High Percentage of MS lesions found to have a central vein using single slice SWI at 7 Tesla

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TARGET AUDIENCE: TARGET AUDIENCE: Researchers and clinicians interested in multiple sclerosis (MS) and MRI.

INTRODUCTION: Post-mortem histopathology studies have consistently demonstrated white matter MS lesions tend to be associated with a central vein. With the advent of ultra-high field (≥ 7T) MRI systems, researchers have been able to more accurately visualize venocentric MS lesions. It has additionally been suggested that venocentric lesions could be used as a biomarker for separating MS patients from controls and from other diseases whose lesions mimic those of MS [1,2] .However, to date, application of central vein analysis method has been time-consuming and labor intensive, limiting its application in clinical practice. In this study we optimized the visualization of veins by incorporating inter-echo variance (IEV) [3] in the generation of susceptibility-weighted images (IEV-SWI) with 7T MRI. SWI images were registered to T2-weighted magnetization-prepared fluid-attenuated inversion-recovery (FLAIR) images to visualize venocentric lesions. If the IEV-SWI is able to pick up smaller veins than previous methods, then one would expect a higher %LCV than previously described.

METHOD: ***Image acquisition:*** Imaging was performed using a 7-T neurospecialized MR imaging system with 16 parallel transmit channels and either 24 or 31-channel receive coils. Main external magnetic field (B_0) and radiofrequency transmit field (B_1^+) shimming were performed in each subject prior to acquisition with the following sequences: (a) a 3D multi-echo GRE sequence to obtain susceptibility-based images, (b) a FLAIR sequence for lesion delineation ($1.0 \times 1.0 \times 1.0$ mm^3 resolution), and (c) a T1-weighted, magnetization-prepared GRE acquisition for anatomic reference and use in tissue segmentation ($1.0 \times 1.0 \times 1.0$ mm^3 resolution). For the multi-echo GRE sequence, we used the axial orientation and the following pulse sequence parameters: TR/TEs = 40/3.77, 7.86, 12.15, 16.64, 21.33, 26.22 ms; flip angle, 13°; in-plane resolution, 0.5×0.5 mm^2; section thickness, 1.25 mm; total imaging time, 15 minutes 55 seconds with GRAPPA factor R = 2 [2].

SWI construction: The complex multi-echo GRE images of all individual channels were used to reconstruct the SWI images. In particular, channel combination at each echo was performed using the inter-echo variance-based technique (IEV): briefly, IEV channel combination first unwraps the phase images, applies a Gaussian filter with a kernel size σ (= 0.006), then calculates the inter-echo variance on a pixel-by-pixel basis and uses it as a weighting factor during channel combination [3]. After channel combination is done, the IEV local frequency-shift (LFS) map is scaled back to a phase image a factor of $2\pi TE_i$, where TE_i is the i^{th} echo time. To reconstruct the SWI images at each echo, a phase mask was generated from the phase maps using the standard approach on a echo-by-echo basis. Lastly, the SWI images from each echo were averaged to increase SNR of the final echo-combined SWI images [4].

FLAIR and SWI registration/overlay: The IEV-SWI and corresponding FLAIR image were registered to each other using the FLIRT tool in FSL. Next, the FLAIR image was overlayed on the SWI image for central vein identification.

Image Analysis: Data from out database for five patients diagnosed with MS were analyzed in this study. For each patient's data, three raters were instructed to independently find lesions on the FLAIR images, defined as hyperintensities not explained by cortical matter or normal anatomy. Raters were then able to toggle to the co-registered IEV-SWI to evaluate the presence of a central hypointensity suggestive of a vein for each lesion. For each rater, the %LCV was calculated for each subject; %LCV is defined as the division of the number lesions with a central vein by the total number of lesions.

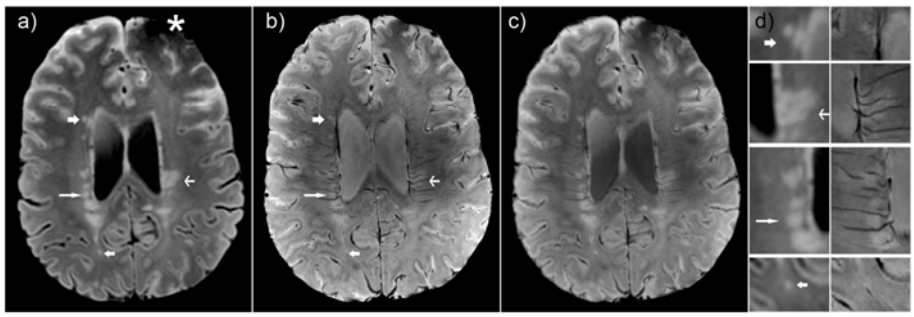

Figure 1. MRI scans from an MS patient a) FLAIR image with white arrows identifying MS lesions b) IEV-SWI showing the veins in highlighted regions c) A co-registered SWI-IEV with FLAIR overlay similar to that used to calculate %LCV d) regions of interest from a) and b) magnified by 2x power (left FLAIR, right SWI).

RESULTS and DISCUSSION: FLAIR images were registered and fused with IEV-SWI images as shown in Figure 1. The FLAIR images were first used to localize the white matter lesions. Then the fused image was then referenced to determine the presence or absence of a vein. This study will determine whether using IEV-SWI technique results in more veins being detected in MS lesions and whether or not this can be used to distinguish MS patients from healthy controls and potentially other diseases with similar white matter hyperintensities. If this is true it would strongly suggest that IEV-SWI is more sensitive in detecting the small penetrating veins found in MS. Three independent observers found a high %LCV in 5 MS patients. Mean with SD was: 94.6 ± 5.1%, 97.4 ± 4.0%, and 86.4 ± 3.8% for observers 1,2, and 3 respectively. Previous work by Grabner et al. also used 3T FLAIR registered with 7T SWI were also able to detect central veins within MS lesions, but to a much lesser extent; 75 veins found within 299 lesions, 25% LCV [5]. Tallantyre et al, also found a very high %LCV in MS patients (80%) compared to healthy controls (19%) and using a cutoff of 40% LCV was able to separate 100% of MS patients form healthy controls using 7T T2*-weighted MRI [1]. Our initial findings support that the IEV-SWI technique is able to detect smaller veins and thus able to identify a higher %LCV which is more reflective of what is expected in MS from post-mortem studies. Ongoing work in our lab is comparing %LCV between MS patients and controls in a larger cohort with the goal of using %LCV to distinguish MS patients from healthy controls and MS mimics.

CONCLUSION: This study used 7T IEV-SWI and found high %LCV in MS patients. Future work will determine whether or not this technique can be used clinically to distinguish MS patients from healthy controls as well as from common MS mimics.

REFERENCES: 1] Tallantyre, et al., Neurology 76 (6): 534-339, 2011 [2] Rudko, et al., Radiology 2014 doi:132475 [3] Lui et. al, Magn Reson Med 2014 doi: 10.1002/mrm.25247 [4] Denk and Rauscher, JMRI 31:185-191, 2010 [5] Grabner et al., JMRI33:543-5, 2011