2	
3	TITLE: Partial range of motion exercise is effective for facilitating muscle hypertrophy
4	and function via sustained intramuscular hypoxia in young trained men
5	
6	RUNNING HEAD: Effects of partial range of motion exercise
7	
8	AUTHOR:
9	Masahiro Goto <sup>1, 2</sup> , Chikako Maeda <sup>2</sup> , Tomoko Hirayama <sup>2</sup> , Shigeru Terada <sup>3</sup> , Shinsuke
10	Nirengi <sup>4</sup> , Yuko Kurosawa <sup>5</sup> , Akinori Nagano <sup>1</sup> , and Takafumi Hamaoka <sup>5*</sup>
11	<sup>1</sup> Graduate School of Sport and Health Science, Ritsumeikan University, Japan
12	<sup>2</sup> Department of Physical Therapy, Aino University, Japan
13	<sup>3</sup> Department of Rehabilitation, Kanazawa Red Cross Hospital, Japan
14	<sup>4</sup> Division of Preventive Medicine, Clinical Research Institute, National Hospital
15	Organization Kyoto Medical Center, Kyoto, Japan
16	<sup>5</sup> Department of Sports Medicine for Health Promotion, Tokyo Medical University, Japan
17	
18	

### \*CORRESPONDING AUTHOR:

- 2 Takafumi Hamaoka, MD, PhD, Department of Sports Medicine for Health Promotion,
- 3 Tokyo Medical University, 6-1-1 Shinjuku, Shinjuku, Tokyo 160-8402, Japan
- 4 Tel: +81-3-3351-6141 E-mail: kyp02504@nifty.com

5

1

## 6 ABSTRACT

- 7 The acute response to and long-term effects of partial range of motion exercise (PRE) and
- 8 full range of motion exercise (FRE) of elbow extensors were compared in young trained men.
- 9 The PRE was expected to increase the intramuscular hypoxic environment, which was
- 10 theorized to enhance muscular hypertrophy. Forty-four resistance-trained men were divided
- into two training groups, PRE (n = 22) or FRE (n = 22) group, and performed the PRE or
- FRE acute exercise protocol. The PRE (elbow range from 45° to 90°) and FRE (from 0° to
- 13 120°) acute protocols consisted of 3 sets of 8 repetitions, with an 8-repetition maximum
- 14 (RM), and an equivalent workload. After the initial testing, the training program for each
- group, comprised three training sessions per week for 8 weeks, was started. The acute
- responses of area under the oxygenated hemoglobin (Oxy-Hb) curve, blood lactate
- 17 concentration, and root-mean-square of electromyography were significantly higher both
- before and after PRE than FRE training. Long-term effects were produced by both PRE and
- FRE, with significant (p < 0.05) increases in cross-sectional area (CSA) of triceps brachii

- and isometric strength. CSA increased significantly greater after PRE ( $48.7 \pm 14.5\%$ ) than
- 2 after FRE ( $28.2 \pm 10.9\%$ ). Furthermore, during the PRE program, a positive correlation was
- 3 detected between the percent increase in CSA and area under the Oxy-Hb curves before and
- 4 after 8-week exercise training (before 8-week exercise training: r = 0.59, after 8-week
- 5 exercise training: r = 0.70, p < 0.01). These results suggest that intramuscular hypoxia might
- 6 facilitate muscular hypertrophy with PRE being more effective than FRE.
- 8 **KEY WORDS:** muscle hypertrophy, resistance exercise, hypoxia, partial range of motion

### 10 INTRODUCTION

7

- 11 Muscle response to resistance exercise is affected by previous exercise training (23). It is
- speculated that certain factors inhibit hypertrophic signaling caused by habitual resistance
- exercise (13). A previous study detected local increases in artery diameter and blood flow
- 14 after eight weeks of resistance exercise (22), resulting in blunted hypoxic muscle stimulation.
- Wessel et al. reported that the increase in muscle oxidative capacity produced by resistance
- training has a negative impact on muscle hypertrophy (26). To obtain effects, such as muscle
- strength enhancement and hypertrophy, in particular for resistance-trained individuals, it is
- important to consider mechanical and metabolic stress caused by the exercise. Therefore, the

- 1 effects of a number of different training strategies have been examined in trained subjects (9,
- 2 25).
- The partial range of motion exercise method (PRE) is an exercise method (3, 4) that
- 4 body-builders and weight lifters often use to increase muscle strength and hypertrophy. As
- 5 PRE uses only the middle range of motion of an exercise, PRE will induce greater active and
- 6 passive muscular tension (4), and can be perform with higher loading compared to FRE (3).
- 7 Furthermore, PRE makes it possible to maintain constant muscular contraction during
- 8 exercise because of its slower movement speed. Constant muscular contraction during
- 9 exercise tends to induce intramuscular hypoxia (24). As higher muscular tension and
- 10 constant muscular contraction is compressing intramuscular capillaries, intramuscular
- 11 hypoxia during PRE is expected. Therefore, PRE might cause greater mechanical and
- metabolic stress in the muscle than FRE.
- McMahon et al. investigated the differences in muscle size and strength, in
- recreationally active subjects, after a same movement velocity 8-week squatting program
- with long and short ranges of motion in the rectus femoris muscle (20). Significant
- 16 post-training differences in strength and distal anatomical cross-sectional area, with training
- at a longer range of motion, which exhibited greater adaptation than training at a shorter
- range of motion, are shown. In contrast, there is a study comparing differences in movement
- kinetics with PRE and FRE in squatting training among recreational weight trainers at 83%

- 1 of 1 RM with non-specified movement velocity (7). Substantially greater muscle contraction
- 2 and power induced during PRE are reported. As mentioned above, the biomechanical
- difference between PRE and FRE has been studied by some researchers. However, there is
- 4 little information available regarding the effect of PRE and FRE on muscle energy
- 5 metabolism. Energy metabolism during squatting exercise is possibly different from that of
- 6 the lying elbow extension. This is because squatting exercise is performed in the basal plane
- 7 and continuous muscle contraction can be performed even at the final range of motion where
- 8 the moment arm reached the longest point (7). Increased product of the moment arm length
- 9 and exercise load during squatting exercise results in greater muscle stretching stimulus
- applied to the quadriceps femoris, and muscular hypoxia is promoted as a result. Therefore,
- the muscle strength and hypertrophy effects of FRE are greater than PRE. On the other hand,
- the point of action is coming out from the basal plane on lying elbow extension and it seems
- to be difficult to keep constant muscle contraction during FRE (27). The increase in muscle
- strength and hypertrophy of PRE and FRE differs according to the exercise type.
- The aim of this study was to compare the acute response to and long-term effects of
- two different exercise methods, PRE and FRE, and to determine if PRE is an effective
- 17 exercise method for increasing muscular strength and muscle size in people with blunted
- 18 hypoxic muscle stimulation resulting from resistance training. We hypothesized that PRE
- would induce greater active and passive muscular tension, and create greater accumulated

- 1 hypoxic conditions, because of continuous vascular compression, than FRE would during a
- 2 single bout of exercise. We also hypothesized that PRE would be a more effective training
- 3 method for increasing muscular strength and size among people with long-term resistance
- 4 training who receive lower hypoxic muscle stimulation, with inadequate hypertrophic
- 5 signaling to the muscle, than untrained individuals.

7

### **METHODS**

# 8 Experimental Approach

- 9 A randomized, counterbalanced two-group (PRE and FRE) pre- and post-test design was
- 10 used to investigate the effects on muscle strength and cross-sectional area (CSA). Forty-four
- trained men with more than one year of resistance training experience were divided into PRE
- group (n = 22) or FRE group (n = 22). Each group performed lying elbow extension exercise
- with different elbow joint range of motion. To compare the acute metabolic and mechanical
- responses to the PRE with FRE, area under the oxygenated hemoglobin (Oxy-Hb) curve,
- 15 blood lactate concentration, and RMS of EMG were evaluated during and after PRE or FRE.
- After assessing the acute effects, PRE or FRE were performed by each group three times a
- week for 8 weeks. To compare the long-term effects of PRE with FRE, CSA and muscular
- strength were evaluated. Furthermore, Pearson's correlations coefficients were calculated to

- 1 clarify the relationship between the percent increase in CSA and intramuscular hypoxia
- during PRE or FRE.

# 4 Subjects

- 5 Forty-four resistance-trained men (members of a resistance weight training club) were
- 6 recruited from among students at Aino University. The inclusion criteria for the subjects
- 7 consisted of at least 1 year of resistance training experience, participating in a resistance
- 8 training program at least 3 days a week, and performing triceps brachii exercises at least
- 9 once a week. Subjects who reported any musculoskeletal injuries of the upper extremities in
- 10 the year before the test were excluded. The subjects were randomly assigned to two
- experimental groups, PRE and FRE (Table 1), and were matched for CSA of the right triceps
- brachii muscle and maximum voluntary contraction (MVC) of elbow extension. All subjects
- were instructed to refrain from vigorous physical activity within 24 hours of an initial testing
- session (18). Before participating in the study, the subjects were informed about the study
- procedures and any possible risks both verbally and in writing before signing informed
- 16 consent forms. The study was approved by the ethics committees of Aino University, and all
- subjects signed an informed consent before participation.

18

# 19 < Table 1 here>

2

3

#### **Procedures**

# PRE and FRE exercise protocols

For the initial testing session, both PRE and FRE groups performed lying elbow extension 4 5 exercises using a bench and a barbell. All eight repetition maximum (RM), PRE, and FRE tests were performed to compare the acute response to PRE and FRE on intramuscular 6 oxygenation and muscle activity. Five minutes of light stretching was performed as warm-up 7 before each testing session. Each subject lay with their back on the bench and both feet on 8 9 the floor. An electrogoniometer (DTS2D goniometer; Noraxon, Arizona, USA) was used to measure the range of motion of the elbow joint during testing. The goniometer was attached 10 to the radial side of the right forearm and the lateral side of the upper right arm. During 1RM 11 and FRE testing, subjects flexed their shoulder joints to 90° with elbow joints in full 12 extension, and grasped the barbell. They flexed their elbow from this starting position to full 13 14 flexion and then returned to the starting position. During PRE testing, the subjects flexed 15 their shoulder joints to 90° with elbow joints flexed by 45°, and grasped the barbell. They 16 flexed their elbow from this starting position to 90° flexion and then returned to the starting 17 position. This eccentric/concentric contraction cycle of triceps brachii was performed at a 18 metronome-controlled tempo of one second per eccentric contraction and one second per 19 concentric contraction. The exercise intensity was determined at the 8RM for each set, but

1 not by % of 1RM, because this method is more commonly used during actual resistance 2 exercises. Both PRE and FRE consist of 8 repetitions per set and 3 sets, with a minute 3 interval between sets. After assessing the acute effects, PRE or FRE using lying elbow extension exercises were performed by each group three times a week for 8 weeks. The 4 5 intensity was increased by 2.5 kg on the first day of every week and adjusted to the 6 maximum weight which can be performed 8 times per set. Table 2 shows the mean exercise intensity used in the periods of the 1<sup>st</sup> week of training, the 4th week of training, and the 8th 7 week of training. Equivalent workloads were used in every period during PRE and FRE. 8 9 < Table 2 here> 10 11 12 **Intramuscular oxygenation measurements** 13 A near-infrared continuous-wave spectrometer (HB14-2; ASTEM Co., Ltd., Kanagawa, 14 Japan) was used to measure peripheral muscle oxygenation and the area under the 15 oxygenated hemoglobin (Oxy-Hb) curve in the right triceps brachii muscle during each 16 exercise. Figure 1 shows a typical example of the Oxy-Hb dynamics detected in the right 17 triceps brachii muscle during the exercise. The wavelength of the emitted light ranged

quantified according to the Beer-Lambert law (5). The distance between the incident point of

between 750~850 nm, and the relative concentration of Oxy-Hb in the target tissue was

18

1	the emitted light and the detector was 30 mm. The laser emitter and detector were fixed in
2	place with adhesive tape. The NIRS signals were stored in a personal computer.
3	The NIRS signals recorded during exercise do not always reflect the absolute levels of
4	intramuscular oxygenation. Therefore, the changes in the oxygenation of working skeletal
5	muscles are expressed relative to the overall changes in the monitored signal, according to
6	the arterial occlusion method (11). In the present study, the Oxy-Hb level observed at rest
7	was defined as 100%, and the minimum Oxy-Hb plateau level induced by arterial occlusion
8	was defined as 0%. A pressure cuff was placed around the proximal portion of the upper arm
9	and manually inflated to 250 mm Hg until the minimum plateau level of Oxy-Hb was
10	obtained (2). The area under the Oxy-Hb curve was used to examine the reduction in the
11	intramuscular oxygen level induced during each exercise, as described by Manfredini et al.
12	(19). The mean area under the Oxy-Hb curve was compared between PRE and FRE, and
13	before and after 8-week exercise training.
14	
15	< Figure 1 here>
16	
17	
18	
19	

### **Electromyographic signal recording measurements**

- 2 The muscle activity of the long head of the triceps brachii was recorded at a sample rate of
- 3 1000 Hz using an EMG system (Myosystem 1200, Noraxon U.S.A. Inc., AZ, U.S.A.).
- 4 Bipolar surface EMG electrodes (model: M-150Ag/AgCl, Nihon Kohden Inc., Tokyo, Japan)
- 5 were used to measure EMG signals from the long head of the triceps brachii during exercise.
- 6 Based on the Surface Electromyography for the Non-Invasive Assessment of Muscles
- 7 (SENIAM) recommendations (12), pairs of EMG electrodes were placed along the muscle
- 8 midline. The bipolar surface EMG electrodes were placed in line with the muscle fibers. The
- 9 center-to-center distance between each pair of electrodes was 2.5 cm. Prior to the placement,
- 10 each subject's skin was shaved, wiped using skin preparation gel (Nihon Kohden Inc., Tokyo,
- Japan), and cleaned with alcohol wipes. A reference electrode was placed over the
- acromioclavicular joint. All of the recorded inter-electrode resistance values were below 10
- 13 k $\Omega$ . Myoelectric signals were relayed from the bipolar electrodes to a TeleMyo device
- 14 (TeleMyo 2400T, Noraxon U.S.A. Inc., AZ, USA). The raw EMG signals were rectified,
- band-pass-filtered, and integrated using commercially available software (MyoResearch XP,
- Noraxon U.S.A. Inc., AZ, U.S.A.). EMG amplitude was measured from EMG signals: (1)
- during MVC measurements, RMS of EMG was calculated based on a 500 ms time window
- centered on the highest force value, (2) during the PRE and FRE, RMS of EMG was
- 19 calculated for each repetition based on a 500 ms time window centered on the highest value.

1 All RMS of EMG measurements were normalized to pre-exercise MVC. The mean RMS of 2 EMG was compared between PRE and FRE, and between before and after 8-week exercise 3 training (10). 4 **Blood lactate concentration measurements** 5 Blood samples were collected at rest, immediately after, and 5 minutes after the exercise. 6 7 Approximately 5 µl of blood was taken from the fingertip with a needle and immediately analyzed for blood lactate concentration using a lactate analyzer (Lactate Pro; Kyoto Primary 8 9 Science Inc., Kyoto, Japan). The mean blood lactate concentration immediately after the exercise was compared between PRE and FRE, and between before and after 8-week 10 11 exercise training (24). 12 13 Cross-sectional area of triceps brachii measurements 14 The muscle thickness (MT) of triceps brachii and the circumference of the upper arm at the 15 60 % proximal between acromion and olecranonat of the right upper arm were measured 16 using an ultrasound imaging unit (Noblus; Hitachi Medical Inc., Tokyo, Japan) and a tape 17 measure at rest. CSA was calculated as the product of MT and circumference (1). A trained

measurement site, and a 2.5 MHz ultrasound probe was placed perpendicular to the tissue

technician performed all the tests. Water-soluble transmission gel was applied to the

18

- 1 interface without depressing the skin. The images were saved to a hard drive. MT
- 2 dimensions were obtained by measuring the distance from the subcutaneous adipose
- 3 tissue-muscle interface to the muscle-bone interface. The mean CSA of triceps brachii was
- 4 compared between PRE and FRE, and before and after 8-week exercise training.
- 5 Furthermore, the relationship between the percent increase in CSA and area under the
- 6 Oxy-Hb curve during PRE and FRE before and after 8-week exercise training was
- 7 calculated.

9

# Measurements of muscle strength

- 10 The maximum isometric contraction torque (MVC) and isokinetic torque-angular velocity
- 11 relationship of elbow extensor muscles were measured using an isokinetic dynamometer
- 12 (Cybex 770-NORM; Cybex International, MA, U.S.A.). To familiarize with the test
- procedure, the subjects performed 10 trials each for isometric at an elbow joint angle of 90°,
- and the isokinetic torque at preset angular velocities of 120° and 200°/sec 5 times a week
- before the muscle strength measurements were taken. They laid down on a bed while
- grasping the lever with their right hand. The pivot point of the lever was accurately aligned
- 17 with the rotational axis of the elbow joint. The isometric torque was measured at an elbow
- joint angle of 90°, and the isokinetic torque was measured at preset angular velocities of
- 19 120° and 200°/sec. The range of angular movement of the elbow joint was limited between

- 1  $0^{\circ}$  and  $90^{\circ}$  (16). Three trials were made for isometric torque and each isokinetic angular
- 2 velocity condition, and the highest torque obtained was used for further analysis. The mean
- 3 muscle strength was compared between PRE and FRE, and between before and after 8-week
- 4 exercise training.

6

## Statistical analysis

- 7 All data are expressed as means  $\pm$  standard deviation. All statistical analyses were performed
- 8 using SPSS for Windows version 21.0 (SPSS Statistics 21.0; IBM, Tokyo, Japan).
- 9 A 2-way [training protocol (PRE: n = 22 vs. FRE: n = 22) × intervention of 8-weeks exercise
- training program (pre-training vs. post-training)] mixed-measures analysis of variance
- 11 (ANOVA), with the Greenhouse-Geisser correction and Bonferroni pairwise comparisons,
- was used to analyze the differences in mean area under the Oxy-Hb curve, blood lactate
- concentration, RMS of EMG, CSA of triceps brachii, muscle strength, and exercise intensity
- of 8RM. Pearson's correlation coefficients were calculated for the relationships between
- percent increase in CSA of triceps brachii and pre- and post-training area under the Oxy-Hb
- 16 curve during PRE and FRE. An alpha level of 0.05 was used to determine statistical
- 17 significance. Sample size was estimated using G\*power. Effects sizes were calculated using
- means and SDs according to the methods of Cohen (6). We used an effect size of 0.40. Using

1	a power of 0.93 and alpha error of 0.05, a sample size of 22 participants per group was
2	suggested.
3	
4	RESULTS
5	Intramuscular oxygenation measurements
6	Figure 1 shows typical examples of changes in relative oxygenation levels in the right tricepa
7	brachii muscle before and during PRE and FRE. In both types of exercise, Oxy-Hb levels
8	decreased immediately as the exercise repetitions started, and then recovered quickly,
9	followed by hypercompensation after the completion of the exercise repetitions. The mean
10	area under the Oxy-Hb curve was significantly higher during PRE than during FRE for both
11	before and after 8-week exercise training ( $p < 0.05$ ). The percent decrease in area under the
12	Oxy-Hb curve was -21.7 $\pm$ 12.7% for PRE and -9.6 $\pm$ 12.5% for FRE (Figure 2). The area
13	under the Oxy-Hb curve during PRE was significantly lower after 8-week exercise training
14	than before 8-week exercise training ( $p < 0.05$ ).
15	
16	< Figure 2 here>
17	
18	
19	

### 1 Electromyographic signal recording measurements

- 2 Figure 3 shows the %MVC-RMS of EMG recorded in the triceps brachii during exercise.
- 3 Both before and after 8-week exercise training %MVC-RMS of EMG were significantly
- 4 higher during PRE than during FRE (p < 0.05). The %MVC-RMS of EMG after 8-week
- 5 exercise training was significantly higher than the value after 8-week exercise training (p <
- 6 0.05). There was no interaction between type of exercise and training period.
- 8 < Figure 3 here>

7

9

10 Blood lactate concentration measurements

- Blood lactate concentration was measured at rest (before 8-week exercise training: PRE 1.6
- $\pm 0.2$  mM, FRE  $1.5 \pm 0.2$  mM, after 8-week exercise: PRE  $1.4 \pm 0.2$  mM, FRE  $1.5 \pm 0.2$
- mM), immediately after exercise (before 8-week exercise training: PRE  $9.9 \pm 2.1$  mM, FRE
- 14 7.3  $\pm$  1.0 mM, after 8-week exercise: PRE 8.9  $\pm$  1.4 mM, FRE 7.0  $\pm$  1.08 mM), and 5
- minutes after exercise (before 8-week exercise training: PRE  $9.8 \pm 1.9$  mM, FRE  $7.1 \pm 1.0$
- 1.0 mM, after 8-week exercise: PRE  $9.0 \pm 1.5$  mM, FRE  $7.2 \pm 1.1$  mM). Both PRE and FRE
- 17 produced significant increases in the blood lactate concentration after exercise compared to
- 18 the resting concentration. No significant differences were observed between the
- immediately-after-exercise value and the 5-minutes-after-exercise value. Figure 4 shows the

- 1 blood lactate concentration immediately after PRE and FRE before and after 8-week exercise
- 2 training. Both before and after 8-week exercise training, the mean blood lactate
- 3 concentration after PRE was significantly higher than after FRE (p < 0.05). There was no
- 4 significant difference between before and after exercise training. Mean blood concentration
- 5 before 8-week exercise training was significantly higher than the value after 8-week exercise
- 6 training (p < 0.05). There was no interaction between type of exercise and training period.
- 7 < Figure 4 here>

### 9 Changes in muscle CSA

- 10 Figure 5 shows CSA before and after the 8-week PRE and FRE training programs. Both
- PRE and FRE significantly increased the CSA of triceps brachii compared with before the
- 8-week exercise training programs (p < 0.05). The percent increase in the CSA of triceps
- brachii was  $48.7 \pm 14.5\%$  after the 8-week PRE program and  $28.2 \pm 10.9\%$  after the 8-week
- 14 FRE program. CSA after 8-week exercise training was significantly larger after the 8-week
- PRE program than the 8-week FRE program (p < 0.05). Furthermore, in the PRE program
- 16 there were significant correlations between the percent increase in CSA and before (r = 0.59,
- 17 p < 0.01) and after 8-week exercise training (r = 0.70, p < 0.01) area under the Oxy-Hb
- curves. However, in the FRE program there were no significant correlations between the

- percent increase in CSA and either before ((r = 0.33, p = 0.13)) or after ((r = 0.18, p = 0.41))
- 2 8-week exercise training area under the Oxy-Hb curve (Figure 6).
- 3
- 4 < Figure 5 here>
- 5 <Figure 6 here>

### 7 Changes in muscular strength

- 8 The force-velocity relations obtained before and after the 8-week exercise training programs
- 9 are shown in Table 3. Both PRE and FRE 8-week exercise training programs produced
- significant increases in the isometric strength and isokinetic strength at 120°/sec compared to
- before the training programs, but there was no significant change in isokinetic strength at
- 12 200°/sec. After the 8-week exercise training programs, isometric strength was significantly
- greater in PRE subjects than in FRE subjects. There was no significant difference in the
- isokinetic strength at 120°/sec and at 200°/sec between PRE and FRE. The maximal elbow
- extension isometric torque per unit CSA of triceps brachii did not change significantly after
- 16 the 8-week PRE and FRE training programs: from  $0.4 \pm 0.1$  to  $0.5 \pm 0.1$  in PRE subjects, and
- 17 from  $0.5 \pm 0.1$  to  $0.5 \pm 0.1$  in FRE subjects.

18

19 < Table 3 here>

2

### **DISCUSSION**

3 In the present study, following a comparison of acute effects, changes in muscle strength and 4 size were compared between two groups, PRE and FRE, after completing two 8-week 5 resistance-exercise training programs. The acute effects on area under the Oxy-Hb curve, blood lactate concentration, and RMS of EMG recorded in the triceps brachii were higher 6 during and after PRE than during and after FRE. PRE was characterized physiologically by 7 higher area under the Oxy-Hb curve, greater motor unit activation, and higher blood lactate 8 9 concentration (Figures 2-4). During PRE, the restriction of muscular blood flow, because of higher muscular tension and constant muscle contraction, might be one reason for the higher 10 area under the Oxy-Hb curve. Higher muscular tension and constant muscle contraction led 11 to mechanical capillary compression, resulting in restricted blood flow to muscles and the 12 13 induction of acute intramuscular hypoxia, and enhanced a glycolytic pathway under hypoxic 14 conditions. This suggested that PRE induced higher intramuscular hypoxia than FRE. 15 Long-term effects produced after both 8-week PRE and FRE programs were 16 significant increases in muscle size (Figure 5) and muscular strength without isokinetic 17 strength at 200°/sec (Table 3). There were greater increases in isometric strength and muscle size after PRE than after FRE. Because the maximal elbow extension isometric torque per 18 19 unit CSA of triceps brachii did not change significantly after PRE and FRE, muscle

1 hypertrophy may be the primary factor influencing increases in isometric strength after the 2 8-week exercise training programs. Furthermore, data showed that intramuscular hypoxia 3 might be the primary factor influencing greater muscle hypertrophy because there were higher correlations between the percent increase in CSA and area under the Oxy-Hb curves 4 5 after 8-week exercise training. A previous study reports that continuous resistance training results in blunted hypoxic stimulation because of local increasing in artery diameter and 6 7 blood flow (22). Our study showed the same results as previous studies. As shown in Figure 8 3, the area under the Oxy-Hb curve during both PRE and FRE decreased after the 8-week 9 exercise training period. Even after 8-week exercise training, under the Oxy-Hb curve during PRE was higher than that during FRE. The Correlation coefficient between area under the 10 Oxy-Hb curve and percent increase in CRA of triceps brachii muscle after 8-week exercise 11 suggested that PRE was more likely to induce intramuscular hypoxia than FRE and was an 12 13 effective exercise protocol for muscle hypertrophy (Figure 6). An effect of mechanical stress, 14 other than hypoxia, as a trigger of muscle hypertrophy might be considered as an explanation 15 for the lack of a relationship between the percent increase in CSA in the FRE program and 16 the area under the Oxy-Hb curve (9). Numerous studies have described the effects of a single 17 bout of resistance exercise under acute hypoxia on muscle strength and hypertrophy in 18 humans. For example, it is reported that performing resistance training under intracellular or 19 environmental hypoxia elicited intramuscular conditions prone to enhancing protein

- synthesis (24), the levels of growth hormone, epinephrine, and lactate (17), and mammalian
- 2 targets of rapamycin (mTOR) signaling (8). In addition, a study using rats reports that
- 3 chronic venous blood flow restriction for 14 days promoted leg muscle hypertrophy due to
- 4 increasing levels of heat-shock-protein-72 and decreasing levels of myostatin protein (15).
- 5 Taken together, these observations demonstrate that performing PRE, under intramuscular
- 6 hypoxia, significantly enhances hypertrophic signaling and muscular size compared to FRE.
- 7 The maintenance of constant muscular tension during exercise may result in hypoxic
- 8 conditions, as reflected by an increasing area under the Oxy-Hb curve, and of energetic
- 9 stress to the muscle, as reflected by the level of blood lactate concentration. Tanimoto et al.
- 10 (24) compared a low-intensity (50% of 1RM) exercise with slow speed knee extensions,
- three seconds for each concentric and eccentric contraction (LS), with a high-intensity (80%
- of 1RM) exercise with normal speed knee extensions, one second for each concentric and
- eccentric contraction (HN). Acute effects of knee extension torque, muscular activity on
- 14 EMG, intramuscular oxygenation, and blood lactate concentration are measured. They report
- 15 that constant muscular tension was maintained during LS, but is difficult to maintain during
- 16 HN. Therefore, intramuscular hypoxia is induced more during LS than during HN. In this
- 17 current study, it was assumed that PRE used only the middle range of motion, which
- activates active and passive muscular tension, and therefore, muscular contraction could be

- 1 maintain during PRE exercises in spite of being performed at almost the same intensity as
- 2 HN (21).
- 3 After 8-week PRE and FRE exercise training programs, isometric strength and
- 4 isokinetic strength at 120°/sec increased significantly, but isokinetic strength at 200°/sec did
- 5 not (Table 3). The reason for the lack of significant increase in isokinetic strength at
- 6 200°/sec can be explained by the results of a previous study that shows muscular strength
- 7 gains are specific to the movement speed used in the training regimens (14). The movement
- 8 speeds were almost 45°/sec in PRE and 120°/sec in FRE, and these speeds were too slow to
- 9 increase isokinetic strength at 200°/sec. The significant difference in isometric strength,
- between PRE and FRE post-training, could be explained by the differences in CSA. In
- regard to the isokinetic strength at 120°/sec, PRE was superior to FRE in muscle size, but
- motor unit activation might be inferior in PRE compared to FRE, due to the specificity of the
- contraction speed during training. Consequently, there was no significant difference in the
- 14 isokinetic strength at 120°/sec between the two methods.
- Previous studies have compared the effects of PRE and FRE using squatting exercise
- in muscle strength and hypertrophy. The moment arm from knee joint to center of gravity
- 17 line during FRE becomes longer in the final range of motion exercise than PRE. Therefore, it
- is reported that FRE is expected to have greater effects of muscle strength and hypertrophy
- than PRE. We used lying elbow extension-flexion exercises with flexed shoulder joints at

90° to compare PRE with FRE on the effects of triceps brachii muscle strength and 1 2 hypertrophy. On this exercise, the point of action is coming out from the basal plane. The 3 length of the moment arm during FRE is longer than PRE. Therefore, the muscle contraction balanced with load might not be sufficiently obtained during FRE. This was confirmed by 4 5 the result that %MVC-RMS of EMG during FRE was lower than PRE. On the other hand, as the PRE of this study used only the middle range of motion, higher %MVC-RMS of EMG 6 was obtained during PRE than during FRE. Furthermore, as the motion speed of PRE was 7 slower with an angular velocity 45° than FRE, sustained muscle contraction might be 8 9 obtained during PRE. This higher muscular tension and sustained muscle contraction throughout the exercise caused intramuscular hypoxia on triceps brachii muscle. As a result, 10 the effects of isometric muscle contraction power and muscle hypertrophy on triceps brachii 11 muscle was higher in PRE than FRE. 12 It was confirmed that PRE is a more effective exercise method to increase isometric 13 14

muscle strength and hypertrophy of the triceps brachii muscle on lying elbow extension. In addition, it was suggested that a muscle strength increase in speed corresponding to the exercise speed used for training can be expected as a training effect. Furthermore, this study revealed that the degree of intramuscular hypoxia during exercise is related to muscle hypertrophy.

19

15

16

17

### PRACTICAL APPLICATIONS

1

- 2 An 8RM load exercise at the middle range of motion was performed in PRE, and it resulted
- 3 in acute physiological effects similar to isometric contraction, such as intramuscular hypoxia
- 4 and higher blood lactate concentration. Furthermore, PRE produced greater increases than
- 5 FRE in triceps brachii CSA after the 8-week exercise-training programs. Therefore, PRE
- 6 might be a valid training protocol, especially, for well-trained individuals with blunted
- 7 hypoxic muscle stimulation due to long-term resistance training. As it is assumed that
- 8 weight-bearing and non-weight-bearing muscles react differently to a particular exercise (28),
- 9 the results of this study might be limited to upper extremity muscles.

### 11 **REFERENCES**

- 12 1. Akagi R, Kanehisa H, Kawakami Y, and Fukunaga T. Establishing a new index of muscle
- 13 cross-sectional area and its relationship with isometric muscle strength. J Strength Cond Res
- 14 22: 82-87, 2008.
- 15 2. Bae SY, Hamaoka T, Katsumura T, Shiga T, Ohno H, and Haga S. Comparison of muscle
- oxygen consumption measured by near infrared continuous wave spectroscopy during
- supramaximal and intermittent pedalling exercise. Int J Sports Med 21: 168-174, 2000.

- 1 3. Baroni BM, Pompermayer MG, Cini A, peruzzolo AS, Radaelli R, Brusco CM, and Pinto
- 2 RS. Full range of motion induces greater muscle damage than partial range of motion in
- 3 elbow flexion exercise with free weights. J Strength Cond Res: in press, 2016.
- 4. Bober T, Kulig K, Burnfield JM, and Pietraszewski B. Predictive torque equations for
- 5 joints of the extremities. Acta of Bioengineering and Biomechanics 4: 49-60, 2002.
- 6 5. Chance B, Dait MT, Zhang C, Hamaoka T, and Hagerman F. Recovery from
- 7 exercise-induced desaturation in the quadriceps muscles of elite competitive rowers. Am J
- 8 Physiol Cell Physiol 262: 766-775, 1992.
- 9 6. Cohen J. Stastical power analysis for the behavioral science. Hillsdale, NJ: Lawrence
- 10 Erlbaum Associates, 1988.
- 7. Drinkwater EJ, Moore NR, and Bird SP. Effects of changing from full range of motion to
- partial range of motion on squat kinetics. J Strength Cond Res. 26: 890-896, 2012.
- 8. Fujita S, Abe T, Drummond MJ, Cadenas JG, Drever HC, Sato Y, Volpi E, and
- 14 Rasmussen BB. Blood flow restriction during low-intensity resistance exercise increases
- 15 S6K1 phosphorylation and muscle protein synthesis. J App Physiol 103: 903-910, 2007.
- 9. Gonzalez AM, Hoffman JR, Townsend JR, Jaitner AR, Boone CH, Beyer KS, Baker KM,
- Wells AJ, Mangine GT, Robinson EH 4<sup>th</sup>, Church DO, Oliveira LP, Willoughby DS, Fukuda
- 18 DH, and Stout JR. Intramuscular anabolic signaling and endocrine response following high

- 1 volume and high intensity resistance exercise protocols in trained men. Physiol Rep 3:
- e12466, 2015.
- 3 10. Goto M, Nirengi S, Kurosawa Y, Nagano A, and Hamaoka T. Effects of the drop-set and
- 4 reverse drop-set methods on the muscle activity and intramuscular oxygenation of the triceps
- 5 brachii among trained and untrained individuals. J Sports Sci Med 15, 562-568, 2016.
- 6 11. Hamaoka T, McCully KK, Quaresima V, Yamamoto K, and Chance B. Near-infrared
- 7 spectroscopy/imaging for monitoring muscle oxygenation and oxidative metabolism in
- 8 healthy and diseased humans. J Biomed Opt 12: 062105, 2001.
- 9 12. Hermens, HJ, Freriks, B, Disselhorst-Klug C, and Rau, G. Development of
- 10 recommendations for SEMG sensors and sensor placement procedures. J Electromyogr
- 11 Kinesiol 10: 361-374, 2000.
- 12 13. Hoffman JR, IM Joohee, Rundell KW, Kang J, Nioka S, Speiring BA, Kime R, and
- 13 Chance B. Effect of muscle oxygenation during resistance exercise on anabolic hormone
- 14 response. Med Sci Sports Exerc 35: 1929-1934, 2003.
- 15 14. Kaneko M, Fuchimoto T, Toji H, and Suei K. Training effect of different loads on the
- 16 force-velocity relationship and mechanical power output in human muscle. Scand J Sports
- 17 Sci 5: 50-55, 1983.
- 18 15. Kawada S and Ishii N. Skeletal muscle hypertrophy after chronic restriction of venous
- 19 blood flow in rats. Med Sci Sports Exerc 37: 1144-1150, 2005.

- 1 16. Knapic JJ, Wright JE, Mawdsley RH, and Braun JM. Isokinetic, isometric and isotonic
- 2 strength relationships. Srch Phys Med Rehabil 64: 77-80, 1983.
- 3 17. Kon M, Ikeda T, Homma T, and Suzuki Y. Effects of low-intensity resistance exercise
- 4 under acute systemic hypoxia on hormonal responses. J Strength Cond Res 26: 611-617,
- 5 2012.
- 6 18. Maehlum S, Grandmontagne M, Newsholme EA, and Sejersted OM. Magnitude and
- 7 duration of excess postexercise oxygen consumption in healthy young subjects. Metabolism
- 8 35: 425-429, 1986.
- 9 19. Manfredini F, Lambeti N, Zambon C, Basaqlia N, Mascoli F, and Zamboni P. Reliability
- of the vascular claudication reporting in diabetic patients with peripheral arterial disease: a
- study with near-infrared spectroscopy. Angiology 66: 365-374, 2015.
- 12 20. McMahon GE, Morse CL, Burden A, Winwood K, and Onambele GL.
- 13 Impact of range of motion during ecologically valid resistance training protocols on muscle
- size, subcutaneous fat, and strength. J Strength Cond Res. 28: 245-255, 2014.
- 15 21. Moritani T, Muramatsu S, and Muro M. Activity of motor units during concentric and
- eccentric contractions. Am J Phys Med. 66: 338-350, 1987.
- 17 22. Okamoto T, Masuhara M, and Ikuta K. Upper but not lower limb resistance training
- increases arterial stiffness in humans. Eur J Appl Physiol 107: 127-134, 2009.

1 23. Peterson MD, Rhea MR, and Alvar BA. Applications of the dose-response for muscular 2 strength development: a review of meta-analytic efficacy and reliability for 3 designing training prescription. J Strength Cond Res. 19: 950-958, 2005. 4 24. Tanimoto M and Ishii N. Effects of low-intensity resistance with slow movement and tonic force generation on muscular function in young men. J Appl Physiol 100: 1150-1157, 5 6 2006. 7 25. Toji H and Kaneko M. Effect of multiple-load training on the force-velocity relationship. 8 J Strength Cond Res 18: 792-795, 2004. 9 26. T van Wessel, A de Hannm W J van der Laarse, and R T Jaspers. The muscle fiber type-fiber size paradox: hypertrophy or oxidative metabolism?. Eur J Appl Physiol 110: 10 11 665-694, 2010. 12 27. Zhang Z, Wang B, Gong H, Xu G, Nioka S, and Chance B. Comparisons of muscle 13 oxygenation changes between arm and leg muscles during incremental rowing exercise with 14 near-infrared spectroscopy. J Biomed Opt 15: 017001-7, 2010. 15 16 17 18 19 20 21

1 Tables

**Table 1.** Physical characteristics of subjects.

5		$\mathbf{PRE}\;(n=22)$		FRE $(n = 22)$
6		Before 8-week ex.	After 8-week ex.	Before 8-weekvex. After 8-week ex.
7	Age (yr)	21.6 ± 1.3	_	20.6 ± 0.9
8	Height (cm)	$170.9 \pm 3.8$	_	169.2 ± 4.1 —
9	Lean body mass (kg)	$64.7 \pm 5.3$	$65.9 \pm 4.8$	$63.3 \pm 5.7$ $63.9 \pm 6.2$

10 Means  $\pm$  SD (n = 22 for both group) were shown.

**Table 2.** Changes in exercise intensity of 8RM during the 8-week exercise training.

2	_	
_	.,	
	_	

3		$\mathbf{PRE}\;(n=22)$	FRE $(n = 22)$
4	Intensity at 1st week (kg)	38.6 ± 7.9	39.3 ± 8.5
5	Intensity at 4 <sup>th</sup> week (kg)	$42.5 \pm 8.3$	41.4 ± 7.1
6	Intensity at 8 <sup>th</sup> week (kg)	$45.2 \pm 8.7$	42.6 ± 7.8

<sup>7</sup> Means  $\pm$  SD (n = 22 for both group) are shown. There was no significant difference between

8 PRE and FRE in the intensity of 8RM used for lying elbow extension.

**Table 3.** Effects of exercise on force-velocity reactions.

	•	1	þ	
ı		•	_	
ľ	7		_	

3	Isometric torque (Nm)	Isokinetic torque	Isokinetic torque
4		at 120 °/sec (Nm)	at 200 °/sec (Nm)
5	Before 8-wk ex. After 8-wk ex.	Before 8-wk ex. After 8-wk ex.	Before 8-wk ex. After 8-wk ex.
6	PRE $59.8 \pm 9.5$ $83.6 \pm 10.2 \dagger \ddagger$	$49.2 \pm 8.7$ $63.8 \pm 11.4 \dagger$	$45.6 \pm 10.5 \qquad 50.1 \pm 10.3$
7	FRE $61.3 \pm 11.4$ $76.2 \pm 12.6$ †	$49.6 \pm 9.7$ $64.7 \pm 12.3 \dagger$	$46.7 \pm 12.1 \qquad 51.9 \pm 13.5$

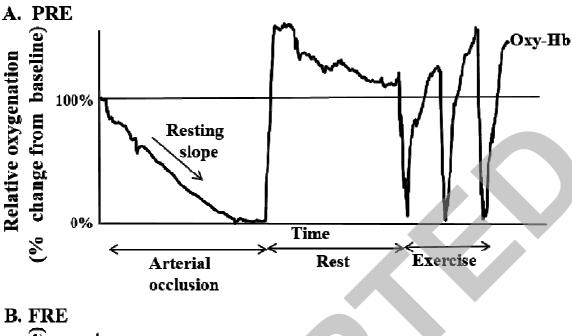
<sup>8</sup> Means  $\pm$  SD (n = 22 for both group) are shown.

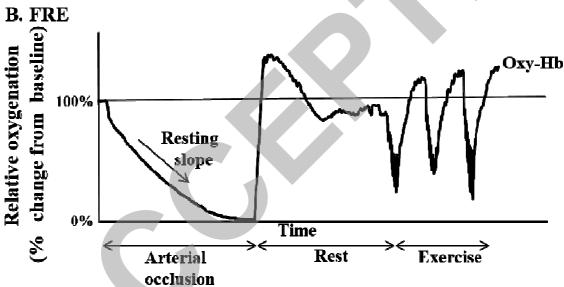
<sup>10 ‡</sup> p < 0.05, PRE vs. FRE.



<sup>9 †</sup> p < 0.05, before 8-week exercise training vs. after 8-week exercise training.

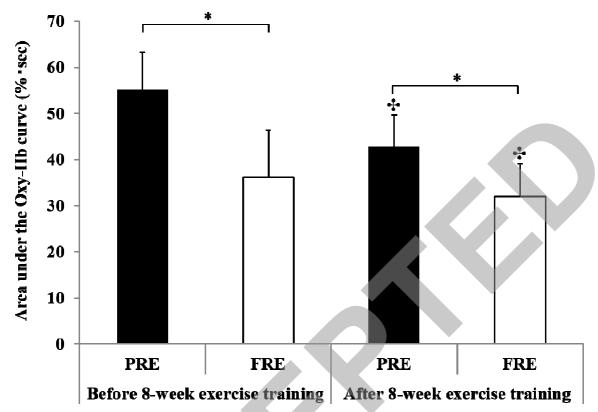
### 1 FIGURE OF LEGENDS





**Figure 1.** Typical examples showing changes in intramuscular oxidative metabolism in the right triceps brachii muscle before and during PRE (A) and FRE (B). The resting and minimum levels of Oxy-Hb were defined as 100% (baseline) and 0%, respectively, according to the arterial occlusion method.





4 Figure 2. Mean values of area under the Oxy-Hb curve during PRE and FRE

- 5 before and after 8-week exercise training.
- 6 Means  $\pm$  SD (n = 22 for both group) are shown. p < 0.05, significant differences between
- 7 PRE and FRE values (\*) and between before and after 8-week exercise training values (\*).

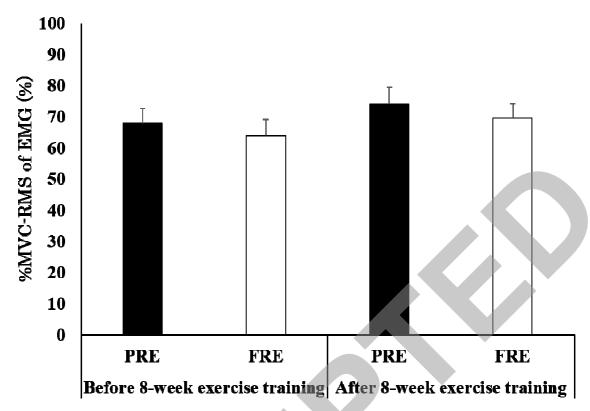
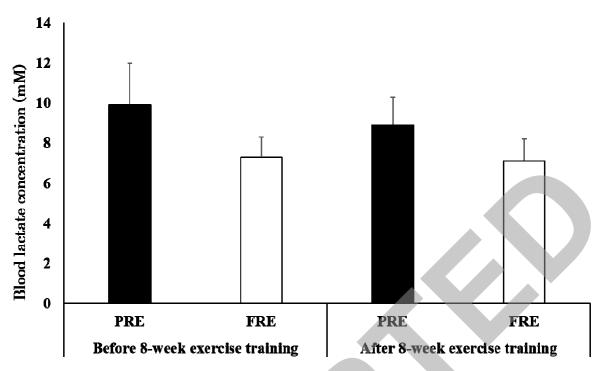


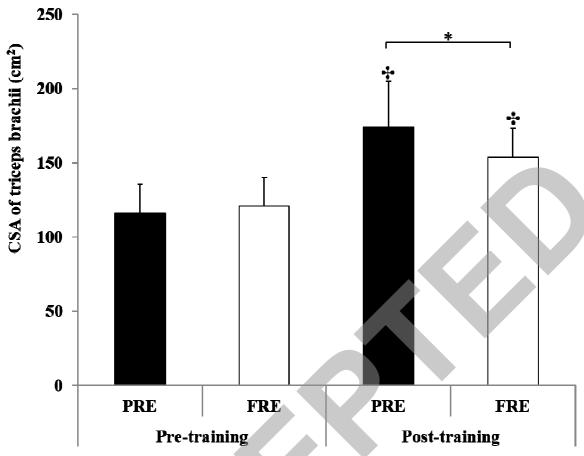
Figure 3. Mean values of %MVC-root-mean-square (RMS) of EMG before and after

- 3 8-week PRE and FRE programs.
- 4 Means  $\pm$  SD (n = 22 for both group) are shown.
- 5 No interaction between type of exercise and 8-week exercise training.
- As a main effect, FRE values  $\langle PRE \rangle$  values  $\langle PRE \rangle$



- 2 Figure 4. Mean values of blood lactate concentrations immediately after PRE and FRE
- 3 before and after 8-week exercise training.

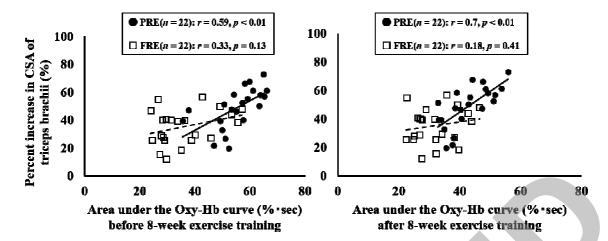
- 4 Means  $\pm$  SD (n = 22 for both group) are shown.
- 5 No interaction between type of exercise and 8-week exercise training.
- 6 As a main effect, FRE values  $\langle PRE \rangle$  values  $\langle PRE \rangle$  and before 8-week exercise training
- 7 values < after 8-week exercise training values (p < 0.05).



**Figure 5.** Cross-sectional area (CSA) of right triceps brachii muscle before and after 8-week PRE and FRE programs.

Means  $\pm$  SD (n = 22 for both group) are shown. p < 0.05, significant differences between PRE and FRE values after 8-week exercise training (\*) and both PRE and FRE values

between before and after 8-week exercise training ( ...).



**Figure 6.** The relationship between area under the Oxy-Hb curve and percent increase in cross-sectional area (CSA) of triceps brachii muscle before (left) and after (right) 8-week PRE and FRE programs.