

# LABELING EFFICIENCY IS CRITICAL IN PSEUDO-CONTINUOUS ASL

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**INTRODUCTION:** Pseudo-Continuous Arterial Spin Labeling (pCASL) (1-3) is a new ASL technique that has the potential of combining advantages of continuous ASL (large brain coverage, high SNR) and pulse ASL (no special hardware). One of the most critical parameters in pCASL is the labeling efficiency, defined as (arterial blood in the control scan – arterial blood in the label scan)/2. Unlike continuous ASL, the labeling process of pCASL is not strictly an adiabatic inversion. Thus the labeling efficiency may be dependent on B0 inhomogeneity, B1 inhomogeneity and flow velocity. As a result, the labeling efficiency may vary for different subjects, for different labeling locations in the same subject, and for different physiologic state at the same labeling location. Here, we performed three sets of studies to: 1) empirically determine the optimal labeling location to achieve best labeling efficiency; 2) experimentally estimate the labeling efficiency using phase-contrast MRI as a normalization factor; 3) demonstrate that labeling efficiency may change with physiologic state and should be estimated for each physiologic condition.

**METHODS:** A total of 21 healthy controls (age 32±8 years) were studied on a 3T scanner (Philips). In the first set experiments (n=8), with the imaging slices in the same location, the labeling position was varied to be 49, 63, 74, 84, 94, 119, and 149mm distal to the anterior-commissure (AC) posterior-commissure (PC) line (bottom panel, Fig. 1). The CBF-weighted signal (control-label) was calculated and compared across different labeling positions.

In the second set of experiments (n=10), the labeling position was chosen to be the above determined optimal location and the imaging slices covered the whole brain (27 slices with slice thickness = 5mm). Importantly, a phase-contrast MRI was performed at the level of left/right internal carotid and left/right vertebral arteries (Fig. 2), from which we can calculate the total amount of blood entering the brain in units of ml/min. We also know the total intracranial volume and mass from a standard T1w MPRAGE image (processed with FSL software). Thus, we can determine the whole-brain-averaged CBF (ml/min/100g brain) = phase contrast (ml/min) / intracranial mass (100g). This value can then be used as a normalization factor to estimate the labeling efficiency in pCASL by solving the equation:

$$\text{Whole-brain-averaged CBF from phase-contrast} = \frac{\lambda \cdot e^{(\delta/T_1)}}{-2\alpha \cdot M_0 \cdot T_1 \left[ e^{\left(\frac{\min(\delta-w,0)}{T_1}\right)} - e^{\left(\frac{-w}{T_1}\right)\left(1-\frac{T_{1RE}}{T_1}\right)} \right]} \times \text{WholeBrainAverage}(\Delta M_{i,j,z}) \quad [1]$$

in which the left side term is from phase-contrast and MPRAGE;  $\Delta M_{i,j,z}$  on the right side terms is from pCASL, the equation is based on an ASL model from Alsop and Detre (4). The only unknown in the equation is the labeling efficiency,  $\alpha$ , and is estimated. Conceptually, this normalization method can be viewed as follows: Adding up all the pCASL signals within the brain gives the total amount of MRI signal (in a.u.); on the other hand, the phase-contrast scan gives the total amount of CBF in ml/min; these two are essentially equivalent; thus one can obtain the “conversion rate” that each unit of MR signal is worth how much CBF. Once the labeling efficiency is known, the absolute CBF map can be calculated with the standard equation (4).

In the third set of experiments (n=3), hypercapnia was induced using 5% CO<sub>2</sub> breathing, and pCASL MRI was acquired during normocapnia (room-air breathing) and hypercapnia. Hypercapnia is known to increase CBF globally. The goal of these experiments is to test whether or not pCASL can accurately quantify CBF changes. Phase-contrast MRI was again used as a gold standard to verify the pCASL results. Other parameters (for all three experiments): voxel size=3x3mm, TR=4s, labeling duration/delay 1.6/1.5s, 30 pairs of controls/labels, RF interval 1ms, RF duration 0.5ms, flip angle 18°.

**RESULTS and DISCUSSION:** Figure 1 shows the results for the labeling position study. The intensities of the CBF weighted images (top, Fig. 1) are highly dependent on the location of the labeling plane. Quantitative analysis revealed that the signal intensity is highest when the label plane is positioned 84mm below the AC-PC line, although similar results are achieved between 63-94mm below the AC-PC line. Next, we set to investigate what the labeling efficiency is at this optimal location (84mm). Phase-contrast MRI (Fig. 2) showed that the whole-brain-averaged CBF is 44.2±7.0ml/min/100g. Using equation 1 above, the label efficiency  $\alpha$  was estimated to be 87±10 (mean±SD) %, in excellent agreement with simulation results reported by Wu et al. (2). However, we note that there are some variations in labeling efficiency across subjects. Therefore, it is important to estimate the labeling efficiency individually rather than assuming a constant value for all subjects. Figure 3 shows the CBF maps during normocapnia and hypercapnia, and their differences. On average, the phase-contrast MRI showed a CBF increase of 63.4±46.8% (n=3) comparing hypercapnia to normocapnia. For confirmation, we also performed phase-contrast in sagittal sinus, which showed similar increases (57.2±53.2%, n=3) in CBF. For pCASL, if we do not consider the possible changes in labeling efficiency between normocapnia and hypercapnia, and just use the (control-label) signals, the CBF increases were 37.6±15.6% (n=3). This is considerably lower than that using phase-contrast MRI. We attribute this discrepancy to the reduction in labeling efficiency in hypercapnia. That is, during hypercapnia, even though CBF has increased, the labeling efficiency at such a high flow velocity has actually decreased slightly, resulting in an under-estimated pCASL signal. This notion is supported by the simulation results (Fig. 4) of labeling efficiency vs. flow velocity. We note that the mean arterial velocity in our data was 17.6±5.0 cm/s (mean±SD, n=3) and 23.0±3.9 cm/s for normocapnia and hypercapnia, respectively. In summary, our results suggest that labeling efficiency is a critical parameter in pCASL MRI not only in terms of achieving highest sensitivity but also in quantification of absolute CBF in ml/min/100g. We propose that the labeling efficiency should be estimated using phase-contrast MRI on a subject-specific and physiologic-condition-specific basis.

**REFERENCES:** 1) Garcia ISMRM, 2005; 2) Wu et al. MRM. 58:1020, 2007; 3) Wong MRM. 58:1086, 2007; 4) Alsop and Detre, JCBFM 16:1236, 1996.

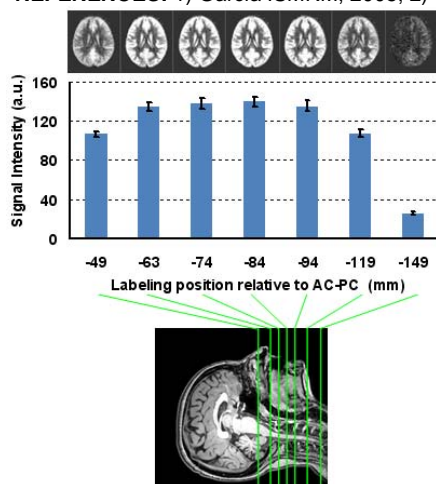


Fig. 1: pCASL signal (control-label) is dependent on the location of the labeling plane. Top: CBF-weighted images. Middle: Averaged signal intensity. Bottom: Illustration of labeling locations.

Fig. 3: Absolute CBF maps (in ml/min/100g) during normocapnia, hypercapnia (5% CO<sub>2</sub> breathing) and their differences.

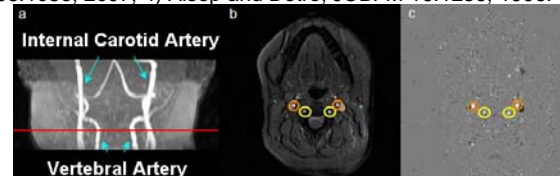
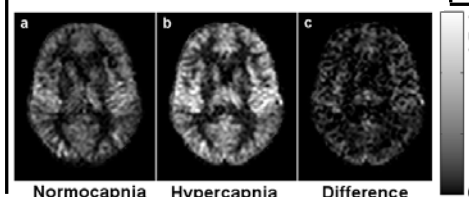


Fig. 2: Phase-contrast MRI. a) position of phase-contrast slice (red line) on a time-of-flight angiogram. b) magnitude image of phase-contrast MRI. Color circles indicate internal carotid and vertebral arteries. c) phase image of phase-contrast MRI.

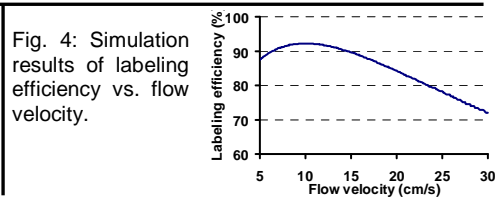


Fig. 4: Simulation results of labeling efficiency vs. flow velocity.