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Physiological Muscle Qualitative Changes In Response To Resistance Training In Older Adults

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PHYSIOLOGICAL MUSCLE QUALITATIVE CHANGES IN RESPONSE TO TO RESISTANCE TRAINING IN OLDER ADULTS

by

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ABSTRACT

Muscle function is determined by structure and morphology at the architectural level**.** In response to resistance training, older adults have demonstrated that the neuromuscular system has a substantial adaptability, which may compensate for muscle size and quality and lead to improved functional capacities and higher quality of life. **PURPOSE:** The purpose of this study was to examine the effect of six weeks of progressive resistance exercise on muscle morphology and architecture in healthy older adults. **METHODS:** Twenty- five healthy men and women were randomly assigned to either six weeks of progressive resistance training (RT) (n=13*; age* = 71.08 ± 6.75, *BMI* = 28.5 ± 5.22) or to serve as a control (CON) (n = 12*; age* = 70.17 ± 5.58, *BMI* = 27.52 ± 5.6). Fat mass (FM), lean mass (LM), and lean thigh mass (LTM) were evaluated using dual x-ray absorptiometry. Lower body strength was estimated by predicting maximal knee extensor strength (1RM). Muscle quality (MQ) was evaluated as strength per unit mass (kg/kg). Cross-sectional area (CSA), muscle thickness (MT), fascicle length (L_f), pennation angle (cosΘ), and echo intensity (EI) of the rectus femoris (RF) and vastus lateralis (VL) were collected using B-mode ultrasound and extended field of view (FOV) ultrasound. EI was quantified using grayscale analysis software. Strength per unit of echo intensity (REI) was determined by dividing 1RM by EI of the thigh. Physiological cross-sectional area (PCSA) was calculated as the ratio of (CSA x cosΘ) / (EI x L_f). A 2x2 (group [exercise vs. control] x time [pre vs. post]) repeated measures ANOVA was used to identify group differences and group x time interactions and stepwise regression was performed to assess variables related to strength. **RESULTS:** 1RM increased by 31.9% ($p \leq 0.01$) in the RT group and was significantly correlated to PCSA of the thigh (r = .579; p = .003) at baseline. MQ increased 31.4% ($p \leq 0.01$) in the RT group consistent with an REI increase of 33.3% ($p \leq 0.01$). There were no significant changes in LTM in either group. VL CSA increased 7.4%, ($p \leq 0.05$) and demonstrated a significant interaction ($p \leq 0.05$) in the RT group. There were no significant changes in the CON group for 1RM, MQ, REI or VL CSA. PCSA demonstrated a significant ($p \leq 0.05$) group x time interaction but did not significantly change in either group. EI did not significantly change in the RT or CON groups.

CONCLUSION: Calculated PCSA of the thigh assessed by ultrasound was related to the force producing capacity of muscle and demonstrated a significant interaction following resistance training. Short term resistance exercise training was effective in increasing 1RM, muscle quality as relative strength, muscle quality as relative echo intensity, and muscle morphology, but not EI. In addition, ultrasonography appears to be a safe, feasible, informative and sensitive clinical technique to aid in our understanding of muscle strength, function, and quality.

This thesis is dedicated to Adrian and Rebecca Scanlon. My accomplishments are a direct result of the tools and foundations that you have given me to succeed.

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LIST OF ACRONYMS/ABBREVIATIONS

1RM	Predicted 1 repetition maximum
ADL	Activities of daily living
ANOVA	Analysis of variance
ASCA	Anatomical cross sectional area
Au	Arbitrary units
BMI	Body mass index
CON	Control
CT	Computed tomography
CV	Coefficient of variation
DEXA	Dual energy x-ray absorptiometry
DOMS	Delayed onset of muscle soreness
EI	Echo intensity
ES	Electrical stimulation
FM	Fat mass
FOV	Extended field of view
HDL	High density lipoprotein
L_f	Fascicle Length
LM	Lean mass
LTM	Lean thigh mass
LV	Logiq view
MHZ	Mega-hertz
MQ	Muscle quality as relative strength
MRI	Magnetic resonance imaging
MT	Muscle thickness
OS	Omni scale
PANG	Pennation angle
PAR-Q	Physical activity and readiness questionnaire
PCSA	Physiological cross sectional area
REI	Relative echo intensity
RF	Rectus femoris
ROI	Region of interest
RPE	Ratings of perceived exertion
RT	Resistance training
SD	Standard deviation
SR	Standard rehabilitation
US	Ultrasound
VL	Vastus lateralis

CHAPTER 1: INTRODUCTION

Aging is associated with a progressive loss of neuromuscular function that often leads to progressive disability and loss of independence (Doherty, 2003). The term sarcopenia, loosely translated, is described as a deficiency of flesh (muscle) (Rosenberg, 1989) and is showcased by total muscle cross sectional area decreases of approximately 40% between the ages of 20 and 60 years (Doherty, 2003). The diagnosis of sarcopenia is arbitrary in the sense that an individual having an appendicular skeletal muscle mass value of two or more standard deviations below that of an age matched population may be classified as sarcopenic however, future efforts aim to establish a more clinical definition. This age associated loss of muscle is problematic and is at the center of strength losses that are generally observed in older adults increasing in age. The muscular size and strength losses are believed to be associated with metabolic, physiologic, and functional impairments and disability (Baumgartner et al., 1998). These changes may be attenuated through regular physical activity for the purpose of preserving muscle quality and strength.

Muscle function is determined by structure and morphology at the architectural level. The aging process leads to changes in muscle quality and quantity (Cadore et al., 2012). Magnetic resonance imaging (MRI) is considered the gold standard for cross sectional and volumetric measurements of muscle size however, ultrasonography of skeletal muscle is more cost efficient and has been shown to be a valid and reliable alternative tool for assessing large individual human muscles (Howe & Oldham, 1996; Narici, Reeves, Morse, & Maganaris, 2004; Noorkoiv, Stavnsbo, Aagaard, & Blazevich, 2010; Thomaes et al., 2012). Changes in muscle quality as seen in sarcopenia include enhanced intramuscular adipose and connective tissue and decreased lean muscle mass and contractile units. These changes have shown that muscle quantity and quality independently contribute to muscle strength in older adults (Fukumoto et al., 2012). Muscle quality can be assessed using ultrasound, where an increase in echo intensity represents changes caused by increased intramuscular connective and adipose tissues (Fukumoto et al., 2012).

Strength training appears to be more beneficial than aerobic endurance training for increasing muscular mass and improving function of the neuromuscular system (Aagaard, Suetta, Caserotti, Magnusson, & Kjær, 2010). It was reported that 80 year old individuals competing in the World Master's Weightlifting Championships were able to produce similar isometric strength and muscular power outputs as a 60 year old sedentary population. This demonstrated that up to 20 years of strength and power losses may be attenuated through regular resistance exercise (Pearson et al., 2002). In response to resistance training, older adults have demonstrated that the neuromuscular system has a great plastic ability which may compensate for not only muscle size and quality changes but also lead to improved functional capacities and a higher quality of life (Aagaard et al., 2010). Data is limited that examines the effect of resistance training in older adults on muscle quality at the structural level; therefore the purpose of this study was to examine the effect of six weeks of progressive resistance exercise on muscle morphology and architecture in healthy older adults.

CHAPTER 2: REVIEW OF LITERATURE

Skeletal Muscle Changes with Aging

Aging is associated with a progressive loss of neuromuscular function that often leads to progressive disability and loss of independence (Doherty, 2003). The term sarcopenia, loosely translated, is described as a deficiency of flesh (muscle) (Rosenberg, 1989) and is showcased by decreases in maximal voluntary strength decreases of 20-40% by ages 70 to 80 (Doherty, 2003). Similar to the arbitrary definition of osteoporosis, diagnosis of sarcopenia is currently defined as having an appendicular skeletal muscle mass of 2 or more standard deviations below the mean of a young reference group (Baumgartner et al., 1998), for lack of a more precise definition, which is currently an area of expanding research. Age associated loss of muscle appears inevitable unless counteracted with physical activity and is likely the most significant contributing factor to the decline in muscle strength (Doherty, 2003). Since the original recognition of the age related decline in lean body mass by Irwin Rosenberg in 1989, the term "sarcopenia" has evolved to become more operational in which the impacts of sarcopenia on physical function, chronic disease, and mortality rate are now considered (Janssen, 2010).

One of the first studies to quantify sarcopenia through the use of anthropometric equation evaluated a population-based survey sample of 883 older adult Hispanic and Non-Hispanic residents of New Mexico (Baumgartner et al., 1998). From this, a subsample of 199 participants was used to develop the anthropometric equation which was then extended to the entire sample population. The results of the study indicated that prevalence of the age related loss of muscle increased from 13-24% for individuals under the age of 70 years and increased to more than 50%

for individuals above 80 years of age. Using this definition of sarcopenia, the authors also revealed that self-reported physical limitation was significantly related and was independent of ethnicity, age, and obesity among other variables and would pave the way for clinicians and researchers to develop standards to define a “deficiency” in muscle mass. It is now evident that losses in lean muscle mass and function are reversible with regular exercise and physical activity, and future research is aimed at exploring what is occurring at the micro level within aging muscle.

Nervous System Effects of Sarcopenia

It is important to note that skeletal muscle fiber losses are not solely responsible for the decrease in strength and size that accompanies the ageing process. In addition, losses are observed in the neural networking that innervates and activates these fibers and in fact, because so many of these motor neurons deteriorate, new motor end fibers must sprout and reach out to existing muscle fibers in an attempt to maintain a respectable innervation ratio (Lieber, 2010). In any case, as a direct result of the loss of neurons, many existing muscle fibers may still fail to become activated, compounding the strength losses observed in older adults. Functional capacity may be improved with regular neuromuscular activity such as exercise, to lengthen the lifespan of neurons (Aagaard et al., 2010).

Age Related Changes to Skeletal Muscle

Changes in muscle quality as seen in sarcopenia include accumulated adipose and connective tissue and decreased lean muscle mass and contractile units. What is interesting is that these changes have shown that muscle quantity and quality contribute independently of each other to muscle strength in older adults (Fukumoto et al., 2012). Pearson et al. (2002) studied the effects of Olympic style weightlifting on maximal isometric knee extensor strength and explosive power in older athletes competing in the World Master's Weightlifting Championships in 1999. Fifty-four elite level master athletes (mean age) were compared to a similar number of control participants that were matched for age. Although muscular power appeared to decline at a similar rate with increasing age, the weightlifters were successful in generating 32% greater peak power and a 32% greater isometric knee extensor strength than the controls. The authors concluded that although rates of decline with age were similar across groups, absolute strength and power differences were so great that 85 year old weight lifters were as powerful as 65 year old control subjects. These results led them to believe that regular weightlifting was successful in attenuating as much as 20 years of muscle power and isometric strength decline (Pearson et al., 2002).

Adaptations to Resistance Exercise

When evaluating older adults it is clear that the neuromuscular and musculoskeletal systems demonstrate a substantial ability to respond positively to strength training. These adaptations appear to compensate for decreases in muscle size and quality and lead to improved functional capacity and higher quality of life (Aagaard et al., 2010). In general, decreases in strength are more gradual for men than in women, who experience a steep decline following menopause (Mangione, Miller, & Naughton, 2010). In addition, one of the widespread misconceptions is that intense physical activity may lead to overuse and injury when working with an older population however, with older individuals progressive strength training is quite effective and substantial adverse effects are not to be expected (Mayer et al., 2011). A recent Cochrane review published in 2010 (Mangione et al., 2010) examined 121 randomized, controlled trials and included over 6,500 total participants. The conclusion from these investigations was that strength training, when performed 2-3 times per week was effective in improving physical function capacities in older adults including improved gait speed, improved ability to perform activities of daily living (ADL), improved chair rise time, as well as decreasing physical disability risk. Furthermore, they noted that the largest overall effect of progressive resistance training was improved strength (Mangione et al., 2010). When examining the benefits of resistance and strength training across genders the results are similar. Tracy et al. (1999) examined the effect of unilateral lower limb strength training on muscle quality (strength divided by muscle volume), leg extensor strength, and muscle volume by MRI. In response to just nine weeks of unilateral strength training as expected, men experienced greater absolute strength gains than women. However, when compared relative to body mass, increases were similar for men and women (27 and 29%, respectively). Muscle volume assessed by MRI exhibited a 12% increase for both participant groups, and men and women increased muscle quality values by 14 and 16% respectively. Interestingly, the untrained leg in both groups also experienced a significant ($p \leq .05$) increase in 1RM leg extension, probably as a result of cross-education, with no significant difference between genders. This demonstrates both the importance of strength training in older adults for preventative and rehabilitative purposes if an injury is incurred to a single limb, and also provides evidence to support the claim that hypertrophic and neuromuscular factors in strength gain may be similar between genders (Tracy et al., 1999).

Resistance Training Recommendations for Older Adults

Older adults participating in regular resistance training activities exhibit clear benefits including slowing the loss of muscle as well as bone mass and strength that are not consistently seen with aerobic training alone (American College of Sports Medicine, 2009). Key training principles must be followed such as overload, specificity, and progression just as if designing a program for a younger healthy population. When considering program variables, it is important to remember that training at 60% of one repetition maximum (1RM) is required to stimulate increases in strength, which corresponds to a repetition range of approximately 15 and a subjective score on the ratings of perceived exertion (RPE) scale of 12-13 (Avers & Brown, 2009). The delayed onset of muscle soreness (DOMS) is an important consideration when working with older adults. With age come increasing aches and pains that can be confounded by the added stress of resistance training. Thus, it is important that the supervising coach or strength professional communicate with the exercise participant to establish an expectant possibility of increased levels of soreness (both general and local) (Avers & Brown, 2009).

The efficacy of resistance training has been well documented as research aimed at combating sarcopenia has increased over the past two decades. It is now evident that in regards to training intensity, resistance training is effective in a dose dependent manner (Steib, Schoene, & Pfeifer, 2010). In a meta-analysis conducted by Steib et al. (2010) 29 trials were evaluated comprising a total of 1313 subjects (age range= 65-81), comparing different training doses to strength and function in old and very old adults. The conclusions were that progressive resistance training intensities ranging from 60-80% of 1RM provided strong evidence to support the claim that higher intensities of training are superior to lower intensities for improving maximal muscular strength. Exercise selection should focus on multi-joint, structural and core type exercises and should also include specific exercises to improve balance (American College of Sports Medicine, 2009). Future research is warranted that investigates the relationship between increases in strength and functional mobility tests (Steib et al., 2010).

Structure-Function Relationship of Skeletal Muscle

Muscle function is determined largely by its structure and morphology at the architectural level. Even more than muscle mass alone, measures of muscle fiber arrangement and muscle composition, among other factors are being investigated. Two major events that occur with aging are the decrease of individual fibers, which contributes to an observed loss in the overall cross-sectional area and volume of muscle, and secondly a preferential decrease of primarily fast muscle fibers that contributes to losses in strength with ensuing years (Lieber, 2010).

This structure-function relationship is apparent when examining different muscles of the lower extremities. When examining the architecture of the hamstrings compared to that of the vastus lateralis it is clear to see why the hamstrings are built for excursion whereas the vastus lateralis is constructed in a way that it is capable of producing very powerful force outputs. Many muscles of the quadriceps femoris muscles are characterized by their large physiological cross sectional areas (PCSA) which are exhibited by steeper pennation angles and relatively shorter fiber lengths (Lieber, 2010). Conversely, the hamstrings contain relatively longer fiber lengths that extend a greater length of the muscle and allow for a faster contraction velocity at the expense of force production. This was demonstrated by Kumagai et al. (2000) in a unique study that used a sample population of elite sprinters that were faster than 11.7 seconds in the 100 meter sprint. Thirty-seven male sprinters were divided into two subgroups based on documented personal-best 100 meter sprint time: 10.00-10.90 seconds (S10: *n*= 22) and 11.00-11.70 seconds (S11: *n*= 15). The findings were remarkable in that every sprinter in the faster group had consistently smaller pennation angles, yet significantly longer fascicle lengths. These correlated to sprint times as well with *r* values ranging from -0.40 to -0.57. The authors concluded that longer fascicle lengths were significantly related to shorter sprint times in the 100 meter sprint (Kumagai et al., 2000). Based upon the structure-function relationship of muscle, interest is growing in methods of assessing architectural and morphological properties of muscle non-invasively and how they relate to function in a multitude of age ranges.

Ultrasonography of Skeletal Muscle Morphology and Architecture

Non-invasive techniques for examining the physiological effects of resistance training *in vivo* are becoming increasingly popular. Real time ultrasonography imaging of the musculoskeletal system provides a method of examination that has been proven to be valid and reliable in comparison to *computed tomography* (CT) (N. Reeves, C. Maganaris, & M. Narici, 2004) as well as *magnetic resonance imaging* (Thomaes et al., 2012) for assessing mass of large skeletal muscles. Bemben et al. (2002) assessed the reliability of ultrasound in three separate demographic groups. The rectus femoris was examined for cross sectional area in 38 post-menopausal women (mean age= 58.9 ± 0.7 years), 85 older men (mean age= 65.0 ± 0.4 years), and 10 young men and women (mean age= 26.1 ± 2.4 years). The intraclass correlations (ICC) for various groups with ultrasound ranged from 0.72-0.99, with coefficients of variation (CV) ranging 3.5-6.7%. The authors concluded that diagnostic ultrasound appeared to be a cost effective method for assessing muscle in both young and old (Bemben, 2002).

Ultrasound (US) imaging compared to CT and MRI is typically associated with a lower cost of administration, does not subject participants to repeated ionization radiation, and does not require a physician prescription (Thomaes et al., 2012). Another beneficial characteristic of ultrasonography is its ability to be used in a multitude of settings including rehabilitation clinics, research facilities, and even aboard manned space flight, in which changes in blood flow rate in the heart as well as the vascular system may be monitored (Thomas, 2002). A survey conducted in 2009 at the International Society of Physical and Rehabilitation Medicine Congress in Istanbul revealed that in a population sample of over 300 physiatrists, 57.8% were currently using musculoskeletal ultrasound in diagnostic processes and furthermore, 75.1% stated that given the availability of the device in their offices they would perform ultrasonography (Özçakar et al., 2010). Barriers that physiatrists believed to hinder ultrasound use were lack of education and lack of ownership of the device however, with proper training, validity of this examination method is found to have an intraclass correlation coefficient of 0.99 to MRI in examining muscle mass and size (N. D. Reeves, C. N. Maganaris, & M. V. Narici, 2004).

Skeletal muscle ultrasound has been employed since the early 1980's primarily to distinguish between differing properties of muscle that are attributed to neuromuscular disorders or for the assessment of injuries (Pillen & van Alfen, 2011) and more recently, the application of these methods to screening and diagnosing athletes, especially at the elite level are coming to light (Lee, Mitchell, & Healy, 2012). Interest is now growing in observing how measures of muscle architecture and muscle quality relate to the ability to perform activities of daily living in older adults. As technological advancements are continually made with ultrasound devices, the quality of imaging also increases. Advancements include higher frequency probes (9-17 MHz) that allow for maximal spatial resolution and an extended field of view (FOV) mode that enables viewing of entire muscle lengths as well as cross-sectional areas and fascicle lengths of larger muscles compared to the limited snap-shot imaging that accompanies B-mode ultrasonography (Noorkoiv et al., 2010). Muscle architectural properties are commonly assessed *in vivo* and in real time and include measures of muscle thickness, cross-sectional area, fascicle length, muscle fiber pennation angle, and more recently echo intensity (EI); the quantification of muscle quality and damage using grayscale analysis functions that are available in many image analysis software packages.

Because the popularity of assessing architectural properties of skeletal muscle using ultrasound has increased in the past 20 years, methodology in anatomical landmark obtainment has been rather inconsistent. Typically, when evaluating the lower limb extensors of the quadriceps femoris, determination of muscle measurement has ranged from 50-60% of the distance from the greater trochanter of the femur to the lateral epicondyle of the femur (Thomaes et al., 2012) (Cadore et al., 2012), to as low as 15 cm above the proximal border of the patella in which significant differences in muscle size have been observed (Bemben, 2002). Differences in methodology may translate to disagreement of results when attempting to generalize findings to larger populations. Agreement between anatomical landmarks and ultrasound machine settings in particular becomes an issue when generalizing results of echo intensity in which normative values may only be used with the same device and setting (Arts, Pillen, Schelhaas, Overeem, & Zwarts, 2010). In cases when different machines will be used, new normative values for echo intensity must be determined using standardized settings that are unique to each respective device.

Muscle Thickness and Cross Sectional Area

Heavy resistance training using at least 70% 1-RM for 10-14 weeks have been shown to increase muscle cross sectional area between 5-12% when evaluated with MRI and CT in older adults (Aagaard et al., 2010). Measurements of muscle cross-sectional area may be more desirable than measures of isolated muscle thickness because they may better reflect the hypertrophy and force-producing characteristics that are associated with increased muscle size (Bemben, 2002). In a review paper of 33 articles that focused on strength training in older adults, ages 60 and above, Mayer et al. (2011) found that when using CT scans for cross-sectional area of the thigh, older men and women were found to increase in muscle size in as little as 6-9 weeks (Mayer et al., 2011). Consistent with the previous results, Suetta et al. (2008) examined the effects of unilateral training leg extension and leg press in 10 unilateral hip replacement men and women (age range= 61-86 years). Thirty-six total participants were randomized into one of three groups: standard rehabilitation (SR), electrical stimulation (ES), or resistance training (RT). Following 12 weeks of rehabilitation, the RT group increased muscle thickness ultrasound measures by 15% ($p \leq 0.05$) and interestingly, delta changes were greater than both the standard rehabilitation and electrical stimulation groups (Suetta et al., 2008). The same results were not reported when examining the effects of 12 weeks of resistance training in men and women that had not trained within the past 12 months by Abe et al. (2000). Men and women (age= 25-50 years) trained 3 days per week for 12 weeks in a progressive whole-body program that included training at 70% 1RM in the knee extension exercise. The time course was found to be the same for increases in muscle thickness in both men and women, but no significant increases in thickness of the quadriceps were reported (Abe, DeHoyos, Pollock, & Garzarella, 2000) in contrast to previous studies that have reported cross-sectional area and thickness of the thigh to occur within 6-14 weeks in older adults (Aagaard et al., 2010; Suetta et al., 2008). With technological advancements, attention has shifted to the evaluation of muscle architecture to include the composite measures of fascicle length, pennation angle, and more recently, echo intensity.

Fascicle Length Evaluation

Muscle fascicle length has been examined as an architectural factor in its contribution to muscular contractile properties. In regards to ultrasound, the ability to evaluate changes in muscle fascicle length (as well as pennation angle) in groups of older adults is acceptable however, on an individual basis may encompass any changes that were observed in training studies because of the relatively large 95% confidence interval (I.S. Raj, Bird, & Shield, 2011). Fascicle length is often calculated as a product of muscle thickness and the cosine of pennation angle, although a relatively new method using an extended field of view mode enables the capture of the entire fascicle within a single image (Noorkoiv et al., 2010). Kubo et al. (2002) examined the muscle architecture differences between gender and age in 121 men and 190 women who were further divided by age (i.e. 20-39 years and 60-85 years). Using B-mode ultrasound, the findings indicated that women had longer fascicle lengths relative to muscle length than did men for the vastus lateralis in both the younger ($p= 0.048$) and older group ($p=$

0.028) (Kubo, 2003). Also, if muscle thickness is decreased or remains unchanged for women compared to men, this may result in a smaller pennation angles in women. Due to changes in muscle architecture, the force-velocity relationship is altered with increasing age. A decrease in fascicle length results in a lower number of sarcomeres per fiber that lie in parallel which lessens the range of motion over which force would be generated. The practical applications of these changes are seen in cases such as the slowing of gait speed with increasing age (Isaac Selva Raj, Bird, & Shield, 2010) which gives meaning for training to induce architectural changes in regards to fiber length. Reeves et al. (2004) found significant increases in fascicle length in response to 14 weeks of resistance exercise in older adults (mean age= 74.3 ± 3.5 years). Nine older adults trained using a whole- body resistance exercise program including bilateral knee extension and leg press exercises. Muscle fiber length increased by 11% ($p= 0.05$) following training (N. D. Reeves et al., 2004). In a follow-up study, Reeves and colleagues (2009) examined the effects of 14 weeks of resistance exercise, comparing eccentric training to conventional training modalities in older adults. They reported muscle fiber length to increase in both groups however, significantly greater gains were reported in the eccentric training group (20%) than the conventional training group (8%, $p=0.05$) (N. D. Reeves, Maganaris, Longo, & Narici, 2009). The difference observed in fascicle length change is interesting when examining the differences between rectus femoris and vastus lateralis in terms of their functional anatomy. The rectus femoris is a bipennate, biarticulate muscle that has been shown to contain fiber to muscle length ratios higher than other muscles of the quadriceps femoris whereas the vastus lateralis is a unipennate muscle that articulates just one function, which indicates that the primary function of this muscle is force production (Moreau, 2009).

Pennation Angle Evaluation

Because changes in pennation angle allow for greater relative changes in single muscle fiber hypertrophy more so than anatomical cross sectional area (Aagaard et al., 2010), ultrasound may be an attractive tool for the obtainment of this variable if the goal is to calculate physiological cross sectional area. Abe et al. (1998) concluded no difference in pennation angle between strength trained females and college age male athletes matched for age and height in relation to their muscle thickness measures in vastus lateralis. They concluded that the observed differences in pennation angle appeared to be related to muscle thickness (Abe, Brechue, Fujita, & Brown, 1998). In a previously cited study, when comparing 121 men and 190 women split by gender and age (i.e. 20-39 and 60-85 years), pennation angles were found to be significantly larger in younger than older adults (p=0.01, for men and women). In response to resistance training, Reeves et al. (2004) found that older adults (mean age= 74.3 ± 3.5) were successful in increasing pennation angle of the vastus lateralis (13%, p=0.01) in response to 14 weeks of resistance exercise. In 2009, Reeves and colleagues also compared the effects of 14 weeks of eccentric training to traditional training in older adults (mean age= 74 ± 3 years). Pennation angle increased by 35% (p=0.05) in the conventional training group, compared to the eccentric group who demonstrated no significant change, leading the researchers to conclude that differences in training protocol may elicit different myogenic architectural responses (N. D. Reeves et al., 2009).

Physiological Cross Sectional Area Calculation

The physiological cross sectional area (PCSA) often exceeds the anatomical cross-sectional area (ACSA) because it accounts for the arrangement of muscle fibers in relation to the force generating axis (Lieber, 2010). Although an increase in pennation angle of muscle fiber decreases the relative force production of a single fiber, it allows the body to lie down more in parallel, which increases potential force generating capacity with angular increases up to about 45 degrees (Aagaard et al., 2001).One of the first studies to combine the methods of MRI, skeletal muscle ultrasound, and muscle biopsy sampling was conducted by Aagard and colleagues (2001). In response to 14 weeks of resistance training, previously untrained male participants (27.0 ± 5.3 years) increased vastus lateralis pennation angle by an average of 35% which in turn related to an increase in single muscle fiber PCSA of 16%. More importantly, this increase was larger than the increase in ACSA of 10% which demonstrated the importance of muscle architecture in making predictions of maximal force output. A point of interest however, was that the length of fascicles was not measured and not estimated in this study which may have applications when calculating force output and contraction velocity.

Recently, estimated PCSA of older males were compared to those of younger male counterparts (Suetta et al., 2009). PCSA was calculated as the product of muscle volume and pennation angle, divided by fascicle length. Older males were found to have PCSA values 17% less than younger males at baseline. When both groups were immobilized for 2 weeks, no decreases were observed in either group. Following the immobilization period, both groups of subject performed a 4- week resistance training program. The young males increased PCSA by 10.6%, but the older adult males demonstrated no significant increase in PCSA, suggesting that older adults may have an attenuated response to training periods as short as 4 weeks compared to a younger population.

Echo Intensity of Skeletal Muscle

Prior to the use of quantitative grayscale analysis software, muscle quality was visually scored on a four point scale, generally by two or more blinded observers (Sipila & Suominen, 1991). Recent technological advancement in image analysis have allowed for a more precise differentiation between lean muscle mass, and connective and adipose tissues (Pillen & van Alfen, 2011). Generally with age, we see an increase in the reflectivity that represents an increase in non-contractile units relative to lean skeletal muscle (Cadore et al., 2012). Echo intensity is the representation of the pixel count that is obtained using ultrasound images and is presented on an arbitrary units scale (Au) ranging from 0-256, (0: black; 256: white) with an increase in echo intensity reflecting a decrease in muscle quality (i.e. greater connective tissue and adipose and decreased lean skeletal muscle). The reflectivity of the ultrasound signal enables the viewing of bundles of muscle fibers because of the reflective nature of the perimysium that surrounds them. Because of this, clinicians and researchers are able to measure muscle fiber fascicle lengths and pennation angles *in vivo.* In terms muscle quality, the most common method of assessment used in previous literature is to divide strength by unit of mass, also referred to as relative strength. However, there are many challenges associated with this common method of muscle quality evaluation, including the need for full central activation, and pain or other neural-inhibitory factors that are not accounted for with this non-invasive method (Doherty, 2003). With the assistance of ultrasound, factors such as the ones previously mentioned may be better represented since the measure of echo intensity is indicative of the architectural characteristics of muscle, including the infiltration of adipose, connective, and other non-contractile tissues into the lean muscle mass. Future research is aimed at the relation between echo intensity and various measures of physical performance not only in older adults, but athletes and children as well. These methods may have implications as a screening tool for quality of muscle and its relation to frailty and ability to perform activities of daily living in older adults. In the athletic population, we may be better able to understand how bilateral discrepancies translate into injury or fatigue throughout the course of a season; and finally, within children these ultrasound methods may be used as an early evaluation tool in identifying neuromuscular disorders and documenting longitudinal changes.

An important consideration to the evaluation of muscle quality via ultrasonography is that values for echo intensity may differ greatly depending on device settings, and sample population. The highest probe frequency available is generally used with the idea of increasing spatial resolution and image quality if the muscles being observed are relatively superficial (Pillen & van Alfen, 2011). As devices have evolved, so have the quality and frequencies of transducer probes. In any case, whenever a new device or setting is used, it is then necessary for new normative values to be established (Arts et al., 2010). Normative values also differ between healthy and myopathic populations (Pillen, Scholten, Zwarts, & Verrips, 2003). Chapman and colleagues (2008) compared the echo intensity of the elbow flexors in young men (mean age= 25 ± 6 years) and older men (mean age= 64 ± 4 years) and found the intraclass correlation coefficients to be higher for the younger men (R= 0.96) than for the older men (R= 0.86). Although the measures were still reliable for both groups (Chapman, Newton, McGuigan, &

Nosaka, 2008), the discrepancy between reliability results may have been a result of the breakdown of surrounding muscle fascia that is commonly observed in many older adults, likely making it difficult to differentiate between lean muscle and connective tissues. Similarly, when investigating the effects of neuromuscular disease on echo intensity, Pillen et al. (2003) found significant differences in echo intensity for children suspected of neuromuscular disease and those that did not ($p \leq .01$ for all outcome measures). Out of 36 total patients (23 boys: median age= 5.3 years; 13 girls: median age= 6.2 years) 13 were found to have a neuromuscular disorder, 6 of which were myopathic and 7 of which were neuropathic. The rectus femoris specifically was chosen to represent the quadriceps femoris because of the fact that the vastus intermedius can be difficult to examine with individuals possessing neuromuscular disorders. The authors concluded that computer-assisted grayscale analysis of echo intensity was a reliable method of detecting possible neuromuscular diseases in children (Pillen et al., 2003). Another group of investigators attempted to establish normative values among adults (age range= 17-90 years) and found values to be higher for females in all muscles evaluated including the biceps brachii, tiabialis anterior, and rectus femoris (Art et al., 2010). One possible limitation however, was that the means were presented as a combination of the age spectrum and the authors did note that echo intensity was found to correlate with age for all muscles examined (Arts et al., 2010).

Recently, studies have evaluated the relationship between echo intensity and measures of fitness and anthropometric measures in older adults. In a cross-sectional study, Cadore et al. (2012) examined the relationship between echo intensity and skeletal muscle power in conjunction with cardiovascular performance in healthy older men (mean age= 65.5 ± 5.0). Lower body isometric and isokinetic peak torque, echo intensity of the rectus femoris, and various measures of cardiorespiratory fitness were evaluated. Mean echo intensity values (mean EI= 126.5 ± 22.9 au) were significantly correlated to values for isometric and isokinetic peak torque (r= -0.48 to r= -0.64; $p \leq .05$), as well as to ventilatory thresholds 1 and 2 (r= -0.46 and r= -0.50, respectively; $p \leq 0.05$) which suggests a connection between intramuscular adipose and connective tissue and cardiorespiratory performance due to decreased cappilarization. In addition, isometric strength was found to correlate to echo intensity (r= -0.40, $p \leq 0.01$). This investigation appeared to be one of the first to demonstrate that echo intensity may have an effect on both muscular strength as well cardiorespiratory performance (Cadore et al., 2012). Another recent study conducted in 2012 examined the relation between measures of echo intensity, strength, and body composition (Fukumoto et al., 2012). In a sample of 92 healthy Japanese women (mean age= 70.4 ± 5.5 years), subcutaneous fat, muscle architecture, and morphology was captured using B-mode ultrasonography, and strength was assessed using knee extensor isometric strength. Echo intensity values were found to significantly correlate with quad strength (r= -0.40, $p \leq 0.01$) independent of age or muscle thickness of the quadriceps femoris. Stepwise regression further revealed that muscle thickness, as well as echo intensity, was independently related to maximal quadriceps strength, and that echo intensity was not related to subcutaneous fat, total body fat, or body mass index. These results suggest that muscle quality, as assessed by echo intensity, directly relates to differences in strength in a population of older adult women (Fukumoto et al., 2012). Although echo intensity has been demonstrated to have a significant relationship with the lower body extensor muscles in older adults, research has been limited to older adults. Whether this relationship exists in younger or athletic populations is not well-understood.

Echo Intensity Response to Resistance Exercise

Investigations examining changes in echo intensity with resistance training have focused on the damaging effects of exercise and how the use of echo intensity might be helpful in quantifying the extent of damage. In 1995, Nosaka et al. led 12 untrained males (mean age= 21.7 ± 2.4) through a damaging protocol consisting of 3 sets of 10 eccentric biceps curls, followed by the same protocol 3 and 6 days after the initial training day. Measures were taken prior to and immediately following each eccentric workout. Results reported that muscle damage as assessed by echo intensity was significantly higher ($p \leq 0.01$) at day one, however; damage was not exacerbated further after 3 and 6 days following the damaging exercise protocol (Nosaka & Clarkson, 1995). These results were substantiated in a follow-up study in 2002 in which no further damage was elicited when using eccentric damaging of the elbow flexors followed by repeating the protocol one week following the initial insult (Nosaka & Newton, 2002). It appears that damage due to eccentric contraction may remain elevated for a minimum of six to seven days, but not further elicited with subsequent bouts in younger healthy trained and untrained men. Eccentric contraction study protocols resulting in elbow flexor damage has been examined in young (mean age= 22 ± 3.2 years) healthy untrained women (Radaelli, Bottaro, Wilhelm, Wagner, & Pinto, 2012). Subjects exercised using a damaging hypertrophic protocol (10 repetitions at 80% of 1RM) in the dominant arm in, while the non-dominant arm was used as a control. Reported results were that echo intensity values remained elevated for 72 hours at each time point with the exception of 0 hours after, although muscle size was increased at 0 hours after. The unexpected finding of no change in echo intensity was attributed to the hyperemic effects of exercise not being detected by ultrasound and that an increase in echo intensity represents changes to inflammatory responses and not hyperemia however, previous research reports that echo intensity is increased immediately after exercise (Nosaka & Newton, 2002). The authors concluded that non-resistance trained females may need more than 72 hours to recovery from a damaging protocol (Radaelli et al., 2012). Taken together, echo intensity has demonstrated reliable results in the assessment of muscular damage in younger men and women, regardless of training status. Results seem to differ however, in the increase of echo intensity immediately following resistance exercise and warrants further investigation.

As interest increases in the use of ultrasound to assess muscular damage and quality so does the application of this method to older adults. It is possible that echo intensity may provide us with a method of documenting not only morphological increases such as muscle thickness and cross sectional area, but also architectural changes observed in grayscale analysis. Chapman et al. (2008) investigated the effects of maximal voluntary eccentric muscle lengthening actions on damage and recovery of the elbow flexors in young versus older men. Ten older men (mean age= 64 ± 4 years) and 10 young men (mean age= 25 ± 6 years) performed 30 maximal voluntary lengthening contractions at an angular velocity of $210°\cdot s^{-1}$. Results revealed that older men showed a significantly slower recovery from the damaging protocol, less development of soreness, and a slower recovery of strength than the younger men (Chapman et al., 2008).

When examining the relation between echo intensity and fitness measures in older adults, Cadore et al. (2012) and Fukumoto et al. (2012) found significant relationships between measures of muscular strength and cardiorespiratory fitness. Currently, research evaluating the effects of a progressive resistance training program on echo intensity in older adults however, are lacking and therefore is warranted for future study.

CHAPTER 3: METHODOLOGY

Participants

Twenty- five healthy men (*n*= 12) and women (*n*= 13) over 60 years of age were recruited to participate in the study on the basis of consent, and health status.

Inclusion and Exclusion Criteria

Study inclusion criteria were as follows: participants must have been at least 60-69 years of age with no positive risk factors on the administered physical activity readiness questionnaire (PAR-Q); those 70 and older were required to obtain physician clearance, may have been male or female, body mass index (BMI) for men must have been greater than 20 but no more than 35, BMI for women must have been greater than 18 but no more than 37, had to be ambulatory, agree to maintain current physical activity level, voluntarily sign an informed consent, had to be able to read, speak and understand English, and must have had the ability to visit the University of Central Florida for testing and training. Any individual was excluded from participation for the following: physically excluded by one or more positive answer on the PAR-Q (ages 60-69 years) or absence of physician's clearance (ages 70 and older), classified as "high risk" by having cardiovascular , pulmonary, or metabolic disease, or having one or more symptoms; undergone major surgery less than 16 weeks prior to enrollment, current active malignant disease (except basal, or squamous cell skin carcinoma or carcinoma in situ of the uterine cervix, or localized prostate cancer not under active treatment), stated immunodeficiency disorder, states presence of partial or artificial limb, known dementia, brain metastases, eating disorder, history of significant psychiatric or psychological condition that may interfere with the study, were currently taking medications or substance that could profoundly modulate metabolism, were regularly participating in a strength or resistance training program in the past 3 months, or anyone that study investigators determined not fit for participation. Individuals who had undergone a procedure with iodine, barium, or nuclear medicine isotopes within the 7 days prior were not able to undergo DEXA scan but may still have participated if we were able to accommodate around scheduled procedures with a sufficient window of at least 7 days to ensure participant safety. Positive risk factors as determined by PAR-Q included: age (men ≥ 45 yrs.; women ≥ 55 yrs.), family history of myocardial infarction, cigarette smoking, sedentary lifestyle, obesity determined by BMI or waist girth, hypertension, dyslipidemia, and pre-diabetes. Negative risk factors included serum high density lipoprotein (HDL) cholesterol (≥60 mg/dL).

Recruitment of subjects occurred through a number of sources including, word of mouth, flyers, newsletter, bulletins as well as electronic media. Initial eligibility was assessed by a scripted phone screening. All participants were required to complete an informed consent document approved by the Universities' Institutional Review Board (APPENDIX B) and had to be physically cleared for participation before taking part in the research study.

Research Design

Procedures

Volunteers were randomized into an exercise group (RT), which began six weeks of resistance training immediately following the pre-test, or a control group (CON), which completed pre-testing prior to six weeks of serving as a non-resistance training control for the RT group. All participants were tested on two occasions separated by six weeks. The study concluded when participants completed the six weeks of resistance training and control and 2-testing sessions. Including testing, the study duration lasted about eight weeks, depending on scheduling availability and each testing period occurred depending on participant availability. (Figure 1).

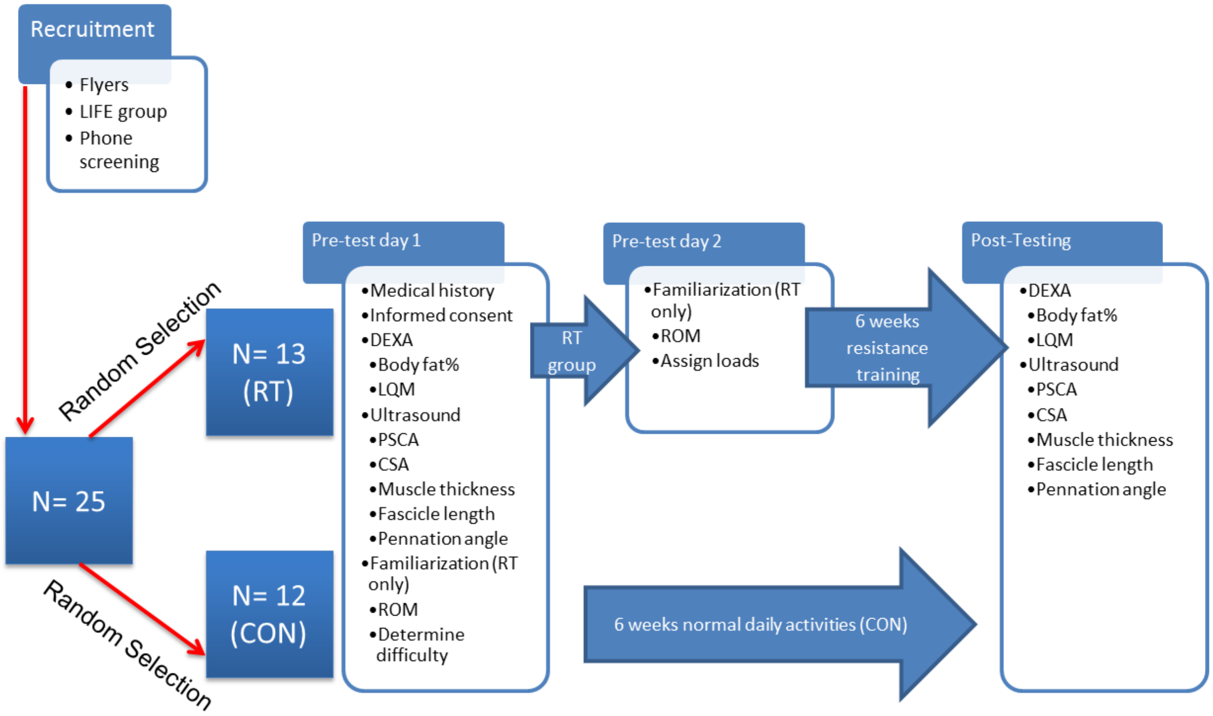


Figure 1. Study Protocol.

Study Endpoints

Each volunteer's participation was considered complete after the second testing session. No investigational agents were being examined and no onsets of disease or adverse side-effects from participation were expected therefore, no reason to terminate the study prior to completion was foreseen. However, if any participant decided to no longer participate for any reason, he/she was able to terminate at any time without consequence. Additionally, if a participant's health status changed during the study, or the participant experienced any event that made participation difficult or risked safety, participation was terminated.

Body Composition

Total and regional body composition was evaluated using dual X-ray absorptiometry (DEXA), providing measures of lean mass (LM), and fat mass (FM). Lean thigh mass (LTM) was collected in kilograms by isolating a region of interest that included the thigh and excluded the lower leg and all other tissues. All DEXA scans were ordered by a licensed physician in the state of Florida and performed in the Faculty Wellness Center by a licensed radiology technician. LTM reliability coefficients (ICC) were 0.98 (SEM = 0.261 kg).

Ultrasonography

Non-invasive skeletal muscle ultrasound images were collected of the rectus femoris and vastus lateralis muscle architecture. This technique uses sound waves at fixed frequencies to create in vivo, real time images of the deep limb musculature. Participants were instructed to wear shorts during the testing day to expose the superficial dermis of the anterior and lateral thigh. Participants were instructed to lay resting supine for 15 minutes to allow fluid shifts to occur. Images were collected after 72 hours without any vigorous physical activity (Cadore et al., 2012). A 12 MHz linear probe scanning head (General Electric LOGIQ P5, Wauwatosa, WI, USA) was used to optimize spatial resolution (Thomaes et al., 2012). The probe was coated with water soluble transmission gel and positioned on the surface of the skin to provide acoustic contact without depressing the dermal layer to collect the image. Measures of cross-sectional area, muscle thickness, and pennation angle were taken using B-mode ultrasound with gain set to 50 and dynamic range set to 72. Image depth was fixed to 5 cm (Cadore et al., 2012). Measures of fascicle length were obtained using a sweep of the muscle in the extended field of view (LV: logiq view) mode to view the entire continuous fascicle. All measures were taken in both rectus femoris and vastus lateralis of the dominant leg. Subsequent measures were taken using the same limb positioning and anatomical site, and were performed by the same examiner. All images were analyzed offline using quantitative grayscale analysis software. ImageJ (National Institutes of Health, USA, version 1.45s) is image analysis software available through the National Institute of Health that contains the ability to quantify muscle quality in the form of Echo Intensity. A known distance of 1 cm shown in the image was used to calibrate the software program (Chapman et al., 2008).

Rectus Femoris

For measures of rectus femoris (RF), the participant was placed supine on an examination table, according to the American Institute of Ultrasound in Medicine, with the leg extended but relaxed and with a rolled towel beneath the popliteal fossa allowing for a 10 degree bend in the knee as measured by a goniometer (Bemben, 2002).

Vastus Lateralis

For measures of vastus lateralis (VL), the participant was placed on their non-dominant leg side on an examination table with the legs together and relaxed allowing for a 10 degree bend in the knee as measured by a goniometer. Toes were angled approximately 45 degrees in relation to the frontal plane.

Cross Sectional Area:

RF Cross Sectional Area

The measurement of RF cross-sectional area (CSA) was taken using the sagittal plane parallel to the long axis of the femur and scanning occurred in the axial plane, perpendicular to the tissue interface at 50% of thigh length. Fifty percent of thigh length was determined as half way from the anterior, inferior iliac to the proximal border of the patella. Three consecutive CSA pictures were taken and further analyzed offline in the ImageJ software, with the average CSA of 3 pictures being used as RF CSA. CSA was measured using the polygon tracking tool in the ImageJ software obtaining as much lean muscle as possible without any surrounding bone or fascia (Figure 2). The ICC for RF CSA was 0.99 (SEM = 0.46 cm^2).

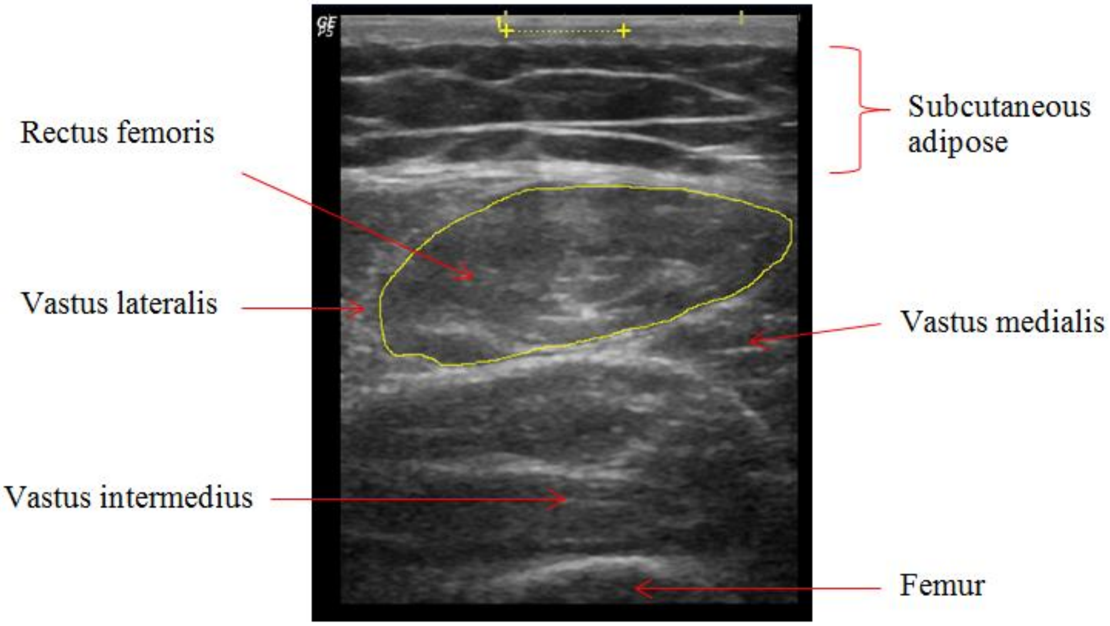


Figure 2. Rectus femoris cross sectional area measured using ImageJ.

VL Cross Sectional Area

VL CSA was measured at 50% of the distance from the most prominent point of the greater trochanter to the lateral condyle. Scanning occurred with a sweep in LV (logiq view/ extended field of view), medial to lateral to obtain the entire muscle, transverse to the muscle tissue interface. Three consecutive sweeps were taken and further analyzed offline in the ImageJ software, with the average of three pictures used as VL CSA. CSA was measured via manual tracking in the ImageJ software. The ICC for VL CSA was 0.99 (SEM = 1.26 cm^2).

Muscle Thickness:

RF Muscle Thickness

The measure of muscle thickness (MT) was taken at the same site described for CSA but with the probe oriented longitudinal to the muscle tissue interface. MT was measured at the site of the muscle's greatest diameter, from the superficial aponeurosis to the deep aponeurosis (Figure 3). Three consecutive pictures were taken and analyzed offline and the average of three pictures determined the RF MT (Thomaes et al., 2012). The ICC for RF MT was 0.96 (SEM = 0.11 cm).

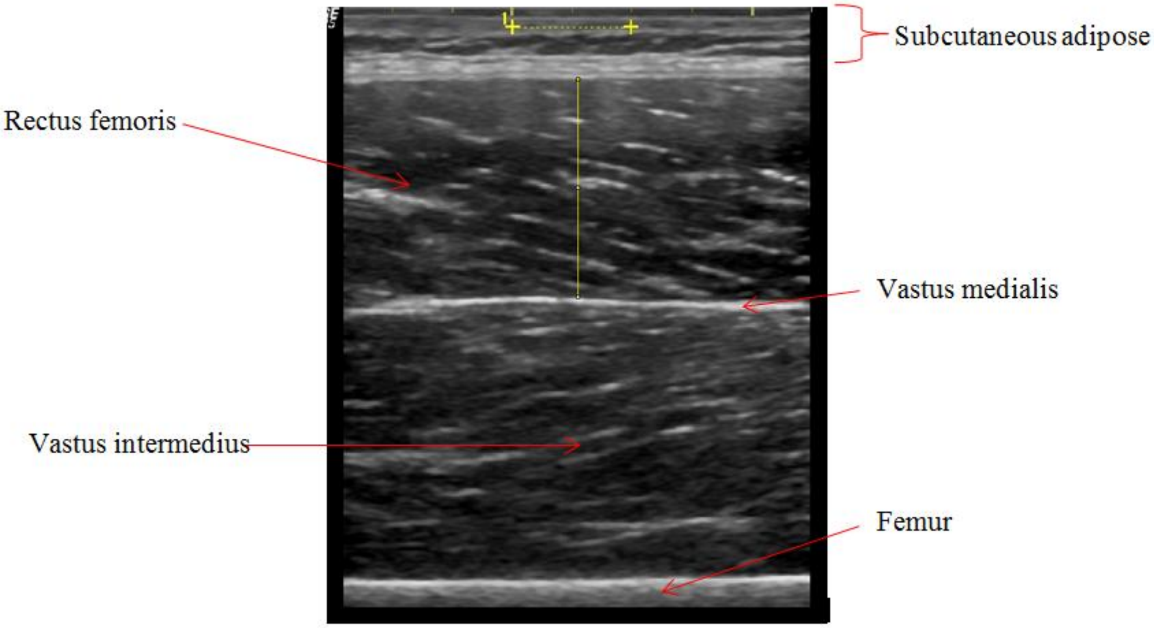


Figure 3. Muscle Thickness.

VL Muscle Thickness

MT of the VL was obtained using the same site as CSA. Thickness was measured at the site of the greatest diameter located within the image as described for RF. The ICC for VL MT was 0.89 (SEM = 0.12 cm).

<u>Fascicle Length:</u>

RF Fascicle Length

Fascicle length (L_f) of RF was measured in LV mode ultrasound. A longitudinal sweep commenced at the distal insertion along the midline of the anterior thigh and terminated at the proximal head of the muscle. L_f was determined in ImageJ by identifying a clear fascicle that extended continuously from the superficial aponeurosis to the deep aponeurosis (Figure 4). 3 consecutive pictures were taken and analyzed offline. The average of 3 pictures determined RF L_f. The ICC for this measure was 0.75 (SEM = 1.13 cm).

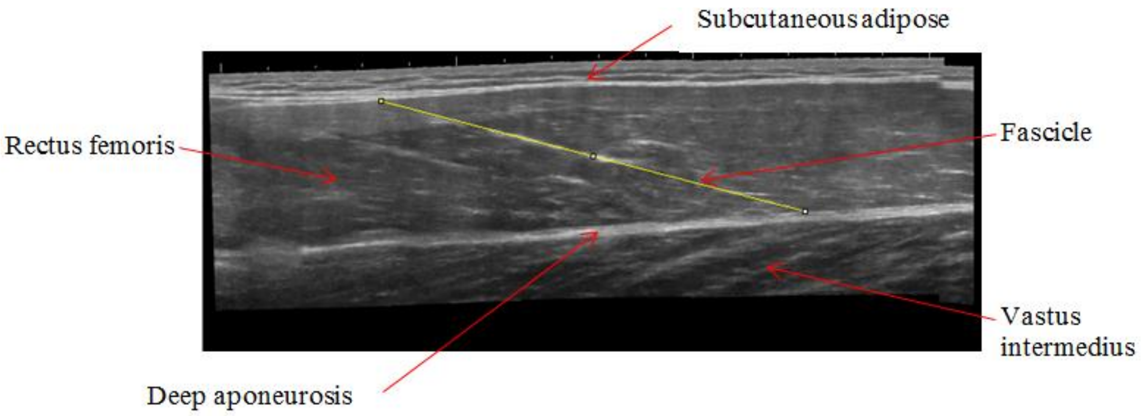


Figure 4. Fascicle length.

VL Fascicle Length

L_f of the VL was measured in LV mode ultrasound. A longitudinal sweep commenced at the distal insertion and terminated at the proximal head of the muscle along the midline of the lateral thigh. The ICC for vastus lateralis L_f was 0.66 (SEM = 1.23 cm).

Pennation Angle:

RF Pennation Angle

Pennation angle (PANG) of RF was measured in B-mode ultrasound at the same site as MT and CSA (Abe et al., 1998). The transducer was placed longitudinal to the muscle tissue interface and 3 consecutive pictures were taken and further analyzed offline in the ImageJ software. Muscle PANG was determined as the intersection of the fascicles and the deep aponeurosis of RF (Figure 5). The ICC for rectus femoris PANG was 0.73 (SEM = 2.8°).

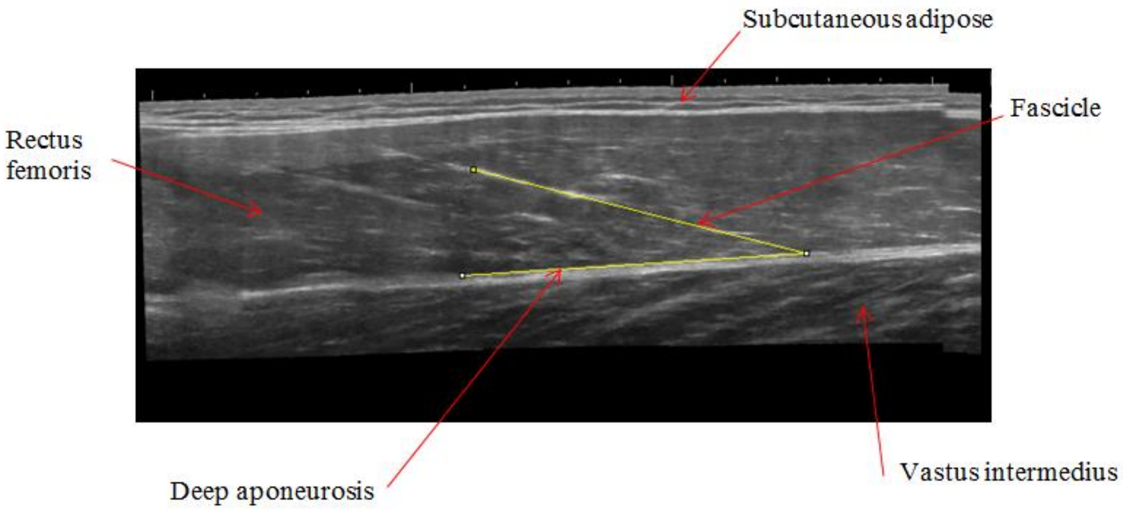


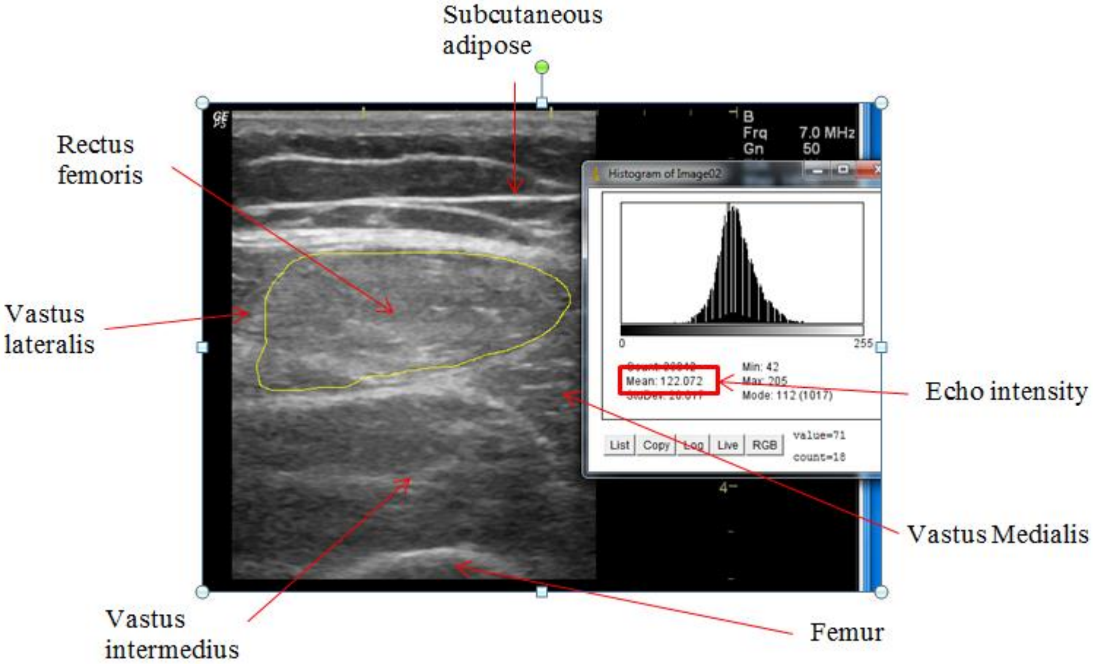
Figure 5. Pennation Angle.

VL Pennation Angle

PANG of VL was measured in B-mode ultrasound with the probe oriented longitudinal to the muscle tissue interface. The same anatomical site was used as for MT and CSA. Three consecutive pictures were taken and further analyzed offline using ImageJ. PANG was determined as described for RF. The ICC for VL PANG was 0.86 (SEM = 1.44°).

Echo Intensity

The echo intensity (EI) of RF and VL were obtained using the same pictures as for CSA and MT, and were the average of 3 consecutive images measured. EI was determined by grayscale analysis using the standard histogram function in ImageJ (Cadore et al., 2012). A region of interest (ROI) within RF was selected by obtaining as much muscle as possible without including any surrounding bone or fascia using the manual tracking tool (Cadore et al., 2012). EI in the ROI were expressed as values between 0-255 (0: black; 256: white) with an increase in EI reflecting an increase in intramuscular connective tissue and adipose relative to lean skeletal muscle (Figure 6). The EI ICCs were 0.91 (SEM = 3.47 au) for RF, and 0.93 (SEM = 5.1au) for VL.



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Mean: 122.072
Min: 42
Max: 205
Mode: 112 (1017)
value=71
count=18
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Figure 6. Measure of echo intensity.

Relative Echo Intensity

Relative EI was calculated by dividing LTM by EI to calculate mass per unit of EI.

Physiological Cross Sectional Area

Physiological cross-sectional area (PCSA) of the RF, VL, and thigh (RF + VL) was calculated using a modified version of Equation 1:

$$PCSA = \frac{mass(g)\ X\ cos\theta}{density\left(\frac{g}{cm^3}\right) X\ fascicle\ length}$$

Equation 1. Calculation of PCSA.

where mass was entered as the CSA in cm^2, PANG was entered as cosΘ, density was entered as EI in arbitrary units, and L_f was entered as cm (Lieber, 2010). The PCSA ICCs were 0.94 (SEM = 0.26 cm^2) for RF, 0.95 (SEM = 0.29 cm^2) for VL, and 0.96 (SEM = 0.43 cm^2) for the thigh.

Resistance Training Protocol

RT group participants completed a six week progressive strength training program (APPENDIX A). The program consisted of workouts twice per week with sessions lasting 1 to 1 ½ hours. The program was an individualized periodized program including exercises of varying progressions of all of the major muscle groups (biceps, triceps, deltoids, chest, back, quadriceps, hamstrings, gluteals, calves, abdominals and lower back). At least 48 hours were allowed between sessions for full recovery. Acute program variables were manipulated throughout the six weeks, but generally consisted of 2 to 4 sets of 8 to 12 repetitions of 6 to 10 exercises at submaximal intensity (Perceived Exertion was not to exceed 5-6 on a 10 point scale) (~70 to 85% of RM) according to the Omni Scale (OS; APPENDIX C) (Gearhart Jr, Lagally, Riechman, Andrews, & Robertson, 2009). Each workout session began with a dynamic warm-up consisting of body weight squats, high knee walking, and limb rotations and terminated with an appropriate cool down. The exercise program followed the recommended guidelines for older adults by the American College of Sports Medicine (American College of Sports Medicine, 2009) and were overseen by a Certified Strength and Conditioning Specialist.

Predicted 1RM

Maximal voluntary isotonic strength of the lower body was assessed with a PLLE Power Lift ® knee extension machine (Conner Athletic Products, Inc., Jefferson, IA). Participants were seated within the machine so that the shin pad was just proximal to the lateral malleolus and the beginning and terminating position of the leg was 90 degrees of knee flexion. Participants performed an initial set of 10 repetitions to assess comfort. Following a three minute rest period, a load was estimated that the participant believed they could complete for 10 repetitions. If more than 10 repetitions were performed, they were stopped and rested for an additional three minutes. Level of perceived exertion was constantly monitored using the OMNI scale as described previously for all resistance exercise sessions. When required, this process was repeated until a load was achieved that the participant could perform a maximum of 10 repetitions or less. Participants performed up to 3 attempts in order to reach the goal. Following repetition maximum evaluation, the Brzycki prediction equation [load in kg / (1.0278 – 0.0278 x repetitions)] was used to predict maximal knee extensor strength (1RM). This method has been previously validated in clinical populations yielding a typical error of 4% (± 3.4kg) (McNair, Colvin, & Reid, 2011).

Muscle Quality as Relative Strength

Muscle quality as relative strength (MQ) was assessed by dividing 1RM in kilograms by the lean thigh mass (LTM) in kilograms, as assessed by DEXA.

Muscle Quality as Strength Relative to Echo Intensity

Muscle quality as strength relative to echo intensity (REI) was assessed by dividing 1RM in kilograms by EI of the thigh in arbitrary units, as assessed by ultrasound.

Statistical Analysis

Results are expressed as mean ± standard deviation unless otherwise noted. A two-way repeated measures analysis of variance (ANOVA) (group [exercise vs. control] x time [pre vs. post]) was used to identify group differences and group by time interactions. Analyses were conducted on the following variables: CSA, MT, L_f, PANG, EI, MQ, REI, and PCSA of RF, VL, and thigh. Stepwise regression was used to assess predictors of 1RM. Independent t-tests were performed to detect differences between groups at baseline. An alpha level of $p \leq 0.05$ was used to determine statistical significance. Data analysis was performed using SPSS v. 20.0.0 (SPSS Chicago, IL).

CHAPTER 4: RESULTS

Participants

Anthropometric results are presented in Table 1. Anthropometric measures did not differ between groups at baseline in any measure. No significant changes in any anthropometric measure were seen in either group following the six week resistance training protocol.

Twenty-five participants completed the study (RT= 13; CON= 12). Adherence rate for training sessions in the RT group was 96%. Results are presented as mean ± S.D.

Leg Extensor Strength and Lean Thigh Mass

Measures of 1RM and measures of relative muscle quality before and after training are presented in Table 2. 1RM increased 31.9% (pre: 39.2 ± 15.9 kg; post: 51.7 ± 17.6 kg; $p = 0.00$; Figure 7) and corresponded with an increase in MQ of 31.5% ($p = 0.00$; Figure 8) as well as an increase in REI of 33.3% (pre: 0.54 ± 0.27 kg/au, post: 0.72 ± 0.32 kg/au; $p = 0.00$; Figure 9) in the RT group. LTM did not significantly change in either group, and demonstrated no significant interaction ($p = 0.84$). 1RM did not change in CON (pre: 31.1 ± 11.8; post: 33.3 ± 14.7; $p = 0.31$; Figure 7). CON group MQ, and REI also showed no significant change; ($p = 0.53$; Figure 8) and ($p = 0.15$; Figure 9), respectively. 1RM was significantly correlated at baseline to thigh PCSA ($r = 0.57$; $p = 0.00$), VL PCSA ($r = .517$; $p = .010$), and RF PCSA ($r = 0.53$; $p = 0.00$; Table 3). Group by time interactions for 1RM, MQ, and REI are presented in Table 4.

Cross Sectional Area

Measures of muscle architecture and size before and after training as well as interactions are presented in Table 5 and 6, respectively. In the RT group, mean CSA of RF did not significantly change (pre: 7.89 ± 2.43 cm^2; post: 8.2 ± 2.78 cm^2; $p = 0.17$; Figure 10). VL CSA increased by 7.4% (pre: 14.99 ± 4.36 cm^2; post: 16.1± 4.87 cm^2; $p = 0.04$; Figure 11). No changes were observed in RF or VL (pre: 7.59 ± 2.76 cm^2; post: 7.64 ± 2.58 cm^2; $p = 0.60$; Figure 10) and (pre: 14.39 ± 4.59 cm^2; post: 14.33 ± 5.01cm^2; $p = 0.33$; Figure 11) respectively, in the CON group. There were no significant interactions in CSA for rectus femoris however, vastus lateralis CSA demonstrated a significant group x time interaction ($p = 0.03$; Table 6).

Muscle Thickness

No significant changes in MT of RF (pre: 1.84 ± .37 cm; post: 1.9 ± .41cm; $p = 0.33$; Figure 12) or VL (pre: 1.51 ± .34; post: 1.4 ± .34 cm; $p = 0.24$; Figure 13) were observed in the RT group. MT remained unchanged in RF for the CON group (pre: 1.75 ± .37 cm; post: 1.70 ± .40 cm; $p = 0.16$; Figure 12) as well as in VL (pre: 1.34 ± .43 cm; post: 1.27 ± .44 cm; $p = 0.06$; Figure 13). There was no significant group by time interaction for MT in either RF or VL (Table 6).

Fascicle Length

No significant changes in L_f were seen in RF (pre: 7.92 ± 1.57 cm; post: 8.2 ± 2.78 cm; $p = 0.33$; Figure 14) or VL (pre: 7.45 ± 1.15 cm; post: 7.9 ± 1.4 cm; $p =.01$; Figure 15) in the RT group. Similarly, the CON group did not change significantly in RF (pre: 7.45 ± 1.96 cm; post: 7.31± 1.78 cm; $p = 0.44$; Figure 14) or VL (pre: 7.27 ± 1.28 cm; post: 7.33 ± 1.12 cm; $p = 0.72$; Figure 15). RF and VL L_f did not demonstrate a significant group by time interaction (Table 6).

Pennation Angle

No changes in PANG were observed in RF or VL in the RT group (pre: 13.52 ± 3.48°; post: 12.9 ± 2.78 °; $p = 0.37$; Figure 16) and (pre: 9.87 ± 1.4°; post: 10.2 ± 1.54 °; $p = 0.43$; Figure 17), respectively. Similarly, no changes in CON were observed from pre to post in either RF (pre: 11.58 ± 3.97°; post: 10.5 ± 2.9°; $p = 0.29$; Figure 16) or VL (pre: 10.98 ± 2.8°; post: 10.13 ± 2.61°; $p = 0.055$; Figure 17). PANG of RF and VL did not demonstrate any significant group by time interaction (Table 6).

Echo Intensity

Mean baseline EI values were 81.3 ± 12.6 Au and 89.1 ± 10.0 Au for RF and VL, respectively for all participants (Table 5). There were no significant changes in EI of RF (pre: 81.5 ± 13.9Au; post: 80.1± 16.0 Au; $p = 0.33$; Figure 18) or VL (pre: 91.8 ± 10.79 Au; post: 90.1 ± 8.1 Au; $p = 0.32$; figure 19) for the RT group. EI for the CON group did not significantly change in RF (pre: 83.66 ± 7.91Au; post: 79.94 ± 7.87 Au; $p =.00$; figure 18) or VL (pre: 86.49 ±

9.22; post: 86.33 ± 9.83 Au; *p* = 0.91; figure 19). There were no significant group x time interactions for RF or VL EI; however, there was a main effect of time for RF in the CON group (Table 6).

Relative Echo Intensity

LTM relative EI did not significantly change in the RT (pre: .0327± .0126 kg/Au; post: .0336 ± .0137 kg/Au; *p* = 0.37) or CON groups (pre: .0313 ± .0114 kg/Au; post: .0323 ± .0127 kg/Au; *p* = 0.09; Figure 20). Relative EI did not demonstrate a significant group by time interaction following training (Table 4).

Physiological Cross Sectional Area

PCSA did not significantly change in the RT group (pre: 3.12 ± 1.44 cm^2; post: 3.39 ± 1.64 cm^2; *p* = 0.09) or CON group (pre: 3.05 ± 1.54 cm^2; post: 2.84 ± 1.48 cm^2; *p* = 0.10; figure 21) however, did demonstrated a significant relationship at baseline in all participants to 1RM (*r* = .897; *p* = 0.00; Table 3). There was a significant group by time interaction in PCSA (*p* = 0.02; Table 6).

Factors Associated with Predicted Leg Extensor Strength

LTM was the best predictor of 1RM at baseline (R^2 = 0.47) and following 6 weeks of training (R^2 = 0.54, Table 7) however, with LTM omitted, MT of RF was the best predictor of

1RM both at baseline ($R^2 = 0.35$) and following training ($R^2 = 0.53$; Table 8). PCSA of VL alone was found to be the single best predictor of change in 1RM ($R^2 = 0.20$, Table 9).

Table 1. Anthropometric measures for participants, before and after training.

Group	Variable	Pre			Post		
Training (*n*= 13)	Height (cm)	171.1	±	10.1	--		--
	Weight (kg)	84.2	±	19.8	84.3	±	20.2
	Body Fat (%)	40.0	±	9.0	40.0	±	8.0
	Age (y)	71.0	±	6.7	--		--
	BMI (m/kg^2)	28.5	±	5.2	28.5	±	5.4
	LBM (kg)	47.6	±	10.6	47.9	±	10.5
	LTM (kg)	5.4	±	1.3	5.4	±	1.3
Control (*n*= 12)	Height (cm)	166.5	±	7.9	--		--
	Weight (kg)	76.5	±	18.2	76.8	±	18.4
	Body Fat (%)	35.0	±	9.0	35.0	±	9.0
	Age (y)	70.1	±	5.5	--		--
	BMI (m/kg^2)	27.5	±	5.6	27.6	±	5.5
	LBM (kg)	49.5	±	13.4	49.5	±	13.2
	LTM (kg)	5.7	±	2.2	5.8	±	2.4

Values reported as mean ± standard deviation (SD); BMI= body mass index, LBM= lean body mass, LTM= lean quad mass.

Table 2. Measures of strength, muscle quality, and size before and after training.

	RT		CON	
Measure	Pre	Post	Pre	Post
1RM (kg)	39.2 ± 15.9	51.7 ± 17.6**	31.1 ± 11.8	33.3 ± 14.7
1RM/LTM (kg)	7.14 ± 1.74	9.38 ± 1.65**	6.04 ± 2.11	6.29 ± 2.21
1RM/Thigh-EI	.542 ± .273	.723 ± .327**	.404 ± .162	.449 ± .221

Values reported as mean ± standard deviation; 1RM= predicted one repetition maximum, LTM= lean thigh mass, Thigh-EI = thigh echo intensity.

**Significantly different than before training, $p \leq 0.01$.

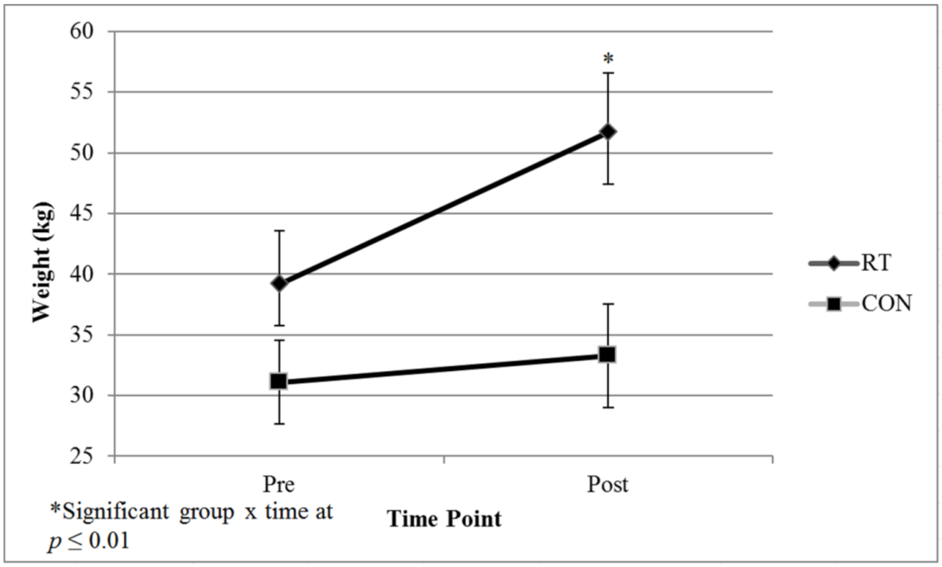


Figure 7. 1RM (kg) before and after training in the RT and CON groups.

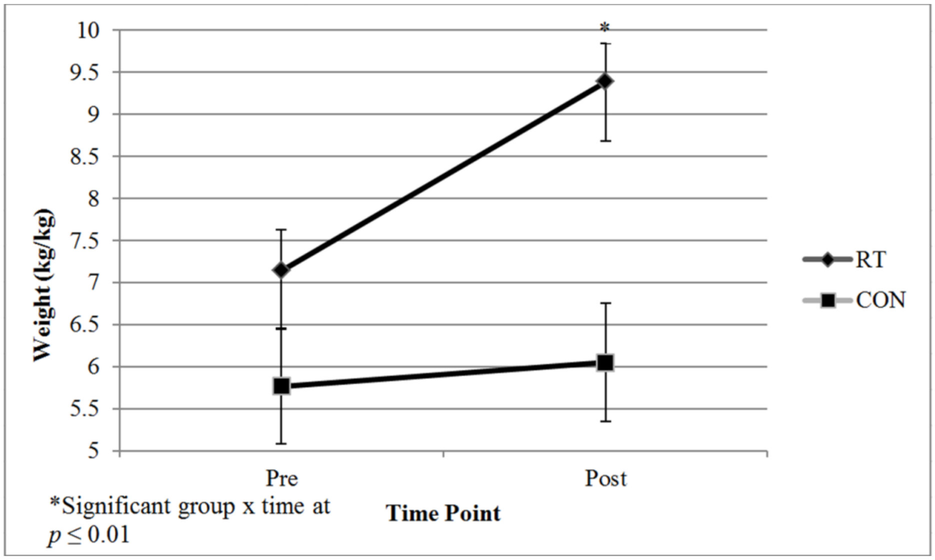


Figure 8. MQ before and after training in the RT and CON groups.

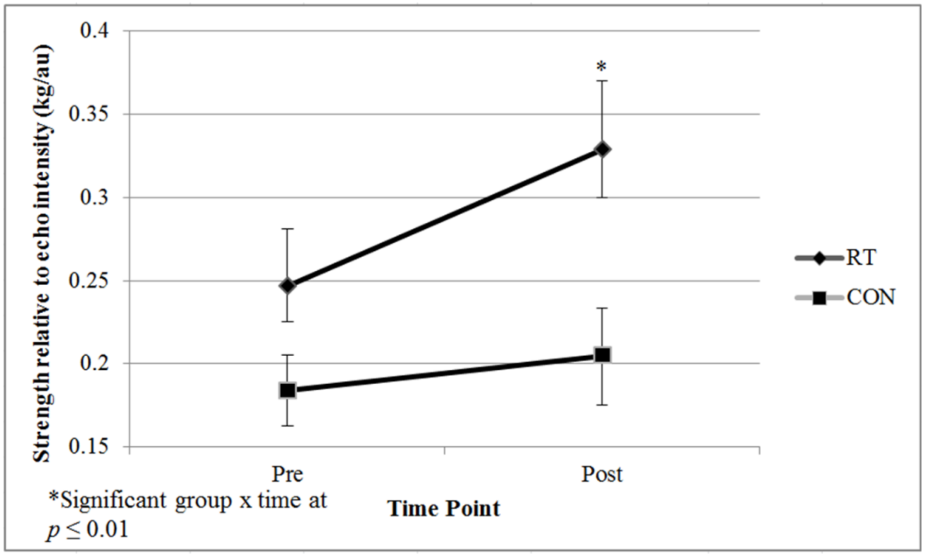


Figure 9. REI before and after training in the RT and CON groups.

Table 3. Correlation between 1RM (kg) and muscle mass and architecture at baseline.

Variable	*r*	*p*
LTM (kg)	0.676	0.000**
Thigh PCSA (cm^2)	0.579	0.003**
RF PCSA (cm^2)	0.532	0.007**
VL PCSA (cm^2)	0.517	0.010**

Values indicate correlation (*r*) and significance (*p*); LTM= lean quad mass, PCSA= physiological cross sectional area, RF= rectus femoris, VL= vastus lateralis; ***p*≤ 0.01.

Table 4. Effect of resistance training on 1RM, MQ, and REI. Effects of time, group, and group x time interactions are reported.

Measure	Group (*p*)	Time (*p*)	Group x Time (*p*)
1RM (kg)	0.037*	0.000**	0.001**
1RM/LQM (kg)	0.007**	0.000**	0.001**
1RM (kg)/Thigh-EI (au)	0.055	0.000**	0.005**
LTM (kg)/THIGH-EI (au)	0.789	0.103	0.922

Values indicate significance (*p*); 1RM= predicted one repetition maximum, Thigh-EI= combined rectus femoris EI + vastus lateralis EI, LTM= lean thigh mass. * *p* ≤ 0.05, ***p* ≤ 0.01.

Table 5. Measures of muscle architecture and size before and after training.

	RT		CON	
Measure	Pre	Post	Pre	Post
RF Muscle Thickness	1.84 ± 0.37	1.9 ± 0.41	1.75 ± 0.37	1.7 ± 0.40
RF Pennation Angle	13.52 ± 3.48	12.9 ± 2.78	11.58 ± 3.97	10.5 ± 2.9
RF Fascicle Length	7.92 ± 1.57	8.2 ± 1.68	7.45 ± 1.96	7.31 ± 1.78
RF Cross-sectional Area	7.89 ± 2.43	8.2 ±2.78	7.59 ± 2.76	7.64 ± 2.58
RF Echo Intensity	81.57 ± 13.94	80.1 ± 16.02	83.66 ± 7.91	79.94 ± 7.87
VL Muscle Thickness	1.51 ± 0.34	1.4 ± 0.34	1.34 ± 0.43	1.27 ± 0.44
VL Pennation Angle	9.87 ± 1.4	10.2 ± 1.54	10.98 ± 2.80	10.13 ± 2.61
VL Fascicle Length	7.45 ± 1.15	7.9 ± 1.4	7.27 ± 1.28	7.33 ± 1.12
VL Cross-sectional Area	14.99 ± 4.36	16.1 ± 4.87*	14.39 ± 4.59	14.33 ± 5.01
VL Echo Intensity	91.8 ± 10.79	90.1 ± 8.1	86.49 ±9.22	86.33 ± 9.83
LTM (kg)	5.42 ± 1.33	5.46 ± 1.39	5.75 ± 2.25	5.80 ± 2.42
Thigh PCSA	3.12 ± 1.44	3.39 ± 1.64	3.05 ± 1.54	2.84 ± 1.48

Values are reported as mean ± standard deviation. RF= rectus femoris, VL= vastus lateralis, LTM= lean thigh mass, PCSA= physiological cross sectional area.
* Significantly different than before training, $p \leq 0.05$.

Table 6. Effects of resistance training on measures of muscle size and architecture. Effects of group, time, and group x time interactions are reported.

Measure	Group (*p*)	Time (*p*)	Group X Time (*p*)
RF Muscle Thickness	0.387	0.903	0.104
RF Pennation Angle	0.087	0.141	0.674
RF Fascicle Length	0.326	0.64	0.205
RF Cross-sectional Area	0.683	0.148	0.293
RF Echo Intensity	0.840	0.005**	0.196
VL Muscle Thickness	0.294	0.058	0.940
VL Pennation Angle	0.527	0.390	0.052
VL Fascicle Length	0.467	0.053	0.150
VL Cross-sectional Area	0.544	0.056	0.033*
VL Echo Intensity	0.238	0.403	0.482
LTM (kg)	0.760	0.609	0.844
Thigh PCSA	0.623	0.762	0.020*

Values indicate significance (*p*); RF= rectus femoris, VL= vastus lateralis, LTM= lean thigh mass, PCSA= physiological cross sectional area; $*p \leq 0.05$, $**p \leq 0.01$.

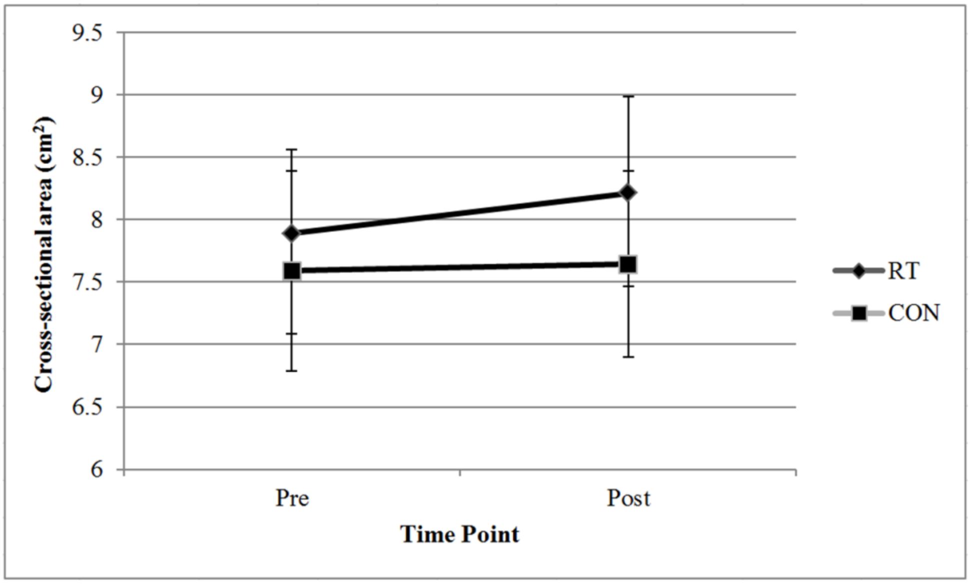


Figure 10. CSA (cm^2) of RF before and after training in the RT and CON groups.

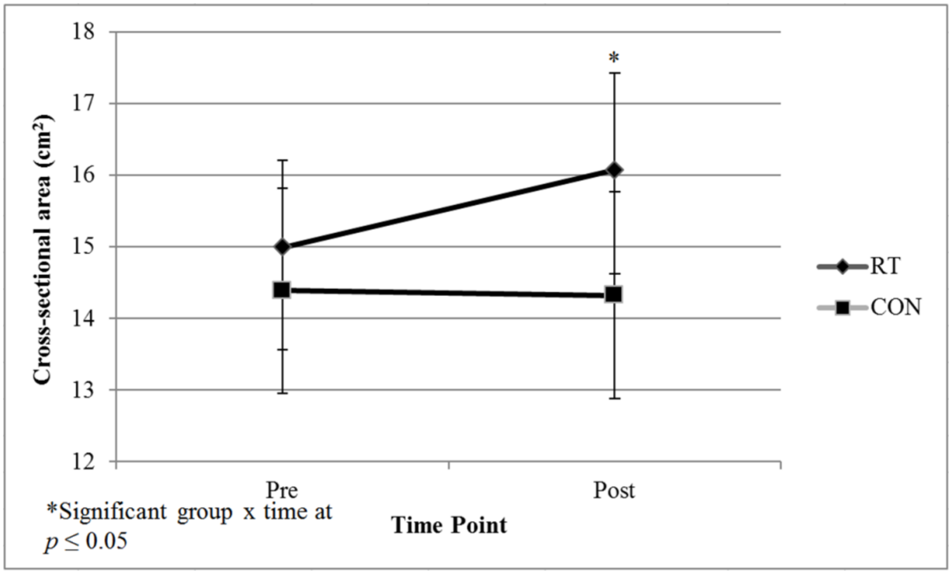


Figure 11. CSA (cm^2) of VL before and after training in the RT and CON groups.

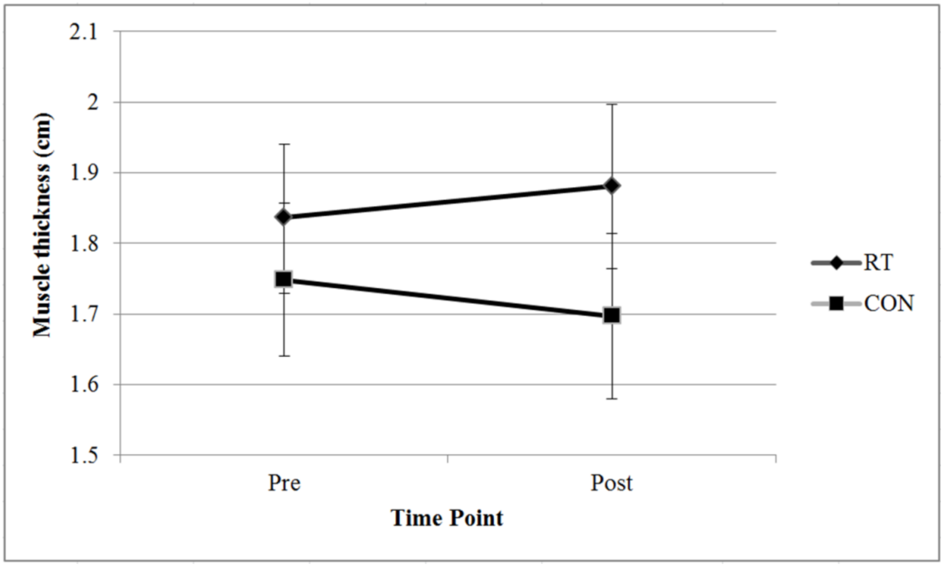


Figure 12. MT (cm) of RF before and after training in the RT and CON groups.

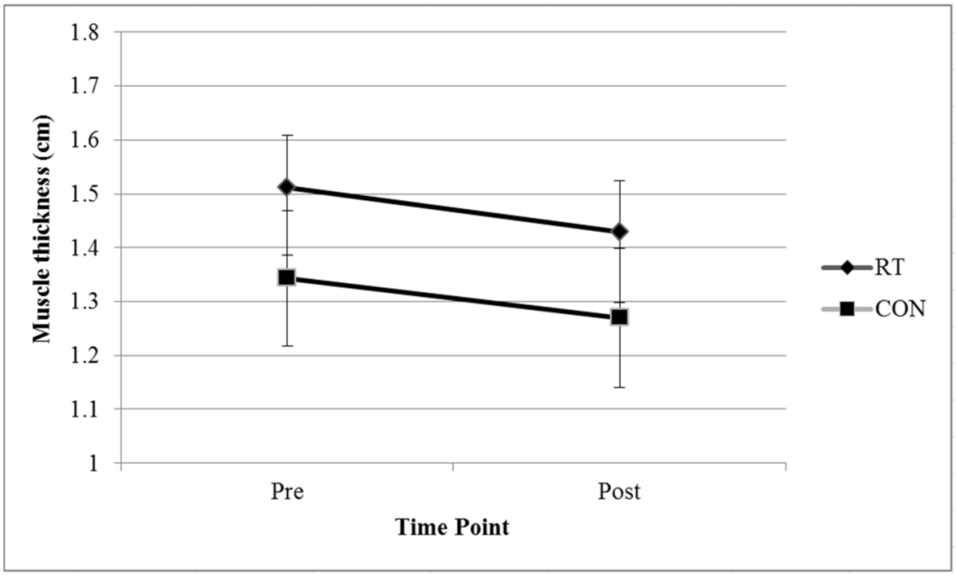


Figure 13. MT (cm) of VL before and after training in the RT and CON groups.

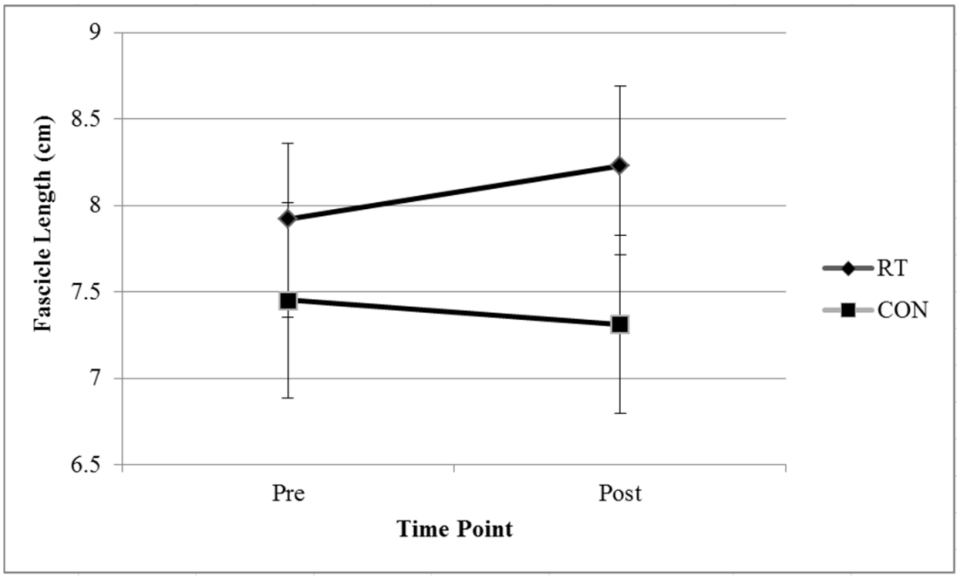


Figure 14. L_f (cm) of RF before and after training in the RT and CON groups.

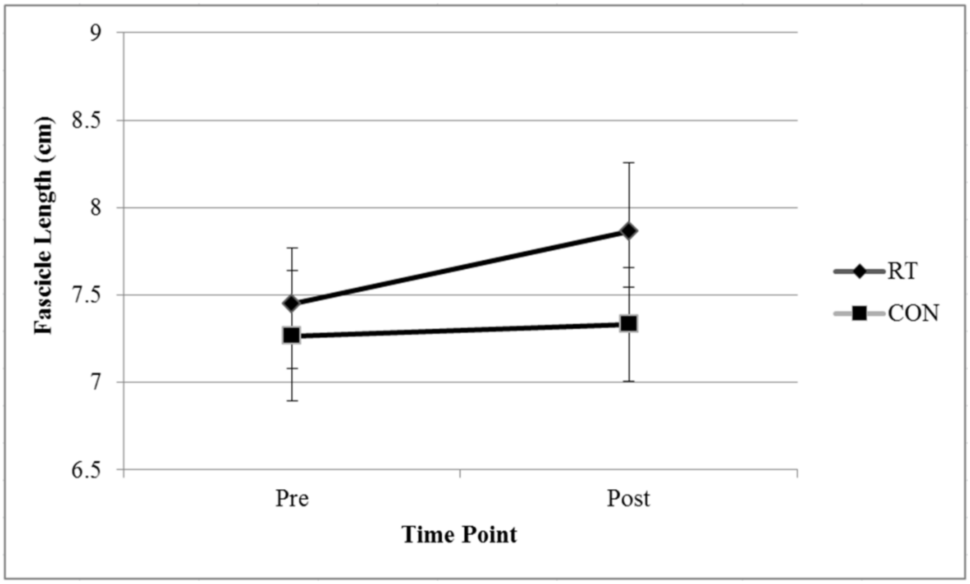


Figure 15. L_f (cm) of VL before and after training in the RT and CON groups.

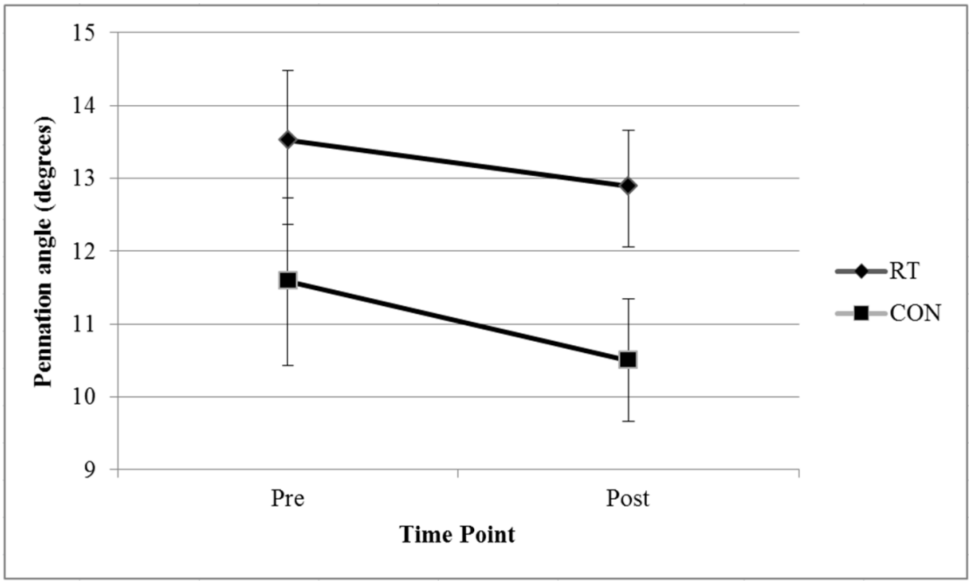


Figure 16. PANG (degrees) of RF before and after training in the RT and CON groups.

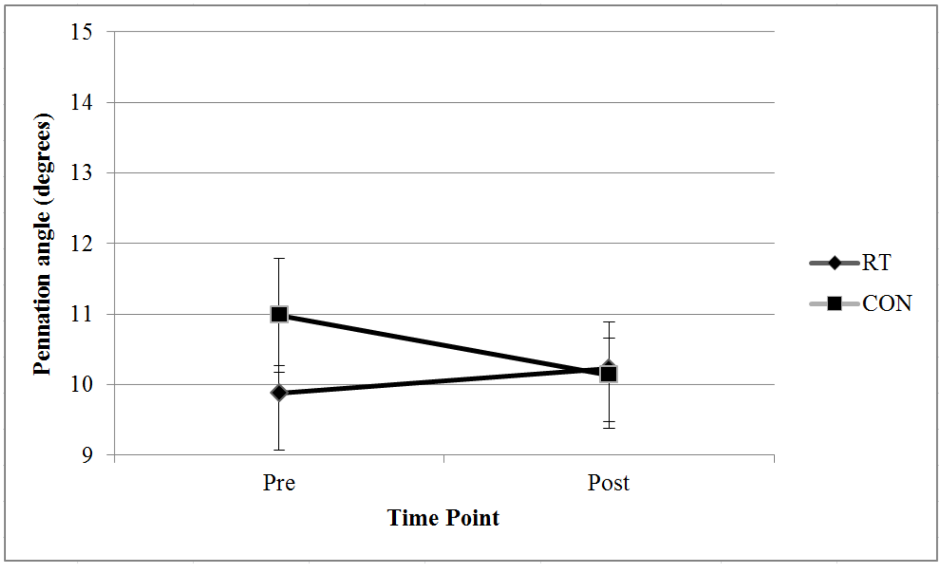


Figure 17. PANG (degrees) of VL before and after training in the RT and CON groups.

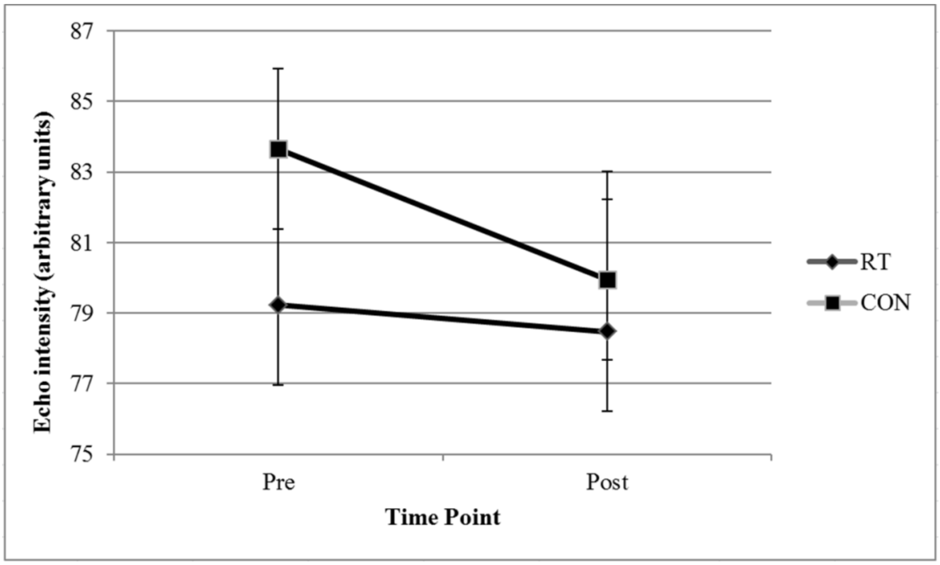


Figure 18. EI (au) of RF before and after training in the RT and CON groups.

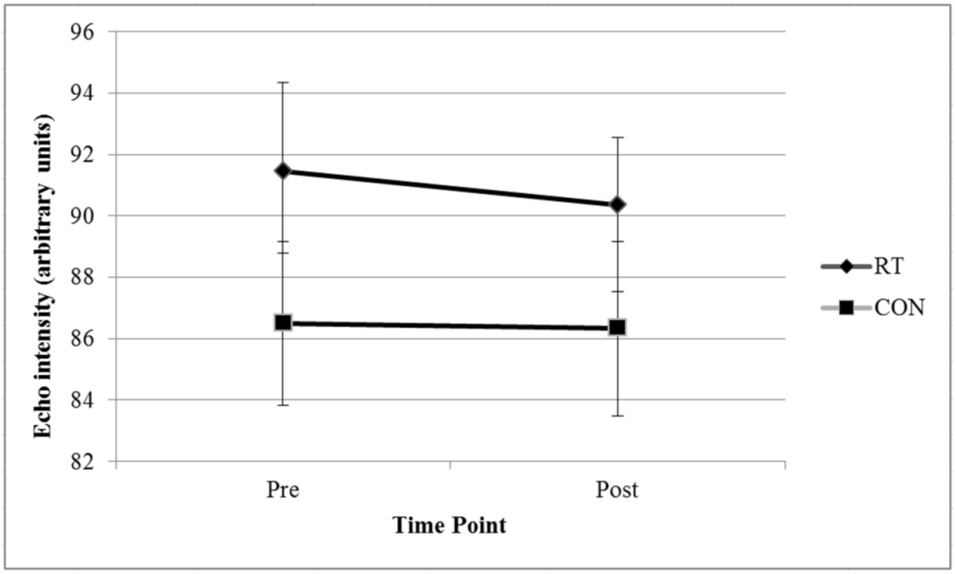


Figure 19. EI (au) of VL before and after training in the RT and CON groups.

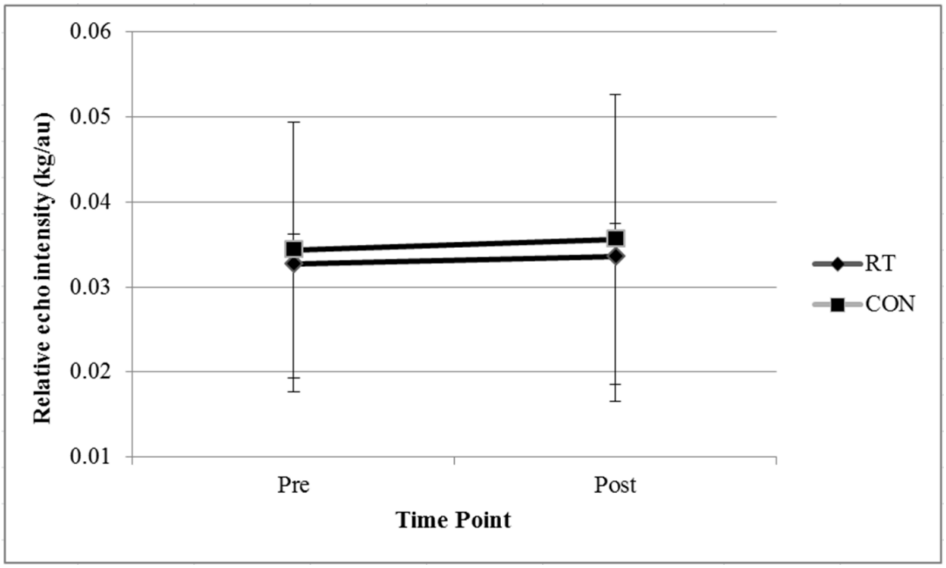


Figure 20. Relative EI (kg/au) of the thigh before and after training in the RT and CON groups.

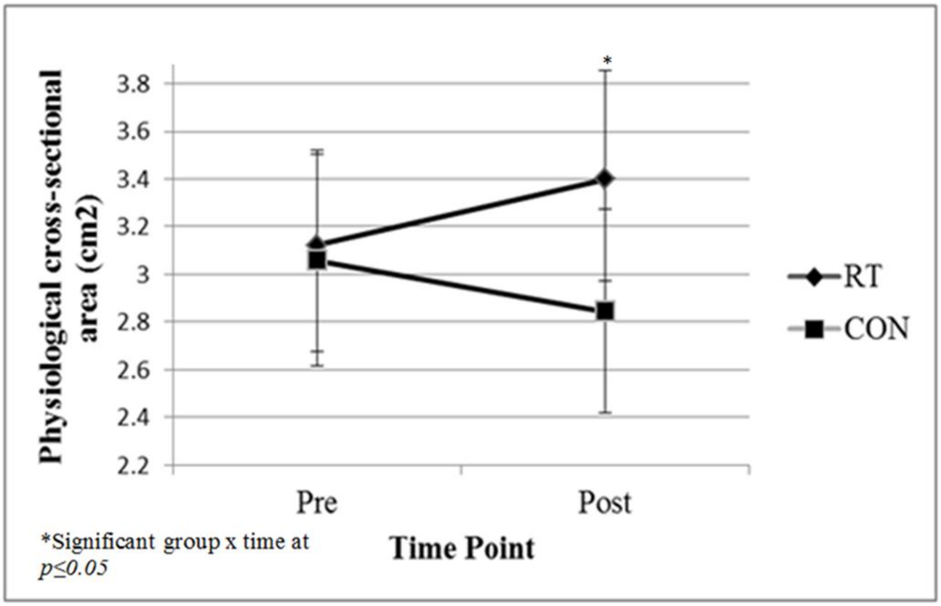


Figure 21. PCSA (cm^2) of the thigh before and after training in the RT and CON groups.

Table 7. Factors associated with 1RM.

Factors associated with Strength

Dependent variables	Independent variables	Coefficient	Standardized coefficient	*t* value	*p* value	95% Confidence interval	
						Lower	Upper
Week 0							
1RM R^2= 0.47	LTM	0.014	0.68	4.4	0.00	0.008	0.021
Week 6							
1RM R^2= 0.54	LTM	0.019	0.73	5.08	0.00	0.011	0.027

1RM= Predicted leg extensor strength, LTM= Lean thigh mass.

Table 8. Factors associated with 1RM when LTM was omitted.

Factors associated with Strength

Dependent variables	Independent variables	Coefficient	Standardized coefficient	*t* value	*p* value	95% Confidence interval	
						Lower	Upper
Week 0							
1RM R^2= 0.35	RF-MT	50.09	0.59	3.5	0.00	20.05	80.13
Week 6							
1RM R^2= 0.53	RF-MT	72.29	0.73	5.06	0.00	42.66	101.92

1RM= Predicted leg extensor strength, RF-MT= Rectus femoris muscle thickness.

Table 9. Factors associated with change in predicted leg extensor strength.

Dependent variables	Independent variables	Coefficient	Standardized coefficient	*t* value	*p* value	95% Confidence interval	
						Lower	Upper
R^2= 0.20	ΔVL-PCSA	20.54	0.447	2.34	0.02	2.39	38.68

Δ1RM= change in 1RM, ΔVL-PCSA= change in vastus lateralis physiological cross-sectional area.

CHAPTER 5: DISCUSSION

To our knowledge this study is the first to examine the effects of resistance training on EI of the lower body musculature in older adults. The main findings of this study suggest that six weeks of progressive resistance exercise may be sufficient to increase measures of muscle morphology and architecture in the vastus lateralis but not rectus femoris. Because increases in 1RM, MQ, and REI were not consistent with values observed for EI in either muscle, other neuromuscular adaptations may be responsible for increases in strength. The novel finding of this study was that a composite ultrasound measure of thigh PCSA demonstrated a significant interaction and was significantly related to maximal voluntary leg extensor strength in older men and women. Results suggest that six weeks of resistance training may increase strength, as well as muscle architectural and morphological measures in older adults, and that the force generating capacity of muscle may be related to architectural characteristics evaluating using ultrasonography.

The focus of the current study was to evaluate early neuromuscular adaptations to as little as six weeks of progressive resistance exercise. This duration of training elicited significant gains in 1RM as well strength relative to LTM and relative to EI. Strength gains in older adults have previously been reported in response to training durations ranging 4 to 22 weeks (Abe et al., 2000; Candow, Chilibeck, Abeysekara, & Zello, 2011; Frontera, Meredith, O'reilly, Knuttgen, & Evans, 1988; N. D. Reeves, Narici, M.V., Maganaris, C.N., 2004; Suetta et al., 2009). Abe et al. (2000) reported increases in younger men and women 25 to 50 years of age in response to 12 weeks of resistance training although absolute gains only reached 19%. It is possible that the larger absolute gains observed in the current study may point to an accelerated loss of muscle with increasing age. The current results demonstrate that strength gains may occur in as early as six weeks in an older population and are supported by previous research in which absolute strength gains in the leg extensors reached 29% , and 16% for strength relative to thigh mass in just 9 weeks (Tracy et al., 1999). Tracy and colleagues (1999) however did report significant gains in thigh mass which may explain the differences observed in relative strength. 1RM testing modality is another possible explanation for differences observed in strength gains between studies since the current study used the Brzycki prediction equation to predict maximal knee extensor strength whereas Tracy et al. (1999) tested maximal isometric contraction strength using an isokinetic device. In addition, it is possible that following training, participants in the current study may have felt more comfortable testing at a lower repetition maximum which may have influenced the strength assessment.

In the current study, no gains were observed in LTM when assessed by DEXA however, ultrasound revealed a significant increase in CSA of VL. Similarly, when performing CT scans of the quadriceps femoris in response to 12 weeks of knee extension and flexion training in older men, significant gains were reported in total quadriceps area of 9.3% and were attributed to significant muscle hypertrophy and myofibrillar protein turnover (Frontera et al., 1988). This may substantiate a claim that in observing gains in response to short term resistance training, the ultrasound device may be more sensitive to small gains in lean muscle mass than DEXA.

Following 6 weeks of resistance training, VL exhibited a significant increase in CSA whereas RF did not. In regards to VL, similar results have been reported in response to resistance exercise ranging 12 to 16 weeks (Ferri et al., 2003; Frontera et al., 1988). Following 12 weeks, CT scans at the mid-thigh level for VL demonstrated significant increases in CSA in older men

(Frontera et al., 1988). In addition, Frontera et al. (1988) reported that 16 weeks of leg press training resulted in knee extensor CSA increases of 7.4% collectively which are similar to our findings for VL which may point to differences in training protocol or sensitivity between evaluation devices. Because similar results were not observed for RF in the current study, it may be possible that the two muscles' respective functional anatomy may indicate a form of selective hypertrophy in the early stages of lower body resistance exercise programs. It is possible that lower body resistance training may not demonstrate significant increases in CSA of RF until after 6 weeks of training (depending upon exercise selection) when the structure-function is considered. RF is the only muscle in the quadriceps that crosses two joints and because of this, if the hip is flexed, it may not be identified as a significant contributor to knee extension. However, with the hip extended RF is more fully activated as seen during toe-off in the gait cycle as well as during the preparatory phase of the kicking motion (Hamill, 2009). Hakkinen et al. 2001 reported similar hypertrophy results in response to 21 weeks of lower body training in older women when examining total thigh as well as individual muscles of the quadriceps femoris. The authors reported that CSA hypertrophy may occur differently between muscles in the quadriceps when examined at the same level and that it may be possible that a multiple slice method may provide further information regarding the hypertrophy of individual muscles (Häkkinen et al., 2001).

The current study observed significant increases in CSA of VL that did not relate to measures of MT however, when reporting MT changes to a greater training duration, Suetta and colleagues (2008) found VL muscle thickness to increase in older men and women by 14.8% in response to 12 weeks of unilateral leg extension and leg press training (Suetta et al., 2008). It is possible that training durations greater than six weeks may be necessary to cause significant change isolated to muscle thickness of the lower limb musculature. In addition, the CSA measure may give an overall larger picture of total muscle hypertrophy since CSA is more desirable in that it may better relate to the hypertrophic and force producing characteristics that are associated with muscular size (Bemben, 2002).

L_f did not significantly change in RF or VL in the current study. Reeves et al. (2004) however, reported significant increases of 11% in L_f in response to 14 weeks of resistance exercise in older adults when training using a full body program with isotonic machines (N. D. Reeves et al., 2004). In a follow-up study in 2009, Reeves et al. examined the effects of 14 weeks of resistance exercise, comparing eccentric training to conventional training modalities in older adults. The reported results were that L_f increased in both groups however, significantly greater gains were reported in the eccentric training group (20%) than the conventional training group (8%, p=0.05) (N. D. Reeves et al., 2009). Our results indicate that architectural changes to L_f may occur in response resistance training durations longer than six weeks. Future research may aim to examine eccentric training versus conventional training in relatively shorter time periods as well which may have application to the architectural response time resulting from resistance exercise.

Rectus femoris and vastus lateralis PANG in the current study demonstrated no significant changes. Previous studies have reported increases in PANG of VL ranging 13 to 22% in response to 14 and 12 weeks of lower body resistance exercise, respectively (N. D. Reeves et al., 2004; Suetta et al., 2008). Data observing responses in PANG of RF are scarce and may be an area of inclusion for future research. The current study did not conclude that six weeks of training was sufficient to elicit a significant response in PANG of either muscle examined. Reeves et al. (2004) found that older adults were successful in increasing PANG of VL (13%, $p=0.01$) in response to 14 weeks of resistance exercise, which may have been attributed to study duration. In 2009, Reeves et al. compared 14 weeks of eccentric and conventional training as previously mentioned and the effects on PANG in older adults. Whereas L_f increases were greater for the eccentrically trained group, the opposite was true for the measure of muscle fiber PANG. PANG increased by 35% ($p=0.05$) in the conventional training group, compared to no change in the eccentric group, leading the researchers to conclude that differences in training protocol may elicit different myogenic architectural responses (N. D. Reeves et al., 2009). The findings of the current study may suggest a longer duration of training needed to exhibit changes in fiber orientation relative to the force generating axis.

Mean EI of RF and VL muscles did not change in either group following training. As this is the first study to our knowledge to report EI values in older adults following progressive resistance training, studies of longer duration may be an area of future research. Cadore et al. (2012) reported average EI values greater than those in the current study however; we used a different ultrasound model as well as a higher probe frequency to maximize spatial resolution. In cases where different ultrasound devices are used, EI values will differ and new normative values must then be established (Arts 2010). This was further demonstrated in a study by Arts and colleagues who found average EI values of the RF for adults age 17 to 90 to average 25.8 au and 30.0 Au for males and females, respectively (Arts 2010). In addition, mean EI for healthy Japanese women age 70.4 (± 5.5) years were found to be 98.8 ± 10.0 au for the RF with a range of 75.3 and 129.9 au which are more closely related to the values that we observed (Fukumoto et al., 2012). The main effect of time for RF EI that was observed in the CON group may be a result of the inability to control for what participants consider vigorous physical activities between testing sessions however, current results would suggest that changes in EI in older adults in response to resistance training may require training durations of greater than six weeks to elicit significant improvements, despite significant changes in strength and muscle architectural. Based upon changes observed in muscle morphology, primarily in VL, changes in muscular size may occur earlier than changes seen within the composition of muscle that pertain to the infiltration of intramuscular connective tissue and/or adipose tissue.

EI relative to LTM did not significantly change in the RT or CON group. Similar to the observations with EI, it may be apparent that within this time frame, neurological adaptations as well as fiber orientation are contributing to a greater degree to the changes in strength that were seen however, this may be an interesting variable for future research to consider.

PCSA of the thigh did not significantly change in either group following training. Similarly, Reeves et al. (2004) noted no significant changes in PCSA in response to 14 weeks of leg press and extension training in older adults however; the method used by Reeves et al. (2004) to calculate PCSA was based upon using the ratio of muscle volume to L_f but neglected the inclusion of PANG. Similarly, Suetta et al. (2009) reported that following immobilization, older males had 17% less PCSA when compared to a younger healthy male population. Following 4 weeks of resistance training after immobilization, young males were able to increase PCSA by 10.4% whereas older males did not experience any significant gains. In line with these results, the current study observed no significant changes in PCSA. Also, the calculation of PCSA is often different between studies in the sense that Suetta et al. (2008) used muscle volume, whereas the current study used a CSA slice from the ultrasound. As with the study by Reeves et al. (2004) another issue is that PCSA calculations must use an assumed muscle density of 1.056 grams·mm^3 which does not account for ethnicity, or individual differences in body composition.

The unique ability of the current study to measure density as EI allows for a more precise estimation of PCSA in our modification to Equation 1 in which mass may be calculated as CSA, PANG can be directly measured, density may be represented as EI, and L_f may be directly measured using extended field of view ultrasound technology. The implications of using ultrasound may give a more composite and inclusive measure when calculating PCSA and may be more accessible and cost effective than MRI or CT. Furthermore, PCSA of the thigh was found to be significantly correlated to maximal leg extensor strength which may have implications in clinical settings where ultrasound is available. This study demonstrates that the force generating capacities of muscle may be related to architectural characteristics as evaluated using non-invasive ultrasound techniques.

LTM was the best predictor of 1RM at all testing points. When LTM was omitted, rectus femoris MT was identified as the strongest predictor of 1RM before and after training. Similar results were reported in which MT of the thigh was found to contribute significantly to strength independently of any measures in middle age and older adults (Fukumoto et al., 2012). Following six weeks of training, delta scores for PCSA of VL were identified as the best contributor to change in strength which may demonstrate that muscle architecture evaluation using ultrasound may be more successful in accounting for variation in leg extensor strength than morphology alone as measured by DEXA, and may support the calculation of PCSA using ultrasonography. Quadriceps thickness is a significant contributor to strength in middle age and older adults and results from the current study may suggest that rectus femoris MT in particular may be a significant contributor. Furthermore, PCSA calculation may be an interesting variable for inclusion when examining strength changes in various populations in response to resistance training.

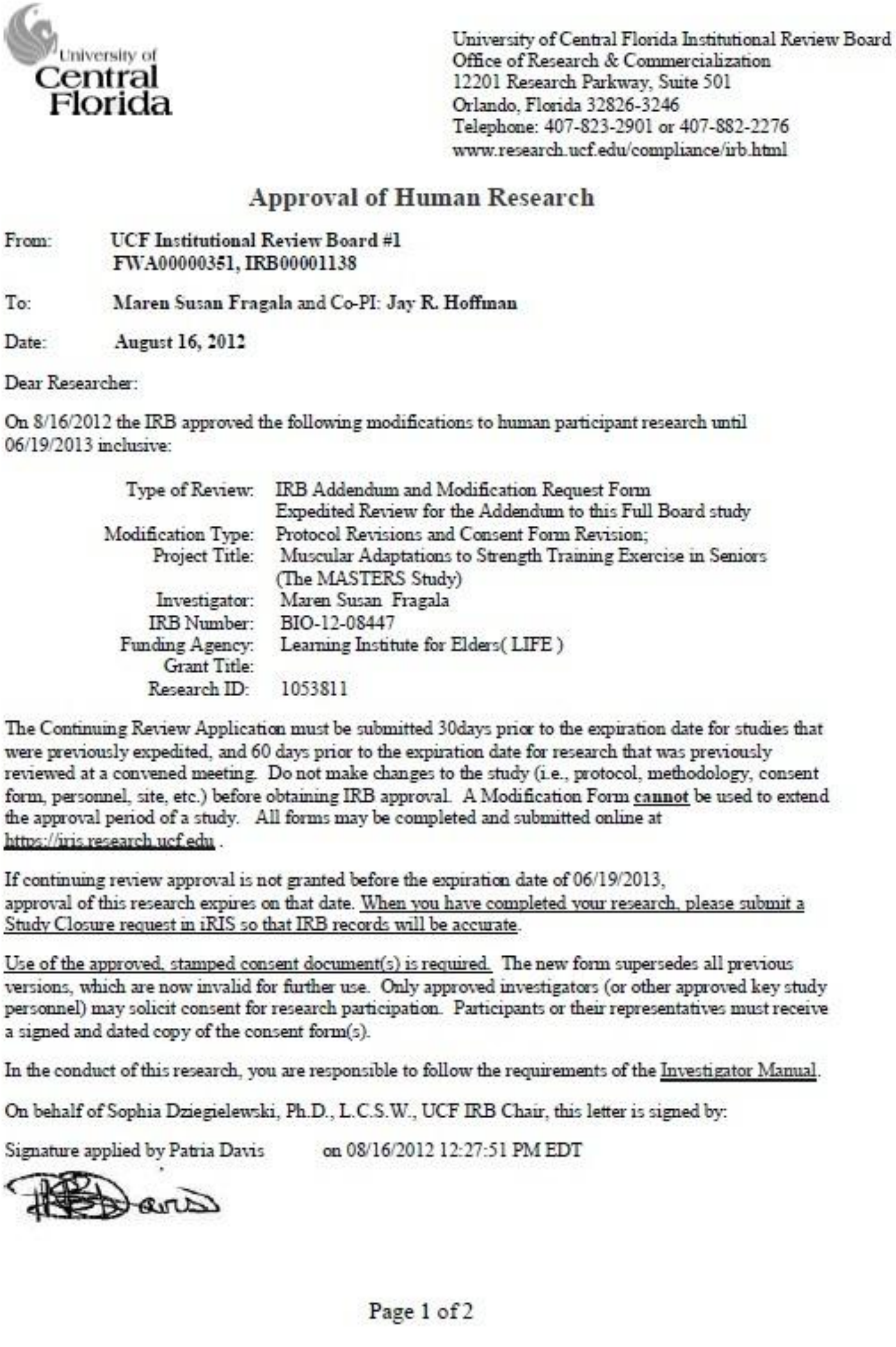
Conclusions

To our knowledge the present study is the first to examine EI values in older adults after engaging in a progressive resistance training program. Six weeks of progressive resistance exercise was effective to increase muscle strength, muscle quality (relative strength) and muscle architecture. Although previous research has attributed earlier strength gains from resistance exercise to primarily neuromuscular adaptation, results from the current study reveal muscle architectural changes observed by US but not DEXA following six weeks of training that are most likely due to the differences in sensitivity to change between the devices. The muscle qualitative changes hypothesized to occur with the EI measurements were not observed however changes muscle quality as relative strength and strength relative to EI were observed. Perhaps the most novel finding of this study was that a composite ultrasound measure of thigh PCSA was found to relate to 1RM in older men and women. In addition, because of the salient features, skeletal muscle ultrasound may be a safe, feasible, informative and sensitive clinical technique to aid in our understanding of muscle strength, function, and quality.

APPENDIX A: RESISTANCE TRAINING PROGRAM

Week 1 (3 X 12-15RM)		Week 2 (3 X 12-15RM)	
Day 1	Day 2	Day 1	Day 2
Squat	Step up	Squat	Lunge
Push up	Lat pull down	Push up	Lat pull down
Leg extension	Calf raise	Hamstring curl	Leg extension
Shoulder press	Bicep curl	Shoulder press	Seated row
Leg curl	Seated row	Triceps extension	Biceps curl
Triceps extension	Upright row	Calf raise	Upright row
Plank	Reverse crunch	Plank	Reverse crunch
		Superman	
Week 3(3 X 10-12RM)		Week 4 (3 X 10-12RM)	
Day 1	Day 2	Day 1	Day 2
Squat	Step up	Squat	Lunge
Push up	Lat pull down	Chest press	Lat pull down
Leg curl	Calf raise	Leg curl	Leg extension
Shoulder press	Seated row	Shoulder press	Seated row
Leg extension	Upright row	Calf raise	Calf raise
Triceps extension	Modified RDL	Triceps extension	Upright row
Plank	Bicep curl	Plank	Bicep curl
	Reverse crunch		Reverse crunch
Week 5 (3 X 8-10RM)		Week 6 (3 X 10-12RM)	
Day 1	Day 2	Day 1	Day 2
Squat	Lunge	Squat	Leg extension
Push up	Lat pull down	Chest press	Lat pull down
Leg curl	Calf raise	Leg curl	Step up
Shoulder press	Seated row	Shoulder press	Seated row
Leg extension	Upright row	Calf raise	Shoulder press
Triceps extension	Biceps curl	Triceps extension	Bicep curl
Plank	Reverse crunch	Modified RDL	Reverse crunch
		Plank	

APPENDIX B: UCF IRB LETTER OF APPROVAL



University of Central Florida

University of Central Florida Institutional Review Board
Office of Research & Commercialization
12201 Research Parkway, Suite 501
Orlando, Florida 32826-3246
Telephone: 407-823-2901 or 407-882-2276
www.research.ucf.edu/compliance/irb.html

Approval of Human Research

From: **UCF Institutional Review Board #1**
FWA00000351, IRB00001138

To: **Maren Susan Fragala and Co-PI: Jay R. Hoffman**

Date: **August 16, 2012**

Dear Researcher:

On 8/16/2012 the IRB approved the following modifications to human participant research until 06/19/2013 inclusive:

Type of Review:	IRB Addendum and Modification Request Form Expedited Review for the Addendum to this Full Board study
Modification Type:	Protocol Revisions and Consent Form Revision;
Project Title:	Muscular Adaptations to Strength Training Exercise in Seniors (The MASTERS Study)
Investigator:	Maren Susan Fragala
IRB Number:	BIO-12-08447
Funding Agency:	Learning Institute for Elders(LIFE)
Grant Title:	
Research ID:	1053811

The Continuing Review Application must be submitted 30days prior to the expiration date for studies that were previously expedited, and 60 days prior to the expiration date for research that was previously reviewed at a convened meeting. Do not make changes to the study (i.e., protocol, methodology, consent form, personnel, site, etc.) before obtaining IRB approval. A Modification Form **cannot** be used to extend the approval period of a study. All forms may be completed and submitted online at https://iris.research.ucf.edu .

If continuing review approval is not granted before the expiration date of 06/19/2013, approval of this research expires on that date. When you have completed your research, please submit a Study Closure request in iRIS so that IRB records will be accurate.

Use of the approved, stamped consent document(s) is required. The new form supersedes all previous versions, which are now invalid for further use. Only approved investigators (or other approved key study personnel) may solicit consent for research participation. Participants or their representatives must receive a signed and dated copy of the consent form(s).

In the conduct of this research, you are responsible to follow the requirements of the Investigator Manual.

On behalf of Sophia Dziegielewski, Ph.D., L.C.S.W., UCF IRB Chair, this letter is signed by:

Signature applied by Patria Davis on 08/16/2012 12:27:51 PM EDT

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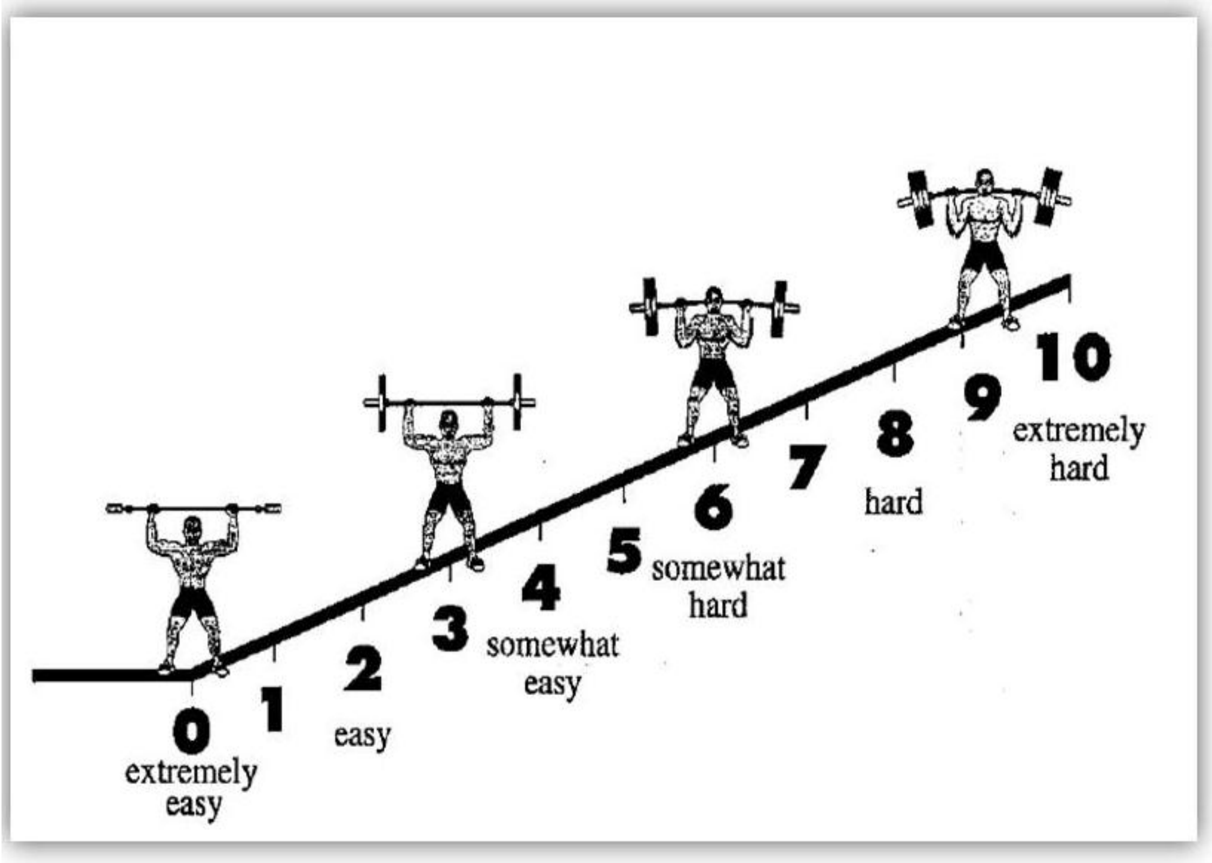
APPENDIX C: OMNI SCALE


0
extremely easy
1
2
easy
3
somewhat easy
4
5
somewhat hard
6
7
8
hard
9
10
extremely hard

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