Comparison of reproducibility between continuous, pulsed, and pseudo-continuous arterial spin labeling

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Introduction
Arterial spin labeling (ASL) is a noninvasive method for measuring cerebral blood flow (CBF). There are two broad categories of ASL: continuous (CASL), which uses a long train of square pulses to approximate a continuous inversion of flowing spins; and pulsed (PASL), which uses a short inversion pulse to label a fixed amount of blood. Theoretically, CASL has higher signal-to-noise ratio than PASL¹, but it is limited to transmit/receive coils due to the high radiofrequency duty cycle. Recently, a modification of CASL called pseudo-continuous ASL (pCASL) was introduced²–³. pCASL combines the SNR advantage of CASL and the lower power deposition of PASL, which makes it possible to use the more sensitive array coils. While initial assessments appear optimistic, there has been no formal comparison of the reproducibility of the various methods including both within and across session measures, which estimate both instrumental and physiological noises. In this study, we investigate the reproducibility of three variants of ASL: CASL, PASL and pCASL.

Methods
Data from twelve healthy subjects (7F, mean age 24) scanned at rest were collected on a 3T whole-body scanner (Siemens Trio, Erlangen, Germany) with both an 8-channel receive-only coil and a transmit/receive head coil (for CASL). Sequence parameters for the different sequences are as follows: 1) PASL (FAIR) – T1=700/1700ms, 40 pairs, 2) pCASL – PLD=1s, τ=1.5s, label offset=80mm, 40 pairs, 3) CASL – PLD = 1s, τ=2s, label offset=80mm, 40 pairs. All data were collected using gradient-echo EPI (TR/TE=4s/17ms, 14 x 6mm slices, 3.75 in-plane resolution). Scans were repeated within-session, after 1 hour and after 1 week. CASL was performed only on a subset of 7 subjects. Other scans include a high-resolution T1-MPRAGE, used for coregistration and normalization, as well as an M0 image for quantification of PASL data. Perfusion images calculated from pair-wise subtractions between control and tag images were converted to quantitative CBF maps using pre-established models⁴. Whole-brain gray and white matter segmentation masks were used to generate the CBF data used for calculating repeatability and within-subject coefficients of variation (wsCV), which were compared between the different sessions.

Results & Discussion
Correlation plots for gray matter (GM) CBF between scan 1 and the subsequent scans for all three sequences are shown to the left. Line of unity is shown to guide the eye. While excellent correlation is seen within session, the 1 hr and 1wk correlations were visibly worse. A summary of the results, including the mean CBF, repeatability in ml/100g/min and wsCV in % are shown in the table below. Raw and temporal signal-to-noise ratios (SNR), normalized to PASL, are also shown in the table. While both pCASL and CASL have similar wsCV within-session, pCASL outperforms CASL at the 1hour and 1week scan. Another advantage of pCASL is that it can be implemented with the more sensitive array coil, evident in the high raw SNR of pCASL compared to CASL (paired t-test, p<0.001). The transmit/receive coil may also account for the poor reproducibility of CASL after 1hr and 1wk, as different positioning of the subjects could result in variability in labeling efficiency, which in turn affects the CBF estimates. Relative to PASL, pCASL has superb wsCV and repeatability within-session (~50% less variability), however, the two methods have similar degrees of wsCV for the 1week scan. It is important to note that pCASL has a significant SNR advantage over PASL (~60% gain in raw SNR, paired t-test, p<0.001 and 20% gain in temporal SNR, paired t-test, p<0.02), likely due to the intrinsic signal advantage of CASL methods. Repeatability in gray matter show a similar trend as the wsCVs, however, better repeatability at the 1wk scan was observed in WM for the CASL-based methods, potentially due to the better labeling efficiency of CASL compared to PASL.

Conclusion
Our results show that pCASL and PASL have the lowest wsCVs of ~13% for scans performed 1wk apart. Additionally, pCASL has higher tSNR and is not limited to transmit/receive coils as traditional CASL. These advantages make pCASL a favorable method for measuring CBF.

<table>
<thead>
<tr>
<th></th>
<th>PASL (N=12)</th>
<th>PCASL (N=12)</th>
<th>CASL (N=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Scan1</td>
<td>Scan2</td>
<td>1Hour</td>
</tr>
<tr>
<td><strong>GM</strong></td>
<td></td>
<td></td>
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<tr>
<td>Mean CBF</td>
<td>54.71</td>
<td>56.68</td>
<td>53.62</td>
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<tr>
<td>(Std)</td>
<td>(6.83)</td>
<td>(7.46)</td>
<td>(8.79)</td>
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<tr>
<td>Repeatability</td>
<td>13.08</td>
<td>9.20</td>
<td>18.67</td>
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<tr>
<td>wsCV</td>
<td>8.7%</td>
<td>6.3%</td>
<td>12.8%</td>
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<tr>
<td><strong>WM</strong></td>
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<td></td>
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<tr>
<td>Mean CBF</td>
<td>36.73</td>
<td>37.98</td>
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<tr>
<td>(Std)</td>
<td>(6.26)</td>
<td>(6.93)</td>
<td>(6.34)</td>
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<tr>
<td>Repeatability</td>
<td>9.91</td>
<td>7.83</td>
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<td>9.8%</td>
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<tr>
<td>Raw SNR</td>
<td>1.0</td>
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<td>tSNR</td>
<td>1.0</td>
<td>1.2</td>
<td>(0.23)</td>
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References