Editorial for “Cardiac Phase and Flow Compensation Effects on REnal Flow and Microstructure AnisotroPy (REFMAP) MRI in Healthy Human Kidney”

Diffusion-weighted MR imaging generally involves a Stejskal–Tanner sequence and a signal decay monoexponential fit to derive an apparent diffusion coefficient (ADC). However, a more elaborate approach is needed when the organ of interest contains other sources of intra-voxel incoherent motion (IVIM) like a substantial vascular compartment in addition to the parenchymal compartment: a biexponential curve is then fitted to the signal data to provide a tissue ADC D, a flow-related pseudo-diffusion coefficient D*, and a perfusion fraction f. When diffusion is anisotropic, diffusion tensor imaging (DTI) is required and a fractional anisotropy (FA) is derived.

The kidney is a complex organ with a medulla and a cortex, including glomeruli, tubules, and blood vessels both with oriented flow, resulting in complex tissue and flow diffusion anisotropy, especially in the medulla. Gaudiano et al found a significantly lower medullar FA in patients with renal function impairment as compared with patients with normal renal function but did not evidence a direct correlation between DTI parameters and the estimated glomerular filtration rate. In this context, Notohamiprodjo et al introduced a sophisticated model combining DTI and IVIM under the hypothesis of a two-compartment cylindrical symmetry, assuming a pseudodiffusion tensor Dp collinear with the tissue tensor Dt. This model involves a scalar perfusion fraction f, axial diffusivities (Dt, axial; Dp, axial) along the eigenvector with the largest tissue diffusivity eigenvalue and radial diffusivities (Dt, radial; Dp, radial). The model demonstrated in healthy subjects the existence of an anisotropic flow diffusion tensor Dp and suggested a possible disentanglement between a reduced medullary flow and irreversible tissue damage in the diagnosis of allograft rejection or diabetic nephropathy; however, without separation between tubular and vascular flows. A subsequent study by Liu et al assessed the (good) reproducibility of these parameters and evidenced in presurgical renal mass patients directional flow changes that were not identified with IVIM analysis alone. A higher medullary Dp, radial pseudodiffusion, and higher Dt, radial and Dt, axial cortical diffusivities were found in the left kidney, but these surprising, if not suspicious, findings might be related to a different sensitivity of right and left kidneys to the cardiac pulsatility and were not reported by a similar but cardiac triggered study. Indeed, cardiac-related IVIM effects, responsible for velocity changes during the application of diffusion gradients, are known to artificially increase the ADC and strongly affect the repeatability of ADC measurements, as previously demonstrated in the liver.

In the present issue, the study entitled “Cardiac phase and flow compensation effects on REnal Flow and Microstructure AnisotroPy (REFMAP) MRI in healthy human kidney” examines combined IVIM-DTI (12 directions, 10b values between 0 and 800 sec/mm²) variables in six healthy volunteers, considering slow and fast diffusion compartments, separately in the renal cortex and medulla. The influence of three cardiac phases (pre-systolic, systole, and diastole provided via cardiac-gated 2DPCA flow velocities of the renal artery) is evaluated in two pulse sequences (flow compensated, FC and bipolar, BP sequences). A small fast flow fraction with maximum pulsatility (likely vascular), a larger intermediate speed flow fraction with little pulsatility (likely tubular), and a dominant slow fraction with minimal pulsatility (tissular) were evidenced. These results suggest a possible separation between vascular and tubular flows. Specifically, the perfusion fraction of the FC sequence is associated with a fast perfusion fraction, while an intermediate fraction is defined by the difference between the perfusion fraction of the BP and FC sequence, and a slow fraction is defined by the tissue fraction (1-fp) of the BP sequence.

Significant differences were observed between BP and FC sequences for most parameters and between cortex and medulla with the BP sequence, except for the mean diffusivity. The FA of the tissue compartment demonstrated maximal values in the medulla at systole but was strongly reduced when using the FC sequence; perfusion fractions were maximum at systole with the BP sequence and significantly lower...
with the FC sequence. These results indicate that cardiac gating is mandatory for a credible assessment of renal diffusion and that tubular flow is compensated by FC, unlike the more pulsatile vascular flow. Indeed, flow compensation cancels the intra-voxel dephasing of spins with constant velocity vectors, including the dephasing in arbitrary oriented capillaries traveled by spins without direction change. However, FC does not eliminate the dephasing due to a turning trajectory from one straight capillary segment to another with a different orientation, neither the dephasing related to the pulsatile cardiac movement. This explains why the dephasing due to the essentially straight tubular flow is almost entirely flow compensated, unlike the vascular flow. Interestingly, realignment followed by denoising was achieved prior to image analysis, as the fitting of so many parameters put heavy demands on SNR; in this setting, a single slice acquisition did not exceed 4 minutes.

Can we expect a clinical use of the methodology demonstrated in the present study? First, new studies including carefully selected renal pathologies should be undertaken and should deal with several remaining challenges, like the complexity of the analysis and biological variability. The price to possibly translate these results in our daily practice includes a very high degree of rigor. The availability of a specific quality-certified software tool is mandatory to alleviate the burden of processing and optimally reduce interobserver variability. The effort is worth because a lot is at stake for patients with renal pathologies.

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References


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