Cerebral Blood Flow and Blood Volume Measured by Magnetic Resonance Imaging Bolus Tracking After Acute Stroke in Pigs

Comparison With $[^{15}\text{O}]\text{H}_2\text{O}$ Positron Emission Tomography

Masaharu Sakoh, MD, PhD; Lisbeth Røhl, MD; Carsten Gyldensted, MD, PhD; Albert Gjedde, MD, PhD; Leif Østergaard, MD, PhD

Background and Purpose—Early and accurate assessments of cerebral ischemia allow therapy to be tailored to individual stroke patients. We examined the feasibility of using a novel method for measuring cerebral blood flow (CBF) of ischemic tissue based on MRI after middle cerebral artery occlusion (MCAO). Moreover, the regional correlations between CBF and cerebral blood volume (CBV) were investigated in the regions with acute ischemic stroke.

Methods—CBF and CBV were measured before and after MCAO or reperfusion by positron emission tomography (PET) in 13 pigs. Just after the PET scans, CBF and CBV were measured by MR bolus tracking and were compared with results obtained by PET at 6 hours after permanent MCAO or reperfusion. The infarction was verified histologically.

Results—The MR method yielded parametric CBF and CBV maps with tissue contrast in good agreement with parametric PET images, which demonstrated hypoperfused and hyperperfused areas after MCAO or reperfusion. Both MRI and PET technology showed that CBF values below 60% of the contralateral value induced a reduction of CBV, which committed the tissue to infarction.

Conclusions—The novel MR method provides accurate measurement of CBF and CBV in acute stroke and hence gives useful information for planning the appropriate therapeutic intervention. (Stroke. 2000;31:1958-1964.)

Key Words: cerebral blood flow ■ magnetic resonance imaging ■ stroke, acute ■ tomography, emission computed ■ pigs

Rapid MRI of the passage of a bolus of magnetic susceptibility contrast agent has recently become an important tool for assessing regional cerebral blood flow (CBF) and cerebral blood volume (CBV). In fact, absolute CBF values have been determined by means of MRI with introduction of an empirical normalization constant in animals and humans. Thus, this technique has gained widespread acceptance in the evaluation of hemodynamic changes in cerebral pathologies, especially stroke, migraine, and central nervous system tumors. For theoretical reasons, however, it is unknown whether this approach provides reliable measurements in the presence of pathological hemodynamics.

In this study, we measured CBF and CBV using both positron emission tomography (PET) and dynamic susceptibility contrast (DSC)-MRI in combination with a newly developed technique for middle cerebral artery occlusion (MCAO) and reperfusion in pigs. The objective of this study was to determine whether rapid DSC-MRI could accurately measure relative CBF and CBV even in the presence of pathological hemodynamics. Moreover, we examined the regional correlations between CBF and CBV in the regions with acute ischemic stroke.

Materials and Methods

Theory

**MRI CBF Measurement**

The following equation, introduced in detail by Østergaard and coworkers, was used to determine relative CBF by DSC-MRI of nondiffusible tracer bolus passage. In brief, the concentration $C_{\text{VOI}}(t)$ of an intravascular contrast agent within a given volume of interest (VOI) can be expressed as a function of time (t):

$$C_{\text{VOI}}(t) = F \cdot \int_0^t C(I)R(t-\tau)\,d\tau$$

where $C(I)$ is the arterial input, $F$ is tissue blood flow, and $R(t)$ is the vascular residue function. By treating the residue function as an unknown variable, this approach circumvents the problems of using intravascular tracers for CBF measurements pointed out by Lassen.
and Weisskoff et al.\textsuperscript{11} R(t) and CBF can be determined with reasonable accuracy, independently of the underlying vascular structure and volume, and with raw image signal-to-noise ratios equivalent to those obtainable in current clinical MRI protocols that use singular value decomposition.\textsuperscript{1,2}

**PET CBF Measurement**

The regional uptake of a diffusible tracer is described by the equation introduced by Ohta et al.\textsuperscript{15}:

\[
C_{\text{voi}}(t) = K_1 \int_0^1 C(r)e^{-k_1t-r}dr + V_p C_e(t)
\]

where, by assumption, \(K_1=\text{CBF for freely diffusible tracers and} k_0=K/V_r\), where \(V_r\) is the partition volume of the tracer. \(V_p\) is the vascular volume for the tracer in the tissue.

**Animal Preparation and Experimental Protocol**

The research project was approved by the Danish National Committee for Animal Research Ethics (DanCARE). Three female country-bred Yorkshire pigs weighing 38 to 45 kg each were divided into the following 2 groups: (1) permanent MCAO (n = 8) and (2) reperfusion after 2-hour MCAO (n = 5). They had free access to water but were deprived of food for 24 hours before the experiment. Pigs were initially sedated by intramuscular injection of 20 mL of midazolam (5 mg/mL). After intravenous injection of a mixture of fentanyl 1 mg, midazolam 50 mg, and pancuronium 4 mg, the pig was intubated and artificially ventilated (Engstrom Ventilator) with a 70% N\textsubscript{2}O-30% O\textsubscript{2} mixture. Anesthesia was maintained by continuous infusion of fentanyl 0.1 mg · kg\textsuperscript{-1} · h\textsuperscript{-1}, midazolam 1.25 mg · kg\textsuperscript{-1} · h\textsuperscript{-1}, and pancuronium bromide 0.2 mg · kg\textsuperscript{-1} · h\textsuperscript{-1} for the first 3 hours during which surgery was performed. Thereafter, fentanyl 0.05 mg · kg\textsuperscript{-1} · h\textsuperscript{-1}, midazolam 1.25 mg · kg\textsuperscript{-1} · h\textsuperscript{-1}, and pancuronium bromide 0.2 mg · kg\textsuperscript{-1} · h\textsuperscript{-1} were used. Indwelling femoral venous and arterial catheters were installed surgically for injection of tracers and arterial blood sampling. Isotonic saline (\(=100\) mL/h) was administered intravenously throughout the experiments. Rectal temperature was kept at 38°C by means of a thermostatically controlled heating blanket.

Focal cerebral ischemia was transorbitally induced by occlusion of the left proximal middle cerebral arteries (MCAs), generally consisting of 2 arteries, and the distal internal carotid artery (ICA). Bipolar coagulation or Sugita microclip (Mizuho; blade length 2 to 4 mm, blade width 0.8 mm, holding force 65 to 70 g) was used to induce permanent MCAO or transient MCAO, respectively. Reperfusion was accomplished by microsurgical removal of the microclips 2 hours after MCAO. The dura was closed with Neuro-Patch (Braun) and fibrin glue (Floseal; Baxter) to avoid leakage of cerebrospinal fluid. The cavity of the orbit was filled with isotonic saline and gauze to avoid susceptibility artifacts in DSC-MRI.

PET studies were performed before and 1 and 6 hours after permanent MCAO. In the reperfusion experiments, PET studies were done before and 1 hour after MCAO, as well as 1 and 6 hours after reperfusion. CBF and CBV were measured in 13 and 9 (ie, 4 for permanent MCAO and 5 for reperfusion) pigs at each time, respectively. Just after the PET scans, relative CBF, CBV, and mean transit time (MTT) with DSC-MRI were measured in the pigs placed in the MCAO scanner, ie, 7 hours after permanent MCAO or reperfusion; the elapsed time between PET and MRI was 1 hour. Then, digital subtraction angiography (DSA) was performed via a femoral catheter that was placed in an ascending pharyngeal artery (corresponding to the distal part of the ICA in humans) near the origin of the rete mirabile to verify the occlusion of the MCA after permanent MCAO and the patency of the MCA after reperfusion. At the end of the experiment, usually 10 to 12 hours after MCAO, histological examination was performed to verify the infarction.

Throughout the experiments, body temperature, blood pressure, heart rate, and expired-air carbon dioxide (CO\textsubscript{2}) levels were monitored continuously, and arterial blood samples were withdrawn and analyzed (ABL 300, Radiometer) every hour to monitor blood gases and whole-blood acid-base parameters. Disturbances in body fluid balance were corrected by appropriate procedures (eg, forced ventilation and/or changes in infusion rates) to maintain physiological parameters within the normal range.

**Positron Emission Tomography**

The pigs were positioned supine in the scanner (Siemens/CTI ECAT EXACT HR) with the head in a custom-made headholder. CBF was estimated by intravenous bolus injection of 800 MBq [\textsuperscript{15}O]H\textsubscript{2}O. Sequences of 21 (12, 6, and 3 samples during the first, second, and third minute, respectively) arterial blood samples and 12 (6, 4, and 2 images per minute, respectively) PET brain images were then obtained. CBV was measured by a single-breath inhalation (1 L) of 1200 MBq [\textsuperscript{15}O]CO, followed by 10-second breath-holding. For all experiments, total radioactivity in blood samples was measured. Brain image and arterial data were corrected for the half-life of [\textsuperscript{15}O]CO (123 seconds). PET image data were reconstructed for 3D images with 2D data acquisition mode, providing 47 contiguous 3.2-mm slices using a Hanning filter with a cutoff frequency of 0.5 pixel\textsuperscript{-1}, resulting in a spatial resolution of 4.6 mm full width at half maximum (FWHM).\textsuperscript{14} Correction for attenuation was made on the basis of a transmission scan.

Raw PET images were applied to the 3×3 uniform smoothing kernel. Then, the [\textsuperscript{15}O] water data were fitted to Equation 2 by nonlinear, least squares regression analysis of each image voxel. CBV was determined by the ratio of cerebral and arterial whole blood [\textsuperscript{15}O]CO levels after initial distribution (30 seconds) of the tracer.

**Magnetic Resonance Imaging**

The pigs were positioned supine in the scanner with the head in a custom-made whole-body holder. Imaging was performed with a GE Signa Horizon 1.0T Imager (GE Medical Systems). After a sagittal scout, an axial T1-weighted 3D gradient-echo sequence (time of repetition [TR] 8 ms, time of echo [TE] 1.5 ms, 20° flip angle) was acquired for later coregistration of MRI and PET data. Then, a T2-weighted fast-spin-echo sequence was obtained with TR/TE of 4000/105 ms. For dynamic imaging of bolus passages, gradient-echo planar imaging (EPI) (TR/TE=1500/45 ms) was performed, starting 15 seconds before injection. A 64×64 acquisition matrix was used with a 14×14-cm axial field of view, leading to an in-plane resolution of 2.2×2.2 mm\textsuperscript{2}, with a slice thickness of 5 mm and an inter slice gap of 2 mm. Six slices were obtained. In all experiments, bolus injection of gadodiamide (0.1 mmol/kg; OMNISCAN, Nycomed Imaging) was performed at a rate of 10 mL/s.

We used susceptibility contrast arising from compartmentalization of the paramagnetic contrast agent\textsuperscript{14} for determining tissue and arterial tracer levels. We assumed a linear relation\textsuperscript{11} between paramagnetic contrast agent concentration and the change in transverse relaxation rate, \(\Delta R_2\), for determining tissue and arterial tracer time concentration curves C(t) according to the equation

\[
C(t)/\Delta R_2(t) = -\log \frac{S(t)}{S(0)} \Bigg/ \text{TE}
\]

where \(S(0)\) and \(S(t)\) are the signal intensities at baseline and time t, respectively. TE is the echo time. We assumed \(T_1\) to be unaltered during the bolus injection. This equation does not provide absolute concentrations. The arterial concentration was determined in each animal from 3 to 4 pixels containing the MCA showing an early and large \(\Delta R_2\) (3 to 10 times that of gray and white matter) after contrast injection.\textsuperscript{15} The integrated area of the arterial input curve was in each measurement normalized to the injected contrast dose (in millimoles per kilogram of body weight) for comparisons within and among animals.\textsuperscript{3}

To determine CBF from Equation 1, the deconvolution was performed over the range of measurements, where the arterial input values exceeded the noise level (usually ~15 seconds). Deconvolution followed smoothing of raw image data by a 3×3 uniform smoothing kernel. The maximum of the deconvolved response curve was assumed to be proportional to CBF. CBV was determined by...
Table 1. General Physiological Variables Before and After MCAO or Reperfusion (Mean±SD)

<table>
<thead>
<tr>
<th></th>
<th>MABP, mm Hg</th>
<th>pH</th>
<th>PaCO₂, kPa</th>
<th>PaO₂, kPa</th>
<th>Hgb, mmol/L</th>
<th>P₇.₅₆, mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (n=13)</td>
<td>103±3</td>
<td>7.48±0.04</td>
<td>5.16±0.10</td>
<td>17.8±1.9</td>
<td>6.1±0.6</td>
<td>4.9±0.6</td>
</tr>
<tr>
<td>MCAO (n=8)</td>
<td>100±8</td>
<td>7.44±0.03</td>
<td>5.13±0.14</td>
<td>17.6±2.7</td>
<td>6.0±0.8</td>
<td>6.1±0.7*</td>
</tr>
<tr>
<td>Reperfusion (n=5)</td>
<td>99±24</td>
<td>7.49±0.06</td>
<td>5.14±0.16</td>
<td>18.4±3.2</td>
<td>5.4±0.4</td>
<td>6.0±1.0</td>
</tr>
</tbody>
</table>

MABP indicates mean arterial blood pressure; pH, arterial blood pH; Hgb, arterial hemoglobin concentration; and P₇.₅₆, plasma glucose concentration.

*Significantly different from baseline value (P<0.05, ANOVA).

Data Analysis

Statistical analysis was performed by 1-way repeated-measures ANOVA to determine whether physiological parameters and/or absolute values for CBF and CBV measured by PET differed significantly with time. A P value of 0.05 was used for statistical significance throughout this report. Pixel maps of CBF and CBV (at similar anatomic locations) generated with PET and MRI were compared on a regional basis for the ischemic regions. For the assessment of correlation between DSC-MRI and PET parameter values, Spearman’s test was used. Linear least squares regression analysis was performed with the ratio of each variable for the ischemic regions in relation to the contralateral value to determine the slope and y intercept of the fit. The statistical significance of the difference between slopes estimated by linear regression was determined by Student’s t test. Moreover, differences between coefficients of correlation after MCAO and reperfusion were measured for CBF and CBV.

Results

General Physiological Variables

All general physiological variables were in the normal range under baseline conditions (Table 1). Most variables remained stable and did not significantly differ before and 6 hours after permanent MCAO or reperfusion, although plasma glucose concentration increased 6 hours after permanent MCAO. In addition, physiological variables did not differ between PET and MRI studies.

Angiographic and Pathohistological Study

After permanent MCAO, the MCAs of 8 pigs angiographically showed complete occlusion. The infarction was verified histologically in 7 of 8 brains. Six of these 7 brains had infarction that included both the ischemic core and the ischemic cortex, but 1 brain had infarction only in the ischemic core. One brain had no infarction because of the collateral flow supplied from the anterior cerebral artery, despite complete occlusion of the MCA.

Reperfusion 2 hours after MCAO was found angiographically to have provided for complete recanalization of the MCA in 5 pigs. Four of the 5 brains had an infarction. Three of these 4 brains showed that the infarction included both the ischemic core and the ischemic cortex, but 1 brain had infarction only in the ischemic core. One brain had no infarction.

PET Study

The absolute values of CBF and CBV were divided into 2 groups on the basis of the tissue damage, ie, infarction or noninfarction in the ischemic core and the ischemic cortex, as shown in Table 2. MCAO induced a significant reduction of CBF in the ischemic core and cortex as soon as 1 hour after occlusion, whereas CBV was significantly decreased in the
TABLE 2. CBF and CBV Values in the Ischemic Core and Cortex (mean±SD)

<table>
<thead>
<tr>
<th></th>
<th>CBF, mL · 100 g⁻¹ · min⁻¹</th>
<th>Core</th>
<th>Cortex</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Infarction (n)</td>
<td>Noninfarction (n)</td>
<td>Infarction (n)</td>
</tr>
<tr>
<td>Baseline (n=13)</td>
<td>...</td>
<td>38.1±1.2 (13)</td>
<td>...</td>
</tr>
<tr>
<td>1-h MCAO (n=13)</td>
<td>14.5±8.6* (11)</td>
<td>31.5±0.7 (2)</td>
<td>19.8±8.5* (8)</td>
</tr>
<tr>
<td>6-h MCAO (n=8)</td>
<td>11.8±8.6* (7)</td>
<td>31.2 (1)</td>
<td>12.8±9.5* (6)</td>
</tr>
<tr>
<td>1-h Reperfusion (n=5)</td>
<td>62.5±19.7* (4)</td>
<td>37.4 (1)</td>
<td>51.7±11.1 (3)</td>
</tr>
<tr>
<td>5-h Reperfusion (n=5)</td>
<td>40.8±12.6 (4)</td>
<td>41.3 (1)</td>
<td>43.0±17.1 (3)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CBV, mL/100 g</th>
<th>Core</th>
<th>Cortex</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Infarction (n)</td>
<td>Noninfarction (n)</td>
</tr>
<tr>
<td>Baseline (n=9)</td>
<td>...</td>
<td>2.69±0.17 (9)</td>
</tr>
<tr>
<td>1-h MCAO (n=9)</td>
<td>2.44±0.61 (8)</td>
<td>3.30 (1)</td>
</tr>
<tr>
<td>6-h MCAO (n=4)</td>
<td>1.54±0.71* (4)</td>
<td>...</td>
</tr>
<tr>
<td>1-h Reperfusion (n=5)</td>
<td>2.75±0.16 (4)</td>
<td>3.03 (1)</td>
</tr>
<tr>
<td>5-h Reperfusion (n=5)</td>
<td>3.11±0.15 (4)</td>
<td>3.20 (1)</td>
</tr>
</tbody>
</table>

*Significantly different from baseline values (P<0.05, ANOVA).

Infarcted ischemic core and cortex only at 6 hours after MCAO. During the MCAO, the ischemic regions with CBV values above the baseline were spared from infarction. Reperfusion 2 hours after MCAO restored CBF and CBV to normal levels after an initial excessive rise in CBF, whereas the saved tissue due to the reperfusion did not show the excessive rise in CBF (Table 2).

MRI Study
Relative CBF, CBV, and MTT maps obtained by DSC-MRI and T2-weighted MRI after MCAO or reperfusion are shown in Figure 2. It is evident that CBF mapping by DSC-MRI was closely correlated to CBF images obtained by PET, even in terms of the different level and volume of ischemia or hyperperfusion. MTT clearly showed a hemodynamic compromise, particularly on mild ischemia, in which CBF and CBV were not completely proportional as MTT=CBV/CBF. T2-weighted imaging showed an obvious tissue injury 7 hours after reperfusion in all 4 pigs with infarction (corresponding to 9 hours after MCAO) in relation to the severity of ischemia, whereas the tissue injury was not yet obvious on T2-weighted images even at 7 hours after permanent MCAO despite the severity of ischemia shown in Figure 2.

Regional Correlation Between MRI and PET of CBF and CBV Measurement
The regional correlations of CBF and CBV measured by DSC-MRI and PET are illustrated in Figures 3A and 3B. The values obtained by DSC-MRI for CBF and CBV were significantly correlated to those obtained by PET during both permanent MCAO and reperfusion (CBF: r²=0.96, P<0.01, df=38; CBV: r²=0.85, P<0.01, df=30). For CBV, however, DSC-MRI detected values lower than PET, especially in severely ischemic territory.

Regional Correlation Between CBF and CBV With PET and MRI
The regional correlations between CBF and CBV obtained by PET are illustrated in Figure 4A. The regional estimates of CBF and CBV were significantly correlated after MCAO (pooled data for 1 and 6 hours: r²=0.89, P<0.01, df=38). In contrast, after reperfusion, CBF was less well related to CBV (r²=0.33, P<0.05, df=14). The correlations between CBF and CBV differed significantly between permanent MCAO and reperfusion (r=3.49, P<0.001), and pairwise comparison of the slope showed a significant difference (t=2.21, P<0.05, df=41). After MCAO, CBV remained above the contralateral value until CBF fell to <70% of the contralateral level. On the other hand, CBF values below 60% of the contralateral value were accompanied by a linear decline in CBV. The reduction of CBV was greater 6 hours after permanent MCAO (r²=0.93, P<0.01, df=11) than 1 hour after MCAO (r²=0.89, P<0.01, df=26), especially in se-
The regional correlations between relative CBF and CBV obtained by DSC-MRI are illustrated in Figure 4B. The estimates were significantly correlated 7 hours after MCAO ($r^2 = 0.91, P < 0.01, df = 23$), whereas after reperfusion, relative CBF was less well related to CBV ($r^2 = 0.35, P < 0.05, df = 14$); the correlations between CBF and CBV differed significantly between permanent MCAO and reperfusion ($z = 3.26, P < 0.001$). DSC-MRI also showed that relative CBV increased at relative CBF values above 70% of the contralateral value 7 hours after MCAO, whereas relative CBV decreased at CBF values below 60% of the contralateral value.

Discussion

The extent of the time window for therapy of acute ischemic stroke depends on the magnitude of residual flow and varies from person to person.7,17–20 Thus, a diagnostic procedure that assesses the magnitude of residual flow allows therapy as a function of time to be tailored to individual patients with acute ischemic stroke. PET has enabled researchers to follow the dynamics of cerebral blood flow and metabolism leading to infarction after stroke, but the technology is of limited use in clinical practice and frequently not available in acute situations.19,21–24 On the other hand, recent results by Østergaard et al1,2,5,6 indicate that DSC-MRI can be used to measure relative and absolute CBF rates in the intact brain of humans or animals. In clinical practice, CBF measurements with MRI, feasible in combination with pathophysiological tomography such as diffusion-weighted imaging, would be of great benefit to patients with acute ischemic stroke.7 Therefore, it is important to know whether abnormal hemodynamics disrupt the reliability of MRI measurements.

Comparison Between DSC-MRI and PET

In the present study, the relative CBF and CBV values obtained with DSC-MRI were in good agreement with the results of PET in the regions that were ischemic after MCAO. Moreover, with the same degree of accuracy as PET, DSC-MRI documented that the hemodynamic abnormalities of acute stroke included changes in both CBF and CBV. Hence, the present results show that cerebral ischemia can be reliably detected and characterized with DSC-MRI, as proposed by previous reports.7,25 This MRI technique for acute ischemic stroke could be improved with more mathematical work, because the technique has far higher resolution and less noise than the PET technique.5

Variability of Cerebral Ischemia: Relation Between CBF and CBV

Classically, the phase of autoregulation in response to decreasing perfusion pressure is characterized by rising CBV at constant CBF, but when maximum vasodilation occurs, CBF falls while CBV remains constant. Gibbs et al21 showed that the ratio CBF/CBV (ie, the reciprocal of the expression for MTT) was an index of diminishing cerebral perfusion pressure and hence residual perfusion reserve.
In the present study, DSC-MRI clearly demonstrated the variability of cerebral ischemia after MCAO, as shown in Figure 1. Especially in the regions with mild ischemia (CBF >30 mL/min/100 g), the MTT maps displayed the compensatory vasodilation in response to the reduced perfusion pressure and hence were highly indicative of a flow-volume mismatch. In the regions with severe ischemia (CBF <30 mL/min/100 g), the MTT maps showed an area at risk that leads to infarction; CBV declined in linear proportion to the reduction of CBF. The CBF thresholds for the reduction of CBV increased with time in acute ischemic regions, in agreement with the findings of Kolhno et al.26 that the CBV thresholds for diffusion abnormality increased with time. Thus, the CBV maps could be a useful predictive tool for the viability of ischemic tissue, because the ischemic regions with decreased CBV proceeded to infarction in the present study, and moreover, a reliable correlation was demonstrated between the lesion volume of diffusion-weighted imaging and the CBV map.7

On the other hand, in the regions with reperfusion, MTT was reduced or normal, although both CBF and CBV were increased. Interestingly, CBV and CBF were uncoupled, indicative of a potentially harmful vasoparalysis. T2-weighted MRI at this time often showed infarction. Hence, the ischemic tissue should be carefully assessed in combination with DSC-MRI to avoid attempts to recanalize vessels supplying spontaneously reperfused tissue. The determination of such variability would allow optimum therapy to be tailored to individual patients with acute stroke. For example, one testable hypothesis suggested by these data is that patients with a severe decrease of CBV (or CBF) would not benefit from thrombolytic therapy, whereas patients with an increase of CBV (or mild reduction of CBF) could benefit from thrombolytic therapy during the occlusion.

Limitations in DSC-MRI

Delays in arrival of contrast agent may be interpreted as a CBF decrease, and therefore collateral flow may not be represented adequately.2,6 In the present study, the region supplied previously by the MCAs was perfused via the collateral flow from the anterior cerebral artery because the MCAs were completely occluded, as shown by angiography. However, DSC-MRI gave the same CBF result as PET, although more mathematical work could improve this technique for ongoing use in the evaluation of patients with acute ischemia, in whom tracer arrival delays may be more severe. In contrast, CBV values obtained by DSC-MRI were underestimated, possibly because the tissue concentration time curve may be delayed and dispersed and difficult to distinguish from the second pass. Thus, the area could be underestimated by our numerical integration routine. This effect affects the PET CBV measurements less, because signals are recorded over 3 minutes, allowing for slow tracer passage. The underestimate of CBV may have caused MTT, ie, the CBV/CBF ratio, to be underestimated by the same amount in the infarcted regions.

Another limitation with this technique is that all intravascular tracer methods require delivery of the tracer to the region of measurement. This limitation also applies to PET, of course. Thus, true CBF and CBV values may be larger than recorded simply because no tracer is reaching dilated but nonperfused blood vessels. However, the present study consistently identified the flow-volume mismatches, although the shortcoming could mask greater mismatches.

Acknowledgments

This study was funded by Danish Medical Research Council grants (9305246, 9305247, 9601888, and 9802833) and the Institute of Experimental Clinical Research, University of Aarhus, Denmark. The authors thank Nycomed Imaging (Oslo, Norway) for providing the contrast agent for this study. We thank Dr Donald F. Smith (Aarhus, Denmark) for his contributions to the improvement of the manuscript, Dr Jens Christian Sorensen (Aarhus, Denmark) for the histological preparations, and the technicians of the PET and MRI centers for their skilful assistance. We are grateful for the helpful contribution and support of Professor Saburo Sakaki (Ehime, Japan) during this project.

References

Techniques that can provide fast and accurate measurements of cerebral blood flow (CBF) and blood volume (CBV) represent an important diagnostic tool for the evaluation of the acute stroke patient. They can yield information about the anatomic location and degree of cerebral ischemia and the success or failure of reperfusion, and they may be potentially useful for planning therapeutic interventions.

The early development of magnetic resonance methods to measure CBF and CBV utilized tracers that were labeled with MR-sensitive nuclei (eg, $^3$H, $^{17}$O, and $^{19}$F). More recently, there has been a flurry of activity to develop CBF and CBV measurement techniques that use high-speed MRI methods to track the passage of a bolus of a magnetic susceptibility contrast agent or magnetic labeling of protons in arterial blood with radiofrequency pulses. However, most of these studies have focused on the theoretical and methodological aspects of the measurements; there have been few that actually attempt to validate the accuracy of the technique by comparing MRI-based CBF and CBV measurements with a well-accepted “gold standard” method.

The study by Sakoh et al uses MRI to measure CBF and CBV in a novel model of middle cerebral artery occlusion and reperfusion in pigs. Measurements obtained by using dynamic susceptibility contrast (DSC)-MRI were evaluated and compared with similar measurements obtained with positron emission tomography (PET) methods to determine whether DSC-MRI could provide accurate measurements of CBF and CBV in stroke. The results demonstrate good agreement between parametric maps of CBF and CBV obtained using the 2 methods, with infarction demonstrated in brain regions having CBF values $<$60% of contralateral levels. Highly significant regional correlations were detected between DSC-MRI and PET measures of CBF, and to a slightly lesser degree CBV, with DSC-MRI showing lower CBV values than PET.

This study offers new and original information about the accuracy of DSC-MRI measurements of CBF and CBV in acute stroke. Although such studies performed with experimental animal models of cerebral ischemia may not exactly reproduce the conditions encountered in human stroke, they will provide an essential link toward the eventual goal of performing these measurements in the clinical setting.

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doi: 10.1161/01.STR.31.8.1958

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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