Multicenter Reproducibility of Continuous, Pulsed and Pseudo-Continuous Arterial Spin Labeling; Can we use General Reference Values of Cerebral Blood Flow?

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Introduction

Cerebral perfusion imaging plays an important role in the evaluation of brain disease. Arterial spin labeling (ASL) is a relatively new and non-invasive perfusion imaging technique that uses magnetically labeled arterial blood water protons as an endogenous tracer of flow. Its non-invasiveness makes ASL an attractive tool compared to standard clinical methods. However, low SNR and uncertainties regarding cerebrovascular kinetics, blood equilibrium magnetization or quantification complicate its clinical use. Sub-optimal labeling efficiencies could for example easily occur due to bad shimming, poor tuning of the RF-chain, or in general a worse performance of the MRI scanner. Several advances like the use of high field systems and the introduction of pseudo-continuous ASL and background suppression have led to increased SNR of resulting perfusion maps. Especially, due to the complicated setup of ASL experiments, it is uncertain whether comparable perfusion values would be obtained in different imaging centers, even when scanning the same subject. To allow for careful patient follow-up and to interpret perfusion data within and across imaging centers, knowledge on reproducibility of different ASL sequences over different imaging centers is indispensible. This will determine whether general reference values, e.g. out of literature, can be used in clinical decision-making or that each hospital should first gauge their own perfusion values, for example in a healthy control group. Therefore, the aim of this study was to assess reproducibility of presently used continuous, pulsed and pseudo-continuous ASL sequences with and without background suppression (CASL, PULSAR, Pseudo-CASL with and without BS) within and between imaging centers (intra- and multicenter) by scanning the same persons multiple times at multiple sites.

Methods

Intra- and multicenter reproducibility was assessed at three imaging centers in the Netherlands, all equipped with a Philips 3T MR scanner with the same implementation of the ASL sequences. Local ethics committees approved this study and the six healthy participants (five male; age 25-50) gave written informed consent. Volunteers were scanned twice at each site with 1 to 3 weeks between sessions. The imaging protocol consisted of: an amplitude modulated CASL sequence [1] (combined with MR angiography for planning of the CASL labeling plane, acquired with a transmit/receive head coil), a pseudo-CASL sequence [2] performed with and without BS, a PULSAR sequence [3], regional perfusion imaging (RPI) [4], inversion recovery for M0 measurements and a high resolution 3D T1-weighted anatomical scan for registration and segmentation purposes (all acquired with a SENSE-8-channel head coil and body coil transmission). Scans were made in a randomized fashion. For imaging parameters of ASL sequences see *Table 1.* All perfusion images and RPI defined basilar (BA) and internal carotid arteries (ICA) flow territories were transformed into anatomical space by registration on corresponding anatomical scans. After quantification of perfusion maps, whole brain (WB) and main flow territory cerebral blood flow (CBF) were calculated. Differences between WB CBF values measured at different imaging centers were tested using paired t-tests (SPSS 16.0.2 Statistics UK). Intra- and multicenter reproducibility were expressed in terms of the repeatability index (RI) defined as the 95% confidence limits for the difference between repeated measurements.

Imaging Parameters	Pseudo-CASL BS	Pseudo-CASL no BS	CASL	PULSAR	RPI
TR/TE	4000 ms/14 ms	4000 ms/14 ms	4500/32 ms	3000 ms/30 ms	4000 ms/14 ms
FOV; Matrix	240×240; 80×79	240×240; 80×79	210×210; 64×45	240×240; 80×79	240×240; 80×79
Slices, thickness	17; 7 mm	17; 7 mm	11; 7 mm	17; 7 mm	17; 7 mm
Sequence	GE EPI	GE EPI	SE EPI	GE EPI	GE EPI
Post labeling delay	1525 ms	1525 ms	1200 ms	1200 ms	1525 ms
Averages	40	40	40	40	40

Table 1: Imaging parameters for ASL techniques

Results

Figure 1 shows representative perfusion images obtained by different ASL sequences. Overall mean WB CBF was 37.9 ± 7.0, 37.9 ± 7.8, 37.2 ± 8.8 and 39.6 ± 7.2 ml/100g/min for Pseudo-CASL with and without BS, CASL and PULSAR respectively. Mean whole brain CBF values per site and technique are shown in *Table 2.* *Figure 2* shows test-retest CBF values for all ASL techniques. Intra- and multicenter RIs for WB CBF were 7.6 and 9.6 for Pseudo-CASL, 12.9 and 10.0 for Pseudo-CASL without BS, 10.1 and 14.9 for CASL and 15.5 and 12.2 for PULSAR. Intra- and multicenter reproducibility for WB CBF measurements and ICA and BA CBF measurements is presented in *Table 3*. The very high RIs for BA CBF measured by PULSAR might be explained by a hyperintense posterior zone (see *Figure 1*) which we commonly encountered on PULSAR perfusion maps.

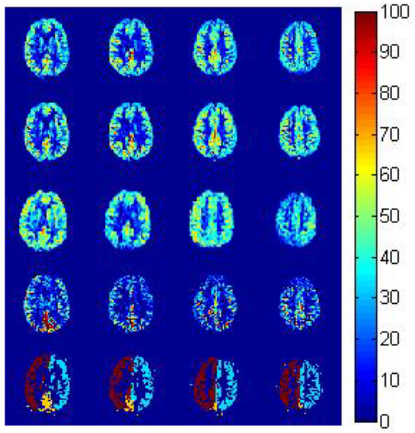

Figure 1: representative perfusion images obtained by Pseudo-CASL BS,Pseudo-CASL no BS, CASL, PULSAR and RPI (top to bottom)

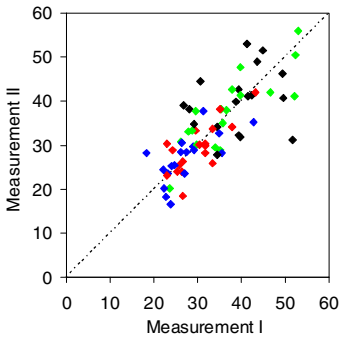

Figure 2: test-retest WB CBF values (ml/100g/min) for CASL (green), PULSAR (black), Pseudo BS (blue) no BS (red)

Mean WB CBF	Pseudo BS	Pseudo no BS	CASL	PULSAR
Site 1	35.7 ± 6.2*	36.5 ± 6.8	41.4 ± 7.5**	36.7 ± 5.1
Site 2	38.5 ± 5.5	38.6 ± 7.0	33.6 ± 9.7	36.0 ± 7.2
Site 3	39.5 ± 9.0*	38.5 ± 9.9	36.6 ± 7.7	46.0 ± 4.4**

*Table 2: Mean whole brain CBF (ml/100g/min) per imaging site. * Mean Pseudo BS WB CBF differed significantly between site 1 and 3. ** Mean CASL WB CBF measured at site 1 and PULSAR WB CBF measured at site 3 differed significantly from WB CBF measured at the other two sites.*

		Pseudo BS	Pseudo no BS	CASL	PULSAR
WB	Intracenter	7.6	12.9	10.1	15.5
	Multicenter	9.6	10.0	14.9	12.2
LICA	Intracenter	14.2	20.5	14.9	15.6
	Multicenter	14.0	18.6	17.1	25.5
RICA	Intracenter	14.9	19.2	15.2	22.5
	Multicenter	18.4	24.2	15.9	24.1
BA	Intracenter	15.5	22.0	15.2	42.7
	Multicenter	19.2	22.6	18.4	41.4

Table 3: Repeatability indices of whole brain CBF measurements

Conclusions

Based on RIs presented in Table 3, one can be 95% sure that WB CBF differences will be less than 25% between imaging centers. This finding could enable the use of general reference values, with CBF deviating less than 25% considered normal. The results of this intra- and multicenter reproducibility study show that in general, intracenter reproducibility surpasses multicenter reproducibility. Also, these data indicate that particularly CASL and PULSAR data gathered at different sites can vary significantly, whereas Pseudo-CASL data are less variable (as is reflected by the lower RIs for WB Pseudo-CASL with BS). Finally, BS further reduces intra- and multicenter variability of Pseudo-CASL data.

References

[1] Alsop and Detre, Radiology 1998;208:410-6, [2] Garcia et al., Proc. ISMRM 2005;#37, [3] Golay et al., MRM 2005;53:15-21, [4] Wong and Kansagra, Proc. ISMRM 2008;#184