^{31}P TRIple TR Saturation Transfer (TRIST) in the Human Heart at 3T

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Introduction: Saturation transfer (ST) ^{31}P MRS techniques enable the study of creatine kinase (CK) reaction kinetics [1,2]. In muscle, the CK reaction is a putative shuttle, transporting high-energy phosphate between the mitochondria, where ATP is created, to the myofibrils, where it is used. The pseudo-first-order rate constant for CK, k_f, in s^{-1}, indexes the rate of generation of ATP from phosphocreatine (PCr). k_f is significantly reduced in human heart failure, suggesting that impaired energy supply plays a role in the disease [3,4]. Those measures were obtained at 1.5T using four flip-angle ST (FAST) which employs adiabatic BIR4 pulses.

While ^{31}P MRS may benefit from increased SNR and spectral dispersion at 3T [5], 3T presents new challenges for surface coil ^{31}P MRS associated with power deposition and power requirements of BIR4 pulses, and T2 decay when the pulses are long. Such problems can be overcome by using adiabatic half-passage (AHP) pulses with a flip-angle of 90° instead of BIR4 pulses [6], but FAST cannot be performed with 90° AHP pulses.

Here we present a new method of measuring k_f, employing just two fully-relaxed and one short-TR acquisition. This triple TR ST, or *TRIST* method, is validated by comparison with conventional progressive saturation (PS) k_f measures in the human calf. It is then combined with 1D chemical shift imaging (CSI) to obtain the first 3T measures of CK kinetics in the normal human heart.

Methods: The CK ST experiment involves saturating the γ-ATP resonance at -2.5ppm using frequency-selective irradiation. We use an amplitude modulated DANTE [7] pulse train to broaden the saturation band. Saturation reduces the PCr signal from a fully-relaxed value of M_0, to M_0' due to chemical exchange with γ-ATP: $k_f=1/T1'(1-M_0'/M_0^c)$, where M_0^c is the fully-relaxed magnetization of PCr with control irradiation at +2.5ppm, and T1' is the T1 of PCr measured with γ-ATP saturated.

TRIST is implemented on a 3T Achieva Philips scanner with a custom cardiac transmit/receive ^{31}P surface coil set, suitable for ^{31}P MRS up to 9cm deep [6]. 5 calf muscles and 6 hearts are studied in healthy volunteers by ^{31}P MRS, after scout MRI and second order shimming [8]. Leg studies are first done non-localized (NL) with TR=25s (control saturation), and with γ-ATP saturated using TRs of 0.75, 1.5, 2.5, 4, 6, 10, and 16s. TRIST 1D CSI (1-cm resolution) is next performed with control saturation at TR=25s, and with γ-ATP saturation at TR=1.5 and 10s.

Heart studies are cardiac triggered (end-systole) with TR=16s control saturation, and TRs of 2 heart-beats and ~10s with γ-ATP saturated.

PCr is measured from peak heights. The 7-point NL PS calf data are fitted to $S(TR)=M_0'(1-\exp(-TR/T1'))$ with two parameters. For TRIST, M_0' and T1' are determined with the dual-TR method [6].

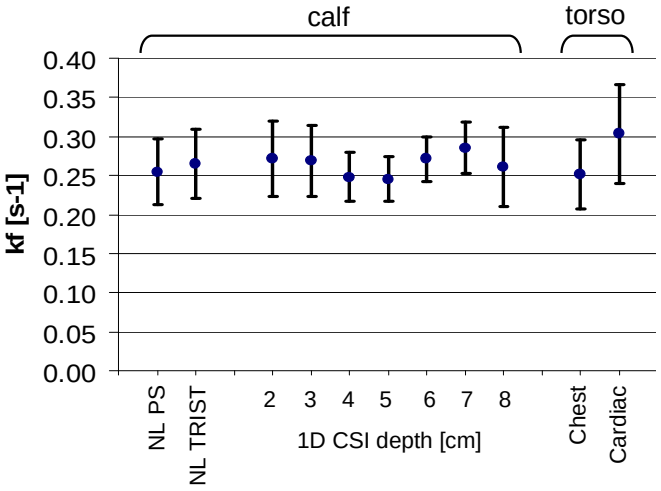

Figure 1: *Mean±SD pseudo-first-order forward rate constant k_f of CK reaction measured in-vivo with TRIST in the calf, chest and heart and with conventional PS in the calf.*

Results: NL k_f (and T1') determined with PS and TRIST in calf muscle are the same at $0.25\pm0.04s^{-1}$ (2.4±0.2s) and $0.26\pm0.04s^{-1}$ (2.3±0.2s), respectively. Fig. 1 plots k_f measured NL in the calf with PS and TRIST, and localized with 1DCSI in the calf and the torso with TRIST. k_f in the chest and the heart were $0.25\pm0.04s^{-1}$ and $0.30\pm0.06s^{-1}$, respectively. Fig. 2 shows TRIST data from the heart.

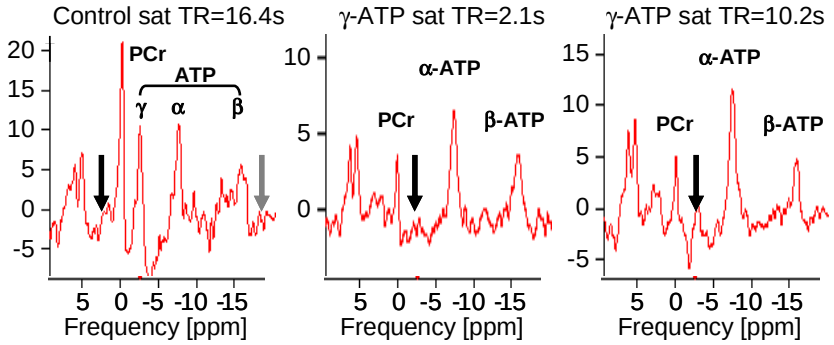

Figure 2: *Cardiac TRIST dataset acquired with control sat at TR=16.4s to determine M_0^c, and γ-ATP sat at TRs of 2.1 and 10.2s to determine M_0' and T1'. Note the different vertical scales; arrows depict saturation.*

Discussion: *TRIST* provides accurate, validated measurements of *in vivo* muscle CK k_f at 3T. k_f values for the human heart measured with *TRIST* agree well with published 1.5T data [3,4]. Together, these data demonstrate that the challenges of higher-field magnets for ST studies can be overcome and that human cardiac CK kinetics can now be quantified at 3T.

References: 1. Forsen S, J Chem Phys 1963; 2. Bottomley PA, MRM 2002; 3. Weiss RG, PNAS 2005; 4. Smith CS, Circulation 2006; 5. Tyler DJ, NMR Biomed 2008; 6. El-Sharkawy AM, ISMRM 2008; 7. Bodenhausen G, JMR 1976; 8. Schär M, MRM 2004;

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