The Hidden Mismatch
An Explanation for Infarct Growth Without Perfusion-Weighted Imaging/Diffusion-Weighted Imaging Mismatch in Patients With Acute Ischemic Stroke

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Background and Purpose—In ischemic stroke, MR perfusion-weighted imaging (PWI) and diffusion-weighted imaging (DWI) mismatch represents tissue at risk for infarction. Infarct growth should only take place in the presence of mismatch, although there have been reports of this occurring. We hypothesized that this observation may be attributable to the presence of undetected “hidden mismatch,” which may become obvious when coregistration techniques are used.

Methods—MR PWI/DWI was performed within 48 hours of stroke onset and a final T2-weighted image at ≈3 months. Volumetric-subtraction mismatch volume was defined as PWI minus DWI volume and infarct growth was defined as T2 minus DWI volume. Coregistration mismatch volume was PWI not overlapped by DWI. Mismatch salvage was the proportion of coregistered mismatch tissue that had not progressed to infarction.

Results—Thirty-four patients were studied with MR at a median of 4.9 hours (interquartile range, 2.9–21.1 hours).

With the volumetric-subtraction technique, 5 patients (14.7%; 95% CI, 0.05%–0.31%) had infarct growth exceeding mismatch volume, 11 patients (32.0%) had no mismatch and, among these, 3 (27.3%) had infarct growth (median volume, 2.2 mL; interquartile range, 1.0–6.5 mL). All patients had mismatch volume identified by coregistration method that was greater than infarct growth volume. The proportion of this volume salvaged was 77.7% (interquartile range, 63.0%–98.9%).

Conclusions—The illogical finding of infarct growth volume being greater than the presence of mismatch volume can be explained by the presence of “hidden mismatch,” which may be detected by coregistration methods. (Stroke. 2011;42:662-668.)

Key Words: diffusion-weighted imaging ■ ischemia ■ ischemic stroke ■ magnetic resonance ■ mismatch ■ perfusion-weighted imaging

The use of MR imaging to select patients likely to benefit from therapy has increased in clinical trials and practice.1 The rationale is that large perfusion-weighted imaging (PWI)/diffusion-weighted imaging (DWI) mismatch volumes are more likely to respond to therapy.2 If no reperfusion occurs, then infarct growth will occur into the PWI/DWI mismatch volume. Conversely, with no mismatch, no expansion should occur. However, some investigators have shown expansion in the absence of PWI/DWI mismatch.2–4

The PWI/DWI mismatch calculation is based on the assumption that the infarct core is always embedded within salvageable ischemic tissue. Hence, the mismatch volume can be obtained by subtracting the DWI from PWI volume (volumetric-subtraction technique). Until now, investigators have used the volumetric-subtraction method exclusively. However, the dynamic stroke process may distort the relationship between the annular penumbra and infarct core. Hence, if the DWI lesion becomes dissociated from the PWI lesion because of reperfusion, the “embedded pattern” will break-down and the volumetric-subtraction method will be in error. Coregistration of DWI/PWI lesions will incorporate precise topographical details, as previously demonstrated.5

We studied this further by assessing patients with acute ischemic stroke using MR and by analyzing mismatch volumes by both volumetric-subtraction and coregistration techniques. Specifically, we hypothesized that in patients with no PWI/DWI mismatch assessed by the volumetric-subtraction technique, mismatch volumes would be identified when the more precise coregistration analysis was...
performed. Further, the infarct growth in these patients may be explained by the existence of the “hidden mismatch.”

Patients and Methods

Patients older than age 18 years who presented with acute middle cerebral artery ischemic stroke within 48 hours of stroke onset without contraindication to MR were recruited. Inclusion criteria included a complete set of initial MR images and final outcome T2 images up to 3 months from stroke onset. Consent was obtained from all participants and the study protocol was approved by the local (Austin Health) Ethics Committee.

Imaging

The MR sequence included T1-weighted sagittal localizer, axial fast spin-echo T2-weighted sequence, diffusion-weighted single-shot echo planar imaging (DWI), and perfusion-weighted sequence performed within 48 hours of stroke onset on a 1.5-T whole body scanner (from 2002–2004, a Sigma Horizontal SR 120 by General Electric was used, and from 2004–2007 this was changed to a Magnetom Avanto Syngo MR2004V by Siemens). The T2 sequence contained 19 slices, with slice thickness of 5 mm and interslice gap of 1.7 mm (repetition time/echo time, 3000/100 ms; field of view, 24×24 cm; matrix, 256×256 pixels). DWI slice (total of 38) was obtained with slice thickness of 5 mm and interslice gap of 1.7 mm (repetition time/echo time, 12 000/100 ms; field of view, 40×20 cm; matrix, 256×128 pixels; b values of 0 and 1000 sec/mm²). A follow-up T2 study was performed up to 3 months after the stroke onset. The perfusion study (a total of 480 slices comprising 12 individual slices) used slice thickness of 6 mm, with interslice gap of 1.0 mm (repetition time/echo time, 2000/60 ms; field of view, 40×20 cm; 40 T2*-weighted measurements at an interval of 2 seconds). Gadolinium 0.2 mmol/kg was injected by a power injector, followed by 15 mL normal saline. The Magnetom Avanto Syngo MR2004V showed values for T2 repetition time/echo time of 3500/100 ms and DWI repetition time/echo time of 1200/100 ms.

Image Analysis

All image analyses were performed blinded to the clinical details of the individual patients.

Core (DWI) Lesion

All the voxels with DWI image intensity reading ≥1.4-times compared to the mean DWI image intensity value of the contralateral cortical hemisphere were included using the Analyze software (Biomedical Imaging Resource; Mayo Clinic; Figure 1). The artifact voxels were removed manually after visual assessment.

Perfusion Defect (PWI Lesion)

Raw perfusion images were processed by StrokeTool (Digital Image Solution; H.J. Wittsack). The chosen arterial input function was the contralateral middle cerebral artery. Smoothing was performed using a smear 3×3 filter and time-direction smoothing using a (1-2-1) mask to reduce noisy data.

$T_{max}$ is the time delay to the maximal residual function. The concentration time course of each voxel was deconvolved with the arterial input function using singular value decomposition algorithm. $T_{max}$ of 2 seconds plus delay was obtained by adding 2 seconds to the mean $T_{max}$ value of the contralateral cortical hemisphere. All the voxels of the affected hemisphere which equaled and exceeded this value were included using Analyze software (Biomedical Imaging Resources, Mayo Clinic, Rochester, MN). The lesions were delineated after the coregistration process. Artifactual voxels were identified and excluded after coregistration process (Figure 1). All regions were screened for severe hypoperfusion (voxels without values) with reference to the opposite side to eliminate the possibility of these being included in mismatch calculation.

Final T2 Lesion

The final infarct lesion was identified on the T2 images up to 3 months from stroke onset. The boundary of the lesions was drawn independently by 2 neurologists using the Analyze software. If acceptable agreement was achieved by the 2 assessors, then only the values of 1 assessor was used as the final T2 lesion volume.

Coregistration of Images

This is an intrasubject registration between different MR imaging modes. The final T2-weighted image was chosen as the target common space. Careful manual coregistration was performed using specific anatomic landmarks with Register software (http://www.bic.mni.mcgill.ca/software/). Up to 10 predetermined anatomic landmarks, such as central gyrus and cerebellopontine angle, were chosen. A $3\times3\times3$ linear transformation matrix was

![Figure 1. Determination of diffusion-weighted imaging and perfusion-weighted imaging lesions. Patient 1 is a 72-year-old woman with MRI performed at 20.8 hours from stroke onset. Patient 2 is 63-year-old man with MRI performed at 4.1 hours from stroke onset.](image-url)
created and resample of the source image was performed. To achieve optimal coregistration, the b1000 image of DWI was used to coregister with the final T2 image and the perfusion image.

Mismatch Volume Calculation
The volumetric-subtraction mismatch volume was calculated by subtraction of the DWI volume from the PWI volume (Figure 2). The coregistration mismatch volume was the region of PWI volume that was not overlapped by the DWI volume when coregistered (Figure 3). Mismatch volume as a percentage of DWI volume was calculated by the following formula:

\[
\frac{\text{Mismatch volume}}{\text{DWI volume}} \times 100.
\]

Mismatch Salvage Percentage Calculation
The coregistration salvage volume was the region of the PWI/DWI mismatch that was not overlapped by the T2 infarction when coregistered (Figure 4). The percentage volume was calculated by the following formula:

\[
\frac{\text{Final mismatch salvage volume}}{\text{Initial mismatch volume}} \times 100.
\]

Infarct Growth
Infarct growth was defined as final T2 volume larger than the initial DWI volume, and its volume was calculated by simple subtraction of DWI volume from T2 volume.

Statistical Analyses
Statistical analyses were performed on a commercial statistical software package (STATA v10). Single proportion test was used to compare proportions of patients whose infarct growth has exceeded mismatch size independently for volumetric-subtraction and coregistration techniques. The agreement of the T2 volume between the 2 assessors was assessed by concordance coefficient and reduced

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**Figure 2.** Determination of mismatch volume by volumetric method. For patient 1, it was 30.1 mL (perfusion-weighted imaging [PWI] volume) minus 36.8 mL (diffusion-weighted imaging [DWI] volume), which equals zero. For patient 2, it was 54.1 mL (PWI volume) minus 23.9 mL (DWI volume), which equals 30.2 mL.

**Figure 3.** Determination of mismatch volume by coregistration method. Patient 1 had a volume of 13.8 mL, which was more than that found by the volumetric method (0 mL). Patient had a volume of 45.4 mL which was more than that found by the volumetric method (30.2 mL).
major axis regression. Nonparametric comparisons using Wilcoxon ranked test were made between groups with and without mismatch using the volumetric-subtraction method.

Results

Patients
A total of 34 (22 males and 12 females) patients fulfilled the inclusion criteria for our prospectively accrued MR image dataset. The median age was 72.0 years (interquartile range [IQR], 61.8–78.3 years) and the median time to MR was 4.9 hours (IQR, 2.9–21.1 hours). The median NIHSS was 7.5 (IQR, 4.0–20.0). Of these 34 patients, 8 (23.5%) have history of stroke, 17 (50.0%) have hypertension, 11 (32.4%) have diabetes, 12 (35.3%) have history of smoking, 11 (32.4%) have ischemic heart disease, 10 (29.4%) have atrial fibrillation, and 9 (26.5%) have hyperlipidemia.

Mismatch Volumes, Infarct Growth, and Tissue Salvage
With the volumetric-subtraction technique, 5 patients (14.7%; 95% CI, 6.0%–31.0%) had infarct growth exceeding mismatch size (Table 1). With coregistration technique, no patients had infarct growth exceeding original mismatch size (0%; 97.5% one-sided CI, 0%–10%; P=0.99).

Eleven patients out of 34 had no mismatch identified by volumetric-subtraction method (32.0%; 95% CI, 17.0%–51.0%). Three out of these 11 patients (27.0%; 95% CI, 6.0%–61.0%) had infarct growth (T2>DWI). The median infarct growth volume was 2.2 mL (IQR, 1.0–6.5 mL). Also, in these 11 patients “hidden mismatch” was identified by coregistration methods with median mismatch volume of 2.8 mL (IQR, 0.9–3.3 mL) and median mismatch salvage proportion of 77.7% (IQR, 63.0%–98.9%).

Based on the volumetric-subtraction method, patients were classified into 2 groups according to the presence or absence of mismatch. Comparing the 2 groups, the patients without mismatch had larger median DWI volumes (23.1 mL and IQR, 2.1–81.6 mL compared to 5.6 mL and IQR 1.4–22.0 mL; P=0.08), smaller median PWI volumes (5.7 mL and IQR 1.2–21.1 mL compared to 54.1 mL and IQR 9.6–107.2 mL; P=0.003), larger median final T2 volumes (8.8 mL and IQR 1.9–31.3 mL compared to 79.1 mL and IQR 3.8–65.5 mL; P=0.9), smaller median mismatch as percentage of DWI volumes (23.5% and IQR 5.8%–47.6% compared to 454.8% and IQR 237.7%–1237.7%; P<0.001), and smaller proportion of salvage (77.8% and IQR 63.0%–97.3% compared to 84.4% and IQR 71.2%–96.8%; P<0.001). There was no difference in the percentage of DWI lesion overlapping the PWI lesion between the 2 groups

Table 1. Patients With Volumetric Mismatch Volume Less Than Infarct Growth Volume

<table>
<thead>
<tr>
<th>Patient</th>
<th>Time of MR From Stroke Onset (hr)</th>
<th>MCA Occlusion</th>
<th>Volumetric Mismatch Volume (mL)</th>
<th>Coregistration Mismatch Volume (mL)</th>
<th>Infarct Growth Volume (mL)</th>
<th>Coregistration Mismatch Salvage Percentage (%)</th>
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</thead>
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<tr>
<td>1</td>
<td>19.2</td>
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</tr>
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<td>2.2</td>
<td>70.1</td>
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<tr>
<td>3</td>
<td>20.8</td>
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<td>6.5</td>
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</tr>
<tr>
<td>4</td>
<td>1.9</td>
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<td>60.1</td>
</tr>
<tr>
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<td>4.1</td>
<td>Yes</td>
<td>30.2</td>
<td>45.4</td>
<td>41.6</td>
<td>59.3</td>
</tr>
</tbody>
</table>

Figure 4. Determination of mismatch salvage and infarct growth. For patient 1, infarct growth was 6.5 mL, which was more than the volumetric mismatch volume of 0 mL but less than the coregistration mismatch volume of 13.8 mL. For patient 2, infarct growth was 41.6 mL, which was more than the volumetric mismatch of 30.2 mL but less than the coregistration mismatch volume of 45.4 mL.
Mismatch volume as percentage of DWI volume (%) 270.4 (47.1–715.0) 454.7 (254.7–1237.7) 23.5 (5.2–47.6) 0.007

Volume of DWI not overlapping with mismatch (mL) 2.6 (1.3–15.2) 1.9 (1.0–6.3) 18.5 (2.3–45.9) 0.007

Percentage of DWI lesion overlapping with PWI (%) 44.1 (10.6–68.9) 48.6 (11.1–75.4) 19.5 (7.9–45.0) 0.123

Final infarct volume (mL) 6.4 (3.3–34.3) 18.0 (3.8–65.6) 8.8 (1.9–31.3) 0.99

Coregistration mismatch volume (mL) 24.7 (3.2–57.9) 44.4 (9.6–90.8) 2.8 (1.0–3.3) <0.0001

DWI volume (mL) 7.2 (2.6–27.6) 5.6 (1.4–22.0) 23.1 (3.7–81.6) 0.08

Volumetric mismatch volume (mL) 13.0 (0–57.4) 33.4 (7.2–75.4) 0 0.0001

Coregistration mismatch volume (mL) 24.7 (3.2–57.9) 44.4 (9.6–90.8) 2.8 (1.0–3.3) <0.0001

Final infarct volume (mL) 6.4 (3.3–34.3) 18.0 (3.8–65.6) 8.8 (1.9–31.3) 0.99

Percentage of DWI lesion overlapping with PWI (%) 44.1 (10.6–68.9) 48.6 (11.1–75.4) 19.5 (7.9–45.0) 0.123

Volume of DWI not overlapping with mismatch (mL) 2.6 (1.3–15.2) 1.9 (1.0–6.3) 18.5 (2.3–45.9) 0.007

Mismatch volume as percentage of DWI volume (%) 270.4 (47.1–715.0) 454.7 (254.7–1237.7) 23.5 (5.2–47.6) <0.0001

DWI indicates diffusion-weighted imaging; PWI, perfusion-weighted imaging.

Table 2. DWI and PWI Lesion Volumes and Overlap Percentage in Different Patient Groups

(48.6% and IQR 11.1%–75.4% compared to 19.5% and IQR 7.9%–45.0%; P=0.123) (Table 2).

Agreement Between Blinded Assessors for Tissue Volumes

Excellent agreement was achieved between the 2 assessors’ estimations of T2 lesion volume, with concordance correlation coefficient of 0.959 (asymptotic 95% CI, 0.934–0.983; P<0.0001), and was further confirmed by reduced major axis analysis (slope, 1.09).

Middle Cerebral Artery Occlusion

Overall, there were 22 patients (64.7%) with patent middle cerebral artery at the time of MRI. Five out of the 14 (35.7%) patients had infarct growth with vessel occlusion, and 7 out of 20 (35.0%) patients had vessel occlusion without infarct growth.

Discussion

We have demonstrated that using the volumetric-subtraction method, 5 patients have mismatch volume less than the infarct growth volume, which defines the ischemic penumbra theory that states that mismatch tissue is the only tissue at risk; all the coregistration mismatch volumes were larger than their corresponding infarct growth volumes. Also, we have demonstrated that in patients in whom PWI/DWI mismatch is absent using the commonly used volumetric-subtraction method of analysis, all have mismatch identified when the more precise coregistration method is used. The median proportion of this mismatch of the DWI volume was 23.5%, approximately the level of inclusion for clinical trials of therapy. This “hidden mismatch” provides an explanation for the puzzling observation by previous investigators that infarct expansion seems to occur even in the absence of PWI/DWI mismatch, although, as in our dataset, at a lower level than among mismatch patients. We were also able to show that the majority of the “hidden mismatch” was salvaged at a rate of 77.7%.

The validity of the volumetric-subtraction technique is dependent on the assumption of the classical pattern of the ischemic penumbra, where the infarct core is always surrounded by penumbral tissue and expands uniformly at the expense of the penumbra. However, this is a rigid interpretation of a dynamic process. Numerous factors can influence the fate of the penumbral tissue, such as the extent of collateral circulation, varying rates and anatomic sites of spontaneous recanalization, and reperfusion and differing tissue infarction threshold. The dynamic interaction of these factors would suggest a heterogeneous and unpredictable fate of the penumbra tissue at different locations and at different times. In addition, neuroimaging such as MR perfusion only provides a static single time point in reference to a dynamic process, which may provide a limited representation of the ischemic penumbra. Nevertheless, these snapshots of the dynamic process have demonstrated the importance of the topographical relationship between the DWI and PWI lesions.

With the classical pattern, one would expect a complete overlap of the DWI lesion by the PWI lesion. However, the median percentage of the volume of DWI lesion overlapping the PWI lesion was only 44.1% (IQR, 10.6%–66.9%). The lesser the area of overlap between DWI and PWI lesions, the less valid the classical pattern is and, hence, the less accurate the volumetric-subtraction method. This was demonstrated by the relatively lower percentage overlap between the DWI and PWI lesions in patients without mismatch volume calculated by the volumetric-subtraction method compared to the group who did have mismatch volume, although this was not statistically significant (P=0.123); however, the difference in volume was significant (P<0.007). In addition, the DWI lesions may contain salvageable tissue with partial or even complete DWI reversal. With the reperfusion of the DWI lesion, the topographically corresponding PWI region would have normal perfusion and use of the volumetric-subtraction technique would incur a “double subtraction” of the DWI lesion volumes and underestimates the mismatch volume. Using a larger cohort of data (which is an extension of this dataset), we have recently demonstrated the volumetric-subtraction method underestimated the mismatch volume by ~30% and such difference increases with time, likely reflective of the unpredictable contribution of various factors stated regarding the penumbral fate.

In clinical neuroimaging studies, a PWI-to-DWI ratio of >1.2 reflects the presence of clinically significant mismatch. In our dataset, 6 out of the 11 patients had >20% proportional mismatch volume to DWI volume when analyzed by the coregistration method despite no mismatch being found using the volumetric-subtraction method. One could argue that these patients should be included in trials of therapy, given that significant amounts of potentially reversible tissue are
present. However, one may need to exercise caution, given that some of these mismatches were of relatively small volume. Compared to the mismatch group, the patients without mismatch had later times of MR scanning and significantly larger baseline median DWI volumes with small PWI volumes, reflective of the breakdown of the ischemic penumbra. Such may explain the comparatively lower percentage compared to the mismatch group (21.7% compared to 615.1%). Despite these differences, the ischemic tissues salvage rate was similar for both groups, suggesting that the “hidden mismatch” can still be salvaged at this later time.

If ischemic penumbra tissue is the only tissue in which infarct expansion could take place, then the infarct growth volume should never exceed the penumbral volume. In Table 1, there were 5 patients with volumetric-subtraction mismatch volume less than infarct growth volume. However, their coregistration volumes were larger than the infarct growth volumes, which could explain this impossible infarct growth. Importantly, these mismatch tissues were partially salvaged spontaneously. As expected, the coregistration volumes of all the patients were larger than the infarct growth volumes. Two patients are shown in Figures 1 to 4. Patient 1 had 0 volumetric-subtraction mismatch volume, but there was infarct growth (6.5 mL) at 3 months, as demonstrated in Figure 4. This infarct growth could be explained by the presence of coregistration mismatch (13.8 mL), with the clear extension of the infarction into the coregistration mismatch. In patient 2, the volumetric-subtraction mismatch volume (30.2 mL) was smaller than the infarct growth volume (41.6 mL). Clearly, again, there was expansion of the infarction into the coregistration mismatch (45.4 mL) to account for such infarct growth.

There are only a few studies in which the issues of mismatch vs nonmismatch patients were addressed. River et al. studied 46 patients within 24 hours of ischemic stroke onset. Using cerebral blood flow squared as the PWI parameter and volumetric-subtraction analysis techniques, they were able to identify 21 patients with no mismatch (PWI-DWI), and 11 out of these 21 patients had infarct growth (final T2>DWI). They found no significant association between lesion growth and the presence or absence of PWI/DWI mismatch and reasonably concluded that patients without mismatch may also benefit from treatment. It seems highly likely that these patients also would have “hidden mismatch,” which would become evident when coregistration techniques were applied. An analysis of 11 neuroimaging studies also showed similar findings. Two recent interventional trials have studied the mismatch concept in acute ischemic stroke, and both of them showed infarct expansion in patients without mismatch; alteplase might attenuate such infarct growth. The Echoplanar Imaging thrombolytic Evaluation Trial (EPITHET) used the inclusion criteria of “distinct penumbra of at least 20%” to assess the existence of clinically significant penumbra. There were 96 of the 359 patients excluded from the study based on these criteria. Again, their median DWI (17–21 mL) and mismatch (83–87 mL compared to our 33 mL) volumes were larger than our values; hence, some of these 96 patient might have existing mismatch if the coregistration method was used. The primary outcomes of both studies were negative and it is possible that by using the coregistration method, the outcome may be different.

This study has a number of limitations. The first is the relatively small sample size of 34 patients. We suggest that these findings are to be substantiated in larger datasets. Second, the median volumes of both DWI and T2 lesions were somewhat smaller compared to those of the previous studies but still were substantial. The coregistration mismatch volume also was relatively small. Such small volume may not be clinically significant, but this will need to be studied further. It is important to note that this study has included patients up to 48 hours from stroke onset and is part of a larger study. The clinical significance of mismatch beyond 9 hours to 12 hours has not yet been clinically studied. If this study were restricted to those 12 hours from stroke onset, then there would be patients with no mismatch shown by using the volumetric-subtraction method but with mismatch shown by using the coregistration method. Two of them would have had mismatch volume >40 mL, which may be clinically important. Third, errors of volume assessment and coregistration are always possible but were kept to a minimum by use of subjective threshold methods in the determination of DWI volumes and meticulous manual coregistration method, even though using manual coregistration method could be time-consuming. There are a number of automated coregistration programs available that could perform coregistration of images with reasonable results. However, this is reliant on good-quality MRI/CT images. With the advance of computer programming and neuroimaging technology, it is likely that an automated coregistration program will be available for clinical use. The use of relative Tmax of 2 seconds plus the penumbral measure may include regions of benign oligemia. A recent study suggested a Tmax threshold higher than 2 seconds was more closely indicative of penumbral tissue. The inclusion of benign oligemic tissue in the penumbral lesion should increase the likelihood of finding mismatch by the volumetric-subtraction method. Patients with previous stroke might affect the acute and infarct lesions assessment; however, by using the DWI and coregistration, one could accurately identify the location of the acute stroke and its subsequent infarct location visually. It has been known that infarct tissue could shrink with time and might result in excessive mismatch salvage at 3 months. Similar error would exist using the volumetric-subtraction method, but the coregistration method would take into account the irregular growth or shrinkage of the infarct over time; therefore, it is likely to be more accurate. The severe lack of blood flow within the infarct core (DWI lesion) may result in lack of voxel signal. We have assessed these regions of severe hypoperfusion and...
demonstrated the presence of voxel signals. Finally, the clinical importance of these “hidden mismatches” will need to be tested in a larger dataset with clinical outcomes.

Conclusions
In summary, we have shown that the application of the more accurate coregistration technique has identified “hidden mismatch” using PWI/DWI mismatch in patients in whom the volumetric-subtraction technique had failed to do so. The presence of this otherwise unidentified mismatch provides adequate explanation for the observed infarct expansion in these patients.

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Disclosure
None.

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La discrepancia oculta: una explicación del crecimiento del infarto sin discrepancia de RM con ponderación de perfusión/RM con ponderación de difusión en pacientes con ictus isquémico agudo

En la actualidad está ampliamente aceptado que la discrepancia de las imágenes con ponderación de difusión (DWI)/imágenes con ponderación de perfusión (PWI) en la RM aporta una aproximación de la penumbra isquémica. Sin embargo, los autores que se muestran críticos con esta exploración citan algunos resultados aparentemente contradictorios para poner en duda toda la teoría de la discrepancia y el valor clínico de las exploraciones de DWI/PWI para facilitar la toma de decisiones en el ictus isquémico agudo. En este número, Ma y colaboradores han analizado la discrepancia de volúmenes en la RM mediante sustracción volumétrica (volumen de la lesión en PWI menos volumen de la lesión en DWI) en comparación con la determinación efectuada con técnicas de registro conjunto (volumen de lesión de PWI no solapado por DWI) y han comparado los resultados con los volúmenes finales de infarto en las imágenes posteriores con ponderación T2 obtenidas hasta 3 meses después. Los autores identificaron a 5 de 34 pacientes con ictus de arteria cerebral media agudos en los que el crecimiento del infarto fue mayor que el volumen de discrepancia observado mediante sustracción volumétrica, pero no al observado con técnicas de registro conjunto. En 11 de los 34 pacientes, se identificó una discrepancia “oculta” tras el empleo de técnicas de registro conjuto, pero no con los análisis de sustracción volumétrica tradicionales. La mediana de la proporción que representaba esta discrepancia “oculta” respecto al volumen de DWI fue del 23,5% (2,8 mL), con una mediana de porcentaje de zona de discrepancia salvada del 78%. Los autores argumentan que el método de registro conjunto utilizado puede corregir las limitaciones de las imágenes y los procesos dinámicos (como la reperfusión parcial) que distorsionan la relación anatómica entre la penumbra y el núcleo. Aun así los datos presentados aportan una explicación atractiva del crecimiento del infarto más allá de los límites de la discrepancia, hay varios aspectos que limitan la posibilidad de extraer conclusiones definitivas. En primer lugar, el tamaño muestral y el volumen total de discrepancia “oculta” fueron pequeños. En segundo lugar, el porcentaje de zona de discrepancia salvada fue elevado, lo cual resulta difícil de interpretar, puesto que no se presentaron datos relativos a la reperfusión/trombolisis, y continúa sin conocerse la relación entre la lesión PWI, el volumen de discrepancia y el volumen final de la lesión en T2. Así pues, serán necesarios nuevos estudios para confirmar la utilidad del enfoque presentado. (Comentario al artículo The Hidden Mismatch: An Explanation for Infarct Growth Without Perfusion-Weighted Imaging/Diffusion-Weighted Imaging Mismatch in Patients With Acute Ischemic Stroke. Henry K. Ma, Jorge A. Zavala, Leonid Churilov, John Ly, Perter M. Wright, Thanh G. Phan, Shuji Arakawa, Stephen M. Davis, and Geoffrey A. Donnan. Stroke. 2011;42:662-668.)
The Hidden Mismatch

An Explanation for Infarct Growth Without Perfusion-Weighted Imaging/Diffusion-Weighted Imaging Mismatch in Patients With Acute Ischemic Stroke

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Background and Objective: Acute ischemic stroke patients with an area of mismatch on perfusion-weighted imaging (PWI) and diffusion-weighted imaging (DWI) have a higher risk of infarct growth on PWI/DWI imaging. However, infarct growth can occur in the absence of PWI/DWI mismatch. We investigated whether infarct growth could occur due to "hidden mismatch.

Methods: Inclusion criteria were age ≥18 years, diagnosis of acute ischemic stroke defined by initial NIHSS >4.5, and PWI/DWI performed within 48 hours. Patients were followed up at 3 months for T2-weighted imaging to assess infarct growth. PWI/DWI mismatch volume was defined as the difference between PWI and DWI lesions. Infarct growth was defined as the difference between T2 and DWI lesions. Mismatch volume挽救率 was defined as the volume of mismatch that did not develop into infarction.

Results: 34 patients were included. The median time from symptom onset to PWI/DWI was 4.9 hours (IQR 2.9-21.1). 5 patients (14.7%, 95% CI, 0.05%-0.31%) had larger infarct growth than the PWI/DWI mismatch volume. Among the 11 patients (32.0%) who did not have DWI lesions, 3 patients (27.3%) had infarct growth (median T2 lesion volume 2.2 mL, IQR 1.0-6.5 mL). All patients had larger mismatch volumes than the infarct growth volume. Mismatch volume挽救率 was 77.7% (IQR 63.0%-98.9%).

Conclusion: "Hidden mismatch" may explain infarct growth in the absence of PWI/DWI mismatch. Mismatch volume挽救率 can be measured using image registration methods.

Keywords: Mismatch, stroke, infarct growth, PWI/DWI, diffusion-weighted imaging, perfusion-weighted imaging.
方法可以精确地合并病变部位的图形细节。本试验拟进一步对 PWI/DWI 影像配准方法进行研究，分别应用体积相减方法和影像配准方法，对急性缺血性卒中 MR 检查不匹配区域的体积进行评估。需要特别指出的是，那些应用体积相减方法评估其缺乏 PWI/DWI 不匹配体积的患者，在应用更精确的影像配准方法分析时，将会发现存在不匹

配体积。这一发现可进一步解释这些患者是因为存在“隐性不匹配”区域而出现了梗死体积的扩大。

研究对象和方法
研究对象为年龄大于 18 岁、发病时间小于 48 小时、无 MR 检查禁忌症的急性大脑中动脉缺血性卒中患者。纳入标准包括：患者发病初期进行一套完整序列的 MR 检查，以及为明确最终的病变体积，在患者发病 3 个月时进行 T2 序列的 MR 检查。所有患者均签署了知情同意书，研究方案获得了当地伦理委员会的批准。

影像检查
应用 1.5T 磁共振扫描仪对发病 48 小时内的患者进行相关序列的扫描，包括 T1 加权矢状定位像、轴位自旋回波 T2 加权序列、弥散加权像 (DWI) 和灌注加权序列 (2002-2004 年，磁共振检查仪为通用电气公司生产的 Sigma Horizontal SR 120；2004-2007 年，更换为西门子公司生产的 Magnetom Avanto Syngo MR2004V)。T2 序列参数：扫描层数 19，层厚为 5 mm，层间隔为 1.7 mm (重复时间 / 回波时间 3000/100 ms，视野 24×24 cm，矩阵 256×256 像素)。

DWI 序列参数：扫描层数 38，层厚为 5 mm，层间隔为 1.7 mm，(重复时间 / 回波时间 1200/100 ms，视野 40×20 cm，矩阵 256×128 像素，b 值为 0 和 1000 s/mm²)。在患者发病 3 个月时进行随访的 T2 序列检查。灌注序列参数：12 个不同层面的 480 张影像，厚度为 6 mm，层间隔为 1.0 mm (重复时间 / 回波时间 2000/60 ms，视野 40×20 cm，T2* 加权成像测量的时间间隔为 2 秒)。给予 0.2 mmol/kg 的钆剂团注，之后注入 15 mL 生理盐水。Magnetom Avanto Syngo MR2004V 扫描仪 T2 序列的重复时间 / 回波时间为 3500/100 ms，DWI 序列的重复时间 / 回波时间为 1200/100 ms。

图像分析
所有图像均在不知晓患者临床资料的情况下进行盲法分析。

核心(DWI)病变
应用分析软件 (生物医学影像实验室，Mayo 医学中心，图 1) 对 DWI 影像进行分析。以对侧大脑半球皮层为参考，DWI 上所有信号强度≥对侧 1.4 倍的体素信号均标记为 DWI 的病变体积。在视觉评判后，用手工方法将伪影去除。

灌注缺损(PWI病变)
原始灌注图像使用单中工具进行处理 (数字化影像处理，H.J. Wittsack)。所选择的动脉输入函数是对侧大脑中动脉。应用 3×3 的滤数和 (1-2-1) 的屏蔽进行减噪平滑处理。

Tmax 是最大残余函数的时间延迟。应用奇异值
分解算法对每个体素的浓度时间过程与动脉输入函数进行卷积展开\(^7\)。通过对侧半球皮层的平均 \(T_{\text{max}}\) 值加 2 秒钟可获得 2 秒钟加延迟的 \(T_{\text{max}}\) 值。采用分析软件 (Biomedical Imaging Resources, Mayo Clinic, Rochester, MN) 分析包括那些受影响半球的所有大于等于这个值的体素。完成配准过程后确定和去除伪影体素并勾勒出病变 (图 1)。参考对侧半球对所有区域进行严重低灌注区 (没有值的体素) 的筛查, 以排除这些区域被计算在不匹配体积的可能性。

最终的 T2 病变

在患者发病 3 个月时，进行 T2 序列的 MR 检查来确定最终的梗死病变体积。两位神经科医师使用分析软件分别单独勾画出病灶边缘。如果二者判断结果达到良好的一致性，则取其中一位医师的判断结果作为最终的 T2 病变体积。

影像配准技术

这是一个在不同磁共振影像模式之间的自体识别过程。最终的 T2 加权影像被选定为共同的靶目标。应用特定的解剖学界标软件进行详细的手工影像配准 (http://www.bic.mni.mcgill.ca/software/)。软件中有 10 个预定的解剖学界标，如中央回和小脑角。创建一个 3×3×3 线性变换矩阵，对源图像进行重新取样。为了实现最佳的影像配准，取 DWI 的 b 值为 1000 的图像与最终的 T2 图像和灌注图象进行配准。

图 2 体积相减方法测量的不匹配体积。患者 1 的不匹配体积是 30.1 mL (PWI 病变体积) 减去 36.8 mL (DWI 病变体积)。相当于零。患者 2 的不匹配体积是 54.1 mL (PWI 病变体积) 减去 23.9 mL (DWI 病变体积)，等于 30.2 毫升。

图 3 影像配准方法测量的不匹配体积。患者 1 的不匹配体积是 13.8 mL，高于体积相减方法测量的不匹配体积 (0 mL)。患者 2 的不匹配体积是 45.4 mL，高于体积相减方法测量的不匹配体积 (30.2 mL)。
不匹配体积的计算

应用体积相减方法计算的不匹配体积是由 PWI 的病变体积减去 DWI 的病变体积所得 (图 2)。影像配准方法测量的不匹配体积是指 PWI 与 DWI 病变部位未重叠区域的体积 (图 3)。DWI 不匹配体积的百分比由以下公式计算:

\[
\text{不匹配体积} / \text{DWI 的病变体积} \times 100.
\]

不匹配组织挽救率的计算

影像配准的挽救体积是指与最终的 T2 梗死病灶与 PWI/DWI 不匹配区域没有重叠的体积 (图 4)。挽救体积百分比的计算公式如下:

\[
\text{最终挽救的不匹配体积} / \text{初始不匹配体积} \times 100.
\]

梗死体积扩大

梗死体积扩大定义为最终的 T2 病变体积大于初始的 DWI 病变体积。计算扩大的梗死体积可由二者间进行简单的减法得到。

统计分析

采用 STATA v10 软件包进行统计分析。对梗死体积扩大超过应用体积相减方法和影像配准方法检测的不匹配体积的患者比例，采用单比率检验方法进行分析。采用一致性系数和压轴回归分析评价两位影像判读者对 T2 病变体积测量结果的一致性。按照体积相减方法的测量结果，分为缺乏和存在不匹配体积两组，两组间应用 Wilcoxon 等级检验进行非参数比较。

结果

共有 34 例 (22 例男性和 12 例女性) 患者完成了我们这组前瞻性设计的 MR 图像资料采集。所有患者年龄中位数为 72.0 岁 (四分位间距 [IQR], 61.8-78.3 岁), 进行 MR 检查的中位时间为 4.9 小时 (IQR, 2.9-21.1 小时)。患者 NIHSS 评分中位数为 7.5(IQR, 4.0-21.1)。在 34 例患者中，8 例患者 (23.5%) 有卒中病史，17 例患者 (50.0%) 有高血压病史，11 例患者 (32.4%) 有糖尿病史，12 例患者 (35.3%) 有吸烟史，11 例患者 (32.4%) 有缺血性心脏病史，10 例患者 (29.4%) 有心房颤动病史，9 例患者 (26.5%) 有高脂血症病史。

<table>
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<tr>
<th>患者</th>
<th>卒中发病至 MR 检查时间 (小时)</th>
<th>MCA 闭塞</th>
<th>体积相减方法测量的不匹配体积 (mL)</th>
<th>影像配准方法测量的不匹配体积 (mL)</th>
<th>扩大的梗死体积 (mL)</th>
<th>救治不匹配体积比率 (%)</th>
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</thead>
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<td>1.0</td>
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<td>0</td>
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<td>2.2</td>
<td>70.1</td>
</tr>
<tr>
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<td>20.8</td>
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<td>6.5</td>
<td>67.3</td>
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<tr>
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<td>1.9</td>
<td>是</td>
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<td>44.4</td>
<td>42.4</td>
<td>60.1</td>
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<tr>
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<td>是</td>
<td>30.2</td>
<td>45.4</td>
<td>41.6</td>
<td>59.3</td>
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</tbody>
</table>
的梗死体积扩大超过了应用体积相减方法测量到的不匹配体积（见表1）。没有患者的梗死体积扩大超过应用影像配准方法测量到的不匹配体积（0%，97.5% 单侧 CI, 0%-10%; P=0.99）。在34例患者中，应用体积相减方法测量出11例患者缺乏不匹配体积（32.0%, 95% CI, 17.0%-51.0%）。在34例患者中，有3例（27.0%, 95% CI, 6.0%-61.0%）出现了梗死体积扩大（T2>DWI）。扩大的梗死体积中位数为2.2 mL(IQR, 1.0-6.5 mL)。此外，这11例应用影像配准方法定义为“隐性不匹配”患者的不匹配体积中位数为2.8 mL(IQR, 0.9-3.3 mL)。不匹配体积挽救率的中位数为77.7%(IQR, 63.0%-98.9%)。

根据体积相减方法的测量结果，将患者分为缺乏不匹配体积和存在不匹配体积两组。将两组进行比较发现，缺乏不匹配体积组患者的 DWI 病变体积中位数更大(23.1 mL 和 IQR, 3.7-81.6 mL; 5.6 mL 和 IQR, 1.4-22.0 mL; P=0.08), PWI 病变体积的中位数更小(5.7 mL 和 IQR, 1.2-21.1 mL; 54.1 mL 和 IQR, 9.6-107.2 mL; P=0.003), 最终 T2 病变体积中位数更大(8.8 mL 和 IQR, 1.9-31.3 mL; 17.9 mL 和 IQR, 3.8-65.5 mL; P=0.9), 不匹配体积与 DWI 病变体积百分比的中位数更小(23.5% 和 IQR, 5.8%-47.6%; 454.8% 和 IQR, 237.7%-1237.7%; P<0.001), 影像配准方法测量的不匹配体积更小(2.8 mL 和 IQR, 0.9-3.3 mL; 44.4 mL 和 IQR, 9.6-90.8 mL; P<0.001)。所有患者、中位数 | 存在不匹配体积组 | 缺乏不匹配体积组 | Mann-Whitney 检验 P 值
---|---|---|---
DWI 病变体积 (mL) | 7.2 (2.6–27.6) | 5.6 (1.4–22.0) | 23.1 (3.7–81.6) | 0.08
PWI 病变体积 (mL) | 31.6 (4.9–72.4) | 54.1 (9.6–107.2) | 5.7 (1.7–21.1) | 0.003
体积相减方法测量的不匹配体积 (mL) | 13.0 (0–57.4) | 33.4 (7.2–75.4) | 0 | <0.0001
影像配准方法测量的不匹配体积 (mL) | 24.7 (3.2–57.9) | 44.4 (9.6–90.8) | 2.8 (1.0–3.3) | <0.0001
最终梗死体积 (mL) | 6.4 (3.3–34.3) | 18.0 (3.8–65.6) | 8.8 (1.9–31.3) | 0.99
DWI 与 PWI 病变重合比率 (%) | 44.1 (10.6–68.9) | 48.6 (11.1–75.4) | 19.5 (7.9–45.0) | 0.123
未与不匹配体积重叠的 DWI 病变体积 (mL) | 2.6 (1.3–15.2) | 1.9 (1.0–6.3) | 18.5 (2.3–45.9) | 0.007
不匹配体积与 DWI 病变体积的百分比 (%) | 270.4 (47.1–715.0) | 454.7 (254.7–1237.7) | 23.5 (5.2–47.6) | <0.0001

DWI，弥散加权成像；PWI，灌注加权成像。

表 2 不同亚组患者的 DWI、PWI 病变体积和 DWI/PWI 病变重叠比例


d的梗死体积扩大超过了应用体积相减方法测量到的不匹配体积（见表 1）。没有患者的梗死体积扩大超过应用影像配准方法测量到的不匹配体积（0%, 97.5% 单侧 CI, 0%-10%; P=0.99）。

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双盲测评员之间病变体积测量结果的一致性

两位测评员对 T2 病变体积的测量，达到了非常好的一致性，一致性相关系数为 0.959(95% 渐近置信区间为 0.934-0.983; P<0.0001)，并进一步得到了压轴回归分析的证实 (线性回归斜率，1.09)。

讨论

本研究结果显示，有5例患者的梗死体积扩大超过了应用体积相减方法测量的不匹配体积，这一发现对缺血半暗带理论所阐述的仅在不匹配区域才可发生梗死提出了质疑。而影像配准方法测量的不匹配体积均超过了扩大的梗死体积。此外，我们还发现应用体积相减方法测量缺乏 PWI/DWI 不匹配区域的患者，当应用更精确的影像配准方法进行测量时，均发现了存在不匹配区域。DWI 病变体积占不匹配体积中位百分比为 23.5%，接近于临床试验治疗的纳入标准[8]。对于缺乏 PWI/DWI 不匹配的患者仍可发生梗死体积的扩大，以往这一问题困惑着众多学者。“隐性不匹配”概念的提出，对该现象提供了解释。尽管我们的研究数据显示，存在隐性不匹配区域的患者中发生梗死体积扩大的患者只占一小部分，但我们也同时发现，绝大部分隐性不匹配区域的组织可以被挽救，其比率达到77.7%。

体积相减方法的有效性依赖于传统的缺血半暗带的假设理论，在缺血半暗带中，梗死中心被半暗带包围，梗死体积的扩大区域应与半暗带一致[8]。然而，这是对卒中动态病程的静态时间点描述。多种因素均可影响缺血半暗带组织的转归，如侧枝循
环的等级[9]，自发血管再通及再灌注的几率和解剖部位的多样化表现、不同组织对缺血的耐受程度等 [10]。在不同部位和不同时点，这些因素的动态交互作用使得缺血半暗带具有特异和不可预测的结局。此外，神经影像，如 MR 灌注影像，仅仅反映了动态病程中一个单独静态时间点的情况，其对缺血半暗带的代表程度非常有限。尽管如此，这些动态病程中单一时间点的影像仍表明了 DWI 和 PWI 病变部位关系的重要性。

以传统的模式来讲，我们都希望 DWI 和 PWI 体积吻合。然而，二者体积吻合的中位比率仅为 44.1%(IQR, 10.6%-66.9%)。DWI 和 PWI 病变体积重叠的越少，传统半暗带理论的有效性就越小，组织相减方法的准确性就越小。这一结论也可以从下述的结果中得到说明。依据体积相减方法的测量结果，将患者分为缺乏和存在不匹配体积两组，与存在不匹配体积组的患者相比，缺乏不匹配体积组者的 DWI 和 PWI 重叠比率更小，尽管差别尚无统计学意义 (P=0.123)，但两组间的重叠体积差别有统计学意义 (P<0.007)。此外，DWI 病变区域可能包含有可挽救的组织[11]，部分甚至全部 DWI 病变部位可以得到逆转[12]。随着 DWI 病变区域得到再灌注，在图形学上相应的 PWI 病变区域亦将恢复正常灌注，此时使用体积相减方法进行不匹配体积测量，将相当于“减去双倍”的 DWI 病变区域，从而低估了不匹配区域的体积。通过更大样本的队列研究数据 (本研究数据库的扩展) 结果显示，体积相减方法大约低估了 30% 的不匹配体积，并且这一差别将随着时间推移而更加明显，这一结果可能对判断受多因素影响的难以预测的缺血半暗带转归有所贡献[5]。

在临床神经影像研究中，PWI/DWI 比例大于 1.2 表示存在明显的不匹配区域[2]。本研究结果显示，体积相减方法测量缺乏不匹配区域的 11 例患者中，应用影像配准方法可发现有 6 例患者存在≥20% 的不匹配体积比率。有学者认为，这些患者存在较大的潜在可挽救组织，因此，应该将此部分患者列为可治疗范围[3]。然而，需要指出的是，这些患者的不匹配体积相对较小。与存在不匹配体积组的患者相比，缺乏不匹配体积的患者具有更大的基线 DWI 病变体积和更小的基线 PWI 病变体积，这也部分说明了传统的半暗带理论的不合理。如此也可以解释，与存在不匹配体积组患者相比，缺乏不匹配体积组患者具有较低的不匹配体积百分比 (21.7%: 615.1%)。尽管存在这些差异，两组间出血组织的挽救率相当，表明了“隐性不匹配”区域的组织仍然可以得到挽救。

如果梗死体积的扩大仅发生在缺血半暗带区域，那么扩大的梗死体积应绝对不能超过缺血半暗带的体积。如表 1 所示，有 5 例患者扩大的梗死体积超过了体积相减法测量的不匹配体积。然而，影像配准方法测量的不匹配体积均大于扩大的梗死体积，这也解释了上述梗死体积扩大的原因所在。重要的事，这些不匹配区域的部分组织可以自行恢复。正如我们所预期的结果，影像配准方法测量的不匹配体积均远远大于扩大的梗死体积。图 1-4 显示了两个患者的情况，用体积相减方法未发现患者 1 存在不匹配体积，而在发病 3 个月检查的 MR 显示发生了梗死体积的扩大 (6.5 mL, 图 4)。该患者梗死体积的扩大可以用影像配准方法测出的不匹配体积来解释 (13.8 mL)。患者 2 体积相减法测出的不匹配体积 (30.2 mL) 小于梗死体积的增大 (41.6 mL)，用影像配准方法测出的不匹配体积同样可以很清楚地解释梗死体积扩大的原因。仅有少数研究同时比较分析了存在和缺乏不匹配体积的患者情况。River 等[2]采用脑血流的平方作为 PWI 的参数，对 46 例发病在 24 h 内的缺血性卒中患者采用体积相减方法进行了研究分析，结果发现有 21 例患者缺乏不匹配体积 (PWI<DWI)，其中 11 例患者出现了梗死体积扩大 (最终 T2>DWI)，并发现梗死体积扩大与是否存在 PWI/DWI 不匹配区域无明显相关，因此得出了缺乏匹配体积的患者也可能从治疗中获益的结论[3]。这些患者极有可能存在着“隐性不匹配”区域，如应用影像配准方法测量可得以明确。对 11 个影像研究进行的综合分析，也得出了类似的结论[4]。近期两项关于急性缺血性卒中不匹配体积的干预性研究也表明，缺乏不匹配体积的患者可以发生梗死体积的扩大[13]。阿替普酶可以减少梗死体积扩大[2]。平面回波溶栓评价研究 (The Echoplanar Imaging thrombolytic evaluation Trial, EPITHET) 的纳入标准为 PWI/DWI>1.2，PWI 减去 DWI 体积大于 10 mL[2]。根据这个标准，在 91 例患者中，有 11 例患者缺乏不匹配体积。如应用影像配准方法，这 11 例患者可能有部分将发现不匹配体积，因为该研究的 DWI 病变体积中位数 (18-21.0 mL；本研究 7.2 mL) 和 PWI 病变体积中位数较大 (146-192.0 mL；本研究 31.6 mL)。目前正在应用影像配准方法对 EPITHET 研究的数据进行重新分析。去氨普酶对急性脑卒中作用研究 (Desmoteplase in Acute Ischemic Stroke, DAS2) 的纳入标准为 PWI/DWI>1.2，这样可能存在临床意义上
的缺血半暗带[14]。基于这个入选标准，359例患者有96例被排除，这些患者的中位DWI体积(17-21mL)和中位不匹配体积(83-87mL：本研究33mL)均大于我们研究的结果。因此，在这96例患者中，如使用影像配准方法测量可能将发现部分患者存在着不匹配体积。这两项研究的主要结论均是阴性，如研究使用影像配准方法，可能会得到不同的结果。本研究存在许多不足之处。首先，34例患者的样本例数相对较少，我们希望本研究结论能够在更大的样本量中得到证实。其次，与之前的研究[15]相比，本研究的DWI和T2病变体积的中位数均偏小，但仍需进一步研究。需着重指出的是，本研究是一项大样本研究的子课题，包括了发病34例患者的样本。如使用影像配准方法测量可能将发现部分患者存在不匹配区域。在应用影像配准方法检测时发现其存在不匹配区域。

结论
综上，本研究显示，对于应用体积相减方法检测缺乏PW/DWI不匹配区域的患者，通过更准确的影像配准方法，可以发现“隐性不匹配”区域。而“隐性不匹配”区域的发现可以解释这些患者发生梗死体积扩大的原因。

参考文献