3D Pseudocontinuous Arterial Spin Labeling in Routine Clinical Practice: A Review of Clinically Significant Artifacts

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1. Identify artifacts associated with the 3D pseudocontinuous ASL sequence.
2. Identify strategies to avoid or attenuate 3D pseudocontinuous ASL artifacts.

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Arterial spin labeling (ASL) is a completely noninvasive magnetic resonance imaging (MRI) perfusion method for quantitatively measuring cerebral blood flow utilizing magnetically labeled arterial water. Advances in the technique have enabled the major MRI vendors to make the sequence available to the clinical neuroimaging community. Consequently, ASL is being increasingly incorporated into the routine neuroimaging protocol. Although a variety of ASL techniques are available, the ISMRM Perfusion Study Group and the European ASL in Dementia Consortium have released consensus guidelines recommending standardized implementation of 3D pseudocontinuous ASL with background suppression. The purpose of this review, aimed at the large number of neuroimaging clinicians who have either no or limited experience with this 3D pseudocontinuous ASL, is to discuss the common and clinically significant artifacts that may be encountered with this technique. While some of these artifacts hinder accurate interpretation of studies, either by degrading the images or mimicking pathology, there are other artifacts that are of clinical utility, because they increase the conspicuity of pathology. Cognizance of these artifacts will help the physician interpreting ASL to avoid potential diagnostic pitfalls, and increase their level of comfort with the technique.

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Arterial spin labeling (ASL) is a completely noninvasive magnetic resonance imaging (MRI) perfusion method for quantitatively measuring cerebral blood flow (CBF).[1–4] It is an alternative to the more established MR bolus technique of dynamic susceptibility contrast (DSC) perfusion.[3,4] Unlike DSC, which requires administration of an exogenous contrast agent to the patient, ASL utilizes an endogenous and freely diffusible tracer: magnetically labeled water.[2–5] Arterial blood water is labeled (or "tagged") by inversion of its longitudinal magnetization in a plane proximal to the brain.[1–4] Following a short time delay, allowing the labeled water to reach the brain parenchyma, imaging is performed.[1–4] As ASL is performed without a gadolinium-containing contrast agent, it is repeatable and can be performed in patients with renal impairment.[2–4]

ASL was first described more than 20 years ago; however, it has historically been confined to the research arena. Adoption of ASL into routine clinical practice was hindered until recently by a lack of consensus in the perfusion imaging community regarding the optimal ASL acquisition methodology and postprocessing algorithms, the complexity of postprocessing, and the inherently low signal-to-noise ratio (SNR) of the sequence.[3–5] However, advances in ASL technique, streamlining of postprocessing, and resolution of licensing issues have led to the major MRI vendors making the sequence available on clinical scanners.[1–3] Additionally, the significant increase in the number of 3T MRI scanners (which provide higher SNR) and the use of multichannel receive coils (enabling faster scanning using parallel imaging) have made ASL feasible in routine clinical practice.

ASL is being incorporated into routine neuroimaging protocols at an increasing number of sites. Therefore, clinicians interpreting these studies should familiarize themselves with the technique and its potential pitfalls. As with all MR sequences, ASL is prone to a number of artifacts that may affect diagnostic accuracy. Findings may be missed or misinterpreted if the clinician is unaware of the presence of an artifact that degrades the study, and either masks pathology or suppresses diagnostic information. Conversely, artifacts may be mistaken for pathology, resulting in an incorrect diagnosis. To avert these pitfalls, physicians interpreting ASL must be cognizant of potential artifacts, and the limitations they impose on a study. While some artifacts detract from study quality, there are certain artifacts that are of diagnostic utility, as they enhance the conspicuity of pathology.

A brief but excellent survey of common ASL artifacts has previously been published by Deibler et al [3] in 2008; however, this discussion was based on a pulsed (flow-sensitive alternating inversion recovery [FAIR]) ASL sequence, with a 2D echo-planar imaging (EPI) readout. The recent consensus guidelines of the ASL community recommend the use of pseudocontinuous ASL (pcASL) with segmented 3D fast spin-echo (FSE) readout.[6] Although some of the artifacts discussed by Deibler et al are common to all ASL implementations, there are some important differences in the type, severity, and manifestation of artifacts seen with 3D pcASL (Table 1).

The following review will therefore provide a discussion of artifacts encountered on pcASL with a 3D FSE readout; this is of high clinical relevance since it is the recommended ASL technique for clinical purposes, and is therefore likely to become increasingly common on most contemporary clinical MRI scanners.

Artifacts can be categorized according to whether they may be attributed to the magnetic labeling period, the time between labeling and imaging, or the image acquisition period. We offer some strategies to avoid and potentially remedy the artifacts that are detrimental to image quality. Artifacts that alert the reader to the presence of certain pathological conditions and therefore have the potential to increase diagnostic sensitivity are subsequently discussed.

Materials and Methods

In ASL, a selective radiofrequency (RF) inversion pulse is applied over a selected region (the labeling plane) proximal to the brain (the imaging plane).[1–4] This pulse magnetically labels water protons within the arterial blood, in the labeling plane, by inverting their longitudinal magnetization.[3] The labeled water flows distally into the brain capillary bed, where it exchanges and mixes with tissue water almost completely.[4] The negative magnetization of these inflowing, magnetically inverted water protons mixes with the positive magnetization of static tissue water protons, resulting in a

TABLE 1. Artifacts Seen in pcASL With a 3D FSE Readout

Artifact		Cause	Manifestation on ASL CBF map
Arising During Labeling			
Ineffective labeling		Tortuosity of vessel in labeling plane[a]	Signal dropout in the affected vascular territory
		Susceptibility variations near labeling plane (eg, metallic material)[a]	
CSF labeling		Pulsatile flow of CSF; CSF tagged in the labeling plane moves into the imaging plane	"Ring of fire": high signal in perimedullary CSF
Arising During Transit			
Loss of spin label		Administration of gadolinium-based contrast agent prior to ASL; tagged arterial spins quickly decay back to equilibrium state, due to decreased T_1 relaxation time, before reaching imaging volume	Complete absence of ASL signal
Intra-arterial ASL signal	*a. Arterial transit artifact (ATA)*	Delayed arterial transit (diminished cardiac output or arterial stenosis). Transit time of arterial blood from labeling plane to imaging plane > PLD; labeled spins still in the intra-arterial compartment at time of imaging.	Intra-arterial ASL signal: linear and serpiginous high ASL signal in basal cisterns and cortical sulci. Low parenchymal CBF- labeled blood has not yet reached parenchymal capillary bed and undergone tissue exchange
	b. Borderzone sign	Characteristic pattern of ATA and low ASL signal in the arterial borderzones resulting from diminished blood flow due to low cardiac output	ATA- high signal in intracranial arteries. Paucity of signal in brain parenchyma in arterial watershed regions especially posteriorly (parieto-occipital)
	c. Trapped ASL signal	Labeled spins still within the aneurysm sac at time of imaging due to turbulent flow	High signal in the aneurysm sac.
Venous ASL signal		Direct and/or rapid transit of blood from arteries into venous structures. Usually seen with arteriovenous shunting (eg, most commonly high-flow vascular malformations), where the normal capillary bed is bypassed, therefore labeled water has not undergone tissue exchange, and there is incomplete T_1 relaxation of labeled blood water.	High ASL signal in venous structures
Arising During Readout			
Motion[b]		Severe patient head motion	High signal intensity spirals[c]
Blurring[c]		Stack-of-spirals acquisition	Smearing of high signal intensity structure along craniocaudal direction
Occipital lobe hyper-perfusion		Physiological occipital lobe activation (patient's eyes open during scan)	High ASL signal in occipital lobes bilaterally

Unless specifically indicated, these artifacts can be seen with all ASL implementations.
[a]Can occur with continuous or pseudocontinuous labeling.
[b]Less severe with 3D FSE readout, due to routine use of background suppression.
[c]Specific to the segmented 3D FSE stack-of-spirals readout.

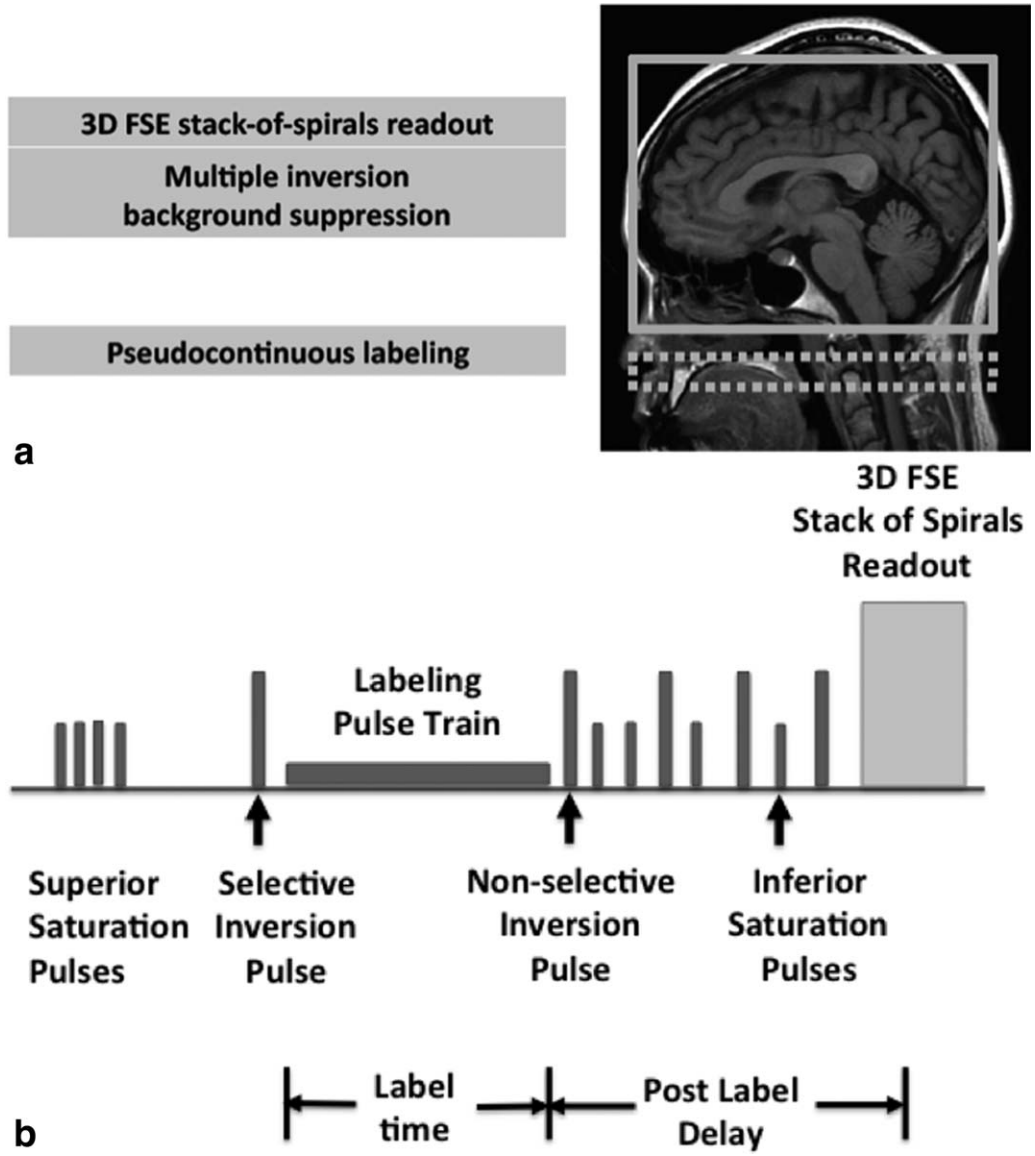

FIGURE 1: Pseudocontinuous ASL technique. a: The labeling and read-out planes. b: Pulse sequence diagram.

small signal intensity decrease of 1–2%.[4] Labeled images are obtained by imaging the brain at a short time interval after labeling; this postlabel delay (PLD), typically between 1 and 3 seconds, allows blood to flow from the labeling plane to the brain parenchyma. A control image of static tissue signal intensity is then obtained by imaging the brain without inverting the arterial blood water proximally. The label image is subtracted from the control image, removing static tissue signal, and producing a CBF-weighted difference image.[4,5]

ASL has an inherently low SNR because the turnover of labeled blood during typical mixing times (<5 sec) constitutes only 1–2% of the volume of the tissue voxel.[4] This is further exacerbated by signal decay due to T_1 relaxation of blood. To improve SNR, multiple label/control image pairs are typically acquired and averaged. Using a global scaling factor, based on the patient's own proton density images, the ASL difference images may be converted into absolute CBF maps in quantitative units (ml/100 g/min).[3]

There are three major labeling strategies in ASL, namely pulsed, pseudocontinuous, and continuous ASL (PASL, pcASL, and CASL, respectively).[1,2,7,8] In PASL, a single RF pulse is used to invert a bolus of inflowing blood proximal to the imaged slices. In CASL, arterial blood is continuously labeled, as it passes through a labeling plane proximal to the brain.[1,2,7] CASL has higher SNR than PASL, but it is beyond the performance limits of RF amplifiers in most clinical MR units, and deposits more RF energy in the patient (usually only a limiting factor at ultrahigh-field strength). pcASL represents a hybrid of these approaches, in which many short pulses simulate the continuous labeling of CASL.[8] pcASL is less hardware-intensive than CASL, yet provides higher SNR than PASL.[8]

The illustrative cases used in this review have been drawn from clinical MRI examinations at our institution, where we routinely perform ASL using a pcASL technique at both 1.5 and 3T (Fig. 1). The typical scan parameters are: repetition time (TR): 5500 msec; echo time (TE): 10.5 msec; number of slices: 24–40;

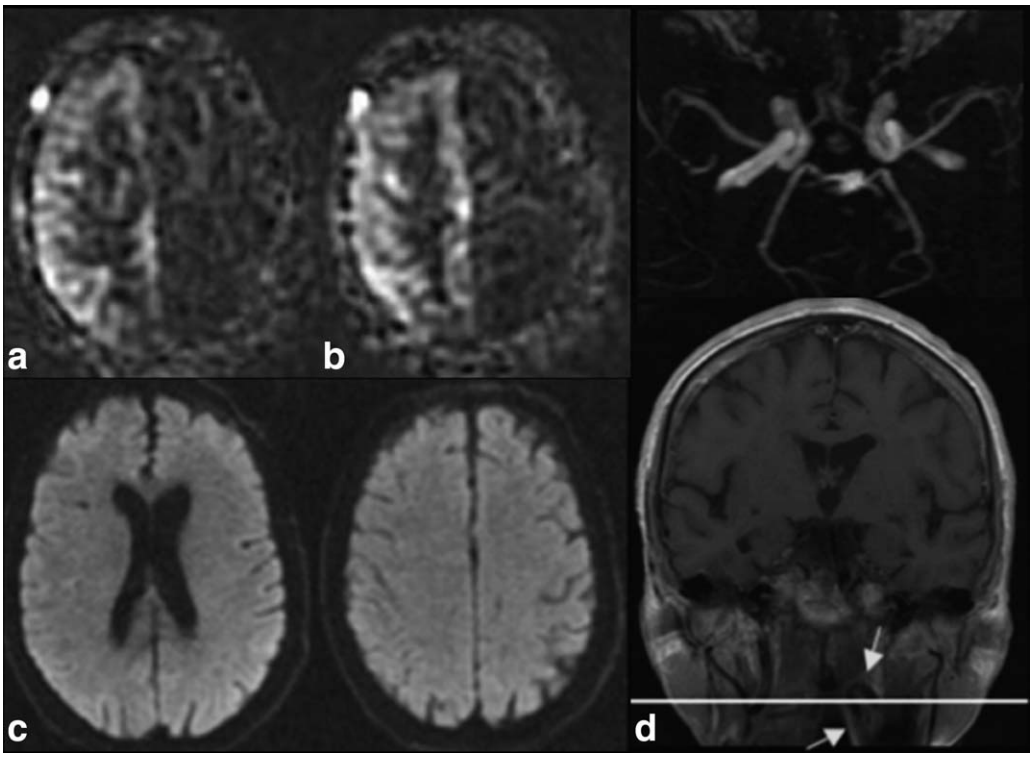

FIGURE 2: Poor labeling due to vessel tortuosity. a: ASL CBF maps demonstrate an absence of signal in the left ICA territory. b: Collapsed TOF MRA demonstrates normal flow signal in the left ICA. c: There is no evidence of acute infarction as diffusion-weighted imaging (DWI) demonstrates. The absence of corresponding abnormality on MRA and DWI suggests that the low ASL signal is an artifact. Unfortunately, a neck MRA, covering the labeling plane, was unavailable for review. d: The distal cervical ICA is, however, visualized on coronal postcontrast T_1-weighted images. Marked tortuosity of the left ICA (arrowed) as it passes through the labeling plane results in the vessel passing through the labeling plane (white line) twice; this in turn results in poor labeling efficiency due to multiple inversions. Decreased signal in the right parietal lobe on the ASL CBF maps is an example of the "ASL borderzone sign" (resulting from decreased cardiac output), discussed later in this review.

label time 1500 msec; postlabel delay time: 2000 msec; in-plane spatial resolution 3–4 mm (achieved using 8 spiral arms in the segmented readout), through-plane spatial resolution 4–6 mm; and scan time: 4–6 minutes. The 3D stack-of-spirals segmented FSE readout uses background suppression but does not use vascular suppressor gradients, concordant with the recommendations of the recent consensus white paper from the ASL community.[6] The 3D readout improves SNR, due to slab excitation and a prolonged image acquisition window, and provides a better-defined background suppression and uniform postlabel delay for all slices.[8] Suppression of static tissue signal increases the relative signal difference between label and control images, markedly improving sensitivity for detecting changes in CBF.[9]

Artifacts

Artifacts associated with 3D pcASL can be classified according to whether they arise primarily from the labeling period, during transit, or from the image acquisition (readout) period.

Artifacts Arising From the Labeling Period

INEFFECTIVE LABELING DUE TO VESSEL TORTUOSITY AND SUSCEPTIBILITY VARIATIONS. For the distribution of ASL signal within brain parenchyma to accurately reflect the pattern of CBF, labeling of protons within arterial blood proximal to the imaging plane must be efficient and uniform. There are two factors that can impede labeling efficiency and uniformity: vessel tortuosity and susceptibility variation within the labeling region. Ineffective labeling is associated with ASL signal dropout in the affected vascular territory.

Obliquity of a target artery relative to the labeling plane can decrease labeling efficiency, particularly if the component of blood flow in the craniocaudal direction is so slow that there is significant decay during the adiabatic passage. Additionally, marked tortuosity, resulting in the artery crossing the labeling plane multiple times, can result in intraluminal blood experiencing multiple inversions; this results in poor labeling efficiency, as seen in Fig. 2. Despite tortuosity of the cervical internal carotid arteries being a relatively common finding, failure of labeling due this is rare (<0.2% in our experience).

Susceptibility variations in the labeling plane can result in dephasing of arterial blood protons, upsetting the conditions required for pseudocontinuous inversion, and result in either poor or absent labeling (Fig. 3). Causes of susceptibility variations in or near the labeling plane include metallic

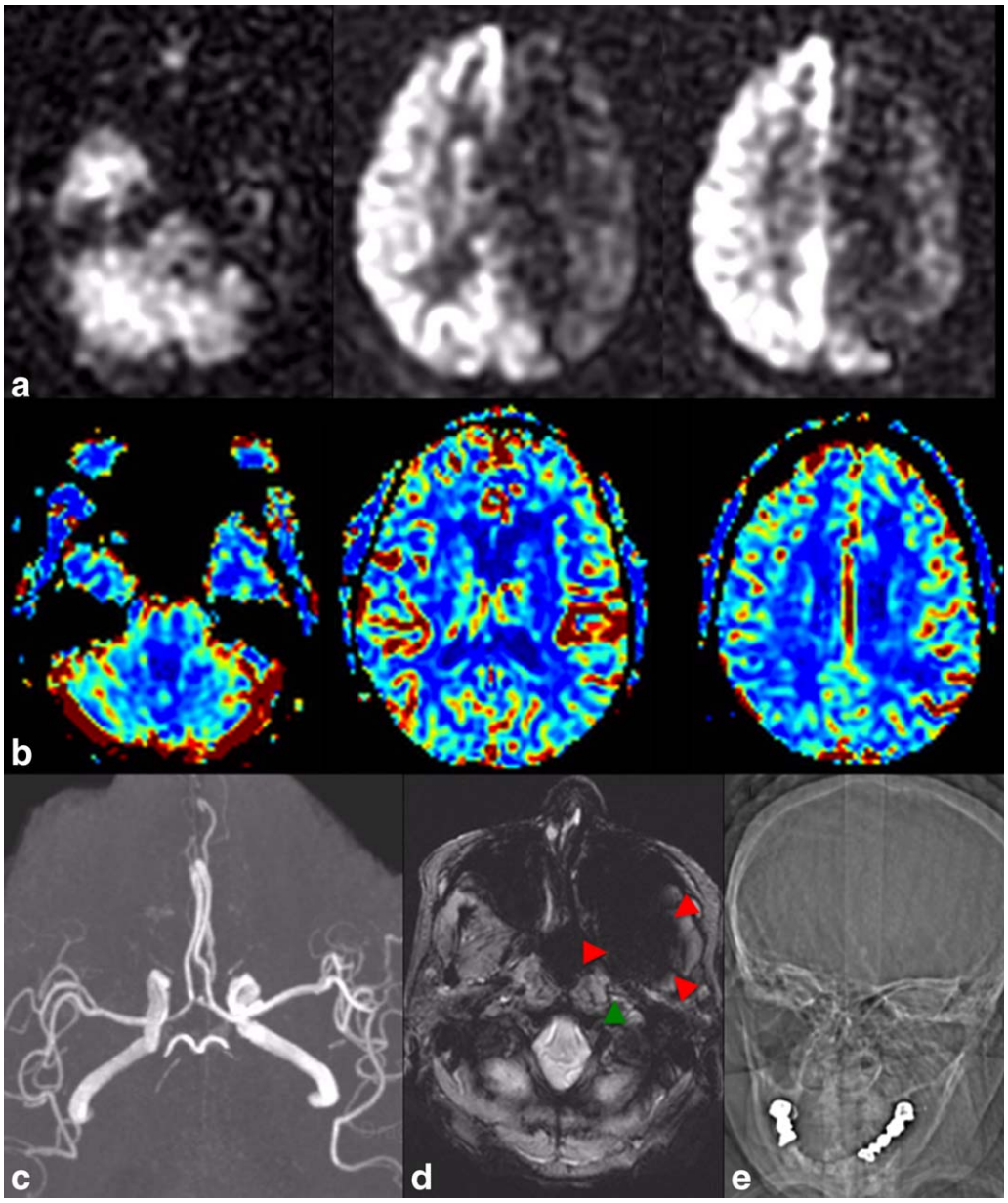

FIGURE 3: Poor labeling due to susceptibility variations in the labeling plane. a: ASL CBF maps demonstrate decreased signal in the left ICA territory. b: However, relative CBF (rCBF) maps, generated from DSC perfusion imaging performed during the same MRI examination, show interhemispheric symmetry of blood flow. c: There is also no evidence of left ICA steno-occlusive disease on the TOF MRA. The normal DSC perfusion CBF maps and MRA indicate that decreased signal on ASL is an artifact (this was also suspected clinically in this asymptomatic patient). d: Axial T_2-weighted gradient-echo image at the level of the maxillary antra: an extensive area of signal loss (red arrowheads) indicates intravoxel dephasing due to susceptibility variation. e: A prior CT scout image reveals the causative dental hardware. Only the left-sided hardware results in a large susceptibility gradient in the labeling plane, which causes dephasing of arterial blood protons within the left ICA (green arrow), hence ineffective labeling—manifested as decreased ASL signal in the left ICA territory. The effect on the local magnetic field experienced by arterial blood protons in the right ICA and vertebral arteries, which are further away from the left dental hardware, is negligible; hence, the ASL maps demonstrate normal CBF in the territories supplied by these vessels.

surgical material (eg, mandibular fixation plates, and clips related to prior carotid endarterectomy), dental hardware, calcification, and air–tissue interfaces due to skull base and facial bone pneumatization. Although these are common, inefficient labeling due to susceptibility effects is rare (<0.2% in our experience), most likely because the susceptibility gradients caused by these materials are either too small or distant to alter the magnetic flux density in the internal carotid and vertebral arteries.

Ineffective labeling is usually easily recognized, based on the characteristic territorial pattern of signal loss, and identification of the causative vessel tortuosity or susceptibility gradients on images of the labeling plane (in the neck). At our institution, it is routine clinical practice to perform

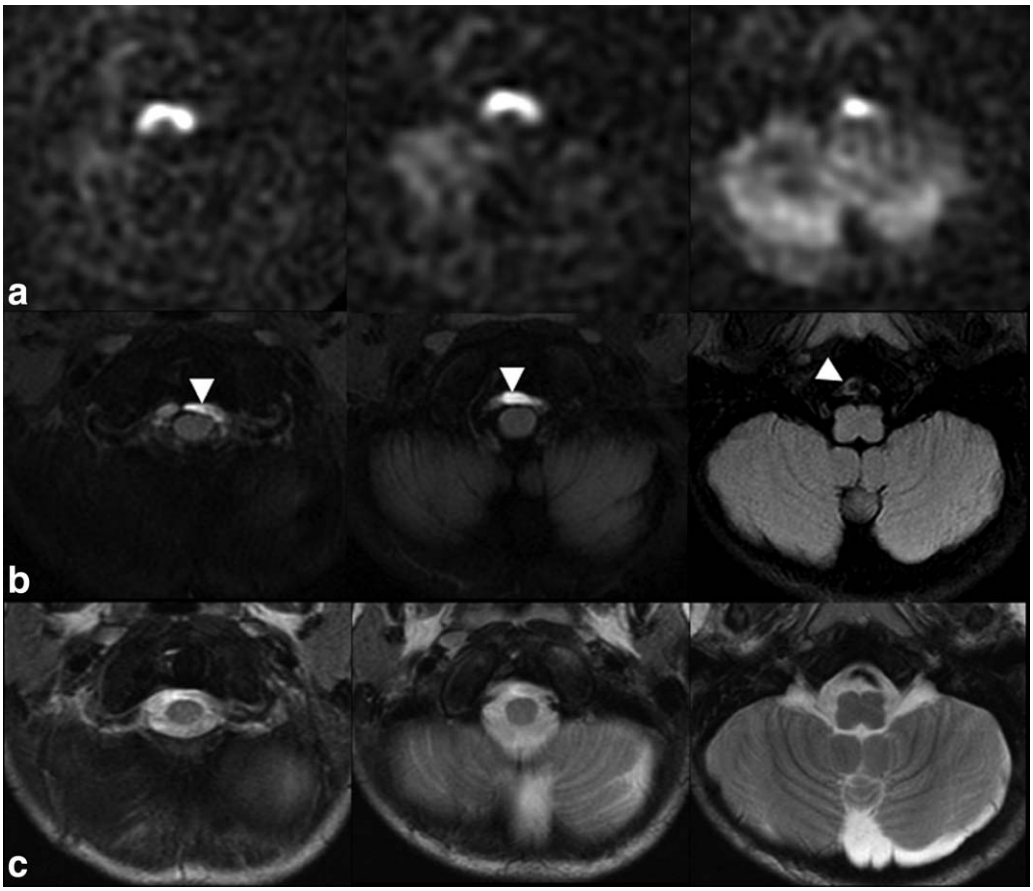

FIGURE 4: CSF labeling. a: High signal is seen anterior to the medulla and the junction of the medulla and upper cervical spinal cord on ASL maps. Fast spin-echo FLAIR (b) and T_2-weighted (c) imaging demonstrates no extra-axial lesion in this location, and confirms that the signal localizes to the CSF space. The characteristic location of high signal within the premedullary CSF cistern, in a ring-like or hemi-annular pattern, alerts the reader that this is an artifact, caused by CSF labeling and pulsation; CSF water protons that are labeled at the skull base due to their pulsatile motion subsequently appear in the inferior imaging sections. CSF pulsation is also evidenced by failure of CSF suppression on the FLAIR images (B, white arrowheads).

imaging of the neck vessels (either computed tomography [CT] or MR angiography [MRA]) in patients with suspected stroke. However, not all patients undergoing ASL will have imaging of neck vessels, as seen in Fig. 2. Therefore, especially in older patients with an increased likelihood of vessel tortuosity, a time-of-flight MRA covering the labeling plane should be considered; this will also reveal any large susceptibility gradients. If either arterial tortuosity or a large susceptibility gradient is detected, the labeling plane should be placed above this level if possible. Alternatively, if one is monitoring the case in real time and identifies the characteristic territorial loss of ASL signal, one can repeat the ASL sequence after adjusting the labeling plane (if possible).

Susceptibility gradients due to intrinsic or implanted material within the neck are unavoidable, but can often be anticipated from the patient's history and prior imaging, allowing adjustment of the labeling plane. Also, in patients known to have metallic hardware, DSC bolus perfusion imaging should be considered, either in addition to or instead of ASL. It should be kept in mind, however, that the gradient-echo EPI readout commonly used for DSC perfusion is very sensitive to off-resonance effects [8,10]; therefore, if there is susceptibility variation in the imaging plane, significant image distortions can occur on DSC, and this must be balanced against the signal loss on ASL resulting from susceptibility variations close to the labeling plane.

CEREBROSPINAL FLUID (CSF) LABELING. Artifacts can also originate from the labeling period due to inversion of water molecules outside the intraarterial compartment, if there is subsequent flow of these tagged nonarterial water molecules into the imaging plane. Water molecules within CSF can be tagged in the labeling plane, and subsequently encroach upon the imaging plane due to pulsatile flow, particularly in the setting of hyperdynamic CSF flow (Fig. 4). Typically this gives a characteristic appearance of high signal around the medulla, sometimes forming a "ring-of-fire" appearance, which is easily recognized as artifact.

A possible preventative measure is placement of the labeling plane further inferiorly, such that tagged CSF water protons have not yet reached the imaging plane at the time

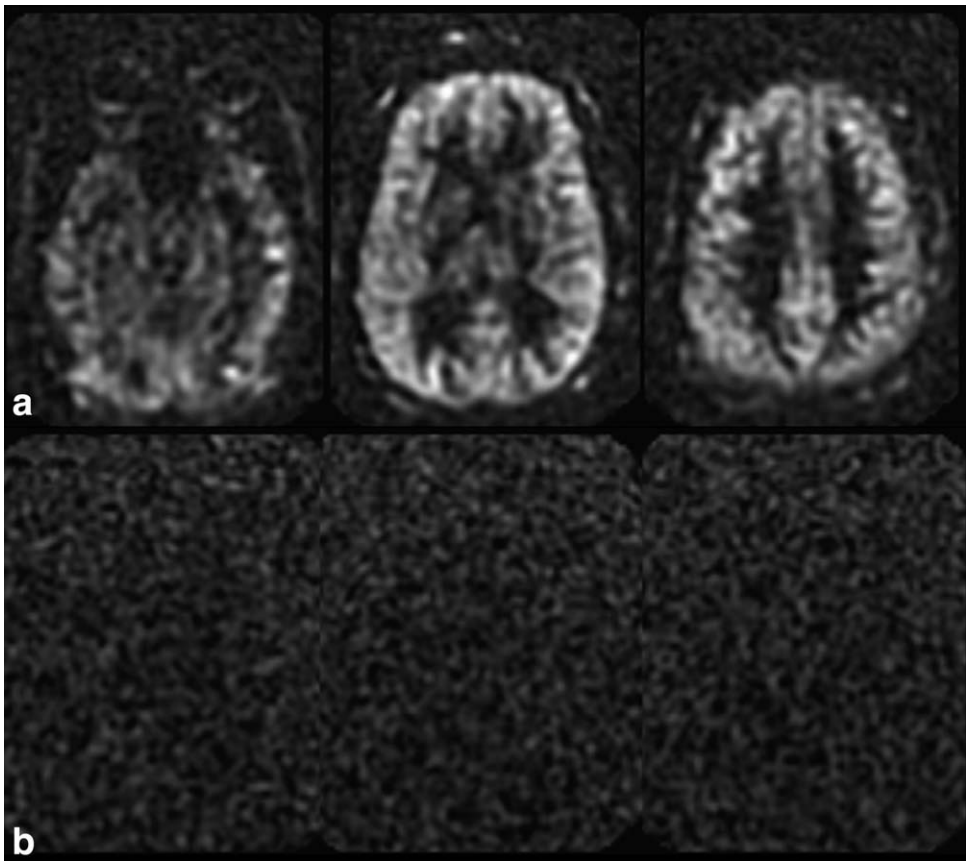

FIGURE 5: Signal loss due to gadolinium-based contrast agent administration. a: ASL images showing a normal signal pattern when the ASL sequence is performed prior to contrast administration. b: Complete absence of signal on CBF maps when ASL is performed following contrast administration. This highlights the importance of performing ASL prior to contrast administration. Gadolinium-based contrast agents cause severe shortening of the blood T_1 relaxation time; labeled spins therefore quickly decay back to their equilibrium magnetization state before reaching the imaging volume, causing absence of ASL signal.

of image acquisition. However, it is usually sufficient to merely recognize that this is an artifact, rather than a representation of pathologically increased CBF.

Inversion of venous blood does not usually pose a problem; under normal physiological conditions, venous blood flows in a craniocaudal direction in the neck, and therefore does not typically appear in the (brain) imaging volume. Venous reflux, with retrograde flow of blood labeled within the internal jugular vein into the sigmoid sinus, could, however, potentially occur in the setting of increased venous pressure due to an upper limb arteriovenous (hemodialysis) fistula, although this is likely quite rare.

Artifacts Arising During Transit

LOSS OF SPIN LABEL. During transit from the labeling plane to the imaging volume, labeled spins decay with the blood T_1, which is usually on the order of 1–2 seconds. Loss of the spin label can arise from any factor decreasing the T_1 relaxation time of blood (hence tagged arterial spins). At a given field strength, the only clinically pertinent factor that significantly decreases the T_1 of intraarterial blood is the administration of gadolinium-based contrast agents. These agents typically reduce the blood T_1 to about 100 msec. Consequently, labeled spins quickly decay back to their equilibrium state before reaching the imaging volume; the resulting CBF maps have a complete absence of signal, as seen in Fig. 5. Therefore, ASL must be performed prior to contrast administration. If one sees this pattern on ASL CBF maps, attention to the imaging protocol is recommended to determine whether contrast was administered before the ASL sequence, perhaps during a separate, recently acquired study.

ARTERIAL TRANSIT ARTIFACT. Conditions in which there is delayed arterial transit, such as heart failure with diminished cardiac output and arterial steno-occlusive disease, can also result in artifact. When the transit time of arterial blood from the labeling plane to the imaging plane approaches or exceeds the combined label time and PLD, imaging is performed too early to capture parenchymal blood flow; labeled spins are still in the intraarterial compartment, and are seen as linear and serpiginous areas of high ASL signal in the CSF cisterns and cortical sulci. This is referred to as "arterial transit artifact" (ATA). The parenchymal CBF distal to the ATA is artifactually low, as the labeled blood has not yet arrived in the parenchymal

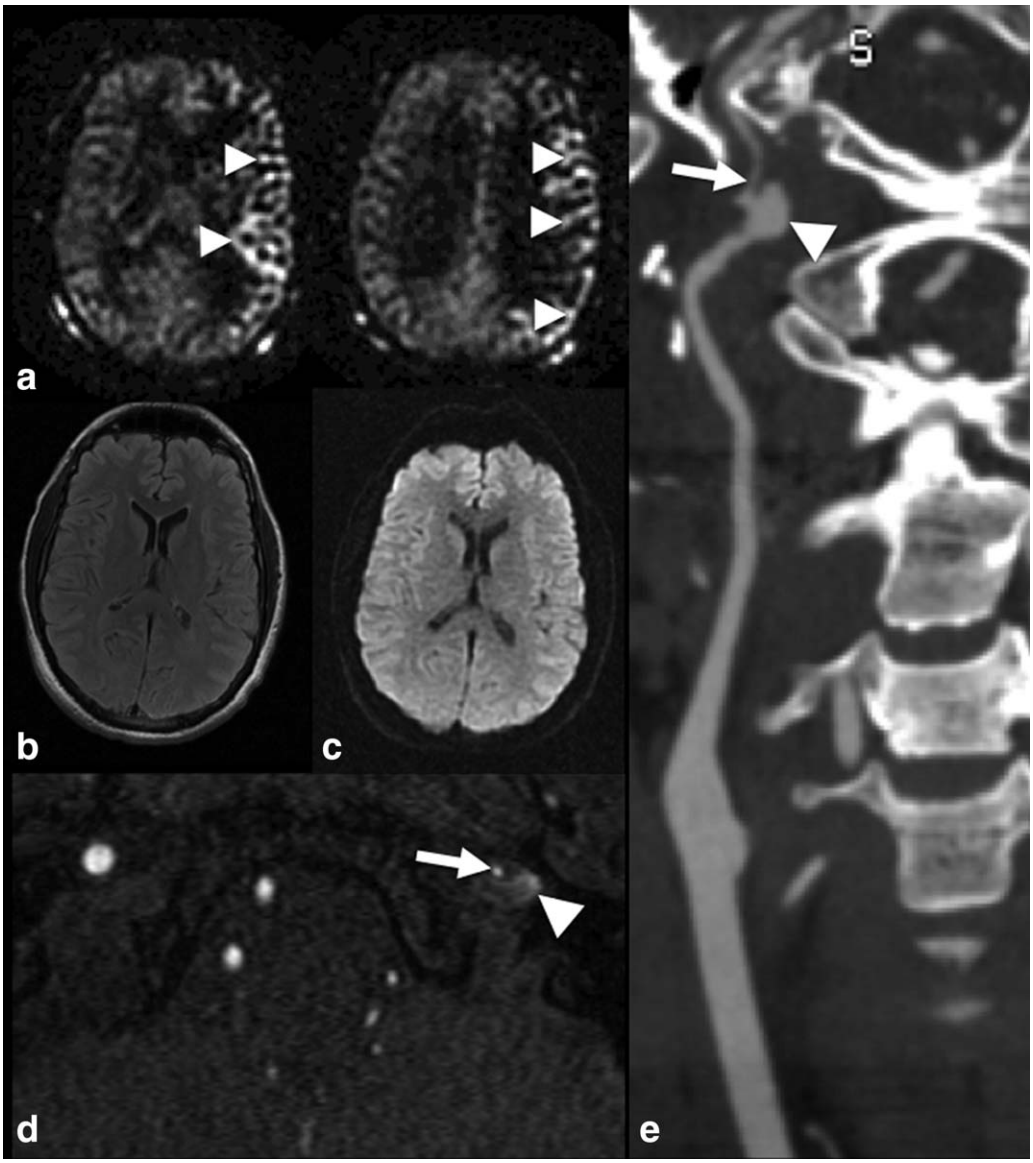

FIGURE 6: Arterial transit artifact (ATA) in a 35-year-old man with a flow-limiting left ICA dissection. a: Serpiginous high signal is seen on the ASL CBF maps, reflecting persistence of labeled spins in the left middle cerebral artery Sylvian branches (arrowheads), due to increased transit time through the dissected left ICA. The parenchymal CBF appears low; however, this is artifactual, as labeled spins have not yet reached the parenchymal capillary bed. b: FLAIR and (c) diffusion-weighted imaging show no parenchymal abnormality. d: TOF MRA source image at the level of the carotid canal demonstrates a left ICA pseudoaneurysm (arrowhead) associated with the dissection, with diminished flow within the lumen (arrow). e: Curved planar reformatted image of the left ICA from the CT angiogram confirms a flow limiting dissection, with psuedoaneurysm (arrowhead) and marked narrowing of the lumen distal to this (arrow).

capillary bed and undergone tissue exchange.[5,9] Therefore, quantification yields inaccurate parenchymal CBF measurements in conditions where there is prolonged transit time due to arterial narrowing or occlusion; this is a significant obstacle to the use of ASL for the prediction of tissue-at-risk, using CBF thresholds, in acute stroke and chronic steno-occlusive disease.[5,9,11–14] It should be noted that ATA can also be seen in patients with normal cardiac output and intracranial arteries if a short PLD (<1500 msec) is used.

In our experience, ATA is present in almost all cases of significant steno-occlusive disease (arterial occlusion or flow-limiting stenosis). In these cases, ATA is confined to the territory of the diseased vessel or vessels (Fig. 6).

Low cardiac output, where there is a significant delay between labeling of spins and their arrival in the imaging plane due to diminished flow, is frequently associated with ATA when a routine PLD is used. As blood flow is globally diminished, ATA is widespread, affecting all vascular territories (Fig. 7). There is a paucity of signal in brain parenchyma, as labeled blood has not yet reached the tissue capillary bed. This latter finding has been termed the "ASL borderzone sign," given its conspicuity and localization to

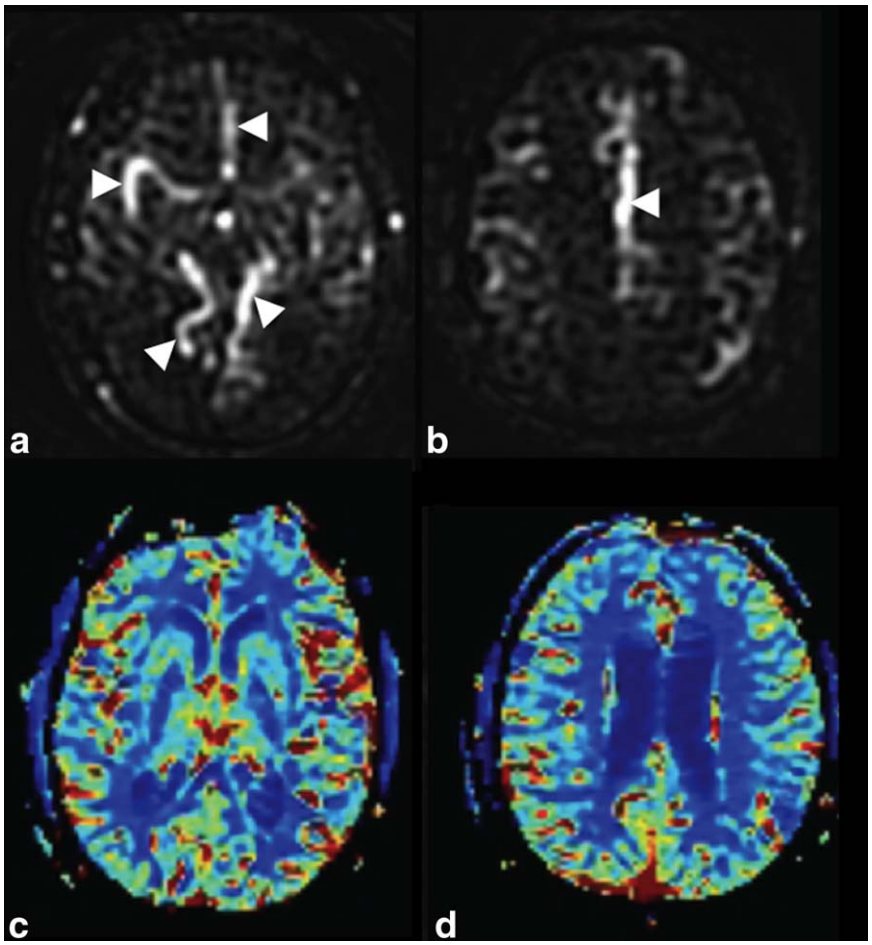

FIGURE 7: ATA and "ASL borderzone sign" in a patient with low cardiac output due to cardiac failure. a,b: ASL images demonstrate high signal due to intraarterial persistence of labeled spins within the anterior, middle, and posterior cerebral arteries (arrowheads), an example of ATA. There is a paucity of signal in brain parenchyma, particularly in the parietal and occipital lobes—a finding known as the "borderzone sign." c,d: DSC relative CBF maps demonstrate no reduction in parieto-occipital blood flow, confirming that the apparent perfusion abnormality on ASL is an artifact arising from delayed arrival of spins in the parenchyma.

the arterial watershed regions, particularly in the parietal and occipital lobes.[15]

Recognition of ATA is important, as it indicates delayed arterial transit time (in the absence of a technical factor to account for this artifact). The reader can then be circumspect in interpreting the findings on ASL CBF maps. Bipolar crusher gradients applied prior to imaging the parenchyma can be used to suppress intraarterial ASL signal; however, this does not address the problem of parenchymal CBF underestimation due to delayed arrival of tagged spins.[5,9] Elimination of intraarterial ASL signal also removes an important clue, which alerts the reader to the presence of delayed transit time. Therefore, in concordance with the recent ASL white paper, we do not advocate the routine use of vascular suppression.[6]

A suggested strategy to compensate for delayed transit time, in patients with known or suspected steno-occlusive disease or low cardiac output, is to increase the PLD (so-called long-delay ASL). However, this compromises SNR, because ASL signal decays exponentially with time due to T_1-relaxation of blood. Therefore, long-delay ASL is typically only feasible at 3T; the improved SNR and longer blood T_1 at high field strength allows the label to persist at longer PLDs.[16] An example of the use of long-delay ASL in a patient with Moyamoya disease is shown in Fig. 8. The sequence parameters of our long-label, long-delay pcASL sequence are the same as for our routine ASL sequence as described previously, with the exception of the labeling time (3000 msec instead of 1500 msec) and PLD (3000 msec instead of 2000 msec). A long labeling time is used to accommodate the different label arrival times in the diseased and normal vascular territories, and optimize tissue signal. Because of the longer labeling and PLD times, the TR and hence the overall time required for the sequence increases (usually between 6 and 8 min).

ARTIFACTS ARISING FROM THE READOUT PERIOD. There are several artifacts originating from the readout period. The manifestation of some of these artifacts, for instance related

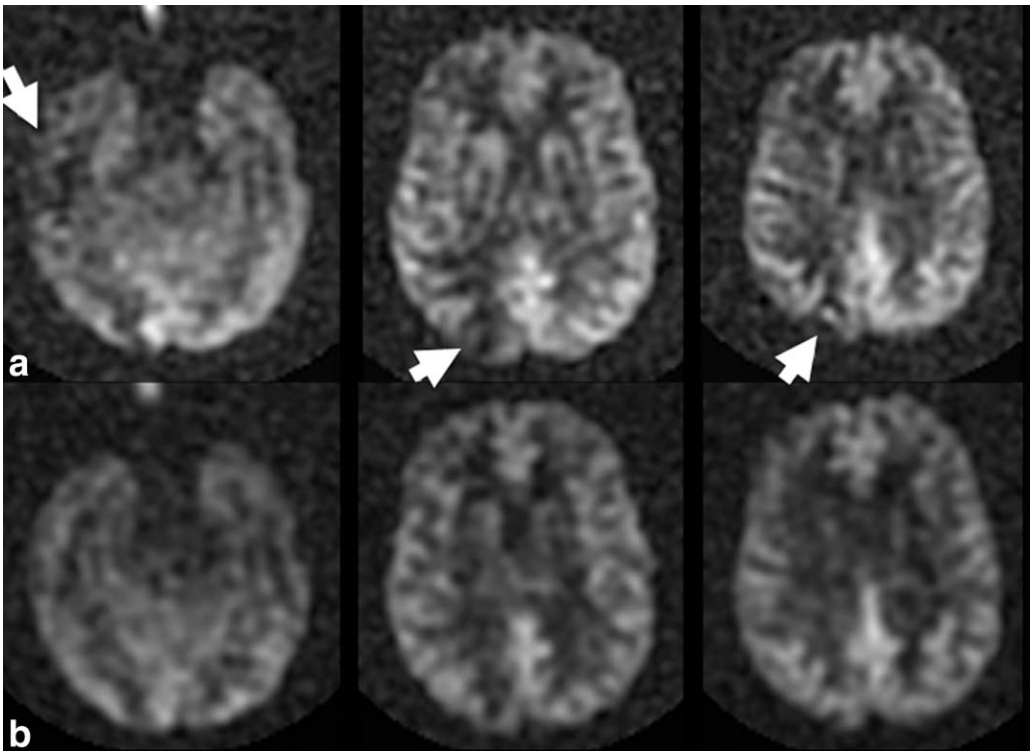

FIGURE 8: Long-label, long-delay (LLLD) ASL in a patient with Moyamoya disease and a 90% stenosis of the right terminal ICA. a: Standard ASL CBF maps demonstrate signal dropout in the right ACA-MCA and MCA-PCA watershed regions (arrows). b: This is alleviated by the use of LLLD ASL, confirming that the signal decrease seen with standard ASL is due to delayed blood flow, rather than a true decrease in parenchymal CBF.

to motion and the presence of susceptibility gradients, depends on the readout technique.

MOTION. The 3D stack-of-spirals FSE readout technique that we routinely use with pcASL is much less motion-sensitive than older EPI readout techniques, due to the implementation of background suppression. The fast and efficient coverage of *k*-space also minimizes the potential for motion between label and control images. Nonetheless, severe patient motion can result in misregistration of signal intensities at the time of readout, appearing as high signal intensity spirals on the CBF maps; this manifestation of motion as high signal intensity spiral artifacts is unique to the spiral *k*-space trajectory.

Recent advances in motion correction, particularly prospective motion correction, have been applied to ASL and can alleviate the effects of even large movements during the scan (Fig. 9).[17,18] If such methods are not available, one can consider repeating the ASL study once the patient is instructed to stay still.

BLURRING. Significant blurring of signal along z-axis occurs in a typical 3D stack-of-spirals readout. This results in the propagation (along the craniocaudal direction) of high signal intensity lesions. For example, in Fig. 10 high ASL signal is seen not only within an aneurysm of the cavernous segment of the right internal carotid artery (ICA), but also in more superior slices, due to smearing of signal along the z-direction.

The source of blurring artifact can be discerned by examining the slices superior and inferior to an area of ASL signal abnormality. Additionally, the smearing effect, and the artifactual nature of the high ASL signal outside the plane of the lesion, can be readily appreciated on coronal and sagittal reformatted ASL images.

When using the stack-of-spirals readout, blurring can be reduced by decreasing the number of slices in the z-direction. Usually it is sufficient just to recognize this as an artifact. If the source of high signal is a vascular structure with flowing blood, such as an aneurysm, one could consider repeating the ASL sequence with vascular suppression gradients, to eliminate the high signal so that it cannot propagate. Use of an alternative readout, such as EPI, would also eliminate this artifact. Finally, reducing the number of slices in the z-direction will also tend to mitigate this artifact.

OCCIPITAL LOBE HYPERPERFUSION. One can observe increased signal intensity in the occipital lobes bilaterally on ASL when patients are scanned with their eyes open (Fig. 11). This regional hyperperfusion is physiological, and corresponds to visual cortex activation.[3] It is important to recognize that this is a physiological phenomenon, in order to avoid mistaking it for pathology. In our experience,

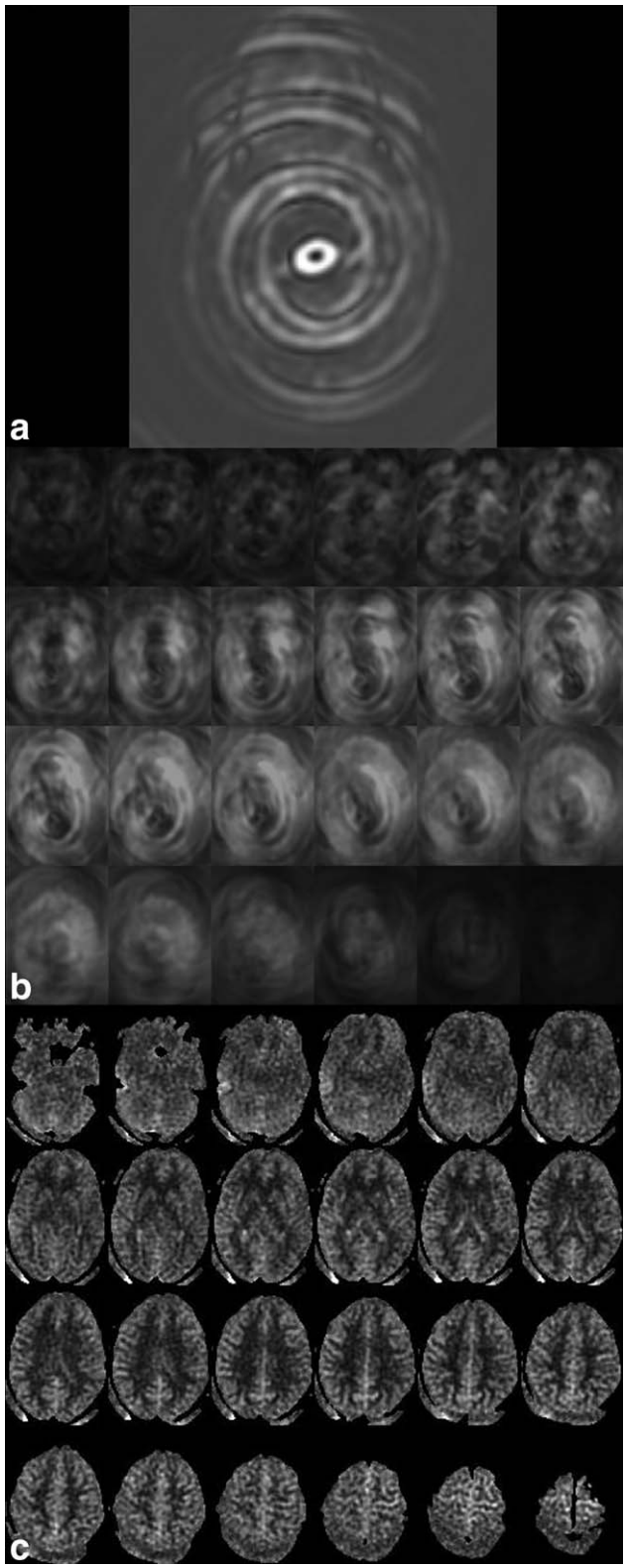

FIGURE 9: Motion artifact. a: Patient head motion results in high signal spiral artifacts on ASL when a 3D stack-of-spirals FSE readout technique is employed. b: Marked head motion due to seizure activity in another patient, again manifesting as spiral artifacts; the ASL images are nondiagnostic due to the severe motion artifact. c: ASL CBF maps of diagnostic quality are obtained in the same patient, despite ongoing head motion, when a prospective motion correction technique is applied.

increased occipital lobe CBF with visual cortex activation is more frequent and conspicuous with 2D PASL (utilizing an EPI readout) than with 3D pcASL, although the reasons for this are unclear.

Although the ability of ASL to demonstrate physiologic increase in CBF with neuronal activation can be utilized for functional imaging, in routine studies it may potentially mask or distract from pathological changes in CBF. Physiological occipital hyperperfusion can be avoided by asking patients to close their eyes during the ASL sequence.

Artifacts That Increase the Conspicuity of Pathology

INTRAARTERIAL ASL SIGNAL. As discussed previously, intraarterial ASL signal is a potentially useful artifact, alerting the reader to the presence of delayed arterial transit time. The distribution of ATA helps differentiate between the causes of this artifact. If ATA is confined to a particular vascular territory, this suggests narrowing or occlusion of the supplying vessel. Structural imaging can then be reviewed to look for evidence of steno-occlusive disease. More extensive ATA indicates the presence of globally delayed arterial transit time, most often due to diminished cardiac output.

Intraarterial ASL signal may also be observed in instances where labeled blood becomes hemodynamically "trapped" due to turbulent flow within an aneurysm. Since only a small volume of the blood flowing in the parent artery becomes trapped, unless the aneurysm is very large, blood flow to the brain parenchyma is neither delayed nor decreased. The high contrast differential between ASL signal in the aneurysm sac and adjacent brain parenchyma or CSF increases aneurysm conspicuity (Figs. 10, 12). In cases where an MRA has not been performed, this conspicuous artifact can alert the reader to the presence of an aneurysm, which may be subtle or occult on the structural sequences.

ASL IN SHUNTING LESIONS. Arterial water is magnetically labeled proximal to the brain in ASL perfusion, and acts as a diffusible flow tracer.[19] In the presence of a normal tissue capillary bed, ~90% of labeled arterial blood water is exchanged at the capillary level with tissue water, giving rise to the parenchymal ASL signal.[20] Because it acts as a diffusible tracer, the labeled spins have a much longer "mean transit time" in the imaging voxel (about 60 sec) compared with intravascular tracers (about 5 sec). Because the T_1 decay of labeled water is much shorter than this mean parenchymal dwell time, most labeled water will relax within tissue and the tissue capillary bed.[21] Consequently, there is minimal venous outflow of labeled spins in a normal human brain, and ASL signal is not typically observed in the venous system.[21]

ASL signal can, however, be seen within venous structures in conditions where there is direct and/or rapid

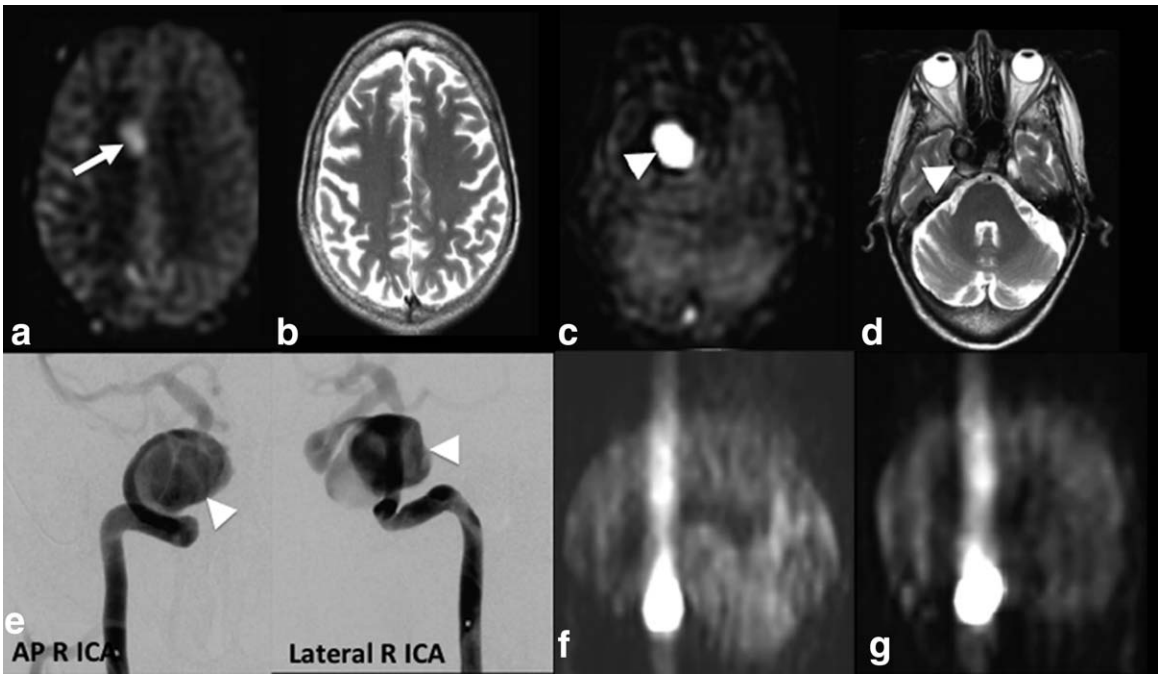

FIGURE 10: Blurring of high signal along the z-axis is another distinctive artifact associated with the segmented 3D stack-of-spirals FSE readout. a: A focal area of high signal (arrow) is seen within the inferior right frontal lobe on the ASL CBF map. b: No structural abnormality is evident at the corresponding level on T_2-weighted images. c: An area of even higher ASL signal intensity is seen further inferiorly, within the right cavernous sinus (arrowhead). d: Corresponding to this, a large, mixed signal intensity lesion is seen within the right cavernous sinus on T_2-weighted images (arrowhead). e: Digital subtraction angiography (DSA) confirms that this lesion is a large aneurysm of the cavernous segment of the right internal carotid artery (arrowheads); the high ASL signal is due to slow and turbulent flow, with trapping of labeled blood within the aneurysm sac. f,g: Coronal and sagittal reformatted ASL images clearly show the smearing of high ASL signal along the z-direction, confirming that the high signal superior and inferior to the plane of the aneurysm is an artifact originating from this smearing.

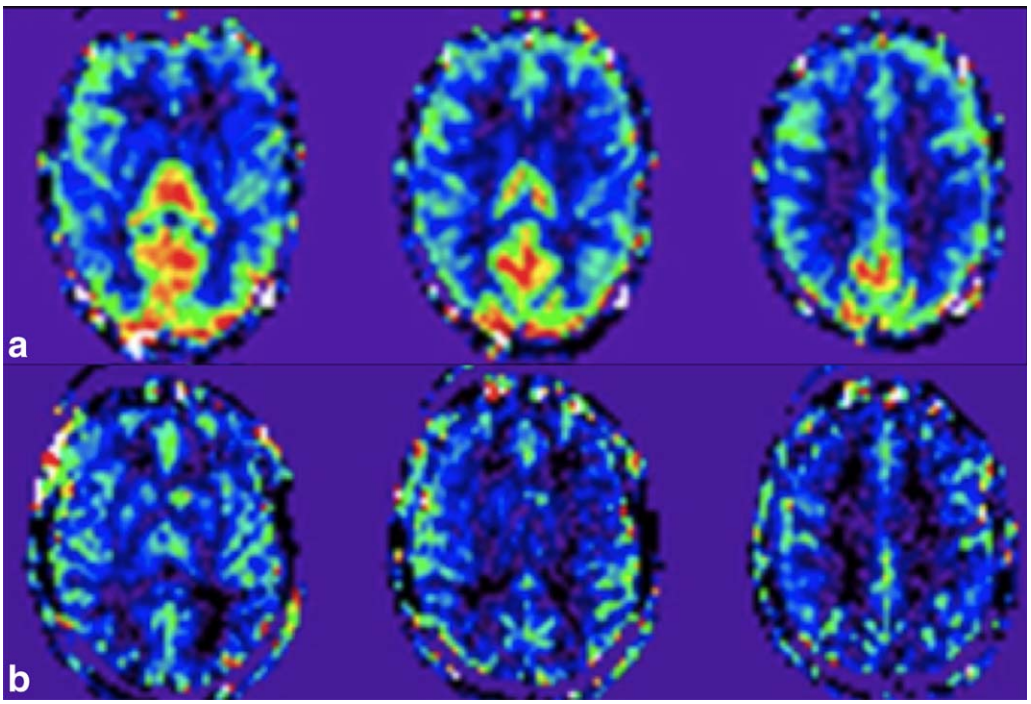

FIGURE 11: Physiological occipital lobe activation in a 20-year-old man. a: ASL CBF maps demonstrate increased signal intensity in the occipital lobes bilaterally when the patient was scanned with his eyes open. This regional hyperperfusion is physiological, and corresponds to neuronal activation in the visual cortex. b: Occipital lobe CBF is seen to have normalized when the ASL sequence was performed again, immediately afterwards, with the patient's eyes closed. Although a 2D PASL technique with an EPI readout was used in this case, the same artifact can be seen with 3D pcASL, albeit less frequently.

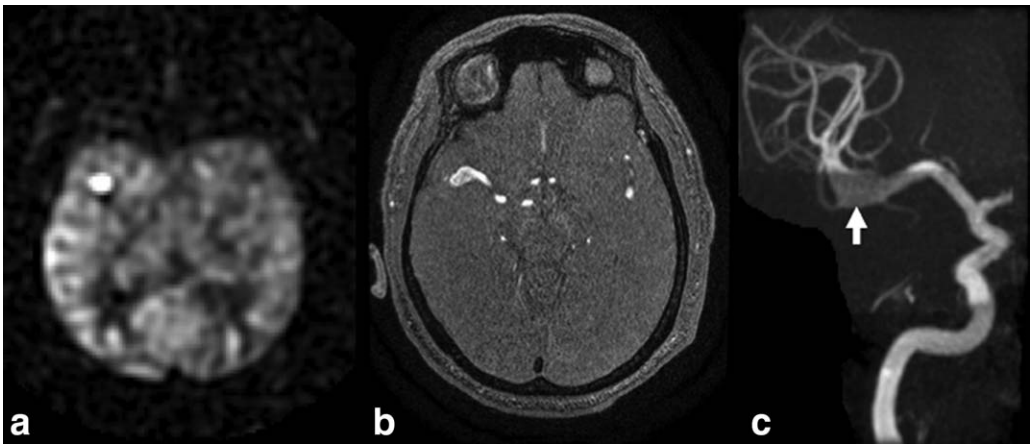

FIGURE 12: High ASL signal in a right MCA aneurysm. a: A focal, rounded area of high ASL signal is seen in the right Sylvian fissure. b: Axial source image. c: Coronal maximum intensity projection (MIP) from this patient's TOF MRA demonstrate a dilated, aneurysmally dilated, dysplastic segment of right MCA (arrowhead). The high ASL signal localizes to this aneurysm. Turbulent, slow blood flow within an aneurysm can lead to labeled blood persisting within the aneurysm sac; this is observed as high signal on ASL images, which serendipitously increases the conspicuity of these aneurysms, aiding detection in cases where MRA has not been performed as a part of the examination.

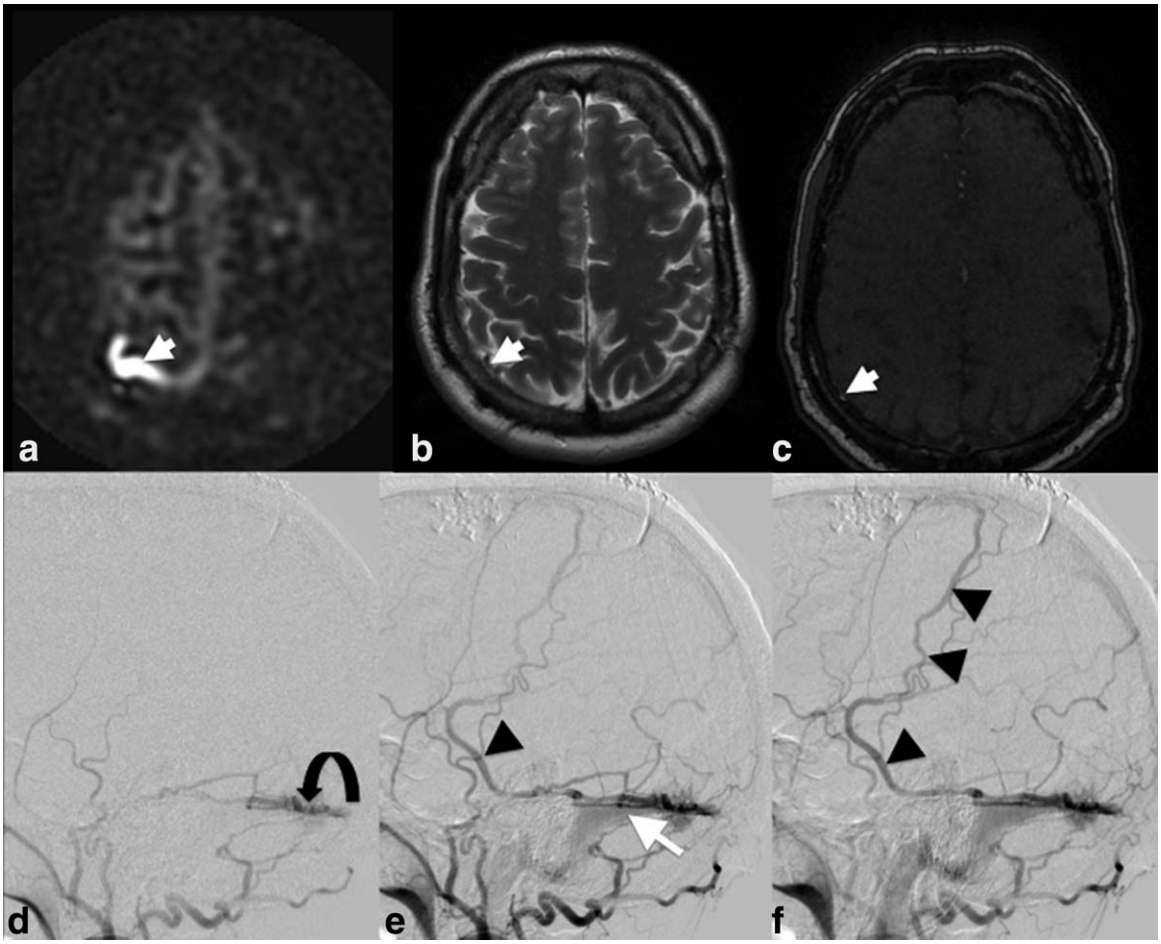

FIGURE 13: Venous ASL signal in a Cognard IIb dural arteriovenous fistula (dAVF). a: ASL CBF map showing serpiginous high ASL signal over the right parietal lobe (arrow). b: Closer inspection of T_2-weighted anatomical imaging reveals that this signal localizes to a cortical vein (vein of Trolard, arrow). c: While difficult to prospectively identify, the 3D TOF MRA demonstrates subtle high signal in this cortical vein (arrow), consistent with fast flow. d: Catheter-based angiography confirms arteriovenous shunting due to a right transverse sinus dAVF (curved black arrow). e,f: Retrograde cortical venous drainage into the veins of Labbe and Trolard (black arrowheads), as well as drainage into the transverse sinus (white arrow) is evident. Retrograde venous drainage from the vein of Labbe into the vein of Trolard accounts for the presence of ASL signal seen in A.

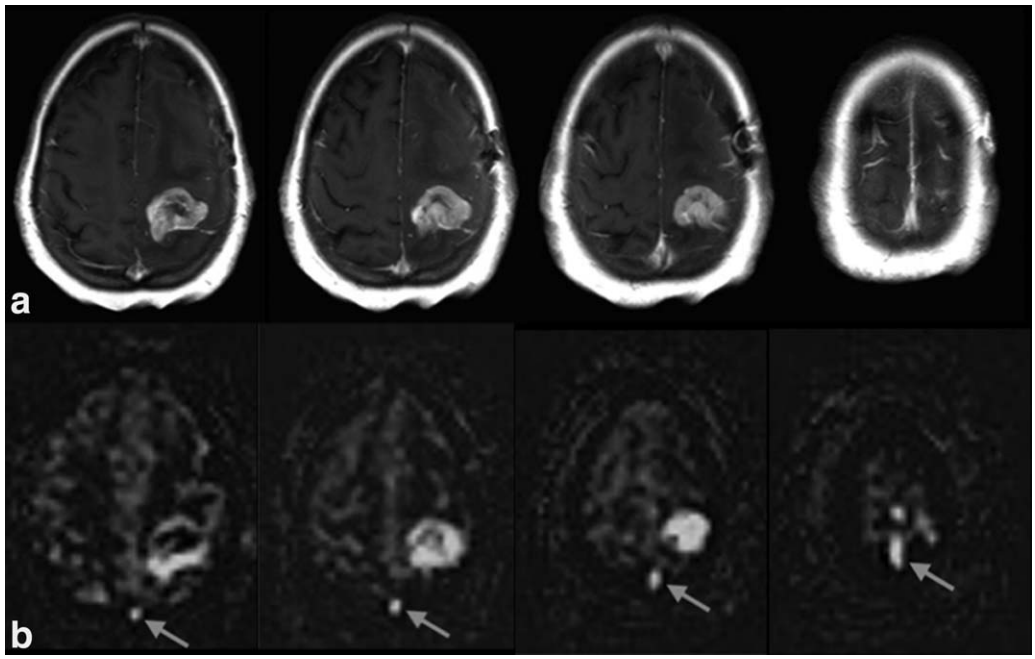

FIGURE 14: Venous ASL signal due to arteriovenous shunting in a glioblastoma. a: Contrast-enhanced T_1-weighted axial images demonstrate an enhancing mass in the left precentral and postcentral gyri, a biopsy-proven glioblastoma. b: ASL images demonstrate high CBF within the tumor. High ASL signal is also seen within the superior sagittal sinus (arrowed), consistent with arteriovenous shunting within the tumor.

passage of blood from arteries into venous structures. In our experience, venous ASL signal is usually observed in the setting of arteriovenous shunting, most often in high-flow vascular malformations. In these conditions, bypass of the normal tissue capillary bed prevents normal tissue exchange of labeled water.[20,21] Also, rapid shunting results in labeled blood water reaching venous structures before significant T_1 relaxation has occurred. Therefore, there is persistence of ASL signal in blood that is shunted into cerebral venous structures.[20,21]

Venous ASL signal was first described as a sign of arteriovenous shunting in arteriovenous malformations (AVMs).[21] In a small series of seven patients, markedly increased signal intensity was observed in the nidus and draining veins of the AVM in all cases.[21] Venous ASL signal has since been described in dural arteriovenous fistulae (dAVFs), which comprise 15% of intracranial arteriovenous shunting lesions.[20] In dAVFs, shunting occurs between dural arteries and intracranial venous structures (dural sinus or cortical vein), and ASL signal may be seen in these draining venous structures.[20] On conventional MRI, dAVFs can be occult. Although 3D time-of-flight (TOF) MRA has been reported to have a high sensitivity and specificity (up to 100%) for the detection of dAVFs, in our experience these lesions can be subtle and difficult to diagnose.[22,23] Conversely, venous ASL signal in shunting conditions is usually a conspicuous finding, comparable to diffusion restriction in acute stroke (Fig. 13). This can be explained by the large size of the nidus and draining veins relative to the image voxel size, and the large fraction of the voxel that is occupied by blood; in comparison, capillary blood constitutes only 1–2% of the volume of the tissue voxel. ASL signal in macrovascular structures is therefore much higher than in parenchyma, giving rise to a large contrast differential.

Given the "light-bulb" conspicuity of venous ASL signal in shunting lesions, it is unsurprising that a pilot study of 26 patients found venous ASL signal to have a high sensitivity for the detection of high-flow vascular lesions, including small AVMs and dAVFs which may otherwise have been occult on MRI.[20] The venous ASL signal alerts the reader to the possibility of a small shunting lesion, which can then be confirmed and delineated on other available sequences, or with digital subtraction angiography (DSA). We feel that ASL is a valuable adjunct to more established noninvasive techniques for the screening of high-flow vascular lesions. If the technique is validated by larger, prospective studies, a lack of venous ASL signal could potentially be used to confidently exclude shunting. On the other hand, the identification of venous ASL signal in a patient with a suspected AVM or dAVF would prompt referral to a neurointerventional service. The venous ASL signal artifact may also be of value for follow-up after treatment of AVMs and dAVFs, as it can indicate shunt recurrence or persistence following therapy.

Venous ASL signal is also infrequently observed in subacute cerebral infarction, where arteriovenous shunting may occur.[20] This can be differentiated from a high-flow vascular malformation on structural imaging, MRA, and

clinical presentation. Venous ASL signal is rarely observed in hypervascular tumors, such as glioblastoma multiforme (GBM) (Fig. 14). Glioblastomas are characterized by angiogenesis, with proliferation of dysplastic neovessels.[24] The frequent intraoperative finding of arterialized veins within these tumors, and the characteristic appearance on catheter angiography of early draining veins, are consistent with arteriovenous shunting in these pathological, low-resistance neovessels.[24] The correlate of this shunting on ASL is venous signal.

Although almost always observed in the presence of arteriovenous shunting, venous ASL signal is not exclusive to these conditions. Venous ASL signal has also been described in normal children with high cerebral flow, and in association with seizures, where there is transient, markedly elevated regional cerebral blood flow.[25–27] This is thought to be due to incomplete tissue exchange of labeled blood during capillary transit, rather than shunting.

Again, it is stressed that the use of vascular suppressor gradients should be avoided, as it eliminates venous ASL signal, which is seen to be a valuable artifact.

Artifacts That Are Attenuated With a 3D FSE Readout

Signal loss and image distortions related to susceptibility variations (eg, due to blood products, surgical material, paranasal sinuses, and pneumatized skull base) are a significant problem associated with EPI readout techniques.[3,6] The 3D FSE readout, however, is relatively immune to off-resonance effects resulting from susceptibility variations near the imaging plane.[6] Consequently, there is improved visualization of the areas adjacent to the skull base and paranasal sinuses, which are usually markedly degraded on EPI-based CBF maps. This is demonstrated in Fig. 3a,b; the inferior right temporal lobe is well seen on the ASL CBF map, while there is pronounced signal loss due to off-resonance effects, obscuring posteroinferior right temporal lobe, on the DSC CBF map obtained using an EPI readout.

Slab excitation and a prolonged image acquisition window with 3D pcASL result in a uniform PLD for all slices.[8] Therefore, artifacts related to variable transit time on pulsed ASL, such as persistent intraarterial ASL signal in the distal slices, are not encountered with 3D pcASL.

In conclusion, pcASL is a relatively new tool for many clinical radiologists, and has a high negative predictive value when normal. However, in order to avoid errors in interpretation of ASL CBF maps, it is important to recognize common artifacts associated with pcASL, as described in this review. This awareness will help avoid misdiagnosis of pathology, and allow potentially remediable artifacts to be addressed. Further, some artifacts can be of diagnostic utility, increasing the conspicuity of pathology. A proper understanding and consideration of ASL artifacts is important to avoid pitfalls and use this unique source of contrast to make the correct diagnosis.

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