Three Dimensional Mapping of Oxidative Capacity in Human Lower Leg Muscles with Compressed Sensing 31P-MRI

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TARGET AUDIENCE: Those interested in muscle physiology, muscle metabolism and bioenergetics, and new imaging methodology for multinuclear MRI.

PURPOSE: The rate of phosphocreatine (PCr) resynthesis following physical exercise is an accepted index of mitochondrial oxidative metabolism and has been studied extensively with ^{31}P-MRS methods and small surface coils. Several diseases such as type 2 diabetes[1] can affect the efficiency of muscles' oxidative metabolism in the mitochondria, which could lead to spatial heterogeneity of the muscles' response to physical exercise. However, very little is known about these spatial gradients of metabolic properties due to the lack of imaging tools with sufficient muscle coverage and temporal resolution to measure oxidative capacity in larger areas of tissue. In this work, we developed and implemented a novel compressed sensing (CS) 3D-^{31}P-MRI technique for imaging PCr resynthesis following exercise.

METHODS: The CS technique uses Principal Component Analysis (PCA) as sparsifying transform (Fig.1). The method was previously validated using 2-fold retrospective undersampling of fully-sampled data from four volunteers acquired with temporal resolution of 24 s, which led to an accurate estimation of the mono-exponential PCr resynthesis rate constant (mean error < 6.4%)[2]. In this study, we recruited five healthy volunteers (three female and two male, 47.4 ± 13.3 years of age). They were all scanned on a 7T MRI system (Siemens Medical Solutions, Erlangen, Germany) using a dual-tuned ^{31}P/^{1}H quadrature transmit-receive knee coil (Rapid MRI, Ohio) with 18 cm inner diameter and 20 cm length. The participants performed plantar flexions using resistance bands for 2 min, at a frequency of 1 repetition per second. The physical exercise was designed to decrease PCr without inducing acidosis, thus avoiding pH effects of mitochondrial ATP synthesis. Images were acquired serially using CS 3D-TSE with 2-fold acceleration, 12 s temporal resolution and 2.1 mL nominal voxel size. Static PCr images were also collected in order to map PCr concentration at rest. Rate constants (k_{PCr}) of PCr recovery were determined by fitting the signal in segmented volumes of interest in different muscles to the following equation: $PCr(t) = \Delta PCr[1-\exp(-k_{PCr}t)]+PCr_{ex}$, where t is the time, PCr_{ex} is [PCr] at the end of exercise, $\Delta PCr = PCr_{rest} - PCr_{ex}$, with PCr_{rest} measured through the static experiment. Oxidative capacity (Q_{max}, mM ATP s-1) was determined as the product of k_{PCr} and PCr_{rest}.

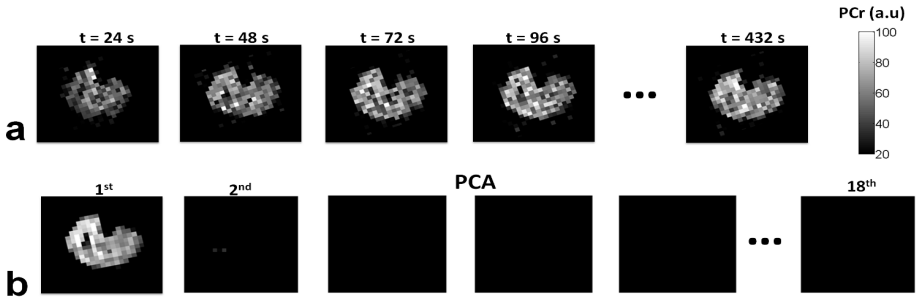

Fig. 1. a) PCr recovery in a cross-section of the lower leg muscles of a 28 year old male volunteer, after execution of plantar flexions. b) Representation of the time series in the PCA domain. These results show that the PCA is a good sparsifying transform for this application.

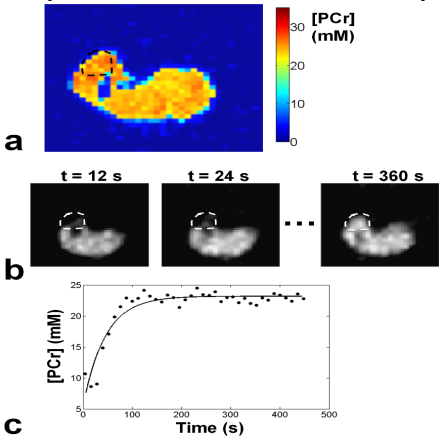

Fig. 2. Measurement of oxidative capacity in the muscle of a 60 yr old female volunteer. a) [PCr] map at rest b) Dynamic imaging of PCr resynthesis post exercise at 12 s temporal resolution. PCr levels in the TA are depleted immediately after exercise (t = 12 s), and fully recover after sufficient time (t = 360 s). c) Evolution of [PCr] in the TA muscle post-exercise, together with the fit of a single exponential growth function to the data in order to estimate k_{PCr}

RESULTS: An example of a resting [PCr] map of a 60 yr old female volunteer is shown in Fig2.a. Following exercise, [PCr] levels are depleted in the tibialis anterior muscle, as can be seen in Fig.2b. After sufficient time, [PCr] levels return to the resting values. By segmenting a VOI within the tibialis anterior, we plotted the PCr resynthesis (Fig.2c) and fitted the single exponential equation to the data. In this example, k_{PCr} was measured at 0.027 s^{-1}. In addition, the oxidative capacity (Q_{max}) in the TA muscle of this volunteer was measured at 0.69 mM ATP s^{-1}. The mean and standard deviation Q_{max} measured in the five subjects was 0.89 ± 0.21 mM ATP s^{-1}.

DISCUSSION: Spectrally selective CS-3D ^{31}P-MRI yields significantly improved spatial resolution compared to existing MRS methods, for the full coverage of all muscle groups and does not require any prior knowledge or assumptions about the muscles involved in the exercise.

CONCLUSION: The results of this work suggest that ^{31}P-MRI studies that suffer from long acquisition times can significantly benefit from the use of CS techniques. CS ^{31}P-MRI can become an important tool for studying spatially the dynamics of muscle function in healthy and diseased populations in a single experiment.

REFERENCES: 1. Kelley DE, He J, Menshikova EV, Ritov VB. Dysfunction of mitochondria in human skeletal muscle in type 2 diabetes. Diabetes 2002;51(10):2944-2950. 2. Parasoglou P, Feng L, Xia D, Otazo R, Regatte RR. Rapid 3D-Imaging of Phosphocreatine Recovery Kinetics in the Human Lower Leg Muscles with Compressed Sensing. Magn Reson Med 2012;DOI: 10.1002/mrm.24484.