Diffusion-weighted Imaging using a Statistical Model as a Functional MRI of the Kidney: Preliminary Experience

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Target audience: Clinicians interested in renal diffusion-weighted imaging.

Introduction: Diffusion-weighted imaging (DWI) was reported as a potential approach to assess renal function and fibrosis. Several studies revealed that the apparent diffusion coefficient (ADC) of the kidney using mono-exponential model had a good correlation with the glomerular filtration rate (GFR). However, this approach is insufficient for describing *in vivo* proton diffusion because a mono-exponential model does not consider heterogeneous biological structures that interfere with free diffusion. Statistical model is a non-Gaussian model of DWI proposed by Yablonskiy et al[1]. Statistical model is an approach that presumes a continuous distribution of diffusion coefficients within an imaging voxel, potentially providing physiological information as demonstrated in the human brain. Recently, Oshio et al. and Shinmoto et al. reported the application of the statistical model in prostate cancer[2,3]. In their reports, histological interpretation of diffusion data seemed possible by introducing the concept of the area fraction for diffusion coefficient D<1.0 mm^2/s (Frac<1) and the fraction of D>3.0 mm^2/s (Frac>3) as parameters representing restricted diffusion and perfusion, respectively. In this study, we used DWI with the statistical model to assess renal function. Thus, the purpose of this study was to evaluate the appropriateness of this model for diffusion signal decays in the kidney and the correlation between the parameters obtained with this model and renal function.

Material and Methods: Nineteen patients (mean age, 67.5±12.0 years) with renal diseases and thirteen healthy volunteers (mean age, 37.4±10.4 years) were included in this study. The mean estimated GFR (eGFR) was 43.7±22.1 ml/min/1.73m^2 in the patients and 90.3±10.8 ml/min/1.73m^2 in the volunteers. The eGFR was calculated using the Modification of Diet in Renal Disease formula, which is recommended by the Japanese Society of Nephrology. Magnetic resonance imaging (MRI) was performed on a 3T MRI scanner (Achieva 3T, Philips, the Netherlands) using a 32-channel phased-array coil. DWI was performed using five b-values (0, 500, 1000, 1500, and 2000 s/mm^2). Other parameters were as follows: TR/TE, 7500/73; 5 mm slice thickness with 0.5 mm gap; FOV, 380 × 380 mm; and matrix size, 256 × 256. Regions of interest were placed in the renal cortex of the right kidney following the consensus of two experienced radiologists. Two DWI models were assessed, including the mono-exponential model, and the statistical model using a truncated-Gaussian distribution. When D is distributed according to a truncated-Gaussian distribution, the diffusion MR signal was represented by equation [1], where Φ is the error function, D_m is the distribution maximum, and σ is the width of the distribution with only D>0 values considered. Goodness of fits between the mono-exponential and statistical models were evaluated by an F-test using R^2 values. Correlation coefficients between ADC and eGFR, and the proposed parameters (Frac<1 and Frac>3) and eGFR were calculated in each model by Spearman's rank correlation coefficient.

$$S(b) = S_0 \frac{1+\Phi\left(\frac{D_m}{\sigma\sqrt{2}} - \frac{b\sigma}{\sqrt{2}}\right)}{1+\Phi\left(\frac{D_m}{\sigma\sqrt{2}}\right)} exp\left(-bD_m + \frac{b^2\sigma^2}{2}\right)\cdots \text{[1]}$$

Results and Discussion: Figure 1 shows the probability density function (PDF) of D in a healthy volunteer (solid line) and in a typical chronic kidney disease (CKD) patient (dotted line). Distribution of D in a CKD patient was shifted towards the lower level compared to that of a healthy volunteer. The fitting results are shown in Table 1. The statistical model provided a statistically better fit compared to the mono-exponential model (P<0.01). Correlation coefficients (R) between the proposed parameters and eGFR are shown in Figure 2. Frac<1 and ADC were strongly correlated with eGFR. Oshio et al. used Frac<1 as a parameter representing restricted diffusion or small cancer cells in prostate cancer[2]. In the present study, it can be assumed that Frac<1 represented the severity of renal tissue fibrosis. In addition, the statistical model enabled the evaluation of perfusion information by taking Frac>3 into consideration. The intravoxel incoherent motion (IVIM) model, which is another non-Gaussian model of DWI with bi-exponential function, is also able to assess tissue pure molecular diffusion and perfusion separately. Recently, Ichikawa et al. reported the relationship between eGFR and parameters calculated by the IVIM model in the kidney[4]. Although IVIM is an informative model and has application for various organs, bi-exponential fitting is considered difficult to perform reliably because of associated mathematical weaknesses[5]. ADC also has good correlation with eGFR; however, it is difficult to evaluate fibrosis and perfusion separately. The results of this study indicated that the statistical model provided additional information regarding renal fibrosis and perfusion of the kidney in relation to histological changes.

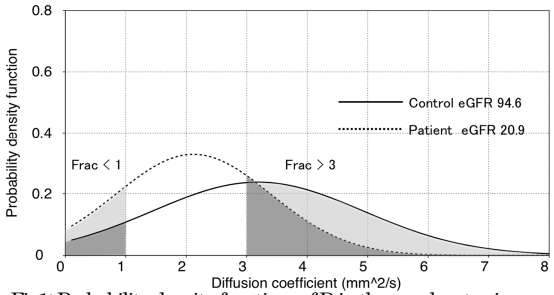

Fig1: Probability density functions of D in the renal cortex in a healthy volunteer and a typical CKD patient.

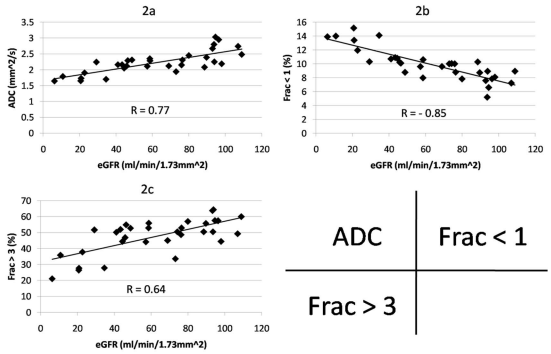

Fig 2: Correlation scatter plots between eGFR and parameters calculated by the statistical model. Correlation coefficients (R) are shown in each plot.

Table 1: Goodness of fits

	Statistical model	Mono-exponential
R^2	0.9999	0.9904
F (vs. statistical model)	—	117.49
p value	—	$p < 0.01$

Conclusion: DWI using the statistical model revealed a good correlation with eGFR, especially with Frac<1. This model might be feasible for interpreting diffusion MR signals with relevance to histological changes in the kidney. However, further investigation is required to clarify the radiological-pathological correlation.

References: 1) Yablonskiy DA, et al. *Magn Reson Med*, 2003;50:664-9. 2) Oshio K, et al. *Magn Reson Med Sci*, 2014;13:191-5. 3) Shinmoto H, et al. *J Magn Reson Imaging*, 2014. doi: 10.1002/jmri.24761. [EPub ahead of print] 4) Ichikawa S, et al. *MRI*, 2013;31:414-7. 5) Oshio K. In: Proceedings of the 20th Annual Meeting of ISMRM, Melbourne 2012. (abstract 3583).