Evaluating transit time and cerebral blood flow estimates in pulsed arterial spin labeling data among patients with carotid stenoses

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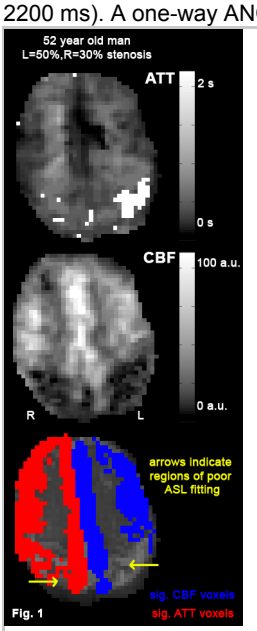
Introduction: Arterial spin labeling (ASL) has gained use in clinical research. Numerous studies show the value of ASL for perfusion imaging[1, 2] and evaluation of hemodynamics[3], and also note that in such studies (e.g., acute stroke[4], diabetes[5], Moyamoya disease or severe carotid stenoses[6 7]) it is prudent to measure the arterial transit time (ATT)[7]. This can be achieved by acquiring a separate low-resolution ATT map that can be used in conjunction with single post-label delay (PLD) ASL scan[8]. Alternatively, as in this study, a multiple inflow ASL acquisition and single-compartment ASL model can be used to calculate the proportion of significant (reliable) grey matter voxels (%-sig-voxels) in each hemisphere. Patients with carotid artery stenosis were studied. We first hypothesized that differences in the left to right (L:R) %-sig-voxels will correlate with L:R carotid disease load. We also hypothesized that patients that were candidates for carotid endarterectomy (CEA) (i.e. high degree of stenosis, >70%) will show a more pronounced L:R %-sig-voxels absolute difference than non-CEA carotid patients (i.e. lower degree of stenosis).

Methods: Twenty-nine patients with carotid disease were recruited (mean [std] age : 73 [9] years). Median [range] carotid stenosis for left and right carotids: 75% [15-100%] and 40% [0-100%] of whom 17 underwent CEA. MRI was conducted using a 3 T scanner (TIM Trio, Siemens, Germany) with a 12 channel head receive coil. Pulsed ASL with 3D gradient and spin echo imaging (3D-GRASE-PASL) was used with the following parameters: 3.4x3.4x5mm voxels, 220 mm FOV, TR/TE=3110/23ms, 22 slices, 8 averages at each of 10 PLDs, starting at 400 and ended at 2200 ms in 200 ms intervals, double inversion background suppression, and Q2TIPS post-tagging saturation for a maximum bolus duration of 1600 ms. T1-weighted anatomical imaging was used for co-registration. Left and right hemisphere lobes were separated using a standard space atlas and warped to ASL space for voxel-wise fitting using a least-squares routine in Matlab (Mathworks, Natick, MA), producing estimates and a 95% confidence intervals (CI) for CBF (a.u.) and ATT (seconds). A CBF voxel was significant if the CBF estimate minus the lower bound 95% CI was greater than zero. An ATT voxel was significant if the ATT estimate plus the upper bound 95% CI was < TI(max) (i.e. 2200 ms). A one-way ANOVA was performed to test for CEA vs non-CEA differences.



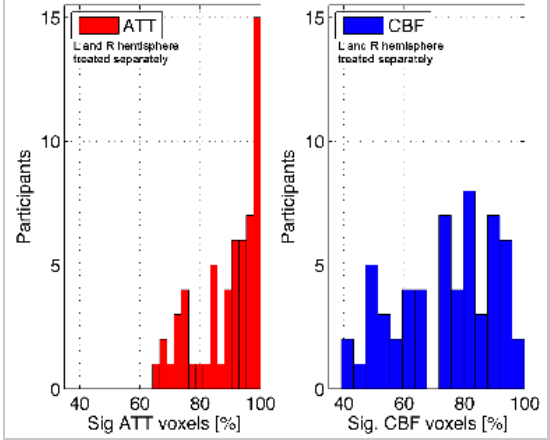


Fig 2. Distribution of significant ATT voxels (left) and CBF voxels (right) from left and right ROIs (L and R %-sig-voxels treated separately). The %-sig-voxels for CBF was wider and consequently significantly reduced compared to ATT (P<0.0001).

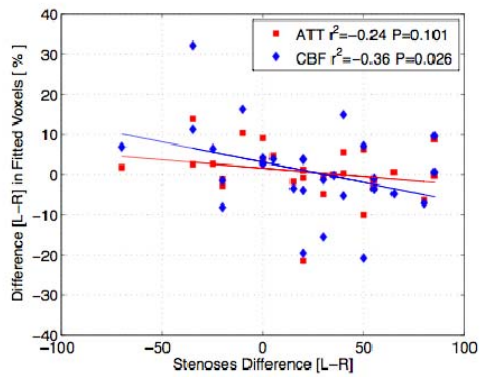


Fig 3. Hemispheric difference in %-sig-voxels (L-R) plotted against the L:R stenoses difference. CBF %-sig-voxels showed a significant trend with carotid stenoses difference (P=0.026).

Results: ***Fig.*** 1 shows ATT and CBF images for a representative carotid. The red mask shows significant ATT voxels, the blue mask shows significant CBF voxels and yellow arrows indicate where the model fitting was not successful. Median proportion of ATT voxels was 92% of all grey matter voxels (range: 64 to 100%) while for CBF voxels it was 77% (range: 39 to 100%). Distributions were significantly different with ATT producing a higher %-sig-voxels compared to CBF (***Fig. 2***, non-parametric U-test, P<0.0001). ***Fig. 3*** shows the L:R %-sig-voxels difference plotted against the L:R difference in stenosis, which was significant for CBF (P=0.026) and showed a trend for ATT (P=0.101). The one-way ANOVA comparing CEA vs non-CEA patients was significant for CBF (P=0.05) but not ATT (P=0.29).

Discussion: Results indicate that carotid stenosis impacts our ability to estimate voxel-wise ATT and CBF as determined from multiple inflow ASL data. The %-sig-voxels for ATT was relatively close to 100% of grey matter voxels, which suggest our choice of PLDs was reasonable and that lower %-sig-voxels for CBF is likely due to an absence of an ASL signal. Future work will incorporate a 2-compartment Bayesian approach to improve the modeling and address the influence of large arteries on our results[9]. We found evidence to support both hypotheses for the CBF estimates. Our interpretation is that a hemisphere downstream from a severe atherosclerosis is more likely to produce inaccuracies in CBF due to voxels that do not fit to the ASL model. In conclusion we have presented a simple method to assess the quality of the ASL estimates, which is an issue that has not been fully explored in clinical ASL.

References: **1.** Firbank MJ, et al. *Neurology.* Apr 26 2011;76(17):1478-1484. **2.** Zaharchuk G, et al. *Radiology.* Sep 2009;252(3):797-807. **3.** MacIntosh BJ, et al. *Stroke.* Apr 2011;42(4):979-984. **4.** Chalela JA,. *Stroke.* Mar 2000;31(3):680-687. **5.** Last D, et al. 2007;30(5):1193-1199. **6.**Hendrikse J, Rutgers DR, Klijn CJ, Eikelboom BC, van der Grond J. *Stroke.* Jul 2003;34(7):1650-1654. **7.** Bokkers RP, et al. *J Cereb Blood Flow Metab.* Jan 2010;30(1):222-229. **8.** Wu WC, et al., Top Magn Reson Imaging. 2010 Apr;21(2):65-73. **9.** Chappell MA, et al *Magn Reson Med.* May 2010;63(5):1357-1365.