Quantifying Cerebral Blood Flow: A Comparison of Two Non-invasive Perfusion Imaging Techniques

Gena Matta[1,2], Andrew D Robertson[1], Sandra E Black[1,3], and Bradley J MacIntosh[1,3]

[1]*Canadian Partnership for Stroke Recovery, Sunnybrook Research Institute, Toronto, Ontario, Canada,* [2]*University of Waterloo, Waterloo, Ontario, Canada,* [3]*University of Toronto, Toronto, Ontario, Canada*

Target Audience: Anyone interested in quantifying CBF using ASL or PCA

Introduction: Arterial-spin labelling (ASL) [1] and phase-contrast angiography (PCA) [2] are two non-invasive methods to quantify the total cerebral blood flow (CBF; ml/100g/min). ASL relies on the use of magnetically labelled blood water as an endogenous tracer to characterize tissue-level perfusion. Total CBF_{ASL} can be calculated by averaging voxels over the entire brain. PCA uses bipolar magnetic gradients that derive contrast between moving blood and stationary tissue to determine blood flow velocity through vessels of interest. Total CBF_{PCA} can be calculated by multiplying the cross-sectional area of the vessels that supply the brain by the mean velocity. Previously, others have used CBF_{PCA} estimates as a means for calibrating the quantification in CBF_{ASL}. This approach involves a characterization of the ASL labeling efficiency empirically, and has occurred primarily in studies of healthy young adults [3,4]. It remains to be seen whether such an approach is also viable in cerebrovascular patients. We therefore compared ASL and PCA in individuals with large artery disease (i.e. survivors of overt stroke) and/or small vessel disease (SVD; i.e. individuals with white matter hyperintensities). The aims of this study were to: 1) assess the agreement of CBF_{ASL} and CBF_{PCA} in these two patients groups, and 2) assess the repeatability of measurements within a stroke cohort.

Methods: MRI was performed on 9 chronic stroke survivors (time post stroke: 21 ± 19 months, age: 62.8 ± 14.4 years) and 24 adults with SVD (age: 73.4 ± 8.3 years). Stroke participants received six separate CBF acquisitions as part of a longitudinal study, whereas SVD adults received a single MRI. The multiple sessions among the stroke participants allowed for an assessment of the repeatability of each modality. Participant were scanned using a 3-Tesla Philips Achieva MRI system using a body coil and an 8-channel head coil receiver. Imaging sequences were obtained with the following parameters: (1) carotid artery time of flight (field of view (FOV): 240x191x168mm^3, voxel dimensions: 0.5x0.5x1.0mm^3; acquisition time: 3.4 min), (2) T1-weighted structural (FOV: 240x191x168mm^3, dimensions: 0.9x0.7x1.2mm^3; 9 min), (3) pseudo-continuous ASL (FOV: 192x192x90mm^3, dimensions: 3x3x5mm^3; 4min), (4) ASL proton density reference (1.5 min), and (5) PCA with cardiac gating (FOV: 150x150x5mm^3, dimensions: 0.5x0.5x5.0mm^3; 1.5min). CBF_{ASL} quantification was performed based on established methods, with constants parameters and proton density estimate, as in Alsop et al. [5] Absolute CBF_{PCA} was normalized by brain mass, which was calculated from the T1-based white and grey matter volume estimates. A tissue density of 1.06 g/mL was used [6]. Linear regression was performed between CBF_{ASL} and CBF_{PCA}. Bootstrapping with 100 samples was performed to compare the regression coefficient (i.e. slope of the line) for the two groups. Figure 1 shows representative ASL (left) and PCA (right) data for one participant.

Results and Discussion: ***Aim1: Agreement*** - Figure 2 shows the total CBF_{ASL} and CBF_{PCA} values for each participant. CBF_{ASL} was greater than CBF_{PCA} in the stroke cohort (ASL: 48.8 ± 11.7 vs. PCA: 40.0 ± 6.9 ml/100g/min; $p<0.0001$) and lower than CBF_{PCA} in the SVD cohort (ASL: 35.9 ± 10.5 vs. PCA: 41.2 ± 11.1 ml/100g/min; $p=0.01$). The histograms in Figure 2 illustrate that the slope between ASL and PCA (i.e. regression coefficients) are significantly different for the two groups ($p<0.0001$). Bland-Altman plots, shown in Figure 3, were generated to visualize the bias between PCA and ASL. In the SVD cohort, we found no significant bias (-5.3 +/ 18.0 mL/100g/min), with consistency across the entire range of CBF. In the stroke cohort, there was a bias towards greater CBF_{ASL} (15.7 +/- 19.3 ml/100g/min) with an increasing bias at greater CBF. ***Aim2: Repeatability*** - The coefficient of variation (CV) was calculated for each stroke participant for both ASL and PCA estimates. Group mean CV were similar between PCA and ASL (CV_{PCA}: 14.62 ± 8.0%; CV_{ASL}: 14.03 ± 5.1%), with a non-significant trend toward greater variance in the posterior vs. the anterior circulation. Low agreement between the two modalities may be due to differences in measurement techniques, which are sensitive to pathology in either large arteries (PCA) or the microcirculation (ASL).

Conclusion: We observed significant differences between the total CBF estimates produced by each modality for these two cerebrovascular groups. These results may be due to differences in the labelling efficiency in ASL, differences in the arterial transit time in ASL, challenges with quantifying intra-arterial velocities in PCA, or combinations thereof. Future work should attempt to address the underlying systematic and physiological causes for these modality differences, as well as put these results in the context of a gold-standard CBF technique. Intra-subject repeatability was high, however, for both approaches.

References: [1] Detre, J.A., et al. Neurology. 1998; 80:633-641. [2] Dumoulin, C.L., et al. MRM. 1989; 9(1): 139-149. [3] Aslan, S., et al. MRM. 2012; 63(3):765-771. [4] Jung, Y., et al. MRM. 2010; 64(3): 799-810. [5] Alsop DC, et al. MRM. Epub 2014 Apr 8, doi: 10.1002/mrm.25197. [6] Lu C., et al. Cortex. 2010; 46(1): 49-67.

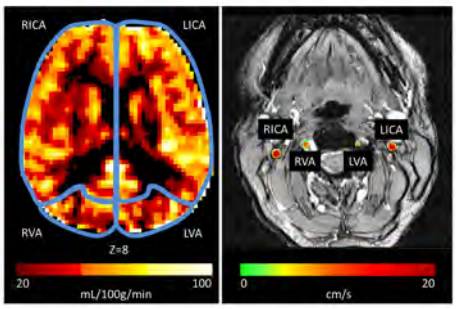

Figure 1: Representative images of CBF (left), and internal carotid (ICA) and vertebral (VA) arteries (right). Colour bars represent absolute CBF and blood flow velocity, respectively. Estimated left and right ICA and VA territories are indicated by blue overlay on CBF image.

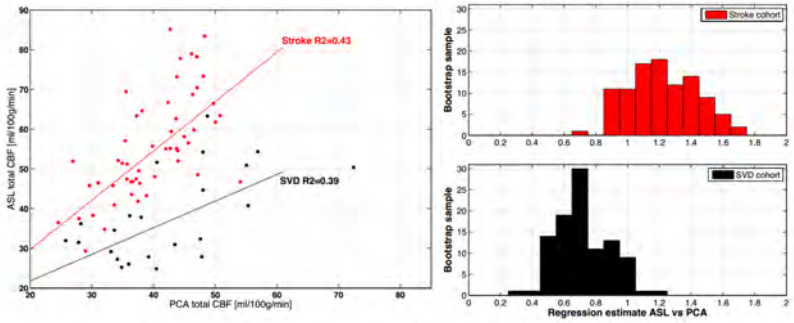

Figure 2: Left scatterplot: Total CBF values from 54 ASL and PCA scans from stroke (6scans/participant, red) and 24 from SVD (1 scan/participant, black). The R-squared values are shown for both scatterplots. Right bar plots: Results of the bootstrapping regression analysis revealed that the group difference in the regression coefficient was statistically significant (unpaired t-test, $p<0.0001$).

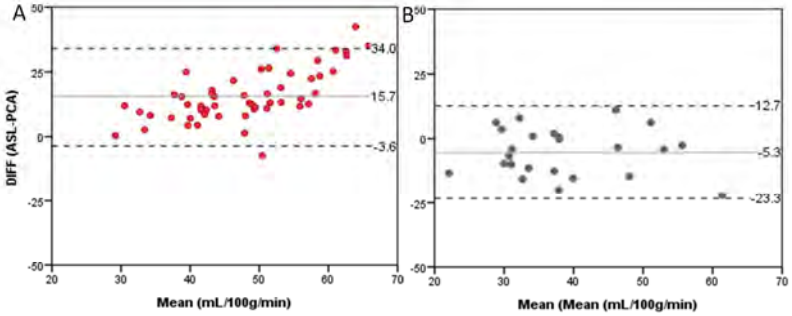

Figure 3: Bland-Altman plots of CBF values measures with PCA and ASL-MRI for (A) stroke and (B) SVD. The difference of the two measures is plotted against the average of the two (ASL+PCA/2). Bias and 95% confidence limits are represented by the solid and dashed lines, respectively