

**THE EFFECTS OF HIGHER- AND LOWER-LOAD RESISTANCE EXERCISE
TRAINING ON LEG AND ARM SKELETAL MUSCLE MASS IN HEALTHY YOUNG
ADULT FEMALES: A RANDOMIZED EQUIVALENCE TRIAL**

by

MATTHEW DAVID FLISS

H.B.Sc., McMaster University, 2019

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF
THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF SCIENCE

in

THE FACULTY OF GRADUATE AND POSTDOCTORAL STUDIES

(Kinesiology)

THE UNIVERSITY OF BRITISH COLUMBIA

(Vancouver)

December 2021

© Matthew David Fliss, 2021

The following individuals certify that they have read, and recommend to the Faculty of Graduate and Postdoctoral Studies for acceptance, a thesis entitled:

The effects of higher- and lower-load resistance exercise training on leg and arm skeletal muscle mass in healthy young adult females

submitted by Matthew D. Fliss in partial fulfillment of the requirements for

the degree of Master of Science

in Kinesiology

Examining Committee:

Dr. Cameron Mitchell, Kinesiology, UBC

Supervisor

Dr. Kristin Campbell, Physical Therapy, UBC

Supervisory Committee Member

Dr. Bill Sheel, Kinesiology, UBC

Supervisory Committee Member

Abstract

Resistance exercise training (RET) is potent stimulus to induce muscle growth. Heavier loads are traditionally more effective compared to lighter loads for inducing muscle growth, but recent research has demonstrated that lighter load (LL) RET can lead to similar muscle hypertrophy as higher load (HL) RET when training to volitional fatigue. While these results have been consistently shown in males, there is limited research on this topic using female participants. The aim of this study was to compare the muscle hypertrophic response to HL and LL RET in the upper and lower body of young adult females. It was hypothesized that there would be an equivalent increase between the HL and LL RET in both the upper and lower body. A randomized repeated measures within-participant design was utilized where each participant had one arm and leg assigned to train with HL and the other limbs assigned to train with LL. Participants trained thrice weekly for 10-weeks, performing unilateral knee extension and unilateral dumbbell bicep preacher curls. Biceps brachii thickness increased following both LL and HL RET ($\Delta_{LL} = 0.3 \pm 0.4$ cm, $\Delta_{HL} = 0.2 \pm 0.4$ cm, Interaction $P = 0.12$), but upper arm lean mass only increased following LL RET ($\Delta_{LL} = 0.1 \pm 0.2$ kg, $\Delta_{HL} = 0.04 \pm 0.2$ kg, Interaction $P = 0.02$). Neither HL nor LL RET induced an increase in any measure of lower body muscle size. LL RET induced a greater training volume compared to HL RET in the arms due to similar absolute loads used during training. In the lower body, training volume must be considered as neither loading condition reached the necessary total training volume required to induce measurable muscle growth.

Lay Summary

Resistance exercise training (RET) is a common method for increasing skeletal muscle size. Recent research has found that if individuals train to the point at which they cannot perform another repetition, similar muscle growth will be observed regardless of the load used. While this result is consistently observed in males, studies using female participants have varied findings. Thus, it is unclear as to the effect of both higher-load (HL) and lower-load (LL) RET on muscle growth in females. The purpose of this project was to contribute to the muscle hypertrophy literature by assessing how performing RET with HL (6-12 repetitions) and LL (20-30 repetitions) impacts muscle growth in females. In the upper body, LL RET induced greater muscle growth compared to HL RET, while neither loading condition was able to elicit growth in the lower body.

Preface

The following thesis project was designed and developed by Matthew D. Fliss with the assistance of Dr. Cameron Mitchell and the other students in the Exercise, Nutrition, and Muscle Metabolism Lab. Scheduling, participant recruitment, and participant testing was conducted by Matthew D. Fliss. Participant training was conducted by Matthew D. Fliss, Jordan Stevenson, Sobhan Mardan-Dezfouli, and Donna Li. Analysis of results was conducted by Matthew D. Fliss with assistance from Dr. Cameron Mitchell. All aspects of the current thesis project were approved by The University of British Columbia's Research Ethics Board (H20-01570) and prospectively with ClinicalTrial.gov (NCT04547972) on September 4th, 2020.

Table of Contents

Abstract	iii
Lay Summary	iv
Preface	v
Table of Contents	vi
List of Tables	x
List of Figures.....	xi
List of Abbreviation	xiii
Acknowledgements.....	xv
Chapter 1: INTRODUCTION.....	1
1.1 Functions of Skeletal Muscle	1
1.2 Maintenance of Skeletal Muscle Mass	1
1.3 Introduction to Resistance Exercise Training	2
1.3.1 The Strength-Endurance Continuum	3
1.3.2 RET Variables	4
1.3.2.1 Training Volume and Frequency & Skeletal Muscle Hypertrophy	5
1.3.2.2 Training Load, Effort & Skeletal Muscle Hypertrophy	9
1.3.3 Measurement of Skeletal Muscle Hypertrophy	10
1.3.4 Training Load and Local Muscle Endurance	12
1.3.5 Training Load and Maximal Strength.....	15
1.3.6 RET and Muscle Architecture	16
1.4 Impact of Biological Sex on RET Adaptations	17
1.4.1 Impact of Biological Sex on Myofiber Characteristics.....	17

1.4.2	Impact of Biological Sex on RET Induced Skeletal Muscle Hypertrophy	20
1.4.3	Impact of Biological Sex on Local Muscle Endurance	22
1.4.4	Impact of Biological Sex on Maximal Strength	25
1.5	Impact of the Menstrual Cycle on Muscular Strength and Endurance	26
1.6	The Unilateral Training Model.....	28
1.7	Equivalence Hypothesis Testing	31
1.8	PURPOSE	33
1.9	HYPOTHESES.....	34
Chapter 2: Body of Thesis.....		35
2.1	METHODS	35
2.1.1	Participants	35
2.1.2	Experimental Design & Resistance Training Program.....	36
2.1.3	Randomization.....	39
2.1.4	Body Composition	40
2.1.5	Strength Testing.....	42
2.1.6	Local Muscle Endurance Testing	43
2.1.7	Muscle Architecture.....	44
2.1.8	Training Volume.....	48
2.1.9	Protein Supplementation	48
2.1.10	Typical Measurement Error Calculations	49
2.1.11	Statistical Analyses	49
2.2	RESULTS	51
2.2.1	Body Composition	51

2.2.2	Strength	53
2.2.3	Relative Muscle Endurance	54
2.2.3.1	KE RME	54
2.2.3.2	DC RME	56
2.2.4	Absolute Muscle Endurance	58
2.2.4.1	KE AME	58
2.2.4.2	DC AME	60
2.2.5	Muscle Architecture	62
2.2.6	Resistance Training Volume	64
2.2.7	Menstrual Cycle Tracking	65
Chapter 3: Discussion & Conclusion		68
3.1	DISCUSSION	68
3.1.1	Main Findings	68
3.1.1.1	Strength	68
3.1.1.2	Hypertrophy and Muscle Architecture	70
3.1.1.3	Local Muscle Endurance	77
3.2	LIMITATIONS	81
3.3	FUTURE DIRECTIONS	83
3.4	CONCLUSION	86
Bibliography		87
Appendices		99
	Appendix A - Consort Flow Diagram	99
	Appendix B - CERT Checklist (187)	100

Appendix C - CONSORT Checklist for Non-Inferiority and Equivalence Trials (188)	101
Appendix D - Familiarization Session Data Recording Sheet.....	103
Appendix E - Sample Testing Session Data Recoding Sheets	104
Appendix F - Sample Training Session Data Recording Sheet	106
Appendix G - Randomization Combinations	107
Appendix H - Graphical Example of Limb Allocation	108
Appendix I - Testing Day One Schematic	109
Appendix J - Testing Day Two Schematic	110
Appendix K - Equivalence Test Outputs.....	111
Appendix L - Participant Information and Informed Consent Sheet	112

List of Tables

Table 1. Participant Baseline Characteristics	36
Table 2. Changes in limb FBFM following higher- and lower-load resistance exercise training	66
Table 3. Changes in strength following higher- and lower-load resistance exercise training	66
Table 4. Changes in knee extension relative muscle endurance following higher- and lower-load resistance exercise training	66
Table 5. Changes in dumbbell preacher curl relative muscle endurance following higher- and lower-load resistance exercise training	66
Table 6. Changes in knee extension absolute muscle endurance following higher- and lower-load resistance exercise training	67
Table 7. Changes in dumbbell preacher curl absolute muscle endurance following higher- and lower-load resistance exercise training	67
Table 8. Changes in muscle architecture following higher- and lower-load resistance exercise training	67
Table 9. Comparison of leg total training volume between studies	72

List of Figures

Figure 1. RET Variables	5
Figure 2. Additional Volume, Hypertrophy, and Benefit Relationship	8
Figure 3. Sex Differences in BB Myofiber Characteristics.....	19
Figure 4. Sex Differences in VL Myofiber Characteristics.....	19
Figure 5. Study Timeline	39
Figure 6. DXA Thigh and Upper Arm Segmentation	41
Figure 7. VL CSA Example Image.....	46
Figure 8. VL Pennation Angle and Fascicle Length Example Image.....	47
Figure 9. VMO Thickness Example Image	47
Figure 10. BB Thickness Example Image	48
Figure 11. Limb FBFM Changes	52
Figure 12. Waterfall Plots of Limb FBFM Changes.....	52
Figure 13. Strength Changes	53
Figure 14. KE RME Changes	55
Figure 15. DC RME Changes	57
Figure 16. Load Specific Improvements in KE AME	58
Figure 17. KE AME Changes.....	59
Figure 18. Load Specific Improvements in DC AME	60
Figure 19. DC AME Changes.....	61
Figure 20. Vastus Lateralis Muscle Size and Architecture Changes	63
Figure 21. Vastus Medialis Oblique and Biceps Brachii Thickness Changes	63
Figure 22. Training Volume	64

Figure 23. Absolute Training Loads Across the Training Period.....64

Figure 24. Volume, Hypertrophy, and Benefit with Limb Change Estimations71

Figure 25. Male, Female, and Scaled Female Leg FBFM Changes75

List of Abbreviation

ACSM	American College of Sports Medicine
AME	Absolute Muscle Endurance
ANOVA	Analysis of Variance
ASIS	Anterior Superior Iliac Spine
ATP	Adenosine Triphosphate
BB	Biceps Brachii
BFFM	Bone- and Fat-Free Mass
CSA	Cross Sectional Area
CT	Computed Tomography
DC	Dumbbell Preacher Curl(s)
DXA	Dual-Energy X-ray Absorptiometry
EMG	Electromyography
FBFM	Fat and Bone-Free Mass
FL	Fascicle Length
FM	Fat Mass
HL	Higher Load
KE	Knee Extension(s)
LL	Lower Load
LME	Local Muscle Endurance
MRI	Magnetic Resonance Imaging
MU	Motor Unit(s)

MVC	Maximum Voluntary Contraction
NSCA	National Strength and Conditioning Association
PA	Pennation Angle
RET	Resistance Exercise Training
RM	Repetition Maximum
RME	Relative Muscle Endurance
ROI	Ranges of Interest
TEM	Typical Error of Measurement
US	Ultrasonography
VL	Vastus Lateralis
VMO	Vastus Medialis Oblique

Acknowledgements

I would like to thank and acknowledge my thesis supervisory committee for their support during this project. Thank you, Jordan, Sobhan, and Donna (a.k.a. the Mitchell Army) for your assistance in carrying out this thesis project and thank you Cam for your invaluable patience and guidance.

To Sean & Rob

Thanks for getting me here

To Mom and Dad

Thank you for everything

Chapter 1: INTRODUCTION

1.1 Functions of Skeletal Muscle

Skeletal muscle mass accounts for approximately 40% of an individual's total body mass while also a reservoir for the majority of total body proteins (1). Skeletal muscle is responsible for key metabolic and mechanical functions that contribute positively to one's overall health and function (2). Metabolically, skeletal muscle acts as the largest storage site for amino acids while also being able to store carbohydrates in the form of glycogen which is necessary for ATP provision (1). Stored amino acids are primarily used to synthesize new proteins whereas the stored glycogen can be broken down within the muscle to act as a source of glucose for the fast glycolytic and oxidative phosphorylation energy systems when necessary (3,4). Mechanically, skeletal muscle converts the chemical energy stored within ATP molecules into mechanical energy that allows for muscle contraction leading to locomotion, postural control, participation in physical activity, and ultimately allowing an individual be physically independent (1,3,4).

1.2 Maintenance of Skeletal Muscle Mass

An individual's skeletal muscle mass is governed by muscle protein synthesis (MPS) and muscle protein breakdown (MPB), with the relationship between these two processes being referred to as net protein balance (NPB) (5,6). When in a positive NPB, also known as an anabolic state, MPS is greater than MPB which leads to an accumulation of skeletal muscle proteins. When in a negative NPB, also known as a catabolic state, MPB is greater than MPS which leads to the degradation of skeletal muscle proteins (6,7).

In order to induce skeletal muscle hypertrophy, a consistent positive NPB must be established in order to continuously synthesize contractile proteins at a greater rate than they are recycled (5). Throughout the day, NPB remains negative and can only reach a positive state

when an individual subjects their skeletal musculature to an anabolic stimulus (8). Resistance exercise training (RET) has been shown to be an potent anabolic stimulus through its ability to stimulate the mechanistic target of rapamycin complex-1 (mTORC1) pathway (9,10) and can assist in driving a positive NPB when combined with endogenous amino acid consumption (11–15). While RET elicits a large increase in MPS, it also increases rates of MPB and when performed in isolation of amino acid intake, the post-RET NPB remains negative (11,15). The concomitant consumption of endogenous amino acids alongside RET has been shown to potentiate RET induced increases in MPS with a simultaneous attenuation of MPB which allows for a positive NPB to be established post-RET (13,14). When consistently conducted over an extended duration, RET in combination with adequate protein intake will allow for consistent positive NPB which will eventually lead to a net accrual of skeletal muscle contractile proteins that ultimately increase the size of the exercising skeletal muscle(s) (5,7,16,17). Specifically, a daily protein intake of 1.6-2.2 g/kg/day has been shown to be an ideal range for assisting RET in inducing muscle hypertrophy (17). However, both males and females show total daily protein intakes around 0.8 g/kg/day in absence of supplementation (18) which is well below the necessary range for optimal hypertrophy (17). If these same individuals were supplemented daily with 50 g of whey protein their daily intakes would increase to ~1.5 and 1.7 g/kg/day, in males and females respectively (18), which highlights the importance of additional protein supplementation in tandem with one's normal diet to reach an amount necessary to induce muscle growth.

1.3 Introduction to Resistance Exercise Training

Resistance exercise training (RET) can be broadly defined as a muscle/muscle group performing work against a load greater than the load(s) one would experience in their normal

everyday activities. RET has been found to reduce the risk of all-cause mortality (19,20), improve insulin sensitivity (21,22), and increase bone mineral density (23). Aside from the general health benefits of RET, it can also be used as the primary means to increase muscle size, strength, and/or local muscle endurance. The positive effect of RET on muscle hypertrophy can be used to aid in recovery from disuse related muscle atrophy (i.e., bed rest, bracing/casting of limbs, etc.), as well as age related muscle loss. Similarly, older adults may be prescribed RET as a means to improve strength/power which can in turn improve independence and physical function. Athletes may also want to increase strength/power in the weight room such that these improvements could translate to improved sport performance. Ultimately, RET is an effective means of exercise that can not only benefit one's overall health, but can also improve one's ability to perform day to day activities or compete in sport.

1.3.1 The Strength-Endurance Continuum

RET can be used to improve skeletal muscle size, local muscle endurance (LME), and muscular strength (24,25). In order to alter our skeletal muscle mass, LME, or strength, RET variables must be manipulated to apply a specific stress to the muscular system (25). The National Strength and Conditioning Association (NSCA) and American College of Sports Medicine (ACSM) have proposed that performing RET under different percentages of an individual's one-repetition maximum (1RM) is the optimal method for selectively targeting skeletal muscle adaptations (24,25). These organizations suggest that moderate loads between ~65-85% 1RM for 6-12 repetitions result in superior skeletal muscle hypertrophy, RET focused on muscular strength should be done with loads greater than ~85% 1RM for 1-6 repetitions, and to best train muscle endurance one should train with loads lower than ~65% 1RM for greater than 12 repetitions (24,25).

1.3.2 RET Variables

When designing a RET program, the manipulation of training volume, effort, and load allow trainers and clinicians the ability to tailor a training plan to the goals of their client/patient. Volume is the total amount of work performed and can be manipulated through the number of sets/repetitions performed (either within a single session or across a week of training) (26–29) or the load prescribed (26,30,31). Load refers to the external load that the muscle/muscle group contracts against and is commonly prescribed as a percentage of 1RM, or sometimes as percentage of MVC in a research setting. Effort refers to the subjective feeling of exertion associated with the muscle/muscle group contraction. It is important to note that when prescribing training volume, effort, or load in a RET program, these variables cannot all be controlled at the same time (Figure 1). As an example, within a single prescribed set with a certain training load (e.g., 50% 1RM) and effort (e.g., train to fatigue) there will be variation in set-volume as the total repetitions performed can vary within and between individuals (26,30). Setting a specific training volume (e.g., 100 kilograms per set or 4 sets of 10 repetitions) and load (e.g., 50% 1RM) will lead to variation in effort, especially when trying to match the training volume performed using different prescribed loads (32,33). The most complex interaction would be to hold volume (e.g., 100 kilograms per set or 4 sets of 10 repetitions) and effort (e.g., train to fatigue) constant as the training load would then need to be adjusted continuously within the same set which would prove difficult as specialized training equipment would be necessary (i.e., an isokinetic dynamometer, or flywheel apparatus).

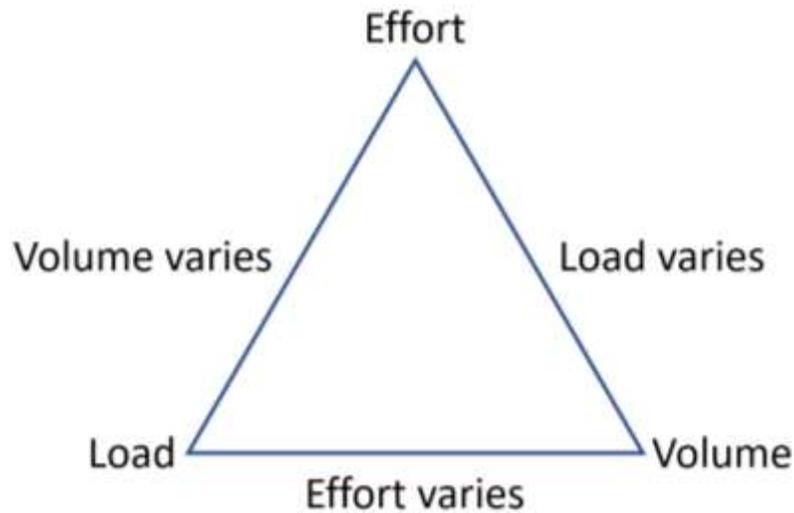


Figure 1. A schematic of the relationship between the manipulation of effort, load and volume when carrying out a resistance exercise set. Only two variables can be held constant during a single set with the third needing to vary.

1.3.2.1 Training Volume and Frequency & Skeletal Muscle Hypertrophy

RET volume is quantified as the product of load used and repetitions completed for each set, and the volume for each set can be summed over a single session or all sets performed over a RET mesocycle (i.e., several weeks of RET) can be summed to yield total volume (16,25,28,34). RET frequency is the number of training sessions dedicated to a muscle or muscle group over a given time interval, typically one week (25,35,36). RET volume and frequency are two RET variables that are presumed to be closely linked with the degree of RET induced skeletal muscle hypertrophy (8,34,37,38), and although they can be individually manipulated, current research has shown an interdependence of these two factors with regards to training for muscular growth (35,39).

Evidence suggests that RET frequency does not play a major role when training to induce skeletal muscle hypertrophy (35,39–41). A recent meta-analysis by Schoenfeld and colleagues concluded that RET frequency is irrelevant when RET volume is equated between training programs, but when volume is unmatched, 3+ days/week of training (ES: 0.15±0.09) was slightly

more effective than 2 days/week (ES: 0.08 ± 0.05) and 1 day/week (ES: -0.03 ± 0.07) likely due to the increased training volume accrued with additional days of training per week (35). It then appears that RET frequency may not be as important when volume is similar between training conditions, but a greater training frequency in unmatched volume training conditions leads to a slightly greater increase in skeletal muscle mass (35).

RET volume may play a more important role in skeletal muscle hypertrophy compared to frequency as several studies have found that additional RET volume induces a greater hypertrophic response (28,29,42,43). A meta-analysis by Krieger found that performing multiple sets was associated with enhanced muscle growth when compared to performing a single set and another meta-analysis by Schoenfeld and colleagues found a dose-response relationship between weekly RET volume and hypertrophy wherein more volume lead to more muscle growth (28,42).

Closer inspection of primary literature shows mixed results for the influence of training volume on muscle growth with some studies finding increases in volume to further stimulate muscle growth (26,29,43,44) and others suggesting it may be of limited importance given effort is maximized (27,30,31,41). The consistent finding across studies showing greater volume leads to greater muscle hypertrophy supports the dose-response relationship put forward by Schoenfeld et al. wherein all groups that performed RET saw an increase in muscle size, but those groups that performed more volume over the training period saw greater improvements (26,29,43,44). However, it has been shown that untrained males can increase myofiber cross-sectional area (CSA) to a similar extent when training with higher loads (HL) or lower loads (LL) even when the LL group performs far greater training volume (30). Similarly, resistance trained males showed comparable improvements in muscle mass in response to either a high- or low-frequency RET program wherein the high-frequency program performed a greater total training volume

(41). If the proposition that greater training volumes always leads to more muscle growth were completely true, then the previously mentioned groups that performed more training volume should have shown greater hypertrophic increases (30,41). Instead, performing additional volume likely follows a diminishing returns pattern where adding more training volume will increase the magnitude of muscle growth up until a point at which more volume leads to no additional increase in hypertrophy (Figure 2). In fact, an argument has been proposed that contrasts the dose-response volume theory which suggests that effort, not volume, could be a more important training variable with regards to muscle growth (16,30,45). Connecting the theory that there is a dose-response relationship with training volume and muscle growth with the finding that muscle hypertrophy can occur independent of load used when training to volitional fatigue, it can be theorized that when one trains to volitional fatigue they are exceeding the minimum dose of training volume required to stimulate growth and could be reaching the upper limit of training volume necessary to grow for that given external load and thus we can see similar growth between loading conditions with substantially different training volumes being performed.

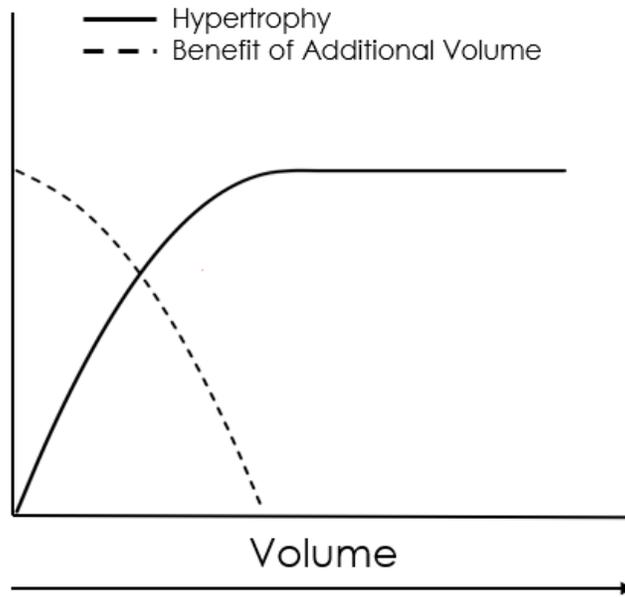


Figure 2. Theoretical model of the relationship between total training volume, hypertrophy, and the benefit of performing additional training volume. Additional volume will increase the degree of muscle growth in a diminishing returns fashion before eventually hypertrophy has plateaued and additional volume provides no benefit.

To summarize, it appears that there is a dose-response relationship between RET volume and skeletal muscle hypertrophy (28,42) when comparing training programs using the same load or when effort is not maximal. However, when effort is matched between different loading conditions the role of RET volume for muscle hypertrophy may be of less importance due to either [1] training to volitional fatigue allowing one to reach a point on the dose-response curve where additional volume does not yield a proportional hypertrophy response, [2] the volume performed does not directly reflect the stress placed on the muscle wherein lower loads require more volume and higher loads require less volume due to the absolute load placed on the muscle (30,41), or [3] the magnitude of hypertrophy plateaus once the upper limit of required training volume is reached and so the benefit of additional training volume decreases (Figure 2).

1.3.2.2 Training Load, Effort & Skeletal Muscle Hypertrophy

Both the NSCA and ACSM have proposed that moderate to heavy loads (67-85% 1RM) are required in order to induced muscle growth (24,25) and this is supported through multiple studies comparing the differential adaptations between different loaded RET protocols (29,31,33,46–49). A study by Lasevicius and colleagues compared the muscle mass changes following HL and LL RET which was not taken to volitional fatigue as well as HL and LL RET that was taken to volitional fatigue (46). Two important results were found in this study, the first being that there was no difference in muscle growth between the two HL RET conditions showing that training to fatigue is not necessary when using HL (46). However, Lasevicius also showed that when using a LL RET program, training to fatigue is necessary to induce skeletal muscle hypertrophy (46).

It has been suggested that the external load used during RET may not be of great importance for muscle hypertrophy when one trains to volitional fatigue (16,38,45,50,51). A key component of studies showing similar muscle hypertrophy between HL and LL is that all groups trained to volitional fatigue (26,30,52–54) which can be described as the inability to move the applied load past the critical joint angle which is generally the joint angle with the greatest moment arm (52–55). Training to volitional fatigue is directly supported by Henneman's size principle as it can be assumed that regardless of load, when an individual trains to task failure, they should be reaching near maximal myofiber recruitment (56). As the initially recruited motor units (MUs) begin to fatigue, other MUs that may not have been required for the initial task are engaged to allow for necessary force to be maintained (56). Empirical evidence through the use of electromyography (EMG) has proposed that HL RET leads to greater activation of the quadriceps compared to LL RET when both trained to volitional fatigue (57). However, through

the analysis of fibre type specific glycogen depletion, which is a more direct measure of myofiber recruitment, performing resistance exercise to task failure leads to similar type I and type II myofiber recruitment independent of the external load (58). The similar gains in muscle mass (26,30,52,59,60) when training to fatigue with HL and LL therefore appears to be supported by the size principle of MU recruitment (56,58).

1.3.3 Measurement of Skeletal Muscle Hypertrophy

To assess the impact of RET on skeletal muscle mass, the measurement tools used must be reliable, valid, and sensitive to allow for accurate assessment of the RET interventions effectiveness. Technologies such as magnetic resonance imaging (MRI), computed tomography (CT), dual-energy x-ray absorptiometry (DXA), and ultrasonography (US) allow for the estimation of skeletal muscle mass with each having their own benefits and drawbacks (61).

MRI is widely considered the gold-standard with regards to the assessment of skeletal muscle mass (62), as it is non-invasive, and is able to produce high resolution muscle cross-sectional area images while also allowing for individual muscles to be assessed within the scanned anatomical compartments (61,63). These images also provide the potential for the assessment of muscle quality through the ability to delineate fat/connective tissue and muscle mass within the muscle compartment as well as individual muscles (61,64). CT scans have similar benefits when compared to MRI with a major limitation being the use of radiation in order to produce these images (61). Taken together, the use of MRI and CT in RET research may not be feasible for every study as they are relatively inaccessible for frequent use and may not be a cost-effective method for tracking skeletal muscle mass changes in a study with a larger sample size (61,63).

DXA and US machines act as non-invasive, accessible, and relatively cheap modes of skeletal muscle mass measurement when compared to MRI and CT scans. Maden-Wilkinson and colleagues assessed the correlation between thigh fat-and-bone free mass (FBFM) measurement via DXA and total thigh muscle volume through MRI in young adults found the two measures were highly correlated ($R^2 = 0.9$) (62). Furthermore, full-body DXA scan can be completed in under 10 minutes and provide a segmental breakdown of body composition immediately without the need for further analysis (65). A major limitation of the output provided by DXA is that it uses a three compartment model wherein the body is split into bone, fat, and lean mass, but this lean mass is considered to be anything that is not bone or fat mass (FM) which means it can include vasculature, organs, and connective tissue in the lean mass estimate(s) (65,66). It is important to note that DXA has the potential for measurement error which can take the form of both technical and/or biological changes that lead to a variance in output values. Kutáč and colleagues reported that DXA typical error of measurement for leg FBFM in females was 2.7-4% which was lower than the 4.05-5.7% observed in males, and suggest that only values greater than the upper limit of these typical error ranges can be considered true changes (67). Granted, changes that are within the range may still represent the change in muscle size observed following training, but they are less reliable than changes above the upper limit. To reduce the error of DXA, fluid balance, participant positioning, and physical activity should be controlled by the research staff when performing repeated scans (67).

US is a non-invasive, inexpensive, and the most accessible means of measuring skeletal muscle mass. Superficial muscles can be easily imaged cross-sectionally as well as longitudinally which allows for many possible metrics to be assessed (61,68). Similar to MRI and CT, US can image muscles such that cross-sectional area and muscle thickness of individual

muscles can be measured (68). Unique to MRI and US imaging is the ability to measure fascicle length and pennation angle which can provide additional insight into how RET impacts skeletal muscle architectural characteristics (61,68,69).

1.3.4 Training Load and Local Muscle Endurance

Repeated muscle contractions lead to a decrease in maximal force production, termed muscle fatigue, with this process being reversible through rest (70). It is important to note that there is a distinct difference between muscle fatigue and task failure wherein these two terms cannot be used synonymously as they refer to separate constructs (71,72). Muscle fatigue directly relates to the drop off in maximal strength/power that occurs soon after the onset of continuous contraction whereas task failure relates to the inability to continue to perform the given task (i.e., performing full range of motion knee extension repetitions with 50 pounds of external load) (71,72). Tightly related to task failure is the RET construct of local muscle endurance (LME) which can be defined as the ability for a muscle/muscle group to resist fatigue when performing muscular work against a submaximal external load (24,25,45,73). It should be noted that this current definition does not align with how fatigue and time to task failure are defined in primary literature (71). As LME is more so concerned with time to task failure, or in the case of dynamic contractions volume to task failure, and not the reduction in maximal force (i.e., fatigue), a more appropriate definition of LME would be ‘the ability for a muscle/muscle group to perform a given task for an extended period of time at a submaximal external load’. When training to improve LME, the NSCA and ACSM both recommend the use of LL/higher-repetition RET (24,25).

The most common method for testing LME is assessing relative muscle endurance (RME) which refers to the number of repetitions/contractions one can perform against a load set

at a percentage of their current maximal strength (50,74). Previous research has shown that RET is capable of improving RME (26,49,51,54,75–77) while only five of these studies have examined the direct impact of RET load on RME (26,49,54,76,77). A consistent result when comparing HL and LL RET in terms of RME is that LL elicits greater improvements which is likely due to lesser increases in maximal strength from LL RET leading to a smaller change in pre-RET and post-RET RME values (26,49,54,77).

Another method of testing muscle endurance is to perform maximal repetitions with the same absolute load for both the pre- and post-testing session (78,79). Similar to RME, the implementation of a RET program is able to improve AME (26,43,78–81), but specific to AME when compared to RME is that improvements are similar between HL and LL RET programs when both train to volitional fatigue (26,43,78–81). Importantly, the relationship between RET load and AME has been observed in both the upper-body (43,78,81) and lower-body (26,79) highlighting that different muscle groups show a similar response. It is also necessary to note that a majority of these studies used a single absolute load (43,78–81) and did not consider how HL and LL RET may impact AME using a heavier and lighter absolute load. Mitchell and colleagues assessed RME at 30% and 80% 1RM, and AME was characterized as the total work (repetitions completed multiplied by the load used in kilograms) of the RME assessments in response to both HL and LL RET (26). RME at 80% 1RM increased similarly between loading conditions, but RME at 30% increased only in the LL condition while decreasing in the HL condition supporting previous literature that LL RET is superior for increasing RME (26). However, AME at 30% 1RM increased similarly between loading conditions, and while AME at 80% 1RM improved in both conditions the HL condition saw a larger improvement (26). The main limitation of this study with regards to its measurement of muscle endurance is that AME was not assessed

through the use of the same absolute loads at both pre- and post-testing sessions, but rather the load product of the RME tests (26).

While RME is the most common method for assessing RET induced LME changes, it has very little application to clinical and performance settings as it is quite rare for an individual to need to perform continual contractions against an external load that is set at a specific percentage of their maximal strength. AME is a more applicable method of quantifying LME as it is more common for an individual to be asked to perform successive contractions against a set load that is not based on the individual's maximal strength. The most obvious example of AME in a performance setting is the NFL combine maximum repetitions at 225 pounds test where each athlete, regardless of their 1RM, must perform as many repetitions as possible against the same absolute load. Running could also be considered an example of performance AME as if a runner's weight stays relatively constant across a season, they will be performing repeated contractions with their legs to move their body weight around a track/course. In a clinical/practical setting, AME can be expressed as the ability for an older individual to climb a series of stairs assuming their body weight remains relatively constant or for a firefighter to carry out a search of a building while wearing their specified gear which will likely remain the same absolute load throughout their career.

In summary, RME can be improved through RET but LL RET appears to induce greater increases likely due to a lower increase in maximal strength and thus a lower load being used to test RME post-training (26,49,54,77). Similar to RME, AME can improve with RET and these improvements are similar between HL and LL RET (26,43,78–81). It remains unclear if HL and LL RET may preferentially improve AME at a heavier or lighter absolute load as previous studies have only every used a single absolute load to measure AME (26,43,78–81). To the

authors knowledge, this will also be the first study to measure RME and AME in the same trial, as well as the first to assess AME using both a heavier and lighter absolute load.

1.3.5 Training Load and Maximal Strength

Increasing strength is a desirable RET adaptation for the general population, athletes, and clinical populations alike. Strength can be generally defined as the ability to produce maximal muscular force through muscle contraction against an external resistance irrespective of the velocity of the movement (25,45). RET is theorized to induce increases in strength through both neural mechanisms (i.e., increased MU recruitment, increased MU firing rate, learning the task) in the short term (16,25,30,82,83) as well as muscular adaptations (i.e., increased sarcomeres in parallel, increased pennation angle) in the long term (25,84,85).

The ACSM and NSCA have stated that when performing RET with the goal of increasing strength, one should train with loads $\geq 85\%$ 1RM for 1-6 repetitions (24,25). In accordance with these recommendations, numerous RET trials directly comparing the effects of different loads on muscular strength have consistently shown HL RET to be superior to LL RET for inducing strength increases (26,29,33,49,51,76,77,79,86). Further supporting the theory that HL RET is better for strength increases, two separate meta-analyses were conducted and concluded LL RET to be an inferior training modality compared to HL RET for improving 1RM strength (38,87). It should be stated that LL RET still leads to improvements in muscular strength, but these improvements are substantially smaller than those observed following HL RET programs (26,44,49,77)

An important consideration for the quantification of strength is how practicing the test can impact the results. Recent studies have shown no differences in 1RM strength between HL and LL RET conditions if the participants 1RMs were assessed periodically throughout the RET

period (30,83,88,89). As many studies perform their 1RM assessments on the same exercises that are being used for the RET program, it would make sense that the HL conditions would perform better as these muscles/participants are used to performing heavier repetitions at loads closer to their maximal strength (16, 20, 88). When periodic 1RM assessments were added into the RET programs, no difference was observed between the LL or HL conditions which could be explained by the LL condition being able to ‘practice’ contracting against a heavier load and thus allowing for strength gains to be equalized (16, 30, 88, 89). In the same fashion, the method of assessing muscular strength can impact the results when comparing differentially loaded RET programs. Morton and colleagues demonstrated that strength increases were similar between HL and LL RET conditions when strength was assessed on a novel task which was a knee extension (KE) maximum voluntary contraction (MVC) (30). Within the same study a traditional KE 1RM test was also assessed and it was shown that the HL condition was superior for increasing 1RM strength, likely due to the ‘practice’ or ‘learning’ of the task (26,30,90). To summarize, strength appears to be dependent on its assessment wherein if the measure of strength is a 1RM test using the same exercise(s) as the RET program, HL RET will lead to greater improvements, but if the strength assessment is novel to both loading conditions the advantage of HL RET is nullified and strength gains are no different between loading conditions.

1.3.6 RET and Muscle Architecture

Muscle architecture relates to the structural composition of a skeletal muscle, specifically pennation angle and fascicle length. Pennation angle refers to the angle between the attachment of the myofiber to its line of pull whereas fascicle length refers to the length of the myofibers as they run from the superficial to deep aponeurosis (91,92). Functionally, fascicle length is related to the velocity of shortening and changes in resting sarcomere lengths and can be altered through

the addition of sarcomeres in series (93). Pennation angle impacts a muscles force production as an increased pennation angle would allow for more fascicles to be packed in parallel to one another along the line of pull (92,94). Both pennation angle and fascicle length are susceptible to change following RET which typically involves an increase in both characteristics (95). However, some studies have reported no change in pennation angle (96–98) following RET, and fascicle length has been shown to be similar when examining the muscles of untrained and trained individuals cross sectionally (99). To the authors knowledge, no study has previously compared how HL and LL RET impact VL pennation angle and fascicle length.

1.4 Impact of Biological Sex on RET Adaptations

1.4.1 Impact of Biological Sex on Myofiber Characteristics

There are notable differences between males and females regarding the distribution and composition of skeletal muscle. Globally, skeletal muscle mass in females has been estimated to account for ~31% of total body mass compared to ~38% in males (100). When differences are examined regionally, females have considerably less muscle mass in both the upper- and lower-body compared to males, but the upper-body difference is much more pronounced than that of the lower-body (100,101). Further, while both sexes have a greater percentage of skeletal muscle mass in their lower- compared to upper-body, females have a larger allocation of muscle mass in their lower-body compared to males (100). Ultimately, women not only have less lean mass relative to total body mass (100) but also a majority of this lean mass is located in the lower body (100,101).

Transitioning to a microscopic view of skeletal muscle, assessments of myofibre CSA, myofibre type distribution (i.e., the percentage of each fibre type in relation to the total number of fibres within a muscle), and the percentage of a muscles CSA occupied by specific myofibre

types has been investigated and compared between sexes. Similar to the relationship between total skeletal muscle mass and sex, all fibre types in males are larger with regard to CSA compared to females in both the biceps brachii and vastus lateralis (102–107). When comparing myofibre CSA within the sexes, it has been shown that type I and type IIa fibres have a similar CSA in women, but in men type IIa fibre CSA is greater than type I CSA (102,104,105,108). Fibre type distribution has been shown to be similar between sexes in the biceps brachii (103,107), but in the vastus lateralis men have a greater distribution of type II myofibres while women have a greater distribution of type I myofibres (102,103,109). Similar to fibre type distribution, no sex differences have been observed when assessing the percentage area occupied by specific fibre types in the biceps brachii CSA (103,107), however type I fibres account for a greater percentage area of the vastus lateralis in women while in men type IIa fibres make up the majority of the vastus lateralis CSA (102–104,108,110). To summarize (Figure 3 and Figure 4), the only observed difference between the myofibre composition of the biceps brachii between the sexes is that females have smaller fibres compared to males, but the distribution of fibres and percentage area are similar between sexes (103,107). Of particular interest, the myofibre characteristics of the vastus lateralis show distinct differences between the sexes with females

having smaller fibres, a greater distribution of type I fibres, and a greater percentage CSA occupied by type I fibres compared to males (102–104,108–110).

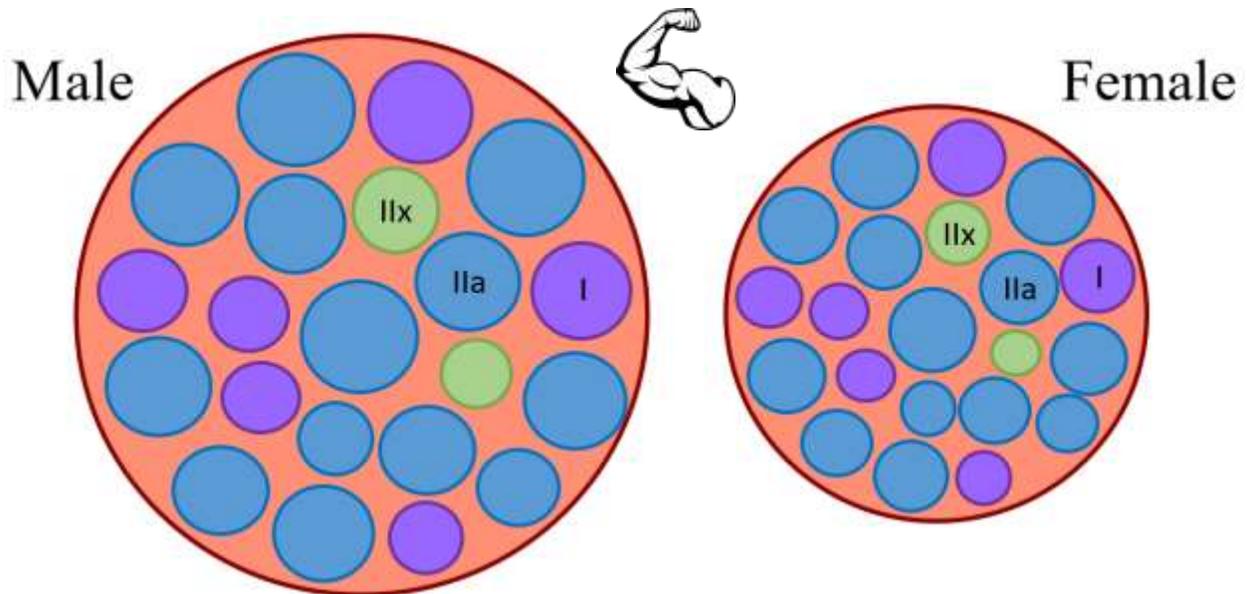


Figure 3. Visualized between sex comparison of biceps brachii myofiber characteristics. All fibre types have a larger CSA in males compared to females. Fibre CSA in both males and females is ranked as IIa > I > IIx. A greater percentage area of total muscle CSA is occupied by type IIa fibres in both males and females followed by type I and then type IIx. Type IIa fibres make up the majority of fibres in both males and females followed by type I and then type IIx.

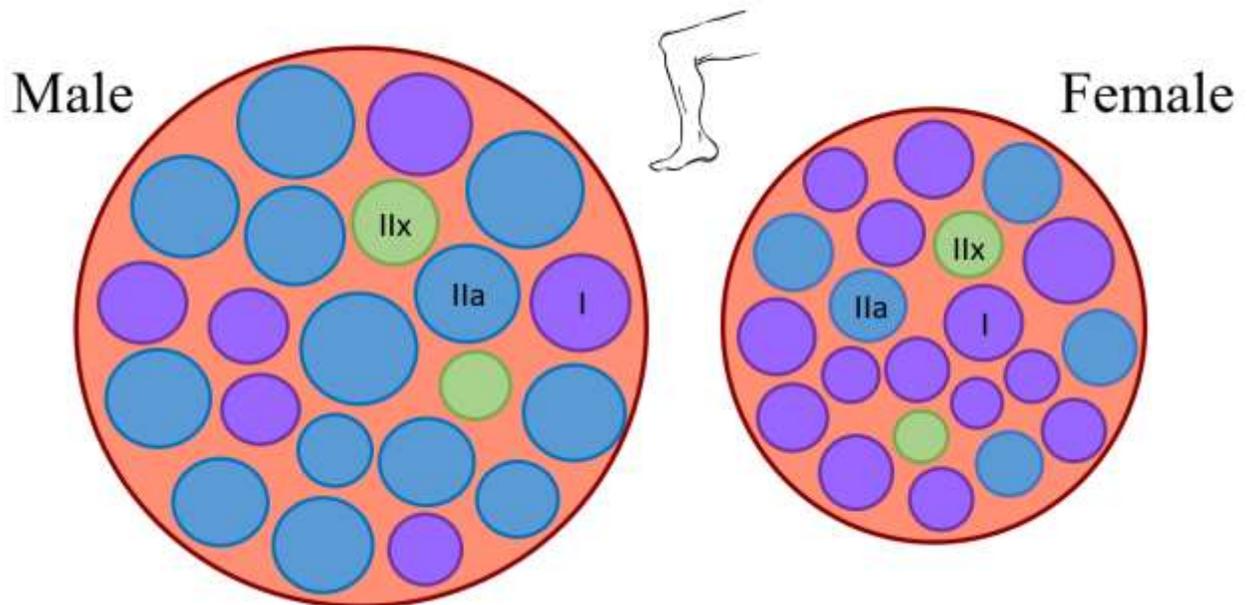


Figure 4. Visualized between sex comparison of vastus lateralis myofiber characteristics. All fibre types have a larger CSA in males compared to females. Fibre CSA in males is ranked as IIa > I > IIx and in females it is ranked as I = IIa > IIx. A greater percentage area of total muscle CSA is occupied by type IIa fibres in males and type I fibres in females. Type IIa fibres make up the majority of fibres in males while type I fibres make up the majority of fibres in females.

1.4.2 Impact of Biological Sex on RET Induced Skeletal Muscle Hypertrophy

While there are apparent sex-differences in skeletal muscle mass distribution (100,101) and myofiber characteristics (102,103,107,108,111), relative muscle hypertrophy occurs in a similar fashion between males and females (112). Absolute gains in muscle size are typically greater in males due to their muscles generally being larger at baseline (112,113), but when muscle hypertrophy is expressed as a relative change males and females show a similar response (112,114–118). It should be noted that one of the largest primary studies comparing hypertrophy between the sexes found upper arm muscle growth to be 20.4% in males (n = 243) and 17.9% in females (n = 342), with this difference reaching significance (118). This is an important consideration as relative changes between sexes are similar, but when a large enough sample is used a statistical difference arises in the capacity for hypertrophy (118).

Numerous studies conducted using males have shown no difference in the amount of skeletal muscle mass gained after performing RET with HL or LL (26,30,49,54,59,119). When similar studies have been conducted using females, the results have shown a great degree of heterogeneity (44,60,77,83,88). To briefly summarize the current findings in females training with HL or LL, one study found both loading conditions lead to no increases in muscle mass (88), three studies found both loading conditions increased muscle mass to a similar degree (60,77,83), and one study found the LL condition led to greater increases in muscle mass (44). As the results of three of these studies in females showed the expected result that there was no difference in the degree of hypertrophy between loading conditions (60,77,83), focus will be placed on examining the two studies that found more unexpected results (44,88). Dinyer et al. showed that both HL and LL conditions were unable to increase total body FBFM (88). One potential explanation is that Dinyer et al. quantified muscle growth using DXA which may not be

sensitive enough to detect the small absolute changes in FBFM observed in females following RET. It can also be speculated that the training volume for both conditions may not have been high enough to stimulate muscle growth as for five of the nine weeks of training, only two sets per exercise were performed at each session and only two sessions per week were carried out across the entire nine week training period (88). A recent meta-analysis concluded there is a dose-response relationship between training volume and muscle growth wherein progressively higher weekly training volume leads to greater muscle gain (42). While differences in training volume between loading conditions may not impact muscle growth as long as effort remains equal, the participants in this study may not have reached a necessary weekly volume regardless of their training regime to induce measurable changes in muscle mass (42,88). Another potential explanation for the results found by Dinyer et al. could be that since females present with a smaller absolute change in muscle mass when undergoing RET induced muscle hypertrophy, the methods of quantification of muscle mass may not be sensitive enough to detect a change (112,113). Under this theory, it could be proposed that the participants may have indeed undergone muscle hypertrophy, but the DXA scanner used by Dinyer and colleagues could not detect a change in the participants due to the sensitivity of this machine and the absolute change in female muscles being smaller compared to males.

In contrast, Franco and colleagues concluded that their LL group saw a greater increase in FBFM compared to the HL group due to the higher training volume accrued through the LL training (44). This conclusion by Franco and colleagues goes against the findings of previous studies comparing different load RET with unmatched training volumes (26,28–30,43) which creates an interesting theory that suggests females may preferentially adapt to LL training. To summarize, males and females show no major differences in relative muscle mass increases

following RET (49,60,112,114–118), but current research remains inconclusive about the comparative effects of both HL and LL RET on skeletal muscle hypertrophy in females (44,60,77,83,88).

1.4.3 Impact of Biological Sex on Local Muscle Endurance

Local muscle endurance is directly related to task failure referring to the point at which an individual can no longer perform a given task (71) and LME being the ability for a muscle/muscle group to perform a task for an extended period of time against a submaximal external load (24,25,45,73). Comparisons of time to task failure and LME have been studied between the sexes under a varying range of external loads, contraction types, and muscles/muscle groups (103,120–125) with multiple reviews being written about this topic as well (110,126–128). A consistent finding among primary research is that females show a greater time to task failure/fatigue resistance when compared to males when performing contractions at relative loads corresponding to 20-70% 1RM/MVC (103,121,122,124,125).

While a general conclusion could be made about sex differences and time to task failure/LME, when research designs are split based on the specific task used to assess task failure/LME the conclusions become less clear for designs employing dynamic contractions (110,121,122,127). As RET exercises are mainly a series of repeated concentric and eccentric dynamic contractions, focus will be placed on studies examining sex differences in dynamic elbow flexor and knee extensor time to task failure/LME where possible, but current research pertaining to this topic is quite sparse (127). Yoon and colleagues found that time to failure when performing repeated elbow flexor dynamic contractions at 20% MVC was greater in females compared to males (122), and Maughan's group showed similar results where females performed more elbow flexor repetitions at loads corresponding to 50%, 60% and 70% 1RM (121). While

these two studies provide preliminary evidence for the presence of a sex difference for dynamic contractions in the elbow flexors (121,122), Maughan and colleagues found no difference in total repetitions completed at 80% and 90% 1RM between females and males suggesting that the apparent advantage females have for dynamic contraction task failure resistance is specific to lower relative loads in the elbow flexors (121). Conversely, Hoeger and colleagues found no difference in the amount of repetitions completed at 40%, 60%, and 80% 1RM between males and females in the elbow flexors (129). The current state of the literature pertaining to sex differences in time to task failure/LME for the elbow flexors appears quite equivocal and no firm conclusions can currently be drawn as to if a difference truly exists between the sexes.

When the knee extensors are used to assess sex differences in time to task failure/LME, Ansdell and colleagues showed that females exhibit a longer time to task failure when compared to males during intermittent isometric contractions at 50% MVC (130). However, Hoeger and colleagues found no difference in the maximum number of repetitions completed at 40% and 80% 1RM between males and females for the knee extensors (129). In support of the results from Hoeger and colleagues study, Miller and colleagues also found no difference in the maximum number of repetitions performed at 60% 1RM for the knee extensors between males and females (103,129). Based on the current research, there appears to be no sex difference in time to task failure/LME between the sexes for a range of relative external loads for the dynamic knee extensor tasks, but the research in this area is limited (103,129,130).

Suggested mechanisms as to why there may be sex differences in time to task failure/LME in dynamic contractions include differences in myofibre characteristics (121,122,126), as well as the theory that larger muscles masses may decrease local blood flow/O₂ perfusion to a greater extent during sustained or repeated contraction(s) (103,126).

Differences in substrate utilization have also been suggested as a potential mechanism to explain sex differences in time to task failure/LME, but this mechanism is of lesser importance for the current thesis as the LME tests that were used in this project were relatively short in duration and as such substrate utilization was thought to be of lesser importance. When comparing VL myofibre characteristics between the sexes, males have larger myofibres than females for all fibre types, type IIa fibres make up the majority of the CSA in males while type I fibres make up the majority of the CSA in females, and males present with a greater proportion of type IIa fibres while females show a greater proportion of type I fibres (102–105,107). When comparing the BB between sexes, the main difference is that males have larger myofibres compared to females, but both sexes have type IIa fibres making up a majority of the CSA and proportion of total fibres (103,107). While current evidence shows a type I dominance in the VL of females compared to males, myofibre characteristics likely play a smaller role in the noted sex differences for time to task failure/LME. Even though males and females have the same distribution and total CSA occupied by type IIa fibres in the BB, studies have shown that females have a greater time to failure/LME when compared to males when the BB is exercised at loads $\leq 70\%$ 1RM/MVC (121,122). Further, the proportion of type I fibres has been found to be greater in the VL of females compared to males, and yet studies have shown no difference between the sexes in time to task failure/LME for the knee extensors (103,129) which provides support that myofibre composition likely plays a minimal role in potential sex differences in time to task failure/LME. Given the current research, distribution of myofibre types within a muscle seem to not impact time to task failure/LME and other factors such as local muscle blood flow and muscle mass distribution may play more important roles (121,122,126).

Adequate blood flow to working musculature allows for the deposition of nutrients (i.e., glucose, triglycerides, and amino acids) and oxygen while simultaneously removing deleterious metabolic by-products (i.e., hydrogen ions) thus allowing for the continuation of muscle contraction. Females present with a greater proportion of type I myofibres which present with a greater capillary density (109) allowing for improved blood flow. Furthermore, occlusion of the local vasculature via muscle contraction can also impact blood flow to the working tissues (126). Occlusion of the local vasculature depends on the absolute force generated across the working muscle (131), and since males have greater muscle mass compared to females (100,101) they will likely create greater intramuscular forces due to a higher muscular strength (103). It can then be postulated that the reason why females have been found to have increased time to task failure/LME when compared to males for lower relative loads is due to the lower absolute forces being produced by the contractions (121,126). To continue on this point, there appears to be a threshold required to occlude blood flow through muscle contraction as Maughan and colleagues found no difference in time to task failure/LME between males and females at loads corresponding to 80% and 90% 1RM (121). These presented works when examined in synthesis show strong support for the theory that the apparent sex difference in time to task failure/LME at lower relative loads may be due to the differences in absolute intramuscular forces that are generated between the sexes (103,126,131)

1.4.4 Impact of Biological Sex on Maximal Strength

As would be expected, numerous studies have shown that males are consistently stronger at baseline and after RET when comparing absolute strength to females in both the upper and lower body (75,132–135) which is attributed to males having greater muscle mass compared to females (100,101). When baseline and post-RET strength is expressed relative to muscle mass

there appears to be mixed results with one study finding similar relative strength in the upper body, but males showing greater lower body relative strength (134). In contrast, Wilmore found no difference in lower body relative strength, but did show that females have greater upper body relative strength compared to males (132).

Early work by Cureton and colleagues demonstrated that following a RET program, both sexes improved absolute strength of the upper and lower body with males showing a far greater improvement, but when these increases were expressed in relative terms there was no observed sex difference (114). While other individual studies have also examined RET induced strength changes between the sexes (75,118,134,135), Roberts and colleagues conducted a systematic review with meta-analysis in order to amalgamate the results of these studies to produce a clearer answer (112). Roberts and colleagues concluded that while males demonstrate greater absolute increases in strength, there are no differences between the sexes for increases in lower body relative strength, and females expressed a greater capacity for increasing upper body relative strength (112).

1.5 Impact of the Menstrual Cycle on Muscular Strength and Endurance

Within the realm of exercise physiology research females are consistently underrepresented compared to their male counterparts. Costello et al. sampled research studies published in the British Journal of Sports Medicine, American Journal of Sports Medicine, and Medicine and Science in Sports and Exercise from 2011-2013 and found that females accounted for ~40% of the total participants (136). It has been suggested that the discrepancy between male and female involvement in exercise physiology studies is due in part to the menstrual cycle (136–138). The menstrual cycle is divided into two distinct phases, follicular and luteal, separated by ovulation and while the median cycle length is 28 days, there is substantial variation

in cycle/phase durations between individuals (139–142). Endogenous changes in the concentrations of estrogen and progesterone allow for the identification of the current phase wherein the early-follicular phase/menstruation is characterized by low concentrations of both estrogen and progesterone, the late-follicular phase is characterized by elevated estrogen and reduced progesterone, and the luteal phase is characterized by elevated estrogen and progesterone (141–143). It is these fluctuations in endogenous hormones, coupled with the potential use of hormonal (or other) contraceptives that may drive exercise physiology research away from a female sample due to the potential confounding effects (138,144).

It has been theorized that estrogen may have the potential to act as a potentiator for muscular strength which then gives rise to the idea that strength and potentially LME may vary across the menstrual cycle due to the fluctuations in endogenous estrogen concentrations (141,143). Regarding differences in maximal strength across the phases of the menstrual cycle, a systematic review with meta-analysis conducted by Blagrove and colleagues found no difference in MVC, rate of force development, or knee-extensor isometric peak torque between any of the phases of the menstrual cycle (141). Further support from a review written by Pereira and colleagues concluded that there was also no difference in perception of effort when performing maximal strength tasks during each phase of the menstrual cycle, showing that subjective reports of strength are also similar across the menstrual cycle (142). Taken together, these two reviews provide an argument to the theory that maximal strength may vary across the menstrual cycle and instead heavily support the notion that there is no impact of menstrual cycle phase on maximal strength (141,142). LME appears to have similar results as maximal strength as Fridén and colleagues found similar muscle endurance of the knee-extensors when comparing the follicular and luteal phases with these phases being confirmed through hormonal assessment

(145). Altogether, distinct phases of the menstrual cycle and their differences in circulating hormone levels appear to have minimal to no direct impact of maximal strength production or muscle endurance (141,142,145).

1.6 The Unilateral Training Model

Within training research, the unilateral within-participant training model gives rise to distinct advantages over traditional between-participant designs when the goal of a study is to compare the peripheral effects of two different training programs. The unilateral training model assigns two conditions to a single participant which reduces the total cost, sample size, and time to complete a training study. Further, as each participant belongs to both interventions, potential confounding factors (e.g., genetic predisposition, epigenetics, diet, training history, hormonal changes, etc.) will impact both conditions equally allowing for the researchers to be confident that the changes in outcomes are due to the training interventions. The primary assumption when utilizing a unilateral training model is that the limbs of a participant are similar in terms of baseline skeletal muscle physiological properties (e.g., muscle size, muscle strength, capillary density, etc.). Indeed, previous studies which utilized a unilateral training model have reported no differences in baseline measures between limbs (26,44). If there were baseline differences between the limbs due to dominance or some other factor, randomization of limbs into the training conditions based on dominance would allow of this limitation to be effectively controlled. The major limitation of the unilateral training model is the theory of the cross-transfer effect which is when the training of one limb can lead to training adaptations in the contralateral limb (48,146,147).

Current research shows minimal support for the cross-transfer effect to induce muscle growth in the non-training limb if the contralateral limb undergoes RET (148–151). The

prominent theory as to how cross-transfer may impact contralateral muscle hypertrophy is that performing RET on one side of the body will induce a rise in endogenous anabolic hormones which could then be circulated to the non-training side and stimulate anabolic pathways (148,149). In order to directly examine if unilateral RET induces contralateral muscle growth and if increases in endogenous anabolic hormones are associated with this muscle growth, Wilkinson and colleagues assigned one leg to perform RET while the other acted as a non-exercising control (149). The researchers found that muscle hypertrophy occurred in the trained limb in absence of increases in systemic hormones with the contralateral limb not exhibiting any muscle growth (149). Another study by West and colleagues had participants training each arm one separate days with one arm only performing bicep curls during its training sessions and the other arm performing bicep curls followed by high-volume lower body RET in the same session (148). Lower body RET was included so that the researchers could examine if the spike in systemic anabolic hormones caused by the lower body RET would lead to increased muscle growth for the arm that trained on the same days (148). West and colleagues concluded that an increase in endogenous circulating anabolic hormones does not lead to enhanced muscle growth compared to a training condition with lower circulating anabolic hormones (148). Countering the results of West and Wilkinson, Hubal and colleagues found an increase in contralateral bicep CSA of $1.4 \pm 0.3\%$ after the trained limb performed 12-weeks of RET (118). While Hubal's findings may support the theory that the cross-transfer effect leads to muscle growth, the trained limb showed an increase of $18.9 \pm 0.4\%$ following RET which is 92.6% more hypertrophy compared to the untrained limb (118). Further, while the $1.4 \pm 0.3\%$ increase in biceps CSA did reach significance, the authors did not report or speak to the potential measurement error of their equipment used when quantifying their changes in skeletal muscle mass (118). While Hubal's

results cannot be completely disregarded, a change of $1.4 \pm 0.3\%$ is quite small which could lead one to believe this result could fall within the biological and technical error margin of skeletal muscle mass quantification (118). As the results of the aforementioned studies (118,148,149) show no-change or minimal change in an non-exercising contralateral limb hypertrophy following contralateral RET, it can be assumed that when participants undergo two distinct RET programs on either limb the results of these RET programs with regard to muscle mass changes will be due to the programs themselves and not due to a cross-training effect.

While the cross-transfer effect does not appear to be involved in muscle hypertrophy (148,149), changes in contralateral limb strength following unilateral RET have been well documented and makes up a much greater percentage of cross-transfer effect research (147,151–154). While this thesis will not provide an in-depth review into the mechanisms of the cross-transfer of strength, theorized sites of adaptation are proposed to occur within the cortical, subcortical, spinal, and peripheral nervous system pathways; essentially stating that cross-transfer of strength is primarily due to neural mechanisms (151,155,156). Recent meta-analyses have estimated the strength increase in the contralateral untrained limb to be between ~9-18% (153,154) with differences between the upper- and lower-body response being reported as well (154). A meta-analysis conducted by Manca and colleagues found that the mean strength increase in the upper-body untrained limb was 9.4% (CI 6.3-12.4%) while the mean increase in strength for the lower-body untrained limb was 16.4% (CI 12.3-20.5%) (154). The difficulty when interpreting the results of these meta-analyses in the context of a within-participant design using two training conditions is that these meta-analyses assessed studies which used a training limb and a non-training limb whereas the current thesis project as well as other previous within-participant RET designs have assigned contralateral limbs to different RET conditions (26,44).

Therefore, a problem arises wherein the direct cause of changes in strength could be attributed to the RET program of each limb, the cross-transfer of adaptation from the contralateral limb, or more likely a combination of both factors. HL RET leads to greater changes in maximal strength when compared to LL RET (47,157) which leads to the theory that HL RET could also lead to greater strength increases in a contralateral untrained limb. Colomer-Poveda and colleagues tested this theory by incorporating a unilateral training design where one leg of each participant either trained with HL, with LL to fatigue, or with HL to fatigue while the contralateral limb acted as a non-exercising control (48). In agreement with previous literature the HL conditions showed the greatest increases in strength with no difference between the HL and HL to fatigue conditions while the LL to fatigue limbs did not improve 1RM strength (48). When maximal strength of the non-exercising limbs was assessed, only the HL training conditions induced contralateral increases in strength in the control limb (48). While this study stands alone in its design and results at the current time, it can be theorized that in the current thesis project that the LL limb conditions could benefit from the HL limb condition training with no reciprocal benefit to the HL limbs. In other words, concurrent training using a unilateral model could lead the LL limbs to see larger increases in strength than would be expected if the LL RET was being carried out in absence of a contralateral HL RET program due to cross-transfer from the HL limb, but there is currently no evidence for cross-transfer to occur when both limbs undergo RET.

1.7 Equivalence Hypothesis Testing

Traditional hypothesis testing involves researchers aiming to support the alternative hypothesis and show a difference is present between variables/interventions. While this method of hypothesis testing is effective when aiming to conclude a difference is present between conditions, if a researcher's goal is to show no difference between groups then equivalence

hypothesis testing is more appropriate. With an equivalence hypothesis test, a researcher is aiming to show that two groups/interventions underwent changes so similar that neither can be considered better or worse than the other (158). The key component of equivalence hypothesis testing is the equivalence limit which sets the upper and lower boundaries of the equivalence region; a larger equivalence limit makes it easier to conclude equivalence was present, but may reduce the credibility of results (158). Once the equivalence limits have been set, if the difference between the two interventions falls within these limits, equivalence can be concluded (159). While this method of hypothesis testing is common among clinical/medical trials likely due to the highly predictable nature of responses following intervention(s), it has never been used in a study comparing the impacts of two different RET programs. This study aims to be the first to utilize equivalence hypothesis testing alongside traditional statistics to compare the effects of HL and LL RET on muscle growth.

1.8 PURPOSE

The primary purpose of this thesis was to examine the effects of HL and LL RET on skeletal muscle mass in the upper and lower body of healthy young adult females. The secondary purposes of the study were to examine the effects of HL and LL RET on muscle strength, local muscle relative and absolute endurance, and muscle architectural characteristics in healthy young adult females.

1.9 HYPOTHESES

Primary:

- I. HL and LL RET will induce an equivalent increase in fat and bone free mass when comparing contralateral upper and lower body limbs
- II. HL and LL RET will induce an equivalent increase in vastus lateralis cross-sectional area, vastus lateralis muscle thickness, biceps brachii muscle thickness, and vastus medialis oblique muscle thickness when comparing contralateral upper and lower body limbs

Secondary:

- I. HL and LL RET will induce increases in absolute muscle endurance in both the upper and lower body with no difference between the loading conditions
- II. HL and LL RET will induce increases in both upper and lower body maximal strength, but the HL limbs will see a greater increase compared to the LL limbs

Tertiary:

- I. HL and LL RET will induce increases in relative muscle endurance in both the upper and lower body, but the LL limbs will have a greater increase compared to the HL limbs
- II. HL and LL RET will induce increases in vastus lateralis pennation angle and fascicle length with no differences between conditions

Chapter 2: Body of Thesis

2.1 METHODS

2.1.1 Participants

16 healthy (i.e., free of any major cardiovascular, muscular, neurological, and/or metabolic disorders) young women volunteered to participate in the study (Table 1). Verbal and written consent were obtained after prospective participants were informed of all study procedures and potential risks associated with the trial. The participants were recreationally active with no formal or regular resistance or aerobic training experience in the 12 months prior to enrolling in the study. Sample size was calculated using the Minitab statistical analysis software (Minitab; Version 20.4.0) packages equivalence trial sample size estimation tool. The values used in sample size estimation were a power of 0.8, an expected difference in hypertrophy of 0.13%, and the equivalence margins were set at -3.5 and +3.5% which represents 70% of the lower limit of the confidence interval of average muscle growth from a recent meta-analysis (38). All participants completed the study between January 2021 to August 2021. The protocol was approved by the University of British Columbia Research Ethics Board (H20-01570), was prospectively with ClinicalTrials.gov as (NCT04547972) on September 4th, 2021 and was written in accordance with the standards set by the Declaration of Helsinki.

Table 1. Participant baseline characteristics

	<i>N</i> = 16
Age (yr)	23±3.2
Height (m)	1.7±0.05
Weight (kg)	61.7±8.6
BMI (kg/m ²)	21.7±2.9
Total Body FBFM (kg)	40±3.8
Total Body FM (kg)	19.6±6.3
Body Fat Percentage (%)	32.4±6.4
Participants Using Oral Contraceptives (n)	4

Values are means ± standard deviation. BMI, body mass index; FBFM, fat and bone free mass; FM, fat mass.

2.1.2 Experimental Design & Resistance Training Program

A within-participant unilateral repeated measure design was utilized where each participant had one arm and one leg assigned to train with HL and the other arm and leg assigned to train with LL (Appendix H). The study was a total of 12-weeks in duration with one week of pre-RET testing, 10-weeks of RET, and one week of post-RET testing (Figure 5). Unilateral knee extension (KE) training and testing was carried out using the Atlantis Strength C-230 Leg Extension/Leg Curl Combo (Atlantis Strength, Laval, QC). Unilateral dumbbell preacher curl (DC) training and testing was carried out using the Atlantis Strength B-256 Seated Preacher Curl Bench (Atlantis Strength, Laval, QC), PowerBlock 5-50-pound adjustable dumbbells (PowerBlock Adjustable Dumbbells, PowerBlock, Owatonna, MN), and two 1.25-pound PlateMate Microload Magnetic Hex Weights. All training sessions were conducted in the Allan McGavin Sports Medicine Clinic at the Chan Gunn Pavilion under the supervision of at least one member of the research team. The study coordinator is a NSCA Certified Strength and

Conditioning Specialist and trained other members of the research team in proper exercise technique/coaching for the training session exercises.

Participants performed three weekly training sessions consisting of unilateral KE and unilateral DC. Three sets were performed for each exercise and each set was carried out until the participant reached volitional fatigue. Each training session lasted between 20-30 minutes. Volitional fatigue was operationally defined as the inability to perform another concentric contraction through the joint angle with the greatest moment arm. Participants performed all sets of KE before moving onto the DC exercise. No encouragement or motivation was provided to the participants by any member of the research team during the training sessions. The HL limbs were given a load that would elicit volitional fatigue between 6-12 repetitions and the LL limbs were given a load that would elicit volitional fatigue between 20-30 repetitions. Initial training loads were set at 80% and 30% of the KE 1RM for the HL and LL legs, and 90% and 60% DC 1RM for the HL and LL arms respectively. Loads were progressed by 2.5-5 pounds when participants performed more than the upper repetition limit for the given condition for the first set of the previous training session (i.e., if a participant performed 32 repetitions with 50 pounds for the knee extension exercise during their first set on Monday, the load for the first set of the training session on Wednesday would be increased to 52.5-55 pounds). Loads were also adjusted between subsequent sets of the same session to ensure participants continued to fatigue within the predetermined repetition ranges.

When performing the KE exercise participants were instructed to remain seated, to move the weight to the greatest achievable knee extension angle and return the load back to the starting position which was $\sim 90^\circ$ of knee extension. Participants were instructed to perform the concentric and eccentric contractions with control as contraction speed would vary across the

sets as peripheral fatigue began to onset. The KE kick pad arm was set at position two, and the backrest was set at position three for every participant. A foam pad was placed behind participants if their knee was not in line with the axis of rotation of the kick pad arm.

When performing the DC exercise, participants were instructed to keep their upper arm in contact with the bench pad and remain seated. The seat height of the preacher curl bench was adjusted for each participant to ensure that correct form requirements were achieved. A complete repetition for the DC exercise required the participant to lower the weight until their forearm was parallel with the floor ($\sim 120^\circ$ of elbow flexion) and then curl the weight back up until their forearm was perpendicular to the floor ($\sim 45^\circ$ of elbow flexion).

Participants were given two minutes of rest between sets and one to two minutes of rest between exercises. For example, once a participant completed a set of HL KE the trainer would start a timer for two minutes and the next HL KE set would begin once the timer is done; during the two-minute rest of one limb the other limb was exercising as long as its rest period was completed. KE were performed prior to DC for all training sessions. Training session attendance was $93.4 \pm 8.8\%$ across the duration of the study. For a session to be considered completed, all sets of both KE and DC had to have been completed under the direct supervision of a member of the research team. One participant dropped out of the study at week six but was able to perform post-RET testing and so her data was included in all analyses consistent with the intention to treat principle (160). No adverse events occurred because of the study protocol and all participants safely completed all aspects of the trial.

tests using the heavier loads first (i.e., 1st RME/AME TEST) (Appendix G). The primary researcher (MDF) generated all randomization sheets, enrolled all participants, and assigned the participants to the loading conditions. Due to the intervention being resistance training, neither the research team nor the participants were blinded to group allocation.

2.1.4 Body Composition

Body composition was assessed using a GE Prodigy iDXA total body scanner (GE Medical Systems Prodigy, Madison, WI). Participants were asked to record what they ate and drank prior to their pre-RET testing scan and were instructed to consume the same food and drink prior to their post-RET training scan. The DXA scanner was calibrated each testing day in the morning prior to the first scan using a QA Block Phantom (GE Medical Systems Prodigy, Madison, WI). Regions of interest were manually placed on the DXA outputs in accordance with the methodology of Burkhart and colleagues (161). Specifically, regions of interest were placed to encapsulate the thigh and upper arm (Figure 6) segments of the scans to most accurately assess the effects of the RET program. The upper arm segment regions of interest (ROI) was defined by drawing [1] a distal line through the elbow joint space in line with the lateral and medial epicondyles of the humerus, [2] a proximal line placed above the shoulder, [3] medial and lateral lines including all soft tissue between the proximal and distal lines (161). Thigh segment ROIs were defined by drawing [1] a distal horizontal line drawn parallel with the knee joint space, [2] an angled line connecting the inferior ramus of the pubis to the lateral aspect of the anterior superior iliac crest, [3] medial and lateral lines including all soft tissue between the proximal angled line and distal horizontal line (161). Typical error of the thigh and upper arm DXA outputs were calculated using whole arm and leg FBFM data from a previous study examining

DXA output typical error and multiplying this error by the percentage of FBFM that makes up the upper arm and thigh out of the entire arm and leg outputs (67,162).

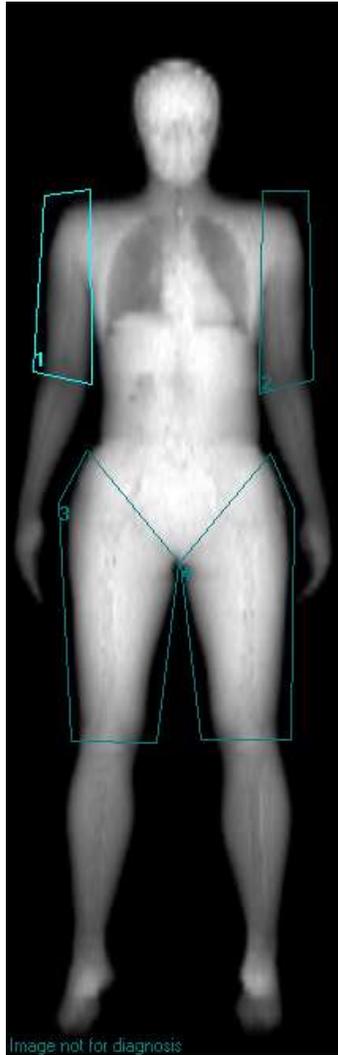


Figure 6. Example image of the custom ranges of interest (ROI) places on the DXA outputs yielding upper and thigh compositions

2.1.5 Strength Testing

Prior to the start of the study participants completed a familiarization session to assess their 3RM for the KE and DC exercises. Participants three-repetition maximums were used to both familiarize them to the exercises/equipment but to also predict their 1RM using an online 1RM prediction equation (<https://www.bodybuilding.com/fun/other7.htm>). Participants returned to the lab between two and seven days after the familiarization session to undergo 1RM testing. Participants performed a brief cycling warmup and a specific warmup of each exercise prior to beginning the 1RM testing procedure. The same 1RM testing procedure was used for the KE and DC exercises and is described as follows. Participants began by performing 5-8 repetitions with ~50% of their predicted 1RM, 2-4 repetitions with ~70% of their predicted 1RM, and 1-2 repetitions with ~85% of their predicted 1RM. The participant then performed single repetitions as the load was gradually increased by 2.5-10 pounds until their 1RM was reached.

A successful 1RM attempt required the participant to move the load through the entire range of motion which was from a starting point of 90° of knee extension to ~170° of knee extension for the KE exercise (only a concentric contraction) and from ~45° to ~120° back to ~45° of elbow flexion for the DC exercise (an eccentric contraction followed by a concentric contraction). Participants were given one minute of rest for the 50%, 70%, and 85% predicted 1RM warmup sets and then given two minutes of rest between all other attempts. For the KE exercise participants were instructed to remain seated, hold onto the support handles on either side of the machine, and to only have motion occurring at the knee joint. For the DC exercise participants were instructed to keep their upper arm in contact with the pad through the entire range of motion, and to only have motion occurring at their elbow joint.

Strength testing was conducted such that each participant performed a complete 1RM test on one leg, then one arm, then the contralateral leg, then the contralateral arm (Appendix I). Participants were randomized as to which loading condition would test 1RM's first (Appendix G) and rested for five minutes before performing the 1RM protocol on the contralateral limb to reduce the cross-transfer effect of strength.

2.1.6 Local Muscle Endurance Testing

Relative muscle endurance (RME) testing had participants performing as many repetitions as possible with 30% and 80% of their current KE 1RM and 60% and 90% of their current DC 1RM. The RME testing was conducted five minutes after the completion of the 1RM testing during the first testing day of the pre- and post-RET testing weeks. The condition testing order and load testing order was randomized for each participant such that half would test RME on their HL limbs first and half would test their LL limbs first and that half would test RME with the lighter relative load first and half would test with the higher relative load first. Participants rested five minutes before performing the RME test on the contralateral limb (Appendix I).

Absolute muscle endurance (AME) testing had participants perform as many repetitions as possible with 30% and 80% of their pre-training KE 1RM and 60% and 90% of their pre-training DC 1RM. The AME testing was conducted after the ultrasound scans on day two of the testing weeks; participants performed a brief cycling warmup followed by an exercise specific warmup prior to the AME testing. The condition testing order and load testing order was randomized for each participant such that half would test AME on their HL limbs first and half would test their LL limbs first and that half would test AME with the lighter absolute load first and half would test with the higher absolute load first. Participants rested five minutes before performing the AME test on the contralateral limb (Appendix J).

2.1.7 Muscle Architecture

Muscle architecture was assessed using a GE Logiq i Ultrasound System (GE Medical Systems Prodigy, Madison, WI). Participants laid supine in anatomical position on a massage table with a pillow was placed under their head for comfort. Participants were instructed to relax the limb that was currently being scanned to ensure the muscle being scanned was in a relaxed/non-contracted state. When scanning the thigh, the participants were instructed to move as close to the edge of the table as possible to ensure the probe could travel across the entire thigh without contacting the table. When scanning the BB participants were instructed to lay with their arm fully extended and to have their forearm supinated.

The VL CSA and PA/FL scans were measured at 60% of the distance from anterior-superior iliac spine (ASIS) to the superior-lateral corner of the patella. Vastus medial oblique (VMO) MT was measured at 80% of the distance from the ASIS to the superior-medial corner of the patella. BB MT was measured at 70% of the distance from the AC joint to the antecubital space. These measurement sites were recorded during visit one and used for both the pre- and post-RET ultrasound scanning sessions to ensure the same site was measured. A small mark was drawn on the skin with a permanent marker at the measurement sites for the VL PA/FL, VMO MT, and BB MT to ensure proper probe placement. For the VL CSA scan, the researchers used a flexible ruler to trace a line perpendicular to the length of the VL which acted as a guide for the probe as this measure required the researcher to move the probe across the thigh. For all scans, a generous amount of ultrasound gel was applied to the measurement site and the probe was applied perpendicular to the skin with minimal pressure to avoid compression and displacement of the tissues. Frequency and Gain were set at 11 Hz and 70 respectively for all ultrasound scans.

Depth was adjusted based on the participants individual anatomy to allow for a complete scan of the necessary muscles. Two scans were taken at each measurement site during each visit.

Ultrasound videos of the VL CSA scans were split into a series of JPG images using a video to JPG software (Free Video to JPG Converter; <https://www.dvdvideosoftware.com/products/dvd/Free-Video-to-JPG-Converter.htm>). These VL CSA JPG images were then manually arranged by a blinded member of the research team using the GIMP software (The GIMP development team; www.gimp.org) to render a panoramic image of the cross-section of this muscle. For the VL PA/FL, VMO MT, and BB MT assessments, videos were viewed by a member of the research team and the clearest frame of the video was used for assessment. Quantification of all muscle architecture characteristics was carried out using the ImageJ software (National Institute of Health, Bethesda, MD, USA). For VL CSA, the polygon tracing tool was used to trace the edges of the VL within the panoramic images (Figure 7). VL (Figure 8), VMO (Figure 9) and BB (Figure 10) MT measurements were taken at the farthest right portion of the imaged muscle belly using the straight-line tool and the line was drawn perpendicular to the bone where one end of the line was placed at the most superficial aspect of the femur/humerus and the other placed at the deepest border of the skin/fascia. Prior to both forms of morphological assessment on ImageJ, images were scaled to actual size using ImageJ's built-in scaling tool and the scale found on the images, as provided from image collection. All scans, image rendering, and image analysis were conducted by the same examiner to reduce inter-rater differences. The examiner was not blinded while performing the ultrasound scans, but was blinded when creating and analyzing the VL panoramic images as well as when selecting and analyzing the images for VL PA/FL, VMO MT, and BB MT. Typical error for the ultrasound scans were calculated by dividing the standard deviation of the change between

familiarization and pre-RET values by the square root of two which represents the number of trials being compared; the ultrasound typical error equation is presented below (162).

$$\text{Typical Ultrasound Error} = SD \text{ of change} / \sqrt{2}$$

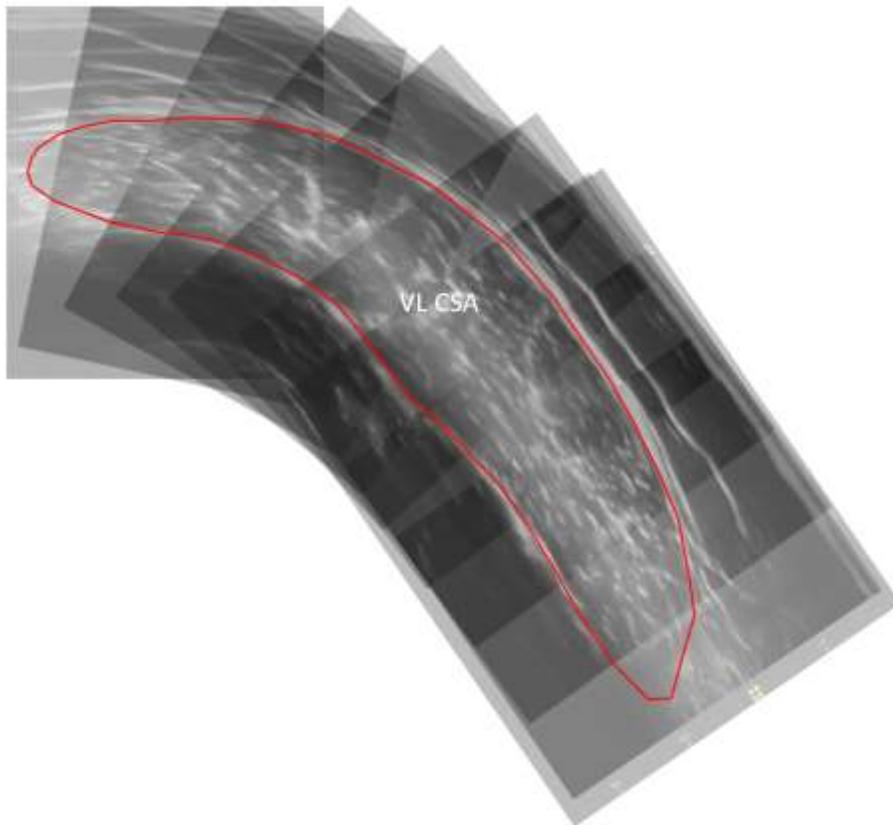


Figure 7. Example stitched image showing the cross section of the vastus lateralis (VL) that was used to quantify VL cross-sectional area (CSA)

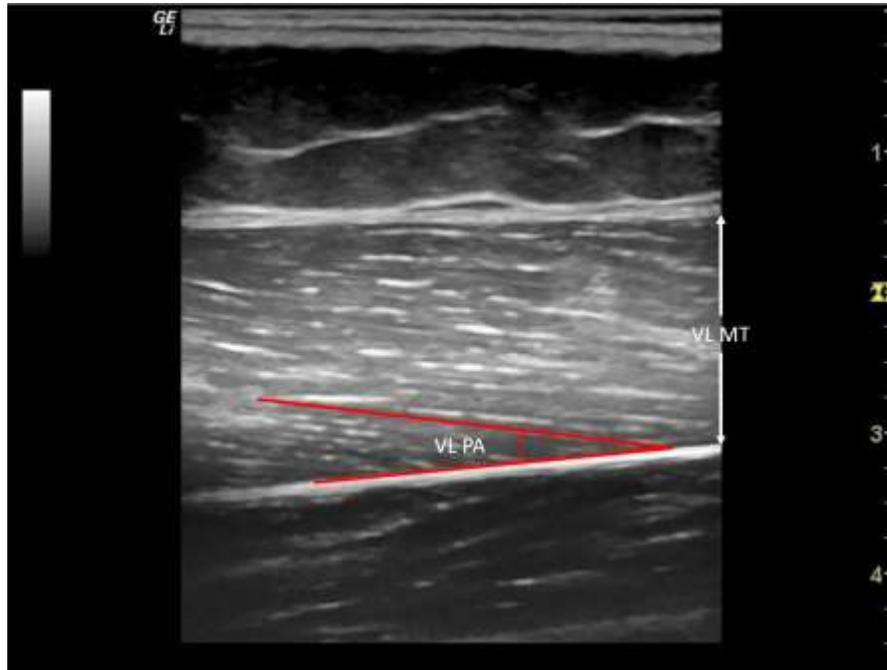


Figure 8. Example image of the vastus lateralis (VL) that was used to quantify VL muscle thickness (MT) and VL pennation angle

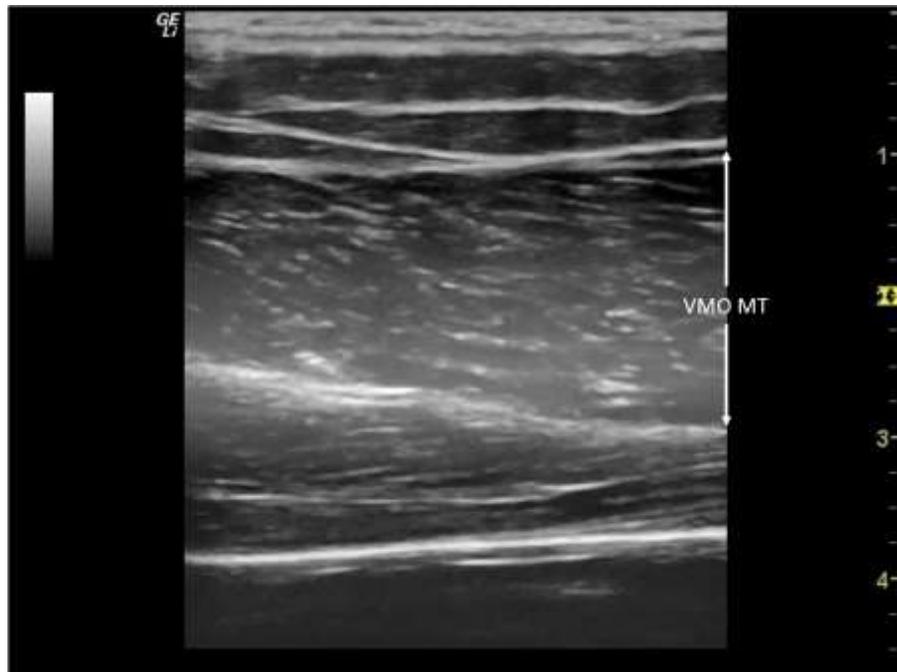


Figure 9. Example image of a participant's vastus medialis oblique (VMO) that was used to quantify VMO muscle thickness (MT)

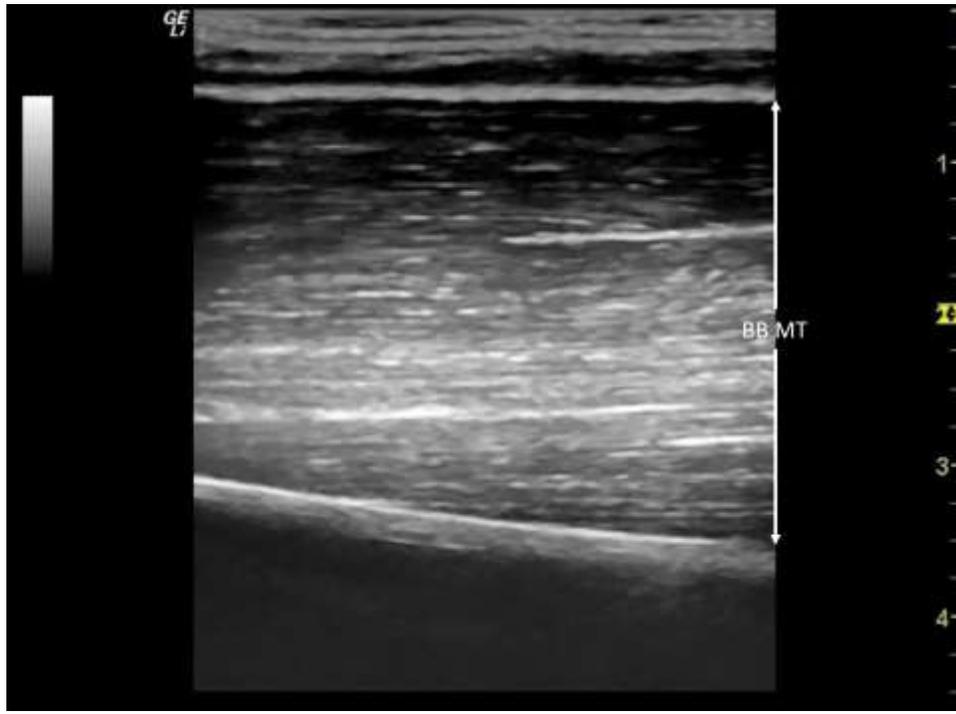


Figure 10. Example image of a participant's biceps brachii (BB) that was used to quantify BB muscle thickness

2.1.8 Training Volume

Set-volume was calculated by multiplying the load used by the number of repetitions completed for each set. Weekly-volume was calculated by summing all set-volumes for each of the three sessions within a single week of training. Total-volume was calculated by summing all weekly-volumes across the entire 10-week training period.

2.1.9 Protein Supplementation

Participants consumed two 30 g boluses of whey protein (Whey Protein Concentrate, 127 kcal, 8.8 g leucine, 24 g protein, 2 g carbohydrate, 2.5 g fat; Canadian Protein, Windsor, ON) or vegan protein (All-Natural Premium Vegan Protein Blend, 122 kcal, 6.2 g leucine, 22 g protein, 6 g carbohydrate, 2 g fat; Canadian Protein, Windsor, ON) every day during the 10-week training period. Vegan protein was only given to participants who could not consume the whey protein option due to dietary or religious reasons or to those who were still in the study when there were

no more whey protein doses. On training days, participants would consume a dose immediately after training and then would consume their second dose either in the morning or in the evening depending on when they trained during the day. On non-training days participants were instructed to consume one dose in the morning and one dose at night. Participants were instructed to avoid consuming a dose with a meal that already had a high protein content and were told they could consume the protein boluses however they chose.

2.1.10 Typical Measurement Error Calculations

Typical measurement error for the ultrasound scans was calculated as the absolute difference between the familiarization and pre-RET scans. Typical measurement error for DXA was calculated using data from a previous study assessing DXA reliability (67). As Kutáč and colleagues presented error values based on total right arm and right leg lean mass, these values were scaled to 50% and 80% to represent the expected lean mass of the upper arm and thigh, respectively. The upper limit of the typical error of the arm was 0.1 kg which was scaled to 0.05 kg, and the upper limit of the typical error of the leg was 0.28 kg which was scaled to 0.22 kg (67).

2.1.11 Statistical Analyses

All data presented in this thesis are in means \pm standard deviation (SD) and were assessed using the Statistical Package for Social Sciences (SPSS) (IBM; Version 28.0.0.0). An intention-to-treat analysis was used for 16/16 participants per condition. Two-factor repeated measures analysis of variance (ANOVA) with time (pre-RET and post-RET) and limb (HL and LL) as factors was used to analyze the limb FBFM, 1RM strength, RME load/repetitions completed/load product, AME load and repetitions completed, VL pennation angle/fascicle length/muscle thickness, VMO muscle thickness, and BB muscle thickness outcomes with Sidak post-hoc tests

being used where necessary to identify significance. Upper- and lower-limb data were assessed independent of each other for the two-factor ANOVA's. Two-sample, two one-sided equivalence test (TOST) was used to assess equivalence of changes in FBFM between loading conditions for both the upper- and lower-body. For the TOST analysis, the equivalence margin was set at -3.5% to 3.5% which was calculated by taking 70% of the lower-limit of the confidence interval for the mean change in muscle mass from Schoenfeld and colleagues systematic review with meta-analysis (38). All data was assessed for normality using the Shapiro-Wilks test. Non-normally distributed data was transformed by \log_{10} and then analyzed. Extreme outliers were removed prior to any analysis and were identified by the SPSS software as being data points greater than three interquartile ranges from the end(s) of the boxplot(s).

2.2 RESULTS

2.2.1 Body Composition

Following the 10-week training intervention total body mass (-0.6 ± 1.6 kg; Time $P = 0.18$), total body FBFM (-0.1 ± 1.1 ; Time $P = 0.86$), total body FM (-0.6 ± 1.5 ; Time $P = 0.12$), and appendicular FBFM (0.1 ± 0.5 kg; Time $P = 0.56$) did not change. HL upper arm FBFM did not change (0.00 ± 0.04 kg) while LL upper arm FBFM increased by 0.06 ± 0.07 kg, with the difference in changes reaching significance (Time \times Limb $P = 0.02$) (Figure 11, panel A). After training, both the HL and LL leg thigh FBFM remained unchanged (HL = 0.1 ± 0.22 kg; LL = 0.04 ± 0.2 kg), with no difference between groups (Time \times Limb $P = 0.21$) (Figure 11, panel B). The 90% confidence interval for the mean change in LL upper arm FBFM minus the mean change in HL upper arm FBFM was (2%, 10.2%) which lies outside of the equivalence limits (-3.5, 3.5%) which means equivalence cannot be claimed (Appendix K, panel B). The 90% confidence interval for the mean change in LL thigh FBFM minus the mean change in HL thigh FBFM was (-3.6, 0.95%) which lies outside of the equivalence limit (-3.5, 3.5%) meaning equivalence cannot be claimed (Appendix K, panel C) (Table 2).

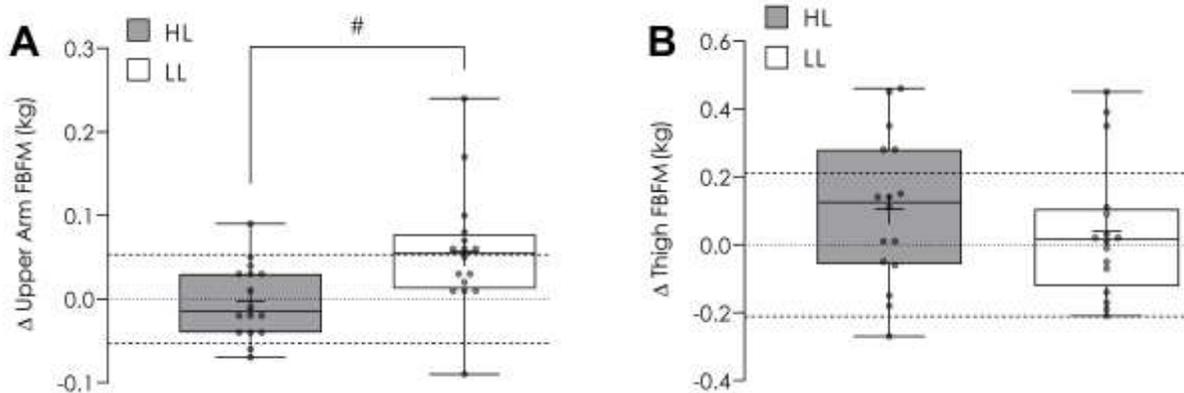


Figure 11. Fat and bone free mass (FBFM) changes following 10 weeks of higher load (HL) or lower load (LL) resistance exercise training (RET). (A) Change in upper arm FBFM. The dashed lines represent the typical error range of the DXA scanner for the upper arm (± 0.06 kg). (B) Change in thigh FBFM. The dashed lines represent the typical error range of the DXA scanner for the thigh (± 0.22 kg). Values are presented as median (lines) with interquartile range (boxes), error bars (minimum and maximum), and mean being represented by +. Each dot represents a single participant. #Significant interaction effect ($P \leq 0.05$) between conditions.

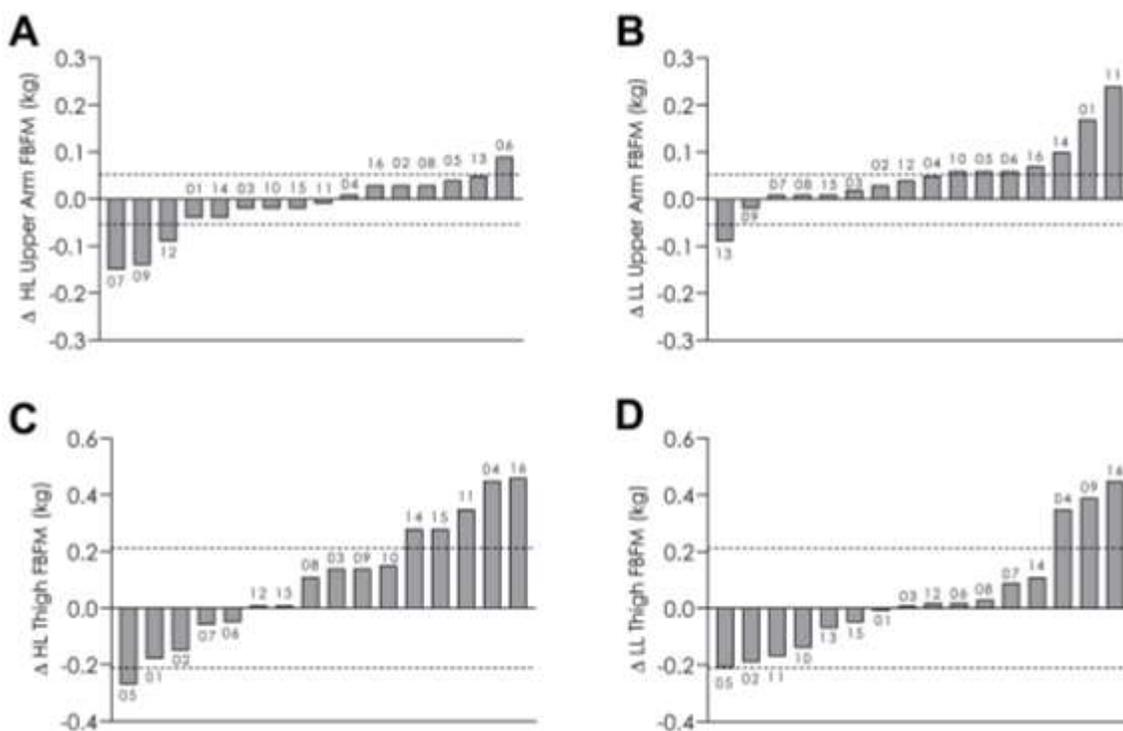


Figure 12. (A) A waterfall plot depicting individual participant HL upper arm FBFM changes. The dashed lines represent the typical error range of the DXA scanner for the upper arm (± 0.06 kg). (B) A waterfall plot depicting individual participant LL upper arm FBFM changes. The dashed lines represent the typical error range of the DXA scanner for the upper arm (± 0.06 kg). (C) A waterfall plot depicting individual participant HL thigh FBFM changes. The dashed lines represent the typical error range of the DXA scanner for the thigh (± 0.22 kg). (D) A waterfall plot depicting individual participant LL thigh FBFM changes. The dashed lines represent the typical error range of the DXA scanner for the thigh (± 0.22 kg). Each bar represents the change in FBFM for an individual participant (i.e., FBFM changes for participant three are depicted with “03” through graphs A-D).

2.2.2 Strength

KE 1RM strength increased by 12.5 ± 4.8 and 6.6 ± 5.8 kg in the HL and LL conditions respectively, with this increase being larger in the HL condition (Time \times Limb $P < 0.01$) (Figure 13, panel A). For DC 1RM strength, the HL condition improved by 5.6 ± 2.2 kg and the LL condition improved by 5.1 ± 1.5 kg with no differences between groups (Time \times Limb $P = 0.46$) (Figure 13, panel B) (Table 3).

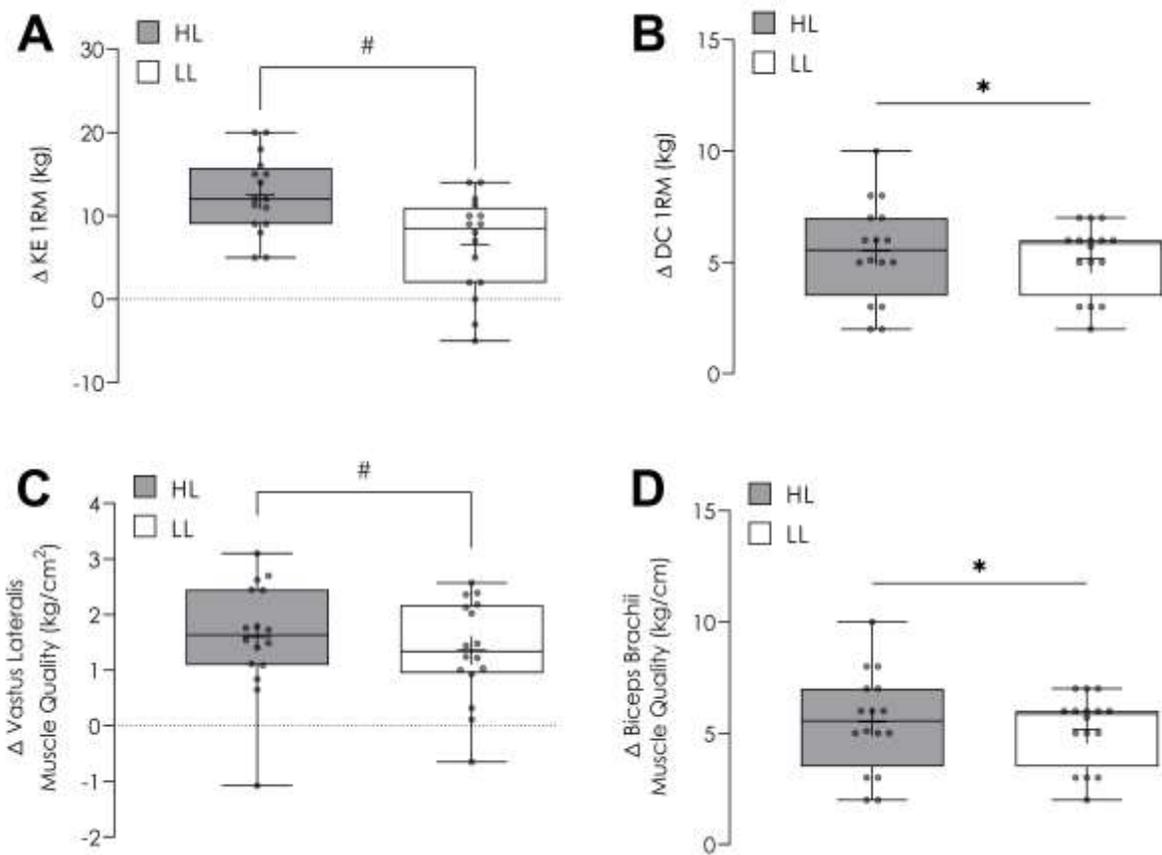


Figure 13. Strength changes following 10 weeks of higher load (HL) and lower load (LL) resistance exercise training (RET). (A) Change in knee extension (KE) 1RM. (B) Change in dumbbell preacher curl (DC) one repetitions maximum (1RM). (C) Change in vastus lateralis muscle quality. (D) Change in biceps brachii muscle quality. Values are presented as median (lines) with interquartile range (boxes), error bars (minimum and maximum), and mean being represented by +. Each dot represents a single participant. *Time main effect for both conditions ($P \leq 0.05$). #Significant interaction effect ($P \leq 0.05$) between conditions.

2.2.3 Relative Muscle Endurance

2.2.3.1 KE RME

Loads used and repetitions performed increased by 9.9 ± 3.7 kg and 1.3 ± 4.3 repetitions in the HL leg, and 5.9 ± 4.1 kg and 1.7 ± 4.3 repetitions for the LL leg for the heavy load RME test with the load increases being different between groups (Time \times Limb $P < 0.01$), but no difference in the change in repetitions completed (Time \times Limb $P = 0.61$). The load product for the heavy load RME test increased by 137.7 ± 207.8 kg for the HL leg and 120.8 ± 167 kg for the LL leg with no differences between conditions (Time \times Limb $P = 0.74$). Loads used and repetitions performed increased by 3.7 ± 1.4 kg and 8.3 ± 9 repetitions in the HL leg, and 2.2 ± 1.4 kg and 20.6 ± 13.9 repetitions in the LL leg for the light load KE RME test with an interaction effect present for both the change in load (Time \times Limb $P < 0.01$), as well as the change in repetitions completed (Time \times Limb $P < 0.01$) between conditions. The load product for the light load KE RME test increased by 264.8 ± 147.2 kg and 397.1 ± 163.4 kg in the HL and LL legs respectively with the LL leg showing a greater increase (Time \times Limb $P = 0.02$) (Figure 14) (Table 4).

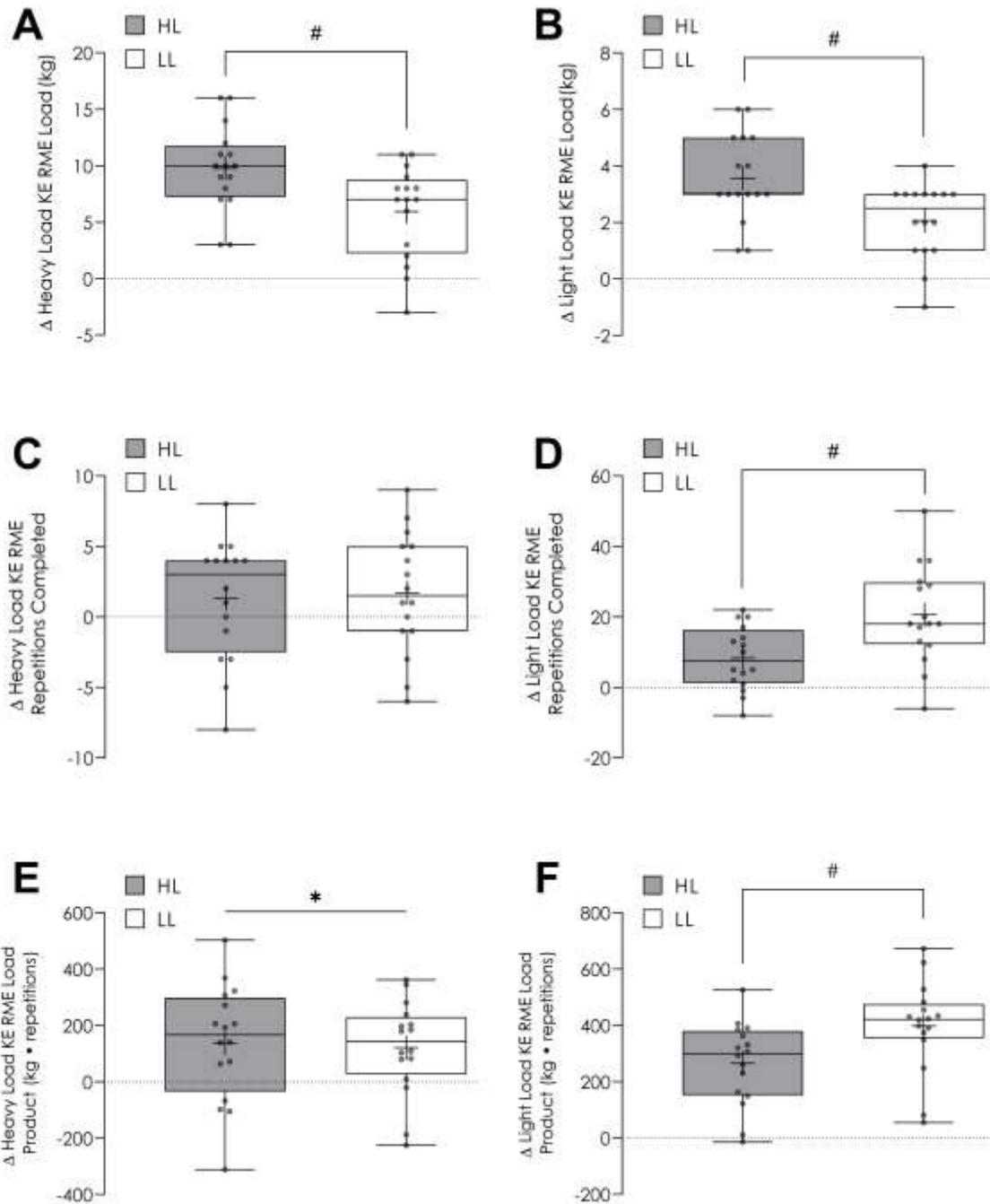


Figure 14. Load and repetitions completed changes for the knee extension (KE) heavy load relative muscle endurance and light load relative muscle endurance (RME) tests following 10 weeks of higher load (HL) and lower load (LL) resistance exercise training (RET). (A) Change in the load used for the heavy load KE RME test. (B) Change in repetitions completed for the heavy load KE RME test. (C) Change in the load used for the light KE lower load RME test. (D) Change in the repetitions completed for the light load KE RME test. (E) Change in load product for the heavy load KE RME test. (F) Change in load product for the light load KE RME test. Values are presented as median (lines) with interquartile range (boxes), error bars (minimum and maximum), and mean being represented by +. Each dot represents a single participant. #Significant interaction effect ($P \leq 0.05$) between conditions.

2.2.3.2 DC RME

There was no observed difference in the increase in load used for the light load DC RME test between the HL (3.3 ± 1.4 kg) and LL (2.9 ± 0.8 kg) conditions (Time \times Condition $P = 0.38$), or the change in total repetitions performed by the HL (7.2 ± 12.8 repetitions) and LL (13.4 ± 11 repetitions) and (Time \times Condition $P = 0.06$) arms. The load product for the light load DC RME test increased by 166.4 ± 119.7 kg and 212.6 ± 102.5 kg in the HL and LL arms respectively with no differences between conditions (Time \times Condition $P = 0.08$). There was no observed difference in the increase in load used for the heavy load DC RME test between the HL (5.3 ± 2.1 kg) and LL (4.9 ± 1.4 kg) conditions (Time \times Condition $P = 0.58$), or the change in repetitions performed for the HL (1.6 ± 5.9 repetitions) and LL (1.7 ± 6.2 repetitions) (Time \times Condition $P = 0.67$). The load product for the heavy load DC RME test increased by 53.8 ± 57.5 kg and 52.9 ± 66.9 kg in the HL and LL arms respectively with no differences between conditions (Time \times Condition $P = 0.95$). (Figure 15) (Table 5).

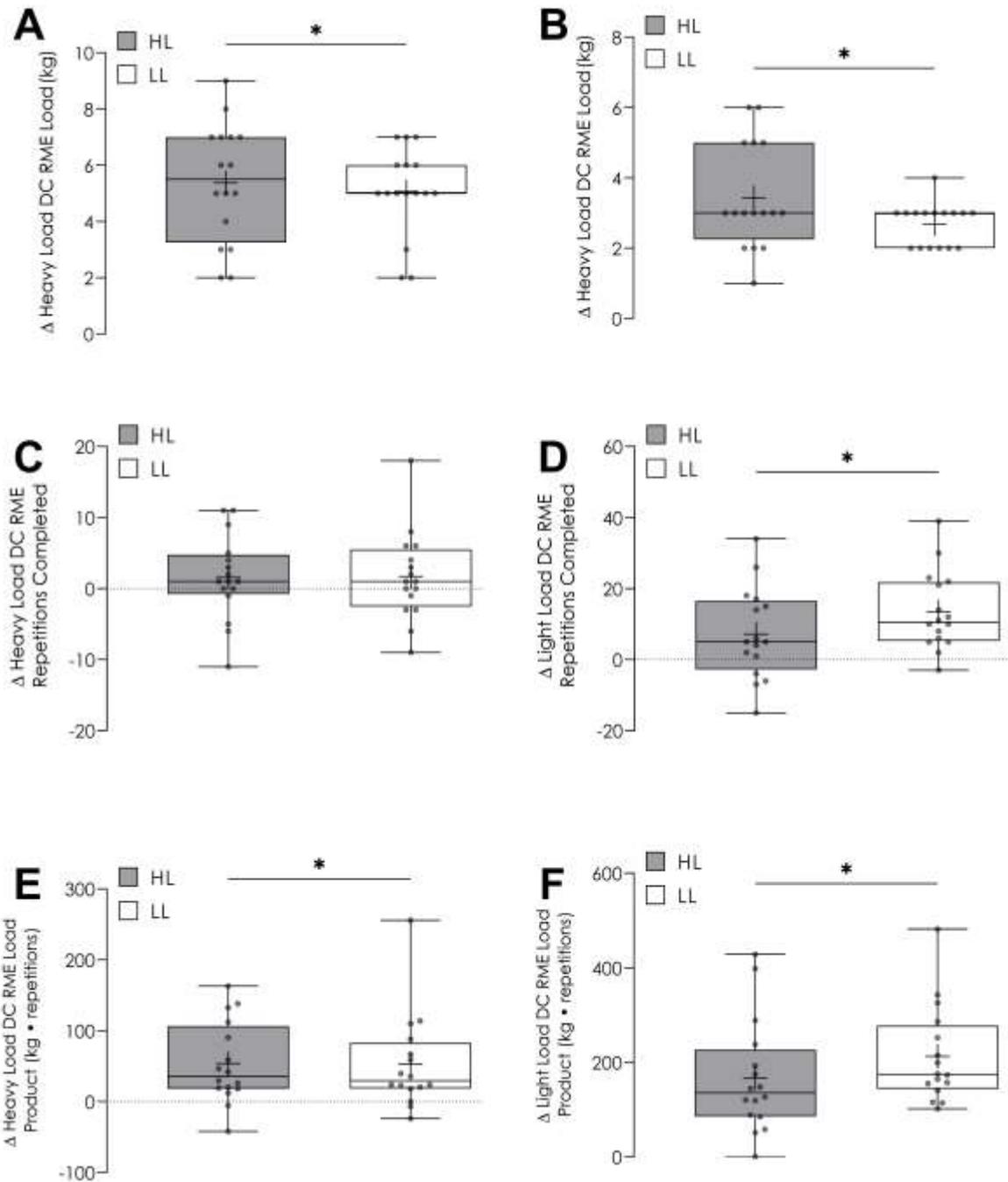


Figure 15. Load and repetitions completed changes for the dumbbell preacher curl (DC) heavy and light load relative muscle endurance (RME) tests following 10 weeks of higher load (HL) and lower load (LL) resistance exercise training (RET). (A) Change in the load used for the heavy load DC RME test. (B) Change in repetitions completed for the heavy load DC RME test. (C) Change in the load used for the light load DC RME test. (D) Change in the repetitions completed for the light load DC RME test. (E) Change in load product for the heavy load DC RME test. (F) Change in load product for the light load DC RME test. Values are presented as median (lines) with interquartile range (boxes), error bars (minimum and maximum), and mean being represented by +. Each dot represents a single participant. *Time main effect for both conditions ($P \leq 0.05$). One extreme outlier was removed from panel C for the HL arm condition.

2.2.4 Absolute Muscle Endurance

2.2.4.1 KE AME

The loads used for the heavy load KE AME tests were 37.6 ± 8.9 kg and 37.6 ± 8.4 kg for the HL and LL conditions respectively with no differences between conditions (Limb $P = 0.81$). Total repetitions performed increased by 9.3 ± 4.3 in the HL leg and 7.5 ± 7.1 in the LL leg with the increase in the HL being greater than that of the LL leg (Time \times Limb $P < 0.01$). The loads used for the light load KE AME tests were 14.2 ± 3.4 kg and 14.1 ± 3 kg for the HL and LL conditions respectively with no differences between conditions (Limb $P = 0.81$). Total repetitions performed increased by 15.2 ± 16.7 in the HL leg and 24.7 ± 22.2 in the LL leg with this difference reaching significance (Time \times Limb $P = 0.04$) (Figures 16 and 17) (Table 6).

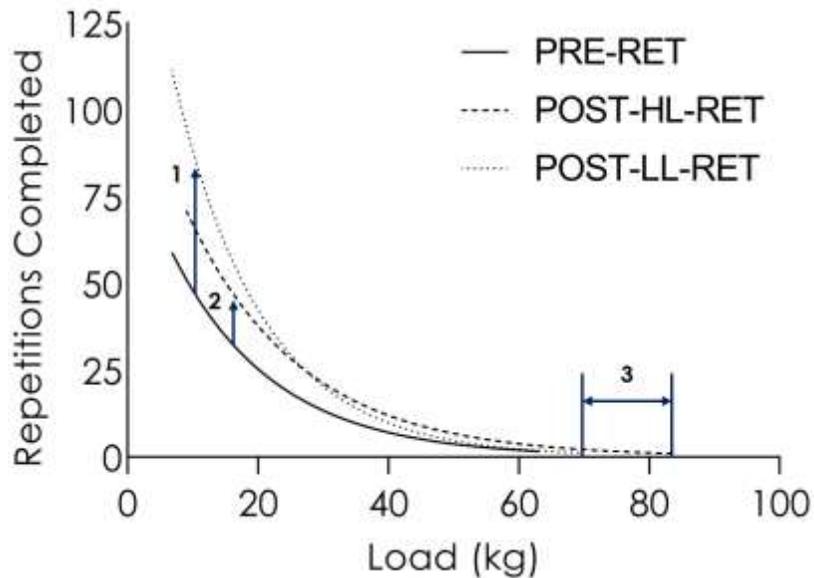


Figure 16. The relationship between the maximum repetitions performed with set absolute load for the knee extension (KE) exercise. Each line represents a semilog curve (x is linear and y is logarithmic) fit to the dataset of each time point (i.e., pre-RET, post HL-RET, and post LL-RET). (1) The improvement in LL AME from LL RET is likely due to increases in metabolite clearance, buffering capacity and/or capillarization alongside smaller increases in strength. (2) increases in LL/HL AME from HL-RET are primarily due to increases in maximal strength. (3) HL-RET improves maximal strength to a greater extent compared to LL-RET.

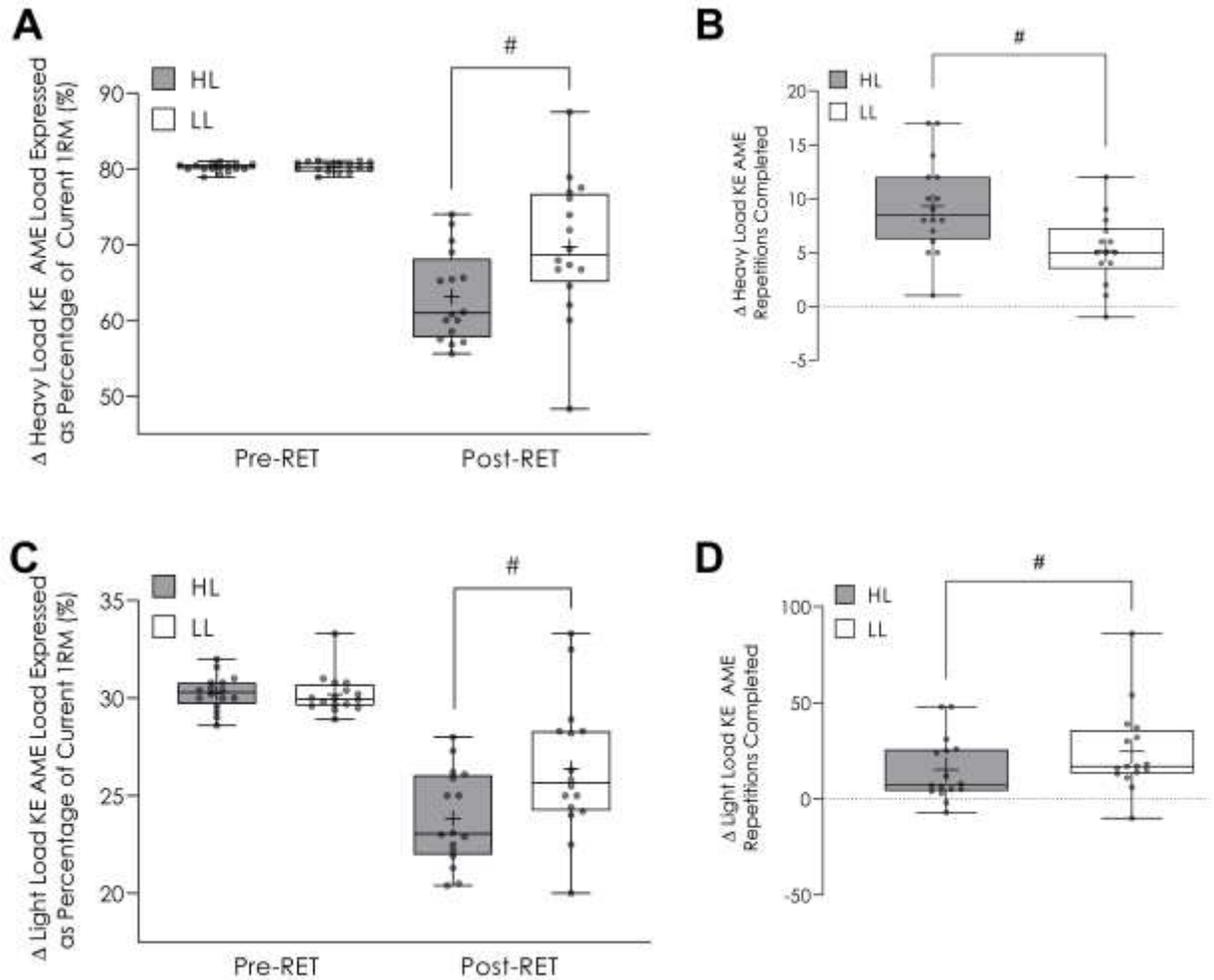


Figure 17. Changes in load expressed as percentage of current one repetition maximum (1RM) and repetitions completed for the knee extension (KE) heavy and light load absolute muscle endurance (AME) tests following 10 weeks of higher load (HL) and lower load (LL) resistance exercise training (RET). (A) Pre- and post-RET absolute load expressed as percentage of current 1RM for the heavy load KE AME test. (B) Change in repetitions completed for the heavy load KE AME test. (C) Pre- and post-RET absolute load expressed as percentage of current 1RM for the light load KE AME test. (D) Change in the repetitions completed for the light load KE AME test. Values are presented as median (lines) with interquartile range (boxes), error bars (minimum and maximum), and mean being represented by +. Each dot represents a single participant. *Time main effect for both conditions ($P \leq 0.05$). #Significant interaction effect ($P \leq 0.05$) between conditions. Two extreme outliers were removed from panel B from the LL leg condition.

2.2.4.2 DC AME

The loads used for the light load DC AME tests were 6.3 ± 1.1 kg and 6 ± 1.2 kg for the HL and LL conditions respectively with no difference between conditions (Limb $P = 0.06$). Total repetitions performed increased by 77.7 ± 73.4 in the HL arm and 113.6 ± 121.6 in the LL arm with no difference in these increases between conditions (Time \times Limb $P = 0.99$). The loads used for the heavy load DC AME tests were 9.1 ± 1.9 kg and 8.8 ± 2 kg for the HL and LL conditions respectively with no differences between conditions (Limb $P = 0.14$). Total repetitions performed increased by 33 ± 16.9 in the HL arm and 35.8 ± 17.4 in the LL arm with no difference in these increases between conditions (Time \times Limb $P = 0.16$) (Figures 18 and 19) (Table 7).

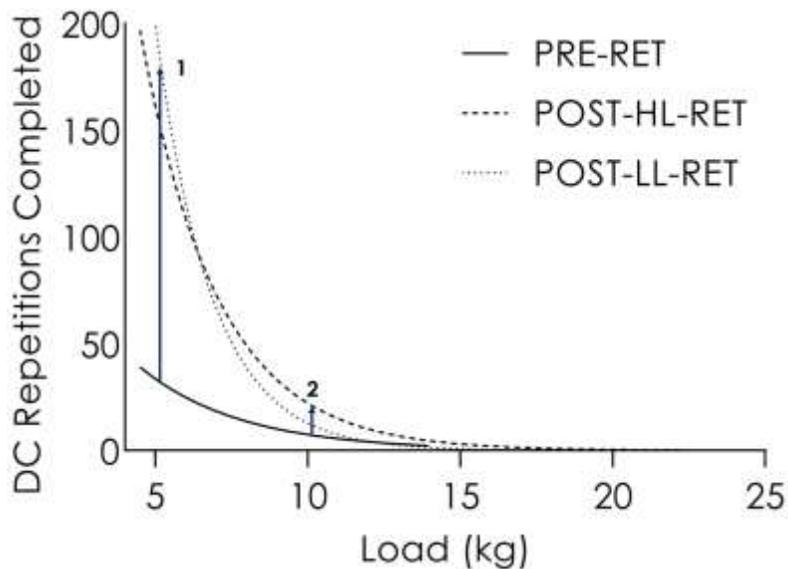


Figure 18. The relationship between the maximum repetitions performed with set absolute load for the dumbbell preacher curl (DC) exercise. Each line represents a semilog curve (x is linear and y is logarithmic) fit to the dataset of each time point (i.e., pre-RET, post HL-RET, and post LL_RET). (1) LL RET shows a trend for preferential improvement for light load AME but high variation in repetitions performed led to similar changes being observed. (2) HL RET appears to preferentially improve heavy load AME, but the changes were similar between conditions due to similar loads being used over the training period.

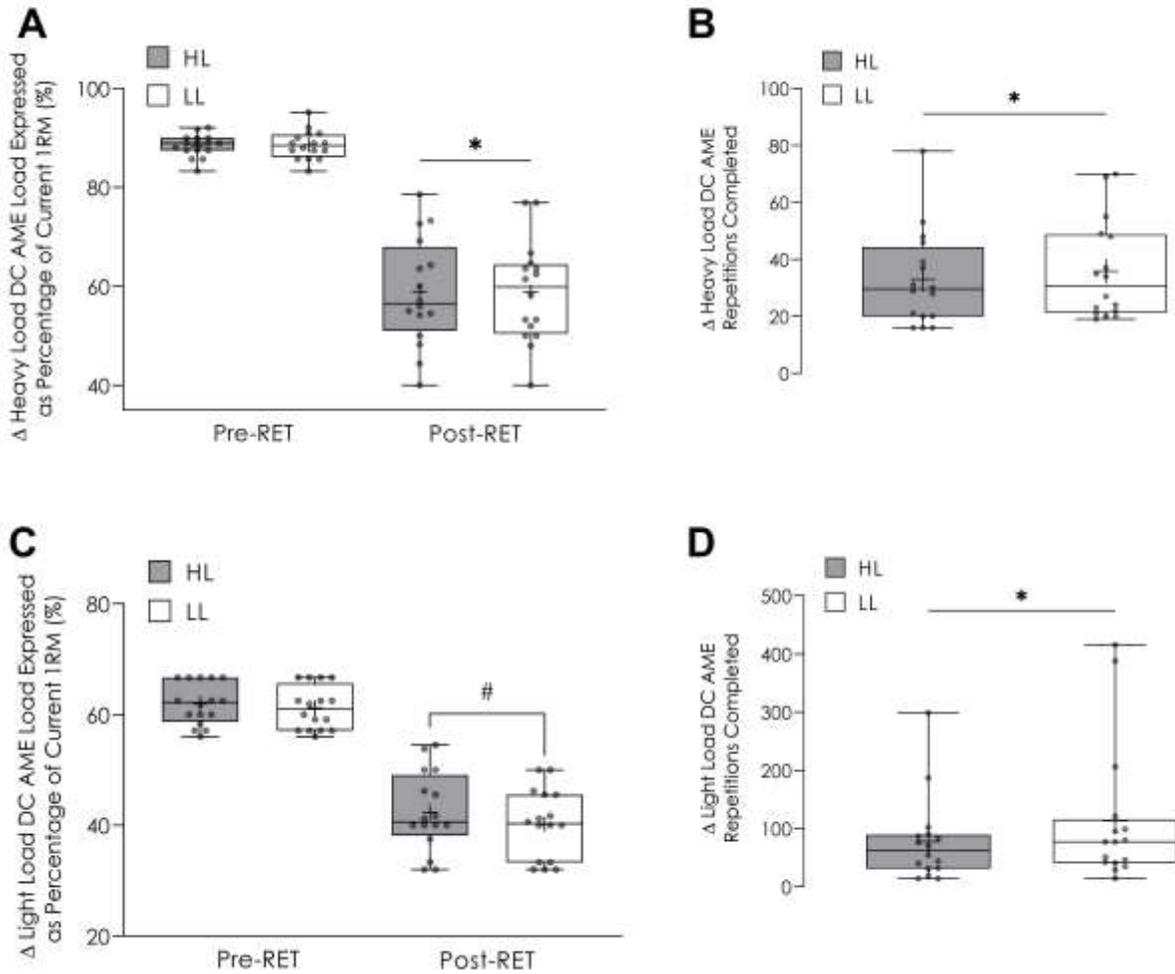


Figure 19. Changes in load expressed as percentage of current one repetition maximum (1RM) and repetitions completed changes for the dumbbell preacher curl (DC) heavy and light load absolute muscle endurance AME tests following 10 weeks of higher load (HL) and lower load (LL) resistance exercise training (RET). (A) Pre- and post-RET absolute load expressed as percentage of current 1RM for the heavy load DC AME test. (B) Change in repetitions completed for the heavy load DC AME test. (C) Pre- and post-RET absolute load expressed as percentage of current 1RM for the light load DC AME test. (D) Change in the repetitions completed for the light load DC AME test. Values are presented as median (lines) with interquartile range (boxes), error bars (minimum and maximum), and mean being represented by +. Each dot represents a single participant. *Time main effect for both conditions ($P \leq 0.05$). #Significant interaction effect ($P \leq 0.05$) between conditions.

2.2.5 Muscle Architecture

VL CSA did not change in either condition following RET (HL = 0.5 ± 3.5 ; LL = 0.3 ± 3 cm²) (Time $P = 0.62$) (Figure 18, panel A). VL MT did not change in either condition following RET (HL = 0.1 ± 0.3 ; LL = 0 ± 0.26 cm) (Time $P = 0.46$) (Figure 20, panel B). VL fascicle length remained unchanged following the RET program (HL = -0.7 ± 5.1 ; LL = 0.3 ± 4.3 cm) (Time $P = 0.92$) (Figure 20, panel C). Pennation angle did not change in either condition following the RET period (HL = 0.5 ± 2.3 ; LL -0.4 ± 3.2 degrees) (Time $P = 0.85$) (Figure 20, panel D). VMO MT did not change following the training program (HL = 0.1 ± 0.5 ; LL = 0.2 ± 0.4 cm) (Time $P = 0.32$) (Figure 21, panel A). HL arm BB MT increased by 0.2 ± 0.4 cm and the LL arm BB MT increased by 0.3 ± 0.4 cm with these increases being similar between conditions (Time \times Limb $P = 0.12$) (Figure 21, panel B). The 90% confidence interval for the mean change in LL BB MT minus the mean change in HL BB MT was (-6.1, 13.7%) which lies outside of the equivalence interval (-3.5, 3.5%) meaning equivalence cannot be claimed (Appendix K, panel A) (Table 8).

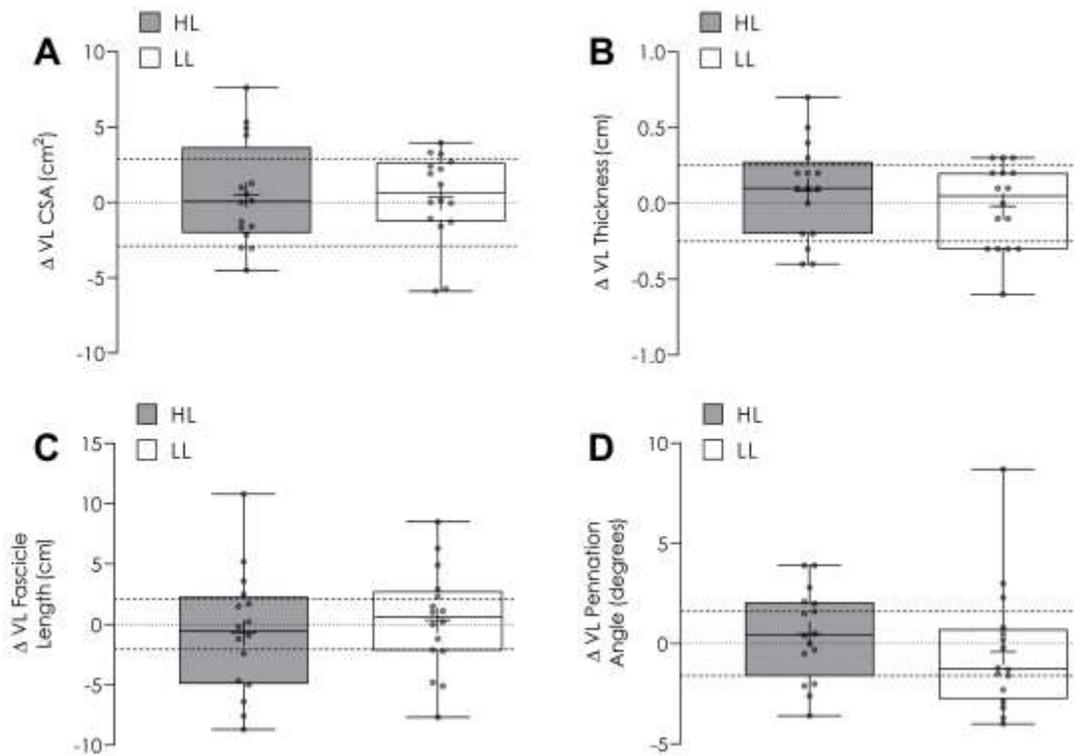


Figure 20. Changes in vastus lateralis (VL) muscle architecture characteristics following 10-weeks of either higher load (HL) or lower load (LL) resistance exercise training (RET). (A) Change in VL cross sectional area (CSA). The dashed lines represent the error of the ultrasound technique for the VL CSA (± 3.17 cm). (B) Change in VL muscle thickness. The dashed lines represent the error of the ultrasound technique for the VL muscle thickness (MT) (± 0.29 cm). (C) Change in VL fascicle length. The dashed lines represent the error of the ultrasound technique for the VL fascicle length (FL) (± 2.14 cm). (D) Change in VL pennation angle. The dashed lines represent the error of the ultrasound technique for the VL pennation angle (PA) (± 1.63 degrees). Values are presented as median (lines) with interquartile range (boxes), error bars (minimum and maximum), and mean being represented by +. Each dot represents a single participant.

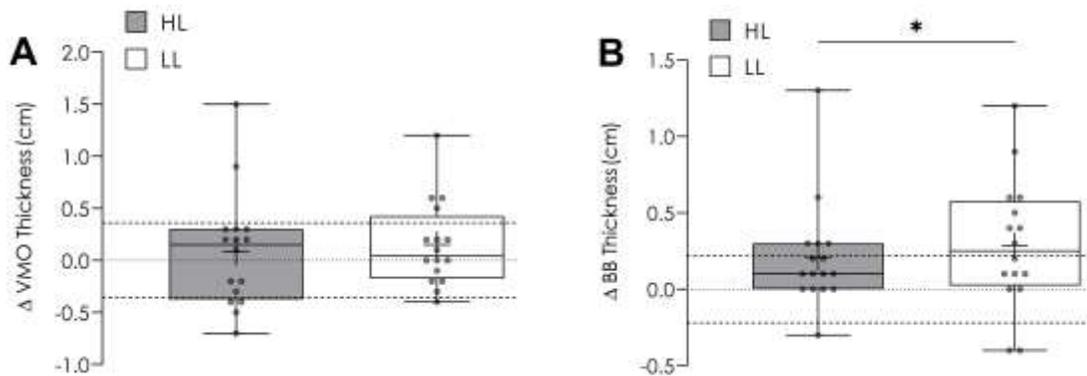


Figure 21. Changes in vastus medialis oblique (VMO) and biceps brachii (BB) muscle thickness following 10-weeks of higher load (HL) or lower load (LL) resistance exercise training (RET). (A) Change in VMO muscle thickness. The dashed lines represent the error of the ultrasound technique for the VMO muscle thickness (MT) (± 0.4 cm). (B) Change in BB muscle thickness. The dashed lines represent the error of the ultrasound technique for the BB muscle thickness (MT) (± 0.24 cm). Values are presented as median (lines) with interquartile range (boxes), error bars (minimum and maximum), and mean being represented by +. Each dot represents a single participant. *Time main effect for both conditions ($P \leq 0.05$).

2.2.6 Resistance Training Volume

Average total training volume was 36309 ± 9713 and 49823 ± 12400 kg for the HL and LL legs respectively with the LL condition performing significantly more volume (Limb $P < 0.01$) (Figure 22, panel A). The HL arm average total training volume was 8794 ± 1894 kg and the LL arm average total training volume was 16598 ± 3948 kg, with this difference reaching significance (Limb $P < 0.01$) (Figure 22, panel B).

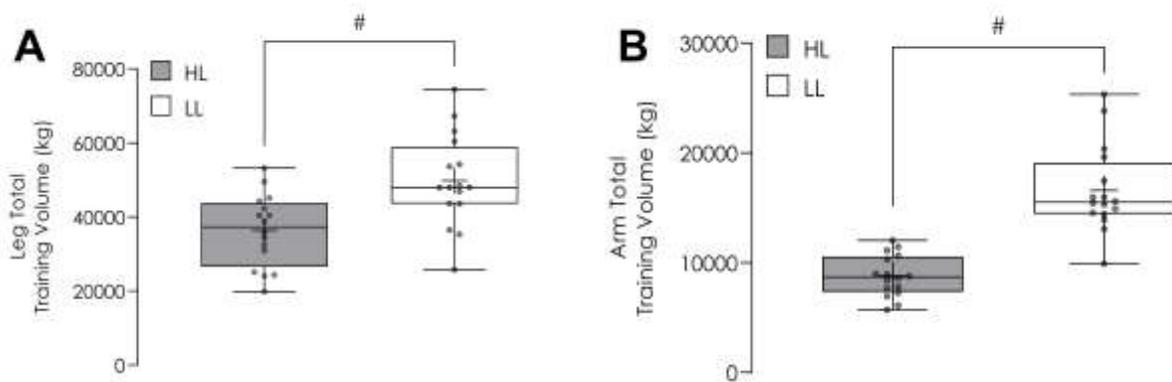


Figure 22. Total training volume summed across the 10-week RET intervention for the higher load (HL) and lower load (LL) arms and legs. (A) Total training volume for HL and LL legs. (B) Total training volume for the HL and LL arms. Values are presented as median (lines) with interquartile range (boxes), error bars (minimum and maximum), and mean being represented by +. Each dot represents a single participant. #Significantly different ($P \leq 0.05$) between conditions.

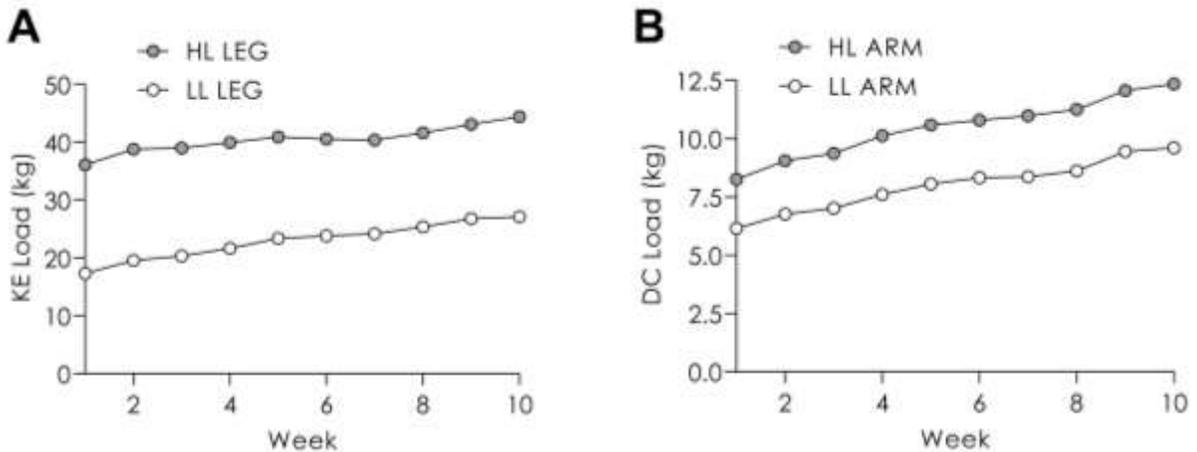


Figure 23. Average absolute load used across the training period for the knee extension (KE) and dumbbell preacher curl (DC) exercises. (A) Average change in training load for KE following higher load (HL) and lower load (LL) resistance exercise training (RET). (B) Average change in training load for DC following HL and LL RET.

2.2.7 Menstrual Cycle Tracking

13 participants (81%) self-reported taking no form of hormonal contraception or other form of birth control when asked at the onset of the study period. All 16 participants self-reported either the current day of their menstrual cycle or hormonal contraception use during the pre-RET testing period. During pre-RET testing, nine participants (56%) were in the follicular phase of their current menstrual cycle and two participants (12.5%) were in the luteal phase of their current cycle. Two participants (12.5%) began menstruation between pre-RET testing days and as such were in their luteal phase for the first day of testing and the follicular phase for their second day of testing. Three participants (19%) were using some form of hormonal contraceptive during pre-RET testing. 11 out of 16 participants self-reported either the current day of their menstrual cycle or hormonal contraception use during the post-RET testing period. During post-RET testing, four participants (36%) were in the follicular phase of their current menstrual cycle and six participants (54.5%) were in the luteal phase of their current cycle. One participant (9%) began menstruation between post-RET testing days and as such were in their luteal phase for the first day of testing and the follicular phase for their second day of testing.

Table 2. Changes in limb FBFM following higher- and lower-load resistance exercise training

	HL			LL			Effect		
	Pre	Post	Δ%	Pre	Post	Δ%	Time	Limb	Time × Limb
Thigh FBFM (kg)	5.62±0.77	5.72±0.77	2±4.4	5.67±0.69	5.71±0.74	0.7±3.6	0.14	0.79	0.21
Upper Arm FBFM (kg)	1.08±0.19 [†]	1.07±0.19	-1.4±6.2	1.05±0.16	1.07±0.19 [‡]	5.3±8.7	0.23	0.1	0.02 [*]

Values are means ± standard deviation. ^{*}Significant main effect or interaction, $P \leq 0.05$. [‡]Different from pre-intervention within the same condition, $P \leq 0.05$. [†]Different between conditions at indicated time point, $P \leq 0.05$. HL, higher load; LL, lower load; FBFM, fat and bone free mass.

Table 3. Changes in strength following higher- and lower-load resistance exercise training

	HL			LL			Effect		
	Pre	Post	Δ%	Pre	Post	Δ%	Time	Limb	Time × Limb
KE 1RM (kg)	46.9±11	59.5±12.5 ^{††}	27±11.2	46.9±10.4	53.5±10.4 [‡]	13.2±12.3	<0.01 [*]	0.04 [*]	<0.01 [*]
VL MQ (kg/cm ²)	2.5±0.6	3.2±0.7 ^{††}	28.5±24.5	2.5±0.6	2.8±0.6 [‡]	14.3±19.5	<0.01 [*]	0.02 [*]	0.02 [*]
DC 1RM (kg)	10.3±2	15.8±2.8 [‡]	59±25.3	9.9±2.1	15±2 [‡]	56.5±23.9	<0.01 [*]	0.07	0.46
BB MQ (kg/cm)	3.8±0.9	5.4±0.9 ^{††}	48±19.5	3.7±0.8	5.1±0.7 [‡]	41.9±31	<0.01 [*]	0.04 [*]	0.16

Values are means ± standard deviation. ^{*}Significant main effect or interaction, $P \leq 0.05$. [‡]Different from pre-intervention within the same condition, $P \leq 0.05$. [†]Different between conditions at indicated time point, $P \leq 0.05$. HL, higher load; LL, lower load; KE, knee extension; 1RM, one repetition maximum; DC, dumbbell preacher curl; MQ, muscle quality.

Table 4. Changes in knee extension relative muscle endurance following higher- and lower-load resistance exercise training

	HL			LL			Effect		
	Pre	Post	Δ%	Pre	Post	Δ%	Time	Limb	Time × Limb
HL RME									
Load (kg)	37.6±8.9	47.5±10 ^{††}	27.7±11.5	37.6±8.4	43.6±9 [‡]	17.8±16.6	<0.01 [*]	0.07	<0.01 [*]
Repetitions	9.6±4.8	10.9±4.9	36.4±74.8	10.3±3.6	12±5.5	22.3±47.3	0.16	0.04 [*]	0.61
Load Product (kg • repetitions)	370.4±217	508.1±226.2 [‡]	73.8±90	384.6±152.6	505.4±208 [‡]	40.9±47.3	<0.01 [*]	0.76	0.74
LL RME									
Load (kg)	14.2±3.4	17.9±3.8 ^{††}	27.2±12.1	14.1±2.5	16.3±3.3 [‡]	17.3±13.6	<0.01 [*]	0.05 [*]	<0.01 [*]
Repetitions	36.3±9.7	44.6±9.8 [‡]	26.7±27.5	37.5±9.3	58.1±18.7 ^{††}	56.5±34.8	<0.01 [*]	<0.01 [*]	<0.01 [*]
Load Product (kg • repetitions)	518.4±496.4	783.1±176.2 [‡]	61.7±40.5	524.4±155.2	921.5±248 ^{††}	82.7±44.7	<0.01 [*]	<0.01 [*]	0.02 [*]

Values are means ± standard deviation. ^{*}Significant main effect or interaction, $P \leq 0.05$. [‡]Different from pre-intervention within the same condition, $P \leq 0.05$. [†]Different between conditions at indicated time point, $P \leq 0.05$. HL, higher load; RME, relative muscle endurance; LL, lower load.

Table 5. Changes in dumbbell preacher curl relative muscle endurance following higher- and lower-load resistance exercise training

	HL			LL			Effect		
	Pre	Post	Δ%	Pre	Post	Δ%	Time	Limb	Time × Limb
HL RME									
Load (kg)	9.1±1.9	14.4±2.6 [‡]	62±28.2	8.8±2	13.7±1.8 [‡]	60.4±25.7	<0.01 [*]	0.04 [*]	0.58
Repetitions	5.8±4.3	7.4±4.1	81.1±131.8	6±4.1	7.7±5.4	70.7±131.8	0.16	0.99	0.88
Load Product (kg • repetitions)	51.3±36.6	105±54.6 [‡]	91.9±65.7	51.8±34.5	104.7±69.2 [‡]	120.5±67.9	<0.01 [*]	0.99	0.95
LL RME									
Load (kg)	6.3±1.2	9.6±1.8 ^{††}	54±25	6±1.2	8.9±1.4 [‡]	50.1±19.7	<0.01 [*]	<0.01 [*]	0.38
Repetitions	30.1±7.2	37.3±13 [‡]	26.9±44.7	31.9±8.8	45.4±11.1 ^{††}	47.2±41	<0.01 [*]	0.02 [*]	0.06
Load Product (kg • repetitions)	191±62.5	357.4±137.7 ^{††}	169.5±165.4	191.4±65.5	404±118.3 [‡]	166±213.5	<0.01 [*]	0.13	0.08

Values are means ± standard deviation. ^{*}Significant main effect or interaction, $P \leq 0.05$. [‡]Different from pre-intervention within the same condition, $P \leq 0.05$. [†]Different between conditions at indicated time point, $P \leq 0.05$. HL, higher load; RME, relative muscle endurance; LL, lower load.

Table 6. Changes in knee extension absolute muscle endurance following higher- and lower-load resistance exercise training

	HL			LL			Effect		
	Pre	Post	Δ%	Pre	Post	Δ%	Time	Limb	Time × Limb
HL AME									
% 1RM	80.2±0.6	64.3±5.9 [†]	-21.1±7.4	80.2±0.7	71.6±7.4 [*]	-13±11.4	<0.01 [*]	<0.01 [*]	<0.01 [*]
Repetitions	9.9±3.2	19.2±5.5 [*]	106.2±60.8	10.9±3.2	18.4±8.3 [*]	73.5±57	<0.01 [*]	0.4	<0.01 [*]
LL AME									
% 1RM	30.1±0.8	24.1±2.5 [†]	-20.6±8	30±0.6	27±3.1 [*]	-12±11.5	<0.01 [*]	<0.01 [*]	<0.01 [*]
Repetitions	38.7±10.1	53.9±21.4 [*]	38.7±36.5	42.8±15 [†]	67.4±30.6 [†]	60.6±45.1	<0.01 [*]	<0.01 [*]	0.04 [*]

Values are means ± standard deviation. ^{*}Significant main effect or interaction, $P \leq 0.05$. [†]Different from pre-intervention within the same group, $P \leq 0.05$. [‡]Different between conditions at indicated time point, $P \leq 0.05$. HL, higher load; AME, absolute muscle endurance; LL, lower load; 1RM, one repetition maximum.

Table 7. Changes in dumbbell preacher curl absolute muscle endurance following higher- and lower-load resistance exercise training

	HL			LL			Effect		
	Pre	Post	Δ%	Pre	Post	Δ%	Time	Limb	Time × Limb
HL AME									
% 1RM	88.3±2.4	57.1±10.5 [*]	-34.6±12.1	88.5±3	58.2±10.2 [*]	-34.6±11.3	<0.01 [*]	0.95	0.93
Repetitions	7.3±3.8	40.3±18.4 [*]	575.3±376.7	7.6±3.1	43.4±17.9 [*]	603.8±571.7	<0.01 [*]	0.44	0.99
LL AME									
% 1RM	61.8±3.8	39±5.3 [*]	-30.7±19.4	61.2±4.1	39.8±6.5 [†]	-34.5±17.7	<0.01 [*]	0.05 [*]	0.12
Repetitions	32.2±7.3	109.9±73.4 [*]	254.6±270.4	34.6±10.4	148.1±122 [*]	351.4±412.3	<0.01 [*]	0.05 [*]	0.16

Values are means ± standard deviation. ^{*}Significant main effect or interaction, $P \leq 0.05$. [†]Different from pre-intervention within the same group, $P \leq 0.05$. [‡]Different between conditions at indicated time point, $P \leq 0.05$. HL, higher load; AME, absolute muscle endurance; LL, lower load; 1RM, one repetition maximum.

Table 8. Changes in muscle architecture following higher- and lower-load resistance exercise training

	HL			LL			Effect		
	Pre	Post	Δ%	Pre	Post	Δ%	Time	Limb	Time × Limb
VL CSA (cm ²)	18.9±3.6	19.4±5.2	2.3±17	19.6±4.8	19.9±4.4	3.2±13.7	0.62	0.4	0.75
VL MT (cm)	1.9±0.6	1.9±0.5	6.7±18.9	1.9±0.4	1.9±0.4	0.8±13.3	0.46	0.82	0.26
VL PA (deg)	13.4±2.9	13.9±2.2	5.9±19.3	14.7±3.1	14.3±3.3	-0.9±24.3	0.85	0.1	0.39
VL FL (cm)	11.8±4.2 [†]	11.1±3.8	-5.25±34.1	9.7±2.9	10±3.2	11.3±41.7	0.92	0.03 [*]	0.41
VMO MT (cm)	1.8±0.6	1.8±0.7	7.1±33.2	1.7±0.4	1.9±0.5	11.4±26.7	0.32	0.29	0.44
BB MT (cm)	2.7±0.3	2.9±0.3 [*]	8.2±15.3	2.7±0.3	3±0.3 [*]	12±17.6	0.02 [*]	0.87	0.12

Values are means ± standard deviation. ^{*}Significant main effect or interaction, $P \leq 0.05$. [†]Different from pre-intervention within the same group, $P \leq 0.05$. [‡]Different between conditions at indicated time point, $P \leq 0.05$. HL, higher load; LL, lower load; VL, vastus lateralis; CSA, cross sectional area; MT, muscle thickness; PA, pennation angle; FL, fascicle length; VMO, vastus medialis oblique; BB, biceps brachii.

Chapter 3: Discussion & Conclusion

3.1 DISCUSSION

3.1.1 Main Findings

The purpose of this thesis was to investigate the effects of 10-weeks of supervised HL or LL RET on changes in skeletal muscle morphology, strength, and endurance in younger adult females. The main findings of this trial were that both HL and LL RET did not induce detectable muscle hypertrophy in the lower body (Figures 11 panel B, 20, & 21, panel A), both HL and LL RET induced hypertrophy of the upper arm which may be greater following LL RET (Figure 11, panel A & Figure 21, panel B), and there were load specific improvements in KE AME (Figures 16 and 17).

3.1.1.1 Strength

In agreement with previous research (26,30,38) both legs increased maximal strength with the HL leg having a larger increase (Figure 13, panel A). In contrast to many previous studies (26,38,44,49,54) and the established strength-endurance continuum concept (25) maximal strength increases for the HL and LL arms were similar between the conditions (Figure 13, panel B). In agreement with this result, Stefanaki and colleagues found similar increases in female elbow flexor strength when training with either HL (80% 1RM) or LL (30% 1RM) (83). Additionally, research in children has shown that LL training induces greater increases in maximal strength compared to HL training which the authors suggested was due to the increased training volume and ability to ‘learn’ the contraction pattern associated with the task (163). Therefore, in smaller individuals such as children and females, training the upper body with LL allows for necessary training volumes to occur which lets these individuals familiarize

themselves with the contraction patterns associated with the movement, which may ultimately lead to increases in maximal strength in the absence of HL training (83,163).

Both HL and LL RET have been found to improve strength, but the magnitude of these changes is consistently greater following HL RET (38) due to the HL conditions performing training with loads that are closer to their maximum (26,30). While the HL limb for both the upper and lower body always used heavier loads, the absolute difference between the loads used for the HL and LL legs was far more pronounced than the absolute difference in loads used for the HL and LL arms (Figure 23). The approximate weekly difference in training loads for the legs was between 15-20 kg which was a large enough difference for the HL leg to gain an advantage in maximal strength (Figure 23, panel A). The difference between the training loads of the arms was consistently 2.25-2.5 kg which may not have been large enough to allow for the HL arm to gain an advantage in strength (Figure 23, panel B). This small absolute difference in training loads for the arms likely allowed the LL arm to also ‘practice’ performing the DC exercise with heavier weights, leading to similar increases in DC 1RM strength (30,89). It should be noted that the percentage 1RM used to denote HL was 80% in the legs and 90% in the arms and for LL it was 30% in the legs and 60% in the arms. The difference in percentage 1RM between the legs was 50% while only being 30% for the arms, which helps to justify why the arms saw similar strength increases but the legs did not. Interestingly, while the percentage 1RMs were different between the legs and arms, similar repetitions were completed highlights the universality of repetition range for RET prescription over the muscle/muscle group/exercise specific percentage 1RM.

Training with HL is recommended when aiming to improve lower body maximal strength as the results of the present study are in accordance with previous research (26,30,38). When

aiming to improve maximal strength of the elbow flexors, training with loads between 60-90% 1RM should be used as similar increases in strength were found between conditions. When considering both strength and hypertrophy as desired RET outcomes, selecting a load that allows 20-30 repetitions to be completed per set for the elbow flexors will allow individuals to get similar strength increases to training with heavier loads, but also allow for enough training volume to stimulate elbow flexor growth.

3.1.1.2 Hypertrophy and Muscle Architecture

In alignment with previous research, HL and LL RET induced elbow flexor muscle hypertrophy to a similar degree (26,30,77,83), when assessed as change in BB thickness (Figure 21, panel B). Only LL RET led to an increase in upper arm lean mass (Figure 11, panel A) which both contrasts (26,30,77,83), and supports (44,83) previous research. Stefanaki and colleagues found BB thickness increases of $6.8\pm 3.2\%$ and $5.9\pm 3.1\%$ following LL and HL RET respectively, but the quality of their results is questionable given the high degree of hypertrophy observed in fewer weeks of training, and with less total training volume compared to the current thesis project (83). Additionally, the presence of edema following RET in the Stefanaki trial could explain their abnormally high degree of muscle hypertrophy observed for their chosen RET program (83,164). Comparison between the current trial and Stefanaki and colleagues may not be meaningful as the results reported by Stefanaki as their reliability may be confounded by muscle edema (83). Franco and colleagues found that LL RET induced a greater increase in leg lean mass which they attributed to the greater training volume accrued performing LL training (44). The LL arm in our study performed significantly greater training volume compared to the HL arm (Figure 22, panel B) which likely explains the greater muscle growth detected in the LL arm.

Neither HL nor LL RET in the lower body induced detectable muscle growth regardless of the measurement technique used (Figures 11, 20, & 21). It was surprising to see that no growth occurred in either loading condition for the legs as previous research has consistently found both HL and LL RET to be capable of stimulating muscle hypertrophy when training to volitional fatigue (26,30,77,83,157). One component of RET program design that may have been missed in this trial was a lack of total training volume necessary to induce growth. While training to volitional fatigue has been proposed as the most important variable for RET induced muscle growth (16,45,165), training volume may be of equal importance as suggested by other works (42,44,166). A dose-response relationship has been presented (Figure 24) wherein the degree of muscle growth increases, up to a point, in relation to the total training volume that has been performed over a RET period (31,43,166).

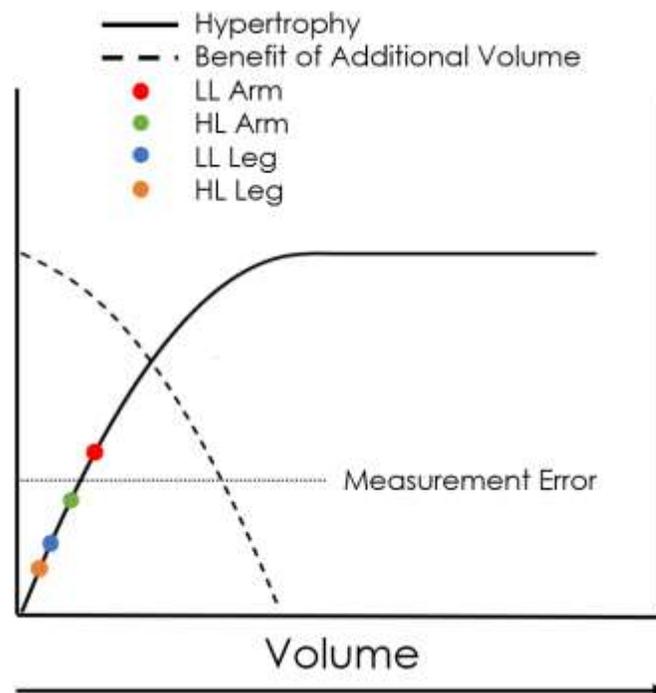


Figure 24. Theoretical model of the relationship between total training volume, hypertrophy, and the benefit of performing additional training volume. It is theorized that the hypertrophy of each limb was limited by the volume performed, with each limb being represented by a dot.

It is possible that neither the HL nor LL legs in our trial reached the minimum necessary training volume to stimulate measurable muscle growth. This theory of a minimum volume threshold for muscle hypertrophy to occur is partially supported by comparing our results to that of Franco and colleagues (Table 9). Both conditions in Franco and colleagues study saw an increase in leg FBFM, likely due to the legs in their study performing a greater total training volume in less weeks compared to our trial, as well as the use of hamstring curls and leg press as additional exercises to train the legs (44). A recent review proposed a volume range of >10 repetitions/muscle/week, but ≤ 15 set/muscle/week. Based on the results of the present study as well as work from Franco and colleagues, the theoretical lower volume limit needed to induce detectable thigh hypertrophy would be ≥ 10 sets/week as the present study found no growth with 9 weekly sets but Franco and colleagues found growth while performing 18 weekly sets (44).

Table 9. Comparison of leg total training volume between studies

	Present Study		Franco et al. 2018		Absolute Difference	Relative Difference
	Volume	Sets/wk	Volume	Sets/wk		
HL Leg Volume	16624±4408 kg	9	~26937±5037 kg	18	~10313 kg	62%
LL Leg Volume	22633±5634 kg		~46710±6586 kg		~24077 kg	106%

Abbreviations: wk, week

Another potential reason why we found no lower body hypertrophy relates the sensitivity of DXA and US to detect changers in muscle size. Both DXA and US scanning techniques have a degree of error in measurement which is the sum of the technical error of the device, the biological error of the participant, and the error of the research team when interpreting outputs. These factors can impact the accuracy of results, and as such the typical error of measurement for each hypertrophy outcome has been calculated and plotted on their respective graphs (Figures

11, 20, & 21). When interpreting these figures, data points that fall within the typical error of measurement cannot be considered to be a true change from baseline (Figures 11, 20, & 21). DXA has an approximate error range between 2.7-4% in females and 4.05-5.7% in males for leg FBFM outputs, and only changes greater than the upper limit of these ranges can be considered true hypertrophy (67).

When comparing the results of this trial to unpublished work in males by Morton and colleagues, males were able to undergo muscle growth following both HL and LL RET whereas the females in our study were unable to do so (Morton personal communications). Briefly, Morton and colleagues study used a male sample ($n = 20$) while using the same HL and LL within-participant design, repetition ranges, sessions per week, number of training weeks, and protein supplementation protocol to that of this trial which were previously explained earlier in this thesis. It has been previously shown that males are capable of slightly greater relative hypertrophy compared to females (118), which may explain why the lower-responders in Morton and colleagues study were able to achieve a positive muscle mass increase even if this value fell below the upper limit of DXA error, meaning their change could not be considered true growth but it had a reduced negative impact on the average change (Morton personal communications). In contrast, the lower-responders in the current trial presented with muscle size changes that were below the upper error limit and at times negative, which would reduce the average change (Figure 11). Furthermore, when female thigh FBFM changes from the present study were scaled to the same relative hypertrophy observed from Morton and colleagues unpublished data while also matching participants for responder ranking (Morton personal communication), the percentage of females showing a detectable response increased from 25% ($n = 8$) to 31% ($n = 10$), and importantly the percentage of participants showing a positive change regardless of it

being within the error range increased from 44% (n = 14) to 72% (n = 23) (Figure 25). This scaling visually represents the impact study methodology may play in detecting small changes in muscle mass, as the two key differences in protocols between this thesis and the trial by Morton and colleagues was the method of reaching/classifying volitional fatigue and the DXA scanning procedures. DXA scans were conducted in the morning after an overnight fast in Morton and colleagues' trial while the participants in the current study had their pre- and post-RET DXA scans at potentially different times of the day making diet control challenging. Participants were encouraged to consume the same food and drink prior to both DXA scans, but if the pre-RET scan was in the morning and the post-RET scan was in the evening, the research team advised the participants to consume additional food to ensure adequate performance could be achieved during the exercise testing. Had the DXA scans from the current trial been conducted using similar procedures as the Morton trial, the variability in results for this project may have been reduced and a greater number of positive responses (i.e., greater than zero) may have been observed, such as those seen in Morton and colleague's trial. Additionally, verbal encouragement during training was used by Morton and colleagues which may have assisted in participants reaching volitional fatigue while also allowing for additional training volume to be achieved (Morton personal communications) while no encouragement was used in this thesis. As such, there is a possibility that participants may have been able to complete 1-5 more repetitions in this trial had they been verbally encouraged, which may have aided in muscle growth due to a slight increase in training volume. Altogether, the small methodical incongruencies between the current thesis and that carried out by Morton and colleagues highlight the importance of utilizing the best possible testing procedures when assessing muscle mass changes to both reduce measurement error but to also ensure an adequate training stimulus has been applied.

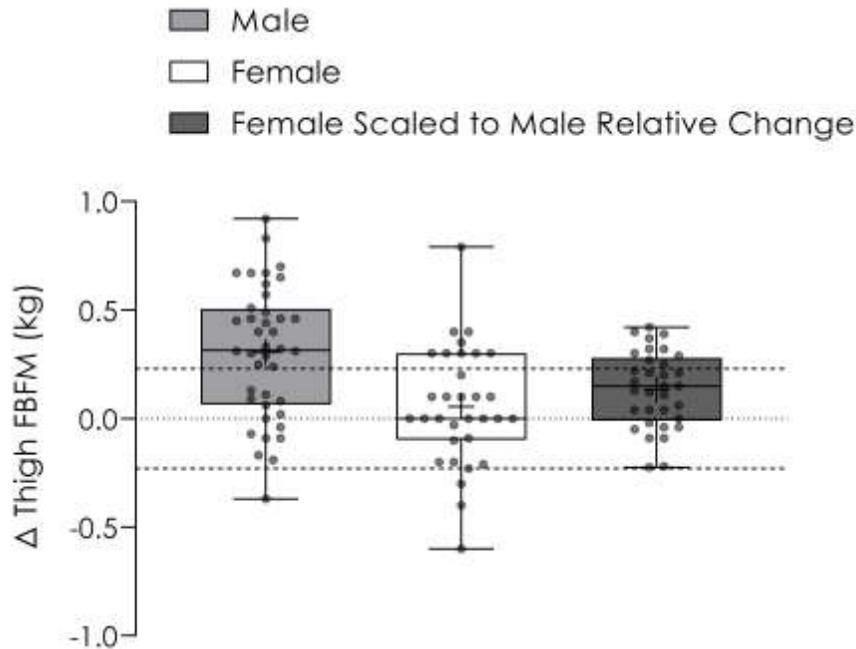


Figure 25. Comparison of absolute change in lower body muscle mass between males and females following 10-weeks of HL and LL RET. The scaled female muscle mass was calculated as the product of the relative change experienced by each similarly responding male and the pre-RET leg FBFM values. When female thigh FBFM hypertrophies to the same relative degree as males, the absolute change from baseline becomes significant ($P < 0.05$).

No changes were observed following HL or LL RET for VL pennation angle (PA) or VL fascicle length (FL) (Figure 20, panels C & D). These results are in agreement with previous research reporting no change in pennation angle or fascicle length following 10-12 weeks of RET (96,97,99). Increases in pennation angle are related to the degree of muscle hypertrophy as an increase in pennation angle allows for a simultaneous increase in sarcomeres in parallel, which would ultimately increase the CSA and/or MT of the muscle (95,167). Since no VL hypertrophy was observed following both HL and LL RET in our study (Figure 20, panels A & B), it is theorized this lack of growth limited the muscles' ability to increase its pennation angle.

Fascicle length has been shown to increase preferentially following eccentric contraction based RET (168–171), but can also increase following conventional RET (i.e., concentric and eccentric contractions being performed) as well (96). Alongside the contraction type, range of

motion and velocity of contraction play direct roles in fascicle length adaptations (95,171). High velocity eccentric contractions have been found to be the most potent stimulus for fascicle length increases (171,172), which could help to explain our results. Our method of contraction during the RET program was conventional (i.e., a concentric followed by an eccentric) following a 1-2 second concentric contraction followed by a 1-2 second eccentric contraction. This contraction type and tempo are not typically associated with larger increases in fascicle length, and the contractions were also performed from ~90-180 degrees of knee extension which could be considered within the normal working range of the vastus lateralis.

Additionally, the current trial failed to demonstrate equivalence between the magnitude of hypertrophy observed between the loading conditions (Appendix K). This is likely due to the high degree of variability in response observed following RET (133) which led to the confidence intervals being larger than predicted and exceeding the set equivalence limits. Equivalence trials are more common in clinical drug trials (158) as the variation in response is quite small and predictable, which is not the case in physiology/training studies. Therefore, using an equivalence test could be possible in future RET research, but greater consideration should be taken regarding response variation when selecting the equivalence limits which would involve accounting for the large variation in muscle growth.

RET recommendations based on the results of this thesis are different when aiming to increase muscle size of the elbow flexors or knee extensors. For the BB, the results suggest that females should train to volitional fatigue with loads that allow for 20-30 repetitions to be completed to achieve a training volume that will induce muscle growth. When aiming to increase quadriceps muscle size, the results of this study do not support a specific loading range over another, but the inclusion of additional sets per exercise, sessions per week, total training weeks,

or other exercises targeting the quadriceps be added to a RET program to increase the total training volume performed is advised. Future studies looking to assess muscle mass changes in female participants should consider the method of muscle mass quantification and aim to use the tool that has the greatest degree of accuracy/reliability. While DXA and US scans are easily accessible and cheaper options, magnetic resonance imaging (MRI) may prove to be useful as this technique is considered the gold standard of muscle mass measurement. However, if a RET is planned to incorporate a large degree of weekly training volume (>12 sets per/muscle/week) then a large enough absolute hypertrophy should occur which would be detected easier by most muscle mass quantification techniques.

3.1.1.3 Local Muscle Endurance

In agreement with previous studies (26,49), LL RET induced greater increases in light load RME for both the upper and lower body, a result due primarily to a smaller increase in maximal strength with LL RET. No improvement was observed for heavy load RME for the upper or lower body following either HL or LL RET, but when these RME tests were expressed as load product (load x repetitions), there was a significant increase from baseline for both conditions (Figures 14 & 15, panels E & F). These heavy load RME results are not surprising as the variability in repetitions able to be completed decreases as percentage 1RM increases (49,121), and improvements in maximal strength have minimal impact on performance as the load used during testing is scaled to one's current strength. Based on our heavy load RME results, an erroneous conclusion could be drawn that both HL and LL training have no impact on LME capacity since no change in repetitions completed was observed, but this claim would be untrue as RME does not accurately quantify true endurance performance. Since RME testing has shown the potential to produce misleading results when examining the effects of RET on LME

(50), AME tests should be used in future studies as it clearly shows improvements in performance while also having a better external validity (173).

Load specific improvements in KE AME were found wherein the HL leg improved heavy load AME to a greater extent, while the LL leg improved light load AME to a greater degree. The primary mechanism responsible for improvements in AME is an increase in maximal strength as the absolute load used during testing becomes a smaller percentage of an individual's current 1RM (Figure 17, panels A & C). This decrease in the absolute load as a percentage of the participants 1RM was greater in the HL compared to the LL leg which aligns with the lower body strength results (Figure 13, panels A). This result supports that the load specific advantage for HL RET to induce greater improvements in the heavy load KE AME test is primarily due to the larger gains in maximal strength (Figures 16 & 17).

The load specific improvement for the light load KE AME test cannot be explained entirely through changes in strength as the LL leg saw a smaller increase in strength compared to the HL leg; therefore, other peripheral mechanisms must be involved (Figures 16 & 17). Indeed, impairments in fatigue/time to task failure following LL training have been found to be peripheral in nature (174), but this study focused on neural metrics of fatigue. Metabolic factors such as improvements in buffering capacity, metabolite clearance (i.e., hydrogen ions, inorganic phosphate, reactive oxygen species), increased capillarization, glycolytic enzyme content, improved mitochondrial function/content, and or increased antioxidant enzymes could also underpin the preferential improvement in light load KE AME observed following LL RET, alongside the previously established neural components (174). Each LL leg RET set took between 25-35 seconds to complete which would require some ATP to be provided through anaerobic glycolysis and potentially oxidative metabolism. As anaerobic glycolysis likely

provides a high percentage of ATP needed to carry out a LL leg set, there would be an accumulation of hydrogen ions which decreases local pH which can lead to a local ‘burning’ sensation as well as a reduction in cross bridge binding (175). Additionally, cross bridges require the release of inorganic phosphate in order to go from a low- to high-force state, but when intramuscular concentrations of inorganic phosphate are elevated due to repeated contraction the total number of cross bridges able to enter a high-force state may be reduced (175,176). Furthermore, a buildup of reactive oxygen species (ROS) can negatively impact muscle contraction as these molecules can target myosin heavy chain as well as troponin C which are key components involved in cross bridge cycling (177–179). Continuous exposure to these byproducts leads to improvements in their clearance which in turn leads to an improvement in performance on subsequent similar tasks due to a reduction in impairment (180,181). An increase in capillary density can occur following RET and allows for improved blood flow to working muscles which can aid in byproduct clearance (182). Increases in anaerobic glycolytic enzymes such as phosphorylase, phosphofructokinase, and/or lactate dehydrogenase could partially explain these improvements as anaerobic glycolytic ATP provision would increase allowing for sustained contraction (25). Improvements in mitochondrial function/content could allow for greater ATP provision during extended sets while also potentially reducing the production of mitochondria generated ROS (178), and increases in antioxidative enzymes such as superoxide dismutase can improve the working muscles ability to deal with the generation of exercise impairing ROS (183). LL RET may induce peripheral adaptations within the leg that are similar to that of high intensity interval training which could explain why LL RET was found to be superior to HL RET when performing light load AME.

In the upper body, a similar improvement was observed for both the heavy and light AME tests demonstrating a lack of load specific increase in the upper body. These results are consistent with previous literature wherein HL and LL RET are capable of improving AME in the upper and lower body (76,78,79,81). Similar to the upper body strength changes, there was likely a similar improvement in upper body AME due to the absolute difference in the loads used between conditions being quite small compared to the difference in loads used in the lower body (Figure 23). Additionally, the high variation in repetitions performed for the light load DC AME test likely interfered with the LL arm presenting with a load specific improvement similar to the LL leg as it is assumed similar intramuscular adaptations occurred between the upper and lower body following LL RET. This finding coupled with the upper body strength changes directly contrast the strength-endurance continuum concept as performing RET with a repetition range of 6-12 and 20-30 have led to similar increases in both strength and muscle endurance (25).

Taken together these results provide insight into how HL and LL RET may have differing effects in the upper and lower body. The recommendation can be made that if an individual's goal is to improve lower body AME for tasks such as hiking or running, they should first identify if the load they will be working against is heavy or light and adjust their training accordingly. This can become difficult when working with individuals of varying strengths as the same absolute load may represent vastly different percentages of multiple individuals' maximal strength. As an example, firefighters may be required to climb multiple flights of stairs with gear that weighs 20-30 kg. The average female KE 1RM is between 20-30 kg while males show a 1RM range between 40-50 kg (184), which means performing successive knee extensions (i.e., climbing stairs) with an additional load of 20-30kg would be quite hard for an average female, but an average male would not find it to be challenging. Ultimately, the gear could be light to a

larger/stronger person, such as the males above, or heavy to a smaller/weaker person, such as the females above, which means differential training prescription would be required to improve both individual's AME. The larger/stronger person may benefit more from LL RET while the smaller/weaker person may benefit more from HL RET if they both are aiming to improve their AME. If an individual is seeking to improve their upper body AME, they should train to volitional fatigue with loads that allow for 6-30 repetitions to be completed.

3.2 LIMITATIONS

As with any trial, limitations were present when completing the outlined study. Participants were able to consume their choice of foods/drinks which does aid in improving the external validity of our study, but diet and especially protein/calorie intake heavily impact the ability for one to undergo hypertrophy. Participants were provided with two 25g doses of whey protein per day for the 10-week training period, but no compliance measures were taken to ensure this supplement was being consistently ingested. While this lack of accountability would not impact the comparison between conditions as taking or not taking the supplement would impact all limbs equally, not taking the supplement consistently would lead to a reduced hypertrophic response as adequate protein ingestion induces additional growth to RET alone (17).

The testing days could have had one day dedicated to testing only the HL limbs and the other day for the LL limbs. The testing schedule of the trial split individual tests across two days (i.e., day 1: DXA, 1RMs, RME; day 2: US, AME) and had the HL and LL limbs perform these tests with brief rest between conditions/tests. While a five-minute rest period between tests was included before moving to the contralateral limb in order to dampen the impact of cross-transfer, performing tests for HL on one day and for LL on a separate day at least 48 hours later would

completely eliminate any impact acute cross-transfer may have had on the dynamic tests (i.e., 1RMs, RME, AME). The methodology of the DXA and US scans was also limited due to availability of equipment, other tests being conducted on the same days, and the scheduling required. Since the DXA and US scans were done on the same days as 1RM and LME testing, scheduling conflicts arose due to other participants needing to perform training sessions on this equipment and as such the testing times could not all be in the morning as many participants trained in the morning. An ideal procedure for body composition scans involves participants coming into the lab in the morning in a fasted state in order to control fluid balance, and limit how much food/fluid is present in the system which can be incorrectly quantified as fat mass or lean mass. DXA and US scans needed to be scheduled to work with the participants schedules as well as other participants training schedules which meant that some scans were performed in the afternoon/evening meaning that one's diet throughout the day could alter the scan outputs.

Limitations also existed with how training sessions were carried out, specifically pertaining to the way participants were coached and how volitional fatigue was defined. Participants were never provided with verbal encouragement when training to standardize this variable between participants, within participants, and within conditions. Encouragement has been shown to improve maximal strength (185) and endurance (186) performance, so there is potential for verbal encouragement to improve participants ability to push themselves to perform more repetitions compared to if they were not encouraged. Volitional fatigue incorporates not only the ability or the muscle to physically contract against the external load, but also the mental component of exercise and pushing oneself to their physical limits. It is plausible that some participants who are less familiar with exercise or sports may not possess the mental ability to push through discomfort compared to those who grew up active and/or in sport.

3.3 FUTURE DIRECTIONS

The role of total training volume as a variable necessary to stimulate hypertrophy requires further study in females. Comparing lower body RET in females who perform differing volumes over a training period is one method to assess the dose-response relationship between growth and volume. Additional sets, sessions, weeks and/or exercises could be added to future studies using our design to easily increase the total training volume performed across the RET period. One such study could incorporate the same RET program variables and within-participant design as this thesis while having both legs and arms train with HL. To investigate the effect of training volume, leg one would train only KE while leg two would train KE as well as unilateral leg press. Similarly, arm one would train just DC while arm two would perform DC as well as unilateral preacher dumbbell hammer curls. In both the upper and lower body, one arm and leg are performing three sets per day for a total of nine sets per week while the contralateral arm and leg are performing six sets per day for a total of 18 sets per week. This study allows for a smaller total sample size to be used due to the within-participant design while also investigating the effects of doubling ones weekly RET volume and the impacts this has on hypertrophy.

Exercise selection could also be improved in future studies through the addition of more than a single exercise for the biceps and quadriceps, but also the inclusion of exercises that target other muscle groups in the same compartments that were measured (i.e., upper arm and thigh), such as the triceps and hamstrings/glutes. Adding more exercises would not only allow for more muscles to be trained, but if multiple exercises target similar muscle groups then the total training volume for those muscles would increase and potentially bring them past the theoretical minimum volume threshold needed for growth. The inclusion of exercises such as tricep

extensions, hamstring curls, and leg press would be ideal as these can all be performed unilaterally, increase the total muscle groups undergoing training, and in the case of knee extensions and leg press, the quadriceps will have an increase in volume performed. Further, while the dumbbell preacher curl is typically considered an isolation exercise, it incorporates both the elbow and wrist joints which could technically classify it as a compound movement. The wrist and finger flexors are put under a constant isometric contraction during the movement and can become the limiting factor when performing repetitions to volitional fatigue. On occasion, participants would have to stop a set not because they reached volitional fatigue of the elbow flexors, but because their wrist/finger flexors could no longer hold the weight. A piece of equipment designed to exclude the wrist during repeated elbow flexion contractions, but the use of such a device would reduce the external validity of any study that uses it. Future studies could also allow for a brief break within the set(s) (i.e., 2-3 seconds) to allow for participants to rest their wrist/finger flexors which could potentially allow for the elbow flexors to train to volitional fatigue or at least get closer to this point before the wrist/finger flexors fail.

Muscle biopsies could be included to better understand the intramuscular mechanisms associated with muscle growth and endurance performance changes observed. Since no muscle samples were taken in this trial, the intramuscular changes proposed as rationale for RET induced changes in performance are purely speculative. Anaerobic glycolytic enzyme content, metabolite (i.e., blood lactate, inorganic phosphate, ROS) buildup and clearance, and capillarization can all be assessed through the analysis of muscle tissue which could help to confirm or refute the proposed theories. Taking pre- and post-RET biopsies would allow for direct comparison of enzyme content and capillary density changes, but to get at metabolite buildup and clearance changes muscle biopsies would need to be taken before and acute bout of

exercise and then sequentially after this bout to assess the buildup and removal of these byproducts. A similar study design to that of this thesis could be used, but the testing days both pre- and post-RET could be switched out for the assessment of the above factors following an acute bout of both light and heavy load AME.

Further research should also aim to expand on the KE AME results by having participants perform the same style of test, but at more than two loads to improve the curve that has been used to model LME performance changes (Figure 16). As KE AME was tested at a single heavy and light load, the current curve may not accurately represent the repetitions completed/load used relationship for very heavy (>80% pre-RET 1RM), very light (<30% pre-RET 1RM), or moderate (<80% 1RM but >30% 1RM) loads. Around ~20-40% 1RM, repetitions completed for a given load begin to exponentially increase which has previously been shown (121), and so testing multiple loads around this point would help to identify an inflection point in the curve.

While comparisons between independent studies can aid in the understanding of sex differences/similarities following RET, conducting the same trial as the one carried out in this thesis but including both males and females would allow for direct comparisons to be made. The present study used an almost identical design to that of Morton and colleagues (Morton personal communications), but these trials were conducted at different institutions, using slightly different exercise equipment, and procedures. Inclusion of both sexes in the same within-participant design would allow for comprehensive comparisons to be made on the effects of HL and LL RET on muscle growth, strength, and endurance both between loading conditions as well as between sexes. Additionally, incorporating muscle biopsies would allow for fibre type changes to be quantified which could contribute to the literature pertaining to load specific and sex specific myofibre hypertrophy/conversion.

3.4 CONCLUSION

LL RET proved to be more effective than HL RET for increasing upper body muscle mass, but neither HL nor LL RET was able to increase lower body muscle mass. These results suggest there is a minimum RET volume that must be reached to elicit measurable hypertrophy, and this minimum threshold may be muscle/muscle group specific. In the lower body, HL RET leads to greater increases in maximal strength while similar strength changes were observed in the upper body likely due to the similarity of training loads used. Additionally, similar improvements in both heavy and light load AME were observed in the upper body which demonstrates that the strength-endurance continuum may exist, but the repetitions ranges denoting each adaptation (i.e., strength, hypertrophy, endurance) may be exercise/muscle group specific. KE AME improved in a load specific fashion wherein HL and LL RET demonstrated preferential improvements in heavy and light load AME respectively. Altogether, these results demonstrate that the upper and lower body may adapt differently to a similar training program and as such RET prescription must consider the muscle/muscle groups being trained and the desired training outcome.

Bibliography

1. Frontera WR, Ochala J. Skeletal Muscle: A Brief Review of Structure and Function. *Calcif Tissue Int.* 2015;45(2):183–95.
2. Mcleod JC, Stokes T, Phillips SM, Phillips SM. Resistance Exercise Training as a Primary Countermeasure to Age-Related Chronic Disease. *Front Physiol.* 2019;10(June).
3. Trovato FM, Imbesi R, Conway N, Castrogiovanni P. Morphological and functional aspects of human skeletal muscle. *J Funct Morphol Kinesiol.* 2016;1(3):289–302.
4. Baker JS, McCormick MC, Robergs RA. Interaction among skeletal muscle metabolic energy systems during intense exercise. *J Nutr Metab.* 2010;2010(Figure 1).
5. Phillips SM. A brief review of critical processes in exercise-induced muscular hypertrophy. *Sport Med.* 2014;44(SUPPL.1):71–7.
6. Breen L, Phillips SM. Skeletal muscle protein metabolism in the elderly: Interventions to counteract the “anabolic resistance” of ageing. *Nutr Metab [Internet].* 2011;8(1):68. Available from: <http://www.nutritionandmetabolism.com/content/8/1/68>
7. Atherton PJ, Smith K. Muscle protein synthesis in response to nutrition and exercise. *J Physiol.* 2012;590(5):1049–57.
8. Joannis S, Lim C, McKendry J, Mcleod JC, Stokes T, Phillips SM. Recent advances in understanding resistance exercise training-induced skeletal muscle hypertrophy in humans. *F1000Research.* 2020;9(141):1–12.
9. Glass DJ. Skeletal muscle hypertrophy and atrophy signaling pathways. *Int J Biochem Cell Biol.* 2005;37(10 SPEC. ISS.):1974–84.
10. Spiering BA, Kraemer WJ, Anderson JM, Armstrong LE, Nindl BC, Volek JS, et al. Resistance Exercise Biology. 2008;38(7):527–40.
11. Chesley A, MacDougall JD, Tarnopolsky MA, Atkinson SA, Smith K. Changes in human muscle protein synthesis after resistance exercise. *J Appl Physiol.* 1992;73(4):1383–8.
12. Phillips SM, Tipton KD, Aarsland A, Wolf SE, Wolfe RR. Mixed muscle protein synthesis and breakdown after resistance exercise in humans. *Am J Physiol Metab [Internet].* 1997;273(1):E99–107. Available from: <http://www.physiology.org/doi/10.1152/ajpendo.1997.273.1.E99>
13. Biolo G, Tipton KD, Klein S, Wolfe RR. An abundant supply of amino acids enhances the metabolic effect of exercise on muscle protein. *Am J Physiol Metab [Internet].* 1997;273(1):E122–9. Available from: <http://www.physiology.org/doi/10.1152/ajpendo.1997.273.1.E122>
14. Biolo G, Maggi SP, Williams BD, Tipton KD, Wolfe RR. Increased rates of muscle protein turnover and amino acid transport after resistance exercise in humans. *Am J Physiol - Endocrinol Metab.* 1995;268(3 31-3):514–20.
15. Tipton KD, Ferrando AA, Phillips SM, Doyle D, Wolfe RR. Postexercise net protein synthesis in human muscle from orally administered amino acids. *Am J Physiol - Endocrinol Metab.* 1999;276(4 39-4):628–34.
16. Morton RW, Colenso-Semple L, Phillips SM. Training for strength and hypertrophy: an evidence-based approach. *Curr Opin Physiol [Internet].* 2019;10:90–5. Available from: <https://doi.org/10.1016/j.cophys.2019.04.006>
17. Morton RW, Murphy KT, McKellar SR, Schoenfeld BJ, Henselmans M, Helms E, et al. A systematic review, meta-analysis and meta-regression of the effect of protein

- supplementation on resistance training-induced gains in muscle mass and strength in healthy adults. *Br J Sports Med.* 2018;52(6):376–84.
18. Sahni S, Mangano KM, Hannan MT, Kiel DP, McLean RR. Higher protein intake is associated with higher lean mass and quadriceps muscle strength in adult men and women. *J Nutr.* 2015;145(7):1569–75.
 19. Artero EG, Lee DC, Ruiz JR, Sui X, Ortega FB, Church TS, et al. A prospective study of muscular strength and all-cause mortality in men with hypertension. *J Am Coll Cardiol.* 2011;57(18):1831–7.
 20. Gale CR, Martyn CN, Cooper C, Sayer AA. Grip strength, body composition, and mortality. *Int J Epidemiol.* 2007;36(1):228–35.
 21. Brooks N, Layne JE, Gordon PL, Roubenoff R, Nelson ME, Castaneda-Sceppa C. Strength training improves muscle quality and insulin sensitivity in Hispanic older adults with type 2 diabetes. *Int J Med Sci.* 2007;4(1):19–27.
 22. Poehlman ET, Dvorak R V., DeNino WF, Brochu M, Ades PA. Effects of resistance training and endurance training on insulin sensitivity in nonobese, young women: A controlled randomized trial. *J Clin Endocrinol Metab.* 2000;85(7):2463–8.
 23. Kelley GA, Kelley KS, Tran ZV. Resistance training and bone mineral density in women: A meta-analysis of controlled trials. *Am J Phys Med Rehabil.* 2001;80(1):65–77.
 24. Ratamess NA, Alvar BA, Evetoch TK, Housh TJ, Kibler BW, Kraemer WJ, et al. Progression Models in Resistance Training for Healthy Adults. *Am Coll Sport Med.* 2009;687–708.
 25. Haff GG, Triplett TN. *Essentials of Strength Training and Conditioning. Vol. 4, Human Kinetics.* 2015. 1–752 p.
 26. Mitchell CJ, Churchward-Venne TA, West DWD, Burd NA, Breen L, Baker SK, et al. Resistance exercise load does not determine training-mediated hypertrophic gains in young men. *J Appl Physiol.* 2012;113(1):71–7.
 27. Starkey DB, Pollock ML, Ishida Y, Welsch MA, Brechue WF, Graves JE, et al. Effect of resistance training volume on strength and muscle thickness. *Med Sci Sports Exerc.* 1996;28(10):1311–20.
 28. Krieger JW. Single vs. Multiple Sets of Resistance Exercise for Muscle Hypertrophy: A Meta-Analysis. *J Strength Cond Res.* 2010;24(4):1150–9.
 29. Martorelli S, Cadore EL, Izquierdo M, Celes R, Martorelli A, Cleto VA, et al. Strength training with repetitions to failure does not provide additional strength and muscle hypertrophy gains in young women. *Eur J Transl Myol.* 2017;27(2):113–20.
 30. Morton RW, Oikawa SY, Wavell CG, Mazara N, McGlory C, Quadrilatero J, et al. Neither load nor systemic hormones determine resistance training-mediated hypertrophy or strength gains in resistance-trained young men. *J Appl Physiol* [Internet]. 2016;121(1):129–38. Available from: <http://jap.physiology.org/lookup/doi/10.1152/jappphysiol.00154.2016>
 31. Mangine GT, Hoffman JR, Gonzalez AM, Townsend JR, Wells AJ, Jajtner AR, et al. The effect of training volume and intensity on improvements in muscular strength and size in resistance-trained men. *Physiol Rep.* 2015;3(8):1–17.
 32. Burd NA, West DWD, Staples AW, Atherton PJ, Baker JM, Moore DR, et al. Low-load high volume resistance exercise stimulates muscle protein synthesis more than high-load low volume resistance exercise in young men. *PLoS One.* 2010;5(8).

33. Lasevicius T, Ugrinowitsch C, Schoenfeld BJ, Roschel H, Tavares LD, De Souza EO, et al. Effects of different intensities of resistance training with equated volume load on muscle strength and hypertrophy. *Eur J Sport Sci.* 2018;18(6):772–80.
34. Schoenfeld BJ, Ratamess NA, Peterson MD, Contreras B, Sonmez GT, Alvar BA. Effects of Different Volume-Equated Resistance Training Loading Strategies on Muscular Adaptations in Well-Trained Men. *J Strength Cond Res.* 2014;28(10):2909–18.
35. Schoenfeld BJ, Grgic J, Krieger J. How many times per week should a muscle be trained to maximize muscle hypertrophy? A systematic review and meta-analysis of studies examining the effects of resistance training frequency. *J Sports Sci [Internet].* 2018;37(11):1286–95. Available from: <https://doi.org/10.1080/02640414.2018.1555906>
36. Damas F, Barcelos C, Nóbrega s R, Ugrinowitsch C, Lixandrão ME, Santos LME, et al. Individual Muscle Hypertrophy and Strength Responses To High Vs. Low Resistance Training Frequencies. *J Strength Cond Res.* 2018;00(00):1–5.
37. Wernbom M, Augustsson J, Thome R. The Influence of Frequency, Intensity, Volume and Mode of Strength Training on Whole Muscle Cross-Sectional Area in Humans. *Sport Med.* 2007;37(3):225–64.
38. Schoenfeld BJ, Grgic J, Ogborn D, Krieger JW. Strength and Hypertrophy Adaptations Between Low- vs. High-Load Resistance Training: A Systematic Reviews and Meta-Analysis. *J Strength Cond Res.* 2017;21(12):3508–23.
39. Saric J, Lisica D, Orlic I, Grgic J, Krieger JW, Vuk S, et al. Resistance Training Frequencies of 3 and 6 Times Per Week Produce Similar Muscular Adaptations in Resistance-Trained Men. *J Strength Cond Res.* 2018;33(7S):S122–9.
40. Gentil P, Fisher J, Steele J, Campos MH, Silva MH, Paoli A, et al. Effects of equal-volume resistance training with different training frequencies in muscle size and strength in trained men. *PeerJ.* 2018;2018(6):1–12.
41. Gomes GK, Franco CMDC, Ricardo P, Orsatti FL. High-Frequency Resistance Training is Not More Effective Than Low-Frequency Resistance Training in Increasing Muscle Mass and Strength in Well-Trained Men. *J Strength Cond Res.* 2018;33(7S):130–9.
42. Schoenfeld BJ, Ogborn D, Krieger JW. Dose-response relationship between weekly resistance training volume and increases in muscle mass: A systematic review and meta-analysis. *J Sports Sci [Internet].* 2017;35(11):1073–82. Available from: <http://dx.doi.org/10.1080/02640414.2016.1210197>
43. Schoenfeld BJ, Contreras B, Krieger J, Grgic J, Delcastillo K, Belliard R, et al. Resistance Training Volume Enhances Muscle Hypertrophy but Not Strength in Trained Men. *Med Sci Sports Exerc.* 2019;51(1):94–103.
44. Franco CMDC, Carneiro MADS, Alves LTH, Junior GNDO, De Sousa JDFR, Orsatti FL. Lower-Load is More Effective Than Higher-Load Resistance Training in Increasing Muscle Mass in Young Women. *J Strength Cond Res.* 2018;33(7S):152–8.
45. Schoenfeld BJ, Grgic J, Every D Van, Plotkin D. Loading recommendations for muscle strength, hypertrophy, and local endurance: A re-examination of the repetition continuum. *Sports [Internet].* 2021;9(February):0–28. Available from: www.mdpi.com/journal/sports
46. Lasevicius T, Schoenfeld BJ, Silva-Batista C, Barros T de S, Aihara AY, Brendon H, et al. Muscle Failure Promotes Greater Muscle Hypertrophy in Low-Load but Not in High-Load Resistance Training. *J Strength Cond Res.* 2019;Publish Ah.
47. Westcott WL, Steele J, Fisher J, Skivington M, Dunn C, Arnold J, et al. Strength and

- hypertrophy adaptations between low- vs. High-load resistance training: A systematic review and meta-analysis. *Sport Med* [Internet]. 2016;26(1):1–8. Available from: <http://jap.physiology.org/cgi/doi/10.1152/japphysiol.00307.2012>
48. Colomer-Poveda D, Romero-Arenas S, Fariñas J, Iglesias-Soler E, Hortobágyi T, Márquez G. Training load but not fatigue affects cross-education of maximal voluntary force. *Scand J Med Sci Sport*. 2021;31(2):313–24.
 49. Campos GER, Luecke TJ, Wendeln HK, Toma K, Hagerman FC, Murray TF, et al. Muscular adaptations in response to three different resistance-training regimens: Specificity of repetition maximum training zones. *Eur J Appl Physiol*. 2002;88(1–2):50–60.
 50. Fisher J, Steele J, Androulakis-Korakakis P, Smith D, Gentil P, Giessing J. The strength-endurance continuum revisited: a critical commentary of the recommendation of different loading ranges for different muscular adaptations. *J Trainology*. 2020;9(1):1–8.
 51. Counts BR, Buckner SL, Dankel SJ, Jessee MB, Mattocks KT, Mouser JG, et al. The acute and chronic effects of “NO LOAD” resistance training. *Physiol Behav* [Internet]. 2016;164:345–52. Available from: <http://dx.doi.org/10.1016/j.physbeh.2016.06.024>
 52. Vargas S, Petro JL, Romance R, Bonilla DA, Florido MÁ, Kreider RB, et al. Comparison of changes in lean body mass with a strength-versus muscle endurance-based resistance training program. *Eur J Appl Physiol* [Internet]. 2019;119(4):933–40. Available from: <http://dx.doi.org/10.1007/s00421-019-04082-0>
 53. Tobalina JC, Calleja-González J, De Santos RM, Fernández-López JR, Arteaga-Ayarza A, Hass CJ, et al. Is repetition failure critical for the development of muscle hypertrophy and strength? *Sport Med*. 2015;26(1):1–8.
 54. Schoenfeld BJ, Peterson MD, Ogborn D, Contreras B, Sonmez GT. Effects of Low- vs. High-Load Resistance Training on Muscle Strength and Hypertrophy in Well-Trained Men. *J Strength Cond Res*. 2015;29(10):2954–63.
 55. van den Tillaar R, Ettema G. The “ sticking period ” in a maximum bench press. *J Sports Sci*. 2010;28(5):529–35.
 56. Henneman E. The size-principle: A deterministic output emerges from a set of probabilistic connections. *J Exp Biol*. 1985;115:105–12.
 57. Schoenfeld BJ, Contreras B, Willardson JM, Fontana F, Tiryaki-Sonmez G. Muscle activation during low- versus high-load resistance training in well-trained men. *Eur J Appl Physiol*. 2014;114(12):2491–7.
 58. Morton RW, Sonne MW, Farias Zuniga A, Mohammad IYZ, Jones A, McGlory C, et al. Muscle fibre activation is unaffected by load and repetition duration when resistance exercise is performed to task failure. *J Physiol*. 2019;597(17):4601–13.
 59. Ogasawara R, Loenneke JP, Thiebaut RS, Abe T. Low-Load Bench Press Training to Fatigue Results in Muscle Hypertrophy Similar to High-Load Bench Press Training. *Int J Clin Med* [Internet]. 2013;4:114–21. Available from: <http://www.ajo.com/article/0002939479906354/fulltext>
 60. Cholewa JM, Rossi FE, MacDonald C, Hewins A, Gallo S, Mickenski A, et al. The Effects of Moderate- Versus High-Load Resistance Training on Muscle Growth, Body Composition, and Performance in Collegiate Women. *J Strength Cond Res*. 2017;32(6):1511–24.
 61. Buckinx F, Landi F, Cesari M, Fielding RA, Visser M, Engelke K, et al. Pitfalls in the

- measurement of muscle mass: a need for a reference standard. *J Cachexia Sarcopenia Muscle*. 2018;9(2):269–78.
62. Maden-Wilkinson TM, Degens H, Jones DA, McPhee JS. Comparison of MRI and DXA to measure muscle size and age-related atrophy in thigh muscles. *J Musculoskeletal Neuronal Interact* [Internet]. 2013;13(3):320–8. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/23989253>
 63. Heymsfield SB, Gonzalez MC, Lu J, Jia G, Zheng J. Skeletal muscle mass and quality: Evolution of modern measurement concepts in the context of sarcopenia. *Proc Nutr Soc*. 2015;74(4):355–66.
 64. Hounsfield G. Computerized transverse axial scanning (tomography): Part I. Description of System. *Br J Radiol*. 1973;45:1016–22.
 65. Bazzocchi A, Ponti F, Albisinni U, Battista G, Guglielmi G. DXA: Technical aspects and application. *Eur J Radiol* [Internet]. 2016;85(8):1481–92. Available from: <http://dx.doi.org/10.1016/j.ejrad.2016.04.004>
 66. Prado CMM, Heymsfield SB. Lean tissue imaging: A new era for nutritional assessment and intervention. *J Parenter Enter Nutr*. 2014;38(8):940–53.
 67. Kutáč P, Bunc V, Sigmund M. Whole-body dual-energy X-ray absorptiometry demonstrates better reliability than segmental body composition analysis in college-aged students. *PLoS One*. 2019;14(4):1–15.
 68. Pillen S, van Alfen N. Skeletal muscle ultrasound. *Neurol Res*. 2011;33(10):1016–24.
 69. Kwah LK, Pinto RZ, Diong J, Herbert RD. Reliability and validity of ultrasound measurements of muscle fascicle length and pennation in humans: A systematic review. *J Appl Physiol*. 2013;114(6):761–9.
 70. Kent-braun JA, Fitts RH, Christie A. Skeletal Muscle Fatigue. *Compr Physiology*. 2012;2(2):997–1044.
 71. Enoka RM, Duchateau J. Muscle fatigue: What, why and how it influences muscle function. *J Physiol*. 2008;586(1):11–23.
 72. Poole DC, Burnley M, Vanhatalo A, Rossiter HR, Jones AM. Critical Power: An Important Fatigue Threshold in Exercise Physiology. *Med Sci Sports Exerc*. 2016;48(11):2320–34.
 73. Ribeiro AS, Dos Santos ED, Nunes JP, Schoenfeld BJ. Acute Effects of Different Training Loads on Affective Responses in Resistance-trained Men. *Int J Sports Med*. 2019;40(13):850–5.
 74. Fisher J, Steele J, Bruce-Low S, Smith D. Evidence-Based Resistance Training Recommendations. *Med Sport* [Internet]. 2011;15(3):147–62. Available from: <http://versita.metapress.com/openurl.asp?genre=article&id=doi:10.2478/v10036-011-0025-x>
 75. Cyrino LT, Cyrino ES, Silva EC de A e., Avelar A, Trindade MC de C, da Silva DRP. Effect of 16 weeks of resistance training on strength endurance in men and women. *Rev Bras Med do Esporte*. 2019;25(5):399–403.
 76. Stone WJ, Coulter SP. Strength/Endurance Effects From Three Resistance Training Protocols With Women. *J Strength Cond Res*. 1994;8(4):231–4.
 77. Rana SR, Chleboun GS, Gilders RM, Hagerman FC, Herman JR, Hikida RS, et al. Comparison of Early Phase Adaptations for Traditional Strength and Endurance, And Low Velocity Resistance Training Programs in College-Aged Women. *J Strength Cond Res*.

- 2008;22(1):119–27.
78. Steele J, Fisher JP, Assunção AR, Bottaro M, Gentil P. The role of volume-load in strength and absolute endurance adaptations in adolescent's performing high- or low-load resistance training. *Appl Physiol Nutr Metab*. 2017;42(2):193–201.
 79. Jessee MB, Buckner SL, Mouser JG, Mattocks KT, Dankel SJ, Abe T, et al. Muscle Adaptations to High-Load Training and Very Low-Load Training With and Without Blood Flow Restriction. *Front Physiol*. 2018;9(October):1–11.
 80. Schoenfeld BJ, Contreras B, Ogborn D, Galpin A, Krieger J, Sonmez GT. Effects of Varied Versus Constant Loading Zones on Muscular Adaptations in Trained Men. *Int J Sports Med*. 2016;37(6):442–7.
 81. Schoenfeld BJ, Contreras B, Vigotsky AD, Peterson M. Differential effects of heavy versus moderate loads on measures of strength and hypertrophy in resistance-trained men. *J Sport Sci Med*. 2016;15(4):715–22.
 82. Sale DG. Neural adaptation to resistance training. Vol. 20, *Medicine and Science in Sports and Exercise*. 1988. p. S135–45.
 83. Stefanaki DGA, Dzulkarnain A, Gray SR. Comparing the effects of low and high load resistance exercise to failure on adaptive responses to resistance exercise in young women. *J Sports Sci [Internet]*. 2019;37(12):1375–80. Available from: <https://doi.org/10.1080/02640414.2018.1559536>
 84. Ema R, Akagi R, Wakahara T, Kawakami Y. Training-induced changes in architecture of human skeletal muscles: Current evidence and unresolved issues. *J Phys Fit Sport Med*. 2016;5(1):37–46.
 85. Kawakami Y. The Effects of Strength Training on Muscle Architecture in Humans. *Int J Sport Heal Sci*. 2005;3(Special_Issue_2):208–17.
 86. Klemp A, Dolan C, Quiles JM, Blanco R, Zoeller RF, Graves BS, et al. Volume-equated high- and low-repetition daily undulating programming strategies produce similar hypertrophy and strength adaptations. *Appl Physiol Nutr Metab [Internet]*. 2016;41(7):699–705. Available from: <http://www.nrcresearchpress.com/doi/10.1139/apnm-2015-0707>
 87. Refalo MC, Hamilton DL, Paval DR, Gallagher IJ, Feros SA, Fyfe JJ. Influence of resistance training load on measures of skeletal muscle hypertrophy and improvements in maximal strength and neuromuscular task performance: A systematic review and meta-analysis. *J Sports Sci [Internet]*. 2021;00(00):1–23. Available from: <https://doi.org/10.1080/02640414.2021.1898094>
 88. Dinyer TK, Byrd MT, Garver MJ, Rickard AJ, Miller WM, Burns S, et al. Low-Load vs. High-Load Resistance Training to Failure on One Repetition Maximum Strength and Body Composition in Untrained Women. *J strength Cond Res*. 2019;33(7):1737–44.
 89. Mattocks KT, Buckner SL, Jessee MB, Dankel SJ, Mouser JG, Loenneke JP. Practicing the Test Produces Strength Equivalent to Higher Volume Training. *Med Sci Sports Exerc*. 2017;49(9):1945–54.
 90. Buckner SL, Jessee MB, Mattocks KT, Mouser JG, Counts BR, Dankel SJ, et al. Determining Strength: A Case for Multiple Methods of Measurement. *Sport Med*. 2017;47(2):193–5.
 91. Stevens DE, Smith CB, Harwood B, Rice CL. In vivo measurement of fascicle length and pennation of the human anconeus muscle at several elbow joint angles. *J Anat*.

- 2014;225(5):502–9.
92. Gans C, De Vree F. Functional Bases of Fiber Length and Angulation in Muscle. *J Morphol.* 1987;192:63–85.
 93. Russell B, Motlagh D, Ashley WW. Form follows function: how muscle shape is regulated by work. *J Appl Physiol.* 2000;88:1127–32.
 94. Chleboum GS, France AR, Crill MT, Braddock HK, Howell JN. In vivo Measurement of Fascicle Length and Pennation Angle of the Human Biceps femoris Muscle. *J Anat.* 2001;169:401–9.
 95. Timmins RG, Shield AJ, Williams MD, Lorenzen C, Opar DA. Architectural adaptations of muscle to training and injury: A narrative review outlining the contributions by fascicle length, pennation angle and muscle thickness. *Br J Sports Med.* 2016;50(23):1467–72.
 96. Alegre LM, Jiménez F, Gonzalo-Orden JM, Martín-Acero R, Aguado X. Effects of dynamic resistance training on fascicle length and isometric strength. *J Sports Sci.* 2006;24(5):501–8.
 97. Rutherford OM, Jones DA. Measurement of fibre pennation using ultrasound in the human quadriceps in vivo. *Eur J Appl Physiol Occup Physiol.* 1992;65(5):433–7.
 98. Blazevich AJ, Cannavan D, Coleman DR, Horne S. Influence of concentric and eccentric resistance training on architectural adaptation in human quadriceps muscles. *J Appl Physiol.* 2007;103(5):1565–75.
 99. Fukutani A, Kurihara T. Comparison of the muscle fascicle length between resistance-trained and untrained individuals: cross-sectional observation. *Springerplus.* 2015;4(1):1–6.
 100. Janssen I, Heymsfield SB, Wang ZM, Ross R. Skeletal muscle mass and distribution in 468 men and women aged 18–88 yr. *J Appl Physiol.* 2000;89(1):81–8.
 101. Abe T, Kearns CF, Fukunaga T. Sex differences in whole body skeletal muscle mass measured by magnetic resonance imaging and its distribution in young Japanese adults. *Br J Sports Med.* 2003;37(5):436–40.
 102. Simoneau J-A, Lortie G, Boulay MR, Thibault M-C, Thériault G, Bouchard C. Skeletal muscle histochemical and biochemical characteristics in sedentary male and female subjects. *Can J Physiology Pharmacol.* 1983;63(1):30–5.
 103. Miller AEJ, MacDougall JD, Tarnopolsky MA, Sale DG. Gender differences in strength and muscle fiber characteristics. *Eur J Appl Physiol.* 1993;66:254–62.
 104. Simoneau J-A, Bouchard C. Human variation in skeletal muscle fiber-type proportion and enzyme activities. *Am J Physiol - Endocrinol Metab.* 1989;257(4):567–72.
 105. Jeon Y, Choi J, Kim HJ, Lee H, Lim JY, Choi SJ. Sex- and fiber-type-related contractile properties in human single muscle fiber. *J Exerc Rehabil.* 2019;15(4):537–45.
 106. Heitzer T, Meinertz T. [Prevention of coronary heart disease: smoking]. *Z Kardiol.* 2005;94 Suppl 3:III/30–42.
 107. Sale DG, Macdougall JD, Alway SE, Sutton JR. Voluntary untrained strength and muscle characteristics in men and women and male bodybuilders. *J Appl Physiol.* 1987;62(5):1786–93.
 108. Staron RS, Hagerman FC, Hikida RS, Murray TF, Hostler DP, Crill MT, et al. Fiber type composition of the vastus lateralis muscle of young men and women. *J Histochem Cytochem.* 2000;48(5):623–9.
 109. Roepstorff C, Thiele M, Hillig T, Pilegaard H, Richter EA, Wojtaszewski JFP, et al.

- Higher skeletal muscle α 2AMPK activation and lower energy charge and fat oxidation in men than in women during submaximal exercise. *J Physiol*. 2006;574(1):125–38.
110. Hunter SK. Sex Differences in Human Fatigability: Mechanisms and Insight to Physiological Responses. *Acta Physiol*. 2015;210(4):768–89.
 111. Alway SE, Grumbt WH, Gonyea WJ, Stray-Gundersen J. Contrasts in muscle and myofibers of elite male and female bodybuilders. *J Appl Physiol*. 1989;67(1):24–31.
 112. Roberts BM, Nuckols G, Krieger JW. Sex Differences in Resistance Training. *J Strength Cond Res*. 2020;34(5):1448–60.
 113. Ivey FM, Hurley BF, Roth SM, Ferrell RE, Tracy BL, Lemmer JT, et al. Effects of age, gender, and myostatin genotype on the hypertrophic response to heavy resistance strength training. *Journals Gerontol - Ser A Biol Sci Med Sci*. 2000;55(11):M641–8.
 114. Cureton KJ, Collins MA, Hill DW, McElhannon FM. Muscle hypertrophy in men and women. *Med Sci Sports Exerc*. 1988;20(4):338–44.
 115. O'Hagan FT, Sale DG, MacDougall JD, Garner SH. Response to resistance training in young women and men. *Int J Sports Med*. 1995;16(5):314–21.
 116. Staron RS, Karapondo DL, Kraemer WJ, Fry AC, Gordon SE, Falkel JE, et al. Skeletal muscle adaptations during early phase of heavy-resistance training in men and women. *J Appl Physiol*. 1994;76(3):1247–55.
 117. Ribeiro AS, Avelar A, Schoenfeld BJ, Fleck SJ, Souza MF, Padilha CS, et al. Analysis of the training load during a hypertrophy-type resistance training programme in men and women. *Eur J Sport Sci [Internet]*. 2015;15(4):256–64. Available from: <http://dx.doi.org/10.1080/17461391.2014.940559>
 118. Hubal MJ, Gordish-Dressman H, Thompson PD, Price TB, Hoffman EP, Angelopoulos TJ, et al. Variability in muscle size and strength gain after unilateral resistance training. *Med Sci Sports Exerc*. 2005;37(6):964–72.
 119. Fink J, Kikuchi N, Yoshida S, Terada K, Nakazato K. Impact of high versus low fixed loads and non-linear training loads on muscle hypertrophy, strength and force development. *Springerplus*. 2016;5(1):1–8.
 120. Wüst RCI, Morse CI, De Haan A, Jones DA, Degens H. Sex differences in contractile properties and fatigue resistance of human skeletal muscle. *Exp Physiol*. 2008;93(7):843–50.
 121. Maughan RJ, Harmon M, Leiper JB, Sale D, Delman A. Endurance capacity of untrained males and females in isometric and dynamic muscular contractions. *Eur J Appl Physiol Occup Physiol*. 1986;55(4):395–400.
 122. Yoon T, Doyel R, Widule C, Hunter SK. Sex differences with aging in the fatigability of dynamic contractions. *Exp Gerontol [Internet]*. 2015;70:1–10. Available from: <http://dx.doi.org/10.1016/j.exger.2015.07.001>
 123. Hunter SK, Enoka RM. Sex differences in the fatigability of arm muscles depends on absolute force during isometric contractions. *J Appl Physiol*. 2001;91(6):2686–94.
 124. Russ DW, Kent-Braun JA. Sex differences in human skeletal muscle fatigue are eliminated under ischemic conditions. *J Appl Physiol*. 2003;94(6):2414–22.
 125. Hunter SK, Schletty JM, Schlachter KM, Griffith EE, Polichnowski AJ, Ng A V. Active hyperemia and vascular conductance differ between men and women for an isometric fatiguing contraction. *J Appl Physiol*. 2006;101(1):140–50.
 126. Hicks AL, Kent-Braun J, Ditor DS. Sex differences in human skeletal muscle fatigue.

- Exerc Sport Sci Rev. 2001;29(3):109–12.
127. Hunter SK. Sex differences in fatigability of dynamic contractions. *Exp Physiol*. 2016;101(2):250–5.
 128. Hunter SK. Sex differences and mechanisms of task-specific muscle fatigue. *Exerc Sport Sci Rev*. 2009;37(3):113–22.
 129. Hoeger WW., Hopkins DR, Barette SL, Hale DF. Relationship between Repetitions and Selected Percentages of One Repetition Maximum - A Comparison between Untrained and Trained Males and Females. *J Appl Sport Sci Res*. 1990;4(2):47–54.
 130. Ansdell P, Thomas K, Howatson G, Hunter S, Goodall S. Contraction intensity and sex differences in knee-extensor fatigability. *J Electromyogr Kinesiol* [Internet]. 2017;37(September):68–74. Available from: <http://dx.doi.org/10.1016/j.jelekin.2017.09.003>
 131. Mitchell JH, Payne FC, Saltin B, Schibye B. The role of muscle mass in the cardiovascular response to static contractions. *J Physiol*. 1980;309(1):45–54.
 132. Wilmore JH. Alterations in strength, body composition and anthropometric measurements consequent to a 10-week weight training program. *Med Sci Sports Exerc*. 1974;6(2):133–8.
 133. Hubal MJ, Gordish-Dressman H, Thompson PD, Price TB, Hoffman EP, Angelopoulos TJ, et al. Variability in Muscle Size and Strength Gain After Unilateral Resistance Training. *Med Sci Sports Exerc*. 2007;36(6):964–72.
 134. Kanehisa H, Ikegawa S, Fukunaga T. Comparison of muscle cross-sectional area and strength between untrained women and men. *Eur J Appl Physiol Occup Physiol*. 1994;68(2):148–54.
 135. Roth SM, Ivey FM, Martel GF, Lemmer JT, Hurlbut DE, Siegel EL, et al. Muscle Size Responses to Strength Training in Young and Older Men and Women. *J Am Geriatr Soc*. 2001;49(11):1428–33.
 136. Costello JT, Bieuzen F, Bleakley CM. Where are all the female participants in Sports and Exercise Medicine research? *Eur J Sport Sci* [Internet]. 2014;14(8):847–51. Available from: <http://dx.doi.org/10.1080/17461391.2014.911354>
 137. Emmonds S, Heyward O, Jones B. The Challenge of Applying and Undertaking Research in Female Sport. *Sport Med - Open*. 2019;5(1).
 138. Mujika I, Taipale RS. Sport Science on Women, Women in Sport Science. *Int J Sports Physiol Perform*. 2019;14(8):1013–4.
 139. Bull JR, Rowland SP, Scherwitzl EB, Scherwitzl R, Danielsson KG, Harper J. Real-world menstrual cycle characteristics of more than 600,000 menstrual cycles. *npj Digit Med* [Internet]. 2019;2(83). Available from: <http://dx.doi.org/10.1038/s41746-019-0152-7>
 140. Macnutt MJ, Souza MJ De, Tomczak SE, Homer JL, Sheel AW. Resting and exercise ventilatory chemosensitivity across the menstrual cycle. *J Appl Physiol*. 2012;112(5):737–47.
 141. Blagrove RC, Bruinvels G, Pedlar CR. Variations in strength-related measures during the menstrual cycle in eumenorrhic women : A systematic review and meta-analysis. *J Sci Med Sport* [Internet]. 2020;23(12):6–13. Available from: <https://doi.org/10.1016/j.jsams.2020.04.022>
 142. Pereira HM, Larson RD, Bembem DA. Menstrual Cycle Effects on Exercise-Induced Fatigability. *Front Physiol*. 2020;11:1–12.

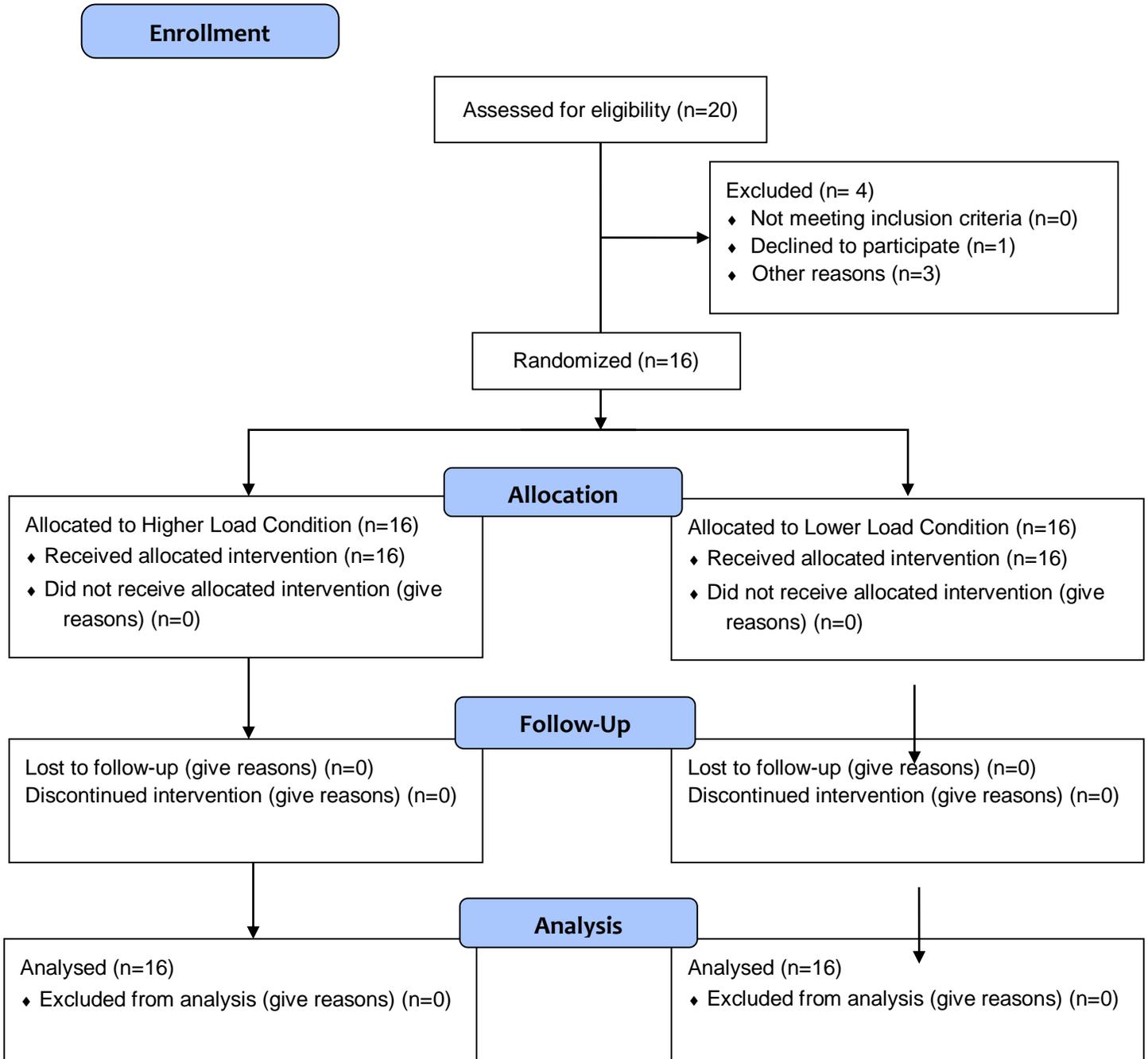
143. Janse De Jonge XAK, Boot CRL, Thom JM, Ruell PA, Thompson MW. The influence of menstrual cycle phase on skeletal muscle contractile characteristics in humans. *J Physiol.* 2001;530(1):161–6.
144. Sims ST, Heather AK. Myths and Methodologies: Reducing scientific design ambiguity in studies comparing sexes and/or menstrual cycle phases. *Exp Physiol.* 2018;103(10):1309–17.
145. Fridén C, Hirschberg AL, Saartok T. Muscle strength and endurance do not significantly vary across 3 phases of the menstrual cycle in moderately active premenopausal women. *Clin J Sport Med.* 2003;13(4):238–41.
146. Andrushko JW, Gould LA, Farthing JP. Contralateral effects of unilateral training: Sparing of muscle strength and size after immobilization. *Appl Physiol Nutr Metab.* 2018;43(11):1131–9.
147. Farthing JP. Cross-Education of Strength Depends on Limb Dominance: Implications for Theory and Application. *Exerc Sport Sci Rev.* 2009;37(4):179–87.
148. West DWD, Burd NA, Tang JE, Moore DR, Staples AW, Holwerda AM, et al. Elevations in ostensibly anabolic hormones with resistance exercise enhance neither training-induced muscle hypertrophy nor strength of the elbow flexors. *J Appl Physiol.* 2010;108(12):60–7.
149. Wilkinson SB, Tarnopolsky MA, Grant EJ, Correia CE, Phillips SM. Hypertrophy with unilateral resistance exercise occurs without increases in endogenous anabolic hormone concentration. *Eur J Appl Physiol.* 2006;98(6):546–55.
150. Housh DJ, Housh TJ, Johnson GO, Chu W-K. Hypertrophic response to unilateral isokinetic resistance training. *J Appl Physiol.* 1992;73(1):65–70.
151. Hendy AM, Lamon S. The cross-education phenomenon: Brain and beyond. *Front Physiol.* 2017;8(May):1–9.
152. Cirer-Sastre R, Beltrán-Garrido J V., Corbi F. Contralateral effects after unilateral strength training: A meta-analysis comparing training loads. *J Sport Sci Med.* 2017;16(2):180–6.
153. Green LA, Gabriel DA. The effect of unilateral training on contralateral limb strength in young, older, and patient populations: a meta-analysis of cross education older , and patient populations : a meta-analysis of cross education. *Phys Ther Rev [Internet].* 2018;23(4–5):238–49. Available from: <https://doi.org/10.1080/10833196.2018.1499272>
154. Manca A, Dragone D, Dvir Z, Deriu F. Cross-education of muscular strength following unilateral resistance training: a meta-analysis. *Eur J Appl Physiol [Internet].* 2017;117(11):2335–54. Available from: <http://dx.doi.org/10.1007/s00421-017-3720-z>
155. Farthing JP, Borowsky R, Chilibeck PD, Binsted G, Sarty GE. Neuro-physiological adaptations associated with cross-education of strength. *Brain Topogr.* 2007;20(2):77–88.
156. Ruddy KL, Carson RG. Neural pathways mediating cross education of motor function. *Front Hum Neurosci.* 2013;7(JUL):1–22.
157. Schoenfeld BJ, Wilson JM, Lowery RP, Krieger JW. Muscular adaptations in low- versus high-load resistance training: A meta-analysis. *Eur J Sport Sci [Internet].* 2016;16(1):1–10. Available from: <http://dx.doi.org/10.1080/17461391.2014.989922>
158. Walker E, Nowacki AS. Understanding equivalence and noninferiority testing. *J Gen Intern Med.* 2011;26(2):192–6.
159. Hahn S. Understanding noninferiority trials. *Korean J Pediatr.* 2012;55(11):403–7.
160. Gupta S. Intention-to-treat concept: A review. *Perspect Clin Res.* 2011;2(3):109.
161. Burkhart TA, Arthurs KL, Andrews DM. Manual segmentation of DXA scan images

- results in reliable upper and lower extremity soft and rigid tissue mass estimates. *J Biomech.* 2009;42(8):1138–42.
162. Hopkins WG. Measures of Reliability in Sports Medicine and Science. *Sport Med.* 2000;30(5):375–81.
 163. Faigenbaum AD, Westcott WL, Loud RL, Long C. The Effects of Different Resistance Training Protocols on Muscular Strength and Endurance Development in Children. *Pediatrics.* 1999;104(1).
 164. Shiromaru FF, de Salles Painelli V, Silva-Batista C, Longo AR, Lasevicius T, Schoenfeld BJ, et al. Differential muscle hypertrophy and edema responses between high-load and low-load exercise with blood flow restriction. *Scand J Med Sci Sport.* 2019;29(11):1713–26.
 165. Fry AC. The Role of Resistance Exercise Intensity on Muscle Fibre Adaptations. *Sport Med.* 2004;34(10):663–79.
 166. Figueiredo VC, de Salles BF, Trajano GS. Volume for Muscle Hypertrophy and Health Outcomes: The Most Effective Variable in Resistance Training. *Sport Med.* 2018;48(3):499–505.
 167. Jorgenson KW, Phillips SM, Hornberger TA. Identifying the Structural Adaptations that Drive the Mechanical Load - Induced Growth of Skeletal Muscle : A Scoping Review. *Cells.* 2020;9(7):1658.
 168. Franchi M V., Atherton PJ, Reeves ND, Flück M, Williams J, Mitchell WK, et al. Architectural, functional and molecular responses to concentric and eccentric loading in human skeletal muscle. *Acta Physiol.* 2014;210(3):642–54.
 169. Baroni BM, Geremia JM, Rodrigues R, De Azevedo Franke R, Karamanidis K, Vaz MA. Muscle architecture adaptations to knee extensor eccentric training: Rectus femoris vs. vastus lateralis. *Muscle and Nerve.* 2013;48(4):498–506.
 170. Reeves ND, Maganaris CN, Longo S, Narici M V. Differential adaptations to eccentric versus conventional resistance training in older humans. *Exp Physiol.* 2009;94(7):825–33.
 171. Davis JF, Khir AW, Barber L, Reeves ND, Khan T, DeLuca M, et al. The mechanisms of adaptation for muscle fascicle length changes with exercise: Implications for spastic muscle. *Med Hypotheses [Internet].* 2020;144(August):110199. Available from: <https://doi.org/10.1016/j.mehy.2020.110199>
 172. Sharifnezhad A, Marzilger R, Arampatzis A. Effects of load magnitude, muscle length and velocity during eccentric chronic loading on the longitudinal growth of the vastus lateralis muscle. *J Exp Biol.* 2014;217(15):2726–33.
 173. Kannus P, Cook L, Alosa D. Absolute and relative endurance parameters in isokinetic tests of muscular performance. *J Sport Rehabil.* 1992;1(1):2–12.
 174. Marshall PW, Forward T, Enoka RM. Fatigability of the knee extensors following high- and low-load resistance exercise sessions in trained men. *Eur J Appl Physiol [Internet].* 2021;(0123456789). Available from: <https://doi.org/10.1007/s00421-021-04832-z>
 175. Woodward M, Debold EP. Acidosis and phosphate directly reduce myosin’s force-generating capacity through distinct molecular mechanisms. *Front Physiol.* 2018;9(JUL):1–6.
 176. Westerblad H, Allen DG, Lännergren J. Muscle fatigue: Lactic acid or inorganic phosphate the major cause? *News Physiol Sci.* 2002;17(1):17–21.
 177. Cooke RE, Franks K, Luciani G, Pate E. The Inhibition of Rabbit Skeletal Muscle

- Contraction by Hydrogen Ions and Phosphate. *J Physiol*. 1988;395:77–97.
178. Westerblad H, Allen DG. Emerging Roles of ROS/RNS in Muscle Function and Fatigue. *Antioxid Redox Signal*. 2011;15(9):2487–99.
 179. Powers SK, Ji LL, Kavazis AN, Jackson MJ. Reactive oxygen species: Impact on skeletal muscle. *Compr Physiol*. 2011;1(2):941–69.
 180. Sharp RL, Costill DL, Fink WJ, King DS. Effects of eight weeks of bicycle ergometer spring training on human muscle buffer capacity. *Int J Sports Med*. 1986;7(1):13–7.
 181. Kraemer WJ, Noble BJ, Clark MJ, Culver BW. Physiologic responses to heavy-resistance exercise with very short rest periods. *Int J Sports Med*. 1987;8(4):247–52.
 182. McCall GE, Byrnes WC, Dickinson A, Pattany PM, Fleck SJ. Muscle fiber hypertrophy, hyperplasia, and capillary density in college men after resistance training. *J Appl Physiol*. 1996;81(5):2004–12.
 183. Powers SK, Jackson MJ. Exercise-Induced Oxidative Stress: Cellular Mechanisms and Impact on Muscle Force Production. *Physiol Rev*. 2008;88(4):1243–76.
 184. Eston R, Evans HJL. The validity of submaximal ratings of perceived exertion to predict one repetition maximum. *J Sport Sci Med*. 2009;8(4):567–73.
 185. McNair PJ, Depledge J, Brett Kelly M, Stanley SN. Verbal encouragement: Effects on maximum effort voluntary muscle action. *Br J Sports Med*. 1996;30(3):243–5.
 186. Andreacci JL, Lemura LM, Cohen SL, Urbansky EA, Chelland SA, von Duvillard SP. The effects of frequency of encouragement on performance during maximal exercise testing. *J Sports Sci*. 2002;20(4):345–52.
 187. Slade SC, Dionne CE, Underwood M, Buchbinder R. Consensus on Exercise Reporting Template (CERT): Explanation and Elaboration Statement. *Br J Sports Med*. 2016;50(23):1428–37.
 188. Piaggio G, Elbourne DR, Pocock SJ, Evans SJW, Altman DG. Reporting of noninferiority and equivalence randomized trials: Extension of the CONSORT 2010 statement. *JAMA - J Am Med Assoc*. 2012;308(24):2594–604.

Appendices

Appendix A - Consort Flow Diagram



Appendix B - CERT Checklist (187)

Consensus on Exercise Reporting (CERT) Checklist			
Section Topic	Item	Checklist Item	Primary paper (page, table, appendix)
WHAT: materials	1	Detailed description of the type of exercise equipment (e.g. weights, exercise equipment such as machines, treadmill, bicycle ergometer etc)	51
WHO: provider	2	Detailed description of the qualifications, teaching/supervising expertise, and/or training undertaken by the exercise instructor	51
HOW: delivery	3	Describe whether exercises are performed individually or in a group	52
	4	Describe whether exercises are supervised or unsupervised and how they are delivered	51
	5	Detailed description of how adherence to exercise is measured and reported	53
	6	Detailed description of motivation strategies	52
	7a	Detailed description of the decision rule(s) for determining exercise progression	n/a
	7b	Detailed description of how the exercise program was progressed	52
	8	Detailed description of each exercise to enable replication (e.g. photographs, illustrations, video etc)	52/53
	9	Detailed description of any home program component (e.g. other exercises, stretching etc)	n/a
	10	Describe whether there are any non-exercise components (e.g. education, cognitive behavioural therapy, massage etc)	n/a
	11	Describe the type and number of adverse events that occurred during exercise	39
WHERE: location	12	Describe the setting in which the exercises are performed	51
WHEN, HOW MUCH: dosage	13	Detailed description of the exercise intervention including, but not limited to, number of exercise repetitions/sets/sessions, session duration, intervention/program duration etc	52
TAILORING: what, how	14a	Describe whether the exercises are generic (one size fits all) or tailored whether tailored to the individual	n/a
	14b	Detailed description of how exercises are tailored to the individual	52/53
	15	Describe the decision rule for determining the starting level at which people commence an exercise program (such as beginner, intermediate, advanced etc)	52
HOW WELL: planned, actual	16a	Describe how adherence or fidelity to the exercise intervention is assessed/measured	53
	16b	Describe the extent to which the intervention was delivered as planned	39

Appendix C - CONSORT Checklist for Non-Inferiority and Equivalence Trials (188)

Paper Section and Topic	Item	Descriptor	Reported on Page #
TITLE & ABSTRACT	1	How participants were allocated to interventions (e.g., "random allocation", "randomized", or "randomly assigned"), specifying that the trial is a non-inferiority or equivalence trial.	iii
INTRODUCTION Background	2	Scientific background and explanation of rationale, including the rationale for using a non-inferiority or equivalence design.	34-35
METHODS Participants	3	Eligibility criteria for participants (detailing whether participants in the non-inferiority or equivalence trial are similar to those in any trial(s) that established efficacy of the reference treatment) and the settings and locations where the data were collected.	37
Interventions	4	Precise details of the interventions intended for each group detailing whether the reference treatment in the non-inferiority or equivalence trial is identical (or very similar) to that in any trial(s) that established efficacy, and how and when they were actually administered.	38-40
Objectives	5	Specific objectives and hypotheses, including the hypothesis concerning non-inferiority or equivalence.	35
Outcomes	6	Clearly defined primary and secondary outcome measures detailing whether the outcomes in the non-inferiority or equivalence trial are identical (or very similar) to those in any trial(s) that established efficacy of the reference treatment and, when applicable, any methods used to enhance the quality of measurements (e.g., multiple observations, training of assessors).	41-47
Sample Size	7	How sample size was determined detailing whether it was calculated using a non-inferiority or equivalence criterion and specifying the margin of equivalence with the rationale for its choice. When applicable, explanation of any interim analyses and stopping rules (and whether related to a non-inferiority or equivalence hypothesis).	38
Randomization – Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (e.g., blocking, stratification)	42
Randomization – Allocation concealment	9	Method used to implement the random allocation sequence (e.g., numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	42
Randomization – Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	42
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	42
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s), specifying whether a one or two-sided confidence interval approach was used. Methods for additional analyses, such as subgroup analyses and adjusted analyses.	51
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	104
Recruitment	14	Dates defining the periods of recruitment and follow-up.	38
Baseline data	15	Baseline demographic and clinical characteristics of each group.	39
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was "intention-to-treat" and/or alternative analyses were conducted. State the results in absolute numbers when feasible (e.g., 10/20, not 50%).	52
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (e.g., 95% confidence interval). For the outcome(s) for which non-inferiority or equivalence is hypothesized, a figure showing confidence intervals and margins of equivalence may be useful.	n/a

Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	n/a
Adverse events	19	All important adverse events or side effects in each intervention group.	39
DISCUSSION Interpretation	20	Interpretation of the results, taking into account the non-inferiority or equivalence hypothesis and any other study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	81
Generalizability	21	Generalizability (external validity) of the trial findings.	82
Overall evidence	22	General interpretation of the results in the context of current evidence.	75-82

Appendix D - Familiarization Session Data Recording Sheet

Version Number – V.03 Study Number - H20-01570

Version Date – 10/20/2020

FAMILIARIZATION SESSION

Are you currently using any form of hormonal contraception?

Please circle one of the following answers: Yes No Prefer not to answer

If yes, please specify delivery system and name: _____

Randomization:

Self-reported dominant arm: _____ **Right Arm:** _____ **Left Arm:** _____

Self-reported dominant leg: _____ **Right Leg:** _____ **Left Leg:** _____

Which condition will test 1RMs and muscle endurance **first:** **HL** **LL**

Which load will be tested **first** for **both** muscle endurance tests: **80/90%** **30/60%**

Ultrasound Landmark Sites:

Vastus lateralis Site: 60% of the distance from the ASIS to the lateral/superior patellar aspect

Vastus Medialis Site: 80% of the distance from the ASIS to the medial/superior patella aspect

Biceps brachii Site: 70% of the distance from the AC joint to the center of the antecubital space

Measurement Site	Measure Site (cm)	Angle of Probe for Penn	CSA/MT Scan Number	Penn Scan Number
Right VL (60%)			0, 1	2, 3
Right VMO (80%)			4, 5	6, 7
Left VL (60%)			10, 11	12, 13
Left VMO (80%)			14, 15	16, 17
Right BB (70%)		n/a	8, 9	n/a
Left BB (70%)		n/a	18, 19	n/a

3RM Testing:

Limb	3RM	Predicted 1RM
<u>High Load Leg</u>		
<u>Low Load Leg</u>		
<u>High Load Arm</u>		
<u>Low Load Arm</u>		

Appendix E - Sample Testing Session Data Recoding Sheets

Version Number – V.03 Study Number - H20-01570

Version Date – 10/20/2020

PRE-INTERVENTION TESTING SESSION 1

Day of current cycle: _____ Notes: _____

DXA Data: Height (m): _____ Weight (kg): _____

Measure	Kilograms (kg)
Total Body FBFM	
Total Body Fat Mass	
Right Arm FBFM	
Left Arm FBFM	
Right Leg FBFM	
Left Leg FBFM	

Equipment Settings: Leg-ext seat back: _____ Leg-ext plate loader: _____ Preacher Curl Height: _____

NOTE: Have the participant **rest 5 minutes** between contralateral limb testing (i.e. after performing the left leg 1RM test have them rest 5 minutes before doing the right leg 1RM)

Which loading condition will perform 1RMs/endurance tests first: **HL LL**

Which endurance load will be tested first: **80/90% 30/60%**

Limb	1RM	80/90% Relative Endurance		30/60% Relative Endurance	
		Load	Reps	Load	Reps
High Load Leg (80/30%) _____					
Low Load Leg (80/30%) _____					
High Load Arm (90/60%) _____					
Low Load Arm (90/60%) _____					

Pre-Intervention Testing Session 2

Day of current cycle: _____ Notes: _____

Ultrasound Scans:

Measurement Site	Measure Site (cm)	Angle of Probe for Penn	CSA/MT Scan Number	Penn Scan Number
Right VL (60%)			0, 1	2, 3
Right VMO (80%)			4, 5	6, 7
Left VL (60%)			10, 11	12, 13
Left VMO (80%)			14, 15	16, 17
Right BB (70%)		n/a	8, 9	n/a
Left BB (70%)		n/a	18, 19	n/a

Equipment Settings: Leg-ext seat back: _____ Leg-ext plate loader: _____ Preacher Curl Height: _____

Which loading condition will perform the muscle endurance tests first: **HL LL**

Which load will be tested first: **80/90% 30/60%**

NOTE: Have the participant **rest 5 minutes** between contralateral limb testing (i.e. after performing the left leg 90% endurance test have them rest 5 minutes before doing the right leg 90% endurance test)

Limb	1RM	80/90% Absolute Endurance		30/60% Absolute Endurance	
		Load	Reps	Load	Reps
High Load Leg (80/30%) _____					
Low Load Leg (80/30%) _____					
High Load Arm (90/60%) _____					
Low Load Arm (90/60%) _____					

Appendix F - Sample Training Session Data Recording Sheet

Version Number – V.03 Study Number - H20-01570

Version Date – 10/20/2020

WEEK ONE **TRAINING SESSION 1**

Day of current cycle: _____ Notes: _____

- 5 min warm-up on bike at ~75 W (optional)
- 120 seconds rest between each set
- Start with HL

Knee Extension

Right Leg	<i>Load (pounds)</i>	<i>Repetitions (#)</i>	<i>Volume (reps x load)</i>
Warm-up (optional)			
Set 1			
Set 2			
Set 3			

Left Leg	<i>Load (pounds)</i>	<i>Repetitions (#)</i>	<i>Volume (reps x load)</i>
Warm-up (optional)			
Set 1			
Set 2			
Set 3			

Biceps Curls

Right Arm	<i>Load (pounds)</i>	<i>Repetitions (#)</i>	<i>Volume (reps x load)</i>
Warm-up (optional)			
Set 1			
Set 2			
Set 3			

Left Arm	<i>Load (pounds)</i>	<i>Repetitions (#)</i>	<i>Volume (reps x load)</i>
Warm-up (optional)			
Set 1			
Set 2			
Set 3			

Appendix G - Randomization Combinations

Dom Leg = HL // Dom Arm = LL // TEST 1ST = HL // 1st RME/AME Test = LIGHT

Dom Leg = HL // Dom Arm = LL // TEST 1ST = HL // 1st RME/AME Test = LIGHT

Dom Leg = LL // Dom Arm = HL // TEST 1ST = HL // 1st RME/AME Test = HEAVY

Dom Leg = HL // Dom Arm = LL // TEST 1ST = LL // 1st RME/AME Test = HEAVY

Dom Leg = HL // Dom Arm = LL // TEST 1ST = LL // 1st RME/AME Test = HEAVY

Dom Leg = HL // Dom Arm = HL // TEST 1ST = LL // 1st RME/AME Test = LIGHT

Dom Leg = LL // Dom Arm = HL // TEST 1ST = LL // 1st RME/AME Test = LIGHT

Dom Leg = HL // Dom Arm = HL // TEST 1ST = HL // 1st RME/AME Test = LIGHT

Dom Leg = LL // Dom Arm = LL // TEST 1ST = LL // 1st RME/AME Test = HEAVY

Dom Leg = HL // Dom Arm = HL // TEST 1ST = LL // 1st RME/AME Test = HEAVY

Dom Leg = LL // Dom Arm = LL // TEST 1ST = HL // 1st RME/AME Test = LIGHT

Dom Leg = LL // Dom Arm = HL // TEST 1ST = LL // 1st RME/AME Test = LIGHT

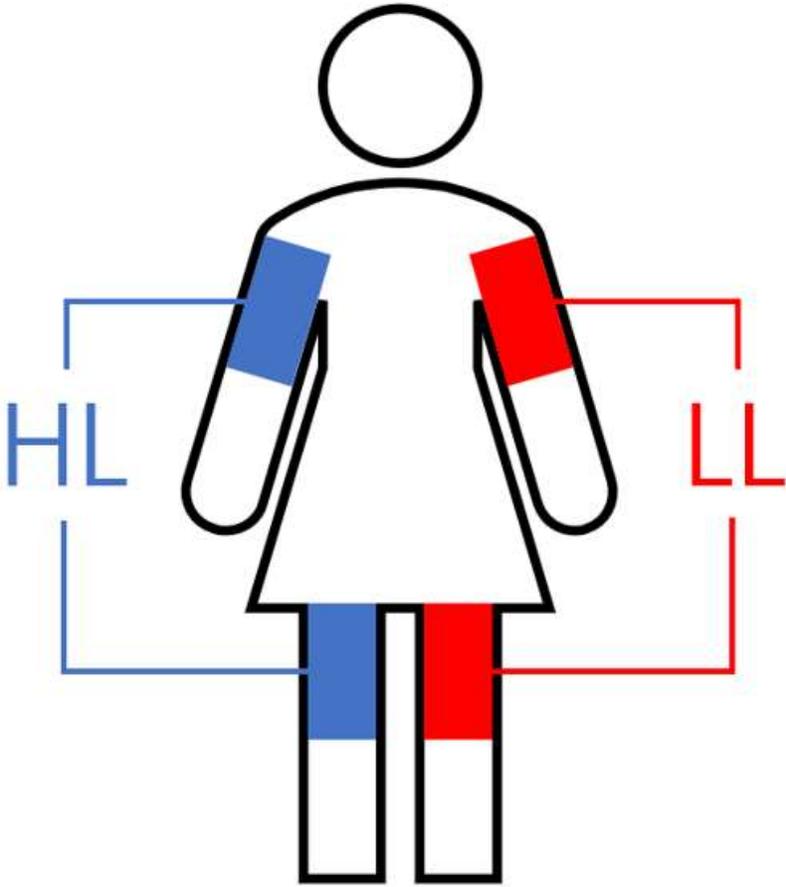
Dom Leg = LL // Dom Arm = LL // TEST 1ST = HL // 1st RME/AME Test = HEAVY

Dom Leg = HL // Dom Arm = LL // TEST 1ST = LL // 1st RME/AME Test = HEAVY

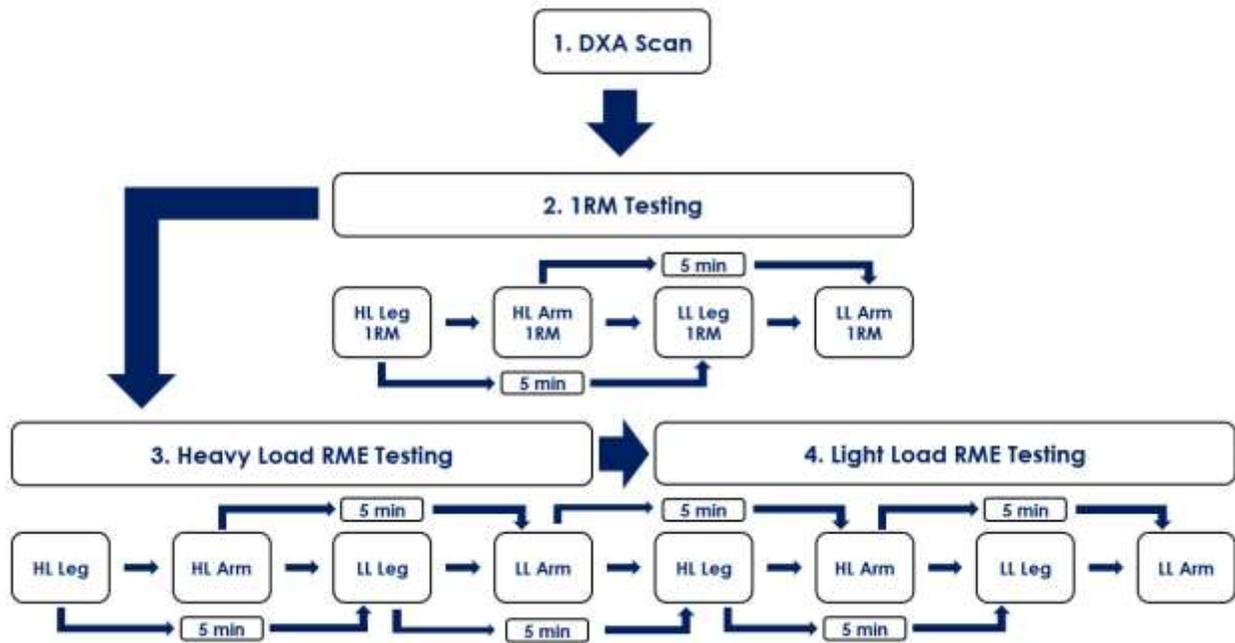
Dom Leg = LL // Dom Arm = HL // TEST 1ST = HL // 1st RME/AME Test = HEAVY

Dom Leg = LL // Dom Arm = HL // TEST 1ST = HL // 1st RME/AME Test = LIGHT

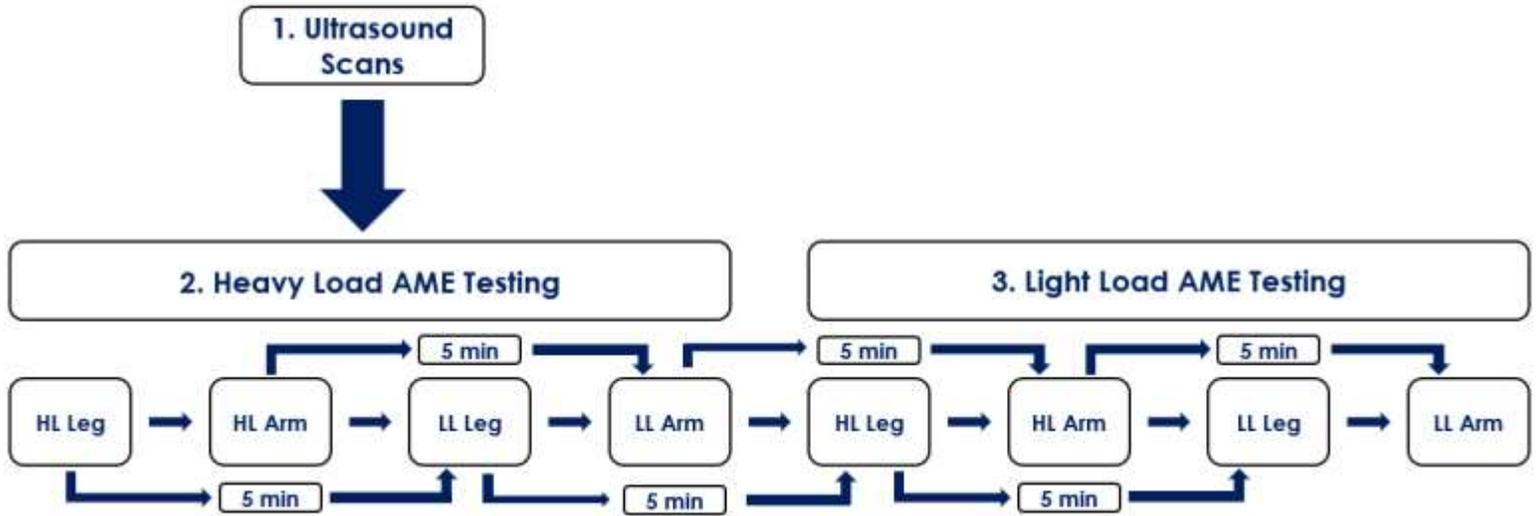
Appendix H - Graphical Example of Limb Allocation



Appendix I - Testing Day One Schematic

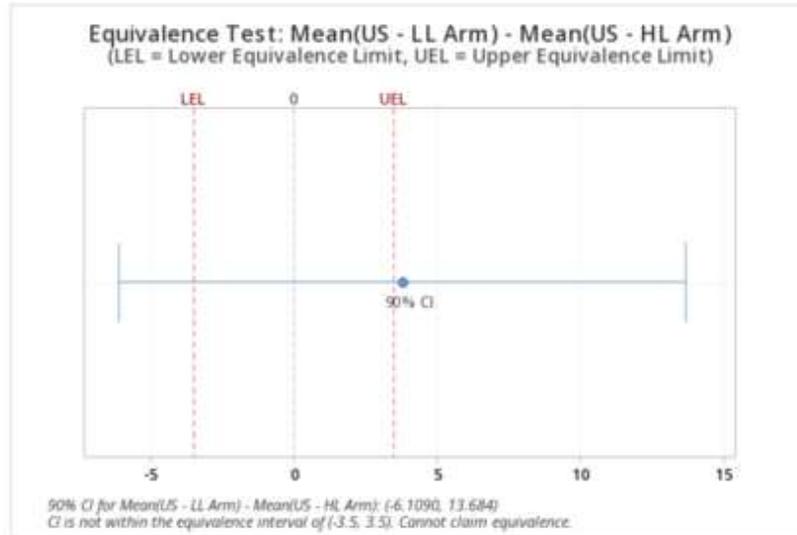


Appendix J - Testing Day Two Schematic

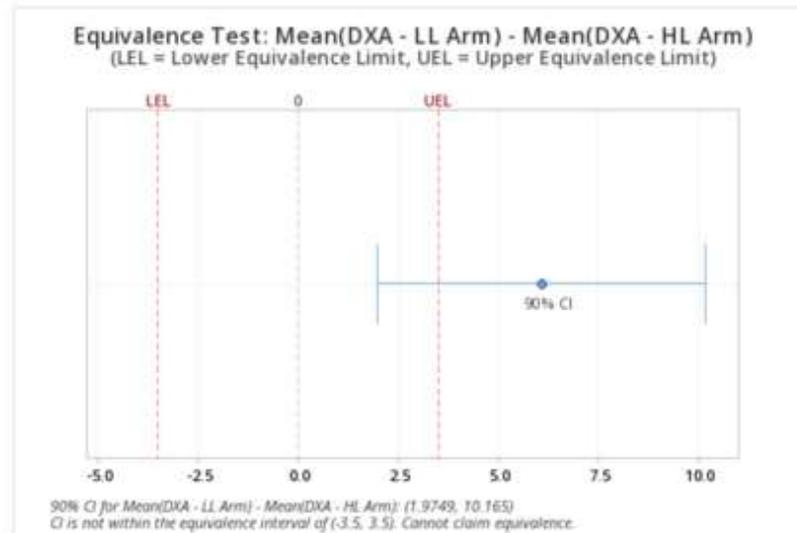


Appendix K - Equivalence Test Outputs

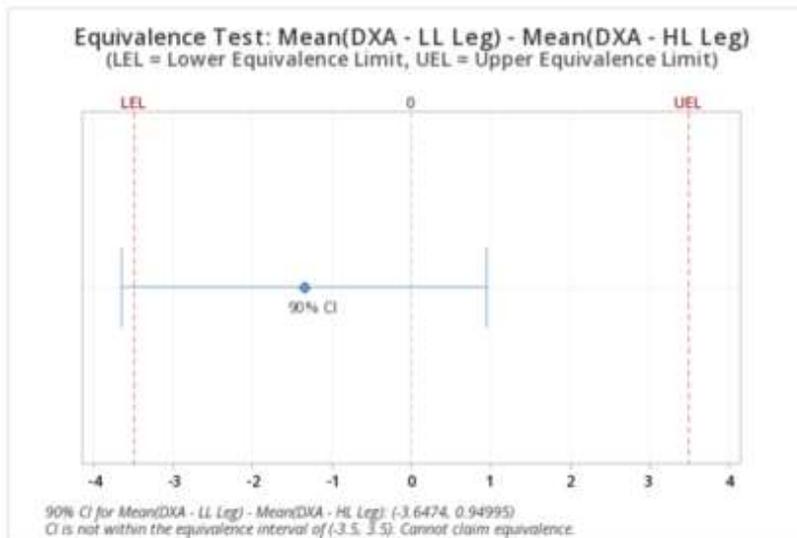
A



B



C



Appendix L - Participant Information and Informed Consent Sheet

Title of Study: The Effects of Higher- And Lower-Load Resistance Exercise Training on Leg and Arm Skeletal Muscle Mass in Healthy Young Adult Females (FHALL)

Principal Investigator: [REDACTED]

Sponsor(s)/Funder: The University of British Columbia, School of Kinesiology

Study Contact Number: [REDACTED]

1. Invitation

You are being invited to participate in a research study investigating the effects of higher- and lower-load resistance exercise training (RET) on upper- and lower-body muscle mass, strength, and muscle endurance changes.

2. Your participation is voluntary

Your participation is voluntary. You have the right to refuse to participate in this study. If you decide to participate, you may still choose to withdraw from the study at any time without any negative consequences to the medical care, education, or other services to which you are entitled or are presently receiving.

3. Who is conducting this study?

This study is being conducted/sponsored by the Exercise, Nutrition, and Muscle Metabolism Research Laboratory under the School of Kinesiology at the University of British Columbia, Vancouver campus.

4. Background

When you perform weightlifting, your body makes new proteins within your muscle. These new proteins can increase the size of the fibers within your muscle to make your muscle larger, a process called hypertrophy. The common convention surrounding gains in muscle mass and strength are that higher-loads (i.e. heavier weights) used for fewer repetitions are better for increasing strength and lower-loads (i.e. lighter weights) used for higher repetitions are better for increasing muscle mass. However, recent research has found that when higher- and lower-loads are used when participants exercise until volitional fatigue (i.e. cannot perform another repetition), muscle mass and strength increases are similar regardless of using a higher- or lower-load. Many of these studies have examined this effect in males with fewer studies examining the effects of higher- and lower-load training in females when assessing changes in muscle mass, strength, and muscle endurance. Further, it has been shown that there is substantial individual variation in response to resistance exercise training where individuals can be broadly categorized as higher- or lower-responders to resistance exercise training. This study aims to explore how the muscle mass, strength, and muscle endurance of females are impacted by both higher- and lower-loads while also exploring how individuals may respond to the training interventions.

5. What is the purpose of this study?

The main purpose of this study is to investigate and compare the effects of higher- and lower-load resistance exercise training on upper- and lower-body muscle mass, strength, and muscle endurance changes. You will be asked to visit the lab a number of times over the period of 12 weeks for body composition scans, strength testing, muscle endurance assessments and exercise training, as outlined below.

6. Who can participate in this study?

You may be able to participate in this study if:

- You are female
- You are 18-30 years of age
- Can fluently read and write in English (you must be able to quickly and concisely communicate with the research staff in case of an emergency and you will be receiving exercise coaching/training advice/cues that must be fully understood and carried out in order to provide a safe and effective resistance exercise training program)
- Are able to commit to three training sessions per week for a continuous 10-week period as well as testing one week before and one week after this 10-week training period
- Have all “No” answers on the CSEP Get Active Questionnaire or a doctors’ approval to participate

7. Who should not participate in this study?

You will not be eligible to participate in this study if you have/are:

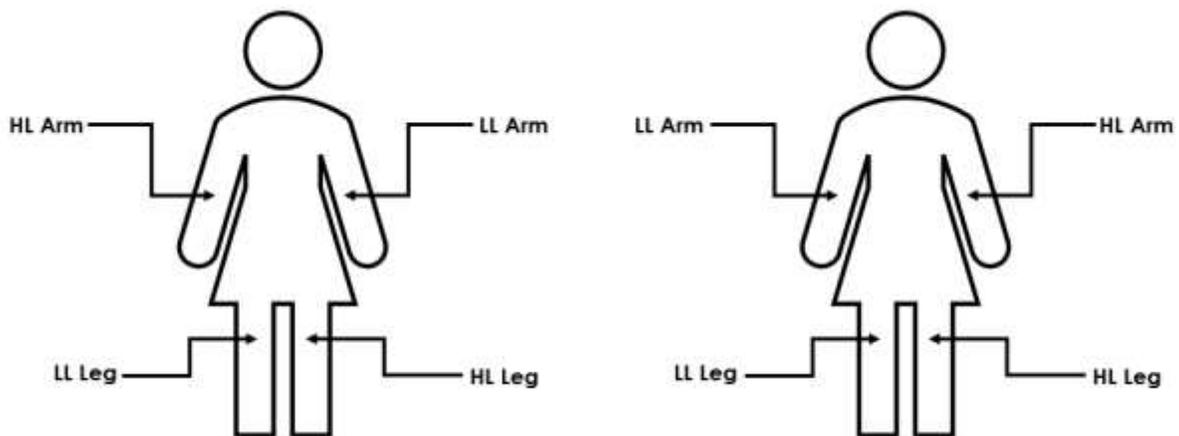
- Allergic to dairy products or are lactose-intolerant (participants will be supplemented with whey protein twice daily for the 10-week training period)
- Allergic to any of the following ingredients which are present in the whey protein concentrate supplement: Bos taurus - Milk, Cocoa, Natural and Artificial Flavours, Xanthan Gum, Sucralose, Non-GMO Sunflower Lecithin
- Any major uncontrolled cardiovascular, muscular, metabolic, and/or neurological disorders
- Lung or kidney disease
- Medical conditions impacting on your ability to undertake strenuous physical activity
- Regular use of any mental health medications that may lead to excessive weight gain or loss (selective serotonin reuptake inhibitors, second-generation antipsychotics, and/or antiepileptic drugs). Check with your primary healthcare physician if you have been prescribed any medication from the above categories to assess if your specific medication can impact weight gain or loss
- Participated in consistent resistance exercise training more than twice per month in the previous 12 months
- Participated in consistent vigorous aerobic training more than twice per week in the previous 12 months
- Significant gain or loss of body mass in the past 6 months (greater than 2 kg)
- Current smoker
- Body mass index (BMI) less than 18 or over 30 (this number is produced through the relationship between your body mass in kilograms and height in meters).

8. What does this study involve?

If you volunteer to participate in this study, we will ask you to do the following things:

You will visit the laboratory of Dr. Cameron Mitchell at the Chan Gunn Pavilion at The University of British Columbia (Vancouver Campus) for 12 weeks for a number of testing and exercise sessions. One of your arms and legs will be randomly assigned to exercise using higher-loads (HL) and your other arm and leg will then exercise using lower-loads (LL) such that you have one arm and one leg assigned to the higher-load condition as well as one arm and one leg assigned to the lower-load condition (Fig. 1) The study will be conducted over a 12-week period and will involve 35 visits to the research lab with 30 training sessions that will each be approximately 30 minutes, as well as 5 testing sessions which range from 70-105 minutes in duration. The total estimated time commitment for your participation in this study is 20 hours spread across the 12-week period.

Figure 1. Limb allocation examples



Each visit will be as follows:

Visit 1 (90 minutes) Participant Registration, Consent, and Familiarization

At least one week prior to the commencement of the pre-RET period, you will visit the lab for screening and familiarisation. This will include an explanation of the study procedures and risks, the inclusion and exclusion criteria, followed by the provision of written and informed consent to participate. Screening for the study will also include the completion of the Canadian Society for Exercise Physiology Get Active Questionnaire (CSEP-GAQ) and you will be asked to track your diet for two weekdays and one weekend day and then provide your report to the research staff for analysis of your macronutrient breakdown. Further, you will undergo landmarking and measurement of ultrasound scans of your biceps and outer thighs, and three-repetition maximum (3RM) testing for the unilateral knee extensions, and unilateral dumbbell bicep preacher curls. This 3RM testing will be used to familiarise you to how strength testing will work and to allow the research staff to predict your one-repetition maximum (1RM) for the 1RM testing session that will occur during visit 2.

Visit 2 (105 minutes) Pre-intervention Testing Session 1

After you consent to participate, you will return to the lab within one-week of enrollment to undergo the first day of pre-intervention testing. For this testing day, you will be asked to record what you consume for breakfast in order to standardize the food and fluids consumed for future testing days. You will be asked to write down exactly what you have for breakfast and give this list the research staff. You will also be asked to consume no more than 500 ml of fluid (the fluid can be your choice but you will be asked to consume no more than 500ml) as excess fluid consumption can lead to changes in dual-energy x-ray absorptiometry (DXA) body composition reporting. Once you arrive at the lab, you will be asked to void your bladder, and then you will undergo a DXA scan. For the DXA scan you will lie on your back on the DXA scanning bed while a scanning arm passes over you and scans your body in segments. The scan will take approximately 7 minutes and all you will be asked to do is lay still for the scan duration.

After the DXA scan, you will undergo 1RM strength assessments. Specifically, you will record your 1RMs for unilateral (single leg) knee extensions, and unilateral (single arm) dumbbell bicep preacher curls. This test will assess the maximum amount of force you can produce with your legs and arms. Prior to completion of the 1RM testing a member of the research staff will demonstrate the exercises and you will also be given time to practice the exercises with a light weight to get used to the movements. You will complete your 1RM testing in a randomised order in terms of loading condition (if your higher-load or lower-load limbs testing first) and you will be given 10 minutes of rest after all 1RM tests have been completed for the first loading condition before being tested on your second loading condition. You will first perform unilateral knee extensions, then unilateral dumbbell preacher curls.

Upon completion of all 1RM tests for both loading conditions, you will be given another 10 minutes of rest and will then perform as many repetitions as possible with 80% and 30% of your 1RM for each limb for both the unilateral knee extensions and unilateral dumbbell bicep preacher curls to assess muscle endurance. For these assessments we will assess the maximum number of consecutive repetitions you can complete with both 30% and 80% of your 1RM that was tested earlier in this session. The order of which load (either 80% 1RM or 30% 1RM) will be tested first will be randomised and after performing this test on all limbs with the first load, you will rest for 10 minutes and then perform the test again with the other load. For example, if you are assigned to perform the 30% 1RM muscle endurance test first, you will perform as many repetitions as possible with 30% of your 1RM on all your limbs for unilateral leg extensions and unilateral dumbbell bicep preacher curls. You will be given 10 minutes of rest after performing this test with one arm and one leg before doing the same test on the other arm and other leg. Once all limbs have performed the test with 30% of your 1RM, you will rest another 10 minutes before following the exact same procedure just explained but with 80% of your 1RM. A breakdown of this testing session is provided below in Table 1:

Table 1. Testing session 1 schedule

Assessment/Measure	Time (minutes)
DXA scan	15
HL limbs 1RM tests	10
Rest	10
LL limbs 1RM tests	10
Rest	10
HL limbs 30% muscle endurance test	5
Rest	10
LL limbs 30% muscle endurance test	5
Rest	10
HL limbs 80% muscle endurance test	5
Rest	10
LL limbs 80% muscle endurance test	5
Total	105

Abbreviations: DXA – dual-energy x-ray absorptiometry

HL – higher-load; LL – lower-load

Visit 3 (70 minutes) Pre-intervention Testing Session 2

Two days after you complete the first day of pre-intervention testing, you will return to the lab to undergo the second day of pre-intervention testing session. For this particular testing day, you will be asked to consume the same breakfast you had during the morning of the first pre-intervention testing day. You will be reminded of what you consumed by the research staff as the research staff will have a written report of exactly what you chose to eat for breakfast during the first pre-intervention testing day. If you consume a breakfast that is completely different from the one consumed prior to visit 2 we will reschedule visit 3. If your breakfast is quite similar with only small differences (e.g., different type of cereal, one extra egg, juice instead of milk, etc.) we will continue with visit 3 as usual but still record what was consumed prior to this testing session. It will be up to the discretion of the study coordinator as to if this session will run or be rescheduled. Once you arrive at the lab, you will undergo ultrasound scans of your outer thighs and biceps. After the ultrasound scans, you will undergo another muscle endurance test where you will perform as many repetitions as possible at either 80% or 30% of your 1RM. The order of load used will be randomised and you will be given 10 minutes rest between tests using either load. This will be the same procedure and test that was done during visit 2. A breakdown of this testing session is provided below in Table 2:

Table 2. Testing session 2 schedule

Assessment/Measure	Time (minutes)
Ultrasound scans	20
HL limbs 30% muscle endurance test	5
Rest	10
LL limbs 30% muscle endurance test	5
Rest	10
HL limbs 80% muscle endurance test	5
Rest	10
LL limbs 80% muscle endurance test	5
Total	70

Abbreviations: HL – higher-load; LL – lower-load

Visits 4-33 (30 minutes each) Training Sessions

You will come to the lab in order to conduct your training sessions. The exercises you will perform are unilateral (single leg) knee extensions and unilateral (single arm) dumbbell preacher curl. You will have one arm and one leg assigned to the higher-load condition and one arm and one leg assigned to the lower-load condition, and these loading conditions also dictate the repetition ranges. You will try to reach volitional fatigue within 8-12 repetitions for the higher-load limbs and 20-25 repetitions for the lower-load limbs. Each exercise will be performed for three sets with 90 seconds of rest between sets and 120 seconds of rest between the exercises.

Visit 34 (105 minutes) Post-intervention Testing Session 1

48 hours prior to this testing session, you will be contacted by the research staff to be reminded of your standard breakfast that should be consumed the morning of this testing session. Once you arrive at the lab, you will be asked to void your bladder, and then you will undergo a DXA scan.

After the DXA scan, you will then undergo 1RM strength assessments. Specifically, you will record your 1RMs for unilateral knee extensions, and unilateral dumbbell bicep preacher curls. You will perform the 1RM strength testing in the same order you performed this testing during the pre-intervention testing session.

You will also perform the muscle endurance test with the same loads that were used during visit 2. The order of loading condition that was used during visit 2 will be the same in this testing session (i.e. if you performed this test first with 80% on visit 2, you will start with 80% for this visit).

Visit 35 (70 minutes) Post-intervention Testing Session 2

48 hours prior to this testing session, you will be contacted by the research staff to be reminded of your standard breakfast that should be consumed the morning of this testing session. Once you arrive at the lab, you will undergo bilateral ultrasound scans of your thigh and upper arm.

After the ultrasound scans, you will undergo another muscle endurance test wherein you will perform as many repetitions as possible using 30% and 80% of your post-intervention 1RM. We will take 80% and 30% of your new 1RM values that you conducted during visit 34. The order of which load you will test first will be the same as the order of the testing during visit 3 (i.e. if you started with maximum repetitions at 30% 1RM during visit 3, you will start with 30% during this testing session).

Figure 2. Schematic of study design

Measure	Visit						
	V ₀	V ₁	V ₂	V ₃	V ₄₋₃₃	V ₃₄	V ₃₅
Initial Phone Contact	x						
Informed Consent		x					
CSEP-GAQ		x					
3RM Strength Testing		x					
Ultrasound		x		x			x
DXA			x			x	
1RM Strength Testing			x			x	
Muscle Endurance Testing			x	x		x	x
Training Sessions					x		

Abbreviations: CSEP-GAQ: Canadian Society for Exercise Physiology Get Active Questionnaire; 3RM: 3-repetition maximum; DXA: dual-energy x-ray absorptiometry; 1RM: 1-repetition maximum

Whey Protein Supplementation:

You will be provided with whey protein concentrate supplements throughout the 10-week training period. You will be asked to consume two 30-gram doses twice daily with one dose being taken in the morning with breakfast and one dose being taken after dinner. You will be provided with a protein shaker bottle which you can use to mix the whey protein doses with your choice of fluid (e.g., water, milk, almond milk, etc.). It is recommended that you mix one dose with roughly 250ml (or 1 cup) of fluid and shake until the whey protein concentrate is incorporated with your chosen fluid.

You will be given 11 pre-measured doses of whey protein concentrate at the beginning of each week. On training session days, you will be given a dose of whey protein concentrate immediately after your training session and this will count as one of your doses for that day. If you train in the morning, the post-exercise dose will count as your morning dose and if you train in the afternoon/evening it will count as your evening dose.

There will be two flavors of whey protein concentrate that will be provided and the ingredients for each are listed here: Chocolate Flavor Ingredients - Whey protein concentrate (whey protein concentrate, Bos taurus - Milk), Cocoa, Natural and Artificial Flavours, Xantham Gum, Sucralose, Non-GMO Sunflower Lecithin. Vanilla Flavor Ingredients - Whey protein concentrate (whey protein concentrate, Bos taurus - Milk), Natural and Artificial Flavours, Xantham Gum, Sucralose, Non-GMO Sunflower Lecithin.

9. What are the possible risks and discomforts?

1. **Exercise Testing:** The potential risks and discomforts associated with resistance exercise training include muscle soreness and muscle strains.
2. **DXA Scanning:** The DXA scan is used in measuring body composition and bone density. The procedure takes approximately 7 minutes and involves lying still on an open bed while the sensor passes over the body. The procedure is completely painless and has no harmful side effects. It uses a very low intensity radioactive beam to measure the amount of muscle and fat. The amount of radiation exposure (effective dose) from a single DXA scan is 0.001 mSv. You will undergo three DXA scans in this study which is equivalent to the natural background radiation you would experience in 9 hours, and 33.3x less radiation than a standard adult chest x-ray (0.1 mSv). The risk from all sources of radiation is cumulative over a lifetime and it could take many years or decades for you to develop cancer related to this study. The latent period for cancer induction is estimated to be 6 to 10 years for blood borne cancers (leukemia, lymphoma) and 10 to 25 years for solid organ cancers.
3. **Gastrointestinal disturbances:** Due to the whey protein supplementation, you may experience bloating, gas, stomach cramps, diarrhea.

10. What happens if I decide to withdraw my consent to participate?

You may withdraw from this study at any time without giving reasons. If you choose to enter the study and then decide to withdraw at a later time, you have the right to request the withdrawal of your information collected during the study. This request will be respected to the extent possible. Please note however that there may be exceptions where the data will not be able to be withdrawn for example where the data is no longer identifiable (meaning it cannot be linked in any way back to your identity) or where the data has been merged with other data. If you would like to request the withdrawal of your data, please let the principal investigator of the study know.

11. How many people will be in this study?

A total of 15 participants will participate in this study.

12. What are the possible benefits for me and/or for society?

We cannot promise any personal benefits to you from your participation in this study. However, the exercise program may result in loss of body fat, an increase in muscle mass, an increase in strength, and/or an increase in physical function. If requested, you will receive the results of the DXA scan (which provides information about your body composition), your strength tests (which provides insight into your upper- and lower-body strength), as well as your muscle endurance assessments (which provide information about how your muscles fatigue) and these data will be summarized into a document and reviewed with a member of the research staff.

13. How will taking part in this study be kept confidential?

Your confidentiality will be respected. However, research records or other source records identifying you may be inspected in the presence of the Investigator or designate and by representatives of UBC's Clinical Research Ethics Board for the purpose of monitoring the

research. No information or records that disclose your identity will be published without your consent, nor will any information or records that disclose your identity be removed or released without your consent unless required by law.

You will be assigned a unique study number as a participant in this study. This number will not include any personal information that could identify you (e.g., it will not include your Personal Health Number, SIN, or your initials, etc.). Only this number will be used on any research-related information collected about you during the course of this study, so that your identity will be kept confidential. Information that contains your identity will remain only with the Principal Investigator and/or designate. The list that matches your name to the unique study number that is used on your research-related information will not be removed or released without your consent unless required by law.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected. You also have the legal right of access to the information about you and, if need be, an opportunity to correct any errors in this information. Further details about these laws are available on request to the study team.

Your de-identified research data may be published or deposited into a publicly accessible location at the time of publication. This data will include your body composition, muscle endurance, and muscular strength testing results as well as the data from your training logs. At no time will identifying information, such as your name or birth date be included in such data. This means that other researchers may analyze the data for different reasons other than those described in this consent form. Once the data is made publicly available, you will not be able to withdraw your data. The extent of the risk of you being identified through public data is unknown, but currently appears to be low.

14. Can participation in the study end early?

If you volunteer to be in this study, you may withdraw at any time. You may also refuse to answer any questions you don't want to answer and still remain in the study. The investigator may withdraw you from this research if circumstances arise which warrant doing so. You will be removed from the study if you miss four (4) total training sessions out of 30. Therefore, you are able to miss three (3) training sessions without being removed from the study. You will however be asked to attend 100% of the testing sessions and these sessions can be rescheduled slightly to accommodate where needed.

15. Will I be paid to participate in this study?

To compensate you for your time and any additional expenses you should incur during participation you will receive \$150. If you withdraw from the study for personal reasons (e.g., no longer interested in study, can no longer commit to sessions, etc.), or are removed from the study due to missing 4 training sessions, the compensation will be adjusted to reflect the amount of time spent in the study based on the number of visits completed out of the 35 total visits. If you choose to withdraw due to a complication from the study (injury from study procedures), you will receive full compensation.

16. Will there be any costs?

Your participation in this research project may include transportation costs in order to get to the research/training facility

17. What happens if something goes wrong?

By signing this form, you do not give up any of your legal rights and you do not release the principal investigator, participating institutions, or anyone else from their legal and professional duties. If you become ill or physically injured as a result of participation in this study, medical treatment will be provided at no additional cost to you. The costs of your medical treatment will be paid by your provincial medical plan.

18. What are the names of the researchers involved in the study?

Locally Responsible and Principal Investigator: [REDACTED]

Study Coordinator: [REDACTED]

19. If I have questions about the study procedures during my participation, who should I speak to?

If you have any questions or desire further information about this study before or during participation, or if you experience any adverse effects, you can contact:

[REDACTED]

[REDACTED]

20. Who do I contact if I have any questions or concerns about my rights as a participant?

If you have any concerns or complaints about your rights as a research participant and/or your experiences while participating in this study, contact the Research Participant Complaint Line in the University of British Columbia Office of Research Ethics by e-mail at RSIL@ors.ubc.ca or by phone at 604-822-8598 (Toll Free: 1-877-822-8598.)

Please reference the study number [H20-01570] when calling so the Complaint Line staff can better assist you.

21. Signatures

The Effects of Higher- And Lower-Load Resistance Exercise Training on Thigh and Arm Lean Mass in Healthy Young Adult Females

Participant Consent

My signature on this consent form means:

- I have read and understood the information in this consent form.
- I have been able to ask questions and have had satisfactory responses to my questions.
- I understand that my participation in this study is voluntary.
- I understand that I am completely free at any time to refuse to participate or to withdraw from this study at any time.
- I understand that I am not waiving any of my legal rights as a result of signing this consent form.
- I understand that there is no guarantee that this study will provide any benefits to me.

I will receive a signed and dated copy of this consent form for my own records.

I consent to participate in this study.

Participant's Signature Printed Name Date

Signature of Person Printed Name Study Role Date
Obtaining Consent

22. Future Contact

Are you interested in learning about other studies conducted by Dr. Cameron Mitchell in the future?

Yes No Initials_____

Note that for any future studies, a separate consent form will be provided to you for review.