Correlation of Quantitative Susceptibility Mapping in Cerebral Cavernous Malformations with Clinical Features

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Target Audience: Radiologists, Neurosurgeons, MR physicists

Introduction: Cerebral cavernous malformation (CCM) is a common hemorrhagic vascular anomaly of the human brain, characterized by vascular leak and repetitive lesional hemorrhages. Our lab has previously demonstrated the feasibility of QSM in a cohort of clinical CCM patients with promising results[1,2]. In this study, we aimed to correlate the baseline characteristics of patients and their clinical activities with QSM measurements in a larger cohort of CCM patients. Specifically, we aimed to test the following hypotheses: 1) older lesions have higher susceptibility; 2) lesions with previous hemorrhagic events have higher susceptibility; and 3) lesional susceptibility over time will have small changes in patients who are stable clinically, and decreases in patients who are recovering from previous hemorrhages.

Methods: Patient population: A total of 84 CCM patients were included for the study with institutional review board approval. Datasets with poor image quality due to patient motion and/or system issues were excluded from the final analysis. The resulting datasets include 65 (49 M, 16F, mean age 39) patients. 15 patients received a second QSM scan 6 – 18 months later following their initial QSM exam. 22 patients were scanned on a Siemens 3T (MAGNETOM Verio) system and 43 patients were scanned on the Philips 3T (Achieva) system. Imaging protocol: A three-dimensional, T2*-weighted, multi-echo, spoiled gradient echo sequence was used for QSM data acquisition with the following common parameters: 8 echo times (TEs) with uniform spacing; flip angle 15 degrees; parallel acceleration of a factor 2. The following parameters are system specific: (Philips) TE [min, max], [5.6, 51] ms; field of view, 224 mm; acquisition matrix 224x224; slab encoding thickness, 1mm; repetition time, 66 ms; (Siemens) TE [min, max], [3.6, 45] ms; field of view, 240 mm; acquisition matrix 256 x 256; slab encoding thickness, 1.5 mm; repetition time, 55 ms. Susceptibility maps were reconstructed using a morphology-enabled dipole inversion algorithm[3]. Quantitative Analysis: Lesional ROIs were defined manually by an experienced physician. All CCM lesions in sporadic cases were included. In familial cases, only lesions identified on T2 weighted images with a maximum cross-sectional diameter greater or equal than 5 mm were included. Mean susceptibility was calculated in a total of 241 lesions (repeated cases included).

Results: We have performed cross-platform validation between the Philip and Siemens 3T systems and high agreements on susceptibility measurements were achieved (correlation coefficient of 0.98, R^2>0.99, $p < 0.01$). Hypothesis 1: since it is difficult to know the accurate duration of lesion presence, we used the age of patient at the time of the MRI scan as the estimator. Pearson's correlation showed that patient age at scan is positively correlated with the mean lesional susceptibility per patient ($p<0.05$, Figure 1). Hypothesis 2: Only hemorrhagic events prior to the most recent MRI exam were considered for this analysis. Student's t-test revealed the mean susceptibility was significantly higher in lesions that previously bled at least once than those without previous bleeds ($p<0.05$, Figure 2). We did not find any significant correlation between the number of prior bleeds and lesional mean susceptibility. Hypothesis 3: In patients who are clinically stable and have received repeated QSM scans, we found little changes in lesional susceptibility (Figure 3).

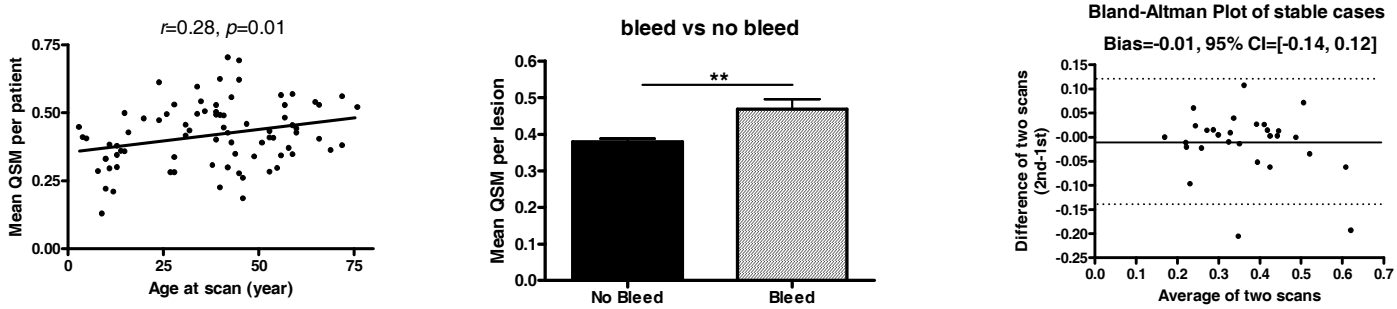

Figure 1-3 (left to right). 1) Patient age at scan vs. mean susceptibility per patient; 2) mean susceptibility between lesion groups with and without previous hemorrhagic events; 3) Bland-Altman plot of lesions without prior bleeds in patients with repeated QSM scans.

Discussion: Our investigation of lesional QSM measurement and the clinical activities in a cohort of CCM patients suggested that: 1) older lesions harbor more iron and/or iron-containing blood byproduct (referred to iron deposition hereinafter); 2) lesions that has bled previously harbor more iron deposition; 3) there are little changes in lesional iron deposition in patients who are clinically stable in a short time frame (< 1.5 years).

Conclusion: QSM offered additional insights into the natural progression of the CCM disease in terms of the accumulation of lesional iron deposition. More longitudinal cases with improved statistical power to fully validate QSM as an imaging biomarker for monitoring CCM disease progression and/or response to treatments.

References: 1) Tan et a. Invest Radiol, 2014. 2) Mikati et al. Stroke, 2014. 3) Liu et al. Magn Reson Med, 2011.