrasound physical quantity imaging. This should include theoretical underpinning of MR fingerprinting and robust statistical methods for quantifying uncertainties of tissue and material properties.
5. To facilitate the take up of PQI techniques developed in the project by clinicians and industry in order to promote their use in clinical trials and support improved medical diagnostic imaging.

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 medical 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.