What is the detectability of arterial transit times in pulsed arterial spin labeling (PASL): a simulation and empirical study

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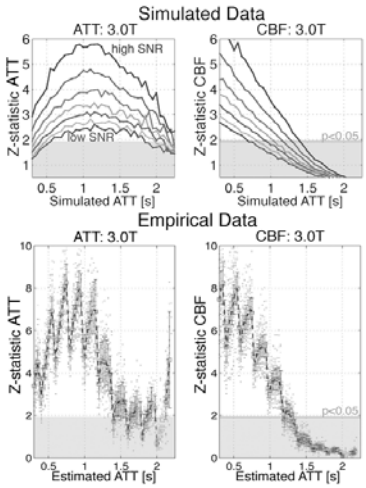
Introduction: Quantitative cerebral blood flow (CBF) measurements using arterial spin labeling (ASL) are highly dependent on the arterial transit time (ATT), which corresponds to the time for blood water spins in the tagging bolus to reach the capillary exchange site. Frequently, an ASL experiment is conducted at a single inversion time (TI), which means an ATT value is assumed. The vascular geometry varies regionally, however, and ATT will vary between brain regions. Furthermore, recent evidence shows that ATT decreases in response to neuronal activation [1, 2], hypercapnia [3], and is affected by disease processes [4]. Accurate knowledge of normal ATT values and variability across the brain would therefore be useful. Regional ATT quantification is complicated, however, when using traditional multi-slice EPI readouts due to limited volume coverage and multiple excitation pulses that yield different TIs for different slices. To overcome these difficulties, we employ a multi-TI pulsed ASL (PASL) approach with a 3D GRASE readout that has demonstrated high SNR and more importantly a single excitation pulse to maintain a single, defined TI for the entire 3D volume [5]. First, we simulate the detectability of the ATT across a range of physiologically plausible values, and second, present an atlas of ATT values across the brain from a cohort of healthy individuals. The results should provide a useful reference for how ATT varies across brain regions in healthy individuals, and should be useful in clinical comparison studies where ATT may be impaired.

Methods: PASL and T_1-weighted anatomical data were acquired on a 3 T Siemens MRI scanner. Empirical data were from 36 healthy volunteers (15 women, 21 men, ages: 20 to 35 years) who provided written consent in accordance with the local ethics committee. The PASL imaging volume was 200 mm x 200 mm x 96 mm (half k_z-space coverage; 64 x 64 x 24 matrix size; voxel dimensions: 3.1 x 3.1 x 5.0 mm^3), TR/TE = 3150 / 40.6 ms, TI=[400:200:2400ms], background suppression, total acquisition time: 11 min 33 s. A two-parameter (CBF and ATT), single compartment ASL model was used to fit the multi-TI data for every voxel using least squares fitting in Matlab. Z_{stats} were used to quantify the confidence in fit estimates at each voxel; e.g. for CBF Z-$stats_{CBF}$ = μ_{CBF}/σ_{CBF}. ATT maps were converted to standard space (MNI) and mean and variance maps were used to create an ATT atlas. ATT values were computed for the different lobes and for males and females using the Oxford-Harvard brain atlas. Simulations of PASL were performed using the identical set of TI values as the empirical data. Simulated CBF levels were kept constant while the ATT values ranged from 0.3 to 2.4 s. Signal-to-noise ratios for the kinetic curves were assumed based on the empirical data. Noise was assumed to be Gaussian and added in increasing increments to simulate a range of SNR scenarios. 500 simulations were performed at each simulated ATT and at each noise level.

Results: Plotting the simulated Z-stats for ATT or CBF as a function of the simulated ATT produced a consistent pattern (Fig. 1-top). ATT Z-stats showed a quadratic dependence on the simulated ATT, while CBF Z-stats showed a decreasing linear trend. The simulated data agreed well with empirical data (Fig. 1-bottom). Figure 2 and the table show the natural variation of ATT across the brain. Women were found to have a significantly reduced ATT compared to men (P<0.003).



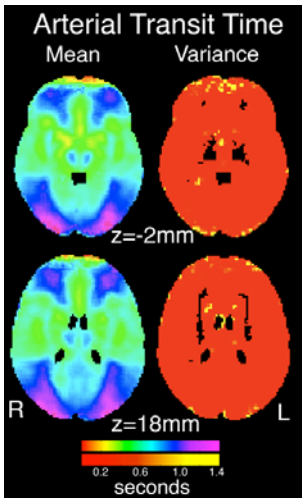


Figure 1: ***Top*** – Statistics from fitting of simulated ASL SNR scenarios (high to low) are represented by the different curves. The gray region corresponds to P > 0.05 (i.e. poor quality fit). CBF Z-stats show a more dramatic decreasing trend with increasing ATT. ***Bottom*** – Empirical Z-stats for ATT (left) and CBF (right) from 3T PASL data.

Figure 2: Mean and variance arterial transit time maps computed across the entire cohort (N=36). The mean ATT map shows the demarcation of the anterior, middle and posterior vascular territories. Variance map is shown with the same scale to demonstrate ATT measurements are robust across the brain.

ATT by Brain Lobes (seconds)

	Temporal	Parietal	Frontal	Occipital
All (N=36)	0.64 ± 0.095	0.80 ± 0.091	0.80 ± 0.126	0.93 ± 0.108
Women (N=15)	0.59 ± 0.089	0.75 ± 0.080	0.72 ± 0.105	0.87 ± 0.091
Men (N=21)	0.68 ± 0.080	0.84 ± 0.081	0.86 ± 0.105	0.98 ± 0.096

Table: ATT by major brain region separated for men and women.

Discussion: This study demonstrates it is possible to measure CBF and ATT reliably in a group of young healthy participants in a time-efficient manner. ATT is known to influence CBF estimates [6, 7] and the ATT atlas that has been created revealed differences across the whole brain that are due to the different vascular territories. Simulated and empirical experiments agreed well and showed ATT was reliably detected as late as 1.4 s at 3.0T with SNR at peak inflow = 6.9 ± 1.2, which was 5 x σ above the mean occipital lobe ATT for instance. An additional interesting finding came from group analysis of ATT. Sex differences were found to be highly significant based on ROI analysis (matched for age; ATT women < men, unpaired t-test P < 0.0003; see Table) and on a voxel-wise level (data not shown).

References:

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