

RARE imaging of post-exercise phosphocreatine recovery - validation and reproducibility

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Introduction: Human skeletal muscle is comprised of multiple fiber types and blood flow is heterogeneous between different muscles and within individual muscles (1). This structural and flow heterogeneity results in a heterogeneity in muscle chemistry and metabolism (2). Exercise training will affect individual muscles differently and the spatial distribution of fiber composition is altered in some diseases, such as diabetes and vascular disease (3). The current standard for non-invasive measurement of muscle metabolic function is surface coil localized phosphorus-31 MRS (³¹P-MRS), which detects signal from only superficial muscles in a non-uniform fashion. A method that can non-invasively measure the phosphocreatine (PCr) recovery rate after exercise in all of the muscles through a cross-section of a human limb may provide insights into muscle function in disease and provide a measure of the response to intervention. In this work we have developed and compared a dynamic ³¹P RARE imaging method to ³¹P MRS for measuring the post-exercise PCr recovery time constant (τ) in 5 normal volunteers and evaluated the reproducibility of the dynamic ³¹P RARE method for measuring PCr recovery.

Methods: Five normal volunteers performed a plantar flexion leg exercise protocol on 3 different days while positioned supine in a 3T clinical MRI system. The protocol consisted of: 1) one minute of rest; 2) exercise until tired (or a maximum of 6 minutes); and 3) 6 minutes of recovery. Phosphorus-31 data were acquired at 10-second intervals throughout the protocol. At the first visit MR spectra were acquired using a ³¹P pulse-and-acquire MRS sequence and a 7-cm circular surface coil placed at the posterior calf adjacent to the gastroc muscle (Fig. 1a). A 2D FSE sequence was modified to acquire ³¹P images with chemical shift selectivity. At the remaining 2 visits the subject's leg was placed in the double-tuned ³¹P/¹H quadrature birdcage coil and PCr RARE (FSE) images were acquired at 10-second intervals with a voxel size of 1.5 cm x 1.5 cm x 2.5 cm (5.6 cm³). The areas of the PCr peaks in the ³¹P MR spectra were calculated and plotted as a function of time. The pixels (target pixels) from the PCr RARE images that corresponded to the same region sampled during the surface coil ³¹P MRS exam were determined by comparing the PCr RARE images to a flip angle map of the surface coil (Fig. 1b). The image pixel intensities of the 8 target pixels were weighted according to the surface coil flip angle map, combined and the results from each image plotted as a function of time. All PCr post-exercise recovery data were normalized to the average pre-exercise value for all 5 subjects and the combined recovery curves were fitted to a monoexponential recovery function. A Pearson correlation analysis was performed to measure the correlation between the combined spectroscopy and each of the 2 combined imaging curves.

Results: A subset of the PCr RARE MR images acquired during exercise recovery are shown in Figure 1c. PCr depletion is clearly apparent at 'Time = 0 seconds' and gradually recovers to nearly pre-exercise levels at 'Time = 6 Minutes'. The combined recovery curves for the 5 subjects are plotted together in Figure 2. The numerical results are presented in Table 1. All correlations were significant ($P < 0.0001$). To demonstrate the utility of RARE PCr recovery MRI, the normalized PCr intensity from pixels in 3 different muscles are plotted together in Figure 3.

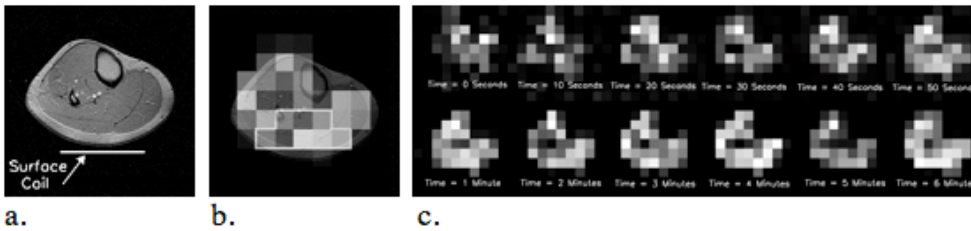


Figure 1. Location of surface coil used for ³¹P MRS (a) and the 8 ³¹P RARE pixels within the sensitive range of the surface coil (bordered by white lines) (b). A representative subset of the ³¹P RARE images acquired during the 6-minute PCr recovery period (c).

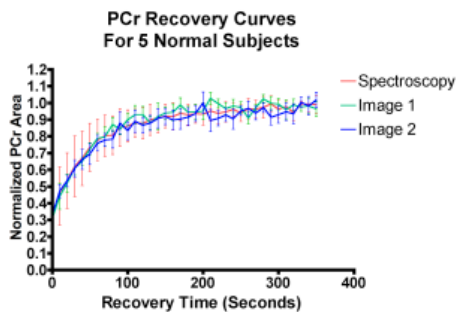


Figure 2. Combined recovery curves for each of the 3 exercise sessions.

Table 1.

PCr Recovery Time Constant (Seconds)			Correlations		
Spectroscopy	Imaging 1	Imaging 2	MRS to MRI-1	MRS to MRI-2	MRI-1 to MRI-2
68.28	79.80	77.33	0.98	0.99	0.97

Discussion: These results demonstrate the high reproducibility of the ³¹P RARE MRI method for measuring post-exercise PCr recovery and show a strong correlation between PCr recovery τ measurement using ³¹P RARE MRI and PCr recovery τ measurement

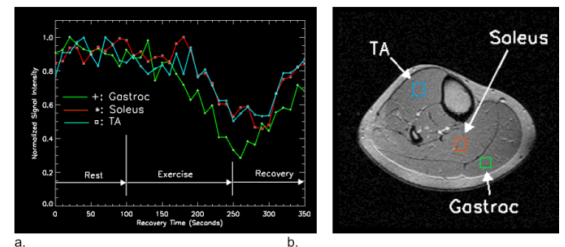


Figure 3. A plot of the normalized RARE PCr pixel intensities throughout the plantar-flexion exercise protocol and the corresponding pixel locations.

results obtained using the traditional method of surface coil-localized ³¹P MRS. In addition, recovery data can be obtained from any region in the cross-section of a human limb. This will allow the study of muscles with different fiber types and blood flow patterns in normal subjects and in disease states.

References: 1) Oberbach, et al. Diabetes Care 2006;29:895-900; 2) Kent-Braun, et al. Radiol Clin North Am 1994;32:313-35; 3) He, et al. Diabetes; 2001;50:817-23