

# Brain Perfusion Territory Imaging: Methods and Clinical Applications of Selective Arterial Spin-labeling MR Imaging<sup>1</sup>

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The ability to visualize perfusion territories in the brain is important for many clinical applications. The aim of this overview is to highlight the possibilities of selective arterial spin-labeling (ASL) magnetic resonance (MR) imaging techniques in the assessment of the perfusion territories of the cerebral arteries. In the past decade, the optimization of selective ASL MR techniques to image the cerebral perfusion territories has resulted in numerous labeling approaches and an increasing number of clinical applications. In this article, the methods and clinical applications of selective ASL MR imaging are described and the importance of perfusion territory information in studying cerebral hemodynamic changes in patients with cerebrovascular disease is shown. In specific patient groups with cerebrovascular disease, such as acute stroke, large artery steno-occlusive disease, and arteriovenous malformation, selective ASL MR imaging provides valuable hemodynamic information when added to current MR protocols. As a noninvasive tool for perfusion territory measurements, selective ASL may contribute to a better understanding of the relation between the vasculature, perfusion, and brain function.

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The ability to visualize the perfusion territories of the cerebral arteries is important for many clinical applications. In acute stroke, the delineation of individual perfusion territories may demonstrate the collateral contribution to the ischemic penumbra and may allow differentiation between a thromboembolic and a hemodynamic etiology of stroke (1–3). In addition, perfusion maps of the brain with a clear demarcation of the individual perfusion territories might also be used to localize the origin of an embolus. In chronic cerebrovascular disease, identification of the perfusion territories may help in the evaluation of the actual territorial contribution of individual collateral arteries, in particular in patients with extracranial steno-occlusive disease (4,5). Further knowledge of the cerebral perfusion territories may explain differences in clinical outcome and potentially expand treatment options for both acute stroke and chronic cerebrovascular disease.

### Essentials

- Selective arterial spin-labeling (ASL) MR is a noninvasive method to visualize the perfusion territories of the individual cerebral arteries.
- In the past decade, the optimization of selective ASL MR techniques to image the perfusion territories in the brain has resulted in numerous labeling approaches and an increasing number of clinical applications.
- In specific patient groups with cerebrovascular disease (such as acute stroke, large artery steno-occlusive disease, and arteriovenous malformation), selective ASL MR provides valuable hemodynamic information when added to current MR protocols.
- As a noninvasive tool for perfusion territory measurements, selective ASL may contribute to a better understanding of the relation between brain vasculature, perfusion, and brain function.

Since Duret (6) described in 1874 the cortical vascular area distribution, many atlases have shown schematic drawings of the areas of supply of the cerebral arteries (7–13). Currently, intraarterial digital subtraction angiography (DSA) is the reference standard for visualizing the cerebral vascular tree and for assessing collateral flow at the level of the circle of Willis or leptomeningeal anastomoses at the brain surface. Intraarterial DSA offers excellent information on the presence of collateral flow, showing also the distal arteries of a collateral pathway. However, intraarterial DSA does not provide quantitative information on the actual perfusion of the brain, and to visualize all the collateral pathways, this technique requires an invasive, selective three-vessel approach.

Recently, selective arterial spin-labeling (ASL) magnetic resonance (MR) imaging has been introduced as the first noninvasive method to visualize the perfusion territories of the individual cerebral arteries. This method enables quantification of the actual contribution of individual collateral arteries to the perfusion of the brain. In the past decade, the optimization of selective ASL MR techniques to image the cerebral perfusion territories has resulted in numerous labeling approaches and an increasing number of clinical applications.

The aim of our overview is to highlight the possibilities of selective ASL techniques to assess the perfusion territories in the brain and to show the importance of this information in studying the cerebral circulation. We focus on patients with obstructive arterial disease.

### ASL MR Imaging

In the past decade, ASL MR imaging has been developed as a noninvasive, multi-section method to assess cerebral perfusion (14–17). This technique uses magnetically labeled blood as an endogenous contrast agent. With ASL MR imaging, the protons of arterial water are magnetically labeled in the feeding vasculature of the brain. The labeled arterial protons flow through the vascular

tree and exchange water with the unlabeled brain tissue. A perfusion-weighted image can be generated by the subtraction of an image in which inflowing arterial spins have been labeled from an image in which spin labeling has not been performed. Several techniques have been implemented to correct for potential magnetization effects in order to obtain complete subtraction of background tissue (18). Quantitative perfusion maps can be calculated when the ASL signal change is combined with other parameters, such as  $R_1$  (longitudinal relaxation rate of tissue),  $R_{1a}$  (longitudinal relaxation rate of blood),  $M_{a,0}$  (equilibrium magnetization of blood), and  $\lambda$  (brain-blood partition coefficient of water) (19,20). Variations in hematocrit level may effect the longitudinal relaxation time of blood and the brain-blood partition coefficient of water (21,22).

The existing techniques can be sorted into two categories: pulsed ASL (PASL) and continuous ASL (CASL) (14,15). In both cases, a certain amount of blood is labeled before it supplies the tissue of interest. PASL is obtained with a large proximal labeling volume at a single time point. With CASL, a thin proximal labeling “slice” is applied during several seconds. A recent approach has been introduced in which arterial water is labeled selectively on the basis of the blood velocity, termed velocity-selective ASL (23,24). The main difference between velocity-selective ASL and the other ASL techniques is that the

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#### Abbreviations:

ACA = anterior cerebral artery  
 ASL = arterial spin labeling  
 CASL = continuous ASL  
 CEA = carotid endarterectomy  
 DSA = digital subtraction angiography  
 ICA = internal carotid artery  
 MCA = middle cerebral artery  
 PASL = pulsed ASL  
 rCBF = regional cerebral blood flow  
 VBA = vertebrobasilar arteries

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arterial water is labeled everywhere, including the volume of interest, therefore minimizing the time for the blood to reach any region of interest (25). Despite differences in advantages and limitations, all of these ASL approaches share one characteristic: The perfusion measurements are completely noninvasive.

### Selective ASL MR Imaging

To date, most perfusion imaging techniques have obtained perfusion maps that include contributions from all the arteries feeding the brain. However, ASL MR imaging offers the potential to selectively label individual brain-feeding arteries and thereby map the perfusion territory of each vessel independently. Edelman et al (26) introduced the use of selective labeling for angiographic examination. However, no perfusion territory mapping was performed in this work. More recently, several authors demonstrated perfusion territory imaging based on the spatially selective application of CASL and PASL MR (Table). Currently, there is no general availability of selective ASL sequences; however, an increasing number of institutions are getting access to selective ASL MR techniques.

### CASL Techniques

By using CASL techniques, local surface coils can be used to selectively label the left or right common carotid artery individually (28–30). However, the labeling efficiency with this technique is dependent on the depth of the targeted artery, which varies for different arteries and individuals and therefore its ability as a universal diagnostic tool is limited (42). Other approaches assessed hemispheric perfusion territories on the basis of oblique positioning of a spatially selective labeling plane, without the need for additional surface coils (27,31). However, no separate labeling of the ICA or VBA can be achieved. Another method, based on pseudo-continuous ASL, provides simultaneous perfusion images of two or more perfusion territories, with the same signal-to-noise ratio as conven-

tional CASL images (33). Recently, continuous artery-selective spin labeling has been introduced on the basis of a rotating labeling frame to obtain a localized effect, limited to a single artery (32). This method allows for perfusion territory mapping of the ICA, VBA, both of the ACAs, and the MCA.

### PASL Techniques

By using PASL techniques, selective labeling of the ICAs and VBA was attained by applying two-dimensional spatially selective radiofrequency pulses, forming a pencil beam (35). However, this method involves serious signal-to-noise limitations and requires very stable hardware. In another study, a sagittal angulated slab inversion scheme was used to lateralize labeling in one hemisphere (34). That approach was used only to extend angiographic methods, rather than generate perfusion data, and lacks the desired selectivity of individual vessel labeling. Others also used a scheme of lateralized pulses for hemispheric labeling (37). However, no separate labeling of the ICA or VBA can be achieved. Another approach uses several different placements of

the inversion slab to distinguish the ACA and MCA perfusion territories based on the directionality of the inflowing blood (36). Hendrikse et al (38) developed regional perfusion imaging based on anatomy-driven spatially selective slabs, which is currently the most applicable technique for imaging the perfusion territories of the ICA and the VBA. Typically the scan time is 3 minutes per perfusion territory. In past years, several improvements in this regional perfusion imaging technique have been made.

First, a modification of the regional perfusion imaging technique suitable for high-field-strength imaging has been developed to control for magnetic field inhomogeneities at a field strength higher than 1.5 T (39). Second, careful positioning of three labeling slabs is required for successful imaging of the perfusion territories (Fig 1). Recently, a method for automatic planning of regional perfusion imaging has been introduced that is both fast and requires only minimal user input (41). Improved time efficiency, as well as better visualization of the perfusion territories, has also been achieved by combining measurements of all territories in one experi-

### Most Important Selective ASL MR Techniques

| Technique, Author, and Year of Publication | Labeling                      | Perfusion Territory   |
|--|-------------------------------|-----------------------|
| <b>CASL</b>                                |                               |                       |
| Detre, 1994 (27)                           | Oblique plane                 | Hemispheric           |
| Zhang et al, 1995 (28)                     | Surface coil                  | Common carotid artery |
| Zaharchuk et al, 1999 (29)                 | Surface coil                  | Common carotid artery |
| Trampel et al, 2002 (30)                   | Surface coil                  | Common carotid artery |
| Werner et al, 2004 (31)                    | Oblique plane                 | Hemispheric           |
| Werner et al, 2005 (32)                    | Anatomy-driven rotating plane | ICA, VBA, ACAs, MCA   |
| Wong, 2006 (33)                            | Anatomy-driven plane          | ICA, VBA              |
| <b>PASL</b>                                |                               |                       |
| Eastwood et al, 2002 (34)                  | Sagittal plane                | Hemispheric           |
| Davies and Jezzard, 2003 (35)              | 2D radiofrequency pulses      | ICA, VBA              |
| Taoka et al, 2004 (36)                     | Sagittal and oblique plane    | ACA, MCA              |
| Song et al, 2004 (37)                      | Sagittal plane                | Hemispheric           |
| Hendrikse et al, 2004 (38)                 | Anatomy-driven plane          | ICA, VBA              |
| Golay et al, 2005 (39)                     | Anatomy-driven plane          | ICA, VBA              |
| Guenther, 2006 (40)                        | Anatomy-driven plane          | ICA, VBA              |
| Zimine et al, 2006 (41)                    | Anatomy-driven plane          | ICA, VBA              |

ACA = anterior cerebral artery, ICA = internal carotid artery, MCA = middle cerebral artery, 2D = two-dimensional, VBA = vertebralbasilar arteries.

ment and by using a single-shot three-dimensional readout technique (40).

### Clinical Applications

Although selective ASL techniques have not entered widespread clinical usage, their utility has been demonstrated for a variety of acute and chronic cerebrovascular diseases. Selective ASL MR imaging has a broad range of clinical applications in the cerebral circulation in both health and disease.

### Healthy Population

Since the post-mortem studies of Duret in 1874 on the cortical vascular area distribution, several studies (6–13) on the areas of supply of the major cerebral arteries in the healthy population have been performed. An extensive review of the literature on the territorial distribution demonstrated that there are many discrepancies between the results of most studies, and that the variability of the cerebral territories is significantly greater than was previously assumed (12). However, these publications concerned post-mortem studies in a limited number of cases.

In a large population, selective ASL MR measurements showed large interindividual variability in perfusion territories (43). In addition, it was shown that the wide variation observed from the entire population is

mainly caused by anatomic variants of the circle of Willis (43). The finding that the configuration of the circle of Willis strongly affects the extent of cerebral perfusion territories seems relevant since about half of healthy control subjects have an anatomic variant type, such as missing A1 segment of the ACA or a fetal-type posterior cerebral artery (Fig 2) (44). Furthermore, numerous intermediate variant types of the circle of Willis exist, in which selective ASL will demonstrate the contribution of each vessel to the regional perfusion (45).

### Cerebrovascular Disease

The anatomic variability of the cerebrovasculature itself will cause intersubject differences in the perfusion territories of the brain-feeding arteries and may limit the potential of the cerebral circulation to compensate for steno-occlusive disease. In addition to the large variability at the level of the circle of Willis, large anatomic variation at the level of the arteries in the neck (eg, a 30% prevalence of hypoplasia of a vertebral artery) is found (44,46). With the presence of a severe stenosis or occlusion, the intersubject differences in the anatomy of the arteries in the neck and the circle of Willis will directly affect the perfusion territories of the major brain-feeding arteries. Furthermore, the combination of stenosis severity, multivessel

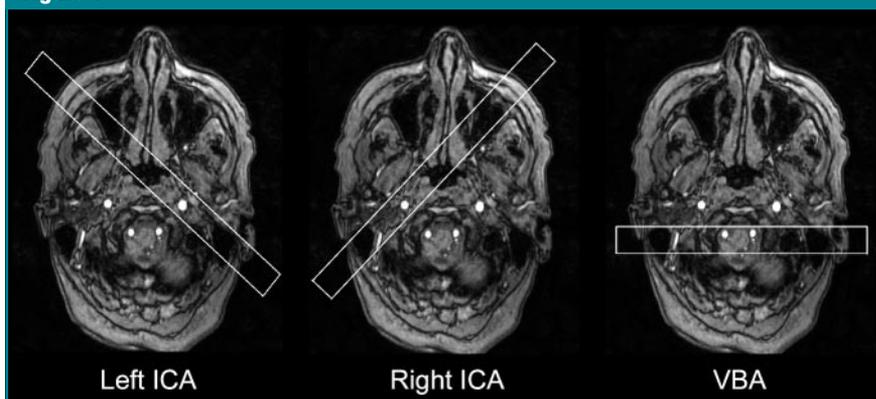
disease, and vascular anatomy will define the ability of the cerebral vasculature to develop effective collateral pathways to compensate for severe steno-occlusive disease.

### Acute Stroke

In patients with stroke, the size and location of the infarct depend on the interaction between embolism originating from an unstable plaque or cardiac thrombus and the regional cerebral hemodynamic status in the perfused territory. Impaired washout of emboli in hypoperfused vascular territories might be an important concept in explaining the development of brain infarction (2). Hypoperfusion and hyperviscosity enhance thrombus formation by promoting embolization of fresh emboli, and hypoperfusion also reduces dissolution of emboli due to reduced flow velocity (47). Brain regions with adequate perfusion may be relatively protected against ischemia and infarction owing to the clearance of emboli from the cerebral circulation in these regions. On the other hand, regions with compromised cerebral hemodynamics and inefficient collateral blood supply may have a higher risk of ischemia and infarction. Selective ASL MR may demonstrate these (border zone) areas with a lower potential to wash-out thromboembolism between the distal end branches of the cerebral arteries (48).

After an acute occlusion of a branch of the intracranial vasculature, the distal branches depend on collateral blood supply. Insufficiency of collateral blood supply will result in areas with critically decreased cerebral blood flow (ischemic core) and areas with decreased cerebral blood flow that are still viable (ischemic penumbra). Selective ASL MR may be used in acute stroke to demonstrate the source of collateral blood supply to the areas surrounding the ischemic core (49). Especially, with the recent development of targeted treatment options such as intraarterial thrombolysis, intraarterial thrombectomy, and administration of neuroprotective agents, the origin of the collateral blood supply may guide treatment (50–52). For instance,

Figure 1



**Figure 1:** Transverse source images of time-of-flight MR angiography (repetition time msec/echo time msec, 23/3.5; 18° flip angle) of brain-feeding arteries show planning of the selective ASL slabs for perfusion territory imaging of left ICA, right ICA, and VBA.

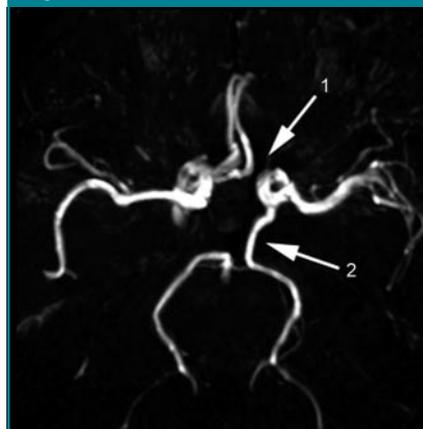
characterization of collateral flow may be used to identify optimal candidates for intervention, and collateral flow may also be an influential factor in the ultimate fate of neuroprotective therapy (52). After therapeutic or spontaneous recanalization of occluded intracranial branches, selective ASL MR may demonstrate the normalization of the perfusion territories of the cerebral arteries.

### Chronic Cerebrovascular Disease

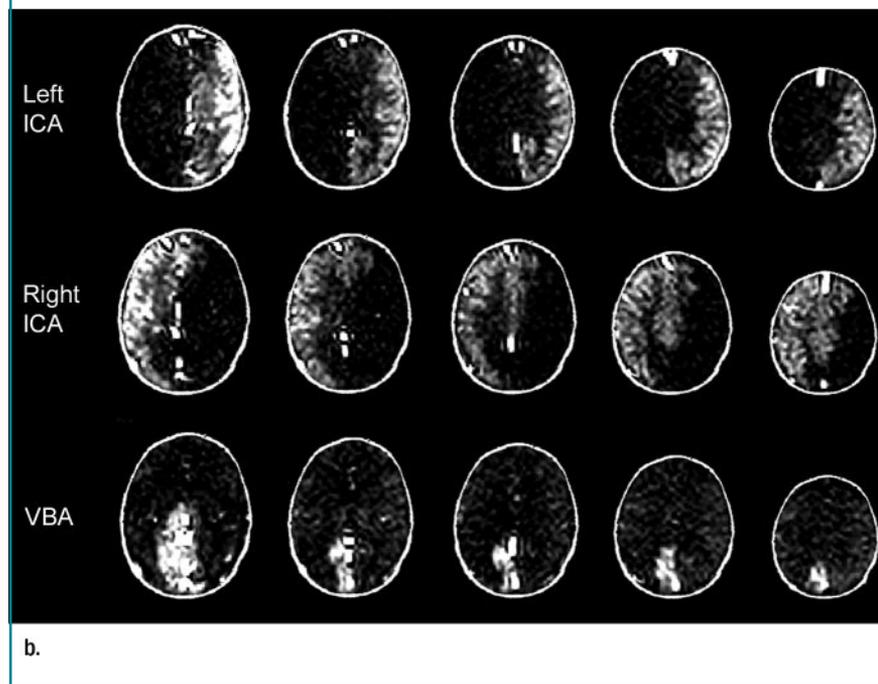
Over the past several years, evidence has been accumulating that in addition to embolism, a compromised cerebral blood flow may play a role in causing transient ischemic attack and stroke in patients with severe extracranial arterial stenosis and occlusion (2). In such cases, ischemia would occur as a result of failure of the collateral blood flow via the circle of Willis, the leptomeningeal collaterals, or the ophthalmic artery (4). Therefore, the status of collateral pathways and cerebral blood supply may be an early indicator of increased risk of future ischemic events. At present, the actual contribution of the individual collateral pathways is difficult to assess and to quantify. MR angiography and transcranial Doppler ultrasonography may depict the presence of collateral flow but not the actual contribution to brain perfusion. Intraarterial DSA offers more information, depicting also the distal arteries of a collateral pathway (53). However, to visualize all the collateral pathways, this technique requires an invasive, selective four-vessel approach. Selective ASL MR is a noninvasive method to quantify the actual territorial contribution of individual collateral arteries to the brain tissue perfusion.

Authors of a recent article (54) describe how selective ASL was used to determine the perfusion territories of the remaining patent arteries supplying blood to the brain in a group of patients with symptomatic ICA occlusion. It is shown that patients with ICA occlusion have a large variation in perfusion territories ipsilateral to the occluded ICA (54). In these patients, the MCA perfusion territory on the side of the occluded ICA is mainly dependent on col-

**Figure 2**



a.



b.

**Figure 2:** Transverse perfusion territory images in healthy subject. (a) Transverse maximum intensity projection of time-of-flight MR angiography of the circle of Willis (30/6.9, 20° flip angle) shows a missing A1 segment of the left ACA (arrow 1) and left-sided fetal-type posterior cerebral artery (arrow 2). (b) When applying selective labeling with regional perfusion imaging sequence (repetition time msec/echo time msec/inversion time msec, 3000/5.6/1600; 90° flip angle) of left ICA, ASL signal is present in left MCA perfusion territory and left posterior part, while ACA perfusion territory is absent. When right ICA is labeled, ASL signal is present in right MCA perfusion territory and left and right ACA perfusion territories. After labeling of VBA, signal is only present in right posterior part of the imaging sections, while left posterior part shows no perfusion signal.

lateral flow originating from the VBA, whereas the contralateral ICA is important for the ACA perfusion territories on both sides (Fig 3) (54). Selective ASL has also been used to demonstrate the effect of ICA stenosis on blood supply to the cerebral hemispheres, as well as the contribution of collateral pathways (55,56). Regional cerebral blood flow (rCBF) in the MCA perfusion territory on the side of the stenosis originating from the ipsilateral ICA ( $54 \text{ mL/min/100 g} \pm 3$  [standard deviation]) was lower than rCBF in the contralateral MCA territory originating from the con-

tralateral ICA ( $59 \text{ mL/min/100 g} \pm 3$ ) (56). The MCA on the side of the ICA stenosis received significant contralateral supply ( $7.0 \text{ mL/min/100 g} \pm 3$ ) (56). Regional CBF thresholds of 17 and 10 mL/min/100 g are routinely used as those values distinguish between normal tissue (including benign oligemia,  $\text{rCBF} > 17 \text{ mL/min/100 g}$ ), penumbra ( $17\text{--}10 \text{ mL/min/100 g}$ ), and infarct core ( $< 10 \text{ mL/min/100 g}$ ) (57).

### Cerebrovascular Intervention

In patients with ICA stenosis, collateral circulation plays a major role in main-

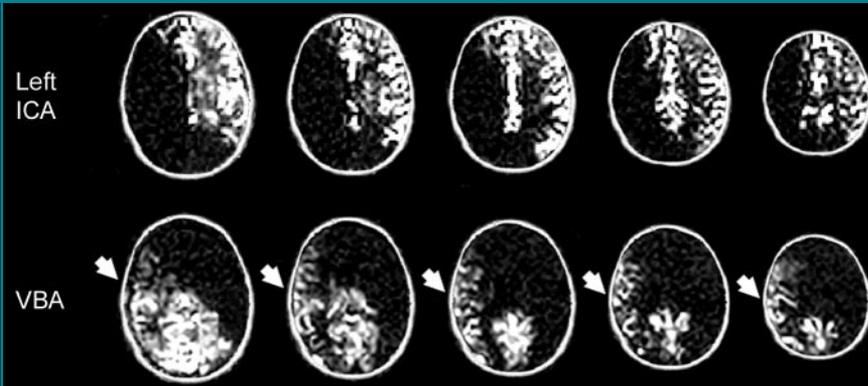
taining cerebral perfusion (2,53). However, the extent and pathways of collateral flow are highly variable, and as a result patients with ICA stenosis form a

heterogeneous population (53,58). Therefore, it would be desirable to directly assess the delivery of arterial blood into the brain as a function of independent

arterial supply from each major branch, rather than make inferences from parameters such as percentage stenosis (59). By using selective ASL, it has been demonstrated that the best predictor of increased rCBF on the side of carotid endarterectomy (CEA) is the contribution of the ipsilateral ICA, while the degree of stenosis was not as predictive (56). The combination of rCBF and degree of stenosis may be more predictive in the risk of recurrent stroke in patients with ICA stenosis.

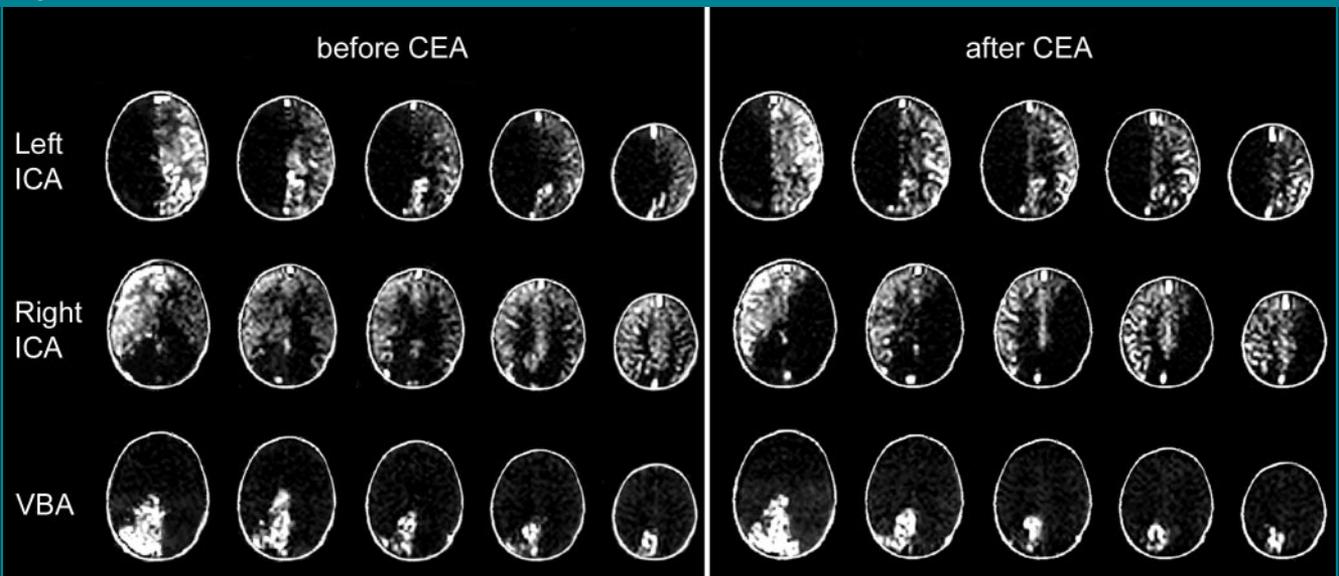
Carotid angioplasty with stent placement may offer an alternative treatment to CEA for high-grade ICA stenosis, and several large randomized trials directly comparing it with CEA are currently underway (60). Selective ASL measurements have shown that carotid angioplasty with stent placement results in a normalization of the territorial distribution and rCBF in a manner similar to that of CEA (61). Although the true role of carotid angioplasty with stent placement in the management of ICA stenosis remains to be determined by large

**Figure 3**



**Figure 3:** Transverse perfusion territory images in a patient with transient ischemic attack associated with right-sided ICA occlusion. Since the right ICA was occluded, only left ICA and VBA were labeled. With selective labeling (3000/5.6/1600, 90° flip angle) of nonoccluded left ICA, signal was observed in left MCA perfusion territory and left ACA perfusion territory, in combination with collateral blood supply to right ACA perfusion territory. After labeling of VBA, signal was detected in posterior part of the imaging sections and collateral blood supply to right MCA perfusion territory (arrows).

**Figure 4**



**Figure 4:** Transverse perfusion territory images in a patient with symptomatic left-sided ICA stenosis of 90% before and after CEA of left ICA. When labeling (3000/5.6/1600, 90° flip angle) left ICA before CEA, signal is observed in left MCA territory and left posterior part of the imaging sections. After CEA, perfusion territory of left ICA has extended into ipsilateral ACA territory. When labeling right ICA before CEA, signal is detected in both the left and right MCA and ACA territories. After CEA, perfusion territory is restricted to the right ACA and MCA territories. When labeling VBA before CEA, signal is only present in the right posterior part of the imaging sections. The left posterior part of the imaging sections is supplied by left ICA via left-sided fetal-type posterior cerebral artery. After CEA, no change in perfusion territory of VBA is observed.

randomized trials, findings (61) suggest that there is no difference in cerebral hemodynamic effect between the two approaches (Fig 4).

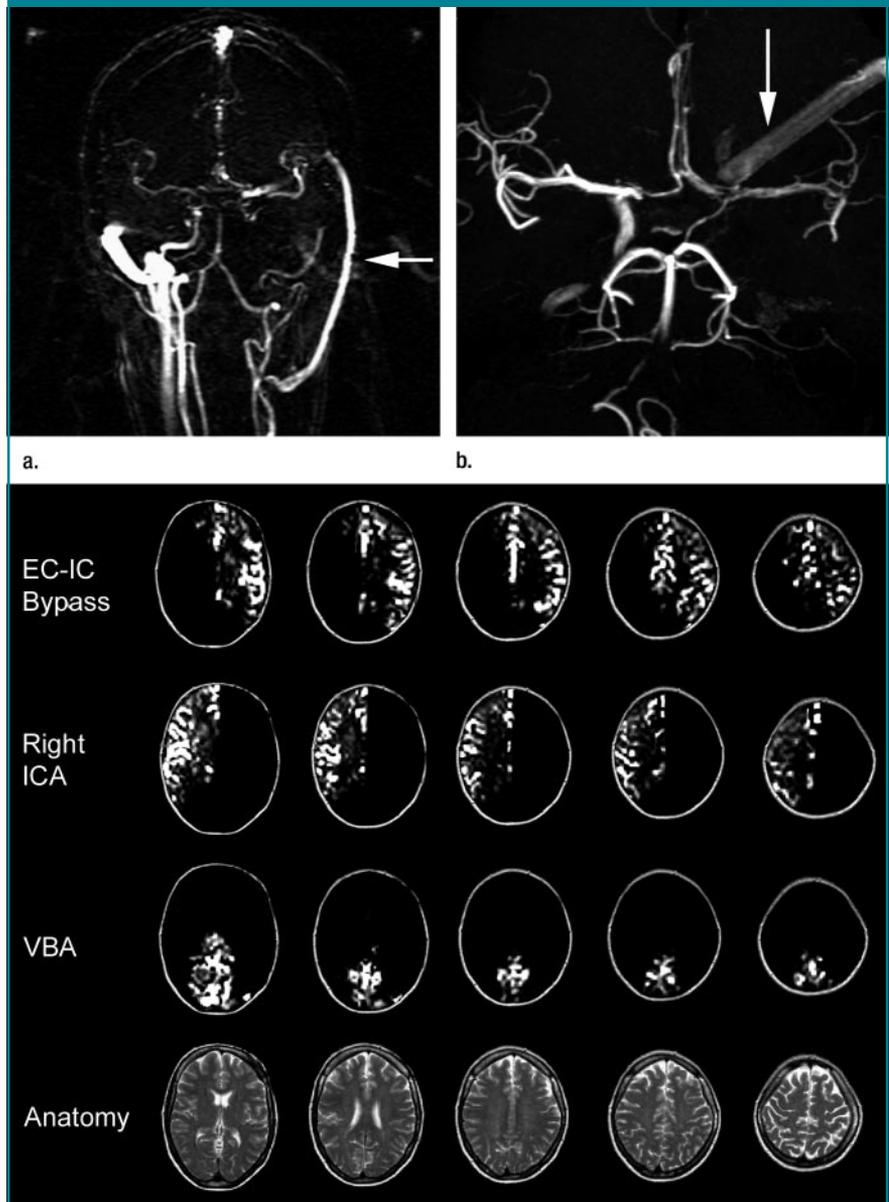
To increase blood flow to the brain in patients with symptomatic ICA occlusion, extracranial-intracranial bypass surgery was introduced. However, in a large randomized trial, extracranial-intracranial bypass surgery did not prevent recurrent ischemic stroke in the average patient with symptomatic ICA occlusion (62). It is unknown, however, whether extracranial-intracranial bypass is effective in the subgroup of patients with insufficient collateral flow and compromised perfusion. Currently, a new extracranial-intracranial bypass study is underway that includes only patients with compromised cerebral hemodynamics (63). Selective ASL assessment of the hemodynamic status of the brain may identify patients at high risk of recurrent ischemic stroke and determine the indication for bypass surgery. Providing perfusion territory and rCBF information, selective ASL also seems well suited for noninvasive follow-up of patients after bypass surgery (Fig 5). In this respect, selective ASL has been used to demonstrate that a smaller perfusion territory is supplied by the bypass with preserved rCBF ( $71 \text{ mL/min}/100 \text{ g} \pm 11$ ) compared with the perfusion territory and rCBF of the contralateral ICA ( $72 \text{ mL/min}/100 \text{ g} \pm 14$ ) (64).

In patients with inoperable giant aneurysms ( $> 2.5 \text{ cm}$ ) of the ICA, therapeutic ICA occlusion is frequently performed (65). However, a subgroup of these patients cannot tolerate ICA test occlusion and develop signs of cerebral ischemia due to insufficient collateral blood supply (66). Noninvasive ASL measurements of rCBF and perfusion territories have been used for the follow-up evaluation of the cerebral hemodynamics before and after therapeutic carotid occlusion in these patients who are vulnerable to a major stroke (55).

#### Other Potential Clinical Applications

Potential future clinical applications may include the evaluation of the extent of arterial perfusion territories in patients with epilepsy who are planning to un-

**Figure 5**



**c.**

**Figure 5:** Transverse perfusion territory images in a patient with a left-sided ICA occlusion after left-sided extracranial-intracranial bypass surgery. **(a)** Coronal ( $14/7$ ,  $20^\circ$  flip angle) and **(b)** transverse ( $14/7$ ,  $20^\circ$  flip angle) phase-contrast MR angiograms show extracranial-intracranial bypass (arrow), right ICA, VBA, and circle of Willis. **(c)** When selective labeling with regional perfusion imaging sequence ( $3000/5.6/1600$ ,  $90^\circ$  flip angle) is applied to extracranial-intracranial bypass, signal is present in left hemisphere, indicating that bypass is supplying the perfusion territory of left MCA and ACA. With selective labeling of right ICA, signal is present in the right hemisphere, indicating that right ICA is supplying the perfusion territory of right MCA and ACA. With selective labeling of VBA, signal is present in the posterior part of the imaging sections.

dergo anterior temporal lobectomy. In these patients, invasive intracarotid Wada testing is performed preoperatively for the evaluation of the lateralization of linguistic functions localization (67). Selective ASL studies may be able to evaluate the hemispheric brain regions perfused by the ICA prior to intracarotid Wada testing. In a functional MR study (68) in healthy subjects, selective ASL has been used to show the relation between the (labeled) brain vasculature, tissue perfusion, and brain function. In patients with arteriovenous malformation, the normal distribution of cerebral blood flow may be disturbed with flow contributions of different brain-feeding arteries (ie, ICAs, external carotid arteries, and VBA) to the nidus of the arteriovenous malformation and the presence of vascular steal. Selective ASL MR may demonstrate preoperatively the presence of these feeders, quantify the extent of arteriovenous shunting, and in addition, demonstrate the effect of therapy (embolization, gamma knife, surgery) on the contributions of different feeding arteries of the arteriovenous malformation (69). In brain tumors, ASL MR may demonstrate hyperperfused regions of tumors potentially corresponding to enhancement after contrast material-enhanced imaging, and previous studies demonstrated the capability of nonselective ASL for tumor grading (70,71). With ASL MR, arterial transit time and arterial blood volume can be derived, which may be a useful marker of capillary density and could direct the neurosurgeon to perform biopsy on the portion of the tumor with the highest grade (72).

### Quantitative Analysis

In addition to visualization of perfusion territories, selective ASL MR has the capacity of quantitative analysis of the rCBF supply from each individual feeding artery (38,39). A review (17) demonstrated the clinical feasibility and utility of quantification of brain perfusion. The main clinical applications of quantitative cerebral perfusion imaging are acute and chronic cerebrovascular dis-

orders, neurodegenerative disorders, epilepsy, and brain tumors.

The quantitative accuracy of ASL MR has been addressed extensively in the literature. Computer simulations and direct comparisons with other brain perfusion imaging techniques (such as positron emission tomography) have been performed (20,73–75). It appears that cerebral blood flow is correctly estimated in the gray matter. In the white matter, ASL measurements show an underestimation, probably caused by an underestimation of the arterial transit time for white matter regions. Quantitative ASL perfusion measurements show a less than 10% change when reimaging the same subject (76). By using long labeling delays, high spatial resolution, and an ASL approach that avoids magnetization effects and venous inflow, ASL CBF maps can be generated that point toward a true measure of gray matter perfusion (75).

Quantification of artery-specific rCBF contributions may demonstrate hemodynamically significant steno-occlusive disease, with rCBF values decreasing below critical values needed to maintain brain metabolism (77). Similar to the quantification of rCBF with nonselective ASL MR, rCBF quantification in patients with steno-occlusive disease requires more advanced selective ASL techniques (78,79). With delayed collateral flow, the label will have a delayed arrival at the brain tissue and ASL techniques with measurements at a single time point will result in an underestimation of the rCBF in the areas with collateral blood supply (20). Two approaches are available to obtain ASL measurements insensitive to these regional differences in arrival time. First, several ASL methods have been developed that apply saturation pulses to obtain a sharply defined and uniform-shaped bolus profile (QUIPPS I, II, Q2TIPS) (80,81). Second, the ASL methods allow acquisition of images at multiple time points, typically between 100 and 2500 msec, after labeling (40,82). In addition to insensitivity to regional differences in arrival time of the label, the acquisition of images at multiple time points allows for quantification of the arrival times. Contrast-en-

hanced perfusion MR techniques do not depend on longitudinal relaxation times with a signal decrease at longer delay times. ASL MR cannot be performed after administration of gadolinium contrast agents because of longitudinal relaxation time shortening.

The use of quantitative selective ASL approaches may demonstrate the combined contribution of different arteries to brain regions (Fig 4). In the study of Jones et al (56) in patients with severe stenosis of the ICA, selective ASL MR at a single time point demonstrated a 7 mL/min/100 g  $\pm$  3 tissue contribution in the MCA perfusion territory from the contralateral ICA before CEA, with a 54 mL/min/100 g  $\pm$  3 tissue contribution in the ipsilateral ICA. Other potential patient groups in whom quantitative selective ASL MR may demonstrate combined contributions of arterial supply to a similar region are the presence of collateral blood supply to the ischemic penumbra surrounding the ischemic core with cerebral artery occlusion in acute stroke. Furthermore, in patients with arteriovenous malformation, selective ASL MR may demonstrate the quantitative contribution of collateral blood supply via multiple collateral arteries to the nidus of the arteriovenous malformation.

### Summary

In the next decade, further technical developments of the selective ASL MR technique will parallel the use of selective ASL techniques in research and clinical studies. The availability of higher field strength magnets will further increase the quality of selective ASL MR; in this respect, ASL MR imaging is one of the MR techniques that benefits most from these higher field strengths (83,84). With increased availability of this technique on clinical MR imagers, an increasing number of patient studies are currently performed. In specific patients groups with cerebrovascular disease, as described above, selective ASL MR may provide valuable hemodynamic information when added to current MR protocols. In the future, this technique may be capable of replac-

ing diagnostic intraarterial DSA in a selected group of patients. Furthermore, selective ASL MR is especially suited for noninvasive follow-up after vascular interventions. Selective ASL MR provides a “perfusion territory weighted” contrast, with the advantage of the possibility to correlate the perfusion territory information with high-spatial-resolution anatomic, angiographic, and diffusion-weighted MR images. As a noninvasive tool for perfusion territory measurements, we believe selective ASL will contribute to a better understanding of the relation between vasculature, perfusion, and brain function.

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