Quantitative magnetic susceptibility improves the detection of multiple sclerosis lesions

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INTRODUCTION: Imaging lesion activity in multiple sclerosis has become widely accepted as a criterion for establishing evidence of disease dissemination in time and space. However, MS can be difficult to diagnose early in the course of the disease because symptoms often come and go. MRI scans can appear normal or near-normal even though substantial clinical disability is present. In the past decade, it has also become increasingly clear that current MRI protocols show only part of MS pathology, failing to reveal important changes occurring at the microscopic level. In addition, distinguishing MRI lesions due to overlapping pathology remains difficult and clinically problematic. This study investigated the utility of quantitative magnetic susceptibility as a means to quantify MS plaques. A group of MS patients and asymptomatic subjects with hyper-intense FLAIR images were scanned. The results indicated that quantitative magnetic susceptibility mapping may potentially improve the sensitivity and specificity for the detection of MS plaques.

METHODS: Seven MS patients were scanned at a 3.0T scanner with IRB approval. PD/T2-weighted images and fluid-attenuated-inversion-recovery (FLAIR) images were acquired following typical clinical protocols. To acquire the phase images, a multi-echo 3D spoiled-gradient-recalled (SPGR) sequence was used with the following parameters: FOV = 22x22 cm^2, matrix = 256x256, slice thickness = 2 mm, TE = 6 ms for the first echo, TR = 60 ms, flip angle = 25º. To assess the specificity, two adult volunteers (age 52 and 60 y/o) with hyperintense FLAIR images but with no history of MS or other known neurological disorders were scanned with the same protocol.

Phase images were reconstructed from the SPGR images. Large background phase was removed with a sphere-mean-value (SMV) filter followed by a deconvolution operation (1). The radius of the filter is varying with reduced width closer to the boundary of the brain tissues. The advantage of this SMV filtering method over conventional high-pass filtering method is that the low frequency component of the local phase is also preserved. The resonance frequency map was calculated from the processed phase image. Quantitative magnetic susceptibility value was computed for each voxel iteratively using the LSQR algorithm (2).

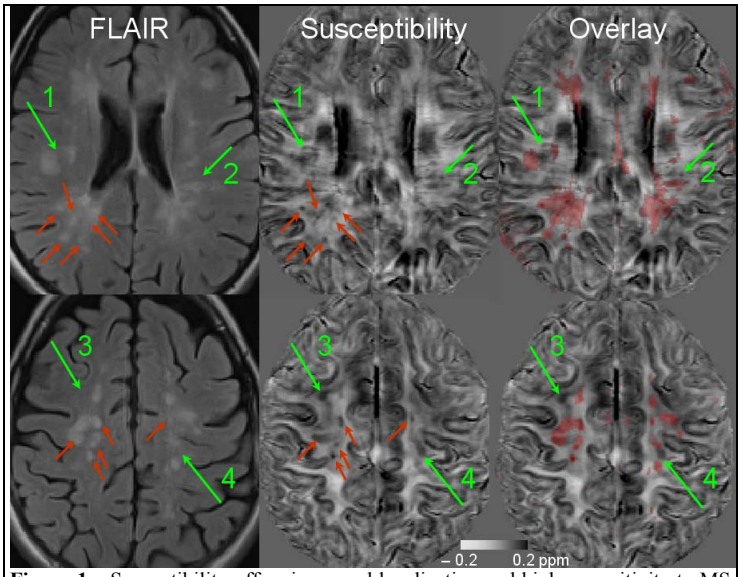

Figure 1. Susceptibility offers improved localization and higher sensitivity to MS plaques. Green arrows: 4 examples of plaques detected by susceptibility only (dark spots in the WM). Red arrows: examples of common lesions (dark spots in susceptibility). Overlay: FLAIR lesions (transparent red) are overlaid on susceptibility map for co-localization of lesions.

RESULTS: Figure 1 shows a comparison between FLAIR images and susceptibility maps of two MS patients. Diffuse hyper-intense regions are clearly seen in the FLAIR images, typical of MS lesions. Plaques seen in FLAIR were all detected by susceptibility (overlay in Fig. 1). A few selected examples are pointed out by red arrows. While lesions tend to be homogeneous in FLAIR, they exhibit much heterogeneity in the susceptibility maps. More importantly, susceptibility detected numerous plaques that were missed by FLAIR (four examples are highlighted by green arrows). In general, WM lesions appear dark in susceptibility maps (0.08 ppm difference on average), consistent with the demyelination pathology. In summary, magnetic susceptibility provides sensitive detection and improved characterization of MS plaques. If it is validated that lesion patterns can be characterized by susceptibility, it may be possible to use this information to guide treatment.

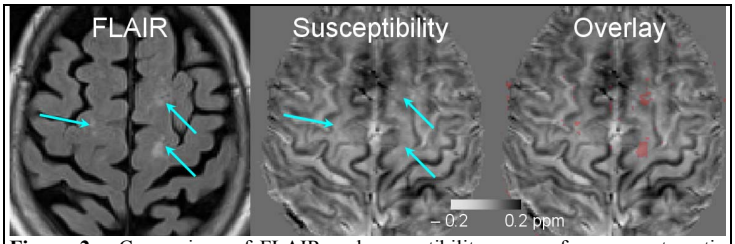

Figure 2. Comparison of FLAIR and susceptibility maps of an asymptomatic subject. Hyperintense spots are seen the FLAIR images while susceptibility maps reveal normal myelination in the same locations consistent with asymptomatic clinical presentation.

Figure 2 compares the FLAIR images with the corresponding susceptibility maps of one asymptomatic volunteer. For this subject, no MS has developed in the past years since the hyperintense FLAIR images were first discovered. Phase images and susceptibility maps were processed with the same methods for the MS patients shown in Fig. 1. The FLAIR images reveal hyperintense regions in the white matter, mimicking those of MS even though the subjects has no history of MS and is asymptomatic. Susceptibility maps, on the other hand, show no abnormalities in the same regions of hyperintense FLAIR, excluding the possibility of demyelination. Magnetic susceptibility can thus potentially improve the diagnostic specificity for MS when combined with standard clinical protocols.

DISCUSSIONS AND CONCLUSIONS: Previous studies have used phase information in susceptibility-weighted imaging to detect iron deposit (3). Phase however is not intrinsic property of brain tissues. Our data demonstrate that magnetic susceptibility is sensitive to demyelination in MS, the hallmark of the disease. This is consistent with recent findings that suggested myelin as the primary source of susceptibility contrast between gray and white matter (4). For example, a recent study demonstrated that, while the phase and susceptibility maps exhibit a strong contrast between gray and white matter in the normal control mouse, this contrast essentially disappears in the myelin-deficient shiverer mouse. Our findings suggest that the relative susceptibility value between lesion and surrounding tissues may provide a sensitive endogenous biomarker for demyelination in MS. In addition, the improved sensitivity to demyelination may allow us to detect lesions that otherwise would have been undetected by conventional imaging methods. Given the critical importance of myelin in MS, it is anticipated that mapping magnetic susceptibility may become a useful tool for the early diagnosis of MS. Imaging susceptibility may also provide a useful prognostic tool for assessing the effectiveness of treatment.

In addition, our data show that the paramagnetic lesions (increased susceptibility) may also be specific to demyelination. In asymptomatic volunteers with hyper-intense FLAIR regions, magnetic susceptibility values appear to be normal. If this finding can be verified on a larger scale of patients, it would be important as a means to differentiating overlapping pathology and improve the diagnostic specificity.

REFERENCES: 1. Schweser F. et al, NeuroImage 54:2789-2807, 2011. 2. Li et al, NeuroImage 55:1645-1656, 2011. 3. Haacke E.M. et al, JMRI 29:537-544, 2009. 4. Liu C. et al, NeuroImage 56:930-938, 2011.