The SCAIFIELD Project

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on behalf of the SCAIFIELD consortium
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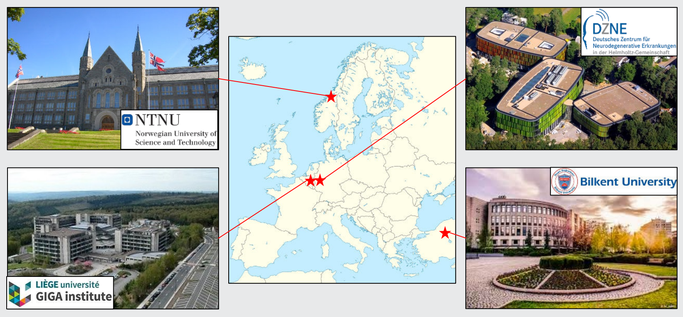
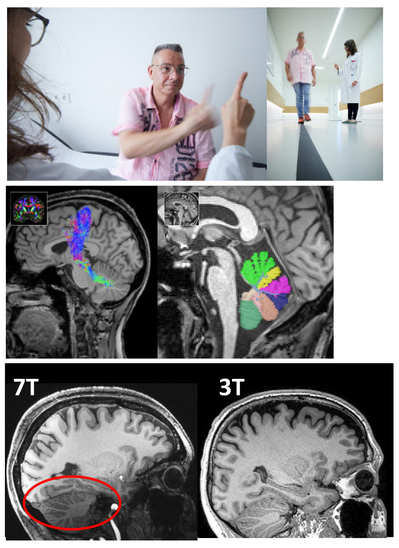


Introduction

- **Spinocerebellar ataxias (SCAs)** are a genetically heterogeneous group of autosomal dominantly inherited disorders and cause 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
- But, field inhomogeneities at 7T degrade image quality of the cerebellum and brainstem.
- This might be overcome with parallel transmission (pTx).
- Rapid **Quantitative MRI (qMRI)** methods with developed direct translational impact for SCAs have been implemented:
  - Multi-parametric mapping (MPM)
  - quantitative susceptibility mapping (QSM),
  - chemical exchange saturation transfer (CEST) mapping
  - magnetic resonance spectroscopic imaging (MRSI)
  - diffusion-weighted imaging (DWI)

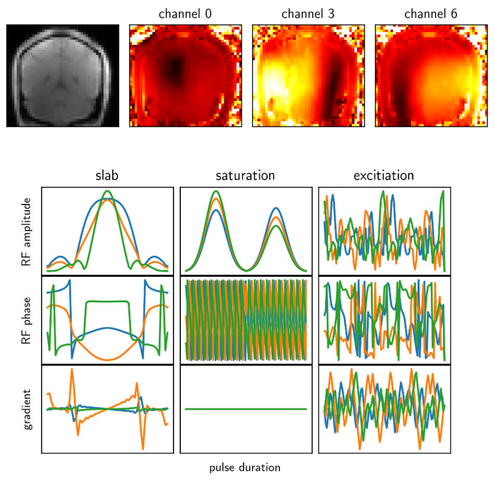


<u>Goal</u>: Multi-center study on Ataxia using *quantitative* MRI at 7 Tesla

<u>Challenge</u>: Cerebellum imaging at 7T

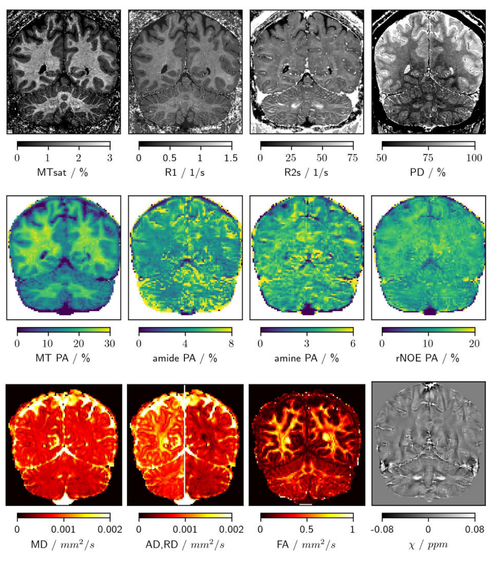
WP1 / WP5 Development of pTx technology

- Development of a coil model for electromagnetic field simulations for safety validation and pulse design.
- **Universal Pulses (UPs)**[5] compensate for excitation field inhomogeneity by calculating pulses, based on a database.
- Establishment of the **BLT** fieldmap database
  - Measure field maps using 3DREAM[6]
  - Contributions from Bonn, Liege and Trondheim
  - More than 70 subjects so far, and still expanding
- Calculation of UPs for:
  - Water-selective excitation[2] (MPM, CEST)
  - homogenous saturation[4] (MPM, CEST)
  - Frequency insensitive slab selection[7] (MRSI)



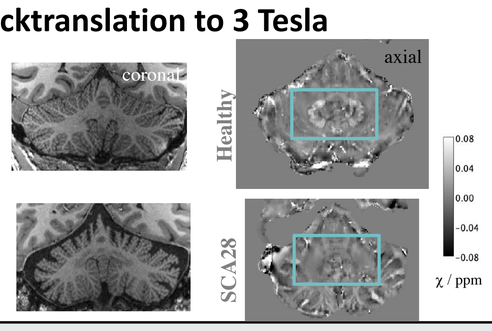
WP 3 multi-model quantitative analysis

- Development of tailored data processing pipelines
  - Adaptation of hMRI[7] toolbox for pTx MT saturation
  - Extraction of QSM map from MPM measurement[9] → no dedicated QSM measurement needed
  - Brain segmentation from MPM measurement[10]
  - Whole cerebellum metabolic profile using MRSI
  - High resolution amide proton mapping using CEST
  - Extraction of DTI, kurtosis and NODDI metrics from DWI
- Combined data analysis pipeline still under development.

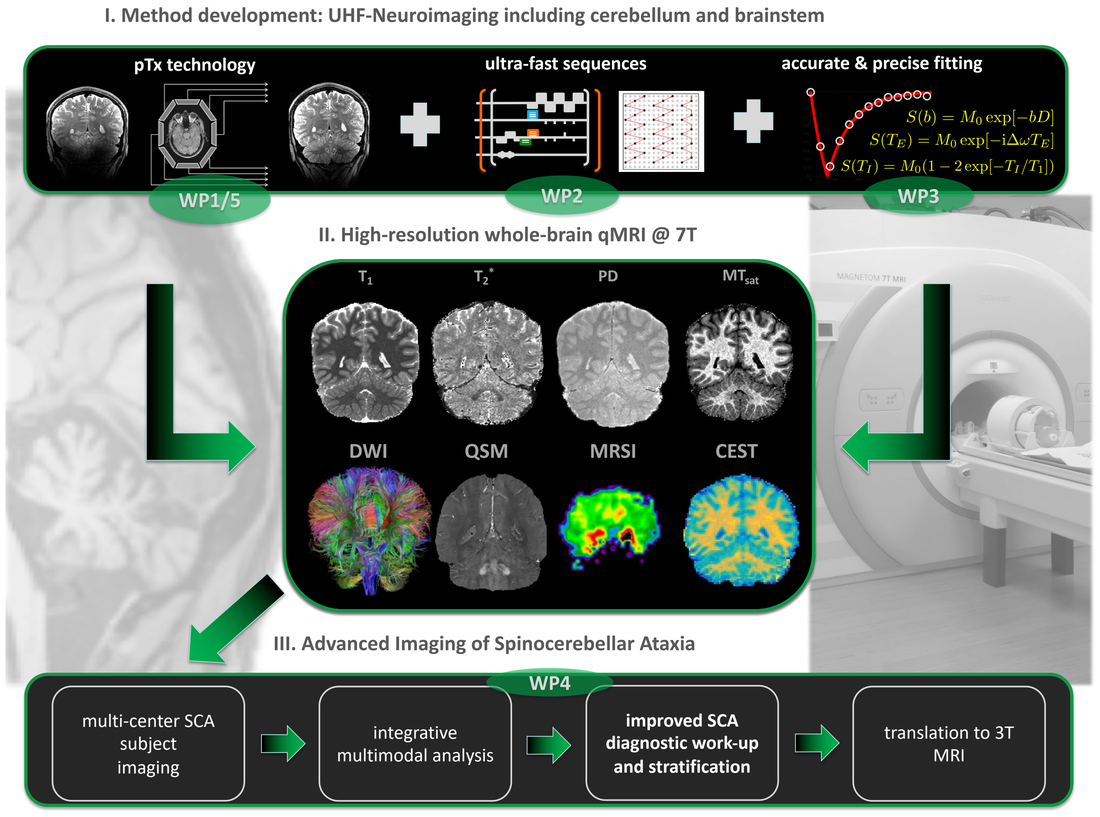


WP4 clinical infrastructure and backtranslation to 3 Tesla

- qMRI protocol successfully established at all sites
- Development of data sharing technology
- Patient study has already begun
- Partial back translation to 3 Tesla started[3]
- Preliminary results show alterations in the deep cerebellar nuclei in some SCA.



Graphical Abstract



WP2 Implementation of qMRI sequences

#	Contrast (Method)	Resolution / mm^3	Coverage	Duration / min	Quantitative Analysis	Purpose / Hypothesis
1	B0 & B1 map (3DREAM)	5.0 x 5.0 x 5.0	whole brain	02:38	Calibration: flip angle maps and multi-channel field maps	qMRI correction
2	MPRAGE	0.6 x 0.6 x 0.6	whole brain	07:24	Tissue segmentation / volumetry	volume loss
3	MPM + QSM (segm. 3D-EPI[1])	0.6 x 0.6 x 0.6	whole brain	13:41	T1, T2*, PD, MT,QSM / volumetry	T1, T2* reduction (PD, MT?) / volume loss / iron load
4	CEST (segm. 3D-EPI)	1.6 x 1.6 x 1.6	whole brain	07:37	Amides	decreased?
5	DWI (SMS-SE-EPI, 2-shell HARDI)	1.5 x 1.5 x 1.5	whole brain	10:44	Microstructure & connectivity: e.g. DTI, NODDI, tractography	reduced connectivity / cerebellar demyelination?
6	MRSI (3D-CRT)	5.0 x 5.0 x 5.0	whole cerebellum	08:56	Neurochemical profile: Cr, Glu, Gln, NAA, ...	MRS Score: SCA classification

All sequences except DWI use UPs

Significance and impact of the work on the field

- A large database of field maps was established for UP calculation. This database is used in other projects.
- Based on our recommendations, the hMRI toolbox for MPM analysis was extended for pTx MT saturation.
- 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

- Patient study is ongoing and will finish in 2025.
- Individual analysis pipelines are ready and the complete automated pipeline is in progress.
- The sequences presented here can be combined in a modular fashion. They are suitable for a wide range of clinical and scientific applications in neurology and neurodegeneration.
- Imaging protocol will be shared with other sites in early 2025.

Accepted SCAIFIELD journal publications

1. Wang et al. “Reproducibility of Rapid Multi-parameter Mapping at 3T and 7T with Highly Segmented and Accelerated 3D-EPI.” *Magnetic Resonance in Medicine* (2022)
2. Löwen et al. “Interleaved Binomial k_T-points for Water-selective Imaging at 7T.” *Magnetic Resonance in Medicine* 88 (2022)
3. Ferreira et al. “Cerebellar Volumetry in Ataxias: Relation to Ataxia Severity and Duration.” *The Cerebellum* 23 (2024)
4. Völzke et al. “Calibration-free whole-brain CEST Imaging at 7T with Parallel Transmit Pulse Design for Saturation Homogeneity utilizing Universal Pulses (PUSHUP).” *Magnetic Resonance in Medicine* (2024)

5. V. Gras, A. Vignaud, A. Amadon, D. Le Bihan, and N. Boulant, “Universal pulses: A new concept for calibration-free parallel transmission,” Magnetic Resonance in Medicine, vol. 77, no. 2, pp. 635–643, 2017
6. P. Ehses, D. Brenner, R. Stirnberg, E. D. Pracht, and T. Stöcker, “Whole-brain B_1-mapping using three-dimensional DREAM,” Magnetic Resonance in Medicine, no. November 2018, p. mrm.27773, 2019
7. Y. Völzke, D. Löwen, E. D. Pracht, L. Hingerl, W. B. Bernhard Srasser Gilbert Hangel, and T. Stöcker, “Universal parallel transmit pulses for pulse-acquire based whole-brain MRSI,” in Proceedings 32. Annual meeting international society for magnetic resonance in medicine, Singapore, 2024
8. K. Tabelow et al., “hMRI - a toolbox for quantitative MRI in neuroscience and clinical research.” Neuroimage, vol. 194, pp. 191–210, Jul. 2019
9. M. Ferreira et al., “Optimized Quantitative Susceptibility Mapping of Deep Cerebellar Nuclei using the phase of 3D-EPI Multi-Parametric Mapping at 7T,” in Proceedings 31. Annual meeting international society for magnetic resonance in medicine, Toronto, Canada, 2023.
10. M.-A. Fortin et al., “High quality brain segmentation from multi-parameter mapping at Ultra-High Field MRI,” in Proceedings 31. Annual meeting international society for magnetic resonance in medicine, Toronto, Canada, 2023.

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