Anatomy of Stroke, Part II
Volumetric Characteristics With Implications for the Local Architecture of the Cerebral Perfusion System

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Background and Purpose—The margin of a stroke is assumed to approximate a trace of the isobar of the perfusion threshold for infarction at the time that infarction occurred. Working from this hypothesis, we have analyzed stroke topography and volume in MR images obtained at a time remote from the stroke event. We have derived parameters from these images that may give information on local perfusion competence and microvascular architecture because they influenced the contour of stroke at the time infarction occurred.

Methods—MR images were obtained months after presumed embolic middle cerebral artery stroke in 21 subjects. Volumetric analyses of image data were undertaken with respect to the tissue shape of stroke and scaling ratios of anatomic partitions involved in stroke.

Results—For stroke confined to a single volume, the 3-dimensional form conforms to a parabola in which the height-to-width ratios are variable. The ratio for cortex is greater than that for underlying white matter. Scaling ratios indicate a close correlation between volume of cortex and radiata destroyed and total volume of stroke, but the relative proportions vary as a function of location within the M4 territory.

Conclusions—Scaling ratios for cortex and radiata to stroke volume are consistent with vascular studies that depict a modular microvascular perfusion architecture for the cortex and underlying white matter. The stroke descriptors are inferred to be related to the competence of collateral perfusion at the time that stroke occurred. This inference may be tested by serial volumetric analysis of the perfusion-diffusion examination mismatch immediately and over the longer-term evolution of stroke. (Stroke. 2002;33:2557-2564.)

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

The topographic features and volumes of stroke resulting from embolism to the middle cerebral artery (MCA) are greatly variable, reflecting the variety of occlusive patterns that may occur within the MCA arterial tree (see elsewhere1 for a review and references). There are, however, regularities in the anatomic patterns of infarction predictable from the general regularity of distribution of the overall MCA system. Thus, infarction secondary to MCA occlusion will be limited to the centro-sylvian region of the hemisphere. Occlusion within the M1 stem will be associated with infarction of deep nuclear and white matter structures; occlusion within the M2 through M4 system will lead to infarction of cortex and radiata. General perfusion failure may lead to infarction within MCA–anterior cerebral artery or MCA–posterior cerebral artery border zones or the internal border zone between the M1 and M2 through M4 subdivisions of the MCA.2–5

In the present MRI-based analysis of MCA embolic stroke, we illustrate 2 further anatomic regularities of stroke, in this instance attributable to the regular volumetric perfusion properties of the MCA: the 3-dimensional form of infarction volume and the volume of infarction of separate anatomic partitions of the cerebrum as scaled to total stroke volume. We postulate the degree of regularity of the first to be an index of the relative competence of perfusion at the margins of infarction under conditions when stroke occurred. We postulate the second to be an index of the modular nature of the microvascular architecture within the separate anatomic partitions involved in infarction. These measures are intended as parameters by which to assess the sensitivity and specificity of stroke contour prediction obtained from perfusion- and diffusion-weighted imaging studies obtained intravitaly in the acute phase of stroke.6–11

Materials and Methods

Subjects
The study is based on a morphometric analysis of brains of 21 subjects (10 men, 11 women; age range, 34 to 75 years; mean,
Imaging, Image Analysis, and Anatomic Segmentation

Acquisition of images, methods of image analysis, and the system of anatomic partition of regions of brain that are involved and not involved in stroke are described in a companion manuscript. In brief, 3-dimensional, spoiled-gradient (T1-weighted) brain images formatted with respect to the Talairach orientation were segmented with respect to forebrain, brainstem, and cerebellum. The forebrain was further segmented with respect to principal gray and white matter anatomic structures. These structures were further subdivided into parcellation units (PUs), respecting the principal gyri and subcortical nuclei. We designate the cortex and radiata the superficial perfusion compartment and the deep white matter and nuclei the deep perfusion compartment, corresponding approximately to the territories of perfusion of the leptomeningeal (M2) and the deep (M1) divisions, respectively, of the MCA. We designate cortex and nuclei as gray matter tissue type and radiata and deep white matter as white matter tissue type.

The same anatomic partitions were observed within infarcted as in noninfarcted regions of the hemispheres. The strokes were already cavitated at the time the images were acquired. The cavity outline and structures within the stroke cavity were segmented by hand-driven cursor; the contours of destroyed structures were estimated and outlined by comparison with the corresponding structure in the opposite hemisphere.

Morphometric Analysis

In the analysis of stroke volumetry, we characterize the 3-dimensional form of stroke as parabola and scale partitions of stroke to overall stroke volume.

Infarct Shape as Parabola

A parabola is defined as the set of all points that are equidistant from a given line (directrix) and a given point (focus) not on the line (Figure 1). Relative to a set of coordinate axes, the parabola can be described in terms of center (c), width (w), and height (h) (Figure 1a and 1b). The standard equation of a parabola with its vertex at the coordinates (h, k) is given as the following: \( (x-h)^2 = 4p(y-k) \). By making the substitutions \( h = c, k = h, \) and \( 4p = w \), we get the following expression: \( (x-c)^2 = w(y-h) \). Now, a second-order polynomial can be expressed as the following: \( y = ax^2 + bx + c \). These last 2 equations let us relate the parabola descriptors \( c, h, \) and \( w \) in terms of the coefficients of the second-order polynomial \( a, b, \) and \( c \); namely, \( c = -b/2a, h = -1/(4a), \) and \( w = 1/a \). When the parabolic nature of the lesion projection is a good representation of the lesion, the volume per slice as a function of slice will fit a second-order polynomial function and have a reasonable \( r^2 (r^2 > 0.6) \).

Scaling by Partition Ratios

We distinguish ratios with which we scale infarction of anatomic partitions to total stroke volume, to noninfarcted corresponding structures of the cerebral hemisphere, and to each other (Figure 2A). Each of the ratios may be applied to average parameters for the series or to single cases. First, for any anatomic partition \( p \), the infarct volume ratio (IR) is the volume within an infarct \( (Ip) \) expressed as a fraction of the total volume of that infarct \( (Ip) : IPR = Ip/Ip \). Second is the noninfarcted hemisphere volume ratio (NHR), which is the volume of any anatomic partition \( p \) of the noninfarcted hemisphere \( (NHp) \) expressed as a fraction of the total volume of the hemisphere \( (NHt) : NHRp = NhHp/NHt \). Third, the infarct to hemisphere scaling ratio (SR) is the infarct volume ratio normalized with respect to the noninfarcted hemisphere volume ratio for a particular partition: \( SRR = IPR/NHRp \). The scaling ratio expresses the representation of a partition in an infarct relative to its representation in the noninfarcted hemisphere and will approximate 1.0 to the extent that representation of the partition in the infarct is the same as in the noninfarcted hemisphere. The scaling ratio for a partition will be \( 1.0 \) to the extent that the partition is overrepresented and \( <1.0 \) to the extent that it is underrepresented in the infarct in relation to its representation in the noninfarcted hemisphere (Figure 2B). We view the noninfarcted hemisphere as a reasonable approximation to the preinfarcted tissue volume in the affected hemisphere because corresponding native structures in opposite hemispheres of normal brain have been previously established to differ volumetrically by \(<10\% \). Finally, the infarct component ratio (ICR) expresses the relative contribution within an infarct of 2 separate anatomic partitions \( (p1 \) and \( p2) \): \( ICR = Ip1/IP2 \).
Results

The 21 strokes in this series were all observed in the centro-sylvian region of the cerebral hemisphere, corresponding to the territory of perfusion of the MCA. Of these, 17 were within the left and 4 within the right hemisphere. The topography of infarction corresponded to the M1 through M4 territories in 14, the M1 only in 1, and the M2 through 4 only in 6. Total volumes of the infarctions were distributed over a 2-order-of-magnitude range, 3.1 to 256 cm$^3$. The volumes of individual infarctions were spread relatively evenly throughout this range.

Shape of Infarction as Parabola

The volumetric extent of each infarction through the succession of coronal image planes in which it appears is represented in Figure 3. For 16 brains, these plots have a parabolic form that extends naturally in all directions through a coherent single volume (Figure 3 and the Table). Whether the shape of stroke plotted this way was parabolic or not was independent of total volume of infarction, its position with respect to the M1 through M4 territories, and whether it extended fully into deep gray structures. Nonparabolic form occurred because infarction in a partition was broken into separate volumes isolated from each other or was quite small in its spatial extent.

For 14 cases involving cortex (the Table and Figure 3), the total infarction volumes as a function of extent along the anterior-posterior axis of the hemisphere fit a second-order polynomial function with $r^2>0.6$. The relative steepness of
the shoulders of the parabola (width-to-height ratio) will reflect the abruptness of transition from infarcted to noninfarcted tissue with respect to the anterior and posterior margins of stroke. This ratio for cortex varies from 0.04 to 0.30 and for total white matter from 0.01 to 0.22, indicating a wide range of variability in the abruptness of transition (the Table and Figure 1c). For both cortex and white matter, the ratios were strongly skewed to the lower half of their respective ranges. Finally, for the 8 strokes with good parabolic fits for the volume of infarction in both cortex and the underlying radiata, the height-to-width ratio for the parabolic form of cortex infarction is on average 1.37 times greater than that for the parabolic form of the infarction of the underlying radiata. That is, for this subset in which the parabolic forms of infarction in cortex and immediately subjacent radiata are compared, the greater height-to-width ratios for cortex suggest that the abruptness of transition from infarct to noninfarcted surround is greater in cortex than in radiata (the Table and Figure 1d).

There were no apparent relationships between the height-to-width ratios and the size or location of the stroke. In particular, high ratios did not predict that the stroke would be small and located within the M2 through M4 territory. Nor did low ratios predict that the stroke would be large with margins in the far distal fields of perfusion of the MCA.

**Stroke Volume and Anatomic Partition**

The infarctions in this series vary greatly with respect to position in the hemisphere, shape, and specific anatomic partitions that they involve (Figure 2 in Reference 1). The relationship between total stroke volume and its impact on superficial and deep compartments is substantially different.

**Superficial Compartment**

The average infarct volume ratios (Figure 4) for cortex and radiata are essentially the same as the average noninfarcted hemisphere ratios for cortex and radiata. For the 2 smallest
strokes in the series, infarction was essentially confined to cortex. If these 2 outliers are ignored, the scaling ratios of cortex and radiata for the individual strokes are relatively invariant, very close to 1.0, over a 2-order-of-magnitude range in infarct volume (Figure 5a and 5b). That is, the volume of cortex and of radiata as a fraction of stroke volume is the same as the volume of cortex and radiata as a fraction of the noninfarcted hemisphere volume. If considered from the perspective of individual strokes, there is a remarkably close correlation between the volumes of cortex or radiata destroyed and the total volume of stroke ($r^2 = 0.97$ and 0.93, respectively; Figure 6a and 6b). The slopes of the regressions for cortex and radiata to total lesion volume are 0.57 and 0.28, indicating that on average twice as much cortex as radiata is destroyed for a stroke of any given magnitude.

Whereas the scaling ratios for cortex and radiata hold very close to 1.0 across the series, there does appear to be systematic regional variability in the relative proportion of radiata to cortex as reflected by the infarct component ratios for individual strokes. Thus, for those PUs in the immediately perisylvian region, the radiata-to-cortex infarct component ratios cluster between 0.40 and 0.60. However, with progression from the perisylvian region to more distal regions of the MCA perfusion field, the radiata-to-cortex infarct component ratios range as high as 1.02. This is seen posteriorly, for example, with the radiata-to-cortex infarct component ratios for PUs in the posterior temporal, lateral occipital, and high parietal regions (PUs: OLI, TO2, or SPL) and the medially extending paracentral and frontal regions (PUs: POG, PRG). This trend is independent of the native proportions of radiata to cortex in these PUs ($r^2 = 0.018$), illustrated for example, by the posterior and far medially extending regions (PUs: SGp, TO2, PRG, POG) in which native radiata-to-cortex ratios are low but radiata-to-cortex infarct component ratios in stroke are high (Figure 7). Because the insula PU is essentially without underlying radiata, it is not included in this correlation.

**Deep Compartment**

The average infarct volume ratios for deep gray and deep white matter, unlike those for cortex and radiata, are greater than their noninfarcted hemisphere ratios (Figure 4). Again, in accordance with pathoanatomic investigations, this implies that perfusion of the MCA is essentially the exclusive source of perfusion for these deep structures. For strokes involving at least 1.0 cm$^3$ of the respective partition (deep gray, 14; deep white, 19), the volume of deep white matter destroyed is moderately well correlated ($r^2 = 0.77$) but deep gray matter is not correlated ($r^2 = 0.05$) with total stroke volume.

## Parabolic Fits for Lesions

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**Figure 4.** Comparison of infarct volume ratio and noninfarcted hemisphere ratios for principal anatomic partitions: total gray matter, total white matter, cortex, radiata, deep white matter, and deep gray matter. Infarct volume ratios are nearly equal to noninfarcted hemisphere ratios for total gray matter, total white matter, and deep gray matter. Infarct volume ratios are nearly equal to noninfarcted hemisphere ratios for total gray matter, total white matter, cortex, and radiata but are greater than noninfarcted hemisphere ratios for deep white and gray matter.
volume (Figure 6c and d). Scaling ratios for both gray and white matter are well above 1.0 and are greatly variable compared with those of cortex and radiata (Figure 5c and d). For the cases with deep compartment infarction volume <10 cm³, infarct component ratios for deep gray to deep white matter were >1. For the cases with deep compartment infarction volume >20 cm³, these ratios were <0.5 We infer that strokes <10 cm³ in volume within the M1 territory preferentially involved deep gray over deep white matter. However, for strokes >10 cm³ in volume, the gray structures at risk are essentially completely destroyed (see also Reference 1). For strokes above this threshold volume, infarction still may spread progressively through deep white but not deep gray structures.

Discussion

Cerebral infarction occurs below a perfusion threshold corresponding to a narrow interval of the full dynamic range of cerebral arterial perfusion, which normally may be as high as 40 to 60 mL · 100 g⁻¹ · min⁻¹. The perfusion threshold for infarction has been estimated to be near the low end of this range. Thus, infarction occurs when perfusion falls below a threshold somewhere between 8 and 10 mL · 100 g⁻¹ · min⁻¹ and is sustained at that low level over minutes. Thus, for the present purposes, the perimeter of an infarction is presumed to approximate a trace of the isobar of the perfusion threshold for infarction at the time that infarction occurred. From this hypothesis, the present volumetric findings are taken to
reflect the local efficiency of perfusion and the microarchitecture of the vascular perfusion system as critical influences on the trace of the infarction isobar through cerebral tissue.

**Shape of Infarction and Competence of Perfusion**

Single volume infarctions have the form of a parabola in which the ratio of height to width reflects the abruptness of transition from infarcted to noninfarcted tissue along their anterior and posterior margins. A gradual slope implies low competence of perfusion support along the margin, ie, an extended zone of marginally competent flow extending well away from the epicenter of ischemia. Conversely, a steeper shoulder implies high competence, ie, an abrupt transition from a competent to an incompetent zone of perfusion.

With respect to the present set of strokes, the ratios of height to width were distributed widely through a 4-fold range but skewed toward low height-to-width ratios. We infer that marginal perfusion by this criterion was relatively poor for most and relatively good for only a few. In the subset of 11 strokes in which stroke volumes in both cortex and radiata were parabolic, the height-to-width ratios of the cortex parabolas were on average 1.37-fold greater than those for radiata. We infer that for these 11 cases, perfusion marginal to infarction was more competent in cortex than in the immediately subcortical radiata.

These criteria for low competence of marginal perfusion are not strongly correlated here with large volume infarctions, having their perimeters at the classic perfusion border zones between the MCA and the posterior or anterior cerebral artery. Nor are criteria for high competence of marginal perfusion correlated strongly with small volume infarctions with perimeters largely within the M2 through M4 territory. On the contrary, infarction size and parabola height-to-width ratios varied largely independently and were detected both at the extremities of and within the M2 through M4 territory (Figure 3 and the Table). Thus, these parameters appear to reflect the state of regional perfusion support both within and at the tangential border zones of the MCA as it operated at the time of stroke. This state is probably influenced in complex ways by the degree of vascular occlusion, whatever the mechanisms, by vasculopathic risk factors, by fluctuations in coagulation and hemodynamics, and by the medical context in which stroke occurred.

**Microarchitecture of the Perfusion System of Cortex and Radiata**

The volume of cortex or of radiata destroyed by infarction correlated closely ($r^2>0.9$) with the total volume of stroke in each subject. That is, with strokes of increasing size, there appears to be a corresponding linear increase in the volumetric increments of cortex and radiata that are recruited to the stroke. These correlations held despite the great variation in the volumes and topographies of the individual strokes in the series.

The inference of a modular form for the M2 through M4 microvascular system implied by these observations is in agreement with microvascular studies of the cerebral cortex. These depict the system as made up of an iterative patterning of arterioles and capillaries arising from the parent leptomeningeal arterial divisions and penetrating radially through cortex and radiate white matter. The interunit interval has been estimated by Marin-Padilla to be $\approx 200 \text{ m}$ throughout the full range of brain growth from fetal life.

The slopes of the regressions indicate that on average the proportion of the module made up of cortex is 2 times that made up of radiata. This is regionally variable, however. Thus, the proportion of radiate white matter to cortex destroyed increases with distal progression in the M2 through M4 perfusion fields. This disparity is expected, given the relatively distal position of radiata with respect to the perfusion module, taken together with the weakening competence of perfusion in the M4 system in border zones.

The present observations suggest a somewhat weaker correlation between volume of deep white matter destroyed and total stroke volume than is seen here for cortex and radiata. If such a correlation exits for infarction in deep gray matter...
structures, the present observations suggest that it must be for strokes <10 cm³ in total volume. A larger series of relatively small strokes is needed to investigate these issues for deep structures.

**Practical Implications**

CT- and MR-based perfusion and diffusion-weighted imaging methods now provide a technology by which to intravascularly partition zones of ischemia that are potentially salvageable and those that are not salvageable. The potential of such technology as an aid to real-time immediate therapeutic decision making and to longer-term predictions of outcome may be expected to substantially affect stroke medicine. The present article and its companion provide an anatomic and practicality of these tools are the subject of investigations in progress.

**Acknowledgments**

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