



## Multi-vendor reliability of arterial spin labeling perfusion MRI using a near-identical sequence: Implications for multi-center studies



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### ABSTRACT

**Introduction:** A main obstacle that impedes standardized clinical and research applications of arterial spin labeling (ASL), is the substantial differences between the commercial implementations of ASL from major MRI vendors. In this study, we compare a single identical 2D gradient-echo EPI pseudo-continuous ASL (PCASL) sequence implemented on 3T scanners from three vendors (General Electric Healthcare, Philips Healthcare and Siemens Healthcare) within the same center and with the same subjects.

**Material and methods:** Fourteen healthy volunteers (50% male, age  $26.4 \pm 4.7$  years) were scanned twice on each scanner in an interleaved manner within 3 h. Because of differences in gradient and coil specifications, two separate studies were performed with slightly different sequence parameters, with one scanner used across both studies for comparison. Reproducibility was evaluated by means of quantitative cerebral blood flow (CBF) agreement and inter-session variation, both on a region-of-interest (ROI) and voxel level. In addition, a qualitative similarity comparison of the CBF maps was performed by three experienced neuro-radiologists.

**Results:** There were no CBF differences between vendors in study 1 ( $p > 0.1$ ), but there were CBF differences of 2–19% between vendors in study 2 ( $p < 0.001$  in most gray matter ROIs) and 10–22% difference in CBF values obtained with the same vendor between studies ( $p < 0.001$  in most gray matter ROIs). The inter-vendor inter-session variation was not significantly larger than the intra-vendor variation in all ( $p > 0.1$ ) but one of the ROIs ( $p < 0.001$ ).

**Conclusion:** This study demonstrates the possibility to acquire comparable cerebral CBF maps on scanners of different vendors. Small differences in sequence parameters can have a larger effect on the reproducibility of ASL than hardware or software differences between vendors. These results suggest that researchers should strive to employ identical labeling and readout strategies in multi-center ASL studies.

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**Abbreviations:** ASL, arterial spin labeling; CBF, cerebral blood flow; DARTEL, diffeomorphic anatomical registration analysis using exponentiated lie algebra; EPI, echo-planar imaging; GM, gray matter; MRI, magnetic resonance imaging; PLD, post-label delay; PCASL, pseudo-continuous ASL; ROI, region of interest; SD $\Delta$ CBF, standard deviation of the paired inter-session CBF difference; SNR, signal-to-noise ratio; WM, white matter; wsCV, within-subject coefficient of variation.

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## Introduction

Through a number of methodological advances, arterial spin labeling (ASL) perfusion MRI has reached a level that allows its application in multiple clinical and research applications for the visualization and quantification of cerebral blood flow (CBF) (Dette et al., 2012; Williams et al., 1992). Since ASL is non-invasive and offers absolute CBF quantification, it is an attractive tool compared to alternative perfusion modalities (Golay et al., 2004; Hendrikse et al., 2012). Furthermore, quantitative ASL CBF maps are reproducible and comparable with perfusion measurements from the “gold standard”  $H_2O^{15}$ -PET (Heijtel et al., 2014; Petersen et al., 2010; Xu et al., 2010). Implementations of ASL are commercially available on all major MRI systems and the number of clinical applications is continuously growing. Measurements of regional CBF promise clinical value in a variety of common neurological disorders, such as cerebrovascular disease, epilepsy, neurodegeneration and brain tumors, and ASL is recognized as a particularly valuable research tool for cognitive and pharmacological neuroscience (Deibler et al., 2008; Wang et al., 2011).

One obstacle that impedes standardized clinical and research applications of ASL, is the substantial differences in the commercial implementations of ASL from the major MRI vendors (Alsop et al., 2015). A variety of possible labeling and readout strategies exists, and each vendor has implemented a different combination of labeling and readout strategies for their commercial ASL release (Alsop et al., 2015). General Electric (GE) Healthcare offers pseudo-continuous ASL (PCASL) with a segmented 3D spiral fast spin-echo (FSE) readout, Philips Healthcare has PCASL paired with a single-shot 2D echo-planar imaging (EPI) readout and Siemens Healthcare provides pulsed ASL (PASL) combined with a segmented 3D gradient and spin-echo (GRASE) readout (Aslan et al., 2010; Gunther et al., 2005; Ye et al., 2000).

These labeling and readout differences between product sequences produce qualitatively different perfusion-weighted images, which can be visually appreciated on a single-subject level as shown in Fig. 1a (Chen et al., 2011; Kilroy et al., 2014). On a group level, it is currently not possible to compare CBF-values from a single region of interest (ROI) in a multi-center study, mainly because of differences in readout between sequences from different vendors (Mutsaerts et al., 2014; Vidorreta et al., 2012). Global CBF-values, however, show quantitative agreement between vendors (Mutsaerts et al., 2014). Furthermore, the inter-vendor global CBF inter-session variation is comparable to the intra-vendor global CBF variation (Chen et al., 2011; Mutsaerts et al., 2014). These observations support the possibility of future multi-center ASL research, if all vendors could implement an identical ASL sequence.

The current study aims to assess multi-vendor ASL CBF variations using a near-identical sequence across vendors, with the same labeling

and readout approach. PCASL was selected as a labeling strategy, because of its wide compatibility with all platforms and superior labeling efficiency for single time-point CBF measurements (Alsop et al., 2015; Chen et al., 2011; Dai et al., 2008). A multi-slice single-shot 2D EPI readout was selected because of its availability on all systems and as it has been used in the majority of previous ASL studies (Alsop et al., 2015). Because of differences in gradient and RF coil specifications between two vendor systems available for our study, two 2D echo-planar imaging (EPI) PCASL sequences were used with slightly different labeling and readout parameters. These will be referred to as study 1 and 2. For one vendor system, both variants of our sequence could be implemented, enabling an additional intra-vendor comparison of these slightly different sequences.

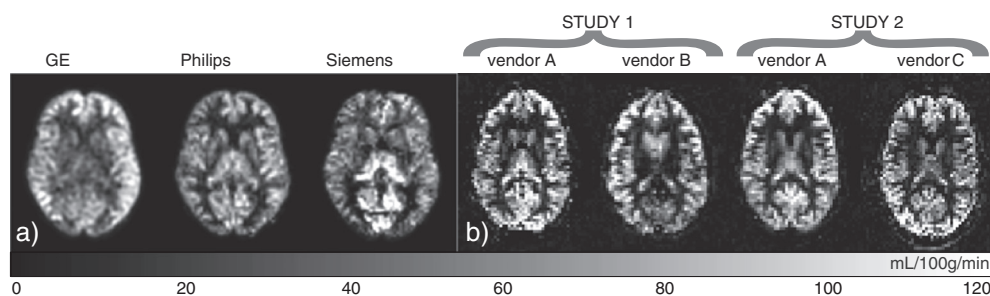
## Materials and methods

### MRI scanners

Three 3 T MRI scanners were used in this single-center multi-vendor comparison: GE Signa HDxt (2006, 60 cm bore opening, General Electric Healthcare, Milwaukee, WI, US), Philips Achieva (2007, 60 cm bore opening, Philips Healthcare, Best, The Netherlands) and Siemens Skyra (2011, 70 cm bore opening, Siemens Healthcare, Erlangen, Germany). None of the vendors were involved in designing or conducting this study, none had access to the data, and none were involved in data analysis or preparation of this manuscript. Because the main purpose of the study was to compare the inter- and intra-vendor reproducibility, without addressing the performance of each vendor system explicitly, vendor and coil names were anonymized by pseudo-randomly reordering the vendor names into vendor A, B and C. Vendor A was included in both studies because its gradient and RF coil specifications allowed sequence implementation identical to both vendor B and C. The scanners of vendor A and B were equipped with 8-channel head coils, whereas the scanner of vendor C was equipped with a 20-channel head-neck coil. Vendor A and C were separated by a five-minute walk, whereas vendor B was located at 20 minutes traveling distance by public transport from the location of the two other scanners.

### Study design

Both the local regional ethics committee and the local University Hospital internal ethical review board approved the study and all subjects provided written informed consent. In addition to standard MRI exclusion criteria, subjects with history of brain or psychiatric disease or use of medication — except for oral contraceptives — were excluded. To minimize physiological perfusion fluctuation, physical exercise and consumption of alcohol or recreational drugs was prohibited for 24 h prior to scanning, except for caffeine or nicotine, which were restricted



**Fig. 1.** a) Perfusion-weighted maps from a single subject scanned with product sequences from GE (PCASL with a 3D spiral FSE readout), Philips (PCASL with a 2D EPI readout) and Siemens (PASL with a 3D GRASE readout). Sequence parameters included PLD = 1525 ms, 4 time points, true axial (GE), PLD = 1525 ms (Philips) and TI = 2300 ms, TI1 = 80 ms, 4 time points (Siemens). Because of differences in voxel size, these maps were linearly registered, re-sliced and skull-stripped. b) Raw perfusion-weighted maps from a single representative subject scanned with the sequence used in the current study (parameters shown in Tables 1 and 2). All perfusion weighted maps were scaled to have a mean gray matter cerebral blood flow of 60 mL/100 g/min.

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