P-31 Chemical Exchange Saturation Transfer (CEST) between ATP and Phosphor-creatine (PCr) at 7T

Jimin Ren[1], Baolian Yang[2], Ivan Dimitrov[2], A.Dean Sherry[1,3], and Craig R. Malloy[1,4]

[1]Advanced Imaging Research Center, University of Texas Southwestern Medical Center, Dallas, Texas, United States, [2]Philips Medical System, Cleveland, Ohio, United States, [3]Department of Chemistry, University of Texas at Dallas, Richardson, Texas, United States, [4]VA North Texas Health Care System, Dallas, Texas, United States

Introduction Phosphate exchange between PCr and γ-ATP is essential for energy homeostasis in skeletal muscle. The reaction, as described by $PCr^{2-} + ADP^{-} + H^{+} \leftrightarrow ATP^{2-} + Cr$, is mediated by creatine kinase (CK), and it has been a research focus for decades for physicists and physiologists, using ^{31}P magnetization transfer. Typically, the technique is comprised of two scans, one on-resonance scan with saturation frequency f_{sat} set on γ-ATP (or PCr), and the other as control with f_{sat} set on the opposite side of PCr (or γ-ATP). The exchange rate k is then evaluated from the difference in PCr (or γ-ATP) between the on-resonance and control scans. The control scan is needed to correct the so-called saturation spillover artifact, manifested as partial saturation at the observation peak PCr (or γ-ATP). However, dependent on experimental parameters (B1 saturation power, duration, pulse shape etc), the extent of the spillover could vary widely, consequently resulting in a large variation in k value, as documented in literatures. Often, severe spillover artifact can even be felt on well-separated peaks such as α-ATP and PDE, which greatly diminishes the dynamic range of CEST effect, while increasing SAR exposure on the subjects.

Purpose To minimize spillover effect while retaining CEST effect, we investigated the feasibility of an alternative saturation strategy, using low power frequency-selective saturation pulses with short saturation time (t_{sat}) and decreased duty cycle. The technique is evaluated by z-spectra of PCr and γ-ATP in human skeletal muscle at 7T.

Methods The right calf of the normal healthy subjects was placed on a partial-volume T/R surface coil, parallel to B_o. High-resolution ^{31}P MR spectra were acquired using FID mode at 7T (Achieva, Philips Medical Systems), with flip angle 50°, TR 3 s, 1 average, NP 4 k, bandwidth 8 kHz. f_{sat} was swept across the spectrum, covering chemical shift range from 11 to -8 ppm, in 10 Hz sweep step. The resultant 240 f_{sat} spectra were used to construct the Z-spectra for PCr, γ-ATP and Pi. The saturation pulse train was comprised of 20 sinc-shaped pulses, each 20 ms in duration with effective B1 of 1 μT, separated each other by 2-10 ms interval. The total length of the pulse train was 450 ms, with a duty cycle of 91%. The SAR value was < 14%. The protocol was approved by the Institutional Review Board. Informed consent was obtained from all participants (n = 4).

Results and Discussion With the low B1 saturation power, reduced duty cycle and short t_{sat}, no spillover was observed on PDE and α-ATP peaks, as shown in the high-resolution on-resonance spectra (Figs 1d and 1e, red traces). The spillover at PCr and γ-ATP was also minimal, judged from the appearance of sharp on-resonance peaks in the Z-spectra (Figs 1b and 1c). Yet, the CEST peaks was clearly illustrated in the Z-sepctra of PCr (Fig 1c) and γ-ATP (Fig 1b), at -2.4 and 0 ppm, respectively, indicative of phosphate exchange between PCr and γ-ATP. Quantitatively, the CEST effect from PCr to γ-ATP (Fig 1b) is nearly 3-fold larger that from γ-ATP to PCr (Fig. 1c), as anticipated from their difference in pool size (PCr : γ-ATP = 4 : 1). The z-profiles also revealed a wider CEST peak in PCr profile than in γ-ATP profile, but a narrower on-resonance peak in PCr profile than in γ-ATP profile, due to difference in T2 relaxation time (220 vs 30 ms, PCr vs γ-ATP). It was noticed that no CEST effect was evident in the Pi profile (Fig. 1a), under the current saturation condition, suggesting that the direct phosphate exchange between Pi and PCr, or between Pi and γ-ATP, is not significant in resting muscle. Thus a simple two-pool model can be used for evaluate the kinetic rate constants. Importantly, it is advantageous to present CEST effect with Z-spectra, which reveals more details of the exchange characteristics and saturation performance. Finally, to obtain PCr and γ-ATP profile from 5 to -5 ppm, it takes only 8 min, under the current condition. Therefore it can be a valuable addition to a clinical muscle protocol.

Conclusion We demonstrated that easy-to-read Z-profile can be obtained for both PCr and γ-ATP using saturation pulses with low B1 power, reduced duty cycle and short saturation time. The high frequency selectivity effectively suppresses the spillover effect. The strategy would be valuable for quantitative measurement of CK activity in skeletal muscle in normal physiology and pathology.

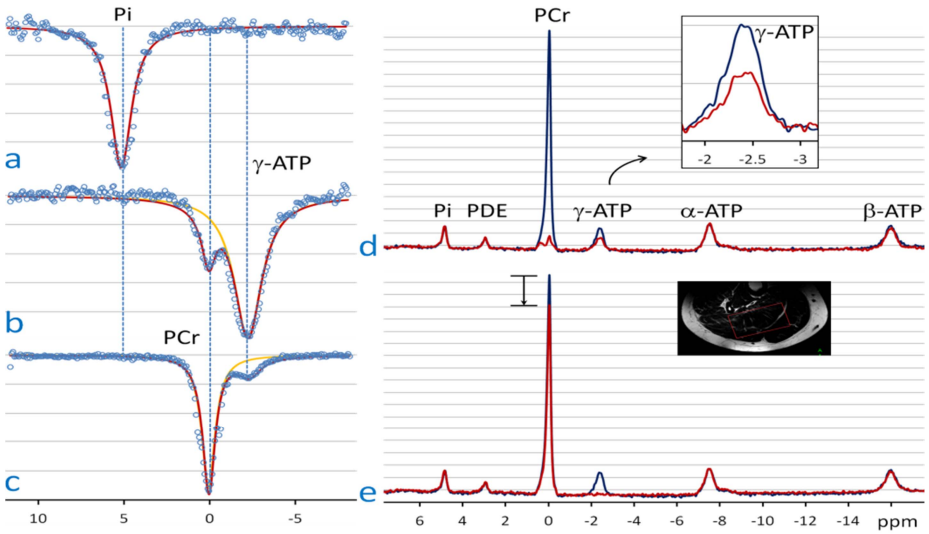

Figure 1. ^{31}P Z-spectra of Pi **a)**, γ-ATP **b)**, and PCr **c)** of human calf muscle, showing the effect of phosphate transfer between PCr and γ-ATP. High-resolution ^{31}P MR spectra of calf muscle with f_{sat} set at PCr **d)**, and γ-ATP **e)** (red trace), and compared to the control (blue trace, f_{sat} set at 11 ppm).