

## Quantitative Susceptibility Mapping of White Matter Hyperintensities in Patients with Traumatic Brain Injury

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### Introduction

White matter hyperintensities (WMH) are areas of focal and diffuse increased MRI signal visualized radiologically on T2-weighted scans. WMH have been related not only to age but also to different risk factors of cardiovascular disorders and neurocognitive disorders (1). Over 60% of the military patients with traumatic brain injury (TBI) scanned at the National Intrepid Center of Excellence demonstrated WMH (data not shown). However, these WMH are nonspecific and could be caused by a variety of pathologies not related to trauma. Further investigation is necessary to explore the potential causes of these WMH. The contrast in quantitative susceptibility map (QSM) is caused by tissue magnetic susceptibility, which is useful for chemical identification and quantification of iron, calcium, and gadolinium (2,3). The presence of iron in WMH could be a marker for microhemorrhage and suggest that the lesions originated from trauma. This paper aims to characterize the apparent susceptibility of the WMH in TBI patients using QSM.

### Methods

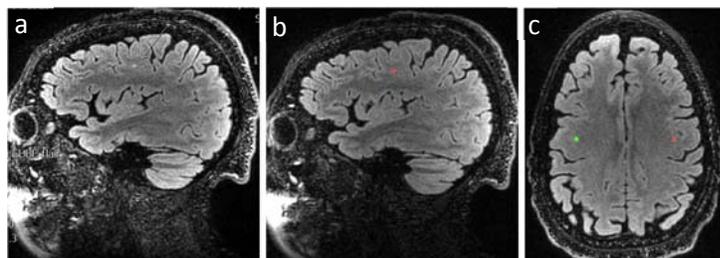
37 military TBI patients ( $33.5 \pm 7.7$  years, 4 female, 32 mild and 5 moderate to severe, 91% from blast) were scanned on a 3T GE 750 with a 32-channel phased array head coil. T2 FLAIR images were acquired with a 3D CUBE sequence: TR/TE = 6500/130 ms, FA = 90°, Resolution =  $0.5 \times 0.5 \times 0.6$  cm<sup>3</sup>, ARC = 2. Multi-echo images were acquired using a 3D flow-compensated multi-echo gradient-echo sequence, with TR = 45 ms, 5 echoes, TE<sub>0</sub> = 13 ms, echo-spacing = 6 ms, FA = 20° and asset-factor = 2. Images were acquired with a  $512 \times 256$  matrix,  $24 \times 24$  cm<sup>2</sup> FOV, and 88 slices at 1.5 mm thickness.

QSM images were calculated from the multi-echo complex imaging data, using the morphology-enabled dipole inversion approach (2,3) implemented in the MEDI software (Dept. of Biomedical Engineering, Cornell University, NY).

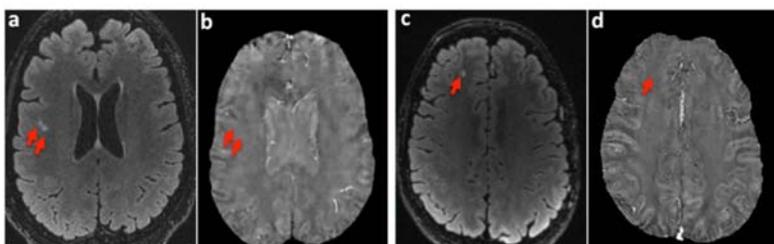
The T2 FLAIR images were read by a trained neuroradiologist and WMH were manually marked. For each WMH, a 1.5 mm sphere-ROI was manually drawn at the center using AFNI's graphical interface. Control ROIs were drawn on the side contralateral to the WMH ROIs on T2 FLAIR images. The magnitude images from the middle echo of the multi-echo images were used to align the QSM images to T2 FLAIR images. WMH ROIs and control ROIs were subsequently applied to the QSM images.

### Results

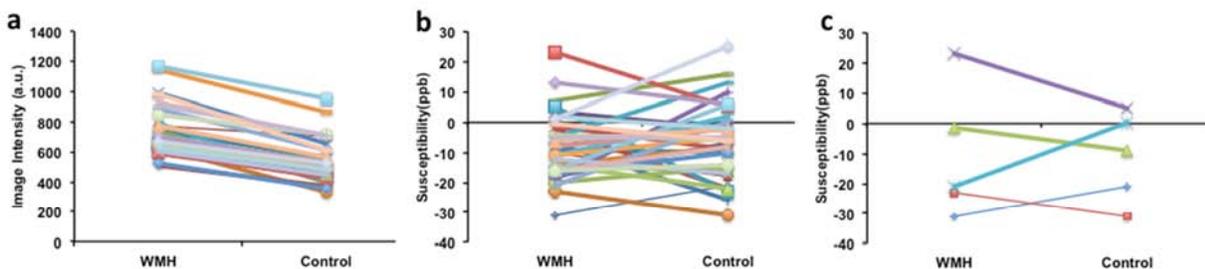
As shown in Figure 2, regions showing hyperintensities on T2 FLAIR images did not demonstrate alterations in apparent magnetic susceptibility on QSM images by visual inspection. The comparison of image intensities on T2 FLAIR images and QSM images between WMH ROIs and control ROIs is illustrated in Figure 3. As expected, image intensities of WMH ROIs were significantly higher than those of the control ROIs' on T2 FLAIR images (Figure 3a,  $730 \pm 155$  vs.  $526 \pm 136$ ,  $p < 0.001$ ). However, WMH ROIs and control ROIs demonstrated similar susceptibilities on QSM images for all 37 patients (Figure 3b,  $-8.06 \pm 10.7$  ppb vs.  $-6.79 \pm 12.3$  ppb,  $p = 0.41$ ). The apparent susceptibilities of the WMH ROIs and control ROIs were also similar in 5 patients with moderate to severe TBI (Figure 3c,  $-10.7 \pm 21.8$  ppb vs.  $-11.1 \pm 14.9$  ppb,  $p = 0.95$ ).



**Figure 1:** a: A T2 FLAIR image on PCAS with a WMH mark from the neuroradiologist. b: WMH ROI (red) manually drawn using AFNI's graphical interface. c: The control ROI (green) manually drawn on the contralateral side.



**Figure 2:** T2 FLAIR images from two patients (a, c) showing WMH (red arrows) and the corresponding QSM images (b,d). Note that no visible alterations were observed at the spots where WMH were located.



**Figure 3:** a: Image intensities of the WMH ROIs and control ROIs on T2 FLAIR images from 37 TBI patients. b: Apparent magnetic susceptibilities of WMH ROIs and control ROIs from 37 TBI patients. c: Apparent magnetic susceptibilities of WMH ROIs and control ROIs from 5 patients with moderate to severe TBI.

### Discussion

The high prevalence of WMH in TBI patients suggests that these WMH may be associated with white matter damage from trauma. ROI analysis from 37 TBI patients with WMH demonstrated that WMH ROIs were not associated with changes in apparent magnetic susceptibility. Because iron and myelin are the two major contributors to the image contrast observed in QSM (4), our results suggest that the WMH observed in TBI patients may not be associated with iron deposition or demyelination and could be due to other sources such as gliosis.

### Reference:

1. Detette S and Markus HS, *BMJ* 2010;341:366. 2. Liu J et al. *Neuroimage* 2012;59:2560-2568. 3. Liu T et al. *Radiology* 2012;262:269-278. 4. Langkammer C et al. *Neurorimage*;2012:1413-1419.