Quantification and Validation of Kidney Perfusion Imaging in the Cortex and Medulla with DCE-MRI Using a Blood Pool Contrast Agent in a Swine Model

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Introduction

Magnetic resonance imaging (MRI) is increasingly used to visualize renal morphology. Supplementing current imaging protocols by renal perfusion measurements may provide missing relevant functional information along with the morphological information for a complete diagnostic work-up of patients with suspected renal artery stenosis. However a method for quantification of total perfusion as well as cortical and medullary perfusion has not been established yet. The prolonged intravascular retention of the so-called blood pool agents is expected to improve robustness of dynamic contrast-enhanced MRI (DCE-MRI) for such an investigation. Therefore, the aim of this animal study was to show the feasibility of quantification of total as well as cortical and medullary renal perfusion with DCE-MRI using an approved blood pool agent, gadofosveset trisodium (Vasovist®).

Material and Methods

A total of 18 female pigs (45-65 kg bw) were investigated. Seven pigs served to optimize the sequences, contrast agent dosage, and acquisition parameters for perfusion and anatomical imaging of the kidney. Additionally, the contrast medium dosage was adjusted for perfusion measurements, and the reproducibility of the MR perfusion technique was investigated. A modified ultrasound transit time flow probe (type 4RB MRI-compatible, Transonic Systems Inc., USA) was placed around the renal vein to measure absolute renal blood flow (RBF). This was done to minimize artifacts on MRI produced by the cable and flow probe. A catheter was inserted into the ear vein for contrast injection prior to scanning.

Imaging was performed on a 1.5 Tesla TwinSpeed system (GE, USA) using an 8-channel cardiac phased-array coil for signal reception. All scans were performed in breath-hold technique in the coronal plane with a field of view of 460 mm. Prior to perfusion imaging, unenhanced morphological 2D-images were acquired with the following sequences: T_1-weighted spoiled gradient echo sequence with fat saturation, T_2-weighted fast spin echo sequence with fat saturation, and a mixed T_1/T_2-weighted steady state free precession sequence.

Each dynamic scan commenced with five sets of 3D T_1-weighted gradient echo images acquired using a TE of 0.88 ms, TR of 2.65 ms, slice thickness 8.8 mm, 4 slices, acquisition matrix 128x128, phase FOV 0.62, reconstruction matrix 256x256, NEX 4, and different flip angles (alpha = 2°, 5°, 10°, 20°, 30°). Immediately after acquisition of these images, the dynamic 3D T_1-weighted gradient echo images were acquired with the same parameters except for alpha=30°, half fourier, and NEX 1. Sixty-four frames were acquired with an interval of 1.65 s between each frame and a total duration of 105.6 s. Three ml of an albumin-binding blood pool contrast agent (0.25 mmol/ml gadofosveset trisodium, Bayer Schering Pharma AG, Germany) was injected at a rate of 3 mL/s followed by 20 mL saline injection at the same rate. Infusion started simultaneously with the acquisition of the fifth 3D image.

Prior to imaging, total baseline kidney blood flow was determined by the ultrasound probe in the scanner room. Perfusion measurement was repeated four times in each pig with a delay of 20 minutes between acquisitions. It was aimed to reduce the kidney blood flow to 60 % of the baseline value at the first acquisition, to 40 % at the second and to 20 % at the third acquisition. The fourth acquisition was performed for control with the stenosis completely opened.

The set of five 3D T_1-weighted gradient echo images with different flip angles (alpha = 2°, 5°, 10°, 20°, 30°) commencing each dynamic scan were used to calculate the intrinsic longitudinal relaxation rate (R_{10}) and magnetization (M_0) maps [1]. Then, R_{10} and M_0 maps were used to convert the dynamic motion-corrected scan into 4D relaxation change maps ($R_1(t)$) [1]. The arterial input function (AIF) was extracted from the voxels which were definitely located completely within the aorta to avoid any partial volume effects. Kidney perfusion was calculated voxelwise using singular value decomposition [2].

The morphological images were used to segment the ipsilateral, i.e. the kidney of which blood flow was reduced to viriable degreees , into cortex, medulla and other parts. The volume contributions of the three segments of each kidney to the total kidney were calculated. The perfusion images were used to define VOIs (voxels of interest) in the medulla and cortex. VOIs were delineated to cover the largest possible volume. The volume and the perfusion of each segment were used to calculate total renal blood flow. It was assumed that only the cortex and medulla significantly contribute to total renal flow.

Results

Two pigs were investigated four times in identical perfusion states. The AIF as well as the averaged tissue signal time curves quantified in units of the dynamic relaxation change could be reproduced with an accuracy of better than 5 %. Additionally, a dose escalation study with single doses up to 5 ml and a total dose up to 18 ml was performed. It was found that the dynamic relaxation change could be reproduced up to a total dose of 15 ml of Vasovist. Therefore, the protocol applied here consisting of four repeated dynamic measurements, each with injection of 3 ml of the contrast agent, is feasible.

In eleven pigs four different perfusion states were investigated sequentially. The reduced kidney perfusion measured by ultrasound highly correlated with the total kidney perfusion determined by DCE-MRI, $P<0.001$ (see Fig. 1A). The correlation coefficient between both measurements was 0.843. Linear regression yielded a slope of 0.777 and a y-axis intercept of 24.1 ml/min. Cortical and medullary flow were also highly correlated with the degree of flow reduction, $P<0.001$ (see Fig. 1B+C). Perfusion values smaller than 50 ml/(min cm^3) were overestimated. The reason might be that the dynamic contrast-to-noise level is low and noise is interpreted as perfusion. High perfusion values were slightly underestimated.

Conclusions

The DCE-MRI technique presented here allows absolute quantification of total kidney perfusion as well as separate determination of cortical and medullary flow. Our results show that the technique has sufficient accuracy and reproducibility to be transferred into the clinical setting.

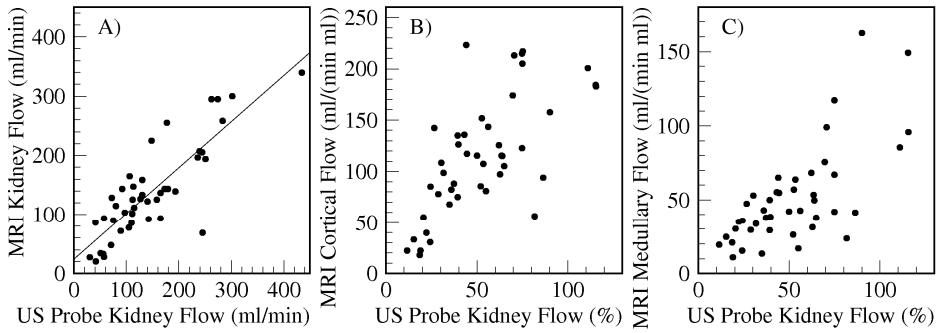

Fig.: A) Correlation of total kidney flow determined by DCE-MRI with the flow of the same kidney determined by the ultrasound probe. B) Average renal cortical flow determined by DCE-MRI in relation to relative total kidney flow. C) Average renal medullary flow determined by DCE-MRI in relation to relative total kidney flow.

References

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