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

Selected Research Topic number: **SRT-h05**
Version: 1.0

Title: *In vivo* quantitative magnetic resonance imaging of tissue relaxation and dielectric properties

Abstract

Quantitative magnetic resonance imaging (MRI) techniques represent the foundation of a paradigm change in medical imaging, as they provide objective tissue parameters that can be used as biomarkers. Some of these techniques have been already experiencing a rapid development, through studies aimed at characterising and optimising the overall quality of the reconstructed maps. However, what they still lack is a metrological framework that moves the uncertainty evaluation to the pixel level and allows to reliably quantify their diagnostic effectiveness *in vivo*. Therefore, there is a need for building a framework for a selection of emerging, high-impact, quantitative MRI techniques.

Keywords

Magnetic Resonance Imaging (MRI), quantitative Imaging, tissue relaxation, dielectric properties, uncertainty evaluation.

Background to the Metrological Challenges

The trend from qualitative to quantitative medical imaging is a radical and general innovation in radiology, promoted by the European Society for Radiology (ESR), that supports the European Imaging Biomarkers Alliance (EIBALL), and by the Radiology Society of North America (RSNA), that established the Quantitative Imaging Biomarkers Alliance (QIBA). This is motivated by the strong potential of quantitative imaging for diagnostic purposes and subject-specific treatment planning and monitoring (e.g., for radiotherapy).

Since each pixel in a quantitative image represents a measured biomarker, an uncertainty evaluation carried out at local level is essential to quantify its real predictive value. For T1-mapping, MRF and EPT, this kind of characterisation is still at its infancy. A full development is required to enter clinical practice, contribute to precision/personalised medicine (which is considered a top priority in the EU) and achieve greater impact. Besides harmonisation in the metrics used to assess the reliability of quantitative MRI results, common publicly available databases are needed for calibrating the optimal parameters of the reconstruction algorithms and for comparing different approaches. Such databases must include a large amount of data collected *in vivo*, to fully catch the complexity of the problem.

During the biophysical parameter's measurement chain, many sources of uncertainty (e.g. noise and inaccuracies due to hardware limitations or physiological motion) occur. Commonly, the propagation of this uncertainty is neglected, e.g., noise or artefacts in the reconstructed images are not taken into consideration during the parameter estimation. Nevertheless, there is a clear clinical need to provide this information for the sake of interpretability, to evaluate robustness, and for quality control. For instance, the Society for Cardiovascular Magnetic Resonance recommends that *image quality should be reviewed during acquisition (e.g., by monitoring sequence sounds and electrocardiographic (ECG) gating), and by looking at source images, error maps, and other quality control maps)*. Hence, strategies to monitor the propagation of the uncertainty from the raw data to the quantitative parametric maps are required to assess the perturbation introduced along with the input, and decide, automatically, if they can impair the reliability of the results.

The relaxation and dielectric properties of tissues, measurable through the emerging quantitative techniques selected in this proposal, have already proven to be effective biomarkers. For instance, changes in the relaxation times have been associated with adverse effects produced by radiation therapy in the myocardium of patients with breast cancer. Similarly, previous studies have shown that the electric conductivity is significantly different between benign and malignant lesions and can be used to differentiate them. Despite this, apart from initial attempts, extended and detailed databases of input data suitable for testing MRF and

EPT algorithms are still not available. In addition, at the state of the art, the quality of the parametric maps is evaluated a posteriori, independently of the input features. Knowledge of how common MRI artefacts affect the parameter quantification is desirable to make the process more efficient. It would allow checking the quality of the input, evaluating automatically whether they are suitable to provide reliable results and allowing corrections, when possible. Finally, even if *in vivo* applications of the selected techniques have appeared in the scientific literature in recent years, a systematic collection of test-retest acquisitions, fundamental to quantify their level of repeatability, is almost completely missing.

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 development of metrology capability in developing a comprehensive framework to associate a pixel-wise uncertainty value to the quantitative parametric maps obtained through Magnetic Resonance Imaging (MRI) techniques and, to provide the groundwork for a standardised approach, fully conceived in a metrological perspective, for developers and users.

The specific objectives are:

1. To develop an approach to associate a pixel-wise uncertainty to the quantitative maps such that each single pixel-wise quantification of the investigated parameters becomes a measurement result, in the strict metrological sense. To tailor and cover different possible approaches to quantitative imaging, including regressions, Bayesian approaches and data driven approaches (machine/deep learning).
2. To create a public database of reference MRI data, which should allow researchers to calibrate the selected techniques and study the propagation of the uncertainty using common (synthetic and experimental) data.
3. To develop sensitivity analysis strategies to monitor the uncertainty propagation from different uncertainty sources in the raw data towards the diagnostic parametric maps. To assess the effect of perturbations in the acquired raw data (e.g., due to hardware limitations or physiological motion) on parametric maps and model uncertainty.
4. To test the stability of MR-based quantitative imaging *in vivo*, checking whether the repeatability and reproducibility of the measurement is consistent with the predicted uncertainty and hence if this repeatability, reproducibility, and uncertainty allows to reliably identify long-term changes within a subject.
5. To facilitate the take up of the technology and measurement infrastructure developed in the project by clinical community, associations that work to standardise quantitative MRI and the MRI manufacturers as well as to address the sustainability and the awareness raising of the public database.

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 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 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.