High resolution sodium imaging of rat and mouse models of stroke at 17.6 T

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Introduction:

Stroke is one of the major causes of death in both men and women in the western world. Various proton MRI techniques, such as diffusion and/or T_2-weighted imaging, have been used to analyze the viability of the affected tissue. Since the sodium concentration is known to increase over time in infarcted regions [1], monitoring the sodium homeostasis provides additional information to characterize the size and progression/regression of the injury [1], [2]. Animal models are particularly useful in assessing disease models and treatment, but since the SNR of sodium images is relatively low, high B_0 fields and optimized sequences are important [3]. In this work three dimensional sodium density weighted chemical shift imaging (DWCSI) [4] was conducted on rodents at 750 MHz. Sodium images of various infarct models in rat and mouse brains (the first such images acquired in mouse) are presented here.

Subjects & Methods:

Experiments were carried out on a Bruker Avance 750 MR system (Bruker Biospin, Rheinstetten, Germany, 17.6 tesla, maximum gradient strength: 200 mT/m for the rat- and 1 T/m for the mouse-experiments) using a linear 38 mm diameter birdcage for rats and a 27 mm quadrature birdcage for mice. In rats, stroke was induced by the permanent occlusion of the middle cerebral artery. Two different stroke models were applied to C57BL6 mice (15 – 18 g). In the first model the coronary artery of one side of the brain was occluded for 90 minutes leading to a massive stroke of almost half of the brain. In contrast, in the second model a much more localized part of the brain is affected, the stroke being induced by activating previously-injected radicals into the brain with a light source. Proton RARE and diffusion-weighted imaging was conducted prior to the sodium imaging. The maximum resolution of the purely phase encoded (32768 phase encoding steps) sodium 3D DWCSI was $(0.8\ mm)^3$ isotropic for the rats and $0.7 \times 0.7 \times 1.0\ mm^3$ for the mice.

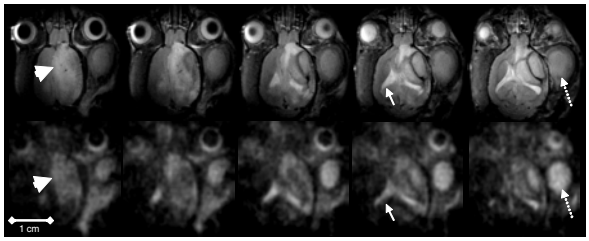

Figure 1: Coronal images from proton 2D RARE (upper row) and corresponding sodium 3D DWCSI data sets of an infarcted rat brair A cyst (dotted arrow) also developed. The images were acquired at day 9 after operation. (arrow head = stroke, small arrow = CSF).

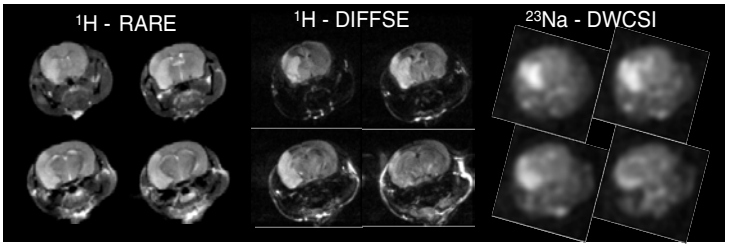

Figure 2: Comparison of proton RARE (left), diffusion weighted spin echo (middle) and sodium DWCSI images of the infarcted mouse brain. The stroke was induced by an occlusion of the coronary artery. The infarcted area can be seen clearly in all three image sequences.

Due to the short relaxation times of sodium the delay between excitation and data acquisition was minimized to 675 µs for the rats and 275 µs for the mouse experiments. The sodium T_1 in the mouse brain was measured with an adapted 3D DWCSI saturation recovery sequence. After saturation, eight time points (20/40/60/80/100/125/200/300 ms) were acquired and a three parameter fit on a pixel-by-pixel basis was conducted on the reconstructed images.

Results:

A good correlation between the proton RARE and sodium DWCSI images of the rat brain can be seen in Figure 1. Figure 2 shows the first sodium images of an infarcted mouse brain (right side, occlusion model) and corresponding slices from the proton diffusion-weighted (middle) and RARE (right side) images. Again the infarcted area can be seen in all images. Measurements of T1 were performed at different times after stroke: results showed little change in the stroke area (Table 1): the healthy brain and CSF provide control values.

10 days after stroke			
	STROKE	BRAIN	CSF
T_1	58 ± 5 ms	40 ± 2 ms	55 ± 4 ms
15 days after stroke			
	STROKE	BRAIN	CSF
T_1	53 ± 3 ms	44 ± 2 ms	56 ± 5 ms

Table 1: Sodium T_1 values of the infarcted mouse brain.

Discussion:

These preliminary results shows that sodium imaging by using high magnetic fields and an optimized pulse sequences is feasible not only for larger rodents such as rats, but also for mice. In future studies, incorporating an external standard should allow quantitative analysis of the total sodium concentration, and how this changes during the progression of the disease/treatment.

References:

[1] Thulborn KR. et al, Radiology 213:156-166, (1999), [2] Lin SP et al, Stroke. 32(4):925-32. (2001), [3] Neuberger et al, Proceedings ESMRMB, 65, (2002), [4] Greiser et al, MRM, 50:1266-75, 2003