Sodium Relaxometry (Part 2): Towards the Characterization of the Sodium NMR Environment in the Human Brain Using a Novel Relaxomety Technique

R. W. Stobbe[1], C. Beaulieu[1]

[1]Biomedical Engineering, University of Alberta, Edmonton, Alberta, Canada

Introduction: Intracellular sodium concentrations may provide significant information pertaining to a diseased cellular state. Intracellular sodium concentrations experience a rapid increase as a result of anoxic depolarization in hyper-acute stroke, may correlate with the rate of cellular proliferation in tumours, and intracellular sodium depletion may be an indicator for apoptosis. Of particular usefulness would be the ability to selectively image intracellular sodium. It has been suggested that the extracellular space, which is said to comprise approximately 20% of the tissue volume is quite sparse facilitating volume transmission. Because sodium relaxation rates correlate with matrix density it has been proposed that these rates differ significantly between the two spaces. Shift-reagent experiments conducted with a tumour implanted in a rat suggest this is the case (1). It would be advantageous to characterize these rates within the human brain – but due to its toxic nature shift reagent work is not an option. Typical multi-echo relaxometry would yield a quadric-exponential curve with one, or two, of the terms being extremely short and would be difficult to analyze. In this abstract, a novel relaxometry technique (introduced in 'part one' abstract) is proposed as a means to characterize these two sodium environments in the human brain.

Methods: Using a set of seven images from two different healthy volunteers acquired with various inversion-recovery delays (TI) and inversion pulse lengths (IPL) (**Figure 1)**, the spectral density parameters governing relaxation were regressed using spin simulation software (see 'part one' abstract). K-space was sampled using 3D-twisted-projection-acquisition with an acquisition voxel size of 6.4 mm isotropic. The excitation pulse was 0.9 ms yielding a TE of 0.52 ms and the magnetization recovery delay following each excitation was 140 ms for the non-inversion experiment, 170 ms for the 5 ms inversion experiment and 260 ms for the 2.5 ms inversion experiment. Using these magnetization recovery delays the SAR for each scan was maintained below 1 W/kg. The total imaging time required to obtain each set of images was 50 minutes.

Image intensities (relative to a no-inversion scan) were measured in an ROI consisting of two volumes (~ 5 mL each) adjacent to the ventricles and containing various nuclei and the thalamus. Care was taken to avoid the inclusion of CSF in the images. Measured data was then regressed using both a one and two compartment model. In the two compartment model the relative contribution from each environment was also included in the regression.

Results: The images obtained from each scan in one volunteer are displayed in **Figure 1**, along with the relative signal intensities measured in the ROI. It is readily apparent from **Figure 1a** that a one compartment model is insufficient to describe the relative image intensities obtained from experiment. Two components of T_1 relaxation appear evident. The partial inversion effect can also not be effectively modelled with only one J_0 parameter. The two-compartment model of **Figure 1b** provides a much closer fit. **Table 1** displays the regressed spectral density parameters and the associated relevant relaxation parameters for both volunteers. While the 95% confidence intervals associated with mean regression are reasonable, the confidence associated with two-compartment regression is very low. This reflects the attempt to regress 5 parameters from six data points. However it is promising that regression yields similar values in each volunteer.

	Volunteer 1	*Volunteer 2*	
1 Compartment Model			
J_0	0.5	0.6	(Hz)
$J_1 = J_2$	0.014	0.013	(Hz)
T_{2fast}	1.8	1.6	(ms)
T_{1ave}	35	37	(ms)
2 Compartment Model			
rapid			
J_0	2.2	2.2	(Hz)
$J_1 = J_2$	0.031	0.025	(Hz)
T_{2fast}	0.45	0.44	(ms)
T_{1ave}	16	20	(ms)
slow			
J_0	0.12	0.15	(Hz)
$J_1 = J_2$	0.012	0.011	(Hz)
T_{2fast}	7.5	6.2	(ms)
T_{1ave}	43	44	(ms)
	(51% rapid)	(49% rapid)	

Table 1 Spectral densities and relevant relaxation parameters derived from regression for both one and two compartment models of brain tissue in two volunteers.

Discussion: Although the one compartment model is insufficient to fit the data points acquired, it can be used to estimate a bulk T_{2fast} and average T_1 in the human brain. An estimation of bulk T_{2fast} has been attempted before with multi-echo relaxometry yielding a value of 1.7 ± 2.3 ms (2). In this experiment the same bulk value is obtained with little difference between volunteers.

Of particular interest is the separation of brain sodium into two compartments. The regressed values for the slow compartment seem to correspond with an environment similar to 2% agar, and may represent extracellular space. The distribution between the rapid and slow compartments may correlate with the sodium distribution between intra- and extracellular space if intracellular space accounts for 85% of tissue volume and the intracellular sodium concentration is 25 mM. Finally, the T_{2fast} component in the rapidly relaxing compartment is smaller than any value measured in-vivo (1 ms has been measured using triple quantum filtering in the presence of shift reagent in rats (3)). The value of J_0 is two orders of magnitude larger than J_1 and J_2 suggesting this compartment could not be modeled by a simple agar environment. This is not surprising as cells contain many very highly ordered structures and negatively charged molecules. Residual quadrupole interactions will also have an effect in these ordered environments. If a significant sodium environmental difference does exist between intracellular and extracellular space – selective intracellular imaging is a distinct possibility.

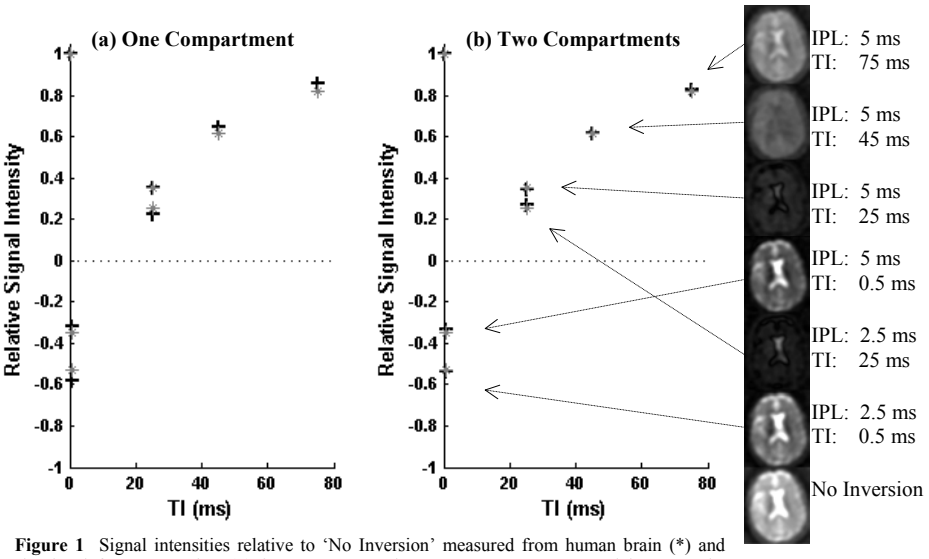

Figure 1 Signal intensities relative to 'No Inversion' measured from human brain (*) and simulated from regression (+) in a one **(a)** and two **(b)** compartment model. Note the systematic inability of the one compartment model to fit the relative signal intensities measured in brain.

References:

(1) Winter, P.M., et. al., Magnetic Resonance in Medicine **45**, 436 (2001). **(2)** Bartha, R., et. al., Magnetic Resonance in Medicine **52**, 407 (2004). **(3)** Winter, P.M., et. al., Journal of Magnetic Resonance **152**, 70 (2001).