The Value of Arterial Spin-Labeled Perfusion Imaging in Acute Ischemic Stroke
Comparison With Dynamic Susceptibility Contrast-Enhanced MRI

Danny J.J. Wang, PhD, MSCE; Jeffry R. Alger, PhD; Joe X. Qiao, MD; Qing Hao, MD; Samuel Hou, MD; Rana Fiaz, MD; Matthias Gunther, PhD; Whitney B. Pope, MD, PhD; Jeffrey L. Saver, MD; Noriko Salamon, MD, PhD; David S. Liebeskind, MD; for the UCLA Stroke Investigators

Background and Purpose—The purpose of this study was to evaluate the potential clinical value of arterial spin-labeled (ASL) perfusion MRI in acute ischemic stroke (AIS) through comparison with dynamic susceptibility contrast (DSC) enhanced perfusion MRI.

Methods—Pseudocontinuous ASL with 3-dimensional background-suppressed gradient and spin echo readout was applied with DSC perfusion MRI on 26 patients with AIS. ASL cerebral blood flow and multiparametric DSC perfusion maps were rated for image quality and lesion severity/conspicuity. Mean ASL cerebral blood flow and DSC perfusion values were obtained in main vascular territories. Kendall coefficient of concordance was calculated to evaluate the reliability of ratings. Spearman correlation coefficients were calculated to compare ratings and quantitative perfusion values between ASL and DSC perfusion maps.

Results—ASL cerebral blood flow and DSC perfusion maps provided largely consistent results in delineating hypoperfused brain regions in AIS. Hyperemic lesions, which also appeared frequently in the AIS cases studied, were more conspicuous on ASL cerebral blood flow than on DSC cerebral blood flow, mean transit time and time to the maximum of the tissue residual function maps.

Conclusions—As a rapid, noninvasive, and quantitative technique, ASL has clinical use in detecting blood flow abnormalities in patients with AIS. (Stroke. 2012;43:00-00.)

Key Words: acute stroke ■ brain imaging ■ ischemia ■ MRI ■ neuroradiology

The role of perfusion neuroimaging in the management of acute ischemic stroke (AIS) is to confirm the presence of reduced regional blood flow and contribute to identification of the ischemic penumbra, regions of hypoperfusion that may be salvaged by thrombolytic and/or endovascular recanalization therapy.1 Dynamic susceptibility contrast-enhanced (DSC) techniques have been the main MR perfusion imaging method used in AIS. In particular, time to the maximum of the tissue residual function (Tmax) has been applied in large case series and clinical trials to define regions of hypoperfusion.2,3 The Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution (DEFUSE) cohort study suggested that specific mismatch patterns between perfusion and diffusion lesions may predict clinical responses to thrombolytic therapy.3,5 Randomized trials, however, have yielded ambiguous findings showing only trends to benefit when using perfusion and diffusion mismatch as a patient selection criterion for thrombolysis.6,7 To date, the value for identifying the ischemic penumbra in the management of AIS remains less than firmly established. The fitful progress is undoubtedly related to the regionally heterogeneous and temporally evolving nature of AIS pathophysiology. However, apart from penumbral identification, there is still a clear use for perfusion imaging with MRI or CT in AIS to confirm the presence of regional hypoperfusion, thereby ruling in acute ischemia and ruling out stroke mimics as the cause of acute deficits. Although diffusion-weighted imaging is often used to confirm the diagnosis of AIS, it can be normal when ischemia is early and only moderate in degree. Perfusion...
imaging provides a direct indication of regional brain ischemia.

Arterial spin-labeled (ASL) techniques provide cerebral blood flow (CBF) measures without the use of a contrast agent. Additional potential advantages of ASL versus DSC perfusion imaging include relative insensitivity to blood–brain barrier permeability changes, which occur frequently in AIS. Perfusion quantification using ASL generally does not rely on the selection of arterial input function. The main limitation of ASL is the short tracer half-life (blood T1 = 1–2 seconds) resulting in limited sensitivity and potential underestimation of perfusion in the presence of prolonged transit delay resulting from arterial occlusion. Recent advances in MRI technology including higher magnetic fields, array receiver coils, pseudocontinuous ASL, and rapid 3-dimensional acquisition techniques rendered it feasible to apply ASL in the setting of acute stroke. Preliminary studies have shown that ASL is able to detect both hypoand hyperperfusion lesions as well as delayed transit effects that may differentiate clinical outcomes in AIS. However, the performance and potential clinical value of ASL versus that of the much more widely used DSC remains unclear. To address this issue, we conducted a systematic comparison of perfusion images obtained using ASL and DSC perfusion MRI in a retrospective cohort of 26 patients with AIS.

Methods

Patient Selection

The present analysis was performed on data collected from June 2010 to November 2010 in an ongoing prospective registry of patients evaluated with diffusion-perfusion MRI at our academic medical center. Image data were included in this study if (1) the patient presented with symptoms of AIS; (2) patients did not have history of previous stroke; (3) baseline MRI was performed within 24 hours of symptom onset; (4) both ASL and DSC perfusion imaging were performed. The University of California at Los Angeles Institutional Review Boards approved the study.

MRI Protocols

All patients underwent MRI on Siemens 1.5-T Avanto or 3.0 T TIM Trio systems (Erlangen, Germany) using 12-channel head coils. The MRI protocol included diffusion-weighted imaging, gradient recalled echo, fluid-attenuated inversion recovery, and perfusion-weighted imaging (PWI) sequences. ASL PWI scans were performed using a pseudocontinuous ASL pulse sequence with background suppressed 3-dimensional gradient and spin echo readout (labeling pulse duration = 1.5 seconds, postlabeling delay = 2 seconds, no flow crushing gradient, field of view = 22 cm, matrix = 64×64, 26×5-mm slices, rate-2 GRAPPA, TR = 4 seconds, TE = 22 ms, 30 pairs of tags and controls acquired in 4 minutes). DSC PWI scans were acquired using a gradient-echo echoplanar imaging sequence (TR = 2.9/1.9 seconds, TE = 45/30 ms for 1.5/3 T, field of view = 22 cm, matrix = 128×128, 26×5-mm slices, scan time = 2 minutes) with an intravenous bolus injection of gadolinium contrast agent (0.1 mmol/kg).

Postprocessing and Evaluation

Data analysis was performed with Interactive Data Language (Boulder, CO) software programs developed in-house. ASL images were corrected for motion, pairwise subtracted between label and control images followed by averaging to generate the mean difference image (ΔM). Quantitative CBF (f) maps were calculated based on the following equation:

\[ f = \frac{\Delta M R_w}{2\alpha M_0 \left[ \exp(-wR_w) - \exp(-\tau + w) R_w \right]} \]

where \( R_w \approx 0.72/0.61 \text{ seconds}^{-1} \) at 1.5/3 T is the longitudinal relaxation rate of blood, \( M_0 \) is the equilibrium magnetization of brain tissue, \( \alpha \approx 0.8 \) is the tagging efficiency, \( \tau \approx 1.5 \text{ seconds} \) is the duration of the labeling pulse, \( w \approx 2 \text{ seconds} \) is the postlabeling delay time, and \( \lambda \approx 0.9 \text{ g/mL} \) is blood/tissue water partition coefficient. Equation 1 assumes that the labeled blood spins remain primarily in the vasculature rather than exchanging completely with tissue water, which is justified in patients with stroke in whom arterial transit times are likely prolonged.

Postprocessing of DSC images yielded multiparametric perfusion maps including CBF, cerebral blood volume (CBV), Tmax, and mean transit time (MTT) according to previously described analysis procedures. Two CBF values were calculated from DSC data, namely CBF0 and CBFR0, based on the value at time 0 and Tmax of the tissue residual function (R[i]), respectively. The calculation of CBFR0 may not represent the standard processing of DSC perfusion MRI but was used to inform the comparison with ASL CBF. In each case, all structural, diffusion, and perfusion images were aligned using SPM8 (Wellcome Dept. of Cognitive Neurology, UCL, UK). Two neuroradiologists and 1 perfusion MRI expert blinded to treatment and clinical information independently and separately reviewed ASL and DSC perfusion maps, which were scored on a scale of 0 to 3 to rate image quality and lesion severity/conspicuity, respectively. Both hypo- and hyperperfusion were noted.

ASL and DSC perfusion images were further normalized into the Montreal Neurological Institute template space using SPM8. Subsequently, segmentation of ASL and DSC perfusion images into major vascular territories was performed using an automated region-of-interest (ROI) analysis based on a published template of vascular territories in both hemispheres. The vascular territories studied were anterior cerebral artery, posterior cerebral artery, and leptomeningeal and lenticulo striate (perforator) distributions of the middle cerebral artery (MCA). In addition, in patients with AIS demonstrating hyperperfusion, ROIs defined by Tmax >6 seconds, 2 seconds < Tmax <6 seconds, and Tmax <2 seconds were used to extract corresponding ASL and DSC CBF values, respectively. Manual restriction of the ROIs was applied when necessary.

Statistical Analysis

Statistical analysis was performed using STATA 10.0 software (College Station, TX). Kendall coefficient of concordance was calculated to evaluate the reliability of ratings across 3 readers. Spearman correlation coefficients were calculated between average ratings of ASL and DSC perfusion maps as well as between mean values of ASL CBF and multiparametric DSC perfusion measures in major vascular territories. The Wilcoxon signed-rank test was applied to compare the mean ratings of ASL and DSC perfusion maps. The significance level was defined as \( P = 0.05 \) (2-sided).

Results

Demographic and Clinical Information

Image data from 26 patients (mean age 71.0±15.7 years; 14 men) with AIS were included. National Institutes of Health Stroke Scale scores at baseline ranged from 1 to 23 with a median of 9.5. The median time from stroke onset to imaging was 5.5 hours (range, 47 minutes to 19 hours). Demographic and clinical information of the 26 patients with AIS are provided in Supplemental Table 1 (http://stroke.ahajournals.org). Serial imaging (up to 3 time points within the subacute period) with combined ASL and DSC was obtained in a subset of 15 cases, resulting in a total of 44 image sets. In addition, 5 patients had repeated perfusion scans before and after endovascular therapies.
Ratings of Hypoperfusion Lesions

Both ASL and DSC perfusion images were of high diagnostic quality (2.44±0.56 and 2.39±0.56 on scale of 0–3, respectively) without a significant difference between the 2 modalities (P=0.38). However, image quality was significantly higher for both ASL (2.61±0.41 versus 2.03±0.64, P=0.0018) and DSC images (2.56±0.47 versus 2.00±0.59, P=0.0017) acquired at 3 T versus 1.5 T. Figure 1 shows a representative AIS case with coregistered diffusion-weighted imaging, ASL, and multiparametric DSC PWI. Both ASL and DSC PWI are of high quality with whole-brain coverage. The Table lists the Kendall coefficient of concordance (W) and associated probability values for conspicuity ratings of ASL and DSC PWI across 3 readers. Excellent interrater reliability (W >0.75) was achieved for ASL hypoperfusion, DSC Tmax, and MTT prolongations. Fair to good interrater reliability (0.75 > W >0.4) was achieved for ASL hyperperfusion and DSC hypoperfusion (CBFr0 and CBFrm images), whereas reliability was poor (W <0.4) for hyperperfusion in DSC CBFr0 and CBFrm images as well as both hypo- and hyperperfusion lesions in DSC CBV images.

Spearman correlation coefficients between average conspicuity ratings of hypoperfusion lesions on ASL CBF maps and multiparametric DSC perfusion maps are listed in Supplemental Table IIA. ASL was most consistent with DSC MTT (r=0.79, P<0.0001), Tmax (r=0.77, P<0.0001), and CBFr0 (r=0.76, P<0.0001) maps in demonstrating hypoperfusion. Note these 4 parameters also demonstrated the highest interrater reliability in the Table. The magnitude of correlations slightly reduced when comparing ASL with DSC CBFrm (r=0.62, P=0.0001) and CBV (r=0.61, P=0.0038) in delineating hypoperfusion. The mean rating of ASL hypoperfusion (1.30±1.16) was significantly higher than those of DSC CBFr0 (0.75±0.84), CBFrm (0.50±0.60), and CBV (0.34±0.50) hypoperfusion (P<0.0001), whereas it was not significantly different from the mean ratings of Tmax (1.34±1.23) and MTT (1.32±1.18). Figure 2 shows serial fluid-attenuated inversion recovery, diffusion-weighted imag-

---

**Table. Mean and SD of Conspicuity Ratings of All 44 ASL and DSC Perfusion Scans and Kendall Coefficient of Concordance (W) of Ratings Across 3 Readers**

<table>
<thead>
<tr>
<th></th>
<th>ASL CBF Hypoperfusion</th>
<th>ASL CBF Hyperperfusion</th>
<th>DSC CBFr0 Hypoperfusion</th>
<th>DSC CBFr0 Hyperperfusion</th>
<th>DSC CBFrm Hypoperfusion</th>
<th>DSC CBFrm Hyperperfusion</th>
<th>DSC CBV Hypoperfusion</th>
<th>DSC CBV Hyperperfusion</th>
<th>DSC Tmax Increase</th>
<th>DSC MTT Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>1.30</td>
<td>0.87</td>
<td>0.75</td>
<td>0.40</td>
<td>0.50</td>
<td>0.37</td>
<td>0.34</td>
<td>0.41</td>
<td>1.34</td>
<td>1.32</td>
</tr>
<tr>
<td>SD</td>
<td>1.16</td>
<td>1.00</td>
<td>0.84</td>
<td>0.49</td>
<td>0.60</td>
<td>0.43</td>
<td>0.50</td>
<td>0.45</td>
<td>1.23</td>
<td>1.18</td>
</tr>
<tr>
<td>W</td>
<td>&lt;0.0001</td>
<td>0.0133</td>
<td>0.0077</td>
<td>0.5315</td>
<td>0.0725</td>
<td>0.7266</td>
<td>0.5521</td>
<td>0.7500</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ASL indicates arterial spin labeling; DSC, dynamic susceptibility contrast-enhanced; CBF, cerebral blood flow; CBV, cerebral blood velocity; Tmax, time to maximum; MTT, mean transit time.

*Rating criteria are: conspicuity: Score 3, the perfusion lesion can be identified definitely; Score 2, relatively clear diagnosis of perfusion lesion can be drawn; Score 1, possible diagnosis of perfusion lesion can be obtained; Score 0, cannot afford any help to diagnosis.
ing, ASL, and DSC PWI of representative AIS cases with primarily hypoperfusion lesions at baseline. By visual appearance, hypoperfusion lesions on ASL CBF maps match best with prolonged Tmax and MTT on DSC PWI. The severity of hypoperfusion lesions appears similar on ASL CBF and DSC CBFr₀ maps, whereas the lesions are less conspicuous on DSC CBFrₘ and CBV maps. In addition, the correspondences between ASL and DSC ratings were stronger at 3 T than 1.5 T as shown in Supplemental Table II.

Ratings of Hyperemic Lesions
Spearman correlation coefficients between conspicuity ratings of hyperperfusion lesions on ASL CBF maps and multiparametric DSC perfusion maps are listed in Supplemental Table IIB. The ratings of hyperemic lesions on ASL images were consistent with those of DSC CBFr₀ \( (r=0.47, P=0.0012) \), CBFrₘ \( (r=0.47, P=0.001) \), and CBV \( (r=0.39, P=0.0087) \) images. Nevertheless, ASL PWI (mean score=0.87±1.00) was significantly more conspicuous than DSC PWI (CBFr₀: 0.40±0.49, \( P=0.005 \); CBFrₘ: 0.37±0.43, \( P=0.005 \); CBV: 0.41±0.45, \( P=0.0087 \)) in delineating hyperemic lesions. Figure 3 shows serial fluid-attenuated inversion recovery, diffusion-weighted imaging, ASL, and DSC PWI of representative AIS cases with hyperperfusion lesions at baseline. As can be clearly seen, hyperemic lesions were much more conspicuous on ASL CBF than DSC CBF or CBV maps. Furthermore, DSC Tmax and MTT maps performed poorly at delineating hyperemic lesions. Note 3 of the 4 cases shown in Figure 3 were treated with recombinant tissue plasminogen activator before the first MRI scans and the hyperperfusion seen in ASL likely reflects hyperemia after thrombolytic reperfusion.

Serial ASL and DSC PWI
Serial ASL and DSC PWI were obtained in 5 patients with AIS pre- and postendovascular procedures. All patients demonstrated partial or full recanalization at angiography. As shown in Figure 4, recanalization resulted in either normal-
ization of perfusion or hyperemic responses within and/or around lesion areas. Again, ASL CBF was more conspicuous than DSC CBF and CBV maps in demonstrating hyperemic flow responses.

Quantitative Vascular Territory Analysis
Spearman correlation coefficients between mean values of ASL CBF and multiparametric DSC perfusion parameters in the 4 major vascular territories are listed in Supplemental Table III. There were significant negative correlations between ASL CBF and DSC Tmax and MTT in the anterior cerebral artery, leptomeningeal MCA, and perforator MCA territories ($r = -0.24$, $P < 0.05$; Supplemental Table IIIA). There were significant associations between ASL CBF and DSC CBFr0 values in the perforator MCA territory ($r = 0.23$, $P = 0.04$). When only patients with predominately MCA strokes were considered, significant negative correlations between ASL CBF and DSC Tmax and MTT in the leptomeningeal and perforator MCA territories as well as a significant positive association between ASL CBF and DSC CBFr0 in the perforator MCA territory were preserved (Supplemental Table IIIB). The findings of quantitative vascular territory analysis are generally consistent with those based on subjective ratings, supporting the associations between ASL perfusion and DSC Tmax, MTT as well as CBFr0 measures across subjects.

ROI Analysis
In the AIS cases demonstrating primarily hypoperfusion lesions, ASL and DSC CBF values within the ROIs of Tmax >6 seconds were significantly reduced compared with those of 2 seconds < Tmax <6 seconds (Supplemental Table IV). When comparing the mean CBF values between the ROIs of 2 seconds < Tmax < 6 seconds, and Tmax < 2 seconds, ASL CBF and DSC CBFr0 values were significantly reduced in the former than the latter ROI, whereas DSC CBFRm values were not significantly different.

Discussion
To summarize the main findings of the present study, ASL and DSC PWI provided largely consistent results in delineating hypoperfusion lesions in AIS. The most consistent associations, as demonstrated by both subjective ratings and quantitative vascular territory analyses, were between ASL CBF and DSC Tmax, MTT, and CBFr0 measures, which also demonstrated the highest interrater reliability. ASL techniques are limited by the relatively short tracer half-life determined by the T1 of blood. Even with advanced pseudo-continuous ASL and 3-dimensional gradient and spin echo readout, the postlabeling delay time is typically <3 seconds in ASL experiments at field strengths of ≤3 T. In the present study, a postlabeling delay of 2 seconds was used in pseudo-continuous ASL scans as a tradeoff between maintaining adequate diagnostic quality at the same time as allowing sufficient delay to visualize tissue perfusion. Our findings suggest that hypoperfusion lesions on ASL CBF maps may reflect delayed transit effects as well as reduced CBF that are manifested as prolonged Tmax and MTT on DSC PWI. Furthermore, significant differences of ASL CBF values were demonstrated between the ROIs of Tmax > 6 seconds, Tmax between 2 to 6 seconds and Tmax <2 seconds, suggesting the potential of ASL to grade hypoperfusion lesions in AIS.

In the present study, 2 DSC CBF measurements, namely CBFr0 and CBFRm, were performed, which represent DSC
CBF calculation without and with consideration of delayed transit effects, respectively. ASL CBF values were more consistent with DSC CBFr0 than CBFr0 or CBV measurements, further supporting that ASL hypoperfusion lesions reflect delayed transit effects in AIS. The CBFr0 images are analogous to CBF images generated using circulating deconvolution (data not shown). Because existing clinical trials have mainly adopted prolonged Tmax to define hypoperfusion regions, the consistency between ASL CBF and Tmax (or MTT) may render ASL an alternative to DSC PWI in patients with renal diseases who cannot be exposed to gadolinium contrast agent. In this regard, the availability of ASL may improve the timing of MRI assessment in AIS by eliminating the need for glomerular filtration rate evaluation. To date, to ideally delineate the penumbra on ASL PWI remains challenging due to the inherent heterogeneity of CBF maps as well as the relatively low signal-to-noise ratio. However, this study demonstrates that ASL provides a rapid contrast agent-free and reliable assessment of the patient’s cerebral hemodynamic status. ASL may also complement DSC in CBF quantification as indicated by a recent study. The second major finding of the present study was that hyperemic lesions appeared more conspicuous on ASL CBF than on DSC PWI maps. The biophysical mechanism underlying this phenomenon is not clear and may be related to differing effects of changes of blood–brain barrier permeability on perfusion quantification using ASL and DSC. Hyperperfusion in acute ischemic stroke arises from spontaneous recanalization, therapeutic recanalization, and, less commonly, improved collateral flow without recanalization. All are present in the cohort studied. Existing ASL studies on stroke have linked hyperperfusion to the “luxury perfusion” seen on positron emission tomographic CBF imaging studies and suggested that hyperperfusion may be associated with positive outcomes in AIS. Hyperperfusion after revascularization has been observed in both CT and DSC perfusion MRI studies. In contrast to regions showing normal perfusion after recanalization, regions presenting hyperperfusion mainly developed infarction and had greater bioenergetic compromise in pretreatment imaging measures.

Whether or not hyperperfusion is a useful prognostic feature of AIS has not been well established. As suggested by positron emission tomographic literature, hyperperfusion may indicate metabolic failures such as low oxygen extraction fraction and therefore the concept of penumbra should include both hypo- and hyperperfusion lesions. Hyperperfusion may reflect vasoparalysis and greater regional vulnerability to hemorrhagic transformation. If so, in the future its recognition might enable timely intervention to avert hemorrhagic complications with blood pressure modulation and blood–brain barrier-stabilizing therapies. Given its superior capability in delineating hyperperfusion lesions and high repeatability, ASL may have unique value in the management of patients with AIS both pre- and posttreatment and may be applied longitudinally to monitor treatment effects.

This study has several limitations. As a cross-sectional study to compare ASL and DSC PWI, the patient cohort was rather “heterogeneous” but represented typical patient population seen at an academic medical center. In 6 patients, the “baseline” ASL and DSC PWI were acquired after recombinant tissue plasminogen activator treatments. Therefore, the correlation between perfusion values and clinical evaluations (National Institutes of Health Stroke Scale at baseline) could not be assessed.

The patient cohort included both anterior and posterior circulation strokes. We performed statistical analyses based on data from all 26 patients with AIS and the 19 patients with predominately MCA strokes, respectively. The results of vascular territory analysis were not affected (see “Results”). Lastly, correlation of perfusion MRI findings with clinical and neuroimaging outcomes was not feasible in this pilot study. Overall, the present study represents an initial step in exploring the clinical value of ASL in the management of AIS through comparison with DSC perfusion MRI.

**Summary**

ASL has clinical uses in detecting both hypo- and hyperperfusion lesions in patients with AIS, which may complement DSC perfusion MRI. The capability of ASL to provide noninvasive and quantitative CBF information without the use of contrast agent offers the potential to include ASL as part of standard neuroimaging protocol in the management of acute stroke both pre- and postrevascularization.

**Sources of Funding**


**Disclosures**

None.

**References**


The Value of Arterial Spin-Labeled Perfusion Imaging in Acute Ischemic Stroke: Comparison With Dynamic Susceptibility Contrast-Enhanced MRI
Danny J.J. Wang, Jeffry R. Alger, Joe X. Qiao, Qing Hao, Samuel Hou, Rana Fiaz, Matthias Gunther, Whitney B. Pope, Jeffrey L. Saver, Noriko Salamon and David S. Liebeskind for the UCLA Stroke Investigators

Stroke. published online February 9, 2012;
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/early/2012/02/09/STROKEAHA.111.631929

Data Supplement (unedited) at:
http://stroke.ahajournals.org/content/suppl/2012/02/10/STROKEAHA.111.631929.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/
## SUPPLEMENTAL MATERIAL

### Supplemental Table 1 Demographic and clinical information of 26 patients with Acute Ischemic Stroke (AIS)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (y) / Gender</th>
<th>MRI reading</th>
<th>Time from onset to scan (hr)</th>
<th>Treatments</th>
<th>NIHSS baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>42/M</td>
<td>Acute infarction of right MCA</td>
<td>1.23</td>
<td>IV tPA, clot retrieval &amp; stenting</td>
<td>13</td>
</tr>
<tr>
<td>2</td>
<td>71/F</td>
<td>Acute infarction of left MCA</td>
<td>10.38</td>
<td>IV and IA tPA, clot retrieval &amp; aspiration</td>
<td>16</td>
</tr>
<tr>
<td>3</td>
<td>64/F</td>
<td>Acute infarction of left MCA</td>
<td>2.03</td>
<td>IV tPA</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>91/F</td>
<td>Acute infarction of left M1</td>
<td>7.32</td>
<td>IV tPA, clot retrieval</td>
<td>22</td>
</tr>
<tr>
<td>5</td>
<td>64/F</td>
<td>Acute infarction of left MCA</td>
<td>4.17</td>
<td>None</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>78/M</td>
<td>Increased DWI signal in cortical left parietal lobe w/o corresponding ADC signal</td>
<td>5.95</td>
<td>IV tPA</td>
<td>5</td>
</tr>
<tr>
<td>7</td>
<td>68/M</td>
<td>Restricted diffusion in left BG, left corona radiata &amp; left parietal WM</td>
<td>1.38</td>
<td>IV tPA</td>
<td>18</td>
</tr>
<tr>
<td>8</td>
<td>59/F</td>
<td>Acute infarction of left MCA</td>
<td>6.48</td>
<td>IA tPA</td>
<td>7</td>
</tr>
<tr>
<td>9</td>
<td>44/M</td>
<td>Acute infarction of right MCA</td>
<td>18.92</td>
<td>None</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>86/M</td>
<td>Ischemia in left MCA territory</td>
<td>0.78</td>
<td>IV tPA, clot retrieval &amp; aspiration</td>
<td>11</td>
</tr>
<tr>
<td>11</td>
<td>75/M</td>
<td>Acute infarction of right MCA &amp; left frontal lobe</td>
<td>18.57</td>
<td>IV tPA, clot retrieval</td>
<td>18</td>
</tr>
<tr>
<td>12</td>
<td>71/M</td>
<td>Acute infarction of right basis pontis</td>
<td>6.18</td>
<td>None</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>----</td>
<td>----</td>
<td>--------------------------------</td>
<td>-----</td>
<td>---------------------</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>93/F</td>
<td>Acute infarction of right BG</td>
<td>1.85</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>66/F</td>
<td>Acute infarction of bilateral cerebellum &amp; left pons</td>
<td>1.05</td>
<td>IV tPA</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>89/F</td>
<td>Acute infarction of left MCA</td>
<td>1.82</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>39/M</td>
<td>Acute infarction of left MCA</td>
<td>1.37</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>90/F</td>
<td>Acute infarction of right MCA</td>
<td>4.38</td>
<td>IV tPA</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>55/M</td>
<td>Acute infarction of right dorsolateral medulla</td>
<td>18.05</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>70/M</td>
<td>Acute infarction of right MCA</td>
<td>8.18</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>87/F</td>
<td>Acute infarction of left MCA</td>
<td>5.40</td>
<td>Clot retrieval</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>57/F</td>
<td>Acute infarction of right MCA</td>
<td>1.83</td>
<td>IV tPA, clot retrieval</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>75/M</td>
<td>Acute infarction of left BG</td>
<td>2.93</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>93/F</td>
<td>Acute infarction of left ACA &amp; MCA</td>
<td>5.62</td>
<td>IV tPA</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>76/M</td>
<td>Acute infarction of left MCA &amp; right parietal lobe</td>
<td>5.42</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>76/M</td>
<td>Acute infarction of right lentiform &amp; caudate nucleus, anterior left temporal lobe</td>
<td>12.98</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>26</td>
<td>57/M</td>
<td>Acute infarction of right MCA</td>
<td>5.50</td>
<td>IV tPA, clot retrieval</td>
<td></td>
</tr>
</tbody>
</table>

MCA=middle cerebral artery, M1=M1 segment of MCA, BG=basal ganglia, WM=white matter, ACA-anterior cerebral artery
**Summary Table 2A.** Spearman correlation coefficients between average conspicuity ratings of hypoperfusion lesions on ASL CBF maps and multi-parametric DSC perfusion maps, p values are listed in parentheses.

<table>
<thead>
<tr>
<th></th>
<th>DSC CBFr0 Hypo-perfusion</th>
<th>DSC CBFrm Hypo-perfusion</th>
<th>DSC CBV Hypo-perfusion</th>
<th>DSC Tmax Increase</th>
<th>DSC MTT Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASL CBF Hypo-perfusion</td>
<td>0.7630 (&lt;0.0001)</td>
<td>0.6173 (0.0001)</td>
<td>0.4229 (0.0038)</td>
<td>0.7695 (&lt;0.0001)</td>
<td>0.7898 (&lt;0.0001)</td>
</tr>
<tr>
<td>ASL CBF Hypo-perfusion (3.0T)</td>
<td>0.8006 (&lt;0.0001)</td>
<td>0.6918 (&lt;0.0001)</td>
<td>0.4269 (0.0017)</td>
<td>0.8212 (&lt;0.0001)</td>
<td>0.8266 (&lt;0.0001)</td>
</tr>
<tr>
<td>ASL CBF Hypo-perfusion (1.5T)</td>
<td>0.6936 (0.0085)</td>
<td>0.4202 (0.1528)</td>
<td>0.2744 (0.3642)</td>
<td>0.7394 (0.0039)</td>
<td>0.7983 (0.0011)</td>
</tr>
</tbody>
</table>

**Summary Table 2B.** Spearman correlation coefficients between average conspicuity ratings of hyperperfusion lesions on ASL CBF maps and multi-parametric DSC perfusion maps, p values are listed in parentheses.

<table>
<thead>
<tr>
<th></th>
<th>DSC CBFr0 Hyper-perfusion</th>
<th>DSC CBFrm Hyper-perfusion</th>
<th>DSC CBV Hyper-perfusion</th>
<th>DSC Tmax Increase</th>
<th>DSC MTT Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASL CBF Hyper-perfusion</td>
<td>0.4679 (0.0012)</td>
<td>0.4734 (0.0010)</td>
<td>0.3867 (0.0087)</td>
<td>-0.2186 (0.1492)</td>
<td>-0.2444 (0.1056)</td>
</tr>
<tr>
<td>ASL CBF (3.0T) Hyper-perfusion</td>
<td>0.5788 (0.0006)</td>
<td>0.6680 (&lt;0.0001)</td>
<td>0.4033 (0.0245)</td>
<td>-0.3063 (0.0937)</td>
<td>-0.3229 (0.0765)</td>
</tr>
<tr>
<td>ASL CBF (1.5T) Hyper-perfusion</td>
<td>0.3458 (0.2471)</td>
<td>0.2547 (0.4010)</td>
<td>0.6409 (0.0183)</td>
<td>-0.0740 (0.8100)</td>
<td>-0.1243 (0.6858)</td>
</tr>
</tbody>
</table>

*Based on the criterion of conspicuity ratings >= 2 in ASL CBF images, there were 21 and 9 scans demonstrating primarily hypo- and hyperperfusion lesions respectively. The rest scans fell between the 2 categories.*
**Supplemental Table 3A.** Spearmen correlation coefficients between average values of ASL CBF and multi-parametric DSC perfusion parameters in major vascular territories of all 44 scans (p<0.05*, p<0.005**)

<table>
<thead>
<tr>
<th></th>
<th>DSC CBFr0</th>
<th>DSC CBFrm</th>
<th>DSC CBV</th>
<th>DSC Tmax</th>
<th>DSC MTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASL CBF ACA</td>
<td>0.0967</td>
<td>0.0738</td>
<td>0.0369</td>
<td>-0.2415*</td>
<td>-0.2445*</td>
</tr>
<tr>
<td>ASL CBF leptomeningeal MCA</td>
<td>0.1892</td>
<td>0.1289</td>
<td>0.0001</td>
<td>-0.3613**</td>
<td>-0.3814**</td>
</tr>
<tr>
<td>ASL CBF perforator MCA</td>
<td>0.2274*</td>
<td>0.1440</td>
<td>0.0204</td>
<td>-0.4273**</td>
<td>-0.4074**</td>
</tr>
<tr>
<td>ASL CBF PCA</td>
<td>0.0733</td>
<td>0.0093</td>
<td>-0.1385</td>
<td>-0.2127*</td>
<td>-0.1740</td>
</tr>
</tbody>
</table>

**Supplemental Table 3B.** Spearmen correlation coefficients between average values of ASL CBF and multi-parametric DSC perfusion parameters in leptomeningeal and perforator MCA territories, based on 35 scans of 19 patients with predominately MCA strokes (p<0.05*, p<0.005**)

<table>
<thead>
<tr>
<th></th>
<th>DSC CBFr0</th>
<th>DSC CBFrm</th>
<th>DSC CBV</th>
<th>DSC Tmax</th>
<th>DSC MTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASL CBF leptomeningeal MCA</td>
<td>0.2068</td>
<td>0.1652</td>
<td>0.0964</td>
<td>-0.2896*</td>
<td>-0.3309**</td>
</tr>
<tr>
<td>ASL CBF perforator MCA</td>
<td>0.2356*</td>
<td>0.1626</td>
<td>0.0832</td>
<td>-0.3628**</td>
<td>-0.3348**</td>
</tr>
</tbody>
</table>
Supplemental Figure 1. Template of vascular territories used in the present study: 1. perforator MCA, 2. PCA, 3. ACA, 4. leptomeningeal MCA
**Supplemental Table 4.** Mean and SD of ASL and DSC CBF values (ml/100g/min) within ROIs defined by Tmax > 6s, Tmax of 2-6s and Tmax < 2s based on 21 scans demonstrating hypoperfusion lesions.

<table>
<thead>
<tr>
<th>Tmax</th>
<th>ASL CBF</th>
<th>DSC CBF&lt;sub&gt;r0&lt;/sub&gt;</th>
<th>DSC CBF&lt;sub&gt;rm&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tmax &gt; 6s</td>
<td>17.1±12.4</td>
<td>5.4±2.6</td>
<td>17.6±5.8</td>
</tr>
<tr>
<td>2s &lt; Tmax &lt; 6s</td>
<td>22.1±13.3</td>
<td>14.6±5.1</td>
<td>21.6±7.1</td>
</tr>
<tr>
<td>Tmax &lt; 2s</td>
<td>32.3±12.5</td>
<td>20.4±7.8</td>
<td>21.7±8.8</td>
</tr>
</tbody>
</table>

P value (Tmax > 6s vs. 2-6s) | 0.0001 | 0.0001 | 0.0012

P value (Tmax < 2s vs. 2-6s) | 0.0001 | 0.0001 | 0.4979