Relationship Between Muscle Swelling and Hypertrophy Induced by Resistance Training

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CITATION:

Hirono, Tetsuya ...[et al]. Relationship Between Muscle Swelling and Hypertrophy Induced by Resistance Training. Journal of Strength and Conditioning Research 2022, 36(2): 359-364

ISSUE DATE:

2022-02

URL:

http://hdl.handle.net/2433/267710

Title

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ABSTRACT

Muscle swelling immediately following resistance exercise may be induced by metabolic stress. The accumulation of metabolic stress is considered to promote muscle hypertrophy after several weeks of resistance training (RT). The purpose of this study was to determine the relationship between muscle swelling immediately after the first session of RT and muscle hypertrophy after a 6-week RT using ultrasonography. Twenty-two untrained young men performed knee extension resistance exercise consisting of 3 sets with 8 repetitions at a load of 80% of one repetition maximum for 6 weeks (3 days / wk). Muscle thickness of the quadriceps femoris was measured using ultrasonography device at three anatomical sites (proximal, medial, and distal sites) of the middle, lateral, and medial part of the anterior thigh. The sum of the muscle thickness at 9 measurement sites was used for analysis. Acute change in muscle thickness immediately after the first session of RT was used as an indicator of muscle swelling. Chronic change in muscle thickness after the 6-week RT was used as an indicator of muscle hypertrophy. A significant increase in muscle thickness was observed immediately after the first session of RT (8.3 ± 3.2 %, $p < 0.001$). After the 6-week RT, muscle thickness increased significantly (2.9 ± 2.6 %, $p < 0.001$). A significant positive correlation was found between muscle swelling and muscle hypertrophy ($\rho=0.443$, $p=0.039$). The present study suggests that the greater the muscle swelling immediately after the first session of RT, the greater the muscle hypertrophy after RT.

KEYWORDS

muscle swelling, muscle hypertrophy, resistance training, knee extension, ultrasound, muscle thickness

INTRODUCTION

Resistance training (RT) is effective in increasing muscle mass or preventing muscle atrophy. High-intensity RT using more than 60% of a one repetition maximum (1RM) load for more than 6 weeks has been recommended to obtain the effect of muscle hypertrophy (1, 4). Regarding the mechanisms of increases in muscle mass, mechanical and metabolic stress caused by muscle tension or muscle damages has been reported to initiate anabolic signaling pathways, which lead to muscle hypertrophy (23). The regular performance of progressive RT positively promotes anabolic signaling to cause a more positive balance of protein synthesis than protein degradation, facilitating gains in muscle mass in 6 weeks (19).

After resistance exercise, metabolic stress products such as growth hormone and reactive oxygen species are produced concurrently and play an important role in activating the mammalian target of rapamycin and muscle protein synthesis (5, 28). Muscle swelling immediately after resistance exercise is also a more novel mechanism that might be involved in the hypertrophic response to metabolic stress (5, 22, 23, 29). Muscle swelling occur as a result of the following: (i) resistance exercise can increase phosphocreatine and hydrogen ion accumulations due to blood lactate and growth hormone production (8) and (ii) the high lactate and hydrogen ion concentrations may accelerate water uptake in muscle cells according to cell permeability (21, 31) because the molecular weights of the lactate and hydrogen ions are smaller than that of muscle glycogen. Peeze Binkhorst et al. (18) reported that exercise-induced muscle swelling is due to increased wet weight because of increased interstitial volume in an animal experiment. In vivo study, Sjogaard et al. (25) also reported that swelling is maximized during exercise that relies heavily on anaerobic metabolism, due to the osmotic changes caused by lactate accumulation. Previous studies that used bioimpedance spectroscopy suggested that changes in intracellular and extracellular water balance after changes in ion concentration were associated with metabolic changes in skeletal muscle cell after exercise (20, 26). Thus, muscle swelling occurs due to the alteration of intracellular and extracellular water balance induced by increased vascular permeability, which can also mediate osmolytes (9, 12, 13, 16). Therefore, muscle swelling can be indirect an indicator of the accumulation of metabolic stress.

Muscle hypertrophy is the result of cumulative periods of positive muscle protein synthesis. Considering that metabolic stress can contribute to muscle hypertrophy adaptations (23), the measurement of acute muscle swelling after resistance exercise may be a good predictor of subsequent muscle hypertrophy. For instance, Bellamy et al. (2) revealed that a significant correlation between acute satellite cell response assessed using muscle biopsies and muscle hypertrophy after RT. With regard to muscle cell swelling, resistance exercise with high training volume induced larger muscle swelling than resistance exercise with less training volume (10). Considering that high training volume causes more severe muscle hypertrophy (24), greater muscle swelling could induce a greater anabolic signaling response and promote muscle hypertrophy. In addition, regarding resistance training with blood flow restriction (BFR), Fahs et al. (6) and Farup et al. (7) investigated acute swelling and chronic muscle hypertrophy. The results revealed similar acute muscle swelling and chronic muscle hypertrophy between the two groups with and without BFR, even with low-load training intensity. Considering these BFR studies, muscle swelling could be related to chronic muscle hypertrophy. However, to the best of our knowledge, no study has examined the relationship between muscle swelling immediately after exercise and muscle hypertrophy induced by several weeks of RT. If greater muscle swelling immediately after resistance exercise can cause greater chronic effects of muscle hypertrophy, assessment of muscle swelling immediately after the first session of RT may predict future effects of muscle hypertrophy. Therefore, the assessment of muscle swelling might lead to more effective RT program prescriptions of physical training for sports athletes.

For measurement of muscle swelling, changes in muscle thickness or cross-sectional area were used in many studies (3, 6, 7, 10, 15, 29, 32). Ultrasound is a relatively inexpensive and noninvasive method for the assessment of skeletal muscle and can be used immediately following exercise. Thus, the purpose of this study was to investigate whether the immediate increase in muscle thickness following resistance exercise, i.e., muscle swelling, is related to muscle hypertrophy after a 6-week RT. We hypothesized that there would be a positive correlation between muscle swelling immediately after the first session of RT and muscle hypertrophy after the 6-week RT.

METHODS

Participants

The sample size was calculated using G*Power 3.1 software (Heinrich Hein University, Düsseldorf, Germany) with an α error = 0.05, power = 0.8, and effect size = 0.5, which showed that 26 subjects were necessary for the correlation analysis. Therefore, 26 healthy young men (24 ± 3 years, range; 20 - 35) participated in this study. None of the included participants were athletes or in regular RT. Participants with a history of neuromuscular disorders or surgery in a training leg were excluded.

The purpose and procedures were explained to the participants before they gave informed written consent for participation in the study. The study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Kyoto University Graduate School and the Faculty of Medicine (C1294). This trial is registered with the UMIN Clinical Trials Registry.

Experimental procedure (Fig. 1)

The RT of knee extension was performed on the dominant leg, which was determined by what they would use to kick a ball. All the participants visited the laboratory for assessment of knee extension strength and muscle thickness of the quadriceps femoris muscle before (PRE) and after (POST) the training program that included 18 sessions of RT over a 6-week training period (RT1–RT18; Fig. 1). The prior assessment session (PRE) was separated more than one week before the first session of RT (RT1). In the first session of RT (RT1), muscle thickness of the quadriceps femoris was measured before (baseline) and immediately (0 min), 5, 10, and 15 min after resistance exercise. The acute change in muscle thickness from baseline was determined as an index of muscle swelling. Following these measurements, RT for knee extensors was performed in 18 sessions, 3 days per week for 6 weeks. The final assessment session (POST) was conducted 3–7 days after the last training session (RT18).

<Figure 1 about here>

Measurements of knee extension strength

The 1RM test was performed using the isotonic mode of a dynamometer (Biodex System 4, Biodex Medical Systems, Inc., Shirley, New York) by increasing load every 5 Nm. The participants sat on the dynamometer seat with belts fastened across their trunk and pelvis. The participants were required to move their leg through the required full range of motion (knee flexion 90°–20°) against the set load. The 1RM was defined as the maximum load in which the participant could complete one repetition through the range of motion. Each trial was separated by adequate rest periods of more than 2 min.

Maximum isometric strength with knee angles at 90° and 70° was measured using the isometric mode of the dynamometer. The participants were instructed to hold maximum voluntary contraction for 3 s. Maximum isokinetic strength through a knee angle range of 110° to 20° with contraction speeds of 90°/s and 180°/s was measured using the isokinetic mode of the dynamometer. Measurements of 1RM, isometric strength, and isokinetic strength were performed randomly one time with interval periods of more than 2 min.

Measurements of muscle thickness

Muscle thickness of the quadriceps femoris was measured using a B-mode ultrasonography device (Noblus; Hitachi Aloka Medical Systems, Tokyo, Japan) with a linear-array probe (4.0 cm). The participants were instructed to lie in the supine position and relax completely. Based on a previous study (11), muscle thickness of the quadriceps femoris was obtained at 9 sites, which consisted of proximal, median, and distal sites on the middle, lateral and medial part of the anterior thigh. Measurements of the middle part were taken at 30, 50, and 70% of the distance from the anterior superior iliac spine to the superior border of the patella. Measurements of the lateral part were taken at 30, 50, and 70% of the distance from the greater trochanter to the lateral condyle of the femur. Measurements of the medial part were taken at 70, 80 and 90% of the distance from the anterior superior iliac spine to the joint space in front of the anterior border of the medial collateral ligament. Wakahara et al. (30) reported that muscle hypertrophy occurred nonuniformly between the proximal and distal parts of the muscle. Therefore, 9 sites of the quadriceps were measured in this study, since muscle swelling might also differ between the proximal and distal parts of the muscle. Muscle thickness was determined as the distance between the muscle fasciae and bone interface, and the sum of measurements of the 9 sites was used in the analysis. To replicate the images between the baseline and after training, we verified that the distances between the landmarks were equal before the measurements. Inter-day reliability of measurement of muscle thickness was assessed by calculating the intra-class correlation coefficient (ICC) (1, 1) using the values of the two measurements at baseline and before the first session. The ICC (1,1) value was 0.961, which was confirmed as having high reliability. In addition, the standard error of the mean (SEM) of the difference in muscle thickness between baseline and immediately before first session was 1.06 mm. The percent change in muscle thickness after the first session of RT was the indicator of muscle swelling. The percent change in muscle thickness after the 6-week training intervention was the indicator of muscle hypertrophy. When we analyzed absolute changes in muscle thickness, we found that the results were similar to those based on of % changes, indicating that using neither absolute changes nor relative changes influenced the interpretation (supplemental figure).

Resistance training

The participants performed resistance exercise on knee extension using a dynamometer (Biodex System

4; Biodex Medical Systems, Inc., Shirley, New York). The training load was set at 80% 1RM, based on the 1RM measurements at PRE session. The participants sat on the dynamometer seat with belts fastened across their trunk and pelvis. The participants performed knee extension through a knee flexion range of 90° to 20° with a speed of 1-s concentric contraction, 1-s eccentric contraction, and 1-s rest period according to 60 bpm made by a metronome. The session of resistance exercise consisted of 3 sets of 8 repetitions with a rest interval of 60 s. The RT was performed 3 days per week for 6 weeks.

Statistical analyses

All data were analyzed using SPSS version 22.0 software (IBM Japan, Inc., Tokyo, Japan). A one-way repeated-measures analysis of variance (ANOVA) with post hoc Bonferroni test was performed to analyze the acute changes in muscle thickness following the first session of RT. Paired t-tests were performed to investigate the effects of RT intervention on 1RM, maximum isometric strength, maximum isokinetic strength, and muscle thickness. The 95% confidence interval and effect size in baseline and after 6-week training were calculated. Additionally, Spearman correlation coefficients were used to examine the association between percent changes in muscle thickness following the first session of RT (0 min, 5 min, 10 min, and 15 min) and percent changes in muscle thickness after the 6-week RT. Statistical significance was set at an alpha-level of 0.05.

RESULTS

Twenty-five participants completed the 6-week RT session. One participant dropped out, and the data of 3 participants could not be obtained completely. Therefore, 22 young men (age; 25 ± 4 years, height; 172 ± 5 cm, weight; 67 ± 10 kg) completed the analyses (Fig. 2).

<Figure 2 about here>

The one-way ANOVA showed a significant main effect of acute changes in muscle thickness of the quadriceps. Post hoc test revealed that muscle thicknesses at 0, 5, 10, and 15 min immediately after the first session of RT were significantly greater compared to baseline (Fig. 3). As for time course of acute change from 0 to 15 min after exercise, significant decreases in muscle thickness were observed between all times.

<Figure 3 about here>

The paired t-tests showed significant increases in 1RM, maximal isometric strength, maximal isokinetic strength, and muscle thickness after the 6-week RT (Table 1).

The Spearman correlation coefficient revealed the significant positive correlations between the change in muscle thickness after the 6-week RT and acute changes in muscle thickness at 0 min (ρ=0.443, p=0.039), 5 min (ρ=0.582, p=0.004), 10 min (ρ=0.596, p=0.003), and 15 min (ρ=0.443, p=0.039) immediately after the first session of RT (Fig. 4).

<Table 1 about here>

<Figure 4 about here>

DISCUSSION

This study investigated the relationship between muscle swelling immediately after the first session of RT and muscle hypertrophy after 6 weeks of RT. Our hypothesis was that muscle swelling in the first session of RT would be associated with muscle hypertrophy. To determine the relationship between acute muscle swelling and chronic muscle hypertrophy, affecting factors should be eliminated as much as possible. As the aim of this study was to investigate the acute effects of the first session of RT on the chronic effects, training load was not changed from the first session. The results showed that resistance exercise with a load of 80% of 1RM caused muscle swelling and that muscle hypertrophy was observed after the 6-week RT program, even though the training load was not changed throughout the intervention.

Furthermore, the present study revealed that each muscle swelling obtained at 0, 5, 10, and 15 min after the first session of RT had significant positive correlations with the muscle hypertrophy caused by the 6-week intervention. These results support our hypothesis. This is the first study to reveal the relationship between muscle swelling immediately after resistance exercise and muscle hypertrophy after RT.

In our study, muscle thickness increased by 2.9 ± 2.6% and 1RM increased by 25.4 ± 9.6% after the 6-week RT. Tanimoto and Ishii (27) investigated the effect of a 12-week knee extension RT at 80% 1RM, which was similar to our RT protocol, and reported that the CSA of the knee extensor muscle increased by 4.3 ± 2.1% and the 1RM increased by approximately 32% (from 104.9 ± 18.6 to 138.3 ± 18.6 kg). Since RT of the present study was performed for only 6 weeks, magnitudes of improved muscle thickness and muscle strength were smaller than those of the previous study.

The present study showed that muscle swelling immediately after the first session of RT was associated with muscle hypertrophy after the 6-week intervention. Muscle swelling immediately after exercise is a response to metabolic stress to the skeletal muscle (14, 23). Even though multiple metabolic stress markers such as hormonal release or reactive oxygen species production can be associated with muscle hypertrophy (5, 23), the result of the present study suggested a possibility that only the acute response assessed with the changes in muscle thickness using an ultrasonography device could affect the subsequent muscle hypertrophy. Acute muscle swelling is caused by water uptake in muscle cell according to phosphocreatine and hydrogen ion accumulation due to blood lactate and growth hormone production (8, 21, 31), which can promote anabolic protein synthesis. Therefore, greater acute muscle swelling might be associated with greater chronic muscle hypertrophy. Since muscle hypertrophy is caused by repeated sessions of RT (19), it is possible that the amount of mechanical or metabolic stress in the skeletal muscle induced by one session of RT could predict muscle hypertrophy following repeated sessions of RT for several weeks. In general, the effects of muscle hypertrophy can be obtained by more than 6 weeks of RT (1, 4). Therefore, to evaluate the effect of muscle hypertrophy, a long-term intervention period is required. The present study revealed a positive relationship between muscle swelling immediately after resistance exercise and muscle hypertrophy induced by the 6-week RT. The results suggest that the assessment of muscle swelling immediately after resistance exercise could possibly predict an effect of muscle hypertrophy in the future. The noninvasive and immediate measurement of muscle swelling may be useful in the prescription of a more effective RT program.

In contrast to our findings, previous studies showed no relationship between acute and chronic effects of RT. Mitchell et al. (17) reported that acute effects of myofibrillar protein synthesis following initial exposure to resistance exercise were not correlated with muscle hypertrophy following chronic RT. Damas et al. (4) also reported that initial RT-induced muscle damage possibly drives myofibrillar protein synthesis toward muscle remodeling, not hypertrophy. The physiological mechanism in exercise-induced muscle damage and remodeling has been incompletely resolved. While Mitchell et al. (17) investigated muscle biopsies obtained from one site of the vastus lateralis, the current study assessed muscle thickness from nine sites on the anterior thigh using an ultrasonography device. There is a difference in the assessments between these studies, but this contradiction is not explained from our data. Further studies are necessary to investigate the mechanism.

This study had some limitations. First, we could not measure the volume of blood flow or blood test data; nevertheless, muscle swelling was affected by physiological functions such as blood flow or metabolic materials (22, 23). In addition, the characteristics of the skeletal muscle such as muscle fiber size and muscle fiber type could also not be examined using muscle biopsy. However, our results showed a positive correlation between muscle hypertrophy and muscle swelling, which suggests that assessment of muscle swelling using ultrasonography images could predict the magnitude of muscle hypertrophy. The second limitation was the small sample size due to data availability. Finally, we examined only the training protocol with load of 80% 1RM and 6-week intervention. Thus, it is unclear whether other training protocols (e.g., low-load training or long duration of intervention) lead to a similar result of this study. Future studies are needed to examine various RT protocols such as low-load RT and high-repetition RT.

In conclusion, this study investigated the relationship between muscle swelling immediately after the first session of RT and muscle hypertrophy after a 6-week RT in untrained healthy young men. The results revealed a significant positive correlation between muscle swelling and muscle hypertrophy. The results of this study suggest that the assessment of changes in muscle thickness immediately after the first session of RT could predict the magnitude of chronic effects of muscle hypertrophy in the future.

PRACTICAL APPLICATIONS

This result suggested that an assessment of immediate change in muscle thickness in the first session of RT using ultrasonography device could be a possible predictor the chronic effect of muscle hypertrophy. Evaluating the change in muscle thickness immediately after exercise may be useful for prescribing the effective training protocol in accordance with the subjects.

ACKNOWLEDGMENTS

We thank all the participants for their cooperation in this study. This study was not funded by any institutions, agencies, or companies.

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FIGURE LEGENDS

Fig. 1. The resistance training of knee extension was performed for 6 weeks. All the participants visited the laboratory for assessments of knee extension strength and muscle thickness before (PRE) and after (POST) 6-week resistance training. Eighteen sessions of resistance training over the 6-week training period were performed (RT1 – RT18). In RT1, muscle thickness of quadriceps femoris was measured before (baseline) and immediately (0 min), 5, 10 and 15 min after resistance exercise in order to assess muscle swelling.

MT, muscle thickness; 1RM, one repetition maximum; RT, resistance training

Fig. 2. Twenty-six healthy young men participated in this study. Twenty-five participants completed the 6-week RT session. One participant dropped out, and the data of 3 participants could not be obtained completely. Therefore, 22 young men completed the analyses.

Fig. 3. Acute changes in muscle thickness immediately after the first session of resistance training. The one-way ANOVA showed a significant main effect of acute changes in muscle thickness of the quadriceps. Post hoc test revealed that muscle thicknesses at 0 min, 5 min, 10 min, and 15 min immediately after the first session of RT were significantly greater compared to baseline. Values are mean ± standard deviation: n = 22. Significance was set at $P < 0.05$: *; Significant difference from baseline. †; Significant difference from 0 min. ‡; Significant difference from 5 min. §; Significant difference from 10 min.

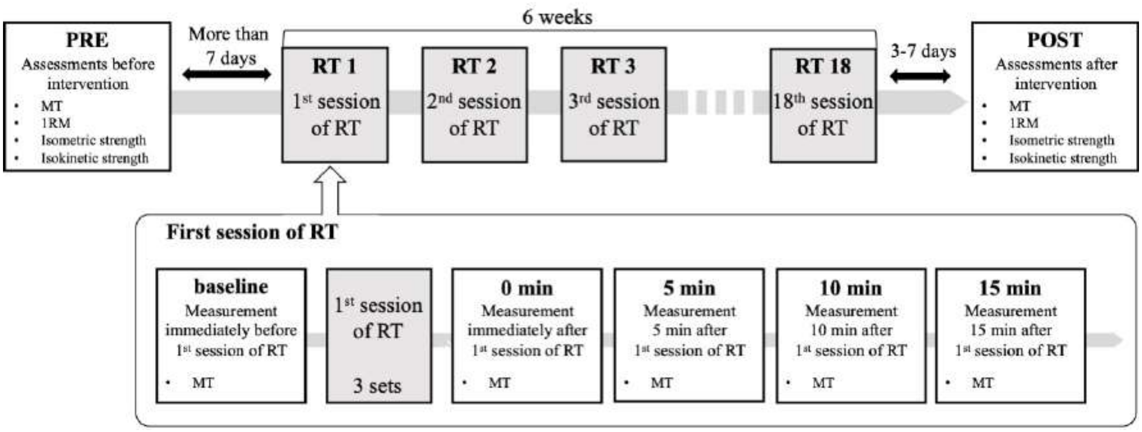
Fig. 4. The relationship between changes in muscle thickness immediately after the first session of resistance training and after 6-week resistance training ($n = 22$). The Spearman correlation coefficient revealed significant positive correlations between the change in muscle thickness after 6-week resistance training and acute changes in muscle thickness at 0 min (A; $\rho = 0.443$, $p = 0.039$), 5 min (B; $\rho = 0.582$, $p = 0.004$), 10 min (C; $\rho = 0.596$, $p = 0.003$), and 15 min (D; $\rho = 0.443$, $p = 0.039$) immediately after the first session of resistance training.

RT, resistance training

Table 1. Changes in muscle strength and muscle thickness after the 6-week resistance training

	Before RT	After RT	P-value	Percent changes [%]	Effect size (r)	95 % confidence intervals
1RM (Nm)	192.3 ± 35.3	240.7 ± 43.9	< 0.001	25.4 ± 9.8	0.93	40.0 – 56.9
Maximum isometric strength at 90° (Nm)	196.4 ± 44.9	237.0 ± 44.5	< 0.001	22.2 ± 15.3	0.87	30.2 – 50.9
Maximum isometric strength at 70° (Nm)	236.7 ± 47.7	266.2 ± 50.7	< 0.001	13.2 ± 12.0	0.74	17.2 – 41.9
Maximum isokinetic strength at 90°/s (Nm)	165.1 ± 32.8	199.3 ± 25.0	< 0.001	24.5 ± 25.9	0.80	22.5 – 46.0
Maximum isokinetic strength at 180°/s (Nm)	132.0 ± 24.0	151.4 ± 18.4	< 0.001	17.0 ± 18.7	0.74	11.5 – 27.3
Muscle thickness of the quadriceps femoris (mm)	340.1 ± 30.2	349.9 ± 29.6	< 0.001	2.9 ± 2.7	0.76	6.0 – 13.6

Values are means ± standard deviation. Muscle thickness of the quadriceps femoris was calculated by the sum of 9 measurement sites. 1RM; one repetition maximum. RT; resistance training


6 weeks
PRE
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1RM
Isometric strength
Isokinetic strength
More than 7 days
RT 1
1st session of RT
RT 2
2nd session of RT
RT 3
3rd session of RT
RT 18
18th session of RT
3-7 days
POST
Assessments after intervention
MT
1RM
Isometric strength
Isokinetic strength
First session of RT
baseline
Measurement immediately before 1st session of RT
MT
1st session of RT
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Measurement immediately after 1st session of RT
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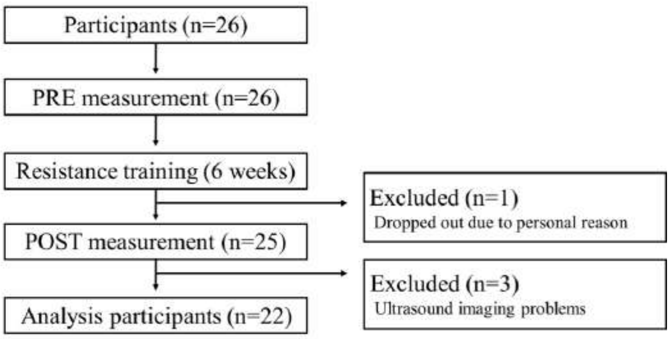
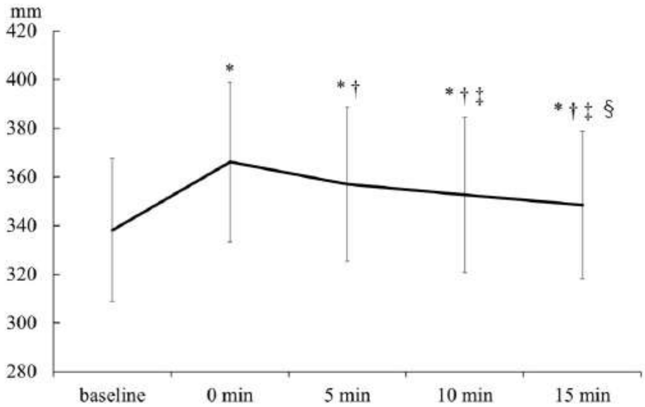

Participants (n=26)
PRE measurement (n=26)
Resistance training (6 weeks)
Excluded (n=1)
Dropped out due to personal reason
POST measurement (n=25)
Excluded (n=3)
Ultrasound imaging problems
Analysis participants (n=22)


mm
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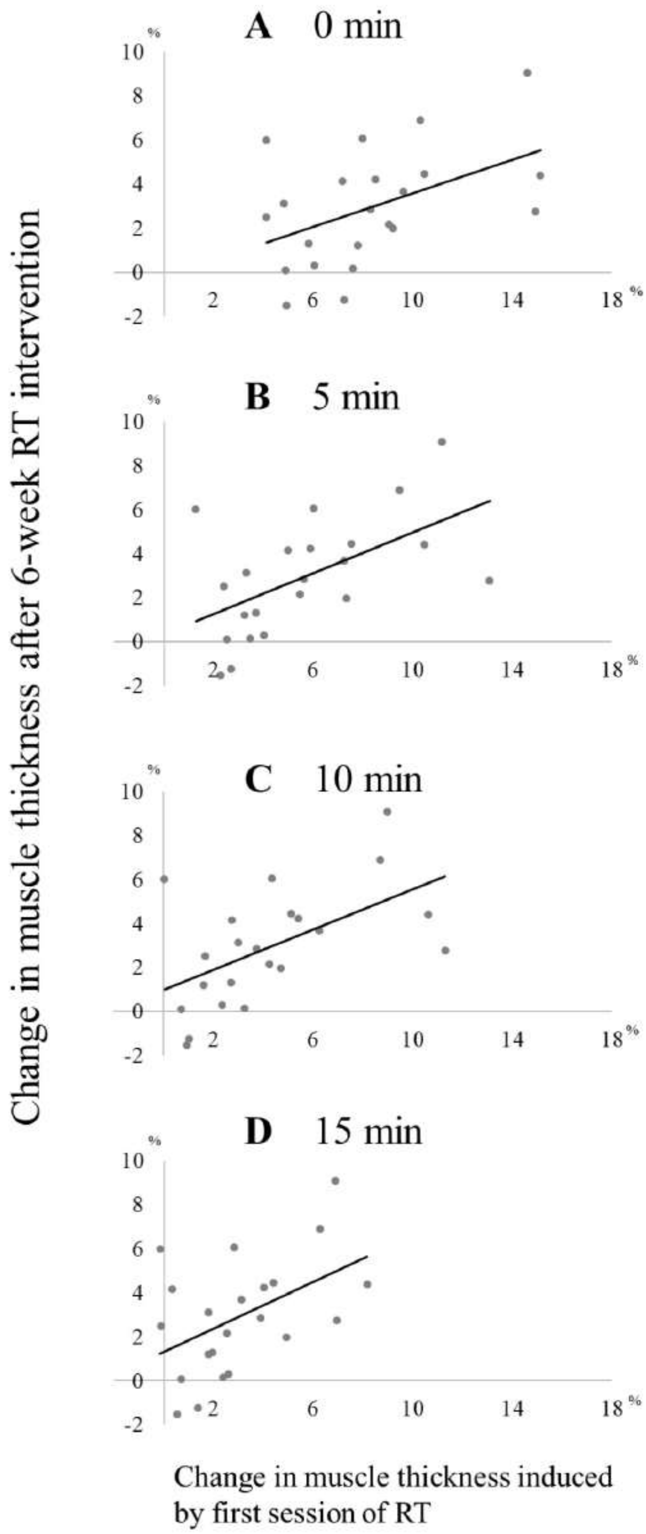
A 0 min
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4
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0
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2
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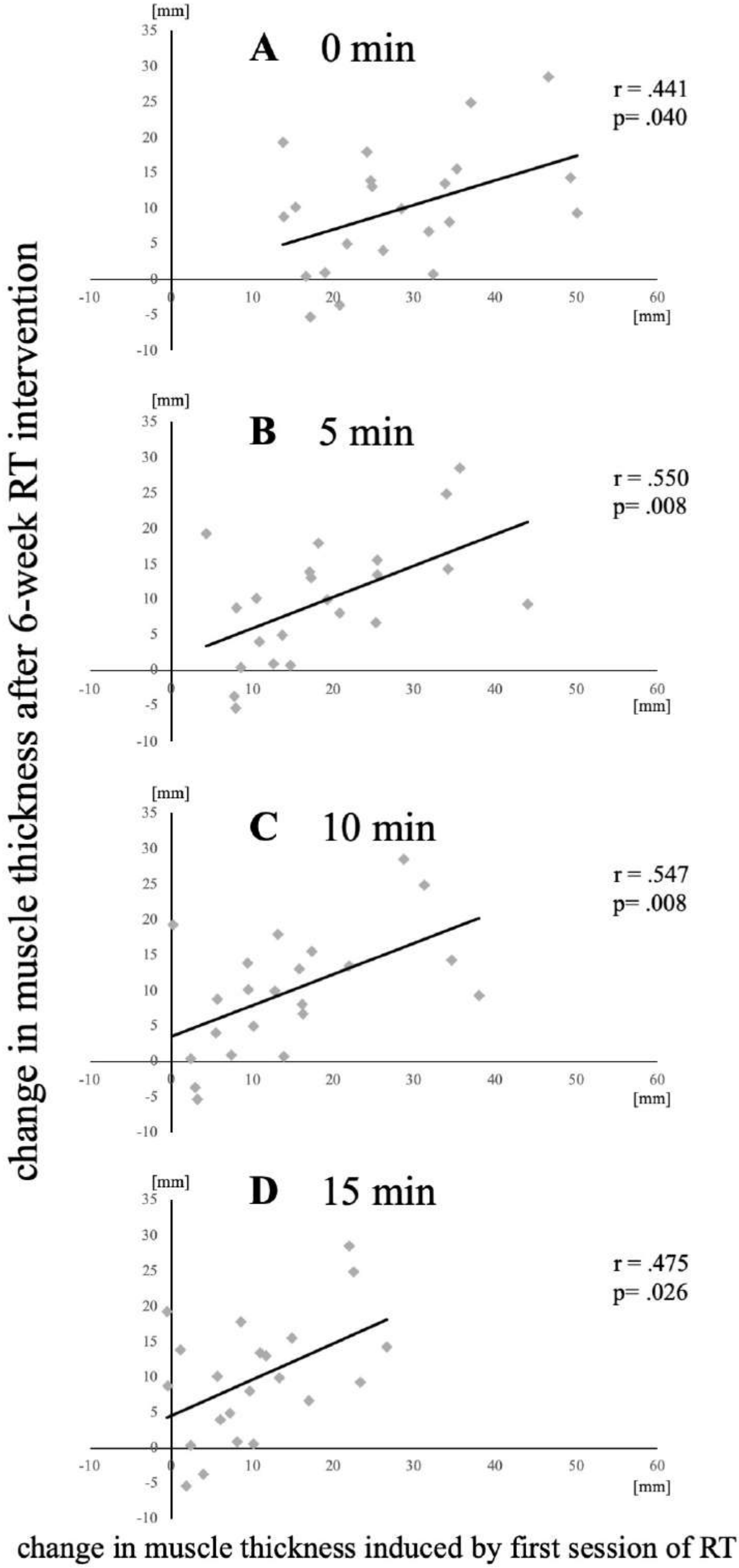
18 %
Change in muscle thickness after 6-week RT intervention
Change in muscle thickness induced
by first session of RT

Supplemental figure legend

The relationship between absolute changes in muscle thickness immediately after the first session of resistance training and after 6-week resistance training (n = 22). The Pearson correlation coefficient revealed significant positive correlations between absolute change in muscle thickness after 6-week resistance training and absolute acute changes in muscle thickness at 0 min (A; r = 0.441, p = 0.040), 5 min (B; r = 0.550, p = 0.008), 10 min (C; r =0.547, p = 0.008), and 15 min (D; r = 0.475, p = 0.026) immediately after the first session of resistance training.

RT, resistance training


change in muscle thickness after 6-week RT intervention
A 0 min
r = .441
p= .040
B 5 min
r = .550
p= .008
C 10 min
r = .547
p= .008
D 15 min
r = .475
p= .026
[mm]
35
30
25
20
15
10
5
0
-5
-10
10
20
30
40
50
60
change in muscle thickness induced by first session of RT