STUDY PROTOCOL

Truly Portable MRI for Extremity and Brain Imaging Anywhere & Everywhere

NextMRI

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1. Executive Summary

Mobile diagnostic imaging devices are invaluable for clinical diagnosis both inside and outside healthcare institutions. Unfortunately, Magnetic Resonance Imaging (MRI), the reference test for numerous neurological and musculoskeletal conditions, is not readily portable. Furthermore, due to its high cost (in the million-euro range) and consequent scarcity, the average waiting time in Europe for MRI assessment is approximately one to several months.

Recently, some companies have taken decisive first steps towards low-field MRI systems that are portable within medical facilities and have a lower cost (approximately EUR 250,000), although the weight and dimensions of these scanners still make transportation difficult. In a previous collaboration among UPV, CSIC, PHYS and IIS La Fe, within the Histo-MRI, PR Scanner and VIEWS projects, in vivo images were acquired using a compact, lightweight, small, low-field extremity MRI scanner outside the hospital environment, including at a patient's home and outdoors while connected to a petrol generator. These results open a path towards highly accessible MRI in circumstances of very limited access and for populations with no access to MRI. In addition, the project proposes training artificial-intelligence models using the generated MRI readings to develop deep-learning algorithms capable of discriminating between normal and damaged tissues.

To advance towards this ambitious goal, the NextMRI project intends to carry out the technical, industrial and business steps required to deploy portable low-field systems in remote and developing regions, rural areas, sports facilities and events, medical and military camps, and home healthcare, thereby improving diagnostic capacity. More specifically, its objectives are:

- to extend the current technology to extremity and brain imaging;
- to improve diagnostic capabilities using machine learning;
- to improve portability and ease of use for the end user;
- to optimise production costs;
- to collect medical evidence on technology performance through clinical studies; and
- to develop a sustainable business case for commercialisation of the technology.

2. Background and Current State of the Art

Detailed source reference: Proposal_HORIZON EIC Transition 2023_NextMRI_#101136407, pages 49-52 (Background).

Mobile diagnostic imaging devices are invaluable for clinical diagnosis both inside and outside healthcare institutions. Standard clinical MRI scanners, the gold standard for the diagnosis and follow-up of numerous conditions, use powerful superconducting magnets (>1.5 T), which provide increased signal-to-noise ratio and resolution. However, they also require cryogenic cooling and are therefore bulky, heavy, environmentally demanding, costly to build, install, operate and maintain, and ultimately represent a substantial barrier to accessibility and portability. Their high cost (in the million-euro range) and consequent scarcity mean that waiting times for MRI assessment in Europe may range from approximately one to several months.

With the aim of creating universal access to this technology, low-field MRI companies (<100 mT), such as Hyperfine, have taken decisive first steps towards portability within medical facilities, with lower-cost systems (approximately EUR 250,000) while maintaining acceptable low-field MRI diagnostic performance.

Within the Histo-MRI FET-Open project, and in research studies involving UPV, CSIC, PHYS and IIS La Fe, the feasibility of a lightweight 0.05 T MRI scanner was demonstrated. A prototype was developed using a series of small permanent magnets arranged in a Halbach configuration to generate sufficiently strong and homogeneous magnetic fields. In the PR SCANNER FET innovation project, progress was made towards the first truly portable MRI system, based on a 0.07 T Halbach magnet. The system is mounted on a wheeled structure 70 cm wide, has a total weight below 250 kg and a component cost below EUR

50,000. Its dimensions allow it to be transported by one person and to pass through standard doors in homes and care facilities (80 cm) and through lifts. These characteristics enabled knee imaging of a volunteer in indoor and outdoor environments, including the first MRI images obtained in a patient's home and outdoors while connected to a petrol generator. The scanner was also installed in the medical facilities of the Ricardo Tormo motorcycle racing circuit during the four days of the Valencia Motorcycle Grand Prix, where medical personnel were able to visualise several injuries and conditions, including traumatic arthritis that had not been detected on radiography.

This first-generation portable scanner constitutes the technological starting point for NextMRI, which will address the final development of a new system intended to democratise MRI use. The use of a much lower field reduces signal-to-noise ratio and resolution, but contrast relative to noise is less compromised and can still support diagnostic use. The system reduces equipment weight by approximately 90% (<250 kg instead of several tonnes) and component cost by approximately 95% (<EUR 50,000 instead of >EUR 1 million), can be powered through a standard household electrical outlet or a fuel generator, and is designed to be easy to transport and install. Its portability and lower cost support potential use in primary care centres, small clinics and sports clubs, which currently have limited or no access to MRI because of cost and infrastructure requirements.

As a secondary objective, NextMRI proposes the development of computational network models using Artificial Intelligence and Machine Learning capable of discriminating between normal and pathological tissues, with the aim of assisting diagnosis and supporting application in routine clinical practice.

The technology is protected by three patents arising directly from the Histo-MRI FET-Open project, co-authored by several founding partners and licensed to PHYS:

- EP20382540.1 - PECOS (PhasE-Constrained Oversampled MRI): a high-efficiency spatial encoding pulse sequence that can substantially accelerate MRI acquisitions and improve the resulting images.
- P202030504 - SliSe-ZTE (Slice-Selective Zero Time Echo): a pulse sequence exploiting spin locking with a magnetic-field gradient to enable slice selection before ZTE pulses, accelerating acquisition and enabling T1rho-weighted imaging for controllable tissue contrast.
- P201930719 - VIEWS (Volumetric Image Encoding Without k-Space): a method using time-varying inhomogeneous magnetic fields and algebraic reconstruction for efficient k-space sampling.

3. Working Hypothesis

Detailed source reference: Proposal_HORIZON EIC Transition 2023_NextMRI_#101136407, pages 50-52 (Background).

The NextMRI project intends to carry out the technical, industrial and business steps required to deploy portable low-field MRI systems in remote and developing regions, rural areas, sports facilities and events, medical and military camps, and home healthcare, and to improve diagnostic capacity.

4. Specific Objectives of the Proposed Research

Detailed source reference: Proposal_HORIZON EIC Transition 2023_NextMRI_#101136407, pages 52-53 (Background).

O1: Improve current portable MRI technology through hardware and software upgrades to increase diagnostic capability.

O2: Reduce production costs of the portable MRI system through the use of low-cost components and manufacture of prototypes for clinical testing.

O3: Evaluate the diagnostic performance of the portable MRI scanner in relevant clinical environments through imaging tests and comparisons with commercial scanners.

O4: Evaluate acceptance of the portable MRI scanner among stakeholders and clinicians, as well as its market adaptation through usability testing and socioeconomic impact assessments.

O5: Secure funding for future commercialisation steps through preparation of a renewed business plan and the search for investors and public funding.

These objectives cover technological improvement, clinical testing, market evaluation and securing funding for commercialisation.

5. Rationale and Relevance of the Proposed Research

Detailed source reference: Proposal_HORIZON EIC Transition 2023_NextMRI_#101136407, pages 54-61 (Background).

The principal technological objective of NextMRI is to improve the technology of the portable MRI prototype in order to expand its clinical capabilities using methods that optimise cost and production, and to test it under clinical conditions. The proposed hardware and software methods are intended to improve the potential for early diagnosis of musculoskeletal and brain conditions and to make the technology available to a larger proportion of the population. The project also addresses market preparation towards commercialisation and implementation, together with regulatory and certification aspects, with the objective of preparing both the technology and the business concept for investment.

6. Methodology

Detailed source reference: Proposal_HORIZON EIC Transition 2023_NextMRI_#101136407, page 53 (Methodology) and pages 69-79 (Essential Information for Clinical Studies in Horizon Europe).

6.1 Study Design

MRI of joints such as the ankle, elbow, wrist and especially the knee has very high sensitivity and specificity for the diagnosis of knee disease, with a negative predictive value close to 100%, and is an effective tool to support diagnosis. Joint MRI is also in high demand, which promotes the use of machines with different field strengths and image quality across clinical environments, producing a wide spectrum of imaging findings, a more complex diagnostic process and a substantial professional workload. At the same time, for some specific lesions and diseases, particularly degenerative or inflammatory conditions, inter-reader variability can be significant and diagnostic accuracy can decrease. Missed and delayed diagnosis can seriously affect prognosis and joint function and lead to progression of organic damage.

In view of this context, NextMRI will conduct a clinical evaluation study involving a multidisciplinary team of radiologists, rheumatologists, physiotherapists, data managers and physicists. At IIS La Fe, the study will include patients with suspected Multiple Sclerosis. The task aims to preliminarily evaluate the diagnostic value of the prototype and its usability for end users, and to generate an Artificial Intelligence training dataset from MRI readings in order to develop deep-learning algorithms capable of discriminating between normal and damaged tissues. These algorithms are intended to assist radiologists in clinical practice and reduce diagnostic time and professional workload.

The clinical validation will be structured in three steps:

1. Radiologists will report the high-resolution MRI images in a structured report as part of their clinical duties.
2. They will subsequently evaluate the MRI images acquired with the low-field scanner.
3. The reference information obtained from the initial radiology report will be used to evaluate performance and to train the deep-learning approach.

6.2 Setting and Relevant Dates

The final objective of NextMRI is to place scanners in clinics worldwide. Three study phases are considered:

- PHASE 1 - Design and development of the prototype, based on the results of Histo-MRI and current advances in the PR SCANNER and VIEWS projects (November 2023-April 2025), together with information collected from clinicians and relevant stakeholders.
- PHASE 2 - Technical and usability validation of the system in laboratory and relevant environments (September 2025-September 2026).
- PHASE 3 - Evaluation of market-acceptance solutions and development of the Business Plan to reach new investors (through December 2026).

For acceptance and usability objectives, the project will develop a Human Factors Plan based on User-Centred Design (UCD). This approach involves end users with different clinical, management, patient and maintenance profiles, as well as other stakeholders such as institutions and procurement managers, in an agile process throughout product development. Including users at each project stage is intended to reduce costs by promoting early identification of design problems and failures and avoiding costly redesigns at later stages.

Following a Human Factors approach is intended to support a product whose performance and use meet the needs, capabilities and expectations of all users and provide functional, safe, comfortable and satisfactory interaction. This process will follow the requirements relevant to CE marking established in Regulation (EU) 2017/745 on medical devices (MDR), including clinical investigation and placing medical devices for human use on the market, together with applicable harmonised standards, so that the final prototype can meet MDR requirements after completion of the project for future commercialisation.

Phase 2, corresponding to technical and usability validation of the prototype, is a prospective, observational and non-interventional study based on an analytical case-control model with comparability of evaluation methods.

6.3 Participants

Participants will be recruited among patients with a diagnosis of Multiple Sclerosis in order to undergo two MRI acquisitions: a standard MRI examination on the 3 T MRI system of the Experimental Radiology Platform (PREBI), and a second comparative low-field MRI examination performed with the NextMRI prototype. The two acquisitions will be performed on the same day, after approval and signature of informed consent by the participant. Both examinations will be reported by a professional radiologist, with an interval of 8 weeks between the two readings, with the aim of reducing bias and allowing comparison of both diagnoses.

Inclusion criterion	Patients with suspected Multiple Sclerosis.
Exclusion criterion	Contraindications to high-field MRI examinations.
Age of the population	Patients aged 18 to 65 years.

6.4 Variables

The variables to be collected in the project are: age, sex, MRI date, MRI type, and main MRI findings, including comparison between radiological readings and potential differences in the reading of Multiple Sclerosis plaques.

6.5 Bias Arising from Variables

Potential biases identified during project execution may arise because MRI examinations can be obtained using different anatomical orientations. Radiologists will therefore be trained to use only well-defined standard orientations.

6.6 Other Sources of Bias

Not applicable.

6.7 Data Sources and Measurements

The proposed study has an open and uncontrolled design. The exploratory nature of device performance means that a specific methodology and the presence of a control group are not considered meaningful. The study may be considered double-blind in the sense that, when evaluating the image obtained with the prototype, the observer will not have prior information on the diagnosis made using the device with regulatory approval.

6.8 Sample Size

Considering that patient recruitment involves two clinical centres (Hospital Universitario y Politécnico La Fe and Bergman Clinics), 50 patients are planned to be recruited in the IIS La Fe group focused on Multiple Sclerosis.

6.9 Statistical Methods

Accuracy metrics will be used and the groups will be compared using receiver operating characteristic (ROC) curve analysis. Unadjusted estimates will be provided together with their precision (95% confidence intervals).

6.10 Schedule and Work Plan

The estimated duration of this validation and patient-recruitment phase is 18 months (WP5: S4 + S5 + S6 = M18-M36).

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Protocol Source and Translation Note

The source document is the approved Spanish institutional research-project application titled “Memoria de Proyecto de investigación propio”, IIS-F-PG-22-02, Edition 4.1, Modification 1, dated 10 February 2025. This English version has been prepared for ClinicalTrials.gov public document submission. It reproduces the study-protocol content of the approved source without incorporating final study results or retrospective changes to the planned methodology. Blank administrative and economic template sections of the source document have been omitted because they contain no additional clinical study procedures or analyses.