

Reliability of Brain Perfusion with Pulsed Arterial Spin Labeling

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Synopsis: Efficiency of pulsed arterial spin labeling (PASL) to tag blood water is one factor besides physiological and instrumental fluctuations that can limit the reliability of brain perfusion studies. This study compares the reliability of different PASL schemes, including EPSTAR, PICORE, and a new scheme termed DIPLOMA to measure perfusion on 13 subjects. DIPLOMA was best, achieving an intra-class correlation (ICC) between test-retest perfusion studies of 0.92 for mean perfusion of whole brain, followed by PICORE (ICC=0.82) and EPSTAR (ICC=0.73). DIPLOMA substantially improved the reliability of perfusion measurements and therefore should provide more power in detecting differences between groups and individuals.

Introduction: Efficiency of pulsed arterial spin labeling (PASL) to tag blood water without introducing magnetization transfer or eddy-current effects different from the untagged experiment is one factor besides physiological and instrumental fluctuations that can limit the reliability of brain perfusion studies. Although PASL is frequently used to study blood flow in different disorders of the brain, the reliability of perfusion measurements have not been rigorously determined. Especially, the extent to which different methods for PASL may improve perfusion reliability, taking into account the variability of cerebral blood flow (CBF) between subjects, has not previously been studied. Recently, we introduced a new PASL scheme termed DIPLOMA (1), which provided perfusion-weighted images (PWI) of superior quality than EPSTAR (2) or PICORE (3) by balancing magnetization transfer and eddy-current effects. Therefore, the objective of this study was to compare DIPLOMA with EPSTAR and PICORE in measuring perfusion reliability.

Methods: The three PASL tagging methods are shown in Figure 1. After PASL, the rest of the pulse sequence structure to image brain perfusion was identical for all three tagging methods and similar to Q2TIPS (4). Thirteen volunteers (mean age 45±14 years, 4 men and 9 women) were scanned with all three PASL schemes twice within two hours on a 1.5T MR system (Siemens Vision). In addition to PWI, volumetric T1-weighted and multi-planar density images (FLASH) were acquired for tissue segmentation and normalization into a standardized space using SPM99 (5) on a Window 2000 system. Reliability of each PASL method was determined by comparing between to within subject variation of perfusion in terms of an intra-class correlation coefficient (ICC) (6). Perfusion measures that were tested included a) overall mean perfusion, b) perfusion of gray matter, and c) perfusion of white matter.

Results: Results from reliability measurements of whole brain, gray matter, and white matter perfusion are listed in Table 1, separately for each PASL scheme. Reliability of mean whole brain perfusion was best with DIPLOMA, achieving an ICC of 0.92, followed by PICORE with 0.82 and EPSTAR with 0.73 for ICC. Similarly, results of gray matter and white matter perfusion showed better reliability with DIPLOMA than with EPSTAR or PICORE. Furthermore, reliability of perfusion was usually higher for gray matter than for white matter.

Discussions and Conclusions: Many sources contribute to noise in perfusion measurements, including biological fluctuations of CBF, instrumental instabilities, and random noise. Furthermore, labeling of blood water by PASL that produces magnetization transfer or eddy-current effects different from those produced in the untagged experiment is thought to be another source of error. The result indicate that using optimized PASL schemes to control magnetization transfer and eddy-current effects is important for reliable measurements of perfusion, despite anticipated large variations of CBF values within and between subjects. Responsible for reliability increase with DIPLOMA compared to PICORE and EPSTAR are likely a) better eddy-current compensation than with PICORE and b) better MT compensation than with EPSTAR. Eddy-current compensation improved, because gradients are applied in both tag and control scan, partially balancing eddy currents. MT compensation improved, because the same RF power is used for tag and control scans, reducing problems with nonlinear MT effect, although MT compensation with DIPLOMA is not perfect (1).

The concept of test-retest studies allows separating the overall measurement variations from variations due to the subjects, thereby providing a gauge of the magnitude of measurement errors. The results from this study show that reliability increased substantially with DIPLOMA, achieving measurements that could be attributed 92% to perfusion and less than 8% to noise. In contrast, noise contributed more than 18% to perfusion measurements with EPSTAR and PICORE. This suggests that DIPLOMA provides more power in detecting differences of CBF between groups and individuals than EPSTAR or PICORE. Another interesting result was higher reliability for gray matter than for white matter perfusion. Although this was expected as perfusion is known to be greater in gray matter than in white matter, resulting in a stronger perfusion signal of gray matter, the finding confirms that signal-to-noise is still an important factor for reliability despite a large biological variability between subjects. This also suggests that reliability of perfusion would benefit from higher magnetic fields, which provide better signal to noise. It should be noted that results from this study could not be applied to determine the reproducibility of perfusion measurements within a subject or CBF changes over time. Previous studies of PASL perfusion (7,8) found significant daily variations of CBF, which could limit the detection of effects on CBF changes over time.

In conclusion, PASL with DIPLOMA should provide superior power in detecting differences of perfusion between subjects and groups than PASL with either EPSTAR or PICORE.

References: 1) Jahng GH et al: 10th ISMRM, Hawaii, 2002, p.1057; 2) Edelman RR, Chen Q: Magn Reson Med 1998;40:800-805; 3) Wong EC et al: NMR in Biomed 1997;10:237-249; 4) Luh et al: Magn Reson Med 1999;41:1246-1254; 5) Ashburner J and Friston KJ: Human Brain Mapping 1999;7(4):254-266; 6) Shrout PE and Fleiss JL: Psychological Bulletin 1979;86: 420-428 7) Blauenstein UW et al: Stroke 1977;8(1):92-102; 8) Yen YF et al: Magn Reson Med 2002;47(5):921-928.

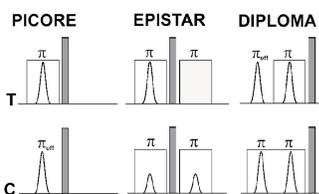


Figure 1

Table 1

MEASURE	DIPLOMA	PICORE	EPSTAR
Mean whole brain	0.92	0.82	0.73
Mean gray matter*	0.73	0.62	<0.5
Mean white matter*	0.68	0.59	<0.5

*ICC values not yet corrected for receiver gain and transmitter voltage variations between test and retest scans.