Human Cardiac Creatine Kinase Flux Measurement at 3T using 31P Magnetization Transfer MRS

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INTRODUCTION: Phosphocreatine (PCr) to adenosine triphosphate (ATP) ratio is generally used as index of myocardial energy metabolism and a reduction in the ratio has been associated with impaired myocardial energy state. However PCr/ATP ratios have not consistently demonstrated myocardial energy metabolism in comparable matched groups (1-3). The creatine kinase (CK) system is central to cellular energy metabolism and facilitates the production and transport of energy in the heart. Animal studies have shown that CK flux is a more sensitive and specific indicator of myocardial energy status (4). Recently Bottomley and coworkers had developed a technique at 1.5 T magnet to measure the CK flux in human subjects however due to technical limitations in their approach it is not applicable at higher field magnets. Therefore this approach cannot take advantage of increased SNR and spectral resolution (5, 6). Here we demonstrate an optimal strategy to measure CK flux in human heart at 3T. Furthermore we investigated the role of CK system for energy metabolism in the heart of subjects with type 2 diabetes (T2DM).

METHODS: Studies were done on Siemens 3 T TRIO magnet (Siemens Erlangen). A 12 cm diameter ^{31}P surface coil was positioned on the chest with the centre of the coil just below the mitral valve level of the heart. Spatial localization was performed in one dimension using 1D image-selected *in vivo* spectroscopy (1D-ISIS) sequence with an adiabatic inversion pulse of 5.12 ms duration. An adiabatic half passage pulse optimized to provide a 90° flip angle at a distance of 6 cm from the coil was used for excitation. CK rate constant was determined using saturation transfer approach where γ-ATP was progressively saturated with saturation times ranging from 0.2 to 6 sec. Other acquisition parameters: 32 signal averages, 6 sec repetition delay, 3000Hz spectral width, and acquisition time of 170 ms, with a total data acquisition time of ~ 30 minutes. An external phantom consisting of 0.15 M phosphate solution was used to quantify the *in vivo* metabolite concentrations. ^{31}P spectra were analyzed using an Advanced Method for Spectral Fitting (AMARES) within jMRUI. The saturation transfer data was fit to a two-site chemical exchange model to determine the CK flux using MATLAB software. The unidirectional forward CK flux was calculated as k•[PCr], where k is the forward rate constant for CK reaction and [PCr] is the PCr concentration.

RESULTS: Examples of spectra and the fitting process to yield the forward rate constant (k) for CK are shown in Figure 1. Results of the CK flux measurements are shown in the table below.

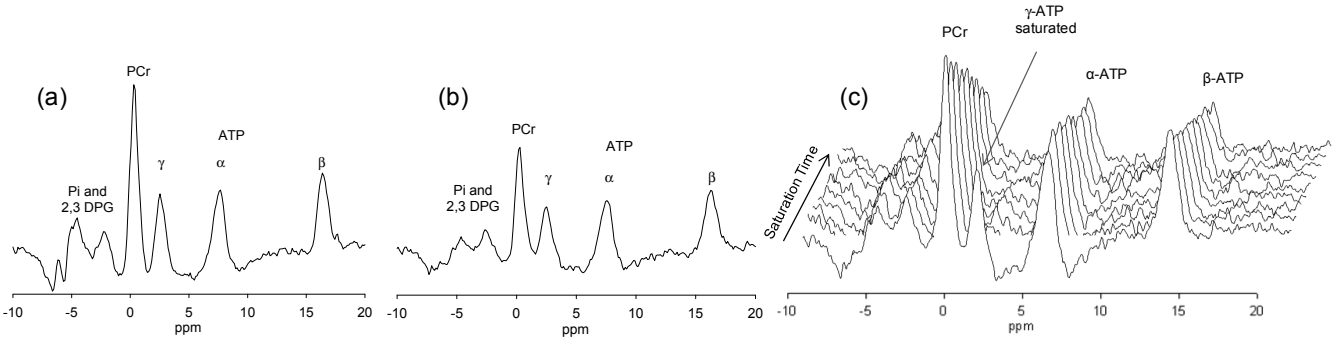

Figure 1: 31P MRS spectrum from normal (a), and T2DM (b) subjects on same scale. A stack of spectra showing the saturation transfer approach (c).

	Age (yrs)	PCr/ATP	PCr (μmol/g)	k (sec^{-1})	Flux (μmol/g.sec)
Non-diabetic (3)	28 ± 9	1.81 ± 0.27	10.5 ± 1.7	0.32 ± 0.02	3.4 ± 0.8
T2DM (2)	66 ± 2	1.46 ± 0.04	6.9 ± 0.5	0.51 ± 0.05	3.2 ± 0.6

CONCLUSIONS: The results demonstrate high quality spectra and CK flux measurements at 3.0 Tesla. We found an optimal TR = 6 s results in best SNR, high dynamic range for rate constant measurements, and low SAR (less than 40% of the FDA recommended limit). The data appear to suggest that myocardial energy production in the male diabetic heart is being maintained by an increase in the forward CK reaction, although this may also be secondary to age and needs to be further investigated. Thus, obtaining measurements of the concentration of PCr and ATP, and CK flux provide a more comprehensive assessment of myocardial energy metabolism than measuring PCr/ATP alone.

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