in vivo Sodium Imaging of Rat Kidney at High Temporal and Spatial Resolutions

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INTRODUCTION: Among all MRI-observable elements in the biological system, sodium is the second most abundant element after hydrogen. Under normal physiological conditions the intracellular and extracellular sodium concentration in living tissue is approximately 15mM and 145mM, respectively. This large ionic concentration gradient across the cellular membrane in tissues is maintained dynamically by the Na-K pump on the cell membrane that consumes ATP. The failure of the Na-K pump due to impaired ATP production will lead to an increase in the intracelluar sodium concentration. Tissue sodium concentration has been exploited as an important indicator of the pathophysiological status of tissue as well as a potential predictor of its fate during an ischemic event or degeneration or other pathological development (1-2). Interestingly, in the kidney, there exists another large corticomedullary sodium concentration gradient at the organ level, which is essential for various normal renal functions, such as the counter-current and the urinary concentration mechanism. It is known that 23Na-MR imaging offers a unique approach to measure tissue sodium concentration non-invasively. Such an imaging technique was demonstrated for mapping kidney sodium distribution in rabbit (3) and recently in rat (4). The main aim of the study was to develop and evaluate the feasibility of both high spatial and temporal 23Na MRI method of rat kidney. Since furosemide inhibits the coupled Na+/K+/2Cl- transport system in the luminal membrane of the thick ascending limb of the loop of Henle, the loop diuretics reduce the reabsorption of NaCl into the interstitium in outer medulla and then abolish this sodium concentration gradient. Another aim of the study was to validate the method by measuring the sodium concentration change induced by the loop diuretic in kidney.

METHODS: All sodium imaging experiments were carried out on a 9.4-T/31-cm Bruker Biospec system (Ettlingen, Germany) and a 12-cm efficient gradient insert (maximum gradient strength =40G/cm; rise time = 80usec). A home-built two-turn circular RF coil (105.9MHz) was used as a T/R antenna. When proton imaging was desired, decoupling between the sodium and a proton linear birdcage was achieved geometrically through maintaining the orthogonality between the B1 polarizations of the two coils. 23Na MRI pulse sequence was based on a 3D gradient-echo (GE) acquisition scheme, in which a short RF pulse (200usec) was used to minimize magnetization relaxations during imaging. Other scan parameters: TR/TE=70/0.90msec, flip angle=60, NSA=4, echo asymmetry=15%. The spatial resolution parameters were: matrix of 64x32x16 corresponding to field of views of 64x40x32mm3. Typical scan time was ~1.50 min. SD rats (n=6) were anesthetized with isofluorane (1.0-1.5% iso/O2) using a nose cone at flow rate of 1 liter/min. A typical sodium imaging study consisted of more than 2 hour repeated volumetric sodium imaging acquisitions, in which a dose of furosemide (6mg/kg, iv) was slowly infused via a femoral vein cannula at the 60min time point.

RESULTS: A representative sodium image of normal rat kidney is shown in Figure 1A. This sodium image clearly revealed a sodium concentration gradient along the corticomedullary axis in kidney, which is also shown on its surface plot. This sodium concentration gradient in kidney was attenuated with an administration of furosemide. Fig. 1B indicates the regions exhibiting either an increase (pink) or decrease (yellow) in sodium concentration after furosemide injection. Fig 1C showed corresponding time courses of sodium signals in the medullary and cortical regions. Approximately 40% decrease in outer medulla region was observed. The rate of the sodium content changes (either decrease or increase) were characterized with time constants, which were found to be 9.5+/-4.4min for medulla or 89+/-26 min for cortex. The difference ($p<0.003$) in kinetics is also consistent with the mechanism of action of furosemide, i.e. inhibition of Na/K/2Cl co-transporter in the thick ascending limb of Henle in the medullary region of kidney.

CONCLUSIONS: The experimental results clearly suggest that high temporal sodium imaging of rat kidney is potentially feasible and practical using a high field NMR scanner. And, the added SNR at 9.4 Tesla allows high resolution imaging with voxel volume as small as 3 micro-liter in reasonable scan time. More importantly, both spatial resolution and SNR of the sodium images were sufficient for resolving the sodium concentration gradient and its kinetics after a 6mpk flurosemide injection in kidney. The results of the study suggest that such a non-invasive sodium imaging platform can be used to gain insights regarding to renal function and mechanism of diuretics.

REFERENCES: 1. Kim RJ, et al. Fast 23Na Magnetic Resonance Imaging of Acute Reperfused Myocardial Infarction: Potential to Assess Myocardial Viability. Circulation 1997; 95: 1877-1885. 2. Thulborn KR, Gindin TS, Davis D, Erb P. Comprehensive MR imaging protocol for stroke management: tissue sodium concentration as a measure of tissue viability in nonhuman primate studies and in clinical studies. Radiology 1999; 213:156-166. 3. Wolff SD, Eng J, Berkowitz BA, James S and Balaban RS. Sodium-23 nuclear magnetic resonance imaging of the rabbit kidney in vivo. Am J Physiol Renal Physiol 258: F1125-F1131, 1990. 4. Maril N, Margalit R, Mispelter J, Degani H. Sodium magnetic resonance imaging of diuresis: Spatial and kinetic response. Magn Reson in Med 2005; 53: 545 – 552.

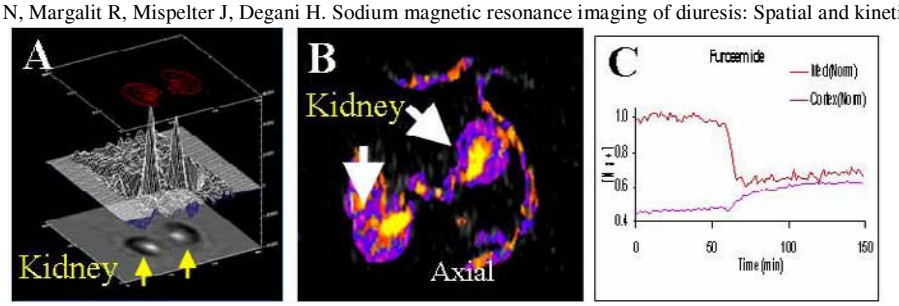

Figure 1. Sodium image and its surface plot / contour plot (A) of a rat kidney taken immediately prior to a furosemide injection (6mpk). A color-coded image (B) indicating the regions in kidney exhibiting an increase (pink) or decrease (yellow) in sodium concentration after the injection, whose corresponding time courses (C) are displayed.