Venous Outflow of Label in ASL Perfusion MRI of Healthy Children and Children with Sickle Cell Disease

W-C. Wu[1], H. Rao[2], M. A. Pawlak[1], K. M. Cecil[3], J. VanMeter[4], T. A. Zeffiro[5], J. A. Detre[2], E. R. Melhem[1], and J. Wang[1]

[1]Dept of Radiology, University of Pennsylvania, Philadelphia, PA, United States, [2]Dept of Neurology, University of Pennsylvania, Philadelphia, PA, United States, [3]Dept of Radiology, Cincinnati Children's Hospital, Cincinnati, OH, United States, [4]Dept of Neurology, Georgetown University Medical Center, Washington DC, United States, [5]Neural system group, Massachusetts General Hospital, Boston, MA, United States

Introduction

Arterial spin labeling (ASL) is an MR technique allowing noninvasive measurement of microvascular blood flow, also referred to as perfusion. An implicit assumption in most quantitative models is that the tagged arterial spins arrive at the capillary network (and the surrounding tissue) without leaving or relaxing prior to data acquisition. Although this assumption generally holds in the brain of adult humans under normal conditions, evidence has suggested a finite permeability of the capillary wall to water (1) and the likelihood that the tagged spins pass through the capillary network without being extracted into the tissue. Both elevated flow and prolonged tracer half-life (blood T1) can accentuate the venous outflow, which has been suspected to confound flow quantification using ASL (2). In this study, continuous ASL (CASL) was employed to measure perfusion in normal adults, normal children and children diagnosed with sickle cell disease (SCD). Healthy children are known to have increased cerebral blood flow (CBF) compared to adults, which is further elevated in SCD children due to their low hematocrit level (3). In the present study, venous outflow was detected as hyperintensities in the sinuses of the dura mater and further quantified as a function of the average flow in gray matter in the pediatric population.

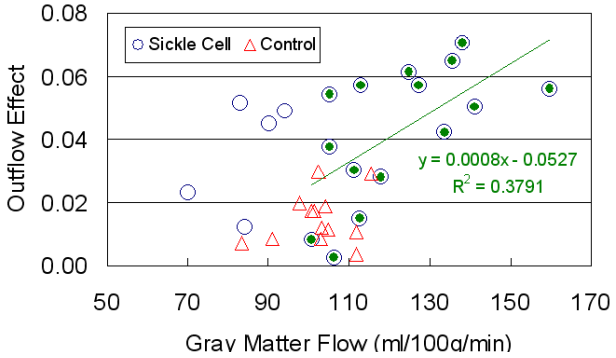
Materials and Methods

Written informed consent was obtained from all adult participants and parents/guardians of child participants, from whom written informed assent was also obtained. Three groups of subjects were studied: healthy young adults (n = 26, F = 11, M = 15, age = 19-30 years, data acquired at the University of Pennsylvania), healthy children (n = 30, F = 14, M = 16, age = 5-12 years, data acquired at Georgetown University and Cincinnati Children's Hospital) and SCD children (All patients had hemoglobin SS genotype and no evidence of vascular abnormalities on structural MRI, n = 24, F = 14, M = 10, age = 2-15 years, data acquired at the Children's Hospital of Philadelphia). All MR scans were conducted on 3.0 T whole body Siemens Trio systems using standard Tx/Rx head coils. Perfusion-weighted images were acquired using a CASL technique with amplitude modulation for control scans (4). Imaging parameters included: FOV = 22 cm, matrix size = 64x64, 16 axial slices with a thickness of 6 mm and an inter-slice gap of 1.5 mm, TR = 4 sec, TE = 17 msec, labeling duration = 2 sec, post-labeling delay = 1.2 sec, 80 pairs of control and tag images. After off-line image alignment, CASL signals were generated by pairwise subtraction of control and label acquisitions, and then converted to CBF absolute units (ml/100g/min), assuming a blood T1 of 1.5s. Masks of vessels were created on the flow map to include the voxels with the top 2% highest intensities. Voxels including veins were manually determined from the vessel mask to include the posterio-superior group of the dura mater sinuses. Average brain perfusion was computed from the region-of-interest of gray matter (our theoretical calculation indicated minimum outflow from white matter due to the relatively low flow). Outflow effect was computed as Σ(venous signal)/Σ(gray matter signal).

Results and Discussion

Hyper-intensities (surpassing the 2% threshold) in the sagittal sinuses were observed in 20 out of 24 sickle cell children, 13 out of 30 healthy children and none of the young adults, indicating that their occurrence is group specific (chi-square test, $p < 0.001$). Fig 1 shows the perfusion images obtained from three representative subjects (top row: a SCD child; middle row: a healthy child; bottom row: a healthy adult). One notices that both global perfusion and hyperintentsities in the sagittal sinus (arrows) increase from the adult to the healthy child and to the child with SCD. As shown in Table 1, SCD children have the highest flow in the three populations studied (ANOVA, $p < 0.01$). When flow rate is above 100 ml/100g/min, on average (4±2%) of the tagged spins pass through the capillary network when images are obtained. In Fig 2, outflow effect is plotted against gray matter flow for both healthy and SCD children. In the latter, outflow effect is found to positively correlate with perfusion. The higher incidence and higher value of outflow effect in SCD children may be attributed to several pathophysiological changes in this population, including higher flow, dilated microvasculature, and potentially prolonged blood T1 (3, 5). By linearly fitting the data above 100 ml/100g/min (green dots in Fig 2), venous outflow of the tagged spins is predicted to occur when gray matter flow exceeds ~70 ml/100g/min. The effect, if not properly accounted for, can lead to flow underestimation in ASL. Thus, caution needs to be exercised when applying ASL to cases with high flow rate (e.g., children, tumors and hypercapnia (6)) and/or prolonged blood T1 (e.g., high magnetic field and children), although outflow effect may not be observable in healthy adults at 3.0T.

Mean Perfusion at Gray Matter (Mean±SD) ml/100g/min	Control Groups		Children with sickle cells
	Young Adults	Children	
	72±10	96±13	108±23



References

1. Herscovitch et al. JCBFM 1987;7:527.
2. St. Lawrence et al. MRM 2000;44:440.
3. Oguz et al. Radiology 2003;227:567
4. Wang J et al. Radiology. 2005;235:218
5. Steen et al. MRI 2004 22:299.
6. Wegenar et al. JMRI 2007;26:855.