Cerebrospinal Arterial and Venous Blood Flow Variability assessed with 4D flow MRI

Eric Mathew Schrauben[1], Kevin Johnson[1], Jason Huston[2], Aaron Field[2], and Oliver Wieben[1,2]

[1]*Medical Physics, University of Wisconsin - Madison, Madison, WI, United States,* [2]*Radiology, University of Wisconsin - Madison, Madison, WI, United States*

Background: The Chronic Cerebrospinal Venous Insufficiency (CCSVI) hypothesis in multiple sclerosis (MS) [1] posits that prolonged reflux of venous flow returning from the deep cerebral veins induces increased iron deposition, neuroinflammation, and ultimately demyelinating lesions. This hypothesis has stimulated interest in using MR for venous flow measurements since the proposed ultrasound-based criteria have been shown to be highly user-dependent and suboptimal for blinded study designs. To be useful in the diagnosis of MS, measurements of deep cerebral, internal jugular (IJV), and azygos vein (AV) blood flow over the cardiac cycle must be reliable and reproducible. Recent venous MR flow studies have simply adopted the MR flow protocols commonly used for arterial flow imaging, despite evidence for venous flow dependencies on various physiological states [2], such as hydration level, respiratory phase, and diurnal changes. Previous work [3] on the repeatability of venous flow quantification has shown that PC-VIPR [4,5], a radially undersampled 4D flow MRI technique, delivers reproducible results in the cerebral veins. The objectives of this test-retest study were to (1) analyze the repeatability of intra- and extra-cranial venous flow measurements with PC-VIPR, (2) compare venous to arterial flow reproducibility, and (3) determine whether blood flow changes in the cerebral veins are related to flow changes in the IJV's.

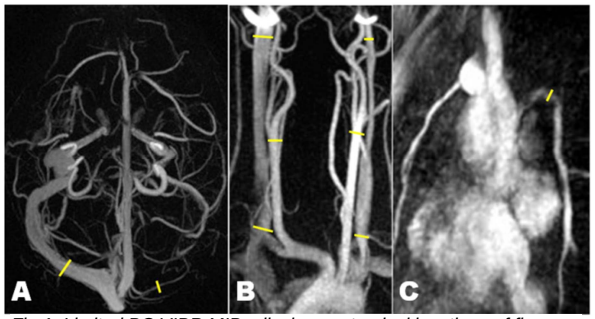
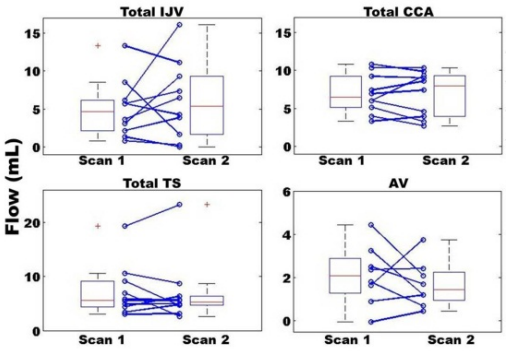


Fig 1. Limited PC VIPR MIPs display anatomical locations of flow measurements: axial cerebral veins (A), coronal IJV and CCA (B), and sagittal AV (C).

Methods: Ten healthy volunteers were imaged on a 3T clinical system (Discovery MR750, GE Healthcare) after obtaining IRB approval and written informed consent. Each volunteer was imaged twice within two weeks (10 volunteers x 2 = 20 total scans) at three different stations in a test-retest fashion (no more than two weeks between scans): the head (cerebral veins), neck (IJV's), and chest (AV). MRI parameters for the PC-VIPR head scan include: 3D radial free-breathing acquisition, flip angle $\alpha = 25^0$; imaging volume = 24 x 24 x 16 cm^3; scan time: 7 minutes 30 seconds. Velocity encoding (VENC) was set at 20 cm/s for head and chest scans, and 70 cm/s for neck scans. Cardiac triggers were recorded for retrospective cardiac gating. The image sets were segmented and exported to an advanced visualization software package (EnSight, CEI). Flow measurements were obtained from reformatted 2D planes interactively placed orthogonally to the direction of flow [6]. To compare blood flow changes throughout the cerebrospinal venous system, total flow over the cardiac cycle was measured in several locations: in the right and left transverse sinuses (TS), at two levels along the right and left IJV's (upper: 2 cm inferior of the jugular bulb and lower: 2 cm above the junction with the subclavian vein), and in the AV (2 cm from the junction with the superior vena cava) (Figure 1). To summarize flow in the cerebrospinal venous system, total flows were added from left and right TS's as well as from the left and right IJV's, providing total flow at a single S/I location. Flows through the common left and right carotid arteries (CCA) were similarly analyzed. Percent change, calculated as difference in total flow from scan 1 and scan 2 normalized to scan 1 flow, was calculated at all locations for each volunteer. Average percent difference between scans and paired t-test p-values were calculated across all volunteers.



	Avg. (± stdev) % Change	p-value
Total IJV	**20.3 ± 14.0**	**0.52**
Total CCA	**5.1 ± 4.2**	**0.99**
Total TS	**6.8 ± 7.6**	**0.71**
AV	**20.4 ± 19.0**	**0.45**

Figure 2. Boxplot result for all measurement locations. Table on right shows average percent change is lowest and least variable in the CCA. No significant changes were observed ($p < 0.05$).

Results and Discussion: Figure 2 includes boxplots of total flow, individual changes from scan 1 to scan 2, and a table with average flow changes. The day-to-day variation in flow in the carotid arteries is very low (5.1 ± 4.2 %), confirming both physiologic reproducibility of arterial flow and technical reproducibility of this 4D flow MRI technique.

In contrast to arterial flow, the venous flow measurements in the IJV's and AV's show much larger variations in excess of 20% and more modest variations in the TS. Individual variations of flow exhibited on the boxplots reveal consistency in carotid flow from one scan to the next while also showing the many varied changes occurring in veins. Figure 3 displays percent change in total flows across all head/neck/chest veins and volunteers. Eight of ten (8/10) volunteers exhibited similar changes (increase/positive or decrease/negative) for 3 of the 4 venous flow measurements, indicating a systematic physiological (i.e. not technical) change affecting venous flow. These results strongly indicate the necessity of controlling for venous flow altering variables such as hydration levels, head position, time of day, etc.

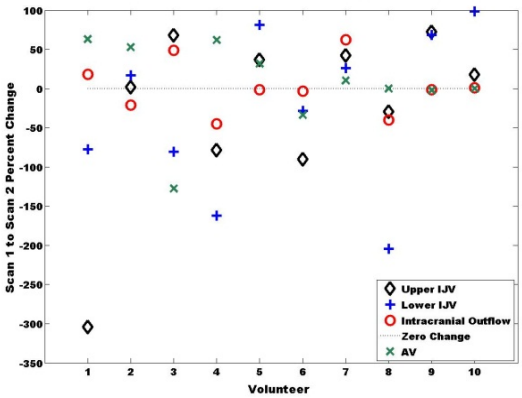


Figure 3. Percent change from scan 1 to scan 2 across volunteers. Volunteers 5-10 have similar directional changes in all measurements.

Conclusions: This test-retest study exhibits the physiologic variations in cerebrospinal venous return using 4D flow MRI. In contrast, arterial flow measurement using the same methods has been shown to be significantly more reproducible. The study demonstrates the need for carefully controlling physiologic variables in experiments attempting to investigate changes in venous blood flow. Further studies are needed to determine which variables are most important and under what circumstances they alter venous flow measurements.

Acknowledgements: We gratefully acknowledge funding from National MS Society #RC1003-A-1, NIH grant 2R01HL072260 and GE Healthcare support.

References: **1.** Zamboni, *JNNP* 2009. **2.** Lu, *AAN* 2011. **3.** Schrauben, *ISMRM Meeting, Abstract #3100,* 2012 **4.** Gu, *AJNR* 2008. **5.** Johnson et al. *JMRI* 2008 **6.** Stalder, *MRM* 2008.