ABSTRACT

Title of Document:	AGING RELATED DIFFERENCES IN HAND INTRINSIC AND EXTRINSIC MUSCLES FOR HAND DEXTERITY- AN MRI INVESTIGATION.
	Jeffrey Hsu, Masters of Arts, 2009
Directed By:	Jae Kun Shim, PhD. Department of Kinesiology

Hand dexterity is crucial for humans to interactions with the external environment. Many activities of daily living (ADLs) such as pressing, grasping, writing and typing would be unattainable without a skillfully and proficiently functioning hand. Sexagenarians and older often experience difficulties in hand dexterity, which seriously impair their ability to perform ADLs. This study described the aging-related changes in hand muscle size and dexterity; and addressed the conflicting literature regarding the extent of atrophy to either the intrinsic or extrinsic hand muscles in the elderly. The overall hypotheses for this study were 1) that elderly adults show an aging-related decrease in hand muscle size and strength, especially a greater decrease in the intrinsic hand muscles, 2) elderly adults show an aging-related decrease in hand dexterity and 3) hand muscle size and strength are positively related to hand dexterity. This study examined hand muscle sizes with magnetic resonance imaging (MRI) and examined hand strength and other functional measures. This study found aging-related decreases in muscle size, muscle strength, hand dexterity. Furthermore, intrinsic muscles showed a greater aging-related decrease in volume and strength as compared to the extrinsic muscles. When examining relationships, muscle strength was positively correlated to multi-finger synergy and finger dependence. Also, muscle size was positively related to performance on clinical hand dexterity tests. This supports the strength-dexterity equivalence hypothesis.

GING RELATED CHANGES IN THE STRUCTURE AND DEXTERITY OF HAND INTRINSIC AND EXTRINSIC MUSCLES- AN MRI INVESTIGATION

By

Jeffrey Hsu

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Advisory Committee:
Jae Kun Shim, PhD Chair
Marcio A. Oliveira, PhD
Ben F. Hurley, PhD

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Chapter 1: Introduction

Interactions with the external environment require a proficiently functioning hand that can perform complex actions, such as prehension, pressing, pinching and gripping. Sexagenarians and older can experience difficulties in hand dexterity, which seriously impair their ability to perform activities of daily living (Kallman et al. 1990; Lateva et al. 1996; Rantanen et al. 1998). Muscle strength, which is often examined with aging, can directly affect measures of hand dexterity such as hand steadiness (Laidlaw et al. 1999), and reaction time (Kauranen et al. 1998) and synergy (Shim et al. 2008).

Hand-finger movements are precisely controlled by over 20 muscles which can be divided into two general groups: intrinsic and extrinsic hand muscles. The overall function of the intrinsic hand muscles was reported to be fine motor control while the extrinsic hand muscles function was reported to be gross motion performance and major hand forces production (Long et al. 1970). Anatomically, intrinsic hand muscles have insertions into the proximal phalanx of individual fingers where as extrinsic hand muscles have insertions into the distal phalanx of multiple fingers. Examining the different tendinous insertions and force generation abilities, previous studies have reported varying degree of intrinsic and extrinsic muscle involvement while pressing with different parts of the finger (Li et al. 2000; Shinohara et al. 2003a). The extrinsic hand muscles are the main force generators at the distal phalanges while the intrinsic hand muscles are the main force generators at the proximal phalanges (Chao et al. 1976; An et al. 1979; Li et al. 2000).

Typically upper limb muscle size has been examined through cadaveric specimens (Chao et al. 1989; Linscheid et al. 1991; Mitsiopoulos et al. 1998). This allows accurate volumetric measurements but lacks the ability to measure function. Relative to the lower limb, few studies have used advanced imaging techniques to measure upper limb muscles. Eng et al (2007) used MRI and surgical measurements of cadaveric forearms to determine the accuracy of forearm muscles. They found errors of approximately 10% from the MRI analysis. Janssen et al (2000) took in vivo measurements of upper body muscle volume in adults across 18-88 years old. Recently, a study (Holzbaur et al. 2007b) used advanced imaging techniques to allow in vivo examinations of upper limb muscles and their functions. They showed a coupled relationship between upper limb muscle volume and isometric moment generating capacity. Despite these findings, there lack studies which examine the size and dexterity of intrinsic and extrinsic hand muscles.

An understanding of the age-related changes of the intrinsic and extrinsic hand muscles' structure and dexterity can have important implications for rehabilitation of decreased hand dexterity. Currently, there are conflicting reports, regarding the extent of sarcopenia in specific muscle groups controlling hand movements. A previous study (Viitasalo et al. 1985) examining muscle strength showed that intrinsic muscles are more affected by age than extrinsic muscles by comparing the reduction in hand grip strength (42% decrease) and elbow flexion (35% decrease). Viitasalo and colleagues considered muscles in the forearm and hand as the intrinsic muscles while muscles in the upper arm as extrinsic muscles. On the other hand, Carmeli et al (2003), argued that intrinsic hand muscles do not show as great a decline in muscle mass as compared to the upper forearm (extrinsic hand muscles). Another study examining finger strength, supported Viitasalo and colleagues but defined intrinsic muscles as those in the hand and extrinsic as those in the forearm (Shinohara et al. 2003a). One of the reasons of the conflicting literature may be the differing working definitions used to define intrinsic and extrinsic hand muscles.

A previously mentioned study (Shinohara et al. 2003a), showed that intrinsic muscles exhibit greater decreases in force production, than extrinsic muscles, with age by measuring forces where specific muscle groups were thought to have differential contributions to the force produced. They performed the study under the premise that forces produced at the distal phalanges were primarily from extrinsic hand muscles and forces produced at the proximal phalanges were primarily from the intrinsic hand muscles. There, however, can be co-activation or dual contribution from the intrinsic and extrinsic muscles at either force application point (Li et al. 2000). The possibility of both muscle groups contributing to force application at a single point along the finger prohibits an independent examination of each muscle group. Finally, the lack of studies examining aging-related changes in hand muscle size also contributes to this debate. This is a major gap in the knowledge of changes in hand muscle size and dexterity with advanced age.

Aim and Hypothesis

This study intended to address the knowledge gap where there lack studies examining aging-related changes in hand muscle size and address the conflicting literature by investigating the age-related differences of young and elderly adult hand muscle volume and its correlates to hand dexterity. This study used magnetic resonance imaging to examine hand muscle sizes and use well established measures of hand dexterity to measure hand dexterity. Specifically, there were three questions addressed. First, what are the aging-related differences in the intrinsic and extrinsic hand muscle size and strength? Second, what are the aging-related differences in hand dexterity and dexterity? Finally, whether hand muscle size and strength are correlated to hand dexterity? The overall hypotheses for this study were 1) that elderly adults show an aging-related decrease in hand muscle size and strength, especially a greater decrease in the intrinsic hand muscles, 2) elderly adults show an aging-related decrease in hand dexterity and 3) hand muscle size and strength are positively related to hand dexterity.

SPECIFIC AIMS AND HYPOTHESIS

AIM 1: To determine aging-related differences between the hand intrinsic muscle and extrinsic muscle sizes

Muscle size has been thought to be directly correlated to strength capability (Hyatt et al. 1990; Doherty 2003). In fact, greater force decreases at points where intrinsic hand muscles are believed to be the focal force generator as compared to points where the extrinsic hand muscles are believed to be the focal force generators (Shinohara et al. 2003a). Thus, it has been suggested that intrinsic hand muscles experience greater aging-related decreases in muscle size than extrinsic hand muscles. Controversially, it has also been reported that intrinsic hand muscles do not show as great a decline in muscle mass as compared to the upper forearm (extrinsic hand muscles) (Carmeli et al. 2003). MRI was performed on the forearm and hand to calculate intrinsic and extrinsic hand muscle sizes, and to test the following hypotheses:

Hypothesis 1a: The hand intrinsic and extrinsic muscle size is smaller in elderly adults as compared to young adults

Hypothesis 1b: The age related decrease of the intrinsic hand muscle volume is greater than extrinsic hand muscle volume

AIM 2: To determine aging-related differences in hand strength

Adequate hand strength is necessary for a fully functional hand. Previous studies have shown an increase in strength from early childhood to adolescence and a decrease in strength from young to elderly adults (Shinohara et al. 2003a; Oliveira et al. 2008a). Muscle quality, a normalized measure of strength, has been shown to decrease as adults age (Lynch et al. 1999). Maximal voluntary isometric force production at the proximal and distal interphalanges (PP and DP, respectively) was recorded to test aging-related differences in the intrinsic and extrinsic muscle strength, respectively.

Hypothesis 2: The age related decrease of intrinsic muscle strength is greater than extrinsic muscle strength

AIM 3: To determine aging-related differences in finger dependence, multi-finger force control accuracy and multi-finger synergy

Finger dependence, force control accuracy and multi-finger synergy are both important measures for skilled hand dexterity. A previous study suggested that the lost of intrinsic muscle function will lead to a considerable functional deficiency of the hand (Ketchum et al. 1978). Another study reported that intrinsic hand muscles decrease in size and strength with adult aging (Shinohara et al. 2003a). Single finger maximal voluntary torque production tasks were performed to measure finger dependence. Multi-finger isometric constant force production at the distal and proximal phalanges was recorded to test the ability of extrinsic and intrinsic muscles, respectively, to control finger forces accurately.

Hypothesis 3a: Finger dependence, force control acccuracy and multi-finger synergy at the intrinsic muscles is smaller in elderly adults as compared to young adults

Hypothesis 3b: Finger dependence, force control accuracy and multi-finger synergy of the extrinsic muscles is smaller in elderly adults as compared to young adults

Hypothesis 3c: The age related difference of finger dependence, force control accuracy and multi-finger synergy of the intrinsic muscles is greater than the difference at the extrinsic muscles.

AIM 4: To determine aging-related differences in overall hand dexterity

Hand dexterity is crucial for humans to perform activities of daily living (ADLs). Deficits will seriously impact people's ADLs. Many previous studies have provided evidence that hand dexterity decreases from young adults to elderly adults (Shiffman 1992; Ranganathan et al. 2001; Carmeli et al. 2003; Shinohara et al. 2004). The Jebsen-Taylor Hand Function Test (JTHF) and Grooved Pegboard (PB) were administered to test overall hand dexterity.

Hypothesis 4: Overall hand dexterity is smaller in elderly adults as compared to young adults.

AIM 5: To determine the relationship between aging-related changes in extrinsic and intrinsic muscle volumes; and aging-related changes in hand dexterity and strength

Shinohara et al (2003) reported that there is a greater weakening of the intrinsic hand muscles as compared to the extrinsic hand muscles. The intrinsic hand muscles are highly important for efficient hand dexterity (Jacobson et al. 1992). A loss of intrinsic muscle function may lead to a considerable functional deficiency of the hand (Ketchum et al. 1978). The overall function of the extrinsic hand muscles is gross motion and major force production (Long et al. 1970). Thus the loss of extrinsic hand muscles can be thought to contribute to a loss in hand strength.

Shinohara and colleagues also claimed that strength and dexterity are mutually exclusive, thus suggesting the strength dexterity-tradeoff hypothesis. However, we (Shim et al. 2008) recently found evidence in young adults that strength and dexterity are additive, thus instead suggesting a strength-dexterity equivalence hypothesis. Regression analysis was performed to test the correlation between hand strength and extrinsic muscle volume as well as hand dexterity, force accuracy control, and multi-finger synergy; and intrinsic muscle volume. This leads to the following hypotheses:

> **Hypothesis 5a:** The loss of hand strength in elderly adults is positively correlated to the loss of extrinsic muscle size.
>
> **Hypothesis 5b:** The loss of hand dexterity (as measured by JTHF and PB), force control accuracy (as measured by RMSE) and multi-finger synergy (as measured by delta variance) in elderly subjects is positively correlated to the loss of intrinsic muscle volume and normalized strength
>
> **Hypothesis 5c:** Strength is positively correlated to measures of hand dexterity.

Chapter 2: Review of Literature

Functional Anatomy of the Hand and Fingers

Hand-finger forces and movements are produced remotely by two groups of muscles- intrinsic hand muscles and extrinsic hand muscles. Extrinsic muscles originate in the forearm, proximal to the hand and insert into the fingers (figure 6A). Intrinsic muscles originate and insert within the hand (figure 6B). There are 11 intrinsic and 15 extrinsic muscles with direct functional roles of the hand (Carmeli et al. 2003). Every finger generally have 6 muscles controlling force movement production- three extrinsic muscles (two long flexors and one long extensor) and three intrinsic muscles (dorsal and palmar interosseous and lumbricles). The amount of extrinsic and intrinsic muscle involvement in finger activity is not uniform and depends on the task.

The amount of intrinsic and extrinsic muscle activity depends on the task, the position of the fingers, and the point of force application. Power grip requires the fingers and thumb to forcibly act against the thumb in order to transmit forces to the object (Napier 1956). During power grip tasks, such as hammer squeeze, the extrinsic hand muscles provided most of the gripping force while the intrinsic muscles, particularly the interossei, acted to rotate the phalanges and flex the MCP. Precision grip involves manipulation of an object between the thumb and the fingertips, not against the palm(Napier 1956). During precision grip tasks, the extrinsic muscles provided gross motion and compressive forces while the intrinsic muscles positioned the finger(Long et al. 1970). The position of the fingers also alters the amount of intrinsic and extrinsic muscle recruitment. During complete finger flexion, simultaneous activity of the extensor digitorum communis and FDP are required and viscoelastic stretching of the interossei. For flexion at the MCP joint with the IP joints straight, interosseus is the main contributor to this motion (Long 1968). Finally, the amount of intrinsic and extrinsic muscle involvement changes for different points of force application along the finger. The different anatomical points of attachment of the muscles (Basmajian and DeLuca 1985) allows for different extrinsic and intrinsic contributions at different force application points (Danion et al. 2000; Z-M Li et al. 2000). For example, producing a force at the distal phalanges (finger tips) will elicit intrinsic muscles as the focal force generators (An et al. 1985; Chao et al. 1976) while producing a force at the proximal phalanges (knuckles) will elicit extrinsic muscles as the focal generators. Maximum force production at the fingertips elicits peak extrinsic muscle force while intrinsic muscle contraction force was measured between 10-30% of their MVF (Harding et al. 1993; Z-M Li et al. 2000). In contrast, when a person presses maximally by proximal phalanges, intrinsic muscles are expected to produce forces close to their MVF, while existing assessments of forces produced by the extrinsic muscles suggest that they require the two major extrinsic flexors to produce below 20% of their maximal forces (Chao and An 1978; Harding et al. 1993; Landsmeer and Lang 1965; Smith 1974).

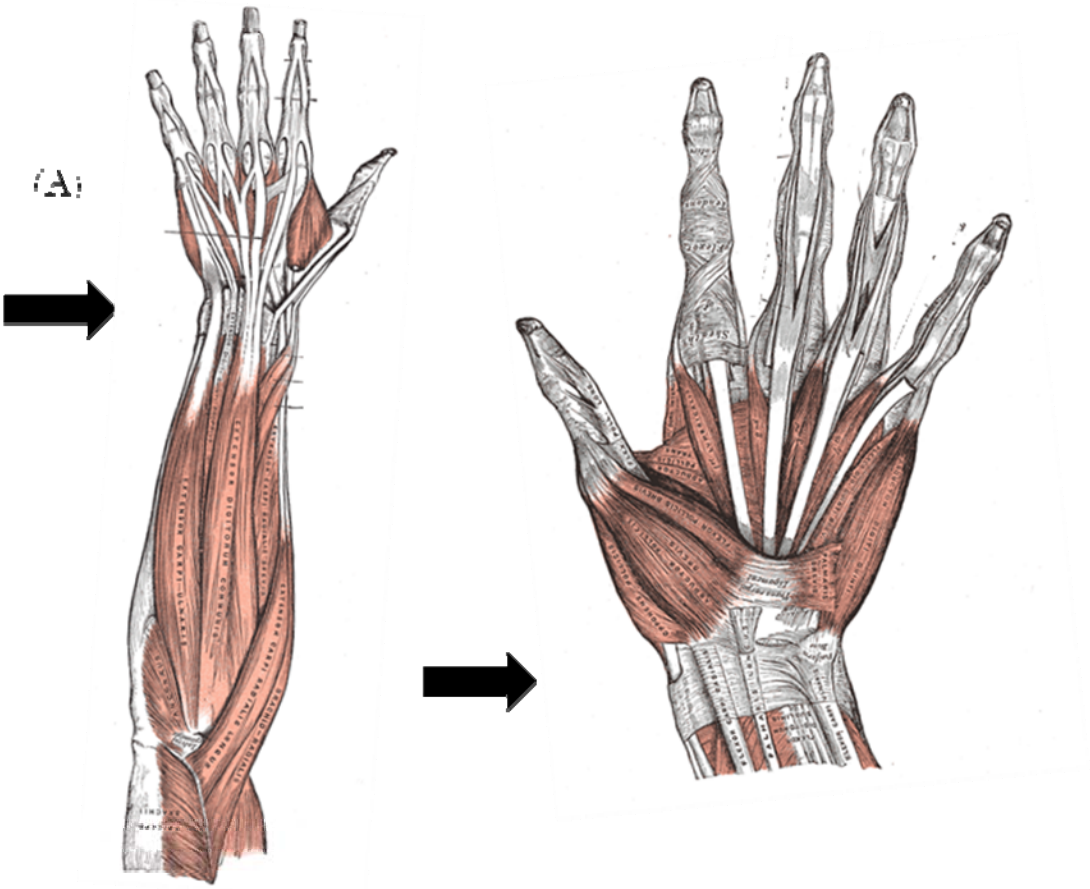

Figure 1- (A)Illustration of the extrinsic hand muscles on the dorsal surface of the forearm. The extrinsic muscles are proximal to the wrist (as designated with the arrow). (B) Illustration of the intrinsic hand muscles in the palm of the hand (right). The intrinsic muscles are distal to the wrist (as designated with the arrow). Reproduced from Gray, 1918 with permission from Bartleby.

Deficits in either of the extrinsic or intrinsic muscle group yield different disabilities. Weakening of the extrinsic hand muscles may hinder multi-finger synergy as the muscles often insert into more than one effector, thus causing a mechanical coupling between fingers. Additionally, the extrinsic hand muscles provide much of the strength in hand manipulation tasks. The intrinsic muscles are mainly known for fine motor control. The interosseous muscles allow flexion and provide stabilization at the MCP joint with extension of the IP joints (Lauer et al.

1999) and they are strong finger abductors and adductors. A deficit in the interosseous muscles may provide severe limitations to keyboard operators but more importantly may cause hand clawing, where there's MCP hyperextension and slight proximal interphalangeal (PP) flexion (Schreuders et al). In hand grip behavior, the intrinsic muscles play an integral role in executing the task. Without intrinsic hand muscles, the power grip is significantly weaker and but attainable. However, the spherical grip, tripod grip, lateral grip, extension grip and tip grip will be hard to attain.

Sarcopenia (Age and Strength)

Since Quetlet's (1835) initial study about the decline in body strength as humans age, this topic has been extensively studied. The term sarcopenia, derived from the Greek word meaning "poverty of flesh" (Doherty 2003), is now frequently used in human aging literature. Sarcopenia was first used to describe the age-associated loss of skeletal muscle mass (Rosenberg 1989). Now, the term is associated with aging-related changes to skeletal muscle, central and peripheral nervous system innervations, hormonal status, inflammatory effects, altered caloric and protein intake (Roubenoff and Hughes 2000).

There are multiple factors contributing to the effects of sarcopenia. The main factor is loss of muscle mass (Doherty, 2003). One possibility contributing to the reduction in muscle mass is atrophy within muscles. Muscle biopsy studies showed Type II muscle fibers diminished between 20-50% while type I fibers diminished between 1-25% (Larsson et al. 1978; Grimby and Saltin 1983; Lexell et al. 1988). The other possibility contributing to the reduction in muscle mass is a decrease in the number of muscle fibers. A muscle biopsy study reported a 50% decrease in the number of muscle fibers in nonagenarians as compared to vicenarians (Lexell 1995). Roubenoff and Hughes (2000) also reported a decrease in the number of myoctes and the protein content in remaining myocyte decreases as well. Other factors contributing to sarcopenia include decreased food intake (Morley 2001b; Morley 2001a) increased catabolic stimuli from proteins (Tilg et al. 1994; Roubenoff et al. 1998) and include physical inactivity (Porter et al. 1995; Roubenoff and Hughes 2000; Vandervoort 2002)

The prevalence of sarcopenia varies depending on the definition, measure of muscle mass, and normative data set used. However, there appears to be a consensus that the prevelance of sarcopenia increases with age (Baumgartner et al. 1998; Iannuzzi-Sucich et al. 2002). One study used DEXA to estimate muscle mass in 883 hispanic and white men and women (Baumgartner et al. 1998). Sarcopenia was defined as muscle mass more than two standard deviations below the mean for healthy young adults. This study found 13-14% of adults 65-70 years old and 50% of adults older than 80 years old to have sarcopenia. Also, men over 75 years of age have higher prevalence sarcopenia than women due to the greater change in quality of lean mass in men (Baumgartner et al. 1998).

Significant losses of skeletal muscle mass can seriously impair general function. In general, the loss of proximal and distal muscle mass in the upper and lower extremities with age is similar on a relative basis across sexes (Doherty, 2003). Muscle cross sectional area (CSA) has been reported to be representative of whole muscle volume. Total muscle CSA decreases by about 40% between the ages of 20 to

60 years (Doherty et al. 1993; Porter et al. 1995; Vandervoort 2002). Janssen and colleagues (2000) used whole body magnetic resonance imaging to determine skeletal muscle mass in a sample of 268 men and 200 women between 18 and 88 yr of age. Men were reported to have significantly greater skeletal muscle mass than women and men had a greater loss of skeletal muscle mass with aging. Also, upper body muscle mass decreased more, on an absolute basis, than the lower body (Janssen et al. 2000).

Aging-related decreases in muscle mass can directly impact strength generation. A study examined hand strength of 552 male manual industrial workers and showed maximum strength occurred in the mid-twenties while strength continued to showed continuous decline after (Fisher 1946). The per decade rates of grip strength decrease, were reported to be 3% per year and 5% per year for men and women, respectively (Bassey and Harries, 1993). Septuagenarians and octogenarians are reported to show, on average, a 20-40% decrease in strength as compared to vicenarians (Larsson et al. 1979; Murray et al. 1985). Additional studies have reported decreases in pinch strength (Boatright et al. 1997), finger pressing strength (Shinohara et al. 2003b; Oliveira et al. 2008b), and hand torque production (Shim et al. 2004) with increasing age.

Muscle quality (MQ) is currently believed to be a more meaningful indicator of muscle function than strength alone (Dutta et al. 1997; Roubenoff and Hughes 2000). Muscle quality is often referred to as strength per unit cross-sectional area (CSA) or per unit of muscle mass (Dutta et al. 1997). Lynch et al (1999) determined the aging-related changes in muscle quality in the upper and lower body. It was reported that the arm MQ decreases (figure 2) at a greater rate than the leg MQ with advancing age. Another study reported no change in CSA of the elbow flexors and extensors however, the MQ decreased for the flexors not the extensors (Klein et al. 2001).

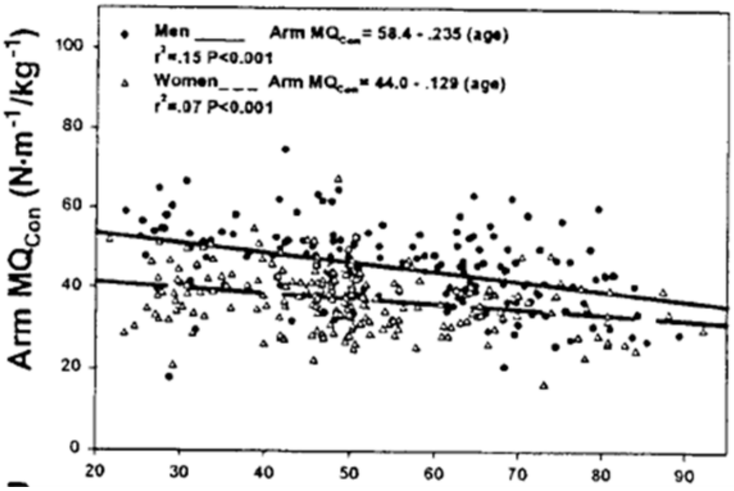

Figure 2. Muscle quality measured from concentric peak torque in the arm. Both sexes reported linear decreases with age, with men showing a greater rate of decrease. Reproduced from Lynch et al 1999 with permission from the American Physiological Society.

Imaging and the Upper Limb

Imaging as a tool for determining muscle volume

Medical imaging has improved significantly in anatomical images. Measurements of tissue volumes have allowed clinicians and researchers to improve their scope of practice. Many studies have used MRI as a method of calculating muscle volume. Heymsfield et al (1995) determined that MRI provides precise and reliable measurements of skeletal muscle in vivo. Other methods, such as bioelectrical impedance analysis (Brown et al 1988) and dual energy x-ray absorption (Shih et al., 2000) only provides an estimate of total limb muscle mass and is not single muscle specific. Many studies that have used MRI focused on the lower extremity, thus the availability of upper extremity literature for upper extremity tissue volume is very limited, nonetheless, the validity and reliability is still being determined.

Janssen et al (2000) was one of the first to use MRI to measure upper body skeletal muscle mass. They imaged over 450 adult men and women across a 70 year adult life span to track changes in upper and lower body skeletal muscle mass with age. They previously reported the correlation coefficient between corresponding MRI and cadaveric measurements approached unity with only a 1.3% difference (Mitsiopoulos et al. 1998). This study took transverse slices at 40mm increments from the intervertebral space between the 4th and 5th lumbar spine to the fully extended upper extremity. They found that gender differences were greater in the upper than lower body. Also, a reduction in relative skeletal muscle starts in the third decade while a noticeable decrease in absolute skeletal muscle mass was not observed until the end of the fifth decade.

Researchers have attempted to validate MRI as a tool to accurately measure upper extremity muscle volume. Rigorous validation from Tingart (2003) found MR-based volume measurements to be highly reliable in measuring the rotator cuff muscles. The authors correlated calculated volumes of the imaged rotator cuff muscles with the dissected rotator cuff muscles. This approach may be oversimplified because it combines muscles with and without-well defined bony compartments into a single volume measurement.

Recently, two studies have directly measured muscles responsible for hand function. Both studies used magnetic resonance imaging (MRI) techniques for the measurement. Holzbaur et al (2007) quantified all the extrinsic hand muscles to provide normative data for future studies. Normative data of upper limb muscle volume allows researchers to study populations with different muscle distributions, such as children, athletes, and stroke patients. They can also help detect changes in muscle dexterity with training or disease. Eng et al (2008) reported that MR imaging provides reliable and valid results for intrinsic hand muscles volume quantification.

Holzbaur et al (2007) quantified the relative sizes of muscles across the upper limb joints in vivo by measuring 32 upper limb muscles in adults. Each muscle was manually outlined in the MRI image (figure 3). This was the most comprehensive study that quantified the forearm muscles. Holzbaur and colleagues assessed the accuracy of the MRI protocol by comparing a known ($77cm^3$) volume of water with the image determined volume. The error was within 1.4%. They found that wrist flexors are twice as large as extensors and the two largest muscles crossing the wrist are the flexor digitorum profundus (figure 4) and the flexor digitorum superficialis. With the imaging, the limb circumference, length, bone length, and PCSA was also determined.

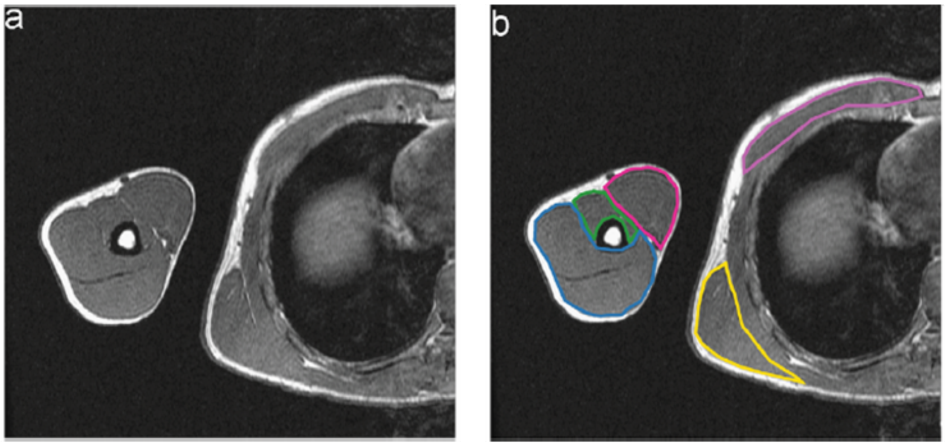

Figure 3- (a)Axial images of the upper arm (b) individual muscle structures are outlined in different colors. Reproduced from Holzbaur et al., 2007 with permission from Elsevier.

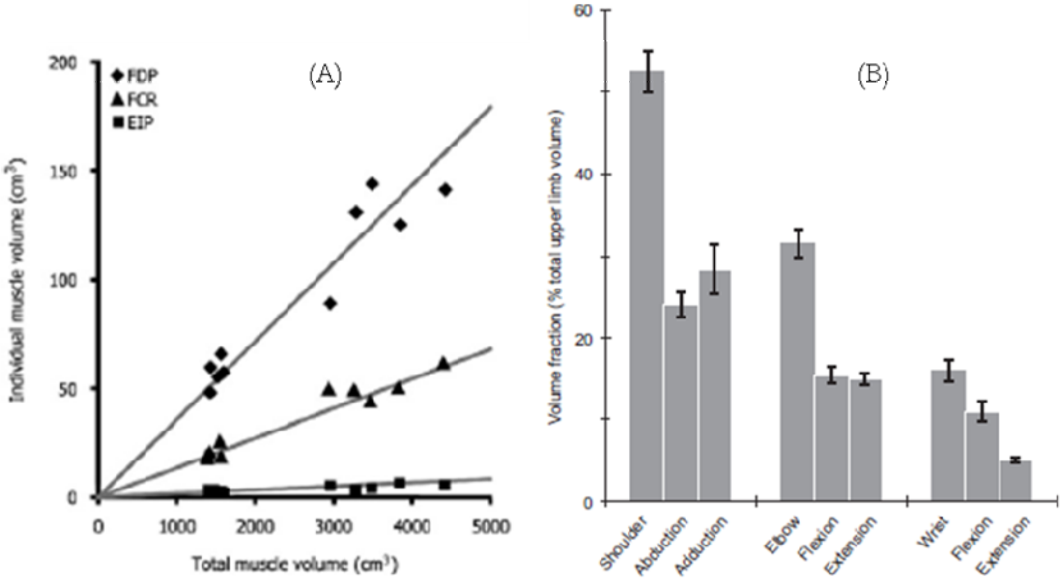

Figure 4- (A) The muscles with the largest volume fraction (diamonds), smallest fraction (squares), and average fraction (triangles). The flexor digitorum profundus (FDP) have the largest volume fraction for muscles crossing the wrist. FCR-flexor carpi radialis; EIP-extensor indicis proprius (B) the volume fraction of wrist flexors are roughly twice the wrist extensors. Reproduced from Holzbaur et al., 2007 with permission from Elsevier.

Eng et al (2007) went further to characterize the hardware and muscle-specific errors associated with measuring muscle volumes in the forearm. This study used cadaveric forearm specimens. To understand imaging errors, the authors placed 15mL placed water phantoms at known positions from the center of the field of view. As the phantom volume was placed further from the field of view center in either direction, the error increased up to 21% (figure 5).

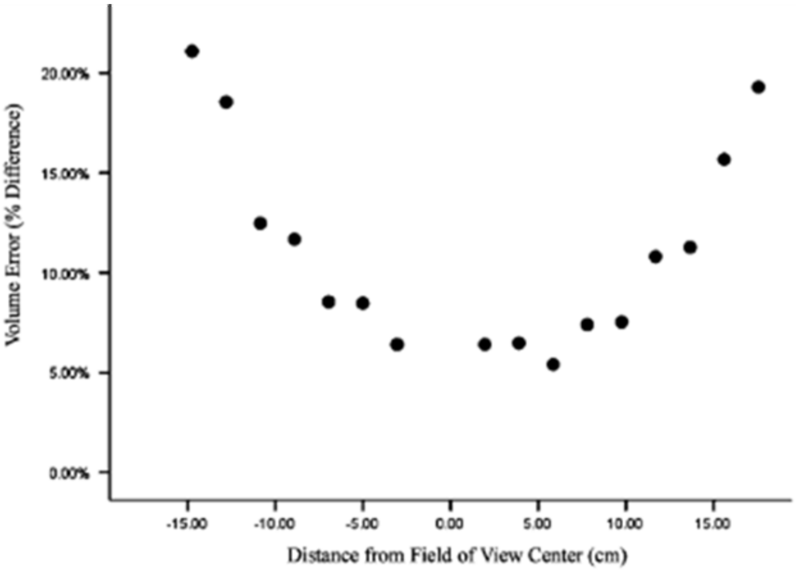

Figure 5- The measured volume error of a 15mL water phantom at various distances from the field of view (FOV) center. The greatest errors (~20%)were measure furthest away from the FOV center. Reproduced from Eng et al., 2007 with permission from Elsevier.

Similar to the Tingart study, the calculated imaged volume was compared with the water displacement determined volume of the cadaveric muscle. They determined that errors were approximately 10%. Longer muscles may be more susceptible to errors due to the greater number of segmentation decisions needed across slices. Thus muscles with smaller surface area to volume ratios have lower errors (figure 6). Also, the error was not dependent upon the location of the muscle in the field of view. Centrally placed muscles were not the most distorted.

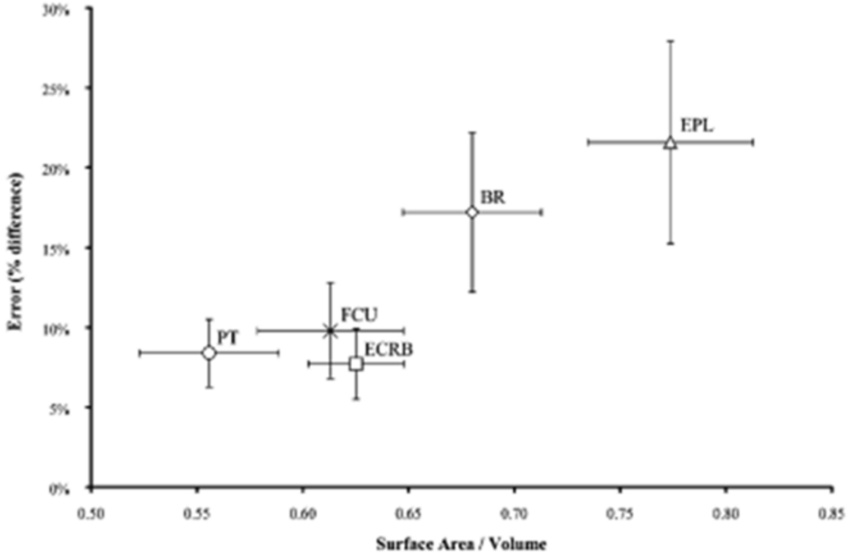

Figure 6. Plot of percent error between MRI and dissection determined measuremtns versus surface area to volume ratio for various forearm muscles. PT- pronator teres; ECRB- extensor carpi radialis brevis; EPL- extensor pollicis longus; FCU- flexor carpi ulnaris; BR- brachoradialis. Reproduced with permission from Eng et al., 2007.

Aging-related Changes of the Hand

Structural Changes (muscular, neural, and tendinous)

Muscular changes

Muscular structural changes are often reported in aging studies. Studies reporting aging-related changes in the hand musculature interpret the changes through behavioral measures such as strength generation and muscle activation. It was reported that intrinsic hand muscles do not show as great a decline in muscle mass as the upper forearm(Carmeli et al. 2003). However, other studies have shown that the loss of distal muscles (intrinsic muscles) is greater than proximal muscles (extrinsic muscles) (Christ et al. 1992; Era et al. 1992; Shinohara et al. 2003a). Aging-related atrophy in the interossei muscles (a group of intrinsic hand muscles) was reported to cause clawing of the hand, where the MCP joint hyper-extends and the PP joint flex. (Carmeli et al. 2003). Janssen et al (2000) directly measured the muscle mass of young and elderly adults in a cross-sectional study with magnetic resonance imaging. They found that upper body muscle mass decreases with age but to a lesser extent than the lower body (figure 7). Currently there is no study directly measuring the aging-related differences in hand extrinsic and intrinsic muscle structure. The lack of studies can be ascribed to the structural complexity of the hand and limitations in imaging techniques. It was within the last 2 or 3 years that scientists have determined accurate in-vivo measurements of the hand muscle structure (Eng et al. 2007; Holzbaur et al. 2007b).

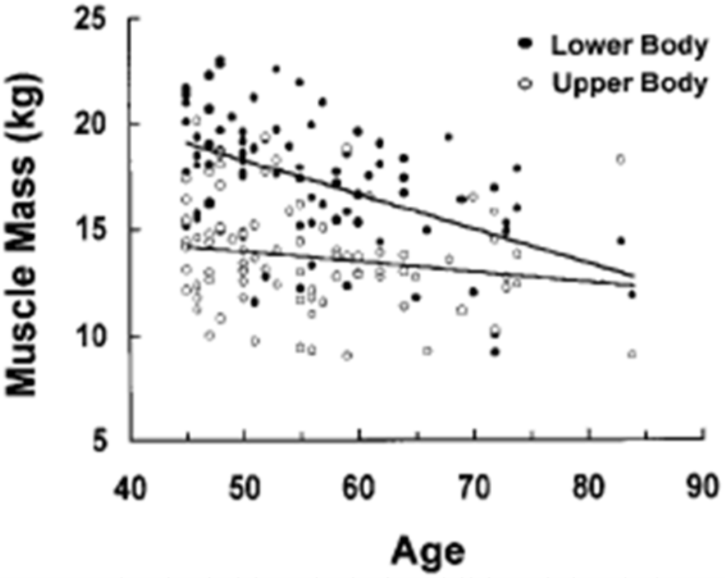

Figure 7- The upper body (white circles) exhibit minimal decreases in muscle mass as compared with the lower body (black circles). Reproduced from Janssen et al 2000 with permission from the American Physiological Society.

Tendon changes

The tendons are a collagen based connective tissue which has poor blood supply. The tendons serve as a connection between the muscle and bone and as a transmitter of muscle contractile force to the bones. The extrinsic hand muscles have multiple tendinous insertions into the distal phalanges while intrinsic hand muscles have single tendinous insertions into the proximal phalanges. The flexor digitorum profundus and flexor digitorum superficialis both have 4 tendons inserting into the distal phalanges. Each lumbrical muscle has one tendon insertion into the proximal phalanges. The multiple tendinous insertion of the extrinsic hand muscles have been associated as a peripheral reason for inter finger-dependency, also known as finger enslaving, during maximal force production (Zatsiorsky et al. 2000; Shim et al. 2007).

Tendons distal to the palm and digits have a minute blood supply. Aging has shown to cause decreased blood supply to this area (Shao et al. 1995), which leads to a decreased range of motion at the joint, and decreased flexion power. The hand tendon tensile strength ranges from 50-150 kg/mm, and this has shown to decrease by 30-50% with age (Tuite et al. 1997). Additionally, type I collagen fibers degrade with age, causing the tendons to become stiffer and denser connective tissue. Functionally, this can be seen as decreased flexibility of the fingers.

Neural changes

Neurological changes play a significant role in the dexterity of the aging hand. The sensory and motor nerves of the hand include cutaneous nerves for the former and ulnar, median, and radial nerves for the latter. Data have shown that approximately 25% of the motor axons in hand muscles are lost with increasing age (Hesselmann et al. 2001). Additionally, the diameter and the number of myelinated nerve fibers diminish after old age. Muscles in the elderly, on average, have larger but fewer motor units (Galganski et al. 1993; Lexell 1995). This change has been an important contributor to the age related decline in motor performance. Elderly adults have fewer but larger and slower motor units. The thenar motor unit has been shown to diminish in size and slow in contractile speed (Doherty and Brown 1997). This reduction in motor units can partially explain the higher fatigue resistance in elderly adults (Chan et al. 2000).

Functional Changes (strength and dexterity)

The aging-related changes of hand dexterity are important for researchers, physicians and therapists to understand. It is well known amongst the scientific community and the general public that ADLs involving precision dexterity such as threading a needle, holding a pen, or pouring a glass of water becomes more difficult with age (Carmeli et al. 2003). Examining the approximate age threshold, it was found that hand function remains stable until age 65, then begins to decline (Shiffman 1992).

Strength is a great limiting factor to the inability of normal hand function in old age. The decreasing strength of the hand with age can be attributed to decreasing muscle mass (Metter et al. 1998). Aging related changes in hand strength has been extensively studied. After 60 years of age, hand-grip strength may decline as much as 20-25% (Kallman et al. 1990; Rantanen et al. 1998). Finger pressing strength, as assessed by MVF, decreases significantly with age in both flexion (Shinohara et al. 2003a; Shinohara et al. 2003b; Oliveira et al. 2008a) and extension (Oliveira et al. 2008a). Thumb abduction strength and pinch strength both decrease after 60 years of age (Boatright et al. 1997). Maximal supination and pronation torque also decrease significantly with age (Shim et al. 2004). The changes are more profound in men than women. Studies have shown that after the age of 60, there is a rapid decline in hand-grip strength by as much as 20-25% (Kallman et al. 1990; Rantanen et al. 1998). A significant portion of this decline is accompanied by loss of muscle fibers and decreased muscle-fiber length, especially in the thenar muscles.

Changes in strength are often coupled with changes in other measures of hand dexterity. Those who examined changes in pressing strength also reported declines in finger pressing control. Multi-finger synergy in constant force pressing and moment production tasks decreased significantly with age (Shinohara et al 2003). Older adults showed worse force and moment stabilizing synergy (Shinohara et al. 2004) at the proximal phalanges versus the distal phalanges. This suggests more functional impairment of the intrinsic hand muscles versus the extrinsic hand muscles. Independent finger force production during single finger maximal voluntary contraction tasks revealed a decreased inter-finger coupling or dependence of forces, as measured by force enslaving (Oliveira et al. 2008a). The decreased force enslaving may be considered improved individual control of finger forces or higher dexterity. Higher grip forces are required for older adults who have less stead performance in object gripping tasks. The higher grip forces are reported along with a greater antagonist activity (Cole and Rotella 2001). Studies reporting an increased variability of movement patterns (Galganski et al. 1993; Enoka et al. 2003) believed an increased safety margin in elderly adults (Kinoshita and Francis 1996; Cole and Rotella 2001; Gilles and Wing 2003) may be an adaptation to the variability.

Chapter 3: Methodology

Experimental Design

A cross-sectional design with comparison group design was used for this study. There were two groups of participants- one control group of young adults and one experimental group of elderly adults. The influence of aging on a number of variables was determined. The main independent variables were age (young or elderly) and muscle (intrinsic and extrinsic). The main dependent variables were muscle volume, multi-finger strength, normalized strength, multi-finger synergy, multi-finger force control, Pegboard time, and Jebsen Taylor Hand Function time. The independent and dependent variables are listed in table 1.

Table 1. The independent and dependent variables of the study

Main independent variables	Main dependent variables
• Age (young or elderly) • Muscle (intrinsic and extrinsic)	• Muscle volume (MV) • Cross sectional Area (CSA) • Multi-finger strength (MVT) • Normalized strength (MVT_{norm}) • Multi-finger synergy index (DV) • Force control accuracy (FC) • Finger dependence (FE) • Jebsen Taylor Hand Function time (JTHF) • Grooved Pegboard time (PB)

Subjects

Nine young adults (age 23.9±1.6 years) and eleven elderly adults (age 71.4±1.6 years) participated in this study (Table 1). All participants were females. Adults over 65 years of age were considered elderly as defined by the World Health Organization.

All subjects were screened for the following- a) right-handedness according to the Edinburgh Handedness Inventory (Ransil and Schachter 1994; Verdino and Dingman 1998; Dragovic 2004) b) low to moderate risk health status according to the American College of Sports Medicine Risk Stratification Guidelines c) no more than 5 years of experience playing musical instruments d) no professional typing experience e) no history of upper extremity disorders (including surgery, arthritis, neurological issues, or neurological disorder). Elderly subjects were recruited from the greater Washington DC area community. All subjects gave informed consent to the procedures approved by the University of Maryland's Institutional Review Board (IRB).

Table 2. Physical Characteristics of Young (n=9) and Elderly (n=11) adult women

	Young	Elderly	P
Age (yrs)	23.9 ± 1.6	71.4 ± 1.6	<0.001
Height (cm)	164.0 ± 1.9	160.0 ± 3.3	0.33
Weight (kg)	59.2 ± 2.5	62.9 ± 4.1	0.48
BMI (kgm^{-2})	22.0 ± 0.7	25.1 ± 1.9	0.178

Mean (SE)

Experiment I- Muscle Size

Experimental Setup

A magnetic resonance imaging (MRI) system (Signa HDe 1.5 T, General Electric Healthcare) was used to quantify intrinsic and extrinsic muscle volumes. The Quad Head Coil (General Electric Healthcare) was used to scan the forearm and hand. A Liberty Docking System (General Electric Healthcare) was used to transport the patient from the preparation room to the MRI system. Styrofoam blocks were used to secure the hand and forearm and prevent any movements that can attribute to movement artifact in the machine. Vitamin E tablets served as markers for identifying anatomical landmarks.

Experimental Procedures

All subjects received scans on the right forearm and hand with a 1.5-T conventional MRI (Signa HDe 1.5 T, General Electric Medical Systems) at the Philip J Bean Medical Center (Hollywood, MD). Subjects were asked to sign the standard medical clearance and consent form. For the forearm scan, subjects laid on the right side of their body on the Liberty Docking system with the right shoulder fully extended (superman position). The hand was supinated such that the palm faces up. Vitamin E tablets were taped on the distal ulna and radial styloid processes, olecranon and lateral epicondyle. Styrofoam blocks were be taped around the hand to ensure full extension of the fingers and wrist and prevent movement of the hand. The arm was placed in the 8 channel head array coil such that 1 inch proximal to the antecubital space was at the proximal edge of the coil. Additional cushions were added for individual comfort of the subjects. The subjects were transported to the center of the system via the docking system.

The MR imaging is based on a previous study (Eng et al., 2007) with slight modifications to the procedures. MR imaging sequences and parameters were established to reduce inter-slice noise, to minimize between and within slice interpolation, to maximize image matrix size, to achieve a balance among anatomic coverage, contrast-to-noise ratio, spatial resolution, and subject tolerance. The following sequences were obtained using a 4-channel HD wrist array coil with a 3-inch internal diameter: transverse T1-weighted spin-echo (TR/TE, 6/1.9; matrix, 1024 x 1024; field of view, 25 x 25 cm; number of acquisitions, ~175; slice thickness, 1 mm; acquisition time 7 min 30 sec) on the dominant limb's hand and T1-weighted spin-echo (TR/TE, 5.8/1.9; matrix, 1024 x 1024; field of view, 40 x 40 cm; number of acquisitions,~150; slice thickness, 2mm; acquisition time 6 min 45 sec) on the dominant limb's forearm. The total acquisition time for the MR imaging was approximately 30 min (14min 15 sec for acquisition and 15 min for set-up). The actual time varied based upon the length of the subject's hand and forearm.

Data Analysis

The MRI data volumes was imported into Analyze Direct 8.1 (Analyze, KY) using the DICOM tool. The data volumes were cropped to minimize the computing memory required. A binary image of all the tissues was created. The original volume was multiplied by the binary image to remove the background noise. The images were then corrected by the "fill holes" operation. Different tissues of the arm have different threshold intensities on the image thus, tissues were separated by the intensities. Three objects were created based on tissue intensity- 1) subcutaneous fat and trabecular bone, 2) muscle, and 3) tendon, ligaments and cortical bones. To determine the threshold, each subject's hand and forearm set was examined and the appropriate threshold for each object was determined on a subject basis. The intensity range for muscle tissue was averaged across all subjects to eliminate bias when examining elderly adults. The averaged muscle intensity range was applied. For the forearm volume, object 1 was defined with the intensity range of 1109.7-max, object 2 was 396.9-1109.6, object 3 was 1-396.8. The muscle and skin was separated by an erode function with a 3 x 3 x 3 element size. For the hand volume, object 1 was defined with the intensity range of 1255.3-max, object 2 was 569.9-1255.3, and object 3 was 1-569.8. The muscle volume (MV) was determined by an algorithm which can first identify the area of muscle voxels in each image then multiplying the voxels by the number of slices and the slice thickness. The extrinsic hand muscles were defined as the muscles in the forearm. The forearm was defined as the region between the first slide that includes the proximal portion of the ulna and the last slide that includes the distal radius, inclusive. The intrinsic hand muscles were defined as muscles within the hand. The hand was defined as the region between the last slide that includes the distal radius and the slide that incorporates the most distal portion of the digits. Each image was then visually inspected to ensure accuracy.

The cross sectional area of the IM and EM were also determined from the MRI data. Data processing to separate different tissues was the same. The intrinsic CSA was taken as the median slice between the carpal metacarpal joint and metacarpal phalangeal joint. The maximal slice was not taken for the intrinsic CSA because it houses many muscles that contribute to the thumb. Since this study examined finger forces produced predominately by the intrinsic hand muscles to the 2nd to 5th digits, the slice was selected to mainly contain the lumbricals and interossei, and be easily identifiable for all subjects. EM CSA was defined as the largest muscle area in a single forearm slice (Klein et al. 2002).

MRI imaging and muscle volume segmentation was be used to determine hand intrinsic and extrinsic muscle volume and cross sectional area. This will address specific aims 1 and 5.

Validity and Reliability

To assess the validity of the MRI analysis, water phantoms were imaged and the volumes were determined by the analysis technique described above. Eight volumes (25, 50, 75, 125, 200, 325, 525, and 825mL) were used. The smallest volume was chosen because it was representative of the estimated intrinsic muscle size. The 825mL volume was chosen because it was representative of the estimated total forearm volume in an adult male. Each intermediate volume used was approximately one magnitude greater than the previous measure. This method is similar to the permutation of the golden ratio. The calculated water volumes very accurately represented the measured water volume. The absolute error from the water phantom volume determination showed no relationship with increasing total water volume. The relative error from the analysis of the water volume phantom showed a negative relationship with increasing total water volume. The greatest error (4.78%) was shown in the smallest volume used. There was high correlation between the measured volume and calculated volume ($r^2 = 0.9997$) (figure 8).

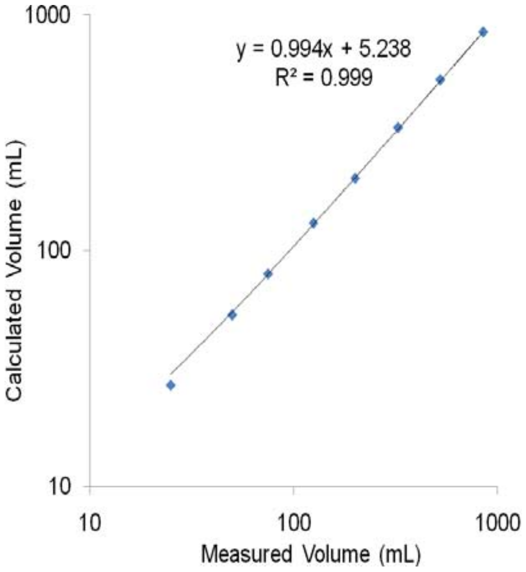

Figure 8. The regression between the measured and calculated water phantom volumes

The MRI tissue segmentation has been used to quantify from gross muscles volumes such as the quadriceps, hamstring, (Ferrando et al. 1995; Akima et al. 2000; Lund et al. 2002; Tate et al. 2006; Olaighin et al. 2007) to fine muscles such as ocular (Tian et al. 2000; Herman et al. 2005; Kvetny et al. 2006; Majos et al. 2007). Much of the data analysis may lead to examiner bias and error. To eliminate inter-examiner error, one examiner performed all the analysis. One subject's intrinsic and extrinsic muscles were each analyzed three times. The correlation of variation for the single examiner was 1.137% for the forearm and 2.113% for the hand. Each subject's hand and forearm volume was independent analyzed twice to determine the muscle threshold. To remove any bias, the muscle threshold used was averaged across all subjects.

Experiment 2- Strength

Experimental Setup

For the strength, finger synergy and force control accuracy tests constant force production tests (experiment 3), a device which includes four force sensors (gray rectangle in Fig. 9A), with amplifiers (Models 208 M182 and 484B, Piezotronics, Inc) for four fingers (2nd-5th digits) was used. Sensors were fixed on a wooden base-layer board with Delran blocks (1cm x 1 cm x 0.5cm) affixed to the top surface. The Delran pieces prevented subjects from directly touching the sensors. The sensors were adjusted in the anterior-posterior and medial-lateral direction to fit the individual hand size of the subjects. A second wooden board was secured above the base-layer board with c-clamps and Velcro. The second board served as a forearm rest which was level with the top surface of the Delran. The height of the two boards stacked was approximately 4.5cm from the top of the table. Three Velcro straps were used at the distal portion of the forearm, wrist and dorsum of the hand to keep the arm and hand stationary. After the position adjustments, the boards were mechanically fixed to the table via c-clamps.

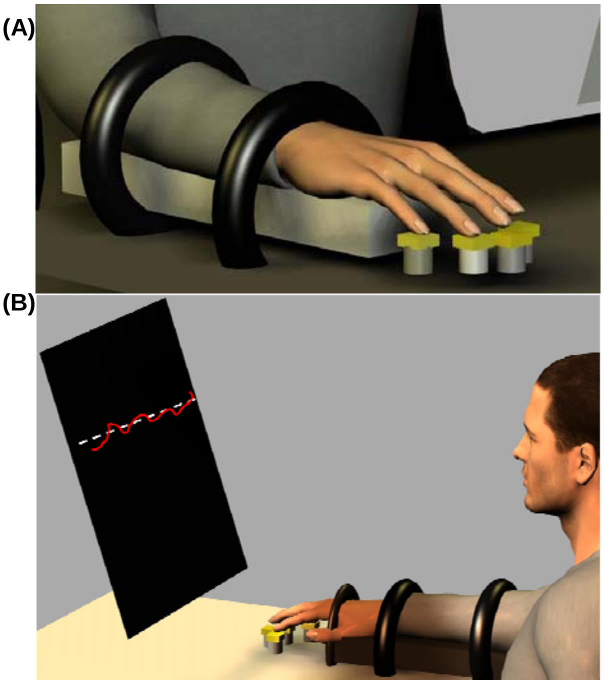

Figure 9 Experimental setting: (A) the experimental settings for the right hand: two-directional (tension and compression) sensors (gray rectangles) were fixed to the table. Delran blocks (yellow objects) are fixed to the tops surface of the sensors. The subject will place either the distal phalange or proximal phalange of each finger on the Delran. The sensor positions are adjustable for different hand sizes. Velcro straps are

used to secure the forearm, wrist and hand (black objects) (B) The subject watches the computer screen to perform a task while sitting in a chair. The dotted line (white) represents a force template. The solid line (red) represents the actual force produced.

Signals from the sensors were conditioned, amplified, and digitized at 100 Hz using a 16-bit A/D board (PCI 6034E, National Instruments Corp.) and a custom software program made in LabVIEW (LabVIEW 7.1, National Instruments Corp.). A desktop computer (Dimension 4700, Dell Inc.) with a 19" monitor was used for data acquisition. The single-finger force (for the task finger) or the total of all-four finger forces applied on the sensors was displayed on the monitor as online visual feedback. After recording the forces, the data were processed and analyzed in MatLAB (MatLAB 7, MathWorks, Inc.).

Experimental Procedures

For testing finger strength, finger synergy and force control accuracy tests constant force production tests, all subjects sat in a chair facing a computer screen with their shoulder abducted 35^{o} in the frontal plane and elbow flexed 45^{o} in the sagittal plane, such that the forearm was parallel to the frame. Subjects rested the forearm on a wooden panel such that the proximal portion of the MCP joint aligned with the edge of the panel. Three Velcro straps secured the forearm, wrist and palm from unwanted movements. Subjects were asked to rest the either the distal phalange or the PP joint of each finger on the Delran piece, attached to the sensor. The top surface of the wooden panel and the Delran was designed to be leveled so the fingers can be fully flexed between the panel and the sensor. In order to remove the gravitational effects of the fingers and any possible favor to finger flexion or extension due to passive stretching of the finger intrinsic and extrinsic muscles, the force signals for the initial 0.5s was averaged for each finger and subtracted from the later signals. Thus, only the force signals after subtraction was shown on the computer monitor as real-time feedback.

Subjects performed five conditions for the isometric MVF test: four single-finger conditions and one four-finger condition using the right hand. The same procedure was repeated at the distal phalange and proximal phalange. For the distal phalange condition, the Delran block was anteriorly translated such that the middle of the phalanges rests on the middle of the block. For the proximal phalange condition, the Delran block was posteriorly translated such that the proximal interphalangeal joint rested on the middle of the block. Subjects were shown a horizontal bar on the screen as force feedback for MVF tasks, and the bar moves vertically downwards when subjects pressed the sensors. Two trials were administered for each condition and the second trial was used for data analysis. During each trial, all fingers remained on the blocks, and subjects were asked to produce maximum isometric force with a task finger (s) in flexion or extension over a 3-s interval while watching the force feedback of the task finger (s) on the computer screen. The order of the tests was counterbalanced to eliminate the order effect and a one-minute break was required between consecutive conditions. The subjects were instructed to concentrate on the task finger and not to pay attention to non-task fingers. The task finger force produced was displayed on-line on the computer screen in front of the subject.

Data Processing

The force data from the MVF and Accurate force production test was digitally low-pass filtered with a 2nd-order, zero-lag Butterworth filter at 25 Hz cutoff frequency (Winter 1990; Shim et al. 2005b). For each trial, the instantaneous maximum force produced by each finger was measured at the moment when the maximum force is reached by the task finger (s). The data were used to detect or calculate the maximum voluntary torque (MVT), and finger enslaving (FE) and MVT_{norm}.

Data Analysis

The MVF value was determined as the maximum instantaneous force produced by the task finger (s). Maximal voluntary torque (MVT) was determined by multiplying the forces, recorded from the individual fingers at both the DP and PP, with the moment arm. The moment arm was defined as the distance between the MCP joint and middle of the distal phalanx and proximal interphalangeal joint, for the DP and PP condition, respectively. The distances were determined by examining the MR images of each subject. Maximal torque was used instead of force since torque considers the different moment arm (s) arising from each subjects varying hand size. Additionally, normalized strength was calculated by taking the ratio of MVT and muscle CSA.

Force enslaving was a measure of finger dependence (FE). FE was calculated as the averaged force produced by non task fingers during a single finger force production task(Zatsiorsky et al. 1998; Zatsiorsky et al. 2000). The results were averaged across all four single-finger conditions.

MVT and MVT$_{norm}$ was used to measure hand strength. These measurements addressed hypotheses 2 and 5a.

Experiment 3- Finger Force Synergy and Accuracy

Experimental Setup

The same setup as the strength task was used.

Experimental Procedures

Subjects were seated and positioned in the same manner as the strength task.

For the constant force production test, a fixed horizontal line which represents 20% of the four-finger MVF value for a particular subject was shown on the computer screen as the force profile template. 20% of the maximum strength was chosen because this force level is easy to achieve, covers the required force level to perform many activities of daily living, and has not been reported by subjects to induce muscular fatigue. The actual force produced on the sensor by the subjects was shown on the computer screen as a different color for force feedback. The line of force feedback moved vertically upwards and downwards as the four-finger force increased and decreased, respectively. Subjects were asked to produce four-finger pressing forces to match the force profile template over a 10s interval. Each subject performed twelve trials with at least one-minute intervals between trials and two-minute intervals between tasks. For both the strength test and the accurate force production test, the experimenter watched the subjects' right hand carefully for any joint movements. Trials with visible finger or wrist joint movements was rejected and performed again by the subjects. At the beginning of each trial, the computer generated a 'get ready' sound and the task finger force was shown graphically on the screen.

Data Processing

The force data from the strength, finger synergy and force control accuracy tests was digitally low-pass filtered with a 2nd-order, zero-lag Butterworth filter at 25 Hz cutoff frequency (Winter 1990; Shim et al. 2005b). For each trial, the force produced between the 5th and 12th second was used to calculate measure the synergy index and force control. The force data from the accurate force production task was used to calculate delta variance and constant error (both measures of synergy).

Data Analysis

Delta Variance (DV) was be calculated as an index of multi-digit synergy strength under the framework of the uncontrolled manifold analysis (UCM) (Schoner 1995; Latash et al. 2001). The exact calculations can be found on a previous study (Shim et al. 2008). When DV > 0, negative covariations among the individual fingers dominate, suggesting increased multi-finger synergy. When DV < 0, positive covariations among the individual fingers dominate, suggesting decreased multi-finger synergy. Root mean square error (RMSE) was be calculated as the average deviation from the force template over 12 trials. The inverse of RMSE quantified force control accuracy (FC).

FC and DV were used to measure hand muscle control. These measurements addressed hypotheses 3and 5b.

Experiment 4- Clinical Hand Dexterity Tests- Lafayette Grooved Pegboard and Jebsen Taylor Hand Function Test

Experimental Setup

The Lafayette Grooved Pegboard (Blum et al., 2006a; Hamby et al., 1997) was used to assess hand manual dexterity. The pegboard (10.1 x 10.1 cm^2) has 25 holes arranged in a 5 by 5 matrix, with each whole having the same shape but a random orientation. Each peg (3mm in diameter 28mm in length) is shaped as a keyhole.

The standard Jebsen Taylor Hand Function Test (Hackel et al., 1992; Stern, 1992; Verdino and Dingman, 1998) equipment was used to assess hand dexterity. This fine motor assessment test is widely used and has been widely validated. The equipment consisted of one wooden board (one pen, one spoon, two paperclips, two pennies, two bottle caps, four checkers, four notecards with pre-written sentences, four 3 x 5 inch note cards, five kidney beans, five empty soup cans and five filled soup cans.

Experimental Procedures

The standard procedures for the Lafayette pegboard (Blum et al., 2006b; Meador et al., 1995) was followed. For the Lafayette grooved pegboard, each subject was asked to place a peg in every hole as fast as possible. Subjects were instructed to perform this task with the right hand by working left to right and moving to the next row upon completion of the previous row. For each subject, the non-task hand was placed at the base of the pegboard, on the table. Subjects were instructed to pick up a single peg at a time and pick up a new peg if a peg dropped. The time from picking up the initial peg to placing the last peg in the hole was the time to complete the test.

The standard procedures for the Jebsen Taylor Hand Function Test (Stern, 1992; Wu et al., 2006) test was followed. There were seven tasks specifically designed to test fine motor, weighted and non-weighted hand performance abilitties. Each task was timed. The tasks were 1) writing (copying a 24-letter sentence), 2) turning over four 3 x 5 inch note card, 3) picking up small common objects such as a paperclip, bottle cap and coin, 4) simulated feeding using a teaspoon and five kidney beans, 5)stacking checkers, 6) lifting large light objects and 7)lifting large heavy objects. The specified instructions for each task of the Jebsen Taylor Hand function test were read verbatim to each subject.

Data Analysis

The time to completion was recorded for the Jebsen-Taylor (JTHF) and grooved pegboard test (PB). The time for individual tasks was summed and examined as one measure rather than 7 individual measures (Hummel et al. 2005). Performance of the JTHF and PB test was quantified by taking the inverse of the total time to complete each task. The units were inverse seconds.

The Jebsen Taylor Hand Function test and Grooved Pegboard test measured general hand dexterity. This measure addressed hypotheses 4 and 5b.

Statistical Analysis

To examine aging-related differences, standard descriptive statistics and two-way repeated measures ANOVA with factors of AGE (two levels: elderly and young) and MUSCLE (two levels: intrinsic and extrinsic) were performed on MV, CSA, MVT, MVT_{norm}, FC, FE, and FS. One way ANOVA with the factor of AGE (two levels: elderly and young) was performed on JTHF and PB.

To examine the association between muscle structure and dexterity, moderator mediated regression analysis was performed to examine the relationship between variables. The moderator variables were MUSCLE (intrinsic or extrinsic) and AGE (elderly or young). Age was considered a categorical variable despite its continuous nature because the study was interested in examining young and elderly adults rather than adults at specific ages. The mediator variables were MV, MVT_{norm}, CSA. This analysis allowed for comparing regression line slope and y-intercept differences across muscle and age groups. The dependent variables were MVT, FC, FE, FS, JTHF, and PB. Appropriate variables were selected for each comparison.

The level of significance was set at $\alpha = 0.05$. Values were presented as mean ± standard error (SE).

Chapter 4: Results

Muscle Size

Averaged muscle volume measurements are shown in table 3 and presented in figure 10A and B.

Table 3. Physical Characteristics of Young (n=9) and Elderly (n=11) female subjects

	Young		Elderly	
	Intrinsic	Extrinsic	Intrinsic	Extrinsic
MV (cm^3)	57.9 ± 3.9	342.3 ± 13.9	43.4 ± 2.7	290.9 ± 9.7
CSA (cm^2)	8.4 ± 0.4	21.3 ± 0.8	7.0 ± 0.5	19.1 ± 0.7
MVT (Ncm)	399.1 ± 26.4	250.9 ± 23.7	270.2 ± 22.9	221.2 ± 21.2
FC (1/RMSE)	168.8 ± 20.2	179.7 ± 27.9	115.1 ± 16.3	132.45 ± 16.8
FE (%)	28.0 ± 5.0	25.1 ± 6.2	31.4 ± 2.9	19.4 ± 2.2
ΔV(norm)	1.31 ± 0.008	1.29 ± 0.016	1.291 ± 0.017	1.263 ± 0.018
MVT_{norm} (Ncm/cm^2)	0.486 ± 0.05	0.118 ± 0.01	0.421 ± 0.06	0.117 ± 0.01
JTHF Performance (1/s)	0.028 ± 0.001		0.018 ± 0.002	
PB Performance (1/s)	0.017 ± 0.001		0.012 ± 0.001	

MV- muscle volume; CSA- cross sectional area; MVT- maximum voluntary torque; FC- force control accuracy; FE- finger dependence; ΔV – delta variance- MVT_{norm}- normalized maximum voluntary torque; JTHF- Jebsen Taylor Hand Function; PB- Pegboard. *indicates a significant AGE by MUSCLE interaction ($p<0.05$)

The extrinsic hand muscles were significantly greater than intrinsic hand muscles for both young [342.3 ±13.9 vs 57.9 ± 3.9 cm^3] and elderly subjects [290.9±9.7 vs 43.4 ± 2.7 cm^3]. Muscle volumes were larger in young as compared to elderly subjects across both muscle groups. The pair wise comparison indicated that there was a greater aging-related difference in intrinsic (25%) than extrinsic (15%) muscle volume. The results were supported by a two-way repeated measures (RM) ANOVA with a main effect of MUSCLE [$F_{(1,18)}=920.1$, $p<0.01$], AGE [$F_{(1,18)}=15.6$, $p<0.01$] and AGE x MUSCLE interaction effect [$F_{(1,18)} = 4.4$, $p<0.05$].

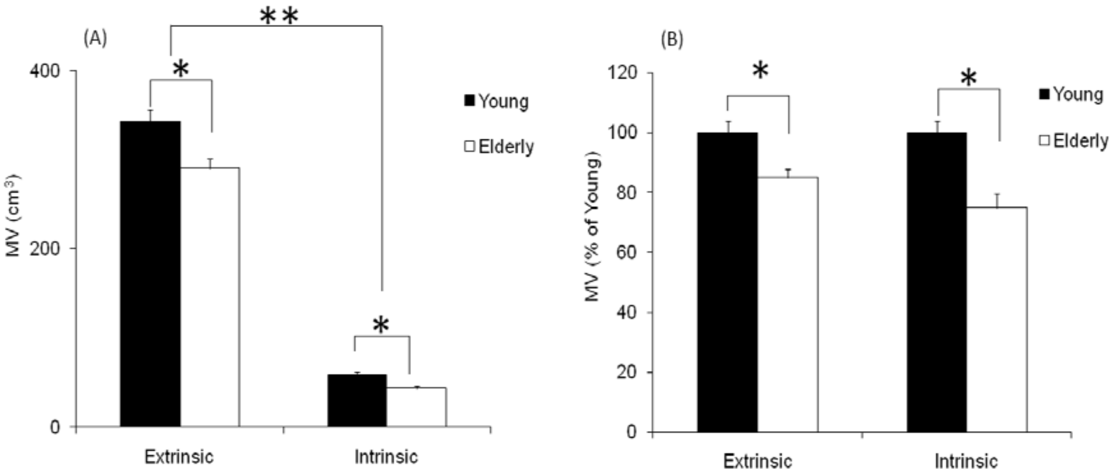

Figure 10. (A) Volume, in absolute units, of extrinsic muscles and intrinsic muscles for young and elderly subjects. (B) Muscle volume normalized by young adult average for both extrinsic and intrinsic muscles. MV- muscle volume; *indicates significant ($p<0.05$) difference between age group; ** indicates significant ($p<0.05$) difference between muscle group.

Muscle cross-sectional area (CSA) was taken as the largest slice in the forearm volume while the intrinsic muscle cross sectional area was taken as the slice representing the middle of the third digit's metacarpal bone. The averaged results across age and muscle group were presented in table 2 and figure 11 A and B. The extrinsic muscle CSA was significantly greater than the intrinsic muscle CSA. The muscle CSA were greater in young subjects for both the intrinsic (17.7%) and extrinsic (10.0%) muscle groups, as compared to the elderly subjects. Averaged across subjects, the extrinsic CSA was 2128.5 ± 75.3 vs 1914.6 ± 67.5 cm^2 while the intrinsic CSA was 844±39.4 vs 695.6 ± 50.0 cm^2 for the young and elderly subjects, respectively. This was supported by a two-way repeated measures (RM) ANOVA with a main effect of MUSCLE group [$F_{(1,18)} = 400.5$, $p<0.001$] and AGE [$F_{(1,18)} =$

9.8, p<0.01]. The interaction effect of AGE x MUSCLE group was insignificant [F $_{(1,18)}$ = 0.3, p=0.61]. Taken together, the results of the volume and CSA support the hypothesis that young subjects have greater muscle volumes as compared to elderly subjects and intrinsic muscle size show a greater aging-related difference than extrinsic muscles.

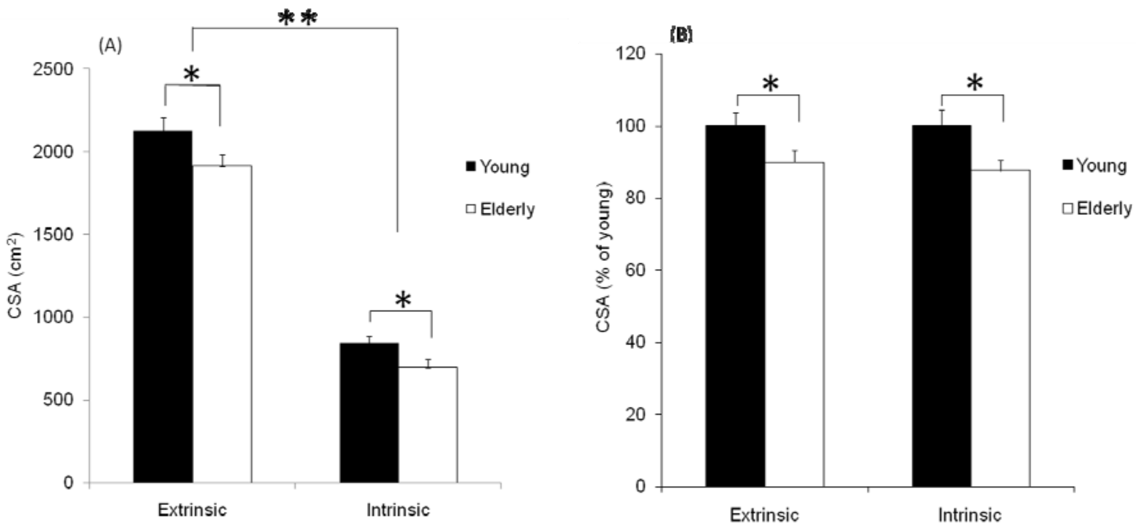

Figure 11. (A) Cross sectional area (CSA), in absolute units, of extrinsic and intrinsic muscle for young and elderly subjects. (B) CSA normalized by young subject average for both extrinsic and intrinsic muscles*indicates significant ($p<0.05$) difference between age group; ** indicates significant ($p<0.05$) difference between muscle group.

Strength

Individual finger forces recorded from the four-finger maximum voluntary contraction were multiplied by the moment arm (from the MCP joint to either the center of the distal phalanx or proximal interphalangeal joint) of each finger and summed to determine the four-finger maximum voluntary torque. The results indicated maximal torque produced by the IM by young subjects was significantly greater (31.2%) than elderly subjects ($p<0.05$). However maximal torque produced at the by the EM by young subjects was not significantly greater (11.8%) than elderly subjects ($p=0.364$). The averaged torque produced by the EM was 250.9 ±23.7 Ncm for young and 221.2±21.2 Ncm for elderly subjects. The averaged torque produced by the IM was 399.1±26.4 Ncm for young and 270.2 ±22.9 Ncm for elderly subjects (figure 12A and B). The torques differed significantly across the DP and PP for both young and elderly subjects ($p<0.05$). The results were supported by a two way RM ANOVA with significant AGE x MUSCLE group interaction [$F_{(1,18)} = 43.1$, $P<0.001$].

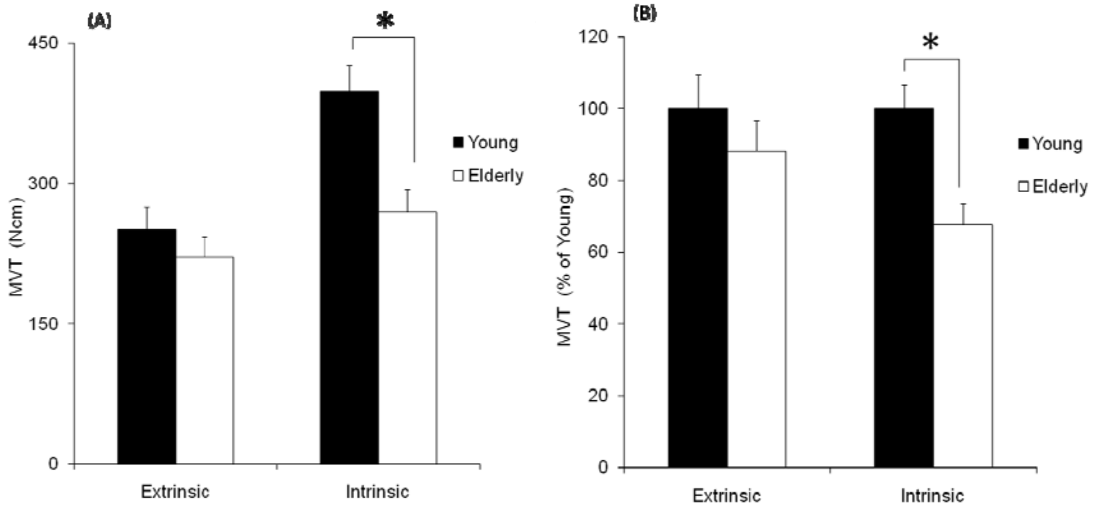

Figure 12. (A) Maximal voluntary torque (MVT), in absolute units, produced by extrinsic and intrinsic muscles of young and elderly subjects. (B) MVT normalized by young subject average for both young and elderly subjects. *indicates significant ($p<0.05$) difference between age group

Normalized strength was calculated as the ratio between MVT and muscle CSA, and MVT and muscle volume. The normalized strength was approximately equal between young and elderly subjects at the EM. The IM normalized strength was

13.4% higher in young subjects, but insignificant (figure 13A and B). However, in both young and elderly subjects, the intrinsic muscles showed a greater normalized strength than EM [F $_{(1,18)}$ = 81.3, $P<0.001$]. Calculating $MVTn_{norm}$ using CSA and volume yielded the same results. The results were supported by a 2-way RM ANOVA with factors of age and muscle.

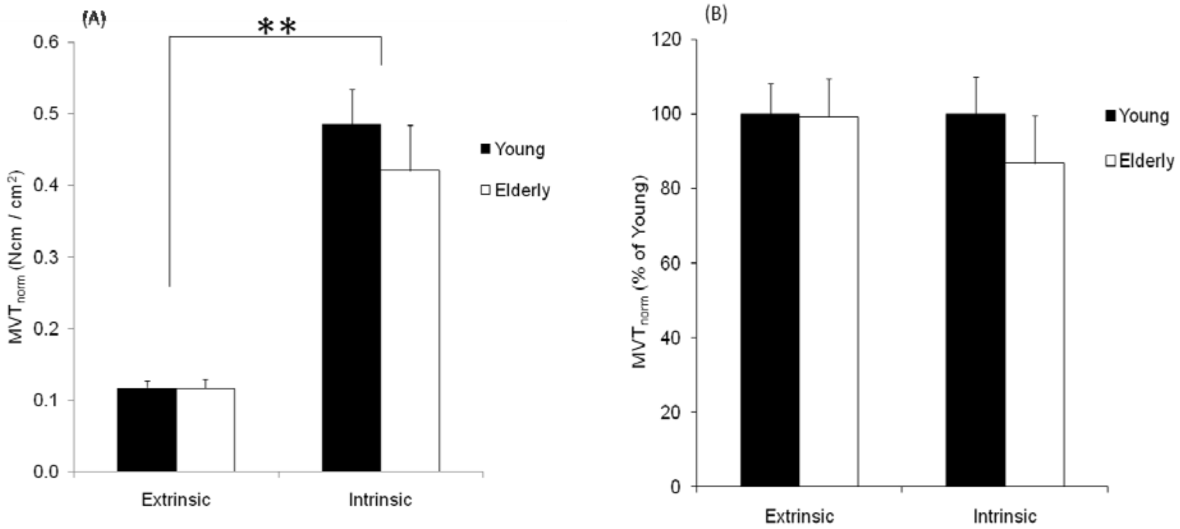

Figure 13. (A) Extrinsic and intrinsic muscle strength normalized by the cross sectional area for young and elderly subjects. MVT_{norm}- normalized maximal voluntary torque; ** indicates a significant ($p<0.05$) difference between muscle group. (B) MVTnorm normalized by young subject average for both young and elderly subjects.

Finger Dependence

During single finger maximal strength tasks, the forces produced by non-task fingers were recorded. The force produced by non-task fingers is known as enslaving. Enslaving examines the dependence of non-task fingers on task finger force production. A 2-way RM ANOVA with factors of age and muscle showed a significant interaction [F $_{(1,18)}$ = 21.4, $P<0.001$]. Pair-wise comparisons showed that the muscle groups did not differ significantly and age groups did not differ significantly either (figure 14A and B).

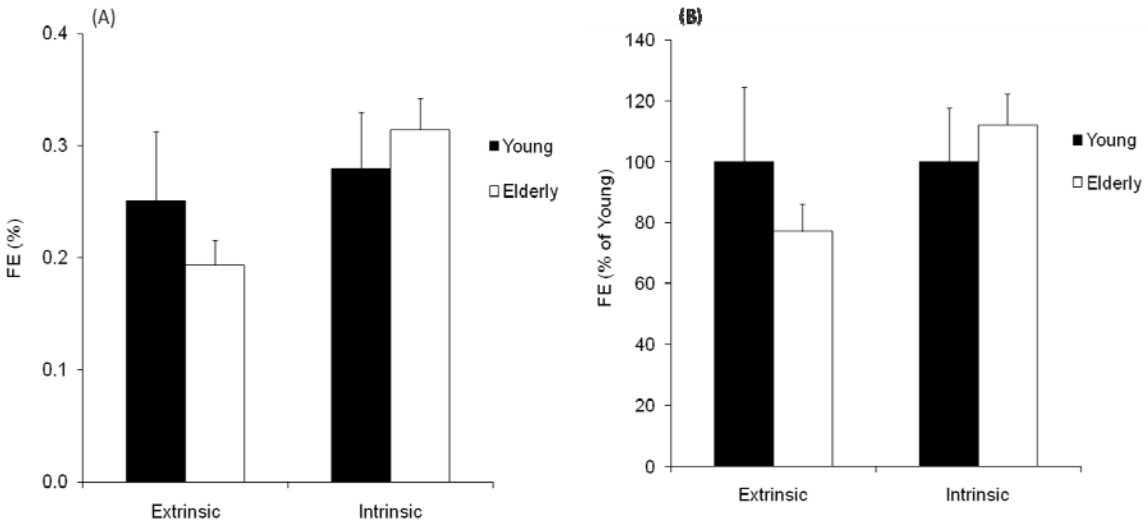

Figure 14. (A) Finger dependence (FE), as a percentage of task finger, in extrinsic and intrinsic muscles for young and elderly subjects (B) FE normalized by young subject average for both young and elderly subjects.

Force Control Accuracy and Synergy

*Force accuracy. D*uring the submaximal constant force production task, errors were quantified by taking the root mean square difference (or error) between the force produced and template force. The RMS errors were averaged across trials of the same condition and normalized by each subject's four-finger MVC force to allow comparisons between subjects. The inverse of the normalized RMS error was calculated to quantify force control accuracy. There was no significant difference between force control by the EM and IM. Despite being statistically insignificant ($p=0.066$), young subjects appeared to have greater force accuracy by the EM (26.3%) and IM (31.8%) (figure 15A and B).

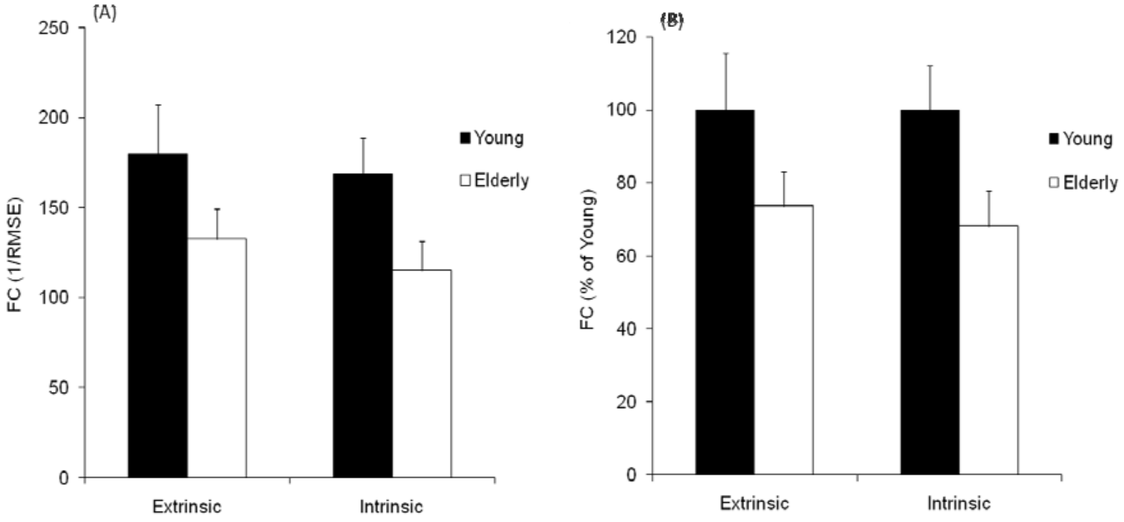

Figure 15. (A) Force control accuracy (FC) of the extrinsic and intrinsic muscle for young and elderly subjects. FC represented as the inverse of root means square error (RMSE). (B) FC normalized by young subject average for both young and elderly subjects.

Delta variance was a measure of multi-finger synergy (Schoner 1995; Latash et al. 2001; Shim et al. 2003; Latash et al. 2004; Shinohara et al. 2004; Shim et al. 2005a; Shim et al. 2008). This was calculated for the four finger constant force production task across the 5th to 12th seconds (constant portion) of the trial. Young and elderly adults did not show a significant difference across both the IM and EM (figure 16A and B).

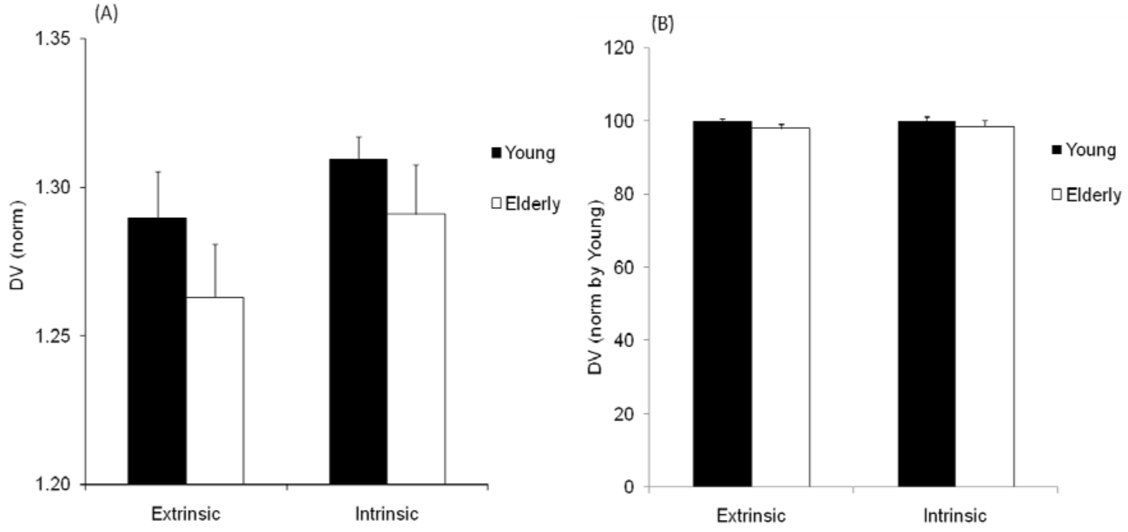

Figure 16-(A) Extrinsic and intrinsic muscle delta variance (DV), for young and elderly subjects. DV is a measure of multi-finger synergy. DV was normalized by each subject's four-finger maximal voluntary force. (B) DV normalized by the young subject average for both young and elderly subjects.

Clinical Hand Dexterity

Grooved pegboard performance was used to determine hand dexterity. Performance was quantified by taking the inverse of time to completion. Young subjects performed 29.1% higher than elderly adults in this test (p<0.001) (figure 17A.). This finding was supported by an one-way ANOVA with the factor of AGE.

The Jebsen Taylor Hand Function Test was used to examine overall hand dexterity. The total time to complete all seven tasks was determined (Hummel et al. 2005) and the inverse of the total time was used to measure performance. Young subjects performed 32.5% higher than elderly adults in this test (p<0.001) (figure 17B). This finding was supported by an one-way ANOVA with the factor of AGE.

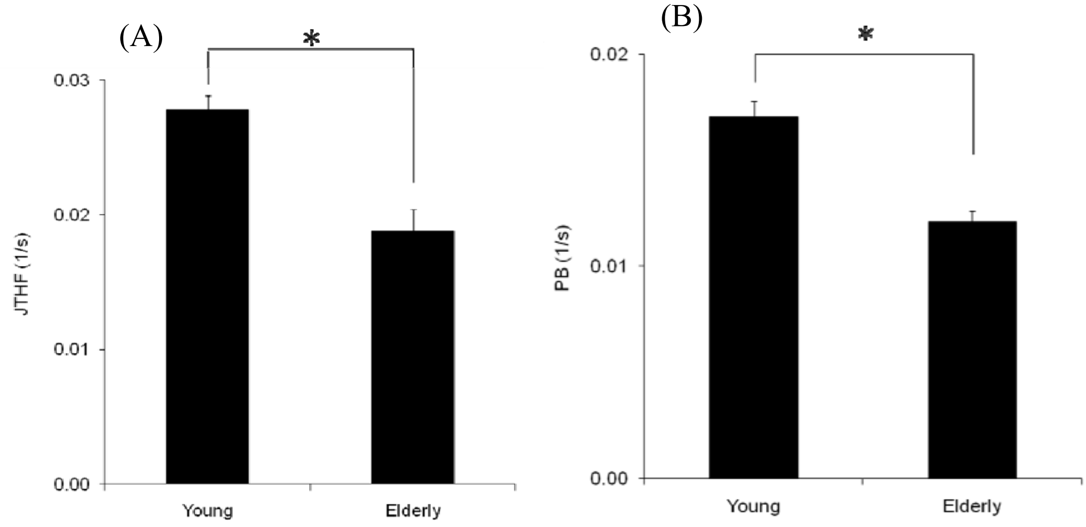

Figure 17 (A) Performance on the Jebsen Taylor Hand Function (JTHF) test for young and elderly adults (B)Performance on the Grooved Pegboard (PB) for yound and elderly adults. S-seconds; * indicates a significant ($p<0.05$) difference between age groups.

Regression Analysis

Regression analysis showed that enslaving and normalized strength were not significantly correlated across age and muscle groups. However for the young intrinsic ($p=0.06$, $r= 0.65$), young extrinsic ($p=0.06$, $r=0.65$), and elderly extrinsic ($p=0.05$, $r=0.060$) groups there was a positive relationship between enslaving and normalized strength. There was no significant difference in the regression y-intercepts. There was a significant difference in the slopes of the regression line between young and elderly adults for the intrinsic ($p<0.05$) and extrinsic ($p<0.05$) muscle groups.

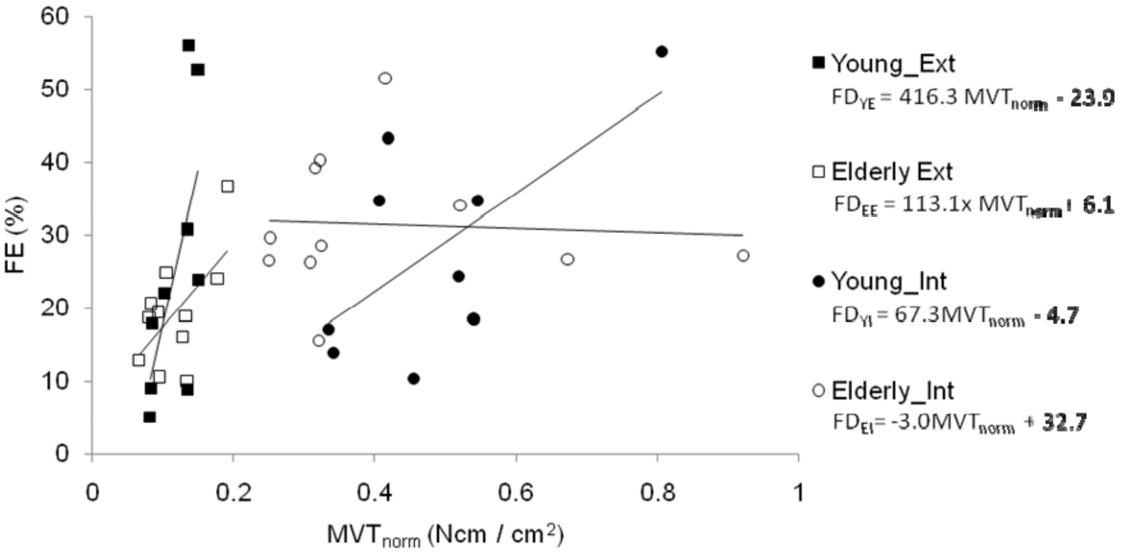

Figure 18. Regression of finger dependence (FE) and normalized strength for young and elderly, extrinsic and intrinsic muscles. Each subjects' data is shown above. The regression line equations are shown below the legend.Ext- extrinsic muscles; Int- intrinsic muscles

Regression analysis showed that delta variance and n was correlated for young extrinsic muscle group ($p<0.05$, $r=0.72$) while the other groups showed insignificant correlations. The young intrinsic muscle group showed a positive trend between the two variables ($p=0.07$, $r=0.63$). There was no significant difference between age and across muscle groups in the regression y-intercepts and regression slopes.

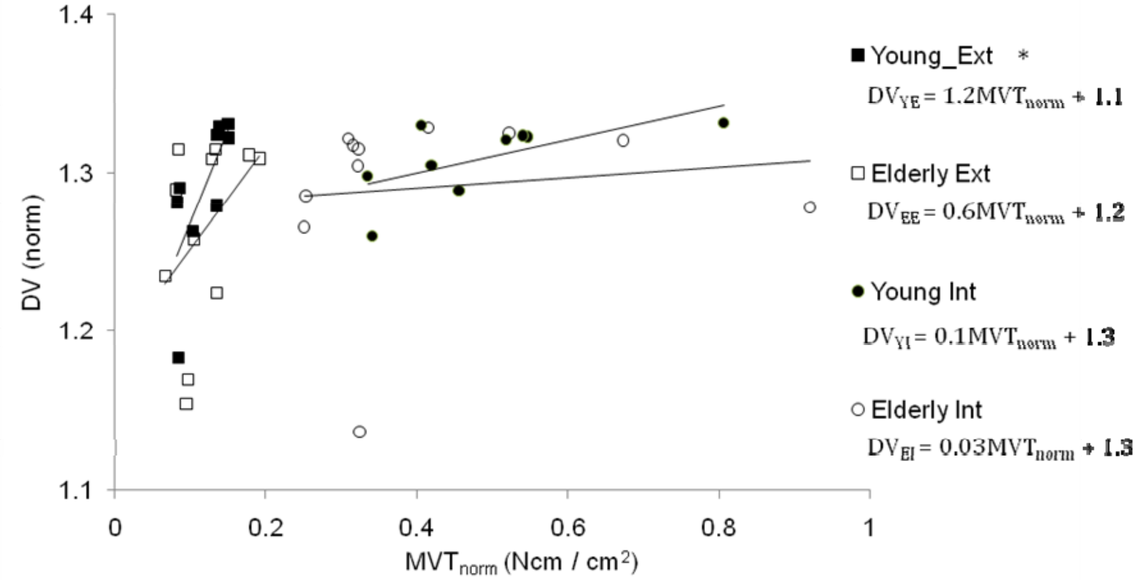

Figure 19. Regression of delta variance (DV) and normalized strength for young and elderly, extrinsic and intrinsic muscles. Each subjects' data is shown above. The regression line equations are shown below the legend. *indicates a significant correlation ($p<0.05$); Ext- extrinsic muscles; Int- intrinsic muscles

Regression analysis showed that extrinsic muscle CSA was correlated with JTHF performance for young adults ($p<0.05$, $r=-0.73$) while the other groups showed insignificant correlations. The elderly extrinsic muscle group showed a positive trend between the two variables ($p=0.05$, $r=0.60$). The slopes between the young and elderly extrinsic muscle groups were different ($p<0.01$) while the slopes did not differ for the intrinsic muscle group. The y-intercepts were greater in young subjects across both muscle groups ($p<0.05$).

All other regression comparisons showed insignificant relationships (not shown).

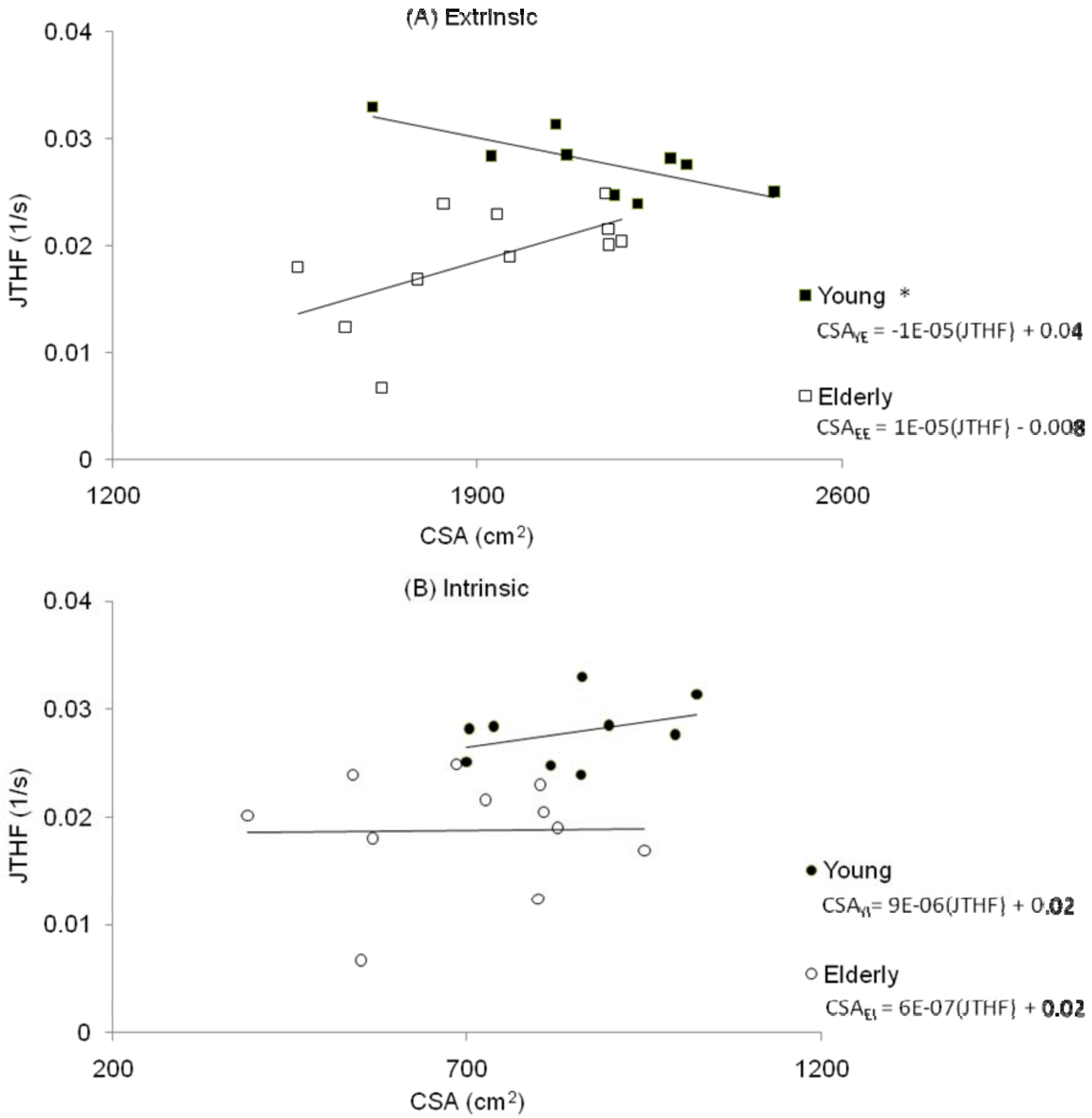

Figure 20. Regression of Jebsen Taylor Hand Function (JTHF) test performance and (A) extrinsic muscle cross sectional area and (B) intrinsic muscle cross sectional area. The regression line equations are shown above. * indicates a significant correlation ($p<0.05$)

Chapter 5: Discussion

Intrinsic and extrinsic hand muscles have been reported to differ in function (Long et al. 1970). It is thus expected that the changes in function is reflected by muscle structural changes. Previous studies have measured force producing capabilities at the fingers (Shinohara et al. 2003a; Shinohara et al. 2004), wrist and elbow (Viitasalo et al. 1985) to examine the aging-related changes in IM and EM. Conflicting reports regarding to the change in muscle structure can be attributed to the varying techniques used to examine IM and EM. Viitasalo et al. identified IM force as those contributing to handgrip strength and EM as those contributing to elbow flexion. Shinohara et al. on the other hand identified IM as those contributing to forces produced at the proximal phalanx while EM force as forces produced at the DP. This study followed a similar working definition as Shinohara and colleagues (Shinohara et al. 2003a).

This is one of the first studies to provide evidence of sarcopenia in muscles responsible for hand and finger force production, in the context of aging-related decrease in both muscle size and strength. This study examined the aging-related difference in hand muscle size and the relationship between muscle size and hand dexterity. Muscle volume and cross sectional area of the extrinsic and intrinsic hand muscles were calculated with MRI data. Hand strength, finger interaction measures and overall hand dexterity was measured, compared between groups and correlated to muscle size. Overall, the results supported the hypotheses that 1) intrinsic muscle size show a greater aging-related difference than extrinsic hand muscles 2) measures of hand dexterity show a general aging-related decrease 3) muscle size is related to the aging-related differences in various measures of hand dexterity.

Muscle Size

This study consistently showed young subjects have greater intrinsic and extrinsic muscle sizes than elderly subjects. This trend is similar to previous findings which showed young subjects having greater muscle size than elderly subjects in the upper extremities (Rice et al. 1989; Klitgaard et al. 1990; Gallagher et al. 1997). The lesser muscle size in elderly adults is indicative of sarcopenia occurring at the muscles controlling the hands and fingers.

The extrinsic hand muscles were 6.0-6.7 times larger than intrinsic hand muscles. This is not surprising as previous studies have suggested that extrinsic hand muscles are for larger force generation and intrinsic hand muscles are mainly for smaller force attenuation (Long 1965; Long et al. 1970). In other words, larger muscles functions to produce greater force than smaller muscles.

The aging-related difference in intrinsic muscle size was more pronounced (25.1%) than extrinsic muscles (15.0%). No study has examined the aging-related difference on hand muscle sizes thus far. Previous literature has addressed sarcopenia, specifically aging related atrophy, by examining the function of specific hand muscle or muscle groups. Shinohara et al (2003) argued have argued through strength measurements that intrinsic hand muscles are affected more with aging than extrinsic muscles. Another reported sarcopenia in the interossei by observing hand postures (Carmeli et al 2003). The results here support the notion that the intrinsic hand muscles undergo sarcopenia at a greater rate than extrinsic hand muscles. It can be interpreted that distal hand muscles were more affected with age than proximal muscles.

The extrinsic muscle volume determined were within one standard deviation reported (538.0 ± 239.5 cm^3) from imaging (Holzbaur et al. 2007b) and cadaveric studies (540.9±260.4cm^3) (Chao et al. 1989). This is one of the first studies to examine intrinsic muscle size with medical imaging, however the reported muscle volumes were similar to those reported from the (76.2±35.9 cm^3) cadaveric studies (Chao et al. 1989). Differences, between this and previous studies, in muscle size can be attributed to the fact that men and women were both examined in the previous studies while this study only examines women. Men are known to have significantly greater muscle sizes than women (Frontera et al. 1991; Tracy et al. 1999; Janssen et al. 2000; Holzbaur et al. 2007b). This can also account for the relatively smaller standard deviation of this study as compared to the previous studies, which lumped men and women in one group. Another factor which can account for the difference is the age of the subjects or specimens used. The human age of the cadaveric specimens were not reported (Chao et al. 1989) while the imaging study (Holzbaur et al. 2007b) reported strictly young adults.

The results for muscle volume and cross sectional area were similar. Reporting cross sectional area (CSA) may be as important as muscle volume. CSA does not consider the muscle fiber length. During muscle contraction, muscle length does not play a significant role in muscle function, as the amount of force generated depends on the number of muscles fibers aligned in parallel, as determined by CSA, than fibers aligned in serial, as determined by volume. Studies have reported that the decrease in CSA is likely the main contributing factor to the aging-related decrease in strength (Young et al. 1984; Klitgaard et al. 1990; Phillips et al. 1992; Jubrias et al. 1997; Macaluso et al. 2002). Measuring MV showed a significant interaction while CSA did not. MV considered the size of the muscle along the whole limb while CSA used one slice to represent the whole forearm or hand. Since it has been suggested (Shinohara et al. 2003b) that proximal and distal muscles show differences in aging-related decreases of strength, distal muscles could also experience greater size decreases than proximal muscles or even disproportionate intra-muscle atrophy may occur. Thus, measuring CSA may not be as sensitive as MV. However, the CSA slice includes the major flexor muscles while MV includes all muscles in the hand and forearm.

The results reported the EM CSA as the slice representing the greatest muscle area in the forearm data set (Klein et al. 2002). On average, the largest EM slice for the subjects in this study was 20% of the distance from the proximal ulna. The EM CSA was also examined by taking the slice representing 20% distance from the most proximal portion of the ulna. This EM CSA determined from this fixed anatomical location revealed similar results to the slice representing the greatest muscle area. For the IM CSA, only the fixed slice was taken. Taking MV and CSA together, the results support the hypothesis where elderly were expected to have an aging-related decrease in muscle size and IM show a greater aging-related decrease than EM.

The scanning parameters were established to mimic previous studies that imaged extrinsic hand muscles (Eng et al. 2007; Holzbaur et al. 2007b) while minimizing the scan time to allow for subject comfort. As a result, this study does not allow the comparison of specific muscles. This can be accomplished by manual segmentation of each image of the forearm or hand. However, the scan time to achieve appropriate quality for individual muscle segmentation would increase the scan time from 6-7 minutes per scan to almost thirty minutes. Elderly adults already reported slight discomfort with the 6-7 minute scan. Sub-millimeter slices with no gaps between slices were used to account for the small extrinsic and intrinsic muscles. Having larger slice thicknesses or adjacent slice gaps would increase the interpolation required and random error. Studies examining the lower extremity have already determined that taking three representative slices in the femur can adequately represent the whole muscle volume (Tracy et al. 2003). However, no study has been done in the upper extremity to confirm this yet. Also having one examiner identify over 30 muscles in about 350 images per subject is not an efficient way to analyze images. The procedures established in this study are extremely user-friendly such that individuals new to image processing can follow and achieve similar results. This study initially incorporated male and female subjects but preliminary data showed female subjects having a smaller inter-sex variability in volume and strength volume as compared to males. Thus only female subjects were incorporated for greater homogeneity within groups.

Strength

Strength

Strength is a measure often employed by researchers to examine the function of muscles (Hyatt et al. 1990; Ivey et al. 2000). Maximal forces were recorded at the DP and PP with the underlying disposition of varying intrinsic and extrinsic muscle activity at the two sites (Chao et al. 1976; An et al. 1979; Li et al. 2000). The forces produced at the distal phalanx elicit near maximal force production by the extrinsic hand muscles and minimal force produced by the intrinsic muscles (Harding et al. 1993; Li et al. 2000). Thus extrinsic hand muscles are considered the focal force generators at the distal phalanx. On the other hand, forces produced at the proximal phalanx have been suggested to be primarily contributed by the intrinsic hand muscles.

Peak torque produced by the elderly subjects was smaller than young subjects at both sites. This result is consistent with many previous findings that elderly subjects have lower strength levels at the hand, whether for pressing (Shinohara et al. 2003a; Oliveira et al. 2008a), pinching (Imrhan and Loo 1989), or prehension (Shim et al. 2004). The aging-related difference in torque production by EM at the DP was 11.8% versus 32.3% by IM at the PP. Only the aging-related difference in torque production by IM was significantly different. These results support the hypothesis that the aging-related difference in IM strength is greater than the EM strength. A previous study which has also examined strength of the intrinsic and extrinsic muscles also reported a greater difference in pressing force by the IM as compared to the EM (Shinohara et al. 2003a). The difference in percentage is similar as well. This also substantiates reports that distal muscles are affected more by age than proximal muscles (Viitasalo et al. 1985; Christ et al. 1992; Era et al. 1992; Shinohara et al. 2003a). However, Doherty (2003) reported that in general, strength in the proximal and distal muscles of the upper and lower extremities experience a similar rate of sarcopenia. The decrease in torque production can be explained by a decrease in muscle size. It has been suggested that the loss of muscle size and muscle fiber loss were primarily responsible for the aging-related decrease in muscle strength (Doherty 2003). Additionally, muscle size has been reported to be directly associated with strength production (Maughan et al. 1983; Frontera et al. 1991). The finding that both IM strength and size undergo a greater aging-related decrease it is possible that the greater sarcopenia of the IM contributes to the greater aging-related difference in strength of the IM.

Taken with the results on differences in muscle volume, the data allows for the assertion that the intrinsic muscles show a greater relative decrease in size and strength with age as compared with the extrinsic muscles. This supports the notion suggested by previous studies (Viitasalo et al. 1985; Christ et al. 1992; Era et al. 1992; Shinohara et al. 2003a) that have examined strength measures of the two muscle groups.

Normalized strength (NS), can be considered a more meaningful indicator of muscle function than strength alone (Roubenoff and Hughes 2000). MVT_{norm} was determined for both the EM and IM. The results showed that both the EM and IM did not significantly differ between young and elderly subjects. However MVT_{norm} of IM was 13.4% less in elderly subjects. Other studies have reported a significant aging-related decrease in MVT_{norm} of the elbow flexors, (Klein et al. 2001), and knee extensors (Frontera et al. 1991; Lynch et al. 1999; Macaluso et al. 2002). The different results found in this study as compared to previous studies can be attributed to different muscles being examined. Previous studies mentioned have examined large muscles which often undergo sarcopenia as a result of overall physical inactivity (Evans 1995; Porter et al. 1995; Roubenoff and Hughes 2000; Vandervoort 2002). However, muscles for the hand and fingers are constantly used in everyday manipulative tasks, such as eating and bathing, despite reports of subjects being physically inactive. It is possible that the similar normalized strength of the EM and IM in the current study, across age groups, can be attributed to the lack of disuse or immobility of the hands and fingers in healthy elderly adults. Lynch et al (1999) also reported that for females, the aging-related decline in MQ was greater in the lower extremity than the upper extremity.

Finger Dependence

Finger dependence, as measured by enslaving (Zatsiorsky et al. 1998; Zatsiorsky et al. 2000; Oliveira et al. 2008a; Shim et al. 2008), can be important in performing common tasks such as typing and dialing telephones. Despite being statistically insignificant, finger dependence by the EM was less (22.9%) in elderly subjects as compared to young subjects. Finger dependence by the IM was slightly higher (12.1%) in elderly adults. The results showed a similar trend with previous studies where elderly adults showed lower finger dependence by the EM (Shinohara et al. 2003a; Oliveira et al. 2008a). The greater dependence by elderly IM differs from previous reports. Shinohara et al (2003) reported IM enslaving with males and females grouped together, and female enslaving with the young and elderly grouped together. The current study however, considered females and reported the young and elderly separately. This may account for differences in IM finger dependence.

Force Control Accuracy and Synergy

Force control accuracy is an important determinant of hand dexterity and performance of ADLs. Previous studies have used various methods to examine force control accuracy, including pressing (Shinohara et al. 2004; Oliveira et al. 2008a), pinching, and prehension (Kinoshita and Francis 1996; Shim et al. 2004). This study employed multi-finger pressing force control accuracy since multiple fingers are often used in everyday activities and the pressing setup allows the experimenter to identify force generation from the intrinsic and extrinsic hand muscles (Li et al. 2000; Shinohara et al. 2003a). Despite being statistically insignificant, elderly adults exhibited 26.3% and 31.8% decreased force control accuracy at the DP and PP, respectively. This suggests a trend of decreased force control accuracy in elderly subjects at both intrinsic and extrinsic muscles, when compared to young subjects. The absence of a significant difference in force control accuracy and multi-finger synergy can be attributed to the relative ease of the task. Subjects were asked to produce a constant force that was 20% of their maximum voluntary isometric force for 10 seconds. Everyday activities often require forces greater than 20% of MVC thus subjects were easily able to achieve this level of force. The level of required force can be increased to elicit the difference. Keogh (2006) reported a more pronounced aging-related difference in force control accuracy as the force production task becomes more challenging. Shinohara et al 2003 used 40% of the subjects' MVC. However the 20% of MVC threshold was previously used a study we conducted (Oliveira et al. 2008a) and the results showed a worsened ability of control accuracy with a constant submaximal force at the DP.

Delta Variance is a measure of multi-finger synergy. The results showed a nearly identical multi-finger synergy level between young and elderly subjects. The difference was less than 3%. A previous study showed a difference in force and moment synergy between young and elderly subjects (Shim et al. 2004; Shinohara et al. 2004). This difference was more pronounced during the increasing portion of the force template and limited during the constant force portion. This study required subjects to produce a constant force and delta variance was examined across a 7-second period of constant force production. A dynamic force template may elicit the aging-related difference in multi-finger synergy more readily since elderly subjects show decreased anticipatory synergy adjustments (Olafsdottir et al. 2007) to the changing force and lower adaptive ability to control changing forces (Sosnoff et al. 2004). Similar to the explanation in force control, the task may be not adequately challenging for healthy adults. The results of the current study concurs with the previous finding where despite young subjects showing a slightly higher trend of synergy, there was no significant difference between the groups during constant force production.

Hand Dexterity

Pegboard and Jebsen Taylor Hand Function Test. Performance on both the grooved pegboard and Jebsen Taylor Hand Function test greatly decreased in elderly subjects. Performance in both measures was determined by taking the inverse of time to completion. On the grooved pegboard, young subjects performed 30.0% better than elderly subjects. When examining the time to completion, the average time for young subjects was similar to the results of right-handed young women in another study (Schmidt et al. 2000). Generally, individual tasks on the Jebsen Taylor Hand Function test matched (results not shown) the previous reported results in young (Jebsen et al. 1969) and elderly subjects (Hackel et al. 1992). The decrease in hand dexterity is not surprising considering many previous studies have already reported various deficits in hand dexterity in elderly subjects, ranging from- decreases in strength (Metter et al. 1998), hand posture stability (Potvin et al. 1980), tactile sensitivity (Ranganathan et al. 2001), and difficulties in movement initiation (Ranganathan et al. 2001).

Regression Analysis

Finger dependence and strength. Regression analysis showed a positive trend between finger dependence and normalized strength. This positive relationship agrees with previous studies reporting that finger dependence is directly related to finger strength (Shinohara et al. 2003a; Shim et al. 2008). Strength can be an indicator of finger dependence. This supports the strength dexterity trade-off hypothesis since finger dependence is often considered a measure of finger dexterity (Shinohara et al. 2003b). There however are additional measures of finger dexterity to consider since relatively few tasks demand individual finger control as compared to multi-finger control.

Force synergy and strength. Our results also showed a significant correlation between force synergy and normalized strength by EM and a positive trend by IM in young subjects. Our previous study examining strength and multi finger synergy also reported increases in strength accompanied by an increase in force stabilizing synergy (delta variance) (Shim et al. 2008). This suggests that strength and multi-finger force synergy in young subjects are not mutually exclusive and supports the strength-dexterity equivalent hypothesis.

Hand dexterity and muscle size We found a significant negative correlation between JTHF performance and extrinsic muscle CSA in young subjects and positive trend between JTHF performance an EM CSA in elderly subjects. A previous study (Lee et al. 2009) examined the upper limb muscle CSA in a child with cerebral palsy and found that strength training induced increases in CSA is associated with motor improvement, specifically on the JTHF test. Taken together, it is believed that the positive trend of extrinsic CSA and JTHF performance is present in individuals with hand dexterity deficits but not in those with normal hand dexterity.

Study Limitations and Implications for Future Studies

There were uncontrolled factors that may have affected the results but were unrealistic to control. There have been reports that strength in the upper (Gauthier et al. 2001) and lower (Wyse et al. 1994) extremity differs depending on the time of day subjects are being tested. Since many subjects were working full time or full time students, the test was administered based upon individual availability. The non-uniform testing time for subjects may contribute to some of the differences between subjects. A standard seat and table was used to test the subjects. Since subjects varied in height, the subject's arm position and perception of the computer screen varied slightly. The amount and type of food consumption has been shown to affect strength. Aging is often associated with lowered food intake. Studies have shown this anorexic effect to impact the progression of sarcopenia (Morley 2001b; Morley 2001a). Also, ingesting half the recommended dietary levels of protein can lead to significant decreases in strength (Castaneda et al. 1995)

The maximum strength recordings were performed under the premise that the focal force generators at the DP are the extrinsic muscles and the focal force generators at the PP are the intrinsic muscle (Landsmeer and Long 1965; Long 1965; Li et al. 2000; Shinohara et al. 2003a). There however, is the possibility that pressing with the DP can recruit both the intrinsic and extrinsic hand muscles. Thus some of the aging-related differences in torque production can be accounted for by other muscle groups. Also, many factors, in addition to muscle size, may contribute to changes in hand dexterity and strength. Neural properties (Morse et al. 2004; Morse et al. 2005) such as a drop in the number of motor units (Sica et al. 1974; Patten et al. 2001), an increase in the size of the motor units and a general slowing down of muscle properties (Chan et al. 1998) was often a contributing factor to the aging-related decrease in strength. The reduction in the specific tension of single muscle (D'Antona et al. 2003; Degens 2007) fibers may also explain the decrease in strength.

The pressing protocol measured forces in flexion, however, the automated segmentation technique did not separate individual muscles or group muscles by function. Rather the muscles were separated by location as described by previous studies (Shinohara et al. 2003a). A future study can group muscles according to function and cross correlate the muscles to function. This has been done in the elbow, shoulder and wrist (Holzbaur et al. 2007a) but not in the fingers. Future studies should attempt to quantify individual muscles contributing to hand-finger function.

The automated segmentation in MRI analysis used to quantify muscle volume takes the grand mean of each subject's intensity ranges to remove any biases during the segmentation. The authors recognize that there's a possibility that changes in muscle configuration and composition with age may cause the intensity of muscle to shift from the intensity of muscle for younger adults. For example, studies (Heymsfield et al. 1993; Heymsfield et al. 2000) have suggested that the hydration levels of fat-free mass (FFM) slightly increases with age. This difference will cause can cause mis-estimation of muscle size. However other studies (Lesser and Markofsky 1979; Chumlea et al. 1999; Visser et al. 2003) have suggested no significant increases in the hydration of FFM. Since the literature is currently inconclusive, the grand mean of the individual intensities were used to report the final muscle volume measurements. Additionally, the automated segmentation technique grouped different tissues by intensities. If a tissue type showed the same intensity as muscle, it was considered as muscle. Based on visual inspection of each subject's hand and forearm volume, there were minimal visible rogue objects. With a stronger magnet, MR images can be obtained with a shorter time and better quality. Improved quality images can allow for the quantification of muscle functional groups or even individual muscles. The ability to quantify individual muscles or even functional muscle groups in the hand can provide greater insight as to the specific muscular atrophy contributions to changes in hand dexterity and strength. A preliminary study using cadaveric specimens to quantify individual intrinsic muscles can examine the quantifiability of individual intrinsic hand muscles with medical imaging.

Since previous studies provided evidence suggesting intrinsic muscles as being primarily responsible for fine motor control. We found a relationship of decreased intrinsic muscle volume, strength and overall hand dexterity with age. This understanding gives rise to the questions of whether specific training of the intrinsic hand muscles can improve fine motor control and whether this improvement would be greater than training only the extrinsic hand muscles. We propose focusing strength training intervention or manual dexterity training where individuals can focus on improving the dexterity of the intrinsic hand muscles. A study designed to specifically train the intrinsic hand muscle may provide greater insight as to how great a role intrinsic versus extrinsic muscles play in fine motor control. A number of devices available for developing hand muscle strength was created without the understanding the disproportionate amount of aging-related decrease in intrinsic hand muscles. A previous study in young adults has already shown that strength training can improve force and moment control. The age related changes in hand muscle structure and dexterity can drive the direction of future intervention research to specifically target deficits elderly adults may encounter.

The current study found that multi-finger synergy, finger dependence and force control were statistically identical between young and elderly subjects. Despite being equivalent, there were similar trends as compared to previously reported studies for all three measures. This can be attributed to the limited sample size of the study and the high operating costs of MRI acquisition. It is expected that with more subjects, the difference between young and elderly subjects will be more pronounced and regression analysis will show more significant correlations.

Chapter 6: Conclusion

This study found aging-related decreases in muscle size, muscle strength, hand dexterity. Furthermore, intrinsic muscles showed a greater aging-related decrease in volume and strength as compared to the extrinsic muscles. This finding provides evidence that distal muscles in the upper extremity were more affected by sarcopenia than proximal muscles. When examining relationships, muscle strength was correlated to multi-finger synergy and finger dependence. Also, muscle size was related to hand dexterity. This supports the strength-dexterity equivalence hypothesis.

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