Using intravoxel incoherent motion MR imaging to predict vesicoureteral reflux in children with upper urinary tract infection: preliminary results

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**Purpose**

Vesicoureteral reflux is the abnormal flow of urine from the urinary bladder to the upper urinary tract. VUR is often diagnosed after urinary tract infection (UTI). VUR predisposes children with UTI to pyelonephritis by facilitating bacteria to spread from the lower urinary tract to the kidney. In children with UTI, renal scarring develops more likely than children without VUR, probably because of the increased risk of renal involvement. Renal scarring may lead to hypertension and chronic renal failure.

Voiding cystourethrography (VCUG) is the method of choice for diagnosis of VUR. VCUG has advantages of allowing a reliable grading of VUR and providing fine anatomic details of the urinary systems, but radiation exposure and invasive catheterization are main problems of VCUG.

Intravoxel incoherent motion (IVIM) diffusion-weighted imaging (DWI) is a concept introduced and developed by Le Bihan et al. to quantitatively assess the microscopic translations that occur in each image voxel during MRI. Using IVIM DWI, pure molecular diffusion parameters and perfusion-related diffusion parameters can be separated. We postulated diffusion parameters of IVIM DWI could be affected by flow in the renal pelvis.

Therefore, the purposes of our study are to compare diffusion parameters of IVIM DWI between "reflux" and "non-reflux" kidneys, and to evaluate feasibility of IVIM DWI in predicting VUR in children with UTI.
Methods and materials

1. Patients

This retrospective study was approved by our institutional review board and the requirement for informed consent was waived. Between May 2011 and September 2013, Sixty-three kidneys of 39 pediatric patients with UTI who underwent MR urography were included and classified into "reflux" and "non-reflux" groups according to the presence of VUR on VCUG.

2. MR methods and IVIM-DWI

Axial diffusion weighted single shot EPI (DWI) (TR/TE, 3420/57 ms; matrix size, 128 X 128; slice thickness and gap; 4/0 mm; b-values of 0, 25, 50, 75, 100, 200, 500, and 800 s/mm2; acquisition time, 3min 36 s) and coronal DWI (TR/TE, 3420/57ms; matrix size, 128 X 128; slice thickness and gap; 3.5/0 mm; b-values of 0, 25, 50, 75, 100, 200, 500, and 800 s/mm2; acquisition time, 3 min 36 s) were obtained with simultaneous use of respiratory triggering method. The acquisition time for DWI was approximately 3 min 30 s to 4 min, respectively.

Diffusion data were calculated by a prototype IVIM postprocessing tool provided by the manufacturer(Siemens, Erlangen, Germany) and by a MATLAB(Mathworks, USA) based SW developed at the institution. Based on the IVIM theory, the relative signal was calculated using the following equation:

\[
\frac{S_b}{S_0} = (1-f) \exp(-bD) + f \exp[-b(D+D^*)]
\]  

Where b represents the strength of the diffusion gradient, S0 is the signal intensity without a diffusion gradient, Sb is the signal intensity at a given b value, f is the microvascular volume fraction, D is the pure diffusion coefficient, and D* is the perfusion-related incoherent microcirculation. Both the Siemens IVIM postprocessing approach and the MATLAB analysis approach use fully bi-exponential nonlinear curve fitting for unknown parameters (D, D*, and f). Considering that D* is significantly greater than D, the effects of D* on the signal decay at large b values (>200 s/mm2) can be neglected. Thus, at higher b values, Eq. [A] can be simplified into a linear fit equation from which D can be estimated:

\[
S_b = S_0 \exp(-bD)
\]

Based on the value of D calculated using Eq. [B], f and D* values can then be calculated by using a partially constrained nonlinear regression algorithm based on Eq. [A]
3. Imaging analysis

All MR images were independently reviewed by one radiologist who were blinded to the VCUG results. All images were evaluated with a 2048 X 2560 PACS (Coronis 5MP; Braco, Belgium) monitor.

Circular regions-of-interest (ROI) were manually positioned on renal pelvis on DW images and ADC maps. All images were displayed synchronously and all ROIs were directly co-localized on all parameter maps. For each ROI, the mean value of each parameter (ADC, D, D*, f) derived from pixel-by-pixel analysis was computed. The value of the ROIs was measured three times and we used mean value of the measurements to compare two groups.

Four indices (D*/ADC, F/ADC, D*/D, and F/D) were also calculated and ROC curve analyses were performed for each index to identify optimal cut-off value that can predict VUR.
Fig. 1: Circular regions-of-interest (ROI) were manually positioned on renal pelvis.

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Fig. 2: All images were displayed synchronously and all ROIs were directly co-localized on all parameter maps

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Results

VURs were detected in 17 kidneys on VCUG.

In "reflux" group, ADC values were significantly lower

\[2.87 \pm 0.27 \text{ vs. } 3.15 \pm 0.39 \times 10^{-3} \text{mm}^2/\text{sec}, \ p = 0.004\], and D* and f values were significantly higher than "non-reflux" group

\[41.50 \pm 12.38 \text{ vs. } 30.01 \pm 10.47 \times 10^{-3} \text{mm}^2/\text{sec}, \ p < 0.001, \text{ and } \]
\[0.31 \pm 0.12 \text{ vs. } 0.22 \pm 0.14, \ p = 0.018, \text{ respectively}\).

Four indeces(D*/ADC, F/ADC, D*/D, and F/D) were all significantly higher in "reflux" group than "non-reflux" group(p=0.004,<0.001,<0.001 and 0.011,respectively). Among them, area under ROC curve for D*/ADC was highest(0.803), and optimal cut-off value of 10.87 corresponded to 82.35% sensitivity and 71.74% specificity for detecting VUR.
Fig. 3: Four indices (D*/ADC, F/ADC, D*/D, and F/D) were all significantly higher in "reflux" group than "non-reflux" group. Among them, area under ROC curve for D*/ADC was highest.

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Fig. 4: ROC curve analysis for D*/ADC. Optimal cut-off value of 10.87 corresponded to 82.35% sensitivity and 71.74% specificity for detecting VUR.

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Conclusion

D* and f values are significantly higher and ADC values are significantly lower in renal pelvis of "reflux" kidney than "non-reflux" kidney. Our new index(D*/ADC) can be useful for predicting VUR.
References
