Relaxation Time Measurements of ^{31}P Metabolites in Human Muscle at 9.4 Tesla

Y. Sui[1,2], H. Xing[2], T. Claiborne[2], K. R. Thulborn[2,3], and X. J. Zhou[2,4]

[1]Department of Bioengineering, University of Illinois at Chicago, Chicago, IL, United States, [2]Center for Magnetic Resonance Research, University of Illinois Medical Center, Chicago, IL, United States, [3]Department of Radiology, University of Illinois Medical Center, Chicago, IL, United States, [4]Departments of Radiology, Neurosurgery and Bioengineering, University of Illinois Medical Center, Chicago, IL, United States

Introduction: Phosphorus (^{31}P) NMR signals from biological tissues carry valuable metabolic information [1]. These signals, however, are difficult to detect on human subjects due to low sensitivity, long T1 relaxation times, and low physiological concentration [2,3]. The advent of 9.4 T human MRI scanner can considerably increase the sensitivity, renewing the interest in ^{31}P spectroscopy and imaging of human subjects [4]. To take full advantage of the sensitivity improvement afforded by ultra-high magnetic fields and optimize data acquisition strategies, it is essential to understand the ^{31}P T1 and T2 relaxation times in human tissues. Although ^{31}P relaxation times on humans have been reported for field strengths of up to 7 T [5,6], to our knowledge they have not been reported at 9.4 T. Measuring ^{31}P relaxation times at 9.4 T *in vivo* faces a number of challenges. First, the long T1 relaxation times of ^{31}P considerably increase the measurement time when conventional inversion recovery technique with TR ≥ 3-5T1 is used, making it prohibitive on human subjects. Second, the B1-field non-uniformity, seen in proton imaging at ≥ 3 T, imposes difficulties in determining the flip angles at 162 MHz (9.4 T) for ^{31}P. This will eventually degrade the accuracy of relaxation time measurements. Third, short RF pulses are needed to cover the broad frequency range (~3.5 kHz) of ^{31}P metabolites at 9.4 T, which can drive the RF power over the limit. The goal of this study is to use multiple techniques, including the Look-Locker method [7,8] and quadratic-phase RF pulses [9], to overcome these obstacles and achieve accurate T1 and T2 relaxation measurements on human subjects at 9.4 T.

Methods:

T1 measurement: To shorten the total scan time, a Look-Locker (LL) method was adapted in this study. In this sequence, the longitudinal magnetization was repeatedly sampled during recovery at a time interval τ with identical small-tip-angle RF pulses (α). The disturbed recovery process produced a modified relaxation time T1*, from which the actual T1 was derived using Eq. (1). This process requires the accurate knowledge of the flip angle α, which is difficult to obtain considering the B1-field non-uniformity at high frequency (162 MHz). To solve this problem, the LL experiment was performed twice with α and 2α (α ≈10°), respectively, while keeping the other parameters the same (TR = 20 s, 16 TIs in the range of 2.6 ms-7.5 sec, τ = 0.5 sec, spectral bandwidth = 5 kHz, 512 points, 20 averages, total scan time = 7 min each). The actual T1 was obtained without explicitly knowing α by solving two simultaneous equations (Eq. (1)). A τ of 0.5 sec was selected so that a sufficient number of points were sampled while not significantly disturbing the relaxation process. To cover the full range of the bandwidth of ^{31}P spectrum at 9.4 T while maintaining the RF peak amplitude within the limit, the adiabatic inversion pulse used in the LL sequence was customized using a quadratic-phase modulation method with a duration of 20 ms, bandwidth of 4 kHz, and B1 peak amplitude of 0.23 Gauss. Compared to a hyperbolic secant pulse with the same bandwidth, the customized pulse reduced the peak amplitude by 43%.

T2 measurement: Although the T2 relaxation times are typically measured using a multi-echo CPMG sequence, we have observed that it was difficult to adequately filter out the disturbing stimulated echoes using variable crushers [10] most likely due to the excessively long T1 times. Thus, a spin-echo (SE) sequence was used for T2 relaxation time measurements with 12 different echo times (TE) ranging from 12.6 ms to 507 ms (TR = 10 s, spectral bandwidth = 5 kHz, 512 points, 10 averages, scan time = 20 min). Again, a quadratic-phase modulation method was employed in designing 90° and 180° pulses (BW = 4 kHz, pulse width = 10 ms) to reduce the RF peak power. The non-linear phase in the frequency domain was effectively canceled with identical shape of the 90° and 180° pulses.

The T1 and T2 measurement methods were implemented on a 9.4 T human MRI scanner with an 80 cm bore-size. After validation on a ^{31}P phantom containing 100 mM inorganic phosphate (Pi), experimental studies were performed on 3 healthy male volunteers (age 29-46 years) using a custom-made ^{31}P RF volume coil (24 cm inner diameter). The right calf of the volunteers was positioned in the RF coil with the gastrocnemius at the center.

The raw data (FID for T1 or echoes for T2 measurement) were zero-filled to 2048 points, followed by constant and linear phase corrections and 30 Hz exponential line-broadening. The peak amplitudes of the absorption spectrum were extracted for T1 and T2 calculations.

Results: Figures 1a and 1b show a set of spectra obtained from a representative LL experiment after successive α-pulses for T1 measurement (a) and the SE experiment with different TEs for T2 measurement (b). Examples of T1* and T2 fitting for PCr are shown in Fig. 1c and Fig. 1d, respectively. Table 1 summarizes the mean and standard deviation of T1 and T2 relaxation times of the major ^{31}P metabolites. The average Pearson's correlation coefficients were $r^2 = 0.9999 \pm 0.0000$ for T1 and $r^2 = 0.9997 \pm 0.0001$ for T2 fit of PCr, and ranged from 0.983 to 0.998 (T1) and from 0.980 to 0.998 (T2) for other metabolites.

	Pi	PDE	PCr	γ-ATP	α-ATP	β-ATP
T1 (ms)	7177±1305	4603±1656	3080±40	2617±105	1410±10	1523±86
T2 (ms)	85±5	220±14	158±8	18.5±1.3	13.4±5.1	N/A*

Table 1 The mean and standard deviation of ^{31}P T1 and T2 relaxation times at 9.4T.
* not measured due to limited SNR.

$$T_1 = \frac{T_1^*}{1 + \frac{T_1^*}{\tau}\ln(\cos\alpha)} \qquad \text{Eq. (1)}$$

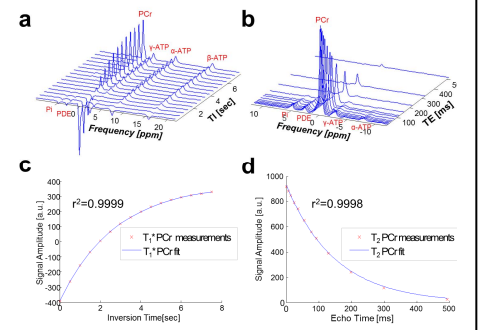

Fig. 1 A set of representative spectra of (a) T1* measurement with 16 TIs (2.6 ms ~ 7.5 sec) and (b) T2 measurement with 12 TEs (12.6 ms~507 ms), and sample fitting curves of T1* (c) and T2 (d) measurement for PCr of a human volunteer.

Discussion and Conclusion: We have integrated a number of techniques to meet the challenges of ^{31}P relaxation time measurements at 9.4 T. With these techniques, we have shown that the total scan time for both T1 and T2 experiments can be limited to ~30 min, the RF peak amplitude can be substantially reduced without compromising the required bandwidth coverage, and the issue with B1-field non-uniformity at high frequency can be addressed using two excitations with different flip angles. By strategically integrating these techniques, ^{31}P relaxation times in human muscle have been determined accurately at 9.4 T. Compared to the previous studies performed at 7 T or below [5,6], it was observed that the T1 and T2 relaxation times decreased at 9.4 T for all ^{31}P metabolites evaluated in this study, except for Pi whose T1 relaxation time increased with the field strength. These trends are generally consistent with the relaxation time changes from 3 T to 7 T [5,6]. Accurate knowledge of the relaxation times at 9.4 T paves the way for optimizing pulse sequence parameters to increase the SNR in ^{31}P spectroscopy and imaging on human subject at ultra-high fields.

References: [1] Arias-Mendoza, *et al.*, Dis Markers, 2003. [2] Barker, *et al.*, J Appl Physiol, 2008. [3] Chao, *et al.*, JMRI, 1997. [4] Sui, *et al.*, ISMRM, 2010: p. 28. [5] Bogner, *et al.*, MRM, 2009. [6] Meyerspeer, *et al.*, MRM, 2003. [7] Look, *et al.*, Phys Review Letters, 1968. [8] Henderson, *et al.*, MRI, 1999. [9] Balchandani, *et al.*, MRM, 2010. [10] Bernstein, King, and Zhou, Handbook of MRI Pulse Sequences. 2004.