

# Flow Territory Mapping of the Cerebral Arteries With Regional Perfusion MRI

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**Background and Purpose**—Conventional contrast-enhanced angiography is the gold standard for visualization of the vascular tree supplied by the major cerebral arteries and assessment of collateral flow. Thus far, however, no methods are available to assess the actual flow territories of the individual cerebral arteries. In the present study, we evaluate a noninvasive arterial spin labeling MRI method for selective mapping of the flow territories of the left and right internal carotid arteries and posterior circulation (basilar artery and vertebral arteries).

**Methods**—A spatially selective labeling approach, regional perfusion imaging, was developed on the basis of selective slab inversion of the arterial water with a pulsed arterial spin labeling sequence. The selectivity of this method was demonstrated.

**Results**—Regional perfusion imaging enables assessment of the perfusion territories of the major cerebral arteries. With selective labeling of an internal carotid artery, signal is present in both the ipsilateral anterior cerebral artery and ipsilateral middle cerebral artery flow territory. With labeling of the basilar artery, perfusion-weighted signal is symmetrically present in both posterior cerebral artery flow territories. Cerebral blood flow values measured with regional perfusion imaging in the complete hemisphere ( $40.1 \text{ mL} \cdot \text{min}^{-1} \cdot 100 \text{ g}^{-1} \text{ tissue}$ ), white matter ( $22.1 \text{ mL} \cdot \text{min}^{-1} \cdot 100 \text{ g}^{-1} \text{ tissue}$ ), and gray matter ( $65.8 \text{ mL} \cdot \text{min}^{-1} \cdot 100 \text{ g}^{-1} \text{ tissue}$ ) are in agreement with data in the literature.

**Conclusions**—We present the first imaging method capable of evaluating both quantitatively and qualitatively the flow territories of the individual brain-feeding arteries in vivo. (*Stroke*. 2004;35:882-887.)

**Key Words:** cerebral blood flow ■ cerebral ischemia ■ circle of Willis ■ collateral circulation  
■ magnetic resonance imaging

Conventional contrast-enhanced (CE) angiography is the gold standard for visualization of the vascular tree supplied by the major cerebral arteries and assessment of collateral flow at the level of the circle of Willis or leptomeningeal collateral flow at the level of the cortical surface.<sup>1,2</sup> MRI provides excellent anatomical information as well as gadolinium injection and arterial spin labeling (ASL) methods for measuring tissue perfusion.<sup>3</sup> At present, however, MRI does not provide selective information on the vascular tree supplied by each major cerebral artery separately. Liebeskind,<sup>4</sup> in a recent review of collateral circulation, said that “current knowledge of collateral circulation is limited due to the absence of non-invasive approaches for the evaluation of collateral blood flow.” Further understanding of the relationship between collaterals and regional perfusion may explain differences in clinical outcome and potentially expand treatment options for acute stroke and chronic cerebrovascular disorders.

ASL perfusion MRI magnetically labels the protons of the arterial water, which is used as endogenous tracer.<sup>3,5,6</sup> After

labeling, a time delay is necessary before the actual MRI acquisition to allow the labeled arterial water protons to flow through the arterial tree and to exchange with the unlabeled tissue water. Thus far, ASL techniques have been used predominantly to measure tissue perfusion of the brain by nonselectively labeling of all the feeding arteries. Recently, 2-dimensional pencil-beam pulses or local surface coils have been developed for selective labeling of the arteries in the neck.<sup>7-9</sup> However, these ASL methods are only partially selective, and significant magnetically labeling of the other arteries in the neck occurs. Furthermore, when local surface coils are used, only superficial arteries in the neck (ie, common carotid artery) can be labeled, excluding separate labeling of the posterior circulation.<sup>7,8</sup> Although labeling of the posterior circulation is possible with a pencil-beam labeling profile, no cerebral blood flow (CBF) values have been obtained with this method so far.<sup>9</sup>

We introduce here a spatially selective labeling approach, regional perfusion imaging (RPI), which is based on selective

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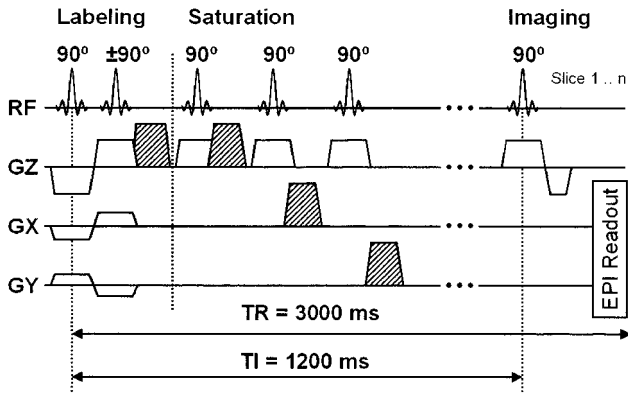
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**Figure 1.** Sequence for RPI. Inversion of inflowing spins is achieved by applying 2 consecutive slice-selective 90° RF pulses in a slab that can be angulated freely with respect to the imaging slice, as seen in Figure 2 (In this illustration, an example of double-angulation is presented). In control scan, the phase of the second 90° pulse is shifted by 180°, as in the TILT sequence. Three 90° saturation pulses, followed by strong dephasing gradients (shaded), are applied after RPI labeling to ensure proper elimination of any remaining static magnetization. After labeling delay time TI (inversion time) of 1200 ms, 5 slices are acquired in a descending slice order. Sequence is repeated every 3 seconds to ensure proper signal-to-noise ratio.

slab inversion of the arterial water with a pulsed ASL sequence. In the present study, we show the ability of RPI to selectively label the left internal carotid artery (ICA), right ICA, and posterior circulation (basilar artery and vertebral

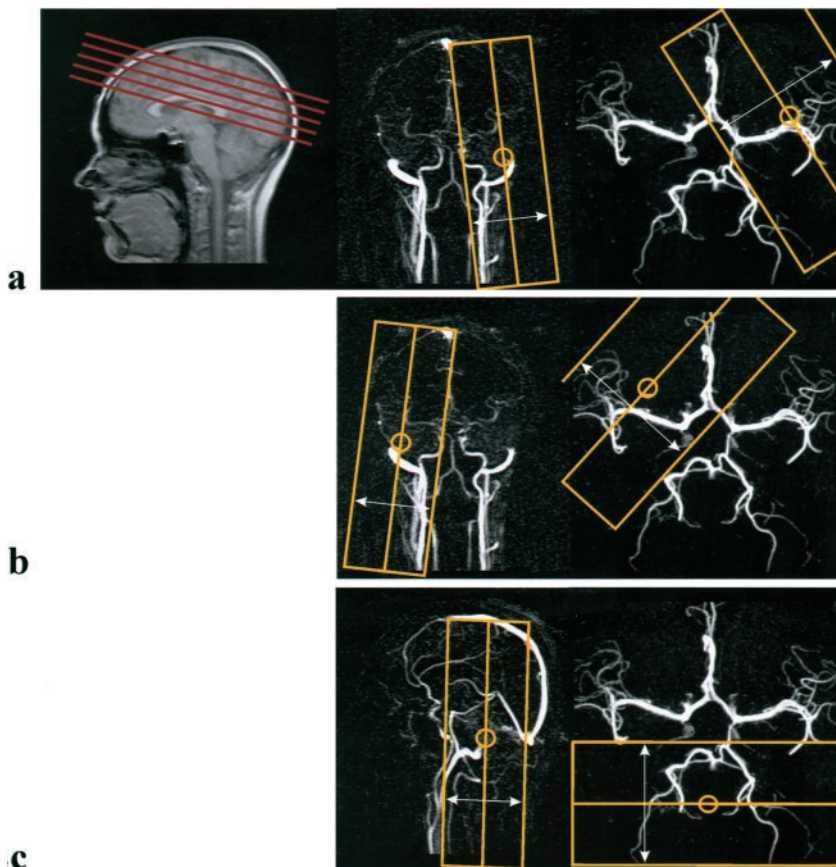
arteries). Furthermore, CBF values are measured in regions of interest (ROIs) within the individual perfusion territories of the selectively labeled cerebral arteries.

## Methods

### MR Pulse Sequence

The RPI sequence is shown in Figure 1. The inversion of inflowing spins is achieved by applying 2 consecutive slice-selective 90° radiofrequency (RF) pulses in a slab. This labeling slab can be in any angulation with respect to the imaging slices, according to the specific arteries one wants to label (eg, see Figure 2). In the control scan, the phase of the second 90° pulse is shifted by 180°, yielding an excellent labeling slice profile and nulling globally the magnetization transfer effects, as shown previously for the pulsed transfer insensitive labeling technique (TILT).<sup>10,11</sup> Subsequently, 3 saturation pulses are applied to remove the effects of the labeling pulses on the imaging slices. Each saturation pulse is followed by a series of strong dephasing gradients in all 3 directions to spoil every remaining transverse magnetization (Figure 1). When this saturation/dephasing scheme is not used, a high-intensity band is present in the perfusion-weighted images (label control) at the intersection of the labeling slab and imaging slices.

In the present study, the range of the saturation slab was set from 10 mm below the lowest imaging slice to 45 mm above the highest imaging slice. This asymmetric saturation slab was used to minimize the gap between the labeling slab and imaging slices (eg, 10 mm) and to reduce the signal contribution of veins. The saturation slab was positioned parallel to the imaging slice, and the total width of the saturated volume was 99 mm. The labeling delay time TI (inversion time) was set to 1200 ms to avoid unwanted macrovascular signal, which will be present at shorter TIs.<sup>12</sup> Other MR parameters were as follows: repetition time (TR), 3000 ms; echo time (TE), 5.6 ms; 62% half-Fourier acquisition; number of slices, 5; slice thickness, 8 mm;



**Figure 2.** Scan plan for selective labeling of left ICA (a), right ICA (b), and posterior circulation (c). Five imaging slices were planned parallel to the orbitomeatal line. Oblique sagittal labeling slab for selective labeling of ICA was planned using the MIP of the circle of Willis and coronal survey (a, b). Coronal labeling slab for selective labeling of the posterior circulation was planned using the MIP of the circle of Willis and the sagittal survey PC (c).

Mean CBF Values and Mean Percentage Signal Change for RPI

Labeled Artery	Brain Region	Expected Perfusion Territory		Nonlabeled Territory $\Delta M/M_0$ , %
		$\Delta M/M_0$ , %	CBF, $\text{mL} \cdot \text{min}^{-1} \cdot 100 \text{ g}^{-1}$	
Left ICA	Hemisphere	0.62±0.04	38.5±2.6	0.00±0.01
	Gray matter	1.03±0.07	64.9±4.5	0.01±0.01
	White matter	0.36±0.03	22.8±1.6	0.00±0.01
Right ICA	Hemisphere	0.66±0.04	41.8±2.9	0.01±0.01
	Gray matter	1.06±0.08	66.8±4.7	0.01±0.01
	White matter	0.34±0.02	21.4±1.3	0.01±0.01
Posterior circulation	Gray matter	1.14±0.09	71.8±5.5	0.06±0.01

Mean±SEM percentage signal change ( $100\% \times \Delta M/M_0$ ) and mean±SEM CBF for selected ROIs in the hemispheres, gray matter, and white matter of the image slices of 8 control subjects.

slice gap, 1 mm; slice order, descending; time between slices, 25 ms; field of view, 240×240 mm; matrix, 64×64; zero filling to 128×128 matrix; averages, 50; and RPI scan time, 5 minutes.

### MRI Experiments

Experiments were performed on a clinical 1.5-T MRI scanner (Philips Medical Systems) using standard body coil transmission and head coil signal reception. Two localizer MR angiography (MRA) scans in coronal and sagittal orientations were performed to visualize the ICAs and basilar artery (coronal: slices, 1; thickness, 60 mm; sagittal: slices, 2; thickness, 50 mm; slice gap, -5 mm [overlapping slices]). Other parameters were as follows: field of view, 250×250 mm<sup>2</sup>; TR/TE, 14/7 ms; flip angle, 20°; velocity sensitivity, 30 cm/s; and averages, 4. To visualize the circle of Willis, a 3-dimensional time of flight (TOF) MRA measurement was performed (TR/TE, 30/6.9 ms; flip angle, 20°; field of view, 100×100 mm; matrix size, 256×256; averages, 2; slice thickness, 1.2 mm; slice gap, -0.6 mm [overlapping slices]; number of slices, 50) with subsequent maximum-intensity projection (MIP) reconstruction. The control and patient studies were performed with the same RPI scan parameters. Total scan time for localizer phase-contrast (PC) surveys (1 minute), MRA (3 minutes), planning of labeling volumes (1 minute), and RPI (15 minutes) was 20 minutes.

Planning of the labeling volume was performed on the basis of PC surveys and TOF MR angiograms (Figure 2). The size of the labeling slab can be adjusted in 1 direction and is infinite in the other 2 directions. The 5 imaging slices were planned parallel to the orbitomeatal angle, and the occipital lobe was included in the lower 2 to 3 slices. For selective labeling of ICAs, an oblique sagittal labeling slab was chosen on the basis of the MIP of the circle of Willis and coronal PC survey. The slab was aligned so that the left (Figure 2a) and right (Figure 2b) ICAs were labeled and signal contribution from the basilar artery and vertebral arteries was avoided by laterally angulation of the posterior and proximal parts of the labeling slab. For the selective labeling of the posterior circulation, a coronal labeling slab was used on the basis of the MIP of the circle of Willis and sagittal PC survey. The slab was aligned so that the basilar artery and vertebral arteries were labeled and signal contribution from the ICAs was avoided by positioning the labeling slab parallel but posterior to the ICAs on the sagittal PC survey (Figure 2c). Because of the anatomical configuration of the vessels in the neck, unwanted labeling of the proximal ICAs will be present in about one third of the subjects. The 5 imaging slices can be freely positioned in any orientation with respect to labeling volume.

All volunteers (n=8; age range, 24 to 57 years; 4 men, 4 women) and the patient (n=1; age, 62 years; female) gave written informed consent before participating in the study. The RPI patient example was scanned 1 month after extracranial-intracranial (EC-IC) bypass surgery and balloon occlusion of the right ICA for treatment of a

giant aneurysm of the right ICA. The study protocol was approved by the Institutional Review Board.

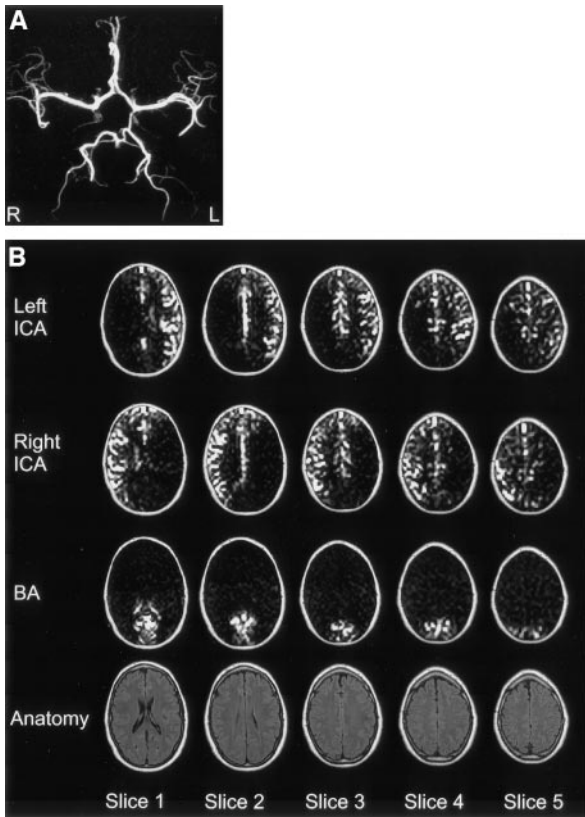
### Data Processing

Data were processed on a Sun Enterprise Server (Sun Microsystems) with MATLAB (Mathworks). Time required for RPI data processing was 15 minutes. Perfusion-weighted images of the flow territories of the selectively labeled cerebral arteries were obtained by subtraction of the labeled from control images. For a better anatomical reference, the fat signal of the anatomical images was projected on the RPI images. For CBF quantification, ROIs were selected in the gray matter, white matter, and complete hemisphere on the basis of the control images. Because of the relatively small flow territory of the posterior circulation, no quantification of the white matter perfusion in the posterior circulation could be performed. To quantify CBF, perfusion-weighted ASL signal was fitted to the perfusion model described by Calamante et al<sup>13</sup> with the following values for the physical constants:  $\alpha$  (efficiency of the inversion pulse)=1.0,  $T_{1\text{gray matter}}=1000$  ms,  $T_{1\text{white matter}}=700$  ms,  $T_{1\text{blood}}=1400$  ms, and  $\lambda=0.9$  mL/g.<sup>14,15</sup>

### Results

The Table shows the mean±SEM percentage signal change ( $100\% \times \Delta M/M_0$ ) and mean±SEM CBF in the cerebral hemispheres, gray matter, and white matter of all 8 control subjects. When the results of the left and the right ICAs were combined, the mean CBFs were 40.1±1.9, 65.8±3.0, and 22.1±1.0 mL · min<sup>-1</sup> · 100 g<sup>-1</sup> tissue for the complete hemispheres, gray matter, and white matter, respectively, compared with a mean gray matter CBF for the posterior circulation of 71.8±5.5 mL · min<sup>-1</sup> · 100 g<sup>-1</sup> tissue. To demonstrate the selectivity of RPI, the mean percentage signal changes ( $100\% \times \Delta M/M_0$ ) are shown for both the expected perfusion territory and the other (nonlabeled) territories defined as the contralateral hemisphere for ICA labeling and the anterior part of the cerebral hemispheres for labeling of the posterior circulation.

Figure 3 shows in a control subject representative perfusion-weighted images according to RPI labeling of the left and right ICAs and posterior circulation (basilar artery and vertebral arteries). When oblique sagittal RPI labeling of the ICA is used, the flow territory of the basilar artery is excluded (Table 1), and no perfusion-weighted signal is present in the posterior part of the imaging slices. When coronal labeling of the basilar artery is used, perfusion-

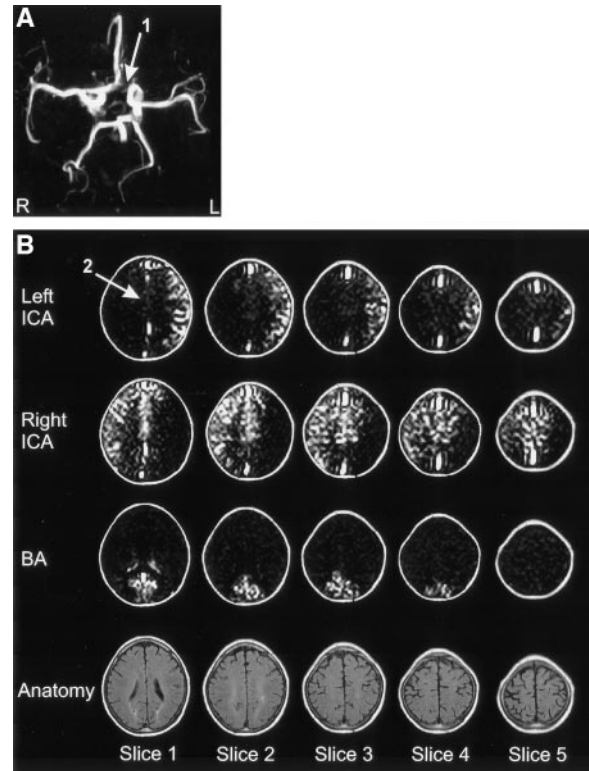


**Figure 3.** a, TOF MRA of a complete circle of Willis. b, Representative perfusion images after RPI labeling of left ICA, right ICA, and posterior circulation (basilar and vertebral arteries) in healthy control subject.

weighted signal is symmetrically present in the posterior part of the imaging slices.

RPI images in a healthy control subject with an incomplete circle of Willis are demonstrated in Figure 4. The MIP reconstruction (Figure 4a) of the TOF MRA from the circle of Willis shows a missing A1 segment of the left anterior cerebral artery (ACA). When RPI labeling (Figure 4b) of the left ICA is applied, perfusion-weighted ASL signal is present in only the left middle cerebral artery (MCA) flow territory, and ACA flow territory is absent. When RPI labeling of the right ICA is applied, perfusion-weighted ASL signal is present in the right MCA flow territory and both the left and right ACA flow territories (signal surrounding midline).

Figure 5 shows the coronal survey PC (Figure 5a) and RPI images (Figure 5b) of the flow territories drained by an EC-IC bypass and the contralateral left ICA in a patient with a balloon occlusion of the right ICA for treatment of a giant aneurysm. The EC-IC bypass is a vein graft connecting the external carotid artery with the distal part of the MCA. When RPI labeling of the EC-IC bypass is used, perfusion-weighted ASL signal is present in the right hemisphere, indicating that the EC-IC bypass is supplying the flow territory of the right-sided MCA. When RPI labeling of the left ICA is applied, perfusion-weighted ASL signal is present in both the left hemisphere and the area surrounding the midline, indicating that the left ICA is supplying the flow territories of the



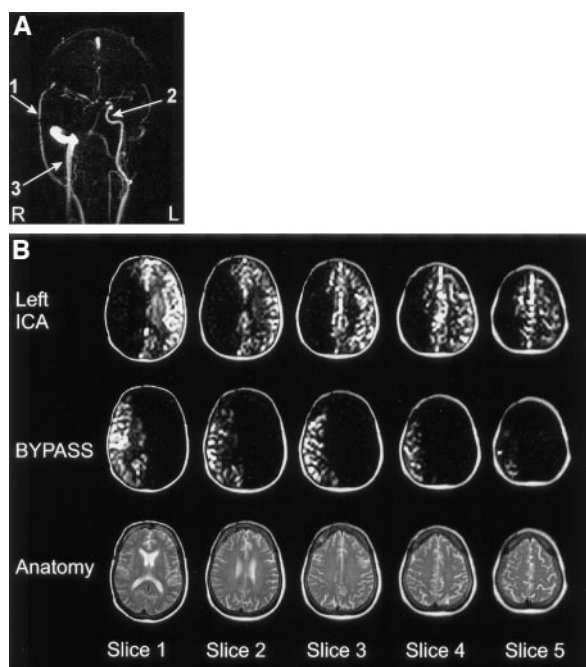
**Figure 4.** a, TOF MRA of the circle of Willis. b, RPI images in a healthy control subject missing the A1 segment of left ACA. 1 indicates missing A1 segment; 2, absent ACA flow territory.

left MCA and both the left and right ACAs. Some labeling of the posterior circulation is present in both RPI series (indicated by arrow 4). No separate posterior RPI images were made in this patient.

### Discussion

We developed a noninvasive method to determine the arterial flow territories with selective ASL labeling of the left ICA, right ICA, and posterior circulation (basilar artery and vertebral arteries). The selectivity of the RPI method was demonstrated in both control subjects and clinical examples. CBF values measured with RPI in the hemisphere ( $40.1 \text{ mL} \cdot \text{min}^{-1} \cdot 100 \text{ g}^{-1} \text{ tissue}$ ), white matter ( $22.1 \text{ mL} \cdot \text{min}^{-1} \cdot 100 \text{ g}^{-1} \text{ tissue}$ ), and gray matter ( $65.8 \text{ mL} \cdot \text{min}^{-1} \cdot 100 \text{ g}^{-1} \text{ tissue}$ ) are in agreement with data from the literature on regional cerebral perfusion.<sup>16,17</sup>

Selective labeling could be achieved because of the sharp labeling profiles of the TILT labeling pulses<sup>11</sup> and the possibility of interactive planning of the spatially selective inversion slabs. Only minimal contamination of the other flow territories is present for the mapping of flow territories of the ICA and posterior circulation (see the Table). Furthermore, because of the use of slab labeling over the whole trajectory (15 to 25 cm) of the cerebral arteries, the RPI method does not lead to a decrease in the signal-to-noise ratio compared with whole-brain ASL. Although selective labeling with sagittal inversion slab has been used for angiography,<sup>18,19</sup> no flow territory mapping or CBF quantification was



**Figure 5.** Coronal survey PC (a) and RPI (b) images of flow territories of EC-IC bypass and left ICA in patient with balloon occlusion of right ICA for treatment of a giant aneurysm. 1 Indicates EC-IC bypass; 2, left ICA; 3, jugular vein; 4, some labeling of posterior circulation.

performed in these studies. Previously, some research articles have been published in which local surface coils were used for selective labeling of the right and left common carotid arteries.<sup>7,8</sup> In these studies, an adiabatic RF pulse scheme was applied with the surface coil with a duration of 2 to 3 seconds for labeling of the arterial blood in the vessels within the sensitivity reach of the coil.<sup>7,8</sup> Because the surface coils allow only superficial labeling of arteries, this method is restricted to selective labeling of either ICA, and no separate labeling of the posterior circulation can be achieved. Recently, another MRI method for selective labeling of ICAs and the basilar artery was proposed in which selective flow labeling was achieved by 2-dimensional labeling pulses forming a pencil-beam profile.<sup>9</sup> When this pencil beam is planned with a gaussian profile parallel to the slices of interest and below the circle of Willis, 2 to 4 cm of the brain feeding arteries could be labeled. However, significant contamination of the perfusion territories of the nonlabeled arteries was still present, and no CBF values were obtained because of the complex labeling scheme used and the absence of global control for magnetization transfer effects.<sup>9</sup> With the pulsed RPI method proposed here, no extra coils are needed, magnetization transfer is compensated for, specific absorption rate (SAR) is kept minimal, and CBF can be quantified by use of well-established perfusion models.<sup>13</sup>

During labeling of the posterior circulation, the curved anatomy of the ICA in the neck will sometimes lead to unwanted labeling of the proximal ICAs. This artifactual residual labeling of the ICAs, however, will be very small because of the poor efficiency of the labeling in this case

(only 1 to 2 cm of the ICAs will effectively be labeled). Consequently, the ICA flow territory will be present as small background signal, which can easily be distinguished from the hyperintense signal in the flow territory of the adequately labeled posterior circulation. Furthermore, during selective labeling of the ICA, care should be taken to exclude the ipsilateral vertebral artery, which is located close to the proximal ICA. With RPI, the signal intensity for the distal flow territory areas is lower compared with the central part of the flow territory. The explanation for the lower signal intensity at the border-zone areas may be found in the increased transit time of the label to these regions. Nevertheless, the present ASL signal in the distal areas allows evaluation of these regions in patients with steno-occlusive carotid disease.

The clinical example shows the ability of RPI to delineate the flow territory of the major cerebral arteries in a patient after EC-IC high-flow bypass surgery. In this example, routine angiography could visualize only the vascular branches supplied by the brain-feeding arteries with no functional information on tissue perfusion. With RPI, qualitative information on the flow territories and quantitative information on the tissue perfusion ( $\text{mL} \cdot \text{min}^{-1} \cdot 100 \text{ g}^{-1}$  tissue) could be acquired in a completely noninvasive manner. This information can be combined with the spatial information provided by routine anatomical MRI scans acquired in the same session.

In conclusion, we demonstrated a noninvasive quantitative MRI approach for separate labeling of a single ICA and posterior circulation and for CBF quantification of the individual perfusion territories. Clinically, perfusion territory mapping with MRI may allow better vascular-anatomic correlations in patients with neurovascular disease and cerebral ischemia. This valuable information can be combined with diffusion/perfusion MRI for a multimodality assessment of ischemic disease.

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