

Serial water changes in human skeletal muscles on exercise studied with proton magnetic resonance spectroscopy and imaging

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In vivo ^1H -magnetic resonance imaging (MRI) enabled us to study the distribution of water in living tissues and to document changes in human skeletal muscles during physical exercise. The purpose of the present study was to determine the total muscle water changes after exercise using water in ^1H -MR spectroscopy and to compare these changes to the signal intensity change on T_2^* -weighted images and/or to the T_2 value change.

Seven young male volunteers were positioned in a 1.5 T Philips MR imaging system. They were then asked to dorsiflex their ankle joint against a 2 kg weight once every 2 seconds for 2 minutes. The peak height of water declined according to the clearance curve after exercise in all seven cases with the ^1H -MRS similar to the signal intensity. The increasing rate at peak height of total muscle water exceeded both the signal intensity and the T_2 value because the water peak height on the ^1H -MRS included the extracellular water. In addition, we measured the changes in signal intensity in both calf muscles after walking race exercise. The time intensity curves were used to draw a clearance curve for each muscle group after exercise. It was possible to discern which muscle was used most from the T_2^* -weighted image that was obtained once after exercise.

Key words: proton, functional imaging, magnetic resonance spectroscopy, skeletal muscle, exercise

INTRODUCTION

IT IS KNOWN THAT SKELETAL MUSCLE EXERCISE increases blood flow. Simultaneously, the water permeability of capillary vessels increases, so that both extracellular and intracellular water components also increase.¹ Additionally, both T_1 and T_2 relaxation times in muscle increase with exercise.²

Active and inactive muscles can be clearly distinguished after exercise. It is reported that the T_2 -weighted spin echo image of an active skeletal muscle has increased signal intensity immediately after exercise.^{2–7} It has also been noted that the image contrast between recently active

and inactive muscles typically persists for approximately 25 to 35 minutes after exercise.⁸ There has been no description of how the time course after exercise of exercise-induced contrast may be of practical clinical use.

The purpose of this study was to determine the total muscle water changes after exercise by using the water peak height as measured by ^1H -MRS and to compare it to the signal intensity change on the T_2^* -weighted image and/or to the T_2 value change. We also measured the changes in signal intensity in every calf muscle after the walking race exercise to determine if exercise-induced contrast may be useful in clinical studies.

SUBJECTS AND METHODS

Untrained male volunteers ($n = 7$, 21 to 30 years of age) were the subjects of this study. Each subject put on a shoe connected to a rope at the medial plantar region. Each was positioned prone in the magnet, then his right lower leg

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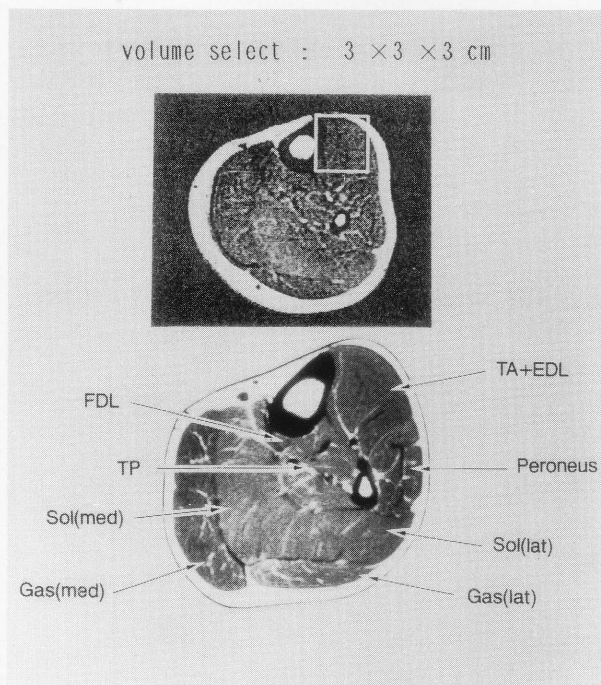


Fig. 1 The size of the localized volume for ^1H -MRS was $3 \times 3 \times 3 \text{ cm}^3$ in the TA and EDL, included partially the fat tissue and bone marrow. An anatomical cross section of the mid-calf was also shown. (TA; tibialis anterior muscle, EDL; extensor digitorum longus muscle, FDL; flexor digitorum longus muscle, TP; tibialis posterior muscle, Gas; gastrocnemius muscle, Sol; soleus muscle)

was fixed in the center of the head coil which was saddle shaped and 30 cm in diameter while his right leg lay out of the coil. The rope was connected to a 2 kg weight.

The MR system used in this study was Philips Gyroscan S15/HP equipped with a superconductive and horizontal-bore 1.5 T magnet.

Each subject exercised his tibialis anterior muscle (TA) and extensor digitorum longus muscle (EDL) to dorsiflex the ankle joint against a 2 kg weight, 10 cm upward 2 seconds at a time for 2 minutes. Three kinds of scans were collected before the exercise and during the recovery period of about 30 minutes. Every volunteer was the subject of three kinds of scans during the test period of one week. Each scan was obtained at the same mid calf site.

Proton spectra were obtained at an operating frequency of 63.77 MHz. The volume measured was $3 \times 3 \times 3 \text{ cm}^3$ on the TA and EDL and included partly subcutaneous fat tissue and bone marrow (Fig. 1). The cubic size was the smallest that enabled the MR system to obtain the spectra. The volume of subcutaneous fat tissue and bone marrow did not change on any exercise. Single voxel volume localization was accomplished with a 90° - 180° - 180° double spin echo pulse sequence.^{9,10} Typical line widths (full width at half maximum) of 10 Hz were achieved. Excitation of the ^1H nuclei was accomplished at 1000 Hz, sampling 512 points. A repetition time of 2000 msec and

an echo time of 136 msec were used. 128 signals were averaged, giving a total acquisition time of approximately 5 minutes. Forty minutes was required to prepare for ^1H -MRS before the first acquisition. Each acquisition was initiated immediately after the exercise and repeated 6 times consecutively.

Second, transaxial T_2^* -weighted mid calf images (10 mm slice thickness) were obtained with a head coil and a fast field echo (FFE) sequence (TR/TE = 500 msec/30 msec, flip angle 30°). A 256×256 matrix, 200 mm field of view and two averages were used, giving a total scan time of approximately 3.5 minutes. One minute was needed to establish the scanning condition. The first scan was collected before exercise. The next scan was initiated one minute after the exercise and repeated 9 times consecutively.

In the third scan, images were obtained for T_1 and T_2 calculation. Longitudinal relaxation time was calculated by means of an inversion recovery sequence (TR/TE/TI = 2240 msec/50 msec/300 msec). Transverse relaxation time was calculated with a spin echo sequence (TR/TE = 760 msec/50 msec). These sequences were the most suitable for this MR system. A 128×128 matrix and one average were used, giving a total scan time of approximately 6.5 minutes. The first scan was collected before exercise. The next scan was initiated one minute after exercise and repeated 5 times consecutively.

The same volunteers were subjected to one other examination. Each was asked to walk rapidly in a walking race and to continue the exercise until he became exhausted. Then the subject was positioned prone in the magnet after the exercise. The scan was initiated about 1.5 minutes after the exercise and repeated 9 times consecutively with the FFE sequence described above.

We set the region of interest (ROI) with care in order to place it within the TA and EDL muscle groups and away from muscle margins and obvious blood vessels. We obtained the dynamic time intensity curve from consecutive scans.

We hypothesized then that intracellular water and extracellular water containing metabolic products would be cleared out by blood flow. We considered the muscle tissue a single compartment model with the background. The time intensity (I) curve as the clearance curve due to the time decay constant was obtained (Fig. 2). The algebraic expression was as follows.

$$I = P(1) \cdot e^{-t/P(2)} + P(3)$$

$P(1)$ = Max intensity
 $P(2)$ = Time constant
 $P(3)$ = Base intensity

The increase ratio and the time constants which could be calculated if $P(1)/P(3)$ was considered to be the increase ratio for each muscle.

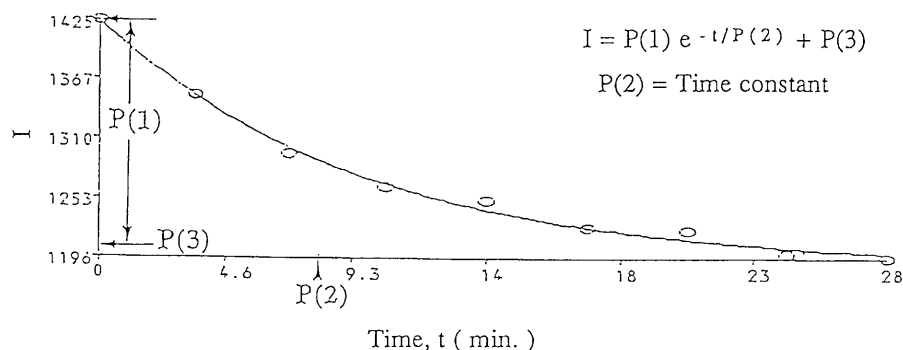


Fig. 2 The time intensity curve was considered as the clearance curve according to the time decay constant which was illustrated by a signal intensity (I) curve. The time (t) was written as the median value at any scan time after exercise.

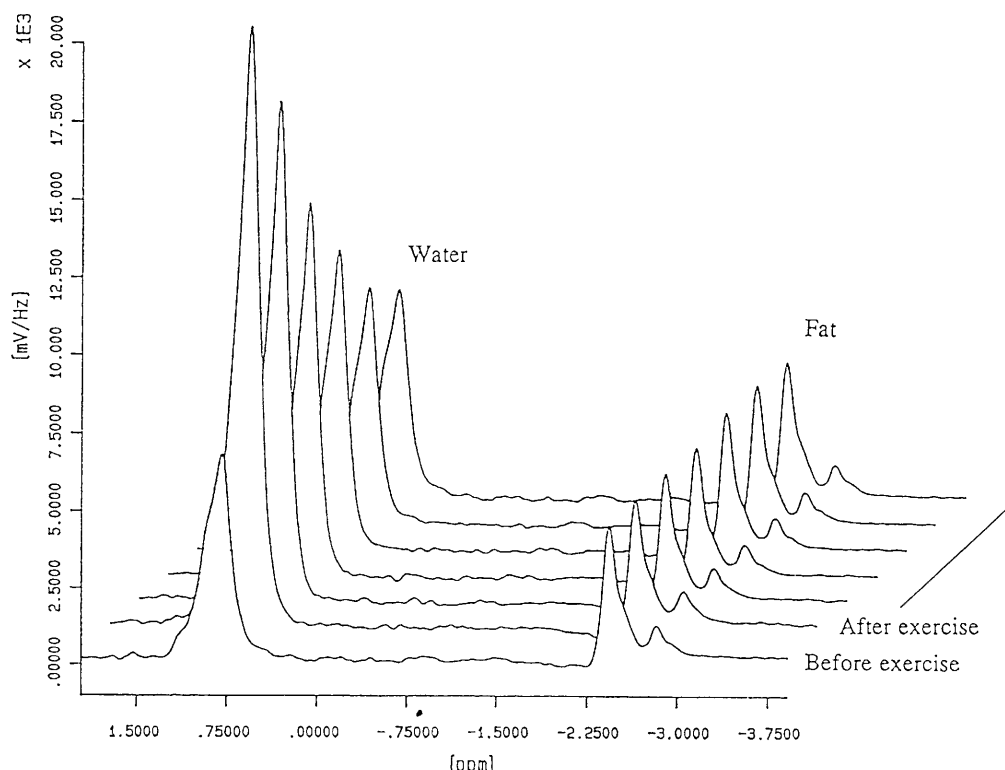


Fig. 3 Two peaks corresponding to water and fat were obtained by ^1H -MRS. The peak height of water increased immediately after exercise and declined thereafter while that of fat did not change.

RESULTS

Two peaks of water and fat were obtained with ^1H -MRS. The peak height of water increased immediately after the exercise and declined consecutively while that of fat did not change (Fig. 3).

The signal intensity of TA and EDL increased immediately after the exercise and declined consecutively with the FFE images. There was no evidence of signal intensity changes within any other muscles.

Transverse relaxation time in the region of interest increased in the same way after exercise and then decreased, drawing a mild slope. The longitudinal relaxa-

tion time curve decreased later after continuous exercise.

Data from all seven subjects were used to reconstruct the clearance curve from the peak-water height (Fig. 4). The area of the spectrum is peak height multiplied by full width at half maximum. Each spectra has same full width at half maximum. We used the peak height. The peak height which was seen immediately after exercise was taken as 100%. The time (t) was considered to be the median value at any scan time after exercise. The peak height at rest was also described.

The time intensity curve for signal intensity in FFE images after exercise was similar to the clearance curve in each case (Fig. 5). The calculated signal intensity

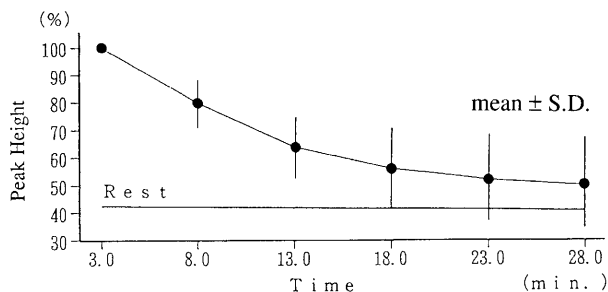


Fig. 4 Peak height changes were obtained by ^1H -MRS. As we processed the water peak height (H) change after exercise, it became clear that all seven cases fitted the clearance curve ($n = 7$). The peak height which was determined immediately after exercise was considered as 100%.

$$H = P(1) \cdot e^{-t/P(2)} + P(3)$$

$$P(1) = 84.5 \pm 28.4\% \text{ (mean } \pm \text{ S.D.)}$$

$$P(2) = 10.8 \pm 6.3 \text{ min.}$$

$$P(3) = 39.9 \pm 26.4\%$$

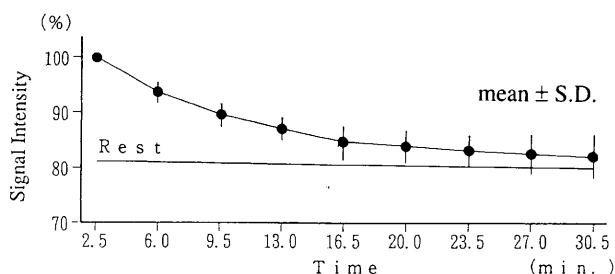


Fig. 5 Signal intensity changes on ^1H -MRI. As we processed the time intensity curves of signal intensities (I) on FFE images after exercise, all seven cases fitted the clearance curve ($n = 7$). The calculated signal intensity which was seen immediately after exercise was considered as 100%.

$$I = P(1) \cdot e^{-t/P(2)} + P(3)$$

$$P(1) = 27.0 \pm 8.5\% \text{ (mean } \pm \text{ S.D.)}$$

$$P(2) = 9.6 \pm 6.3 \text{ min.}$$

$$P(3) = 80.0 \pm 8.2\%$$

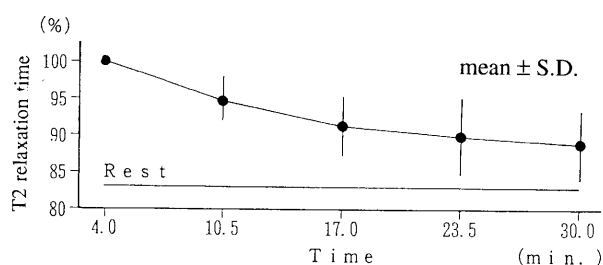


Fig. 6 The T_2 change was measured from T_1 , T_2 mixed calculated images. The T_2 value change fitted the clearance curve in six of the seven cases ($n = 6$). The T_2 relaxation time which was measured immediately after exercise was considered as 100%.

$$T_2 = P(1) \cdot e^{-t/P(2)} + P(3)$$

$$P(1) = 22.1 \pm 10.0\% \text{ (mean } \pm \text{ S.D.)}$$

$$P(2) = 13.8 \pm 7.1 \text{ min.}$$

$$P(3) = 86.7 \pm 6.2\%$$

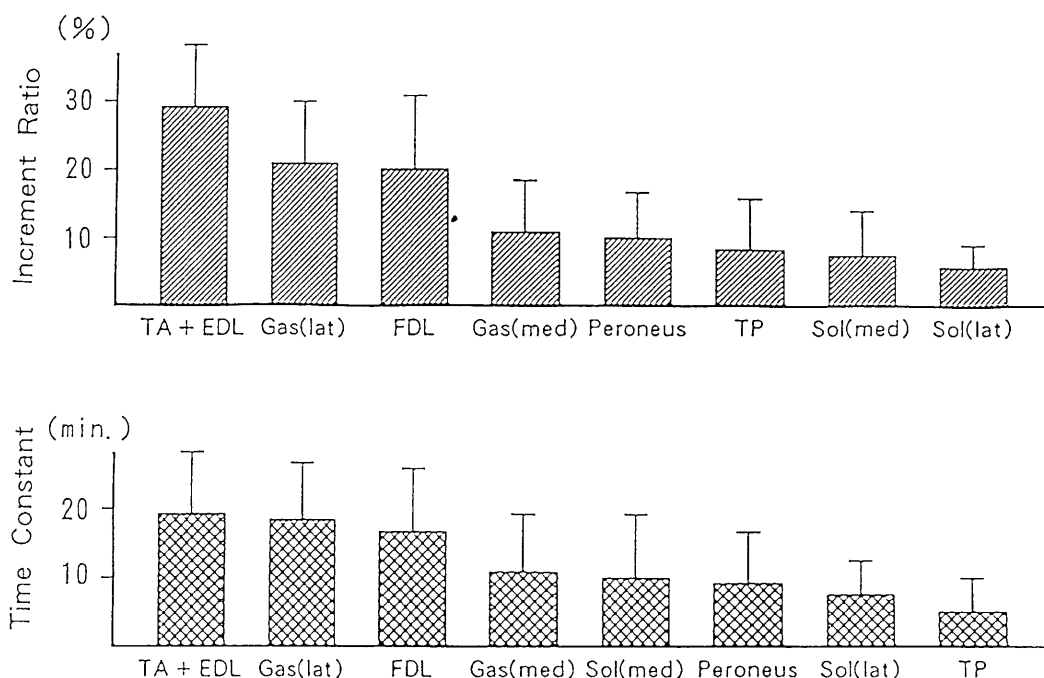


Fig. 7 The time intensity curves of all or most muscles fitted the clearance curve for each muscle group after the walking race exercise. The increment ratios and the time constants were able to calculated (mean \pm S.D.). The muscle groups with higher increment ratios tended to have longer time constant. (TA; tibialis anterior muscle, EDL; extensor digitorum longus muscle, FDL; flexor digitorum longus muscle, TP; tibialis posterior muscle, Gas; gastrocnemius muscle, Sol; soleus muscle)

immediately after exercise was taken as 100%. The signal intensity at rest was also described.

The longitudinal relaxation time change did not fit the curve, but the T_2 change fitted the clearance curve in six of the seven cases (Fig. 6).

We obtained the interrelation of time constants (min.) to each other. There was some correlation between water peak height and T_2^* signal intensity. The correlation coefficient was 0.57. Simple regression was as follows:

$Y = -0.18 + 0.80X$ (X = Signal intensity, Y = Water peak height)

There was little correlation between water peak height and T_2 relaxation time. The correlation coefficient was -0.31 .

$Y = 15.62 - 0.29X$ (X = T_2 relaxation time, Y = Water peak height)

It was thought that more exhausted muscle produced more metabolic products, so T_2 relaxation time was made shorter. Otherwise, the calculated T_2 value might have been incorrect.

The time intensity curve for each muscle group fitted the clearance curve after the walking race exercise. The increase ratios and time constants were obtained (Fig. 7).

DISCUSSION

It has been proposed that about 10% of tissue water is associated with the extracellular space and that 90% is in the intracellular space in skeletal muscle. The water associated with the macromolecules composes approximately 8% of total tissue water and does not exchange rapidly with the rest of the intracellular water.¹¹ There has been no non invasive method to catch the tissue water although the blood flow is calculated by ^{133}Xe . Submaximal exercise increases total muscle water content, primarily in the extracellular space, while severer exercise increases intracellular water.¹²⁻¹⁴ The major change in water content during exercise is an increase in the extracellular water content.² Fisher et al. postulated that the single T_2 value was primarily a function of myoplasmic or intracellular water.⁸ We demonstrated that the changes in the peak heights for tissue water on ^1H -MRS were similar to those of the signal intensities on the FFE images in the present study. T_2^* signal intensity was thought to reflect the water concentration which was seen as proton spectra, because it was obtained directly from a free induction decay signal. Sejersted et al. proposed that immediately after end of shortlasting exercise the volume of swollen muscle cells rapidly decreased. Fluid would accumulate in the interstitium since reuptake of fluid into the capillaries was a much slower process.¹⁵ The increasing rates of peak total muscle water exceeded both the signal intensity and the T_2 value because water peak height on ^1H -MRS included not only intracellular water but also extracellular water (e.g. slow venous flow).

Not only TA and EDL muscle groups, but also other

muscles of the mid-calf underwent a change in contrast on FFE images after the walking race exercise. The muscle group with a higher increase ratio had a greater time constant. This was thought to be due to the fact that after more severe exercise, a muscle took longer to recover because the exercise produced metabolic products of anaerobic metabolism and these accumulated. Each subject felt TA and EDL muscle pain a day after race walking.

The time decay constants were about 10 minutes after ankle dorsiflexion as the submaximal exercise in the present study. The constants varied from about 5 minutes to 20 minutes after race walking.

In conclusion, exercise-induced contrast should be of practical use in clinical studies. Deep active muscles are not able to be examined by electromyogram although subcutaneous muscles are able to be examined. It would be possible, with this method, to determine which muscle was used most when the T_2^* -weighted image is obtained once after exercise. We hope this method will be useful for clinical evaluations in rehabilitation or in sports medicine.

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