The Feasibility of Measuring Phosphocreatine Recovery Kinetics in Muscle Using a Single-shot ^{31}P RARE MRI Sequence

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Rationale and Objectives: Heterogeneity of skeletal muscle structure, composition, and perfusion results in spatial differences in oxidative function between muscles and muscle regions. The simultaneous measurement of the postexercise phosphocreatine (PCr) recovery rate across all muscles of a human limb cross-section may provide new insights into normal physiology and disease states. The objective of this work was to assess the feasibility of acquiring PCr rapid acquisition with relaxation enhancement (RARE) images with sufficient temporal and spatial resolution to accurately measure PCr recovery kinetics in a cross-section of a human limb.

Materials and Methods: One normal subject performed a finger exercise until fatigued. At cessation of exercise surface coil localized pulse-and-acquire phosphorus-31 MR spectra (^{31}P- magnetic resonance spectroscopy [MRS]) of the forearm were acquired at 6 S intervals for 4 minutes. The exercise protocol was repeated 7 days later and axial PCr RARE images of the forearm were acquired following exercise with 5.6 cm^3 voxels at 6-second intervals for 4 minutes.

Results: The PCr recovery time constants for the PCr RARE and ^{31}P-MRS measurements were 91.0 and 91.1 seconds, respectively, based on a monoexponential fit. A Pearson correlation test showed that the PCr recovery data that resulted from the RARE PCr imaging were highly correlated with the data resulting from the ^{31}P-MRS ($r = 0.91$, $P < .0001$).

Discussion: Data from selected regions of RARE PCr images acquired at 6-second intervals compare well to those acquired using surface coil ^{31}P MR spectroscopy and can provide an accurate assessment of PCr recovery kinetics.

Key Words: MRI; phosphocreatine recovery kinetics; RARE MRI; muscle function; phosphorus MRI.

Substantial variation in the biochemical properties, vascular supplies, and composition (eg, fiber type) among human skeletal muscles has been well-documented (1–6). These characteristics influence the mitochondrial capacity to varying degrees in different muscles in normal and athletically trained individuals (2,4). Further changes in these characteristics occur because of normal aging (7) and some disease states, which may result in a heterogeneous pattern of altered metabolic function (4–6).

The rate of resynthesis of phosphocreatine (PCr) in skeletal muscle following exercise is an index of the capacity of the mitochondria to carry out oxidative metabolism (2,8,9). Phosphorus-31 magnetic resonance spectroscopy (^{31}P-MRS) with surface coil localization is an accepted method for measuring the postexercise recovery rate of skeletal muscle PCr (9,10) and can provide insights into normal physiology and pathophysiology in disease states (2). A limitation of surface coil ^{31}P-MRS is that it does not provide precise spatial information and is limited to superficial muscle regions. It is also uncertain whether the acquired signal is from only a single muscle or from multiple muscles with different characteristics within the sensitive region of the surface coil (2). Current ^{31}P-MRS localization methods require times that are too long for the precise assessment of postexercise PCr recovery kinetics (2,11,12).

Forbes and coworkers measured the rate of PCr recovery simultaneously across several muscles in the human lower leg using a low-intensity gated exercise protocol (13,14) and ^{31}P chemical shift imaging (11,12). Although low-intensity gated exercise protocols allow the measurement of PCr recovery without the confounding effects of muscle acidification, the ^{31}P-chemical shift imaging method is time consuming and results in a long data acquisition period.

A fast imaging method for acquiring dynamic PCr recovery information through a cross-section of a human limb may provide more information about altered metabolic function

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by allowing the simultaneous assessment of recovery kinetics in all of the muscles in the cross-section. Such a method may reveal patterns of disease progression and information that would help elucidate the mechanisms responsible for metabolic changes that occur as a result of exercise training, aging, and disease.

It has been demonstrated that the rapid acquisition with relaxation enhancement (RARE) pulse sequence can be used to produce magnetic resonance (MR) images that reflect the ^{31}P content in resting skeletal muscle with much smaller voxel sizes and shorter scan times than other localized ^{31}P MRS methods at 3T and higher field strengths (15,16).

In this work we investigated the use of the ^{31}P RARE pulse sequence at 3T for the measurement of postexercise PCr recovery kinetics in a cross-section of the human forearm. A novel aspect of this study is the demonstration of the feasibility that PCr recovery kinetics can be measured with a temporal resolution and a signal-to-noise ratio (SNR) that is comparable to that of surface coil localized ^{31}P-MRS but with a spatial resolution that is comparable to current ^{31}P-MRS localization methods that are used in resting muscle studies (2,11,12).

MATERIALS AND METHODS

Study Subject

One healthy 56-year-old man was recruited for this study. The subject was recreationally active but was not involved in any training programs to specifically strengthen the forearm and did not use any medications. The subject provided written informed consent approved by the local institutional review board. Data were acquired on a 3T whole body clinical MR imaging system (General Electric, Waukesha, WI) equipped with broadband transmit and receive channels. PCr RARE MR images and ^{31}P MR spectra were acquired in two separate sessions 7 days apart after an identical exercise protocol.

Exercise Protocol

The same exercise protocol was used for ^{31}P MRS and PCr RARE MR imaging measurements. The subject lay prone on the scanning table with his right forearm extended above his head. One ^{31}P spectrum or one PCr RARE image was acquired with the forearm muscles at rest for baseline information. The exercise protocol consisted of repeatedly squeezing a firm rubber block between the thumb and index finger. Audio cues for the contraction and rest periods were provided by a computer-based metronome. The duration of the contractions and rest periods were 1 second each. The subject was signaled to begin exercise and continued to exercise until exhaustion was experienced. The subject reported exhaustion at approximately 90 seconds after beginning exercise for both the ^{31}P spectroscopy and imaging studies. Forty-one images or spectra were acquired at 6-second intervals beginning immediately at the cessation of exercise. The total postexercise measurement time was 240 seconds. Healthy muscle with resting levels of PCr will appear bright on a PCr image. As the concentration of PCr is reduced during exercise the signal intensity of muscle tissue appears darker until it is at the level of the background noise during sustained exhaustive exercise. Squeezing the rubber block with only the thumb and index finger results in depletion of PCr in only a subset of the forearm muscles, mainly the flexor muscles near the location of the surface coil, used for the ^{31}P MRS portion of this study (volar surface of the forearm). Muscles not recruited in the exercise protocol, will appear consistently bright throughout the recovery period and provide a visual reference during times when the regions of muscle that are exercised intensively have signal intensities near the noise level.

MRS

A 7.5-cm circular ^{31}P transmit/receive surface coil was placed on the volar surface of the mid-forearm in close proximity to the flexor digitorum as shown in Figure 1b. The center of the coil was 5 cm distal to the elbow joint. Spectra were acquired using a pulse-and-acquire free induction decay (FID) sequence. The MRS acquisition parameters were: sweep width, 2048 Hz; number of complex points, 1024; TR, 3 S; signal averages, 2; time per acquisition, 6 S. The acquisition range was limited to 2.5 cm in the axial direction by a slice selection gradient.

Mapping the region of sensitivity of the ^{31}P surface coil. To determine the region of sensitivity of the ^{31}P surface coil a map of the RF (B1) field was generated, as previously described (17,18), by placing one of the flat end surfaces of a 16 cm diameter × 25 cm long cylindrical phantom containing a solution of 50 mM inorganic phosphate (Pi) onto the 7.5-cm circular ^{31}P surface coil. The spatial resolution of the radiofrequency (RF) field map was chosen to match that of the PCr RARE images.

MR Imaging

A double-tuned (^{31}P/^{1}H) low-pass quadrature birdcage RF coil with a diameter of 12 cm and a length of 12 cm was used for all image acquisitions for this study (17). All imaging was performed in an axial plane located 5 cm distal to the elbow joint.

Measurement of RF excitation pulse width. The bandwidth of the 15 ms RF excitation pulse (19) was measured by acquiring a series of images of a 500-mL bottle containing an 85% solution of phosphoric acid (A242-500, Fisher Scientific, Fair Lawn, NJ) placed within the double-tuned birdcage coil. The scanner's transmit/receive frequency was incrementally stepped in 10 Hz increments from 300 Hz below to 300 Hz above the sample's center frequency and an image was acquired at each step resulting in 61 images. The following scan parameters were prescribed to acquire an axial view of the sample: slice thickness = 25 mm, field of view (FOV) = 30 cm, acquisition matrix = 32 × 32, receiver bandwidth