Sodium chemical shift imaging of induced diuresis in a mouse renal model

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Introduction:

Sodium plays a major role in fluid and electrolyte homeostatsis. In the last few years renal tissue sodium concentrations (TSC) in healthy as well as in pathological models of the rat using MRI have been described [1-3]. In this study we report the effect of furosemide induced diuresis on the TSC in mice. We show that, despite the small size of the mouse, the low gamma of sodium and the low sodium concentration, functional information not available from proton MRI can be obtained at high resolution.

Subjects & Methods:

Experiments were performed on a Bruker 17.6 T widebore spectrometer with a maximum gradient strength of 1T/m. A custom built sodium quadrature birdcage with an inner diameter of 27 mm was used to acquire three dimensional density weighted chemical shift image (DWCSI) data sets [4]. The DWCSI method allows a short (<500 μs) gradient-encoding time, enabling signal detection from the very short T_2 values of intravascular sodium and also optimizes the shape of the spatial response function for a given total data acquisition time. After positioning the mouse (20-25g) in the magnet, a first dataset with a spatial resolution of 1.0 x 1.0 x 2.5 mm^3 and a temporal resolution of 4.7 minutes was acquired. Subsequent to this reference scan, the mouse was given a bolus tail-vein injection of 10 mg/kg of 1 mg/mL furosemide ('Lasix', Hoechst, Frankfurt, Germany) and a series of eleven 3D DWCSI sodium data sets with the same parameters as the reference scan were acquired.

Results:

Changes in the renal sodium distribution during the administaration of furosemide could be observed with a temporal resolution of 4min 40sec. Twelve axial slices at different time points, one before and eleven after injection of furosemide, are shown from A to L in Figure 1. A decrease in the sodium signal in the medulla and an increase in the renal cortex can be seen. Figure 2 shows the profiles along the corticomedullary axis as indicated in Figure 1 (blue bar in A). Fifteen minutes after the bolus injection the increase of the sodium signal in the renal cortex is about 20%. Thirty minutes later, however the signal is below that measured before the administration of furosemide. The sodium signal in the medulla, in contrast, decreases to about 55% of the initial signal height after approximately 25 minutes (data set F-G). During the next 25 minutes the signal intensity of the medulla stays unchanged. This decay of the signal in the medulla could be exponentially fitted with a time constant of 6 +/- 1 minutes (data not shown).

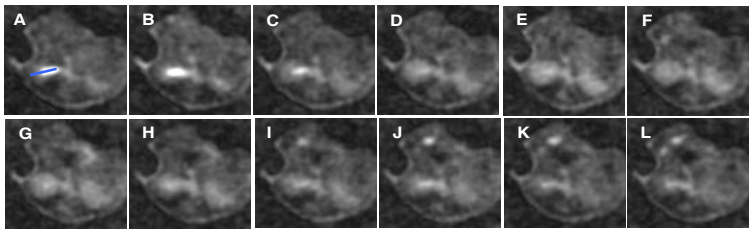

Figure 1: Series of axial images of the same slice during diuresis. The diureticum was administered after the first data set. With a resolution of 1.0 x 1.0 x 2.5 mm^3, each data set takes 4.7 minutes. A decrease in the medulla and a slightly increase in the cortex of the sodium signal can be observed. Blue bar in A: Corticomedullary axis of a mouse kidney.

Discussion:

This study shows the application of sodium MRI during the administration of a loop diuretic on the mouse. It shows the potential of sodium MRI in improving the understanding of the effects of pharmacological agents on renal function. Furosemide has two main effects on sodium concentration in the kidney. Due to the inhibition of the absorption of Na^+ and Cl^- in the macula densa cells and the following reactions, the total sodium concentration increases in the renal cortex [5]. The second effect takes place in the medulla where the cotransport of $Na^+/K^+/2Cl^-$ is inhibited and the reabsorption of Na^+ and Cl^- is reduced resulting in a lower total sodium concentration [6]. Both of these effects could be observed in our study. The profiles along the corticomedullary axis show a huge decrease of the sodium signal in the medulla and a moderate increase in the cortex. The temporal and spatial resolution is sufficient for further studies of physiological or pathological models. Using an external standard, absolute quantification of the TSC should also be possible. This work adds a valuable tool to renal diagnosis, previously available only in larger rodents.

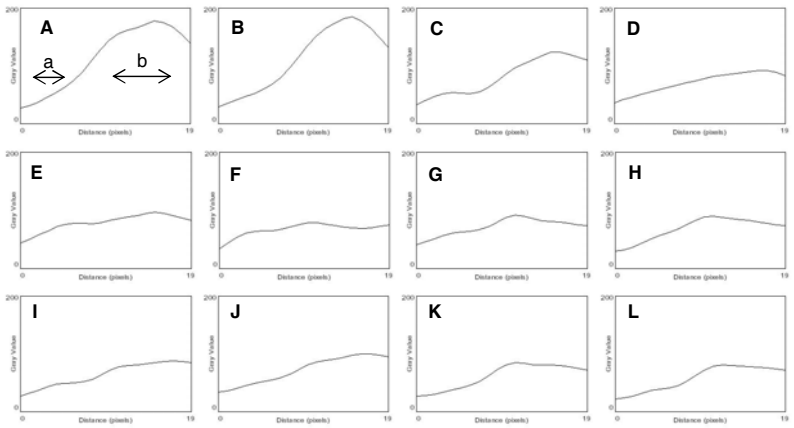

Figure 2: Profiles along the corticomedullary axis of a mouse kidney during diuresis. The diureticum was administered after the first data set. A decrease in the medulla (b) and a slightly increase in the cortex (a) of the sodium signal can be observed. Even 45 minutes after administration a steady state has not yet been re-established.

References:

[1] Maril et al [2004] KidneyInt 65(3):927–935. **[2]** Maril et al [2005] MRM 53: 545-552. **[3]** Maril et al [2006] KidneyInt 69:765–768. **[4]** Greiser et al [2003] MRM 50(6):1266–1275. **[5]** Greger [1997] Nephrol Dial Transplant 12:2215-2217. **[6]** Greger [2000]Am J Med Sci 319:51-62