Noninvasive Monitoring of Acute Tubular Necrosis Induced by Ischemia/Reperfusion in a Rat Model using ^{23}Na MRI

B. Atthe[1], A. Babsky[1], and N. Bansal[1]

[1]Department of Radiology, Indiana University School of Medicine, Indianapolis, Indiana, United States

INTRODUCTION:

Acute tubular necrosis (ATN) accounts for some 50% of cases of acute renal failure (ARF) in hospitalized patients. It can be caused by limited blood flow and oxygen supply to the tubules in conditions such as sepsis, hypotension, heart failure and a large variety of other hemodynamic conditions. The clinical detection of evolving acute tubular necrosis and differentiating it from other causes of renal failure are currently limited. The maintenance of the corticomedullary sodium gradient, an indicator of normal tubular function in the kidney, is presumably lost early in the course of ATN [1]. Herein, ^{23}Na MRI is applied to study the early alteration in renal sodium distribution in the rat kidney with ATN using the ischemia-reperfusion injury model.

METHODS:

All ^{23}Na MRI experiments were performed on a Varion 9.4-Tesla, 31-cm horizontal bore system equipped with a 12-cm gradient insert (maximum gradient strength = 38 G/cm). A home-built loop-gap resonator tuned to 105.9 MHz was used as antenna. 3D ^{23}Na MRI were collected using a gradient-echo (GE) imaging sequence and following imaging parameters: 50 ms repetition time, 4.5 ms echo-time, 64 x 64 x 16 data points over a field of view of 6 x 6 x 6 cm. Weighted signal summation (WSS) was used to increase the SNR [2]. On average, 9.67 transients were collected per phase-encoding step. Typical scan time was ~10 min. Wistar rats were anesthetized with 1.0-1.5% isofluorane in medical air using a nose cone at flow rate of 1 liter/min. A 3-0 silk suture (SOFSILK) was placed around the vascular pedicle of the left kidney using an atraumatic needle. The ends of the thread were passed through a 1 m long plastic tubing to form a snare. In-magnet ischemia was induced for 0 (control), 10, 30 or 50 minutes on different group of rats (n = 3 for each group) by pulling the snare taut and clamping it in position. After occlusion, the snare was released for reperfusion, with the ligature left loose on the surface of the renal vascular pedicle. The time-domain data were zero-filled to 128 x 128 x 16 and Fourier transformed. Medulla to cortex sodium gradient was determined by drawing regions of interest around the medulla and cortex (Fig 1A), and taking their average ^{23}Na MRI signal intensity (SI) ratio.

RESULTS:

Selected sections from 3D ^{23}Na MRI of the normal rat kidneys for a control rat at 10 and 120 min time points during the MRI experiment are shown in Fig 1A and 1B. The images show ~80% higher ^{23}Na MRI SI in the medulla compared to the cortex. There was no change in the sodium gradient over 2 hr in the control rats. Fig 1C, 1E, and 1G show sodium distribution in the left kidney after 10, 30 and 50 min of ischemia, respectively. Fig 1D, 1F and 1H show the sodium distribution after 60 min of reperfusion for each of the ischemic kidney, respectively. Changes in the renal sodium distribution can be clearly seen after the induction of ischemia and re-perfusion. The time course of the changes in the medulla to cortex sodium gradient for 0, 10, 30 and 50 min ischemia groups are shown in Fig 2. There was a slight decrease in the sodium gradient after 10 min of ischemia but the gradient was quickly recovered on reperfusion. The medulla to cortex sodium gradient decreased from 1.81 ± 0.08 to 1.68 ± 0.10 after 30 min of ischemia and from 1.77 ± 0.03 to 1.38 ± 0.04 after 50 min of ischemia. On reperfusion the ratio continued to decrease and plateaued at 1.45 ± 0.16 and 1.27 ± 0.02 for 30 and 50 min ischemia groups, respectively. The steep decrease in the medulla to cortex sodium gradient during ischemia with no recovery after 1 hour of reperfusion, especially in the 50 min ischemia group, suggests irreversible tubular dysfunction of the kidney.

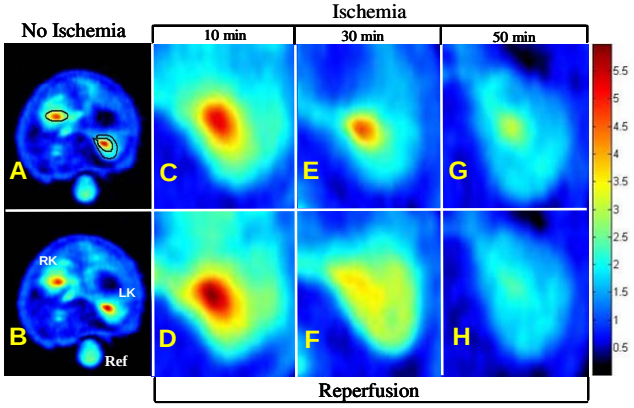

Fig. 1. Images A and B show selected sections from 3D ^{23}Na MR images of a control (no ischemia) rat at 10 (A) and 120 (B) min time points (RK – right kidney, LK – left kidney, Ref - Reference). Images C, E and G show zoomed ^{23}Na MR image of the left kidney after 10 (C), 30 (E) and 50 (G) minutes of ischemia, respectively. Images D, F and H show zoomed ^{23}Na MR images of the left kidney after 60 min of reperfusion for each of the ischemic kidney respectively.

CONCLUSION:

Renal ^{23}Na MRI revealed a marked change in medulla to cortex sodium gradient during the early evolution of ATN caused by ischemia-reperfusion injury. The sodium images clearly demonstrated the inability of the ATN kidneys (30 min and 50 min ischemia-reperfusion injured kidneys) to maintain the corticomedullary sodium gradient. Therefore, this noninvasive imaging technique may enable the detection of evolving ATN in the setup of acute renal failure and to differentiate it from other renal diseases where tubular function is maintained.

REFERENCES:

1. Maril N, Margalit R, Rosen S, Heyman SN, Degani H. *Kidney International*. 69:765-8, 2006.

2. Bansal N, Seshan V. *J. Magn. Reson. Imaging*, 5:761-767, 1995.

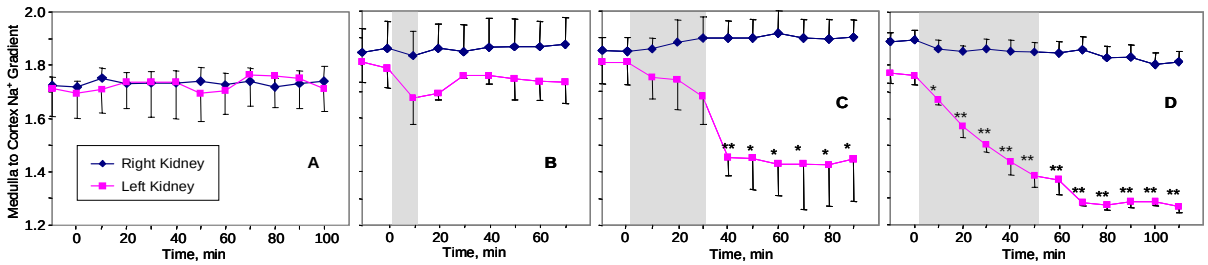

Fig. 2. Effect of 0 (A), 10 (B), 30 (C) and 50 (D) min of ischemia and reperfusion on the medulla to cortex Na^+ gradient in the rat kidney. Shading indicates the ischemia periods. Mean ± SE, n = 3 significance * - $p \leq 0.05$ *vs.* right kidney, ** - $p \leq 0.05$ *vs.* both right kidney and pre-ischemic baseline