Comparison of PASL, pCASL and background suppressed 3D pCASL in a Clinical Population

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Target Audience: Anyone interested in ASL methods and clinical applications of ASL MRI of the brain.

Introduction:

Arterial Spin Labeling (ASL) [1] uses magnetically labeled arterial blood water as an endogenous tracer to measure cerebral blood flow (CBF) noninvasively. Various strategies exist for labeling the arterial blood and for measuring the effects of labeling on brain signals [2]. Pseudo continuous ASL (pCASL) [3] is currently the recommended labeling strategy [2] while pulsed ASL (PASL) [4] has been available for almost 2 decades and is more readily implemented. ASL can be sampled using any imaging sequence, but background suppression (BS) of static brain tissue signals [5] has been shown to increase data quality. BS ASL is optimally combined with 3D imaging sequences. Most experience with ASL MRI to date has been with the more widely available unsuppressed 2D echoplanar imaging (EPI) readouts, particularly in clinical populations. Here we compare ASL MRI acquired from patients with mild cognitive impairment (MCI) and elderly control subjects using PASL 2D EPI, pCASL 2D EPI and BS pCASL 3D spiral imaging [6]. All imaging schemes were single-shot. The goal of this comparison was to assess the effects of different labeling and acquisition strategies on individual subject data as well as investigating the sensitivity of the methods in detecting group differences between patients and controls.

Materials and Methods:

ASL data from 14 Controls and 12 MCI patients (26 total) were acquired at the hospital of the University of Pennsylvania after obtaining their written consent and using protocols pertaining to the institutional review board (IRB). All ASL variants were obtained in a single scanning session. PASL 2D EPI was acquired following the ADNI PASL protocol (http://adni.loni.usc.edu/methods/documents/mri-protocols/) using a FAIREST scheme with TI1/TI=700/1900ms, slices=24, voxel=4x4x4mm^3, TR/TE=3.4s/12ms, BW=2368 Hz/px and 64x64 matrix. PCASL 2D EPI was acquired with voxel size=3.4x3.4x6mm^3, 18 slices, 64x64 matrix, TR/TE=4s/18ms, bandwidth=3004 Hz/pix, labeling plane offset=9 cm, labeling duration=1.5s, post-labeling delay (PLD)=1.5s. 3D-pCASL was obtained with voxel size: 3.4x3.4x5 mm^3, TR/TE=4.5s/11ms, 26 partitions with slice PF=6/8, labeling plane offset=8cm, labeling duration=1.5s, PLD=1.5s, and a BS scheme as detailed in [6]. In addition, a high resolution T1 MPRAGE scan was obtained for each subject with voxel size=1mm isotropic, TR=1.9s, TE=2.89 ms, flip angle 9^0 and bandwidth=170 Hz/px. Data from two subjects were rejected because of unusable pCASL BS 3D spiral data, leaving 13 Controls and 11 MCI patients (24 total) for the final analysis. Data were processed using SPM8 and ASLtbx [7]. Label-control time series were motion corrected, smoothed using an isotropic Gaussian kernel of FWHM=5mm, subtracted, averaged and converted into CBF maps using the quantification models in [2]. The mean CBF maps were subsequently coregistered to the anatomical space and normalized to the MNI space for group comparison.

Table 1: Correlations (p values) between different modalities for different ROIs

ROIs	3D pCASL vs 2D pCASL	2D pCASL vs PASL	3D pCASL vs PASL
GM CBF	0.73(5x10^{-5})	0.77(9x10^{-6})	0.49(0.015)
Global	0.76(1x10^{-5})	0.82(9x10^{-7})	0.53(0.008)
Hippocampus	0.55(0.005)	0.71(1x10^{-4})	0.34(0.10)
Precuneus	0.83(4x10^{-7})	0.69(1x10^{-4})	0.74(4x10^{-5})
PCC	0.72(8x10^{-5})	0.69(2x10^{-4})	0.64(9x10^{-4})
Motor Cortex	0.66(4x10^{-4})	0.39(0.06)	0.42(0.04)
Visual Cortex	0.77(1x10^{-5})	0.71(1x10^{-4})	0.45(0.03)

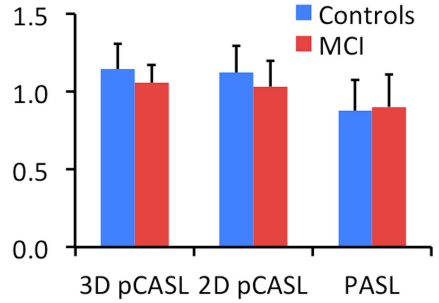
Results:

First, the mean CBF values in different ROIs, obtained using the three methods, were compared. Table 1 lists the correlations (with corresponding p-values) between the measurements obtained using the different methods. The correlation between 3D-pCASL vs 2D-pCASL and 2D-pCASL vs PASL were higher and more significant compared to that between 3D-pCASL and PASL. Next, the temporal signal-to-noise ratio (TSNR) and the grey matter to white matter contrast ratio were compared for the different schemes and the values are reported in Table 2. TSNR was computed as the mean of the whole brain perfusion signal in the time series divided by its standard deviation. TSNR increased for pCASL vs. PASL and more dramatically for BS 3D pCASL vs. non-BS 2D pCASL. The GM-WM contrast ratio was the highest in non-BS pCASL and much lower in PASL and BS-pCASL. Finally, the sensitivity of each method in detecting a group difference between Controls and MCI patients groups was evaluated by comparing the relative mean CBF values within the posterior cingulate cortex (PCC), a region previously shown to differ in relative CBF between Controls and patients with incipient Alzheimer's disease [8]. The relative CBF values were computed by normalizing the absolute ROI values by the mean global CBF for the specific scan. Figure 3 shows the mean relative CBF values and standard deviation within the Controls and the patients for the three methods. The pCASL methods demonstrate higher values in Controls compared to the patients. The PASL showed a weaker reverse trend with larger standard deviations within group. The p values in two sample T tests with unequal variances were 0.14, 0.22 and 0.77 for 3D-pCASL, 2D-pCASL and PASL respectively.

Table 2: TSNR and GM-WM contrast ratio values (mean±standard deviation across subjects)

	pCASL (BS/3D)	pCASL (nBS/2D)	PASL (nBS/2D)
TSNR	6.32±2.53	2.53±1.33	2.15±0.75
GM-WM contrast	1.48±0.18	2.80±0.66	1.68±0.45

Figure 1: Comparison of mean CBF in PCC between controls and patients for different methods



Discussion and Conclusions:

Since ASL MRI directly measures a biological parameter (CBF), the CBF values obtained should be independent of the ASL strategy used. Here we found significant correlations between CBF measured using 3 common approaches, but correlations were highest when obtained either with the same labeling (pCASL) or imaging strategy (2D). TSNR between ASL approaches increased as expected from PASL to 2DpCASL and to BS 3DpCASL. The low GM-WM contrast in 3D pCASL and PASL can be attributed to through-plane blurring and noisier data, respectively. Statistically significant patient<control differences in PCC CBF were not observed with any of the methods likely due to the small sample size, but relative group differences increased with the use of pCASL BS 3D vs pCASL nBS 2D and were not evident in PASL nBS 2D data. Based on the observed trends, 44 subjects for pCASL BS 3D and 58 subjects for pCASL nBS 2D would be required to achieve significant group effects. This study demonstrates the benefits of improved ASL MRI acquisition strategies in clinical research.

References: [1] Detre et al. Magn Reson Med 1992; 23(1): 37-45; [2] Alsop et al. Magn Reson Med 2014; *http://onlinelibrary.wiley.com/doi/10.1002/mrm.25197/pdf*; [3] Dai et al. Magn Reson Med 2008; 60(6):1488-97; [4]Wong et al. Magn Reson Med 1998; 39: 702-708; [5] Ye et al. Magn Reson Med 2000; 44: 92-100; [6] Vidorreta et al. Neuroimage 2013; 66: 662-671; [7] Wang et al. Magn Reson Imag 2008; 26(2): 261-269 [8] Xekardaki et al. Radiology, http://dx.doi.org/10.1148/radiol.14140680

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