EIBALL - QIBA ASL Perfusion Biomarker Committee: 2018 Overview

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SUMMARY AND GOALS OF THE ASL-MRI BIOMARKER COMMITTEE

The Arterial Spin Labeling (ASL) Perfusion MRI Biomarker Committee (ASL-MRI BC) is a joined committee from the European Imaging Biomarker Alliance (EIBALL) Committee from the European Society of Radiology (ESR), together with the Quantitative Imaging Biomarker Alliance (QIBA) from the Radiological Society of North America (RSNA), supported by the European Institute for Biomedical Imaging Research (EIBIR). The ASL-MRI BC has been recently formed out of the RSNA QIBA Perfusion, Diffusion, and Flow MRI Biomarker Committee (PDF-MRI BC), which became too large to continue as an umbrella MRI QIBA committee. It is composed of scientists representing imaging device manufacturers, image analysis laboratories, biopharmaceutical industry, academia, government research organizations, imaging core labs, and professional societies. The goal of the ASL-MRI BC is to define technical performance standards (QIBA Profiles) for data acquisition, data processing, and quality control procedures that enable consistent and reliable quantitative imaging biomarkers for assessment of the physiologic measures related to the use of ASL perfusion, primarily in the brain.

The efforts of the ASL-MRI BC are a continuation of the work done previously by the "ASL in Dementia" Action supported by the European Commission through the European Cooperation in Science and Technology (COST) mechanism and by the Perfusion Study Group from the International Society for Magnetic Resonance in Medicine (ISMRM), which both came together to publish a recommendation paper on the use of ASL in clinical practice[1]. These efforts are motivated by the emergence of ASL perfusion as a quantitative imaging biomarker of early diagnosis, staging and response to therapy in several brain diseases, including but not limited to e.g. stroke, dementia, brain tumors or epilepsy. as a means of diagnosing pathologies, staging disease, and evaluating responsiveness to therapy. Following the publication of the "ASL White Paper" in 2015, we are now pleased to report that the three main MRI vendors have all implemented the recommended pseudo-continuous ASL perfusion technique, followed by a segmented 3D-readout as a standard on their most recent software level. Thus, there appears to be a promising future for the use of ASL for both clinical research and in routine clinical practice, particularly in the era of precision medicine. However, in order to fulfill this promise, it is essential that common quantitative endpoints are used and that results are reproducible and unbiased across imaging platforms, clinical sites, and time.

Summary of ASL-MRI Biomarker Committee Goals

To develop consensus technical performance standards (QIBA Profiles), based on existing literature and and other funded projects, regarding the appropriate data acquisition, data processing, and quality control procedures necessary to provide reproducible quantitative ASL Perfusion MR imaging biomarker measures of normal and diseased tissues.

Organizational Updates, Profile and Conformance Progress

- The ASL Task Force was dissolved, and a ASL-MRI Biomarker Committee was created, after the dissolution of the PDF-MRI Biomarker Committee. It is supported by the European Institute for Biomedical Imaging Research (EIBIR)
- A version 1.0 of the ASL Profile was established. The main decisions taken are:
  1. Only focus on the **brain** and on a single Quantitative Imaging Biomarker (QIB): **The Cerebral Blood Flow (CBF)**.
  2. Separate primary vascular disease from primary metabolic-related disease in the brain.
  3. Start with simple performance claims (i.e. ASL can measure Cerebral Blood Flow).
  4. The early publication of the White Paper1 in 2015 allowed the ASL-MRI BC to simply use the main recommendations from this paper as input for most of the Profile Activities. In particular, a subset of indication is given below.
- A weekend workshop is programmed on March, 9-10, 2019 at University of Michigan and led by L. Hernandez-Garcia for the community of users and developers of ASL MRI techniques to network, share new findings, discuss developments & experience, with the intent of mapping out further technical recommendations for clinical translation.

Table 1
Recommended Labeling Parameters

Parameter	Value
PCASL labeling duration	1800 ms
PCASL PLD: neonates	2000 ms
PCASL PLD: children	1500 ms
PCASL PLD: healthy subjects <70 y	1800 ms
PCASL PLD: healthy subjects >70 y	2000 ms
PCASL PLD: adult clinical patients	2000 ms
PCASL: average labeling gradient	1 mT/m
PCASL: slice-selective labeling gradient	10 mT/m
PCASL: average B_1	1.5 μT
PASL TI_1	800 ms
PASL TI	Use PCASL PLD (from above)
PASL labeling slab thickness	15–20 cm

Table 2
Recommended Imaging Parameters

Parameter	Value
Spatial resolution	3–4 mm in-plane, 4–8 mm through-plane
3D RARE stack of spiral or 3D GRASE	4–15 ms readouts, turbo-factor of 8–12, echo train of up to 300 ms
2D EPI or spiral	Single shot, minimum echo time
Scan time	4 min for acute cases, 2 min with lower spatial resolution
Field strength	Use 3T when available; for 1.5T, use lower spatial resolution
Vascular crushing gradients	Not recommended under most circumstances; when applicable, use VENC = 4 cm/s in the Z-direction

Table 3
Values To Be Used in Quantification of ASL Data

Parameter	Value
λ (blood–brain partition coefficient)	0.9 mL/g (74)
$T_{1,blood}$ at 3.0T	1650 ms (10)
$T_{1,blood}$ at 1.5T	1350 ms (75)
α (labeling efficiency) for PCASL	0.85 (17)
α (labeling efficiency) for PASL	0.98 (19)

Ongoing Projects: Round Robin ASL Perfusion Phantom

A multi-site round-robin assessment study was conducted to assess the effective reproducibility of CBF estimates by ASL using a recently developed Perfusion phantom[2] (Figure 2.) at 11 different sites with a range of scanner manufacturers (total 17 systems). We present here the preliminary data from a subset of 5 Philips 3T MRI scanners, all running software release R5.3, detailed in Figure 1.a.
ASL measurements were made using the product Philips 2D EPI pCASL sequence (detailed in 1.b). Measurements were made at two flow rates; 200ml/min and 350ml/min, and computer software monitored and recorded the phantom flow rates during scanning. M0 images were registered to a structural atlas image (generated from CAD) from which an ROI mask of the entire porous material was generated, CBF maps were computed using the single subtraction equation for pCASL[1], and the mean/standard deviation CBF were calculated within this ROI.
Qualitatively, CBF maps from all systems are very similar. Quantitatively, the coefficient of variance of the mean CBF was 9.2% at 200ml/min and 11.7% at 350ml/min. At the higher flow rate the difference between systems is accentuated, as shown in Figure 4. System 2 has a noticeably higher mean CBF than other systems, potentially due to increased labelling efficiency.
In general, measurements across all systems are in good agreement with each other; however, further analysis and measurements are required to determine statistically significant differences between systems.

a.

MRI SYSTEM NO.	MRI VENDOR	MODEL	SOFTWARE VERSION	RECEIVE COIL
1	Philips	Ingenia	R5.3.1	32ch
2	Philips	Achieva	R5.3.1	8ch
3	Philips	Ingenia	R5.3.1	32ch
4	Philips	Ingenia	R5.3.0	32ch
5	Philips	Achieva dStream	R5.3.1	32ch

b.

IMAGING PARAMETER	VALUE
LABEL DURATION	1800ms
POST LABELLING DELAY	1800ms
LABEL PLANE LOCATION	60mm from centre of FOV, parallel alignment.
NO. DYNAMICS	3
NO. SHOTS	4
SENSE FACTOR	2.3
FOV	256x192x59mm
PE DIRECTION	AP
ACQUISITION MATRIX (PER SLICE)	128x96
NO SLICES	12
SLICE THICKNESS/GAP	4mm/1mm
TR	5000ms
TE	Min TE selected, given per MRI system 1-5: 11.271, 10.166, 11.283, 11.269, 10.16 ms
BACKGROUND SUPPRESSION	4 pulse product default

Figure 1. MRI scanner details (a) and protocol parameters (b).

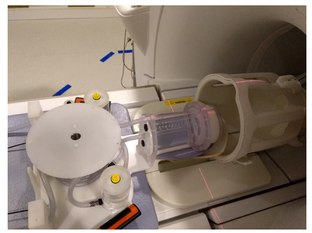


Figure 2. Care was taken to ensure standardized positioning and alignment of the phantom in each MRI scanner.

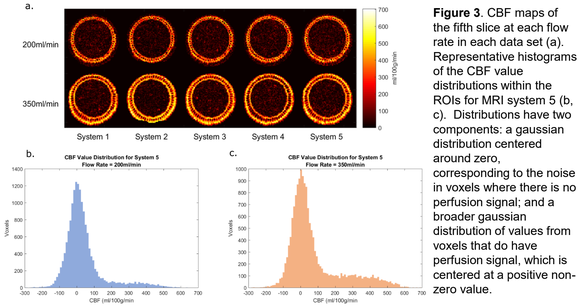


Figure 3. CBF maps of the fifth slice at each flow rate in each data set (a). Representative histograms of the CBF value distributions within the ROIs for MRI system 5 (b, c). Distributions have two components: a gaussian distribution centered around zero, corresponding to the noise in voxels where there is no perfusion signal; and a broader gaussian distribution of values from voxels that do have perfusion signal, which is centered at a positive non-zero value.

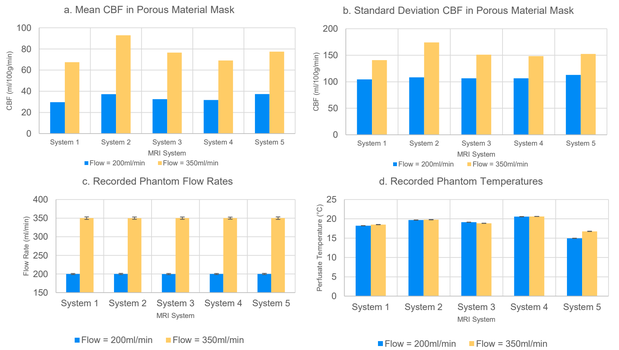
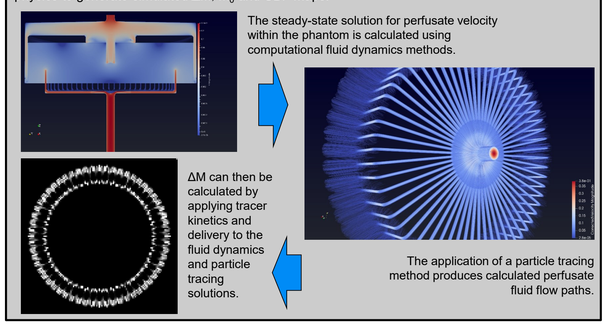


Figure 4. Mean CBF (a) and standard deviation of the CBF values (b) within the porous material masks. Trends in variation between the MRI systems visually correspond at flow rates, with variation at the higher flow rate more pronounced. In all cases, the mean CBF at 350ml/min is more than double that measured at the 200ml/min, despite the flow rate ratio being 1.75. This is because 200ml/min not all of the labelled bolus has yet entered the porous material. c) Recorded Flow rates delivered by the pump. d) Recorded temperatures of the fluid during scanning. Note the lack of correlation between fluid temperature and mean perfusion values.

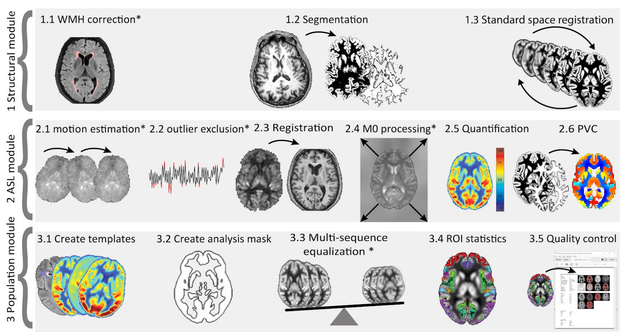
While the round robin assessment has shown there is a small difference between the Philips 3T systems, it does not give an indication of the precision, bias and linearity of an ASL measurement. To do so requires comparison against a ground truth. We have been developing a simulated ASL simulation of the phantom, combining computational fluid dynamics, tracer kinetics, and MR physics to generate simulated ΔM, M_0 and CBF maps.



Ongoing Project: ExploreASL

To provide a potential standardised platform for data analysis of ASL scans, the ASL-MRI BC is collaborating with a group of scientist led by H. Mutsaerts for the development of **ExploreASL**.

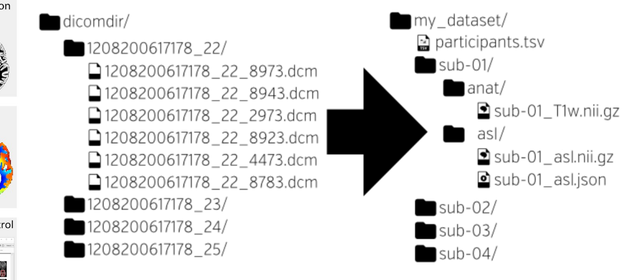
ExploreASL is de facto an emerging standard for ASL image processing and quality control. This multi-OS, open source software package was designed as a comprehensive pipeline for reproducible multicenter ASL image processing[3]. Initiated by the European COST action "ASL in Dementia"[1], ExploreASL focuses on improving compatibility between data from different MRI vendors and ASL sequences[4]. To date, ExploreASL has been developed over more than 30 clinical studies including more than 8000 ASL scans from three MRI vendors - i.e. GE, Philips, Siemens - with different ASL sequences, 2D and 3D readouts, and a variety of populations.



Ongoing Project: ASL-BIDS

In addition, members of the ASL-MRI BC have also worked on the standardization of the image inputs necessary for the treatment and organisation of ASL data. This work has also been coordinated by H. Mutsaerts within the the **Brain Imaging Data Structure (BIDS)**.

ASL-BIDS is an extension on the the Brain Imaging Data Structure (BIDS): an emerging standard for the organisation of neuroimaging data (https://bids.neuroimaging.io). The plethora of existing ASL sequences, as well as the significant differences between product sequences as implemented by different vendors and/or clinical centres, make ASL a challenging data type for standardization[4]. ASL-BIDS provides a simple, hierarchical folder structure, with key study parameters documented in text-based metadata files, allowing to aggregate heterogeneous multi-centre datasets with a common structure for present and future clinical ASL studies and open-data repositories.



PUBLICATIONS AND PRESENTATIONS

1. Alsop DC, Detre JA, Golay X, Guenther M, et al. Recommended Implementation of Arterial Spin-Labeled Perfusion MRI for Clinical Applications: A Consensus of the ISMRM Perfusion Study Group and the European Consortium for ASL in Dementia. Magnetic Resonance in Medicine 2015; 73: 102-116.
2. Oliver-Taylor A et al. A Calibrated Perfusion Phantom for Quality Assurance of Quantitative Arterial Spin Labelling. Proceedings of the 24th meeting of the ISMRM, 2017, Abstract #0681.
3. Mutsaerts, H. et al. Comparison of arterial spin labeling registration strategies in the multi-center GENetic frontotemporal dementia initiative (GENFI). J. Magn. Reson. Imaging 47, 131–140 (2018).
4. Mutsaerts, H. J. M. M. et al. Multi-vendor reliability of arterial spin labeling perfusion MRI using a near-identical sequence: Implications for multi-center studies. Neuroimage 113, (2015).

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