

ASL Perfusion Imaging: Clinical Experience in Patients with Cerebrovascular Steno-Occlusive Disease

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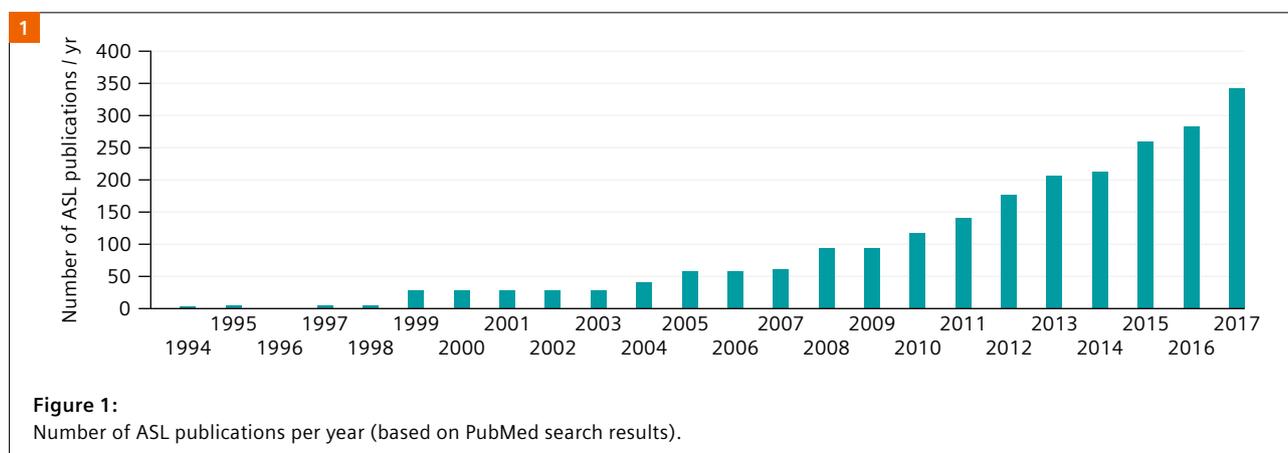
Introduction

Arterial spin labeling (ASL) is an MR perfusion technique which uses magnetically labeled arterial blood as tracer for measuring local tissue perfusion [1–4]. Quantitative brain imaging – i.e., absolute measurements of regional cerebral blood flow (CBF) – is achievable with simple, conventional kinetic modeling of labeled blood [5]. The greatest benefit of ASL is that it is completely noninvasive, with no need for radioactive tracers as in other modalities or exogenous contrast agents. However, despite numerous research efforts since the initial reports on continuous ASL (CASL) were published in 1992 [6, 7], it is only quite recently that ASL has been adequately applied in clinical settings. The primary problem was that ASL images had an intrinsically low signal-to-noise ratio due to the rapid T1 decay of labeled blood. This situation changed radically in the 2010s, with the introduction of pseudo-continuous ASL (PCASL) [8, 9] combined with rapid 3D readout sequences on commercially available MR scanners. These technical innovations greatly improve the image quality, and therefore encourage routine clinical use of ASL. Increased use of ASL imaging is evidenced by the recent rapid rise in the number of research publications on the topic (Fig. 1). To address the diversity of ASL methodologies and implementations, various research communities,

the Perfusion Study Group of the International Society for Magnetic Resonance in Medicine (ISMRM), and the European consortium ASL in Dementia (AID) held workshops in 2012 to formulate a consensus statement on current recommendations for ASL imaging. This was then published as a consensus paper, or white paper, in 2015 [2]. The statement strongly recommends PCASL acquisition combined with a segmented 3D readout sequence and a background suppression (BS) technique. The recommended ASL implementations are currently available as a prototype¹ on Siemens Healthineers MR scanners.

Quantitative imaging for cerebral circulation plays a critical role in the understanding of brain pathophysiology and in making decisions about treatment courses for patients with cerebrovascular steno-occlusive disease [10–12]. Imaging modalities used in modern clinical practice – i.e., molecular imaging methods including positron emission tomography (PET) and single photon emission tomography, and bolus-tracking techniques with computed tomography or MR imaging – have various advantages and disadvantages [13]. Although ASL is entirely noninvasive and has the potential to replace the other methods, its technical limitations and pitfalls are not yet fully understood. In addition, the clinical

¹WIP, the product is currently under development and is not for sale in the US and in other countries. Its future availability cannot be ensured.



value of ASL imaging has yet to be widely accepted. Under these circumstances, we believe that a comparative study with the other imaging modalities will be of great value for gaining a deeper understanding of ASL. Among the imaging modalities, PET with ¹⁵O-labeled compounds (¹⁵O PET) is regarded as the gold standard for assessing cerebral circulation and oxygen metabolism [12, 14]. It can quantitatively measure CBF, cerebral blood volume (CBV), oxygen extraction fraction (OEF), and cerebral metabolic rate of oxygen (CMRO₂) in a single examination session and thereby enable a comprehensive assessment of the patient's cerebral perfusion status. In this report, we use direct comparisons with ¹⁵O PET in patients with cerebrovascular steno-occlusive disease to present the clinical benefits and some key pitfalls of brain ASL imaging.

Arterial spin labeling methods

Two types of labeling have been used in ASL imaging: CASL and pulsed ASL (PASL) [15]. With the Siemens prototype package¹, both of these techniques – i.e., PCASL and FAIR Q2TIPS – are available combined with a segmented 3D GRASE readout and BS module [16, 17]. Bolus duration (TI₁) and inversion time (TI) are major sequence parameters. In PCASL, TI₁ and the difference between TI and TI₁ are usually referred to as, respectively, labeling duration (LD) and post-labeling delay (PLD) (Fig. 2).

Pseudo-continuous Arterial Spin Labeling (PCASL)

CBF maps for PCASL with single PLD are calculated with the standard equation

$$f = \frac{\lambda \Delta M R_{1a}}{2\alpha M_0 (\exp(-wR_{1a}) - \exp(-(\tau+w)R_{1a}))}$$

where *f* is regional CBF in mL/100g/min, λ is blood/tissue water partition coefficient (0.9 mL/g), α is inversion efficiency (85% for PCASL), M₀ and ΔM are respectively fully relaxed image intensity and signal difference (control/label), τ is LD (or TI₁), w is PLD (or TI–TI₁), and R_{1a} is longitudinal relaxation rate of blood (0.606 s⁻¹ at 3T).

Pulsed Arterial Spin Labeling (PASL)

In PASL, multiple inversion time (multi-TI) acquisition is available. CBF and arterial transit time (ATT) maps are calculated by analyzing the time series of ASL images using a simple kinetic model [5]. ATT can be a useful measure for evaluating hemodynamic ischemia, as we will show below.

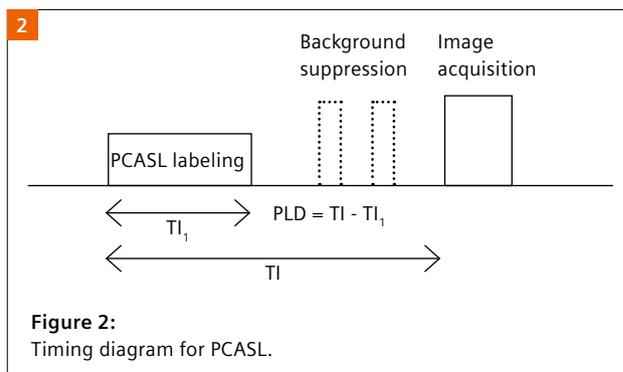


Figure 2: Timing diagram for PCASL.

Scanner	MAGNETOM Verio	
ASL module	PCASL	PASL
LD (PCASL) / TI ₁ (PASL)	1800 ms	700 ms
PLD (PCASL) / TI (PASL)	2000 ms	470–3770 ms (16 time-points)
Readout module	3D GRASE	
TR / TE	4600 / 18 ms	4600 / 21.8 ms
Number of repetitions	6	1
GRAPPA acceleration factor	2	
EPI factor	21	31
Turbo factor	12	
Field-of-view	256 x 256 x 144 mm	
Voxel size	4.0 x 4.0 x 6.0 mm ³	
Acquisition time	4 min 6 sec	5 min 11 sec

Table 1: Imaging parameters.

Our imaging protocol includes two sequential ASL acquisitions [18]: A single-PLD PCASL with a high number of averages for sufficiently high-quality CBF maps, and a multi-TI PASL for obtaining ATT maps. The 3T scanner, a MAGNETOM Verio with a 32-channel head coil, used the imaging parameters presented in Table 1, at the recommended setting [2].

Case reports: Comparisons with ¹⁵O PET

In our institute, patients with occlusion or severe stenosis of major cerebral arteries – the internal carotid artery (ICA) and the middle cerebral artery (MCA) – are routinely examined by ¹⁵O PET, mainly to assess indications for revascularization surgery. We present five representative cases that highlight the utility and pitfalls of clinical ASL imaging.

Case 1: Chronic infarction due to occlusion of the right MCA

PCASL images show a marked hypoperfused lesion in the right parietal lobe. Corresponding T2-weighted images show a marked hyperintense lesion in the ischemic core. CBF and CMRO₂ (both measured by

¹⁵O PET) are severely reduced in the right parietal lobe. The lesion with markedly decreased signal in the PCASL images is almost identical to the perfusion defect in the PET CBF and CMRO₂ maps.

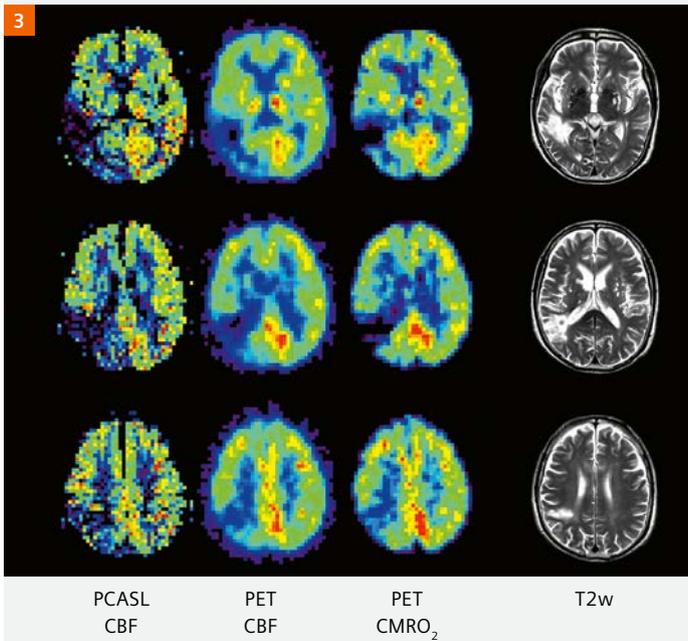


Figure 3:
A patient with right MCA occlusion; left to right: PCASL CBF, PET CBF, PET CMRO₂, T2-weighted images.

Case 2: Severe stenosis of the right ICA

PCASL images show hypoperfusion in the right cerebral hemisphere. Subtle but definitely increased vascular signal is visible in the hypoperfused lesion. ATT is slightly prolonged in the right cerebral hemisphere. MRA shows severe stenosis of the terminal segment of the right ICA (arrow). PET CBV is increased

in the right cerebral hemisphere. CBF is reduced more than CMRO₂, and OEF is mildly increased. These ¹⁵O PET findings indicate misery perfusion. PCASL imaging can clearly visualize a hypoperfused lesion with vascular signal in cases with severe stenosis of a major artery.

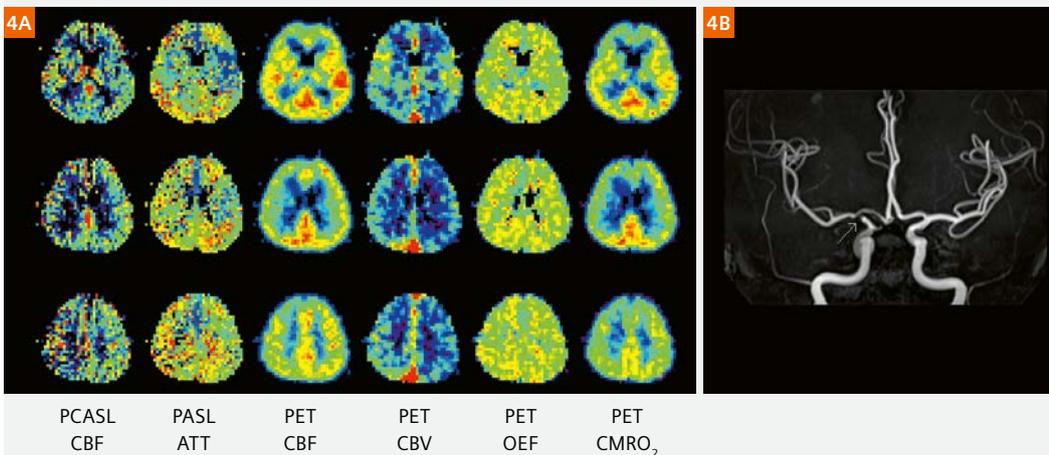


Figure 4:
A patient with right ICA stenosis; left to right: PCASL CBF, PASL ATT, PET CBF, PET CBV, PET OEF, PET CMRO₂, MRA.

Case 3: Moyamoya disease

PCASL imaging shows relative hypoperfusion with small foci of high signal in the right cerebral hemisphere. ATT is relatively prolonged in the right cerebral hemisphere. MRA shows multiple large-vessel occlusions in both anterior and posterior circulation with abnormally prominent collateral formation. Cortical branches of the right MCA are poorly visualized on MRA images, indicating hypoperfusion in the right MCA territory. The collateral pathway via leptomeningeal anastomosis is thought to be poorly developed because distal branches of the bilateral posterior

cerebral arteries (PCAs) are insufficiently visualized with MRA. ¹⁵O PET images show higher CBV and OEF, and lower CBF in the right cerebral hemisphere. Increased OEF with minimally decreased CMRO₂ may lead to a diagnosis of misery perfusion. Arterial transit artifact (ATA) in PCASL images, which is characterized by increased high vascular signal, occurs with misery perfusion because decreased perfusion pressure results in labeled blood stagnating in the vasculature before it enters tissue capillaries [18–20], which is consistent with prolonged ATT.

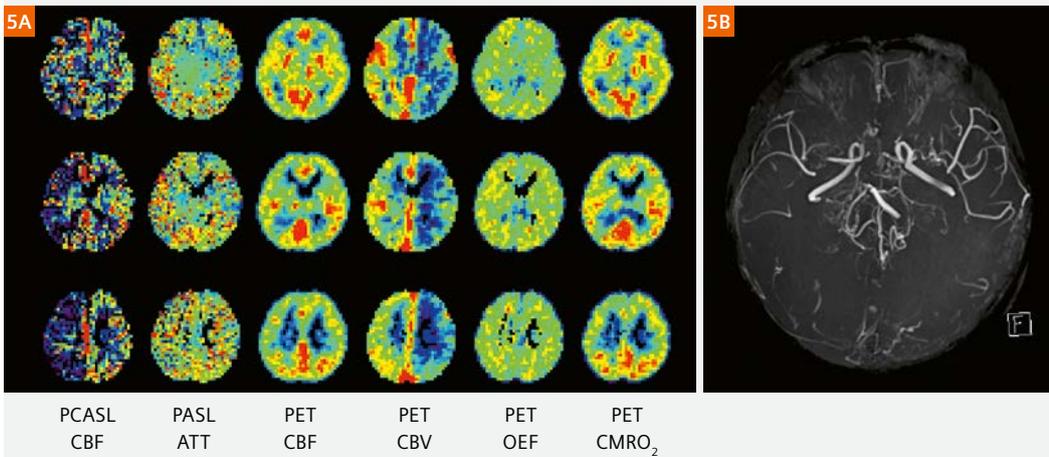


Figure 5: A patient with moyamoya disease; left to right: PCASL CBF, PASL ATT, PET CBF, PET CBV, PET OEF, PET CMRO₂, MRA.

Case 4: Occlusion of the right ICA

PCASL images show increased signal mimicking hyperperfusion in the right cerebral hemisphere. ATT is markedly prolonged in the right cerebral hemisphere. Areas with delayed ATT correspond to high signal foci with PCASL. MRA shows occlusion of the right ICA with prominent PCA reflecting good collateral circulation through leptomeningeal anastomosis.

¹⁵O PET images show higher CBV and OEF, and lower CBF with a minimal decrease in CMRO₂ in the right cerebral hemisphere, suggesting misery perfusion in the right cerebral hemisphere. ATA frequently appears in focal misery perfusion on PCASL images. Increased signal due to ATA should not be misdiagnosed as hyperperfusion.

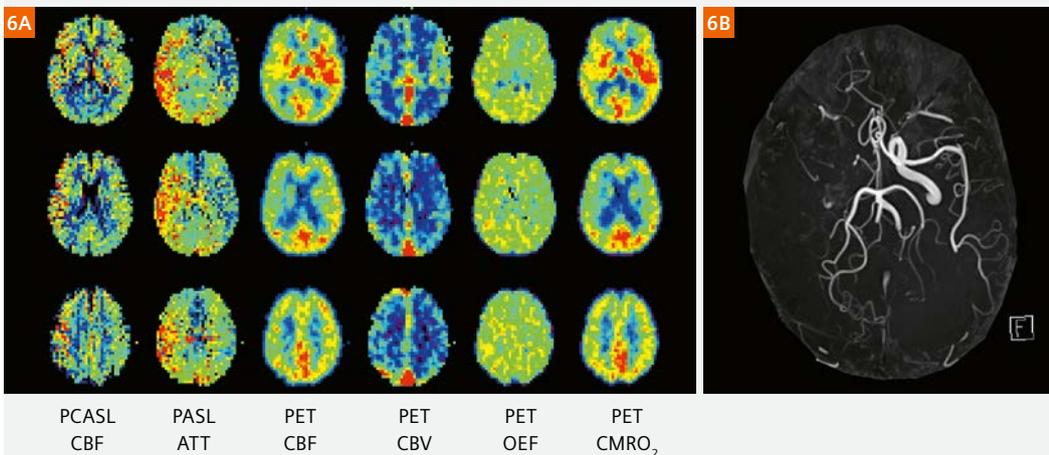


Figure 6: A patient with right ICA occlusion; left to right: PCASL CBF, PASL ATT, PET CBF, PET CBV, PET OEF, PET CMRO₂, MRA.

Case 5: Right ICA aplasia

MRA shows filling of the right distal ICA via the right posterior communicating artery with non-visualization of the right proximal ICA. PCASL imaging shows relatively decreased signal in the right cerebral hemisphere. ATT is not prolonged in the right cerebral hemisphere. CBF measured with ^{15}O PET is normal.

In PCASL imaging, blood-flow-velocity-dependent and/or vessel-geometry-related variations in labelling efficiency are possible sources of error [21]; labeling efficiency in the vertebral artery might be different from that in the carotid artery, and this difference might produce left-right asymmetric PCASL images.

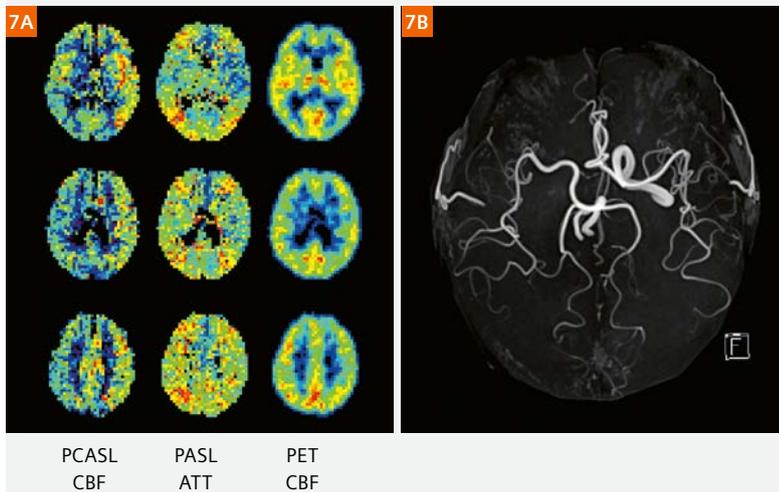


Figure 7:

A patient with right ICA aplasia; left to right: PCASL CBF, PASL ATT, PET CBF, MRA.

Summary

ASL, a completely non-invasive perfusion imaging technique, has now become a clinical tool for evaluating cerebral ischemia. In this report, we presented our clinical experiences of 3D ASL imaging in patients with cerebrovascular steno-occlusive disease, and emphasized comparisons with the gold standard ^{15}O PET. We can summarize the clinical utility and some pitfalls of current ASL imaging in the evaluation of hypoperfusion state accompanied by severe stenosis or occlusion of a major artery:

1. ASL imaging can clearly visualize lesions of territorial or superficial divisional MCA infarction as areas with severe hypoperfusion and significantly reduced CBF.
2. In a patient with severe stenosis or occlusion of major arteries, delays to the regional arrival time of labeled bloods occur frequently in hypoperfused areas. This is clearly visualized as prolonged ATT with multiple inversion time ASL acquisition. Delayed arrival results in bright vascular signals in CBF maps with single-PLD PCASL acquisition. This ATA sign should not be misdiagnosed as hyperperfusion.
3. In PCASL imaging, variations in labeling efficiency between feeding vessels are a possible source of error, but they are rarely detected without additional clinical and other imaging information. The variations in labeling efficiency may cause an asymmetrical PCASL CBF map in a case of unilateral ICA aplasia or occlusion.
4. When unexpected, uninterpretable CBF maps occur, the above methodological errors (i.e., ATA and labeling efficiency variations) should be considered. MRA findings can provide important information about the pathway of the labeled bloods and thereby help us to better interpret ASL images.

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