Quantification of sodium in healthy cervical cord using prior knowledge

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Target audience: Scientists and clinicians interested in the quantification of sodium using magnetic resonance spectroscopy (MRS).

Purpose: Evaluating the most accurate technique for fitting in vivo sodium MRS data.

Introduction: Sodium MRI has the possibility to report on several pathologies affecting the spinal cord including spinal cord injury and multiple sclerosis. 23Na MRI is challenging in the cord due to short T2 relaxivities and partial volume effects. In tissue 23Na T2 relaxation is bi-exponential, resulting in a short T2 fraction (T2s=3-4ms), which constitutes 60% of the signal, and a long T2 fraction (T2L=20-25ms). Recently two 23Na MRS protocols were presented, both based on the ISIS localization sequence, to overcome these challenges and measure sodium in the spinal cord: 1) using hypersecant (HS) inversion pulses (FAHS) and 2) a Fast Ultra Short TR Sensitive (FUSS) sequence, using shorter sinc-gauss inversion pulses. Both sequences result in a single resonance and similar SNR. However, the accuracy of the sodium concentrations found using these methods has not been explored. A single resonance is often fit to a single peak, however as the bi-exponential behavior of sodium in tissue is known this information can be factored into the analysis. Here we investigate different analysis techniques for 23Na MRS and their effect on accuracy and variation within a group.

Methods: In vivo MRI: 6 healthy subjects were recruited (4 female, 2 male). Scanning was performed on a 3T Achieva TX system (Philips Healthcare, Best). A fixed quadrature sodium transceive coil (Rapid, Germany) was used for 23Na (33.8MHz). Using the Q-Body coil, 1H images were taken in the sagittal and coronal planes for MRS planning. FUSS and FAHS spectra were acquired from an effective voxel size of 9x12x35mm3 centered on the C2-3 intervertebral disc, using inner volume saturation to suppress signal from CSF and bone, TR 300ms, BW 6000Hz, number of points 1024, TE=0.26ms, and n=800.

Quantification:

Immediately following the 23Na MRS scan volunteers were removed, and replaced with an external concentration reference phantom (44.8mM NaCl), on which an identical scan was run. All data were line broadened to 5Hz, zero-filled to 2048 and phased in JMRI. The spectra were then fitted in each of the following 3 ways using the AMARES algorithm: a) a mono exponential fit with no prior knowledge (1 peak Mono Fit b) a bi-exponential fit (2 peaks), using prior knowledge for the amplitude ratios [60-40] and soft constraints on the linewidths (15-17Hz and 90-110Hz corresponding to T2s and T2l respectively) (Bi-fit c) a combination fit, using the bi-exponential fit for in vivo data together with a mono-exponential fit for the reference phantom (Combo Fit), Figure 1. Amplitudes were corrected for T2 and T2l. The sum of the peak amplitudes was used in the quantification for Bi-fit. Data was quantified using equation 1 where Smono and Sbi are the measured signal amplitudes respectively, Na is the reference concentration and Cload is the correction factor for loading.

Quantification of sodium (mean±standard deviation (SD)) was compared for each fitting method using a paired t-test. T2 relaxation times derived from spectral fitting were also recorded, for each fitting method.

Results:

In vitro- The agar data shows that FUSS Bi-Fit yields the most accurate quantification with only a 3% error in the calculated concentration (Table 1). High sodium concentrations are found using Comb-Fit. In vivo- Mean concentrations for each fitting method are shown in Table 1. When using the same fitting method, FUSS and FAHS gave similar sodium concentrations (p>0.05 for all). Differences in sodium concentration do however, vary across fitting methods. In vivo the lowest concentrations are found using the Mono-Fit (p<0.05) and the highest with Comb-Fit (p<0.05). Coefficients of variation (CV) were 0.2 for in vivo sodium concentration across all fitting methods, with the exception of the FUSS Bi-Fit (CV=0.3).

Discussion:

In vitro FUSS and FAHS give the most accurate concentrations in vitro supporting the bi-exponential nature of bound sodium. In vitro data from agar suggests that FUSS Bi-Fit is the most accurate fitting method, if this translates to in vivo an estimate of 23Na concentration in the spinal cord of 34±11mM can be made. This agrees well with the reported values in brain using 23Na-MRI. T2-values derived using FUSS Bi-Fit also support those measured in the brain for 23Na (T2s=3.08ms and T2l=21.2ms), however given the soft constraints on the linewidth this is somewhat expected. The larger CV with FUSS Bi-Fit is however concerning, and the source of this variation needs further investigation. The larger variation in 23Na concentration found using Bi-Fit can be seen in figure 2, at least two subjects appear to have a underestimation (1 and 4). Improvements, beyond natural between-subjects’ variability, could perhaps include cardiac triggering the sequence and increasing the SNR through more averages. Alternatively, FAHS Bi-Fit gives a concentration similar to FUSS Bi-Fit (p>0.05) but with a smaller CV (0.2), and only a small deviation in the accuracy of the agar phantom concentration measurement. This may in part be due to the fact that the HS pulses in FAHS are less susceptible to the inherent B0 inhomogeneity in the spinal cord, a factor that does not affect the phantom measurements. Monosodium Bi-Fit is high indicating the mono-exponential fit of the saline phantom maybe underestimating its amplitude, resulting in higher calculated concentrations (possibly due to using shim current values optimized for the agar scan).

Conclusions:

Sodium MRS data is fitted most accurately using a bi exponential fit. Using the sinc gauss inversion pulses (FUSS) together with Bi-Fit gives the most accurate results in vitro. Using Bi-Fit has the added advantage of the estimation of T2s and Ts. This method could be extended to estimate changes in the 60:40 ratio. Changes in the ratio could be related to an expansion in extracellular space (increased amount of T2s) or an increase in intracellular sodium (increased amount of T2l). Hence, we present a method with which to accurately quantify total sodium concentration in the spinal cord, whilst allowing changes in the proportion of bound and unbound sodium in vivo to be estimated.