# Ultra-high field MRI longitudinal MS lesion study

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## Purpose

Multiple sclerosis (MS) is a common neurodegenerative disease that often manifests as periods of demyelination and remyelination, predominantly in the white matter. Our study utilized ultra-high field (7T) magnetic resonance imaging (MRI) quantitative image techniques including quantitative susceptibility mapping (QSM) and effective relaxation rate ($R_2^*$), in a prospective study of patients with relapsing remitting MS (RRMS). QSM is a relatively new imaging technique that is sensitive to iron and myelin within the brain.[1,2] It has been shown that only a subset of MS lesions appear in QSM, and these are hypothesized to be active lesions.[1,3] By using QSM, myelin (diamagnetic, negative susceptibility) can, in principle, be separated from the paramagnetic (positive susceptibility) iron contained in the macrophages.[1] Separating these contributions should give a better understanding of how RRMS lesions evolve temporally, and may result in earlier diagnosis and better management of the disease.

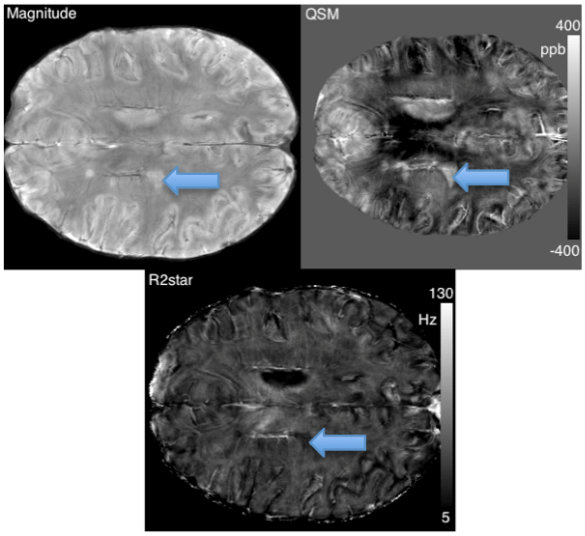


**Fig. 1:** Typical magnitude echo, QSM, and $R_2^*$ images used in our study. The blue arrow shows a large periventricular lesion, visible in all three contrasts.

## Methods

Patients diagnosed with RRMS from a major tertiary care hospital were selected for the longitudinal study, along with age-matched controls. Each patient underwent scanning in a 7T MRI system every four months over the course of two years. Imaging data was acquired using a 3D multi-echo GRE sequence for calculation of the susceptibility-based images and $R_2^*$ images. Mono-exponential $R_2^*$ maps were generated using an interior-point, least squares fitting in MATLAB. QSM was calculated by unwrapping the phase wraps, followed by (sophisticated harmonic artifact reduction for phase (SHARP) filtering to remove the background field contributions, generating the local frequency shift (LFS) map.[4,5] The QSM maps were calculated from the LFS map using a k-space regularized inversion in MATLAB.[6] Figure 1 contains typical images from our study. All of the lesions for each patient were manually segmented using a custom MATLAB GUI developed in house. Segmentation involved tracing each lesion and separating the ring-like portion of the lesion from the inactive core, if possible. The reference tissue was taken to be the normal appearing white matter (NAWM) directly surrounding the lesion. Using the QSM and $R_2^*$ images, we attempted to characterize the relaxation rate and susceptibility of the lesions that appeared or disappeared over the course of the study. Several lesions were analyzed in greater detail by resampling the resolution to 0.125 x 0.125 x 0.300 $mm^3$.

## Discussion

Only one third of the lesions visible in the $T_1$ and $T_2$ weighted images were visible in the QSM images. We found mixed results with regards to the evolution of QSM and $R_2^*$ prior to, during, and after the formation of a lesion. The change in $R_2^*$ slowly decreased in value as the lesion formed, whereas the QSM value had a sudden increase as the lesion became initially visible, followed by a gradual drop off. Following the lesion formation (month 8) shown in figure 2, there is an increased $R_2^*$ and susceptibility of the outer lesion, perhaps indicating the presence of iron. The reduced $R_2^*$ and susceptibility inside the lesion suggests increased edema, and may also indicate initial demyelination followed by the start of remyelination. Several lesions exhibited a ring-like appearance. The ring-like portion was separated from the inner core, allowing us to analyze both independently. The ring-like portion and the core both followed the same time course, indicating that both respond similarly to the biological changes occurring throughout the lesion and surrounding tissue. The $R_2^*$ changes appeared to precede the QSM changes, but the QSM changes were substantially larger.

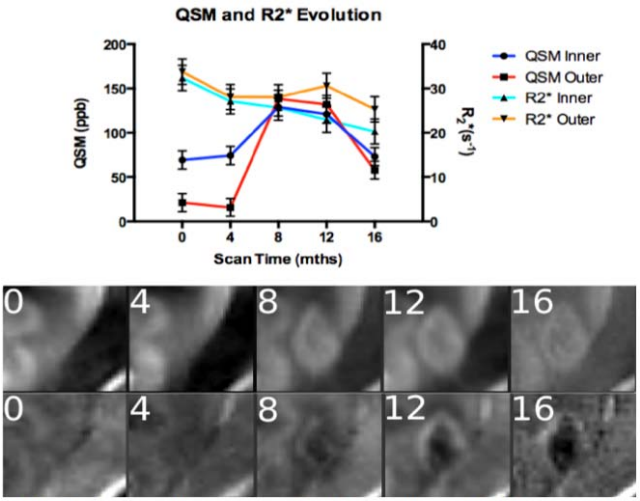


**Fig. 2:** Longitudinal images (0 – 16 months) of QSM (top) and $R_2^*$ (bottom). Graph contains the QSM and $R_2^*$ values for both the ring structure (outer), and the "inactive" core (inner).

## Conclusion

A group of 16 RRMS patients and 16 age-matched controls underwent scanning every four months for two years. We found that the $R_2^*$ tends to slowly decrease prior to obvious lesion formation, whereas the QSM value increases occur more rapidly, right around the time of lesion formation. This suggests that QSM and $R_2^*$ are sensitive to different biological processes in MS lesions and that $R_2^*$ changes may help predict future lesion formation. The increase in QSM is suggestive of increased paramagnetism, and could be a marker for iron containing macrophages in a newly active lesion. This study will continue to follow subjects for several more years in order to increase the number of observed lesions that appear and disappear over time.

## References

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