ABSTRACT

Title of Document: THE EFFECTS OF HIGH VOLUME HEAVY RESISTANCE EXERCISE TRAINING ON REGIONAL HYPERTROPHY OF THE QUADRICEPS MUSCLE IN YOUNG AND OLDER MEN AND WOMEN

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The purpose of this study was to examine the effects of nine weeks of unilateral high volume, heavy resistance strength training (HRST) and 31 weeks of detraining on the three regions (proximal, middle, distal) of the quadriceps in young (25 yrs) and older (69 yrs) men and women. Quadriceps CSA was assessed as a difference of the trained leg minus the untrained leg (T-UT). A multi-way ANOVA with repeated measures revealed that after HRST, young men had significantly higher CSA (T-UT) compared to young women in all three regions (6.7 ± 1.4, 9.3 ± 1.4, 7.8 ± 1.2 versus 2.3 ± 1.5, 3.4 ± 1.5, 1.7 ± 1.3 cm^2). Older men displayed significantly higher CSA (T-UT) in the proximal region compared to older women after HRST (6.4 ± 1.3 versus 2.4 ± 1.3 cm^2). Both age groups had similar CSA (T-UT) values after HRST and after 31 weeks of detraining. Thus, age did not influence the magnitude of the increase in regional CSA (T-UT) after HRST nor did it influence the degree of loss after 31 weeks of detraining.

THE EFFECTS OF HIGH VOLUME HEAVY RESISTANCE EXERCISE TRAINING ON REGIONAL HYPERTROPHY OF THE QUADRICEPS MUSCLE IN YOUNG AND OLDER MEN AND WOMEN

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Dedication

For my mother and father. It’s done! And to Julia, for always being there.

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Chapter 1: Introduction

Sarcopenia describes the loss of neuromuscular function and skeletal muscle mass, which is accompanied with a loss of muscular strength, as a result of the process of aging. Studies have estimated the strength loss past the 4th decade to be 5% on average per decade and this loss may increase further past the age of 65 yr (27). With an estimated 39 million Americans over the age of 65 yr and a projected increase by 6 million within ten years (87), sarcopenia represents a major health issue and public concern, as loss of strength and muscle mass negatively affects activities of daily living, physical independence, and quality of life.

Physical inactivity is one of the contributors to sarcopenia and it has been shown that older men and women who are less physically active have less skeletal muscle mass and an increased prevalence of disability (19). To combat this loss of skeletal muscle mass, numerous resistance exercise training studies have been performed to analyze the effects of training on the cross-sectional area (CSA) of skeletal muscle. These studies utilized various methods including ultrasound (98), anthropometry (55), computer-assisted tomography (75), and magnetic resonance imaging (MRI) (41). Of these methods, MRI has been found to be the preferred method due to its safety (subjects are not exposed to radiation) and its ability to distinguish between soft-tissues (i.e., adipose tissue and skeletal muscle) (41). Magnetic resonance imaging also allows the investigator to examine axial slices along the entire muscle which enables analysis of different regions or the ability to calculate muscle volume.

Although MRI provides the means to distinguish different regions of a muscle, most resistance training studies assess hypertrophy of the quadriceps at only one cross-section (13, 18, 30-33, 35, 75, 79, 95, 98) with a limited number of studies examining multiple regions (36, 37, 40, 41, 69, 71, 72). Narici *et al.* were the first investigators to examine the CSA of the knee extensors with MRI at five regions of the thigh in men ages 24-31 years. These regions were spaced approximately five centimeters apart and the investigators noted that maximum anatomical CSA of the knee extensor muscles was found to be at the middle region in young males (71). Three studies have examined the effects of resistance training on regional CSA of the quadriceps in young men (41, 69) and have found significant increases in regional CSA in all regions measured. Two studies have also examined skeletal muscle CSA in young (40) and older women (36) and have demonstrated significant increases in regional CSA after resistance exercise training that have utilized varying contraction types (isokinetic concentric, isokinetic eccentric, isokinetic, and isotonic). Analysis of the quadriceps muscle group has revealed that the quadriceps displays increasing CSA values up to the mid-point of the femur and then CSA values decrease distally towards the knee. This non-uniform CSA of the quadriceps is due to the four constituent muscles that make up the quadriceps group (vastus lateralis, medialis, intermedius, and rectus femoris) having maximal CSA values at different regions along the thigh. In reference to analysis of older subjects, only one study has examined more than one region of the quadriceps in 3 elderly men and 8 elderly women (37). However, this study found no significant differences between the three regions measured (proximal, middle, and distal) and therefore reported changes in only one region. No comparisons were made between genders in this investigation due to the relatively small sample size (37).

No strength training study examining multiple regions of the quadriceps has included subject groups of young and older men and women and only two studies have included a detraining period (31, 72). Narici *et al.* (72) included a 40 day detraining period in a study on young men and found that the middle region of the quadriceps decreased ($-0.10\%\cdot day^{-1}$), which was similar to the increase that occurred after 60 days of unilateral isokinetic knee extension ($0.14\%\cdot day^{-1}$). Häkkinen *et al.* (31) examined the distal region of the quadriceps in middle-aged and elderly subjects. After 24 weeks of full body resistance training an increase of 7% and 3% occurred in the distal region for middle-aged and elderly subjects, respectively. After 24 weeks of detraining, decreases of 9% and 11% occurred in the distal region of the quadriceps in middle-aged and elderly, respectively. No comparisons were made between age groups in this study (31).

Recently, a study examined MRI data of the knee extensors in young and older women (26 ± 2, 68 ± 3 years) before and after a nine-week, high volume, heavy resistance strength training program (HRST) that consisted of unilateral knee extensions (80). Young and older women demonstrated increases in muscle CSA of 4%, 6%, and 8%, and 5%, 10%, and 9%, respectively, at the three regions of interest (proximal, middle, distal). A period of 31 weeks of detraining resulted in a loss of 7%, 7%, and 4% in young and 9%, 10%, and 11% decrease in CSA of the knee extensors of older women with respect to the three regions (80).

A shortcoming of most of the regional hypertrophy studies in the literature is that they do not include an untrained limb or a control group to act as a control. However, even a control group would lead to possible genetic differences between groups. This genetic difference would be accounted for when using a trained and untrained limb. Unilateral strength training studies that due not include a control limb may lead to variability in the data due to seasonal variations or increased activity outside of the study design. In terms of assessing a non-uniform distribution of hypertrophy due to individual muscles hypertrophying in different regions along the thigh, one can account for this in two ways: one would be to calculate the total volume of the muscle or examine specific regions, such as the proximal, middle, and distal regions. Only two studies have examined quadriceps muscle volume (44, 85). Ivey *et al.* (44) were the first to publish a study on quadriceps muscle volume changes after nine weeks of HRST and 31 weeks of detraining in young and older, men and women. The investigators found significant quadriceps muscle volume gains after nine weeks of HRST with men displaying significantly greater increases in muscle volume than women (204 ± 20 vs. 101 ± 13 cm^3) with no statistically significant differences between age groups. After 31 weeks of detraining, no significant differences were found in the amount of muscle volume lost between young and older groups, but a significantly greater loss was observed in men than in women (151 ± 13 vs. 88 ± 7 cm^3) (44). Roth *et al.* examined age and gender responses after six months of a whole body resistance exercise training program and found no significant differences in quadriceps muscle volume between gender or age groups (20-30 yrs, 65-75 yrs) (85). This conflicts with the findings of Ivey *et al.* (44) due most likely to the lack of a control limb as well as the differences in the resistance training stimulus (knee extensions versus full body).

Assessing the volume of a muscle by calculating the CSA of each axial slice of the thigh is a time-intensive and arduous process (92). Thus from a practical standpoint and the fact that most studies assess the CSA of a muscle at the point of maximal CSA or in multiple regions, it would be important to identify regional changes in CSA at the proximal, middle, and distal points along the muscle.

The current literature on regional changes in quadriceps CSA in response to strength training are lacking in that studies have examined multiple regions of only young men (41, 69, 72) only young women (40), only elderly women (36), or elderly men and women (37), and have not made any comparisons in regards to age or gender. In reference to the effects of detraining on regional quadriceps CSA, only two studies have been published. Narici *et al.* (72) analyzed young men and Häkkinen *et al.* (31) studied middle-aged and elderly men and women, but only examined the distal region, with no comparisons made between age or gender groups.

While no study to our knowledge has specifically compared regional hypertrophy responses to resistive training in young and older, men and women, studies have compared the degree of hypertrophy in one cross-sectional slice through ultrasound (30, 32, 33, 98), computed tomography (13, 18, 75), or MRI (31, 35, 79, 95) and fewer studies have examined the detraining effect (31, 44, 72). Currently, the literature shows that young men and women have increases in regional CSA ranging from 4-15% after 8 to 12 weeks of resistive exercise training. Older men and women show similar percent increases ranging from 6-11%. The current study will focus on young and older, men and women to allow for a broader based comparison between age groups and gender in response to an HRST program and more importantly, to ascertain the degree of loss in quadriceps CSA after 31 weeks of detraining on the three regions of the quadriceps.

Statement of Purpose

This study was designed to determine the age and gender differences that exist in the regional CSA of the quadriceps muscle group to nine weeks of unilateral HRST and 31 weeks of detraining in young and older women and men.

Hypotheses

1. Older subjects will experience a greater decrease in CSA (T-UT) than young subjects in all three regions of the quadriceps (proximal, middle, and distal) after 31 weeks of detraining.
2. (a) Young men will show a greater decrease in CSA (T-UT) than young women in all three regions of the quadriceps (proximal, middle, and distal) after 31 weeks of detraining. (b) Older men and women will show similar losses in CSA (T-UT) in all three regions of the quadriceps (proximal, middle, and distal) after 31 weeks of detraining.
3. There will be a greater increase in CSA (T-UT) of the middle region as opposed to the proximal and distal regions of the quadriceps.
4. There will be no differences in CSA (T-UT) between young and older subjects in all three regions of the quadriceps (proximal, middle, and distal) after nine weeks of HRST.

5. (a) Young men will show a greater increase in CSA (T-UT) than young women in all three regions of the quadriceps (proximal, middle, and distal) after nine weeks of HRST. (b) Older men and women will show similar increases in CSA (T-UT) at all three regions of the quadriceps (proximal, middle, and distal) after nine weeks of HRST.

Delimitations

1. The participants in this study were healthy, sedentary males and females of two age groups (20-30 and 65-75 years of age).
2. Subjects refrained from any physical activity for at least 6 months prior to beginning the study.
3. All subjects were non-smokers, had no musculoskeletal or physical limitations, and were free of any coronary disease as determined by a graded exercise test.

Limitations

1. All subjects are volunteers and not randomly selected. Therefore any generalization of the results will be applicable only to healthy men and women ages 20-30 and 65-75 yrs old.
2. Changes in diet and physical activity outside of the HRST were monitored by self-report.

Definitions

Absolute increase: Reference to increases in CSA of skeletal muscle by comparing area values (e.g. 41 cm^2 versus 45 cm^2)

Axial scan: An image taken in the transverse plane of the body producing a cross-sectional image

Coronal scan: An image taken in the frontal plane of the body producing a longitudinal image.

CSA: Cross-sectional area. The area (cm^2) taken by outlining the muscle of interest in the cross-section.

Distal (Region 3): Proximal to the patella, the region that is 70% of the length of the femur. This is determined by taking the total number of slices containing quadriceps muscle tissue and multiplying by 0.7, then counting down from the head of the femur the number of slices calculated.

HRST: High volume, heavy resistance strength training program that consists of five sets of unilateral knee extensions of 5, 5,10, 15, and 20 repetitions three times per week for nine weeks.

Middle (Region 2): The midpoint of the quadriceps muscle. This is determined by taking the total number of slices containing quadriceps muscle tissue and multiplying by 0.5, then counting down from the head of the femur the number of slices calculated.

MRI: Magnetic resonance imaging. A non-invasive technique that produces images of the body's interior.

Proximal (Region 1): Proximal to the hip, the region that is 30% of femur length. This is determined by taking the total number of slices containing quadriceps muscle tissue and multiplying by 0.3, then counting down from the head of the femur the number of slices calculated.

Regional hypertrophy: The amount of muscle growth in a specific region of a muscle.

Sarcopenia: The decline of muscle mass and strength associated with aging.

Slice: An image generated through magnetic resonance imaging is referred to as a slice. There are three possible slices located in a scan plane: sagittal, axial, and transverse.

T-UT: Refers to any variable (cross-sectional area or muscle volume) that is computed by subtracting the untrained leg from the trained leg.

Unilateral strength training: Performing a resistance training exercise with one limb while the other limb serves as a control which performs no resistance training.

1RM: One repetition maximum or the maximum amount of weight capable of being lifted one time and no more with proper form.

5RM: Five repetitions maximum or the maximum amount of weight capable of being lifted five times and no more with proper form.

Chapter 2: Literature Review

Introduction

Sarcopenia is defined as a reduction in muscle mass with a decrease in muscle volume and cross-sectional area. This leads to a reduction in force generating capacity (58) and is a consequence of aging. Due to the increasing elderly population with currently over 33 million Americans > 65 years, sarcopenia is a major public health issue (87). This issue must be addressed due to associations of strength loss with an increased risk of falls, leading to hip fractures, a decrease in the quality of life, and a reduction in activities of daily living (ADL) (73). Numerous mechanisms have been postulated for the causes of this muscle wasting disease and these mechanisms vary from changes in the neurological system, muscle fiber type distribution, muscle architecture, and muscle cross-sectional area (CSA). This literature review chapter contains the following major sections of background information: (1) loss of muscular strength, (2) loss of muscle mass, (3) mechanisms of loss (4) activities of daily living, (5) adaptations to resistance training (6) regional hypertrophy (7) gender and age comparisons in resistance training, (8) summary of the various techniques for assessing muscle mass, and (9) magnetic resonance imaging validation and reliability, concluding with a summary.

Loss of Muscular Strength

Having adequate muscular strength and power is a basic requirement for daily function. Increasing age is accompanied by a loss of muscular strength and this has been demonstrated in multiple cross-sectional and longitudinal studies (10, 15, 48, 83). Studies analyzing muscular strength have used simple measurement techniques such as hand-held dynamometers due to the ability to test a large subject pool in a time-efficient manner. In a study by Reed *et al.*, the testing population consisted of middle-aged (55-64 yrs), young-old (65-74 yrs), and old-old (75+ yrs) men and women. The results showed that there was an age-related trend of decreasing muscle strength per unit of lean body mass with increased age in both upper and lower body musculature. Cumulative strength losses were estimated to be 18 and 22% for men and women, respectively between middle-aged and old-old age groups (83). Lauretani *et al.* performed a similar study on a broader age range of subjects (second to eighth decade) and found an 8% decrease in handgrip strength in men when comparing age groups from the second to third decade. On average, a 7% decrease in handgrip strength occurred up until age 40. After the fourth decade, handgrip strength decreased by as much as 20% from the fifth to sixth decade of life (56).

While handgrip strength measurements can be time efficient, the importance of relating strength to the amount of skeletal muscle mass can offer a more accurate assessment of strength. Many investigators (63, 64) have examined muscle quality, which is strength per unit of muscle mass. A large, comprehensive study done by Lindle *et al.* examined changes in concentric and eccentric peak torque and muscle quality in 654 subjects taken from the Baltimore Longitudinal Study of Aging (63). Isokinetic testing was performed on the knee extensors to assess isometric, concentric, and eccentric peak torque at two velocities (0.5 and 3.1 rad/s). For men, there was a significant age-related decline when analyzing muscle quality as a function of eccentric peak torque but not in women. When examining muscle quality in terms of concentric peak torque, significant age related decreases were evident in both men and women. A curvilinear relationship was noted between strength and age with a noticeable decline occurring in concentric and isometric peak torque at the onset of the fourth decade (63). These findings were confirmed in a later study by Lynch *et al.* (64) on muscle quality related to eccentric and concentric peak torque and it appears that concentric peak torque decreases at a rate of 8-10% per decade after the fourth decade.

From these studies, it is evident that there is an age-related decline in muscular strength with strength losses noticeable as early as the third decade (56). When examining strength as a function of muscle quality, there is an age-related trend of decreasing muscle quality over time in both men and women, with the exception of eccentric peak torque in women. Women tend to maintain eccentric strength due to their ability to maintain greater elastic properties in skeletal muscle. In reference to the age-related decrease in muscle strength, losses appear to be significant after the fourth decade, with greater losses occurring in the eighth or ninth decade of life (3, 19, 45, 64).

Loss of Skeletal Muscle

CSA and Volume

Decreases in muscle volume or a reduction in the CSA of skeletal muscle is a main factor contributing to strength loss. Studies using imaging methods such as MRI and computer-assisted tomography have allowed investigators to measure changes in muscle CSA with aging. Jubrias *et al.* examined MRIs of the thigh on a broad age range (23-80 yrs) of 57 subjects and found that quadriceps CSA decreased linearly with age with reductions as high as 21% from the twentieth to eighth decade (47). Also using MRI imaging, Kent-Braun *et al.* demonstrated significantly greater muscle CSA of the tibialis anterior in healthy young (32 yrs) versus healthy elderly (72 yrs) subjects. One interesting finding was that despite subjects having similar levels of physical activity as estimated through an accelerometer and seven day recall questionnaire, reductions in CSA were still evident between age groups. The MRI measurements in this study also accounted for intramuscular fat content of the tibialis anterior (52). This is important as authors have reported elderly subjects (65-80 yrs) have more than twice the amount of quadriceps muscle fat content when compared to young (23-57 yrs) subjects (47). In terms of a quantifying the amount of muscle mass lost, Narici *et al.* found significant 19 and 25% reductions in anatomical CSA and muscle volume, respectively of the gastrocnemius medialis muscle between older (70-81 yrs) and young (27-42 yrs) subjects (70).

Muscle Fiber Area

Measurements of CSA and volume are one way to assess changes in skeletal muscle over time. A second technique is to examine skeletal muscle fibers at the microscopic level through muscle biopsies. Biopsy samples may be used to assess changes in muscle fiber distribution (type I, type II), fiber area, fiber diameter, fiber size, as well as the ratio of type I to type II fibers.

Numerous investigations have been performed by Lexell *et al.* on cross sections taken from whole vastus lateralis muscle (59, 61, 62). The first study examined two groups of subjects, mean age 72 and 30 yrs, and demonstrated that calculated skeletal muscle CSA and mean fiber counts were significantly lower in older compared to young subjects (364,000 ± 50,000 versus 478,000 ± 56,000 fibers). The investigators attributed this difference to a preferential loss of type II fibers in older subjects. However, there was no significant difference in the percentage of type I fibers in both age groups (54 ± 5 and 51 ± 3 %, older vs. young). Differences in muscle fiber CSA in the aged subjects were attributed to a decrease in fiber number as opposed to fiber area. This decrease was also found to be 60% attributable to the loss of type II fibers even though the proportions of type I and II fibers remained the same in both age groups (61).

Expanding their prior study, Lexell *et al.* examined whole vastus lateralis muscle from 43 men designated to five different age-groups of 20, 30, 50, 70 and 80 yrs (62). Assessment of the vastus lateralis showed an emergent relationship between the numbers of total muscle fibers and type I fiber area. Those with a few number of muscle fibers tended to have a large type I fiber area whereas those with a large number of muscle fibers displayed a smaller type I fiber area. This study also demonstrated that a reduction in muscle fiber size can begin as early as 25 years of age (62).

While previous studies by Lexell *et al.* examined cadavers, a longitudinal study was performed by Aniansson *et al.* (6). Investigators examined a cohort, initial mean age 69 yrs, with two follow-ups occurring at mean ages 76 and 80 yrs. Repeat muscle biopsy samples were taken from the vastus lateralis and analysis revealed a non-significant reduction in the percentage of type IIB muscle fibers of 11% as well as a significant decrease in the area of type IIA (by 14%) and IIB (by 25%) fibers at the first follow-up (6). Upon the second follow-up, the subjects showed increases in type I and type II fiber area by 30% and 40%, respectively. The authors speculated that this was due to subjects taking walks or other moderate physical activities = 4 hours / wk, an amount that may be uncommon in this age group (5).

A more recent study by Klein *et al.* (54) demonstrated that a difference in fiber area may be the cause for loss of strength as opposed to a decrease in the total number of muscle fibers. This study involved examining the total number of muscle fibers in the biceps brachii in young (21 yrs) and older (82 yrs) healthy men. Based on muscle biopsy samples, it was discovered that the type II fiber percentages were not significantly different between age groups (62% and 59%, young versus older). The older men displayed a lower proportion of type II fibers and a significantly reduced type II fiber area when compared to the young group with no significant differences in type I fiber area. Mean fiber diameters of type II muscle fibers were significantly lower in older men than the young men (61 versus 72 µm). The estimated total number of fibers in the biceps brachii ranged from 201,360-312,708 in the young men and 149,301-291,501 in the older men, but these numbers were not significantly different (54).

Skeletal muscle CSA, muscle volume, and muscle fiber area are reduced with age. This reduction in muscle CSA has been demonstrated in studies comparing broad age ranges (52, 70). Specifically, reductions in muscle CSA may be attributed to a decrease in muscle fiber area of type IIA and IIB fibers with age (54). This loss of skeletal muscle CSA is one factor that can further progress or induce the development of sarcopenia and strength loss in the elderly.

Mechanisms of Skeletal Muscle Loss

Inactivity and Disuse

One of the mechanisms postulated to be a cause of skeletal muscle atrophy is a reduction in physical activity (10, 39, 82) as studies have shown decreases in physical activity occurring with age (42, 82). In a longitudinal study by Hughes *et al.*, subjects initially 47-68 years old showed slight declines in physical activity after nine years. It was hypothesized that losses in strength after nine years would be attributed to a decrease in activity, however the main factor was a decrease in muscle mass (42). When comparing younger and older women, Hunter *et al.* discovered older women were significantly less active and women classified as inactive showed significantly less muscle strength in the knee extensors than active women (43). Guo *et al.* found in subjects aged 40-66 yrs with follow-ups every two years that those with higher physical activity levels had smaller total body fat and percentage body fat values (28).

Models involving prolonged periods of bed-rest demonstrate the effect of disuse on muscle CSA and strength. For example, in young healthy men, six weeks of bed rest resulted in a 14% decrease in knee extensor CSA with a 13% loss in maximum torque per knee-extensor CSA and a 19% decrease in electromyographic activity (11). Changes in electromyography indicated that loss of strength was partially attributed to the denervation of muscle fibers as a result of inactivity.

Aging and the Neuromuscular System

Changes occur both functionally and structurally in the neuromuscular system as a result of aging. Functional changes include a decline in the number of active motor units (17) and motor unit firing rates (49). Most studies agree that this occurs after the sixth decade of life (12, 17, 22, 49, 88). Studies have also analyzed the number of motor units in the spinal cord (90) as well as changes in motor axon sizes in the lumbar spinal column (51).

Doherty *et al.* examined the effects of motor unit loss on strength in 20 older adults and 24 young adults that were active and participated in walking/jogging and/or exercise classes (22). Measurements of the maximum M-potential (reading taken when the electrode is placed over the musculocutaneous nerve) of the biceps brachii and brachialis were recorded as were the mean single motor unit action potentials. The maximum M-potential amplitude and mean single motor unit action potentials amplitude were lower in older subjects indicating a reduced number of motor units. The authors suggested that maximal voluntary contraction in older adults (>60 yrs) is reduced by one-third, with a loss of approximately one-half the number of motor units as compared to young adults (22). In a similar study, Doherty and Brown demonstrated motor unit losses in the thenar muscle of the thumb. Through use of multiple point stimulation methods on young (20-40 yrs) and older (63-81 yrs) adults, the authors found 288 ± 95 and 139 ± 68 motor units in young and older respectively (20). These results suggest that older adults have approximately half the number of thenar motor units as compared to young adults.

Further analysis of functioning motor units in the hand were assessed by using a quantal method by Sica *et al.* (88). Ninety-two subjects ranging in age from five to 97 yrs showed an average mean motor unit loss of 77% ± 14, 77% ± 9, and 58% ±11 for the extensor digitorum brevis, thenar, and hypothenar muscles, respectively when comparing subjects > 70 years to those aged five to 60 years. Statistically, the results showed no significant losses of motor units up until the sixth decade. After the sixth decade, the number of units declined with less than half present (42%) by the ninth decade (88).

In studying the extensor digitorum brevis muscle of the foot in subjects aged 3 to 96 years, the number of motor units began to decline past the age of sixty (17), as estimated according to the methods of McComas et al (65). There was no evidence of this decline between the ages of 3 and 58 years and of the surviving motor units in the elderly subjects, properties indicated an increase in motor unit CSA that was attributed to either adoption of denervated muscle fibers, fiber hypertrophy or both (17). This increase in motor unit CSA is most likely due to an adoption of denervated muscle fibers (type II) or an increase in type I fibers.

Tomlinson and Irving examined postmortem, the lumbosacral spinal cords of 47 subjects (age 13-95 yrs) and saw no significant drop in number of motor neurons up to 60 years of age (90). After 60, there was a significant decline, with as much as a 50% reduction in motor neurons. Kawamura *et al.* measured the number of large and intermediate diameter myelinated fibers in the lumbar (L3, L4, & L5) spinal roots of men aged 17-81 yrs (51). Total number of fibers in relation to age was studied with linear regression and the results indicated that total fiber number decreases with age in L3, L4, and L5.

Furthermore, Doherty *et al.* examined the conduction velocity of nerve impulses in young (24-53 yrs) and older (64-74 yrs) subjects (21). A computerized technique based on F-response measured conduction velocities of single median motor fibers. The results indicated that the axonal conduction velocities were consistently slowed with aging with a conduction velocity range of 48-68 m/s in young and 38-61 m/s in older subjects. The slower conduction impulses suggested a slower population of motor fibers. This is consistent with the fiber grouping evident in histochemical studies (24, 74, 91).

A study by Kamen *et al.* measured motor unit discharge rates of the first dorsal interosseous muscle in seven young (21-33 yr) and older (>67 yr) adults (49). Measurements were taken from the first dorsal interosseous muscle by a transducer at 50% and 100% of maximal voluntary contraction. It was demonstrated that with increasing age, motor unit discharge rates decrease, suggesting a reduction in maximal force capability in older adults. Specifically, the maximal discharge rate in the older adults was 31 impulses/s with the young subjects demonstrating 51 impulses/s. It is this age-related decrease in motor unit firing rate that contributes to limiting maximal voluntary activation of agonist muscle (49).

Decreases in neuromuscular activity through loss of motor units and/or motor unit firing rates will negatively impact strength. Physiological adaptations will then occur in the muscle to minimize decreases in strength. This may occur by having type I motor neurons expand to some of the denervated type II muscle fibers or by increasing existing type I muscle fiber size. This allows for a muscle fiber grouping of type I fibers not evident in young skeletal muscle (17). As a consequence, muscular strength of the elderly is weakened due to a preferential type II muscle fiber loss, decline in conduction velocity (due to fast fatigability properties of type II fibers), and loss of motor units.

Nutritional Intake

Resting metabolic rate declines with age as a consequence of a loss of muscle mass (93). As resting metabolic rate declines, so too does food intake in the elderly and despite these reductions in energy requirements, fat mass tends to increase with age (67). A specific reduction in dietary protein intake is of importance as maintaining positive nitrogen balance is a requirement for maintaining muscle mass (27, 97). A study assessing 946 healthy men and women over 60 years of age found that 50% consumed less than the recommended 1.0-1.25 g of protein per kg of bodyweight (68). Because muscle protein is in constant turnover, protein synthesis rates must exceed protein breakdown as this helps to maintain and repair skeletal muscle. Several authors have demonstrated a reduction in protein synthesis rates with age (7, 27, 94). Welle *et al.* found in healthy, older (> 60 yrs) and young (< 35 yrs) subjects, total myofibrillar protein synthesis rates were 44% slower in those > 60 years when compared to young subjects (1.4 vs. 2.5 g/h) (94). Thus decreased protein synthesis rates may contribute to a decrease in muscle mass with aging.

Muscle Architecture

Recently Narici *et al.* evaluated the effect of ageing on skeletal muscle architecture. Variables other than muscle volume or CSA including muscle fascicle length and pennation angle were investigated. This is important as changes in fascicle length and pennation angle can affect force generation capacity of skeletal muscle. For this study, morphometric measurements were compared between 14 young (27-42 yrs) and 16 older (70-81 yrs) physically active men, who were matched for activity, height and body mass. Computer-assisted tomography was used to measure anatomic CSA and volume, and ultrasonography evaluated gastrocnemius medialis fascicle length and pennation angle. Narici showed that there were significant differences for all measured variables between young and older subjects. Specifically, anatomical CSA decreased by 19%, muscle volume decreased by 25%, fascicle length fell by 10%, pennation angle was decreased by 13%, and physiological CSA decreased by 15%. Due to the strong relationship between force and physiological CSA, the decrease in physiological CSA can be attributed to being a primary factor for a decrease in contractile force-generating potential in old age (70).

Effects of Sarcopenia on Activities of Daily Living

Aging often leads to an increase in fat-mass, which results in a reduction of fat-free mass, specifically, loss of skeletal muscle. This ultimately results in the loss of muscular strength (53). Muscle weakness leads to an increased risk of falling, hip fracture, and gait disorders in the elderly (89, 96). Loss of muscular strength, especially in the knee extensors is of particular relevance, as the ability of these muscles to generate force rapidly is critical when performing several activities of daily living including climbing stairs, walking, and in the prevention of falls and trips (9). Thus, the muscular strength of the knee extensors has been correlated with walking speed, balance, time to rise from a chair, ability to climb stairs, incidence of falls, and survival rates (26).

Whipple *et al.* showed the importance of the strength of the muscles of the knee and ankle in the elderly by studying nursing home residents with a history of falls. The authors measured knee and ankle muscle strength with an isokinetic dynamometer at low (60°/s) and high (120°/s) angular velocities. The most prominent sign of weakness was in the ankle muscles as opposed to the knee muscles and peak torque and power differences were greatest at the high angular velocity. Ultimately, it was discovered that those residents experiencing falls had lower peak torque and power of the knee extensors, flexors, and ankle plantar and dorsiflexors when compared to non-fallers (96).

Bassey *et al.* examined leg extensor power and functional performance in very older men (89 yrs) and women (87 yrs) (9). A custom rig was built to measure the power available in a single extension of one leg (8). The rig consisted of a seat with a low back so that the subject pushed a foot pedal as quickly as possible with the maximum power output being recorded from both legs. The measurement took place in less than one second; therefore power was solely attributed to the ability to command the nervous system from within the muscle cells as opposed to circulatory or respiratory factors (9). Other measurements were also taken, including time to rise from a chair, stair climbing, and walking 6.1 meters. All three performance tests were correlated with leg extensor power (r = 0.65, 0.81, and 0.80).

The decrease of peak torque and power of the knee extensors, flexors, and ankle plantar and dorsiflexors is a consequence of muscle weakness in association with aging. Loss of muscular power and strength leads to an increased risk for falls, which may lead to injury. To combat these risks, Buchner *et al.* tested the effects of resistance and endurance training on risk of falls and found that exercise training may have a beneficial effect on fall rates in older adults between 65 and 85 years of age (14). Inactivity, reduced nutritional intake, and structural and functional changes to the neuromuscular system affect muscle mass and strength. This leads to a diminished function to perform activities of daily living. Some of these mechanisms have been previously identified and proper countermeasures included increasing physical activity levels through resistance training to combat muscle strength loss.

Adaptations to Resistance Training

Numerous studies have examined the benefits of resistance training on muscle CSA, muscle fiber area, 1-repetition maximum (1RM) values, and electromyography (EMG) data to assess neuromuscular adaptations. Authors examining muscle biopsies have found significant increases in both type I and type II fibers after a resistance training stimulus (60, 81). Lexell *et al.* (60) examined the effects of heavy resistance training (85% 1RM) on elbow flexors and knee extensors in six men and ten women aged 70-77 yrs. Measurements on muscle biopsies from the biceps brachii indicated significant increase in both type I and type II fiber area of 13% and 17%, respectively. No significant changes occurred in the percentage of type I and II muscle fibers in vastus lateralis after resistance training. Although Lexell found no significant changes in vastus lateralis fiber area, a study by Pyka *et al.* demonstrated significant increases in type I (3,872 ± 259 to 5742 ± 187 μm^2) and type II (3,245 ± 183 to 5,246 ± 264 μm^2) muscle fiber area of the vastus lateralis after 30 weeks of full body resistance training (75% 1RM) on older subjects (61-78 yrs) (81).

Häkkinen *et al.* also demonstrated significant changes in 42 men and women of two age groups (40 and 70 years) who performed six months of full body resistance training, two days/week, involving loads of 50-70% 1RM. The authors demonstrated a significant increase in vastus lateralis mean muscle fiber area of type I and II fibers in women but the increases did not prove significant in men. However, men demonstrated significantly larger mean type II muscle fiber area than women before the start of the resistance training program (34).

Jozsi *et al.* examined muscular power changes after a resistance training program in 34 young (21-30 yrs) and older (56-66 yrs) men and women. Subjects performed five exercises, three sets of eight to twelve repetitions, twice a week at 80% of 1RM on Keiser pneumatic resistance machines. All subjects increased power in the arm pull and knee extension exercise at 40 and 60% 1RM, but only in knee extension power did men show greater absolute gains than women. There were no significant interactions between age x time and gender x time for changes in arm pull power or leg extensor power. Therefore changes in arm and leg extensor power can improve similarly in young and older individuals, thus improving functional performance regardless of age (46).

Studies Assessing Muscle Volume

Very few studies have analyzed changes in muscle volume after resistance training likely due to the time and labor involved (92). One study by Roman *et al.* assessed the elbow flexors in five older males after 12 weeks of heavy resistance training noting a significant increase of 360 ± 28 to 409 ± 24 cm^3 (84). Overend *et al.* used anthropometric and computed tomography methods to determine muscle plus bone CSA and muscle volume in young and older men. It was found that there was no difference in total thigh CSA between young and older men but there was a significant difference in muscle plus bone CSA between young and older (182.2 cm^2 versus 158.5 cm^2). Muscle plus bone volume was also significantly different between young and older (4,219 cm^3 vs. 3,355.1 cm^3) (76).

More recently, Ivey *et al.* examined quadriceps muscle volume changes after nine weeks of unilateral high volume, heavy resistance strength training on young and older, men and women. The investigators found significant quadriceps muscle volume gains after nine weeks of HRST with men displaying significantly greater increases in muscle volume than women (204 ± 20 vs. 101 ± 13 cm^3) and no significant differences between age groups. (44). Roth *et al.* examined age and gender responses after six months of a whole body resistance training program and found no significant differences in muscle volume between gender or age groups (20-30 yrs, 65-75 yrs) (85).

Regional Hypertrophy Studies

Due to the four constituent muscles of the quadriceps (vastus lateralis, vastus intermedius, rectus femoris, and vastus medialis), hypertrophy may occur in varying degrees along the entire quadriceps muscle group. In 1988, Narici *et al.* performed a study that showed that the quadriceps reaches a maximal anatomical CSA at the middle region and then decreases distally towards the knee (71). Narici later completed a study that utilized a 60 day unilateral strength training program four times/week with six sets of ten maximal isokinetic knee extensions on the dominant leg of four young men aged 23-34 years (72). Measurements of maximal voluntary contraction, integrated EMG, and quadriceps muscle CSA were taken every 20 days and after 40 days of detraining. Six of the seven regions scanned increased significantly with the largest percent increases occurring at the most proximal scan (12%) and then decreasing distally towards the knee (3.5%). At the middle region, quadriceps CSA increased by 8.5% in the trained leg. No significant differences were seen in the untrained leg after resistance training or detraining. The detraining loss (-0.10%·day^{-1}) appeared to be similar to that of the training gain (0.14%·day^{-1}) (72).

Housh *et al.* (41) performed a similar study compared to Narici's (71, 72) with the following modification: isokinetic concentric only contractions were performed on the non-dominant arm and knee flexor / extensor muscles of men (age 25 ± 6 years). After eight weeks of resistance training, increases of 6%, 11%, 11% were seen in the knee extensors at the proximal, middle, and distal regions, respectively (41).

Previous studies examining regional hypertrophy prior to 1996 examined only isokinetic resistance training. Narici *et al.* again examined quadriceps CSA using isotonic contractions for six months. Seven men (age 29 ± 4 yrs) completed unilateral knee extensions at 80% of 1RM with the dominant leg (69). Significant increases were seen in the three regions (proximal, middle, and distal) of 19%, 13%, and 19%, respectively. Isotonic contractions were then separated into the two respective actions, eccentric and concentric, by Higbie *et al.* (40). Sixty women (20 ± 1 yrs) were assigned to concentric only, eccentric only, or a control group with MRI used to assess quadriceps muscle CSA at seven regions along the thigh (40). The increases in CSA at the middle and distal regions of the quadriceps were significantly greater in the eccentric training group when compared to the concentric resistance training group and both resistance training groups were significantly greater than the control group (40). A recent longitudinal study examining junior elite Olympic lifters through use of MRI revealed significant increases in quadriceps CSA in the distal region only after an 18-month follow-up survey (50). While this study offers limited insight into regional hypertrophy due to the focus on a small number of elite wrestlers, it illustrates preferential hypertrophy in the distal region of the quadriceps. Thus showing that assessing changes in CSA at various regions may be preferred as changes may go unnoticed if only one region of the quadriceps was examined.

Specific training types (isokinetic, isotonic, Olympic lifting) and loads (%1RM) can affect the degree of hypertrophy along the quadriceps muscle group (40, 41, 50, 69, 72). Typically, studies analyze changes in muscle CSA at the point of maximal anatomical CSA but this may not be adequate due to the non-uniform hypertrophic response and distribution of individual muscles.

Resistance Training, Effects of Gender and Age

Many studies have examined changes occurring in muscle strength and size relative to gender and age groups (18, 30, 37, 44, 57, 75, 85). Cureton *et al.* studied 22 young men and women (22 to 37 yrs) before and after completing a 16-week protocol of progressive heavy-resistance weight training utilizing 70-90% of 1RM. A non-significant increase in of 3% occurred in the quadriceps of men and women as measured by computer-assisted tomography. Women displayed significantly greater increases in the CSA of the upper arm (23% versus 16% in the men). Absolute increases were not significantly different (7 cm^2 vs. 5 cm^2) for men and women respectively (18). Contrary to the findings of Cureton *et al.* (18), O'Hagan *et al.* (75) found no significant differences in relative and absolute measures of muscle CSA measured in the arm flexors of six men and seven women (20 ± 0.8 yrs) after resistance training. Prior to the resistance training program, woman possessed 51% of elbow flexor CSA of the men. The training program included 20 weeks of resistance training three days/wk at 70-90% of 1RM. The data from computer-assisted tomography indicated that the absolute (3.3 vs. 3.1 cm^2) and relative (15 vs. 26%) increases in men and women, respectively for the arm flexors were not significantly different (75).

A study by Häkkinen *et al.* (30) found significant increases in quadriceps CSA as assessed by ultrasound after six months of heavy-resistance training combined with explosive exercise. There were four subject groups, young (43-57 yrs) and older (64-73 yrs) men and women. Relative increases in CSA were similar between all four groups (30). A later study by Häkkinen *et al.* (32) examined similar age groups from the previously mentioned study (30) except relative increases were reported. Ultrasound measurements revealed increases of 5% and 2% in men aged 39 and 67 years, and 10%, and 6% in women aged 39 and 67 years, respectively (32). The larger relative increases that occurred in woman are in part due to smaller absolute CSA values at baseline.

Harridge *et al.* studied eight women (85-97 yrs) and three men (85-92 yrs), examining muscle strength and quadriceps CSA before and after a resistance training stimulus of three times per week for 12 weeks (37). The exercise program included knee extensor and flexor training with three sets of eight repetitions with loads of 80% of 1RM. The results from the MRI scans showed a 10% increase in muscle CSA, no comparisons were made in regards to gender.

Lemmer *et al.* studied the effects of age and gender on unilateral high volume, heavy resistance knee extension exercise, three times/wk for nine weeks in young and older, men and women. Young subjects displayed significantly greater relative increases in 1RM strength when compared with older subjects (34% vs. 28%) but absolute changes in 1RM strength were not significantly different for age or gender. This was the first study to demonstrate that age may affect 1RM strength values but gender does not (57).

Ivey *et al.* found that gender plays a role in the amount of muscle volume gained after nine weeks of unilateral knee extension exercise in the dominant leg. Young and older, men and women underwent nine weeks of resistance training. Quadriceps muscle volume measurements assessed through MRI revealed greater absolute increases in muscle volume in men than women (204 ± 20 vs. 101 ± 13 cm^3) with no significance differences between young and older (44). Contrary to these findings, Roth *et al.* assessed quadriceps and thigh muscle volume after six months of a full body resistance training program consisting of exercises of all major muscle groups three days/week. Subjects included young and older, men and women. At baseline, men displayed significantly higher muscle volume measurements than women and young subjects displayed significantly higher quadriceps muscle volume than older subjects. Despite these initial differences, significant increases in muscle volume occurred in all groups after strength training with no statistically significant differences detected between groups after six months of training. The difference between Roth and Ivey may be that there was greater control in the Ivey study due to the unilateral program and inclusion of a control limb.

Studies that have assessed changes in muscle CSA appear to show similar relative and absolute increases in muscle CSA when comparing gender groups. However when studies assess muscle volume, men show large absolute changes after resistance training when using a unilateral resistance training program. Full body resistance training programs revealed no significant differences in gender or age for muscle volume. In reference to relative increases and CSA measured at one region, it would appear that similar relative increases occur regardless of age or gender, although some studies have shown otherwise. When accounting for absolute changes, men typically show larger values.

Methods for Assessing Skeletal Muscle Size

There are numerous imaging methods available to assess changes in skeletal muscle CSA and volume. Proper identification of methods that are reliable and valid is important in order to make accurate comparisons after resistance training and detraining and also between age and gender groups.

Ultrasound

Ultrasound utilizes high-frequency (1-5 megahertz) sound pulses that are emitted from a transducer probe. The pulses are transmitted through the tissues of the body and then reflected back to the probe where they meet a boundary between fluid and soft tissue or soft tissue and bone. The reflected waves are transmitted to a machine that calculates distances from the probe to the tissue using the speed of sound (1,540m/s) and the time of each echo's return. With this information the computer calculates a two-dimensional image.

Dual-Energy X-Ray Absorptiometry

Dual-energy X-ray absorptiometry is a common method used to analyze body composition and estimate bone and soft-tissue, both muscle and adipose through photo transmission and detection. When photons are emitted they are either scattered or absorbed by the tissue and this reduces the beam intensity. This method is referred to as attenuation and attenuation is observed at two energy levels, high and low, and the ratio of the two energy levels is expressed as R. The R values are then used to identify hard and soft-tissue through knowledge of atomic elements. Fat consist of predominantly hydrogen, carbon, and oxygen, low-atomic number elements whereas bone mineral consist of calcium, a high-atomic number element.

To measure body composition, dual-energy X-ray absorptiometry assumes humans consist of three components distinguishable by X-ray attenuation properties: fat, bone mineral, and lean soft tissue. Pixels are generated and then further separated based on computing the R value for every pixel. Pixels are then separated into those with only soft tissue (fat + lean tissue) and those with soft tissue + bone mineral. A threshold R value is then set to determine which pixels include bone and soft tissue. This threshold is determined by the subject's body composition and bone density.

There is some concern for fluid levels in tissue and as these levels increase or decrease R values may change. However these changes are predictable and can be adjusted for during experimentation (77).

Computer-Assisted Tomography

Computerized tomography is a radiological imaging technique that produces transverse topographic images. An x-ray beam rotates around an object at multiple angles within a scanner or by radiation detectors set at different angles. This creates an image or slice of tissue. The x-rays that pass through the object are attenuated (absorbed or scattered) with the amount of attenuation dependent upon the type of tissue the x-ray beam passes through. The attenuations are recorded as a value or density. A complex computer algorithm is then used to reconstruct an image of the internal structure of the analyzed object. The image is made up of black, white, and shades of grey colors that are assigned to squares made up of pixels. Each pixel represents a block of tissue with the color assigned to each pixel dependent upon the attenuation of the tissue. Air appears black, bone is white and water appears as the central grey color. Based on this color or contrast capability, images may be generated allowing for excellent soft tissue contrast (16, 38).

Biophysics of Magnetic Resonance Imaging (MRI)

Magnetic resonance imaging utilizes radio waves and the fact that atoms are comprised of protons (positively charged), neutrons (neutrally charged), and electrons (negatively charged). Where most atoms have a balance between the number of protons and electrons, the only difference is the number of neutrons. If the nucleus of an atom has an uneven number of protons or neutrons it has a net spin and angular momentum. This net spin depicts a current loop with a north and south pole. The angular momentum describes the rotational motion and must be a nonzero number for the MR imaging to work. When a magnetic field is applied, the dipole moments are aligned with the field in a parallel or anti-parallel fashion. The parallel condition is the low energy state or the ground state, the anti-parallel condition is the high energy or excited state. Slightly more protons align in the low-energy state and the use of this knowledge allows a spin echo image to be generated (86).

Spin echo imaging is the most common form of MR imaging. The protons in each atom must be manipulated in order to successfully generate an image. Three manipulations take place, (1) the protons magnetic vector is flipped 90 degrees; (2)

the protons must spin in phase; and (3) the spins must be moved into a higher energy state so that there are an equal number in both high and low energy states (86). These conditions are met by applying a second magnetic field 90º offset from the main magnetic field. The oscillations of the magnetic field generate a radiofrequency. When the second magnetic field is turned off, the protons move from a high to low energy state releasing radiofrequency energy which is the MR signal. The number of spins in the sample or its proton density is proportional to the amplitude of the MR signal.

The MRI is generated by three magnetic field gradients. A slice-select gradient locates the position and thickness. The frequency-gradient locates protons by its spin frequency and the phase-encoding gradient specifies the location in space of a proton according to the phase of its spin. Any of these three gradients may be in the X, Y, or Z axis.

The radiofrequency is received at lower amplitude than when generated due to signal losses within the sample. These signal losses are designated T1 and T2 relaxation times and given in milliseconds. A T1 relaxation is also called longitudinal or spin-lattice relaxation. It indicates the relationship of the nucleus of the atom with its environment. The T2 relaxation stands for transverse or spin-spin relaxation. It is due to randomly varying inconsistencies in the magnetic field created by adjacent nuclei within the sample. Unlike T1, T2 relaxation is independent of magnetic field strength.

The intensity of the MR signal is a reflection of T1 and T2 relaxation values. Therefore T1 and T2 relaxation times may be manipulated to suit the needs of the image. Images that emphasize T1 and minimize T2 characteristics are said to be T1-weighted. This T1-weighted imaging is used to identify abnormal tissue within structures of high fat content, such as marrow and subcutaneous fat (86). A T2-weighted image allows for detecting differences between normal and abnormal tissue as well as tendons and ligaments.

Magnetic Resonance Imaging Reliability & Validity

Magnetic resonance imaging provides superior differentiation between tissues (skeletal muscle, adipose, and connective) which allows for accurate measuring of muscle CSA. Unlike computer assisted tomography, it is safe because the subject is not exposed to radiation. A study by Engstrom *et al.* utilized three cadavers to examine the precision and relative accuracy of MRI in comparison to the anatomical CSA of individual thigh muscles (23). MRI measurements were within ± 7.5% of the anatomical CSA standard. Linear regression determined a correlation coefficient of 0.97 and a test-retest reliability measurement had correlation coefficients between paired observations with 95% of the comparisons exceeding an r of 0.94, thus indicating good reliability.

Mitsiopoulos *et al.* analyzed adipose tissue free skeletal muscle mass (66). Correlation coefficients between duplicate measurements of subcutaneous fat, adipose free skeletal muscle, and intra-abdominal tissue in MR images were 0.97, 0.99, and 0.92, respectively. These investigators also demonstrated that adipose free skeletal muscle area was significantly less than anatomic skeletal muscle ($p < 0.01$) (66). It was noted that this difference reflected the fact that intra-abdominal tissue represented ~ 24% of the skeletal muscle area for the 119 cadaver sections. This shows the importance of correcting intramuscular fat deposits within muscle when determining skeletal muscle CSA. Based on these two studies, MRI may be used as a reliable and valid method to assess skeletal muscle CSA

Summary

Sarcopenia is a consequence of aging and may lead to an increase in falls, hip fractures, and a reduction in functional performance. A review of the literature has shown that decreases in skeletal muscle CSA, volume, fiber area, motor units, and motor unit firing rates occur with increased age. Through physical activity, especially resistance training, these negative effects can be negated and often reversed.

Studies using resistance training as an intervention have typically analyzed one region of muscle in either knee or arm flexor/extensors. Results indicate that significant changes can occur in skeletal muscle through varying resistive exercise training protocols through analysis of one region of a muscle. Investigators that have examined multiple regions in the quadriceps have shown modest relative increases on the order of 3-10% with the largest increases occurring in the middle region. More importantly, studies analyzing multiple regions have only included a limited subject population of only one gender or age group and have not used a control limb.

With regional hypertrophy studies lacking diverse subject groups (men and women, young and older) it is important to identify if resistance training benefits all age and gender groups similarly across all regions of the quadriceps. It is also important to identify if muscle loss occurs similarly across all groups after a period of detraining. A unilateral resistance training program that provides a stimulus significant to induce hypertrophy along with a sufficient detraining period will provide answers as to what changes occur in the quadriceps muscle in young and older, men and women.

Chapter 3: Methods

Subjects

Subjects in this study were volunteers recruited through advertisements in the Prince George's Journal, The Washington Post Health section, and in the University of Maryland campus newspaper. Participants included 10 young females and 11 males (20-30 yrs), and 11 older females and 12 males (65-75 yrs). All subjects underwent a medical history, physical exam, and a graded exercise test (GXT), supervised by a physician prior to participating to ensure the health of the participants and for screening purposes. Subjects were excluded from the study if found to be smokers or have any type of cardiovascular, metabolic, or musculoskeletal disorder. Only sedentary subjects who did not exercise for the past 6 months (less than 2x/wk; <30min) participated. All subjects provided written informed consent prior to participation and the project was approved by the Institutional Review Board at the University of Maryland, College Park. Subjects underwent the nine week HRST program and 31 weeks of detraining between 1995 and 1999. Subject's strength and MRI data is archived and no new subjects were tested for this thesis.

Testing Procedures

Graded Exercise Test (GXT)

The GXT was performed according to guidelines established by the American College of Sports Medicine for clinical exercise testing and according to standard 12-lead ECG protocol (4). The skin was prepared by abrading the skin and wiping clean with an alcohol swab to reduce skin resistance. A Quinton 3000 – electrocardiograph recorded resting supine, sitting, and standing ECG tracings. A standard blood pressure cuff, mercury manometer, and stethoscope in the supine, seated, and standing positions recorded blood pressure. The GXT followed the standard Bruce Protocol with blood pressure and heart rate being monitored at the end of each 3-minute stage. Subjects were encouraged to continue the test until exhaustion. Abnormal responses or instruction by the physician to halt testing concluded the GXT. Only healthy subjects given a negative GXT were permitted to participate in the study.

Body Composition

Total body fat free mass and total body fat mass was measured by dual x-ray absorptiometry using a Lunar DXP-L (Lunar Corporation, Madison, WI) before and after HRST. Dual x-ray absorptiometry scans were completed in the morning after an overnight fast. To ensure reliability of the measurements, a calibration standard was scanned daily. A water/oil phantom sample containing 41% fat was also scanned monthly. Previous studies have reported coefficients of variance of 5.7% (29).

Strength Testing

Subjects underwent three familiarization sessions prior to starting HRST. These sessions familiarized the subject to the warm-up and stretching procedures as well as seat position and familiarity with the use of the Keiser K-300 air powered knee extension machine (Keiser Sport/Health Equipment, Fresno, CA). During these three sessions, subjects experienced little to no resistance on the Keiser knee extension machine.

One-repetition maximum (1RM) strength testing of the knee-extensors of both legs was assessed prior to starting the HRST. Prior to the start of the test, subjects warmed-up for 3 minutes on a cycle ergometer and were supervised in stretching the knee flexors and extensors. Subjects sat on the Keiser machine with a pelvic strap in place to ensure muscle recruitment of only the knee extensors. Seat position was recorded to have consistency in future sessions. The initial resistance chosen was thought to be slightly less than the subjects 1RM. Each following set included increased resistance where the subject performed one or two repetitions at each weight. One minute rest intervals took place between sets and the weight continued to be increased until a true 1RM was achieved. The trials for this test were minimized (approximately 7) to ensure a true 1RM. The test was performed on both legs (trained and untrained) and a 5RM test was performed in the same manner as the 1RM test. The same investigator performed the 1RM at both time points.

Resistance Training Protocol

Unilateral, HRST knee extensor training of the dominant leg was performed three times per week on Monday, Wednesday, and Friday for nine weeks. The dominant leg was trained. Prior to each session the subject performed a warm-up on a cycle ergometer for three minutes followed by supervised stretching of the knee flexors and extensors.

A total of five sets of knee extension were completed at each training session. The first set was a warm-up of 5 repetitions at 50% of the subject's original 1RM with a rest interval of 30 seconds. The second set consisted of 5 repetitions at the 5RM resistance with 90 seconds of rest prior to starting the next set. The third set consists of 10 repetitions. The first 5 repetitions are completed at the subjects 5RM. The resistance is then decreased so that the subject can complete 2 more repetitions and then decreased again until completion of the full set of 10 repetitions. For the fourth and fifth set, the same procedure was followed as the third set except 15 and 20 repetitions are completed on the fourth and fifth set respectively. Rest intervals for the third, fourth set are 150 and 180 seconds. Upon completion of the training session a total of 55 repetitions were performed.

The concentric portion of the exercise (knee extension) was performed in approximately 1-second and the eccentric portion (knee flexion) was performed in 2-seconds. Subject's 5RM values were re-adjusted individually every week allowing for increases in strength throughout the duration of the training program. The design of this training program allowed for heavy resistance (5RM) and high volume (high number of repetitions) in the same training session. This was done by having each repetition at or near maximal on every repetition. Subjects were directly supervised by study personnel during the HRST sessions. If a subject missed a session, the number missed was added to the end of the nine weeks so that a minimum of twenty-seven sessions were completed by all subjects. Body weight was measured on a detecto balance beam scale at each exercise training session.

Detraining

After completion of the nine-week HRST program, participants were instructed to resume their normal lifestyle while avoiding any form of regular exercise for 31 weeks. Subjects were contacted each month during this period to ensure compliance. At 15 and 31 weeks, strength tests were performed measuring 1RM values. At the end of 31 weeks, MRI scans were taken.

Magnetic Resonance Imaging (MRI)

Magnetic resonance images were taken before HRST, after HRST, and after detraining. A Picker Edge 1.5 Tesla MRI scanner obtained a series of axial slices from the superior border of the patella to the anterior superior iliac spine surrounding the entire quadriceps femoris muscle group. Fifty-two axial scans, 9mm thick (1mm gap), T1-weighted, with an echo time of 14ms and a relaxation time of 700ms, encompassing the entire quadriceps muscle group were produced. Scans were performed between eight and ten in the morning. Subjects did not eat after midnight prior to the MRI scanning and all scans took place at least 72h after the subjects last training session.

The MRI technician checked the calibration daily and made adjustments as needed. A lean beef phantom measurement ensured scanning reproducibility via repeat volume measures. Dimensions of the lean beef phantom were one that approximates dimensions of the human quadriceps muscle. A 0.12% difference was reported in repeat volume measurements. Engstrom *et al.* compared MRI measurements against anatomical CSA of the human thigh in cadavers and found that MRI measurements of CSA provided accurate values generally within ± 7.5% of the anatomical CSA standard (23).

Magnetic Resonance Imaging Analysis

NIH Image version 1.61 was used to analyze the MRI scans on a Macintosh PC (Apple, Inc.). The axial scans are cross-sectional slices of the muscles and the images are viewed as if looking at a cross-section of the human thigh. Three regions are of interest; region 1, proximal to the hip from the midpoint, region 2, the midpoint of the quadriceps group, and region 3, proximal to the knee from the midpoint. The CSA of each region was determined by outlining the quadriceps muscle group and subtracting any visible fat and bone with the use of a trackball. To determine the regions of interest, the following methods were used: Two bony landmarks marked the proximal and distal points of all slices containing quadriceps muscle tissue. This involved using the first slice that showed a clear image of the head of the femur and the last slice contained the superior border of the patella. The total number of slices containing muscle tissue was multiplied by 0.5. Counting down this number from the slice including the head of the femur will result in a region that represents 50% of femur length. The first region (proximal to the hip) is 30% and the third region (proximal to the knee) 70% was determined by multiplying the total number of slices by 0.3 and 0.7 respectively.

The same investigator measured the regional CSA of both the trained and untrained leg in male subjects before and after HRST as well as after 31 weeks of detraining. Calculations of the female subjects CSA had been previously measured by Pouliot at all three time points (80). The men's data was then combined with the women's data as measured by Pouliot (80). To ensure reliability between the two data sets, a regression analysis was performed where the primary investigator analyzed 51 axial scans computed by Pouliot (80). The results indicated an R^2 value of 0.93. A pilot study was also carried out to ensure test-retest reliability such that the investigator performed repeat measurements on different days of 50 axial scans, blinded to subject's gender, age, and time point (before or after HRST and after detraining). The test-retest correlation was, $R^2 = 0.94$.

Data Analysis

Changes in CSA at all three time points were calculated by subtracting the control leg from the trained leg. The importance of this allowed for controlling for seasonal variations (subject's trained at different periods during the year) as well as if the subjects were active outside of the requirements for this study. If subjects did perform physical activity outside of the HRST program, these changes were accounted for through use of the control leg. Specifically, changes in CSA after nine weeks of HRST were calculated by subtracting the CSA of the control leg after HRST from the CSA of the trained leg after HRST. Changes in CSA after detraining were calculated by subtracting the CSA of the control leg after detraining from the detrained leg after 31 weeks of detraining. These differences were calculated for both genders and age groups for all three regions of the quadriceps muscle. A multi-way ANOVA with repeated measures assessed significance between gender and age. The differences in the CSA after training and detraining were examined for significance. Factors in the ANOVA included age, gender, time point, and region. Percentage increases and decreases in the trained leg were calculated from the mean values of the trained leg covaried for the untrained leg. Statistical analyses were performed using SAS version 9.1.2 for Windows with data being expressed as means ± SE. The level of significance was set at an alpha of 0.05.

Chapter 4: Results and Discussion

Results

Physical Characteristics

Table 1 shows the physical characteristics of the subjects. In comparison to older subjects, young subjects were significantly taller (173.5 ± 5.0 versus 167.9 ± 5.0 cm, $p < 0.005$) and had a significantly lower amount of body fat, both before (27 ± 8 versus 34 ± 7 %, $p < 0.0001$) and after HRST (27 ± 8 versus 34 ± 7 %, $p < 0.0001$). Young men and older men were significantly taller, weighed significantly more before and after HRST and also had significantly lower body fat before and after HRST when compared to young and older women, respectively. Men were significantly taller than women (177 ± 8 vs. 164 ± 7 cm, $p < 0.0001$) and had a significantly higher VO_2max (33 ± 11 vs. 26 ± 8 $ml \cdot kg^{-1} \cdot min^{-1}$, $p < 0.0001$). Body weights at both time points (before and after HRST) were significantly higher in men than women, (before HRST, 81 ± 14 vs. 66 ± 10 kg, $p < 0.001$; after HRST, 82 ± 14 vs. 66 ± 10 kg, $p < 0.001$) and body fat was significantly higher in women than men both before (26 ± 7 vs. 35 ± 7 %, $p < 0.0001$) and after HRST (26 ± 7 vs. 35 ± 7 %, $p < 0.0001$). Body fat and body weight did not change significantly after HRST in any of the subject groups.

Table 1. Subject Characteristics Before and After 9 weeks of HRST.

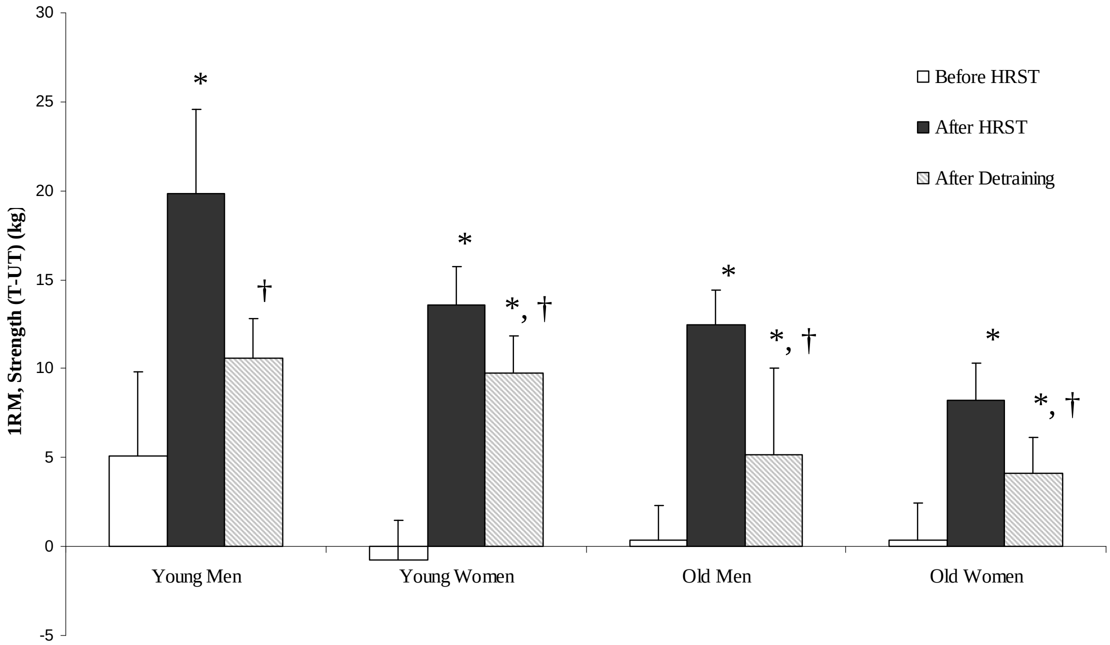
	Young							
	Men (n=11)				Women (n=10)			
	Before		After		Before		After	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (yrs)	25	3	-	-	26	2	-	-
Height (cm)	179 *	9	-	-	168	6	-	-
Weight (kg)	82 *	19	83 *	19	64	12	64	12
% Bodyfat	23 *	8	23 *	8	31	7	31	5
VO_2max (ml·kg-^{1}·min-^{1})	44 *	4	-		33	7	-	-
	Older							
	Men (n=11)				Women (n=11)			
	Before		After		Before		After	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (yrs)	69	3	-	-	68	3	-	-
Height (cm)	174 †	5	-	-	161	7	-	-
Weight (kg)	80 †	8	81 †	8	68	9	68	8
% Bodyfat	29 †	5	29 †	4	39	6	38	6
VO_2max (ml·kg-^{1}·min-^{1})	23 †	5	-	-	20	3	-	-

All values are means. SD = standard deviation. Before = Before HRST, After = After HRST. * Significantly different from young women. † Significantly different from older women. $p < 0.05$.

Muscle Strength

Mean strength differences, expressed as 1RM of the trained leg minus the 1RM of the untrained leg, are presented in Figure 1 for each subject group at each of the three time points (before HRST, after HRST, after 31 weeks detraining). No significant differences were present between older men versus older women and young men versus young women at any of the three time points. There was a significant main effect for time as muscle strength differences increased significantly after HRST (1.3 ± 1.5 kg to 13.5 ± 1.5, $p < 0.0001$) and significantly decreased after detraining (13.5 ± 1.5 to 7.4 ± 1.5 kg, $p < 0.0001$). Young subjects displayed significantly greater strength differences than older subjects only after HRST (16.7 ± 2.6 vs. 10.4 ± 1.4 kg, $p < 0.05$).

Figure 1. Changes in Quadriceps Muscle Strength Differences After HRST and Detraining in the Four Subject Groups.



Data are means of differences ± SED. 1RM = 1 repetition maximum. (T-UT) = 1RM of the trained leg minus 1RM of the untrained leg. * Significantly different from before HRST, $p < 0.05$. † Significantly different from after HRST, $p < 0.05$.

All four subject groups demonstrated significant increases in 1RM strength of the trained leg after HRST as well as significant reductions after detraining (after HRST, 27-35% increase; after detraining, 7-14% decrease). All groups except older women maintained a significantly greater 1RM of the trained leg after detraining (data not shown). In the untrained leg, all groups displayed modest but significant increases in 1RM strength (10-11%) after HRST. After detraining, 1RM strength of the untrained leg was significantly reduced in only older men when compared to 1RM strength achieved after HRST. Only young men maintained 1RM strength values that were significantly higher than before HRST (data not shown).

Muscle CSA

Regional mean CSA values of the trained leg are presented in Table 2 for all four subject groups. All groups significantly increased CSA in the proximal, middle, and distal regions after HRST for the trained leg with the exception of young women, whom increased CSA significantly in only the middle and distal regions. Regional CSA also significantly decreased in all four groups in all three regions after detraining. Only young men maintained a significantly larger CSA in the proximal and middle regions after detraining when compared to before HRST. Overall, absolute increases for the middle region in the trained leg were 7.6, 4.6, 5.1, and 5.4 cm^2 for young men, young women, older men, and older women, respectively. After detraining, CSA of the middle region in the trained leg was reduced by 3.9, 5.3, 4.1 and 6.0 cm^2 for young men, young women, older men, and older women, respectively.

Table 2. Regional CSA of the Quadriceps (Trained leg)

Young Men

Region	Before	After	Detrained	% increase	% decrease
1	67.2 ± 2.9	73.2 ± 3.0 *	70.2 ± 3.0 *,†	12	5
2	83.7 ± 2.9	91.3 ± 3.0 *	87.4 ± 3.0 *,†	15	9
3	65.5 ± 2.9	72.0 ± 3.0 *	67.3 ± 3.0 †	14	9

Young Women

Region	Before	After	Detrained	% increase	% decrease
1	42.3 ± 3.1	44.4 ± 3.1	41.4 ± 3.1 †	4	6
2	57.9 ± 3.1	62.5 ± 3.1 *	57.2 ± 3.1 †	8	7
3	47.2 ± 3.1	51.9 ± 3.1 *	48.4 ± 3.1 †	7	4

Older Men

Region	Before	After	Detrained	% increase	% decrease
1	53.0 ± 2.9	58.7 ± 3.0 *	53.3 ± 3.0 †	11	10
2	63.5 ± 2.9	68.6 ± 3.0 *	64.5 ± 3.0 †	11	8
3	48.1 ± 2.9	51.7 ± 3.0 *	48.9 ± 3.0 †	7	5

Older Women

Region	Before	After	Detrained	% increase	% decrease
1	34.9 ± 2.9	37.3 ± 3.0 *	33.3 ± 3.0 †	5	10
2	45.2 ± 2.9	50.6 ± 3.0 *	44.6 ± 3.0 †	9	9
3	37.8 ± 2.9	42.9 ± 3.0 *	36.9 ± 3.0 †	10	11

Data are mean ± SE in cm^2. Region 1 = proximal, 2 = middle, 3 = distal. Before = Before HRST, After = After HRST, Detrained = after 31 weeks of detraining. * Significantly different from before HRST. † Significantly different from after HRST ($P < 0.05$).

Regional mean CSA values for the untrained leg are presented in Table 3. Minimal changes occurred in the untrained leg after HRST and after detraining when compared to before HRST. However, a statistically significant reduction was found in the middle region of the untrained leg in older men after HRST. Yet after detraining, this region returned to a value similar to before HRST. Statistically significant increases were also detected in the middle and distal regions of older women after detraining and in the middle region of young men when compared to after HRST, but their values were not significantly different from before HRST.

Table 3. Regional CSA of the Quadriceps (Untrained leg)

Young Men					
Region	Before	After	Detrained	% change (Before to After	% change (After to Detrained)
1	67.1 ± 2.8	66.5 ± 2.7	67.4 ± 2.8	-1	1
2	83.3 ± 2.8	82.0 ± 2.7	85.0 ± 2.8 †	-2	4
3	65.6 ± 2.8	64.2 ± 2.7	65.7 ± 2.8	-2	2
Young Women					
Region	Before	After	Detrained	% change (Before to After	% change (After to Detrained)
1	42.1 ± 2.9	42.2 ± 2.8	41.6 ± 3.0	0	-1
2	58.6 ± 2.9	59.0 ± 2.8	57.8 ± 3.0	1	-2
3	48.5 ± 2.9	50.1 ± 2.8	48.5 ± 3.0	3	-3
Older Men					
Region	Before	After	Detrained	% change (Before to After	% change (After to Detrained)
1	52.7 ± 2.8	52.3 ± 2.7	53.9 ± 2.8	-1	3
2	63.6 ± 2.8	61.6 ± 2.7 *	64.0 ± 2.8 †	-3	4
3	47.9 ± 2.8	47.7 ± 2.7	47.6 ± 2.8	-1	0
Older Women					
Region	Before	After	Detrained	% change (Before to After	% change (After to Detrained)
1	33.7 ± 2.8	34.9 ± 2.7	34.7 ± 2.8	4	-1
2	45.3 ± 2.8	46.7 ± 2.7	44.3 ± 2.8 †	3	-5
3	38.6 ± 2.8	40.2 ± 2.7	37.2 ± 2.8 †	4	-7

Data are mean ± SE in cm^2. Region 1 = proximal, 2 = middle, 3 = distal. Before = Before HRST, After = After HRST, Detrained = after 31 weeks of detraining. * Significantly different from before HRST. † Significantly different from after HRST. ($P < 0.05$).

Table 4 shows the mean CSA differences of the trained leg minus the untrained leg (T-UT). For all subjects, CSA (T-UT) after HRST (4.4 ± 0.7, 6.0 ± 0.7, 4.1 ± 0.6 cm^2) was significantly different from before HRST (0.5 ± 0.6, -0.1 ± 0.6, -0.5 ± 0.7 cm^2, $p < 0.05$) and after detraining (0.2 ± 0.6, 0.7 ± 0.6, 0.6 ± 0.6 cm^2, $p < 0.05$) for all three regions. Cross-sectional area (T-UT) was not significantly different when comparing any of the three regions before HRST versus after detraining. No significant differences existed between age groups at all three time points in all three regions. When groups were compared by age and gender, young men displayed significantly higher CSA (T-UT) than women in all three regions. Older men also displayed significantly higher CSA (T-UT) but only in the proximal region when compared to older women. There also was a significant gender x time interaction. Further analysis revealed that men had significantly higher CSA (T-UT) in all three regions (6.6 ± 1, 8.2 ± 1, 5.9 ± 0.8 cm^2) when compared to women (2.3 ± 1.0, 3.7 ± 1.0, 2.2 ± 0.9 cm^2, $p < 0.05$) after HRST.

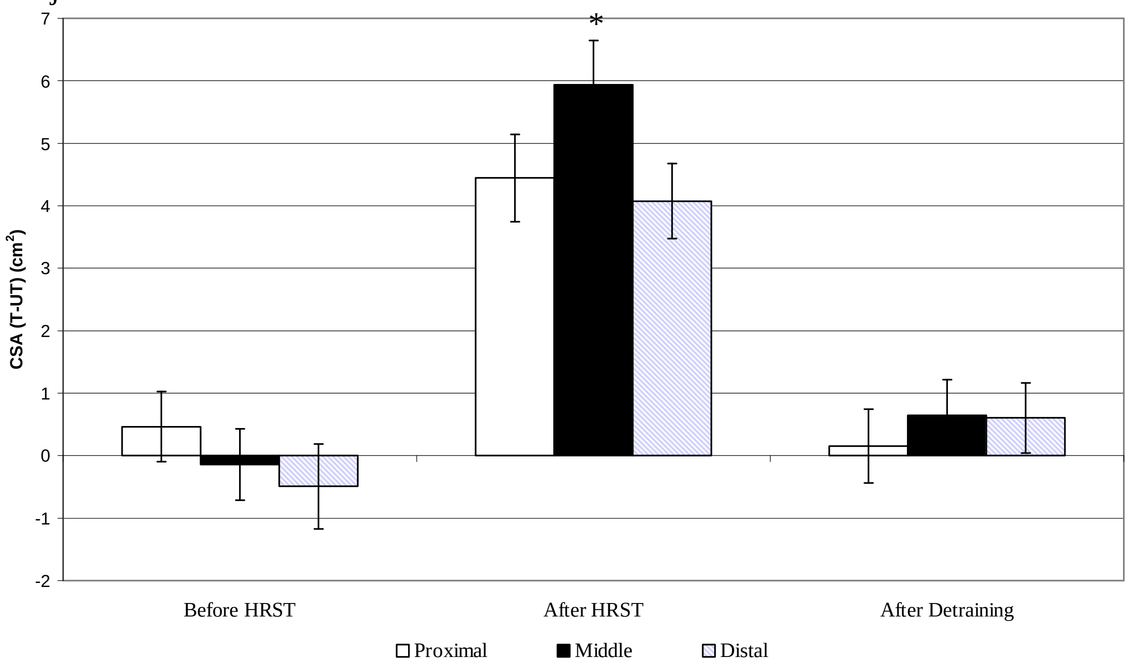
Table 4. Regional CSA Differences of the Quadriceps (T-UT)

Young Men (n=11)	Region	Before	After	Detrained
	1	0.1 ± 1.1	6.7 ± 1.4 *	2.8 ± 1.2
	2	0.4 ± 1.1	9.3 ± 1.4 *	2.4 ± 1.1
	3	-0.1 ± 1.3	7.8 ± 1.2 *	1.6 ± 1.1
Young Women (n=10)	**Region**	**Before**	**After**	**Detrained**
	1	0.2 ± 1.2	2.3 ± 1.5	-0.1 ± 1.2
	2	-0.8 ± 1.2	3.4 ± 1.5	-0.5 ± 1.2
	3	-1.3 ± 1.4	1.7 ± 1.2	-0.2 ± 1.2
Older Men (n=11)	**Region**	**Before**	**After**	**Detrained**
	1	0.4 ± 1.1	6.4 ± 1.4 †	-0.6 ± 1.2
	2	-0.1 ± 1.1	7.1 ± 1.4	0.4 ± 1.1
	3	0.2 ± 1.3	4 ± 1.2	1.2 ± 1.1
Older Women (n=11)	**Region**	**Before**	**After**	**Detrained**
	1	1.2 ± 1.1	2.4 ± 1.4	-1.4 ± 1.2
	2	-0.1 ± 1.1	4 ± 1.4	0.3 ± 1.1
	3	-0.8 ± 1.3	2.7 ± 1.2	-0.3 ± 1.1

Data are means of differences ± SED in cm^2. T-UT = CSA of the trained leg minus CSA of the untrained leg. Region 1 = proximal, 2 = middle, 3 = distal. Before = Before HRST, After = After HRST, Detrained = after 31 weeks of detraining. * Significantly different from young women at same region. † Significantly different from older women at region 1. ($P < 0.05$).

Figure 2 shows the mean changes in regional hypertrophy averaged across all four groups. The analysis of CSA (T-UT) indicated a significantly greater increase in the middle region (5.9 ± 0.7 cm^2) as opposed to the proximal (4.4 ± 0.7 cm^2) and distal region after HRST (4.1 ± 0.6 cm^2, $P < 0.0001$).

Figure 2. Changes in Regional CSA Differences of the Quadriceps Muscle of all Subjects



Data are means of differences ± SED in cm^2. * Significantly different vs. proximal and distal after HRST. ($P < 0.05$)

Discussion

The main purpose of this study was to examine the changes in muscle CSA in the three regions of the quadriceps group after nine weeks of unilateral HRST and 31 weeks of detraining in young and older men and women. It was hypothesized that the older subjects would show significantly greater losses in regional CSA (T-UT) than younger subjects after detraining. No prior studies have answered this question in regards to regional CSA, but one study has examined muscle volume changes. Specifically, Ivey *et al.* (44) examined muscle volume changes over a prolonged detraining period and found no significant differences between young and older subjects. The results of the present study indicated that no significant differences existed in quadriceps CSA (T-UT) loss for all three regions between young and older subjects indicating age was not a factor for the degree of regional CSA loss after cessation of resistive exercise training.

Overall, all four subject groups showed significant increases in quadriceps muscle strength of the trained leg after 9 weeks of HRST (27-35%), but not all were able to maintain those strength levels after 31 weeks of detraining as only young women (YW) maintained strength levels similar to those achieved after 9 weeks of HRST. Interestingly, all groups except young men (YM) maintained a 1RM (T-UT) significantly greater than baseline after 31 weeks of detraining. A reason for the YM not maintaining strength levels above their baseline values is mostly likely due to the high standard error associated with the YM's baseline 1RM (T-UT). Before the HRST program, there were no significant muscle strength differences between age groups ($p = 0.53$), after HRST, young subjects had significantly higher T-UT muscle strength than older subjects. At the conclusion of detraining, 1RM (T-UT) was not statistically significant between the two age groups ($p = 0.07$).

There have been a limited number of regional hypertrophy studies and only one study by Häkkinen *et al.* (31) included men and women, middle-aged (43-57 years) and elderly (64-73 years). Häkkinen *et al.* (31) showed a non-significant 3% and 7% increase in the distal region of the quadriceps as measured by ultrasound, in both elderly and middle-aged subjects, respectively, after a twice weekly, 24 week full body resistance training program with work loads ranging from 50-80% 1RM. In the current study, the distal region of the quadriceps in the trained leg increased by 14%, 7%, 7%, and 10% for YM, YW, older men (OM), and older women (OW) respectively in only nine weeks of high volume heavy resistance training. Clearly the HRST program was sufficient to produce significant increases in regional quadriceps CSA due to the heavy loads with each repetition at or near the subject's 1RM. (discuss reasons for differences in the train leg?)

Other regional hypertrophy studies utilized unilateral isotonic (36, 40, 41, 69) and isokinetic (72) resistive training programs but only tested YM (41, 69, 72),or YW (40). All studies found significant increases in CSA in one or more regions of the quadriceps measured through MRI in the trained limb after a resistance training stimulus. In YM, Narici *et al.* (72) demonstrated increases of 9% in CSA of the middle region of the quadriceps whereas Housh *et al.* (41) showed an 11% increase in CSA of the middle region of the quadriceps in YM. Both studies used isokinetic resistance training at the same speed (2.09 rad/sec) for approximately eight weeks. The only exception was that Housh *et al.* (41) used solely concentric contractions.

Despite this difference in contraction type, the results compare to the present study's findings of a 15% increase in the CSA of the middle region of YM. Another notable regional hypertrophy resistive exercise training study was completed in YW by Higbie *et al.* (40). After ten weeks of unilateral isokinetic resistance training, quadriceps CSA increased by 9%, 9%, and 5% and 6%, 6%, and 4% in the eccentric isokinetic group and concentric isokinetic group, respectively, for the proximal, middle, and distal regions of the quadriceps. These findings are similar to the relative increases in quadriceps CSA of the YW in the present study of 4%, 8%, and 7%. Older women (64 yrs) were studied after 24 weeks of a total body, low volume resistance exercise training program by Häkkinen *et al.* (36) and the women increased CSA significantly in all regions of the quadriceps from proximal to distal, with increases ranging from 6 to 11%. The older women in the current study increased regional CSA by 5%, 9%, 10% for the proximal middle, and distal regions.

The length of the resistance training interventions in the aforementioned studies (40, 41, 72) were six to ten weeks and percent increases in regional quadriceps CSA after resistance training were similar to those found in the present study. One notable exception was an extensive six month resistance training study by Narici *et al.* (69) which showed much higher increases in quadriceps CSA on the order of 18%, 13%, and 21% for the proximal, middle, and distal regions. Young men performed resistance training every other day for 24 weeks with loads of 80% of 1RM. The higher relative increases are expected due to the length of the resistive training program as well as a high frequency of sessions (every other day).

In the present study, when comparing YM and YW, the YM had significantly higher CSA (T-UT) differences in all three regions after HRST in the current study. This indicates that the trained leg increased to a greater extent in YM compared to YW. However, only the proximal region was significantly higher in OM compared to OW. A reason for this may be due to the fact that in terms of absolute increases in the trained leg, the proximal region increased by only 2.4 cm^2, whereas the middle and distal regions increased by 5.4 and 5.1 cm^2. This would compare to absolute increases in the trained leg of OM of 5.7, 5.1, and 3.6 cm^2. Examination of CSA (T-UT) between genders revealed that men had significantly higher CSA (T-UT) after HRST in all three regions compared to women. While gender influenced the magnitude of increase in regional CSA (T-UT) after HRST, CSA (T-UT) values were similar between age groups after HRST. Therefore the present results indicate that individuals both young and older can achieve similar increases in regional quadriceps CSA after resistance training.

There have only been two studies examining the regional CSA response of the quadriceps to detraining. Narici *et al.* (72) found a decrease of 4% in CSA after 40 days of detraining in the middle region of the quadriceps in YM. As expected, the increased detraining period in the current study resulted in a 9% decrease in the middle region of YM. When examining the subjects in the current investigation by age, young subjects decreased CSA by 8% and 7% in the middle and distal regions whereas older subjects showed a 9% and 8% decrease in CSA. Häkkinen *et al.* utilized a fairly similar detraining period of 24 weeks in the CSA of the distal region of the quadriceps and observed a 9% and 11% decrease in middle aged (37-44 years) and elderly (62-77 years) subjects, respectively (31). Analysis of CSA (T-UT) for all three regions showed that no region had a larger difference than any other. In terms of percent decreases in regional CSA, the current study's findings are similar to the results of Häkkinen but clearly larger than the decrease found by Narici *et al.* (72) due to the short 40 day detraining period, as 31 weeks invoked larger decreases in regional CSA. In the current study, no significant differences were detected in CSA (T-UT) between men and women or young and older groups in all three regions of the quadriceps after 31 weeks of detraining.

The present study is unique in that it is the first regional hypertrophy study to include young and older, men and women, while also using a unilateral, high volume, heavy resistance training stimulus. Due to the nature of the HRST program, the same relative resistance training stimulus was applied to the quadriceps muscle of all four subject groups. Also, the unilateral resistance training design allowed for inclusion an untrained leg that provided much greater control over outside variables during the nine weeks of unilateral training. No previous study assessing regional changes in skeletal muscle CSA has specifically utilized a control limb to compute CSA (T-UT). A control limb was not possible in the study by Häkkinen *et al.* (31) due to the nature of a full body resistance training program and Narici *et al.* (72) and Housh *et al*. (41) mentioned that while CSA was calculated on the untrained limb, no such data was reported in the paper. In the present study, the original hypotheses proposed that older subjects would lose significantly more CSA (T-UT) after 31 weeks of detraining and also that YM would lose significantly more muscle mass than YW with no significant differences occurring between OM and OW. Analysis of CSA (T-UT) after detraining revealed no significant differences between the three regions of YM versus YW as well as OM versus OW. Cross-sectional area (T-UT) was similar between genders and age groups for all three regions after detraining. Although it was hypothesized that older subjects would show significantly smaller CSA (T-UT) due to effects of age, this did not occur. Therefore the two major hypotheses involving detraining were not supported by the data.

The data in the current study was examined for regional CSA (T-UT) at three regions in the quadriceps (proximal, middle, and distal). Ivey *et al.* (44) published the original examination of the data, but summed all possible regions along the quadriceps to determine quadriceps muscle volume on both legs, as well as calculated a muscle volume (T-UT) variable. Both the current study and Ivey *et al.* (44) concluded that men and YM made significantly greater gains than women and YW, respectively, after HRST. Ivey *et al.* (44) also found that after HRST and after detraining, no significant differences occurred between young and older subjects. Examination of gender within age groups by Ivey *et al.* (44) revealed no significant differences between OM and OW after HRST for muscle volume (T-UT), whereas regional CSA (T-UT) analysis of the present study revealed that OM had significantly higher CSA (T-UT) in the proximal region only when compared to old women after HRST. After 31 weeks of detraining, Ivey *et al.* (44) found significant differences between YM and YW, OM and OW whereas the present study found no significant differences.

It has been demonstrated that men and women, young and older, can increase skeletal muscle CSA with resistance training (13, 18, 25, 32, 37, 75) and that hypertrophy of the quadriceps occurs in a regional manner such that individuals muscles hypertrophy to the greatest degree at points of maximal CSA. While the current study did not examine the individual muscles of the quadriceps, Narici *et al.* (72) confirmed this through assessment of the four individual muscles of the quadriceps and identified maximal CSA in the vastus intermedius (VI) at the middle region, vastus lateralis (VL) mid-way between the proximal and middle regions, vastus medialis (VM) at the distal region, and rectus femoris (RF) at the proximal region. After a resistance exercise training stimulus, Häkkinen *et al.* (36) showed that CSA of VL increased significantly in the proximal region whereas CSA of VM increased significantly in the distal region (36). In Häkkinen's analysis, significant increases occurred in regions of maximal CSA for VL and VM but not so for RF and VI.

It is clear that there is a difference in the degree of hypertrophy occurring across all regions of the quadriceps (36, 69, 72). Recently, investigators have utilized electromyography (EMG) (78) and MRI (1) to study muscle recruitment patterns of the individual muscles of the quadriceps based on the mode of exercise used (e.g. leg press, knee extension, etc.) (2) and joint angle (78). Knowledge of the specific recruitment and activation patterns of the quadriceps may further explain the regional hypertrophic response. This would be especially useful if different regions or particular muscles of the quadriceps are activated during functional activities such as rising from a chair or climbing stairs. It has been demonstrated that isometric maximal voluntary contractions at knee joint angles of 0°, 10°, 30°, 50°, 70°, and 90° flexion indicate increasing EMG activity of VM from 0 to 90° flexion , whereas this pattern did not occur in VL and RF (78). Pincivero *et al.* (78) also examined peak torque at these joint angles and calculated a muscle recruitment efficiency ratio of allometric-modeled average torque ($N{\cdot}m{\cdot}kg^{-n}$) which was normalized to values at 0º flexion to normalized EMG. Allometric torque uses a ratio of absolute torque and body mass and thus helps to control body mass as a covariate. Recruitment efficiency improved significantly more for VM from 70º to 90º flexion compared to RF and VL. The authors suggested that the improved recruitment efficiency suggests that VM may provide greater knee-extensor torque than the RF and VL at 90º flexion. Because standing from a seated position places the legs initially in 90° flexion, there may be added benefit to a larger CSA and/or greater neural activation in VM in the distal region. Based on the VM having significantly higher normalized EMG data at 90º (78) compared to RF and VL, and that it reaches maximal CSA in the distal region (36, 72), identification of resistive exercises than can produce significant increases in the distal region of the quadriceps, specifically VM, may provide a greater functional benefit. However, other investigators have not found increasing EMG activity of VM from 10 to 90° of knee flexion (99) thus weakening the argument that VM may contribute greater torque generating potential when the knee is in 90° flexion, such as when rising from a chair.

Further evidence has recently been generated to describe the recruitment pattern in neuromuscular compartments within the RF muscle. While previous investigators have found no significant differences in quadriceps EMG activity between leg press and knee extension (2), Akima *et al.* (1) showed that the neural recruitment of the rectus femoris during isokinetic knee extension is different between the proximal and distal portions of the neuromuscular compartments of RF. However, during isotonic knee extension, this finding did not occur (Akima, personal communication). If there are different recruitment patterns with isokinetic exercise, there may possibly be a difference in the hypertrophic response to a resistive training stimulus based on the type of contractions performed.

All subject groups showed significant increases in CSA (T-UT) in all three regions (proximal, middle, and distal) of the quadriceps after HRST in the present study. Young men had significantly greater absolute CSA (T-UT) at all three regions compared to YW after HRST whereas OM had significantly greater absolute CSA (T-UT) only at the proximal region when compared to OW. Both age groups had similar CSA (T-UT) values after HRST and after 31 weeks of detraining, thus indicating that age per se did not influence the amount of gain or loss in regional CSA of the quadriceps muscle due to inactivity.

Chapter 5: Summary, Conclusions, and Recommendations

Summary

The purpose of this study was to examine the effects of nine weeks of HRST and 31 weeks of detraining on the three regions of the quadriceps in young and older men and women. It was hypothesized that young men would show higher CSA (T-UT) values than young women and that older men would show similar CSA (T-UT) values compared to older women after nine weeks of unilateral HRST. In reference to 31 weeks of detraining, it was hypothesized that older subjects would have significantly smaller CSA (T-UT) compared to young subjects, older men and women would show similar losses, and that young men would show greater CSA (T-UT) loss after detraining. It was also hypothesized that the middle region would have the largest increase in CSA (T-UT) compared to the proximal and distal regions. Analysis of the data revealed that all hypotheses were supported with the exception of the following two hypotheses. First, after 31 weeks of detraining, no significant differences occurred between age groups. And second, young men did not show greater losses than young women after 31 weeks of detraining.

Subjects for this study included healthy young men (n=11) and women (n=10), respectively, between the ages of 19 and 29 years and healthy older men (n=11) and women (n=11), between the ages of 64 and 73 years. All subjects were sedentary, non-smokers, and free from any type of cardiovascular, metabolic, or musculoskeletal disorders. Subjects underwent body composition (DEXA), maximal oxygen consumption testing, 1RM strength testing, and bilateral MRI scans to measure quadriceps muscle CSA by region. The high-volume, heavy resistance strength training (HRST) program consisted of five sets of 55 repetitions performed three days/wk for nine weeks. Unilateral knee extension exercise was completed for the dominant leg on the Keiser K-3000 knee extension machine and resistance was adjusted accordingly each week throughout the program to accommodate for strength gains. Cross sectional images of the quadriceps muscle group were identified in three regions (proximal, middle, and distal), outlined with a trackball, and measured in cm^2 using NIH Image version 1.6 software for the before HRST, after HRST, and after 31 weeks of detraining time points.

Muscle strength was significantly increased in all four subject groups after HRST (27-35%) and was maintained after detraining with the exception of older women. In the untrained leg, modest but significant increases in 1RM strength (10-11%) occurred after HRST. After detraining, 1RM strength of the untrained leg was significantly reduced in only older men when compared to 1RM strength achieved after HRST and only young men maintained 1RM strength values that were significantly higher than before HRST.

After nine weeks of HRST, CSA (T-UT) increased significantly in all three regions of the quadriceps with the greatest increase occurring in the middle region. Young men made significantly greater gains in CSA (T-UT) in all three regions compared to young women. Older men also made significantly greater gain in CSA (T-UT) than older women, but only in the proximal region. Overall, all groups made similar relative increases in the CSA of the trained leg. Thirty-one weeks of detraining resulted in the CSA of the trained leg returning to values before HRST with the exception of the proximal and middle regions in young men which were significantly higher than values before HRST. When adjusting for the control leg, CSA (T-UT) after detraining was not significantly different between young men versus young women and older men versus older women. Also, age did not influence the amount of CSA (T-UT) lost in any of the three regions of the quadriceps after detraining.

Conclusions

In conclusion, this study has determined that a high volume, heavy resistance strength training program can induce significant gains in regional hypertrophy of the quadriceps, with the largest increases occurring in the middle region. Young men had significantly higher CSA (T-UT) in all three regions when compared to young women after HRST. No differences existed between young men and women after detraining. For older men and women, CSA (T-UT) of the proximal region was significantly higher in older men after HRST. Cessation of resistance training for 31 weeks resulted similar CSA (T-UT) values when comparing young men and women as well as older men and women. Age did not influence the magnitude of the increase in regional CSA (T-UT) after HRST nor did it influence the degree of loss after 31 weeks of detraining.

Recommendations

The following recommendations are suggested for future studies:

1. A resistance training study that identifies if different contraction types, isokinetic (eccentric, concentric, both) and isotonic induce different regional hypertrophic responses in the quadriceps.

2. Analysis of subjects with a high incidence of falls to determine possible differences in their regional CSA of the quadriceps versus matched subjects with no incidences of falls.

Appendix I: Raw Data

Subject Characteristics, Women

Subject	Group	Age	Height	Pre-Weight	Post-Weight	Pre Fat %	Post Fat %	VO2max
1	4	26	172.72	72.1	74.0	30.7	31.5	32.03
2	4	26	170.18	63.0	62.8	34.4	33.0	15.95
3	4	25	170.18	74.8	76.7	35.9	36.2	35.90
4	4	28	165.1	49.6	49.4	24.9	26.4	35.40
5	4	26	172.72	68.9	69.0	32.6	33.3	30.80
6	4	27	157.08	55.3	59.3	22.8	24.2	33.88
7	4	26	167.64	59.3	59.5	29.5	30.9	32.54
8	4	28	175.26	67.3	67.2	29.0	28.2	37.70
9	4	25	160.02	45.7	45.0	23.3	25.4	42.80
10	4	23	165.1	83.0	81.2	44.9	41.9	29.00
11	2	67	165.1	79.1	78.5	43.4	42.9	15.95
12	2	64	154.94	69.4	67.9	43.4	43.5	26.03
13	2	64	165.1	58.0	60.7	26.1	27.4	17.50
14	2	66	165.1	61.0	61.1	41.0	38.7	21.69
15	2	72	160.02	52.5	53.0	28.3	26.6	24.50
16	2	65	160.02	74.4	71.7	42.0	40.8	16.90
17	2	71	154.94	65.6	65.7	41.8	41.8	19.62
18	2	66	162.56	69.2	74.7	35.6	38.7	18.10
19	2	70	149.86	66.3	64.1	43.1	44.2	18.70
20	2	73	162.56	66.9	66.1	37.5	35.9	21.40
21	2	70	175.26	83.0	81.4	42.9	39.8	18.54

Subject Characteristics, Men

Subject	Group	Age	Height	Pre-Weight	Post-Weight	Pre Fat %	Post Fat %	VO2max
22	1	69	175.26	88.0	89.8	35.9	34.3	21.01
23	1	73	177.8	80.5	83.0	25.3	25.3	27.60
24	1	71	180.34	78.5	.	28.8	.	23.06
25	1	66	172.72	82.5	81.2	32.1	30.2	24.35
26	1	72	177.8	74.5	75.9	29.4	29.4	20.14
27	1	68	167.64	72.7	73.4	22.8	22.3	24.59
28	1	65	177.8	96.5	97.2	34.8	35.8	32.20
29	1	71	170.18	65.5	67.1	22.1	23.4	19.04
30	1	65	177.8	80.0	79.5	30.6	30.6	29.30
31	1	67	165.1	79.6	80.1	26.5	27.3	18.74
32	1	72	175.26	83.4	82.9	31.1	30.1	17.04
33	3	27	165.1	65.2	65.7	25.1	24.8	39.50
34	3	26	170.18	67.8	68.3	19.3	19.9	41.70
35	3	29	175.26	65.2	66.7	20.0	19.2	38.50
36	3	29	195.58	105.4	107.3	30.3	30.1	39.10
37	3	22	185.42	75.7	77.8	13.1	15.0	47.90
38	3	27	167.64	59.2	59.4	14.2	13.4	47.70
39	3	19	185.42	106.0	106.4	36.5	35.7	46.30
40	3	26	180.34	105.7	106.0	28.1	29.6	41.60
41	3	24	182.88	75.7	75.7	19.3	19.3	47.00
42	3	24	175.26	76.2	78.2	12.4	14.7	47.50
43	3	23	187.96	102.9	103.8	33.2	34.2	41.90

1RM Strength, Women
(kilograms, T = Trained leg, UT = Untrained leg)

Subject	Group	T Before	T After	T Detrained	UT Before	UT After	UT Detrained
1	4	65.45	90.91	90.91	63.64	73.64	81.82
2	4	56.82	81.82	77.27	55.00	63.64	63.64
3	4	90.91	115.91	109.09	84.09	90.91	93.18
4	4	38.64	54.55	47.73	36.36	43.18	40.91
5	4	75.00	95.45	95.45	72.73	81.82	77.27
6	4	56.82	72.73	.	68.18	72.73	.
7	4	58.64	79.55	79.55	53.64	61.36	61.36
8	4	59.09	79.55	63.64	59.09	59.09	59.09
9	4	47.73	77.27	63.64	52.27	65.91	59.09
10	4	70.45	86.36	77.27	81.82	86.36	70.45
11	2	47.73	59.09	52.27	45.45	47.73	47.73
12	2	39.55	45.45	38.64	41.36	42.27	38.64
13	2	47.73	70.45	63.64	47.73	56.82	61.36
14	2	34.09	46.36	43.18	35.45	38.64	34.09
15	2	38.64	47.73	40.91	38.64	40.91	38.64
16	2	47.73	54.55	40.91	47.73	50.00	31.82
17	2	50.00	63.64	56.82	45.45	52.27	54.55
18	2	31.82	45.45	34.09	18.18	27.27	20.45
19	2	43.18	45.45	47.73	52.27	56.82	50.00
20	2	38.64	56.82	50.00	43.18	45.45	50.00
21	2	47.73	65.91	50.00	47.73	52.27	45.45

1RM Strength, Men
(kilograms, T = Trained leg, UT = Untrained leg)

Subject	Group	T Before	T After	T Detrained	UT Before	UT After	UT Detrained
22	1	75.00	97.73	77.27	73.64	86.36	70.45
23	1	68.18	81.82	68.18	56.82	59.09	56.82
24	1	70.45	84.09	75.00	72.73	75.00	75.00
25	1	90.91	106.82	97.73	95.45	97.73	93.18
26	1	79.09	102.27	102.27	76.36	92.27	100.00
27	1	69.55	93.18	86.36	78.64	90.91	86.36
28	1	65.91	104.55	68.18	65.91	88.64	63.64
29	1	72.73	90.91	86.36	68.18	70.45	75.00
30	1	86.36	109.09	86.36	86.36	90.91	79.55
31	1	68.18	79.55	68.18	77.27	81.82	72.73
32	1	79.55	95.45	84.09	70.45	75.00	70.45
33	3	88.64	97.73	100.00	90.91	90.91	90.91
34	3	90.91	125.00	118.18	86.36	102.27	115.91
35	3	88.64	134.09	106.82	81.82	90.91	81.82
36	3	56.82	79.55	.	115.91	131.82	.
37	3	90.91	120.45	111.36	90.91	100.00	95.45
38	3	72.73	84.09	77.27	79.55	90.91	84.09
39	3	51.14	73.86	56.82	53.98	56.82	56.82
40	3	68.18	79.55	68.18	68.18	62.50	56.82
41	3	109.09	122.73	120.45	106.82	111.36	109.09
42	3	62.50	79.55	85.23	62.50	68.18	82.39
43	3	93.18	134.09	127.27	97.73	111.36	118.18

CSA in cm^2
Proximal region, Women

		Before HRST		After HRST		After Detraining	
Group	Subject	T	UT	T	UT	T	UT
4	1	51.38	50.62	53.71	51.57	47.42	48.48
4	2	45.59	44.4	48.41	42.8	42.5	40.02
4	3	42.23	41.01	44.67	36.77	43.23	43.22
4	4	28.69	28.11	30.44	31.05	25.9	25.71
4	5	61.38	60.92	63.49	61.28	62.37	61.24
4	6	33.61	39.67	34.87	40.47	34.32	42.04
4	7	42.11	37.38	45.7	38.95	44.1	38.72
4	8	39.18	39.33	41.66	40.66	40.17	42.65
4	9	33.8	32.65	35.02	32.65	33.45	33.15
4	10	44.86	46.69	46.46	45.32	40.86	40.51
2	11	37.61	33.87	40.7	32.65	34.71	34.48
2	12	36.31	35.52	37.73	33.68	34.33	44.75
2	13	43.35	38.87	47.57	51.97	39.22	38.22
2	14	27.89	29.17	28.8	29.64	28	28.69
2	15	34.71	32.35	36.66	31.85	33.15	33.53
2	16	42.11	40.25	45.74	38.72	35.55	33.19
2	17	37.57	34.41	39.49	33.61	37.16	36.58
2	18	26.51	27.66	27.31	29.51	26.22	27.17
2	19	33.07	32.27	35.59	35.51	33.43	34.39
2	20	29.91	32.2	32.81	34.33	29.87	29.97
2	21	35.02	34.22	37.65	32.54	34.33	40.36

CSA in cm^2
Proximal region, Men

		Before HRST		After HRST		After Detraining	
Group	Subject	T	UT	T	UT	T	UT
1	22	56.04	56.08	68.44	56.19	58.4	54.89
1	23	49.9	49.78	51.57	49.78	51.54	51.57
1	24	45.78	45.55	54.09	46.5	47.23	48.9
1	25	54.66	51.23	62.87	52.57	55.31	54.32
1	26	48.75	53.52	58.36	54.59	51.73	54.09
1	27	50.13	55.73	61.72	54.7	49.74	55.27
1	28	59.51	57.56	58.14	53.75	57.07	57.41
1	29	51.04	46.35	58.14	45.05	51	48.83
1	30	57.98	53.37	61.49	55.62	55.85	57.6
1	31	52.64	56.11	54.28	57.68	53.71	55.85
1	32	57.03	54.24	56.65	49.1	54.47	54.17
3	33	58.06	58.48	64.74	57.26	65.12	62.03
3	34	58.33	63.21	65.19	61.99	65.08	64.35
3	35	49.25	49.25	58.63	48.98	48.98	46.81
3	36	84.3	88.35	87.59	89.76	84.46	85.33
3	37	65.92	58.94	72.56	56.34	69.47	58.9
3	38	49.74	52.53	55.58	52.53	49.97	49.9
3	39	71.11	69.27	74.27	68.63	70.69	68.59
3	40	92.24	90.68	91.86	83.16	89.49	86.14
3	41	60.92	59.43	63.78	61.07	72.67	67.48
3	42	84.04	79.65	93.77	79.19	85.18	80.11
3	43	64.74	67.9	77.29	72.29	70.8	71.75

CSA in cm^2
Middle region, Women

		Before HRST		After HRST		After Detraining	
Group	Subject	T	UT	T	UT	T	UT
4	1	67.89	67.83	69.82	64.77	64.74	65.38
4	2	61.68	61.23	65.65	58.78	57.5	58
4	3	64.74	62.6	69.96	65.31	69.39	65.04
4	4	47.42	46.92	49.32	47.11	44.98	45
4	5	74.24	69.96	80.38	69.78	70.65	69.05
4	6	46.12	51.23	50.74	55.69	47.15	53.1
4	7	58.02	57.21	65.8	56.88	57.79	56.19
4	8	56.92	59.89	58.75	59.05	57.37	56.12
4	9	42.38	46.92	48.63	47.84	43.72	46.54
4	10	59.28	62.58	65.57	65.27	58.9	63.13
2	11	44.33	44.21	49.17	43.95	42.92	41.05
2	12	44.82	49.82	51.65	48.1	43.53	45.89
2	13	61.38	58.78	67.6	69.43	60.5	65.02
2	14	36.35	38.15	40.21	39.75	36.39	37.51
2	15	42.99	42.08	47.34	41.28	41.58	41.08
2	16	55.69	52.19	58.44	49.21	52.38	49.21
2	17	49.51	47.23	54.59	47.72	49.51	46.69
2	18	32.32	31.81	34.71	37.21	32.19	32.29
2	19	39.46	42.23	50.77	49.02	41.01	41.97
2	20	44.14	46.96	52.22	45.66	45.01	44.56
2	21	45.97	44.63	50.39	42.04	45.36	41.69

CSA in cm^2
Middle region, Men

		Before HRST		After HRST		After Detraining	
Group	Subject	T	UT	T	UT	T	UT
1	22	62.64	60.27	65.23	58.52	63.63	57.33
1	23	60.12	58.36	68.63	57.91	65.5	61.42
1	24	59.55	64.01	68.89	60.39	59.62	66.57
1	25	62.64	59.13	69.58	59.59	63.74	60.69
1	26	62.71	65.19	69.54	57.98	63.17	66.26
1	27	59.32	65.57	66.83	64.93	61.04	61.8
1	28	73.66	71.18	75.45	69.47	72.75	71.79
1	29	60.2	61.11	65	58.9	54.44	58.36
1	30	66.57	64.24	72.59	63.74	68.32	66.64
1	31	61.04	64.51	61.11	64.32	65.42	67.98
1	32	70.04	65.84	72.21	61.68	71.72	65.61
3	33	68.97	75.3	79.38	74.27	73.09	74.5
3	34	73.97	77.74	80.57	78.7	80.15	86.21
3	35	60.31	56.27	69.62	59.85	61.61	59.51
3	36	109.29	111.16	116.92	108.99	110.51	113.26
3	37	82.86	72.25	94.76	73.39	88.73	75.19
3	38	61.23	68.66	72.75	67.94	63.13	66.83
3	39	92.16	88.12	92.66	85.49	91.59	85.72
3	40	111.01	107	117.72	101.17	111.5	105.71
3	41	77.02	74.12	79.08	73.85	84.15	80.64
3	42	104.22	99.79	108.34	95.71	106.7	99.72
3	43	79.96	86.4	92.89	83.08	90.45	88.23

CSA in cm^2
Distal region, Women

		Before HRST		After HRST		After Detraining	
Group	Subject	T	UT	T	UT	T	UT
4	1	53.06	51.99	60.5	55.96	55.01	54.63
4	2	49.36	45.55	56.15	51.57	49.67	47.8
4	3	50.96	51.12	55.77	55.85	54.82	55.24
4	4	44.82	42.04	44.82	40.55	42.99	38.91
4	5	59.59	58.75	61.53	59.01	59.81	59
4	6	40.89	44.82	44.33	47.34	40.32	45.81
4	7	41.77	40.77	48.6	42.42	41.5	38.18
4	8	48.86	52.87	52.6	52.83	51.16	51.04
4	9	30.98	34.07	38.15	36.24	33.87	35.29
4	10	51.8	62.68	56.23	59.43	54.78	59.55
2	11	41.05	36.54	45.97	37.57	36.85	31.81
2	12	37.57	39.52	44.93	42.19	36.66	37.72
2	13	48.79	45.32	52.35	56.76	49.63	54.64
2	14	28.27	30.91	35.91	32.81	30.94	32.2
2	15	35.02	32.69	36.28	34.6	35.55	35.06
2	16	43.6	40.7	45.09	37.99	35.48	33.57
2	17	40.08	40.68	47.3	42.46	42.17	41.64
2	18	26.78	33.62	28.27	32.95	26.89	28.2
2	19	34.48	42.61	43.03	42.53	35.23	37.03
2	20	36.67	40.76	45.28	41.5	38.33	40.7
2	21	43.79	41.54	47.57	40.66	38.61	36.93

CSA in cm^2
Distal region, Men

		Before HRST		After HRST		After Detraining	
Group	Subject	T	UT	T	UT	T	UT
1	22	45.55	45.32	47.19	43.64	46.12	43.72
1	23	46.01	44.63	54.51	46.84	43.68	36.93
1	24	51.38	52.49	50.24	44.56	49.06	49.51
1	25	49.71	49.1	49.1	46.35	50.47	49.67
1	26	47.49	49.13	52.03	44.36	49.29	48.29
1	27	45.81	47.68	49.1	48.29	45.93	47.26
1	28	56.27	55.92	62.48	55.35	53.86	54.93
1	29	38.03	38.8	45.59	45.89	41.77	43.41
1	30	49.06	51.54	56.42	52.26	51.69	52.91
1	31	43.75	49.51	46.04	48.94	48.29	48.45
1	32	56.08	43.14	56	47.91	57.45	48.6
3	33	52.83	59.59	55.31	53.33	45.51	54.28
3	34	59.47	62.18	65.42	62.94	66.38	69.2
3	35	39.52	40.09	50.24	43.56	43.22	38.72
3	36	90.56	93.38	94.41	89.53	93.12	94.49
3	37	60.88	56.84	74.54	57.75	68.32	58.06
3	38	55.39	59.66	56.19	53.41	51.61	53.37
3	39	80.38	74.42	78.66	70.8	72.29	71.68
3	40	81.75	75.45	94.15	80.49	84.3	76.41
3	41	60.77	59.28	64.01	58.06	66.76	66.99
3	42	78.93	75.91	88.65	75.99	81.1	74.08
3	43	60.2	64.81	70	59.93	67.56	65.38

MRI Raw Data

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
71358	17	56.04	56.08	87810	18	68.44	56.19
	26	62.64	60.27		26	65.23	58.52
	34	45.55	45.32		34	47.19	43.64
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
13013	15	49.9	49.78	25376	15	51.57	49.78
	24	60.12	58.36		23	68.63	57.91
	32	46.01	44.63		31	54.51	46.84
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
85912	20	45.78	45.55	59343	16	54.09	46.5
	29	59.55	64.01		25	68.89	60.39
	38	51.38	52.49		34	50.24	44.56
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
39817	14	54.66	51.23	57869	17	62.87	52.57
	23	62.64	59.13		25	69.58	59.59
	32	49.71	49.1		33	49.1	46.35
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
55510	14	48.75	53.52	8585	15	58.36	54.59
	23	62.71	65.19		23	69.54	57.98
	31	47.49	49.13		31	52.03	44.36
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
1715	18	50.13	55.73	83949	19	61.72	54.7
	27	59.32	65.57		27	66.83	64.93
	35	45.81	47.68		35	49.1	48.29
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
47453	16	59.51	57.56	49018	15	58.14	53.75
	25	73.66	71.18		24	75.45	69.47
	33	56.27	55.92		32	62.48	55.35
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
59440	18	51.04	46.35	93923	18	58.14	45.05
	26	60.2	61.11		26	65	58.9
	34	38.03	38.8		34	45.59	45.89

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
55494	17	57.98	53.37	50205	18	61.49	55.62
	26	66.57	64.24		27	72.59	63.74
	35	49.06	51.54		36	56.42	52.26
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
60307	18	52.64	56.11	90334	19	54.28	57.68
	26	61.04	64.51		27	61.11	64.32
	34	43.75	49.51		35	46.04	48.94
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
79192	21	57.03	54.24	49971	16	56.65	49.1
	29	70.04	65.84		25	72.21	61.68
	37	56.08	43.14		33	56	47.91
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
27326	17	58.06	58.48	39484	20	64.74	57.26
	25	68.97	75.3		28	79.38	74.27
	32	52.83	59.59		36	55.31	53.33
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
61076	17	58.33	63.21	76357	17	65.19	61.99
	25	73.97	77.74		25	80.57	78.7
	33	59.47	62.18		33	65.42	62.94
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
77611	18	49.25	49.25	20804	17	58.63	48.98
	26	60.31	56.27		25	69.62	59.85
	34	39.52	40.09		33	50.24	43.56
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
35657	15	84.3	88.35	51860	10	87.59	89.76
	25	109.29	111.16		20	116.92	108.99
	34	90.56	93.38		29	94.41	89.53
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
88701	16	65.92	58.94	68678	17	72.56	56.34
	25	82.86	72.25		26	94.76	73.39
	34	60.88	56.84		35	74.54	57.75

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
15284	16	49.74	52.53	4047	18	55.58	52.53
	24	61.23	68.66		26	72.75	67.94
	31	55.39	59.66		34	56.19	53.41
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
39146	20	71.11	69.27	91259	17	74.27	68.63
	29	92.16	88.12		26	92.66	85.49
	38	80.38	74.42		35	78.66	70.8
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
64964	18	92.24	90.68	24378	18	91.86	83.16
	26	111.01	107		26	117.72	101.17
	34	81.75	75.45		34	94.15	80.49
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
42582	16	60.92	59.43	34522	15	63.78	61.07
	25	77.02	74.12		24	79.08	73.85
	34	60.77	59.28		33	64.01	58.06
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
61363	17	84.04	79.65	95852	18	93.77	79.19
	25	104.22	99.79		26	108.34	95.71
	33	78.93	75.91		34	88.65	75.99
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
28367	17	64.74	67.9	29865	15	77.29	72.29
	26	79.96	86.4		24	92.89	83.08
	34	60.2	64.81		32	70	59.93
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
500	17	40.7	32.65	40382	16	48.41	42.8
	24	49.17	43.95		24	65.65	58.78
	32	45.97	37.57		32	56.15	51.57
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
33573	17	37.73	33.68	73940	16	44.67	36.77
	24	51.65	48.1		25	69.96	65.31
	31	44.93	42.19		33	55.77	55.85

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
43022	20	47.57	51.97	25382	15	30.44	31.05
	28	67.6	69.43		23	49.32	47.11
	36	52.35	56.76		31	44.82	40.55

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
30118	16	28.8	29.64	16501	16	63.49	61.28
	23	40.21	39.75		24	80.38	69.78
	31	35.91	32.81		32	61.53	59.01

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
39414	18	36.66	31.85	38398	16	34.87	40.47
	26	47.34	41.28		24	50.74	55.69
	34	36.28	34.6		32	44.33	47.34

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
13315	16	45.74	38.72	42118	15	45.7	38.95
	23	58.44	49.21		23	65.8	56.88
	31	45.09	37.99		31	48.6	42.42

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
64985	16	39.49	33.61	23783	16	41.66	40.66
	23	54.59	47.72		24	58.75	59.05
	30	47.3	42.46		32	52.6	52.83

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
82683	20	27.31	29.51	61787	16	35.02	32.65
	27	34.71	37.21		23	48.63	47.84
	35	28.27	32.95		31	38.15	36.24

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
26920	18	58.4	54.89	46281	16	37.61	33.87
	27	63.63	57.33		23	44.33	44.21
	35	46.12	43.72		31	41.05	36.54

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
80473	20	51.54	51.57	59248	20	36.31	35.52
	29	65.5	61.42		27	44.82	49.82
	37	43.68	36.93		34	37.57	39.52

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
24796	18	47.23	48.9	64531	20	43.35	38.87
	27	59.62	66.57		28	61.38	58.78
	36	49.06	49.51		36	48.79	45.32
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
35062	16	55.31	54.32	43998	16	27.89	29.17
	24	63.74	60.69		23	36.35	38.15
	32	50.47	49.67		31	28.27	30.91
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
63725	17	51.73	54.09	16651	16	34.71	32.35
	26	63.17	66.26		23	42.99	42.08
	34	49.29	48.29		31	35.02	32.69
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
85793	17	49.74	55.27	19901	16	42.11	40.25
	26	61.04	61.8		24	55.69	52.19
	34	45.93	47.26		32	43.6	40.7
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
89281	19	57.07	57.41	53071	17	37.57	34.41
	28	72.75	71.79		24	49.51	47.23
	36	53.86	54.93		31	40.08	40.68
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
63112	17	51	48.83	45640	15	26.51	27.66
	25	54.44	58.36		23	32.32	31.81
	32	41.77	43.41		30	26.78	33.62
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
26493	14	55.85	57.6	18442	21	33.07	32.27
	23	68.32	66.64		29	39.46	42.23
	32	51.69	52.91		35	34.48	42.61
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
93129	19	53.71	55.85	39689	18	29.91	32.2
	27	65.42	67.98		26	44.14	46.96
	35	48.29	48.45		34	36.67	40.76

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
45268	16	54.47	54.17	26624	17	35.02	34.22
	25	71.72	65.61		25	45.97	44.63
	33	57.45	48.6		33	43.79	41.54

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
29944	20	65.12	62.03	64027	15	51.38	50.62
	27	73.09	74.5		23	67.89	67.83
	35	45.51	54.28		31	53.06	51.99

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
8374	15	65.08	64.35	55815	20	45.59	44.4
	23	80.15	86.21		28	61.68	61.23
	31	66.38	69.2		36	49.36	45.55

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
8164	17	48.98	46.81	50972	14	42.23	41.01
	26	61.61	59.51		23	64.74	62.6
	34	43.22	38.72		31	50.96	51.12

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
67528	16	84.46	85.33	48002	17	28.69	28.11
	26	110.51	113.26		25	47.42	46.92
	35	93.12	94.49		33	44.82	42.04

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
54591	15	69.47	58.9	59117	16	61.38	60.92
	24	88.73	75.19		24	74.24	69.96
	33	68.32	58.06		32	59.59	58.75

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
61839	18	49.97	49.9	49989	15	33.61	39.67
	26	63.13	66.83		23	46.12	51.23
	34	51.61	53.37		31	40.89	44.82

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
10077	17	70.69	68.59	57289	14	42.11	37.38
	26	91.59	85.72		22	58.02	57.21
	35	72.29	71.68		30	41.77	40.77

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
33149	19	89.49	86.14	9830	15	39.18	39.33
	27	111.5	105.71		23	56.92	59.89
	35	84.3	76.41		31	48.86	52.87
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
78029	14	72.67	67.48	73402	17	33.8	32.65
	23	84.15	80.64		24	42.38	46.92
	31	66.76	66.99		33	30.98	34.07
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
55647	18	85.18	80.11	99901	19	44.86	46.69
	27	106.7	99.72		26	59.28	62.58
	35	81.1	74.08		33	51.8	62.68
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
94033	14	70.8	71.75	36298	17	62.37	61.24
	23	90.45	88.23		25	70.65	69.05
	32	67.56	65.38		33	59.81	59
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
72844	14	28	28.69	64427	16	34.32	42.04
	22	36.39	37.51		24	47.15	53.1
	30	30.94	32.2		32	40.32	45.81
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
52092	17	33.15	33.53	26053	15	44.1	38.72
	24	41.58	41.08		23	57.79	56.19
	31	35.55	35.06		31	41.5	38.18
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
86141	17	35.55	33.19	1706	17	40.17	42.65
	25	52.38	49.21		24	57.37	56.12
	33	35.48	33.57		31	51.16	51.04
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
2850	18	37.16	36.58	23398	17	33.45	33.15
	26	49.51	46.69		24	43.72	46.54
	34	42.17	41.64		32	33.87	35.29

ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
22443	19	26.22	27.17	80696	15	40.86	40.51
	27	32.19	32.29		23	58.9	63.13
	34	26.89	28.2		31	54.78	59.55
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
13346	14	33.43	34.39	12143	16	34.71	34.48
	21	41.01	41.97		24	42.92	41.05
	28	35.23	37.03		32	36.85	31.81
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
94909	15	29.87	29.97	37836	22	34.33	44.75
	23	45.01	44.56		28	43.53	45.89
	31	38.33	40.7		33	36.66	37.72
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
45786	15	34.33	40.36	84636	14	39.22	38.22
	22	45.36	41.69		22	60.5	65.02
	29	38.61	36.93		30	49.63	54.64
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
99346	17	35.59	35.51	80791	15	46.46	45.32
	24	50.77	49.02		23	65.57	65.27
	31	43.03	42.53		31	56.23	59.43
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
33033	19	32.81	34.33	49501	14	47.42	48.48
	27	52.22	45.66		22	64.74	65.38
	35	45.28	41.5		31	55.01	54.63
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
26877	15	37.65	32.54	1581	15	42.5	40.02
	23	50.39	42.04		24	57.5	58
	32	47.57	40.66		32	49.67	47.8
ID #	slice #	T. LEG	UT. LEG	ID #	slice #	T. LEG	UT. LEG
31800	16	53.71	51.57	86745	15	43.23	43.22
	24	69.82	64.77		24	69.39	65.04
	32	60.5	55.96		32	54.82	55.24

ID #	slice #	T. LEG	UT. LEG
54832	16	25.9	25.71
	24	44.98	45
	32	42.99	38.91

Appendix II: Statistics

SAS Statiscal procedure for CSA (T-UT) as the dependent variable

```
proc mixed data=master covtest;
class gender age subject period region;
model diff = gender age gender*age
        region    region*age region*gender         region*age*gender
        period    period*age period*gender period*region period*age*gender
        region*gender*period region*age*period
        gender*age*period*region / DDFM=KR outp=resids;
random subject(gender age) region*subject(gender age);
lsmeans     gender age gender*age
        region    region*age region*gender         region*age*gender
        period    period*age period*gender period*region period*age*gender
        region*gender*period region*age*period
        gender*age*period*region /pdiff;
repeated region period / subject=subject type=UN@CS r rcorr group=period;
ods listing exclude lsmeans;
ods output lsmeans=lsmeans;
ods listing exclude diffs;
ods output diffs=pdiffs;
run;quit;
```

Type 3 Tests of Fixed Effects for CSA (T-UT)

Effect	Num DF	Den DF	F Value	Pr > F
GENDER	1	41.8	4.59	0.038
AGE	1	41.8	0.25	0.6165
GENDER*AGE	1	41.8	0.76	0.3876
REGION	2	72	1.85	0.1641
AGE*REGION	2	72	0.03	0.9706
GENDER*REGION	2	72	0.08	0.9202
GENDER*AGE*REGION	2	72	0.23	0.7991
PERIOD	2	43.2	66.87	<.0001
AGE*PERIOD	2	43.2	2.54	0.0904
GENDER*PERIOD	2	43.2	8.16	0.001
PERIOD*REGION	4	52.8	7.39	<.0001
GENDER*AGE*PERIOD	2	43.2	0.61	0.5498
GENDER*PERIOD*REGION	4	52.8	0.98	0.4277
AGE*PERIOD*REGION	4	52.8	2.05	0.1005
GEND*AGE*PERIO*REGIO	4	52.8	2.23	0.0784

Tests of Specific Hypotheses for CSA (T-UT)

Hypothesis # 1
Older versus Young After 31 Weeks of Detraining

Region	Diff	StdErr	DF	T-Value	Prob
1	-2.326	1.1732	61	-1.98	0.0519
2	-0.54	1.1452	66.9	-0.47	0.639
3	-0.23	1.1115	63.7	-0.21	0.8365

Hypothesis # 2A
Young Men versus Young Women After 31 Weeks of Detraining

Region	Diff	StdErr	DF	T-Value	Prob
1	2.9165	1.6793	61	1.74	0.0875
2	2.9078	1.6392	66.9	1.77	0.0806
3	1.7438	1.5909	63.7	1.1	0.2771

Hypothesis # 2B
Older Men versus Older Women After 31 Weeks of Detraining

Region	Diff	StdErr	DF	T-Value	Prob
1	0.7736	1.6388	61	0.47	0.6386
2	0.1345	1.5997	66.9	0.08	0.9332
3	1.5536	1.5526	63.7	1	0.3208

Tests of Specific Hypotheses for CSA (T-UT)

Hypothesis # 3

Regional Comparisons After HRST

Region v Region	Diff	StdErr	DF	T-Value	Prob
1 v 2	-1.492	0.6182	51.4	-2.41	0.0194
1 v 3	0.3689	0.6085	52.2	0.61	0.5469
2 v 3	1.8606	0.4566	44	4.07	0.0002

Hypothesis # 4

Old versus Young After 9 Weeks of HRST

Region	Diff	StdErr	DF	T-Value	Prob
1	-0.136	1.3952	76	-0.1	0.9224
2	-0.839	1.4128	70.7	-0.59	0.5546
3	-1.398	1.1945	67.1	-1.17	0.2461

Hypothesis # 5 A

Young Men versus Young Women After HRST

Region	Diff	StdErr	DF	T-Value	Prob
1	4.4417	1.997	76	2.22	0.0291
2	5.8815	2.0222	70.7	2.91	0.0049
3	6.0511	1.7098	67.1	3.54	0.0007

Hypothesis # 5 B

Old Men versus Old Women After HRST

Region	Diff	StdErr	DF	T-Value	Prob
1	4.0164	1.9488	76	2.06	0.0427
2	3.0827	1.9735	70.7	1.56	0.1227
3	1.3045	1.6686	67.1	0.78	0.4371

Appendix III: Reliability Study

Test-retest Measurements at Time Point 1 (x1) and Time Point 2 (x2)

File #	Slice #	x1	x2
99572	19	65.77	48.83
	26	56.69	48.59
	34	39.57	39.9
99389	20	85.79	99.6
	27	95.41	100.05
	33	76.71	80.87
94909	18	41.16	36.51
	25	46.69	43.03
	32	40.55	42.46
94033	15	72.36	73.47
	23	85.99	86.9
	30	72.78	75.07
91417	16	57.03	55.81
	23	68.13	66.71
	31	49.13	50.16
91072	19	56.53	56.77
	27	62.11	63.17
	34	48.64	49.09
90331	19	61.15	61.34
	27	72.94	74.24
	34	62.52	59.62
89330	19	36.97	36.47
	26	45.12	46.24
	33	43.6	42.61
89281	19	55.58	55.92
	27	73.47	70.61
	34	62.6	62.06
86745	19	56.27	55.85
	26	67.03	67.45
	34	48.07	49.55

File #	Slice #	x1	x2
85649	15	67.52	66.8
	23	76.83	77.1
	31	56.99	56.53
85271	19	70.65	70.42
	26	82.48	79.92
	33	72.74	70.15
84636	17	50.16	49.06
	24	60.85	59.05
	31	48.71	45.62
80473	20	49.24	48.49
	28	58.33	56.61
	36	41.2	43.26
78029	15	74.16	72.56
	23	83.81	83.12
	30	69.54	67.86
85793	18	49.82	52.52
	26	59.2	58.71
	33	50.93	48.52
86141	20	45.28	45.74
	27	51.61	47.38
	34	38.56	36.43

Reliability Statistics

Test-retest

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F-Value	Pr > F
Model	1	9547.04	9547.04	805.36	<.0001
Error	49	580.863	11.8543		
Corrected Total	50	10128			

Root MSE	3.44301	R-Square	0.9426
Dependent Mean	60.0975	Adj R-Sq	0.9415
Coeff Var	5.72905		

Parameter Estimates

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	1	6.95548	1.93365	3.6	0.0007
JCSA	1	0.89305	0.03147	28.38	<.0001

Appendix IV: Correlation Study

Comparison of Pouliot Measurements Versus Melnyk

File #	Scan #1 Rose	Scan #2 Jason
45786	40.36	40.86
	41.69	43.03
	36.93	37.42
36298	61.24	67.41
	69.05	71.64
	59	55.66
37836	44.75	43.95
	45.89	48.18
	37.72	38.06
1581	40.02	41.69
	58	55.12
	47.8	52.26
2850	36.58	39.56
	46.69	50.68
	41.64	43.76
12143	34.48	35.86
	41.05	41.81
	31.81	36.13
86745	43.22	42
	65.04	65.99
	55.24	52.22
86141	33.19	33.68
	49.21	48.94
	33.57	36.66
13346	34.39	35.06
	41.97	39.18
	37.03	34.9
22443	27.17	29.68
	32.29	35.71
	28.2	30.63

File #	Scan #1 Rose	Scan #2 Jason
26053	38.72	41.47
	56.19	57.3
	38.18	38.83
54832	25.71	26.82
	45	43.72
	38.91	41.62
72844	28.69	27.16
	37.51	34.64
	32.2	30.29
25382	31.05	31.81
	47.11	47.84
	40.55	44.82
38398	40.47	36.54
	55.69	50.35
	47.34	43.37
84636	38.22	40.13
	65.02	60.39
	54.64	51.16
23398	33.15	32.46
	46.54	42.19
	35.29	33.23

Correlation Statistics

Pouliot versus Melnyk

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F-Value	Pr > F
Model	1	5089.812	5089.81	667.14	<.0001
Error	49	373.8357	7.6293		
Corrected Total	50	5463.648			

Root MSE	2.76212	R-Square	0.9316
Dependent Mean	42.57647	Adj R-Sq	0.9302
Coeff Var	6.48743		

Parameter Estimates

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	1	0.10822	1.68908	0.06	0.9492
X	1	0.99176	0.0384	25.83	<.0001

Appendix V: Human Subjects

UNIVERSITY OF
MARYLAND
INSTITUTIONAL REVIEW BOARD

2100 Lee Building
College Park, Maryland 20742-5121
301.405.4212 TEL 301.314.1475 FAX

April 15, 2004

Dr. Marc Rogers
Mr. Jason Melnyk
Department of Kinesiology

REFERENCE:
04-0194; "The Effects of High Volume, Heavy Resistance Exercise Training on Regional Hypertrophy of the Quadriceps in Men and Women"

This is to affirm that the Institutional Review Board (IRB) concurs with the departmental Human Subjects Review Committee's (HSRC's) preliminary review of the application concerning the above referenced project. The IRB has approved the application and the research involving human subjects described therein. We ask that any future communications with our office regarding this research reference the IRB HSR identification number indicated above.

We also ask that you not make any changes to the approved protocol without first notifying and obtaining the approval of the IRB. Also, please report any deviations from the approved protocol to the Chairperson of your departmental HSRC. Thank you.

Sincerely,

Phylis Moser-Veillon
Co-Chairperson, Institutional Review Board

ADDITIONAL INFORMATION REGARDING IRB/HSRC APPROVALS

EXPIRATION OF IRB APPROVAL—Approval of non-exempt projects expires one year after the official date of IRB approval; approval of exempt projects expires three years after that date. If you expect to be collecting or analyzing data after the expiration of IRB approval, please contact the HSRC Chairperson in your department about submitting a renewal application. **(PLEASE NOTE: If you are not collecting data from human subjects and any on-going data analysis does not increase the risk to subjects, a renewal application would not be necessary.)**

STUDENT RESEARCHERS—Unless otherwise requested, the IRB will send copies of approval paperwork to the supervising faculty researcher (or advisor) of a project. We ask that such persons pass on that paperwork or a copy to any student researchers working on that project. That paperwork may be needed by students in order to apply for graduation. **PLEASE BE ADVISED THAT THE IRB MAY NOT BE ABLE TO PROVIDE COPIES OF THAT PAPERWORK, particularly if several years have passed since the date of the original approval.**

Enclosures (where appropriate), will include stamped copy of informed consent forms included in application and any copies of the application not needed by the IRB; copies of this memorandum and any consent forms to be sent to the Chairperson of the Human Subjects Review Committee

UNIVERSITY OF MARYLAND, COLLEGE PARK

HUMAN SUBJECTS REVIEW COMMITTEE (HSRC)

Departmental Application for Review of Research Using Human Subjects

Please check one: [x] Initial Application [ ] Renewal Application

Name of Principal Investigator or Project Faculty Advisor (NOT a student or fellow: must be UMD employee) Dr. Marc Rogers Tel. No. 301-405-2484

Name of Co-Investigator ______ Tel. No. ______

Administering Department of Project Kinesiology

E-Mail Address of P.I. mrogers1@umd.edu E-Mail Address of Co-I. ______

Where should IRB send approval letter? ______

Name of Student Investigator Jason Melnyk Tel. No. 443-610-3724

Student Identification No. & E-Mail Address 217-31-9574 jmelnyk@umd.edu

Name of Student's Advisor (if different from above) ______

Signature of Student's Advisor ______

Project Duration (mo/yr – mo/yr) 3/04 – 8/04

Project Title The Effects of High Volume, Heavy Resistance Exercise Training on Regional Hypertrophy of the Quadriceps in men and women.

Sponsored Project Data Funding Agency ______ ORAA Proposal ID Number ______

(PLEASE NOTE: Failure to include data above may result in delay of processing sponsored research award at ORAA.)

CONFLICT OF INTEREST: Investigators [ ] do [x] do not have a real or potential COI. See question #7 on page 2.
MEMBERS OF HEALTH CENTER: Investigators [ ] are [x] are not members of Health Center. See question #8 on page 2.

For initial application, please attach a copy of your responses to question 1 - 8 of the instructions on page 2 of this document, including all related documents (such as questionnaires, interview questions, surveys).

OPTIONAL: Complete appropriate box below to indicate whether you are requesting an exemption from further human subjects review and to list the number of any exemption categories (described on page 4 of this document) which you believe applies to your project: [x] Exempt---List Exemption Category Numbers 4 Or [ ] Non-Exempt

If exempt, please briefly describe the reason(s) for exemption. Your notation is simply a suggestion to the HSRC.

Study has been completed and data is stored for further analysis

Date ______ Signature of Principal Investigator or Faculty Advisor *(PLEASE NOTE: Person signing above accepts responsibility for project, even when data collection is performed by other investigators)*

Date ______ Signature of Co-Principal Investigator

30 MAR 04 [signature]

Date Signature of Student Investigator

4/1/04 [signature]

Date Signature of Human Subjects Review Committee Chairperson or Designee.
(Please also print name of person signing above)
(PLEASE NOTE: When HSRC Chairperson is also a project investigator or the Student Investigator's advisor, this line should be signed by another member of the HSRC.)

(rev 11/03) * PLEASE ATTACH THIS COVER PAGE TO EACH SET OF COPIES*

* SEND (3) COPIES WITH ONE CONTAINING ORIGINAL SIGNATURES *

You may send e-mail to irb@deans.umd.edu to inquire about the status of applications delivered to the IRB.

Please return completed applications to the Chairperson of the Human Subjects Review Committee in your academic department. Thank you

Jason Melnyk

Departmental application for Review of Research Using Human Subjects

The Effects of High Volume, Heavy Resistance Exercise Training on Regional Hypertrophy of the Quadriceps in Men and Women

1. **Abstract.** The data for the current study was originally collected between 1996 and 1999 (Effects of Age and Strength Training on Muscle Strength, Body Composition and Health Status, IRB approval #00098 1994, P.I. Dr. Ben Hurley). The objective of this study is to compare regional hypertrophy of the quadriceps muscle after high volume, heavy resistance training (HRST) and 31 weeks of detraining. Forty-four men and women completed unilateral knee extensor training three times per week for nine weeks with their dominant leg. In each session, subjects completed 55 repetitions at near maximal or maximal effort. Magnetic resonance images (MRI) were taken before and after HRST and after 31 weeks of detraining on both legs. The MRIs will be analyzed using NIH Image version 1.61 for the Macintosh PC. Three regions of interest will be identified and the cross-sectional area (CSA) of the muscle will be calculated at 3/10, 5/10, and 7/10 femur length. Comparisons will be made on the differences in CSA of the quadriceps muscle in men and women, young and old, at three time points: before HRST, after HRST, and after detraining.

2. **Subject selection.** The data collection portion of the study has been completed and no new subjects will be tested. The subject pool consisted of 21 women and 22 men

who were enrolled in the study and had MRI and strength measurements before and after HRST as well as after 31 weeks of detraining.

3. **Procedures.** No new subjects will be tested. The MRI data will be analyzed in the graduate assistance office room 2132 at the Health and Human Performance Building. Briefly, cross-sectional images will be outlined on a Macintosh PC with a trackball and the areas (cm2) will be calculated. A multi-way ANOVA with repeated measures will assess significance between gender and age. The differences in CSA after training and detraining will be specifically examined for significance. Factors in the ANOVA include age, gender, time point, region, and leg.

4. **Risks and Benefits.** There are no benefits to the subjects and the risk is minimal since all data collection and intervention with subjects has been completed.

5. **Confidentiality.** The MRI data is stored on a Macintosh PC that is locked in the graduate assistant office, room 2132 HHP Building. All data is identified by subject numbers. Other data is stored in locked file cabinets in the Exercise Physiology Lab, HHP Building.

6. **Information and Consent Form.** Research study involves analysis of existing data.

7. **Conflict of Interest.** There is no conflict of interest in this study, financial or otherwise.

8. **HIPAA Compliance.** Protected health information via the University of Maryland Student Health Center is not being used in this study.

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