

Arterial Spin Labeling and Diffusion Tensor Imaging of Early Kidney Changes in Pediatric Sickle Cell Disease Patients

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Introduction: Sickle cell disease (SCD) affects ~100,000 African Americans and is characterized by abnormal, or “sickled”, red blood cells (RBCs). SCD patients are at an increased risk for acute clinical events such as stroke and acute chest syndrome. In addition, one third of SCD patients suffer from chronic kidney disease (CKD) which starts in childhood and results in increased morbidity and mortality. Unfortunately current clinical assessments of kidney function are either 1) insensitive to focal early-stage CKD (i.e., serum creatinine) or 2) require injectable radiotracers undesirable for pediatric imaging studies. Therefore, improved techniques to non-invasively and sensitively assess early-stage CKD in sickle cell disease patients are needed to eventually develop effective therapies. In this initial study, we are using Diffusion Tensor Imaging (DTI) and Arterial Spin Labeling (ASL) MRI techniques to assess renal microstructure and blood flow in pediatric SCD patients in comparison to healthy control subjects. It is believed that CKD is due to chronic and acute vaso-occlusion/ ischemia which should be detectable by ASL and/or DTI. Overall, our goal is to provide a quantitative and non-invasive basis to sensitively detect early-stage structural and functional kidney changes in pediatric SCD patients.

Methods: Six pediatric SCD patients with early-stage CKD (age: 12-18, eGFR 110-185 ml/min/1.73m²) and six healthy young adult controls were scanned according to our approved Institutional Review Board (IRB) protocol. The patient and healthy controls were scanned in the supine position with no sedation in a Siemens Espree 1.5T MRI scanner. The DTI data were acquired using respiratory-gated, single-shot echo planar imaging (EPI) sequence (FOV, resolution, b= 0, 400 s/mm, 6 directions + null). Apparent Diffusion Coefficient (ADC) and Fractional Anisotropy (FA) maps of the kidney were calculated using established methods.¹ Renal ASL data were acquired using a novel ASL-FISP acquisition which combines a conventional flow-sensitive alternating inversion recovery (FAIR) ASL preparation with a centrically-encoded FISP readout to limit artifacts from EPI and True FISP acquisitions.^{2,3} Quantitative ASL-based perfusion maps (in ml/min/100g of tissue) were calculated using previously reported models.⁴ Conventional coronal T2-weighted MRI images were acquired to delineate medullary and cortical kidney regions to calculate the mean ADC/FA and perfusion for the renal medulla and cortex for each subject. A Student’s t-test was performed to compare the mean renal DTI and ASL results between the pediatric SCD patients and healthy controls.

Results: **Figure 1** shows ADC/FA maps comparing healthy controls to SCD patients. Distinct medullary regions of high FA value (FA > 0.3) are visible for the healthy controls as described previously⁵. For the SCD patients, the medullary FA values are visually decreased (FA < 0.3) suggesting degradation of medullary microstructure (tubules/vessels). Both cortical ADC (p < 0.02) and medullary FA (p < 0.01) were significantly reduced in these images indicative of microstructural changes associated with CKD in sickle cell disease patients. No other significant differences in ADC/FA were observed. ASL perfusion maps for a SCD patient and a healthy control are shown in **Figure 2**. Visually reduced cortical perfusion was observed for the SCD patients in comparison to healthy controls. Mean cortical perfusion values were also significantly reduced in pediatric SCD patients in comparison to controls (*p < 0.05).

Discussion and Conclusion: These are the first ever reported ASL and DTI results demonstrating early kidney changes in pediatric sickle cell disease patients. Our initial results demonstrated a significant reduction in cortical ADC, medullary FA, and cortical blood flow in pediatric sickle cell patients in comparison to healthy volunteers. These observed focal kidney changes are in accordance with the working understanding of CKD in sickle cell disease resulting from chronic and acute renal vaso-occlusion. It is also important to note that these quantitative assessments were successfully obtained in two pediatric SCD patients undergoing chronic transfusions and therefore had significant renal iron loading. Overall, these initial results also suggest that ASL and DTI techniques can provide a quantitative assessment of CKD in sickle cell disease patients that has the potential to complement current clinical assessments of kidney function.

References: [1] Basser PJ Biophys J. 1994 66(1):259-67. [2] Lu, L. Magn Reson Med. 2012 Sep;68(3):868-73. [3]Shah,T. Magn Reson Med. 2011 Feb;65(2):432-7. [4] Kim SG, et al, Magn Reson Med 1997. [5]Sigmund, EE. Radiology. 2012 Jun;263(3):758-69.

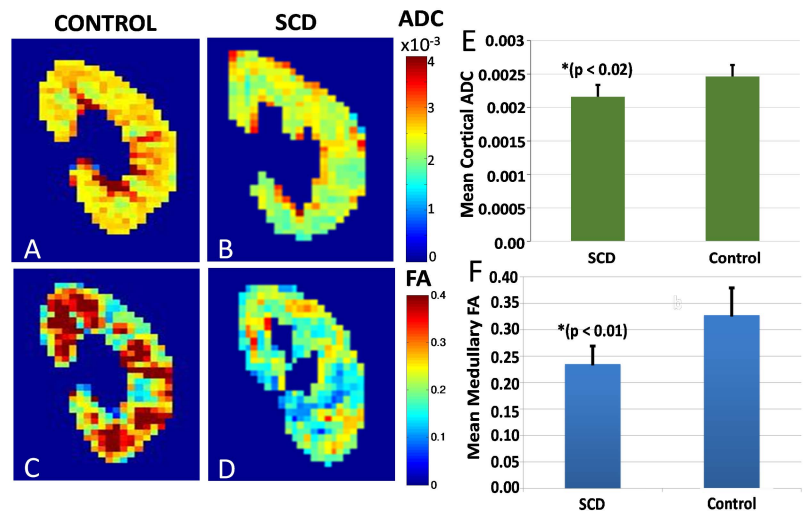


Figure1: Representative kidney ADC maps (A,B) and FA maps (C,D) from a healthy control and pediatric SCD patient. Comparison of mean cortical ADC (E) and medullary FA (F) values for all pediatric SCD patients (n=6) and healthy controls (n=6). Note the significantly reduced cortical ADC values (p < 0.02) and medullary FA values (p < 0.01) for the SCD patients.

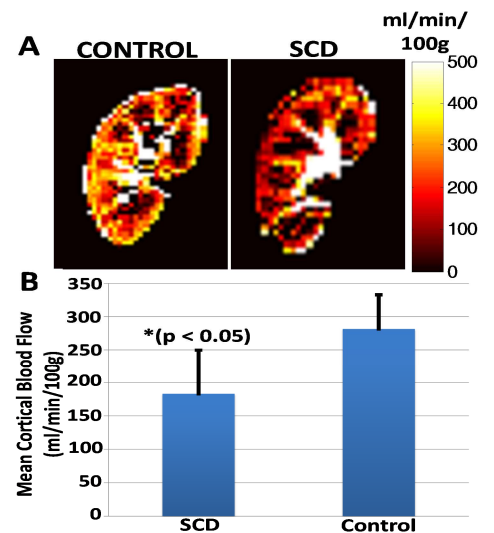


Figure 2: (A) Representative kidney ASL perfusion maps from a healthy control and a pediatric SCD patient. (B) Mean cortical perfusion (in ml/min/100g of tissue) MRI for ALL pediatric SCD patients (n=6) and healthy controls (n=4). Note the significantly reduced cortical perfusion in SCD patients (p < 0.05).