

Iron-Sensitive Quantitative Methods for Multiple Sclerosis: Lesion Evolution and Deep Grey Matter Iron Deposition

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Introduction: From post-mortem pathological studies, it is well known that multiple sclerosis (MS) patients often exhibit a buildup of iron in deep grey matter and within lesions (1). Quantitative MRI methods to follow this iron variation would be valuable. Susceptibility phase imaging has extremely high sensitivity to iron, however it is also prone to artifact from phase reconstruction and tissue orientation. R2* mapping provides a higher degree of robustness but with lower iron sensitivity than phase imaging. However, both R2* and phase mapping can fail in areas of high field variation near air-tissue interfaces. R2 mapping can overcome this limitation, providing substantially higher image quality through RF refocusing, but also greater RF heating and less specificity to iron. All three methods have major limitations, but together may provide a comprehensive evaluation into iron and MS. Moreover by using a high magnetic field strength, the iron sensitivity is further enhanced. In this work, we apply three iron-sensitive methods with high field adaptations for tracking iron-based changes in the brain of relapsing-remitting (RR) MS patients.

Methods: Iron sensitive imaging was performed on 9 RR MS patients using three separate techniques. Patients were imaged monthly for five scans. Each method was evaluated for lesion visibility, lesion evolution and deep grey matter measurement. All methods were performed on a 4.7 T magnet which provides a substantial intrinsic SNR and iron-sensitivity boost over 3.0 T, while still enabling RF intensive pulse sequences that are constrained at 7.0 T. The key parameters for each imaging method were: 2D phase susceptibility method, 62° flip, TE/TR 15/1540ms, 512x256, 50 slices, 2mm thickness, 6.6min acquisition and standard phase filtering. R2 mapping was performed with a 2D multi-spin echo sequence TE1/TR 10/3500ms, 256 x 145 matrix, 2 slices with 4mm thickness, 20 echoes with 10 ms echo spacing, 5 min acquisition. Note, in its current form, R2 mapping provides only two slices in 5 min owing to RF heating limitations. R2* mapping was performed using a 3D multiecho sequence TE1/TR 3.2/44ms, 256 x 192 matrix, 80 slices with 2 mm thickness, 10 echoes with 4.1 ms echo spacing, 8.9 min. To account for high field effects, R2* maps were reconstructed with susceptibility compensation (2,3), while R2 maps used stimulated echo compensation (4).

Results: Although lesion visibility varies significantly between methods, evolution of visible lesions can be followed with all methods. For example, in phase imaging the hypointense lesion in Fig 1 remains visible throughout the time course and can be quantified (Table 1). Deep grey matter maps are shown in Fig 2, where each method provides unique contrast. Consensus interpretation of phase hypointensity with R2 and R2* enhancement provides increased confidence of iron specificity.

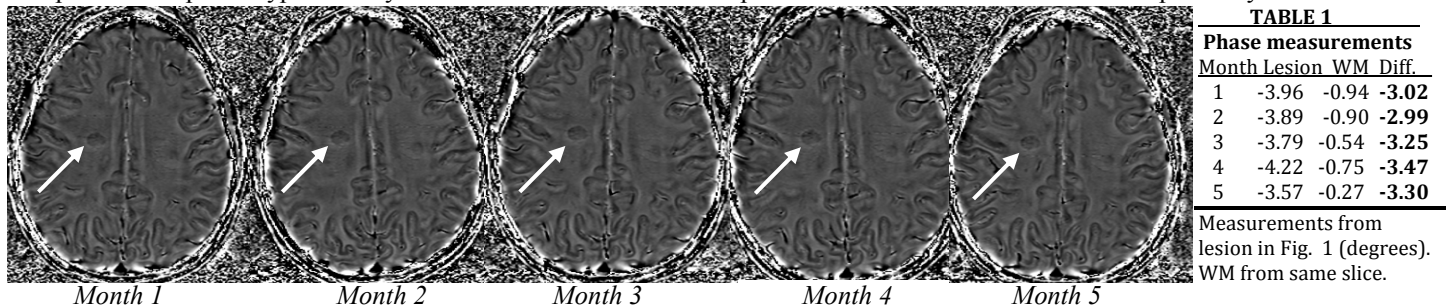


Fig 1 (above) Lesion evolution in monthly phase susceptibility (TE 15ms) from a 28 year old RR MS patient illustrating a persistent hypointense lesion (arrows), with relative phase angle quantified (Table 1).

Fig 2 (right) Deep grey matter structures illustrating (a) T2-weighting, (b) R2, (c) phase susceptibility, and (d) R2* mapping in a 29 year old RR MS patient.

Conclusions: Remaining high field limitations include slice limitations in R2 due to RF heating and air-tissue susceptibility artifacts in R2* and phase imaging. Nevertheless, with appropriate high field compensation, phase, R2 and R2* mapping at 4.7 T provides three separate iron-sensitive measures to track lesion and deep grey matter changes in MS. Together these methods can provide new insight into MS progression.

- References:**
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