3T magnetic resonance diffusion tensor imaging in chronic kidney disease

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Abstract

Objective: To investigate the relationship of apparent diffusion coefficient (ADC) and fractional anisotropy (FA) values with renal function on 3T diffusion tensor imaging (DTI) in chronic kidney disease.
Materials and methods: Twenty healthy volunteers and 29 patients with CKD underwent DTI. The relationship among ADC, FA, and renal function was analyzed.
Results: Cortical and medullary ADC and FA values of patients with chronic kidney disease were lower than those of healthy volunteers ($P = 0.000$). Both the renal ADC and FA values correlated inversely with serum creatinine and blood urea nitrogen ($P < 0.05$).
Conclusion: DTI is a feasible and non-invasive means to reflect the severity of renal function damaged.

Key words: Magnetic resonance—Diffusion-weighted imaging—Diffusion tensor imaging—Kidney

Diffusion-weighted imaging (DWI) is a non-invasive functional magnetic resonance imaging (MRI) examination to detect diffusion of water molecules in living tissues [1]. The structural integrity of kidneys has been assessed by evaluating the degree of water molecule diffusion using the apparent diffusion coefficient (ADC) [2, 3]. Diabetic nephropathy, renal allograft, renal artery stenosis, ureteral obstruction, and lupus nephritis have been found to have reduced renal ADC values [1–8]. Correlation between ADC and glomerular filtration rate (GFR) has been reported [9–11]. Diffusion tensor imaging (DTI) was developed on the basis of DWI to show the direction in addition to speed of water molecule diffusion, thereby indirectly reflecting the structural integrity. The most commonly used indices for DTI evaluation are fractional anisotropy (FA) and ADC. There are few reports on DTI of normal kidneys [12–17], renal tumors, renal artery stenosis, and diabetic nephropathy [18–20]. The purpose of this study was to research the relationship between ADC and FA value with the renal function state, investigate the value of DTI in chronic kidney disease (CKD).

Materials and methods

Twenty healthy volunteers (10 women, 10 men; age range: 23–45 years, average: 31 years) and 29 patients with CKD (15 women, 14 men; age range: 20–50 years; average: 36 years) were enrolled in this study. All volunteers had no history of kidney or vascular disease, diabetes, or hypertension and had normal renal function tests in the past year, as well as normal conventional MRI of the kidneys. Fifteen patients with CKD were confirmed by ultrasound-guided renal biopsy, and the remaining 14 patients were diagnosed by clinical criteria. Patients with renal tumor, stone or other obstructive nephropathy on imaging examination were excluded. The study protocol was approved by the institutional ethics committee and informed consent was obtained from all subjects. The Modification of Diet in Renal Disease (MDRD) equation was used to calculate the estimated GFR (eGFR) $= 170 \times$ (serum creatinine)$^{-0.999} \times$ (age)$^{-0.176} \times$ (urea nitrogen)$^{-0.170} \times$ (albumin)$^{0.318} \times 0.762$ (female). Table 1 lists the renal function of patients with CKD classified into five stages according to the kidney disease outcome quality initiative guidelines [21].

MRI was performed using a 3T system (Magnetom Trio Tim; Siemens Medical Solutions, Erlangen, Germany) with

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Table 1. Renal function of patients with chronic kidney disease

CKD stage	Number of patients	Age (years)	Serum creatinine (μmol/L)	Urea nitrogen (mmol/L)	eGFR (mL/min)
1	5	31.6 ± 9.2	63.6 ± 12.7	5.1 ± 0.6	115.6 ± 13.2
2	6	33.8 ± 8.8	86.0 ± 20.7	6.2 ± 2.3	77.3 ± 9.8
3	7	35.6 ± 10.9	164.9 ± 33.5	10.1 ± 2.8	37.4 ± 9.4
4	4	40.3 ± 13.0	356.0 ± 29.5	13.9 ± 3.3	16.2 ± 1.7
5	7	39.0 ± 7.0	755.1 ± 244.7	26.1 ± 8.3	7.7 ± 3.2

phased array body and spine surface coils. Morphologic imaging included axial T1-, T2-, axial and coronal fat-saturated T1-, and coronal T2-weighted sequences. DTI was performed using coronal breath-held single-shot spin-echo, echo-planar imaging sequence with 6 diffusion directions and $b = 0, 400$ s/mm^2. The parameters were TR 2200 ms, TE 70 ms; 7 slices, 5-mm thick, 1-mm intersection gap; left-to-right phase encoding direction, 38 cm field-of-view, 154×154 matrix, 1 excitation, and 24-second acquisition time. The images were transferred to a workstation (Siemens Healthcare Sector, Erlangen, Germany) with DTI post-processing software generating DWI trace images, ADC maps and FA maps automatically. Identical circular regions of interest (ROIs) were drawn on the b = 0 s/mm^2 images, ADC and FA maps of two contiguous slices close to the renal hila of both kidneys. A total of 6–9 ROIs were drawn on the upper, middle, and lower portions of bilateral renal cortex and medulla. Renal sinus, visible blood vessels, and artifacts were not included in the ROIs. The ADC and FA values were obtained for each ROI, and the average was calculated. Free curves on the medulla between cortex and renal sinus as seed points were drawn manually and diffusion tensor tractography (DTT) maps displaying the directions of renal collecting systems were automatically generated using the DTT software with FA threshold of 0.20, angle threshold of 30° and color coding of directions with blue color indicating cranial-caudal, red color indicating left-right, and green color indicating dorsal-ventral directions. Statistical analysis was performed with SPSS 17 (SPSS Inc., Chicago, USA). The variability of ADC and FA of bilateral kidneys was compared using paired t-test. One-way ANOVA analysis was used to compare the variability of ADC and FA of cortices and medullae. Paired comparison among the different CKD stages was performed using the least significant difference method. The correlations of renal ADC and FA values with serum creatinine, blood urea nitrogen, and eGFR were analyzed with the Pearson correlation analysis. Statistical significance was defined as $P < 0.05$.

Results

The boundaries between renal cortices and medullae were sharp and clearly defined on the ADC and FA maps of the central renal slices in patients with stages 1 and 2 CKD; unclear on those of patients with stages 3, 4, and 5 CKD (Figs. 1, 2, 3, 4, 5). Corresponding DTT maps showed that the diffusion directions of renal collecting systems were radial towards the renal hila. There was no significant difference between the average left and right cortical ADC (2.414 ± 0.070, 2.392 ± 0.067), medullary ADC (2.005 ± 0.063, 1.991 ± 0.057), cortical FA (0.275 ± 0.019, 0.280 ± 0.018), medullary FA (0.454 ± 0.021, 0.446 ± 0.016) values of healthy volunteers ($P > 0.05$). There was also no significant difference between the average left and right cortical ADC (2.247 ± 0.169, 2.223 ± 0.187), medullary ADC (1.884 ± 0.140, 1.858 ± 0.148), cortical FA (0.251 ± 0.022, 0.254 ± 0.024), medullary FA (0.411 ± 0.035, 0.409 ± 0.031) values of patients with CKD ($P > 0.05$).

With declining renal function from normal to CKD stage 5, the average cortical and medullary ADC values showed a significant ($P = 0.000$) downward trend with $F = 41.775$ and 33.041, respectively (Fig. 6; Table 2). There was no significant difference among the cortical and medullary ADC values of healthy volunteers and patients with CKD stages 1–2 ($P > 0.05$). The average cortical ADC values of patients with CKD stages 3–5 were significantly different from those of healthy volunteers and patients with other CKD stages ($P < 0.05$). The average medullary ADC values of patients with CKD stages 4–5 were significantly different from those of healthy volunteers and patients with other CKD stages ($P < 0.05$). The average medullary ADC value of patients with CKD stage 3 was significantly ($P < 0.05$) lower than that of healthy volunteers and not significantly lower than those of patients with CKD stages 1–2 ($P > 0.05$).

With declining renal function from normal to CKD stage 5, the average cortical and medullary FA values also showed a significant ($P = 0.000$) downward trend with $F = 25.082$ and 42.735, respectively (Fig. 7; Table 3). There was no significant difference among the average cortical FA values of healthy volunteers and patients with CKD stages 1–2 ($P > 0.05$). The average cortical FA values of patients with CKD stages 3–5 were significantly lower than those of healthy volunteer and patients with CKD stages 1–2 ($P < 0.05$). The average cortical FA value of patients with CKD stage 5 was significantly lower than that of patients with CKD stage 3 ($P < 0.05$), whereas the average cortical FA values were not significantly ($P > 0.05$) different between CKD stages 3 and 4 and between CKD stages 4 and 5. The average medullary FA values of patients with CKD stages 3–5 were significantly
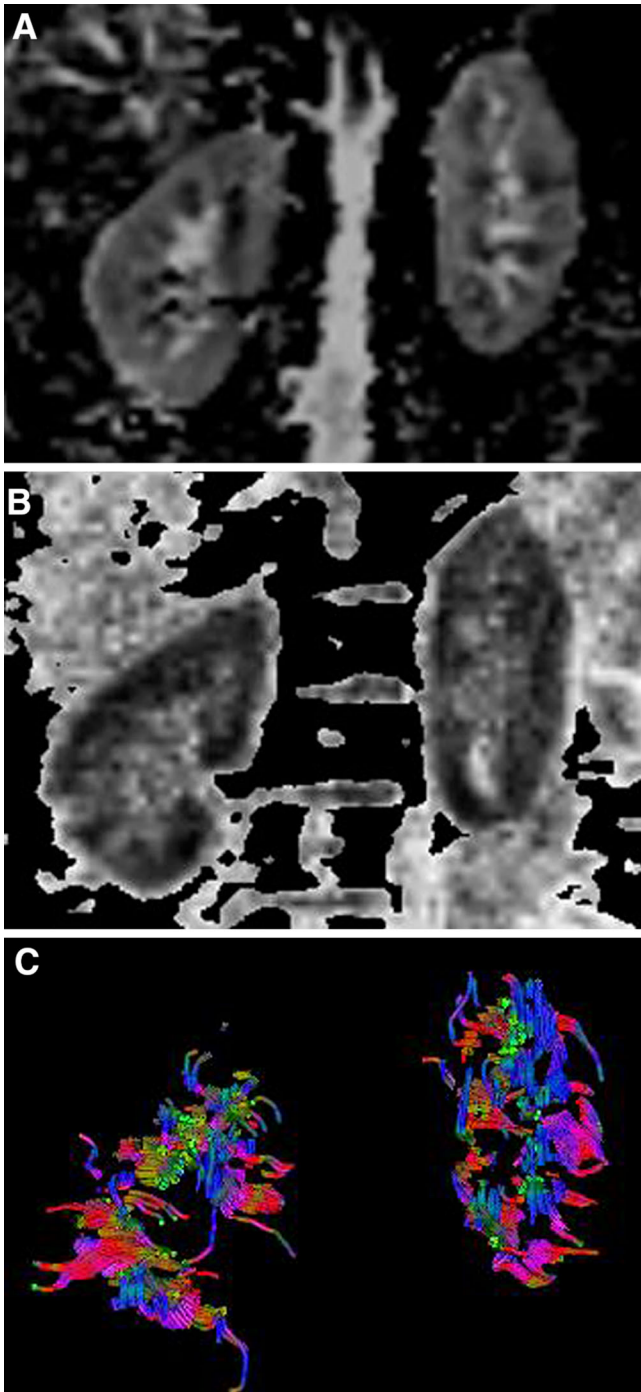
Fig. 1. The ADC (**A**), FA (**B**), and DTT maps (**C**) of CKD 1

Fig. 2. The ADC (**A**), FA (**B**), and DTT maps (**C**) of CKD 2

different from those of healthy volunteers and patients with other CKD stages ($P < 0.05$). There was no significant difference ($P > 0.05$) between the average medullary FA values of healthy volunteers and patients with CKD stage 1, between those of CKD stages 2 and 3, whereas the average medullary FA value of patients with CKD stage 2 was significantly lower than that of healthy volunteers ($P < 005$).
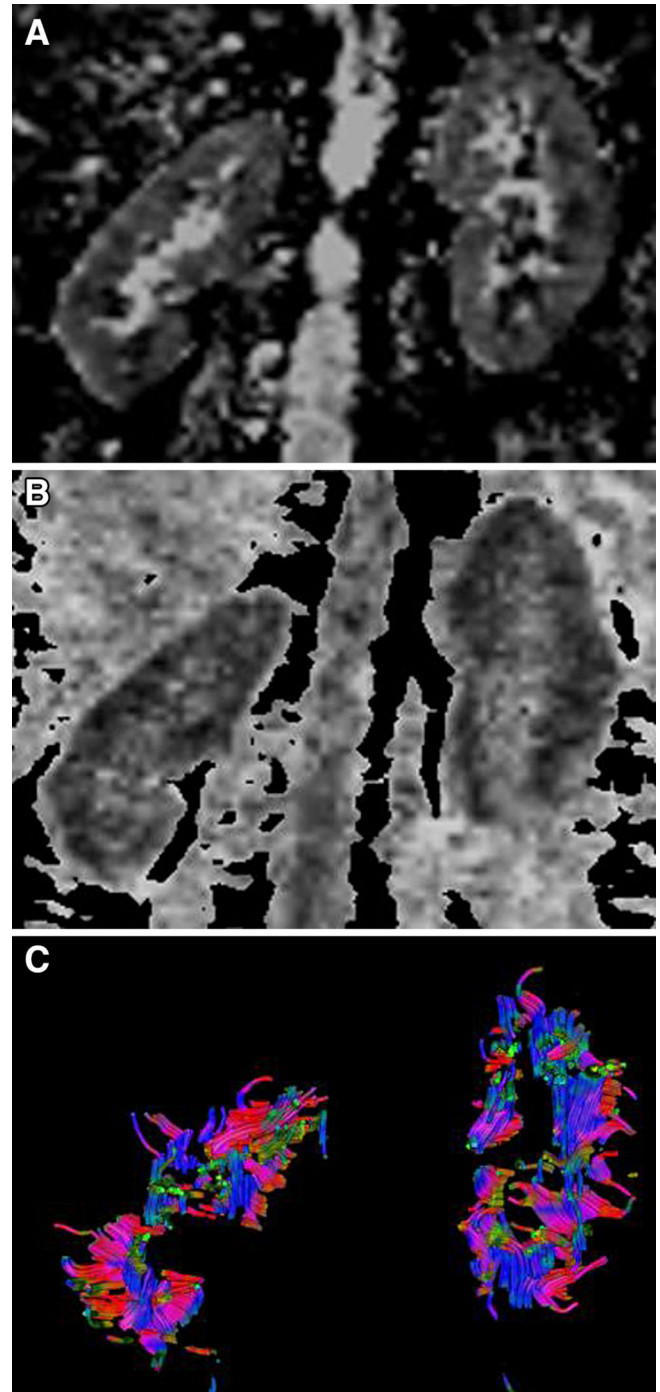
There was negative correlation ($P = 0.000$) between the cortical and medullary ADC values with serum creatinine ($r = -0.752$, -0.783) and blood urea nitrogen ($r = -0.695$, -0.706); between the cortical and medullary FA values with serum creatinine ($r = -0.622$, -0.691) and blood urea nitrogen ($r = -0.627$, -0.682). There was positive correlation ($P = 0.000$) between the cortical and medullary ADC values ($r = 0.695$, 0.639)
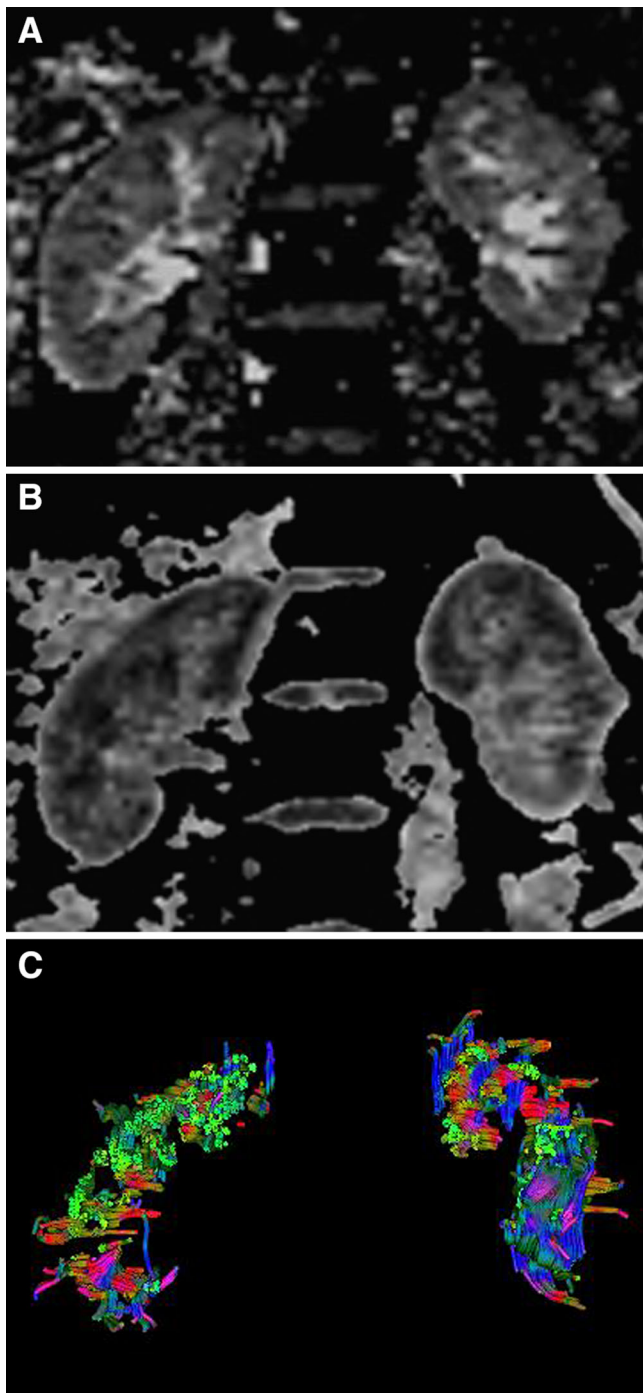
Fig. 3. The ADC (**A**), FA (**B**), and DTT maps (**C**) of CKD 3

Fig. 4. The ADC (**A**), FA (**B**), and DTT maps (**C**) of CKD 4

with eGRF; between the cortical and medullary FA values ($r = 0.756, 0.696$) with eGFR.

Discussion

The kidney is an organ with high blood perfusion and water content with main functions of water filtration, reabsorption, and concentration. The renal ultrastruc-
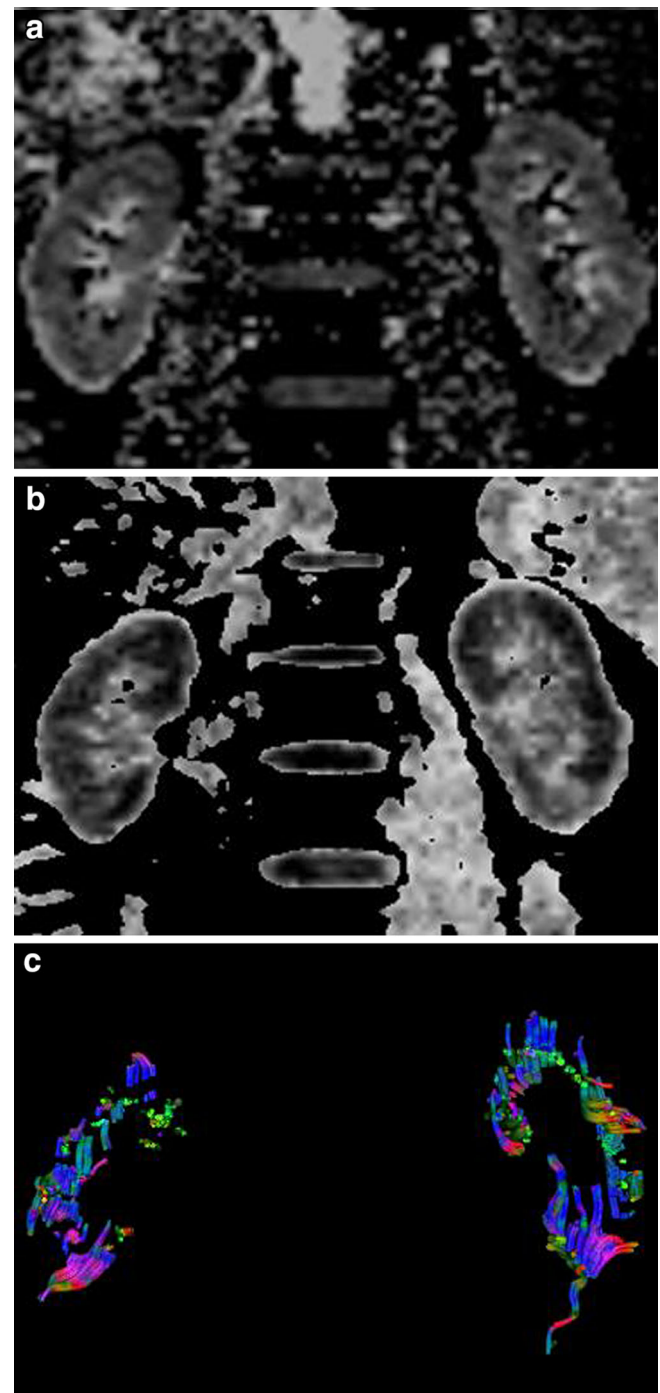
ture can be demonstrated by water molecule diffusion in DTI. DTI provides diffusion measurements in at least six directions. Compared with DWI, DTI shows the direction in addition to the speed of water molecule diffusion. We found no difference in the cortical and medullary ADC values between the right and left kidneys. Similar to findings reported in the literature [4, 11, 22], the cortical and medullary ADC values of CKD were lower
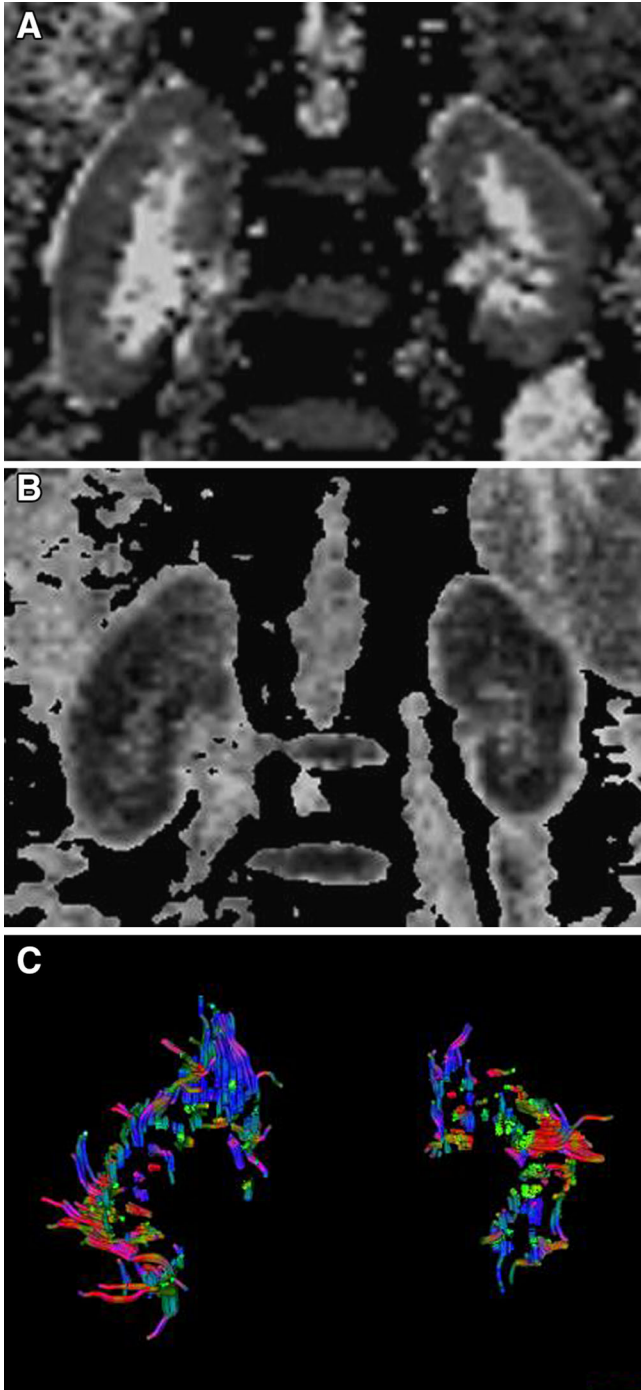
Fig. 5. The ADC (**A**), FA (**B**), and DTT maps (**C**) of CKD 5

Fig. 6. The bar graph of the average renal cortical and medullary ADC values from normal to CKD stage 5 ($\times 10^{-3}$ mm^2/s).

Table 2. Comparison of average renal ADC values in healthy volunteers and patients with CKD ($\times 10^{-3}$ mm^2/s)

	Cortex	Medulla
Normal	$2.403 \pm 0.069^{d,e,f}$	$1.998 \pm 0.060^{d,e,f}$
CKD 1	$2.377 \pm 0.122^{d,e,f}$	$1.978 \pm 0.051^{e,f}$
CKD 2	$2.374 \pm 0.087^{d,e,f}$	$1.972 \pm 0.087^{e,f}$
CKD 3	$2.287 \pm 0.139^{a,b,c,f}$	$1.918 \pm 0.141^{a,e,f}$
CKD 4	$2.122 \pm 0.114^{a,b,c,d,f}$	$1.792 \pm 0.060^{a,b,c,d,f}$
CKD 5	$2.029 \pm 0.071^{a,b,c,d,e}$	$1.705 \pm 0.076^{a,b,c,d,e}$
F	41.775	33.041
P	0.000	0.000

[a] $P < 0.05$ compared with normal volunteer
[b] $P < 0.05$ compared with CKD 1
[c] $P < 0.05$ compared with CKD 2
[d] $P < 0.05$ compared with CKD 3
[e] $P < 0.05$ compared with CKD 4
[f] $P < 0.05$ compared with CKD 5

than those of normal kidneys because of limited water diffusion movement in the extravascular and intercellular space by glomerulosclerosis, interstitial fibrosis, and tubule atrophy. Xu et al. [11] reported a positive correlation between renal ADCs and GFR. Our study got the similar result. In our study, the ADC values of patients with stages 1–2 CKD were not significantly lower, whereas thos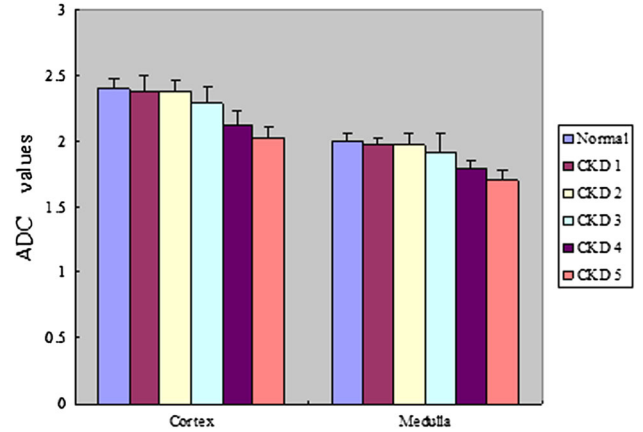e of stages 3–5 CKD were significantly lower than that of healthy volunteers. Our findings suggest that renal ADC measurement is only useful for detecting moderate to advanced renal damage.

Both cortical and medullary ADC values of patients with CKD correlated inversely with serum creatinine and blood urea nitrogen. The decreasing ADC values from stages 1 to 5 CKD reflected severity of renal damage and are in accordance with literature reports [11, 22, 23].

There was no difference in the cortical and medullary FA values between the right and left kidneys. Lu et al. [20] observed medullary FA was significantly lower in diabetics compared to healthy controls, and medullary FA correlated significantly with eGFR. Hueper et al. [24] have attempted to assess renal allograft dysfunction with DTI, and reported that the renal FA reduced in renal allograft patients. In our study, compared to normal kidneys, the cortical and medullary FA values of patients with CKD were lower, and the numbers of radially oriented collecting tubules on the DTT maps were also reduced and shortened. The statistically insignificant
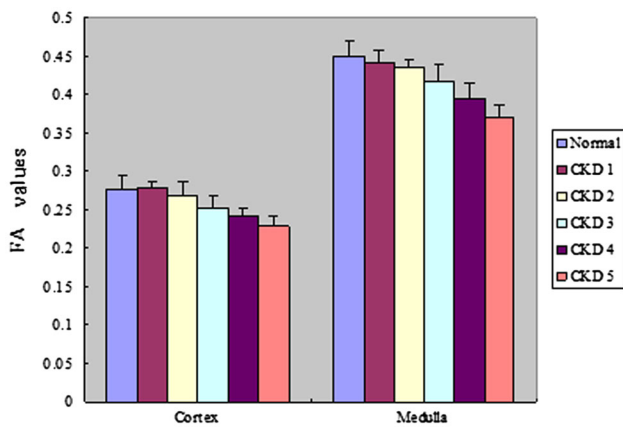
Fig. 7. The bar graph of the average renal cortical and medullary FA values from normal to CKD stage 5.

Table 3. Comparison of average renal FA values in healthy volunteers and patients with CKD

	Cortex	Medulla
Normal	$0.277 \pm 0.018^{d,e,f}$	$0.450 \pm 0.019^{c,d,e,f}$
CKD 1	$0.278 \pm 0.010^{d,e,f}$	$0.441 \pm 0.017^{d,e,f}$
CKD 2	$0.270 \pm 0.016^{d,e,f}$	$0.434 \pm 0.012^{a,d,e,f}$
CKD 3	$0.251 \pm 0.018^{a,b,c,f}$	$0.417 \pm 0.023^{a,b,c,e,f}$
CKD 4	$0.241 \pm 0.011^{a,b,c}$	$0.394 \pm 0.020^{a,b,c,d,f}$
CKD 5	$0.229 \pm 0.012^{a,b,c,d}$	$0.369 \pm 0.018^{a,b,c,d,e}$
F	25.082	46.735
P	0.000	0.000

[a] $P < 0.05$ compared with normal
[b] $P < 0.05$ compared with CKD 1
[c] $P < 0.05$ compared with CKD 2
[d] $P < 0.05$ compared with CKD 3
[e] $P < 0.05$ compared with CKD 4
[f] $P < 0.05$ compared with CKD 5

decrease in FA values of patients with stages 1–2 CKD may be result of mild renal damage as reflected by the normal serum creatinine and blood urea nitrogen. Glomerulosclerosis, interstitial fibrosis, and tubule atrophy or destruction in patients with stages 2–5 CKD may account for the reduction and shortening of tubules demonstrated on DTT maps. The cortical or medullary FA values correlated inversely with serum creatinine and blood urea nitrogen. The FA values decreased with the increasing stages of CKD reflecting severity of renal damage.

Our study is limited by the low image resolution of renal DTI and small sample size of CKD. Future studies with improved MRI hardware and software, as well as larger patient samples will be helpful to confirm our current findings of inverse relationship of ADC and FA values with severity of renal damage. Renal DTI may be a useful non-invasive imaging tool for detecting changes in renal structure without radiation and contrast injection.

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