Effect of Intravenous Gadolinium-DTPA on Diffusion-Weighted Images
Evaluation of Normal Brain and Infarcts

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Background and Purpose—Diffusion-weighted imaging (DWI) is usually done before administration of intravenous contrast agents. Repetition of DWI is occasionally necessary after administration, but the effects of contrast material on DWI and apparent diffusion coefficient (ADC) values have not yet been fully examined. The present study assesses whether administration of gadolinium-based contrast material significantly affects DWI and ADC values.

Methods—We examined DWI data from 39 patients (mean age, 67.9 years; range, 34 to 87 years) who were evaluated with a stroke protocol at our institute. All patients were scanned at the acute or subacute stages of infarct from 3 hours to 5 days after symptom onset. We obtained DWI images using single-shot echo-planar imaging with a $b$ value of 1000 s/mm$^2$. Patients were injected with 0.1 mmol gadopentetate dimeglumine per 1 kg body weight. We examined the signal-to-noise ratio of the normal brain and the infarct and evaluated the contrast-to-noise ratio of each lesion. In addition, we compared the ADC values calculated from the DWI images before and after administration of contrast. The statistical significance of differences between precontrast and postcontrast administration was determined by use of a paired $t$ test.

Results—The signal-to-noise and contrast-to-noise ratios of the DW images were not significantly different before and after administration of contrast agent. The ADC values were slightly lower after administration of contrast agent for both normal brain ($P=0.0011$) and infarcts ($P=0.038$). The estimated differences in the ADC values were $\approx 1.3\%$ and $3.5\%$ for normal brain and infarcts, respectively.

Conclusions—The lack of a significant difference between the signal-to-noise and contrast-to-noise ratios of DW images before and after administration of contrast agent indicates the feasibility of postcontrast DWI. (Stroke. 2002;33:1799-1802.)

Key Words: brain injuries gadolinium DTPA infarcts magnetic resonance imaging perfusion

Diffusion-weighted imaging (DWI), which allows visualization of intravoxel incoherent motion of water molecules, has become indispensable in the evaluation of stroke patients.1-6 This technique uses echo-planar imaging (EPI) and thus is relatively resistant to motion. However, when bulk movement of the head occurs, the images are significantly degraded by ghost artifacts. In an acute clinical setting with limited time for imaging, DWI repetition may not be feasible before perfusion-weighted images are obtained because the perfusion-weighted imaging study could be compromised by prolonged imaging time.

Repeated DWI after administration of contrast material may also be necessary in circumstances other than motion. For example, when the results of the DWI are negative or equivocal, a further workup with a different DWI approach may be necessary. DWI taken from different slice orientations, at higher spatial resolution, at different $b$ values, or by multishot EPI may be able to detect or confirm the presence of lesions.

Despite the emerging clinical need to occasionally repeat DWI after perfusion-weighted imaging, to the best of our knowledge, the effect of contrast media on DWI or the measured apparent diffusion coefficient (ADC) has not been fully examined. The present study examines whether repeated DWI before and after administration of contrast produces comparable image quality.

We considered that contrast agent could affect DWI 2 ways. The ADC may decrease slightly because the contrast agent will decrease the intravascular signal intensity. This might lead to suppression of the perfusion effect on the
calculated ADC. Or, the T2-shortening effect of contrast may slightly decrease the signal intensity of both the $b=0$ and $b=1000$ s/mm$^2$ DWI images. The combination of these factors may alter the signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) of the brain lesions. If the SNR or CNR changes, the question of whether visualization of the brain infarcts increases or decreases arises. To address these issues, we assessed DWI images from patients who were evaluated according to the stroke protocol at our institute over a 6-month study period. Additional DWI images were acquired after dynamic susceptibility-contrast perfusion-weighted images were obtained from patients who seemed stable enough to undergo an additional imaging sequence. This procedure added only 2 minutes to the routine stroke study applied at our institute.

Materials and Methods

Patient Population
Prospective data were collected between December 15, 2000, and June 15, 2001. To be included, patients must have (1) presented at our institute with symptoms indicative of stroke, (2) followed the MR stroke protocol with perfusion-weighted imaging, (3) been sufficiently stable to tolerate a repeated DWI after the routine stroke protocol, and (4) refused aggressive treatment for brain infarction, including intraarterial thrombolytic therapy.

Imaging data from a total of 39 patients who fit the inclusion criteria were accepted for the study. The age of the patients ranged from 34 to 87 years (mean, 67.9 years). All patients were scanned at the acute or subacute stage of infarct, a period ranging from 3 hours to 5 days (mean, 2.3 days) after symptom onset. Written, informed consent was obtained from all patients or their next of kin.

Imaging Methods
Images were obtained with a whole-body, 1.5-T imager (Gyroscan Intera, Philips Medical Systems). The routine stroke protocol at our institute requires 14 minutes and consists of DWI, T1-weighted images (repetition time [TR] = 611 ms, echo time [TE] = 13 ms), T2-weighted images (TR = 4754 ms, TE = 100 ms), fluid level–attenuated inversion recovery images (delay time [TI] = 2200 ms, TR = 8000 ms, TE = 100 ms), T2*-weighted images (TR = 666 ms, TE = 23 ms), MR angiogram (TR = 30 ms, TE = 2.3 ms), and dynamic susceptibility-contrast perfusion imaging with single-shot spin-echo EPI (TR = 1500 ms, TE = 90 ms), followed by postcontrast T1-weighted images. We also added another DWI sequence after perfusion imaging. The DWI images were acquired with a single-shot EPI sequence with motion-probing gradients in 3 or 6 orthogonal directions. The DWI sequences had TR = 4000 ms, TE = 95 ms, and flip angle = 90°, with a $128 \times 77$ acquisition matrix in a 23×23-cm field of view. A $b$ value of 1000 s/mm$^2$ was used with averaging of 1 or 2 times. The DWI sequences scanned the entire brain with a slice thickness of 5 mm and interslice gaps of 1 mm. The amount of injected gadopentetate dimeglumine (Magnevist; Nihon Schering) was 0.1 mmol/kg body weight.

Image Analysis
SNRs and CNRs of the DWI images and T2-weighted EPIs and the ADC were calculated for both precontrast and postcontrast studies. SNR and CNR were calculated from the following equations: $\text{SNR} = S/\text{SD}_{\text{noise}}$ and $\text{CNR} = (S_{\text{infarct}} - S_{\text{normal}})/\text{SD}_{\text{noise}}$, where $S$ is signal intensity and $\text{SD}_{\text{noise}}$ is the SD of the background noise. To calculate ADC, 3 or 6 orthogonal ADC components were averaged to produce the apparent diffusion tensor trace. Data from normal tissues were taken from a slice through the centrum semiovale without overt infarction on DWI. Regions of interest were designated with an automated segmentation program to select out the cerebrospinal fluid in the sulci and ventricles.

Among the 39 patients studied, 2 had no lesions detectable by DWI, so a total of 37 brain lesions were available for analysis. Lesions with overt motion between the 2 scans ($n=3$) were excluded from the measurements. In addition, lesions <50 pixels ($\approx162$ mm$^2$; $n=2$) were excluded from the study because small lesions tend to be affected by partial volume averaging even when motion is minimal between the 2 scans. A total of 32 lesions were analyzed. All regions of interest were placed by a single operator (K.Y.).

Statistical Analysis
Differences between the 2 sets of data were assessed with Student’s paired 2-tailed $t$ test. A value of $P<0.05$ was considered significant.

Results
The imaging quality of all the MR studies was technically satisfactory, and significant artifacts resulting from Nyquist ghosts or susceptibility effects were absent. Visual inspection of the T2*-weighted images failed to reveal lesions with overt hemorrhage. We did not find any lesions with apparent enhancement on contrast-enhanced spin-echo T1-weighted images.

SNR and CNR of DWI
Figure 1A shows the SNRs of the DWIs for both normal brain and infarcted tissues. SNRs do not differ significantly between tissue with and without contrast administration. B, CNR for brain infarcts. No significant difference was noted between the 2 conditions. Horizontal bars through boxes indicate median values of data points. Error bars indicate 90th percentile of all observations.

Figure 1. SNR and CNR of DWI. A, SNR of DWI for normal and infarcted brain tissue. SNRs do not differ significantly between tissue with and without contrast administration. B, CNR for brain infarcts. No significant difference was noted between the 2 conditions. Horizontal bars through boxes indicate median values of data points. Error bars indicate 90th percentile of all observations.
SNR and CNR of T2-Weighted EPIs

Figure 2 shows the SNRs and CNRs of T2-weighted EPIs for normal brain and infarcts. The mean SNRs of precontrast and postcontrast T2-weighted images for normal brain tissue were 28.64 ± 8.53 and 28.29 ± 7.33, respectively. The SNRs of brain infarcts for the precontrast and postcontrast T2-weighted images were 47.38 ± 9.75 and 47.38 ± 9.13. The paired t test applied to the values before and after administration of contrast agent did not reveal a statistically significant difference between the 2 conditions (P = 0.44 and P = 0.99 for normal and diseased SNRs, respectively).

Figure 2B shows the CNR of the brain infarcts with and without contrast agent. The CNRs from infarcts at precontrast and postcontrast T2-weighted images were 19.11 ± 6.39 and 19.86 ± 6.47. Once again, the paired t test found no significant difference between the 2 conditions (P = 0.13).

ADC Values

Figure 3 shows the precontrast and postcontrast ADC values for both normal brain and infarcts. The mean precontrast and postcontrast ADC values from the normal brain were 779.44 ± 35.36 and 769.77 ± 35.17 mm²/s. The precontrast and postcontrast ADC values for infarcted tissue were 523.94 ± 100.05 and 505.33 ± 92.30 mm²/s. A paired t test comparing the values before and after administration of contrast agent revealed a significant difference between the 2 conditions for both normal brain (P = 0.0011) and infarcts (P = 0.038). The estimated differences between ADC for normal brain and infarcts were 1.3% and 3.5%, respectively.

Discussion

Our study represents the first systematic evaluation of the diagnostic value of DWI scans performed after gadolinium-based contrast media administration. The SNR and CNR from the DWI images taken before and after administration of contrast for both normal brain tissue and infarcted tissue were not significantly different. These data indicate that DWI can be repeated after gadolinium-enhanced MR studies. Therefore, when motion is detected on the initial DW scan or when repeated DWI images with different imaging techniques are needed, they can be performed after perfusion-weighted imaging without a significant change in the SNR or CNR of the brain lesions.

An important point derived from our data is the slight but statistically significant decrease in ADC after administration of contrast agent. The presumed mechanism for this decrease is the suppression of the intravascular contribution, namely the flow. The ADC reflects not only the diffusion coefficient of water molecules but also the physiological motion of the intravascular movement of saline. This perfusion factor may have a positive influence on the ADC, so that an increase in blood movement may result in a higher ADC. This perfusion factor has been the accepted explanation for the higher ADC value of brain tissue in vivo compared with in vitro, and it dominates the change in signal for DWI images taken at low b values (0 to 300 s/mm²).
Before this study, we conjectured that the intravascular contrast agent would result in a lower ADC value because of suppression of the signal from the perfusion. We also predicted that this reduction in ADC would be minimal because blood makes up only a small percentage of the volume of brain tissue. A few articles related to functional MR imaging have assessed the effect of intravascular contrast agent.13–16 Zhong et al15 found that administration of gadolinium-DTPA in humans (0.2 mmol/kg) reduces the ADC by 2.4%. Our results showed a 1.3% decrease in ADC with half the dose used by Zhong et al, which apparently agrees with their findings. Zhong et al also demonstrated a change in 1/T2 of \( \approx 1.3\% \). This minimal change may be responsible for our inability to detect a significant change in the signal of T2-weighted EPIs.

Whereas the perfusion factor for normal brain tissues should be constant from location to location, it may differ in areas with brain infarcts because the perfusion status may be different across the lesions. For instance, an infarct with oligemia may be less influenced by the perfusion factor, leading to a reduced change in ADC after administration of contrast. In contrast, the ADC of lesions with paradoxically high perfusion (luxury perfusion) may be more significantly changed. The higher variability in the ADC values from infarcts compared with normal tissue (as indicated by the large error bars in Figure 3) may be explained by the increased variation in the perfusion factor. We did not perform exploratory subgroup analysis that might have detected a difference between lesions with oligemia and hyperemia because the number of lesions in our study was limited. Further study using a larger population should shed light on this hypothesis.

The findings reported here should be viewed in the context of several methodological limitations. First, the number of the samples was small, which may explain why we did not detect significant differences on DWI or T2-weighted images between precontrast and postcontrast conditions. In particular, from the results of Zhong et al,15 we anticipated a decrease in the signal of T2-weighted images by \( \approx 1\% \), but it was not realized. Second, this study focused on the DWI of infarcts at the acute and subacute stages because these groups of patients tend to have a limited amount of time available for the imaging study. Because there would be no significant blood-brain barrier breakdown at the acute or subacute stage of disease, our data cannot be directly extrapolated to chronic lesions, in which blood-brain barrier breakdown may be significant. What might happen to patients with blood-brain barrier breakdown is difficult to predict because the changes would be a combination of perfusion term and tissue concentration of leaked contrast agent. Further study may be needed to clarify this issue. Third, the slice locations for the 2 DWI sequences may not have been perfectly matched. Care was taken to avoid the possibility of misregistration by eliminating those lesions for which motion was suspected between the precontrast and postcontrast DWI. Even then, the effect of misregistration may not be completely avoided.

Conclusions
DWI images can be acquired after administration of contrast agent without compromising the SNR of normal brain or the CNR of brain infarcts. The slight change in the ADC value that we reported, presumably caused by suppression from the perfusion factor, was below the level of clinical significance. Further study may be required to evaluate whether DWI is reliable in patients with blood-brain barrier breakdown.

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