

# Regional White Matter Perfusion Measurement Using an Optimized Pseudo-Continuous ASL MRI

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**Introduction:** Measuring white matter perfusion using arterial spin labeling (ASL) MRI is challenging for various reasons [1]: perfusion in white matter is low compared to that in gray matter, resulting in a lower intrinsic signal to noise ratio (SNR); the relative low resolution of ASL MRI images causes partial volume effects and overestimation of white matter perfusion due to contamination from the neighboring gray matter; finally, the wide spread of transit time across white matter regions introduces bias in the perfusion measurements. Previous attempts in measuring white matter perfusion have used both pulsed ASL and continuous ASL. Despite having the advantage of higher SNR over pulsed ASL, continuous ASL suffers from low tagging efficiency which partially cancels its SNR advantage [2]. Our group has recently worked on an optimized pseudo-continuous ASL (PCASL) method that greatly improves the tag efficiency (see Theory section). The goal of this study is to utilize the SNR gain of this optimized PCASL method in measuring the transit time and perfusion in major white matter regions across the brain.

**Theory:** The tagging efficiency of PCASL is impaired by phase errors due to both gradient imperfections and local field frequency offset at the labeling plane [3]. Conventional PCASL uses two constant RF phase offsets ( $0^\circ$  and  $180^\circ$ ) to alternate between tag and control conditions assuming zero phase errors. We can instead estimate the phase errors by acquiring MRI signal at multiple phase offsets (i.e.  $-90^\circ$ ,  $0^\circ$ ,  $90^\circ$ ,  $180^\circ$ ) and fitting the data to a signal equation describing the PCASL labeling process. The estimated phase error can then be compensated by adding a constant phase offset to the labeling RF pulses. However, the labeling plane typically contains several blood vessels, each of which may have a different phase error due to the local field inhomogeneities, causing non-uniform tagging across blood vessels. This can be addressed by adding small XY shim gradients during labeling period whose amplitudes are determined by the magnetic field difference between the vessels. Therefore, by properly compensating for the phase errors, we can achieve uniform and optimal tagging efficiency in PCASL.

**Methods:** A healthy human subject was studied. All data were acquired on a General Electric (GE) Signa HDx 3.0 Tesla research scanner with a standard 8 channel head coil (GE, Milwaukee, Wisconsin). The labeling plane was placed in a relatively straight part of the internal carotid artery approximately 30 mm inferior to the bottom slice as guided by a quick angiography scan. The perfusion scans were done using an in-house PCASL pulse sequence [4] with single shot spiral acquisition. The scan parameters were: TR 5 s, TE 3 ms, 22 slices, 4mm thick with no gap, FOV 22cm,  $64 \times 64$  matrix, labeling duration 1.6sec. Data with six different post-labeling delays {0.1, 0.5, 0.9, 1.3, 1.7, 2.5 sec} were acquired. Perfusion signals were calculated by surround subtraction of the tag-control series [5] at each post-labeling delay. A field map was collected and used to correct the off resonance effect in the individual spiral images using an iterative approach [6]. A diffusion tensor imaging (DTI) dataset with 25 directions, b value of  $1000 \text{ s/mm}^2$ ,  $64 \times 64$  matrix and echo planar readout was also acquired to assist in localizing major white matter tracts. Geometric distortions in the DTI data were corrected using the same field map. Additionally, a series of inversion recovery experiments with different recovery time were acquired in order to map the T1 values of white matter for accurate perfusion quantification. Finally a high resolution T1 weighted FSPGR (GE) dataset was collected and later segmented into partial volume maps of gray, white and CSF tissue types.

The field map corrected perfusion data, DTI and T1 map data were motion corrected and registered to the FSPGR images. Transit time and mean perfusion were then estimated by fitting the measured perfusion signal to a single compartment perfusion model [7]. Both voxel-based and region of interest (ROI) based curve fitting were performed. In order to minimize partial volume effects, the analysis is performed only in voxels with white matter partial volume  $> 0.9$  based on the white matter segmentation maps. The DTI fractional anisotropy (FA) and directional maps were used to guide the drawing of the white matter ROIs. A threshold of  $\text{FA} > 0.4$  was applied in selecting white matter ROIs in addition to the white matter partial volume threshold (0.9).

**Results:** Figure 1 shows the transit time fitting results in various white matter ROIs from the ROI-based analysis. The results indicated a wide spread of the white matter transit time ( $\delta t$ ) and the perfusion values ( $f$ ). The mean transit time and perfusion in whole brain white matter obtained from the voxel-based analysis were 1394 msec and 23.6 ml/100g/min, respectively. As a comparison, the mean transit time and perfusion were 1190 msec and 50.9 ml/g/min in whole brain gray matter.

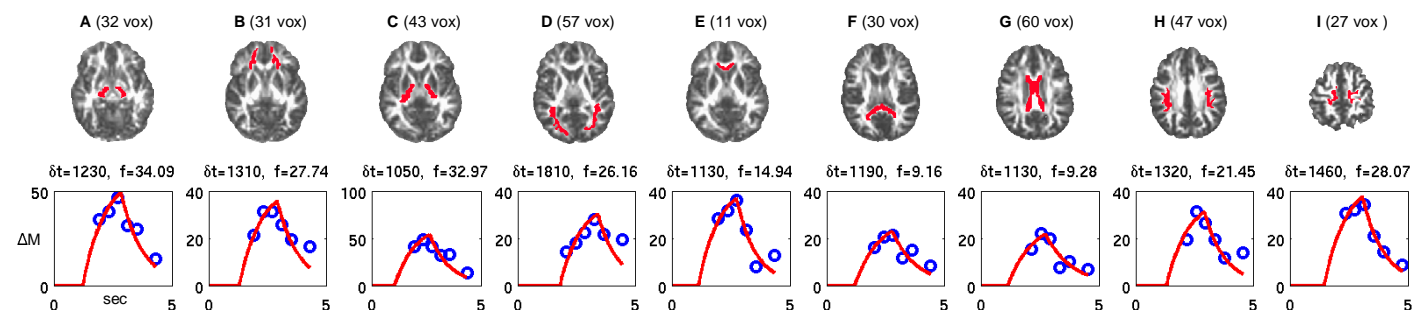


Figure 1: The top row shows the white matter ROIs overlaid on top of the fractional anisotropy maps and number of voxels contained in each ROI. The bottom row shows the ROI-based transit time curve fitting results.  $\Delta M$  is the raw perfusion signal,  $\delta t$ (msec) is the estimated transit time, and  $f$ (ml/100g/min) is the quantified perfusion. (A. cortical spinal tract B. anterior portion of the inferior fronto-occipital fasciculus C. posterior limb of the internal capsule D. optic radiata E. genu of corpus callosum F. splenium of corpus callosum G. body of corpus callosum H. superior longitudinal fasciculus I. superior region of corona radiata)

**Discussion:** The three main challenges of measuring white matter perfusion using ASL MRI are: low SNR, partial volume, and transit time effects. We have shown that our optimized PCASL method has sufficient SNR to detect perfusion in major white matter tracks. The adverse effects of partial voluming can be limited by carefully selecting voxels containing mostly white matter. Our results indicate significant variability of the white matter transit time across brain regions. Therefore it may be recommended that separate ASL experiments are carried out with parameters tailored to the specific targeted white matter regions to ensure optimal signal and accurate measurements.

**References:** [1] van Gelderen P et al, Magn Reson Med 59, p788, 2008. [2] Wu WC, Magn Reson Med 58, p1020, 2007. [3] Luh WM, et al, 16th ISMRM: p3339, 2008. [4] Wong EC, Magn Reson Med 58, p1086, 2007. [5] Liu TT et al, Neuroimage 24, p.207, 2005. [6] Sutton BP et al, IEEE Tran Med Imag 23, p178, 2003. [7] Buxton RB et al, Magn Reson Med 40, p383, 1998.