Publishable Summary for 18HLT05 QUIERO
Quantitative MR-based imaging of physical biomarkers

Overview

With more than 30 million scans per year in European countries, Magnetic Resonance Imaging (MRI) is one of the most important tomographic tools adopted in clinical practice. Nevertheless, standard MRI results mostly had a qualitative nature, to be interpreted by a specialist on visual inspection, that limited their objectivity and comparability. The project evaluated the suitability of two promising MR-based techniques, **Electrical Properties Tomography** (EPT) and **Magnetic Resonance Fingerprinting** (MRF), to bring a "quantitative revolution" in MRI, so that each image pixel could be associated with the measurement (including uncertainty) of one or more tissue parameters.

The project implemented EPT and MRF algorithms (some of which were distributed as open source software), characterized them both on synthetic data and on the phantoms developed in the project itself, and used such algorithms to identify minimum thresholds for the detection of a selection of brain and cardiac pathologies.

Need

Traditional MRI was qualitative and MRI results obtained at different times and locations were difficult to compare. In addition, conventional MRI could not provide direct information about the nature of the pathology. The development of quantitative imaging approaches like EPT and MRF started some years ago with the aim to eliminate interobserver variability and reduce the need for invasive procedures (e.g. biopsies). The idea behind this field of research was to enable new biomarkers to be identified and boost early disease detection, optimising the clinical path, improving the quality of life of patients and reducing the associated economic burden.

At the beginning of the project, a comprehensive characterisation of the reliability of EPT and MRF procedures had not yet been achieved. To start considering their clinical use, the medical community needed to know the level of confidence associated with EPT and MRF results, but this required a systematic analysis of their performance.

In particular, a specific characterisation of EPT and MRF was required for those contexts that have significant implications for health and, at the same time, are challenging from the imaging viewpoint (e.g. the cardiac region, where the physiological motion of the tissues affects the image acquisition).

Characterisation of EPT and MRF in terms of repeatability and reproducibility required artificially constructed test objects, known as "phantoms", with traceable, validated, and monitored components.

For *in vivo* applications, the physiological variability of parameters from subject to subject (which could act as a misleading element in the diagnostic phase) required to be carefully evaluated. From this viewpoint, the possible synergy between EPT and MRF, and the use of artificial intelligence to analyse the corresponding biomarkers, were worth exploring to maximise the diagnostic power of quantitative MRI.

Objectives

The overall objective of the project was to promote the development and possible combination of EPT and MRF, two MR-based techniques able to produce objective, quantitative and traceable images, and their adoption in clinical practice through a systematic characterisation of their reliability.

The specific objectives of the project were:

1. **To develop, improve and implement numerical algorithms for use in EPT and MRF and to characterise their performance**. For EPT, both local relationships and global inversion methods were considered and compared; for MRF, statistical template-free methods were evaluated as an alternative to traditional dictionary-based techniques.

2. **To make EPT and MRF suitable for practical use in the analysis of "high impact" clinical conditions**. Basic EPT techniques had to be improved to handle the partial knowledge of the phase of the magnetic field and mainly applied to the analysis of diseases that cause significant changes in dielectric properties (e.g. cerebral ischemia). The application of MRF to the heart region required methods able to suppress artefacts caused by physiological motion and moving fluids.

3. **To evaluate the accuracy of EPT and MRF procedures in magnetic resonance experiments under controlled conditions**. Heterogeneous phantoms, composed of soft semisolid materials mimicking the properties of human tissues (e.g. conductivity, relative permittivity, longitudinal and transverse relaxation times in the order of 1 S/m, 50, 1000 ms and 50 ms respectively), had to be specifically developed and used for this purpose. The target uncertainties were 20 % for EPT and 10 % for MRF.

4. **To fully characterise EPT and MRF as diagnostic tools under real-world conditions**, including determining, for the target organs selected, the inter- and intrasubject physiological variability and minimum threshold for the detection of anomalies due to diseases. The variability of tissue properties had to be taken into account and advanced statistical techniques and *in vivo* assessments applied. The synergistic use of EPT and MRF was worth exploring to optimise diagnosis, and specific computer-aided diagnostics approaches had to be developed.

5. **To facilitate the take up of the technology and measurement infrastructure developed in the project** by the measurement supply chain (accredited laboratories, MRI manufacturers), the relevant technical committees and end users (e.g. hospitals and health centres).

Progress beyond the state of the art

Most authors of EPT and MRF algorithms had the exclusive use of their computational codes. This consortium implemented its own codes, some of which were released as freeware. This allowed comparison of the performance of different EPT/MRF approaches under identical conditions and their characterisation against synthetic data.

Traditional EPT and MRF implementations were not fully suitable to tackle the specific technical challenges required by some "high impact" pathologies (e.g. cerebral and cardiac diseases). The project consortium worked to overcome such restrictions, by producing: 1) MRF procedures designed to address the heart motion and novel approaches that do not require a pre-calculated "dictionary" of MR signals; 2) more efficient EPT implementations. In addition, the possibility to "hybridise" the two techniques was explored during the project.

Most commercial test objects (phantoms) did not (and still do not) replicate the heterogeneity of real tissues. Moreover, metrological support for characterisation of tissue mimicking materials and MRI phantoms was quite limited. The project improved this unsatisfactory state of the art, through the preparation and characterisation of materials that mimic realistic tissue properties and the development of 3D-printed anthropomorphic phantoms. Such phantoms were used to test EPT/MRF algorithms multiple times both in the same scanner and in different scanners, to obtain a characterisation of the results in terms of repeatability and reproducibility.

To reach clinical maturity, EPT and MRF should be able to spot anomalous values of the parameters in the presence of a physiological variability. Therefore, *in vivo* acquisitions were performed in the project to quantify the dispersion of the parameters in healthy humans. Then, this information was exploited to evaluate the suitability of the investigated parameters to act as biomarkers. Moreover, the project explored the use of artificial intelligence to interpret the distribution of such biomarkers automatically.

Results

Objective 1: Development, improvement and implementation of numerical algorithms for use in EPT and MRF and their characterisation

In order to test the EPT and MRF algorithms, a number of digital models (both phantoms and anatomical models, with focus on the brain and heart regions) were prepared and used to perform realistic simulations involving body coils (at 1.5 T or 3 T) or a head coil (parallel transmission at 7 T). The obtained transmit and receive sensitivities, in turn, were used to perform Bloch simulations.

For MRF, dictionary-based methods were implemented, using both Bloch simulations and the Extended Phase Graph (EPG) formalism. Moreover, a new technique that estimates the parameters (in particular, the relaxation times) directly from "k-space" (i.e. raw MR data) was implemented. In addition, the project developed a specific Bayesian MRF approach that provides a whole probability distribution for the relaxation times, and hence their uncertainty. Analysis of the implemented MRF methods showed that k-space–based approaches were promising and improved the estimation at low signal-to-noise ratios, but they still required reconstruction times that were too long to be readily adopted into clinical practice. In terms of accuracy and precision, a parametric analysis of the performances of the MRF techniques showed that a combination of high maximum flip angles without T2 preparation pulses was able to produce accurate T1 and T2 estimation.

The project developed *EPTlib*, an extensible, open-source, C++ library collecting the EPT methods that were under study within the project itself. The library was made publicly available through an open-access repository on GitHub and, for the first time ever, gave access to open implementations of EPT algorithms. *EPTlib* contains implementations of the Helmholtz-EPT (H-EPT), the convection-reaction-EPT (CR-EPT) and the gradient-EPT (gEPT). To have a benchmark to test the EPT algorithms, a novel tool (called *b1map-sim*), able to produce synthetic B1-mapping and generate realistic MR acquisitions, was also made available. The implemented algorithms were characterised through virtual experiments. Their intrinsic bias was evaluated with different choices of the operative parameters to determine the set of parameters that provide the best results. Finally, the propagation of the uncertainty when the techniques were applied with the selected optimal parameters was assessed. In addition to traditional EPT approaches, a technique that estimates the dielectric properties from T1 maps (exploiting their correlation with the water fraction) was implemented. As a collateral outcome of the research on EPT, the possibility to estimate subject-specific local SAR based on B1-mapping sequences and EPT algorithms was investigated at 1.5 T. The investigation showed that it is possible to obtain satisfactory results using a suitable tissue-dependent correction factor, preliminarily calibrated based on numerical results. The robustness of this correction factor in the presence of noisy input was also assessed.

Having these results, the project successfully achieved the objective.

Objective 2: Making EPT and MRF suitable for practical use in the analysis of "high impact" clinical conditions

Based on a preliminary analysis, fast gradient echo sequences, improved by suitable preparation pulses, were selected for cardiac MRF acquisitions of the relaxation times, because they allowed for fast imaging, were robust to field inhomogeneity and applicable at different field strengths. A study on the effect of different cardiac and respiratory motion types on the accuracy and precision of the estimation of T1 and T2 was carried out using a simulation software developed in the project, published as an open-source software package on GitHub together with a range of different open-source tutorials written as Jupyter Notebooks. Different non-rigid respiratory and cardiac motion fields were included into the numerical MRF simulations, using this information to transform the underlying anatomy during the acquisition. A motion-correction approach (able to correct for cardiac motion and minimise motion-related artefacts for a wide range of different heart rates) was developed. Cardiac triggering combined with breath holding was identified as the most reliable reference method for cardiac parameter mapping.

B1-mapping based on MRF was checked. The quality of the maps, especially in the presence of cardiac/respiratory motion artefacts, was too low to be used to perform EPT, which is very sensitive to input noise. However, since MRF can provide information useful to improve the EPT reconstructions (in particular, an independent segmentation of the tissues), *EPTlib* was equipped with a specific post-processing algorithm.

To explore the possibility of using EPT results in the brain and MRF results in the heart to detect pathologies, specific populations of virtual human models were developed, including both healthy and pathological models (with pathologies of the white matter in the brain or cardiac fibrosis in the heart). For both EPT and MRF, the reconstructions were performed on synthetic data intentionally corrupted by the presence of noise. Traditional statistical approaches were applied to study the capability of the techniques to identify lesions, using the area-under-curve metric as a performance indicator. CR-EPT performed satisfactorily, while MRF produced good to excellent classifications. Moreover, a Convolutional Neural Network (CNN) was implemented to classify the quantitative maps, obtaining good results when applying it to MRF data. On the contrary, the large amount of noise did not allow using the CNN for EPT. Hence, a smart post-processing approach, based on the combined use of H-EPT and CR-EPT, was developed, obtaining good classification performance.

Having these results, the project successfully achieved the objective.

Objective 3: Evaluating the accuracy of EPT and MRF procedures in magnetic resonance experiments under controlled conditions

A protocol for the preparation of phantoms was developed and used to produce simple-geometry homogeneous and heterogeneous phantoms, exhibiting dielectric and relaxation properties similar to those of the white and grey matter. Then, a new generation of brain phantoms with anthropomorphic structures (some of which included "pathological lesions") was produced. In particular, one biphasic anthropomorphic phantom was realised using realistic 3D-printed brain-shaped moulds. In addition, tools and strategies for the realisation of a low-cost soft-matter printer were developed and conducted, and a new 3D printer (equipped with two pneumatic valves, extrusion modules, additional motor axes and 30 ml-cartridge holders) was developed. After a preliminary test using a blend based on alginate/hydroxycellulose for setting printing conditions, several large phantom samples consisting of one or more material phases were prepared, with dimensions up to 100 mm x 60 mm x 44 mm. In particular, using the new printer, a larger biphasic brain-shaped phantom was printed and characterised. Finally, a triphasic 3D-printed phantom, including a hydrogel grey/white matter structure in combination with 350 mL of $CaCl_2$ solution mimicking the cerebrospinal fluid, was built.

The characterisation of the relaxation times of the tissue mimicking materials adopted in the phantoms was carried out using both MRI scanners and spectrometers. At the same time, the characterisation of the dielectric properties was performed through the measurement of their complex electrical reflectance over the frequency range 50 MHz – 300 MHz. Added value was introduced in these characterisations in the framework of a research mobility grant, by repeating the measurements at different temperatures. In order to monitor the stability of the tissue mimicking materials, the measurements were repeated periodically, showing, to a large extent, a good stability over relatively long times for both dielectric and relaxation properties.

The implemented EPT and MRF algorithms were applied to MRI data acquired on the phantoms mentioned above. For EPT, despite some artefacts (ascribable to the relatively small size of the phantoms), the average value of the estimated conductivity was within the range of the expected values. In the case of the brain mould-based phantom the artefact was not present, the EPT map allowed to recognize precisely the boundary between the two compartments and the measured data were in good agreement with the expected values. For MRF, the relaxation results obtained in different sites of simple mould-based phantoms were in good agreement with each other. Larger variations were observed when scanning the 3D-printed anthropomorphic phantoms, probably because of their much more heterogeneous structure (due to the printing process).

Having these results, the project successfully achieved the objective.

Objective 4: Full characterisation of EPT and MRF as diagnostic tools under real-world conditions

The clinical study of brain diseases involved 53 patients (five of which underwent two different MR sessions) and 32 age-matched healthy controls, scanned at 1.5 T. Ten patients were also scanned at 7 T. MRF data of these subjects were acquired and used to perform water-content-based EPT starting from T1 maps. In addition to this clinical study, 3D MRF maps of twelve healthy volunteers were obtained in the framework of a repeatability/reproducibility study involving eight different sites (1.5 T and 3.0 T scanners, single vendor). Each subject/site dataset included two acquisitions, to assess repeatability of the measurements. The analysis of these datasets demonstrated high repeatability and reproducibility in grey and white matter. The corresponding parametric maps are publicly available in QUIERO's repository on Zenodo. After segmentation of the EPT data, the median conductivity of white and grey matter was calculated. In healthy people, it was observed that the evolution with the age of this parameter can be modelled through an exponential decay. A statistical analysis provided a quantification of the intra- and inter-subject variation of the calculated conductivity. Correcting the effect of the age in the data allowed to quantify a significant patient-control effect and a threshold for the detection of anomalies in white matter with 95 % confidence level.

The clinical study of heart diseases involved four healthy volunteers (two at 1.5 T and two at 3 T) and 15 patients (all at 3 T). The patient cohort included 7 people with hypertrophic cardiomyopathy, 4 with muscular dystrophies and 4 with severe aortic stenosis. Both conventional and MRF-based mapping acquisitions were carried out. Also in this case, the intra- and inter-subject variability of the parameters was calculated and thresholds for the detection of pathologies based on T1 and T2 values were identified.

To evaluate the possibility of using EPT and MRF maps for the automatic detection of pathologies, various machine learning approaches were tested. Unfortunately, for both techniques the results were unsatisfactory, due to few training samples (and large variability of the underlying diseases, especially for EPT). However, since a proof of concept for the automatic detection was given in the project working on synthetic data, it is expected that it will become doable in the future, when a larger amount of in vivo data will be available.

Having these results, the project successfully achieved the objective.

Impact

The progress of the project was publicised via the project website (https://quiero-project.eu/) and two dedicated pages on LinkedIn and ResearchGate. In addition, a short video describing the work plan of the project was made available on YouTube (https://youtu.be/I3wNZpzUoog), and was promoted on the EURAMET website and by DG Science & Innovation.

A newsletter summarising the project achievements was regularly provided to the stakeholder committee, whose members represented 17 different affiliations, including relevant international societies and committees, MRI scanner manufacturers, scientific and clinical institutes. Members of the stakeholder committee participated at the formal project meetings, where specific time slots were devoted to round table discussions.

To date, thirteen scientific papers have been published in the form of open access articles; one of them originated a dataset made available under the project community on the Zenodo repository. Other scientific articles are currently accepted, under review and in preparation. In addition, 45 presentations (20 posters and 25 orals, six of which invited) were presented at scientific conferences, including the Mathematical and Statistical Methods for Metrology (MSMM) workshop in 2021 (where a special session was devoted to the project) and the 2020, 2021 and 2022 editions of the annual meeting of the International Society for Magnetic Resonance in Medicine. Moreover, in 2022 the project coordinator chaired the Joint Workshop on MR Phase, Magnetic Susceptibility and Electrical Properties Mapping, where seven technical presentations were given by members of the consortium.

Impact on industrial and other user communities

The project consortium has cooperated with all three main manufacturers of MRI scanners, i.e. GE Healthcare, Philips Healthcare and Siemens Healthcare. The latter, based on the work done in the project to produce and characterise tissue mimicking materials and phantoms, asked to be periodically informed about the progress of the consortium in this field and attended some of the official project meetings. More in general, the expertise in the characterisation of the dielectric and relaxation properties of tissue mimicking materials will allow INRIM, PTB and TUBITAK to offer corresponding measurement services to their external customers. Other uptake by external users could originate from the new low-cost soft-matter 3D printer designed and built by TUD, whose development, in order to promote open science, was described within an open access scientific article.

The dissemination activities carried on by the consortium during the project lifetime attracted the attention of some potential end users of the investigated quantitative methods. Among them, we may cite the University of Verona and the Istituto Neurologico "C. Besta", that showed interest in applying EPT to clinical data. The evaluation of uncertainty in EPT experiments will be the subject of a scientific paper under preparation, co-authored by consortium members and a researcher from Philips Healthcare.

A summary of the values of the parameters measured in vivo through EPT and MRF will be made available shortly after the end of the project (as soon as the data will be published in open access scientific articles) on the project website and other widely accessible repositories. Relevant stakeholders (e.g. the IT'IS Foundation, that maintains a popular online database of tissue properties) will be specifically informed about this action, to encourage uptake of this research product.

Impact on the metrology and scientific communities

The *EPTlib* library developed within the project gave public access to EPT algorithms for the first time. In particular, it was recognised as the first EPT package available on the internet by the Electro-Magnetic Tissue Properties Study Group of ISMRM, which represents the reference community for EPT. The adoption of *EPTlib* by external users was promoted in many occasions, including the 2021 edition of the ISMRM congress (where a work describing EPTlib was awarded with the ISMRM Magna Cum Laude Merit Award) and the 2022 Joint Workshop on MR Phase, Magnetic Susceptibility and Electrical Properties Mapping (where a specific educational lecture, attended by about 100 scientists, was given). Similarly, the MRF approaches developed and made available as open source software by consortium members allowed external users to access the

MRF world. To facilitate this kind of uptake, a tutorial on the use of the simulation framework for cardiac MRF was held during an online workshop, with more than 20 participants (mainly early career researchers), organised in July 2022 by PTB and Charité. The work done in the project created the opportunity to start a number of scientific collaborations with research groups that did not belong to the project consortium. Among them, we may cite a cooperation with the University Medical Centre in Utrecht, which manages a Dutch national project on EPT (for whose advisory board, QUIERO's coordinator was invited to become a member). The exploitation of the freeware developed and made available during the project took place also in the framework of other EMPIR projects. In particular, EPTlib was exploited within the 17NRM05 EMUE project to develop an example of evaluation of the uncertainty associated with the repeatability of EPT experiments, whereas MRF approaches were used in the 18HLT09 Neuromet2 project to acquire in vivo brain data.

Five consortium members belong to MATHMET, the European Metrology Network for Mathematics and Statistics, and regularly updated this community on the project outcomes. Moreover, specific presentations were held by consortium members at the conferences organised by MATHMET in 2019 and 2022. Periodic reports on the progress of the project were also provided by consortium members to the Working Group on the Expression of Uncertainty in Measurement of the Joint Committee for Guides in Metrology.

The work performed within the project created the occasion for the development of four Master theses and two Bachelor theses. A specific lecture on EPT was given within a course on MR dosimetry, for PhD students, at Politecnico di Torino (April 2021). EPT was also presented during lectures on MR dosimetry within a qualifying course in health physics at the University of Torino (December 2020 and 2021). One seminar on EPT, held by a consortium member, was hosted within INRIM's program of internal seminars. Furthermore, to assist NMI capacity building, a short online training course for project partners was provided to transfer knowledge on the use of EPT methods.

Impact on relevant standards

To date, EPT and MRF are still not subject to specific standards. The route to their standardisation requires a number of preparatory steps, involving those organisations responsible for the relevant standards and good practice. To promote long-term uptake of EPT and MRF and pave the way for the creation of future standards, the consortium established contacts with targeted bodies, including the European Imaging Biomarkers Alliance (EIBALL), the Quantitative Imaging Biomarkers Alliance (QIBA) and the International Society for Magnetic Resonance in Medicine (ISMRM), which were periodically informed of the project's progress. After receiving the first project newsletter, the Chairperson of the EIBALL invited the project coordinator to give a presentation on the project work plan during their business meeting held in May 2020. Moreover, members of the consortium have been invited to join the advisory board that will supervise the first international "challenge" organised with the aim of performing an extended intercomparison of EPT implementations in the framework of the ISMRM Study Group on Electro-Magnetic Tissue Properties.

In terms of MRI safety, EPT is the key to assessing the subject-specific, local exposure to radiofrequency electromagnetic fields, which depends on the spatial distribution of the actual electrical properties throughout the body. Working in this direction, the consortium informed the committee that maintains standard IEC 60601-2-33 (the international standard on MRI equipment and safety, which prescribes limits of exposure) about the investigation performed in the project on subject-specific SAR assessments based on EPT reconstructions.

Longer-term economic, social and environmental impacts

Patients will be the principle long-term beneficiaries of the full characterisation of EPT and MRF as diagnostic tools. MR-based quantitative imaging will boost early disease detection, fundamental to increased survival rates. Besides their intrinsic value for the detection, characterisation and monitoring of pathologies, fast and quantitative MRI methods will also cut down the use of (unnecessary) invasive procedures, reducing patients' stress and the corresponding cost for the healthcare system.

For **clinicians**, the use of biomarkers provided by EPT and MRF will pave the way for new diagnostic strategies. Furthermore, the exploitation of EPT and MRF will foster personalised medicine. Finally, the increasing availability of images bringing reliable quantitative information will contribute to the development of large databases of reference clinical data at an international level, promoting knowledge transfer, training and decision-making in a global context.

From the **economic** viewpoint, the use of MRF has the potential to reduce scan times and allow a larger number of exams to be performed in one day (or, equivalently, to cut the cost of each single exam). Due to the increased confidence in the results of quantitative MRI, the number of redundant scans will be also reduced. In addition, quantitative MRI will stimulate the extended use of artificial intelligence in diagnostics, with further time and money savings in the longer-term.

List of publications

1) A. Arduino, O. Bottauscio, M. Chiampi, L. Zilberti, *Uncertainty propagation in phaseless electric properties tomography*, Proceedings of the 2019 International Conference on Electromagnetics in Advanced Applications (ICEAA), https://arxiv.org/abs/1911.02809.

2) J. Mayer, R. Brown, K. Thielemans, E. Ovtchinnikov, E. Pasca, D. Atkinson, A. Gillman, P. Marsden, M. Ippoliti, M. Makowski, T. Schaeffter, C. Kolbitsch, *Flexible numerical simulation framework for dynamic PET-MR data*, Physics in Medicine and Biology, 2020, https://doi.org/10.1088/1361-6560/ab7eee.

3) G. Buonincontri, J. W.Kurzawski, J. D. Kaggie, T. Matys, F. A. Gallagherd, M. Cencini, G. Donatelli, P. Cecchi, M. Cosottini, N. Martini, F. Frijia, D. Montanaro, P. A. Gómez, R. F. Schulte, A. Retico, M. Tosetti, *Three dimensional MRF obtains highly repeatable and reproducible multi-parametric estimations in the healthy human brain at 1.5T and 3T*, NeuroImage, 2021, https://doi.org/10.1016/j.neuroimage.2020.117573. A dataset linked to this publication is publicly available on the Zenodo repository, at http://doi.org/10.5281/zenodo.3989799.

4) P. A. Gómez, M. Cencini, M. Golbabaee, R. F. Schulte, C. Pirkl, I. Horvath, G. Fallo, L. Peretti, M. Tosetti, B. H. Menze, G. Buonincontri, *Rapid three-dimensional multiparametric MRI with quantitative transient-state imaging*, Scientific Reports, 2020, https://doi.org/10.1038/s41598-020-70789-2.

5) S. Metzner, G. Wübbeler, S. Flassbeck, C. Gatefait, C. Kolbitsch, C. Elster, *Bayesian uncertainty quantification for magnetic resonance fingerprinting*, Physics in Medicine and Biology, 2021, https://doi.org/10.1088/1361-6560/abeae7.

6) A. Arduino, *EPTlib: An Open-Source Extensible Collection of Electric Properties Tomography Techniques*, Applied Sciences, 2021, https://doi.org/10.3390/app11073237.

7) S. Metzner, G. Wubbeler, C. Kolbitsch, C. Elster, *A comparison of two data analysis approaches for quantitative magnetic resonance imaging*, Measurement Science and Technology, 2022, https://doi.org/10.1088/1361-6501/ac5fff.

8) J. Ludwig, K. M. Kerkering, P. Speier, T. Schaeffter, C. Kolbitsch, *Pilot tone-based prospective correction of respiratory motion for free-breathing myocardial T1 mapping*, Magnetic Resonance Materials in Physics, Biology and Medicine, 2022, https://doi.org/10.1007/s10334-022-01032-4.

9) D. Kilian, W. Kilian, A. Troia, T. Nguyen, B. Ittermann, L. Zilberti, M. Gelinsky, *3D Extrusion Printing of Biphasic Anthropomorphic Brain Phantoms Mimicking MR Relaxation Times Based on Alginate-Agarose-Carrageenan Blends*, ACS Applied Materials & Interfaces, 2022, https://doi.org/10.1021/acsami.2c12872.

10) S. Hufnagel, S. Metzner, K. M. Kerkering, C. S. Aigner, A. Kofler, J. Schulz-Menger, T. Schaeffter, C. Kolbitsch, *3D model-based super-resolution motion-corrected cardiac T1 mapping*, Physics in Medicine and Biology, 2022, https://doi.org/10.1088/1361-6560/ac9c40.

11) J. Martinez, A. Arduino, O. Bottauscio, L. Zilberti, *Evaluation and Correction of B^+_1-Based Brain Subject-Specific SAR Maps Using Electrical Properties Tomography*, IEEE Journal of Electromagnetics, RF, and Microwaves in Medicine and Biology, 2023, https://doi.org/10.1109/JERM.2023.3236153.

12) C. Gatefait, S. Ellison, S. Nyangoma, S. Schmitter, C. Kolbitsch, *Optimisation of data acquisition towards continuous cardiac Magnetic Resonance Fingerprinting applications*, Physica Medica, 2023, https://doi.org/10.1016/j.ejmp.2022.102514.

13) A. Arduino, F. Pennecchi, U. Katscher, M. Cox, L. Zilberti, L. *Repeatability and Reproducibility Uncertainty in Magnetic Resonance-Based Electric Properties Tomography of a Homogeneous Phantom.* Tomography 2023, https://doi.org/10.3390/tomography9010034.

This list is also available here: https://www.euramet.org/repository/research-publications-repository-link/

Project start date and duration:	01 June 2019, 42 months
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Internal Funded Partners:	External Funded Partners:	Unfunded Partners:
1. INRIM, Italy 2. IMBiH, Bosnia and Herzegovina 3. LGC, United Kingdom 4. LNE, France 5. PTB, Germany 6. TUBITAK, Turkey	7. Charité, Germany 8. SM, Italy 9. TUD, Germany 10. UL, Slovenia 11. UNITO, Italy	
RMG1: INRIM, Italy (Employing organisation); PTB, Germany (Guestworking organisation)		