Do Acute Diffusion- and Perfusion-Weighted MRI Lesions Identify Final Infarct Volume in Ischemic Stroke?

C.S. Rivers, MSc; J.M. Wardlaw, MBChB, MD, FRCR, FRCP, FmedSci; P.A. Armitage, PhD; M.E. Bastin, Dphil; T.K. Carpenter, PhD; V. Cvoro, MBChB, MD, MRCP; P.J. Hand, MBChB, MD, MRCP; M.S. Dennis, MD, FRCP

Background and Purpose—An acute mismatch on diffusion-weighted MRI (DWI) and perfusion-weighted MRI (PWI) may represent the “tissue-at-risk.” It is unclear which “semiquantitative” perfusion parameter most closely identifies final infarct volume.

Methods—Acute stroke patients underwent DWI and PWI (dynamic-susceptibility contrast imaging) on admission (baseline), and T2-weighted imaging (T2WI) at 1 or 3 months after stroke. “Semiquantitative” mean transit time ($MTT_{sq}$), cerebral blood volume ($CBV_{sq}$), and cerebral blood flow ($CBF_{sq}$) were calculated. DWI and PWI lesions were measured at baseline and final infarct volume on T2WI acquired ≥1 month after stroke. Baseline DWI, CBF$_{sq}$, and MTT$_{sq}$ lesion volumes were compared with final T2WI lesion volume.

Results—Among 46 patients, baseline DWI and CBF$_{sq}$ lesions were not significantly different from final T2WI lesion volume, but baseline MTT$_{sq}$ lesions were significantly larger. The correlation with final T2WI lesion volume was strongest for DWI (Spearman rank correlation coefficient $\rho = 0.68$), intermediate for CBF$_{sq}$ ($\rho = 0.55$), and weakest for MTT$_{sq}$ ($\rho = 0.49$) baseline lesion volumes. Neither DWI/CBF$_{sq}$ nor DWI/MTT$_{sq}$ mismatch predicted lesion growth; lesion growth was equally common in those with and without mismatch.

Conclusions—Of the 2 PWI parameters, CBF$_{sq}$ lesions most closely identifies, and MTT$_{sq}$ overestimates, final T2WI lesion volume. “DWI/PWI mismatch” does not identify lesion growth. Patients without “DWI/PWI mismatch” are equally likely to have lesion growth as those with mismatch and should not be excluded from acute stroke treatment. (Stroke. 2006;37:98-104.)

Key Words: cerebrovascular disorders imaging, diffusion-weighted imaging, perfusion-weighted magnetic resonance imaging stroke
Previous studies of PWI data (<24 hours after stroke) and final lesion extent (Table 1) have produced rather confusing results. Of the 13 studies, only 3 compared CBFq and MTTq (total n=53):11–13 2 found that CBFq and 1 that MTTq related best to final infarct volume. None directly compared CBFsq and MTTsq. In the remainder, TTP correlated strongly with final infarct volume4,6 and MTT sq and MTT q overestimated final infarct volume.14–21 Only 4 studies included pa-

### TABLE 1. Studies Comparing Acute PWI Lesions With Final Infarct Volume (≥1-month T2WI)

<table>
<thead>
<tr>
<th>Paper</th>
<th>n</th>
<th>PWI Measure</th>
<th>PWI Parameter</th>
<th>Lesion Measurement</th>
<th>Statistical Analysis of Volumes Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baird14</td>
<td>18</td>
<td>Index</td>
<td>MTT</td>
<td>Manual outline</td>
<td>MTT volume &gt; final infarct volume in 8 of 14 patients; MTT may overestimate</td>
</tr>
<tr>
<td>Barber4</td>
<td>18</td>
<td>Summary</td>
<td>TTP (likely)</td>
<td>Manual outline</td>
<td>Pearson r TTP volume correlated well (r=0.83) with final infarct volume</td>
</tr>
<tr>
<td>Barber16*</td>
<td>45</td>
<td>Absolute</td>
<td>MTT</td>
<td>MTT delay &gt;4-s threshold</td>
<td>Tissue with MTT delay &gt;4 s overestimates final infarct volume</td>
</tr>
<tr>
<td>Beaulieu6</td>
<td>21</td>
<td>Summary</td>
<td>TTP</td>
<td>Manual outline</td>
<td>Pearson r TTP volume correlates well (r=0.86) with final infarct volume</td>
</tr>
<tr>
<td>Butcher17$</td>
<td>35</td>
<td>Absolute</td>
<td>MTT</td>
<td>Manual outline of final infarct; MTT delay &gt;2-s threshold</td>
<td>Tissue with MTT delay &gt;2 s overestimates final infarct volume as all patients have areas of “salvage” (part of acute PWI lesion but not final infarct)</td>
</tr>
<tr>
<td>Parsons18</td>
<td>38</td>
<td>Absolute</td>
<td>MTT</td>
<td>Manual outline of final infarct; MTT delay &gt;4-s and &gt;6-s thresholds</td>
<td>Tissue with MTT delay &gt;4 s appears to overestimate final infarct volume, tissue with MTT delay &gt;6 s appears to more closely match final infarct volume</td>
</tr>
<tr>
<td>Parsons12</td>
<td>23</td>
<td>Absolute</td>
<td>CBF &amp; MTT</td>
<td>% thresholds of signal intensity on CBF and MTT</td>
<td>Spearman ρ and Wilcoxon rank sum test Compared with final infarct volume, tissue with: lowest 30% of CBF signal intensities correlated (ρ=0.70), and was not significantly different in volume; highest 50% of MTT signal intensities correlated (ρ=0.77), but was significantly larger; and highest 70% MTT signal intensities correlated (ρ=0.87), but was significantly smaller.</td>
</tr>
<tr>
<td>Rahl11</td>
<td>11</td>
<td>Absolute</td>
<td>CBF &amp; MTT</td>
<td>Autothreshold of DWI, visual assessment of CBF for mismatch with final infarct</td>
<td>CBF values distinguish between infarct (part of acute PWI lesion and final infarct) and salvage (part of acute PWI lesion but not final infarct) more sensitively and accurately than MTT values</td>
</tr>
<tr>
<td>Rahl19</td>
<td>22</td>
<td>Absolute</td>
<td>MTT</td>
<td>Semiautomated autosegmentation</td>
<td>Spearman ρ MTT volume correlates well (ρ=0.90) with final infarct volume; in 19 of 21 patients acute MTT lesion volume &gt; final infarct volume</td>
</tr>
<tr>
<td>Rose20</td>
<td>19</td>
<td>Absolute</td>
<td>MTT</td>
<td>“Region growing” technique from DWI region seed</td>
<td>? Pearson r (unspecified) MTT volume correlates well (r=0.88) with final infarct volume; 10 of 12 patients MTT lesion volume &gt; final infarct volume</td>
</tr>
<tr>
<td>Rose13</td>
<td>19</td>
<td>Absolute</td>
<td>CBF &amp; MTT</td>
<td>Manual outline</td>
<td>Spearman ρ CBF correlates well (ρ=0.87) with final infarct volume. MTT correlates well (ρ=0.84) with, but significantly overestimates, final infarct volume. Bolus-delay correction improves correlation</td>
</tr>
<tr>
<td>Simonsen21</td>
<td>23</td>
<td>Absolute</td>
<td>MTT</td>
<td>Manual outline</td>
<td>Wilcoxon signed rank test MTT volume significantly overestimates final infarct volume by 75%</td>
</tr>
<tr>
<td>Ueda15</td>
<td>18</td>
<td>Index</td>
<td>MTT</td>
<td>Manual outline</td>
<td>MTT overestimates final infarct volume by 282%</td>
</tr>
</tbody>
</table>

*Likely includes the 18 patients reported previously in Barber et al4; $may include 18 of 38 patients reported previously in Parsons et al.18
tients who did not receive thrombolyis or experimental agents.11,12,15,20 The small sample sizes (Table 1), different PWI lesion measurement methods, inappropriate statistical tests (parametric versus nonparametric), and total absence of data comparing CBF_{sq} and MTT_{sq} (more rapidly calculated than “quantitative” data acutely) indicate that more data are required to determine which PWI parameter identifies “tissue-at-risk.”

We aimed to determine whether CBF_{sq} or MTT_{sq} on acute DSC PWI most closely identified the final T,WI infarct extent, the relationship of “DWI/PWI mismatch” and lesion growth, and to identify possible reasons for discrepancies in previous studies.

**Methods**

**Patients**

We prospectively recruited patients from the hospital stroke service with moderate to severe ischemic stroke. We performed imaging urgently (maximum for the study of 24 hours after stroke onset [baseline]). Baseline clinical assessment including the National Institutes of Health Stroke Scale (NIHSS) score and Oxfordshire Community Stroke Project (OCSP) classification were performed by a trained stroke physician. Functional outcome (modified Rankin scale [mRS]) was measured at 3 months. A panel of experts determined a final diagnosis of stroke. We recorded any acute treatments that the patients received (treatment did not affect inclusion in study).

**Imaging**

We used a GE Sigma LX 1.5T (General Electric) MR scanner with a self-shielding gradient set (22 mT/m maximum) and “birdcage” quadrature head coil. We included fast spin-echo T,WI and gradient-echo T,WI echo-planar (EP) imaging diffusion tensor protocol (DT-MRI), and DSC PWI. For DT-MRI, sets of axial diffusion-weighted EP images (b=0 and 1000 s/mm²) were collected with diffusion gradients applied sequentially along 6 noncollinear directions (5 acquisitions including baseline T,WI EP image and 6 diffusion-weighted EP images per slice position). PWI was measured by tracking gadolinium diethylenetriamine pentaacetic acid, injected intravenously by MR-compatible pump injector, for 85 s using a single-shot gradient-echo EP sequence. The DWI/PWI sequences used: 15 axial slices, 5-mm slice thickness, 1-mm slice gap, 128×128 image matrix, and 24×24 cm field-of-view.

**Image Processing**

“Semiquantitative” PWI parameters were calculated in each voxel from the signal intensities in the component EP images8 by fitting the data to a χ-variate curve. Maps of CBV_{sq} (area under fitted concentration/time curve), MTT_{sq} (first moment of fitted concentration/time curve), and CBF_{sq} (CBV_{sq}/MTT_{sq}) were generated for each voxel, converted into Analyze (Mayo Foundation) format and presented as a color-coded map. Voxels in which the data did not reach a maximum value of >2× the maximum precontrast baseline signal SD and then begin to fall before the end of the imaging time (85 seconds) were assigned as error voxels, visible as white areas on the perfusion color maps (there were extremely few patients with any of these), indicating very low flow areas in the infarct.

**Baseline PWI and DWI and Final T,WI Lesion Volume Analysis**

A neuroradiologist, blind to all clinical and other imaging data, guided the tracing by an experienced neuroscientist of the visible lesions on DWI, CBF_{sq} and MTT_{sq} maps, using a Sun Ultra Sparc Station 10 (Sun Microsystems) in Analyze (ie, a consensus of 2 experienced observers). Image brightness and contrast were optimized between areas of abnormal diffusion or perfusion and normal-appearing brain. The neuroradiologist also traced the final infarct on the latter of the 1- or 3-month T,WI as described above. Lesion volumes were obtained by summing the number of outlined voxels and multiplying by the slice thickness on each slice on which the lesion was visible.

**Statistical Analyses**

Baseline DWI, CBF_{sq}, MTT_{sq} and final T,WI lesion volumes were not normally distributed (Kolmogorov–Smirnov test; P<0.01), so median lesion volumes were compared using Wilcoxon signed rank sum tests, and correlations between baseline DWI, CBF_{sq} and MTT_{sq} volumes with final T,WI lesion volume were assessed with Spearman rank correlation coefficients (r). We also calculated mean volumes (±SD) for comparison with previous studies (Table 1), and Pearson product moment correlation coefficients (r, appropriate for parametric data) to compare baseline DWI, CBF_{sq} and MTT_{sq} with final T,WI lesion volume, to determine whether use of Pearson r might explain differences between previous studies. “Lesion growth” was defined as final T,WI lesion volume>baseline DWI lesion volume, and “DWI/PWI mismatch” as PWI lesion volumes>DWI lesion volumes. χ² tests were used to test whether DWI/CBF_{sq} or DWI/MTT_{sq} “mismatch” predicted “lesion growth.”

**Results**

**Patients**

A total of 46 patients were included; 28 of 46 (61%) were male, with an average age of 72 years (range 37 to 94 years). Mean NIHSS score on admission was 8 (median 8; range 0 to 25). For OCSP classifications, 12 of 46 (26%) patients had a total anterior circulation infarct, 29 of 46 (63%) had a partial anterior circulation infarct, 4 of 46 (9%) had a lacunar infarct, and 1 of 46 (2%) had a posterior circulation infarct. All patients were treated with aspirin, but none received thrombolysis or investigational drugs. Mean mRS score at 3 months was 2 (median 2); 2 of 46 (4%) patients were dead (mRS=6), and 13 of 46 (28%) patients were dependent (mRS=3 to 5). Mean (±SD) time from stroke onset to

**TABLE 2. Baseline DWI, CBF_{sq} and MTT_{sq} Lesion Volumes Compared With Final T,WI Volume**

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Median Volume (cm³)</th>
<th>% of Median Volume (cm³)</th>
<th>Minimum Volume (cm³)</th>
<th>Maximum Volume (cm³)</th>
<th>Mean Volume (cm³)</th>
<th>SD (cm³)</th>
<th>% of Mean Volume (cm³)</th>
<th>Final T,WI Volume</th>
<th>n&gt;T,WI Volume</th>
<th>% of T,WI Volume</th>
<th>P</th>
<th>ρ</th>
<th>χ²</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final T,WI</td>
<td>18.47</td>
<td>…</td>
<td>0.24</td>
<td>304.80</td>
<td>39.61</td>
<td>57.84</td>
<td>…</td>
<td>…</td>
<td>…</td>
<td>…</td>
<td>…</td>
<td>…</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1 or 3 months)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline DWI</td>
<td>13.28</td>
<td>72%</td>
<td>0.33</td>
<td>154.49</td>
<td>25.61</td>
<td>32.78</td>
<td>65%</td>
<td>0.14</td>
<td>20/46</td>
<td>44%</td>
<td>0.68</td>
<td>0.53</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline CBF_{sq}</td>
<td>23.74</td>
<td>129%</td>
<td>0</td>
<td>287.60</td>
<td>44.14</td>
<td>58.62</td>
<td>111%</td>
<td>0.82</td>
<td>18/46</td>
<td>39%</td>
<td>0.55</td>
<td>0.41</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline MTT_{sq}</td>
<td>50.60</td>
<td>274%</td>
<td>0</td>
<td>582.02</td>
<td>96.41</td>
<td>118.16</td>
<td>243%</td>
<td>0.00</td>
<td>30/46</td>
<td>65%</td>
<td>0.49</td>
<td>0.66</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P=exact significance result of Wilcoxon signed rank sum tests; ρ=Spearman rank, r=Pearson product moment, correlation coefficients between mean baseline DWI, CBF_{sq} and MTT_{sq} and final T,WI lesion volumes; n>T,WI volume=No. of DWI/CBF_{sq}/MTT_{sq} lesions >final T,WI volume.
baseline MRI was 10±7 hours; 18 of 46 (39%) patients were imaged within 6 hours, 11 of 46 (24%) at 6 to 12 hours, and 17 of 46 (37%) at 12 to 24 hours. Final T2WI was performed at 1 month (mean 32±4 days) in 6 of 46 (13%) patients and at 3 months (mean 96±7 days) in 40 of 46 (87%) patients.

Baseline PWI Lesion Volumes (Table 2)
Baseline CBFsq lesion volumes (median 23.74 cm³) were significantly smaller than baseline MTTsq lesion volumes (median 50.60 cm³; \( P<0.01 \)). Eleven patients (24%) had no visible lesion on baseline CBFsq and 10 patients (22%) had no visible lesion on baseline MTTsq; 6 (13%) had no visible lesion on either baseline CBFsq or MTTsq.

Baseline DWI Lesion Volumes (Table 2 and Figure 1)
All patients had a visible baseline DWI lesion. Baseline DWI lesion volumes (median 13.28 cm³) were significantly smaller than baseline CBFsq (\( P=0.01 \)) and MTTsq volumes (\( P<0.01 \)) but were not significantly different from final T2WI lesion volume (\( P=0.14 \)).

Figure 1. Scatter plots of final T2WI volumes vs baseline DWI (a), CBFsq (b), and MTTsq (c) volumes. Note volumes are in mm³; 1000 mm³=1 cm³.
Baseline PWI Versus Final T2WI Lesion Volumes (Table 2 and Figure 1)
All patients had a visible lesion on final T2WI (median 18.47 cm³) corresponding with the lesion indicated on baseline DWI. Overall, baseline CBFsq lesion volume was not significantly different from final T2WI lesion volume ($P = 0.82$). Baseline MTTsq volume was significantly larger ($P = 0.01$) than final T2WI lesion volume.

Correlation Between Baseline DWI, PWI, and Final T2WI (Table 2 and Figure 1) 
Final T2WI lesion volume most strongly correlated with baseline DWI ($\rho = 0.68$), followed by baseline CBFsq ($\rho = 0.55$) and baseline MTTsq ($\rho = 0.49$) lesion volumes (all $P<0.01$). Using Pearson’s $r$, final T2WI lesion volume was most strongly correlated with baseline MTTsq ($r = 0.66$), followed by baseline DWI ($r = 0.53$) and baseline CBFsq ($r = 0.41$) lesion volumes (all $P<0.01$).

“DWI/PWI Mismatch” and Final T2WI Lesion Volume
There was no significant association between “lesion growth” (final T2WI lesion > baseline DWI lesion) and the presence or absence of “DWI/PWI mismatch” (Table 3). On CBFsq, 15 of 25 patients with “mismatch” had “lesion growth,” and 10 of 25 patients did not; 11 of 21 without “mismatch” had “lesion growth,” and 10 of 21 did not ($\chi^2 = 0.27; P = 0.60$; Table 3). On MTTsq, 21 of 33 with “mismatch” had “lesion growth,” and 12 of 33 did not; 5 of 13 without “mismatch” had “lesion growth,” and 8 of 13 did not ($\chi^2 = 2.40; P = 0.12$; Table 3). Thus, about half of patients without “mismatch” had lesions that grew, and “mismatch” was as common among patients with lesions that grew as among those with lesions that did not grow (Figure 2).

Discussion
Because there were no previous studies testing the relationship between acute CBFsq and MTTsq and final infarct volume, we asked: which “semiquantitative” PWI parameter, if any, best predicts final infarct extent? In this large systematic study, we found that acute CBFsq lesions more closely identified final T2WI lesion extent than acute MTTsq lesions, which clearly overestimate final lesion extent. We also demonstrate that “lesion growth” was equally common among patients with lesions that grew as among those with lesions that did not grow (Figure 2).
the patients without a “mismatch” had “lesion growth”; half of those with “mismatch” did not. Although “DWI/PWI mismatch” is being used to identify patients for inclusion in trials of stroke treatments, our results imply that patients without “mismatch” may also benefit and should not be denied that possibility by being excluded.

Our findings concerning “semiquantitative” PWI parameters agree overall with the few previous “quantitative” studies directly comparing CBF$_{sq}$ and MTT$_{sq}$ 11-13 Some disparities among previous studies may result from different statistical analyses; use of Pearson $r$ instead of Spearman $\rho$ completely changed the strength and order of correlation between baseline CBF$_{sq}$ and MTT$_{sq}$ lesions and final T$_2$WI lesion volume. Previous studies also support the conclusion that acute MTT (MTT$_{sq}$ or MTT$_{q}$) lesions overestimate final lesion extent, 12-21 although some studies found stronger correlations between MTT and final infarct volumes than we did (eg, $\rho=0.77$ to 0.90 12,13,19,20); these studies used MTT$_{sq}$ were small (mean n=21; Table 1), and tested some very restricted perfusion thresholds (eg, highest 70% of MTT signal intensities12). Furthermore, it is important to distinguish between “correlation” and “size equivalence”; a good correlation between baseline MTT volume and final T$_2$WI lesion volume is not incompatible with MTT significantly overestimating the final infarct volume.

In contrast to some previous studies, 4,11-13,16,19,20 we found no significant association between DWI/CBF$_{sq}$ or DWI/MTT$_{sq}$ “mismatch” and “lesion growth” (Table 3). However, some of these studies only included patients with “mismatch.” 11,12 A recent study using “DWI/PWI mismatch” as an inclusion criteria in a thrombolysis trial 22 failed to show an association between “DWI/PWI mismatch” and lesion expansion but did show that reperfusion was inversely associated with “lesion growth.”

The superiority of “quantitative” over “semiquantitative” PWI measures is not yet proven. “Quantitative” measures are still only estimates 7 and require considerably more complex image processing than “semiquantitative” measures so are less appropriate to the acute setting. Newer perfusion measures including flow heterogeneity 21 and bolus-delay corrected maps 13 appear promising, but further validation is required to determine their overall usefulness. There is a further question concerning the use of the term “perfusion-weighted imaging” itself, which is somewhat misleading because MR perfusion maps are actually calculated parameter maps.

The strengths of the current study include the large sample, inclusion of patients with and without “DWI/PWI mismatch,” careful clinical characterization, blinded image analysis and outcome assessment, and careful use of statistics. We included patients up to 24 hours, and interestingly most (75% to 80%) had a perfusion lesion on CBF, MTT, or both, with only just >10% not having a perfusion lesion. We used manual rather than “threshold” measurement methods because the former is currently the most rapid method to apply in the clinical setting. Thresholds might reduce observer variation, but the hemodynamics underlying ischemic stroke are complex and variable. Baseline perfusion values greatly overlap between tissue that does and does not infarct, 12,17 and PWI parameter thresholds are time dependent; a threshold for ischemic but viable brain at 3 hours may be very different from that at 6 hours. None of our patients received thrombolysis or any investigational drugs, therefore this series represents a baseline measure of the presence or absence of spontaneous lesion expansion and could be used to estimate sample sizes for future acute stroke treatment trials using imaging markers of outcome. However, our data emphasize the need for further study to identify which, if any, alternative imaging markers might identify patients in whom treatments such as thrombolysis might prevent infarct growth. For example, it is unclear precisely how large artery patency relates to the PWI lesion. Are middle cerebral artery or internal carotid artery occlusions always accompanied by PWI lesions, and do these lesions resolve completely and rapidly as the artery reperfuses, or is there a time lag between arterial reperfusion and PWI lesion disappearance?

In conclusion, acute DWI, CBF$_{sq}$, and MTT$_{sq}$ lesion volumes all correlated well with final infarct volume, but acute MTT$_{sq}$ lesion volume significantly overestimated final infarct volume. Of the 2 “semiquantitative” PWI measures, the acute CBF$_{sq}$ lesion most closely identifies the final T$_2$WI lesion. There was no clear association between the presence of a “DWI/PWI mismatch” and lesion expansion, questioning the value of the “DWI/PWI mismatch” as a clinical marker of “tissue-at-risk.” About half of patients without “DWI/PWI mismatch” have “lesion growth” so they may benefit from acute stroke treatments and should probably not be excluded from clinical trials.

Acknowledgments
This study was funded by the Scottish Executive’s Chief Scientist Office (Reference No. C2B/4/14) and the Row Fogo Charitable Trust. C.S.R. is funded by a Royal Society of Edinburgh/Lloyds TSB Foundation studentship. The work was conducted at the SHeFC Brain Imaging Research Centre for Scotland.

References


Do Acute Diffusion- and Perfusion-Weighted MRI Lesions Identify Final Infarct Volume in Ischemic Stroke?

Stroke. 2006;37:98-104; originally published online December 1, 2005;
doi: 10.1161/01.STR.0000195197.66606.bb
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2005 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/37/1/98

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/