Comparison of Cerebral Blood Flow and Arterial Transit Time mapping methods: Look-Locker ASL, Hadamard Encoded ASL, and Multi-TI ASL with Variable Bolus and TR

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Target Audience: The target audience is clinicians and researchers interested in cerebral blood flow imaging and arterial transit time mapping with ASL.

Purpose: Arterial Spin Labeling (ASL) has been established as a quantitative and completely non-invasive cerebral blood flow (CBF) technique, though the challenge of predicting the optimal post-labeling delay (PLD) remains. Multiple ASL scans with different TIs has been used, acquiring ASL images at multiple PLDs and then estimating CBF and arterial transit time (ATT)[1], to address this issue but this method is not time optimal due to a long, fixed TR and sensitive to motion between acquisitions with different TIs.. A new PCASL acquisition scheme is proposed here involving varying the bolus duration, TI, and TR through the use of pre-saturations immediately prior to the labeling bolus. This method also allows for estimation of T_1 and M_0 on a voxel-wise basis from the ASL data itself; the method is titled multi-TI ASL with variable bolus and TR, referred to as "Multi-TI Integrated ASL." Multi-TI Integrated ASL leads to more accurate CBF and ATT estimation without the need for a separate T_1 scan, thus eliminating registration of a separate T_1 acquisition. Multi-TI Integrated ASL is implemented and compared with other existing CBF and ATT estimation methods: ASL with Look-Locker acquisition[2] and Hadamard Encoded ASL[3].

Methods: All images were acquired on a 3T Siemens Skyra MRI with a 32 channel head coil. Five healthy subjects were imaged (2 M/3 F, 28.6 +/- 3.2 years old). A 1 mm isotropic T_1-weighted MPRAGE structural image was acquired to allow for tissue segmentation. All ASL images used pseudo-continuous labeling and a 2D EPI acquisition with GRAPPA parallel imaging (acceleration factor = 2), 24 slices (full brain coverage), 5 mm slice thickness, 1 mm slice gap, in-plane resolution 3.4x3.4 mm, and matrix size of 64x64x24. ***Look-Locker*** parameters included 1600 ms labeling bolus, 5 TI values ranging from 1700 ms to 4900 ms in increments of 800 ms, leading to PLDs of 100 ms to 3300 ms in the same increment. The TI increment was minimized while still maintaining full brain coverage. TR was 5700 ms. ***Hadamard Encoding*** parameters included 4200 ms labeling bolus divided into 8 sub-boluses of 600 ms encoded as label or control according to the Hadamard encoding scheme[3]. A 100 ms delay before the image acquisition led to effective 7 PLDs ranging from 100 ms to 4300 ms in increments of 600 ms, TR was 5100 ms. ***Multi-TI Integrated ASL*** parameters included 7 TI times ranging from 100 ms to 4300 ms in 700 ms increments with a 1600 ms labeling bolus when the TI allowed, otherwise the labeling bolus was 100 ms shorter than the TI time. TR was minimized for each different TI, ranging 900 ms to 5100 ms, average 3000 ms. TI times were interleaved to minimize sensitivity to subject motion. For all methods except Multi-TI Integrated ASL, a separate M_0 volume was collected for quantification. All methods had as many averages as possible within a 6 minute scan time; see additional parameters in **Table 1**. Images from all methods were registered to the first volume, smoothed using a 5 mm Gaussian kernel. From the Multi-TI Integrated ASL data, T_1 and M_0 maps were created from the average of control and label images at each TI time, fitting to the saturation recovery equation on a voxel basis. The shortest TI time is used for T_1 and M_0 estimation only, CBF and ATT estimation used the remaining 6 TI times. For all methods, CBF and ATT were estimated using an unconstrained nonlinear optimization function in Matlab (fminsearch) to find a solution minimizing the difference between the data and the ASL kinetic model. Tissue T_1 estimated from the Multi-TI Integrated ASL data was used for CBF and ATT estimation. Tissue T1 of 1500ms was assumed for the other two methods. A correlation between the data and the model fit of the data was calculated on a voxel basis and the correlation coefficient (rho) and the p-value were found. Voxels with a p-value of greater than 0.05 were rejected.

Results: A representative slice of the CBF and ATT maps from three subjects representing the range of map quality are shown in **Figure 1** for each method having rejected voxels with a poor fitting (p-value >0.05). The mean and standard deviation of the averaged GM CBF, averaged GM ATT, both after p-value masking across all 5 subjects are listed in **Table 2** as well as averaged GM rho value (before p-value masking), and the GM percentage of p-value masking survival. Multi-TI Integrated ASL has the largest average GM rho value before p-value masking and percent survival after p-value masking for all subjects.

Table 1 *Summary of ASL parameters*

	Look Locker	Hadamard Encoding	Multi-TI Integrated ASL
TR (ms)	5700	5100	3000 (avg)
Bolus Duration (ms)	1600	600	0/700/1400/1600
Flip Angle (deg)	45	90	90
TI increment (ms)	800	600	700
Number of TIs (time points)	5	8	7 for T_1 mapping 6 for Perfusion
Scan Time (min)	5:53	5:31	5:39
Avgs in 6 min	31	8	8

Table 2 *Summary of method comparison*

	Look-Locker	Hadamard Encoded	Multi-TI Integrated ASL
Mean GM CBF (ml/100g/min) (mean±std)	58.77±31.4	53.24±20.8	66.94±20.4
Mean GM ATT (ms) (mean±std)	1651.5±631	1461.4±554	1477.2±495
MeanGM Rho (mean ± std)	0.843±0.173	0.795±0.184	0.851±0.149
GM % survival p-value mask (mean±std)	50.7±10.4%	59.3±13.9%	67.3±7.5%

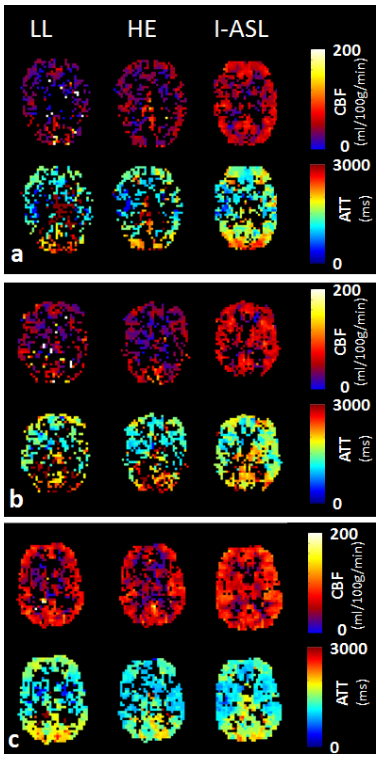

Figure 1 *Slices from CBF (row 1) and ATT (row 2) maps after p-value masking from subject 1 (F, 31 yr) (a), subject 2 (M, 27 yr) (b), and subject 3 (F, 25 yr) (c). Left column Look-Locker ASL, middle column Hadamard Encoded ASL, right column Multi-TI Integrated ASL.*

Discussion: The use of measured tissue T1 in multi-TI integrated ASL may correct underestimation of CBF values when an assumed T1 used. As shown in Figure 1, Look-Locker method produced more voxels with longer ATT (>3sec) within the gray matter mask, which contributed to the higher average GM ATT. The correlation coefficient and p-value rejection represents the goodness of fit to the model. It is known that ATT does not vary widely across small regions of the brain[4], so the large wide variation within small regions seen in the Look-Locker and Hadamard Encoded methods are likely less accurate.

Conclusion: The study shows that Multi-TI Integrated ASL can be a time efficient method for simultaneous CBF and ATT estimation without the need for a separate acquisition for T_1 mapping which fits the perfusion model well.

References: **1.** Gonzalez-At et al. MRM 43, 739-746, 2000 **2.** Gunther, et al., MRM 46, 974-984, 2001. **3.** Dai, et al., MRM 69, 1014-1022, 2013. **4.** Dai, et. al., MRM 67, pp. 1252-1265, 2012.