

## Case Report

# Intravenous administration of gadolinium diethylene trianminepentaacetic acid affects diffusion-weighted imaging of focal liver lesions

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**Abstract:** Objectives: The present study is to investigate whether intravenous administration of gadolinium-diethylene-trianminepentaacetic acid (Gd-DTPA) significantly affects diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) values of focal liver lesions (FLLs). Methods: A total of 26 patients with 26 FLLs, including 6 hemangioma and 20 hepatocellular carcinoma, underwent DWI with b value of 600 s/mm<sup>2</sup> before and after intravenous administration of Gd-DTPA. Signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) of FLLs were calculated on DWI. ADC values of FLLs were measured on ADC maps. The statistical significance of differences between precontrast and postcontrast data was determined using paired t-test. Results: On DWI, the SNR and CNR of FLLs on postcontrast DWI were significantly higher than those on precontrast DWI ( $P=0.036$  and  $P=0.008$ , respectively). ADC values of the lesions were significantly lower on postcontrast DWI than on precontrast DWI ( $P=0.019$ ). Conclusions: The SNR and CNR of FLLs on DWI were significantly increased after Gd-DTPA injection. However, ADC values of FLLs were significantly decreased after Gd-DTPA injection. If ADC measurements are taken into account, DWI should be performed before Gd-DTPA injection.

**Keywords:** Focal liver lesions, magnetic resonance imaging, diffusion-weighted imaging, apparent diffusion coefficient, gadolinium diethylene-trianminepentaacetic acid

## Introduction

Diffusion-weighted imaging (DWI) is a functional imaging, which measures the free motion of water molecule within normal tissues and lesions [1]. The motion of water molecule is restricted in tissues and lesions with high cellularity and intact cellular membrane. Restricted diffusion demonstrates higher signal intensity on DWI and lower ADC values [1]. The primary application of DWI is in brain imaging, mainly for the assessment of the acute stroke, intracranial tumors, and demyelinating disease [2-4]. With the development of echo-planar imaging technique, DWI is increasingly used for the evaluation of focal liver lesions (FLLs) [5-7]. Several studies have investigated the importance of DWI in the detection and characterization of FLLs [8-10]. Results of these studies show that DWI has improved detection and increased sensitivity of FLLs compared with T2-weighted imaging and extracellular agent-

enhanced MRI. DWI can also be used as a quantitative tool for lesion characterization by means of apparent diffusion coefficient (ADC) measurement [11-13].

DWI is usually performed before administration of intravenous contrast medium. However, repeated DWI after administration of intravenous contrast medium may occasionally be necessary in the presence of motion artifacts or the need of additional DWI with different b values, different spatial resolution or different slice orientations [1, 14]. Several studies have been carried out to investigate the effect of gadolinium diethylene-trianminepentaacetic acid (Gd-DTPA) on DWI or the measured ADC [14-18]. These studies have shown that the image quality has no significant difference before and after the administration of Gd-DTPA on DWI. However, their findings on ADC measurement are contradictory. To our knowledge, the effect of Gd-DTPA on DWI or the measured

ADC at FLLs has not been fully established. The present prospective study investigates whether intravenous administration of Gd-DTPA significantly affects DWI and ADC values at FLLs.

### Materials and methods

#### *Patients*

From November 2013 to June 2014, a total of 31 patients who were diagnosed as FLLs underwent Gd-DTPA-enhanced magnetic resonance (MR) imaging (MRI) with DWI before and after intravenous injection of contrast medium. Hypervascular lesions were included in the study according to enhancement patterns. The exclusion criteria were as follows: i) lesions were smaller than 10 mm; ii) there were artifacts in DWI results. Some patients had multiple lesions, in which the largest lesion was chosen for the evaluation. Finally, a total of 26 patients (19 males and 7 females) with 26 lesions (6 hemangioma and 20 hepatocellular carcinoma) were included in the study. The age range of the patients was 37 to 67 years (average age,  $54.50 \pm 9.12$  years). The maximal diameter of the lesions ranged from 2.1 to 18 cm (mean,  $7.17 \pm 4.03$  cm). The diagnosis of hemangioma was based on typical MRI findings, in which two lesions were confirmed by surgery. Hepatocellular carcinoma was diagnosed by surgery or biopsy. All procedures were approved by the Ethics Committee of Shandong University. Written informed consents were obtained from all patients or their families.

#### *MRI*

MRI was performed with a 3.0T system (GE Signa Excite, GE Healthcare, Milwaukee, WI, USA), equipped with eight-channel phased-array surface body coils.

Axial T2-weighted imaging (T2WI) was performed using respiratory-triggered fast spin echo sequence with the following parameters: repetition time (TR), 6500-7000 ms; echo time (TE), 85-90 ms; slice thickness, 7 mm; interslice gap, 1.5 mm; matrix,  $320 \times 224$ ; field of view,  $27 \text{ cm} \times 36 \text{ cm}$ ; number of excitation, 4; acquisition time, approximately 2-2.3 min. Axial T1-weighted imaging (T1WI) was performed using breath-hold fast spoiled gradient echo sequence, with the following parameters: TR/

TE, 230/2.3 ms; slice thickness, 7mm; interslice gap, 1.5 mm; matrix,  $320 \times 192$ ; field of view,  $27 \text{ cm} \times 36 \text{ cm}$ ; flip angle,  $80^\circ$ ; number of excitation, 1; acquisition time, approximately 19-21 s. DWI was obtained with a breath-hold single shot spin-echo imaging (EPI) in three orthogonal directions (x, y, and z). Post-contrast DWI was performed at approximately 4min after injection of the contrast agent. Pre-contrast and post-contrast DWI were acquired using the same parameters as follows: b value, 0 and  $600 \text{ s/mm}^2$ ; TR/TE, 1400/72.3 ms; slice thickness, 7 mm; interslice gap, 1.0 mm; matrix,  $128 \times 128$ ; field of view,  $38 \text{ cm} \times 38 \text{ cm}$ ; number of excitation, 4; acquisition time, approximately 22 s. Dynamic contrast-enhanced MRI was performed using a breath-hold three dimensional (3D) T1-weighted fat-suppressed spoiled GRE sequence with the parameters as follows: TR/TE, 4.1/1.9 ms; field of view,  $27 \text{ cm} \times 36 \text{ cm}$ ; thickness, 6.0 mm; interslice gap, 0 mm; matrix,  $256 \times 192$ ; NEX, 1; flip angle,  $20^\circ$ ; acquisition time, 19-21 s. Dynamic contrast-enhanced images were obtained at 18-20 s, 55-60 s, 3 min, and 5 min after the injection of Gd-DTPA (0.1 mmol/kg or 2 ml/kg; Magnevist, Bayer Schering, Berlin-Wedding, Germany). Gd-DTPA was injected at a rate of 2-2.5 ml/s and immediately followed by a 20 ml saline flush through a power injector.

#### *Image analysis*

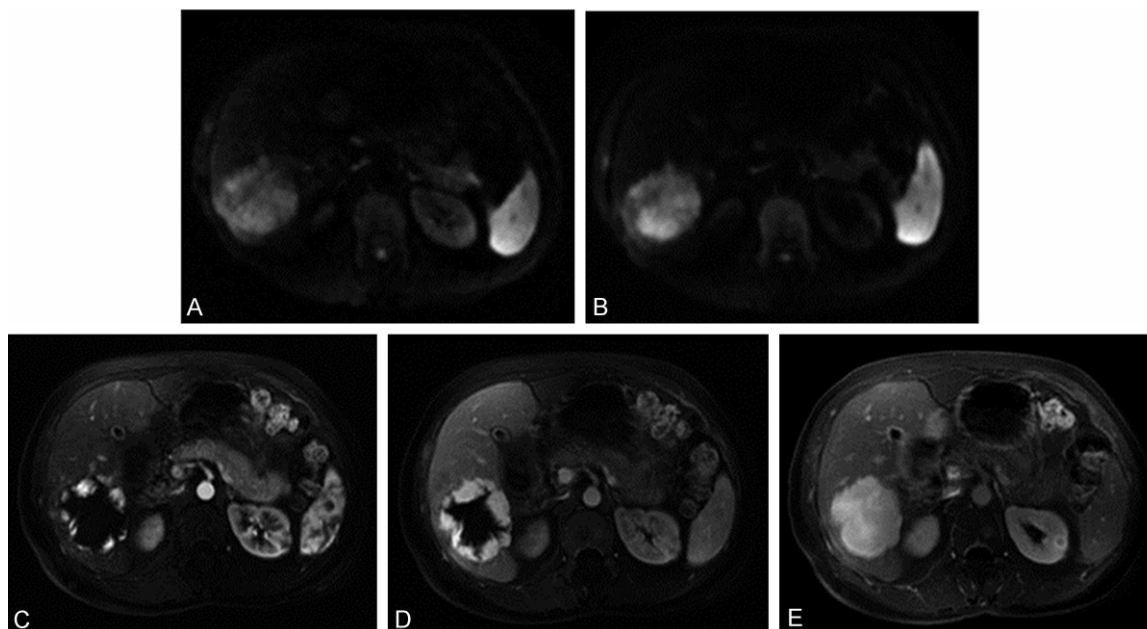
MR images were reviewed by two experienced radiologists independently in a blinded fashion. Each final decision was made only with the agreement between these two radiologists. Quantitative analysis was performed in the GE workstation. Region of interest (ROI) was a circle area of 110 pixels, and all ROIs were uniform. On DWI at b values of  $600 \text{ s/mm}^2$ , ROIs were placed in the focal lesion and hepatic parenchyma to measure signal intensity (SI). According to lesion size, 1-4 uniform ROIs were placed in the solid parts of focal lesions, avoiding necrotic and hemorrhagic areas as indicated by T2WI, T1WI, and enhanced images. The ROI of the liver was placed in the posterior right hepatic lobe, excluding the great vessels. Additional ROIs were placed on the surrounding air along the phase encoding direction to estimate the noise level. Signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) of each lesion on DWI were calculated using the following for-

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**Table 1.** SNR, CNR and ADC values of lesions measured on pre-contrast and post-contrast DWI

	No. of lesions	SNR	CNR	ADC value ( $\times 10^{-3}$ mm <sup>2</sup> /s)
Pre-contrast	26	12.97 $\pm$ 5.43	20.83 $\pm$ 17.57	1.56 $\pm$ 0.50
Post-contrast	26	16.39 $\pm$ 8.38	31.18 $\pm$ 26.65	1.33 $\pm$ 0.38
<i>t</i>		2.356	3.170	2.717
<i>P</i>		0.036	0.008	0.019

Note: SNR, signal-to-noise ratio; CNR, contrast-to-noise ratio; ADC, apparent diffusion coefficient; DWI, diffusion-weighted imaging.



**Figure 1.** A 55-year-old woman with hemangioma in the posterior right hepatic lobe. The lesion shows hyperintensity on axial (A) precontrast and (B) postcontrast diffusion-weighted images. (C) Axial arterial phase, (D) portal venous phase and (E) delayed phase T1-weighted images showing lesions with peripheral nodular and interrupted enhancement and progress centripetally to uniform.

formula:  $SNR = S_{\text{lesion}} / SD_{\text{noise}}$ ,  $CNR = |S_{\text{lesion}} - S_{\text{liver}}| / SD_{\text{noise}}$ . Where  $S_{\text{lesion}}$  is the SI of the lesion,  $S_{\text{liver}}$  is the SI of the liver, and  $SD_{\text{noise}}$  is the standard deviation of the background noise. The mean SNR and CNR values of the lesions were calculated from precontrast and postcontrast DWI. ADC values of the lesions were automatically calculated on ADC maps, with the location identical to that of the DWI image. The mean ADC values of the lesions were calculated from pre-contrast and postcontrast DWI.

### Statistical analysis

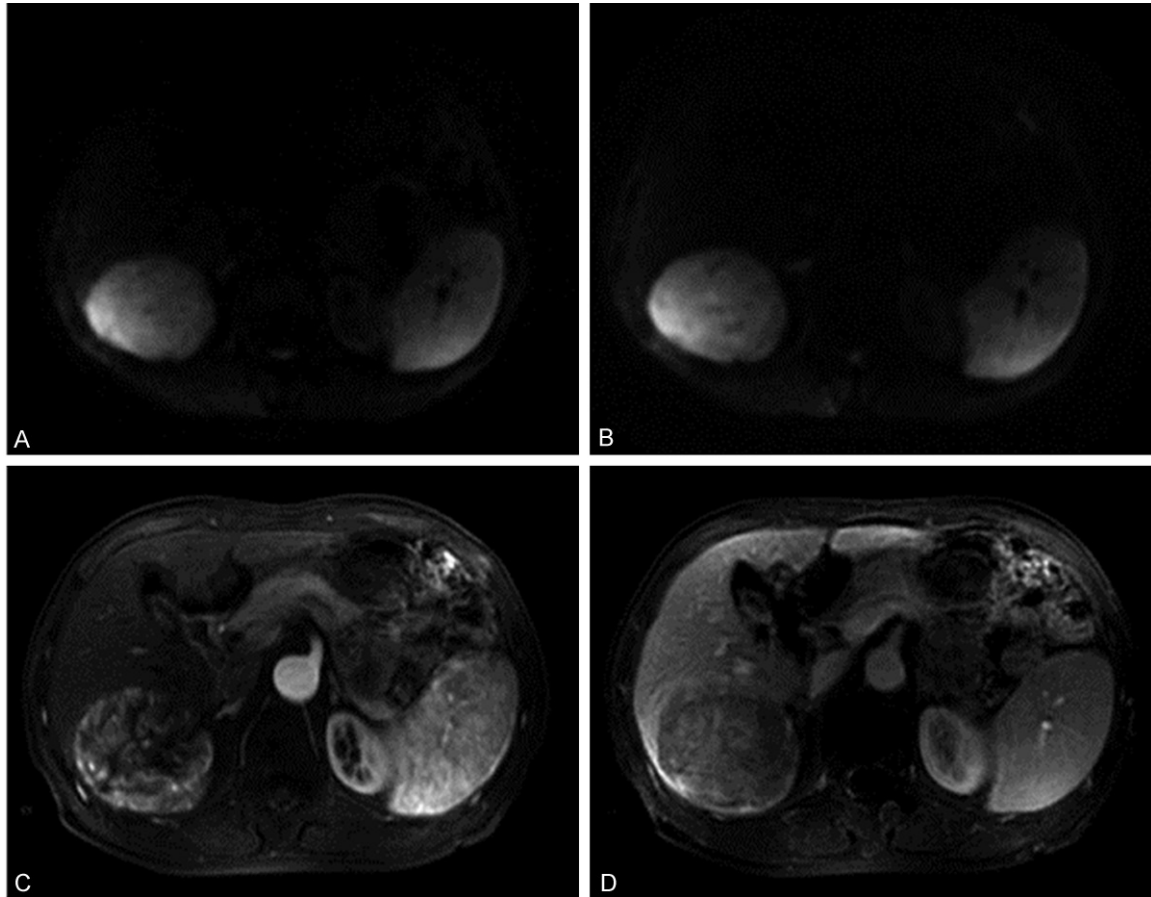
All statistical analyses were performed using the statistical software SPSS16.0 (IBM, Armonk, NY, USA). SNR, CNR and ADC values obtained on precontrast and postcontrast DWI were analyzed using paired *t*-test.  $P < 0.05$  was

considered statistically significant in all statistical analyses.

### Results

*Post contrast DWI shows higher SNR and CNR, and lower ADC value of FLLs compared with precontrast DWI*

To measure the SNR, CNR, and ADC of the lesions, precontrast and postcontrast DWI was performed. Both SNR and CNR of lesions were significantly higher on postcontrast DWI than those on precontrast DWI ( $t = 2.356$ ,  $P = 0.036$ ;  $t = 3.170$ ,  $P = 0.008$ ; respectively). There was approximately 26% and 49% increase in mean SNR and CNR on postcontrast DWI compared with precontrast DWI, respectively (**Table 1**; **Figures 1** and **2**). In addition, ADC value of the



**Figure 2.** A 65-year-old man with hepatocellular carcinoma in the posterior right hepatic lobe. The lesion shows hyperintensity on axial (A) precontrast and (B) postcontrast diffusion-weighted images. (C) Axial arterial phase T1-weighted image showing the lesion with heterogeneous enhancement. (D) Portal venous phase T1-weighted image showing the lesion with washout.

FLLs on postcontrast DWI were significantly lower than that on precontrast DWI ( $t=2.717$ ,  $P=0.019$ ), showing an approximately 15% decrease in mean ADC on postcontrast DWI compared with precontrast DWI (**Table 1**). These results suggest that the image quality of DWI is improved after injection of Gd-DTPA, and ADC values of FLLs on postcontrast DWI are significantly lower than those on precontrast DWI.

### Discussion

In this study, the mean SNR and CNR of FLLs on postcontrast DWI were significantly higher than those on precontrast DWI. There was approximately 26% and 49% increase in mean SNR and CNR on postcontrast DWI compared with precontrast DWI, respectively. This result indicates that the image quality of DWI was in-

creased after injection of contrast medium, and DWI can be acquired after intravenous injection without losing clinical information. Especially, increases in CNR of FLLs on postcontrast DWI may be helpful for improving lesion conspicuity. Because ADC value derives from signal intensity on DWI, image quality of DWI is essential for ADC value calculation.

Our data also show that ADC values of the FLLs are significantly lower on postcontrast DWI than on precontrast DWI. This finding shows that Gd-DTPA has a significant effect on ADC values after the injection, which is in accordance with a previous study [14]. These authors consider that decrease in ADC values after contrast medium injection is due to the suppression of intravascular contribution, namely the flow. Previous studies demonstrate that ADC values have been affected by both perfusion and diffu-

sion [19, 20]. We speculate that contrast medium may lead to decrease in blood movement, resulting in a lower ADC value. We also presume that ADC values of the hypervascular lesions may be more significantly changed than that of hypovascular lesions, so hypervascular lesions were selected in this study. Additionally, Yamada et al. find a 3.5% reduction in ADC values in infarcts after injection of contrast medium at 0.1 mmol/kg body weight [14]. However, our results show a 15% decrease in ADC after injection of contrast medium at 0.1 mmol/kg body weight. This difference may be caused by multiple factors such as different DWI sequences, magnetic field strengths, and types of lesions.

By contrast, Fitzek et al. [15] find no changes in ADC values in brain lesions. Chiu et al. [17] show that the ADC values of FLLs tend to decrease after injection, but without statistical significance. The contradictory results may be due to the time interval between contrast medium injection and DWI acquisition. In our study, the time interval between contrast medium injection and DWI acquisition was approximately 4min. However, in the study by Chiu et al. [17], repeated DWI was performed approximately 5 min after contrast medium injection. In the study by Fitzek et al. [15], the time interval between contrast medium injection and DWI acquisition in some groups was approximately 40 min. We hypothesize that, as time interval prolongs, the concentration of contrast medium in the blood decreases, and the effect of contrast medium in blood flow reduces, resulting in insignificant change in ADC values. Additionally, a few studies have demonstrated that the effect of contrast medium presents a time-dependent pattern in brain lesions, which further supports the above-mentioned analysis [16, 18]. However, there are several limitations in our study. Firstly, the study population is relatively small. Secondly, the slice locations of pre-contrast and postcontrast DWI may not be completely matched. In conclusion, we find that the SNR and CNR of the FLLs on DWI are significantly increased and ADC values of the FLLs are significantly decreased after Gd-DTPA injection. If ADC measurements are taken into account, DWI should be performed before Gd-DTPA injection.

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### Disclosure of conflict of interest

None.

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