Potential of ^{23}Na-MRI in muscular sodium channel diseases

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Introduction

Sodium MRI has the potential to noninvasively detect sodium content changes *in vivo* [1, 2]. The *in vivo* ^{23}Na signal decays biexponentially with a short component of T_{2s} = 0.5-8 ms and a long component of T_{2l} = 15-30 ms [3]. Thus pulse sequences that enable short echo times are necessary. In this work we used a density adapted 3D Radial sampling scheme to measure the sodium concentration in the lower leg muscles of a patient with confirmed paramyotonia congenita (PC), a muscular sodium channelopathy, and a healthy volunteer. In PC, cooling causes an increased open probability of the mutant sodium channels resulting in intracellular sodium accumulation and muscle weakness. The purpose of this study was to show the feasibility of ^{23}Na-MRI for the examination of patients with PC and testing for specific therapies.

Methods

A patient with confirmed PC and a healthy volunteer were examined on a 3.0 T clinical MR system (Magnetom Tim Trio, Siemens Medical Solutions, Erlangen, Germany). ^{23}Na-MRI was performed with a density adapted 3D Radial (DA-3D-RAD) sequence (Fig. 1; TA = 15 min, TE = 0.2 ms, TR = 60 ms, 3 averages, t_0 = 0.5 ms, G_0 = 6.78 mT/m, 6.67 ms readout window, resolution of 4x4x4 mm^3). The sequence's readout gradients are switched constantly up to a k-space radius $k < k_0$. Beyond this radius the gradient's amplitude is reduced in a way that the sampling density in all spherical shells is kept constant. This technique leads to a higher SNR compared to conventional radial sequences [4]. Additionally, ^{1}H-imaging with T_1 (2D-FLASH) and T_2 (TSE) weighted sequences was performed. Images were acquired using a double-resonant (32.59 MHz/ 123.2 MHz) birdcage coil (Rapid Biomed GmbH, Würzburg, Germany). Image reconstruction was performed offline with Matlab (Mathworks, Natick, MA, USA). A Kaiser-Bessel gridding kernel was used [5], followed by Hanning-filtering and a conventional FFT with three identical measurements. In between the first and second measurement one leg was cooled (>20 min), between measurement two and three a medication of zinc (30 mg i.v.) was applied and the contralateral leg of the patient was cooled. For the volunteer zinc medication and a third measurement were omitted. For each measurement the mean sodium concentration was determined in 15 consecutive slices in the tibialis anterior muscle. ROI's were selected in the ^{1}H-images to prevent a biased selection (Fig. 2a). Prior to each measurement the muscle strength of the patient was measured.

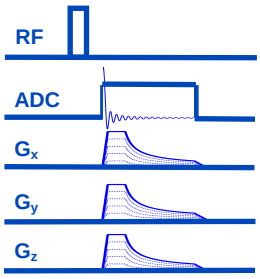

Fig. 1: gradient scheme of the DA-3D-RAD sequence

Results

After cooling the right lower leg, a sodium concentration increase of about 22%, compared to the reference scan and the non-cooled leg (within the same measurement), was measured in the tibialis anterior muscle (Fig. 2e; Fig. 3a). Medication of zinc and cooling the other leg led to a concentration increase of 14% in the cooled leg (compared to the reference scan), whereas the former cooled leg showed still a 7% higher concentration (Fig. 2f; Fig. 3a). The differences within one measurement in the concentration between right and left side without provocation are well below 5%. The differences in the healthy volunteer with cooling of one leg are also below 5% (within one measurement), e.g. no significant difference between cooled and non-cooled leg was measured, although a slight increase in concentration from the first to the second measurement was detected (Fig. 3b). Besides the effect the cooling induced, the patient showed a higher sodium concentration than the healthy volunteer in the triceps surae muscle (Fig. 2c). The measured muscle strength of the patient decreased after cooling (table 1).

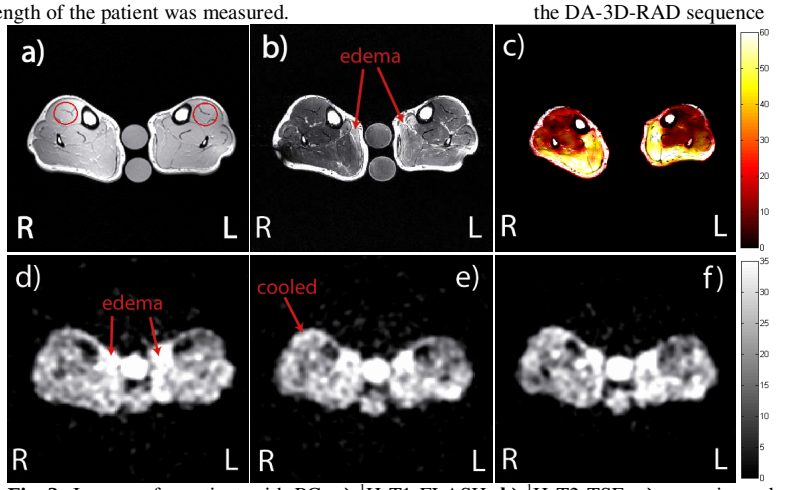

Fig. 2: Images of a patient with PC: **a)** ^{1}H T1-FLASH; **b)** ^{1}H T2-TSE; **c)** co-registered ^{23}Na- and ^{1}H T2 weighted image; edema in triceps surae muscle; the scale is given in mmol/l; **d) – e)** slice of a DA-3DRAD ^{23}Na data set; the scale is given in mmol/l; **d)** reference image (before cooling and medication); **e)** after cooling of the right lower leg; **f)** after zinc medication and cooling of the left lower leg

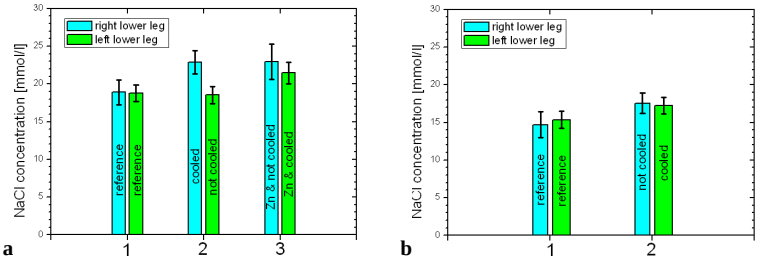

Fig. 3: ROI analysis of the patients leg (a) and the volunteers leg (b) **1**: reference measurement; **2**: one lower leg cooled; **3**: zinc medication and other lower leg cooled

	Foot Dorsiflexion		Foot Dorsiflexion		Toe Dorsiflexion		Toe Dorsiflexion	
Measurement	right	left	right	left	right	left	right	left
1 (reference)	5	5	5	5	4	5	4	5
2 (cooled right)	2	5	3	5	2	5	4	5
3 (Zn & cooled left)	4	5	4	5	4	5	4	5

Table 1: Muscle strength in patient with PC. The strength was scored according to the grading system proposed by the British Medical Research Council.

Discussion

The slight increase of the intracellular sodium concentration between the two measurements in the volunteer might be due to the new positioning and a possible temperature change of the references. So the differences between the right and left side within one measurement should be more reliable. The change of the sodium concentration in the patient's cooled leg was seen within one measurement and also compared to the reference scan. This change can be attributed to an increase in intracellular sodium concentration and is well in accordance with the lower muscle strength in the cooled leg (table 1). The muscle strength of the left leg did not change after cooling in combination with medication of zinc (table 1). This implies that zinc can prevent intracellular accumulation of sodium ions. From the MRI measurement at least a smaller increase of the sodium concentration was determined. To investigate this in more detail we will use a larger number of patients. The second cooling followed about 1h after the first one. To prevent a bias of the non-cooled leg from the former cooling, it would also be beneficial to have at least one day between the second and third measurement. Furthermore the higher sodium concentration in the patient (triceps surae muscle) compared to the volunteer is due to muscular edema evidenced also by ^{1}H MRI. A larger number of subjects is needed to investigate this effect with higher significance. These preliminary results are a promising base for further investigations of patients with muscular channelopathies and testing for specific therapies.

References

[1] Nielles-Vallespin et al.; MRM (2007); 57: 74-81
[2] Weber et al.; Radiology (2006); 240: 489-500
[3] Constantinides et al.; Radiology (2000); 216: 559-568
[4] A.M. Nagel et al.; Submitted Proceedings ISMRM 2008
[5] Jackson et al.; IEEE Transact. on Med. Imaging; (1991) 10(3); 473-478