

ORIGINAL ARTICLE

# Reliability of Three Dimensional Pseudo-continuous Arterial Spin Labeling: A Volumetric Cerebral Perfusion Imaging with Different Post-labeling Time and Functional State in Health Adults

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**Key words:** pseudo-continuous arterial spin labeling; magnetic resonance imaging; intraclass correlation coefficient; reliability

**Objective** To evaluate the reliability of three dimensional spiral fast spin echo pseudo-continuous arterial spin labeling (3D pc-ASL) in measuring cerebral blood flow (CBF) with different post-labeling delay time (PLD) in the resting state and the right finger taping state.

**Methods** 3D pc-ASL and three dimensional T1-weighted fast spoiled gradient recalled echo (3D T1-FSPGR) sequence were applied to eight healthy subjects twice at the same time each day for one week interval. ASL data acquisition was performed with post-labeling delay time (PLD) 1.5 seconds and 2.0 seconds in the resting state and the right finger taping state respectively. CBF mapping was calculated and CBF value of both the gray matter (GM) and white matter (WM) was automatically extracted. The reliability was evaluated using the intraclass correlation coefficient (ICC) and Bland and Altman plot.

**Results** ICC of the GM (0.84) and WM (0.92) was lower at PLD 1.5 seconds than that (GM, 0.88; WM, 0.94) at PLD 2.0 seconds in the resting state, and ICC of GM (0.88) was higher in the right finger taping state than that in the resting state at PLD 1.5 seconds. ICC of the GM and WM was 0.71 and 0.78 for PLD 1.5 seconds and PLD 2.0 seconds in the resting state at the first scan, and ICC of the GM and WM was 0.83 and 0.79 at the second scan, respectively.

**Conclusion** This work demonstrated that 3D pc-ASL might be a reliable imaging technique to measure CBF over the whole brain at different PLD in the resting state or controlled state.

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**A**RTERIAL spin labeling (ASL) is a non-invasive cerebral perfusion imaging technique to be used to measure cerebral blood flow (CBF) *in vivo* without exogenous tracers.<sup>1-3</sup> In clinical practice, ASL sequence is used to diagnose and monitor stroke,<sup>4</sup> brain tumor,<sup>5</sup> and cognitive disorders.<sup>6</sup> Initially, flow-sensitive alternating inversion recovery (FAIR) technique is applied in the functional imaging to measure CBF.<sup>7</sup> This approach could label the water molecules of flowing blood as a tracer to obtain the CBF information. However, this technique suffered from low signal intensity, limited spatial coverage of the brain and rapid T1 decay of the labeled spins.<sup>8</sup>

Three dimensional (3D) spiral fast spin echo (FSE) pseudo-continuous ASL (3D pc-ASL) is a novel non-enhancement perfusion sequence on MR750 3.0T. The advantage of this technique includes 3D acquisition, spiral k-space filling, FSE pulse sequence, which would further expand the clinical application of ASL. Therefore, the assessment of the reliability of 3D pc-ASL seems important before the large scale application.

Previous studies<sup>9-10</sup> demonstrated that continuous and pulsed ASL had a good test-retest reliability of CBF on 1.5T scanners. And compared with <sup>15</sup>O-water positron emission tomography (PET) in Alzheimer's disease, 3D pc-ASL provided a reliable whole brain CBF measurement in young and elderly adult on 3.0T scanner.<sup>6</sup> A reliability study of pseudo-continuous ASL was also performed at 1.5T and 3.0T, suggesting the fluctuations in perfusion signal seen over the longer term at both 1.5T and 3.0T are likely to reflect genuine fluctuations in resting-state perfusion, and the physiological contributions to the variability of the regional ASL perfusion signal should be furtherly clarified.<sup>11</sup>

Although some reliability studies focused on the different short term inter-scan interval<sup>12-14</sup> and different scanners,<sup>15</sup> the reliability of 3D ASL with different post-labeling was not investigated up to now, which would be helpful for the best choice for the different post-labeling time. Besides, it was not assessed that whether the different cerebral functional state may influence the reliability of 3D pc-ASL. In the current study, we hypothesize that a good reliability of 3D pc-ASL could be confirmed with different post-labeling time and functional state. To address this hypothesis, we performed the study as follows: (1) investigate the reliability of 3D pc-ASL with different post-labeling delay time (PLD) at the resting state and right finger tapping state over one week interval; (2) clarify the

signal fluctuation by different PLD contributions to the test-retest reliability changes of CBF over the whole brain.

## SUBJECTS AND METHODS

### Subjects

Eight health adults (6 men and 2 women) were recruited from our medical school in April 2016, with a mean age of 23.8 years (ranging from 21 to 33 years). All the subjects were right-handed and highly educated. The exclusion criteria included: cranium trauma, central nervous system inflammatory disease, and use of psychoactive drugs or hormone. All the subjects were scanned twice at the same time each day for one week interval, and none was permitted to do heavy exercise and has caffeinated beverages within one hour of scanning session. Written informed consent was obtained from all subjects and the study was approved by the ethics committee of the local institution.

### MR imaging

All the MR data were acquired on a DISCOVERY MR750 3.0T MR system (GE Healthcare, Milwaukee, WI, USA), with a conventional eight-channel phased array head coil. First, fast fluid-attenuated inversion recovery (FLAIR) images with repetition time (TR)/echo time (TE)/inversion time (TI) = 8802 ms/124.3 ms/2200 ms, slice thickness = 4 mm, gap = 1 mm, matrix = 256×256, field of view (FOV) = 24 cm×24 cm, and number of acquisition (NEX) = 1 were obtained for general assessment. The structural imaged data were acquired with a high resolution 3D T1-weighted fast spoiled gradient recalled echo (3D T1-FSPGR) sequence, which was used to generate the 244 contiguous axial slices with parameters as follows: TR/TE = 8.6 ms/3.5 ms, flip angle = 12°, FOV = 22 cm×22 cm, matrix = 256×256, slice thickness = 1.2 mm, and NEX = 1. Volumetric perfusion imaging was obtained using a pc-ASL tagging scheme with a 3D interleaved spiral FSE readout (3D spiral FSE ASL) with parameters of TR/TE = 5128 ms/15.9 ms, flip angle = 111°, FOV = 20 cm×20 cm, x, y matrix = 1024×8 (spiral acquisition), and slice thickness = 3.0 mm. The labeling duration was 1.5 seconds, and PLD was 1.5 seconds and 2 seconds respectively. The first ASL data acquisition was performed with PLD 1.5 seconds, and the second ASL data acquisition with PLD 2 seconds in the uncontrolled resting state for all the subjects, and the third ASL

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