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Communication

In vivo ^{39}K, ^{23}Na and ^{1}H MR imaging using a triple resonant RF coil setup

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ABSTRACT

The maintenance of a gradient of potassium and sodium ions across the cell membranes is essential for the physiological function of the mammal organism. The measurement of the spatial distribution of pathologically changing ion concentrations of ^{23}Na and ^{39}K with magnetic resonance imaging offers a promising approach in clinical diagnostics to measure tissue viability. Existing studies were focused mainly on ^{23}Na imaging as well as spectroscopy with only one post-mortem study for ^{39}K imaging. In this paper a triple resonant RF coil setup for the rat head at 9.4 T is presented for imaging of both nuclei (^{23}Na and ^{39}K) and the acquisition of anatomical proton images in the same experiment without moving the subject or the RF coil. *In vivo* MR images of ^{39}K and ^{23}Na in the rat brain were acquired as well as anatomical proton images in the same scanning session.

1. Introduction

Na^+ and K^+ are the most important ions for the normal cell function in the mammal organism. The maintenance of a specific gradient of these ions across the cell membrane by the active Na/K pump is a crucial basis not only for the osmotic pressure of the cell bodies and the excitability of nerve cells but also for the intra- and extracellular environment which is inevitable for the regular cell function. It is obvious that the ability to determine the viability or the non-viability of tissue by investigating these two elements non-invasively with magnetic resonance imaging (MRI) offers a tremendous potential in clinical diagnosis of some of the most widespread diseases like myocardial infarction, stroke or cancer.

Impressive advances have been made to extend the application of MRI of tissue sodium and its pathological changes from animal models to clinical use in humans [1–7]. The most abundant natural isotopes ^{23}Na and ^{39}K have a nuclear spin of 3/2 and therefore exhibit an electrical nuclear quadrupole moment. Compared to the well established MRI of water protons (^{1}H) MRI of quadrupolar nuclei suffers from the low sensitivity caused by the intrinsic gyromagnetic ratio and from high quadrupolar relaxation rates. Typical reported relaxation times of the spin-lattice relaxation T_1 are 23 ms at 8.4 T for ^{23}Na [8] and 14 ms at 7 T for ^{39}K [9]. The relaxation constants of the biexponential transverse signal decay T_2^I and T_2^{II} are reported as 2 ms and 17 ms at 8.4 T for ^{23}Na in the frog heart [8] and as 2.4 ms and 12.9 ms at 7 T for ^{39}K in the rat brain [9].

In addition to the fast relaxation the *in vivo* concentration of ^{23}Na and ^{39}K is much lower compared to water protons, resulting in MR signals which are 20,000 times (^{23}Na) and 2.1 million times (^{39}K) lower than ^{1}H signals [10].

Several efforts have been made to assess the detectability and the physical properties of these nuclei which are important for their quantification in different tissues by means of NMR [8–15]. In the year 1999, Fieno et al. presented ^{39}K MR images of isolated hearts of rabbits [16].

In order to investigate the feasibility of *in vivo* ^{39}K MRI we developed a triple resonant RF coil setup that allows the acquisition of *in vivo* MR images of tissue ^{39}K and ^{23}Na as well as anatomical ^{1}H images in one scanning session without changing the setup. To the best of our knowledge here we present the first *in vivo* MR images of ^{39}K of the rat head. Multinuclear MRI of ^{1}H, ^{23}Na and ^{39}K with a triple resonant coil setup might help to gain a deeper insight into pathologies like stroke, ischemia or cancer.

2. Materials and methods

2.1. RF coil setup

Fig. 1 demonstrates the triple resonant RF coil setup with a rat head placed inside and the corresponding circuit layouts. The RF coil for ^{39}K imaging at 9.4 T was built with 0.8 mm copper wire. Two Teflon carriers each with four windings with 1 mm spacing and a diameter of 35 mm formed a Helmholtz pair at 40 mm distance. The coil was coupled to the signal line through the capacitors C1 = 5.6 pF, C2 = 1–10 pF and C3 = 8.2 pF and tuned to the resonance frequency of 18.7 MHz by C4 = 10 pF in parallel to 56 pF, C5 = 10 pF in parallel to 33 pF and C6 = 1–40 pF.

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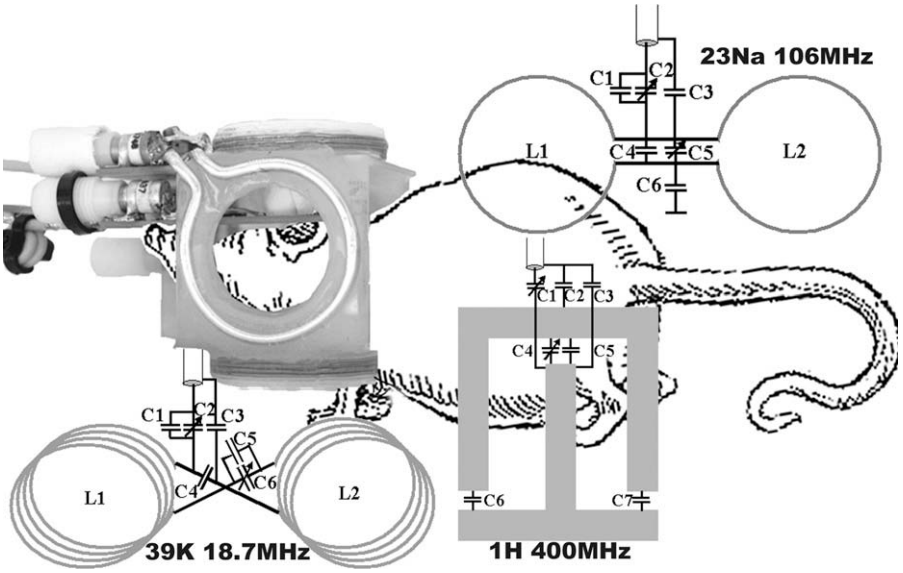

Fig. 1. Image of the triple resonant RF coil setup with a rat head placed inside and the corresponding circuit layouts of the three separate coils. The inductances of the coil for ^{39}K imaging at 18.7 MHz are at the top and bottom with the tune and match network soldered to a printed circuit board in the back (C1 = 5.6 pF, C2 = 1–10 pF, C3 = 8.2 pF, C4 = 10 pF parallel to 56 pF, C5 = 10 pF parallel to 33 pF, C6 = 1–40 pF). The inductances of the coil for ^{23}Na imaging at 106 MHz are in the front and in the back with the tune and match network soldered to a printed circuit board on the top (C1 = 8.2 pF, C2 = 1–10 pF, C3 = C6 = 6.8 pF, C4 = 10 pF, C5 = 1–40 pF). The coil for proton imaging at 400 MHz is designed on a printed circuit board placed 10 mm below the top of the K/N coil cube with C1 = 1–10 pF, C2 = C3 = 5.6 pF, C4 = 0.5–4 pF, C5 = 5.6 pF and C6 = C7 = 4.7 pF.

For ^{23}Na imaging we added a saddle coil made of two single loops of 3 mm silver wire with a diameter of 35 mm with the B_1 field perpendicular to that of the ^{39}K coil. The ^{23}Na coil was tuned to the resonance frequency of 106 MHz with C4 = 10 pF and C5 = 1–40 pF. The matching network consisted of C1 = 8.2 pF, C2 = 1–10 pF and C3 = C6 = 6.8 pF. The tune and match elements of these two coils were soldered on printed circuit boards which were then glued together with epoxy glue to form a cube with holes that allowed access to the animal for stereotactic positioning.

For the proton resonance frequency of 400 MHz we introduced a 32 × 32 mm flat two mesh structure coil which operates in counter rotating mode. The values for the capacitors within the matching network were C1 = 1–10 pF, C2 = C3 = 5.6 pF, whereas the values of the tune capacitors were C4 = 0.5–4 pF and C5 = 5.6 pF. In order to reduce the voltage drops across the coil elements a capacitor was added in each mesh (C6 = C7 = 4.7 pF). The coil was constructed on copper plated printed circuit board which was placed perpendicular to the B_1 field of the ^{39}K coil 10 mm above the center of the circuit board cube. This arrangement ensured the placement of the ^{1}H coil directly on the rat head while the head was positioned in the center of the other two coils. The inductive elements consisted of 5 mm wide and 37 μm thick copper. All variable capacitors used were purchased from Voltronics® (Denville, NJ, USA), while the fixed capacitors were purchased from American Technical Ceramics® (Huntington Station, NY, USA).

2.2. Experimental setup

Imaging experiments were performed at 9.4 T on a Bruker Biospec 94/20USR small animal system equipped with 740 mT/m *x*,*y*,*z*-gradients. A glass vial filled with 12 ml of a solution containing 150 mM NaCl and 150 mM KCl was used for phantom experiments.

In vivo imaging was performed on Sprague–Dawley rats (250–300 g) which were anesthetized with 1.2–1.5% isoflurane. The respiration frequency and the body temperature were monitored throughout the experiment and the latter was maintained with a water heating pad. All experiments were approved by the local authorities (Regierungspraesidium) and were in full compliance with the guidelines of the European community (EUVD 86/609/EEC) for the care and use of the laboratory animals. After a total experiment time of about four hours the animals were allowed to recover from anaesthesia.

2.3. MR imaging

Proton imaging was accomplished with a FLASH sequence with TE = 4.3 ms and TR = 250 ms. The field of view (FOV) was 9.6 × 9.6 mm^2 at a matrix of 384 × 384 with 8 slices of 6 mm thickness to match the potassium images. Additionally, ^{1}H images were acquired in 1 min with a RARE sequence with effective TE = 32 ms, TR = 500 ms, rare factor = 8, FOV = 3.2 × 3.2 mm^2, matrix = 256 × 256, 3 slices of 2 mm thickness.

The scan parameters of the 2D-FLASH sequence used for ^{23}Na imaging were TE = 1.32 ms, TR = 50 ms, 0.4 ms gauss pulse, readout bandwidth 3 kHz, echo position 5%, field of view = 64 × 64 mm^2, matrix 32 × 32, slice thickness 2 mm, 3 slices, 256 averages, 6 min 50 s scan duration.

In vivo ^{39}K MR imaging was done using a 3D-FLASH sequence with TE = 2.06 ms, TR = 50 ms, 1 ms gauss pulse, readout bandwidth 2 kHz, echo position 5%, field of view = 96 × 96 × 48 mm^3, matrix 32 × 32 × 8, 256 averages, 54 min 37 s scan duration.

The optimal transmit power for the RF pulse was determined by manually adjusting the attenuation of a reference rf pulse in an FID experiment. The signal to noise ratio (SNR) was calculated by dividing the difference between the mean signal in the head and the mean magnitude of the background noise by the standard deviation of the noise.

3. Results

All three coils were easily tuned to the corresponding resonance frequencies and matched to 50 Ω coaxial lines. The frequency shift was negligible when the coil setup was inserted into the magnet. No coupling between the coils was observed. The ^{1}H coil showed sufficient spatial coverage for shimming and for the measurement

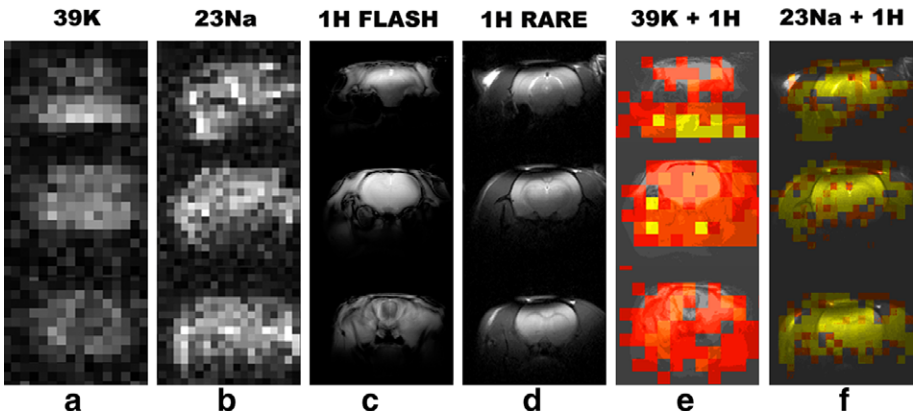

Fig. 2. Three raw unprocessed ^{39}K (a) and ^{23}Na (b) MR images of a rat head. ^{1}H images with a FLASH (c) and a RARE (d) sequence. Overlay of the thresholded and cropped ^{39}K images with the coronal ^{1}H FLASH images (e). Overlay of the thresholded and cropped ^{23}Na images with the coronal ^{1}H RARE images (f).

of anatomical images of a rat brain. We were able to acquire ^{23}Na and ^{39}K images as well as anatomical ^{1}H images of the rat head without changing the setup. To the best of our knowledge no previous publication of *in vivo* MR images of ^{39}K exists.

In the ^{39}K experiments on phantoms a strong dependency of the SNR per scan time not only on TR and TE, but also on the readout sampling bandwidth was observed. In a phantom experiment on the 150 mM solution of KCl, a reduction of the receiver bandwidth from 5 to 2.5 kHz resulted in an increase of the SNR of about 25%. It should be noted, that the reduction of the receiver bandwidth involved an *increase* of TE from 1.6 to 1.9 ms.

Fig. 2a shows three raw unprocessed ^{39}K MR images of a rat head with an SNR of about 4 after 54 min scan time at a resolution of $3 \times 3 \times 6$ mm^3. The corresponding coronal anatomical images are shown in Fig. 2c. Fig. 2b shows three raw unprocessed ^{23}Na MR images of a rat head with an SNR of 6 after less than 7 min acquisition time at a resolution of $2 \times 2 \times 2$ mm^3. The corresponding ^{1}H images are shown in Fig. 2d. Fig. 2e displays an overlay of the thresholded and cropped ^{39}K images on the proton images. In Fig. 2f, the thresholded sodium images are fused with the corresponding ^{1}H images.

4. Discussion

In this study we demonstrate the possibility to image physiological ^{23}Na and ^{39}K concentrations by means of MRI. Furthermore, we show that the triple resonant coil setup used in our study enables measurement of ^{1}H anatomical images as well as ^{23}Na and ^{39}K images without changing the setup. To the best of our knowledge, we show the first *in vivo* ^{39}K MR images of a rat head.

In good agreement with the suggestions of Parrish et al. [10] we observed a strong dependence of the signal to noise ratio per scan time in ^{39}K experiments not only on the repetition time and echo time in the FLASH sequence but also on the readout sampling bandwidth. From this observation we conclude, that optimization of rf pulse sequence parameters is essential for obtaining maximum SNR in context with ^{39}K imaging.

Although the low SNR in the presented ^{39}K images is evident, it is noteworthy that *in vivo* images originating from ^{39}K nuclei, which are 2.1 million times less sensitive to MRI than protons, can be obtained in a reasonable measurement time. The presented rf coil setup allows the detailed examination of the Na/K interplay in various pathological states which can lead to new diagnostic applications. Further studies will be devoted to the optimization of the rf coil setup and imaging pulse sequences in order to maximize the achievable SNR.

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