Field Dependence of PCr and ATP Linewidths and its Impact on *In Vivo* ^{31}P MRS Studies

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Introduction *In vivo* ^{31}P MRS is unique for studying high-energy phosphate compounds of adenosine triphosphate (ATP) and phosphocreatine (PCr), and for noninvasively imaging the ATP_{ase} fluxes in the brain [1]. It can benefit greatly from high/ultrahigh field for overcoming the intrinsic sensitivity limitation [2,3]. With increasing field strength (B_0), one key factor in determining the improvements in both sensitivity and spectral resolution is the resonance linewidth at half peak height (LW or T_2^* =1/(πLW)) and its field dependence; since the line-broadening accompanying with the increased B_0 can reduce both the signal-to-noise ratio (SNR) and spectral resolution. The field dependence of linewidth or T_2^* of ATP and PCr relies on several factors: susceptibility change, different relaxation mechanisms and their relative dominance at a given B_0. Interestingly, both dipole-dipole interaction and chemical shift anisotropy (CSA) can contribute to the ATP and PCr T_2 (or T_2^*) relaxation processes and their relative contribution depends on B_0 and molecular environment inside the cells. Theoretically, the CSA contribution can become dominant due to its square power dependence of $1/T_2$ on B_0, and could result in significant broadening of linewidth at high/ultrahigh fields, thus potentially limiting the high-field advantages. To address this concern, we quantitatively compared the linewidths of PCr, α-ATP and γ-ATP peaks acquired from the human and cat brains covering a wide B_0 range from 1.5T to 16.4T.

Methods *In vivo* brain ^{31}P spectra were acquired from either human on 4T/90cm bore (Oxford) and 7T/90cm bore (Magnex Scientific) magnets or from cat on 9.4T/31cm bore (Magnex Scientific) and 16.4T/26cm bore (Magnex Scientific) magnets interfaced with the Varian console (Varian, Palo Alto, CA). A set of ^{31}P RF surface coils were home-built and applied to collect the ^{31}P signals from the cat and human visual cortices at different field strengths (4T, 7T, 9.4T and 16.4T). Single-pulse-acquisition sequence was applied to collect *in vivo* brain ^{31}P spectra. A relatively long repetition time and a large number of signal averaging were used for achieving sufficient SNR. All ^{31}P spectra were processed without line broadening before Fourier transformation. Linewidths of PCr, γ-ATP and α-ATP spins were determined for each spectra acquired at different magnetic field strength. To further extend the B_0 range, the linewidth results of 1.5T and 2.0 T were taken from the literature [2], and were applied for the comparison in the present study.

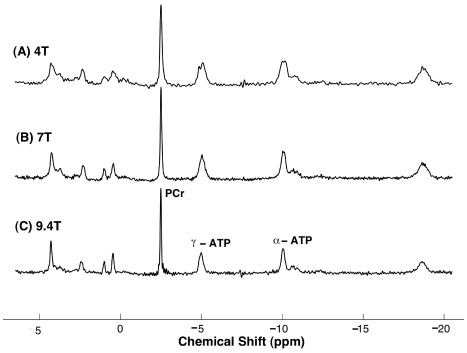

Fig. 1 *In vivo* ^{31}P spectra of visual cortex acquired at (A) 4T and (B) 7T (human brain), and (C) 9.4T (cat brain).

Results Figure 1 demonstrates typical *in vivo* ^{31}P spectra obtained from either human visual cortex at 4T (1A) and 7T (1B) or cat visual cortex at 9.4T (1C). It clearly shows that the linewidths in ppm scale reduced when increasing the field strength, thus, improved the spectral resolution and separation of adjacent resonance peaks. Figure 2 shows the linewidth dependence on B_0 for three phosphate resonance peaks (PCr, γ-ATP and α-ATP) in the unit of Hz (top panel in Fig. 2), indicating a strong linear correlations for all peaks: LW_{PCr}(Hz)=0.41B_0+10.6, R^2=0.50; $LW_{\alpha\text{-ATP}}$(Hz)=1.45B_0+28.7, R^2=0.99; and $LW_{\gamma\text{-ATP}}$(Hz)=3.02B_0+22.3, R^2=0.99. However, such linear relations between *LW* and B_0 became an inverse relation when the units of the LW were converted from Hz to ppm as shown in Fig. 2 (low panel).

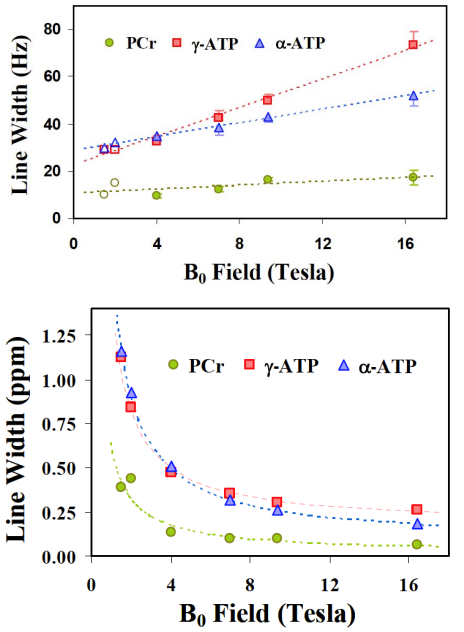

Fig. 2 Field dependence of PCr, γ-ATP and α-ATP linewidth in unit of Hz (top panel) and ppm (low panel). The data pints of 1.5T and 2T were taken from Boska et al (Ref. 2).

Discussion and Conclusion In this study, we investigated the field dependence of brain PCr and ATP linewidths across a large B_0 range from 1.5T to 16.4T. In general, all linewidths in Hz unit are positively correlated to B_0 with high linearity. However, the regression slopes were substantially different with a smallest slope for PCr and largest slope for γ-ATP (see top panel in Fig. 2). Interestingly, the γ-ATP slope was higher than that of α-ATP within the same ATP molecule, and the two lines only across at ~4T with equal linewidths. These results suggest distinct relaxation behaviors between the α-ATP and γ-ATP (doublet) resonances, they may reflect their different spin environments in the cells. We also observed that the interceptions for both γ-ATP and α-ATP peaks at zero field strength were larger than that of ^{31}P-^{31}P J-coupling constant (~20 Hz). Importantly, the acceleration rates of linewidth broadening as a function of B_0 were much slower than that of B_0 itself for all resonance peaks studied, e.g., increasing B_0 from 4T to 16.4T (> 4 times) only doubles the linewidth for γ-ATP. Therefore, the linewidths in the ppm scale that reflect "true" spectral resolution become significantly improved, in particular, for the ATP resonances as demonstrated by Fig 2, low panel. This B_0 dependence results in substantial improvements in both SNR and spectral resolution at high/ultrahigh fields, especially from 1.5T towards 9.4T, however based on Fig. 2, further improvements are expected to be less substaintial when B_0 > 16.4T. The overall results of the present study provide a quantitative explanation about large sensitivity and spectral resolution improvements at high/ultrahigh fields, and they don't support the notion about a dominant (or sole) CSA mechanism in ^{31}P T_2 relaxation at high/ultrahigh fields.

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References [1] Zhu et al. Methods Mol Biol 2009;489:317-357; [2] Boska et al. Magn Reson Med 1990;13:228-238; [3] Qiao et al. Magn Reson Imaging 2006;24:1281-1286.