Detecting Iron Deposition In Multiple Sclerosis Using Susceptibility Contrast Imaging

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TARGET AUDIENCE: Radiologists, neurologist, physicians, MR physicists.

PURPOSE: Hypointensity of deep brain gray matter (GM) structures in T_2-weighted images (T2WI) of multiple sclerosis (MS) patients has been reported and suggested to represent increased iron deposition[1]. However, these findings are difficult to generalize because the contrast in T2WI depends on a number of MR parameters including TE, TR, and others. The goal of this study is to explore the use of quantitative susceptibility contrast imaging including R2* and Quantitative Susceptibility Map (QSM) to identify characteristic regions suggestive of increased iron deposition in MS patients.

METHODS: Ten clinically definite MS patients (F/M = 8/2, age = 56.0±8.3 y/o, EDSS score = 0-6.0) and ten healthy volunteers (F/M = 5/4, age = 37.5±12.5 y/o) participated in this study. A 3D multi-echo gradient-echo acquisition was performed on a 3T Siemens Skyra scanner with a standard 20-ch head/neck coil. The parameters were as follows: TE = 8.49/16.86/25.23/33.60/41.97 ms, TR = 49 ms, resolution = 0.9×0.9×2 mm^2, flip angle= 20°, bandwidth= ±38.4 kHz. A total of 52 axial slices were acquired to cover the whole brain. A GRAPPA of 2 was used to shorten the scan time down to 5 minutes. Quantitative R_2^* maps were derived from exponential fitting over the 5 echo data. The Laplacian algorithm was used to unwrap the raw phase and remove the phase background. The susceptibility maps were then calculated using the LSQR algorithm based on the unwrapped phase maps[2] and averaged over three echo data (25.23, 33.60 and 41.97 ms). Six regions of interest (ROIs) including substantia nigra (SN), red nucleus (RN), globus pallidus (GP), putamen (PU), caudate nucleus (CN) and thalamus (TH) were manually drawn on the magnitude images. A registered MP-RAGE image was used as an additional reference for the ROI drawing. Each ROI was drawn on multiple successive images to almost entirely cover each structure. R_2^*, and susceptibility values were averaged in each ROI, respectively, and then averaged across all the subjects in the group. Results in the patient group and control group were compared by two-way ANOVA and corrected for multiple comparisons.

RESULTS: Two representative axial slices of the MR images containing the ROI regions from one MS patient and one control volunteer are shown in **Fig. 1**. The SN, RN, GP, PU and CN are readily identifiable in the magnitude, and R_2^* maps as dark and bright regions, respectively. Comparing to the magnitude and R_2^* maps, these iron-rich structures are clearly visible and distinguishable with clear boundaries in the QSM. TH has moderate contrast in the three image types but is still visible, especially in the QSM. Two diffused lesions in the optical fibers were detected in R2* maps (yellow arrows) but less visible in magnitude and QSM maps. **Fig. 2** shows a comparison between MS patients and controls in different ROI regions. An overall greater values in both R_2^* and susceptibility were observed in the MS group for all the regions except TH. The differences in both R_2^* and susceptibility are significant in CN, GP and SN regions ($p < 0.05$). The group difference in PU is significant in the R_2^* maps and the difference in SN is significant in QSM.

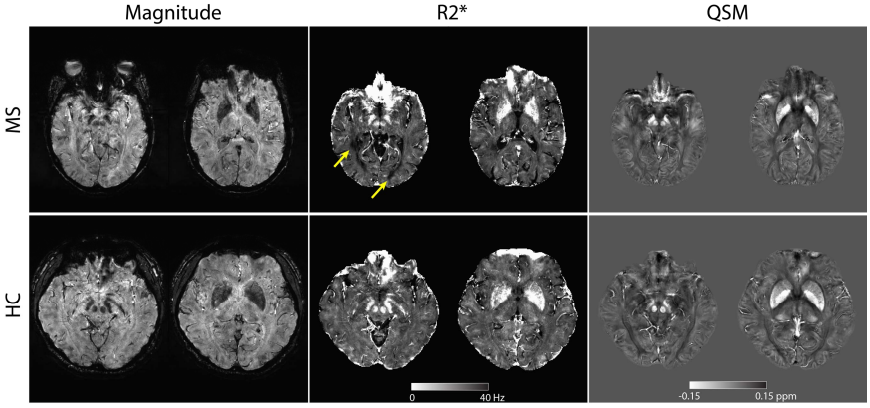

Fig. 1: *Representative axial slices in Magnitude (TE = 33.6 ms), R_2^*, and QSM maps, respectively, containing SN, RN, GP, PU, CN and TH regions from one MS patient (top row) and a healthy volunteer (bottom row). Yellow arrows point at visible lesions.*

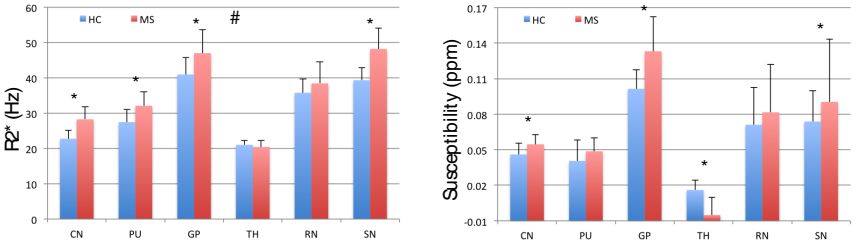

Fig. 2: *A comparison of the R_2^* and susceptibility values between MS patients (MS) and healthy controls (HC) in different brain regions. "*" indicates a significant difference between patient and healthy groups ($p < 0.05$); "#" indicates a significant interact difference between groups and ROI regions.* The *error bars are standard deviations.*

DISCUSSION AND CONCLUSION: The overall higher R_2^* and susceptibility values in the patient group may indicate a higher iron deposition in most of the iron-rich regions in the brain. These results are supported by recent findings from neuropathology at autopsy, which show that the substantial degeneration of deep grey matter structures corresponds with iron accumulation and oxidative damage[3]. In fact, increased iron deposition is found to be correlated with measurements to patient disability[4]. Interestingly, not like the other regions, TH shows no significant difference in R_2^* between the two groups but a significantly lower values of susceptibility in patient. Our interpretation is that thalamus is a region mixed of gray matter and white matter tissues. The myelin component in the white matter, fiber orientation and etc. also play significant roles in contributing contrasts in R_2^* and QSM. The final contrasts in R_2^* and QSM are a combination of all these factors. A fine segmentation within the structure may be necessary to evaluate this.

REFERECES: [1] Bakshi R et al, Arch Neurol 59:62, 2002; [2] Li W et al, *Neuroimage* 55:1645, 2011; [3] Haider L et al, JNNP, doi:10.1136/jnnp-2014-307712, 2014; [4] Rudko DA et al, Radiology, 272:851, 2014