Relation Between Cerebral Perfusion Territories and Location of Cerebral Infarcts

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Background and Purpose—The perfusion territories of the brain-feeding arteries are difficult to assess in vivo and therefore standard cerebral perfusion territory templates are often used to determine the relation between cerebral infarcts and the feeding vasculature. In the present study, we compared this infarct classification, using standard templates, with the individualized depiction of cerebral perfusion territories on MRI.

Methods—The ethics committee of our institution approved the study protocol. A total of 159 patients (92 male, 67 female; mean age, 58.9 years) with first-time clinical symptoms of cerebral ischemia were included in the study. Diffusion-weighted imaging was used for depiction of the area of ischemia and the perfusion territories of the left internal carotid artery, right internal carotid artery, and verteobasilar arteries were visualized with territorial arterial spin labeling MRI. Infarct locations with respect to cerebral perfusion territories were evaluated with and without territorial arterial spin labeling MRI images.

Results—In 92% of the patients, the territorial arterial spin labeling images were of diagnostic quality. One hundred thirty-six patients showed areas of ischemia on diffusion-weighted images. The additional information from the territorial arterial spin labeling images changed the classification in 11% of the cortical or border zone infarcts (6 of 56), whereas no territorial changes were observed in lacunar, periventricular, cerebellar, and brainstem infarcts.

Conclusion—The diagnostic information provided by perfusion territory imaging in patients with stroke is valuable for the classification of cortical and border zone infarcts, whereas no change of the textbook-based classification was observed for other infarct types. (Stroke. 2009;40:1617-1622.)

Key Words: cerebral hemodynamics ▪ collateral circulation ▪ magnetic resonance imaging ▪ perfusion ▪ stroke

The classification of cerebral infarcts into different subtypes is based on the clinical presentation, anatomic location of the infarcts, and the presumed perfusion territories of the major brain-feeding arteries. For instance, the classification of clinical strokes according to the Oxfordshire Community Stroke Project makes a distinction among anterior circulation infarcts, posterior circulation infarcts, and lacunar infarcts. In addition, the classification of an infarct into the subtype of large artery atherosclerosis, according to the Trial of Org 10172 in Acute Stroke Treatment criteria, implies knowledge of the brain tissue area supplied by these large arteries. The location of cerebral infarcts can easily be assessed from anatomic MRIs or CT and the even more sensitive MR-based diffusion-weighted images (DWIs). Still, the perfusion territories of the brain-feeding arteries are difficult to assess. Standard perfusion territory templates are frequently used to determine the relationship between an infarct and the feeding vasculature. Because of the large between-subject variability in the perfusion territories of the brain-feeding arteries, especially in patients with cerebrovascular disease, these standard perfusion territory templates may fall short.

Recently, territorial arterial spin labeling (TASL) MRI has been introduced as a technique for the assessment of the perfusion territories of the individual brain-feeding arteries. With TASL MRI, the blood water protons in a single brain-feeding artery are magnetically labeled and a delay allows the magnetically labeled blood to travel to the brain tissue before image acquisition. Subsequent subtraction of this image from a control image in which no magnetic labeling is performed will show the perfusion territory of that single artery. The advantage of TASL, as compared for instance with digital subtraction catheter angiography, resides in its noninvasiveness and excellent correlation with cross-sectional anatomic and DWI MRI images. Thus far, TASL MRI has been mainly applied in patient populations with extracranial or intracranial atherosclerotic disease. To the best of our knowledge, no previous study has combined TASL MRI with DWI in patients with stroke. TASL MRI in combination with DWI may link the anatomic location of
infarcts with the perfusion territories of the individual brainfeeding arteries.

The aim of the present study is to investigate the feasibility of TASL within routine stroke imaging and to study the relationship between infarct location and perfusion territories depicted with DWI and TASL MRI, respectively. Furthermore, we investigate the number of patients in which the perfusion territory information provided by TASL MRI changed the infarct classification based on standard perfusion territory templates.

Materials and Methods

Patients

The ethics committee of our institution approved the study protocol and written informed consent was obtained from all patients. A total of 159 patients (92 male, 67 female; mean age, 58.9 years; age range, 25 to 89 years) with clinical symptoms of cerebral ischemia and no history of previous cerebrovascular disease were included in the study. Patients were recruited from the Department of Neurology and the average time between the start of the ischemic symptoms and the research MRI examination, including the TASL MRI scans, was 3 days 10 hours ± 2 days 5 hours (mean ± SD). Clinical stroke scoring was performed by a stroke neurologist according to a clinical classification of acute ischemic stroke.

Magnetic Resonance Imaging

All MRI studies were performed on a 3.0-T Philips Achieva System (Philips Medical Systems, Best, The Netherlands). Images were acquired using the quadrature body coil for transmission and an 8-element phased-array head coil for MR signal reception. The scan protocol for each patient, including conventional MR localizer and SENSE reference scan, consisted of a time-of-flight MR angiogram followed by TASL MRI scans for consecutive labeling of the 3 vascular territories of the left and right internal carotid artery (ICA) as well as the posterior circulation. For the arterial spin labeling (ASL) perfusion territory MRI, we used the recently developed QUAntitative STAR labeling of Arterial Regions (QUASAR) pulse sequence. This sequence is capable of acquiring images at multiple time points and is therefore provides dynamic information about the bolus and its arrival to the tissue. The readout was performed using a conventional multislice single-shot gradient echoplanar imaging with a small flip angle. This resulted in the following scan parameters for the QUASAR sequence for perfusion territory imaging: 7 slices; thickness = 8 mm; gap = 1 mm; matrix = 64 × 64; field of view = 240 mm; α = 35°; TR/TE = 4000/23 ms; TI/ΔTI = 50/390 ms; time points = 10; SENSE = 3; 96 averages (32 for each territory); scan time 6:40 minutes. The planning of the labeling volume for the vascular territories was performed according to Hendrikse et al13 on the basis of the maximum intensity projections and native data from the time-of-flight MR angiogram covering an area spanning from the carotid bifurcation to the circle of Willis. The size of the oblique labeling slab can be adjusted in one direction and is infinite in the other 2 directions. Labeling slabs covering the ICAs were planned on the basis of the axial and coronal maximum intensity projections and aligned such that each ICA was labeled independently (Figure 1). Signal contribution from the contralateral ICA as well as the basilar and vertebral arteries was avoided by appropriate angulations. The posterior circulation was planned using both axial and sagittal maximum intensity projections of the circle of Willis. The planning for all territories was verified on the native time-of-flight images to minimize the amount of contamination by the other territories, although it was not always completely avoidable. The MRI studies, including the planning of the perfusion territory MRI scans, were performed by a group of 4 well-trained MR technicians. The scan parameters for the DWI were: 21 slices; thickness = 5 mm; gap = 1 mm; matrix = 256 × 256; field of view = 240 mm; α = 90°; TR/TE = 2412/80 ms; b = 1000/s/mm² in 3 directions; SENSE = 2; scan time 53 seconds.

Postprocessing

All images were exported on a Windows PC running IDL 6.1 (Research Systems Inc, Boulder, Colo). The labeled and nonlabeled perfusion territory ASL images were first subtracted to produce ΔM images of the difference perfusion signal, one for each of the individual territories. These images were subsequently combined into a red--green--blue frame to demonstrate simultaneously the individual blood supply from the left ICA, right ICA, and posterior circulation to the brain tissue. The left ICA is visualized in green, the right ICA in red, and the posterior circulation in blue. Areas demonstrating mixing of perfusion from more than one vessel will show a combined color, e.g., perfusion contributed by both ICAs may be visualized as yellow and perfusion contributed by the posterior circulation and the left ICA will be visualized as cyan, whereas contributions from the posterior circulation and the right ICA will be visualized as magenta. The color ΔM images described are saved with all the inversion times behind each other as a movie file to visualize the dynamic aspects of the bolus such as time of arrival and the duration of the bolus, which can differ between regions due to, for example, collateral perfusion. The TASL images in the patient examples are shown at a single inversion time of 1220 ms. All territories were manually masked based on the TASL data and subsequently registered to Montreal Neurological Institute-based atlas14 to provide an overview image of the extent and variability of the TASL perfusion territories.

Infarct Location

In a first step, the infarct location, with respect to the perfusion territories of the brain-feeding arteries, was evaluated based on the DWI images in combination with standard textbook perfusion territory templates. Based on these templates, the location of the areas of high signal intensity on the DWI images were judged to be located in the anterior circulation, fed by the left ICA or the right ICA, or the posterior circulation, fed by the vertebrobasilar arteries. Intraobserver reproducibility of the DWI-based scoring of perfusion territories was assessed using a kappa test. In a second step, the infarct location was re-evaluated based on the DWI images in combination with the individual perfusion territory ASL images acquired in each patient. The location of the high signal intensity area on the DWI images was visually matched to the artery feeding that specific area on the perfusion territory images. A distinction

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Figure 1. Positioning of the labeling slab for TASL using the axial, sagittal, and coronal maximum intensity projects of the time-of-flight MR angiogram. Right ICA labeling in red, left ICA labeling in green, and posterior circulation labeling in blue.
between anterior circulation, fed by either the left ICA or right ICA, and the posterior circulation could be made directly on the basis of these images. In Step 1, the reviewer was unaware of the TASL MRI images and in Step 2, the reviewer was blinded to the results of the first assessment based on the DWI images alone. The first and second steps were separated by more than 3 days.

### Statistical Analysis
The number of infarcts located in a specific perfusion territory (left ICA, right ICA, and posterior circulation) were counted for the evaluation of the DWI images alone using standard textbook perfusion territory templates (Step 1) and the evaluation of the DWI images in combination with the TASL MRI perfusion territory images of each patient (Step 2). The number and percentage of discrepancies between Step 1 and Step 2 were calculated.

### Results
In 3 of the 159 patients, the complete TASL data were not acquired due to logistic reasons. In 143 of the remaining 156 patients (92%), the TASL images were of diagnostic quality. In the other 13 patients, the TASL images were degraded due to severe patient motion and these patients were excluded from further analysis. A clinical syndrome of a total anterior circulation infarction was found in 10 of the 143 patients (7%), a partial anterior circulation infarction in 43 patients (30%), a lacunar infarction in 49 patients (34%), a posterior circulation infarction in 36 patients (25%), and a transient ischemic attack in 3 patients (2%). Clinical stroke scoring was incomplete in 2 patients. The MR angiographic images showed an occlusion of the anterior cerebral artery in 3 of the 143 patients, an occlusion of the middle cerebral artery in 3 patients, and an occlusion of the posterior cerebral artery in 3 patients. Furthermore, 3 patients showed an occlusion of the internal carotid artery and 2 an occlusion of the vertebrobasilar arteries. The prevalence of a fetal-type posterior communicating artery was 22% (31 of 143 patients) and the prevalence of an absent or hypoplastic A1 segment was 13% (19 of 143 patients).

Figure 2 shows for the 143 patients a summary image of the extent and variability of the TASL MRI perfusion territories maps (n=143 patients) for the left ICA, the right ICA, and the vertebrobasilar arteries, respectively. Colors correspond to the color bar, which indicates the percentage of patients who demonstrated perfusion in that region of the brain. The last row shows the combined TASL perfusion territory maps using the color coding with the left ICA in green, right ICA in red, and vertebrobasilar arteries in blue.

![Figure 2](https://example.com/figure2.png)

The locations of infarcts based on the DWI changes are listed in the Table. DWI showed no infarcts in 7 of the 143 eligible patients and recent infarcts at multiple (2 or more) locations in 22 patients.

<table>
<thead>
<tr>
<th>Infarct Locations</th>
<th>n=143 Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>No infarct on DWI</td>
<td>7</td>
</tr>
<tr>
<td>Two or more infarct locations</td>
<td>22</td>
</tr>
<tr>
<td>Cortical territory infarct</td>
<td>54</td>
</tr>
<tr>
<td>Lacunar infarct</td>
<td>44</td>
</tr>
<tr>
<td>Subcortical infarct</td>
<td>26</td>
</tr>
<tr>
<td>Border zone infarct</td>
<td>2</td>
</tr>
<tr>
<td>Pons or brainstem infarct</td>
<td>23</td>
</tr>
<tr>
<td>Cerebellar infarct</td>
<td>12</td>
</tr>
</tbody>
</table>

Based on the hyperintense regions on the DWI scans and standard textbook perfusion territory maps, 52 infarcts were classified as posterior circulation infarcts. Furthermore, 98 infarcts were classified as anterior circulation infarcts, of which 55 were classified to the left ICA and 43 to the right ICA. Fourteen patients showed infarcts in multiple (2 or more) territories. The kappa for the intraobserver reproducibility of the DWI-based scoring of perfusion territories (right ICA, left ICA, and posterior circulation) was 0.85. The additional knowledge of the TASL images changed the classification in 11% of cortical or border zone infarcts (6 of 56), whereas no territorial change was observed in the infarcts classified as lacunar (Figure 3), periventricular, cerebellar, and brainstem. Infarct classification changed in 3 patients with anterior circulation infarcts being supplied by the contralateral ICA (Figure 4) and in 3 patients with posterior circulation infarcts being supplied by the ipsilateral ICA (Figure 5). Although the infarcts were reclassified in only a minority of the patients, in a series of patients, the TASL perfusion territory images clearly depicted that the infarcts were located in a cerebral border zone region between different perfusion territories (Figure 6).

### Discussion
In the present study, we show that TASL MRI can be successfully added to a routine MRI protocol of patients with
stroke for the noninvasive assessment of the perfusion territories of the brain-feeding arteries. In only a minority of the patients the textbook-based classification of cerebral infarcts changed with additional knowledge of the perfusion territories in the individual patients with stroke.

To the best of our knowledge, this is the first ASL study in patients with stroke with the TASL MRI method to show the relationship between infarct location and the perfusion territories of the individual brain-feeding arteries. TASL MRI can depict the perfusion territories of the individual brain-feeding arteries noninvasively, comparable to digital subtraction catheter angiography. An advantage of TASL MRI, compared with catheter angiography, is the possibility to perform a comparison of cross-sectional MRIs such as DWI images with the perfusion territory images.

In our study, we found a large interpatient variability in perfusion territories in patients with stroke as has been reported previously for a population without cerebrovascular disease. However, this variability in perfusion territories changed the classification of cerebral infarcts in only a minority of our patients. The correct classification of infarcts based on textbook perfusion territory maps alone can be partly explained by the presence of lacunar infarcts, periventricular infarcts, brainstem and cerebellar infarcts in the majority of our patients. It is very unlikely that in these types of infarcts the textbook-based judgment will change because these infarcts are in the middle of a perfusion territory. Changes in infarct classification, based on the knowledge of the actual perfusion territories, were only found in the subgroup of patients with either a cortical territory or border zone infarct. For this subgroup of patients, TASL MRI may also clarify if an infarct is located at the border of the perfusion territories of 2 brain-feeding arteries. We hypothesize that the number of infarcts at the borders of perfusion territories will be larger than the 2% to 5% that is currently reported in the literature. We observed that in patients with cortical territory infarcts, the DWI changes were often located at the borders of perfusion territories. Information about the location of cerebral infarcts at a border of perfusion territories may add to the knowledge of underlying pathophysiology of cerebral infarcts and potentially have consequences for patient management.

A potential drawback of ASL, mentioned in previous reviews, is the low sensitivity for low-flow conditions. Therefore, the general belief is that ASL is not the MR perfusion method of choice in patients with stroke compared with perfusion methods with contrast injection. Thus far, only a few ASL studies have been performed in small series of patients with acute stroke and none of these studies used the TASL MRI method. For the TASL MRI method, low-flow conditions in patients with stroke and absence of ASL...
signal in areas at the boundaries of the perfusion territories could result in an underestimation of perfusion territories. In the present study, we found that the TASL MRI method performed at field strength of 3.0 Tesla showed complete depiction of the perfusion territories even under low-flow conditions. Another advantage of the current pulsed TASL MRI method, using the QUASAR technique, is the acquisition of perfusion territory images at a series of delay times. This series of inversion times provides dynamic information and shows the inflow of the blood at the early time points and the tissue perfusion at the later time points. With potential delayed arrival of the magnetic label to the brain tissue in patients with stroke, these TASL images at multiple time points will also show the perfusion in the areas with delayed arrival at the borders of the perfused territories. A potential limitation of TASL MRI in patients with stroke is the need to average a series of acquisitions in time to obtain images with an adequate signal-to-noise ratio. In the present study, 32 images are averaged resulting in a total scan time for the 3 perfusion territories of 6:40 minutes. Patient movement during the acquisition of the TASL images will degrade the images because the head will be in a different position for the series of acquisition. Furthermore, in the presence of severe motion, the location of the labeling slab may have an incorrect position with respect to the arteries in the neck, resulting in a labeling error. Despite these potential difficulties of TASL labeling in patients with stroke, only 8% of the TASL images in the present study had to be discarded because of motion artifacts. This success rate is in line with a previous study, in which 89% of the perfusion territories were successfully depicted using a similar technique. This figure can be expected to be reduced even further in future studies with the recent introduction of prospective motion correction methods by the scanner vendors.

A limitation of the present study is the patient inclusion outside the 3-hour timeframe required for intravenous thrombolysis in acute stroke settings. Future work will aim at moving these techniques to the acute phase of stroke in which the value of TASL MRI could eventually be investigated using the perfusion territory data in outcome prediction algorithms. Additional hemodynamic information on perfusion territories, not provided by the anatomic scans, may add information about the potential cause of an infarct, which may have implications for therapy and the future development of therapeutic options. For the present study, the longer delay between the start of the ischemic symptoms and the TASL MRI scans may have resulted in altered perfusion territories compared with the acute phase of ischemia in some patients. Recent improvements of the ASL technique will result in shortening of the acquisition time for the TASL MRI scans compared with the 6 minutes 40 seconds in the present study. With shortening of the acquisition time of the TASL MRI scans, the implementation of TASL MRI scans in the MR protocol in patients with acute stroke will become easier.

Information of the perfusion territories of the brain-feeding arteries from the TASL MRI scans may also be possible to infer from a detailed analysis of the MR angiography scans usually acquired in stroke imaging protocols. However, a recent study, in which 89% of the perfusion territories were successfully depicted using a similar technique. This figure can be expected to be reduced even further in future studies with the recent introduction of prospective motion correction methods by the scanner vendors.
slice-by-slice comparison of the extent of the perfusion territories and ischemic changes, as has been demonstrated in the present study with TASL MRI and DWI, is not possible on the basis of MR angiograms alone. With the TASL MRI technique used in the present study, we were only selective for the left ICA, right ICA, and posterior circulation. Recently introduced territory ASL MRI techniques also allow for the distinction of the anterior and middle cerebral artery territories. The additional knowledge provided by these techniques relative to the present TASL MRI technique has to be investigated in future studies.

In conclusion, we showed that the additional diagnostic information provided by the TASL MRIs in patients with stroke proved valuable in the classification of cortical and border zone infarcts, whereas no change of the textbook-based classification was observed for other infarct types. TASL MRI clearly showed the location of infarcts with respect to the collateral perfusion and the borders of the different perfusion territories. Future studies in patients with acute stroke (<3 hours) are needed to elucidate whether the characterization of collateral flow with TASL MRI may predict tissue fate and clinical outcome.

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Disclosures

At the time of this study, E.T.P. and X.G. were on the speaker’s bureau of Philips Medical Systems.

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