Simultaneous measurement of GFR by DCE-MRI and FITC-sinistrin clearance in rats at 3.0 T

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Introduction

Recent clinical techniques for the estimation of glomerular filtration rate (GFR), such as clearance of inulin or sinistrin, scintigraphy with radio-labeled markers, and creatinine clearance are limited [1]. Investigative techniques to overcome some of the limitations of the above mentioned methods are dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) [2] or transcutaneous approaches based on fluorescent tracer molecules [3]. Both approaches allow for a non-invasive, radiation free and less time consuming way to estimate GFR. The goal was to investigate if a simultaneous measurement of MRI-GFR and optical-GFR is feasible and how these two techniques correlate.

Materials and Method

For the experiments healthy Sprague Dawley rats (n=6; 382 ± 62g b.w.) were used. All measurements were performed on a 3T scanner using an eight-channel receive-only volumetric rat array (RAPID Biomedical GmbH, Rimpar, Germany) for signal detection.

For transcutaneous FITC-sinistrin clearance, the miniaturized fluorescent sensor (NIC-Kidney, Mannheim Pharma & Diagnostics GmbH, Mannheim, Germany, Fig. 1) was fixed on the depilated back of an anesthetized rat; the fluorescence background level of the skin was recorded for one minute. Thereafter a bolus of 5 mg/100g b.w. in a solution of 40 mg/ml of FITC-sinistrin (Mannheim Pharma & Diagnostics GmbH, Mannheim Germany) was intravenously injected followed by a saline flush. The measurement time was 2 hours with measurement intervals of 1 second.

Immediately afterwards, the MRI acquisition was started. After localization, high resolution morphological T2w images were acquired using a 2D turbo spin echo sequence (TR/TE/FA = 6980ms/80ms/140°, ETL = 28, FOV = 65 x 87 mm², averages = 12, matrix = 320 x 240, 20 slices. DCE-MRI was performed using a time-resolved angiography with stochastic trajectories (TWIST) sequence [4] with the following parameters: TR/TE/FA=3.4ms/1.4ms/20°, matrix = 192 x 84, FOV = 114 x 50 mm², GRAPPA 2 and 28 slices. The nominal temporal resolution was 0.9s per volume. Images were continuously acquired for 6 minutes. After the 15th volume, 0.05ml of contrast agent (Dotarem, Guerbet, France) was manually administered in the femoral vein, followed by a saline flush.

The excretion half-life ($t_{1/2}$) of FITC-sinistrin was calculated using a one compartment model and converted into GFR as in [3]. Quantification of DCE-MRI kidney filtration was performed by fitting a two compartment filtration model [5]. GFR for each kidney was estimated by GFR = tubular flow * cortex volume. Cortex volumes were segmented from the T2w images.

Results

Fig. 2 shows a T2w image and a corresponding parametric map of tubular flow obtained by DCE-MRI of one animal as example. Mean tubular flow was 75 ± 22 ml/100ml/min and 70 ± 14 ml/100ml/min for the right and left kidney, respectively. Mean total GFR was 4.3 ± 2.2 ml/min for the FITC-sinistrin clearance and 2.3 ± 0.7 ml/min for DCE-MRI (Table 1).

Discussion

Simultaneous measurement of the GFR by two non-invasive techniques namely, DCE-MRI and transcutaneous FITC-sinistrin clearance in rats at 3.0 T is feasible. Sadick et al. [6] compared these techniques previously; however, large differences (factor of 10) between the methods were detected. Also, optical-GFR and MRI-GFR were not measured simultaneously but on different days. In our approach, these differences could be reduced to a factor of 2 by removing the influence of anaesthesia to the GFR [7] and by better coverage of the kidneys compared to [6]. In conclusion, transcutaneous and MRI GFR measurements may be a powerful combination to diagnose renal failure and monitor progression and treatment outcome.

References

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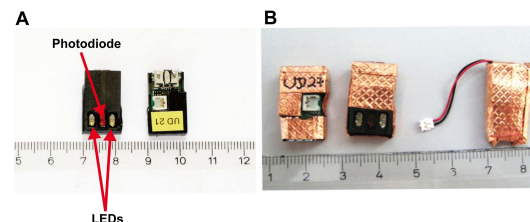[7] Fusellier M et al., Am J Vet Research, 68:807-811, 2007

Fig.1: Optical devices for FITC-sinistrin clearance measurement. A: original devices with LEDs and photodiode for signal exaltation and reception (bottom side) and electronics (upper side). B: the devices are shielded by copper foil, for use inside the scanner.
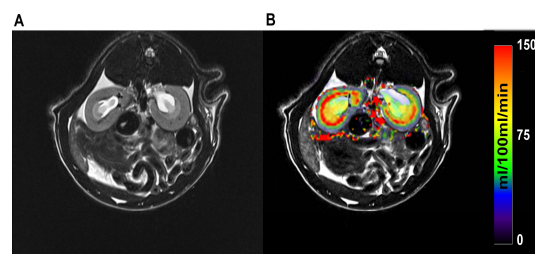

Fig. 2: Example of a T2w image (A) and a corresponding parametric map of tubular flow (B) calculated using a two compartment model. In (B) the parametric map was overlaid to the image in (A).

animal	GFR [ml/min]	
	FITC-sinistrin clearance	DCE-MRI
1	7.2	2.3
2	4.7	2.3
3	5.5	2.7
4	2.6	3.2
5	1.7	1.4
6	3.2	1.5
mean (sd)	4.3 (2.2)	2.3 (0.7)

Tab. 1: Comparison of total GFR obtained by MRI and FITC-sinistrin in healthy SD rats.