Motion Artifact Reduction of Diffusion-Weighted MRI of the Liver: Use of Velocity-Compensated Diffusion Gradients Combined With Tetrahedral Gradients

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Purpose: To assess the effect of motion artifact reduction on the diffusion-weighted magnetic resonance imaging (DWI-MRI) of the liver, we compared velocity-compensated DWI (VC-DWI) and VC-DWI combined with tetrahedral gradients (t-VC-DWI) to conventional DWI (c-DWI) in the assessment of apparent diffusion coefficients (ADCs) of the liver.

Materials and Methods: In 12 healthy volunteers, the liver was scanned with c-DWI, VC-DWI, and t-VC-DWI sequences. The signal-to-noise ratio (SNR) and ADC of the liver parenchyma were measured and compared among sequences.

Results: The image quality was visually better for t-VC-DWI than for the others. The SNR for t-VC-DWI was significantly higher than that for VC-DWI ($P < 0.05$) and comparable to that for c-DWI. ADCs in both hepatic lobes were significantly lower for t-VC-DWI than for c-DWI ($P < 0.01$). Although ADC in the left lobe was significantly higher for VC-DWI ($P < 0.01$), no significant differences in ADCs were found between the right and left lobes for VC-DWI and t-VC-DWI.

Conclusion: The use of a t-VC-DWI sequence enables us to correct ADCs of the liver for artificial elevation due to cardiac motion, with preserved SNR.

Key Words: magnetic resonance imaging; diffusion-weighted imaging; apparent diffusion coefficient; liver; cardiac motion; velocity compensation

DIFFUSION-WEIGHTED (DW) magnetic resonance imaging (MRI) with the calculation of apparent diffusion coefficient (ADC) values is a valuable MRI technique for the detection and characterization of liver lesions (1–5). However, previous reports demonstrate that DW MRI (DWI) of the liver is affected by cardiac and respiratory motion (6–12).

DWIs of the liver may be performed during a breath hold to freeze respiratory motion, or during free breathing with multiple signal acquisitions or with respiratory triggering to reduce the effects of respiratory motion. The use of free breathing with multiple signal acquisitions offers images with high signal-to-noise ratio (SNR). High-quality DW images of the liver can be obtained using a free-breathing technique because cyclical respiration is a coherent motion that does not cause additional attenuation of the signal from the liver (13). However, free breathing with multiple signal acquisitions impairs the reliability and reproducibility of ADC measurements for characterizing liver lesions, because data for different axes of diffusion gradients are acquired at different respiratory phases (6). Therefore, it is useful to perform DWI of the liver in combination with respiratory triggering, although the use of respiratory-triggered acquisition increases the acquisition time.

Furthermore, a typical pulse sequence for DWI adds a bipolar gradient in three orthogonal directions, after excitation and before readout. These pulsed gradients will induce a phase shift due to cardiac motion as well as cause attenuation of the echo signal due to diffusion of the spins (7–9). Such a phase shift can cause signal loss on DWI and artificial elevation of ADC values in the liver (7,8), and the problems are

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Contract grant sponsor: Kitasato University School of Allied Health Sciences; Contract grant number: Grant-in-Aid for Research Project, No. 2011-1040.

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Received November 25, 2011; Accepted July 31, 2012.
DOI 10.1002/jmri.23796
View this article online at wileyonlinelibrary.com.
larger at higher b-values. One method of minimizing such artifacts is the use of cardiac triggering at image acquisition (10). When cardiac triggering is employed, higher reliability and reproducibility of ADC measurements in the liver may be obtained. However, the use of cardiac triggering, as well as respiratory triggering, increases the acquisition time. Combining cardiac and respiratory-triggered acquisition further increases the acquisition time and is not suitable for routine clinical use.

The use of a velocity-compensated (VC)-DWI sequence is another method to depress artifacts due to cardiac motion (Fig. 1) (14–16). VC diffusion gradients use dual bipolar gradients to remove all phase sensitivity to first-moment velocity motion during the diffusion-weighting period without cardiac triggering. One limitation of VC-DWI is that, for a given b-value, the duration of the VC diffusion gradient pulses becomes ~1.6 times longer than that of the conventional Stejskal-Tanner (ST) diffusion gradients pulses, which leads to a reduction in the SNR (13). The VC-DWI sequence is appropriate for neonatal brain imaging because of the long $T_2$ values of the brain (17). However, the short $T_2$ values of the liver make it difficult to acquire images of sufficient SNR using a VC-DWI sequence in clinical settings.

In a conventional DWI sequence, orthogonal x, y, and z diffusion gradient pulses are separately applied, and isotropic DW images are obtained by using three orthogonal images. This method is referred to as the orthogonal-gradients method (Fig. 2a). Orthogonal x, y, and z diffusion gradients pulses may be simultaneously applied, which shortens the duration of diffusion gradient pulses without reducing the b-value, resulting in a higher SNR. This method can generate four different vectors arranged in tetrahedral directions, called tetrahedral gradients (Fig. 2b). Isotropic DW images are obtained by using four different tetrahedral vector images (18). Recent reports have shown that the tetrahedral gradients provide a higher SNR than orthogonal gradients (19,20). Therefore, incorporating tetrahedral gradients into a VC-DWI sequence can be expected to improve SNR.

In the present study, we compared a VC-DWI sequence and a VC-DWI sequence combined with tetrahedral gradients (t-VC-DWI) to conventional DWI (c-DWI) in the assessment of liver ADC values.

**MATERIALS AND METHODS**

**Subjects**

This study was approved by the local Institutional Review Board and written informed consent was obtained from all participants. Twelve healthy adult volunteers (eight men and four women; mean age, 30.7 years; age range, 22–38 years) with no prior history or findings related to liver disease at the time of the study prospectively underwent DWI of the liver. Exclusion criteria were general contraindications to MRI, such as implanted pacemaker and claustrophobia.

**Imaging Procedures**

All examinations were performed on a clinical MR scanner (Signa HDxt optima edition 1.5T, GE Healthcare, Milwaukee, WI). The system provides a maximum gradient strength of 33 mT/m with a peak slew rate of 120 mT/m/msec. The coils used here were a 12-element body phased-array coil. DWI of the liver was performed in each subject using all three sequences: c-DWI, VC-DWI, and t-VC-DWI. The parameters of single-shot spin-echo echo planar imaging were as follows: axial-plane image acquisition, repetition time (TR) 12,610–20,000 msec (with respiratory triggering), echo time (TE) 76.3 msec (c-DWI), 121.6 msec (VC-DWI), or 95.5 msec (t-VC-DWI), slice thickness/slice gap 10/0 mm, number of slices 15, receive bandwidth $\pm 250$ kHz, b-values 0 and 1000 s/mm$^2$, field of view (FOV) 400 mm, matrix 128, signal averaging 4 (for the orthogonal gradients) or 3 (for the tetrahedral gradients), and spectral spatial radiofrequency fat suppression. Orthogonal gradients were used for c-DWI.

**Figure 1.** Pulse sequence charts of conventional diffusion sequence (a) and velocity-compensated diffusion sequence (b). The radiofrequency (RF) pulses (excite and refocus), diffusion gradients ($G_{\text{diff}}$) and echo planar imaging (EPI) readout are shown; other sequence elements are omitted for simplicity. Dual bipolar diffusion gradients enable velocity compensation (b).

**Figure 2.** Schematic presentation of orthogonal gradients (a), and tetrahedral gradients (b). The x, y, and z directions indicate the left, anterior, and caudal directions, respectively, for a patient placed in the magnet head-first and in the supine position. Since the tetrahedral gradients have strength equal to the square root of 3 times the orthogonal input components, this technique shortens the duration of the diffusion gradient pulse (18).
and VC-DWI. Mean nominal acquisition time was 231 seconds (range, 187–306 sec) for c-DWI, 239 seconds (range, 168–306 sec) for VC-DWI, and 232 seconds (range, 183–306 sec) for t-VC-DWI.

**Visual Assessment**

Images obtained with c-DWI, VC-DWI, and t-VC-DWI sequences were visually evaluated by two board-certified radiologists in a random and blinded manner. Severity of signal loss in the right hepatic lobe, severity of signal loss in the left hepatic lobe, and degree of noise were assessed using a three-point grading scale (1 = severe, 2 = mild, 3 = negligible), and overall image quality was assessed using another three-point grading scale (1 = poor, 2 = fair, 3 = good). Discrepancy was resolved by the third board-certified radiologist. The visual assessment was performed on the monitor of Advantage Workstation (GE Healthcare), and the observers were allowed to adjust the window level and width of the DW images.

**Quantitative Analysis**

ADC maps were generated from isotropic DW images and $T_2$-weighted images with a $b$-value of 0 s/mm$^2$ using the following equation: $\text{ADC} = - \ln (S_{b}/S_{0})/b$, where $b$ is the $b$-value and $S_{b}$ and $S_{0}$ are the signal intensities on images with $b$-values of 1000 and 0 s/mm$^2$, respectively.

For SNR and ADC measurements, regions of interest (ROIs) were placed in the liver parenchyma, excluding visible vascular and biliary structures, on the slice including the umbilical portion. SNRs were calculated by the method proposed by Steckner (21) (Appendix).

ROIs for measuring SNR were set to the smallest possible size in order to minimize the effect of spatially variant noise caused by parallel imaging reconstruction techniques. Three ROIs were set in the right hepatic lobe (anterior, lateral, and posterior portions) (Fig. 3a), and the SNR was calculated for each ROI. Because the signal in the left hepatic lobe was...
affected by artifacts, SNR was not computed for the left lobe. For ADC measurement, three circular ROIs (49 pixels) were placed for each of the right and left hepatic lobes (Fig. 3b). The ADC value for each lobe was defined as the average of the ADC values determined from the three ROIs. All image analyses were performed with MatLab (MathWorks, Natick, MA).

Statistical Analysis
ADC values were compared between the right and left hepatic lobes using a paired t-test, and ADC values and SNRs were compared among c-DWI, VC-DWI, and t-VC-DWI using one-way repeated measures analysis of variance (ANOVA) and the post-hoc Tukey test, because the data fitted a normal distribution (Kolmogorov–Smirnov test). Visual grades were compared among c-DWI, VC-DWI, and t-VC-DWI using the Kruskal–Wallis test and the post-hoc Steel–Dwass test, and visual grades regarding the severity of signal loss were compared between the right and left hepatic lobes using the Wilcoxon signed-rank test, because the data did not fit a normal distribution.

Differences were considered significant when \( P < 0.05 \). All statistical analyses were performed on a personal computer with JMP v. 9.0 (SAS Institute, Cary, NC).

RESULTS
DWI image sets using the three sequences were successfully acquired in all 12 subjects with no need for retry (Fig. 4). Table 1 presents results of visual assessment regarding the severity of signal loss in the right hepatic lobe, severity of signal loss in the left hepatic lobe, degree of noise, and overall image quality. All four visual grades were significantly better for t-VC-DWI than for c-DWI and for VC-DWI, although no significant differences were found between c-DWI and VC-DWI. Table 2 shows the results of comparison of visual assessments regarding the severities of signal loss between the right and left hepatic lobes. Visual grades regarding the severity of signal loss in the left hepatic lobe were significantly worse than those in the right hepatic lobe for VC-DWI and t-VC-DWI, although no significant differences were found for c-DWI.

Figure 5 shows SNRs for each pulse sequence. The SNR was lower for VC-DWI than for c-DWI, and statistically significant differences were found in the anterior and lateral portions of the right hepatic lobe. No significant differences in SNRs in any of the three portions were found between c-DWI and t-VC-DWI. The SNRs in all the three portions were significantly higher for t-VC-DWI than for VC-DWI; the ratio of mean SNR for t-VC-DWI to that for VC-DWI was 2.33 in the anterior portion, 1.87 in the lateral portion, and 1.94 in the posterior portion.

Figure 6 shows ADC values for each pulse sequence. ADC values in both hepatic lobes were significantly lower for t-VC-DWI than for c-DWI and for VC-DWI. ADC values in the left hepatic lobe were significantly lower for VC-DWI than for c-DWI. Table 3 shows the results of comparison between ADC values in the right and left hepatic lobes. Although ADC values in the left hepatic lobe were significantly higher than that in the right hepatic lobe for c-DWI, no significant differences in ADC values were found between the right and left hepatic lobes for VC-DWI and t-VC-DWI.

DISCUSSION
DWI is a useful technique for the detection of liver lesions (1–5). Furthermore, the ADC value may be helpful for characterizing liver lesions, quantifying liver fibrosis, and predicting or assessing response to chemotherapy (22,23). Typical DWI sequences are intrinsically sensitive to diffusion. However, they are generally also highly sensitive to other kinds of motion such as bulk motion, which may produce artifacts.
Such artifacts may influence the accuracy of ADC values (7–9).

First, the present study showed that ADC values were significantly higher in the left hepatic lobe than in the right hepatic lobe for c-DWI. Nasu et al (7) demonstrated signal loss in the left hepatic lobe on DWI and ascribed it to artifacts due to cardiac motion. The right-to-left difference in ADC observed in our study appears to be attributable to artificial elevation of ADC values of the left hepatic lobe due to cardiac motion. In contrast, no significant right-to-left differences in ADC values were observed for VC-DWI and t-VC-DWI, which indicates that VC-DWI and t-VC-DWI sequences allow correction for artificial elevation of ADC values due to cardiac motion.

Moreover, ADC values in the right hepatic lobe were significantly higher for c-DWI than for t-VC-DWI. This result suggests that signal loss on DWI and artificial elevation of ADC values also occurs in the right hepatic lobe, albeit to a lesser degree than in the left hepatic lobe, and that the artificial elevation was reduced by the use of a t-VC-DWI sequence. Kwee et al (8) indicated that signal loss due to cardiac motion also occurs in the right hepatic lobe. Nasu et al (12) demonstrated signal loss in the right hepatic lobe on respiratory-triggered DWI. They ascribed this phenomenon to artifacts originating from respiratory motion and called them “pseudo-anisotropy artifacts.”

In our study, all DW images were acquired in combination with respiratory triggering. The artificial elevation of ADC values in the right hepatic lobe for c-DWI may have occurred due to cardiac motion and pseudo-anisotropy artifacts.

The SNR for the t-VC-DWI sequence was higher than for VC-DWI. For evaluating SNR, the sum of the axes of diffusion gradients and signal averaging was set to be equal among different pulse sequences. The use of VC gradients decreases the SNR of the liver parenchyma, despite a reduction in motion artifacts, because the resulting prolongation of effective TE leads to T2 suppression in the liver with relatively short T2 relaxation time. In contrast, the use of tetrahedral gradients shortens the duration of diffusion gradients with the diffusion b-value kept constant, and thus provides a shorter TE, which would be expected to increase the SNR (18–20). Actually, the SNR was improved by approximately two times for t-VC-DWI compared to VC-DWI, which could be explained by the different effective TEs: 95.5 msec with t-VC-DWI sequence and 121.6 msec with the VC-DWI sequence. Although the effective TE was longer for t-VC-DWI than for c-DWI, no significant differences in SNRs were found between c-DWI and t-VC-DWI. This observation may be attributable to signal loss due to bulk motion (eg, cardiac motion) in images acquired with a c-DWI sequence, and compensation...
of signal loss in images acquired with a t-VC-DWI sequence. Furthermore, higher ADC values for VC-DWI than for t-VC-DWI may be responsible to the severe SNR for VC-DWI. The severe SNR for a VC-DWI sequence would prevent its clinical application in liver imaging, although imaging with a lower b-value may provide an acceptable SNR. In contrast, the t-VC-DWI sequence has the capability of providing high-quality DW images during a reasonable acquisition time even with a b-value of 1000 s/mm\(^2\) and appears to be suitable for practical use.

Visual grades were significantly better for t-VC-DWI than for c-DWI and for VC-DWI. These results appear to support the utility of a t-VC-DWI sequence; however, some discrepancies were noted between quantitative analysis and visual assessments. Although quantitative evaluation of the SNR did not indicate significant differences between c-DWI and t-VC-DWI, visual evaluation of degree of noise gave significantly better results for t-VC-DWI. Quantitative evaluation was performed for the right hepatic lobe, and visual evaluation was performed considering the entire liver. This difference may be responsible for the difference in results. Additionally, although the use of a t-VC-DWI sequence eliminated the right-to-left differences in ADC values, visual signal loss was severer for the left hepatic lobe. ROIs for quantitative analysis were placed only on the slice including the umbilical portion. The signal loss tended to be reduced on more caudal slices mainly delineating the right hepatic lobe, which may have contributed to the assignment of better visual grades to the right hepatic lobe. The right-to-left differences in visual signal loss suggest the need for further improvement. The use of the tracking only navigator echo technique (24), instead of respiratory triggering, provides sharp DW images in a shorter acquisition time. The combination of such a technique appears to be worth investigating.

We used b-values of 0 and 1000 s/mm\(^2\) in this study because recent studies indicated the utility of DWI with this combination for the characterization of liver tumors (26, 27). A b-value of 1000 s/mm\(^2\) is relatively high for DWI of the liver (4), which should have decreased the SNR. It should also be noted that the fast diffusion fraction related to capillary perfusion and the slow diffusion fraction reflecting tissue diffusion were not separated in calculating ADC values using this combination of b-values. The slice thickness was set at 10 mm in this study to compare DW images with different sequences. In clinical practice, the acquisition of thinner slices is recommended.

This study had several limitations. First, t-VC-DWI has not been proven yet to provide accurate ADC values, because of the lack of standard ADC values. However, t-VC-DWI provided approximately equivalent ADC values between the right and left hepatic lobes and enabled the assessment of the left lobe, which should be beneficial for clinical application. Second, only a small number of healthy volunteers were included in this study; future patient studies are necessary to determine the clinical utility of a t-VC-DWI sequence in detecting and characterizing hepatic lesions.

In conclusion, this study demonstrated that the t-VC-DWI sequence is able to compensate for artificial elevation of ADC values in the liver due to cardiac motion with maintenance of an acceptable SNR. The use of a t-VC-DWI sequence enables the acquisition of high-quality DW images even at a high b-values and has the potential to contribute to clinical liver imaging.

### APPENDIX

We calculated SNRs by the method proposed by Steckner (21). In this method, both the signal intensity and noise are determined using a given ROI. Noise is estimated excluding the contribution of artifacts such as the ringing artifact and ghost artifact to the variability of the signal intensity.

The standard deviation (SD) was calculated using the following equation:

\[
SD = \left[ \frac{1}{n(n-1)} \sum_{i=1}^{n-2} (X_{i+1} - X_i)^2 \right]^{1/2} (1)
\]

where \(n\) is the number of pixels evaluated and \(X_i\) and \(X_{i+1}\) represent signal intensities of successive pixels.

In addition to the underlying noise variance of interest (\(\sigma\)), additional variance due to issues found exclusively in the read (\(\sigma_r\)) or phase (\(\sigma_p\)) direction, including the ringing artifact and ghost artifact, was considered as the source of the standard deviation. The directionally unique standard deviations are determined as follows:

\[
SD_r = \sqrt{\sigma^2 + \sigma_r^2} \quad (2)
\]

\[
SD_p = \sqrt{\sigma^2 + \sigma_p^2} \quad (3)
\]

\[
SD_d = \sqrt{\sigma_r^2 + \sigma_p^2} \quad (4)
\]

where SD\(_r\), SD\(_p\), and SD\(_d\) are standard deviations in the read, phase, and diagonal directions, respectively.

The SD\(_r\), SD\(_p\), and SD\(_d\) were calculated using the acquired images and Eq. [1], and the value of \(\sigma\) was computed using the SD\(_r\), SD\(_p\), SD\(_d\), and Eqs. [2–4].

The SNR was calculated using the following equation:

\[
\text{SNR} = \frac{SI}{(\sigma/\sqrt{2})} \quad (5)
\]

where SI is the mean signal intensity in the ROI.
REFERENCES