Quantitative Assessment of Mixed Cerebral Vascular Territory Supply With Vessel Encoded Arterial Spin Labeling MRI

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Background and Purpose—Recent advances in arterial spin labeling MRI have permitted noninvasive evaluation of vascular territories. In the present study, we quantitatively assess mixing of internal carotid and basilar artery blood through cerebrovascular anastomoses using vessel-encoded arterial spin labeling and a new postprocessing method.

Methods—Vessel-encoded arterial spin labeling was used to determine the territories of the internal carotid and basilar arteries in 14 healthy subjects and one patient with asymptomatic high-grade carotid artery stenosis before and after endarterectomy. Contributions to individual vascular territories were quantified using a voxelwise supply fraction algorithm and the results were correlated with MR angiography.

Results—Vascular territories were consistent with cerebrovascular anatomy and the presence of pathology. The supply fraction method allowed quantification of mixed territorial supply arising from collateral flow and showed vascular supply changes in a patient with carotid artery stenosis after endarterectomy.

Conclusions—Vascular territories obtained with vessel-encoded arterial spin labeling correlate with cerebrovascular anatomy and allow quantitative assessment of mixed territorial supply in subjects with and without pathology. (Stroke. 2008;39:2980-2985.)

Key Words: carotid endarterectomy  cerebral blood flow  collateral circulation  imaging techniques  magnetic resonance imaging

The selection of appropriate treatment for ischemic stroke depends critically on accurate classification by etiologic subtype. In practice, etiology is inferred from clinical presentation and the pattern of ischemic lesions seen with brain imaging.1–7 Unfortunately, interpretation of lesion patterns is confounded by significant vascular territory variations between individuals.8–13 In this regard, methods to image arterial perfusion territories are likely to have considerable value. Such techniques may also facilitate evaluation and management of cerebrovascular stenosis, mapping of blood supply to arteriovenous malformations, and planning of targeted intra-arterial chemotherapy.14–17

Arterial spin labeling (ASL) MRI offers a method by which to quantitatively and noninvasively assess cerebral perfusion.18–23 ASL uses magnetically labeled protons in arterial water as an endogenous tracer of perfusion to the brain. Although most ASL techniques to date have been designed to measure whole-brain perfusion by simultaneously labeling all feeding arteries, the development of vessel-selective ASL methods in recent years has made it possible to assess perfusion from individual arteries.24–34

In the present study, we use vessel-encoded ASL to image the perfusion territories of the left internal carotid artery (ICA), right ICA, and basilar artery (BA) and analyze these territories using a new postprocessing method based on fractional supply. The purpose of our study was to identify potential clinically relevant information obtainable with vessel-encoded ASL by demonstrating that (1) vascular territory maps are consistent with cerebrovascular anatomy; (2) postprocessing based on supply fraction permits quantification of mixed territorial supply that results from flow through anastomoses; and (3) pre- and postoperative vascular territory mapping in a patient undergoing carotid endarterectomy reveals changes in vascular supply patterns.

Materials and Methods

Subjects and Consent

Fourteen healthy subjects (7 male, 7 female; ages, 22 to 52 years) without known cerebrovascular disease and one patient (female; age 48 years) with asymptomatic high-grade (>90%) stenosis of the right ICA were scanned as part of this study. The patient was scanned twice, 1 month before undergoing uncomplicated carotid endarterectomy and again 9 months after the surgery. The local Institutional Review Board approved the study protocol and informed consent was obtained from all participants in the study, which was conducted in accordance with institutional guidelines.
Data Processing and Analysis

Data were processed using MATLAB (Mathworks, Natick, Mass). Perfusion-weighted images comprised of multiple selected arterial territories were decoded into individual territories based on vessel-specific labeling efficiencies that are measurable from ASL data. This decoding process produced 3 quantitative perfusion territories specific labeling efficiencies that are measurable from ASL data.32,35

Data were processed using MATLAB (Mathworks, Natick, Mass). After a sagittal localizer scan for anatomic reference, we conducted a 3-dimensional time-of-flight MR angiography (MRA) to locate cerebral arteries for labeling in subsequent scans and to identify anatomic variations of the circle of Willis. The MRA was performed with the following parameters: TE 2.7 ms, TR 20 ms, flip angle 15°, field of view 220×165×1 mm with an in-plane resolution of 324×228, and one average. From the MRA slices, we identified an axial labeling plane approximately 30 mm below the circle of Willis in which the ICAs and vertebral arteries had an approximately trapezoidal arrangement and the direction of flow was predominantly inferior to superior.

With the labeling plane chosen, we prescribed 2 serial vessel-encoded ASL scans, the first to separate left ICA and right ICA perfusion and the second to distinguish ICA and BA perfusion (Figure 1). Image slices were positioned parallel to the labeling plane. Parameters of the vessel encoded ASL scan were as follows: TE 3 ms, TR 3400 ms, field of view 220×220×8 mm with slice gap of 2 mm and in-plane resolution of 64×64, 80 averages, single-shot spiral acquisition with fat saturation, 974 tagging radiofrequency pulses, Hanning window shaped with an amplitude of 0.05 G, 800-μs duration, and 1.64-ms spacing for a total tagging time of 1600 ms, a slice selective gradient of 0.8 G/cm amplitude during the radiofrequency pulses and mean gradient of 0.06 G/cm, and 1000 ms postlabeling delay. Total scan time for localizer (1 minute), MRA (7 minutes), and vessel-encoded ASL (each 4.5 minutes) was 17 minutes.

Vascular Mixing

Vascular mixing was characterized by calculating the supply fraction in each voxel. In any voxel perfused by 2 arterial sources with corresponding signals \( S_1 \) and \( S_2 \), the supply fraction is calculated as the ratio of an individual arterial contribution to the total contribution from both arteries, \( S_i/(S_1+S_2) \times 100\% \). This quantity is 0% or 100% except in those voxels supplied in part by both arteries, where it adopts intermediate values. Supply fractions were calculated in each voxel and combined into a map of supply fractions. A histogram of these supply fractions was also constructed, demonstrating peaks at 0% and 100% with additional peaks at intermediate values for each mixed territory.

The extent of mixing in vascular territories was quantified by computing the mean supply fraction in each territory. In territories with mixed supply, the mean supply fraction was measured as the mean of Gaussians that were fitted to each peak in the supply fraction histogram using automated routines in MATLAB. The correspondence of each histogram peak to a given vascular territory was verified against the average supply fraction within manually selected regions of interest covering the approximate extent of each vascular territory. These region of interest-based supply fraction estimates were used only for verification of mean supply fraction calculated from the histogram, but nonetheless yielded excellent agreement in each territory. In territories with pure, unmixed supply that did not produce intermediate peaks in the supply fraction histogram suitable for fitting, the lack of mixing was verified using the region of interest method only.

Vascular territories and supply fraction data were visually compared against time-of-flight MRA of the circle of Willis. A territorial supply was considered nonstandard if greater than 5% was derived from a source other than the ipsilateral ICA in the case of the anterior cerebral artery or middle cerebral artery territories or the BA in the case of the posterior cerebral artery territories. The 5% threshold was chosen empirically based on the level of noise present in the supply fraction maps.

Results

Vascular Territory Maps

Vascular territory maps and corresponding MRAs from 3 subjects showing 3 different degrees of mixing are pictured in Figure 2. If there is no flowthrough communicating arteries, the anterior cerebral artery (ACA) and middle cerebral artery (MCA) territories are supplied by the ipsilateral ICA, and the posterior cerebral artery (PCA) territories are supplied bilaterally by the BA. With congenital absence of the left A1 segment, the left ACA territory is completely supplied by the contralateral ICA through the anterior communicating artery (ACoA). In an intermediate case, the right ACA territory is partially supplied by the left ICA and the right PCA territory is supplied primarily by the ipsilateral ICA, the latter due to a right fetal P1 variant in which the proximal PCA is narrowed and the ipsilateral posterior communicating artery (PCoA) is enlarged.

The sharp transitions between adjacent territories, as is seen along the interhemispheric fissure in subjects with no ACoA flow, reflect the quality of vascular separation possible with vessel-encoded ASL. The small artifacts visible outside the boundaries of the brain are due to inadvertent labeling of extracerebral vessels that were not specifically included in our analysis.

Supply Fraction Analysis

Quantification of territorial supply is accomplished by calculating supply fraction maps and drawing histograms of the supply fraction in each voxel (Figure 3). In a subject lacking the left A1 segment, comparison of ICA and BA
perfusion reveals that most voxels receive pure supply from either the ICA or BA as indicated by a lack of large-scale territorial mixing that would otherwise produce additional histogram peaks with intermediate supply fraction. Those few voxels that are perfused by both arteries occur at territorial interfaces, where the source of perfusion transitions. Comparing left and right ICA perfusion yields similar results with the notable finding that the left ACA territory receives 95% of its supply from the right ICA. The difference between the measured and theoretical supply fraction of 100% to this territory is attributable to noise in the supply fraction map.

In a subject with a right fetal P1 and double ACoA, the right PCA territory receives only 24% of its supply from the BA with the remaining 76% drawn from the right ICA. In addition, the right ACA territory receives 58% of its supply from the left ICA. Because mixing in these 2 cases affects entire territories, there is a sufficient number of voxels with
similar supply fraction to create additional peaks in the supply fraction histograms.

Anatomic Correlation of Vascular Territories

Supply fraction maps calculated in 15 subjects correlated well with vascular anatomy seen with time-of-flight MRA (Table). Of these subjects, 11 of 15 (73.3%) possessed at least one arterial territory with a nonstandard vascular supply.

The ACA territory is supplied by either the ipsilateral A1 segment or the ACoA. In the 2 of 15 (13.3%) subjects with unilateral A1 absence, the ipsilateral ACA territory receives essentially all of its supply from the contralateral ICA through the ACoA. Flow through the ACoA is not limited to just these cases, however, because 6 of 13 (46.2%) subjects with bilaterally intact A1 segments have partial ACA supply from the contralateral ICA. We found no instances in which both ACA territories received blood from the contralateral ICAs. This finding is expected on the grounds that flow through a single ACoA must be unidirectional, but holds true even for the 2 of 15 (13.3%) subjects with double ACoA.

ICA supply to the ipsilateral PCA territory occurs through the PCoA and was seen in 6 of 15 (40.0%) subjects. The ICA contribution to PCA supply was greatest in the 3 of 15 (20.0%) subjects with fetal P1 configuration. There was no evidence of ICA supply in any of the 8 of 30 (26.7%) PCA territories with ipsilateral PCoA absence. Additionally, there were no cases of ICA supply to the contralateral MCA or PCA territories.

The BA represented a nonstandard blood source in one of 15 (6.7%) subjects. In this case, the mean BA supply fraction in the affected ACA and MCA territories was equal, consistent with the observed PCoA origin 7 mm inferior to the ICA bifurcation leading to delivery of mixed blood to both the ACA and MCA territories.

Endarterectomy

Pre- and postoperative vessel-encoded ASL imaging performed in a patient with right fetal P1 configuration and asymptomatic high-grade (>90%) stenosis of the right ICA revealed the hemodynamic effect of the stenosis as well as improvement of perfusion patterns after successful carotid endarterectomy (Figure 4). Preoperatively, the right ACA territory received 95% of its supply from the left ICA, and the

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**Table. Quantification of Atypical ICA and BA Contributions to ACA, MCA, and PCA Territories**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Anatomical Variations</th>
<th>Left ACA</th>
<th>Left MCA</th>
<th>Left PCA</th>
<th>Right ACA</th>
<th>Right MCA</th>
<th>Right PCA</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>2</td>
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<td></td>
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<tr>
<td>3</td>
<td>None</td>
<td>16% left ICA</td>
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<tr>
<td>4</td>
<td>None</td>
<td>49% left ICA</td>
<td></td>
<td></td>
<td>12% BA</td>
<td>12% BA</td>
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<tr>
<td>5</td>
<td>None</td>
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<td></td>
<td>52% left ICA</td>
<td>26% right ICA</td>
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<tr>
<td>6</td>
<td>Absent left A1</td>
<td>95% right ICA</td>
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<td></td>
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<tr>
<td>7</td>
<td>Absent right A1, absent right PCoA</td>
<td></td>
<td></td>
<td></td>
<td>94% left ICA</td>
<td></td>
<td></td>
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<tr>
<td>8</td>
<td>Right fetal P1, double ACoA</td>
<td></td>
<td></td>
<td></td>
<td>58% left ICA</td>
<td>76% right ICA</td>
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<tr>
<td>9</td>
<td>Left fetal P1</td>
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<td></td>
<td></td>
<td>96% left ICA</td>
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<tr>
<td>10</td>
<td>Double ACoA, absent left PCoA</td>
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<td>26% right ICA</td>
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<tr>
<td>11</td>
<td>Absent left PCoA</td>
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<td>38% right ICA</td>
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<tr>
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<td></td>
<td>47% right ICA</td>
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<tr>
<td>13</td>
<td>Absent left PCoA</td>
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<td></td>
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<tr>
<td>14</td>
<td>Absent bilateral PCoA</td>
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</tr>
<tr>
<td>15-1†</td>
<td>Right fetal P1, absent left PCoA</td>
<td></td>
<td></td>
<td></td>
<td>95% left ICA</td>
<td>50% right ICA</td>
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</tr>
<tr>
<td>15-2†</td>
<td>Right fetal P1, absent left PCoA</td>
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<td></td>
<td>16% left ICA</td>
<td>83% right ICA</td>
<td></td>
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</tbody>
</table>

*Empty entries indicate <5% supply fraction from an atypical source.
†15-1 and 15-2 are collected from the same subject before and after carotid endarterectomy, respectively.

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Figure 4. Vascular territories in a patient with right fetal P1 undergoing carotid endarterectomy for asymptomatic high-grade right ICA stenosis. A, Preoperatively, collateral supply is manifested as left ICA supply to the right ACA territory and partial BA supply to the right PCA territory despite the fetal P1 anatomy. B, Postoperatively, there is normalization of right ICA perfusion with corresponding reduction of collateral supply to the right ACA and PCA territories.
right PCA territory received 50% of its supply from the right ICA and 50% from the BA. The stenosed right ICA supplied 37% of the total cerebral blood flow. In light of the fetal P1 anatomy, mixed supply to the ACA and PCA territories was interpreted as collateral flow compensating for impairment of right ICA perfusion. Postoperatively, there was normalization of flow with the right ACA territory receiving only 16% of its supply from the left ICA, and the right PCA territory drawing a much smaller 17% of its supply from the BA, consistent with the variant anatomy. The right ICA supply had increased to 46% of total cerebral blood flow.

Discussion

There are 3 primary findings of the present study. First, vascular territory maps generated in vivo using vessel-encoded ASL can be processed using a supply fraction algorithm into quantitative maps of territorial supply. Second, territory and supply fraction maps are consistent with cerebrovascular anatomy. Third, characterization of pre- and postoperative vascular territory supply in a patient undergoing carotid endarterectomy can provide information about perfusion changes.

In subjects with anatomic variations of the circle of Willis, we found corresponding variations in ICA and BA supply territories relative to standard territory maps. However, we also identified a high proportion of subjects with flow through nonvariant communicating arteries, manifest in our analysis as territorial mixing.

Variations of vascular territory supply have been the subject of interest for many years. As the most recent investigations using a pulsed ASL method have demonstrated many of the same territorial variations that are reported in the present study. However, in our study, we are able to quantify the fractional contributions of the major feeding arteries on a territory-by-territory basis instead of indicating only presence or absence of supply. Furthermore, although we have not done so here, our technique permits absolute quantification of individual arterial contributions to each vascular territory in terms of blood flow per unit tissue. Such measurements require only the inclusion of calibration scans, which contribute minimally to total scan time.

Two independent mechanisms permitted the sharp discrimination of vascular territories that is essential to accurately quantify mixed territorial supply. First, in contrast to pulsed ASL techniques, vessel discrimination with vessel-encoded ASL depends only on the distance between arteries as they traverse a 20-mm thick plane. As such, geometric confounders such as vascular curvature do not interfere with selective labeling. Second, the method corrects for vessel-specific labeling efficiencies and allows for significantly improved separation of vascular contributions. Without these mechanisms in place, vessel-selective labeling is susceptible to inadvertent labeling of nontargeted vessels, which is likely to produce inaccurate estimates of mixed territorial contributions.

Application of the vessel-encoded method in a patient with asymptomatic high-grade carotid artery stenosis before and after surgical intervention demonstrates a large shift in vascular distribution. Earlier studies of postendarterectomy perfusion using bolus-tracking methods have shown that changes in inflow transit times are complex and continue to evolve as late as 1 year after the intervention. We assessed perfusion changes in a distinct way in terms of alterations in vascular supply, but our data should nonetheless be interpreted with caution because cerebral blood flow changes after surgical or endovascular intervention are not fully understood.

Assessment of territorial supply with ASL adds insight into physiological perfusion that is not obvious from MRA alone. In particular, MRA can reveal the course and caliber of the feeding arteries, but not the destination of blood contained within each vessel. In this sense, the information provided by our method is more similar to conventional contrast angiography but can be obtained entirely noninvasively without contrast or placement of a catheter that can potentially disrupt physiological flow patterns.

The primary limitation of this study is the lack of validation of supply quantification with alternate imaging modalities. Findings in each subject are compatible with MRA and, as a group, appear to be consistent with previous studies of territorial variability. Nevertheless, because most imaging was conducted in healthy subjects, there was no justification for more invasive techniques that may have permitted independent verification of supply quantification on a subject-by-subject basis.

In summary, vessel-encoded ASL produces vascular territory maps that contain quantitative information about mixed arterial supply to cerebral vascular territories consistent in each case with circle of Willis anatomy and the presence of pathology. Additional testing in healthy subjects and patients with cerebrovascular disease, including separation of arterial sources above the circle of Willis, will further clarify the clinical role of this new method.

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Disclosures

None.

References

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