

# Quantitative Biomarkers in Renal MRI: From Morphology to Physiology - Diffusion -

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## Highlights

- Signal decay in renal diffusion-weighted imaging (DWI) deviates from monoexponential characteristics and is influenced by both pure diffusion and perfusion.
- Diffusion-tensor imaging (DTI) demonstrates high fractional anisotropy in the renal medulla
- Both DWI and DTI allow for functional assessment of native and transplanted kidneys as well as characterization of renal masses
- Diffusion-kurtosis imaging (DKI) is feasible in human kidneys and may provide additional information on renal microstructure

**Target Audience:** Abdominal radiologists and MRI physicists with interest in renal MRI

## Objectives

1. To provide an overview of different mathematical models for the evaluation of the signal decay in renal DWI.
2. To demonstrate promising clinical applications for renal DWI and DTI.
3. To provide an outlook on novel renal imaging strategies, as for example DKI.

## Background

MR imaging is shifting from pure visualization towards functional evaluation of kidneys. Besides Arterial Spin Labeling (ASL) and Blood-Oxygen-Level Dependent (BOLD) MRI, Diffusion-weighted imaging (DWI) and Diffusion-tensor imaging (DTI) have emerged as major functional imaging techniques [1]. DWI measures the motion of water molecules in the extracellular space, which is usually quantified by the apparent diffusion coefficient (ADC). Diffusion-tensor imaging (DTI) represents an extension of DWI and allows for the assessment of the directionality of diffusion. Due to the radial orientation of tubules and vessels in the medulla, the kidney is probably the most interesting abdominal application for DTI.

## Methods

Several mathematical approaches have been applied to model the DWI signal decay, including a monoexponential model, non-Gaussian model and biexponential model (also referred to as "Intravoxel Incoherent Motion" (IVIM)) [2]. According to the IVIM model, DWI signal decay is influenced by both pure diffusion and microperfusion. While the signal decay at b-values  $> 200$  s/mm<sup>2</sup> is believed to reflect pure diffusion, at b-values  $\leq 200$  s/mm<sup>2</sup> it is mainly attributed to microperfusion. Therefore, the choice of b-values has a substantial impact on calculated diffusion parameters [1]. Different calculation algorithms can be used to determine IVIM parameters ( $ADC_D$ ,  $ADC_P$ ,  $F_P$ ), as for example simultaneous fitting of three free parameters (Levenberg-Marquardt (LM) algorithm), a segmented algorithm or a fixed  $ADC_P$  algorithm [3]. For further evaluation of the IVIM model, an ECG-gated temporally-resolved EPI sequence was recently introduced, which enables DWI acquisitions at different time points during the cardiac cycle [4].

For DTI, EPI sequences with a least 6 diffusion encoding directions are applied. DTI yields the fractional anisotropy (FA) as a measure of directionality of diffusion. DTI allows for the assessment of microstructural changes in the renal medulla in native and transplanted kidneys [5]. Diffusion-kurtosis imaging (DKI) can be considered as an extension of DTI, which accounts for the deviation of water diffusion from a Gaussian distribution and provides information regarding tissue complexity. However, DKI requires EPI-sequences with at least 15 diffusion encoding directions [6].

## Results

DWI signal decay in renal tissue deviates from a monoexponential behavior. For example, the biexponential model improves the mathematical fitting significantly. However, for calculation of IVIM parameters a sufficiently high Signal-to-Noise Ratio (SNR) is required when the LM algorithm is applied [2]. The use of other calculation algorithms might lead to substantial variations of renal IVIM parameters [3]. ECG-gated temporally-resolved DWI detects differences in monoexponential ADC and IVIM parameters related to microperfusion during systole and diastole, highlighting the influence of blood flow on DWI signal decay [4]. DWI can be applied in clinical practice for characterization of renal masses or functional evaluation of kidneys under several pathological conditions [7, 8]. DTI enables functional assessment of transplanted kidneys and holds promise for the differentiation between reversible and irreversible functional restriction of renal allografts [9]. In addition, initial studies have proven that DKI is feasible in human kidneys, yielding reproducible results [10].

## Discussion

DWI and DTI are increasingly used for functional assessment of native and transplanted kidneys. As nonenhanced imaging techniques, they can also be applied safely in patients with contraindications for gadolinium-based contrast material. The choice of b-values has a substantial impact on diffusion parameters. In addition, the applied calculation algorithm has to be considered when comparing biexponential diffusion parameters reported in previous studies. Novel promising imaging techniques (e.g. DKI or ECG-gated time-resolved DWI) have been recently introduced. The clinical potential of these novel techniques has to be determined in future studies.

## References

- [1] Thoeny HC, De Keyzer F. Diffusion-weighted MR imaging of native and transplanted kidneys. *Radiology*. 2011;259:25-38.
- [2] Wittsack HJ, Lanzman RS, Mathys C, Janssen H, Modder U, Blondin D. Statistical evaluation of diffusion-weighted imaging of the human kidney. *Magn Reson Med*. 2010;64:616-22.
- [3] Heusch P, Wittsack HJ, Pentang G, Buchbender C, Miese F, Schek J, et al. Biexponential analysis of diffusion-weighted imaging: comparison of three different calculation methods in transplanted kidneys. *Acta Radiol*. 2013;54:1210-7.
- [4] Wittsack HJ, Lanzman RS, Quentin M, Kuhlemann J, Klasen J, Pentang G, et al. Temporally resolved electrocardiogram-triggered diffusion-weighted imaging of the human kidney: correlation between intravoxel incoherent motion parameters and renal blood flow at different time points of the cardiac cycle. *Invest Radiol*. 2012;47:226-30.
- [5] Notohamiprojo M, Glaser C, Herrmann KA, Dietrich O, Attenberger UI, Reiser MF, et al. Diffusion tensor imaging of the kidney with parallel imaging: initial clinical experience. *Invest Radiol*. 2008;43:677-85.

- [6] Jensen JH, Helpert JA. MRI quantification of non-Gaussian water diffusion by kurtosis analysis. *NMR Biomed.* 2010;23:698-710.
- [7] Chandarana H, Kang SK, Wong S, Rusinek H, Zhang JL, Arizono S, et al. Diffusion-weighted intravoxel incoherent motion imaging of renal tumors with histopathologic correlation. *Invest Radiol.* 2012;47:688-96.
- [8] Thoeny HC, Binser T, Roth B, Kessler TM, Vermathen P. Noninvasive assessment of acute ureteral obstruction with diffusion-weighted MR imaging: a prospective study. *Radiology.* 2009;252:721-8.
- [9] Lanzman RS, Ljimini A, Pentang G, Zgoura P, Zenginli H, Kropil P, et al. Kidney transplant: functional assessment with diffusion-tensor MR imaging at 3T. *Radiology.* 2013;266:218-25.
- [10] Pentang G, Lanzman RS, Heusch P, Muller-Lutz A, Blondin D, Antoch G, et al. Diffusion kurtosis imaging of the human kidney: a feasibility study. *Magn Reson Imaging.* 2014;32:413-20.