

Optimized Quantitative Susceptibility Mapping of Deep Cerebellar Nuclei using the phase of 3D-EPI Multi-Parametric Mapping at 7T

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Synopsis:

RF transmit field inhomogeneities at 7T usually degrade the image quality in regions such as the cerebellum and brainstem, which has so far delayed its use to study cerebellar ataxias with higher fields. We present an optimized pipeline that maximizes the QSM contrast of nuclei in the cerebellum based on multi-echo MPM data. We show that averaging the individual susceptibility maps increases the signal-to-noise ratio (SNR) and reduces the group standard deviation. We introduced a weighted averaging based on the individual acquisition SNRs. Final maps presented high contrast of the dentate nucleus and a high delineation of its denticulated silhouette.

Summary of main findings:

We present a pipeline that maximizes the QSM contrast within a whole brain MPM protocol at 7T based on 3D-EPI and universal pTx pulses. Final maps show, in high detail level, the denticulated silhouette of the dentate nuclei in the cerebellum.

Abstract:

Introduction

Quantitative Susceptibility Mapping (QSM) can quantitatively assess iron concentration in the brain. In spinocerebellar ataxias (SCAs), iron concentration in deep cerebellar nuclei is of particular interest¹. Ultra-high field (UHF) MRI allows an increased resolution compared to 3T. However, RF-transmit field inhomogeneities at 7T prevented its exploitation to study cerebellar-related disorders, such as SCAs, to a larger extent. Overcoming these challenges by utilizing universal pTx pulses² at 7T may have direct translational impact on SCAs. In the current pilot study, we hypothesize that high-resolution QSM will enhance the sensitivity and specificity to delineate cerebellar structures. We here optimized a pipeline for QSM processing of Multi-Parametric Mapping (MPM) data with a focus on infratentorial structures, in particular, to explore high-resolution quantitative imaging of deep cerebellar nuclei at 7T.

Methods

Three female healthy controls (31, 35, and 26 years old) were imaged on a Siemens MAGNETOM 7T Plus scanner using a 32-channel receive, 8-channel transmit coil (Nova Medical). Data was acquired using a multi-echo skipped-CAIPI [2] 3D EPI-based MPM³ sequence with magnetization transfer (MT), proton density (PD) and T1 contrasts. Each subject was measured once using CP-mode water excitation pulses⁴ and once using universal interleaved binomial kT-points excitation pulses⁵. Sequence parameters were: 0.6 mm isotropic resolution; TA=15:04 min; TE=[5.3,12.2,19.1,26.0] ms; TR of 48, 34.5, 34.5 ms and nominal flip angle (FA) of 6, 4, 25° for MTw, PDw, and T1w images, respectively. For each contrast, the susceptibility maps were individually calculated using the following steps: 1) quantitative unwrapping and multi-echo phase combination with ROMEO⁶ (using the spatially unwrapped first echo as the template for temporal unwrapping; mask generation using

the “robust mask” and phase offset correction); 2) conversion from ΔB_0 to wrapped phase at a nominal TE of 10ms; 3) QSM reconstruction with QSMxT⁷ (in which brain masks were generated for each contrast, based on the corresponding magnitude data with a threshold of 25, 25 and 40% for MTw, PDw, and T1w, respectively). Finally, we averaged the three QSM maps with different weight combinations, aiming to reduce noise and therefore to increase susceptibility contrast-to-noise ratio. We compared averaged maps with equal weighting and magnitude-SNR-based weights, where the SNR was estimated in two selected WM regions.

Whole-brain white matter (WM) and gray matter (GM) segmentation was performed using with SPM12⁸ based on the T1w images.

Results

SNR estimates for each subject are shown in Figure 1. Figure 2 shows the standard deviations (SDs) of the susceptibility values for GM and WM. In all subjects, the dentate nucleus can be easily identified, and a high detail level of the denticulated silhouette can be seen in Figure 3. Motion artifacts were found in subject 2. For each pair of QSM maps of different MPM contrasts (diagonal, Figure 4), the Pearson correlation coefficient (r) of the susceptibility was calculated within the WM and GM masks. Similarly, differences between the weighted averaged QSM map and each individual QSM map were calculated.

Discussion

In Figure 1, the image magnitude SNR was found to be higher for both PDw and MTw when using pTx compared to CP excitation. In T1w, CP leads to higher SNR in the whole brain (including the cerebellum) than pTx, as the actual CP-mode FA is closer to the signal-maximizing Ernst angle. This effect is less pronounced in the cerebellum.

The final QSM maps were averaged to minimize noise. We included equal weighting and SNR-based weights and calculated the standard deviations of the susceptibility values in GM and WM using CP and pTx. GM was found to have a higher standard deviation compared to WM (Figure 2). Increased variance due to residual inversion artifacts close to the outer brain boundary may play a larger role in the standard deviation in the GM mask than in the WM mask.

Averaging the individual QSM maps with SNR-based weights resulted in a lower standard deviation in WM compared to equal weights, albeit not as clearly for the pTX data as for the CP data. Interestingly, overall WM susceptibility standard deviation was larger for pTX data than for CP data, both based on the individual contrasts and after averaging. Further investigations are required on this. In all subjects, the dentate nucleus could be identified and a high detail level of the denticulated silhouette was found (Figure 3). Visually, differences between equal weighting and SNR-based weights were little.

WM was shown to have higher r than GM in all comparison pairs. This could be driven by the overall increased standard deviation level of GM. The lowest differences were found between the SNR-based averaged QSM maps and the QSM map reconstructed from PD. T1 was shown to have the lowest r in GM as well as the highest susceptibility differences (bottom row). This could be due to arterial blood signal contributing much stronger in the T1 contrast than in the other contrasts. The major differences between the pairs center adjacent to the silhouette of the dentate nucleus and the superior cerebellar peduncles, likely with contributions from the rhomboidal artery.

Conclusions

The developed pipeline maximizes QSM contrast-to-noise ratio of a multi-echoes MPM measurement. We have shown high delineation of the silhouette of the dentate nucleus.

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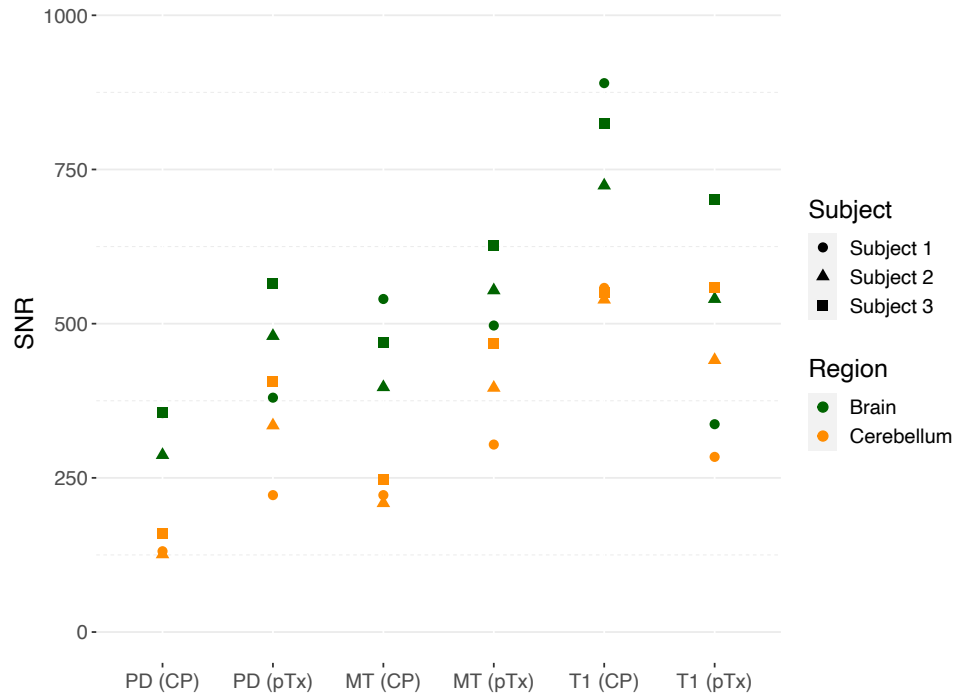


Figure 1 -SNR for each subject in 2 selected WM regions (brain in green and cerebellum in orange) for each MPM acquisition using CP and pTx excitation pulses.

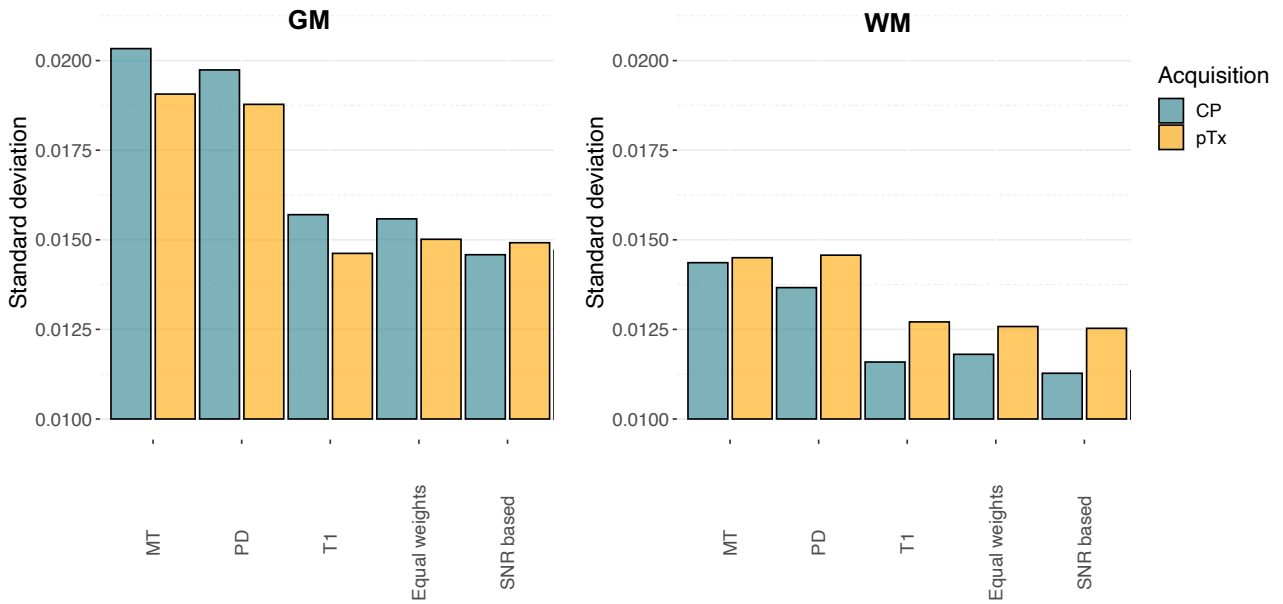


Figure 2 - Comparison of the group mean of the standard deviations of the susceptibility values in the whole brain GM (left) and in the whole brain WM (right) for each individual and averaged QSM map.

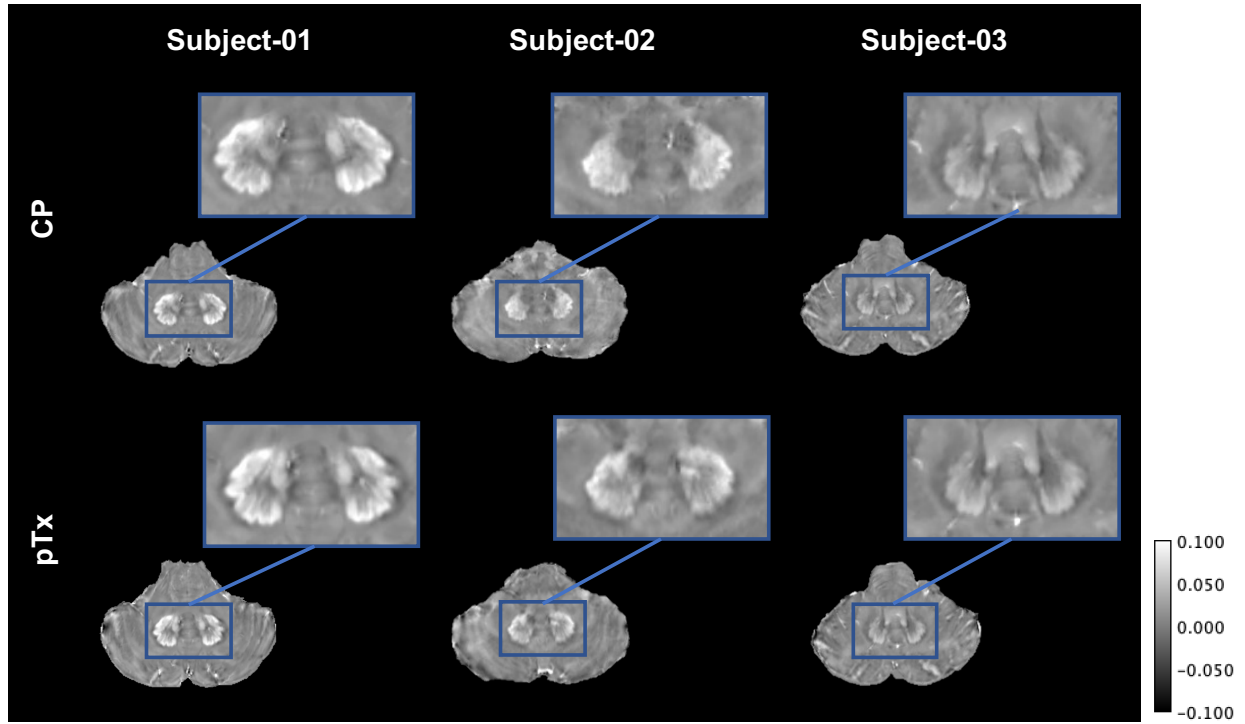


Figure 3 - Axial slice through the cerebellum of the SNR-based averaged QSM maps with CP (upper row) and pTx (lower row) excitation pulses, for all 3 subjects. The detail drawing highlights the dentate nucleus (images scaled from -0.1 to 0.1 ppm).

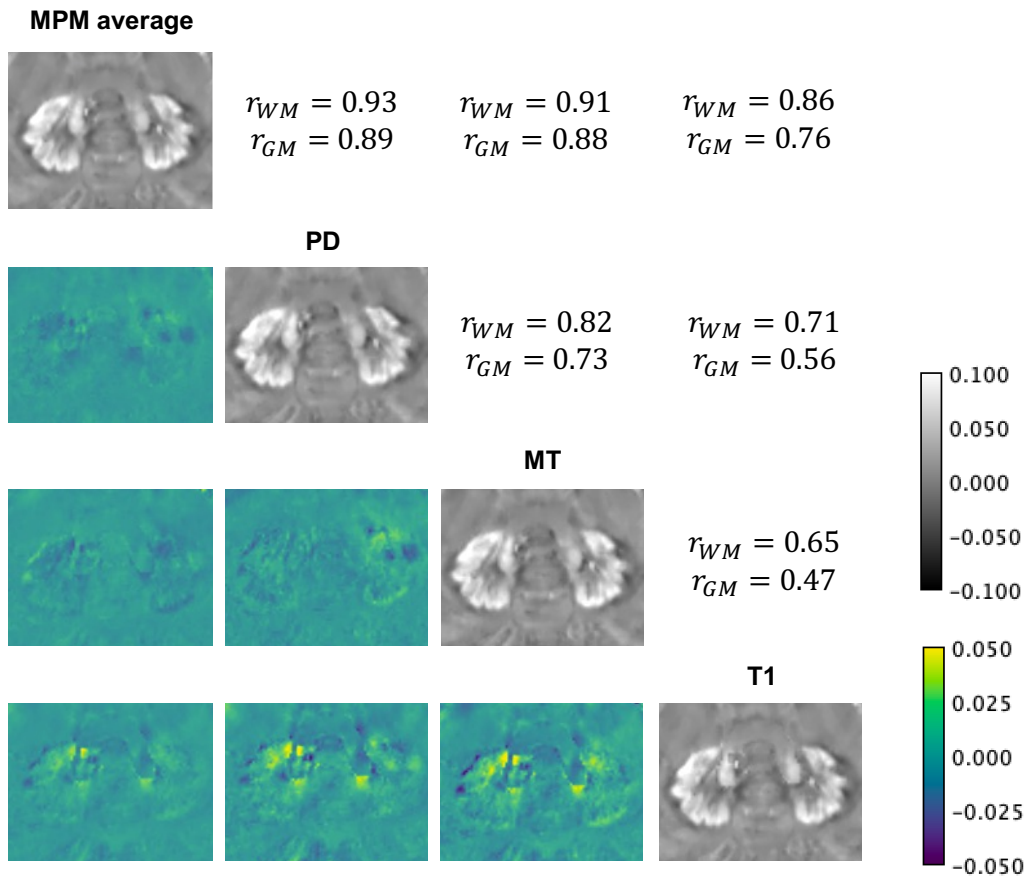


Figure 4 - In the diagonal: susceptibility of the dentate nucleus for the SNR-based averaged map and for each contrast (images scaled from -0.1 to 0.1 ppm); in the lower triangle: the differences between each pair of images; and, in the upper triangle: the Pearson correlations of the susceptibility values in WM and GM between each pair of images, for subject-01 acquired with pTx excitation pulses.

References:

- (1) Deistung, A.; Jäschke, D.; Draganova, R.; Pfaffenrot, V.; Hulst, T.; Steiner, K. M.; Thieme, A.; Giordano, I. A.; Klockgether, T.; Tunc, S.; Münchau, A.; Minnerop, M.; Göricke, S. L.; Reichenbach, J. R.; Timmann, D. Quantitative Susceptibility Mapping Reveals Alterations of Dentate Nuclei in Common Types of Degenerative Cerebellar Ataxias. *Brain Commun.* **2022**, 4 (1), fcab306. <https://doi.org/10.1093/braincomms/fcab306>.
- (2) Gras, V.; Vignaud, A.; Amadon, A.; Bihan, D.; Boulant, N. Universal Pulses: A New Concept for Calibration-free Parallel Transmission. *Magn. Reson. Med.* **2017**, 77 (2), 635–643. <https://doi.org/10.1002/mrm.26148>.
- (3) Weiskopf, N.; Suckling, J.; Williams, G.; Correia, M. M.; Inkster, B.; Tait, R.; Ooi, C.; Bullmore, E. T.; Lutti, A. Quantitative Multi-Parameter Mapping of R1, PD*, MT, and R2* at 3T: A Multi-Center Validation. *Front. Neurosci.* **2013**, 7. <https://doi.org/10.3389/fnins.2013.00095>.
- (4) Stirnberg, R.; Brenner, D.; Stöcker, T.; Shah, N. J. Rapid Fat Suppression for Three-Dimensional Echo Planar Imaging with Minimized Specific Absorption Rate: Rapid, Minimum-SAR Fat Suppression. *Magn. Reson. Med.* **2016**, 76 (5), 1517–1523. <https://doi.org/10.1002/mrm.26063>.
- (5) Löwen, D.; Pracht, E. D.; Stirnberg, R.; Liebig, P.; Stöcker, T. Interleaved Binomial k_T -points for Water-selective Imaging at 7T. *Magn. Reson. Med.* **2022**, 88 (6), 2564–2572. <https://doi.org/10.1002/mrm.29376>.
- (6) Dymerska, B.; Eckstein, K.; Bachrata, B.; Siow, B.; Tractnig, S.; Shmueli, K.; Robinson, S. D. Phase Unwrapping with a Rapid Opensource Minimum Spanning Tree Algorithm (ROMEO). *Magn. Reson. Med.* **2021**, 85 (4), 2294–2308. <https://doi.org/10.1002/mrm.28563>.
- (7) Stewart, A. W.; Robinson, S. D.; O'Brien, K.; Jin, J.; Widhalm, G.; Hangel, G.; Walls, A.; Goodwin, J.; Eckstein, K.; Tourell, M.; Morgan, C.; Narayanan, A.; Barth, M.; Bollmann, S. *QSMxT: Robust Masking and Artefact Reduction for Quantitative Susceptibility Mapping*; preprint; Neuroscience, 2021. <https://doi.org/10.1101/2021.05.05.442850>.
- (8) *Statistical Parametric Mapping: The Analysis of Functional Brain Images*, 1st ed.; Friston, K. J., Ed.; Elsevier/Academic Press: Amsterdam ; Boston, 2007.