

Examining large vessel flow and microvascular perfusion in pediatric sickle cell patients with and without Moyamoya disease

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**Introduction.** Pediatric sickle cell anemia (SCA) patients are at increased risk of stroke compared to the pediatric population at large. Both large and small vessels are implicated in strokes and cerebrovascular events; thus, when considering stroke risk it is useful to assess both large vessel blood flow and microvascular perfusion. However, large vessel flow ratios do not always coincide with tissue perfusion patterns and may be influenced by acquisition timing [1]. A subset of SCA patients also have Moyamoya syndrome, and in these patients, large vessel surgeries are used to improve brain tissue perfusion. This pilot study examined large vessel flow ratios and tissue perfusion distributions in the context of large vessel distributions in SCA patients with and without corrective surgery for Moyamoya syndrome. We hypothesized that large vessel flow and microvascular perfusion asymmetries would agree in SCA patients that had undergone surgery for Moyamoya syndrome.

**Methods.** Data were acquired from four pediatric SCA patients, and informed assent and consent from the patients and their guardians, respectively, were obtained. As part of the informed consent, clinical records were examined for relevant information. Patients (Pts.) 1 and 3 each had a history of Moyamoya disease, and each had undergone superficial temporal artery to middle cerebral artery (STA-MCA) and encephalo-duro-arterio-myosynangiosis (EDAMS) revascularization on the right side (Pt. 1: 10 mo. prior to the MR scan; Pt. 3: 23 mo. prior to the MR scan). The scans were performed using a 3T Achieva MR scanner (Philips Healthcare) equipped with a 16-channel neurovascular coil. Data from each patient included two 3D time-of-flight (TOF) MRA scans (TR/TE=23 ms/3.45 ms; flip angle=20°; 100 slices and 30 slices for phase contrast MR (PCMR) planning; acq. voxel=0.5×0.51×0.6 mm<sup>3</sup>; recon. voxel=0.4×0.4×0.6 mm<sup>3</sup>; SENSE factor=2); PCMR (TR/TE=15/7.68-8.24 ms; flip angle=10°; acq. voxel=0.33×0.33×5 mm<sup>3</sup>; recon. voxel=0.31×0.31×5 mm<sup>3</sup>; 21 phases over the cardiac cycle; VENC=125 or 150 cm/s); FLAIR (TR/TE=11000/125 ms; 24 slices; gap=1 mm; acq. voxel=0.65×0.8×4 mm<sup>3</sup>; recon. voxel=0.45×0.45×4 mm<sup>3</sup>); and pseudo continuous arterial spin labeling (pCASL) (TR/TE=4000/17.3; 15 slices; voxel=2.88×2.88×7 mm<sup>3</sup>; for Pt. 1: TR/TE=4000/10.32; 15 slices; voxel=2.75×2.75×6 mm<sup>3</sup>). **TOF.** Intensity-based segmentation was used to automatically segment/reconstruct large vessels in ITK-SNAP 2.0.0 (itknap.org) [2]. Minor manual adjustments were made where necessary. **PCMR.** PCMR-measured velocities were measured in the common carotid artery (CCA) and in the vertebral arteries (Pts. 1 and 4). Using Amira 5.2.0 (Visage Imaging, Inc.), the CCA was segmented and masked. Velocity values were summed across the vessel at each time point to produce the flow rate, and the flow rates were summed over all time points using MATLAB 7.8.0 (Mathworks). These values were used to calculate the flow ratio between the left and right sides. The mean external carotid flow was assumed to be 30% [3]; thus allowing estimation of the internal carotid artery (ICA) flow ratios over the cardiac cycle. **FLAIR.** Brain lesion burden (mm<sup>3</sup>) was quantified using itk-snap [2]. **pCASL.** The cerebral blood flow (CBF) (ml/100 g/min) was determined using the single compartment, flow-modified Bloch equation.

**Results.** The CBF was asymmetric in all subjects: in Pts. 1, 3, and 4, CBF was higher in the left hemisphere, and in Pt. 2, CBF was higher in the right. In the subjects with a history of Moyamoya disease (Pts. 1 and 3), there were fewer large vessels, particularly in the right hemisphere. However, smaller collateral vessels were dispersed throughout the tissue. PCMR large vessel flow over the cycle in Pts. 1, 2, and 3 was higher on the left, and in Pt. 4, flow was higher on the right. Lesions were evident in the FLAIR data of two subjects, and the lesion burdens of Pts. 1 and 3 were approximately 15,000 and 200 mm<sup>3</sup>, respectively.

**Discussion.** The redundancy – or the lack thereof in Pts. 1 and 3 – of large vessels in the Circle of Willis affects the relationship between ICA flow ratio and CBF distributions. More redundant structures allow greater mixing of blood from the contributing arteries as a compensatory mechanism to maintain tissue perfusion to offset ICA flow asymmetries. Further, areas of infarcted tissue, particularly in Pt. 1, limit the local tissue perfusion. In addition, basilar artery flow may sway left/right ICA flow distributions. In Pt. 1, the basilar flow (the sum of vertebral artery flow) contributes 38% of the total flow, and in Pt. 4, it contributes 35%; in both cases, the basilar flow is at least as large as the dominant ICA flow and is expected to influence the CBF distributions. Limitations include the assumption that 70% mean flow from the CCA is directed to the ICA and the small number of subjects. However, this pilot study suggests that it is crucial to consider large vessel configurations when interpreting the relationship between large vessel flow and CBF in pediatric SCA patients. Further, pre-/post- surgery studies will be valuable for determining the efficacy of large vessel rerouting surgeries in improving central nervous system status and in assessing the role of infarcted tissue in limiting microvascular perfusion in SCA patients with Moyamoya syndrome.

1. Gevers S *et al.*, ISMRM 373, 2011. 2. Yushkevich PA, *et al.*, Neuroimage, 2006. 3. Ku DN, *et al.*, Ultrasound in Med. & Biol, 1985.

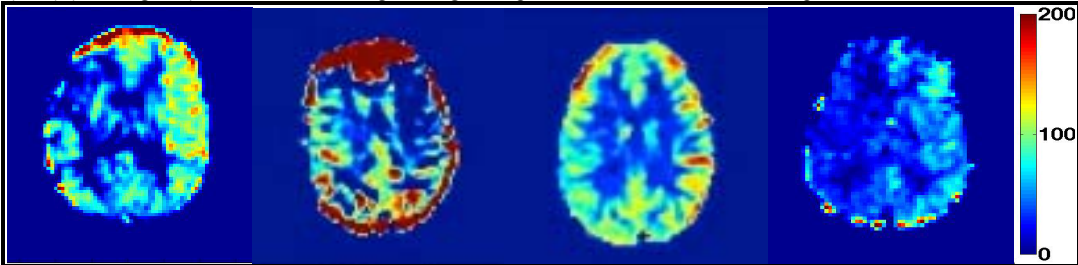


Figure 1. Representative CBF (ml/100 g/min) of each subject. Left to right: Patients 1, 2, 3, and 4.



Figure 2. Vessel reconstructions from TOF data. Left to right: Patients 1, 2, 3, and 4. Axes: X=R; Y=A; Z=H.

	Patient			
	1	2	3	4
Flow Ratio	1.07 L:R	1.25 L:R	1.60 L:R	1.23 R:L

Table 1. PCMR-measured flow ratio (L:R) over the cardiac cycle in each patient

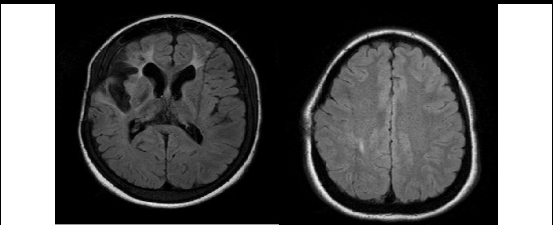


Figure 3. FLAIR data showing lesions in Patients 1 (L) and 3 (R).