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Original contribution

Assessment of time-resolved renal diffusion parameters over the entire cardiac cycle

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ABSTRACT

Object: To assess changes diffusion properties of renal cortex over the entire cardiac cycle using electrocardiogram-gated respiratory-triggered dynamic diffusion-weighted imaging (DWI).
Materials and methods: 20 healthy volunteers were investigated on a 1.5 T MR scanner. Blood flow velocity within the renal arteries was determined by electrocardiogram-gated phase-contrast measurements. For dynamic renal DWI, an electrocardiogram-gated respiratory-triggered coronal single-slice EPI sequence was acquired at 14 times at 20, 70, 120, 170, …, 570, 620, 720 ms after the R-wave over the cardiac cycle. ROI measurements were performed by two authors in the renal cortex on apparent diffusion coefficient (ADC) maps. A pulsatility index was calculated for ADC as maximal percentage change. Five subjects were measured twice to assess scan-rescan reproducibility.
Results: Flow measurements exhibited a minimum velocity of 15.7 ± 4.3 cm/s during the R-wave and a maximum of 43.2 ± 10.4 cm/s at 182.5 ± 48.3 ms after the R-wave. A minimal mean ADC of $2.19 \pm 0.09 \times 10^{-3}\,mm^2/s$ was observed during the R-wave. A maximum mean ADC of $2.85 \pm 0.20 \times 10^{-3}\,mm^2/s$ was measured 193 ± 57 ms after the R-wave. The mean ADC pulsatility index in the renal cortex was 29.9 ± 5.8%. ADC variation exhibited a significant correlation with pulsatile blood flow velocity. The scan-rescan reproducibility in this study had a low deviation of 0.3 ± 0.1%. The inter-reader reproducibility was 2.9 ± 0.6%.
Conclusion: Renal ADCs exhibit pulsatile characteristics. Due to the significant difference of systolic and diastolic ADCs, the pulsatility index can be calculated.

1. Introduction

Diffusion-weighted imaging (DWI) has emerged as a major functional MR imaging technique. DWI measures the motion of water molecules in the extracellular space, yielding the apparent diffusion coefficient (ADC) as a quantitative parameter. In the abdomen DWI is mainly used for the detection and characterization of tumors [1–4] or for functional evaluation of different organs [5–8]. Several studies have focused on renal DWI [7,9–14]. For both native and transplanted kidneys a significant correlation between diffusion parameters and renal function has been demonstrated [9,13,14]. Besides pure diffusion, renal ADC is also influenced by micro-perfusion and both contributions can be separated according to the IVIM (Intravoxel Incoherent Motion) model [15–17]. While the signal decay at b-values > 200 s/mm^2 is believed to reflect pure diffusion, at b-values ≤ 200 s/mm^2 it is mainly attributed to micro-perfusion. Recently, an ECG-gated temporally-resolved EPI sequence was introduced, which enables DWI measurements at different times of the cardiac cycle [18]. First results have shown that ADC values obtained at the time of maximum blood flow (systole) and minimum blood flow (diastole) differ significantly [18,19], highlighting the influence of perfusion on ADC values. So far, temporally-resolved DWI has only been acquired at two different times (systole and diastole) of the cardiac cycle. The purpose of this study was to obtain diffusion parameters over the entire cardiac cycle at multiple time points using

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dynamic DWI measurements with a temporal resolution of 50 ms.

2. Material and methods

Our study has been approved by the local ethics committee and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All volunteers included in this study gave written informed consent prior to their inclusion in the study.

Twenty healthy subjects (10 men, 10 women, mean age = 26.2 ± 7.2 y) were included in this study and imaged on a 1.5 T whole-body clinical MRI scanner (Magnetom Avanto, 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.

Coronal and axial T2-weighted single shot turbo spin echo (HASTE) were acquired (repetition time (TR) = 2000 ms, echo time (TE) = 79 ms, flip angle = 150°, 24 slices, thickness = 4 mm, field of view (FOV) = 380 mm, matrix = 320 × 260, parallel imaging factor = 2) for anatomical orientation.

For quantification of blood flow velocity in the renal arteries, ECG-gated phase-contrast flow imaging (gradient echo sequence, TE = 2.6 ms, TR = 71.6 ms, flip angle = 30°, matrix = 256 × 128, field of view = 320 mm, parallel imaging factor = 2, slice thickness = 6 mm, 20 phases within cardiac cycle) was performed in the parasagittal plane orthogonal to the renal arteries during breath-hold. Only one renal artery was measured per subject.

For dynamic DWI, an ECG-gated, respiratory-triggered echo-planar imaging (EPI) sequence was acquired in the coronal plane with 4 b values (0, 50, 100, 300 s/mm^2) using the following parameters: spin echo planar imaging sequence, TE = 66 ms, TR = 3000 ms, matrix = 192 × 192, FOV = 400 mm, 3 scan trace, 4 averages, 1 slice with 6 mm thickness, parallel imaging factor = 2. The acquisition was performed at 14 defined points at 20, 70, 120, 170, …, 570, 620, 720 ms after the R-wave of the ECG signal and data acquisition was only performed when the required respiratory state and the ECG-signal coincided. The acquisition time of a single image was about 100 ms and therefore short enough to enable temporally resolved measurements. Additionally, respiratory navigation assured that the images section of the kidneys was identically throughout the complete DWI scan, and no further image registration was needed. The total scan time ranged from 50 to 68 min (mean 58.6 ± 5.7 min) due to double triggering depending on the heart rate and respiration frequency. The quantitative analysis of the renal blood flow velocity was performed using Syngo Argus software (Syngo Argus, Siemens Medical Systems, Erlangen, Germany). Velocity time curves of the blood flow within the renal arteries were plotted.

Parametric images of the apparent diffusion coefficient (ADC) were calculated from the DWI data inline by the MRI scanner software as well as on an external workstation (Syngo MultiModality Workplace, Siemens Healthcare, Erlangen, Deutschland) using a mono-exponential model.

Image analysis was performed independently by two authors (A.L. 5 years of experience with abdominal MR imaging, R.S.L. 10 years of experience with abdominal MR imaging). To analyze ADC results in dependency of the underlying b-values, ADCs were calculated from subsets of images with b = 0, 50, 100 s/mm^2, b = 0, 300 s/mm^2, b = 0, 50, 300 s/mm^2, b = 0, 100, 300 s/mm^2 and b = 0, 300 s/mm^2 in three arbitrary subjects. Signal to noise ratio (SNR) of the ADC in renal cortex was determined as quality criteria with $SNR = \frac{\overline{ADC}}{\sigma_{ADC}}$, where $\overline{ADC}$ is the mean and σ_{ADC} is the standard deviation of a measured region. A comparison of the ADCs determined by sub-sets and full data was performed. This analysis was conducted with respect to reduce total measurement time for possible future investigations in patients.

Regional analysis of the ADC maps was conducted using home build software based on MATLAB (MathWorks, Natick, Massachusetts, USA). One continuous region of interest (ROI) (70–100 pixels) was drawn manually covering the whole cortical region (inter-reader variation < 10%). The mean value of the ROI was determined and plotted against the time within the cardiac cycle. Further an index of ADC pulsatility (PI_{ADC}) was calculated as

$$PI_{ADC} = \frac{ADC_{\max} - ADC_{\min}}{ADC_{\min}} \cdot 100\%,$$

where ADC_{max} and ADC_{min} are the maxima and minima of ADC values within the cardiac cycle. PI_{ADC} therefore reflects the maximal percentage change of ADC within the cardiac cycle. An analogous measure was defined for the blood flow velocity in the renal arteries:

$$PI_{flow} = \frac{F_{\max} - F_{\min}}{F_{\min}} \cdot 100\%,$$

where F_{max} and F_{min} are the global maximum and minimum blood flow velocities over the cardiac cycle.

The defined points in time within the cardiac cycle from the phase contrast flow measurement are depending on the individual heart cycle time using the pre-defined number of 20 measured phases. Therefore the points in time differed from the points in the DWI. For comparability of phase contrast flow measurements and dynamic diffusion parameters, the measured blood flow velocities were interpolated linearly to the pre-defined time points of DWI measurements using MATLAB R2011a (The MathWorks, Inc., Natick, Massachusetts, US).

In five subjects the MRI investigation was repeated to determine the reproducibility of measurements.

All calculated values are provided as mean and standard deviation. *t*-Test statistic was used to analyze differences between maximal and minimal ADC and blood flow velocity during the cardiac cycle. Further these differences were visualized in whisker plots. Pearson's correlation analysis was employed to compare ADC and blood flow velocity over the heart cycle. A p-value < 0.05 was defined as statistically significant.

3. Results

Dynamic DWI could be performed successfully in all 20 subjects. Cardiac cycle time varied between 754 ms und 1162 ms in our subjects.

Differences in the DWI signal decay and corresponding changes of ADC values in the renal cortex were observed at different times of the cardiac cycle (Figs. 1, 2).

Maximum ADC (ADC_{max}) determined numerically over all measurements in the renal cortex was 2.85 ± 0.20 × 10^{-3} mm^2/s at 193 ± 57 ms after the R-wave, while minimum ADC (ADC_{min}) found at 20 ms after R-wave was significantly lower at diastole (2.19 ± 0.09 × 10^{-3} mm^2/s) ($p < 0.001$). The mean of ADC over all points in time was ADC_{mean} = 2.43 ± 0.15 × 10^{-3} mm^2/s.

The maximum flow velocity within the renal arteries of 20 subjects was 43.2 ± 10.4 cm/s at 182.5 ± 48.3 ms after the R-wave, while the minimum flow velocity was significantly lower during diastole (15.7 ± 4.3) ($p < 0.001$).

Table 1 is containing the minimum and maximum data of ADC and blood flow velocity of all 20 subjects. The data are visualized in a boxplot in Fig. 3.

Mean pulsatility index (PI_{ADC}) measured over all subjects with 4 b-values was 29.9 ± 5.8% and mean pulsatility index of blood flow velocity in the renal artery (PI_{flow}) was 181.7 ± 51.8%.

Changes in ADC values in renal cortex exhibited a highly significant correlation with the pulsatile blood flow velocity in the renal arteries ($r^2 = 0.95$, $p < 0.0001$) (Figs. 4, 5).

3.1. b-Value optimization

The SNR differed between the ADCs resulting from sub-sets of images. Further the pulsatility index PI_{ADC} showed variations