Measurement of CBF with the aid of SPECT is useful for making diagnostic and treatment decisions in patients with cerebrovascular disease. Current-ly, SPECT does not provide selective information on the vascular territories supplied by separate major cerebral arteries. The MCA is the largest of the cerebral arteries, supplies substantial portions of the brain, and is the vessel most frequently affected by cerebrovascular diseases. Therefore, establishing a consistent evaluation system for cerebral perfusion in the MCA territory is especially important.

Previous mapping of cerebral artery territories mostly involved the use of injection techniques in cadavers. However, overflow of injection material through leptome-

probabilistic cortical surface map of the middle cerebral artery territory for single-photon emission computed tomography studies

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Object. The middle cerebral artery (MCA) is the intracranial vessel most frequently affected by cerebrovascular diseases. A more accurate knowledge of the topography of this vessel may have an impact on treatment strategies for ischemic cerebrovascular diseases. The aim of this study was to construct a topographic map of the MCA territory for single-photon emission computed tomography (SPECT) using statistical brain mapping.

Methods. The margin of the perfusion deficit associated with infarction due to arterial occlusion, as seen on SPECT imaging, is presumed to approximate the borders of the territory of the artery. Basing the study on this hypothesis, SPECT images obtained in 12 patients with large MCA infarctions due to angiographically confirmed MCA trunk occlusion were selected, anatomically standardized, and compared with SPECT images obtained in healthy volunteers to construct probabilistic cortical surface maps of the MCA territory. Crossed cerebellar diaschisis was used as a primary cutoff marker for creation of the map. This MCA map (Method C) was compared with the conventional region of interest (ROI) method (Method A) and previously reported predefined cortical templates (Method B) for preliminary clinical application.

The probabilistic cortical surface map of the MCA territory showed that regions with the highest ratio of MCA territory included the transverse temporal gyrus (100%), supramarginal gyrus (100%), and inferior parietal lobule (91–92%). For preliminarily clinical application, this map (Method C) was compared with the conventional ROI method (Method A) in predicting hyperperfusion after carotid endarterectomy by performing a receiver operating characteristic (ROC) analysis, which demonstrated the statistically significant superiority of the MCA map (area under the ROC curve [A] = 0.91) to the ROI method (A = 0.75; p = 0.025). The ROC analysis also demonstrated a diagnostic value of the MCA map (A = 0.95) that equaled predefined cortical templates (Method B) (A = 0.93).

Conclusions. The probabilistic cortical surface map of the MCA territory used for SPECT, which was created using statistical brain mapping techniques, would be useful for an objective assessment of the cerebral perfusion status of patients with cerebrovascular diseases.

Key Words • infarction • middle cerebral artery • cerebral blood flow • hyperperfusion • carotid endarterectomy • single-photon emission computed tomography

MEASUREMENT OF CBF with the aid of SPECT is useful for making diagnostic and treatment decisions in patients with cerebrovascular disease. Currently, SPECT does not provide selective information on the vascular territories supplied by separate major cerebral arteries. The MCA is the largest of the cerebral arteries, supplies substantial portions of the brain, and is the vessel most frequently affected by cerebrovascular diseases. A more accurate knowledge of the topography of this vessel may have a positive impact on treatment strategies for ischemic cerebrovascular diseases such as CEA for carotid stenosis, extracranial–intracranial bypass surgery, and administration of recombinant tissue plasminogen activator for acute ischemic stroke. Therefore, establishing a consistent evaluation system for cerebral perfusion in the MCA territory is especially important.

Previous mapping of cerebral artery territories mostly involved the use of injection techniques in cadavers. However, overflow of injection material through leptome-
ningeal and choroid anastomoses can lead to inconsistent findings. Accordingly, we need to develop an alternative strategy for determining the borders of cerebral artery territories. The margin of the perfusion deficit associated with an infarction due to arterial occlusion on a SPECT image is presumed to approximate the margin of the territory of the artery that supplies part of the brain. Basing this study on this hypothesis, we analyzed the topography of an MCA infarction as demonstrated on SPECT images that had been obtained a considerable time after the ischemic event. The statistical brain mapping technique used for this analysis, 3D SSP\(^1\), enables spatial normalization of images into standardized coordinates and a more objective comparison with images obtained in healthy volunteers. This analysis may provide information on MCA territorial perfusion and vascular architecture because these factors influence the contour of the infarction at the time ischemia occurs.

In the current study, we compared brain SPECT images obtained in patients harboring large MCA infarctions with images obtained in healthy volunteers by performing a 3D SSP analysis to create a probabilistic cortical surface map of blood flow from the MCA. To confirm the diagnostic value of the cortical surface map, we preliminarily compared the usefulness of this method with the conventional ROI method and with predefined cortical templates in the prediction of hyperperfusion after CEA.

Clinical Material and Methods

Between August 1997 and March 2002, 12 patients who presented at the Hyogo Brain and Heart Center with a first-time, single embolus-based infarction and who met specific inclusion criteria were enrolled in the study. The inclusion criteria were the following: a large infarction in the MCA territory, which was shown on CT and/or MR images to completely cover three MCA subterritories (the superficial anterior, superficial posterior, and deep territories); complete occlusion of the origin of the MCA without recanalization, as confirmed by angiography (Fig. 1); no occlusion and/or stenosis of any other major arteries (Fig. 1); and SPECT performed 4 weeks or longer after onset of injury. Seven of the 12 patients were male and five were female. The mean age of the patient population was 62.9 ± 10.3 years (range 45–80 years). We obtained informed consent from all patients or their next of kin.

For a comparison with a control group, data obtained in 21 healthy volunteers (seven men and 14 women) were used. The mean age of this group was 65.1 ± 10.7 years (range 50–85 years). The healthy volunteers displayed no clinical evidence of cognitive deficits or neurological disease and were not taking any short- or long-term medications at the time of SPECT scanning. There were no statistically significant differences in age and sex between the control and MCA infarction groups.

Cerebral Blood Flow Data Collection

Details of the SPECT procedure, which was undertaken using \(^{123}\)I-IMP, were described previously. In brief, \(^{123}\)I-IMP SPECT images were obtained using a rotating dual-headed gamma camera (GAMA View SPECT 2000 H-20; Hitachi). At first, 111 MBq (3 mCi) of \(^{123}\)I-IMP was injected intravenously into the patient. The acquisition of SPECT images was begun 15 minutes after \(^{123}\)I-IMP injection and lasted 35 minutes. Data were accumulated in 64 steps, and at each step data collection lasted 30 seconds. Data were collected in 64 × 64 matrices, and were reconstructed in transaxial sections that were parallel to the orbitomeatal line and 8 mm thick. For the measurement of absolute CBF values, we used arterial blood sampling and a microsphere model. After the SPECT images had been acquired, activity across the entire brain in the anterior view was documented over a 30-second period. The original data were prefiltered with the aid of a Wiener filter and then reconstructed using a Ramachandran backprojection filter, resulting in a resolution of 13 mm full width at half maximum. The median time between onset of the infarction and the SPECT study was 39 days (range 28–117 days).

![Fig. 1. Typical neuroimages obtained in a patient and used for the construction of an MCA territory map. A: A CT scan showing a large MCA infarction. B: An SPECT scan demonstrating a large perfusion deficit due to the MCA infarction. C: Angiogram depicting complete occlusion of the MCA trunk. Note that the margin of the SPECT perfusion deficit in a patient with a large MCA infarction involves not only a perfusion deficit in the infarcted area, but also moderate to severe hypoperfusion in the area of the margin of the MCA territory.](image)
Construction of the MCA Territory Map Using the Statistical Mapping Method

We used the NEUROSTAT software program (version: 2/8/06; University of Washington) for anatomical standardization of SPECT images because the program’s anatomical standardization algorithm is robust against perfusion deficits, as described previously. The imaging sets were transformed to a standard stereotactic space by using the portion of the NEUROSTAT program that generates standardized 3D SSP data sets for individual persons. For construction of the cortical surface map of the MCA territory, we used qualitative SPECT images in the manner described earlier.

An automated algorithm was used to estimate the location of the bicommissural line on the midsagittal plane and to realign the image set to the standard stereotactic orientation. The variation in an individual’s brain size was removed by linear scaling, and regional anatomical differences were minimized using a nonlinear warping technique. As a result, each brain was standardized anatomically to match a standard atlas brain while preserving regional activity. Subsequently, maximum cortical activity was extracted to adjacent predefined surface pixels on a pixel-by-pixel basis by using the 3D SSP technique.

The extracted data on cortical activity were used in the following analyses. A normal control database for the 3D SSP technique was constructed by averaging image sets collected from the 21 healthy volunteers described earlier. Pixel values of an individual’s image set were normalized to values in the thalamus before the analysis as follows: normalized CBF = (individual CBF)/(thalamic CBF).

The normalized activity in each patient was compared with the reference control database by means of a Z score. A Z score was calculated for each surface pixel as follows: Z score = [(normal mean value) – (individual value)] / (normal standard deviation). A positive Z score represents CBF in a patient that is reduced relative to the control mean value. Because the entire procedure is fully automated, no interference by the user was necessary. The comparison of CBF between the group of patients with an MCA infarction and the control (healthy volunteer) group generated Z-score maps for the construction of the probabilistic map of the MCA territory. We explored various Z-score thresholds for this purpose. Crossed cerebellar diaschisis was used as the primary cutoff marker to remove nonspecific perfusion reduction.

We also performed a quantitative evaluation of the MCA territory according to anatomical segmentation by using the stereotactic extraction estimation method. This method provides a reference table in which the brain coordinates that are obtained correspond to anatomical information and the Z-score association between coordinates in the prepared reference table and the case coordinates. Subsequently, we calculated the rate of all coordinates with a Z score exceeding the threshold of the Z score set as a significant finding in the total coordinates in respective segments and the average Z score coordinates with a Z score that exceeded the threshold.

Methods Used to Evaluate Hyperperfusion

To validate the constructed MCA territory map, we compared the predictive value of three different methods for evaluating hyperperfusion after CEA: Method A, the conventional ROI method; Method B, the use of predefined cortical templates developed with 3D SSP; and Method C, the MCA territory map analysis that we are testing. Using Method B, the 3D SSP analysis of preoperative CBF reduction (represented as a Z score) demonstrated a higher diagnostic value than the conventional ROI method for predicting hyperperfusion after CEA.

Between March 1999 and February 2003, 90 consecutive patients underwent CEA at the Hyogo Brain and Heart Center; 46 of these fulfilled the specific criterion used for the current comparison study. The inclusion criterion for the comparison study was unilateral ICA stenosis of 70% or greater. Exclusion criteria included contralateral carotid stenosis of 30% or more, intracranial artery stenosis or occlusion, and/or major disabling stroke. Thirty-nine of the 46 patients were male and seven were female. The mean age of the patients was 70.3 ± 7.4 years (range 49–84 years). Thirty-nine patients had hypertension and 16 had diabetes mellitus. Transient ischemic attacks associated with the relevant ICA were the only symptoms for eight patients. Four patients had sustained transient ischemic attacks with subsequent strokes, and 15 patients had sustained strokes only. All stroke patients had made good functional recoveries. Nineteen patients exhibited asymptomatic ICA stenosis. Quantitative measurements of CBF in these patients were performed as described earlier and were used for a validation study whose description follows. Data obtained in these patients using Methods A and B were reported in a previous study.

In Method A (conventional ROI analysis), we measured CBF by placing six to 10 ROIs (each 16 × 16 mm) in bilaterally symmetrical regions of the MCA territory on the SPECT imaging plane in which the asymmetry was most prominent. The pairs that exhibited the largest differences in values were used. A region in which infarction was observed on CT and/or MR imaging was carefully excluded from the evaluation. Normal control values of CBF on the ROI analysis were obtained in a manner described previously. The reduction in CBF was defined as a percentage reduction in comparison with CBF measured in healthy volunteers. Hyperperfusion after CEA was defined as an absolute CBF value increase of ≥100% on the 1st postoperative day because that amount of increase was reported to be a significant risk factor for intracerebral hemorrhage.

In Method B (use of predefined cortical templates), stereotactic grid coordinates were used for the frontal, primary sensorimotor, parietal, temporal, occipital, mediofrontal, and medioparietal cortices, and for the cerebellum on the surface format. These predefined regions were created by using a statistical mapping method (NEUROSTAT) according to the stereotactic atlas of the human brain published by Talairach and Tournoux. The mean values of each region were quantified using a fully automated algorithm. The mean value of the Z scores in a predefined region that showed the highest mean value was selected as the value of the Z score for each patient. For Method B, we defined hyperperfusion as a mean increase in the value of CBF that was 100% or greater in at least one region and 70% or greater in at least two regions, in accordance with data in a previous study.

For Method C (use of the MCA territory map), the mean value of the Z score in the MCA territory was used to pre-
dict postoperative hyperperfusion. The mean value of the Z score in the MCA territory was quantified using a fully automated algorithm. For visual inspection, the Z-score surface map of the MCA territory was superimposed on NEU-ROSTAT T1-weighted MR imaging templates and displayed on a pixel-by-pixel basis. Hyperperfusion after CEA was defined as an absolute CBF value increase of 70% or greater on the 1st postoperative day for the MCA map analysis, because the MCA territory (1507 pixels) was much larger than the conventional ROI (16 × 16 mm) used in the ROI analysis (Method A) and was larger than the frontal lobe (1206 pixels), parietal lobe (469 pixels), sensorimotor cortex (461 pixels), temporal lobe (648 pixels), and occipital lobe (844 pixels) shown using Method B.

Statistical Analysis

Descriptive statistics are presented as mean values ± standard deviations. To determine which method is most useful for identifying patients at risk for hyperperfusion, an ROC analysis was also performed using the ROCKIT program. The area under the ROC curve was used to compare classifiers. The ROCKIT program also provides a critical test result value, which separates positive results from negative results and can be used as a candidate for the optimal cutoff value for the proportion analysis. For the comparison study, we used the Student t-test. The Fisher exact test was used for the proportional analysis. Probability values less than 0.05 were reported to be significant.

Results

Construction of a Probabilistic Cortical Surface Map of the MCA Territory

The stereotactic anatomical standardization of SPECT images was successful in all patients with a large MCA infarction. After cortical extraction in three dimensions, the mean relative perfusion values in the MCA infarction group were compared with values in the control group to determine the most appropriate cutoff value of the Z score for the MCA territory. We compared several cutoff values of the Z score. As shown in Fig. 2, crossed cerebellar diaschisis was prominently visualized on the probabilistic map when a Z score of 2 or 3 was used as a cutoff value. The crossed cerebellar diaschisis area could be removed for the most part when a Z score of 4 was used as a cutoff value. Nevertheless, a few crossed cerebellar diaschisis areas and some nonspecific positive spots in remote regions were still recognized. A Z-score map with a cutoff value of 5 demonstrated almost no crossed cerebellar diaschisis-related spots and very few nonspecific remote spots. A Z-score map with a cutoff value greater than 5 appeared to be too strict and insensitive (Fig. 2), and therefore a Z score of 5 was chosen as the cutoff value. We deleted very few sparse nonspecific positive spots in the Z-score map with a cutoff value of 5 to make the probabilistic cortical surface map of the MCA territory. Each side of the map was created separately, and then combined (Fig. 3).

Using the stereotactic extraction estimation method, the

Fig. 2. A comparison of MCA cortical surface maps associated with various cutoff values of the Z score. Note that the Z-score map with a cutoff value of 5 demonstrated almost no crossed cerebellar diaschisis–related areas and very few nonspecific remote spots. ANT = anterior; INF = inferior; L. LAT = left lateral; L. MED = left medial; POST = posterior; R. LAT = right lateral; R. MED = right medial; SUP = superior.
anatomical extent of the MCA territory was obtained (Table 1). The regions with the highest ratio of MCA territory were the transverse temporal gyrus (100%), supramarginal gyrus (100%), and inferior parietal lobule (91–92%).

Validation of Applicability of the Cortical Surface Map of MCA Territory

To clarify the usefulness of the probabilistic cortical surface map of the MCA territory (Method C), it was compared with the conventional ROI analysis (Method A) and the predefined cortical templates analysis (Method B) for the prediction of hyperperfusion after CEA. Using Method C, Z-score surface maps of the MCA territory superimposed on MR imaging templates clearly demonstrated the CBF status of the MCA territory in a patient with carotid stenosis on a pixel-by-pixel basis (Fig. 4).

In six of 46 patients, postoperative ipsilateral hyperperfusion was observed on all three analyses of the CBF percentage increase 1 day after CEA, although postoperative CT scans displayed normal findings. The ROC analysis demonstrated a significant improvement in the predictive value of CBF reduction using the map of the MCA territory (Method C; A_z = 0.91) in comparison with using the ROI method (Method A; A_z = 0.72) (p = 0.025) (Fig. 5A). On the other hand, there was no significant difference between the map of the MCA territory (Method C; A_z = 0.95) and the predefined cortical templates (Method B; A_z = 0.93) (Fig. 5B).

According to the results of the ROC analysis, the optimal cutoff values of CBF reduction (Z score) were selected for prediction of postoperative hyperperfusion. For the cortical surface map of the MCA territory, patients were categorized into two groups based on the severity of the preoperative CBF decrease: Type A (ipsilateral Z score < 1.26) and Type B (ipsilateral Z score ≥ 1.26). Using the probabilistic map of the MCA territory, the incidence of hyperperfusion was significantly higher in Type B (five [63%] of eight patients) than in Type A (one [3%] of 38 patients) (p = 0.0002). The sensitivity was 83% and the specificity was 93%.

### Table 1

Main anatomical extension of the MCA territory

<table>
<thead>
<tr>
<th>Region</th>
<th>Lt Side</th>
<th>Rt Side</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ratio of MCA Territory (%)</td>
<td>Mean Z score</td>
</tr>
<tr>
<td>transverse temporal gyrus</td>
<td>100</td>
<td>7.15</td>
</tr>
<tr>
<td>supramarginal gyrus</td>
<td>100</td>
<td>6.37</td>
</tr>
<tr>
<td>inferior parietal lobule</td>
<td>92</td>
<td>6.12</td>
</tr>
<tr>
<td>inferior frontal gyrus</td>
<td>64</td>
<td>6.28</td>
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<tr>
<td>superior temporal gyrus</td>
<td>63</td>
<td>6.36</td>
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<tr>
<td>precentral gyrus</td>
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<td>5.99</td>
</tr>
<tr>
<td>angular gyrus</td>
<td>55</td>
<td>5.42</td>
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<tr>
<td>postcentral gyrus</td>
<td>54</td>
<td>6.11</td>
</tr>
<tr>
<td>middle temporal gyrus</td>
<td>52</td>
<td>5.67</td>
</tr>
<tr>
<td>middle frontal gyrus</td>
<td>39</td>
<td>6.15</td>
</tr>
<tr>
<td>inferior temporal gyrus</td>
<td>34</td>
<td>5.79</td>
</tr>
<tr>
<td>fusiform gyrus</td>
<td>17</td>
<td>6.36</td>
</tr>
<tr>
<td>superior parietal lobule</td>
<td>14</td>
<td>5.23</td>
</tr>
</tbody>
</table>

* Rate of total coordinates with a Z score greater than 5 in all coordinates of the respective region.
† Mean Z score of coordinates having a Z score greater than 5.

Fig. 3. Cortical surface map of the MCA territory superimposed on NEUROSTAT T1-weighted MR imaging templates. **Upper** (left to right): Right lateral, left lateral, superior, and inferior views. **Lower** (left to right): Anterior, posterior, right medial, and left medial views.
Discussion

An MCA territory infarction is the most common type of cerebral infarction. According to one large study, the CA territory was involved in 68% of patients with cerebral infarctions, and 96% of the CA territory infarctions involved the MCA territory. Therefore, the quantification of regional CBF in the MCA territory is very important. Nevertheless, the manual and observer-dependent techniques of image analysis that have been used in most CBF studies have several disadvantages such as incomplete data sampling and inter- and intraobserver variability, which result from the reliance on an observer to draw the ROI. To overcome these shortcomings, observer-independent approaches to image analysis for positron-emission tomography and SPECT, such as 3D SSP, have been developed. The measurement of CBF on SPECT images by applying MCA probabilistic maps constructed using these new analytical techniques may provide more specific and objective information on cerebral perfusion in patients with ischemic cerebrovascular diseases. For example, an accurate assessment of hemodynamics in the MCA territory may provide a better indication for CEA and extracranial–intracranial bypass surgery during the chronic stage of cerebral ischemia as well as postoperative management and evaluation in these cases. A recent study on the use of recombinant tissue plasminogen activator therapy for acute ischemic stroke yielded data suggesting that patients with early ischemic changes in more than 33% of the MCA territory had an increased risk for fatal brain hemorrhage. Nevertheless, to date there has been no clear definition of the MCA territory. An MCA territorial map would be useful to determine the extent of the MCA's involvement.

Methodological Consideration for the Construction of an MCA Territory Map

Anatomical standardization of SPECT images showing a large MCA infarction is a critical step in the generation of the probabilistic map of the MCA territory. We used the NEUROSTAT program because the anatomical standardization algorithm is robust against perfusion deficits, as we previously showed in CA stenosis studies. In fact, the procedure provided satisfactory results of standardization, even in cases in which there was a large defect in the uptake of radiotracers due to a large infarction.

Repeated CBF studies showed a transition through a hyperemic phase with an increase in CBF in the area of complete infarction on Days 5 through 9 and demonstrated that the hyperemia lasted for 2 or 3 weeks. It is most likely that the CBF increase was due to fragmentation and lysis of an embolus with recanalization of previously occluded vessels. In the current study, the median time between onset of infarction and the SPECT study was 39 days (range 28–117 days). In addition, no recanalization of the occluded MCA trunk was observed. These findings ensured that cerebral perfusion had stabilized in the patients in the current study. Occlusion of the MCA trunk without recanalization was confirmed by cerebral angiography in all patients in the current study; this assured that there was no anterograde blood flow into the brain through the MCA. This means that the defect on SPECT images represents portions of the brain that are mainly supplied by the MCA. As shown in Fig. 1, the margin of the SPECT perfusion deficit in patients with large MCA infarctions fundamentally involves not only the perfusion deficit in the infarcted area itself but also moderate to severe hypoperfusion in the margin of the cortical area of the MCA territory. The regional uptake of radiotracer-
ers in SPECT images of portions of the brain supplied by collateral flow depends on how much blood flow other cerebral arteries provide. The specific MCA territory had to be demarcated and nonspecific parts had to be removed. One obvious problem was that reductions in perfusion could be caused by “remote effects” beyond the vascular territories. Crossed cerebellar diaschisis is a good example, but the ipsilateral striatum, contralateral hemisphere, and other locations may also display diaschisis. Nevertheless, the magnitude of perfusion reductions associated with diaschisis is relatively mild compared with perfusion reductions caused by occlusion or infarction. In addition, in previous studies investigators found no statistically significant change in crossed cerebellar diaschisis among the acute, subacute, and chronic stages of MCA infarction. Therefore, we used crossed cerebellar diaschisis as a major cutoff marker to delineate the specific MCA territory. With a Z score of 5 as the cutoff value, a satisfactory cortical surface map of the MCA territory was obtained without a crossed cerebellar diaschisis–related area and nonspecific remote positive spots. Consequently, the constructed probabilistic cortical surface maps of the MCA territory represent cortical CBF distributions via the MCA. With a Z score of 4, some variability in the MCA territory and in collateral flow might be displayed.

One limitation of the current study is that no attempt was made in the control population to perform other imaging studies, such as angiography and MR angiography, to make sure that the healthy volunteers did not have any baseline stenotic areas that would have affected the distribution of blood flow. None of the healthy individuals underwent angiography and only some underwent MR angiography, although normal findings were found on MR angiography in these patients. Regardless, the healthy volunteers did not display any cerebral ischemic symptom and close observation of their SPECT raw images and cortical surface maps demonstrated no abnormal findings, such as asymmetrical uptake or low regional uptake of radiotracers. Therefore, we believe that it is appropriate to regard the volunteers as representative of the healthy population.

Comparison With Previous Territorial Maps

Previously, most techniques of anatomical mapping of cerebral artery territories relied on various injection techniques. Different injection materials and conditions under which the investigations were performed as well as the phenomenon of overflow of injection material through leptomeningeal and choroid anastomoses have caused discrepancies among those maps. The technique used in this study has the flexibility to grasp the variability of the MCA territory. The final map we obtained may represent a core MCA territory. By setting a modest cutoff value, 3D SSP images allow a simple recognition of regions that might vary in the MCA territory and/or be supplied not only by the MCA but also by collateral flow, as indicated in the maps in which the cutoff value of the Z score was lower than 5 (Fig. 2).

Some MR imaging studies that focus on the location of the MCA infarction have been reported. The map developed by Caviness and associates was different from the current map in that the MCA territory reached the frontal pole anteriorly and almost reached the occipital pole posteriorly. Those investigators used clinical features such as dysphasia as inclusion criteria and did not confirm MCA occlusion, which suggests that cases were included in which there was embolism of the anterior or posterior cerebral arteries in addition to the MCA. On the other hand, Phan and colleagues used the finding of occlusion of the MCA trunk...
and/or the \( M_1 \) and \( M_2 \) branches on MR angiography as inclusion criteria. Their map seems to be similar to ours, although our approaches are very different. The regions with the highest ratio of MCA territory in the current study are similar to regions on their map. However, it is difficult to compare the two maps exactly because Phan et al. provided a transaxial map on MR images, whereas we developed a cortical surface map on SPECT images. Because our focus was the distribution of cortical CBF, we constructed a cortical surface map of the MCA territory. Combination of the current map and 3D-SSP technique enables not only the calculation of mean values of the CBF parameter in the MCA territory, but also the calculation of the rates of all coordinates with a value exceeding the threshold set as a significant finding in all the coordinates of the MCA territory. As far as we know, this is the first probabilistic map of the MCA territory for SPECT studies.

Another MR imaging approach, was recently introduced—regional perfusion imaging—in which selective labeling of the major brain-feeding arteries is used for flow territory mapping by relying on a direct anatomical correlation. Regional perfusion imaging is based on a selective slab inversion of arterial water with a pulsed arterial spin labeling sequence, in which the protons of the arterial water in the feeding vasculature of the brain are labeled magnetically and are used as an endogenous tracer. Regional perfusion imaging enables the assessment of perfusion territories of the major cerebral arteries; however, it provides information on the entire ICA territory rather than on the MCA territory alone because it is difficult to selectively achieve spin labeling for the MCA.

Recently, a probabilistic map of the ICA was constructed by performing SPECT during an intracarotid amobarbital procedure. However, the SPECT images used to create the map were obtained in patients with medial temporal lobe epilepsy. In addition, amobarbital could induce hyperperfusion. These methods might cause some studies to be limited in scope and results.

**Preliminary Clinical Application of the MCA Territorial Map**

In the current study, we preliminarily investigated the usefulness of the probabilistic maps in the clinical assessment of cerebrovascular diseases during the chronic stage. The analysis involved with the MCA map is fully automated and the computational time was a few minutes per case. The method, therefore, is not tedious but convenient to perform. The diagnosis was decided solely on the mean values of CBF in the MCA territory. Using this technique, both inter- and intraobserver variability are completely eliminated, because no interference by the user is necessary. In addition, this approach also enables visual inspections of CBF status in the MCA territory on a pixel-by-pixel basis by superimposing a Z-score map on MR imaging templates. The results demonstrated that the current MCA map (Method C) is diagnostically superior to the conventional ROI method (Method A). However, there was no significant difference in the predictive value of the CBF reduction (Z score) for hyperperfusion after CEA between the current map of the MCA territory (Method C) and predefined cortical templates (Method B), which already have demonstrated a high diagnostic value. The sensitivity (83%) and specificity (93%) of the MCA territory map were also similar to those (83% and 98%, respectively) shown in a previous study of postoperative hyperperfusion in which predefined cortical templates (Method B) were used. However, the current method is simpler and more straightforward than that performed using the predefined cortical templates (Method B) because the current approach requires calculation of a Z score only in the MCA territory. In contrast, the predefined cortical templates approach (Method B) requires this calculation in all eight predefined regions and the selection of the highest mean value. In addition, an assessment of MCA stenosis or occlusion might have resulted in a more preferable outcome for the map of the MCA territory. On the other hand, the validity of the current MCA map in the assessment of early changes associated with ischemic stroke should also be investigated in the future because the pathophysiology of chronic ischemia is not quite the same as that of an acute ischemic insult.

**Conclusions**

In the present study, we constructed a cortical surface map of the MCA territory by using SPECT images of an MCA infarction and statistical brain mapping analysis. Preliminary clinical application of this map demonstrated its high diagnostic value in comparison with the conventional ROI method for the prediction of hyperperfusion after CEA, and a diagnostic value equal to that of predefined cortical templates developed by the statistical brain mapping method. This map for SPECT studies can be used for the objective assessment of CBF in the MCA territory in various cerebrovascular diseases.

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