Inter- and Intra-subject variability of CBF Measurements Using PCASL Method

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Introduction: With the recent technical development in pulsed continuous arterial spin labelling (PCASL), non-invasive whole-brain cerebral blood flow (CBF) quantification has become practically feasible. PCASL techniques have become very attractive for pharmacokinetics studies and clinical applications where repetitive, longitudinal, and quantitative CBF measurements are desirable. For such applications, one important issue need to addressed is the inter- and intra-subject variability of the measured CBF results. In this study, we experimentally investigated this issue using an optimized PCASL protocol at 3T.

Materials and Method: Twenty normal adult volunteers (female/male=8/14, aged of 38±7 years old) participated in the study. All MRI measurements were performed by using a Siemens 3T clinical MRI scanner equipped with a 32 channel phased-array coil for brain imaging. To investigate the inter-subject variability of the CBF measurements, whole-brain PCASL measurements were conducted in 17 subjects. The essential Acquisition parameters used for PCASL measurements was based on previously established protocol and are listed below. The distance from the center of imaging slices to the labeling plane was 90mm for all the adult subjects. Post label delay duration that allows the tagged blood to flow into the imaging slices was 1200ms. The mum RF blocks was 80 and each block has 20 RF pulses of 1ms each, so the total labeling duration was 1600 ms. 18 transverse slices of 6mm thick with 1 mm gap, acquisition bandwidth was 2600Hz/pixel, FOV=22cm, matrix=64x64 TE/TR=18/3515 ms. A total of 140 dynamic time frames corresponding to a total acquisition time of 8:20 min. Three subjects volunteered for the intra-subject variability study, who performed up to 6 sets of PCASL measurements on different days. The PCASL protocol was identical as what was used for the inter-subject study. The post-processing of the PCASL data was performed off-line using shell scripts calling C-programs from the AFNI package. The main steps included: 1) 1) motion correction by 3D rigid-body image registration; 2) creation of brain mask, 3) voxel-wise computation according to previously established equation; 4) brain normalization to align individual CBF data to brain atlas template by using affine transformation and mutual information as cost function. 5) Voxel-wise statistical analyses including average (mean), standard deviation (stdev), coefficient variance (CVAR), minimum, and maximum; 6) whole-brain statistics.

Results: Figure shows the inter- (1st row) and intra-subject (2nd row) statistical maps for the middle slice. For displaying, the standard deviation and coefficient of variance were scaled up by a factor of 50 and 100, respectively. Although both the inter- and intra-subject results were interpolated to the same spatial resolution of 3 mm isotropic voxel size, the inter-subject averaged CBF maps displayed more blurring than the intra-averaged CBF. Besides the edges, CSF and white matter regions demonstrated much larger variations. For voxels in the gray matter region, the inter-subject CVAR is typically in the range of 30-60%, whereas the intra-subject XVAR is 5-15%. Region of interest (ROI) based statistics can also be meaningful . For simplicity, we computed the mean, stdev, and CVAR based on the whole brain. The results for the inter-subject and 3 sets of intra-subjects measurements were detailed in Table 1. As shown, the inter-subject variability is about twice of that for the intra-subject value.

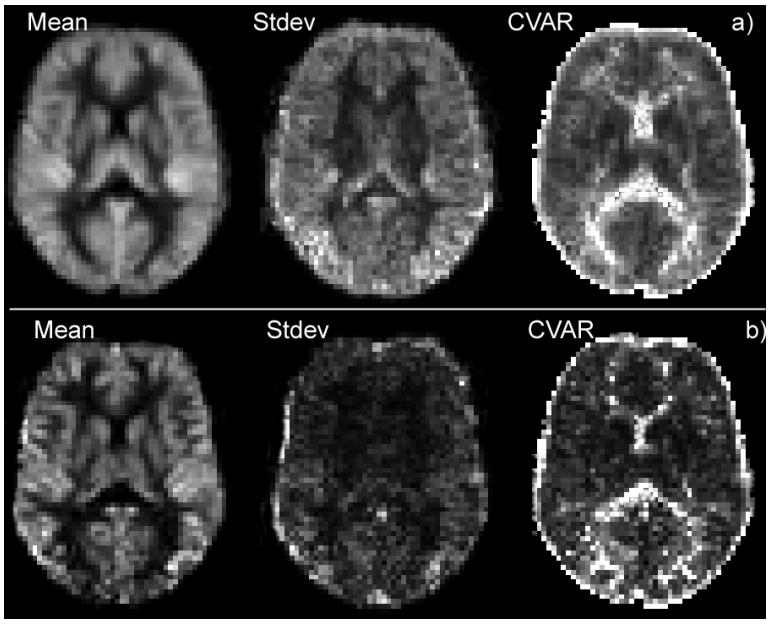

Table 1:Inter- intra-subject statistics

Subject	Mean	Stdev	CVAR
17 (inter)	35.6	26.8	91%
A (intra)	38.9	17.2	52%
B (intra)	34.9	14.1	45%
C (intra)	34.7	13.8	47% .

Discussion: Using an up-to-date PCASL protocol with optimized acquisition parameters, we evaluated the inter- and intra-subject variability of CBF measurements based PCASL technique. The inter-subject variability is about 2-3 time of that for intra-subject depending the chosen ROI size (from voxel to whole brain). If the expected pharmacokinetic effect on CBF for an individual is larger than 15%, PSCAL can be a useful method for longitudinal and quantitative studies.

References: [1] Wu W. et al. *Magn Reson Med* **58**:1020 (2007); [2] Wong1 E.C. *Magn Reson Med* **58**:1086 (2007); [3] Dai W. *Magn Reson Med* **60**:1488 (2008). [4] Wang Z. *Magn reson. Iamging* **26**:261 (2008); [5] Saad S. et al. *NeuroImage* **4**4:839 (2009)