Correction for T1 effects on MRI estimation of muscle sodium levels

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Introduction: Sodium ion homeostasis is of major importance in cells and is maintained by coupled exchange with potassium ions between intra- and extra-cellular spaces using the Na^+/K^+-ATPase (sodium-potassium pump) [1, 2]. The pump maintains a constant concentration gradient across cell membranes that results in an intracellular sodium concentration of 10 -15mM and extracellular concentration ~140mM in normal tissues [3, 4]. To quantify tissue sodium content (TSC), calibration standards (phantoms) are typically scanned together with the body part so the TSC can be calculated by comparing signal intensities between tissue and the reference standards. Significant differences in relaxation times between the tissue and calibration phantoms would affect the reported TSC values, which are usually reported lower than true values. In this study, we evaluated the influence of T_1 effects on estimates of calf muscle TSC *in vivo* at 3T.

Methods: Lower legs (calf muscles) of two healthy volunteers (both aged 37) were scanned on a Philips 3T Achieva system (Philips Healthcare, Cleveland OH, USA) with a Rapid sodium quadrature knee coil (Rapid Biomedical GmbH, Rimpar, Germany). Four calibration phantoms (NaCl aqueous solutions with [Na]: 10mM, 20mM, 30mM, and 40mM) were scanned together with each calf. Imaging parameters: 3D GRE, FOV= 192×192mm^2, 7 slices at a thickness of 30mm, bandwidth=434Hz/pixel, TE=0.99ms. Based on our previous work, calf sodium T_1 is ~15ms, and phantom T_1 ~27ms. To examine the effect of TR on the reported TSC value, a series of scans with different TRs [=50ms, 70ms, 90ms, 110ms, 130ms, 150ms, 160ms] were performed with a flip angle (Ernst angle) adjusted according to the TR and calf T_1. Each scan took ~15 minutes by adjusting the number of signal acquisitions. Regions of interest (ROIs) were drawn manually on the reference phantoms as well as the calf (Figure 2 A), from which TSCs were estimated at each TR. Finally, we assumed the longest TR (=160ms) had no T_1 effect, because at this TR, sodium ions in both phantom and tissue should be fully relaxed, and the relative errors of the measurements at other TRs were then evaluated.

Results: Figure 1 (A) shows the sodium images at different TRs, the corresponding proton structural image is displayed in (B). The calibration phantoms are shown at the bottom of the image with [Na] 10mM – 40mM (left to right). The TSC maps are illustrated in (C).

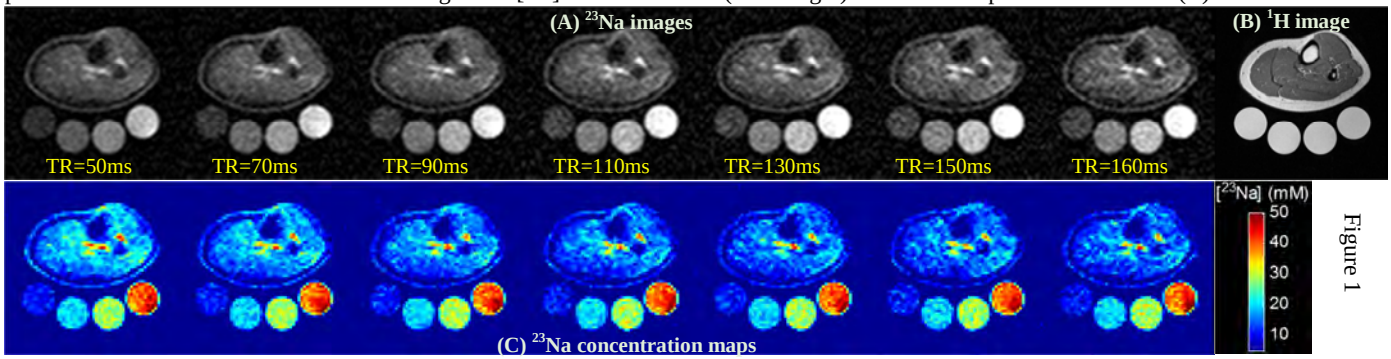
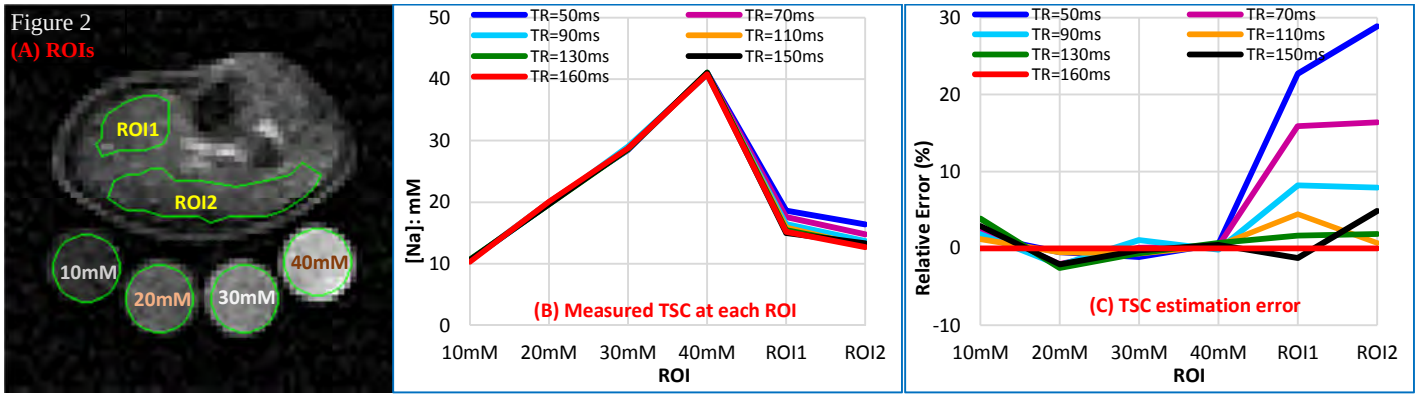


Figure 1

Figure 2 (A) denotes the ROI locations, and (B) plots the TSCs at each ROI and compares them between different TRs. For the calf ROIs (ROI1 and ROI2), it is seen that the TSC is higher at shorter TR, but it essentially converges as TR increases. From Figure 2 (C), when TR=130ms, the relative error < 5% if assuming TR=160ms provides a true TSC (T_1 effect should be eliminated from both tissue and phantom).



Discussion: According to our other measurements, sodium T_1 is ~15ms in calf, and ~27ms in calibration phantoms. To eliminate T_1 effect in calf, presumably a TR = $5\times T_{1_calf} \approx 75$ms should be used. However, our results indicate here that a TR=75ms still leads to more than 10% error in the reported TSC. The error is because the sodium ions in the calibration phantoms are still partially saturated, and their full recovery would need a TR = $5\times T_{1_phantom} \approx 135$ms. This is verified by our data, where we find that the relative error is less than 5% when TR is greater than 130ms.
In summary, unless the relaxation times of the reference phantoms and tissue are well matched, to eliminate T_1 effects from TSC measurements a TR should be chosen so that sodium ions are fully relaxed in both tissue and calibration phantoms.

References:

[1] Madelin *et al*. Sci Rep 2014; 4:4763. [2] Rose *et al*. Clinic Chem 1994; 40:1674. [3] Inglese *et al*. Brian 2010; 133:847. [4] Madelin *et al*. JMRI 2013; 38:511.