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Diffusion kurtosis imaging of the human kidney: A feasibility study☆,☆☆

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ABSTRACT

Purpose: To assess the feasibility and to optimize imaging parameters of diffusion kurtosis imaging (DKI) in human kidneys.
Methods: The kidneys of ten healthy volunteers were examined on a clinical 3 T MR scanner. For DKI, respiratory triggered EPI sequences were acquired in the coronal plane (3 b-values: 0, 300, 600 s/mm^2, 30 diffusion directions). A goodness of fit analysis was performed and the influence of the signal-to-noise ratio (SNR) on the DKI results was evaluated. Region-of-interest (ROI) measurements were performed to determine apparent diffusion coefficient (ADC), fractional anisotropy (FA) and mean kurtosis (MK) of the cortex and the medulla of the kidneys. Intra-observer and inter-observer reproducibility using Bland-Altman plots as well as subjective image quality of DKI were examined and ADC, FA, and MK parameters were compared.
Results: The DKI model fitted better to the experimental data ($r = 0.99$) with $p < 0.05$ than the common mono-exponential ADC model ($r = 0.96$).
Calculation of reliable kurtosis parameters in human kidneys requires a minimum SNR of 8.31 on b = 0 s/mm^2 images.
Corticomedullary differentiation was possible on FA and MK maps. ADC, FA and MK revealed significant differences in medulla (ADC $= 2.82 \times 10^{-3}$ mm^2/s $\pm$ 0.25, FA $= 0.42 \pm 0.05$, MK $= 0.78 \pm 0.07$) and cortex (ADC $= 3.60 \times 10^{-3}$ mm^2/s $\pm$ 0.28, FA $= 0.18 \pm 0.04$, MK $= 0.94 \pm 0.07$) with $p < 0.001$.
Conclusion: Our initial results indicate the feasibility of DKI in the human kidney presuming an adequate SNR. Future studies in patients with kidney diseases are required to determine the value of DKI for functional kidney imaging.

1. Introduction

Diffusion tensor imaging (DTI) is a powerful method to assess the directionality of diffusion of water molecules in biological tissue known as Brownian motion [1]. It provides valuable information for the non-invasive characterization of tissue microstructural properties in vivo [2]. However, conventional DTI has limitations. Because of structural hindrances in biological tissue like membranes or directional structures as in renal medulla, the diffusion of water molecules is restricted and does not follow a Gaussian distribution. To describe the diffusion process more correctly, mathematical models considering the deviation from the Gaussian behaviour have been proposed.

Diffusional kurtosis imaging (DKI) is an extension of the conventional DTI model [3–8]. Along with the conventional diffusion tensor (DT), DKI estimates the kurtosis tensor (KT), which contains information about the deviation of the diffusion from the Gaussian form. DKI provides different diffusion parameters, such as kurtosis anisotropy (KA), mean kurtosis (MK), radial kurtosis (RK) and axial kurtosis (AK). DKI can better reflect the microstructural complexity of tissue because it considers the non-Gaussian behaviour of water in biological tissues.

Consistently, Raab et al. have shown that DKI is superior to DTI for grading of cerebral gliomas [9]. A recent study of Falangola et al. [10] applied DKI for assessing aging-related changes in brain microstructure and showed a distinct signature for cerebrospinal fluid (CSF), grey matter (GM) and white matter (WM). DKI was also successfully applied for the detection of ischemic stroke and pathological changes in neural tissues as in Alzheimer disease [4].

Another major challenge of DKI in body imaging relates to the difficulty in obtaining sufficient SNR at high b-values. A parameter

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optimization is necessary to prevent low SNR, inherent in the diffusion technique, from impacting the result of key diffusion parameters [11]. Strategies that may be used to increase SNR include imaging at a higher field strength (3 T vs. 1.5 T); minimizing echo time (<100 ms); increasing the number of signals acquired, which must be balanced against the resulting increase in imaging time.

DKI has so far been applied to human and small animal brain studies. Non-Gaussian diffusion weighted imaging (DWI), not determining the complete kurtosis tensor, was used rarely in abdominal organs [12]. The human kidney is well suited for the application of DKI due the presence of anisotropy in renal tissue [13,14].

Thus the aim of this study was to assess the feasibility and reproducibility of DKI of the human kidney and to optimize imaging parameters.

2. Methods

2.1. Study population

The institutional review board approved our protocols and written informed consent was obtained from all volunteers before entering the study. Ten young healthy volunteers (6 men, 4 women, mean age 28.50 ± 3.34 years, range 28–34 years) without any history of renal disease, previous renal surgery, or any known systemic disease potentially involving the kidneys were included in this study.

2.2. Magnetic resonance imaging (MRI)

MRI examinations were performed on a 3 T whole-body clinical MRI scanner (Magnetom Trio, a TIM system; Siemens Medical Systems, Erlangen, Germany) using a 6 channel array body coil and a 24 channel phased array spine coil integrated into the scanner table.

For DKI, a single shot EPI sequence was applied in the coronal plane using respiratory triggering via a respiratory belt with 3 b-values (0, 300 and 600 s/mm^2), 30 diffusion directions and 8 signal averages. The other imaging parameters were as follows: echo time (TE) = 90 ms, repetition time (TR) = 1500 ms, matrix = 192 × 192, field of view (FOV) = 400 mm, 10 slices with a slice thickness of 5 mm. GRAPPA (generalized autocalibrating partially parallel acquisition) as parallel imaging method was applied with an acceleration factor of 2. The mean acquisition time of the respiratory triggered DKI sequence was 32:08 ± 4:37 min (range, 23:56–36:30 min).

2.3. Image analysis

Initially, all diffusion-weighted (DW) images were reviewed including a subjective motion analysis by one of the authors, with more than 10 years' experience in image processing and MR diffusion imaging, to assess whether the MR image quality was satisfactory for further analysis. For this purpose, a landmark was set on the first b = 0 s/mm^2 non DW image of the kidney of each volunteer that served as reference and then in the following b = 300, 600 s/mm^2 DW images. The displacement between the reference landmark and the landmarks in the DW images was measured to quantify motion. The results were averaged over all the subjects to obtain minimal and maximal values.

All the acquired datasets were transferred to a workstation and processed to calculate the statistics of the diffusion and kurtosis parameters using in-house developed MATLAB algorithms based on [5,6]. A constrained linear least square formulation of the kurtosis model was used to fit the signal intensities S (see Eq. (1)) on a voxel-by-voxel basis [4].

$$\ln\left[\frac{S(n,b)}{S_0}\right] = -b\sum_{i=1}^{3}\sum_{j=1}^{3} n_i n_j D_{ij} + \frac{1}{6}b^2\overline{D}^2\sum_{i=1}^{3}\sum_{j=1}^{3}\sum_{k=1}^{3}\sum_{l=1}^{3} n_i n_j n_k n_l W_{ujkl} \quad (1)$$

$S(n,b)$ is the measured signal intensity for direction n depending on the diffusion-weighting value b, S_0 is the signal intensity for $b = 0$, D_{ij} and W_{ijkl} are the elements of the second order diffusion tensor (DT) $\mathbf{D_T}$ and fourth-order KT $\mathbf{W}$ respectively, and $\overline{D} = (1/3)tr(D_T)$ is mean diffusivity, where tr(D_T) denotes the matrix trace. Diffusivity D (n) and kurtosis K(n) along direction n are given by

$$D(n) = \sum_{i=1}^{3}\sum_{j=1}^{3} n_i n_j Di_{ij}, \quad (2)$$

and

$$K(n) = \frac{\overline{D}^2}{D(n)^2}\sum_{i=1}^{3}\sum_{j=1}^{3}\sum_{k=1}^{3}\sum_{l=1}^{3} n_i n_j n_k n_l W_{ijkl}. \quad (3)$$

Further, the conventional ADC determined by a logarithmic linear regression fit using the following equation was calculated [15]:

$$\ln\left[\frac{S(b)}{S_0}\right] = -\sum_{i=1}^{3}\sum_{j=1}^{3} b_{ij} D_{ij} \quad (4)$$

The estimated tensors were utilized to determine the diffusion and kurtosis measures for each subject corresponding to the parameters ADC, FA, MK according to the methods of Tabesh et al. [5] and Le Bihan et al. [15] respectively (see Eqs. (1) and (4)).

Although values of RK and AK could be determined from our data, we chose not to report these in the present work, but either concentrate on investigating the relevance of MK measures for human kidney DKI.

To optimize the DKI sequence by the means of acquisition time versus SNR, parametric images of ADC, FA and MK were calculated from subsets of the measured DWI including 2, 4, 6 and 8 signal averages. ROIs were manually drawn on the averaged b = 0 images for different signal averages. The b = 0 image was chosen for the measurements because of the lower SNR in the DW images [16]. SNR was calculated by dividing the mean signal intensity S within the ROI by the standard deviation (SD) of the background noise $SNR = \frac{S}{SD}$.

Eight separate, manual drawn ROIs of 9 to 13 pixels were placed on FA maps because of its proven high corticomedullary discrimination [17]. The ROIs were drawn over the cortex and medulla on the upper pole, mid-zone and lower pole of the right kidney in each subject by one author experienced in genitourinary imaging and DTI measurements (Fig. 1). We selected the right kidney for analysis because of the relatively limited cardiac and respiratory motion artefact due to the presence of the liver above the right kidney [18]. The positions of the ROIs were reviewed by another author in consensus mode. These two authors were genitourinary radiologists with more than 5 years' experience in MR imaging of the kidneys. ROIs on FA maps were copied onto the corresponding position on the ADC and MK maps. The mean and SD of the FA and MK values respectively as averaged values of the 4 ROIs on the cortex and the 4 ROIs on the medulla were calculated for all the signal averages to quantify the corticomedullary differentiation.

As a marker of measurement error or reproducibility, the intra-observer and inter-observer variability of FA and MK values were examined using the free hand ROI technique [19]. Intra-observer repeatability analysis was based on data of one volunteer imaged on