Mapping the Creatine Kinase Reaction Rate in Muscles of the Lower Leg Using Progressive Saturation 31P-MRI at 3.0 T.

Prodromos Parasoglou1, Ding Xia1, Greg Chang1, and Ravinder R Regatte1
1Radiology, NYU School of Medicine, New York, New York, United States

TARGET AUDIENCE: Those interested in muscle physiology, muscle bioenergetics, or in technical developments in multinuclear MRI.

PURPOSE: To develop and implement a progressive saturation 31P-MRI method for imaging the unidirectional conversion rate of phosphocreatine (PCr) to adenosine triphosphate (ATP) through the creatine kinase (CK) reaction at relatively high spatial resolution. The 31P-MRI method provides full coverage of the lower leg muscle on a high-field (3.0 T) clinical scanner within experimental times that can be relevant for clinical application (~ 45 min). METHODS: The CK reaction can be written as:

\[ PCr + ADP + H^+ \overset{k_f}{\leftrightarrow} ATP + Cr \quad (1) \]

where \( k_f \) and \( k_r \) the pseudo first-order forward and reverse rate constants. One way of measuring \( k_f \) is through the progressive saturation transfer (ST) experiment, in which the \( \gamma \)-ATP resonance is saturated for different durations (\( t_{sat} \)), resulting in PCr signal decrease. Under fully-relaxed conditions, assuming close to complete saturation of the \( \gamma \)-ATP resonance, the magnetization of PCr as a function of \( t_{sat} \), is described by the following equation:

\[ M(t_{sat}) = c \left[ 1 + k_f T_1 e^{-\frac{1}{T_1} k_f t_{sat}} \right] \quad (2) \]

Where \( M(t_{sat}) \), the magnitude of the PCr signal as a function of \( t_{sat} \), and \( c \), a parameter accounting for direct spill-over effects. By measuring the PCr signal at several \( t_{sat} \), we can estimate \( k_f \) through a three-parameter (i.e. \( c, k_f \) and \( T_1 \)) fit of the data to Eq.2. The constant \( k_f \) is multiplied by the PCr concentration to estimate the unidirectional flux of PCr to form ATP, \( V_f \). PCr concentration is measured using reference phantoms and the water/fat content of the muscle is accounted for. Ten healthy volunteers (seven men, three women, mean ± standard deviation age 32.0 ± 3.5 years of age), underwent 3.0 T MRI examination, which included saturation transfer 31P-MRI using the pulse sequence shown in Fig.1, and chemical shift-based water/fat separation imaging5. Mean \( k_f \) and \( V_f \) measurements were compared (one-tailed Student t-test for paired samples) among four major muscles of the lower leg [i.e. Gastrocnemius Lateral (GL), Gastrocnemius Medial (GM), Soleus (S), and Tibialis Anterior (TA)]. Differences with \( P \) less than 0.05 were considered significant.

RESULTS: Figure 2a shows an anatomical cross-section of the lower leg muscles of a volunteer (BMI = 30.4) together with the fat fractions. The decrease of PCr due to aging and disease 8,9. The advantage of our method compared to existing 31P-MRS methods is the large volume coverage and the ability to measure metabolic activity in muscles with different fiber content both in normal aging and diseased populations.