Sodium quantification of transplanted kidney using dual-tuned proton/sodium MRI

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[Introduction] When renal function of a transplanted kidney is compromised, a biopsy of the kidney is frequently required for further diagnostic evaluation. Since the biopsy is invasive and may potentially expose patients to a risk of serious complications, a non-invasive method to assess pathophysiologic changes of the transplanted kidney would be desirable[1]. Renal function, including water reabsorption and urine concentration is directly related to the creation and maintenance of a cortico-medullary sodium (^{23}Na) gradient (CMSG) as well as the [^{23}Na] [2]. A few studies of sodium MRI of human kidneys were published with normal volunteers [3,4], including only one study of a transplanted kidney from a patient with normal renal function [5]. Recent technical advancements, including highly-sensitive, multi-array receivers, dual-tuned MR techniques [6,7], and ultra-short echo-time (UTE) pulse sequence [8], facilitate the acquisition of sodium MR images with improved signal sensitivity at relatively high pixel resolution (e.g., > 3 mm^3) as well as proton (^{1}H) MR images for co-registered structural information. In this study, we evaluated and compared quantitative sodium MRI characteristics between the native and transplanted kidneys that were imaged using dual-tuned ^{1}H/^{23}Na coil at 3 T.

[Methods and materials] All MRI was performed with a whole-body 3-T scanner equipped with multi-nuclei spectrometer (Siemens Medical Imaging, Erlangen, Germany). All procedures followed the guidelines of approved IRB. Six healthy volunteers and six renal transplant patients were included in the study. *Dual-tuned ^{1}H/^{23}Na RF coil:* Two dual-tuned coils were used for this study (**Fig. 1**). Overall reflection (S11) and transmission (S12) coefficients of ^{23}Na coils were -17 – -32 dB. ^{23}Na markers (4% agar, 153-mM [^{23}Na]) were attached to the coil frame for ^{23}Na concentration calibration and fiducial markers for co-registration of ^{23}Na images of kidney and calibration body phantom. *Dual-tuned proton/sodium MRI protocol:* Normal healthy subjects were scanned in the prone position and transplanted kidney patients were scanned in the supine position with the coil centered over the kidney during free breathing. To assess the reproducibility of sodium measurements, all healthy subjects were scanned twice within 48 hours. Proton MRI protocol included the following sequences; coronal T_2-weighted half Fourier acquisition single shot turbo spin echo (HASTE) (repetition time (TR)/echo time (TE) = 1,000/90 ms, resolution = 1.76 × 1.4 × 3.0 mm^3 and 75-mm depth coverage) (**Fig. 2A**). Without repositioning the subject, sodium MRI was performed using 3D UTE spiral trajectory sequence (hard RF pulse for 500 µs – 900 µs, TR/TE = 100/0.27 – 0.5 ms, flip angle = 90°, isotropic resolution = 3 mm^3, and total acquisition time = ~27 min) (**Fig. 2B**). The 5-mm low resolution sodium image of a homogeneous saline body phantom was also acquired for B_1-inhomogeneoty correction. *Imaging and data analysis:* Data processing and imaging analysis were performed using in-house programs and SPM (*www.fil.ucl.ac.uk/spm*). B_1-inhomogeneoty was corrected by the division of sodium image of abdomen with that of homogeneous body phantom. Point spread function (PSF) of sodium MRI at 3-mm^3 nominal imaging resolution was measured. For each subject, renal signal to noise ratio (SNR) and [^{23}Na] (within the medullary region, see black-dotted contour in **Fig. 3A**) as well as CMSG were measured. *Statistical analysis:* Mean ± STD of SNR, [^{23}Na] and CMSG of each kidney were computed. SNR, [^{23}Na] and CMSG of the healthy and transplanted kidneys were compared using Mann-Whitney test. The difference was considered significant if the P value was < 0.05.

[Results and conclusions] In-vivo ^{1}H/^{23}Na MR images of human abdomen were successfully acquired using our new dual-tuned ^{1}H/^{23}Na coil (**Fig. 2**). Both nucleus images were anatomically well co-registered. In the ^{23}Na image, kidney, spine discs and cerebral spinal fluid were mostly hyper-intensive (**Fig. 2B**). The PSF of sodium MRI was measured as ~5 mm at 3-mm nominal pixel resolution, suggesting lowering [^{23}Na] in sodium MR image. In the kidney, ^{23}Na image intensity increased from the cortex to the medulla (**Fig. 3A**). The peaks of local maximal signal intensity consistently corresponded to renal pyramids depicted on the corresponding proton image. SNR measurement of ^{23}Na image was acceptable (e.g., > 20) and reproduced; with 22.2 ± 4.8 (1st session) vs. 22.4 ± 4.2 (2nd). In addition, [^{23}Na] of the native kidneys was also reproduced with 192.9 ± 9.6 mM (1st) vs. 187.3 ± 4.7 mM (2nd). Interestingly, [^{23}Na] of the transplanted kidneys was 153.5 ± 11.9 mM, significantly lower than that of the healthy native kidneys (P = 0.002). The mean CMSG of the healthy native kidneys (10.5 ± 0.9 mM/mm) was significantly higher than that of the transplanted kidneys (8.9 ± 1.5 mM/mm) (P = 0.041).

In conclusion, we developed ^{1}H/^{23}Na MRI technique to image human kidney with dual-tuned RF coils at 3 T and to quantify [^{23}Na] and CMSG within the kidneys. The renal [^{23}Na] and CMSG of the transplanted kidneys were significantly lower than those of the healthy native kidneys. A further study with a larger population would be required to validate our findings.

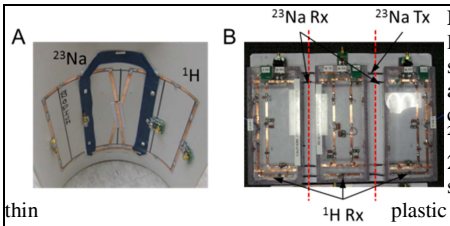

Fig. 1 Dual-tuned ^{1}H/^{23}Na RF coils – a quadrature saddle type coil (coil 1, **A**) and a flexible coil with 3-channel ^{1}H and 2-channel ^{23}Na coil (coil 2, **B**). Coil 2 consists of three segments on the foldable thin plastic sheet (see red dotted lines). The coil 1 was operated as both Tx and Rx, and in the coil 2, 3-channel ^{1}H coils works as Rx (operated with scanner body Tx coil), and 1-channel large surface ^{23}Na Tx and 3-channel surface ^{23}Na Rx coils.

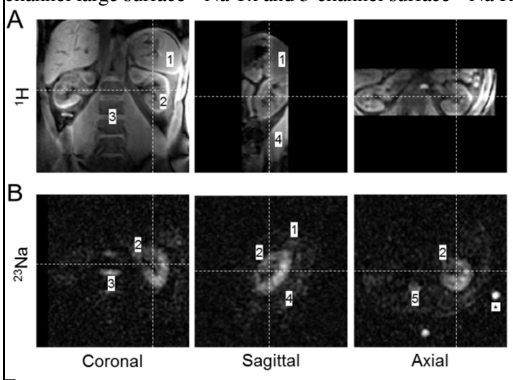

Fig. 2 Representative dual-tuned ^{1}H (**A**) and ^{23}Na MR images of abdomen (**B**). Two nucleus MR images were acquired at same experimental condition. Intensity is in arbitrary unit. 1 – liver, 2 – kidney, 3 intervertebral disc, 4 – muscle, 5 – cerebral spinal fluid, and * – reference marker.

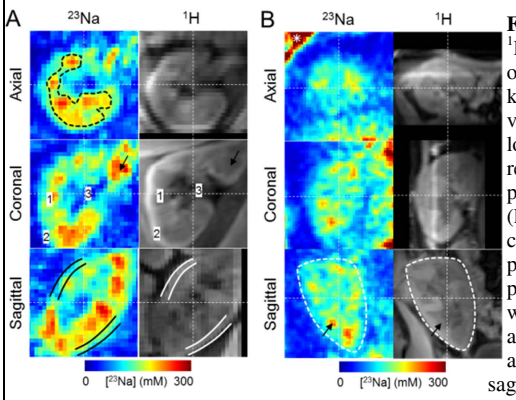

Fig. 3 Dual-tuned ^{1}H /^{23}Na imaging of the native kidney of a volunteer (**A**) and lower quadrant renal allograft in a patient (**B**). ^{23}Na (left panels) and corresponding proton (right panels) T_1-weighted images are displayed on axial, coronal and sagittal plane (white dotted lines). 1 – medulla, 2 – cortex and 3 – pelvis. White/black-solid curves are the approximated cortex boundary based on proton image. Black-dotted region is determined by threshold method to measure SNR and [^{23}Na] of the kidney. White-dotted contour is the boundary of kidney based on proton anatomy image and overlaid on sodium image. Black arrows indicate the medullary regions co-registered in both proton and sodium images.

[Reference] **1**. Chandarana et al, *AJR*, 2009. **2**. Jamison et al, *Oxford University Press*, 1982. **3**. Maril et al, *MRM*, 2005. **4**. Haneder et al, *Radiology*, 2011. **5**. Rosen et al., *Acad Radiol*, 2009. **6**. Kim et al., *MRI*, 2012. **7**. Moon et al., *JMRI*, 2013. **8**. Zhao et al., *ISMRM*, 2009.

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