A Digital Map of Middle Cerebral Artery Infarcts Associated With Middle Cerebral Artery Trunk and Branch Occlusion

Thanh G. Phan, FRACP; Geoffrey A. Donnan, MD, FRACP; Peter M. Wright, FRACP; David C. Reutens, MD, FRACP

Background and Purpose—Knowledge of the topographic distribution of infarcts of the middle cerebral artery (MCA) may give insight into the limits of the arterial territory and infarct mechanism and may influence the decision to use thrombolytic therapy. We describe the creation of a digital atlas of MCA (DA-MCA) infarction associated with MCA branch and trunk occlusion using magnetic resonance (MR) techniques.

Methods—Hemispheric infarcts, with evidence of MCA trunk or branch occlusion, were manually segmented into binary images, linearly registered into a common stereotaxic coordinate space, and averaged to yield the probability of involvement by infarction at each voxel. Comparisons were made with existing maps of the MCA territory.

Results—Twenty-eight patients with median age of 74 years (range, 26 to 87 years) were studied. On the DA-MCA, the highest frequency of infarction was within the striatocapsular region, centrum semiovale, and the insula. The mean and maximal MCA infarct volumes were 195.5 cm³ and 366.3 cm³, respectively. Comparison with published maps showed that the most common difference from the DA-MCA was in the superomedial extent of the MCA territory. Some maps showed the MCA territory reaching the interhemispheric fissure, whereas in the DA-MCA it did not. There was a lower variability in the anterior boundary of the MCA territory compared with its posterior counterpart.

Conclusion—We have created a digital atlas of MCA infarction using MR imaging techniques. This approach may be useful to establish the distribution of the MCA and other arterial territories and the border zones between them with greater certainty. (Stroke. 2005;36:986-991.)

Key Words: magnetic resonance imaging ■ middle cerebral artery ■ stroke

Accurate knowledge of the territory infarcted after the occlusion of a specific cerebral artery provides important information about stroke mechanism and aids the planning of investigations and subsequent therapy. Delineation of the arterial territory or territories involved by ischemic stroke can help the clinician to narrow or widen the scope of investigations. For example, involvement of multiple territories prompts the search for a more proximal embolic source. In addition, accurate knowledge of arterial territory allows the distinction between infarcts located within an arterial territory and infarcts located in the border zone between arterial territories to be made. The latter may suggest a different infarct mechanism. More recently, information on the spatial extent of infarction has been incorporated into therapeutic decision-making for middle cerebral artery (MCA) infarcts; the percentage of the vascular territory affected by early ischemic changes has been correlated with an increased risk of hemorrhage after the administration of recombinant tissue plasminogen activator. However, the MCA template and the volume on which this recommendation is based is unclear. Absence of a clear operational definition of the MCA territory may be partly responsible for the low agreement between raters on the extent of involvement.

Available maps of cerebral arterial territories are largely perfusion maps based on injection studies in cadavers. These territories may not be comparable with the area affected by arterial occlusion in subjects with ischemic stroke because of the younger age of subjects used to create cadaveric maps, and the presence of atherosclerotic disease in patients and potential collateral blood supply, which may influence the region at risk of infarction. Hence, there is a need for an alternate strategy in which the topography of infarcts caused by known occlusions of specific arteries is mapped. The correspondence between these 2 mapping modalities is unknown but may not be close. Further, previously
published maps have a limited number of slices and may be difficult to use in clinical practice if the site of infarction is not at the same level as the one depicted.4–6,9,10

To map the topographical distribution of MCA infarcts, we have created a digital atlas of MCA infarcts from T2-weighted magnetic resonance imaging (MRI) scans in patients with demonstrated occlusion of the MCA trunk or M1 or M2 segments. This map was then compared with existing maps of the MCA territory.

Patients and Methods

Patient Selection

The reports of MRI scans performed in our institution between January 1999 and December 2002 were reviewed for the presence of MCA trunk or branch occlusion on time of flight MR angiography (MRA). MR images were then inspected and the clinical notes reviewed.

Patients were included in the study if they had images demonstrating “occlusion” of the MCA trunk and/or M1 and M2 branches on the initial MRA as defined by loss of signal on the maximum intensity projection and the corresponding source images of the MR angiogram, and if they had T2-weighted MR scans performed >48 hours after stroke onset.

In 9 of the 28 patients fulfilling these criteria, MR scanning was performed on a single occasion. The remaining 19 patients had serial MR scans as part of an observational study of infarct evolution. In these patients, MCA occlusion was identified on the initial MR scan and infarct segmentation was performed on the final MR scan.

Patients who had new infarcts or concurrent infarcts in the posterior cerebral artery and anterior cerebral artery territory were excluded. The mechanism of infarction was determined according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria as large-artery atherosclerosis, cardioembolism, small-vessel occlusion, or MCA trunk or branch occlusion. The volume of tissue at a distance of 1 cm from the infarct edge was not measured due to the limited number of slices.11 No patient received recombinant tissue plasminogen activator.

Imaging Techniques

MRI scans were performed on a 1.5-Tesla superconducting imaging system (General Electric Medical Systems) with echo-planar imaging capabilities. Fast-spin echo T2 images were acquired using thickness 6 mm/1.7 mm, matrix 256×256, and repetition time [TR]/echo time [TE]/echo train length 2000 ms/102 ms/12. Diffusion-weighted imaging was performed using echo-planar imaging techniques with 6 mm/1.7 mm thickness, matrix 128×256, field of view 230 mm, and TR/TE 10 000/102 ms. Diffusion-gradient values (b values) of 0 s/mm² and 1000 s/mm² were applied in 3 directions. The images with the 1000 s/mm² diffusion gradient are referred to here as diffusion-weighted imaging images. Isotropic ADC maps were calculated using the Stesjkal and Tanner equation on a voxel-by-voxel basis. The 3-dimensional time of flight MRA was performed using TR/TE 38 ms/6.9 ms, 25° flip angle, thickness 1.4 mm, slab thickness 60 mm, matrix 256×224, and field of view 180 mm.

Registration and Segmentation

Alignment of corresponding anatomical structures in images (before segmentation) from different subjects was achieved by registration to a standard brain template comprising images from 152 subjects placed into the stereotaxic coordinate space of Talairach and Touroux (MNI 152 brain template available at http://www.bic.mni.mcgill.ca/software/).12 Manual internal and external landmark-based registration to the template yielded a 9-parameter linear transformation matrix allowing rotation, translation, and scaling along each of the 3 principal axes.13 Hence, registration also had the effect of correcting for overall differences in brain size.

Phan et al A Digital Map of MCA Infarcts 987

Registration errors were assessed by applying a known linear transformation matrix, here termed the simulation matrix, to T2-weighted phantom images generated in standard stereotaxic coordinate space with dimensions and field of view corresponding to the patients’ T2-weighted images. The resultant image was then manually registered to an isotropic T1-weighted image yielding a transformation matrix, here termed the registration matrix. Multiplication of the 2 transformation matrices yielded the matrix describing registration errors. Registration errors were calculated for 20 randomly chosen voxel positions and 10 simulation matrices. The mean Euclidean distance between original voxel position and the position after registration was calculated.

Segmentation was performed on the subacute and chronic MR scans. Infarcts were manually segmented on T2-weighted images using interactive mouse driven software and standardized intensity windows.

Creation of Digital Atlas

To create a composite map, the images from subjects with infarcts in the right hemisphere were also flipped along the y-axis so that all infarcts lay on the left side of the image according to the radiological convention.

Registered binary images of the infarcts were averaged to create the digital atlas of MCA (DA-MCA). Anatomical interpretation was facilitated by the use of an existing database relating Talairach coordinates to anatomical structures (Talairach Daemon; http://ric.uthsc.edu/projects/talairachdaemon.html).14 Calculation of the volume of MCA territory infarcts was restricted to patients with MCA trunk occlusion. The volume of tissue at a number of probability thresholds was calculated. Voxels with probabilities exceeding the minimum probability (ie, the maximum extent of the infarct territory) and mean probability comprised the maximum and the mean infarct volumes, respectively. The mean and standard deviation of these measurements of MCA territory infarct volume were calculated by a “leave one out” or jack-knife analysis.15

Comparison With Existing Maps

Comparisons with existing vascular territory maps were performed both qualitatively and quantitatively. Maps chosen for comparison were those widely cited in the literature. Maps by van der Zwan et al,16 Beevor,6 Gibo et al10 and Tatoo et al18 were based on arterial injection studies in cadavers unaffected by stroke. Caviness et al16 created a map based on MR imaging of stroke patients with cortical features as the inclusion criteria. The map of Damasio9 is a composite map derived from textbooks on the cerebral circulation.

Results

Assessment of Registration Errors

In the phantom study to assess registration errors, the mean error in registration was 2.3 mm±1.1 mm.

Clinical Characteristics

There were 28 patients (13 males) with a median age of 74 years (range, 26 to 87 years; interquartile range, 64 to 78 years). Fifteen patients had right-side and 13 had left-side MCA territory infarcts. Of these, 19 patients were also enrolled in another observational study of infarct evolution and hence had serial MR scans. Nine patients had MR imaging performed as part of routine stroke workup. As a result of this the T2-weighted MRI scan that was used for segmentation was performed at a median interval 55 days (range, 2 to 150 days; interquartile range, 6 to 90 days) after stroke onset. The stroke mechanisms and sites of arterial occlusion are displayed in Table 1. The mean and maximum infarct volumes are shown in Table 2.
The regions with the highest probability of MCA infarction were striatocapsular ($P = 0.73$), centrum semiovale ($P = 0.73$), and the insula ($P = 0.50$) (Figure 1). The mean and median probabilities of infarction were 0.17 and 0.15, respectively.

### Table 1. Clinical Characteristics Including Time of MR Scan, Severity of Neurological Deficit, Stroke Mechanism, and Sites of Arterial Occlusion

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Sex</th>
<th>NIHSS on Admission</th>
<th>Initial MR Scan, h from Stroke Onset</th>
<th>Final MR Scan, d from Stroke Onset</th>
<th>Side of Infarction</th>
<th>TOAST Classification</th>
<th>ICA Occlusion</th>
<th>MCA Trunk Occlusion</th>
<th>MCA Branch Occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>77</td>
<td>M</td>
<td>9</td>
<td>3.7</td>
<td>120</td>
<td>L</td>
<td>Large artery</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>67</td>
<td>F</td>
<td>21</td>
<td>1.6</td>
<td>90</td>
<td>L</td>
<td>Large artery</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>70</td>
<td>M</td>
<td>4</td>
<td>...</td>
<td>3</td>
<td>L</td>
<td>Large artery</td>
<td>+</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>71</td>
<td>M</td>
<td>16</td>
<td>2.5</td>
<td>90</td>
<td>R</td>
<td>Large artery</td>
<td>–</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>83</td>
<td>M</td>
<td>25</td>
<td>21.8</td>
<td>13</td>
<td>L</td>
<td>Large artery</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>63</td>
<td>M</td>
<td>4</td>
<td>3.7</td>
<td>85</td>
<td>R</td>
<td>Large artery</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>84</td>
<td>F</td>
<td>25</td>
<td>...</td>
<td>4</td>
<td>R</td>
<td>Large artery</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>26</td>
<td>F</td>
<td>13</td>
<td>8.5</td>
<td>91</td>
<td>R</td>
<td>Large artery</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>38</td>
<td>F</td>
<td>24</td>
<td>...</td>
<td>93</td>
<td>R</td>
<td>Large artery</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>75</td>
<td>M</td>
<td>20</td>
<td>...</td>
<td>26</td>
<td>R</td>
<td>Large artery</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>78</td>
<td>F</td>
<td>5</td>
<td>3</td>
<td>69</td>
<td>L</td>
<td>Large artery</td>
<td>+</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>83</td>
<td>F</td>
<td>11</td>
<td>4.7</td>
<td>7</td>
<td>R</td>
<td>Large artery</td>
<td>+</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>40</td>
<td>F</td>
<td>13</td>
<td>...</td>
<td>2</td>
<td>R</td>
<td>Large artery</td>
<td>+</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>78</td>
<td>M</td>
<td>10</td>
<td>...</td>
<td>4</td>
<td>R</td>
<td>Cardioembolic</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>72</td>
<td>F</td>
<td>21</td>
<td>65</td>
<td>90</td>
<td>L</td>
<td>Cardioembolic</td>
<td>–</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>62</td>
<td>F</td>
<td>20</td>
<td>4.2</td>
<td>90</td>
<td>L</td>
<td>Cardioembolic</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>74</td>
<td>M</td>
<td>12</td>
<td>8.5</td>
<td>30</td>
<td>R</td>
<td>Cardioembolic</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>60</td>
<td>M</td>
<td>6</td>
<td>...</td>
<td>19</td>
<td>R</td>
<td>Cardioembolic</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>75</td>
<td>F</td>
<td>5</td>
<td>120</td>
<td>40</td>
<td>R</td>
<td>Cardioembolic</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>73</td>
<td>F</td>
<td>21</td>
<td>20.8</td>
<td>90</td>
<td>L</td>
<td>Cardioembolic</td>
<td>–</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>78</td>
<td>M</td>
<td>5</td>
<td>5.3</td>
<td>90</td>
<td>R</td>
<td>Cardioembolic</td>
<td>–</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>81</td>
<td>F</td>
<td>23</td>
<td>28.6</td>
<td>150</td>
<td>L</td>
<td>Unknown</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>67</td>
<td>F</td>
<td>12</td>
<td>3.4</td>
<td>7</td>
<td>L</td>
<td>Unknown</td>
<td>–</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>87</td>
<td>F</td>
<td>21</td>
<td>1.95</td>
<td>120</td>
<td>L</td>
<td>Unknown</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>57</td>
<td>M</td>
<td>7</td>
<td>2</td>
<td>3</td>
<td>L</td>
<td>Unknown</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>75</td>
<td>F</td>
<td>6</td>
<td>...</td>
<td>4</td>
<td>R</td>
<td>Unknown</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>63</td>
<td>M</td>
<td>15</td>
<td>4</td>
<td>90</td>
<td>L</td>
<td>Unknown</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>77</td>
<td>M</td>
<td>9</td>
<td>...</td>
<td>3</td>
<td>R</td>
<td>Unknown</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
</tbody>
</table>

F indicates female; ICA, internal carotid artery; L, left; M, male; MCA, middle cerebral artery; NIHSS, National Institute of Health Stroke Scale; R, right; TOAST, Trial of Org 1–172 in Acute Stroke Treatment.

Comparison With Existing Maps

The maximum infarct volume of the DA-MCA was similar to that of the map by van der Zwan (Table 2). The anatomical location of the boundaries of the MCA infarct territory in each map is provided in Table 3. The maximal extent of the digital map resembles the Beevor, Damasio, and Gibo maps more closely than the Tatu and van der Zwan maps.

### Table 2. Comparison of the MCA Territory Infarct Volume for the Digital Atlas and Maps by van der Zwan and Caviness

<table>
<thead>
<tr>
<th>MCA Territory Volume</th>
<th>DA-MCA (n=28)</th>
<th>Van der Zwan Map (n=23)</th>
<th>Caviness Map (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximal extent: voxel probability &gt; 0 (mean volume ± SD)</td>
<td>366.3 ± 13.1 cm³</td>
<td>408.3 cm³</td>
<td>264.0 cm³</td>
</tr>
<tr>
<td>Voxel probability &gt; mean probability (mean volume ± SD)</td>
<td>195.5 ± 19.0 cm³</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Mean infarct volume ± SD</td>
<td>...</td>
<td>284.4 cm³ ± 65.2 cm³</td>
<td>103.3 cm³</td>
</tr>
</tbody>
</table>

Infarct volumes are shown for predetermined probability thresholds for the digital atlas. Maximal and mean infarct volumes reported for the other maps are shown for comparison.

Discussion

Accurate visualization of cerebral infarct location remains a key pointer to underlying mechanism. Until recently, location
of infarcts within a vascular territory depended on information obtained from cadaver studies of normal vascular anatomy. We have used a more direct approach by creating a digital atlas of MCA territory infarcts. One advantage of this approach is the absence of a priori constraints on infarct size, shape, and location. To be certain of the vascular territory involved, the presence of MCA trunk or branch occlusion on MRA was an essential inclusion criterion.

Previous anatomical maps of the MCA territory have depended on a variety of injection techniques. However, overflow of injection material through anastomosing arteries, variability in the physical properties of the injectate, and the difficulties of distinguishing between territories when all the arteries were injected with the same dye have hampered the interpretation of the maps. Earlier maps and templates depicted the arterial territories as being symmetrical and invariant.3 The digital approach used here captures the variability in infarct location more realistically. van der Zwan and Hillen3 have highlighted the importance of territorial variability and have pointed out the inconsistencies between previous cadaver studies. The most common discrepancy between studies was in the superomedial extent of the MCA territory, with some maps showing the maximal extent of the MCA territory reaching the interhemispheric fissure.6,16,17 In the DA-MCA, the development or presence of leptomeningeal collaterals may have modified the MCA infarct territory because the posterior extent of the territory was variable and the superomedial extent did not reach the interhemispheric fissure. Variable involvement of the precentral gyrus after MCA infarction has been explained by its supply from branches of the anterior cerebral artery and MCA.18

A recent MRI study of MCA infarct location by Caviness et al16 was significantly different from the current map and that by previous investigators in that the MCA territory was shown to reach the frontal pole anteriorly and almost reached the occipital pole posteriorly.6,16,17 The discrepancy may have been caused by the use of clinical features such as dysphasia as inclusion criteria by Caviness et al. This may have led to inclusion of cases with embolism to the anterior or posterior cerebral arteries in addition to the MCA.6,10,16,17 The inclusion criteria that we used allowed us to exclude such patients.

In the DA-MCA, the highest probability of involvement was in the striatum, centrum semiovale, and insula, suggesting that collateral blood supply was most likely to be inadequate in these regions. This finding is consistent with the observation that the striatocapsular and insular regions
show the earliest signs of ischemia on CT and these regions are the most susceptible to ischemia in the reversible MCA occlusion model in the baboon. Previous anatomical studies indicate that the arterial supply of the insula is derived solely from the MCA. The perforating medullary branches of the MCA have a dominant role in the arterial supply of the putamen and globus pallidus and do not appear to have a significant collateral supply.

Two previous anatomical studies are similar to ours in that the investigators have attempted to capture the variability in vascular territory. The resultant maps are difficult to interpret, however, because of the limited number of brain sections depicted and the expression of variability in terms of maximum and minimum territorial maps. We have used voxel-based maps of infarct probability to circumvent these constraints. Nonetheless, there are several similarities between the findings of our study and the arterial injection studies by van der Zwan. These include the lower variability in the anterior boundary of the MCA territory compared with its posterior boundary.

In addition to the technical difficulties affecting injection studies, previous anatomical maps have generally relied on a stylized brain template and manual superimposition of the arterial territory. Although the accuracy of this process is difficult to quantify, this issue has evoked surprisingly little comment. In our study, errors in registration to a standard brain template were small. Furthermore, previous maps of the MCA territory have used templates in different planes, often with a limited number of brain slices for comparison. This poses additional difficulties for comparison of infarct territories. In contrast, the DA-MCA can be transformed and resampled into other orientations or slice thickness.

In this study, MCA occlusion was defined on time of flight MRA. Although it is possible that in some cases MCA occlusion was not complete but that there was trickle flow, this is not likely to affect the results of the study significantly given that it is still indicative of severe hypoperfusion. Infarcts were segmented at a median delay of 55 days after stroke onset, MCA infarct extent may have been underestimated as a result of the effects of atrophy. We cannot exclude the occurrence of other infarcts within the MCA territory subsequent to the initial MRA. However, 2 patients with infarcts clearly within the posterior cerebral artery or anterior cerebral artery territory were excluded.

We have created a digital atlas of MCA territory infarction using MRI techniques. This approach may be useful to establish the distribution of the MCA and other arterial territories and the border zones between them. Further, the
DA-MCA can be used to objectively define the arterial territory using a predetermined threshold probability.

Acknowledgments
We thank Lichun Quang and Indra Lim for their assistance in preparing the figures. T.G.P. is supported by a postgraduate medical research scholarship awarded by the National Health and Medical Research Council, Australia.

References
A Digital Map of Middle Cerebral Artery Infarcts Associated With Middle Cerebral Artery Trunk and Branch Occlusion
Thanh G. Phan, Geoffrey A. Donnan, Peter M. Wright and David C. Reutens

Stroke. 2005;36:986-991; originally published online April 7, 2005;
doi: 10.1161/01.STR.0000163087.66828.e9

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/36/5/986