FAST ^{31}P measurements of the creatine kinase synthesis rate at 11.7T

Andrew Bresnen[1] and Timothy Q. Duong[1]
[1]*UTHSCSA - Research Imaging Institute, San Antonio, Tx, United States*

Target Audience Researchers interested in ^{31}P measurements of metabolic rates.

Purpose The aim of this project was to develop and implement a fast and robust protocol to measure the forward creatine kinase rate of ATP synthesis ($k_{f,CK}$) in the in vivo rat brain at 11.7T. In vivo ^{31}P MT experiments suffer from low SNR resulting in long scan times, often on the order of hours, limiting in vivo applications. A high magnetic field and surface coil were used to maximize SNR. The ^{31}P Four Angle Saturation Transfer[1] (^{31}P FAST) experiment was implemented to minimize the TR (by using low flip angles) and the number of data points required to calculate to $k_{f,CK}$. The optimized protocol provides robust measurements of $k_{f,CK}$ in ~5mins.

Methods Male Sprague-Dawley rats (n=6, 225-250g) were studied under 1.2% isoflurane using an 11.7T Bruker scanner, using a concentric loop ^{1}H/^{31}P (500/202.5 MHz) 2.0/1.5-cm diameter transceiver surface coil. The ^{1}H coil was used for positioning and shimming prior to ^{31}P acquisition. ^{31}P magnetization transfer (MT) data was acquired using the FAST method, where $k_{f,CK}$ is calculated[1] using four spectra acquired with 30° and 60° FA's with and without γ-ATP saturation (TR=1100s, NA=64, DS=6). Accurate FA's throughout the brain were set using BIRP[2] plane rotation adiabatic RF pulses. Narrowband ATP saturation with negligible bleed over was achieved using the BISTRO[3] saturation scheme with 8x50ms hyperbolic secant RF pulses. Pulse sequence and RF pulses were optimized using the inorganic phosphorus (Pi) signal from dead rats.

Results We developed a ^{31}P MT protocol to measure $k_{f,CK}$ in about ~5mins. $k_{f,CK}$ was measured by observing the changes in the PCr signal and T_1 with and without saturation of the γ-ATP resonance (**Fig 1).** BIR4 adiabatic pulses were used to provide accurate and homogeneous FA throughout the brain using surface coils. The long BIR4 pulses (5ms) eliminated signal from the short T2 phospholipids (**Fig 2**), allowing accurate quantification of the ^{31}P metabolites. The adiabatic BIR4 pulses provided accurate user selected FA over a wide range of attenuation (**Fig 3).** Optimization of the power and duration of the BIR4 pulses showed that performance of the BIR4 pulses most closely matched theoretical expectations at 6dB and 5ms pulse duration (**Fig 4**). We then adopted the BIRP excitation scheme, that averaged phase alternated acquisitions using positive and negative BIR4 pulses, to further improve flip angle accuracy. By summing phase alternated acquisitions flip angle and phase error from spectra acquired with BIR4 pulses canceled out (**Fig 5**). The BIRP excitation significantly improved the T1 measurements of ^{31}P metabolites compared to BIR4 excitation alone. The $k_{f,CK}$ in normal rats (n=6) was measured to be $0.26\pm0.02 s^{-1}$.

Discussion Our results for measurement of $k_{f,CK}$ closely matched previously reported values from rats under similar conditions ($k_{f,CK}=0.24\pm0.02 s^{-1}$)[4,5]. We were able to make measurements of the forward creatine kinase rate, however, measurements of the forward ATPase rate, though theoretically possible were limited by SNR. In future studies we would like to 1) incorporate localization by both single voxel and CSI for analysis of ATP synthesis by region, and 2) study ATP synthesis via the ATPase ($k_{f,ATPase}$) pathway. We will apply these techniques to study acute changes in metabolism in disease models such as stroke, traumatic brain injury and responses to therapy.

Conclusions We successfully developed and implemented hardware, pulse sequence and parameters to measure $k_{f,CK}$ in in vivo rat brains. We tested and optimized a new ^{31}P/^{1}H surface coil and animal holder for experiments. The unique BIR4 pulses, BIRP excitation scheme and BISTRO saturation were implemented on the 11.7T scanner. The dual-angle T1 measurement was tested. The ^{31}P FAST pulse sequence was demonstrated to measure the creatine kinase rate in rat brains in vivo.

REFRENCES 1) Bottomley et al. MRM 2002 2) Bottomely PA, et al. J Magn Reson., Ser A 1993. 3) de Graff et al. J Magn Reson B 1996 4) Du F, et al. PNAS 2008. 5) Sauter and Rudin J Biol Chem 1993.

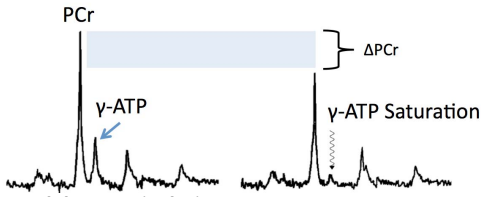

Figure 1. Whole Brain: w/ and w/o Y-ATP Saturation

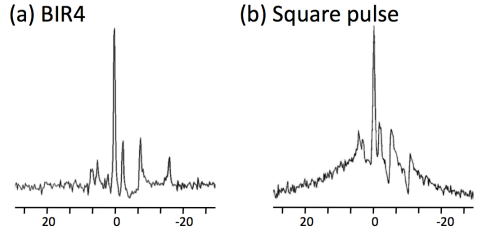

Figure 2. BIR4 RF Pulse compared to square pulse in living rats.

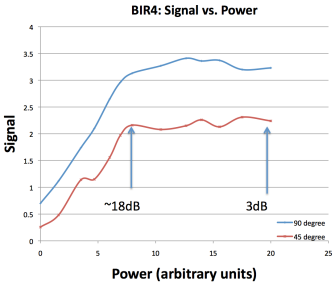

Figure 3. Signal vs. Power for BIR4-45 and -90 RF Pulse. The B1 insensitivity of BIR4-45 and -90 pulses is evident over 3-18dB

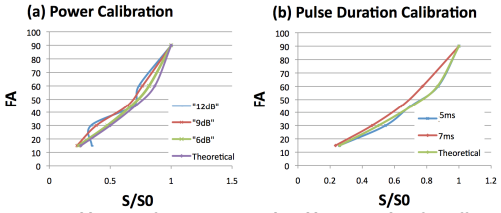

Figure 4. Calibration of Various FAs Produced by BIR4 Pulses for Different Powers (a) and Pulse Durations (b).

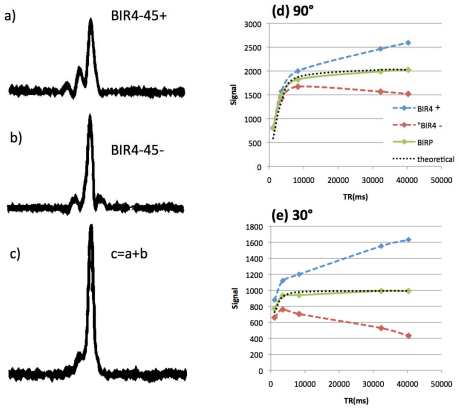

Figure 5. Results from acquired in dead rat. (a) BIR4+, (b) BIR4-and (c) BIRP. Fitting T1 using BIRP and BIR4 with 90° (d) and 30° (e) flip angles.