Evaluation of Susceptibility Weighted Imaging in Children with Sickle Cell Disease

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Introduction: One of the most devastating complications in children with sickle cell disease (SCD) is stroke.[1] Stroke risk arises from occlusive contributions caused by vascular injury from sickle red blood cells (sickle vasculopathy), and hemodynamic contributions from the anemia-associated hyperemia.[2] SCD patients at risk for and those patients who have already experienced particularly stroke routinely undergo MR imaging to assess the integrity of their cerebrovascular system. MR angiography is useful in SCD patients to detect stenosis and determine stroke risk.[2] There is active research in perfusion imaging for prospective identification of children with SCD at risk for developing subclinical infarction.[3,4] Similarly, three-dimensional gradient echo (3D-GRE) susceptibility-weighted imaging (SWI)[5] which is used to visualize the venous vasculature and is known to be affected by perfusion[6] could be a marker of stroke risk. In this study, we investigate the role of SWI in SCD. We use a hessian-based vessel segmentation algorithm to quantify the venous contrast in patients and compare group results to normal controls. Furthermore, we correlated the visible venous volume calculated in each SWI data set with physiological parameters to investigate if this quantitative SWI measure can be used as a biomarker of disease progression.

Methods: 30 non-sedated patients with SCD (17 F, mean age 12.8±4.0 years; 13 M, mean age 13.5±3.2 years) and gender/age-matched healthy controls (17 F, mean age 12.8±4.3years; 13 M, mean age 13.5±2.9 years) who received SWI as part of their MR exam were analyzed in this retrospective Institutional Review Board approved study. Physiological parameters such as hemoglobin level, absolute reticulocyte count, and hematocrit were also collected in the SCD group if the blood tests were performed within seven days of the MR exam (n=27). In the SCD group, 18 exams were performed at 1.5T (Siemens Avanto and Symphony) and 12 exams at 3T (Siemens Trio and Skyra). All control exams were acquired at 3T. A 3D T2*-weighted GRE SWI sequence with the following parameters was used: TE/TR 25/56 ms (3T) and 40/60 ms (1.5T), flip angle 20º, FOV 210×210 mm^2, slice thickness 2 mm, matrix size 384×257×72, and a parallel imaging acceleration factor of 2. Using minimum intensity projection (mIP) images after SWI processing, brains were extracted using BET[7] and a 2D Hessian matrix was calculated. The second eigenvalues of the Hessian matrix were patient specifically thresholded to create a segmented vein map. A normalized visible venous volume (NVVV) was calculated by dividing the volume of voxels identified as veins above the level of the middle cerebral artery (MCA) by the total intracranial volume above the MCA. In addition, basilar vessel tortuosity (τ) was measured according to [8] on an MRA acquired during the exam since high basilar τ has been associated with higher blood flow in children with SCD.[9] Group differences were assessed using Wilcoxon rank sum test. Linear dependencies of physiological markers with NVVV were evaluated using the Pearson's correlation coefficient.

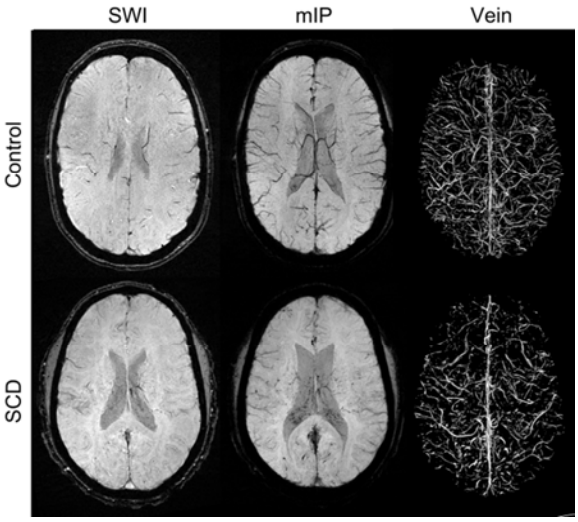

***Figure 1**: Representative images selected from the SCD and control group. Note the mIP and vein mask show decreased venous contrast in the SCD patient.*

Results: Figure 1 shows a representative example of the SWI, mIP, and maximum intensity projection of the segmented vein images from the control and SCD groups. There was a significant difference in NVVV between the SCD (0.011±0.005) and the controls (0.038±0.012) ($p<0.001$). Using the group of SCD patients (n=12) examined at 3T, there was also a significant difference in NVVV in comparison to the controls (0.012±0.004, 0.041±0.013, respectively) ($p<0.001$). There was no difference in NVVV between 1.5T and 3T in the SCD group (0.011±0.006, 0.012±0.004, respectively) ($p=0.43$) or gender differences in the SCD group ($p=0.80$) and control group ($p=0.96$). There was no significant correlation of SCD's NVVV with the hematocrit ($p=0.37$), hemoglobin ($p=0.41$), or absolute reticulocyte count ($p=0.85$). There was a significant, inverse correlation between NVVV and vascular tortuosity (Figure 2).

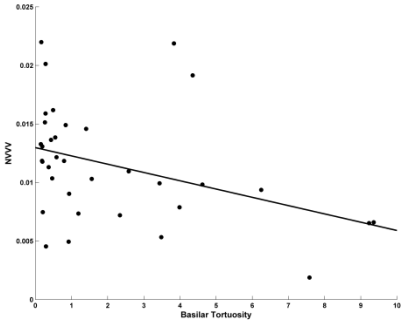

***Figure 2:** Correlation between basilar tortuosity and NVVV(R=-0.38, P=0.024).*

Discussion/Conclusion: SWI can be used in SCD to monitor vascular integrity. However, the conspicuity of venous contrast in SCD is qualitatively less than in controls and NVVV shows a significant quantitative decrease. NVVV was independent of gender or field strength (with TE optimized to field strength). Given that SCD can affect the concentration of paramagnetic deoxyhemoglobin, which is the source of contrast in SWI, it was expected that certain physiological parameters, such as hemoglobin levels and absolute reticulocyte count, would correlate with the amount of venous contrast in SWI. However, none of the physiological parameters correlated with NVVV. As SCD produces a complex physiological response to maintain adequate cerebral oxygenation, several other factors, particularly elevated flow velocities and perfusion[6], may play a major role in the decreased SWI contrast. The inverse association between basilar τ and NVVV may also attribute to this fact. Further studies are needed to investigate the mechanism of decreased venous contrast as seen in SWI of SCD patients to determine its prognostic utility as an imaging biomarker of disease progression or stroke risk.

References: [1] Ohene-Frempong K et al (1998) *Blood* 91: 288-94. [2] Debaun MR et al (2006) Ment Retard Dev Disabil Res Rev 12: 192-9. [3] Oguz KK et al (2003) Radiology 227:567-74. [4] Helton KJ et al (2009) Pediatr Blood Cancer 52:85-91. [5] Reichenbach JR et al (2001) *NMR Biomed* 14:452-67. [6] Sedlacik J et al. (2010) *AJNR* 31:901-6. [7] www.fmrib.ox.ac.uk/fsl [8] Steen, R et al (1998) J Stroke Cerebrovasc Dis 7:32-43. [9] Steen, R (1998) J Stroke Cerebrovasc Dis 7:330-38.