TEMPORALLY-RESOLVED IMAGING OF RENAL SODIUM-23 CHANGES AFTER FUROSEMID INJECTION

Raffi Kalayciyan[1], Friedrich Wetterling[1], Sabine Neudecker[2], Norbert Gretz[2], and Lothar R. Schad[1]
[1]*Computer Assisted Clinical Medicine, Heidelberg University, Mannheim, Germany,* [2]*Medical Research Center, Heidelberg University, Mannheim, Germany*

Introduction:
Furosemide is a commonly used loop diuretic which reduces NaCl reabsorption in the loop of Henle. Hence, the corticomedullary osmotic gradient is abolished resulting in reduced medullary ^{23}Na signal [1, 2] and increased urine production. Since renal function is highly correlated with renal tissue ^{23}Na concentration, ^{23}Na-Kidney-MRI can be used to monitor the spatial changes in ^{23}Na along the corticomedullary axis after diuretics administration [2]. Furthermore, the temporal changes in the medulla and cortex ^{23}Na signals could be studied, if sufficient spatial and temporal resolution is achieved. The aim of this study was to measure the temporal ^{23}Na signal before and after furosemide-injection in four rats via bilateral renal ^{23}Na-MRI (n=8). In order to maximize ^{23}Na signal at 9.4 T, a 3D-Ultrashort Echo Time (3D-UTE) sequence was used in conjunction with a home-built transceiver surface resonator.

Methods:
The saddle-shaped transceiver surface coil was geometrically adapted to the size of the target object in order to maximize the measured signal intensity in kidney (see Fig. 1 a). For balancing purposes at 105.9 MHz, the resonance circuit was designed with two fixed value capacitors and a variable capacitor. Furthermore, a custom built ^{1}H transceiver birdcage resonator (see Fig. 1 a - left) was used in order to acquire ^{1}H reference images: a linearly-polarized volume resonator of Bruker BioSpin MRI GmbH.
^{23}Na-MR measurements were carried out on a 9.4 T system (Bruker BioSpin GmbH, Ettlingen, Germany) using 3D-UTE with TE/TR = 85 µs / 50 ms, nominal voxel size = (1 x 1 x 4) mm^3, and an acquisition time of 2min/2550 projections (rat no 1 and 2), and 3.5min/4206 projections (rat no 3 and 4). ^{1}H reference image was acquired prior to ^{23}Na scanning using 3D-RARE sequence with TE/TR = 3ms/10ms, and a resolution of (0.5 x 0.5 x 2) mm^3. Baseline measurements via ^{23}Na-MRI took about 30 min prior to the furosemide injection. A bolus of furosemide (10 ml/kg body weight) was administered intravenously in four Wistar rats (280 ± 20 g) at approximately 30min after the first MR image was acquired. ^{23}Na scans were acquired for up to one hour after bolus injection. Additionally, urine and blood samples were taken using urinary and arterial blood catheterization once before furosemide and every 15 min after furosemide injection.
After co-registration of ^{1}H-MR images with ^{23}Na images, mean signal was analyzed for manually-marked regions of interest (ROI). Temporally resolved sodium change was visualized using time course plots and parameter maps for each experiment. The ^{23}Na signal values during the slope phase were fitted by a line and the ^{23}Na slope values were computed in every pixel. Parameter maps of each scan were then generated for each slice. In total, 8 kidneys were investigated in 4 rats.

Results:
An abdominal ^{1}H MR image is presented in Fig. 1 b for one representative rat (no. 1). The co-registered ^{23}Na-MR images prior to and after furosemide injection are shown in Fig. 1 c-d. Note the strong decrease in ^{23}Na signal within the medulla. The time course data for the ^{23}Na signal in inner and outer medulla as well as in cortex are plotted in Fig. 2. Three main phases of diuresis are indicated respectively: baseline, range of changing ^{23}Na signal, and steady-state. Fig. 3 contains the parameter map for the right kidney and the corresponding ^{1}H image. ROIs in the inner and the outer medulla as well as in cortex could be easily placed in those images due to the excellent tissue contrast achieved with used RARE sequence. Furthermore, ^{23}Na slope values clearly delineated the three ROIs. The ^{23}Na slope values for each investigated kidney are tabulated in Table 1. According to these values, a negative slope in the inner (-4.6±1.3 %/min) and outer (-1.4±0.9 %/min) medulla, but a positive slope of +1.76±0.9 in cortex were observed (n=8). In medulla tissue, steady state conditions were always reached within 10min after furosemid injection. However in cortex, there was a distinct signal decrease measured afterwards in all kidneys characterized by a negative slope of -0.97±0.4 (n=8) until the initial ^{23}Na cortex signal was reached – normally within 1h after furosemid injection. ^{23}Na Urine concentration increased from 50 ± 3 mM to 160 ± 10 mM. However, blood plasma concentration of Na^+ remained constant at 138.5 ± 2.5 mmol/l. Thus, the kidney ^{23}Na ions were mainly washed out through the bladder after furosemid injection.

Discussion and Conclusion:
High resolution ^{1}H and ^{23}Na images were acquired with a combination of two single tuned resonators without the need to exchange resonators inbetween the ^{1}H and ^{23}Na scans. Furthermore, short TE (<100µs) and sensitivity-optimized surface resonator enabled fast acquisition of ^{23}Na kidney images within 2min per scan, which allowed to study the fast ^{23}Na change after furosemid injection. The improved temporal resolution of renal ^{23}Na slope maps provided additional contrast between cortex and medulla which is most likely correlated with renal filtration rate. The ^{23}Na decrease in medulla and ^{23}Na increase in cortex has been measured before and herein reported values match those literature values exceptionally well. However, the superior spatial and temporal resolution in renal cortex tissue further enabled to monitor a ^{23}Na decrease back to the initial ^{23}Na cortex signal within 1h after furosemid injection. This was measured in every rat. A physiological explanation remains to be clarified in future experiments, for instance, by investigating this effect under application of different furosemid volumes. In conclusion, ^{23}Na-MRI provides a powerful technique for investigating renal tissue function and hence could offer a non-invasive method for assessing renal tissue function in various pathologies such as Acute Tubular Necrosis (ATN), and transplanted kidney.

References: [1] Maril et al., Kidney Int. 65:927-935 (2004); [2] Maril et al., Kidney Int. 55:545-552 (2005).

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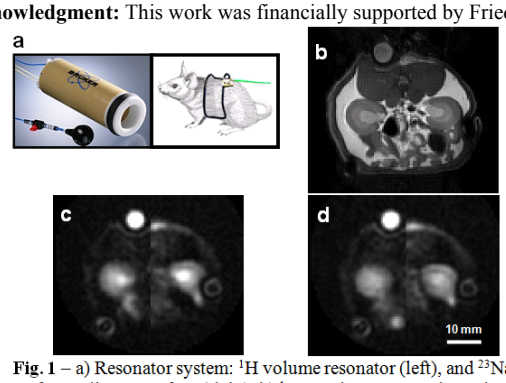

Fig. 1 – a) Resonator system: ^{1}H volume resonator (left), and ^{23}Na surface coil on top of rat (right), b) ^{1}H-MR image co-registered with baseline c) and steady-state d) ^{23}Na-MR-images.

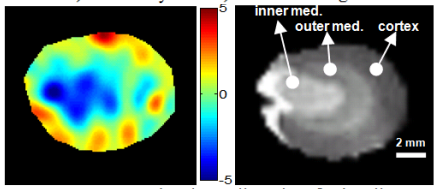

Fig. 3 – Parameter map showing sodium slope [% baseline per min] on left, and 1H-MR-image as reference on right.

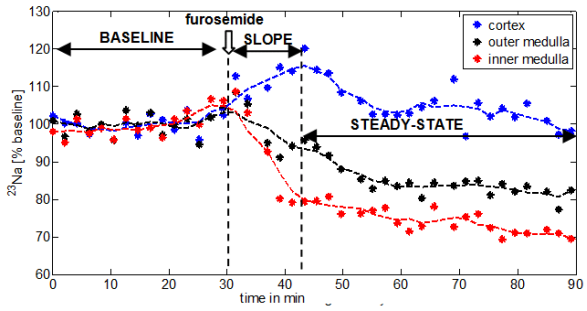

Fig. 2 – ^{23}Na signal as a function of time for three different ROIs in the right kidney of rat no. 1. Note the decrease in cortex ^{23}Na signal during the steady state period.

Animal number	CORTEX		OUTER MEDULLA		INNER MEDULLA	
	left	right	left	right	left	right
1	+3	+1.75	-1.75	-2.9	-3.5	-4.6
2	+1.75	+1.25	-0.4	-2.0	-2.6	-3.8
3	+0.8	+2.0	-1.5	-2.0	-4.7	-4.7
4	+3.0	+0.5	-0.5	-0.3	-7.2	-5.4
std. deviation	**+1.76±0.9 %/min**		**-1.4±0.9 %/min**		**-4.6±1.3 %/min**	

Tab. 1 – Sodium slope values [% baseline / min] for 4 rats (n=8).