Diffusion-weighted imaging of the kidney: beyond mono- and bi-exponential models

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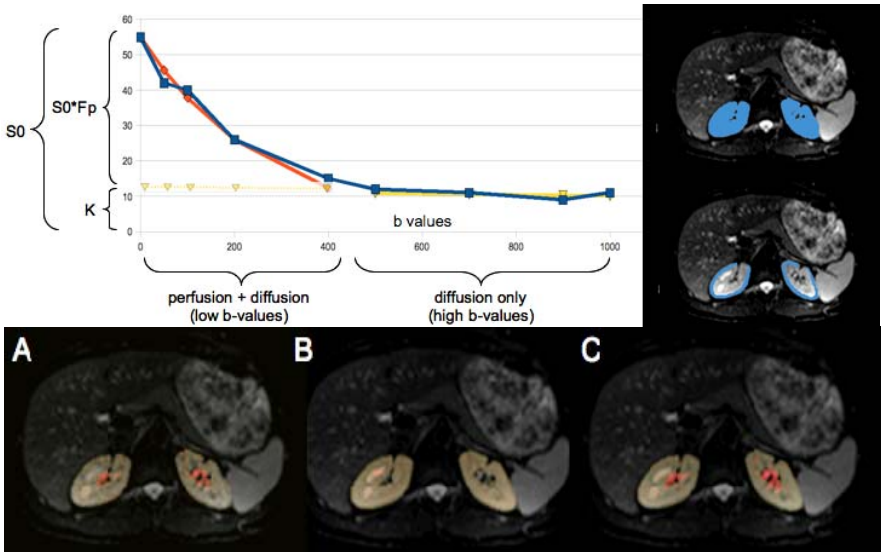
Introduction. Signal attenutaion in diffusion-weighted MR images (DWI) has often been simplistically described as depending on the applied b-value according to the monoexponential equation: $S(b) = S(0)e^{-bADC}$, where S(0) is the unweighted signal, ADC is the apparent diffusion coefficient of a voxel of tissue, and b defines the diffusion encoding of the applied magnetic field gradients. Past studies have shown that a single exponential does not accurately predict signal decay in DWI of the kidney. A biexponential model, $S(b) = S(0)(fe^{-bADC1}+(1-f)e^{-bADC2})$, assuming diffusion to be the combination of a slow (ADC1) and a fast (ADC2) component, is more accurate than the monoexponential model, but requires fitting three parameters at a time, and results are not representative of the perfusion+diffusion and diffusion components in the kidney, as no sharp bend between perfusion and diffusion is seen. Studies assessing reproducibility of the ADC coefficients have been limited to repeating the examination on separate days (few days to 6 months later), and not a single acquisition session. Nor has the effect of a meal on DWI in the kidney been assessed; two studies investigating the effect of hydration reached opposite findings [1,2]. The first aim of this study was to identify a model able to accurately predict diffusion signal decay in the kidney, taking into account the complexity of the renal microstructure. Further aims of this study were to accurately assess reproducibility of the diffusion coefficients, and to investigate the effect of a meal on ADC values in the kidney.

Materials and Methods. Ten healthy volunteers (age: 33±11 years, 2 F) underwent DWI after at least 4 hours of fasting and between 45 and 75 minutes after consuming a meal. A standard T2-weighted scan was acquired in the pre-meal session to rule out pathology. DWI were acquired in both sessions with the following parameters: 30 axial slices, FoV 340 x 280mm, matrix 256 x 192 (after interpolation), thickness/gap 7/1mm, TE/TR 71/3200ms, b-values: 0, 50, 100, 200, 400, 500, 700, 900, 1000 s/mm^2, three diffusion encoded direction with 4 averages and fat suppression performed during gentle free breathing. In half of the subjects the DWI was acquired twice in the pre-meal session, and in the other half it was acquired twice in the post-meal session.

To assess the fitting of DWI data of the kidney, a monoexponential, a biexponential and a "piece-wise" exponential model (Figure 1, top left), consisting of two separated mono-exponential equations: $S(b) = S(0)e^{-bADClow}$, indicative of combined diffusion and perfusion, fitted to the low b-values (b=0,50,100,200), and $S(b) = Ke^{-bADChigh}$, indicative of diffusion-only, fitted to higher b-values (b=500,700,900,1000), were compared. A "perfusion fraction" (Fp) was computed as 1 – K/S0 in all voxels where K/S0<1, and 0 otherwise. As an initial estimate, both ADChigh and ADClow were set to the ADCtot coefficient estimated from the monoexponential fitting using all b-values. The parameters ADClow, ADChigh and K were then estimated voxel-wise using Levenberg-Marquardt fitting. All image-processing steps were performed with in-house software based on the Insight Toolkit version 3.10 and programmed in the C++ programming language.



For each acquisition, whole kidney and cortex regions of interest (ROIs) were manually traced on the pertinent b=0 DW image using the 3D Slicer software (Figure 1, top right). Mean values were computed averaging individual ADChigh, ADClow and Fp maps over the pertinent ROIs.

To investigate repeatability, root mean square (RMS) and concordance correlation coefficient (CCC) were computed.

Differences in diffusion parameters between pre- and post-lunch and between repeated acquisitions were assessed by nonparametric Wilcoxon's test. All statistical analyses were performed using the R software.

Figure 1. Top left) Piece-wise exponential: diffusion signal (blue), diffusion (high b-values, yellow) and diffusion+perfusion exponential (low b-values, red). Top right) Whole kidney and cortex regions of interest. Bottom) Color-coded ADClow (A), ADChigh (B) and Fp (C) maps overlaid on the T2-weighted (b=0) image of the kidney.

Results. All DW images acquired had a good resolution, with diffusion signal reasonably above noise level even for b=1000. One of the patients was excluded due to the presence of a cyst in the left kidney. Both kidneys in all the remaining patients were included in the study.

An example of ADClow, ADChigh and Fp maps resulting from the piece-wise exponential fitting is shown in the bottom row of Figure 1. This model was stable, accurately fitted the diffusion signal attenuation both for low and high b-values, and took into account different diffusion components. All parameters showed high repeatability, with low root mean squares and high concordance correlation coefficients: RMS was 0.011 and 0.015 for ADChigh cortex and whole kidney, 0.041 and 0.005 for ADClow cortex and whole kidney, 0.003 and 0.007 for Fp cortex and whole kidney; CCC=0.91 (0.94) for ADChigh cortex (whole kidney), 0.83 (0.91) for ADClow cortex (whole kidney), CCC=0.75 (0.78) for Fp cortex (whole kidney).

Mean ADChigh was significantly different between pre- and post-meal conditions both in the cortex ($1.662\pm0.098*10^{-3}$ vs $1.733\pm0.105*10^{-3}$ p=0.039) and in the whole kidney ($1.677\pm0.101*10^{-3}$ vs $1.747\pm0.117*10^{-3}$, p=0.039), while ADClow and Fp were not significantly different in either the cortex (ADClow: $3.533\pm0.340*10^{-3}$ pre-meal vs $3.877\pm0.474*10^{-3}$ post-meal, p=0.301; Fp: $0.324\pm0.039*10^{-3}$ pre-meal vs $0.327\pm0.047*10^{-3}$ post-meal, p=1) or the whole kidney (ADClow: $4.031\pm0.385*10^{-3}$ pre-meal vs $4.190\pm0.429*10^{-3}$ post-meal, p=0.129; Fp: $0.329\pm0.034*10^{-3}$ pre-meal vs $0.329\pm0.047*10^{-3}$ post-meal, p=0.722). For both the cortex and the whole kidney, the pre-meal individual mean values of all parameters were significantly correlated with their post-meal values.

No significant differences were found in ADChigh, ADClow and Fp between repeated acquisitions; differences between repeated acquisitions were almost significantly lower than the differences between pre-post meal conditions for ADChigh (p=0.055) but not for ADClow and Fp.

Discussion. The piece-wise exponential model was stable and accurately fitted diffusion signal attenuation in the kidney both for low and high b-values. Looking at the signal decay as a function of b-values in the kidney, no sharp bend between perfusion and diffusion is seen, so that the biexponential fitting is not representative of the perfusion+diffusion and diffusion components; monoexponential fitting is not optimal (initial results, not shown, suggest this remains the case for b-values <100). Since the kidney is a very dense structure where pure perfusion (e.g. in peritubular capillaries and glomeruli), slow convection (in tubules and collecting structures), ultrafiltration (from the glomerulus to the Bowman space into the tubule), and reabsorption occur, different kinds of transport contribute to signal decay in a complex way. Thus, the combined contributions of perfusion and diffusion may extend to b-values in the 500-1000 range, and higher b values would be needed to isolate pure diffusion. The piece-wise exponential model could be extended to isolate single transport components.

Diffusion parameters showed high reproducibility, and differences in repeated acquisitions were much smaller than differences between pre and post meal, suggesting the importance of monitoring fasting during diffusion acquisitions. All diffusion parameters increased after a meal. The significant increase in ADChigh could be due to the effect of the meal on perfusion, or on transport (likely due to altered protein level). Further investigation of the mechanisms contributing to DWI signal loss in the kidney may raise the potential for the use of DWI in highlighting physiopathologies.

References. [1] Damasio et al. Radiol Med 2008; 113:214–224. [2] Muller et al. Radiology 1994; 193:711-715.