Simultaneous Dynamic PCr and Pi Imaging of the Calf Muscle During Exercise and Recovery Using ^{31}P Gradient-echo MRI at 7 T

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Abstract. *Acquisition of dynamic changes in phosphocreatine (PCr) during exercise by ^{31}P-MRI has been recently show beneficial for evaluation of oxidative muscle metabolism in diverse muscle groups. In this study, a 3-D gradient-echo sequence for simultaneous dynamic ^{31}P-MRI of both PCr and inorganic phosphate (P_i) resonances was developed and tested at 7 T. The developed sequence allowed for multiple frequency-selective excitations of the PCr and P_i signals in an interleaved sampling scheme. The achieved spatial resolution was ~2 ml with an acquisition time of 5.8 s. Seven healthy subjects performed plantar flexions in an exercise-recovery experiment in between ^{31}P-MRI acquisitions. This allowed to observe differences in the mean PCr depletions during exercise between gastrocnemius (medialis: 44±14 %, lateralis: 40±11 %) and soleus (15±8 %). As expected from the low concentration of P_i, the P_i images had inherently low SNR at rest, but its signal was clearly detected in voxels of actively exercising muscles. In conclusion, simultaneous acquisition of PCr and P_i images with high temporal resolution, suitable for measuring PCr and P_i kinetics in exercise-recovery experiments, was demonstrated using a 3-D gradient-echo sequence at 7 T.*

Keywords: high energy phosphate, dynamic X-nuclei imaging, exercise, skeletal muscle

1. Introduction

Phosphorus magnetic resonance spectroscopy (^{31}P-MRS) is an established non-invasive method for studying muscle metabolism [1]. In particular, PCr and P_i kinetics in exercise-recovery experiments allow quantification of mitochondrial function or capacity, and provide insights into physiology, training status [2] and pathophysiology, e.g., in diabetes mellitus [3] or peripheral arterial disease [4]. Recently, the importance to spatially resolve differently exercising muscles (e.g., soleus and gastrocnemius) became more apparent [5].

In particular, ^{31}P-MRI with spectrally selective excitation has been proposed for spatially resolved detection of ^{31}P metabolites, e.g., PCr, at rest [6-8]. The 2-D spin-echo approach, originally proposed by Ernst et al. [6], was improved first by using TSE sequences and expanded to 3-D acquisition [8]. Techniques have been proposed even for simultaneous acquisition of multiple ^{31}P metabolites, e.g. interleaved excitation [7]. Recently, PCr imaging with temporal resolution in the order of seconds has been demonstrated by Greenman et al. [9] and Parasoglou et al. [10].

The aim of this study was to acquire both, PCr and P_i, images simultaneously with even higher temporal resolution. ^{31}P imaging experiment is used for simultaneous acquisition of both PCr and P_i time-courses during exercise-recovery experiments.

2. Subject and Methods

Seven healthy subjects (3f/4m, age 25.6±2.6 y, BMI=22.5±1.9 kg/m^2) participated in this study. All measurements were performed using a 7 T MR system (Siemens Healthcare, Erlangen, Germany) equipped with a ergometer, designed for plantar flexions [5]. An in-house built form-fitted 3-channel ^{31}P/ 2-cahnnel ^{1}H transceive coil was used.

For simultaneous acquisition of PCr and P_i data, a 3-D gradient-echo sequence was modified to perform multiple frequency-selective excitations in an interleaved scheme (Fig. 1). The excitation and readout frequency offsets were adjusted to the chemical shifts (PCr: 0 Hz, P_i: 570 Hz). The acquisition of a k-space line at the second frequency is shifted by $T_R/2$. This means that both images are shifted in time by only $T_R/2$. The excitation pulse was a 5 ms long sinc with truncated side lobes and with a bandwidth of 600 Hz.

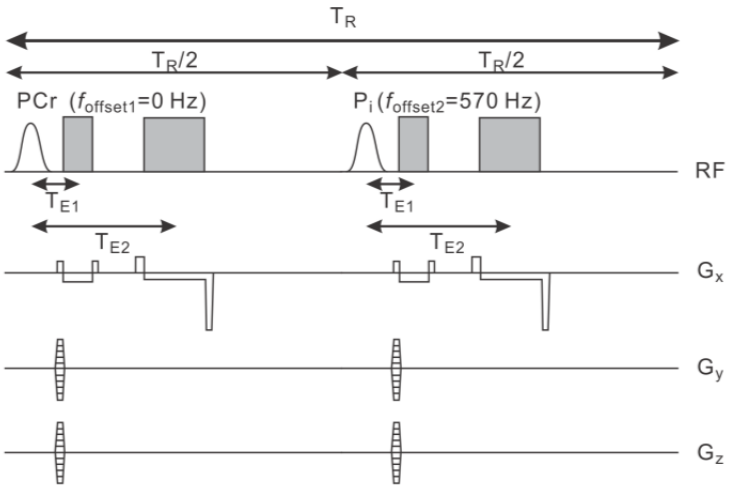

Fig. 1 Schematic of the interleaved, multi-frequency-selective 3-D gradient-echo sequence. $f_{offset1}$=0 Hz (PCr) and $f_{offset2}$=570 Hz (P_i). Corresponding sample images are shown in Fig. 2.

For dynamic ^{31}P imaging, the measurement parameters were as follows: T_R=60 ms; two echoes were acquired, to test the influences of the echo time and the receiver bandwidth on the temporal SNR of the PCr and Pi images, with T_E=3.8 ms and 14 ms; bandwidth 280 and 120 Hz/pixel, respectively. The matrix size was 16×16×6 with nominal spatial resolution of 9.4×9.4×20 mm^3. The resulting acquisition time for both PCr and P_i images was 5.8 s.

The maximum voluntary contraction (MVC) force of subjects was determined individually, before MR experiments, to set the workload to ~40% MVC. The dynamic ^{31}P-MRI protocol consisted of rest/exercise/recovery, lasting 1/3/4 minutes, respectively. The time between two complete sets of images was set to 10 s (5.8 s MRI + 4.2 s delay). During the exercise part of the protocol, subjects performed during the delay two plantar flexions.

Three ROIs were drawn, in the medial and lateral gastrocnemius and soleus, based on the anatomy images, resampled and applied to the ^{31}P images. The temporal SNR was calculated in the ROIs during the last two minutes of recovery. The temporal SNR of the P_i images was calculated during the second minute of exercise. The time-courses integrated over the ROIs were used to calculate PCr depletion and the time-constant of exponential recovery.

3. Results

Both PCr and P_i gradient-echo images with high temporal and spatial resolution were acquired with the proposed protocol. PCr was visible without averaging in as little as 5.8 s, in all three investigated muscles (Fig. 2a and 2b). The mean temporal SNR of PCr was 17.0±4.6 at T_E=3.8 ms and 18.6±3.2 at T_E=14 ms ($p<0.05$, paired t-test). P_i has an inherently low signal at rest since its concentration is much lower than that of PCr. It was therefore only visible in voxels from exercising muscles. The mean temporal SNR of P_i in gastrocnemius muscles was 3.5±1.6 at TE=3.8 ms, with no detectable signal at TE=14 ms. PCr and P_i images during exercise are displayed in Fig. 2c and 2d, respectively.

A decrease in PCr and an increase in P_i were observed in six volunteers during exercise. The mean PCr signal dropped by 44±14% and 40±11% in medial and lateral gastrocnemius muscles, respectively, while only by 15±8% ($p<0.01$, ANOVA, Tukey post hoc) in the soleus. One subject was excluded from further analysis due to poor compliance with the protocol and resulting low PCr depletion. The calculated τ_{PCr} values were 55.7±11.7 s and 57.1±14.1 s for gastrocnemius medialis and lateralis, respectively. Single subject data are given in Table 1. No assessment of recovery time-constant was performed in soleus due to low PCr depletion.

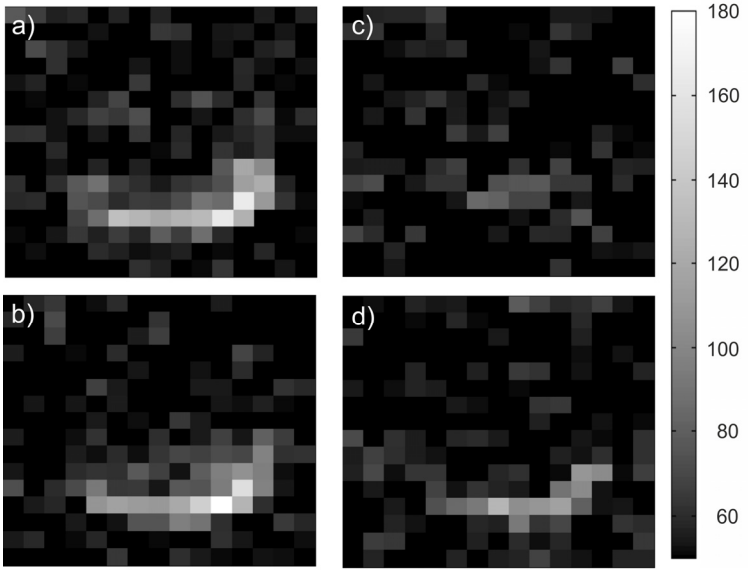

Fig. 2. ^{31}P MR images acquired during the exercise-recovery experiment (averaged over 3 acquisitions). (a) PCr at rest, and (b) at the end of recovery are similar. (c) Lower PCr signal during exercise is accompanied by (d) detectable P_i signal in gastrocnemius muscles. Note that no resting P_i image is provided due to low SNR, caused by its low concentration.

Table 1. Exercise intensities (%MVC), PCr depletion (ΔPCr) and recovery time-constants (τ_{PCr}) are shown for each analyzed subject. The bottom line shows the group average ± standard deviation (SD).

		gastrocnemius medialis		gastrocnemius lateralis		soleus
Subject	%MVC	ΔPCr [%]	τ_{PCr} [s]	ΔPCr [%]	τ_{PCr} [s]	ΔPCr [%]
1	42	31	39.1	37	33.9	3
2	38	66	57.2	40	48.0	20
3	43	42	46.3	19	63.1	11
4	39	56	71.9	46	58.3	17
5	35	38	56.4	48	73.0	16
6	41	30	63.2	47	66.4	25
Mean ± SD	40 ± 3	44 ± 14	55.7 ± 11.7	40 ± 11	57.1 ± 14.1	15 ± 8

4. Discussion

In our study, we present a frequency-selective 3-D gradient-echo sequence for simultaneous acquisition of PCr and P_i images. We have successfully used the designed sequence for dynamic localized measurements of oxidative muscle metabolism during and after exercise, providing time-courses of both PCr and P_i from the calf in a group of healthy volunteers.

The PCr depletion in the gastrocnemius, measured at 40% MVC, is in the range of literature values from localized MRS examinations [5]. The reported τ_{PCr} values are also in agreement with literature values from ^{31}P-MRI measurements [10]. The temporal resolution of 10 s, achieved in this study, is higher than previous reports of 24 s on fully sampled k-space, and still slightly better than 12 s using compressed sensing with TSE approach at 7 T [10]. The spatial resolution in this study (1.76 ml) was comparable to the spatial resolution of dynamic ^{31}P imaging (PCr only) using 3-D TSE imaging at 7 T (1.6 ml) by Parasoglou et al. [10].

The sequence described here has additionally the benefit of acquiring the PCr and P_i images simultaneously, thus providing more information on muscle metabolism at the same time.

Interleaved excitation of PCr and P_i was recently published using TSE sequence at 3 T, but low temporal resolution (4 minutes) rendered dynamic studies impossible [7].

5. Conclusions

The combined high temporal and spatial resolution achieved with the designed sequence at 7 T presents a valuable alternative to MRS for simultaneous PCr and P_i imaging during exercise-recovery experiments. Simultaneous and rapid measurements potentially allow for identifying local injuries, myopathies or functional deficits, in e.g., peripheral arterial disease.

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