Effect of Intravenous Gadolinium-DTPA on Diffusion-Weighted Magnetic Resonance Images for Evaluation of Focal Hepatic Lesions

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Objective: Diffusion-weighted imaging (DWI) is usually performed before administration of intravenous contrast agents. Repetition of DWI is occasionally necessary after contrast administration, but the effects of contrast material on DWI and apparent diffusion coefficient (ADC) values in the abdomen have not yet been fully examined. The purpose of this work is to assess whether administration of gadolinium-based contrast material significantly affects DWI and ADC values at the focal hepatic lesions.

Methods: The results of DWI at 3.0 T (Signa VH3; GE Medical Systems, Milwaukee, WI) were examined in 20 patients (age range: 33–86 years, mean age = 68 years) who were evaluated by means of a hepatic protocol at our hospital. Among the 20 patients studied, a total of 57 lesions were detected. Diffusion-weighted imaging was obtained using single-shot echo planar imaging with a *b* value of 500 s/mm^2. Patients were injected with 0.1 mmol/kg gadopentetate dimeglumine. The signal-to-noise ratio (SNR) of the liver and the hepatic lesions was examined, and the contrast-to-noise ratio (CNR) of each lesion was evaluated. In addition, the ADC values calculated from the DWI were compared before and after administration of contrast agent. The statistical significance of differences between precontrast and postcontrast administration was determined by use of a paired *t* test.

Results: The SNR and CNR of the DWI were not significantly different before and after administration of contrast agent. The ADC values tended to decrease after administration of contrast agent for each focal hepatic lesion and the liver, although they did not reach statistical significance.

Conclusion: There was no significant difference before and after administration of contrast agent in the SNR or CNR of DWI. This indicates the feasibility of postcontrast DWI as a substitute for an unsuccessful precontrast-enhanced study in clinical practice.

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Diffusion is the thermally induced motion of water molecules in biologic tissues, also referred to as Brownian motion.[1–3] The microscopic motion includes molecular diffusion of water and microcirculation of blood in the capillary network (microperfusion). With the addition of diffusion gradient pulses, magnetic resonance (MR) imaging by means of apparent diffusion coefficient (ADC) measurement[1–3] is currently the best imaging method for in vivo quantification of the combined effects of capillary perfusion and diffusion. The primary application of diffusion-weighted imaging (DWI) has been in brain imaging, mainly for the evaluation of acute ischemic stroke, intracranial tumors, and demyelinating disease.[4–8] With the advent of the echo planar MR imaging technique,[9–12] DWI of the abdomen with faster imaging times has become possible, minimizing the effect of gross physiologic motion from respiration and cardiac movement.

Investigators in a few preliminary studies measured the ADCs of abdominal organs and focal hepatic lesions using a single-shot echo planar MR imaging sequence.[13–16] Results of these studies showed principally that DWI, by means of ADC measurement, can be used to characterize focal hepatic lesions. Repeated DWI after administration of contrast material may also be necessary in certain circumstances. For example, when the results of the DWI are negative or equivocal, a further workup with a different DWI approach may be necessary to detect or confirm the presence of lesions.

Despite the emerging clinical need to repeat DWI occasionally after injection of contrast agent, to the best of our knowledge, the effect of contrast media on DWI or the measured ADC has not been fully examined. The present study evaluates whether repeated DWI before and after administration of contrast agent produces comparable image quality.

We considered that contrast agent could affect DWI in 2 ways. For example, the ADC may decrease slightly because the contrast agent decreases the intravascular signal intensity. This might lead to suppression of the perfusion effect on the calculated ADC. Second, the T2 shortening effect of contrast

agent may decrease the signal intensity of the DWI images at $b = 0$ and $b = 500$ s/mm^2. The combination of these factors may alter the signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) of the focal hepatic lesions. If the SNR or CNR changes, the question of whether better or worse visualization of the focal hepatic lesions arises. To address these issues, we assessed DWI images from patients at our institution who were evaluated according to the hepatic protocol over a 6-month period. Additional DWI images were acquired after dynamic contrast perfusion images from patients who had focal hepatic lesions. This procedure added only a few minutes to the routine hepatic protocol applied at our institution.

MATERIALS AND METHODS

Patients

The protocol in our study was approved by our institutional review board, and informed consent was obtained from all patients. During a period of 6 months, 20 patients (age range: 33–86 years, mean age = 68 years) suspected of having hepatic lesions were prospectively examined with DWI before and after injection of contrast agent. In these 20 patients, 57 focal hepatic lesions (mean diameter = 4 cm, range: 1.5–10.0 cm) were evaluated on DWI images. When a patient had different types of lesions, all types were included in the study.

Metastasis

Twenty-six metastatic lesions were evaluated in 4 patients. The primary tumors were colorectal carcinoma. The diagnosis of metastasis was confirmed by means of surgery and follow-up imaging examinations, including ultrasonography, computed tomography (CT), and MR imaging, which showed progression of the lesions.

Hemangioma

Fifteen hemangiomas were evaluated in 5 patients. The diagnosis of hemangioma was established by means of hyperintensity on T2-weighted images and the typical enhancement pattern seen in CT or MR imaging (slightly irregular or globular peripheral enhancement after injection of a bolus of contrast medium, with gradual filling of the center of the lesion on delayed images).

Hepatocellular Carcinoma

Twelve hepatocellular carcinomas were evaluated in 8 patients. The diagnosis of hepatocellular carcinoma was made on the basis of MR imaging, CT, or ultrasonographic findings and confirmed by means of histologic findings or the elevation of serum α-fetoprotein levels in patients. All patients with hepatocellular carcinoma had concomitant cirrhosis related to chronic viral hepatitis B or hepatitis C. The diagnosis of cirrhosis was made on the basis of clinical findings and histologic findings in the patients.

Cholangiocarcinoma

Two cases of cholangiocarcinoma were diagnosed in 2 patients. The diagnosis of cholangiocarcinoma was made on the basis of MR imaging, CT, ultrasonography, and invasive cholangiography findings (infiltrating mass with infiltration of the portal hepatis and dilated intrahepatic biliary duct) and confirmed by means of histologic findings.

Liver Abscess

Two liver abscesses were evaluated in 1 patient. The diagnosis of liver abscess was assigned on the basis of MR imaging and CT findings (rim enhancement) and confirmed by means of catheter drainage and by antibiotics producing complete resolution of the abscess.

MR Imaging

Patients were examined with a 3.0-T superconducting MR system (GE Medical Systems, Milwaukee, WI). All patients underwent DWI in addition to imaging with a routine hepatic MR protocol to identify and select hepatic lesions suitable for ADC measurement. The additional postcontrast-enhanced DWI was obtained according to a hepatic protocol approximately 5 minutes after injection. The hepatic protocol included a T1-weighted spin echo sequence (repetition time/echo time [TR/TE] = 130/1.4 milliseconds, 8-mm thickness, 40 × 40 field of view, 256 × 128 matrix, number of excitations = 2.0), a T1-weighted dual fast gradient-recalled echo sequence (in-phase and out-of-phase sequences; TR/TE = 120/2.1 milliseconds [in-phase], TR/TE = 120/1.3 milliseconds [out-of-phase], 60° flip angle, 40 × 40 field of view, 256 ×128 matrix, number of excitations = 1.0, 8-mm section thickness), a T2-weighted fast spin echo sequence with spectral fat saturation (TR/TE = 13,333/102.9 milliseconds, 8-mm section thickness, 40 × 40 field of view, 512 × 256 matrix, number of excitations = 2.0), and a T1-weighted gradient echo sequence (TR/TE = 3.7/0.908 milliseconds, 10° flip angle) after dynamic injection of gadopentetate dimeglumine at a rate of 0.1 mmol/kg of body weight through a power injector at a rate of 2 mL/s.

Diffusion-Weighted MR Imaging

Before and after contrast agent injection, 2 breath-hold DWI sequences were performed with the single-shot echo planar imaging technique with motion-probing gradients in 3 directions. The following parameters were used to acquire 20 sections in a 24-second breath-hold (2 b values: 0 and 500 s/mm^2, TR/TE = 1000 /61.1 milliseconds, 8-mm thickness, 40 × 40 field of view, 128 × 256 matrix, number of excitations = 1.0).

Image Analysis

All MR images were analyzed retrospectively by consensus of 2 experienced radiologists (J.S.H. and G.C.L) who were aware of the results of CT or ultrasonography. The focal hepatic lesions were identified on the T1- and T2-weighted images, and their signal intensities, sizes, and patterns of enhancement after injection of contrast agent were noted. Because of the limited resolution of the DWI, only lesions larger than 1 cm in diameter were evaluated. The ADCs were measured in lesions (>1 cm) in all patients. Quantitative ADC maps were derived automatically on a voxel-by-voxel basis using commercially available software (Advantage Workstation 4.0; GE Medical Systems). The ADC was calculated with a linear regression analysis of the function

TABLE 1. SNRs of DWI in the Liver and Different Hepatic Lesions

Disease	Patients	Nodules	Precontrast	Postcontrast	*P*
Liver	20	57	35.37 ± 14.14	32.48 ± 10.1	0.365
Metastatic disease	4	26	59.55 ± 10.20	62.60 ± 19.84	0.591
Hemangioma	5	15	69.66 ± 16.70	56.00 ± 6.99	0.098
Hepatocellular carcinoma	8	12	73.72 ± 11.79	70.45 ± 17.84	0.485
Cholangiocarcinoma	2	2	73.20	63.48	None
Liver abscess	1	2	66.92	67.62	None

There is no significant difference between pre- and post contrast-enhanced DWI. The SNRs of hepatic lesions and the liver are expressed as arithmetic mean ± SD.

$S = S_0 \cdot \exp(-b \times \text{ADC})$, where b is the diffusion factor, S is the signal intensity after application of the diffusion gradient, and S_0 is the signal intensity at $b = 0$ s/mm^2.

One of the 2 radiologists (H.R.S.) established regions of interest in each lesion on the mapping images, and ADC values were obtained by using commercially available software (Advantage Workstation). All regions of interest (ie, round shape, at least 10 mm in diameter) were placed within the confines of the lesions. For heterogeneous lesions, regions of interest included the solid part. To ensure that the same areas were measured, the regions of interest were copied and pasted onto the T1-weighted, T2-weighted, and diffusion-weighted images and ADC maps. In livers, regions of interest were always placed in the posterior segment of the right hepatic lobe so as to avoid artifacts from the great vessels. The SNRs and CNRs of the DWI and the ADCs were calculated for precontrast and postcontrast studies. The SNR and CNR were calculated from the following equations: $\text{SNR} = \text{S}/\text{SD}_{\text{noise}}$ and $\text{CNR} = (\text{S}_{\text{lesion}} - \text{S}_{\text{liver}}) / \text{SD}_{\text{noise}}$, where S is signal intensity and SD_{noise} is the standard deviation of the background noise. The ADCs were each measured 3 times, and the measurements were averaged.

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

Signal-to-Noise Ratio and Contrast-to-Noise Ratio of Diffusion-Weighted Imaging

The SNRs of DWI for the liver and focal hepatic lesions are summarized in Table 1. There was no significant difference in the SNRs of DWI before and after administration of contrast agent. The CNRs of focal hepatic lesions with and without contrast agent are summarized in Table 2. There was no significant difference in the CNRs of DWI before and after administration of contrast agent (Fig. 1).

Apparent Diffusion Coefficient Value

The precontrast and postcontrast ADC values for the liver and focal hepatic lesions are summarized in Table 3. The ADC values tended to decrease after administration of contrast agent for each focal hepatic lesion and the liver, although they did not reach statistical significance.

DISCUSSION

Diffusion is the microscopic random translative motion of molecules, and water molecular diffusion can be measured in vivo using DWI and an ADC.[1] In many biologic tissues, particularly those that have regular and ordered microstructure, the diffusion coefficient depends on the direction along which it is measured. Magnetic resonance imaging can only measure differences directionally, and dependent components must be measured separately. The liver, unlike the brain[4–8] and kidney,[17] has an isotropic diffusion pattern, probably because of its randomly organized structure.[18] This information indicates that the use of multidirectional diffusion gradients is unnecessary for the design of hepatic diffusion studies. In this study, we used DWI with motion-probing gradients in 3 directions. Our study represents the first systematic evaluation of the diagnostic value of DWI scans performed after gadolinium-based contrast media administration in the abdomen. The SNR and CNR from the DWI taken before and after administration of contrast agent for the liver and focal hepatic lesions were not significantly different. These data indicate

TABLE 2. CNRs of DWI of the Different Hepatic Lesions

Disease	Patients	Nodules	Precontrast	Postcontrast	*P*
Metastatic disease	4	26	26.82 ± 14.77	33.51 ± 22.26	0.219
Hemangioma	5	15	37.32 ± 7.81	25.86 ± 6.46	0.069
Hepatocellular carcinoma	8	12	38.35 ± 11.75	37.95 ± 18.02	0.895
Cholangiocarcinoma	2	2	12.53	18.92	None
Liver abscess	1	2	56.60	51.47	None

There was no significant different between pre- and postcontrast-enhanced DWI. The CNRs of hepatic lesions and the liver are expressed as a arithmetic mean ± SD.

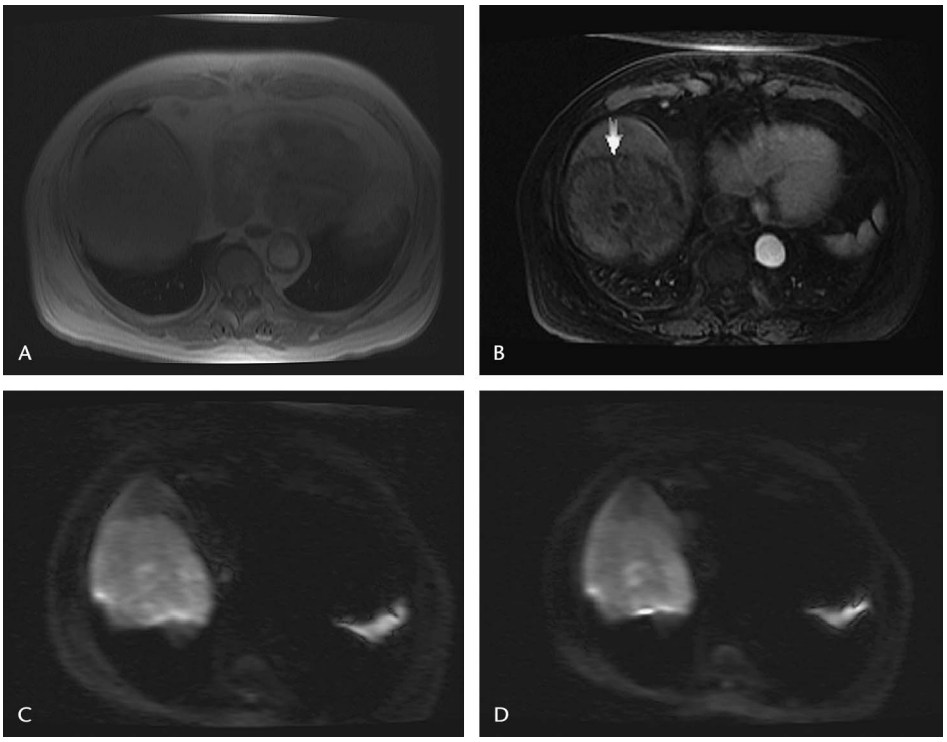

FIGURE 1. Images in a 75-year-old man with hepatocellular carcinoma (arrow). Precontrast T1-weighted spin echo image (A), postcontrast T1-weighted gradient echo image (B), precontrast apparent diffusion coefficient (ADC) map (C), and postcontrast enhanced ADC map (D) are shown. The overall appearance of the liver and lesion conspicuity are not significantly different between the precontrast and postcontrast ADC maps.

that DWI can be repeated after gadolinium-enhanced MR imaging studies. Therefore, when motion is detected on the initial DWI scan or when DWI needs to be repeated with different imaging techniques, it can be performed after routine hepatic MR protocol imaging without a significant change in the SNR or CNR of the hepatic lesions.

The ADC of hepatic lesions tended to decrease after administration of contrast agent, although the change did not reach statistical significance. Yamada et al[19] demonstrated that the intravascular contrast agent would result in a lower ADC value because of suppression of the signal from the perfusion. Other articles related to functional MR imaging have assessed the effect of intravascular contrast agent.[20–22] Zhong et al[21] found that administration of gadolinium-DTPA in human beings (0.2 mmol/kg) reduces the ADC by 2.4%. Yamada et al[19] showed a 1.3% decrease in ADC (0.1 mmol/kg). Our results agree with their findings. Whereas the perfusion factor for liver tissues should be constant from location to location, it may differ in areas with focal hepatic lesions, because the perfusion status may be different across the lesions. The ADC of lesions with paradoxically high perfusion (luxury perfusion) may be more significantly changed. Higher variability in ADC values from focal hepatic lesions compared with the liver (as indicated in Table 3) may be explained by the increased variation in the perfusion factor.

The findings reported here should be viewed in the context of several methodologic limitations. First, the subjects in this study were a heterogeneous group, and the sample was relatively small. Second, slice locations for the DWI sequences may not have been perfectly matched. Care was taken to avoid the possibility of misregistration by eliminating those lesions for which motion between the precontrast and postcontrast DWI was suspected. Even then, the effect of misregistration may not have been completely avoided. Third, another

TABLE 3. Comparison of Precontrast and Postcontrast ADC Value's ($\times 10^{-3}$) in the Different Hepatic Lesions

Disease	Patient	Nodules	Precontrast	Postcontrast	*P*
Liver	20	57	1.63 ± 0.16	1.58 ± 0.14	0.49
Metastatic disease	4	26	2.15 ± 0.17	2.05 ± 0.19	0.65
Hemangioma	5	15	2.25 ± 0.12	1.77 ± 0.29	0.07
Hepatocellular carcinoma	8	12	1.66 ± 0.15	1.54 ± 0.18	0.31
Cholangiocarcinoma	2	2	1.85	1.15	None
Liver abscess	1	2	1.73	1.46	None

There was a slight decrease in the ADC of each focal hepatic lesion or the liver, although decrease did not reach statistical significance. The ADCs of focal hepatic lesions and the liver are expressed as arithmetic mean ± SD.

potential source of error was the placement of the region of interest cursor. Inhomogeneity of hepatic lesions and motion may have affected the accuracy of calculations. Fourth, differences in timing of the images obtained after contrast agent injection may have skewed the ADC calculations. These sources of error are likely to produce random rather than systemic errors, however.

CONCLUSION

Diffusion-weighted images can be acquired after administration of contrast agent without compromising the SNR of the liver or the CNR of focal hepatic lesions. The mild change of the ADC value in our study was presumably caused by the contrast agent decreasing intravascular signal intensity. This may have led to suppression of the perfusion effect on the calculated ADC.

REFERENCES

1. Le Bihan D, Turner R, Douek P, et al. Diffusion MR imaging: clinical applications. *AJR Am J Roentgenol*. 1992;159:591–599.
2. Le Bihan D, Breton E, Lallemand D, et al. Separation of diffusion and perfusion in intravoxel incoherent motion MR imaging. *Radiology.* 1988; 168:497–505.
3. Le Bihan D. Diffusion/perfusion MR imaging of the brain: from structure to function. *Radiology.* 1990;177:328–329.
4. Schaefer PW, Grant PE, Gonzalez RG. Diffusion-weighted MR imaging of the brain. *Radiology.* 2000;217:331–345.
5. Tsuruda JS, Chew WM, Moseley ME, et al. Diffusion-weighted MR imaging of extraaxial tumors. *Magn Reson Med*. 1991;19:316–320.
6. Lutsep HL, Albers GW, DeCrespigny A, et al. Clinical utility of diffusion-weighted magnetic resonance imaging in the assessment of ischemic stroke. *Ann Neurol*. 1997;41:574–580.
7. Sorensen AG, Buonanno FS, Gonzalez RG, et al. Hyperacute stroke: evaluation with combined multisection diffusion-weighted and hemodynamically weighted echo-planar MR imaging. *Radiology.* 1996;199: 391–401.
8. Bammer R, Stollberger R, Augustin M, et al. Diffusion-weighted imaging with navigated interleaved echo-planar imaging and a conventional gradient system. *Radiology.* 1999;211:799–806.
9. Keogan MT, Edelman RR. Technologic advances in abdominal MR imaging. *Radiology.* 2001;220:310–320.
10. Muller MF, Prasad P, Siewert B, et al. Abdominal diffusion mapping with use of a whole-body echo-planar system. *Radiology.* 1994;190:475–478.
11. Edelman RR, Wielopolski P, Schmitt F. Echo-planar MR imaging. *Radiology.* 1994;192:600–612.
12. Butts K, Riederer SJ, Ehman RL, et al. Echo-planar imaging of the liver with a standard MR imaging system. *Radiology.* 1993;189:259–264.
13. Chan JH, Tsui EY, Luk SH, et al. Diffusion-weighted MR imaging of the liver: distinguishing hepatic abscess from cystic or necrotic tumor. *Abdom Imaging*. 2001;26:161–165.
14. Kim T, Murakami T, Takahashi S, et al. Diffusion-weighted single-shot echoplanar MR imaging for liver disease. *AJR Am J Roentgenol*. 1999; 173:393–398.
15. Ichikawa T, Haradome H, Hachiya J, et al. Diffusion-weighted MR imaging with a single-shot echoplanar sequence: detection and characterization of focal hepatic lesions. *AJR Am J Roentgenol*. 1998;170: 397–402.
16. Namimoto T, Yamashita Y, Sumi S, et al. Focal liver masses: characterization with diffusion-weighted echo-planar MR imaging. *Radiology.* 1997;204:739–744.
17. Ries M, Jones RA, Basseau F, et al. Diffusion tensor MRI of the human kidney. *J Magn Reson Imaging*. 2001;14:42–49.
18. Taouli B, Vilgrain V, Dumont E, et al. Evaluation of liver diffusion isotropy and characterization of focal hepatic lesions with two single-shot echo-planar MR imaging sequences: prospective study in 66 patients. *Radiology.* 2003;226:71–78.
19. Yamada K, Kubota H, Kizu O, et al. Effect of intravenous gadolinium-DTPA on diffusion-weighted images: evaluation of normal brain and infarcts. *Stroke*. 2002;33:1799–1802.
20. Darquie A, Poline JB, Poupon C, et al. Transient decrease in water diffusion observed in human occipital cortex during visual stimulation. *Proc Natl Acad Sci USA*. 2001;98:9391–9395.
21. Zhong J, Kennan RP, Fulbright RK, et al. Quantification of intravascular and extravascular contributions to BOLD effects induced by alteration in oxygenation or intravascular contrast agents. *Magn Reson Med*. 1998;40: 526–536.
22. Does MD, Zhong J, Gore JC. in vivo measurement of ADC change due to intravascular susceptibility variation. *Magn Reson Med*. 1999;41: 236–240.