Chemical Shift Sodium Imaging in a Mouse Model of Thromboembolic Stroke at 9.4 Tesla

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Introduction

Sodium imaging in stroke models is of growing interest because of its availability for the use as intrinsic marker for brain integrity [1]. The main interest thereby lies in the distinction between viable and nonviable tissue involved in stroke. An increase of the tissue sodium concentration (TSC) after loss of membrane integrity is an established marker for dead tissue [1] that makes the quantification of TSC a promising approach for localized measurements of cell viability. Most animal studies of stroke use a rat model in which the middle cerebral artery (MCA) is occluded by the insertion of a threat into the artery. Orset et al. [2] presented a mouse model of in situ thromboembolic stroke that allows early reperfusion using plasminogen activator and therefore is very close to the human treatment strategy. Nevertheless, the very small size of the murine brain complicates many MR-imaging techniques. In particular sodium MRI with low signal-to-noise ratio (SNR) suffers from small-sized voxels required for imaging of the mouse brain at adequate spatial resolution. Furthermore, the short relaxation rates of the ^{23}Na nucleus preclude MRI with standard acquisition techniques. Thus, radial projection imaging techniques commonly are used for sodium MRI. Although data acquisition thereby starts in the center of k-space, the echo time TE is still in the range of 300 to 400 µs [3]. Because of the fast transversal relaxation, an increase of the sodium signal, detected with imaging sequences with non-zero echo times, may not only be explained by an increase in TSC, but also by a longer T2*. While the relaxation rate T2* of sodium still remains a limiting factor, the fast longitudinal relaxation T1 allows the use of short repetition times. Thus, we propose to use ^{23}Na chemical shift imaging for both, generic sodium imaging and the reconstruction of relaxation parameter maps from the acquired free induction decays (FIDs). It is shown that 3D sodium imaging of the whole murine brain of small anatomical sizes is possible in an adequate measurement time. This technique was applied to a mouse stroke model.

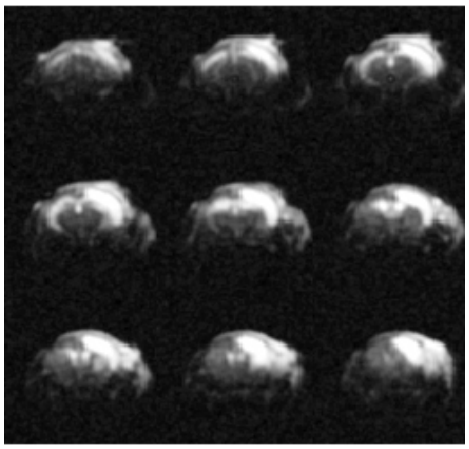

Figure 1: *Sodium image, reconstructed by integration of the first 6 ms of the FIDs.*

Methods

Three male C57 black/6J mouse were scanned 24 hours after middle cerebral artery occlusion (MCAo), which was induced as described by Orset et al [3]. All measurements were performed on a 9.4 Tesla Biospec 94/20 USR (Bruker, Germany) small animal system equipped with 740 mT/m gradients. A two-winding (12 and 20 mm i.d.) 105 MHz surface resonator element was developed with variable tuning (0.5 to 6 pF, Voltronics NMQM6GE) to maximize the SNR. Inductive coupling was achieved via a longitudinally displaceable coupling loop (18 mm i.d.), which was mounted in 10 mm distance above the surface coil. Na-CSI measurements were performed with a Hanning-weighted k-space acquisition [4] in three dimensions to reduce blurring and ringing and to increase SNR. 65536 phase encoding steps (two averages) were measured at a TR of 60 ms. Both factors lead to a total acquisition time of 1 h 5 min. 150 data points were acquired in an acquisition time of 30 ms. The first 30 data points (6 ms) of each FID were integrated to reconstruct sodium images. A matrix size of 47 x 47 x 37 was used, corresponding to a matrix size of 32 x 32 x 32 in a non-weighted acquisition case. The field of view was set to be 19.2 x 19.2 x 38.4 mm^3 leading to a spatial resolution of 0.6 x 0.6 x 1.2 mm^3. To measure the changes in the sodium density and in the transverse relaxation time T2*, two regions of interest (ROI) were manually defined in five slices, by comparison with histology. One ROI contained ischemic tissue. The second ROI was put on the contralateral side, equally shaped and at the same distance to the surface coil. The mean signal intensity of both ROIs was calculated for each time point of the FID and a monoexponential fit function of the form $S(t) = S0 \exp(-t/T2^*) + \text{const}$ was estimated by least squares. The weighted mean of T2* and of the S0 increase were calculated in all slices with the weightings $w_i = 1/\text{Std}(T2^*)^2$ and $w_i = 1/\text{Std}(S0_{inc})^2$, respectively.

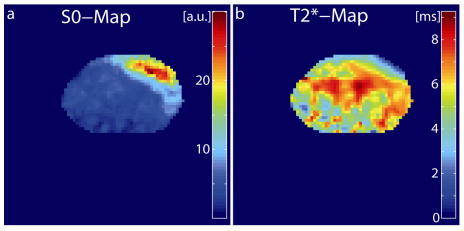

Figure 2: *S0 and T2* parameter maps, estimated by an exponential fit approximation of the FID's. The S0-Maps shows a significant signal increase in the infarcted area.*

Results

Infarcted regions appear hyperintense in the sodium image (Fig. 1) and are equally shaped as in the less stained area in hematoxylin-eosin stained coronal brain slices (not shown). The center slice of each scan was used for further data analysis to calculate S0 and T2* parameter maps. The S0 map (Fig. 2a) reveals a strong signal increase in the infarcted region indicating an increase in TSC. The T2*-map in Fig. 2b shows that the sodium relaxation parameter T2* ranges from about 3 to 10 ms in the mouse brain. There is a slight T2*-increase in the infarcted hemisphere, but the infarcted area does not significantly stand out against healthy tissue. The ROI-based data analysis is more precise because the mean of all data points in the ROI was used. The results are shown in Table 1. The increase in sodium concentration in the stroke area compared to healthy tissue is ranging from 160 to 260 % (2.6 to 3.6 fold). The T2* in healthy brain tissue varies from 4.6 to 7.5 ms and is increased in stroke in all mice. Although the increase in T2* is much smaller than the S0 increase, ranging from 110% to 175% it is still significant.

	T2* stroke	T2* contralateral	S0 increase
Mouse 1	(8.3 ± 0.1) ms	(7.5 ± 0.3) ms	(220 ± 7)%
Mouse 2	(5.3 ± 0.2) ms	(4.6 ± 0.3) ms	(260 ± 7)%
Mouse 3	(8.7 ± 0.3) ms	(6.7 ± 0.6) ms	(160 ± 12)%

Table 1: *T2* -values of stroke and healthy tissue and S0-increase.*

Discussion

In this work, it has been demonstrated that ^{23}Na-CSI is feasible for sodium imaging at adequate resolution for the small anatomical size of the murine brain. The combination of the high field of 9.4 Tesla, the inductive coupled surface coil and the weighted ^{23}Na-CSI sequence enable a spatial resolution of 0.6 x 0.6 x 1.2 mm^3. To the best of our knowledge, this is the highest reported resolution in sodium magnetic resonance imaging measured below 21 Tesla. Furthermore, the acquired data allows the calculation of S0 and T2* parameter maps and therefore a quantitative evaluation of the sodium signal change in stroke. Although theoretically the signal decay is biexponential, the monoexponenial function sufficiently fits the FID's. Earlier presented methods to measure local T2* values, based on a gradient echo sequence [5], are applicable for sodium long component T2*-mapping, but the influence of the short T2*-component cannot be taken into account with the long echo times achieved with these techniques. The presented measurements show an approximately threefold sodium density increase in the infarcted area and indicate that T2* also increases in infarcted tissue. This effect should be taken into account for the estimation of the TSC using imaging techniques with non-zero echo times.

References

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