Utility of Apparent Diffusion Coefficients in the Evaluation of Solid Renal Tumors at 3T

Hiroto SASAMORI*, Makoto SAIKI, Jumpei SUYAMA, Yoshimitsu OHTSUKI, Masanori HIROSE, and Takehiko GOKAN

Department of Radiology, School of Medicine, Showa University
1–5–8 Hatanodai, Shinagawa-ku, Tokyo 142-8666, Japan

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Purpose: We assessed the usefulness of apparent diffusion coefficients (ADCs) for solid renal tumor imaging using diffusion-weighted magnetic resonance imaging (DWI) at 3T.

Methods: This retrospective study assessed ADCs of 31 patients with renal tumors that were imaged using preoperative DWI. DWI was performed with the b values of 50, 500, and 1000 s/mm², using a 3T magnetic resonance imaging (MRI) system (MAGNETOM Trio, 3T, Siemens Healthcare, Erlangen, Germany). The ADC map was calculated using the b values of 50 and 1000 s/mm². ADCs of the different tumors were compared according to the Tukey–Kramer test.

Results: The tumors were diagnosed as clear cell renal cell carcinoma (RCC; n = 20), papillary RCC (n = 1), infiltrating urothelial carcinoma (UC) of the kidney (n = 4), cystic RCC (n = 1), poorly differentiated carcinoma (n = 1), and angiomyolipoma (AML; n = 4). The mean ADC of clear cell RCC was significantly higher than that of infiltrating UC of the kidney (1.423 vs. 0.931 × 10⁻³ mm²/s; P < 0.05), and the mean ADC of AML was significantly lower than that of clear cell RCC (0.674 vs. 1.423 × 10⁻³ mm²/s; P < 0.01).

Conclusion: ADCs used in DWI at 3T may be useful for differentiation of different types of solid renal tumors.

Keywords: apparent diffusion coefficients, diffusion-weighted MRI, renal tumor, 3T

Introduction

Recent advances in CT and magnetic resonance imaging (MRI) have made it possible to histologically characterize renal tumors on the basis of density or intensity on unenhanced images, as well as enhancement pattern.1–14 Despite these advancements, some cases still remain for which CT or MRI cannot be used for the histological characterization of a renal tumor. For example, the differentiation of RCC from AML and infiltrating UC of the kidney can be difficult in some cases. With regard to MRI, diffusion-weighted MRI (DWI) has recently been used to differentiate different subtypes of RCC and fat poor AML and clear cell RCC.15–20 However, almost all these studies were performed using MRI at 1.5T. To date, only 2 studies, which examined only RCC but not benign renal tumors, have used MRI at 3T.21,22 The purpose of this study was to assess the usefulness of the apparent diffusion coefficients (ADCs) for differentiating different types of solid renal tumors with DWI at 3T.

Materials and Methods

Patients

A retrospective review of clinical and imaging data was performed with approval of our institutional review board, therefore waiving the need for informed consent. The retrospective review included all patients who underwent evaluation of solid renal tumors using 3T MRI between March 1, 2007 and February 28, 2013 and who had a subsequent pathological confirmation of the diagnosis. During this period, 41 patients underwent evaluation of renal tumors using DWI. Of these, in one

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*Corresponding author, Phone: +81-3-3784-8573, Fax: +81-3-3784-8360, E-mail: 21110022m@grad.showa-u.ac.jp

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patient, a CT-guided needle biopsy was performed. The remaining 40 patients underwent surgical resection of renal tumors. One patient had two renal tumors, and 41 patients had 42 renal tumors. Eleven of these 42 tumors were excluded because of the unavailability of DWI at the time of evaluation \( (n = 8) \) or difficulty in calculating the ADC because the tumors were less than 1 cm in size \( (n = 3) \). The remaining 31 patients with 31 tumors were included in this study.

**MRI protocol**

MRI examinations were performed using a 3T MRI system (MAGNETOM Trio, Siemens Healthcare, Erlangen, Germany). Patients were imaged in the supine position using body- and spine-phased array coils. The standard imaging protocol comprised unenhanced in- and opposed-phase T1-weighted images, T2-weighted images, T2-weighted images using HASTE, fat-suppressed T2-weighted images, and fat-suppressed dynamic contrast-enhanced MR images. Gadobenate dimeglumine (Magnevist, Bayer Health Care, Leverkusen, Germany; Omniscan, Daiichi-Sankyo, Tokyo, Japan; Prohance, Eisai, Tokyo, Japan; or Magnescope, Terumo, Tokyo, Japan) was intravenously injected at a rate of 2 mL/s using a power injector (Sonic Shot GX, Nemoto Kyorindo Co., Ltd., Tokyo, Japan), followed by a 20-mL saline flush. The dose of gadolinium was 0.1 mmol/kg of body weight.

**Image analysis**

Two reviewers independently analyzed the images while being blinded to the histological or radiological follow-up findings. At the time of the study, one reviewer was a resident radiologist with 3 years’ experience in measuring the ADC values in renal tumors. The other reviewer was a fellowship-trained abdominal radiologist with 25 years’ experience in MRI interpretation. As large as possible circular regions of interest (ROIs) were placed over the renal tumors while avoiding regions of necrosis and cystic degeneration, which are typically not enhanced on contrast-enhanced MRI.

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**Table. Imaging parameters**

| parameter                        | In- and opposed-phase T1-weighted image | T2-weighted image | Fat-suppressed T2-weighted image | Diffusion-weighted image | Fat-suppressed dynamic contrast-enhanced MR image |
|----------------------------------|----------------------------------------|-------------------|----------------------------------|--------------------------|-----------------------------------------------|
| Repetition time (ms)             | 3.91                                   | 4000              | 1500                             | 4000                     | 3000                                          | 3.29 |
| Echo time (ms)                   | 1.25/2.45                             | 88                | 74                               | 84                       | 73                                            | 1.22 |
| Flip angle (degrees)             | 15                                     | 120               | 120                              | 120                      | —                                             | 15.0 |
| Slice thickness (mm)             | 3.50                                   | 5.0               | 5.0                              | 5.0                      | 5.0                                           | 3.00 |
| Gap between slices (mm)          | —                                      | 1.0               | 1.0                              | 1.0                      | 1.0                                           | —    |
| Receiver band width (Hz/pixel)   | 890                                    | 401               | 434                              | 300                      | 2442                                          | 520  |
| Field of view (mm)               | 360                                    | 350               | 350                              | 380                      | 350                                           | 50   |
| Matrix                           | \( 192 \times 256 \)                    | \( 214 \times 320 \) | \( 230 \times 384 \)             | \( 224 \times 320 \)     | \( 67 \times 128 \)                          | \( 202 \times 320 \) |
| Acquisition time (s)             | 0.20                                   | 0.40              | 1.36                             | 0.48                     | 2.24                                          | 0.22 |

Free-breath DWI was obtained by using echo-planar sequence and b values of 50, 500, and 1000 s/mm². HASTE: half-Fourier acquisition single-shot turbo spin-echo.
MRI (Fig. 1). In this study, one of the four AML cases was classical AML with an apparent fatty component. The ROI was placed over the fatty component because the tumor intensity was homogeneous. The ADC values were measured three times by each reviewer, and the mean values measured by each reviewer was used for analysis.

Statistical analysis

Statistical analysis was performed using SPSS software (version 17.0, SPSS). The Tukey–Kramer test was used to determine the significance of differences in ADCs between solid renal tumors. All reported P values were 2-sided and considered to be statistically significant when less than 0.05.

Results

Lesion and patient characteristics

Thirty-one tumors ranging in diameter from 1.6–8.9 cm (median, 3.9 cm) were evaluated. Each patient had a single tumor. The mean patient age was 61.6 years (range, 23–79 years). Patients included 23 men (mean age, 62.2 years; range, 35–79 years) and eight women (mean age, 59.6 years; range, 23–78 years). The tumors were diagnosed as clear cell RCC (n = 20), papillary RCC (n = 1), cystic RCC (n = 1), infiltrating UC of the kidney (n = 4), poorly differentiated carcinoma (n = 1), and AML (n = 4). Three of the four AML cases were fat poor AML, which have too few fat cells to be detected with imaging. Of these one was diagnosed using CT-guided biopsy. The remaining AML case was classical AML with an apparent fatty component, and this tumor was surgically resected at the risk of rupture, because it was larger than 7 cm in diameter. Two of the three fat poor AML were shown as hyperattenuating masses when compared with the surrounding renal parenchyma on unenhanced CT (hyperattenuating type). The remaining fat poor AML did not undergo unenhanced CT. The three fat poor AML showed low signal intensities on T2-weighted MR images.

ADC values

The mean ADC ± 2 SD of clear cell RCC was $1.423 \pm 0.548 \times 10^{-3} \text{mm}^2/\text{s}$, with a range of $0.749–1.881 \times 10^{-3} \text{mm}^2/\text{s}$. The ADC of papillary RCC was $0.605 \times 10^{-3} \text{mm}^2/\text{s}$. The ADC of cystic RCC was $2.194 \times 10^{-3} \text{mm}^2/\text{s}$. The mean ADC ± 2 SD of infiltrating UC was $0.931 \pm 0.256 \times 10^{-3} \text{mm}^2/\text{s}$, with a range of $0.805–1.079 \times 10^{-3} \text{mm}^2/\text{s}$. The ADC of poorly differentiated carcinoma was $1.088 \times 10^{-3} \text{mm}^2/\text{s}$. The mean ADC ± 2 SD of AML was $0.674 \pm 0.248 \times 10^{-3} \text{mm}^2/\text{s}$, with a range of $0.541–0.817 \times 10^{-3} \text{mm}^2/\text{s}$. The mean ADC ± 2 SD of fat poor AML was $0.719 \pm 0.172 \times 10^{-3} \text{mm}^2/\text{s}$, with a range of $0.606–0.817 \times 10^{-3} \text{mm}^2/\text{s}$.

The mean ADC of infiltrating UC of the kidney was lower than that of clear cell RCC ($0.931$ vs. $1.423 \times 10^{-3} \text{mm}^2/\text{s}$; $P < 0.05$), and the mean ADC of all AML was lower than that of clear cell RCC ($0.674$ vs. $1.423 \times 10^{-3} \text{mm}^2/\text{s}$; $P < 0.01$). Box-and-whisker plots for the ADCs of the different tumor groups are shown in Fig. 2.
Discussion

In this study, we found that the mean ADC of infiltrating UC of the kidney was significantly lower than that of clear cell RCC, thus possibly reflecting the high cellularity of UC. The ADC is a measure of the free movement of water molecules and is influenced by a number of factors including cellularity, cell membrane integrity, the nuclear-to-cytoplasmic ratio, and viscosity. Among these features, cellularity is the most widely studied and has been shown to be strongly associated with the ADC in biological tissues. Cellularity is believed to be the principal reason for the restricted diffusion observed within malignancies.²³–²⁵

It is generally possible to differentiate clear cell RCC from UC. Clear cell RCC is a well-defined mass with expansive growth. Its enhancement pattern is an early wash-in and delayed wash-out.¹⁴ In contrast, UC grows in an infiltrative manner and is hypovascular. However, it is sometimes difficult to differentiate necrotic clear cell RCC with extension into the renal pelvis from infiltrating UC of the kidney with renal parenchymal invasion. In such cases, DWI may be useful for the differentiation (Figs. 3 and 4).

The mean ADC of AML was also significantly lower than that of clear cell RCC in this study. AML shows various imaging findings depending on the amount of fat. Classic AML is the most fre-
quent and easily diagnosed by the detection of fat on imaging. Fat poor AML, which is divided into hyperattenuating type and isoattenuating type, is less frequent and contains too few fat cells to be detected with imaging (Fig. 5). In this study, three of the four AML cases were the hyperattenuating type fat poor AML, composed mainly of muscle component, and the other was classic AML, composed mainly of fat. Thus, both muscle component and fat component will cause the decrease of ADC value as previously reported.

Our findings indicated that DWI might contribute to a differentiation of clear cell RCC from hyperattenuating type fat poor AML and papillary RCCs is more difficult on the conventional findings of CT and MRI, because both show a prolonged enhancement and low T2 intensity. In this study, there was only one case of papillary RCC was observed, which had an ADC of 0.605 × 10⁻³ mm²/s, similar to the mean ADC of hyperattenuating type fat poor AML (0.719 × 10⁻³ mm²/s). Two studies have examined the ADC of papillary RCC using 3T MRI. One obtained values of 1.087 × 10⁻³ mm²/s (b values of 0 and 500 s/mm²) and 0.884 × 10⁻³ mm²/s (b values of 0 and 800 s/mm²), and the other obtained a value of 1.053 × 10⁻³ mm²/s (b values of 0 and 800 s/mm²). However, so far, no study has compared the ADC value between AML and papillary RCC. Further studies will be necessary to evaluate whether the ADC value will be useful for the differentiation of these two tumors.

We used a 3T MRI system to improve the DWI quality, as this approach theoretically doubles the signal-to-noise ratio in comparison to the standard 1.5T system. ADCs of renal tumor obtained with 3T MRI tended to be lower than those obtained with 1.5T MRI. The ADC of clear cell RCC with 1.5T MRI was reported to be within the range of 1.54–1.85 × 10⁻³ mm²/s and between 1.381–1.698 × 10⁻³ mm²/s with 3T MRI; In our study, the ADC was 1.423 × 10⁻³ mm²/s. The ADC of AML with 1.5T MRI was reported to be within the range of 0.74–1.58 × 10⁻³ mm²/s. The ADC of AML with 3T MRI was not previously reported, but it was 0.674 × 10⁻³ mm²/s in our study. The ADC of UC with 1.5T MRI was reported to be within the range of 1.59–2.70 × 10⁻³ mm²/s. The ADC of UC with 3T MRI was not previously reported, but it was 0.931 × 10⁻³ mm²/s in our study. Some authors have reported that ADCs of liver and brain tissues are significantly different when obtained using MRI at 3T vs. 1.5T. However, other studies have reported no significant differences in ADCs of abdominal organs obtained using MRI at 3T vs. 1.5T. Further studies will be necessary to fully evaluate the differences in ADC between 3T and 1.5T MRI.

In addition to the field strength, the actual ADC values were affected by the method of ROI placement and the b factors used to calculate the ADC. In this study, the circular ROI was placed over as much of the renal tumor as possible, and the mean values were used for the analysis. In previous studies, the ROI measurement methods varied; for example, some included a ROI that was as large as possible, and some included a ROI with measurements of approximately 100 mm² or 30–120 mm². Furthermore, we used the mean ADC value, but others used the minimum value. Differences in the ROI measurement method can consequently cause differences in the results. In this study, an ADC map was calculated using the b values of 50 and 1000 s/mm². In previous studies, the b factor varied (e.g., b = 0, 400, 600, 800, or 1000 s/mm²).
The ADC values with high b-values are lower than those with low b values. This reduction in the ADC can result from any source of incoherent motion, particularly capillary perfusion. 32–35

Our study had several limitations. First, our sample size was small. Second, as with all retrospective studies, a possibility of unintended selection bias was present. Finally, the Fuhrman RCC grades were not considered, because of the relatively small patient sample size.

Conclusion

We found that the ADCs using DWI at 3T may be useful for differentiating between solid renal tumors.

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