In vivo measurement of T_1 relaxation times of ^{31}P metabolites in human brain at 3T

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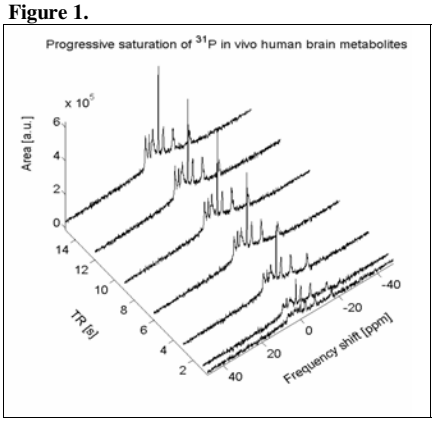
Introduction: ^{31}P MRS has been lauded as a powerful quantitative tool that offers several advantages over other methods of in vivo biochemical investigations because it is noninvasive, non-ionizing, and does not require the use of tracer ligands or contrast media[1]. As such, the ^{31}P nucleus has been used to study many neuropsychiatric disorders over the past ten years. It is particularly important today in studies of schizophrenia[1] that have shown altered phospholipid metabolism during the early course of the illness. More specifically, bipolar subjects have shown deficits in membrane phospholipid precursor levels and high-energy phosphates[2,3] – these characteristics are also consistent with major depression[4]. However, the development of quantitative techniques that maximize the signal of these identified disease/disorder biomarkers at 3T, is hampered by the lack of knowledge of ^{31}P brain metabolite relaxation times. Apparent T_1 estimates are important for signal-to-noise (SNR) optimization, the accurate quantitation of spectral data, and also for the correction of partially saturated MRS data. Though the relaxation times of ^{31}P human brain metabolites have been the subject of a few studies at 1.5T, 2T and 7T[5,6,7,8], values measured at 3T have not yet been published.

Materials & Methods: All phantom experiments were conducted with a 2555 ml ^{31}P brain phantom, containing 18 mM ATP + 38 mM PCr + 50 mM Pi + 50 mM PE, on a GE 3T SIGNA scanner (GE Healthcare, Waukesha, WI) using a dual-tuned ^{1}H-^{31}P head coil (Clinical MR Solutions, Brookfield, WI). To validate our techniques, in vitro T_1 relaxation times were measured using a progressive saturation technique with TR = 1, 2, 3, 6, 9, 12, 17 seconds. In vivo measurements were acquired for five healthy subjects who gave written informed consent (IRB#98-05). After fast ^{1}H MR 3-plane localizers were obtained for ROI placement and shimming, all first- and second- order shim currents were adjusted on tissue water with an automated shim protocol. Linewidths of the PCr resonance observed from the 240mm × 240 mm × 20 mm axial slice placed above the brain ventricles were 7-10 Hz without Gaussian line broadening. ^{31}P acquisitions were taken at six TR times (TR = 0.5, 1, 3, 6, 12, 15 s) using a progressive saturation spin-echo experiment with a TE of 2.5ms. For each measurement, 128 scans were acquired with 2048 data points and a spectral width of 5000 Hz. The half echoes were summed, reconstructed (Gaussian filtered, Fourier transformed and zero-order phase corrected) and the spectral peak areas fit with TDFDFIT[9]. Peak integrals were fit with a one-parameter monoexponential function by the sum of least squares minimization algorithm.

Results & Discussion:

Figure 1.



In vitro peak integral fits yielded R^2 values greater than 0.997 in all cases. T_1 relaxation times were measured to be 4.55 ± 0.08s, 9 ±0.22s, 5.98 ± 0.91s, 6.87 ± 0.49s, 6.87 ± 0.49s, and 6.87 ± 0.50s for PCr, PE, Pi, α-ATP, γ-ATP and β-ATP respectively. These T_1 times are uncharacteristically long when compared to those measured in vivo[6,7,8,9], but this phantom data allowed us to evaluate our in vivo protocol and quantification/fitting techniques beforehand. Figure 1 shows a typical progressive saturation time series for one of the in vivo measurements.

Table 1: Summary of human brain T_1 times in the literature compared to those measured in this study

Research group	Field strength	PME	Pi	PDE	PCr	γ-ATP	α-ATP	β-ATP
Merboldt et al (1990)	2 T (n=6)	4s	2.5s	2s	3s	0.7s	0.7s	1.0s
Hubesch et al (1990)	2 T (n=3)	1.7s	1.4s	1.3s	2.7s	0.6s	1.0s	0.7s
	1.5 T (n=7)	1.4s	1.4s	1.3s	3.1s	0.6s	0.8s	0.8s
Luyten et al (1988)	1.5 T (n=1)	2.74s	1.47s	1.64s	3.29s	1.36s	0.97s	1.03s
Lei et al (2003)	7T (n=9)	PE= 4.78s PC=NM	3.19s	GPE=4.06s GPC=4.01s	3.37s	1.27s	1.26s	1.02s
Blenman et al	3T (n=5)	PE= 4.88s PC=NM	2.20s	GPE=3.94s GPC=3.11s	3.57s	0.98s	0.98s	0.98s

In vivo brain relaxation times were measured to be 3.57 ± 0.65s (mean ± std), 4.88 ± 0.54s, 2.2 ± 0.4s, 3.94 ± 1.43s, 3.11 ± 0.7s for PCr, PE, Pi, GPE and GPC, and 0.98 ± 0.11s for α-, β-, and γ-ATP respectively. Table 1 summarizes the T_1 relaxation times measured in this study as compared to other human brain T_1 times in the literature. As expected, these T_1 estimates measured at 3T are longer than those measured at lower field strengths. However, some measurements do not fall below those measured at 7T. Certainly, the measurement cohort is small enough that any outliers significantly affect the T_1 estimates and the accuracy of the measurement itself can be affected by many factors. These include reliable quantitative separation of overlapping resonances and underlying baseline distorting resonances, the inherent SNR of the measured data, and quality of the spectral data fits. This ^{31}P in vivo spectral data was modeled with Voigt lineshapes and a priori knowledge, such as frequency shifts and relative intensities, was incorporated into TDFDFIT for optimal fitting. Short T_2 ^{31}P components detected at the short TE used, distort the spectral baseline and make the fitting of overlying resonances more difficult. The use of a longer TE would remedy this distortion, but signal would suffer from T_2 decay. R^2 values for the individual fits of the metabolite peak integrals to a monoexponential curve were typically greater than 0.95.

Conclusion:

This study has presented previously unpublished in vivo T_1 relaxation times of ^{31}P human brain metabolites measured at 3T (PCr=3.57 ± 0.65s,PE=4.88 ± 0.54s, Pi=2.2 ± 0.4s, GPE=3.94 ± 1.43s, GPE=3.11 ± 0.7s and α-,β-,γ-ATP = 0.98 ± 0.11s). Future work will include the recruitment of a larger measurement cohort of normal volunteers, the use of higher spectral resolution data for the accurate measurement of PC and the implementation of saturation bands to null ^{31}P signals arising from scalp, skin, meninges and muscle located on the outer edges of the selected slice.

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