Effects of Ischemia-Reperfusion Injury on $^{23}$Na Relaxation Times and its Implications on Quantification of Corticomedullary Sodium Concentration by $^{23}$Na MRI

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INTRODUCTION

The maintenance of the corticomedullary sodium gradient, an indicator of normal tubular function in the kidney, is presumably lost early in the course of acute tubular necrosis (ATN) [1]. Ischemia remains the major cause of ATN in the adult population. $^{23}$Na MRI has been applied to study the alterations in renal sodium distribution in the rat kidney during ischemia-reperfusion (IR) injury [2]. The observed changes in $^{23}$Na MRI signal intensity (SI) of the renal medulla and cortex during ischemia and reperfusion can be caused by a) a change in sodium concentration, and/or b) changes in $^{23}$Na relaxation times. In this study, $^{23}$Na MRI and MRS are applied to evaluate the effects of renal ischemia and reperfusion on $^{23}$Na relaxation times in renal medulla and cortex, and the changes in $[Na^+]$ due to IR injury are quantified by applying $T_1$ and $T_2$ corrections.

METHODS

$^{23}$Na MRI: All $^{23}$Na MR experiments were performed on a Varian 9.4-Tesla, 31-cm horizontal bore system equipped with a 12-cm gradient insert. Effect of ischemia and reperfusion on $^{23}$Na MRI SI was investigated in Wistar rats (n=5) using a home-built 50 mm diameter loop-gap resonator tuned to 105.9 MHz. A 10 mm diameter tube containing 50 mM NaCl was positioned next to the rat and used as a signal intensity reference. A 3D $^{23}$Na gradient-echo (GE) imaging sequence with the following parameters was used: 50 ms repetition time (TR), 4.5 ms echo-time (TE), 64 × 64 × 16 data matrix over a field of view of 6 × 6 × 6 cm. Weighted signal summation (WSS) was used to improve SNR. On average, 9.67 transients were collected per phase-encoding step. $^{23}$Na images were collected every 10 minute during baseline, 50 min ischemia and 50 min reperfusion periods. In-magnet ischemia was induced by a snare taut placed around the vascular pedicle. Reperfusion can be caused by a) a change in sodium concentration, and/or b) changes in tissue water content.

$^{23}$Na fast- and slow T$_2$ ($T_{2f}$ and $T_{2s}$, respectively) and $T_1$ of the whole kidney were measured by MRS on separate cohort of rats (n=4) using a 10-mm-diameter surface coil directly placed on exposed kidney. $^{23}$Na T$_2$ was measured using a pulse-burst saturation recovery pulse sequence consisting of 10 saturation pulses followed by an incremental delay (16 values ranging from 0.05 to 200 ms, each) and 50 ms delay following saturation. A 3D $^{23}$Na GE imaging sequence with similar imaging parameters as describe above was used. For $T_2$ measurements, the image matrix size was reduced to $64 \times 32 \times 8$ and five $^{23}$Na images were collected with a 4.5 ms TE and 10, 20, 50, 80 and 120 ms TR. $T_2$ measurements were repeated every ~16 min during normal perfusion, 50 min ischemia and 50 min reperfusion. $T_1$ of the medulla and cortex was computed by least square fitting the SI of the regions of interest (ROI) to a mono-exponential function. For $T_2$ measurements, the image matrix size was reduced to $64 \times 32 \times 8$, the readout gradient was increased by a factor 10 to allow shorter TE and ten $^{23}$Na images were collected with a 50 ms TR and 1.5, 2.2, 3.5, 4.5, 6, 8, 11, 15, 19 and 25 ms TE. $T_2$ measurements were repeated every ~25 min during normal perfusion, 50 min ischemia and 50 min reperfusion. Least squares curve fitting of the $T_2$ image data to a bi-exponential function did not give a reproducible value for $T_{2s}$ because the $T_{2s}$ in tissue is very short. Thus $T_2$ and the relative fractions of the fast and slow components for the whole kidney from the spectroscopy experiments were used to calculate $T_{2f}$ of the cortex and medulla by bi-exponential curve fitting of SI.

RESULTS

$^{1}$H MRS and $^{23}$Na MRI SI were investigated in Wistar rats (n=5) using a home-built 50 mm diameter loop-gap resonator. A 3D $^{1}$H MRI with similar imaging parameters as describe above was used. For $T_2$ measurements, the image matrix size was reduced to $64 \times 32 \times 8$, the readout gradient was increased by a factor 10 to allow shorter TE and ten $^{1}$H images were collected with a 50 ms TR and 1.5, 2.2, 3.5, 4.5, 6, 8, 11, 15, 19 and 25 ms TE. $T_2$ measurements were repeated every ~25 min during normal perfusion, 50 min ischemia and 50 min reperfusion. $T_1$ of the medulla and cortex was computed by least square fitting the SI of the regions of interest (ROI) to a mono-exponential function. For $T_2$ measurements, the image matrix size was reduced to $64 \times 32 \times 8$, the readout gradient was increased by a factor 10 to allow shorter TE and ten $^{23}$Na images were collected with a 50 ms TR and 1.5, 2.2, 3.5, 4.5, 6, 8, 11, 15, 19 and 25 ms TE. $T_2$ measurements were repeated every ~25 min during normal perfusion, 50 min ischemia and 50 min reperfusion. $T_1$ of the medulla and cortex was computed by least square fitting the SI of the regions of interest (ROI) to a mono-exponential function. For $T_2$ measurements, the image matrix size was reduced to $64 \times 32 \times 8$, the readout gradient was increased by a factor 10 to allow shorter TE and ten $^{23}$Na images were collected with a 50 ms TR and 1.5, 2.2, 3.5, 4.5, 6, 8, 11, 15, 19 and 25 ms TE. $T_2$ measurements were repeated every ~25 min during normal perfusion, 50 min ischemia and 50 min reperfusion. Least squares curve fitting of the $T_2$ image data to a bi-exponential function did not give a reproducible value for $T_{2s}$ because the $T_{2s}$ in tissue is very short. Thus $T_2$ and the relative fractions of the fast and slow components for the whole kidney from the spectroscopy experiments were used to calculate $T_{2f}$ of the cortex and medulla by bi-exponential curve fitting of SI.

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$^{23}$Na MRI SI during the early evolution of ATN caused by ischemia-reperfusion injury.

CONCLUSION

$^{23}$Na MRI revealed a marked decrease in medulla and cortex $^{23}$Na MRI SI during the early evolution of ATN caused by ischemia-reperfusion injury. $^{23}$Na relaxation time measurements by $^{23}$Na MRI and MRS showed that sodium relaxation characteristics are similar in renal medulla and cortex in normal kidney. Ischemia causes a significant decrease in the relaxation times which affects the calculation of medulla and cortex $[Na^+]$ from $^{23}$Na MRI data. However, the changes in relaxation times for the medulla and cortex are identical, thus the medulla to cortex $^{23}$Na SI ratio represents $[Na^+]$ in the two compartments during ischemia and reperfusion.

REFERENCES