Original Contributions

Anatomy of Stroke, Part I
An MRI-Based Topographic and Volumetric System of Analysis

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Background and Purpose—The clinical diagnosis and treatment of stroke, as well as investigations into the underlying pathophysiology of the disease, hinge on inferences from the anatomy of the stroke lesion. We describe an MRI-based system of topographic and volumetric analysis that considers distribution of infarct with respect to neuroanatomic structures, superficial and deep perfusion compartments, and gray and white matter tissue types.

Methods—MRI-based 3-dimensional topographic and volumetric analysis of presumed MCA embolic stroke was performed months after the acute event in 21 subjects ranging in age from 34 to 75 years.

Results—The topography of infarction was greatly variable, with virtually all regions of the MCA territory involved in at least 1 stroke in the series. In 14, there was involvement of the M1 as well as the M2 through M4 territories; in 6, there was involvement of only the M2 through M4 territories; and in 2, there was involvement of only the M1 territory. The volumes varied from 3.1 to 256 cm³, corresponding approximately to a range of 1% to 90% of the total MCA territory.

Conclusions—The system of topographic and volumetric analysis is generally applicable to all strokes in the forebrain and an increase in tissue tolerance to ischemia. MRI directed toward both reestablishment of flow after occlusion from the anatomy of the stroke lesion. Treatment has been lying pathophysiology of the disease, hinge on inferences from the anatomy of the stroke lesion. Treatment has been directed toward both reestablishment of flow after occlusion and an increase in tissue tolerance to ischemia. MRI affords approximate estimates of stroke topography and size with respect to numerous aspects. Coordinated diffusion and perfusion studies go even further to provide a view of the evolution of stroke contour in relation to a perimeter of relative hyperperfusion. Although quantitative uses at present are limited, MRI is also suitable for volumetric study of stroke and the brain damaged by stroke.

We present here an MRI-based system for topographic and volumetric study of cerebral stroke with images obtained months after the acute event. Infarctions all involve the territory of perfusion of the middle cerebral artery (MCA) and are presumed, but not demonstrated, to have occurred consequent to an embolus within the MCA system. Images were obtained from an ongoing study of subjects recruited for investigations of aphasia. However, the association of a language or indeed other neurological deficits with stroke was only incidental to the purposes of the present analysis, which were strictly those of anatomic analysis. The analysis follows standard neuroanatomic subdivisions of the brain and partitions further with respect to differential arterial perfusion compartments and tissue types. A companion manuscript illustrates its application in an analysis that has theoretical implications for patterns of perfusion within the territory of stroke. Intended applications include correlation with predictions from acute-phase diffusion- and perfusion-weighted imaging and investigations of the potential benefit of therapeutic agents. (Stroke. 2002;33:2549-2556.)

Key Words: embolism • image processing, computer assisted • magnetic resonance imaging • stroke, cardioembolic

Thromboembolic stroke may occur at any moment in the human life cycle. It is a principal cause of morbidity and death in middle and late life. The clinical diagnosis and treatment of stroke, as well as investigations into the underlying pathophysiology of the disease, hinge on inferences from the anatomy of the stroke lesion. Treatment has been directed toward both reestablishment of flow after occlusion and an increase in tissue tolerance to ischemia. MRI affords approximate estimates of stroke topography and size with respect to numerous aspects. Coordinated diffusion and perfusion studies go even further to provide a view of the evolution of stroke contour in relation to a perimeter of relative hyperperfusion. Although quantitative uses at present are limited, MRI is also suitable for volumetric study of stroke and the brain damaged by stroke.

We present here an MRI-based system for topographic and volumetric study of cerebral stroke with images obtained months after the acute event. Infarctions all involve the territory of perfusion of the middle cerebral artery (MCA) and are presumed, but not demonstrated, to have occurred consequent to an embolus within the MCA system. Images were obtained from an ongoing study of subjects recruited for investigations of aphasia. However, the association of a language or indeed other neurological deficits with stroke was only incidental to the purposes of the present analysis, which were strictly those of anatomic analysis. The analysis follows standard neuroanatomic subdivisions of the brain and partitions further with respect to differential arterial perfusion compartments and tissue types. A companion manuscript illustrates its application in an analysis that has theoretical implications for patterns of perfusion within the territory of stroke. Intended applications include correlation with predictions from acute-phase diffusion- and perfusion-weighted imaging with respect to tissue that is infarcted and tissue that is potentially viable, as well as correlation with measures of long-term neurological outcome and adaptation.

Materials and Methods

Subjects
There were 21 subjects (10 men, 11 women; age range, 34 to 75 years; mean age, 57.5±12.5 years). Nineteen were right handed; 1 was left handed; and for 1, hand preference was not determined.
There were 3 entry criteria. First, dysphasic disturbance was of acute onset and considered by the clinical staff to be consequent to an embolus in the MCA territory of the language-dominant hemisphere. Second, there had been no clinically (by history or examination) recognized prior stroke or other cerebral disorder that might have impaired cognitive and language processing. Third, a language disturbance persisted at the time of imaging. The study was conducted within the guidelines of Institutional Review Board approval and with patients’ and their families’ informed consent. The median interval between the acute stroke and the imaging sequence was 16 months.

Magnetic Resonance Imaging

MRI was performed on a General Electric 1.5-T Signa MR system. The acquisitions included a conventional sagittal scout, a coronal T2-weighted sequence, and a coronal 3-dimensional, T1-weighted, spoiled gradient echo pulse sequence (repetition time, 50 ms; echo time, 9 ms; flip angle, 50°; field of view, 24 cm; contiguous 3.0-mm coronal slices; 60 matrices; 256×256; average, 1).

Image Processing

The routine of image analysis that precedes the anatomic analysis operation from 3-dimensional T1-weighted images has been previously detailed. A coordinate system is defined for the MR images for each brain so that the anterior-posterior axis corresponds to the anterior commissure–posterior commissure line. The superior-inferior axis is set orthogonal to the anterior-posterior axis, passing through the interhemispheric fissure, and the medial-lateral axis is orthogonal to the other axes. A new set of coronal planes is reconstructed according to the above coordinate system at the plane thickness of the original acquisition.

The brain was segmented into forebrain, brainstem, and cerebellum. The forebrain was further segmented by standard algorithms into cerebral cortex, cerebral white matter, caudate, putamen, pallidum, thalamus, hippocampus, and amygdala. The principal cerebral cortical gyri were parcellated by a semiautomated method into 48 parcellation units (PUs) per hemisphere with reference to a set of anatomical landmarks and the course of fissures (Figure 1). The terminology of the parcellation system and its abbreviations follow the canonical gyral nomenclature in which F, T, O, and P refer to the location in the frontal, temporal, occipital, and parietal lobes and L (lateral), M (medial), I (inferior), S (superior), and numbers designate relative positions or order within a lobe or partition of a gyrus. A PU was considered to be involved by MCA stroke only if it was among the 30 in our parcellation system that fall within the classically accepted territory of perfusion of the MCA and if at least 10% of the native volume of the PU was involved.

The perimeter of the principal infarction was traced “by eye” but using the full dynamic range of signal intensity allowed by the imaging parameters (Figure 1). Frank cavitation and a surrounding rim of altered signal intensity were readily distinguished from adjacent brain tissue. When the perimeter extended to the surface of the hemisphere, a “veil” of somewhat thickened and presumably scarred leptomeningeal membrane invariably preserved the outlines of fissures and gyri involved in the stroke. Volumetric concordance of bilaterally represented structures is normally within 10%, 1, 13, 19, 20 Therefore, pre-stroke contours of structures destroyed within the stroke perimeter were reconstructed on image overlays by a hand-driven cursor by reference to corresponding undamaged structures in the opposite hemisphere. We assume that the assigned perimeter somewhat underestimates the true boundary between normal and damaged tissue, in part because some tissue components, eg, neuronal somata or oligodendroglia, are more vulnerable than others, eg, astrocytes. This accepted, we expect the margin of error to be small relative to the substantial total volume of these strokes and to be more or less systematic across the series of brains. Volumes for brain regions and PUs were computed from the imaging parameters and the number of voxels assigned to that PU in the course of the segmentation and parcellation routines.

For subsequent analysis, we distinguish a “superficial” compartment corresponding to the perfusion territory of the leptomeningeal branches (M2 through M4) of the MCA (cortex and subjacent white matter radiata and a “deep” compartment (basal ganglia, thalamus, amygdala, and white matter of the capsules and commissures) corresponding to the perfusion territory of the M1 division of the MCA system. We also distinguish a partition into gray (cortex and deep nuclei) or white (radiata and deep) matter tissue types.

Results

A principal infarction was located in the centro-sylvian region in each of the 21 brains (Figure 2). In 11 brains, there were also ≥1 relatively small secondary subcortical foci of ischemic leukomalacia (2.5±3.4 cm³) at the depth of the sagittal strata. There was a small lacunar infarction within the caudate head in a single brain.
Stroke and Vascular Topography

Of the principal infarctions, 17 were within the left (15 right-handed people, 1 left-handed person, 1 whose handedness not determined) and 4 within the right (all right handed) hemisphere. In all but 3, these fell exclusively within the classically accepted territory of perfusion of the MCA. In 3, infarctions also involved the accepted territories of perfusion of the anterior (the medial frontal and cingulate cortical fields, patients 5 and 8) or the posterior (the medial occipital and occipital polar fields, patient 1) cerebral arteries.

The collective set of infarctions considered, all cerebral regions within the M2 through M4 perfusion territory were involved (Figure 2). There was, however, a preponderant emphasis on the insular and adjacent opercular region (M2 and M3 territories) and the cortical regions supplied by the precentral, central, and anterior parietal branches of the M4 system. With reference to the subdivisions of the MCA, we distinguish by case number the 4 general patterns of distribution of infarction. Infarction may be (1) limited to the M1 territory (patients 20 and 21), (2) limited to the M2 through M4 territory (patients 11, 12, 15 through 17, and 19), (3) distributed within both the M1 and M2 through M4 territories where the tissue volumes involved are continuous (patients 2, 4, 6, 8, 9, and 18), and (4) distributed within both the M1 and M2 through M4 territories where the tissue volumes involved are discontinuous (patients 1, 5, 7, 10, 13, and 14). Patterns 1 and 2 illustrate the commonplace occurrence in which infarction occurs independently either in the deep nuclear and capsular (M1 alone) or in the superficial cortical territories of the MCA (M2 through M4 alone).

Stroke Volume and Brain Topography

The total volumes of the infarctions are distributed over a 2-order-of-magnitude range, 3.1 to 256 cm³, with a mean of 103.3 cm³ (left, 104.8 cm³; right, 95.6 cm³; Table 1). The volumes of individual infarctions spread relatively evenly (a uniform distribution) through this range (Figure 3A). With respect to the full series, ~60% and 20% of the total stroke
volume are assigned to cortex and radiate white matter, respectively (Figure 3B). Estimates of lesioned structure volumes were on average 12.8% less than the measured volumes of the corresponding unlesioned structure in the hemisphere contralateral to the principal lesion. For the cortex on the lesioned side, the difference was negligible. However, for deep nuclear structures, the estimate of the volumetric extent on the side of stroke was variably 15% to 20% less than the measured volumes of the corresponding unlesioned structures in the opposite hemisphere (Table 1).

<table>
<thead>
<tr>
<th>Anatomic Region</th>
<th>Structural Volume, cm³</th>
<th>Lesion Volume, cm³</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>Cerebrum</td>
<td>557.3±61.7</td>
<td>543.2±60.0</td>
</tr>
<tr>
<td>Cortex</td>
<td>301.1±34.3</td>
<td>298.8±32.9</td>
</tr>
<tr>
<td>White matter</td>
<td>209.9±28.9</td>
<td>193.0±27.4</td>
</tr>
<tr>
<td>Thalamus</td>
<td>6.5±1.4</td>
<td>5.2±1.4</td>
</tr>
<tr>
<td>Ventral DC</td>
<td>4.1±0.8</td>
<td>3.4±0.7</td>
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<tr>
<td>Caudate</td>
<td>2.9±0.9</td>
<td>2.4±0.6</td>
</tr>
<tr>
<td>Accumbens</td>
<td>0.5±0.1</td>
<td>0.4±0.2</td>
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<tr>
<td>Putamen</td>
<td>4.1±0.6</td>
<td>3.6±0.6</td>
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<tr>
<td>Pallidum</td>
<td>1.4±0.3</td>
<td>1.2±0.2</td>
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<tr>
<td>Hippocampus</td>
<td>4.3±0.6</td>
<td>3.7±0.7</td>
</tr>
<tr>
<td>Amygdala</td>
<td>1.7±0.4</td>
<td>1.6±0.4</td>
</tr>
<tr>
<td>Lateral ventricle</td>
<td>20.1±11.3</td>
<td>29.4±9.6</td>
</tr>
</tbody>
</table>

DC indicates diencephalon. Values are mean±SD.
We attribute this disparity in part to an error in the estimate of structure contour with stroke and in part to secondary atrophy within surviving deep white and gray matter.

Gyral PUs within the classic territory of perfusion of the MCA were infarcted in 19 of the 21 brains (90%) (Table 2). A small number of PUs in only 3 subjects were excluded when infarction was judged to extend into the territories of perfusion of the anterior or posterior cerebral arteries (patients 1, 5, and 8; Figure 2). For this subset of 19 brains, the probability that 1 of the MCA PUs will be involved ranges from 0.84 to 0.16 (Figure 4), with a mean of 0.54. For 19 (63%) of the PUs, specifically those of the insula, opercular, paracentral, inferior and frontal and the junction of the temporal, parietal, and occipital regions, this probability is at least 0.5. For only 6 MCA PUs, principally at the inferior and posterior temporal and superior frontal regions this probability is less than 0.3. The mean volume of tissue destroyed in the MCA PU ranges from 0.4 to 10.5 cm³, corresponding to a range of 30.6% to 88.3% of the individual PU, with mean of 57.6% (Table 2).

In 15 brains in which stroke involved the deep perfusion compartment, putamen, pallidum, and caudate were involved with probabilities of 1.0, 0.80, and 0.87. The average fraction of nucleus damaged was 53%, 67%, and 48%, respectively, for the 3 nuclei. That is, the putamen was involved in all and the other 2 in most of the cases that included the M1
compartment. In all 15 cases, there was also injury to the deep white matter of the capsules. The ventral diencephalon was involved in only 1 case, the thalamus and amygdala in 2 cases each, and the accumbens in 3 cases. The fractional damage to both diencephalic structures was \( \approx 20\% \) and to accumbens and amygdala \( \approx 50\% \) each. In each of these brains, the patterns of neocortical PU involvement indicated that there had been associated infarction in the territory of either the anterior or posterior cerebral artery territories.

**Discussion**

The principal infarctions in this series of strokes are presumed to be due to occlusions within the MCA arterial system because of the mixed patterns of superficial and deep infarctions typical of stroke within the territory of perfusion of the MCA.\(^{28,29}\) We assume that most were caused by embolus but have not excluded thrombotic propagation from the internal carotid. Because each stroke was associated with stable dysphasia, this selection criterion would have favored infarction to the centro-sylvian region of the left hemisphere. Despite these expected biases, the topographic patterns of infarction in this series appear to be largely representative of those encountered in large acute neurology services in a number of ways.\(^{28,30-32}\) First, MCA strokes involve the M1 and the M2 through M4 territories much more frequently than the M2 through M4 or the M1 alone. Moreover, separate or clustered branches of the M4 subdivision appear to be involved independently. That is, infarction in the territory of the M1 stem was not generally associated with infarction throughout the M2 through M4 territory. The largest stroke encountered here, 254 cm\(^3\), approaches 90\% of the total perfusion territory of the MCA or \( \approx 50\% \) of the hemisphere.\(^{19,33}\) Only 2 (10\%) were pervasive throughout the MCA territory, a percentage of the total similar to the 7.6\% proportion for massive strokes encountered in the general Lausanne Stroke Registry.\(^{34}\)

The occurrence of infarction in the territories of the individual M4 branches with or without infarction in the

**Figure 4.** Infarction probability for the MCA PU. Intensity of shading of a PU represents the probability that it was lesioned by >10\% of its volume in the full series of cases.
territory of the M1 stem, we suggest, unlikely to be caused by a single vascular occlusive event. On the contrary, it suggests the occurrence of multiple occlusive events either concurrently or in series. Certainly, complex patterns of this type resulting from embolus have established precedent not only within a given principal territory but also targeting multiple principal territories.29,35–37 Thus, in the present series, there are 3 cases (15%) in which the topographic evidence suggest embolus to the anterior or posterior cerebral arteries, as well as to the MCA. Again, this is a pattern with precedent in other series.29,35,37

Stroke Volume and Vascular Topography

Overall in the series, the volumes of tissue destroyed by infarction in the superficial perfusion compartment greatly exceed those destroyed in the deep perfusion compartment. This disproportion in topographic distribution of stroke reflects the disproportion in volume of the perfusion territories whereby that of the M2 through M4 area is much greater than that of the M1 subdivisions of the MCA system. With respect to deep structures of the hemisphere, the present topographic patterns affirm the location of striatum, pallidum, and capsules but not that of the thalamus and amygdala to be within the M1 territory.18

Finally, the partition with respect to tissue type highlights an overrepresentation within the lesion volume of gray matter structures with respect to white in strokes caused by embolic occlusive disease within the MCA system. In particular, the analysis identifies putamen and caudate as the tissue most sensitive to occlusion in the M1 system. Thus, the likelihood of infarction of the putamen was 100%; that of the caudate was nearly as high. In this regard, infarction in the putamen detected by CT scan has become a sensitive index of the risk of hemorrhage when tissue plasminogen activator is given for lysis of clot occluding the M1 system.38,39

In terms of the comprehensiveness of its treatment of neuroanatomic structure, its distinction of superficial and deep perfusion compartments and gray and white matter tissue types, and its volumetric treatment of anatomic partitions, the anatomic analysis of these strokes goes beyond that usually undertaken for diagnostic and therapeutic reasons. We envision 2 general domains of application for this system of anatomic analysis. First, as a strictly anatomic method of analysis, it is a tool for studies of forebrain tissue infarction as differentially reflected in vascular territories and with respect to tissue compartments and tissue types within territories. The implications for such quantitative patterns of infarct distribution are considered more fully in a companion manuscript.40 Second, we intend that it be adapted to the operations and purposes of real-time short- and long-term stroke medicine. In particular, it is intended that this system of analysis will be extended to MR and CT imaging modalities, including diffusion and perfusion studies obtained in early phases of stroke evolution. It will be used to increase the precision of calibration of the “already destroyed” and “penumbra salvageable” predictions made from these early-phase studies. To the extent that the approach does augment confidence of prediction, it will aid therapeutic choices regarding thrombolysis, aggressive anticoagulation, and perhaps in time, tissue protective agents. In time, this approach, enhanced by improvements in imaging and automated image analysis technology and correlated with studies of neurologic outcome and adaptation, may increase the predictive power of early-phase studies regarding long-range outcome from stroke in the individual patient.41

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References

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