SCAIFIELD

Spinocerebellar ataxias: Advanced imaging with ultra-high field MRI (SCAIFIELD)

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Introduction

The spinocerebellar ataxias (SCAs) are a genetically heterogeneous group of autosomal dominantly inherited disorders that are clinically characterized by progressive loss of balance and coordination. Brain pathology of SCAs centers around the cerebellum and brainstem. Ultra-high field MRI (UHF-MRI) has an enormous potential to detect and monitor structural and chemical brain changes at an unprecedented level of detail that cannot be achieved with 3T. However, technical shortcomings caused by field inhomogeneities at 7T that degrade image quality of the cerebellum and brainstem have so far prevented the exploitation of UHF-MRI to study SCAs. Overcoming these technical challenges by utilizing novel parallel transmission (pTx) MRI technology, the application of quantitative MRI at 7T in SCAs will mark a breakthrough with direct translational impact for SCAs.

Aims of the project

The aim of the SCAIFIELD project is the development of a multi-modal MR protocol, tailored to SCA and the quantification of potential biomarkers. From a multi-center patient study, these biomarkers will be accessed and a potential translation to 3Tesla will be investigated. To achieve this, the project is divided into 5 working packages (WP) that have significant overlap.

Methods implemented by the consortium

WP1 focuses on the homogenization of the magnetization in the whole brain, including the cerebellum and the brain stem. It uses universal ptx-pulses (UP)[1], which are RF-pulses, calculated on a database of field maps and used unchanged for all subsequent subjects.
The results of WP1 are used in WP2, which implements quantitative MRI (qMRI) sequences: Multi-parametric mapping (MPM), Chemical exchange saturation transfer, MR spectroscopic imaging (MRSI) and diffusion weighted imaging (DWI).
WP3 develops and optimizes the quantification of biomarkers that can be extracted from the qMRI sequences, developed in WP2.
In WP4 we have set up the clinical research infrastructure at all sites.
WP5 characterizes the pTx technology in high detail using temperature measurements and Maxwell simulations. These results might improve the UPs, created by WP1.

Results

A database of field maps was required for WP1. Using the fast 3DREAM sequence [2], the so-called BLT database was obtained with data from more than 70 subjects from Bonn, Liege and Trondheim. This is the largest and first multi-center field map database and it is still growing. Based on the BLT database UPs for homogeneous, water-selective [3], homogeneous saturation[4] and slab-selective excitation [5] have been developed.

Based on our custom 3D-EPI sequence and the novel UPs, fast sequences for high-resolution (0.6mm) MPM [6] and high-resolution (1.6mm) CEST [4] were developed. In collaboration with the university Vienna, UPs were also implemented in a pulse-acquire based MRSI sequence [5]. Additionally, an SCA tailored DWI protocol was included, using a vendor-provided sequence.

WP3 resulted in tailored data analysis for all measurement modalities. This included the extraction of quantitative susceptibility maps (QSM) from the phase information of the MPM images [7]. Therefore, no additional QSM-specific measurement was required. A combined analysis pipeline is still under development. Segmentation was performed on the MPM images [8].
In WP4 we have set up the clinical research infrastructure at all sites with access to database, scales training and provided the clinical protocol. The backtranslation to 3T has been implemented and assessed for the iron-sensitive QSM sequences. Full UHF protocol is distributed and started to be used at each site. Preliminary data underline the hypotheses of alterations in the deep cerebellar nuclei.

Significance and impact of the work on the field
A large field map database was created which forms the basis for advanced pTx pulse design. Based on this database, pulses for other projects have already been designed and successfully used [9,10]. This will most likely continue.

The novel pTx pulses for MT saturation enabled for the first time rapid whole-brain MPM at 7T. Based on our recommendations, the hMRI [11] toolbox for MPM analysis was extended for this purpose.

In SCAIFIELD, we developed fast sequences for homogeneous whole-brain 7T qMRI with high spatial resolution and high image quality. The developed protocol can be applied without any expert knowledge and is ready for clinical research, paving the way for increased routine use of 7T MRI.

Next steps and future challenges
UHF MRI has been implemented at each site and patient scanning has started and will be completed in 2025, aimed to be completed by end of Q2. The analysis pipeline is already set up. Preliminary data has been shown on the worldwide ataxia conference (ICAR, International Conference for Ataxia Research, London, November 2024) and several 7T sites across the globe expressed their interest in joining. Thus, at the beginning of 2025 we are planning to roll out the MRI protocol to other ataxia sites.

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