Original Article

Preliminary study on intravoxel incoherent motion imaging and diffusion kurtosis imaging based on magnetic resonance imaging of normal kidneys in children

Zhe Yan[1,2], Lihua Chen[3], Wen Shen[3], Lu Dong[2], Chunxiang Wang[2], Yong Guan[4], Meimin Zheng[2], Ying Li[2], Chen Zhang[5], Robert Grimm[6]

[1]Department of Radiology, First Central Clinical College, Tianjin Medical University, Tianjin, China; [2]Department of Radiology, Tianjin Children's Hospital (Tianjin University Children's Hospital), Tianjin, China; [3]Department of Radiology, Tianjin First Central Hospital, School of Medicine, Nankai University, Tianjin, China; [4]Department of Urology Surgery, Tianjin Children's Hospital (Tianjin University Children's Hospital), Tianjin, China; [5]MR Scientific Marketing, Siemens Healthineers, Beijing, China; [6]Siemens Healthcare GmbH, Erlangen, Germany

Contributions: (I) Conception and design: Z Yan; (II) Administrative support: W Shen, C Wang, Y Guan; (III) Provision of study materials or patients: M Zheng, Y Li; (IV) Collection and assembly of data: L Dong, C Zhang, R Grimm; (V) Data analysis and interpretation: Z Yan, L Chen; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Wen Shen. Department of Radiology, Tianjin First Central Hospital, School of Medicine, Nankai University, 24 Fukang Road, Nankai District, Tianjin 300192, China. Email: shenwen66happy@126.com.

Background: Renal disease in children may lead to a continuous decline of renal function. Multimodal functional magnetic resonance imaging (fMRI) technology can provide quantitative evaluation of renal function information. We investigated the feasibility of intravoxel incoherent motion imaging (IVIM) and diffusion kurtosis imaging (DKI) based on 3.0T MRI for the assessment of normal renal function in children and then analyzed the changes in functional parameters during development.

Methods: A total of 132 children with normal function of both kidneys were grouped according to age: ≤1 year old, 1–≤2 years old, 2–≤3 years old, 3–≤10 years old, and 10–≤14 years old. All subjects received renal IVIM examinations to obtain the measured values of true diffusion coefficient (D), pseudo diffusion coefficient (Dp), perfusion fraction (f), and DKI examinations to obtain the mean diffusivity (MD) and mean kurtosis (MK) parameters of both kidneys. The differences of IVIM and DKI function indexes between the upper, middle and lower poles of the normal ipsilateral kidney, between the left and right kidneys, and between the renal cortex and medulla were compared. The correlations between the above parameters and age were analyzed.

Results: There was no significant difference in the IVIM and DKI parameters between the upper, middle and lower poles in the ipsilateral kidney. There was no significant difference between bilateral kidneys. The D, MD, and MK values of the renal cortex and medulla at the same age were statistically different. The D and MD values of the renal cortex were higher than those of the medulla; the MK value of the renal medulla was higher than that of the cortex. The Dp and f values of the renal cortex and medulla were not statistically different. Except for Dp, all functional parameters of the remaining renal cortex and medulla were related to age.

Conclusions: IVIM and DKI functional imaging of children's normal kidneys can reflect the physiological characteristics and differences in the renal cortex and medulla, and their functional parameters have particular regularity with growth and development, suggesting that this technique has potential application value in children's kidney diseases.

Keywords: Child; normal kidney; intravoxel incoherent motion imaging (IVIM); diffusion kurtosis imaging (DKI)

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Introduction

With the development of functional magnetic resonance imaging (fMRI), diffusion-weighted imaging (DWI) and diffusion tensor imaging (DTI) technologies are becoming more mature and have been increasingly applied to various diseases of the kidney (1). Intravoxel incoherent motion imaging (IVIM) reflects the degree of water molecule diffusion more realistically than traditional DWI (2). Diffusion kurtosis imaging (DKI), as an extension of DTI technology, reflects the diffusion state of the non-Gaussian distribution of water molecules and the complexity of tubule structures (3,4). In additional, clinical detection methods for evaluating renal function include serum biochemical indicators (such as creatinine), isotope tracer detection of glomerular filtration rate (GFR), but there are deficiencies such as low early sensitivity. Imaging methods, such as ultrasound, CT urography and intravenous pyelography, mainly reflect the morphological changes of the kidney and can provide limited information on renal function. Therefore, our study provides a new non-invasive examination for clinical evaluation of renal function. Based on the functional imaging of IVIM and DKI in normal children's kidneys, this study investigated the characteristics of the normal renal cortex and medulla function parameters in children at different developmental stages and how their changes correspond to the physiological structure of the kidney in order to evaluate the feasibility of using IVIM and DKI sequences in children's kidney diseases. We hope that our findings can provide guidance for further research on kidney disease. We present the following article in accordance with the MDAR reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-22-558/rc).

Highlight box

Key findings
- IVIM and DKI functional imaging of children's normal kidneys can reflect the physiological characteristics and differences in the renal cortex and medulla, and their functional parameters have particular regularity with growth and development.

What is known and what is new?
- The potential value of IVIM and DKI imaging in evaluating renal function have confirmed.
- Our study explored the changes in IVIM and DKI function parameters in the normal renal cortex and medulla during childhood and found that these changes were related to age.

What is the implication, and what should change now?
- IVIM and DKI function parameters can provide relative quantitative levels for different age groups, which may have potential application value in children's kidney diseases.

Methods

Study population

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics board of Tianjin Children's Hospital (No. EC-20190802-1151), and informed consent was obtained from the children's legal guardians before examination.

A total of 132 children under 14 years old with normal morphology and function of both kidneys were enrolled, including 75 males and 57 females. They were divided into five groups according to age: ≤1 year (n=26), >1–2 years (n=20), >2–3 years (n=32), >3–10 years (n=25) and >10–14 years (n=29).

The inclusion criteria were as follows: children (I) without primary or secondary renal disease; (II) without abnormalities in renal function or routine urine examination after admission; (III) without abnormalities in renal ultrasound or routine MRI examination; (IV) who had not taken medications affecting kidney function (such as diuretics).

The exclusion criteria consisted of children (I) with primary or secondary renal disease; (II) with pre-renal or post-renal factors affecting renal metabolism (such as fever, dehydration, renal artery stenosis, or nutcracker syndrome); (III) with abnormalities evident on renal ultrasound and routine MRI examination; (IV) who had taken drugs affecting renal function (such as diuretics); (V) who were premature or growth retarded; (VI) with contraindications for MRI.

Imaging protocol

Subjects were instructed not to drink water 1 hour before the examination. If they could not cooperate with the examination, a 6.5% chloral hydrate (0.8 mL/kg) solution was taken orally for sedation. Subjects who were able to cooperate with the examination in the awake state underwent prior breathing training. The MRI was performed with a Siemens Skyra 3.0T scanner (Siemens Healthcare, Erlangen, Germany). Subjects were laid in the supine position, and their body surface was covered with an 18-channel body coil with the renal region as the center. The scanning sequence included coronal T2-weighted imaging (T2WI), axial T1-weighted imaging (T1WI), fat-suppressed T2WI, IVIM, and DKI. Simultaneous multi-slice (SMS) was used to complete the IVIM and DKI sequences in one scan and combined with a single shot-echo planar imaging (SS-EPI) sequence with multi-b values (0, 10, 20, 30, 50, 100, 200, 300, 500, 800, 1,000, 1,500, and 2,000 s/mm^2) for coronal scanning with the level of the renal hilum as the center (5).

Image processing and data analysis

The multi-b value raw images were imported into a post-processing software package (MR Body Diffusion Toolbox V1.4.0; Siemens Healthcare, Erlangen, Germany) for measurement and analysis, followed by the generation of functional parameter maps related to IVIM and DKI, respectively. In the IVIM analysis, 0, 10, 20, 30, 50, 100, 200, 300, 500, and 800 s/mm^2 were selected using the software to generate the true diffusion coefficient (D), pseudo diffusion coefficient (Dp), and perfusion fraction (f) maps. In the DKI analysis, 0, 500, 1,000, 1,500, and 2,000 s/mm^2 were selected using the software to generate the mean diffusivity (MD) and mean kurtosis (MK) maps.

All images were measured in a double-blind manner by two chief physicians. The region of interest (ROI) was selected on the coronal plane near the renal hilum at a b value of 0 s/mm^2. Subsequently, the cortex and medulla of the upper, middle, and lower poles in both kidneys were manually delineated, avoiding the artifacts caused by the interference of blood vessels, renal sinuses, and intestinal gas. The ROI was automatically copied to other functional parameter maps in the same layer.

Statistical analysis

The data were analyzed by SPSS 25.0 statistical software. The intra-class correlation coefficient (ICC) was used to analyze the interrater consistency. An ICC greater than or equal to 0.75 was considered to represent good consistency, an ICC between 0.40–0.75 indicated medium consistency, and an ICC less than 0.40 was considered to represent poor consistency. The measurement data are presented as means ± standard deviations (SD). The paired samples *t*-test was used to compare the functional parameters between the cortex and medulla of normal kidneys in the same age group. A one-way ANOVA and independent-samples *t*-test were used to compare the functional parameters of the normal renal cortex and medulla between different age groups and genders. A Pearson linear correlation analysis was used to investigate the association between the functional parameters and the subjects' age. A P value <0.05 indicated that the difference was statistically significant.

Results

IVIM and DKI MRI of normal kidneys

The multi-b value imaging of normal kidneys in children of different ages was of good quality and had no obvious artifacts (*Figure 1*). When the b value was less than 1,000 s/mm^2, images showed that the renal cortex and medulla demarcation was clearly discernible, and the cortex signal was higher than that of the medulla (*Figure 1*).

The IVIM parametric maps (D, Dp, and f) and DKI parametric maps (MD and MK) were of good quality with no obvious artifacts, and the outline of the kidneys was clearly visible. Among them, the cortex and medulla were roughly distinguished in the f and MD maps, and the demarcation of the cortex and medulla on the D, Dp, and MK maps was unclear (*Figure 2*).

Reliability investigation of IVIM and DKI functional parameters

The D value derived from IVIM and the MD and MK values derived from DKI had good consistency, with a mean ICC of 0.812, 0.887, and 0.865, respectively. However, the consistencies of the Dp and f values derived from IVIM were medium, with a mean ICC of 0.675 and 0.713, respectively. It is worth noting that the parameters for children under 1 year old or even under 3 months old were also stable, indicating that the reliability for younger children was also high.

Analysis of IVIM and DKI functional parameters in the cortex and medulla of the kidneys

The results showed no significant difference in the IVIM and DKI parameters of the medulla between the upper, middle, and lower poles in the ipsilateral kidney (*Table 1*). Additionally, the IVIM and DKI parameters of the cortex and medulla between the left and right kidneys were not statistically different (*Table 2*). Therefore, the average value of each parameter was used as the final measurement result

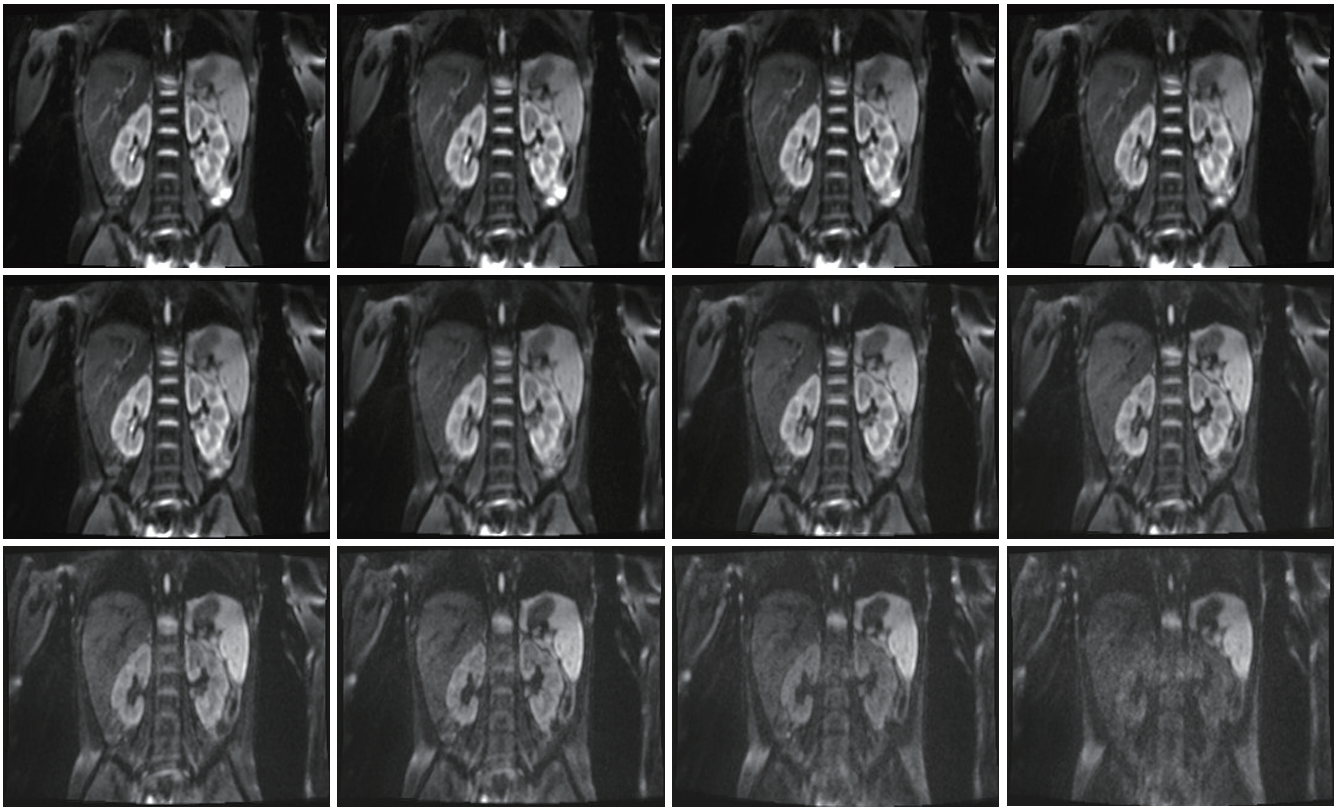

Figure 1 DWI images of normal bilateral kidneys with different b values in 3-year-old children. The images with multi-b values (10, 20, 30, 50, 100, 200, 300, 500, 800, 1,000, 1,500, 2,000 s/mm^2) are shown from left to right and from top to bottom. When the b value was less than 1,000 s/mm^2, the renal cortex and medulla were clearly demarcated, and the cortex signal was higher than that of the medulla. At higher b values, the kidney contour was clear, indicating that the multi-b values DWI image quality for young children may be superior. DWI, diffusion weighted imaging.

of the entire cortex and medulla of both kidneys for the subsequent statistical analysis.

Analysis of IVIM and DKI functional parameters between the normal renal cortex and medulla in the same age group

As displayed in *Table 3*, the D, MD, and MK values between the renal cortex and medulla were statistically different in the same age group ($P<0.05$). Of these, the D and MD values of the renal cortex were significantly higher than the medulla, while the MK value of the renal medulla was higher than the renal cortex. Additionally, the Dp and f values of the renal cortex were slightly higher than those of the medulla, but the differences were not statistically significant ($P>0.05$).

Correlation analysis between IVIM and DKI functional parameters of normal kidneys and age or gender

As displayed in *Tables 4,5*, there were statistical differences in the values of various functional parameters between the normal renal cortex and renal medulla in different age groups, and the differences between groups gradually decreased with age. There were no statistical differences in the functional parameter values between the normal renal cortex and medulla and gender. With growth and development, the D, MD, Dp, and f values of the renal cortex and medulla gradually increased. In contrast, the MK value of the renal cortex and medulla gradually decreased. The Dp value had no significant correlation with age, but the D, f, and MD values of the renal cortex and medulla were positively correlated with the subject's age. The MK values of the renal cortex and medulla were negatively

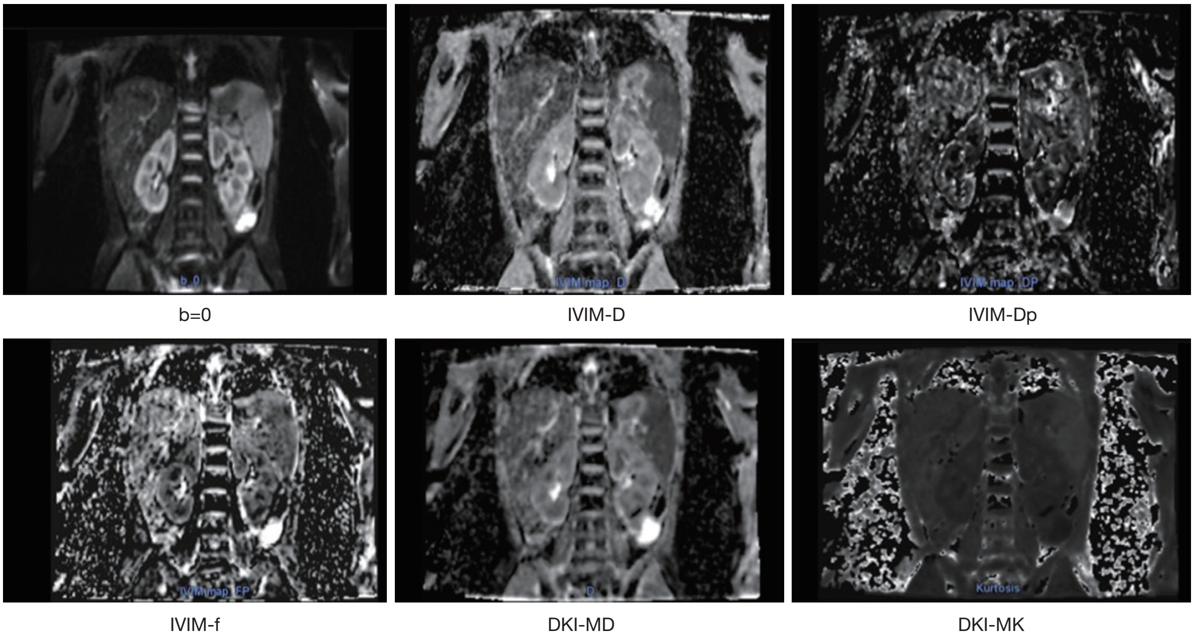

Figure 2 The IVIM and DKI parameters of normal kidneys in 3-year-old children. The image quality of D, Dp, and f values of the IVIM sequence and the MD and MK values of the DKI sequence of the normal kidney are good, and the outline of the kidney is clear. The f and MD images can roughly distinguish the cortex and medulla, while the boundaries of the D, Dp, and MK maps are not clear. IVIM, intravoxel incoherent motion; DKI, diffusion kurtosis imaging; D, true diffusion coefficient; Dp, pseudo diffusion coefficient; f, perfusion fraction; MD, mean diffusivity; MK, mean kurtosis.

Table 1 Comparison of IVIM and DKI parameters in the normal renal medulla

Location	IVIM-D (10^{-3} mm^2/s)	IVIM-Dp (10^{-3} mm^2/s)	IVIM-f (%)	DKI-MD (10^{-3} mm^2/s)	DKI-MK
LU	1.35±0.25	17.01±4.17	16.81±2.92	1.80±0.34	0.68±0.06
LM	1.38±0.25	17.25±4.00	16.82±2.94	1.80±0.35	0.68±0.07
LL	1.35±0.26	17.22±4.60	16.54±3.14	1.83±0.40	0.67±0.08
RU	1.39±0.25	17.76±4.35	16.97±3.16	1.78±0.38	0.68±0.08
RM	1.39±0.24	18.01±4.51	16.98±3.26	1.76±0.41	0.68±0.09
RL	1.41±0.26	17.86±5.02	17.25±3.27	1.81±0.50	0.70±0.14
F	1.352	1.103	0.746	0.452	1.617
P	0.240	0.358	0.589	0.812	0.153

Data are presented as mean ± standard deviation except for F or P. IVIM, intravoxel incoherent motion; DKI, diffusion kurtosis imaging; D, true diffusion coefficient; Dp, pseudo diffusion coefficient; f, perfusion fraction; MD, mean diffusivity; MK, mean kurtosis; LU, left-upper; LM, left-middle; LL, left-lower; RU right-upper; RM, right-middle; RL, right-lower.

Table 2 Comparison of IVIM and DKI parameters in the cortex and medulla of normal bilateral kidneys

Location	IVIM-D (10^{-3} mm^2/s)	IVIM-Dp (10^{-3} mm^2/s)	IVIM-f (%)	DKI-MD (10^{-3} mm^2/s)	DKI-MK
Cortex					
L	1.55±0.22	18.34±3.35	18.33±5.30	2.13±0.37	0.61±0.06
R	1.58±0.20	18.47±4.27	17.35±5.75	2.17±0.54	0.60±0.08
t	1.404	0.304	1.445	0.723	1.568
P	0.161	0.761	0.150	0.471	0.118
Medulla					
L	1.36±0.25	17.16±4.12	16.72±2.86	1.80±0.34	0.68±0.06
R	1.40±0.25	17.88±4.51	17.07±3.06	1.79±0.41	0.69±0.08
t	1.445	1.346	0.942	0.327	0.999
P	0.150	0.180	0.347	0.744	0.319

Data are presented as mean ± standard deviation except for *t* or P. IVIM, intravoxel incoherent motion; DKI, diffusion kurtosis imaging; D, true diffusion coefficient; Dp, pseudo diffusion coefficient; f, perfusion fraction; MD, mean diffusivity; MK, mean kurtosis; L, left kidney; R, right kidney.

correlated with age. The D and MD values of the renal cortex and the MK value of the renal medulla strongly correlated with age, as shown in *Figure 3*.

Discussion

As we know, the embryonic kidney comprises a cortex and medulla, and the total number of nephrons is generally formed at about 36 weeks of gestational age (6). There is no obvious difference in the structure, composition, or distribution between the embryonic and adult kidney. Additionally, the physiological function of children's kidneys is no different from that of adults. Specifically, the renal cortex is richer in blood supply than the medulla, and the structure is arranged without obvious regularity. The activity of water molecules is very active due to the formation of original urine in the glomeruli and water reabsorption by the proximal and distal convoluted tubules. However, the renal medulla comprises renal tubular loops, collecting ducts, and other structures, which are regularly arranged radially, leading to water molecule activity with obvious directionality. There is a specific difference in the degree of water molecule diffusion between the cortex and medulla, and these anatomical and physiological characteristics have laid the foundation for renal function imaging. Children are in a stage of growth and development, and kidney function in the neonatal period has not yet fully matured. After birth, kidney function continues to improve, reaching the adult level at about 2 years old (7). Those changes may be related to individual factors such as age (8), and we can follow these growth rules to explore the functional characteristics of the kidney-related microstructures.

Regarding the IVIM functional parameters of normal kidneys in children, most studies have confirmed the potential value of IVIM imaging in evaluating renal function, and its parameters (D, Dp, and f values) can reflect water molecule diffusion and perfusion information (9,10). In the current study, the IVIM results showed that the D value of the normal renal cortex in the same age group was higher than that of the medulla, and this difference was statistically significant. This finding may be related to the relatively free diffusion of water molecules in the urine generated by glomerular filtration of the renal cortex and the limited diffusion of water molecules in the radially arranged tubules of the renal medulla, consistent with previous reports (11). However, the Dp and f values between the cortex and medulla of normal kidneys were not remarkably different. The abovementioned parameters differed from previous study, which may be associated with the low stability of the Dp and f values (6). Although the stability of the Dp and f values were lower than other parameters in our study, the large number of low-b values were set in order to improve accuracy. Because the blood flow of the renal cortex is richer than that of the medulla and there is a secondary capillary network, the Dp and f values of the renal cortex are slightly higher than those

Table 3 Comparison of IVIM and DKI parameters between the normal renal cortex and medulla in the same age group

Groups	IVIM-D (10^{-3} mm^2/s)	IVIM-Dp (10^{-3} mm^2/s)	IVIM-f (%)	DKI-MD (10^{-3} mm^2/s)	DKI-MK
≤1 year					
Cortex	1.37±0.13	16.90±2.97	15.47±1.54	1.68±0.18	0.67±0.05
Medulla	1.16±0.15	15.73±3.07	14.78±1.40	1.5±0.14	0.78±0.03
t	0.543	1.397	1.679	4.114	10.111
P	0.000	0.169	0.099	0.000	0.000
>1–2 years					
Cortex	1.44±0.15	17.38±3.15	16.39±3.22	1.99±0.20	0.61±0.04
Medulla	1.30±0.12	17.14±4.49	15.65±1.67	1.74±0.28	0.72±0.01
t	3.299	0.193	0.916	3.270	11.727
P	0.020	0.848	0.365	0.002	0.000
>2–3 years					
Cortex	1.53±0.08	18.46±2.96	17.85±2.19	2.14±0.16	0.60±0.02
Medulla	1.39±0.13	17.45±2.90	16.83±2.23	1.77±0.18	0.68±0.01
t	5.283	1.383	1.845	8.485	22.202
P	0.000	0.172	0.070	0.000	0.000
>3–10 years					
Cortex	1.69±0.15	19.26±3.41	18.91±3.52	2.28±0.26	0.58±0.02
Medulla	1.45±0.12	18.11±3.82	17.86±2.46	1.88±0.26	0.64±0.01
t	6.035	1.121	1.222	5.547	14.493
P	0.000	0.268	0.228	0.000	0.000
>10–14 years					
Cortex	1.78±0.14	19.67±3.25	20.05±4.20	2.57±0.18	0.57±0.03
Medulla	1.55±0.15	18.94±4.74	18.89±3.23	2.04±0.22	0.60±0.02
t	6.030	0.682	1.185	9.674	4.545
P	0.000	0.498	0.241	0.000	0.000

Data are presented as mean ± standard deviation except for *t* or P. IVIM, intravoxel incoherent motion; DKI, diffusion kurtosis imaging; D, true diffusion coefficient; Dp, pseudo diffusion coefficient; f, perfusion fraction; MD, mean diffusivity; MK, mean kurtosis.

of the medulla. These findings are consistent with the physiological characteristics of renal blood flow distribution.

On the other hand, DKI is utilized to reflect the non-Gaussian diffusion state of water molecules, especially in the renal medulla region. The MD and MK values derived from DKI can more accurately evaluate the true diffusion of water molecules (12). Our study indicated that the MD and MK values between the cortex and medulla of normal kidneys in the same age group were statistically different, which was also consistent with the multidirectional arrangement of tubules in the medulla. Among them, the MD value reflects the degree of water molecule diffusion in the non-Gaussian distribution, and the MK value reflects the complexity of the microstructures (13). The complexity of the tubule arrangements in the medulla makes the diffusion of non-Gaussian water molecules more restricted than that in the cortex, so the MD value of the cortex is higher than that of the medulla, and the MK value of the medulla is higher than that of the cortex, which is consistent with our results (14). As a functional imaging

Table 4 Comparison of IVIM and DKI parameters in the normal renal cortex between different age groups

Groups	IVIM-D (10^{-3} mm^2/s)	IVIM-Dp (10^{-3} mm^2/s)	IVIM-f (%)	DKI-MD (10^{-3} mm^2/s)	DKI-MK
≤1 year[1]	1.38±0.13[3,4,5]	16.90±2.97[4,5]	15.47±1.54[3,4,5]	1.68±0.18[2,3,4,5]	0.67±0.05[2,3,4,5]
>1–2 years[2]	1.44±0.15[3,4,5]	17.38±3.15[4,5]	16.39±3.22[4,5]	1.99±0.20[3,4,5]	0.61±0.04[4,5]
>2–3 years[3]	1.53±0.08[4,5]	18.46±2.96	17.85±2.19[5]	2.14±0.16[4,5]	0.60±0.02[5]
>3–10 years[4]	1.69±0.15[5]	19.26±3.41	18.91±3.52	2.28±0.26[5]	0.58±0.02
>10–14 years[5]	1.78±0.14	19.67±3.25	20.05±4.2	2.57±0.18	0.57±0.03
F	43.636	3.650	9.516	75.105	34.626
P	0.000	0.008	0.000	0.000	0.000

Data are presented as mean ± standard deviation except for F or P. Superscript numbers represent P<0.05 between age groups. [1], stands for ≤1 year old; [2], stands for >1–2 years old; [3] stands for >2–3 years old; [4], stands for >3–10 years old; [5], stands for >10–14 years old. IVIM, intravoxel incoherent motion; DKI, diffusion kurtosis imaging; D, true diffusion coefficient; Dp, pseudo diffusion coefficient; f, perfusion fraction; MD, mean diffusivity; MK, mean kurtosis.

Table 5 Comparison of IVIM and DKI parameters in the normal renal medulla between different age groups

Groups	IVIM-D (10^{-3} mm^2/s)	IVIM-Dp (10^{-3} mm^2/s)	IVIM-f (%)	DKI-MD (10^{-3} mm^2/s)	DKI-MK
≤1 year[1]	1.16±0.15[2,3,4,5]	15.73±3.07[4,5]	14.78±1.40[3,4,5]	1.50±0.14[2,3,4,5]	0.78±0.03[2,3,4,5]
>1–2 years[2]	1.30±0.12[3,4,5]	17.14±4.49	15.65±1.67[4,5]	1.74±0.28[4,5]	0.72±0.01[3,4,5]
>2–3 years[3]	1.39±0.13[5]	17.45±2.90	16.83±2.23[5]	1.77±0.18[5]	0.68±0.01[4,5]
>3–10 years[4]	1.45±0.12	18.11±3.82	17.86±2.46	1.88±0.26	0.64±0.01[5]
>10–14 years[5]	1.55±0.15	18.94±4.74	18.89±3.23	2.04±0.22	0.60±0.02
F	32.281	2.618	13.073	23.313	473.105
P	0.000	0.038	0.000	0.000	0.000

Data are presented as mean ± standard deviation except for F or P. Superscript numbers represent P<0.05 between age groups. [1], stands for ≤1 year old; [2], stands for >1–2 years old; [3] stands for >2–3 years old; [4], stands for >3–10 years old; [5], stands for >10–14 years old. IVIM, intravoxel incoherent motion; DKI, diffusion kurtosis imaging; D, true diffusion coefficient; Dp, pseudo diffusion coefficient; f, perfusion fraction; MD, mean diffusivity; MK, mean kurtosis.

technique to quantify the movement of non-Gaussian water molecules, the DKI model is closer to the human internal environment, suggesting that MD and MK can better reflect the differences in the physiological characteristics of the renal cortex and medulla than IVIM functional parameters.

Especially in children under 2 years old, the renal structure and physiological mechanisms continue to mature, and their functional parameters may change accordingly (4,5). Similarly, the calculation formula of the glomerular filtration rate in children also suggests that it is related to factors such as age and height. Therefore, in our study, the age groupings were more detailed in the younger years, and the age span was broadened for older children. Our study preliminarily explored the changes in IVIM and DKI function parameters in the normal renal cortex and medulla during childhood and found that these changes were related to age. Beyond that, we concluded that there was no statistical difference in the functional parameters of the normal renal cortex and medulla between different genders.

With increasing age, the renal blood flow increases, the parenchyma thickens, the area of filtration and reabsorption increases, and the amplitude and speed of water molecule movement increases. Therefore, the D and MD values reflecting the degree of water molecule diffusion and the Dp and f values reflecting renal perfusion information all increase with age. The MK value was used to quantify the deviation degree of diffusion displacement of water molecules. We found that the MK values of the subjects' cortex and medulla decreased slightly with

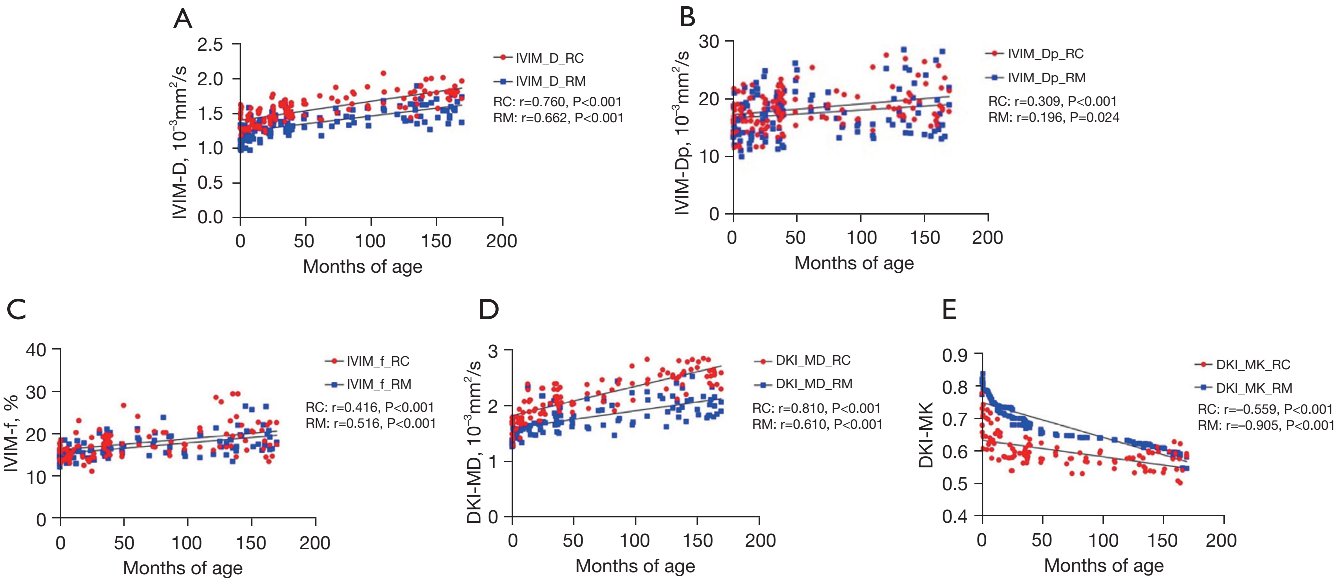

Figure 3 Correlations between the IVIM and DKI parameters of the normal kidney cortex and medulla and age. IVIM, intravoxel incoherent motion; DKI, diffusion kurtosis imaging; D, true diffusion coefficient; Dp, pseudo diffusion coefficient; f, perfusion fraction; MD, mean diffusivity; MK, mean kurtosis; RC, renal cortex; RM, renal medulla.

age, which may be related to the widening of the pipe diameter of the water molecules flow pipe, the reduction of the pipe wall's restriction on its movement, and the more dispersed diffusion direction. The results indicated that the correlation of the D and MD values of the renal cortex and the MK value of the renal medulla with age was more pronounced. We should pay more attention to these parameters in future research and speculate that they can provide quantitative information on corticomedullary function during growth and development.

The limitations of this study should be noted. First, this study was conducted in a single center with a small sample size. Second, the selection of the b values was based on empirical assignment. The number of its settings and how to further ensure the signal-to-noise ratio of images for high b values needs to be further studied (15). Lastly, the manual delineation of the ROI may have led to measurement errors.

IVIM and DKI as imaging techniques to comprehensively evaluate the shape and function of children's kidneys, are highly repeatable and have great clinical application prospects. With the further improvement of functional sequence and the gradual standardization of post-processing software, the combined application of multimodal fMRI technology can provide more valuable information on renal function. For children, the scanning scheme should be reasonably configured to shorten the scanning time as much as possible. In our research, SMS technology is used to achieve one-time acquisition of functional images and ensure adequate image quality. It is feasible to study IVIM and DKI of normal kidney in children. On the basis of IVIM and DKI studies on children's normal kidneys, combined with clinical data such as biochemical indicators of renal function, it is possible to effectively carry out relevant studies on children's kidney diseases, but further clinical validation of multi center and multi method is still needed.

Conclusions

IVIM and DKI reflect the physiological and microstructure characteristics of different parts of children's kidneys and provide a relative quantitative level for different age groups. These findings indicate that fMRI may have potential application value in the pathological state of children's kidneys.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics board of Tianjin Children's Hospital (No. EC-20190802-1151), and informed consent was obtained from the children's legal guardians before examination.

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