MUSCLE TO BONE RELATIONSHIP IN THE FOREARM AT MIDLIFE

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By

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ABSTRACT

Larger and stronger muscles are positively associated with bone strength in the growing skeleton; however, less is known about the role of muscle properties on bone strength later in life. The primary objective of this study was to examine the relationship between muscle cross sectional area (MCSA), muscle force and rate of torque development (RTD) with bone strength indices (bone strength index (BSI) and strength strain index (SSI)) in the radius of healthy middle-aged adults. All bone and muscle measurements were determined in the non-dominant forearm in a sample of 40 healthy adults (23 men, 17 women: mean age 49.5, SD 2.3 yrs). Peripheral quantitative computer tomography (pQCT) was used to scan the distal and shaft sites of the radius bone in the forearm. MCSA was determined from the forearm shaft scan. Forearm muscle force was measured by hand grip dynamometry and RTD was obtained from isometric wrist flexion from an isokinetic dynamometry protocol. Hierarchical regression analyses were used to identify whether muscle properties (MCSA, grip force, and RTD) independently predicted radius bone strength indices (BSI and SSI), after adjusting for the confounders of sex, height and weight. Steps of the regression models that included sex, height, weight and a muscle property explained between 66% and 71% of variance in distal radius BSI and between 74% and 78% variance of estimated bone strength (SSI) at the shaft site (all steps $p<0.001$). MCSA explained a significant amount of variance in BSI ($R^2=0.08$; $p<0.01$) and SSI ($R^2=0.04$; $p<0.05$) at the radius. Grip force was also a significant predictor of SSI (R2=0.05; $p<0.01$) but not distal radius BSI ($R^2=0.03$; $p=0.07$). Conversely, RTD explained a significant amount of variance in bone strength at the distal radius ($R^2=0.04$; $p<0.05$), but not at the shaft ($R^2=0.01$; $p=0.17$). These cross sectional findings support the

theory that regional muscle size, force, and rate of torque development are related to estimated bone strength in the forearm at midlife. Further research should focus on targeted interventions to help determine which muscle property elicits a greater osteogenic response to optimize bone strength at distal and shaft sites of the radius.

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LIST OF ABBREVIATIONS

aBMD	Areal Bone Mineral Density
BMC	Bone Mineral Content
BMD	Volumetric Bone Mineral Density
BMU	Bone Multicellular Unit
BSI	Bone Strength Index
CoA	Cortical Area
CoD	Cortical Density
CV	Coefficient of Variance
DXA	Dual Energy X-ray Absorptiometry
MCSA	Muscle Cross Sectional Area
MES	Minimum Effective Strain
MVC	Maximum Voluntary Contraction
pQCT	Peripheral Quantitative Computed Tomography
PVE	Partial Volume Effect
RTD	Rate of Torque Development
SGDS	Saskatchewan Growth and Development Study
SSI	Strength Strain Index
ToA	Total Area
ToD	Total Density

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INTRODUCTION

The risk of wrist fracture increases sharply after the age of 55, especially in women (Larsen & Lauritsen, 1993). Muscle properties, such as size and strength, are positively associated with bone strength in the growing skeleton (Kontulainen, Sievanen, Kannus, Pasanen, & Vuori, 2002; Macdonald et al., 2005; Macdonald, Kontulainen, Petit, Janssen, & McKay, 2006; Schoenau, Neu, Beck, Manz, & Rauch, 2002; Schoenau, Neu, & Manz, 2004); however, less is known about the role of muscle properties on bone strength later in life. It is hypothesized that larger and stronger muscles elicit higher strains on bone than small or weak muscles, which in turn leads to adaptations within the bone tissue that increase its resistance to fracture (Frost, 1987; Burr, 1997). Therefore a possible strategy of optimizing fracture prevention among aging adults is to explore the muscle properties that are related to bone strength in mid-adulthood to improve bone strength prior to the period of increased risk of fracture (Owen, Melton, Johnson, Ilstrup, & Riggs, 1982).

Bone strength, or its ability to resist fracture, can be described as the product of i) bone size and shape (bone geometry); and, ii) its material distribution (Martin et al., 1998). A stronger bone is therefore larger in cross section and has more mass than a weak bone. Although bone tissue is influenced by a plethora of factors, including genetics, nutrition, and hormone status, muscle contractions result in the largest physiological strains on bone tissue (Burr, 1997; Martin et al., 1998). The influence of muscle contractions on bone strength is particularly important because of the modifiable nature of skeletal muscle. Training regimens can be designed to increase muscle size

(hypertrophy), muscle strength (the ability for a muscle group to contract and generate force), and muscle power (the rate at which a muscle force is generated). Frost's (1987) mechanostat theory hypothesizes that bone tissue undergoes structural adaptations in response to external loads to maintain material strains within an acceptable range. Once external loads exceed a predetermined minimum effective strain (MES), a physiologic response in the bone tissue facilitates adaptation, whereas bone that is exposed to loading below the MES fails to initiate an adaptive response in the bone tissue (Frost, 1987). This theory is supported by research that has observed no osteogenic response to gravitational forces in the lower limb, yet significant osteogenic effects of high or odd impact loading as would be experienced during hurdling or soccer, respectively (Dalsky et al., 1988; Heinonen et al., 1996; Nikander, Sievanen, Uusi-Rasi, Heinonen, & Kannus, 2006a).

Animal models have demonstrated bone elicits a greater response to magnitude of loading rather than repetitious low-intensity loading (Rubin & Lanyon, 1985). Furthermore, peak strain rates have also demonstrated a greater osteogenic response than low or moderate strain rates (Lanyon & Rubin, 1984; Mosley & Lanyon, 1998). As skeletal muscle contracts, dynamic strains are not only localized at sites of musculo-tendinous origin and insertion but are also distributed along the shaft and appear to be the primary stimulus of bone adaptation (Burr et al., 1996; Turner, 1998). Muscle power serves as an indicator of how quickly a muscle can produce force, or the efficiency of a contraction. The association of peak power of the lower extremity and tibia bone geometry has been previously examined in a cross sectional analysis of elderly women (Ashe, Liu-Ambrose, Cooper, Khan, & McKay, 2008). The results indicated that muscle power is a significant predictor of bone strength, explaining up to 8.9% of variance in

estimated bone strength at the shaft site. Currently, there is no known literature demonstrating a relationship between muscle power and bone strength at the radius. The radius is a clinically important site to study because of the high incidence of reported fracture, particularly in adults 65 years of age and older who are more susceptible to experiencing falls (Hausdorff, Rios, & Edelber, 2001; Cummings & Melton, 2002; Kannus, Uusi-Rasi, Palvanen, & Parkkari, 2005).

Analysis of bone and muscle *in vivo* has been facilitated by development of precise non-invasive peripheral quantitative computer tomography (pQCT). This imaging technique permits estimation of long bone strength indices, which consider bone size, shape and material distribution from a single tomographic slice. Two bone strength indices are commonly employed to estimate strength: strength strain index in torsion (SSI_p) and bone strength index in compression (BSI_c). SSI_p, proposed by Schiessl et al. (1996a) considers density distribution and represents a long bone's ability to resist torsional stresses in the normal plane (Kontulainen et al., 2008). BSI_c, the product of total area and squared total density of the bone cross section, estimates bone strength at the distal site of long bones, which are primarily loaded in compression (Ferretti, Capozza, & Zanchetta, 1996; Kontulainen et al., 2008).

The association between muscle properties and bone parameters has been assessed in both upper and lower extremities. Muscle cross sectional area (MCSA), an adequate surrogate of muscle force (Ikai & Fukunaga, 1968; Maughan, Watson, & Weir, 1983), was associated with estimated bone strength in children (Macdonald et al., 2006; Remer et al., 2003; Schoenau, Neu, Mokov, Wassmer, & Manz, 2000) and adolescents (Schoenau et al., 2004). The most obvious limitation of MCSA is its failure to assess the

functional abilities of skeletal muscle, such as dynamic force generation and power output. Muscle force assessment by hand-held grip dynamometry has demonstrated a positive association with estimates of bone strength at the forearm (Hasegawa, Schneider, & Reiners, 2001; Kaji et al., 2005; Schoenau, 1998); however, none of these studies have focused on healthy individuals in mid-adulthood. Evaluating the relationship between muscle properties and bone strength at the radius is the first step in determining whether a training intervention could be beneficial in midlife to reduce the rate of fractures observed in later adulthood.

This cross sectional study aimed to assess the relationship between muscle properties and estimated bone strength at distal and shaft sites of the radius in healthy adults, after accounting for the influence of sex and body size. It was hypothesized that MCSA, grip force and RTD will each be significantly related and independently predict estimated bone strength.

1.0 REVIEW OF LITERATURE

In this chapter I present the key concepts of physiology, strength and adaptation of bone and skeletal muscle to provide a framework of knowledge necessary to understand associations between the tissues. The review of the literature is intended to provide background information pertaining to musculoskeletal strength measurement techniques and tissue adaptations to mechanical loading.

1.1 Bone Physiology

Bone is a dynamic tissue continually regenerating as a result of environmental influences and metabolic demands (Dempster, 2006). Bones serve many critical functions: systemic mineral homeostasis, hematopoesis, a protective barrier for vital organs, and structural support to facilitate precise movements and locomotion (Dempster, 2006). The material composition of bone reflects its need to be stiff enough to resist deformation under mechanical loading, yet sufficiently flexible to absorb energy when tension or compression stresses are applied. Stiffness is attributed to the matrix of crystalline calcium hydroxyapatite, the principle inorganic compound of bone consisting of calcium and phosphate (Robey & Boskey, 2006). Type I collagen, the predominant organic material of bone, provides bone with flexibility (Rubin & Rubin, 2006). The proportion of organic and inorganic compounds of bone is critical, since imbalance could compromise its structural integrity and systemic mineral status (Rubin & Rubin, 2006).

Long bones are essentially hollow rods and are composed of two types of calcified bone tissue: cortical (also called *compact* bone) and trabecular (also called *cancellous* bone). Classified by their porosity and microstructure, cortical bone encloses the medullary cavity and forms the dense, external portion of the long bone shaft

(Dempster, 2006). Trabecular bone is a more porous material composed of an intricate network of vertical and horizontal plates (Martin et al., 1998). Distal regions of long bones are characterized by an increase in trabecular bone, thinning cortical shell, and absence of the medullary cavity.

Cortical bone is characterized by two distinct surfaces: periosteal and endosteal. The periosteum covers the outermost perimeter and bone "added" here (increasing its diameter) is the most effective way to increase the bone's resistance to bending and torsion (Robling, Castillo, & Turner, 2006). The endosteum is the inner surface of cortical bone that lines the medullary cavity. Both periosteal and endosteal surfaces remain metabolically active throughout the lifespan as a consequence of bone remodeling, yet periosteal apposition is suppressed in adults due to the deafened response mature bone exhibits to biomechanical loading (Robling et al., 2006). The structural units of cortical bone are cylindrical osteons, which are comprised of a Haversian canal surrounded by concentrically organized fibers along the long axis of the bone (Bonewald, 2008). This arrangement is optimal for resisting deformation from torsion and compression loading along its longitudinal axis (Martin et al., 1998).

There are three types of bone cells – osteoclasts, osteoblasts, and osteocytes. Osteoclasts are multinucleated, phagocytic cells that secrete enzymes to dissolve the bone matrix (Bonewald, 2008). Osteoblasts are bone cells found on the outer surfaces and within cavities of bone. They are responsible for producing osteoid, which is the predominant organic component of collagen and assists in bone apposition (Dempster, 2006). Osteoid is a cartilage-like material where calcium salts precipitate (Dempster, 2006). Osteoblasts that become entrapped in the osteoid are called osteocytes. Osteocytes

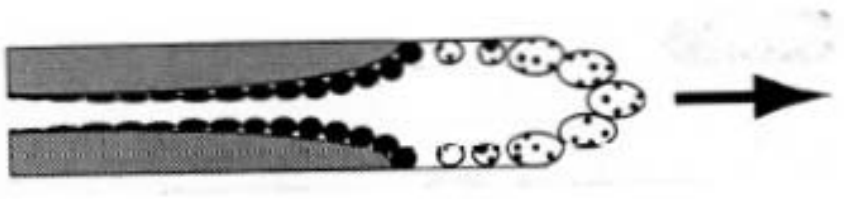
are mature bone cells and the most numerous cell type composing the adult skeleton (Bonewald & Johnson, 2008). They were once thought to be quiescent, but have demonstrated roles in monitoring mineral content of surrounding osteoid and responding to mechanical strains that are important for bone remodeling (Lanyon, 1993).

1.1.2 Modeling and Remodeling

Bone modeling is a process that facilitates bone growth and adaptations in bone strength by increasing bone diameter and accumulating additional mass (Forwood, Owan, Takano, & Turner, 1996). Remodeling is the process whereby basic multicellular units (BMUs) replace old pockets of bone with new bone to maintain bone mass and strength (Karsenty & Elefteriou, 2008). The BMU links microscopic cellular activities to the entire bone macromorphology. It is responsible for the coupled function of new bone deposition by a team of several hundred osteoblasts and old bone removal (resorption) by a few active osteoclasts (Karsenty & Elefteriou, 2008).

There are three principle stages to the remodeling process: activation, resorption, and formation (Parfitt, 1979). Activation is initiated by metabolic or mechanical stimuli and signals for cellular recruitment of the BMU to begin resorbing bone at a specific location (Robling et al., 2006). As depicted in Figure A, osteoclasts are the leading cells of the BMU that excavate an intracortical tunnel by adhering to the packet of old bone, which stimulates synthesis and release of acidic enzymes (Robling et al., 2006). Leaving only mononucleated cells in its wake, the BMU now creates a matrix high in sulfur and mineral-deficient where several osteoblasts remain and synthesize unmineralized bone (osteoid) (Robling et al., 2006). Once the final stages of osteoid deposition are complete, a new osteon with a central Haversian canal is formed and awaits mineralization (Robling

et al., 2006). In this fashion, the BMU ensures that old bone tissue is removed and new material is laid down to maintain structural integrity of the whole bone (Parfitt, 2000).



direction of BMU

Formation……..…..←…….Resorption…←…Activation

Figure A. Schematic representation of BMU remodeling stages. The large multinucleated cells on the right are osteoclasts, which are activated from precursor cells at the point of BMU origin. The small black cells on the left are osteoblasts, which appear around the tunnel periphery and fill in the excavation made by osteoclasts. The direction of the BMU always follows the same sequence in normal bone remodeling. Adapted from Martin et al. (1998)

In adulthood the rate of remodeling slows down and bone adaptation strives to conserve bone strength in response to environmental and physiological stimuli (Seeman, 2003). When the rate of bone resorption exceeds bone formation there is a resulting net loss in bone material. In aging adults, the periosteal surface of bone results in a positive bone balance (or net gain) compared with the endosteal surface that experiences an overall net loss of bone material (Dempster, 2006). The outcome of the coupled positive and negative bone balance is an enlarged circumference and an enlarged medullary cavity with increasing age (Dempster, 2006). This modification in bone geometry becomes important in resistance to fracture, since geometry (size and shape) is a determinant of bone strength at both distal and shaft sites of long bones (Martin et al., 1998).

1.2 Mechanostat

It was in 1867 that Culmann and Von Meyer (1867) postulated that the trabecular structure of bone tissues coincided with principle stress directions (von Meyer, 1867). This is the earliest credited notion that structural adaptation occurs with mechanical loading. This idea was further developed by Wolff who postulated that bone structure would change if the mechanical stress directions were altered (Wolff, 1892). Now referred to as Wolff's Law, this theory has helped lead to the development of the mechanostat hypothesis. Advanced by Frost in 1987, the mechanostat hypothesis suggests that bone undergoes structural adaptations in response to external loads in attempts to maintain strain levels within an acceptable range (Frost, 1987). This is currently the most widely established hypothesis of bone adaptation, and with it the notion that muscular forces generate the highest levels of physiological strain on the skeleton (Frost, 1988; Genant, Geusens, Rosen, Zhao, & Jiang, 1999). Although the mechanostat bone response is governed by biomechanical usage, it can be modified by several modulators, including nutrition, environment, and hormones (Frost, 1987).

The mechanical loading that drives osteogenic adaptations of bone strength can be classified into minimum effective strain (MES) "windows" based on the strain levels achieved by the bone tissue (Figure B) (Forwood & Turner, 1995). Strain magnitude dictates and stimulates the remodeling, modeling, or repair responses of bone tissue (Frost, 1987). Likewise, strains not reaching the remodeling MES threshold (disuse) fail to elicit a response and the result is resorption rate exceeding remodeling rate, which leads to a net loss of bone mass and subsequently diminished bone strength (Frost, 1987). On the other end of the spectrum, exposure to high magnitude strains in the pathological

window can lead to eventual bone failure (fracture) due to microcracks coalescing, as in repetitive loading (Burr et al., 1998; Matheson et al., 1987)

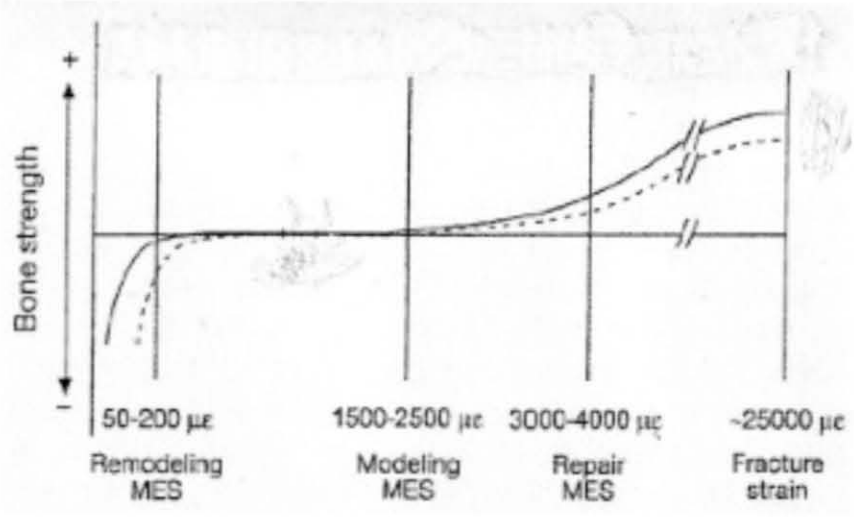


Figure B. A schematic representation of Frost's mechanostat hypothesis. The solid curve reflects "normal" conditions of minimum effective strain (MES) windows and microstrain (με) ranges hypothesized to elicit osteogenic responses. The dash line represents the estrogen deficient hypothetical strain curve. Adapted from Suominen (2006)

Bone tissue senses and responds to peak strains and strain rates resulting from the dynamic loading of muscle contractions, the largest physiological loads on bones (Bonewald & Johnson, 2008; Jee, 2000; Martin et al., 1998). The osteogenic response to mechanical loading seems to be site specific, thus bone will be added where strain distribution is the greatest (Robling, Hinant, Burr, & Turner, 2002). However, the beneficial responses of bone to mechanical loading are dampened with advancing age (Rubin, Bain, & McLeod, 1992; Turner, Takano, & Owan, 1995). Declines in bone response associated with aging have triggered research focus in the direction of new types of loading that may be sufficient and safe to elicit a bone response in adults.

1.3 Peripheral Quantitative Computer Tomography

Peripheral QCT is a non-invasive research imaging tool capable of capturing a cross sectional image of bone and muscle tissues at several sites of the appendicular skeleton, such as the forearm or lower leg. The emergence of pQCT in the early 1990's permitted analysis of whole bone cross sectional geometry (i.e. bone size and shape), distribution of trabecular and cortical bone, and aspects of bone material properties (i.e. volumetric bone mineral density) using an X-ray source (Khan et al., 2001). Volumetric bone mineral density (BMD, mg/cm^3) of cortical and trabecular bone is accounted for by considering the porosities of the tissues and their normal material density ($1200mg/mm^3$). The ability of pQCT to independently analyze tissues of high and low density is particularly important, especially when distinguishing between cortical and trabecular bone or isolating skeletal muscle from bone (Genant, Fuerst, Faulkner, & Gluer, 1996).

The capabilities of pQCT are not without limitation. pQCT scans are limited by their slice thickness. Although in-plane resolution or voxel (pixel) size selections for the scan range from 0.1mm to 0.8mm, the slice thickness cannot be adjusted and is approximated 2.3±0.2mm (Stratec, 2008). As a result, the pQCT image generates a voxel that is not a perfect cube and augments the likelihood of influence by the partial volume effect (PVE). The problem of PVE is most pronounced at distal scan sites where the cortical shell is thin and the in-plane resolution includes lower density trabecular bone within the same voxel (Rauch, Neu, Manz, & Schoenau, 2001). Thus PVE can result in underestimation of the density of cortical bone. Scan times and radiation doses are also a concern for imaging techniques. Compared with dual energy x-ray absorptiometry

(DXA), the scan times and radiation doses are similar to those of pQCT. DXA forearm scans (6 minutes in duration) have a radiation dose between 20-30 μSv and an effective (absorbed) dose of 0.07 μSv whereas a pQCT forearm scan (7 minutes) has a reduced effective dose of 0.02 μSv per scan even though the radiation dose is higher (30-100 μSv) (Augat, Fuerst, & Genant, 1998; Lewis, Blake, & Fogelman, 1994). Both peripheral sites scanned by pQCT (i.e. tibia and radius) and whole body scans by DXA contribute to only a fraction of annual background radiation doses of 2400 μSv (Augat et al., 1998).

1.4 Estimating Whole Bone Strength

Direct measurement of long bone strength can only be assessed by breaking the structure and is therefore only feasible for cadaver specimens. Thus the development of algorithms, which estimate whole bone strength have received considerable attention among researchers and have facilitated quantitative estimated assessment *in vivo* (Augat et al., 1998). The assessment of bone acquired by pQCT permits the estimation of bone strength index (BSI_c) and stress strain index (SSI_p) that are commonly used to estimate bone strength in compression and torsion, respectively. This section will highlight methods of estimating bone strength *in vivo* using pQCT, which combine aspects of size (area), density, and spatial distribution of density.

1.4.1 Bone Strength Index

Bone strength index (BSI, mg^2/cm^4) is a non-invasive strength index for epiphyseal sites because they are primarily loaded in compression (Ferretti et al., 1996). Total strength in compression is dependent upon total area and therefore BSI_c is the product of total bone area (ToA) and squared total density (ToD). The BSI_c reflects

mechanical rigidity and has been validated as an indicator of bone's resistance to compressive loading at the distal tibia (Kontulainen et al., 2008).

$$BSI = ToA * ToD^2$$

1.4.2 Strength Strain Index

The bone shaft can be loaded in many directions and subsequently experiences strains different from the distal region. Section modulus is a measure of material strength in torsion where increases in the distance from the bending axis (or centre of mass) of the cross section require less material for the same torsional stiffness (Kontulainen, Hughes, Macdonald, & Johnston, 2007). Technology which captures bone geometry (size and shape) and volumetric density has enabled the quantification of estimated long bone strength. Polar strength strain index (SSI_p, mm^3) is an algorithm, which estimates bone strength by incorporating the bone's cross section strength in torsion (section modulus, $(a * d^2)/d_{max}$) and the ratio of pQCT measured cortical density (CoD) to normal physiological density (ND, $1200mg/mm^3$) of cortical bone (Schiessl, Ferretti, Tysarczyk-Niemeyer, & Willnecker, 1996b). Figure C illustrates a schematic image of the variables incorporated in the calculation of SSI_p. A close association between SSI_p and failure load has been demonstrated in the radius and tibia (Liu et al., 2007; Lochmuller, Lill, Kuhn, Schneider, & Eckstein, 2002; Muller, Webber, & Bouxsein, 2003)

$$SSI_p = \Sigma \frac{[(a * d^2)(CoD/ND)]}{d_{max}}$$

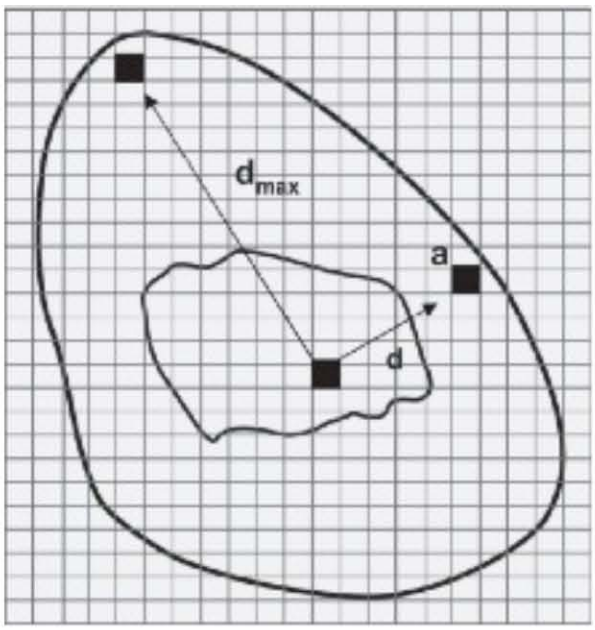


Figure C. An illustration of a bone shaft cross section and variables used in calculating polar SSI, where *a* is the area of a voxel, *d* is the distance between the voxel and the neutral axis, and d_{max} is the farthest distance of a bone voxel from the neutral axis. Adapted from Macdonald et al. (2007)

1.5 Skeletal Muscle

Skeletal muscle provides forces necessary to perform physical activities, maintain posture, and locomote. Muscle is a tissue specialized for contracting or shortening of its component cells along its longitudinal axis. As skeletal muscle contracts, strains are detected by bone cells and adaptations occur to either maintain or increase bone mass. The importance of maintaining skeletal muscle function is therefore an important component of preventing bone fragility. Although the peak force generated by a muscle group is attributed to a multitude of factors, in this section of the literature review I will provide a brief background on skeletal muscle physiology.

1.5.1 Physiology

Each muscle fiber is a single, elongated cell surrounded by a thin layer of connective tissue called endomysium. A bundle of muscle fibers are wrapped together by a membrane called the perimysium and these bundles become attached to bone by a tendon. The contractile machinery of each muscle fiber is the sarcomere, a structure consisting of actin and myosin proteins. The number of sarcomeres lined up in parallel (stacked one next to the other) will determine the muscle thickness, whereas muscle length will be dictated by how many sarcomeres are lined up in series (Malina, Bouchard, & Bar-Or, 2001).

Reductions in muscle mass and function seem to be unavoidable consequences of the aging process. The term sarcopenia was coined to describe this age-associated loss of muscle force and mass evident with advancing age (Roubenoff, 2000). It is generally accepted that muscle force is well preserved throughout adulthood until the age of 45, at which point performance outcomes begin to deteriorate (Aoyagi & Shephard, 1992). Accelerated declines in muscle force and power are evident in adults after 60 years of age (Grabiner & Enoka, 1995; Hakkinen & Hakkinen, 1991). It is believed the diminishing levels of sex hormones (i.e. estrogen and testosterone) influence the anabolic pathways in skeletal muscle (Brown, 2008). The increasing prevalence of sedentary lifestyle habits causes an infiltration of lipids, particularly intramuscular adipose, which threatens skeletal muscle quality and function (Taaffe et al., 2009). Although it remains unclear whether muscle wasting with aging is a result of inactivity, endocrine function, or intrinsic muscle properties (i.e. muscle architecture), both disuse and aging are likely responsible for marked reductions in strength (Hekimi et al., 2001).

1.6 Measuring Muscle Properties

A muscle's ability to generate force is not merely attributable to its size, but a complex synthesis of many factors including co-ordination, neuromuscular activation, fiber type distribution, and pennation angle. In this section I outline some key measurement tools currently available to measure muscle properties, including: isokinetic dynamometry, handgrip dynamometry and muscle cross sectional area.

1.6.1 Isokinetic Dynamometry

Isokinetic dynamometry is a method of measuring muscular torque across a range of motion while maintaining a constant contraction velocity. The devices employ computer assisted resistance equipment to assess concentric, eccentric and isometric contractions; and can be configured to isolate and measure the torques of different joints. Benefits of assessing muscle forces using isokinetic dynamometry include the ability to standardize joint positioning to permit a constant range of motion. This tool is also useful because its settings restrict muscle contributions or body movement that could help or hinder force acquisition at the desired joint axis. Although isokinetic dynamometry is heralded as the gold standard for the relatively safe and controlled quantitative assessment of functional muscle capacity (Mercer & Gleeson, 1996), the methodology is not without disadvantage. The most frequently cited shortfall of isokinetic dynamometry rests in its external validity. Isokinetic dynamometry produces highly controlled, repeatable results, but the assessment does not necessarily mimic the natural biomechanics of naturally occurring contractions (Baltzopoulos & Brodie, 1989).

1.6.2 Hand Grip Dynamometry

Hand grip dynamometry is an established predictor of health complications, demonstrating an ability to reasonably predict future outcomes of premature mortality, development of disability, as well as increased length of hospital stay (Bohannon, 2008). The convenience, portability and simplicity of administering grip force testing are likely responsible for making this tool so valuable across the age range. Hand grip force has often been utilized as an assessment of total body capacity for muscular force generation because of its ability to correlate well with force generation of other muscle groups and their associated functional tasks (Rantanen et al., 1998). Poor grip force results have also demonstrated a relationship with low aBMD at the clinically important femoral neck and lumbar spine in adults over 50 years old (Dixon et al., 2005). Isometric gripping induces considerable strain on the forearm bones and has therefore been a useful tool for assessing the muscle-bone relationship at the radius (Ducher, Jaffre, Arlettaz, Benhamou, & Courteix, 2005; Hasegawa et al., 2001; Van Pottelbergh, Goemaere, Nuytinck, De Paepe, & Kaufman, 2001; Yamazaki et al., 1995).

1.6.3 Muscle Cross Sectional Area

MCSA is considered an adequate surrogate of muscle force in healthy populations (Fukunaga et al., 2001; Ikai & Fukunaga, 1968; Maughan et al., 1983). The MCSA and muscle force relationship remains evident in cases of hypertrophy (Hubal et al., 2005) and muscle atrophy (Frontera, 2008). Relatively convenient methods of calculating MCSA are now included within musculoskeletal imaging software packages, which accompany hardware such as Stratec's pQCT scanner. These measures are advantageous because they are not reliant upon participant motivation levels; however, they are limited

by the accuracy and precision of the data acquisition and analysis protocols. Although muscle size is highly correlated with its ability to generate force, the importance of screening populations by gender and age are emphasized in order to attain accurate representations of the muscle-force relationship (Jones, Bishop, Woods, & Green, 2008).

1.6.4 Muscle Power

Power generated by skeletal muscle is the product of force and displacement, or work, divided by the time elapsed to do the work (McGinnis, 2005). Stated more simply, power describes the rate at which work is done, since it represents the force and shortening velocity of a muscular contraction (Foldvari et al., 2000). Most of the literature pertaining to muscle power has evaluated older adults and has highlighted lower extremity muscle power as an important determinant of functional independence (Foldvari et al., 2000; Runge, Rittweger, Russo, Schiessl, & Felsenberg, 2004). Since there are physiological changes in skeletal muscle associated with atrophy and aging, muscle power declines at a quicker rate than muscle force and MCSA (Foldvari et al., 2000; Runge et al., 2004). Measurement of isometric muscle power is possible by obtaining a rate of torque development (RTD) from a muscular contraction. RTD has been previously reported as an adequate surrogate of muscle power because it reflects the maximal amount of force that can be achieved during a muscle contraction (Aagaard, Simonsen, Andersen, Magnusson, & Dyhre-Poulsen, 2002). Although the RTD of an isometric contraction does not result in displacement in the line of action of the force, it remains an indicator of the ability for fast force generation (Kraemer et al., 2002).

1.7 Forearm Muscle-Bone Association

Assessment of the muscle-bone relationship independent of gravitational influences is made possible by measuring non-weight bearing segments of the appendicular skeleton, such as the upper extremity. Regional muscle forces of the forearm have been previously reported as grip force (Hasegawa et al., 2001; Kaji et al., 2005) MCSA (Hasegawa et al., 2001; Rittweger et al., 2005; Sumnik, 2006), and elbow flexor moment (Nikander, Sievanen, Uusi-Rasi, Heinonen, & Kannus, 2006b)

The upper extremity muscle-bone relationship has been assessed among adult men and women aged 18-86 years of age (Kaji et al., 2005; Hasegawa et al., 2001). In simple regression analyses Kaji et al. (2005) reported very weak, yet significant, correlations of grip force with cortical density (CoD), cortical area (CoA), cortical thickness (CoTh), and SSI_p at the radius shaft (r values ranging from 0.16 to 0.43). These low correlations may be attributed to a sample with little variation in handgrip strength and bone geometry. The Pearson correlations were higher in the women than men, which could have been a result of combining pre- and post- menopausal participants (Kaji et al., 2005). Hasegawa et al. (2001) used MCSA in addition to grip force to determine the independent contribution of these variables on the SSI_p. Although MCSA and SSI_p were correlated ($r = 0.58$, $p<0.05$) in both genders, the stepwise multiple regression revealed sex and grip force as the only non-bone parameters significantly contributing to the age adjusted model predicting SSI_p (adjusted $R^2=0.82$, $p<0.05$) (Hasegawa et al., 2001).

In a sample of premenopausal women and middle aged men, height and MCSA explained 22% of variability in pQCT measured bone mineral content (BMC) at the distal

radius shaft (Sumnik, 2006). The Long Term Bed Rest (LTBR) study also found a low but significant correlation ($r = 0.47$, $p<0.05$) between MCSA and BMC at the distal radius after three months immobilization (Rittweger et al., 2005). Although the LTBR study had a small sample size, it is important to note that this result suggests the pivotal role of biomechanical loading. The relationship between MCSA and BMC found after a period of immobilization suggests muscle strains of the forearm may be critical for maintaining distal radius bone strength. Elbow flexor moments of elite female athletes significantly predicted variance at the 30% site of the radius BMC, cortical thickness, and ToA (Nikander, Sievanen, Uusi-Rasi, Heinonen, & Kannus, 2006a). Interestingly, CoD has shown no significant correlations with muscle force (or its surrogates) at the shaft site of the radius (Kaji et al., 2005; Nikander, Sievanen, Uusi-Rasi, Heinonen, & Kannus, 2006a). Thus it seems that both muscle size and function are related to bone size and geometry, yet density is not predicted by muscle force measures in the forearm. Bone strength improves most by expansion at the periosteal surface thus increasing in cross sectional area and distribution of mass away from the center of gravity (Robling et al., 2006).

Muscle power has recently been studied in concert with measures of bone strength in the lower extremity. From a functional perspective, low femoral neck aBMD measured by DXA has demonstrated an association with poor functional test performance in women (Blain et al., 2001). This is an important point, since poor functional performance may lead to increased likelihood of falls and subsequent fracture. Ashe et al. (2008) conducted a cross sectional study of women aged 65-75 years to assess the association between lower extremity muscle power and bone strength in the tibia. They reported leg

extensor muscle power predicted up to 8.9% of variance in tibia shaft SSI_p. Similarly, Rantalainen and colleagues (2008) showed that peak eccentric plantar flexor torque and muscle volume of the lower leg are related to BSI at the tibia shaft. This highlights the potential association between the explosive nature of muscle power to positively affect bone geometry parameters in the upper extremity, which has not yet been reported in the literature.

1.8 Objective

The objectives of this study were to determine the relationships and predictive capacity of forearm muscle properties (MCSA, grip force, and RTD) and estimated bone strength (BSI_c and SSI_p) at the distal and shaft sites of the radius in healthy adults in midlife.

2.0 HYPOTHESIS

After accounting for sex and body size, I hypothesize MCSA, grip force and RTD will each be significantly related and independently predict estimated bone strength indices (BSI_c and SSI_p) in the radius of healthy adults in midlife.

3.0 METHODS

3.1 Participants

This cross-sectional study was a part of a larger longitudinal study, the Saskatchewan Growth and Development Study (SGDS, 1964-2010). My first instance of recruitment involved individuals returning for SGDS follow-up measurements. A detailed description of this population has been reported previously (Thompson, Baxter-Jones, Mirwald, & Bailey, 2002). A total of 314 participants, 46-52 years of age, were therefore eligible for follow-up measurements. Most updated address listings were used to mail out an informative letter inviting all SGDS participants for follow-up measurements. Additional eligible participants who were not members of the SGDS were recruited by online campus announcements and emails within the College of Kinesiology.

Participants who did not meet the age criteria (45-55 years) or reported a musculoskeletal or neurologic condition (i.e. osteoarthritis, Parkinson's disease, multiple sclerosis, or rheumatoid arthritis) that may be associated with decreased functional capacity, decreased muscle strength or poor bone health were excluded. Women who were peri- or post-menopausal (had not menstruated within the last twelve months) were also excluded.

I recruited and evaluated 48 healthy adults (26 men, 22 women). Self-reported menopausal status revealed 17 women were pre-menopausal and were included in data analysis. Women who had not menstruated within last twelve months (n=4) or had undergone a partial hysterectomy (n=1) were excluded from analyses. Although the five women were excluded from the present analysis, they were evaluated because they were

members of the SGDS. A total of 33 adults (21 males) were recruited from the SGDS and the remainder (n=15, 5 males) were additional recruits.

3.2 Background Characteristics, Anthropometry and Health

Height was measured using a wall-mounted stadiometer (Holtain Ltd., Britain) accurate to ±1 mm and weight was measured using a scale (Toledo, Windsor, ON) accurate to ±0.05 kg. A standard questionnaire (Appendix A) was used to identify current medical conditions, including medications, menopause status, and bone and joint health (Dequeker, Ranstam, Valsson, Sigurgevisson, & Allander, 1991). Informed consent was obtained from all participants prior to testing (Appendix B). The study protocol was approved by the University of Saskatchewan Biomedical Research Ethics Board (Appendix F).

3.3 Muscle Measurements

I conducted peak torque testing of the non-dominant arm using an isokinetic dynamometer (Humac Norm, CSMi, Stoughton, MA). Force was tested with the forearm supinated ensuring the middle third of the forearm was resting on a padded holder. To limit contribution of the trunk and shoulders a waist buckle was fastened and Velcro straps were fit snugly to stabilize and limit postural compensations. A cotton forearm sleeve with a thumb hole was worn by the participant during testing to prevent rubbing from the Velcro strap or discomfort from the padding.

The programmed dynamometry protocol included isometric (0 degrees) flexion of the forearm about the wrist joint. The protocol consisted of three maximum exertions each separated by 30 seconds of rest. Prior to the three recorded trials a practice contraction was programmed and performed to be sure the participant was clear on

instructions and was aware of what to expect. Ten seconds rest was provided after the practice contraction. Verbal encouragement was provided to promote maximal exertion. Peak torque (Nm) and time to peak torque (seconds), as calculated by dynamometer software, were used to calculate rate of torque development (RTD, Nm/s). RTD was defined as the peak torque attained by the isometric wrist flexion divided by the time elapsed to attain the peak torque. RTD is considered a surrogate of muscle power (Aagaard, Simonsen, Andersen, Magnusson, & Dyhre-Poulsen, 2002). Lab precision (CV, %) of muscle strength measurements using dynamometry for the left arm was previously reported at 5.8% (Farthing, Chilibeck, & Binsted, 2005).

Maximal grip force of the non-dominant arm was determined using a hand-held dynamometer (JAMAR, Jackson, MI). I instructed participants to adjust the instrument's grip setting so the second joint of the fingers fits snugly under the handle and takes the weight of the instrument. Participants stood in anatomical position with their non-dominant arm about 45 degrees away from their body. Once ready, they were told to squeeze the grip as hard as possible for 3 seconds. Approximately 30 seconds rest was permitted between repetitions. Three maximal contractions were assessed, but only the highest force (MVC, kg) was used for analysis. Short-term precision (CV,%) of hand held dynamometry measures has been previously reported to be 6.3% (Trutschnigg et al., 2008).

3.4 Peripheral Quantitative Computer Tomography

Peripheral QCT (Stratec XCT 2000, Pforzheim, Germany) was used to measure bone geometry (i.e., bone size and shape), density, and estimated strength of the non-dominant radius. Scanning protocol is described in Appendix C. A single 2.3 mm slice

was acquired at a voxel size of 0.4 mm from distal (4%) and shaft (65%) sites of the radius. These sites correspond with radius length between Radiale (point at the proximal and lateral border of the head of the radius) and Stylion (most distal point of the lateral margin of the styloid process of the radius) (International Society for the Advancement of Kinanthropometry, 2001). Planar scout views over the joint line were used to accurately place the reference line at the medial tip of the distal radius endplate. The 4% site was chosen to estimate bone strength at a clinically relevant location, whereas the 65% site represents bone strength at the shaft and muscle cross sectional area (Figure D). Radiation dose (< 0.5 µSv) to participants was minimal and approximately equal to background radiation exposure during a return flight between Saskatoon and Toronto (Department of Transport UK, 2003).

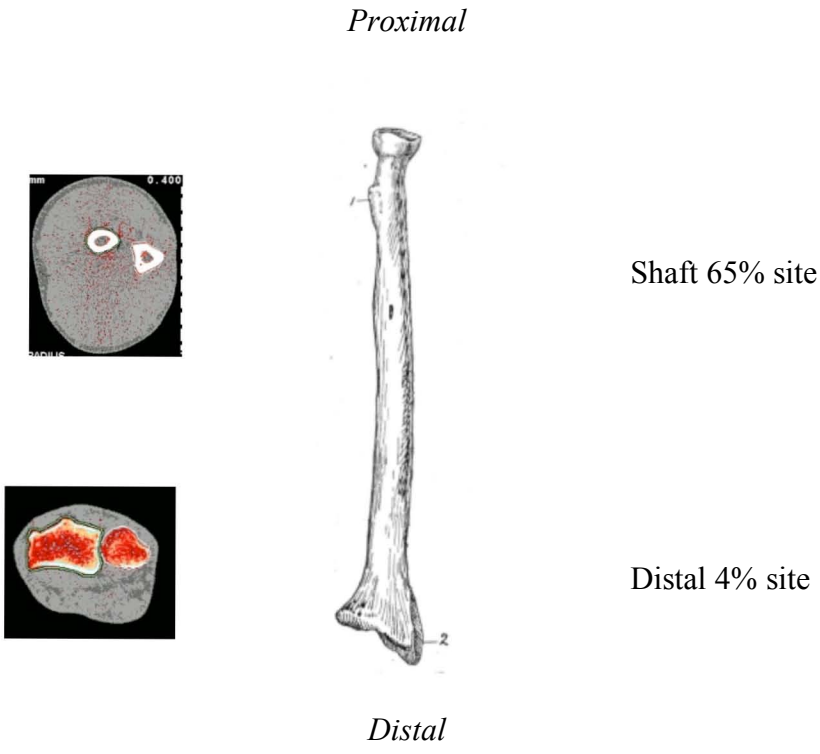


Figure D. Diagram showing the distal and shaft pQCT scan sites of the radius and sample scan images of the forearm.

3.4.1 pQCT Data Analysis

I analyzed all scans using Stratec software, Version 6.0. The 4% site images were analyzed for total bone area (ToA, mm^2) and density (ToD, mg/cm^3). The 65% site assessed cortical bone area (CoA, mm^2), cortical density (CoD, mg/cm^3) and muscle cross sectional area (MCSA, mm^2). Estimates of radius bone strength were calculated at the distal site as bone strength index in compression (BSI_c, mg^2/cm^4) and stress strain index in torsion (SSI_p, mm^3) at the shaft.

All scans of the 4% site radius were analyzed using contour mode 1, 280 mg/cm^3 to separate bone from surrounding soft tissue. Peel mode 2 with the inner threshold of 480 mg/cm^3 was used to obtain trabecular bone. Scans from the 65% site of the radius were analyzed using separation mode 4 with inner and outer threshold of 480 mg/cm^3. The MCSA was analyzed at this site using manufacturer recommended contour mode 1 bone edge detection threshold set to 40 mg/cm^3. Muscle filter C02 was used to smooth and enhance muscle tissue detection. Precision of these scan acquisition and analysis protocols have been previously assessed in our laboratory using a separate sample of adult participants. Bone strength precision as calculated by coefficient of variation (CV_{rms}, %) (Gluer et al., 1995) for BSI_c and SSI_p were 6.25% and 4.33%, respectively at the radius (unpublished data). Upper extremity MCSA precision (CV_{rms}, %) was 1.4% (unpublished data).

3.5 Statistical Analysis

I reported mean and standard deviation (SD) for descriptive characteristics and select outcome variables. I first reported Pearson correlation coefficients for both genders pooled to determine which variables were most highly correlated with estimated bone

strength. Next, I constructed hierarchical linear regression models (enter method) to assess the independent variance muscle measures (MCSA, grip force, RTD) accounted for in estimates of bone strength (BSI_c and SSI_p). In these models, body size and gender were statistically controlled for by forcing height, weight and sex (entered as 0=male, 1=female) variables into the regression model prior to muscle measures. MCSA was then entered into the regression model. The regression model was then constructed with grip force replacing MCSA. The last model replaced grip force with RTD. For each model, the unstandardized β coefficient, standard error, variance in estimated bone strength (R^2), and standardized β coefficient are reported. Normal distribution of data was checked by assessing skewness, kurtosis, and homoscedasticity. The significance level was set at $p<0.05$. I used SPSS Version 17.0 for Windows (SPSS, Chicago, IL, USA) for all data analysis.

3.5.1 Sample Size Justification

Required sample size was determined using studies that previously assessed muscle forces and bone strength outcomes in the lower extremity within adult samples (Ashe et al., 2008; Rantalainen et al., 2008). In the calculation, I assumed a significant total $R^2=0.35$ (effect size of 0.54) because this was the least amount of bone strength index variance explained in a body size adjusted linear regression model by Rantalainen and colleagues (2008). Each linear regression model had three forced predictors (sex, height, and weight) and a measure of muscle properties (MCSA, grip force, or RTD). In line with similar models, age was not entered as a predictor, since all participants were within a close age range (Rantalainen et al., 2008). Therefore, a sample size of 40 provided a power of 0.95 at an alpha level of 0.05 (Soper, 2009).

4.0 RESULTS

4.1 Descriptive data

Descriptive variables for all participants are presented (Table A). All data was normally distributed. Three male participants were excluded from analysis as a result of movement artifact during pQCT scanning (n=2) and no RTD captured by dynamometry system (n=1). The final sample included in analysis consisted of 40 healthy adults (23 males, 17 females) (Table A). Values for muscle force measures and bone outcome variables are presented in Table B.

Table A. Description of the participants

Variables	Males n=23	Females n=17
Age (years)	50.87 ± 1.25	47.76 ± 2.11
Height (cm)	179.18 ± 7.41	164.89 ± 5.58
Weight (kg)	90.67 ± 18.97	67.35 ± 12.29
BMI	28.08 ± 4.61	27.74 ± 4.20

Data presented as mean ± SD

Table B. Bone and muscle variables

Variables	All N=40
Total area (ToA, mm^2)	404 ± 84
Total density (ToD, mg/cm^3)	340 ± 40
Bone strength index (BSI_c, mg^2/cm^4)	4813 ± 1668
Cortical area (CoA, mm^2)	110 ± 22
Cortical density (CoD, mg/cm^3)	1090 ± 54
Strength strain index (SSI_p, mm^3)	417 ± 132
MCSA (mm^2)	4179 ± 1295
Grip force (kg)	42 ± 13.6
Rate of torque development (Nm/s)	12 ± 12

Data presented as mean ± SD

4.2 Correlations

Bivariate correlations (Pearson's r) are provided in Table C. Additional correlations are presented in Appendix E. Pooled gender Pearson correlation coefficients for sex were significant with both distal and shaft site bone strength variables (-0.67 and -0.74, respectively; $p<0.01$). Correlations were positive and significant for both height and weight on BSI_c and SSI_p (0.72-0.78; $p<0.01$).

Table C. Bivariate Correlations (Pearson's r)

	Sex	**Age** (yrs)	**Height** (cm)	**Weight** (kg)
ToA (mm^2)	-0.78**	0.54**	0.76**	0.74**
ToD (mg/cm^3)	-0.35*	0.02	0.41**	0.41**
BSI_c (mg^2/cm^4)	-0.67**	0.29	0.72**	0.72**
CoA (mm^2)	-0.73**	0.44**	0.68**	0.69**
CoD (mg/cm^3)	0.12	-0.07	-0.06	-0.10
SSI_p (mm^3)	-0.74**	0.42**	0.78**	0.77**

*$p<0.05$, **$p<0.01$

4.3 Hierarchical Linear Regression Models

Hierarchical linear regression models were used to quantify the contribution of muscle properties on estimated bone strength variables. Results are summarized in Tables D and E. All assumptions of hierarchical linear regression modeling (linearity, normality of residuals, homoscedasticity of residuals) were met. Predictor variable and multivariate outliers were tested by assessing leverage values adjusted for a small sample size, 3p/n (p = number of predictor variables, n = sample size). Values did not exceed 0.225. There

were no extreme scores (>1), as tested by Cook's distance. Colinearity was not detected, since all tolerance values were >0.1 and Variance Inflation Factors were <10.

Step one in the hierarchical linear regression models revealed that baseline adjustments for height, weight and sex significantly explained between 63.2% ($p<0.001$; BSI_c) and 72.5% ($p<0.001$; SSI_p) of variance in bone strength at the radius.

Sex was a significant predictor of both BSI_c and SSI_p, albeit only in the baseline models (Step 1, Tables D and E) and in the step with RTD as a predictor (Step 4, Tables D and E). Weight predicted 14.4 – 21.4% of variance in BSI_c ($p<0.001$) and 5.4 – 7.9% of variance in SSI_p ($p<0.01$) at all steps that did not include MCSA. Conversely, height was not a significant predictor for either of the outcome variables (Tables D and E).

Both models (Steps 1-4, Tables D and E) were significant in the overall prediction of estimated bone strength ($p<0.001$). MCSA was a significant predictor of BSI_c ($R^2=0.085$; $p<0.01$) and SSI_p ($R^2=0.042$; $p<0.05$) (Figures E and F). Although grip force was not a significant predictor of BSI_c ($R^2=0.032$, p=0.075), a significant amount of variance in SSI_p ($R^2=0.060$; $p<0.01$) was accounted for by isometric grip force. The variance accounted for by RTD was significant in predicting BSI_c ($R^2=0.049$, $p<0.05$), yet did not reach statistical significance in predicting midshaft radius SSI_p ($R^2=0.144$, $p=0.174$).

Table D. Hierarchical linear regression model investigating the contribution of muscle forces to BSIc at 4% site

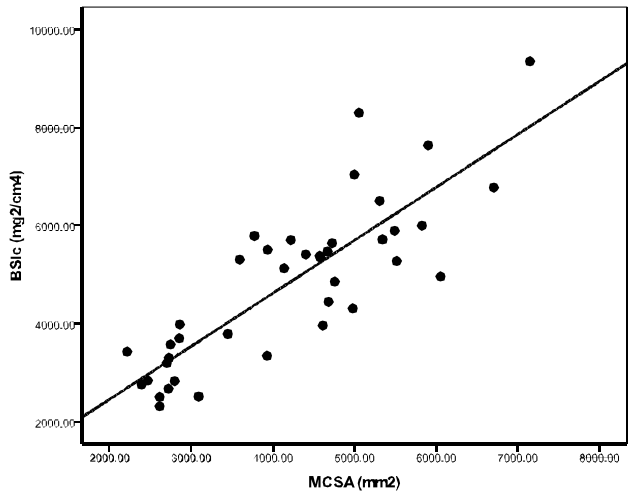
Independent Variable	Overall R^2	R^2 Change	B	SE of B	β	*p* value
STEP 1	0.632					
Sex			-1699.999	497.977	-0.510	0.002
Height (cm)			-48.335	30.986	-0.282	0.128
Weight (kg)			52.198	12.598	0.627	<0.001
STEP 2	0.717	0.085				
Sex			167.416	725.087	0.050	0.819
Height (cm)			-27.663	28.264	-0.162	0.334
Weight (kg)			9.316	17.301	0.112	0.594
MCSA (mm^2)			1.169	0.360	0.908	0.003
STEP 3	0.664	0.032				
Sex			-1083.794	588.044	-0.325	0.074
Height (cm)			-59.858	30.670	-0.350	0.059
Weight (kg)			48.087	12.409	0.577	<0.001
Grip Force (kg)			40.200	21.936	0.328	0.075
STEP 4	0.681	0.049				
Sex			-2083.053	498.065	-0.625	<0.001
Height (cm)			-55.710	29.419	-0.325	0.067
Weight (kg)			59.686	12.320	0.717	<0.001
RTD (Nm/s)			-37.620	16.178	-0.267	0.026

MCSA = muscle cross sectional area
RTD = rate of torque development

Table E. Hierarchical linear regression model investigating the contribution of muscle forces to SSIp at 65% site

Independent Variable	Overall R^2	R^2 Change	B	SE of B	β	*p* value
STEP 1	0.725					
Sex			-94.288	34.100	-0.357	0.009
Height (cm)			2.508	2.122	0.185	0.245
Weight (kg)			2.779	0.863	0.421	0.003
STEP 2	0.767	0.042				
Sex			9.366	52.160	0.035	0.859
Height (cm)			3.655	2.033	0.269	0.081
Weight (kg)			0.399	1.245	0.060	0.750
MCSA (mm^2)			0.065	0.026	0.635	0.017
STEP 3	0.785	0.060				
Sex			-27.757	37.286	-0.105	0.462
Height (cm)			1.264	1.945	0.093	0.520
Weight (kg)			2.335	0.787	0.354	0.005
Grip Force (kg)			4.340	1.391	0.446	0.004
STEP 4	0.740	0.015				
Sex			-77.916	35.678	-0.295	0.036
Height (cm)			2.823	2.107	0.208	0.189
Weight (kg)			2.459	0.882	0.372	0.009
RTD (Nm/s)			1.608	1.159	0.144	0.174

MCSA = muscle cross sectional area
RTD = rate of torque development



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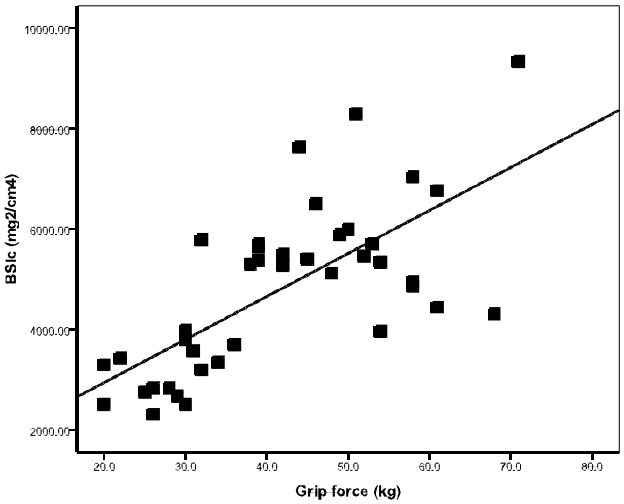

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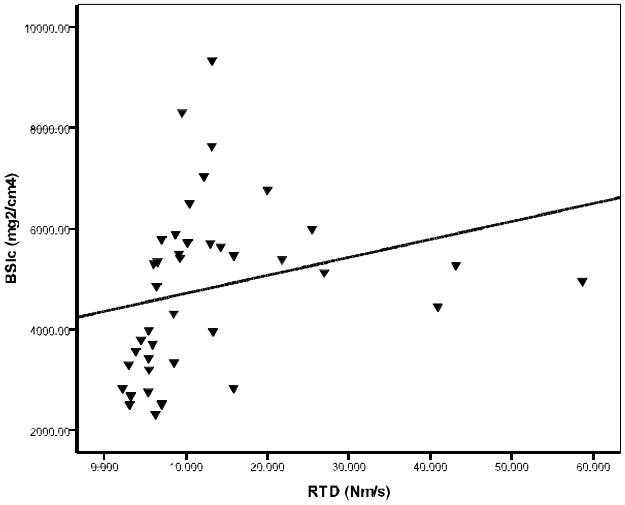
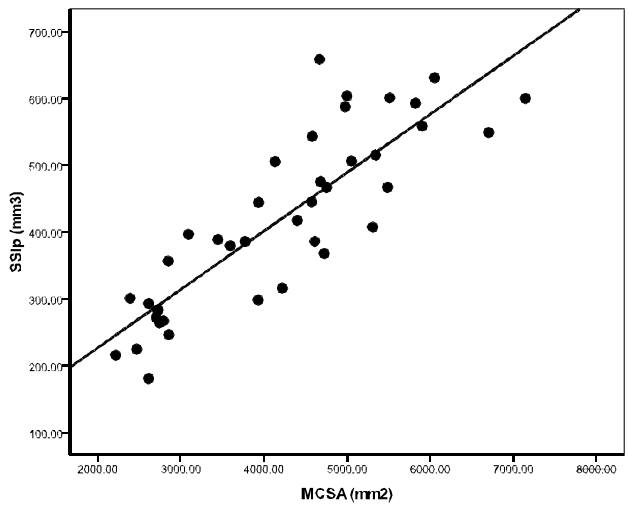


C.

Figure E. The relation between muscle cross sectional area (MCSA) (A), grip force (B) and rate of torque development (RTD) (C) and estimated bone strength (BSI_c) at the radius 4% site. The line of fit is based on bivariate correlations: **A**: R^2=0.702; **B**: R^2=0.487; **C**: R^2=0.064



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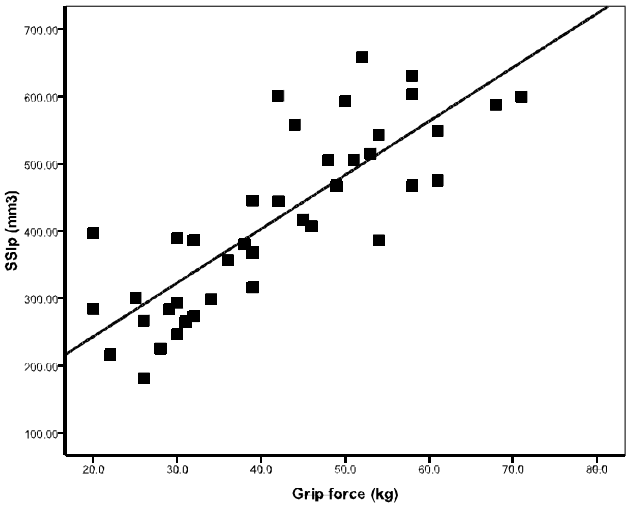

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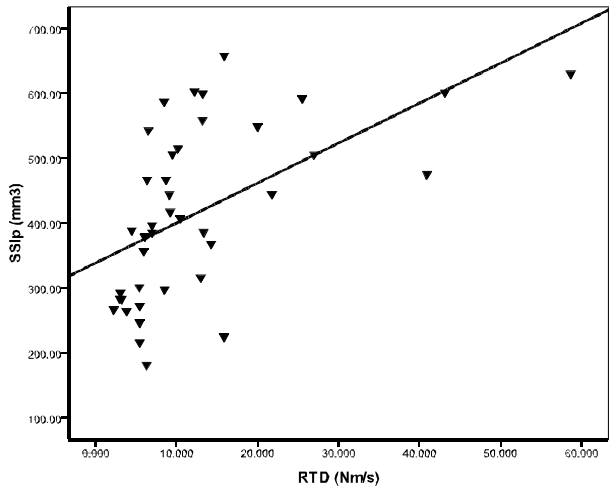

C.

Figure F. The relation between muscle cross sectional area (MCSA) (A), grip force (B) and rate of torque development (RTD) (C) and estimated bone strength (SSI_p) at the radius 65% site. The line of fit is based on bivariate correlations: **A**: R^2=0.73; **B**: R^2=0.675; **C**: R^2=0.304

5.0 DISCUSSION AND CONCLUSIONS

5.1 Discussion

The aim of this study was to identify the relationship between forearm muscle properties and pQCT measured bone strength at the distal and shaft sites of the radius of healthy individuals in mid-adulthood. I hypothesized that muscle properties (MCSA, grip force and RTD) would each independently be significant predictors of estimated bone strength indices (BSI_c and SSI_p) in the radius of healthy adults, after adjusting for sex, height, and weight.

Results revealed RTD was a significant predictor of BSI_c at the distal radius and a significant positive correlate with SSI_p, which agrees with previous human research of the lower extremity (Ashe et al., 2008; Binkley & Specker, 2008). The model predicting BSI_c suggested that bone strength increases with a quicker RTD, however the bivariate correlation indicated no association between the two variables. Within the isokinetic dynamometry protocol a trend was observed, whereby individuals attaining the highest peak torque values tended to take longer to reach their peak, thus resulting in a slower RTD. The trend may partially explain the non-significant contribution of RTD predicting SSI_p and indicates that different components of force development should also be investigated. This was the first known study to investigate the relationship between an indicator of explosive muscle force and bone strength in the forearm. Animal studies have shown that generating high strain rates (large muscle forces in a short time) can stimulate increases in cross sectional area of bone (Lanyon & Rubin, 1984). Presuming these quick strains have similar effects on human bone, one would expect individuals capable of generating an increased amount of power to have larger bone cross sectional

area and therefore improved bone strength. Evidence from human studies has suggested that lower extremity muscle power is associated with bending strength at the tibia shaft of older adults and has been shown to predict up to 9% of estimated bone strength (Ashe et al., 2008; Binkley & Specker, 2008). Although Ashe et al. (2008) demonstrated peak muscle power correlated well with SSI_p at the tibia shaft, others have reported muscle power to have less predictive contribution to estimated bone strength than measures of muscle size (Binkley & Specker, 2008; Ashe et al., 2008). The importance of muscle power in the lower extremity is associated with functional tasks of daily living such as gait speed and chair rise time, whereas the importance of forearm muscle power is important for daily tasks such as opening doors, bottles, and jars (Hazell, Kenno, & Jakobi, 2007). My results seem to indicate that larger muscle forces are positively associated with greater bone strength in the upper extremity, yet the RTD may be larger in these same individuals. The independent contribution of RTD predicting distal radius BSI_c was significant, yet at the radius shaft RTD was not a significant predictor on the criterion variable SSI_p. There are no muscle insertions at the distal site of the radius, but ten muscles cross the wrist joint and load the distal radius in compression when they contract. The strains on bone at the shaft site likely differ from those at the distal radius and these may play a critical role in bone strength adaptation. Maintaining the force generating ability of these wrist flexion muscles as adults get older could have an important osteogenic effect on bone strength at the clinically relevant site. Since the risk of distal radius (Colles') fractures for a woman in her 50's can reach up to 60% (Cummings et al., 1999), these preliminary results warrant further experimental research

to focus on establishing methods of fracture prevention by assessing muscle properties that may be most effective for optimizing osteogenic response to loading.

My results indicated that grip force was a significant predictor of SSI_p in the radius after controlling for confounders of sex and body size. This result is supported by literature demonstrating a close association between radius estimated bone strength indices and isometric muscle force in adults (Hasegawa et al., 2001; Kaji et al., 2005; Specker, Binkley, & Fahrenwald, 2004). Grip force has been shown to be strongly related to sex and age (Hasegawa et al., 2001), yet the site-specific relationship between muscle force and SSI_p seems to be stronger in women than men (Kaji et al., 2005). I found that the contribution of grip force did not remain significant in the regression model predicting BSI_c, which could be a potential outcome of analyzing a small sample with sexes pooled. Although unclear from this study design why such a relationship exists, it could be attributed to the muscle strains generated by isometric gripping eliciting an influential effect on bone remodeling at the radius shaft. An investigation of rural and non-rural dwellers found that daily activities involving gripping and forearm strength may lead to increased bone and muscle strength at the forearm (Specker, Binkley, & Fahrenwald, 2004). The close relationship observed between grip force and bone strength is important since it suggests that maintaining function of muscle is associated with bone strength. To further correlate grip force with health related outcomes, Rantanen et al. (1998) found that midlife grip force was well correlated with physical functional capacity 25 years later. Grip force may therefore help screen for individuals who may be at increased risk of physical disability due to low muscle strength and serve as an indicator of individuals who could also be at higher risk of bone fragility. The correlations I have

reported may not represent a convincing relationship between muscle force and bone strength; however, a closer look at the muscle to bone relationship among healthy adults is warranted. Prior to muscle force measures being considered an indication of bone strength, further investigation should focus on assessing how bone geometry can change to improve its ability to resist fracture. Identifying the most influential muscle property capable of inducing remodeling at the radius may one day be beneficial in reducing the incidence of Colles' fractures among aging adults.

The use of MCSA as a surrogate of muscle force has been criticized because it ignores intrinsic muscle properties known to affect functional performance, such as fiber type and pennation angle (Rittweger et al., 2000). My results indicated that MCSA was closely associated with estimated strength of the radius at both distal and shaft sites. MCSA has previously demonstrated significant positive relationships with bone size at the weight bearing tibia of children (Binkley & Specker, 2008; Macdonald et al., 2006) and adults (Rittweger et al., 2000). Significant associations with BMC and MCSA have been demonstrated in the forearm of growing boys and girls (Schoenau, Schwahn, & Rauch, 2002), yet there remains a paucity of literature concerning the forearm MCSA association with bone geometry and strength in healthy adults. Sumnik et al. (2006) revealed MCSA and height were strong predictors of BMC at the radius 65% site among healthy adults, but BMC has been criticized for its inability to represent long bone strength in torsion (Burr, 1997). Using SSI_p as an indicator of bone strength in torsion is particularly relevant to the radius shaft because it likely more representative of biological loading conditions. Due to limitations in study design I cannot prove that muscle size is

improving bone strength, yet my results are preliminary evidence highlighting a relationship between muscle size and bone strength at the radius.

MCSA, grip force, and RTD resulted in higher correlations with estimated bone strength at the shaft than at the distal radius. Furthermore, MCSA correlations with BSI_c were larger than those with grip force or RTD. Anatomically, many muscles are involved in hand gripping tasks, which include flexors of the interphalangeal joints and wrist that are responsible for the grip force in addition to forearm extensor muscles that account for wrist stabilization. Origins of these muscles are primarily at the proximal half of the forearm, while their insertions are at the phalanges. Peak muscle forces generated by mechanical loading induce proportionately predictable strains (deformation) on bone tissue (Forwood, 2001), particularly at the shaft site where the strain gradient is a result of mechanical loading. MCSA could be more influential on long bone shaft strength due to the higher strains occurring near midshaft attachments that subsequently stimulate a site specific osteogenic response. These findings suggest an important role for local muscle size and function on bone geometry and strength. The highest dynamic strains are experienced at the cortical surface of the bone (Robling et al., 2006), which is a component of bone strength estimates. Since the distal radius is predominantly composed of trabecular bone, cortical enlargement may occur to a lesser extent than expected at the midshaft. This is consistent with literature indicating that adding material to the periosteal surface is the most effective means of increasing long bone strength (Robling et al., 2006). In support of this notion, Kontulainen et al. (2002) found that in a sample of female racquet-sport players there were no significant differences in cortical density between dominant and contra-lateral arms but side-to-side differences in other bone

characteristics were significant at the distal radius. The increased amount of mechanical loading on the dominant arm is therefore associated with bone geometry. It has been proposed that bone material properties (i.e. density) differ to a lesser extent than architectural (structural) characteristics across populations (Ferretti, Cointry, Capozza, & Frost, 2003). This is supported by similar evidence in the lower extremity. Previous findings by Rantalainen and colleagues (2008) found that BSI_c at the distal tibia was not significantly associated with muscle volume, eccentric torque, or ground reaction force in women; however in men these relationships were significant and positive. This may be an indication of a depressed osteogenic response or a smaller range of muscle properties and their performance in women, which could prevent a significant association to be observed. Having a small sample size and analyzing my data as a pooled sample of men and women may have limited the range of muscle properties and subsequently masked a relationship with bone strength at the distal radius for some variables.

The middle-aged group of adults measured for this study was important for several reasons. These participants were also younger than the 55 years of age, which is the critical age at which incidence of Colles' fractures rises significantly (Larsen & Lauritsen, 1993). They were also healthy adults between 45-55 years of age that do not yet exhibit signs of sarcopenia, meaning that the size and strength of their skeletal muscle has not yet begun to diminish. Finally, women of this age are approaching menopause but most still experience normal menstruation cycles. The pre-menopausal status was important because this would indicate that these women have normal estrogen levels, which is important for bone remodeling (Pacifici, 1996). Evaluating musculoskeletal relationships and interactions among healthy adults at midlife may assist in the

development of methods aimed at optimizing bone geometry for fracture prevention and establishing non-pharmacologic interventions for individuals nearing the age of increased fracture risk.

5.2 Summary

Altogether these results indicate that bone strength of the non-dominant radius of healthy adults is predicted by muscle size, grip force and RTD of the forearm. This outcome parallels findings from studies that have reported a muscle-bone relationship at various anatomical sites in other populations. Additional assessment of site specific muscle properties and their interactions with bone geometry is warranted to gain understanding of how bone strength may be improved by training skeletal muscle.

5.3 Strengths and Limitations

This study provided a glimpse into the muscle-bone relationship in healthy adults. I used some of the most advanced measurement equipment for both bone and muscle strength data acquisition. The Humac dynamometer permitted RTD to be calculated from a muscle contraction and pQCT facilitated estimation of distal and shaft site bone strength derived from structural and geometric properties. Desired sample size was also calculated prior to initiating recruitment to ensure I would be sufficiently powered to observe a significant regression model with a large effect size ($f^2 = 0.54$). This sample of participants permitted me to study a group of adults approaching the age at which there is a high prevalence of Colles' fractures. Focusing on the distal radius and forearm shaft sites was important, since it facilitated the examination of the relationship muscle properties have with bone, independent of weight bearing and gravitational influence, in addition to its importance in the clinical realm.

On the other hand, I acknowledge there are limitations to this study. First of all, the cross sectional study design does not permit the identification of causal relationships between muscle forces and bone geometry. The intent of this study was instead to gather preliminary observations of the muscle-bone association in the forearm to explore the contribution of muscle size or function to predicting bone strength. The second limitation lies in the reliability of RTD as a surrogate measure of muscle power at the wrist. In particular, the muscle contraction from which RTD was obtained was isometric, which is indicative of no displacement about the joint, thus no work was done. Since muscle power had not yet been investigated in the forearm, the use of RTD was attempting to capture a meaningful indicator of how quickly the local muscles are able to produce force. Finally, I recognize the challenges associated with analyzing pooled data of men and women, without contrasting sexes for confounding differences. Sex has been demonstrated to be a significant variable of radius bone strength (Mueller et al., 2009). However, pooling men and women in this study was important for maintaining adequate power according to my sample size justification. I attempted to overcome this limitation by excluding all women who self-reported themselves peri- or post-menopausal, in order to eliminate participants who may have a shift in their MES due to estrogen removal (Frost, 1987). In addition, I used gender as a predictor in the regression models to assess its overall explanatory power at each step.

5.4 Future Directions

Future research is necessary to comprehend the site specific osteogenic adaptations occurring as a result of mechanical loading incurred by muscle forces, particularly at non-weight bearing sites of the appendicular skeleton. Other clinically

relevant sites, the proximal femur and vertebrae, should also be examined to explore the potential differences between loaded and non-loaded sites in their response to targeted muscle force training interventions. In terms of muscle function analysis, methods of accurately capturing muscle power of the forearm should be investigated and validated because this may facilitate further inquiry to be made about an individual's functional status and how it may relate to bone strength. As technology contributes to the advancement of musculoskeletal imaging equipment the need to utilize these tools with enhanced image resolution to assess bone geometry and architecture should be used to examine specific components of bone strength, such as tissue porosity and trabecular microstructure.

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APPENDICES

APPENDIX A – HEALTH HISTORY QUESTIONNAIRE

Subject ID: _____

Date: _____ (dd/mm/yy)

Medication questionnaire

Please answer the following questions to the best of your ability. If you answer yes to any of the questions please provide the drug name and dosage to the best of your ability.

1. Are you taking medications for high blood pressure?
Yes
No
Not Sure

Name: _____ **Name: _____** **Name: _____**
Dosage: _____ **Dosage: _____** **Dosage: _____**

2. Are you taking medications to lower your blood cholesterol?
Yes
No
Not Sure

Name: _____ **Name: _____** **Name: _____**
Dosage: _____ **Dosage: _____** **Dosage: _____**

3. Are you currently taking asprin at least three times a week?
Do not include Tylenol (acetaminophen) or Advil (ibuprofen) use.

Yes
No
Not Sure

Name: _____ **Name: _____** **Name: _____**
Dosage: _____ **Dosage: _____** **Dosage: _____**

4. Are you taking any other prescription medications?
Remember to include prescribed medications such as insulin, nicotine patches and birth control (pills, patches or injections)
Yes
No
Not Sure

If yes, how many prescription medications are you taking?

_____

Name: _____ **Name:** _____ **Name:** _____
Dosage: _____ **Dosage:** _____ **Dosage:** _____

5. Are you taking any over-the-counter medications?
Pain killers, antacids, allergy pills and hydrocortisone creams are all examples of over-the-counter medications.

Yes
No
Not Sure

If yes, how many over-the-counter medications are you taking?

_____

Name: _____ **Name:** _____ **Name:** _____
Dosage: _____ **Dosage:** _____ **Dosage:** _____

6. Are you taking any health products or herbal remedies?
Vitamins, minerals, fish oils and other oils, and botanical or homeopathic preparations are all example of health products or herbal remedies.

Yes
No
Not Sure

If yes, how many health products or herbal remedies are you taking?

_____

Name: _____ **Name:** _____ **Name:** _____
Dosage: _____ **Dosage:** _____ **Dosage:** _____

Subject ID: _____

The following questions 7-9 are for women only.
Menopausal Status

7. Regarding menopause, do you think you are?

a. Without any sign
b. Just beginning
c. In the middle
d. Near the end
e. All through

8. Have you had your uterus (hysterectomy) or both ovaries removed?

Yes
No
Not Sure

9. Have you menstruated in the past 12 months?

Yes
No
Not Sure

If yes, have you menstruated in the past 3 months?

Yes
No
Not Sure

If yes, has the length of your cycle become less predictable in the past year?

Yes
No
Not Sure

If no, when did you stop menstruating?

Date: (mm/yy) _____/_____

10. Have you used any female hormones in the preceding 3 months?

Yes
No
Not Sure
If yes, please fill in the question #4.

Subject ID: _____

Bone and Joint Health Questionnaire

1. Have you ever had a wrist fracture?

Yes
No
Not Sure

If yes, please indicate the body site and date:

Left or Right (circle) Date: (mm/yy) _____/_____

2. Have you ever had any other broken bone or stress fracture?

Yes
No
Not Sure

If yes, please indicate the bone and date:

Bone _____

Left or Right (circle) Date: (mm/yy) _____/_____

3. Have you ever been treated for or diagnosed with arthritis or other painful joint disease?

Yes
No
Not Sure

If yes, please explain_____
_____
_____

APPENDIX B – CONSENT FORM

Title: The bone to muscle relationship in the forearm at midlife.

College of Kinesiology, University of Saskatchewan
Consent Form

Investigators:
Principal Investigator: Saija Kontulainen, Ph.D., College of Kinesiology, University of Saskatchewan, phone: 966-1077
Student Investigator: Amanda Lorbergs, M.Sc Candidate (supervised by Dr. Kontulainen), College of Kinesiology, University of Saskatchewan, phone: 966-1123

Participant:
You are invited to participate in a research study to determine the relationship between bone and muscle strength in the forearm at midlife. The findings of this study may provide valuable information about the association between of bone and muscle properties.

Before you decide to participate, it is important for you to understand what the research involves. This consent form will tell you about the study, why the research is being done, what will happen to you the study and the possible benefits, risks and discomforts.

If you decide to participate, you will be asked to sign this consent form. Your participation is entirely voluntary. If you do decide to take part in this study, you are free to withdraw at any time without giving any reasons for your decision. Please take time to read the following information carefully and feel free to ask any questions you might have.

Purpose of the study:
There is an increased risk of fracture after the age of 55, especially in women. To optimize fracture prevention we need to determine those factors such as muscle size or strength that can be modified to improve bone strength prior to the time of increased risk of fracture. A strong bone has a greater ability to resist fracture than a weak bone. The proposed study aims to assess the association of muscle and bone parameters in the forearm with the aim of developing fracture prevention interventions in the future. This study will examine muscle size, strength, and power among men and women between the ages of 45 and 50 to assess whether there is a relationship to various bone properties of the forearm.

Procedures:
All testing procedures will occur at the Physical Activity Complex and will take approximately one hour to complete. If you agree to participate in this study the following will happen:

a) Questionnaires: You will be required to complete questionnaires regarding current medications, menopausal status (women only), and bone and joint health.
b) Anthropometry: Your standing height and weight will be measured.

c) Muscle Strength: Arm and hand muscles force and power will be measured by two dynamometers. The first measurement will assess your grip strength. You will be asked to squeeze a hand-held grip dynamometer as hard as you can. The second set of measurements will assess your ability to flex and extend your wrist joint.
d) Bone Strength: Bone structural properties and strength will be measured by scanning the non-dominant wrist and forearm by peripheral quantitative computer tomography (pQCT). You will be asked to sit quietly with your arm extended through the pQCT scanner. Approximate time of the scanning procedure is seven minutes. Measurements are done by a qualified technician.

Possible benefits of the study:
There may be no direct benefits from participation in this study.

Foreseeable risks, side effects or discomfort:
The strength tests will be performed at maximal intensity and therefore may result in muscle fatigue and/or muscle soreness. Radiation dose associated with the pQCT measurements is minimal. The effective dose is 0.2 μSv per pQCT scan. The combined dose of two pQCT scans is less than 0.5 μSv. This is similar to the background radiation exposure resulting from a flight from Saskatoon to Halifax on a commercial airline.

Research-Related Injury:
There will be no costs to you for participation in this study. You will not be charged for any research procedures. In the event that you become ill or injured as a result of participating in this study, necessary medical treatment will be made available at no additional cost to you. By signing this document you do not waive any of your legal rights.

Confidentiality:
The researchers will protect your privacy, and safeguard the confidentiality of information collected about you during the course of this study. Absolute confidentiality cannot be guaranteed. You will be identified in this study only by your assigned study number. All testing procedures will take place in an enclosed space in the Physical Activity Complex. All imaging data will be recorded on password protected digital media in the Growth and Development Laboratory. It is the intention of the research team to publish results of this research in scientific journals and to present the findings at related conferences and workshops, but your identity will not be revealed.

Voluntary Withdrawal:
Your participation in this research is entirely voluntary. You may withdraw from this study at any time. If you decide to enter the study and to withdraw at any time in the future, there will be no penalty or loss of benefits to which you are otherwise entitled. If you choose to withdraw from the study there will be no penalty or loss of benefits to which you are otherwise entitled, and your future medical care will not be affected.

If you choose to enter the study and then decide to withdraw at a later time, all data collected during your enrolment in the study will be retained for analysis. All information provided and data collected will be stored in a locked office for a minimum of five years after the completion of the study.

If you have questions concerning the study you can contact Dr. Kontulainen at 306-966-1077.

If you have questions about your rights as a research participant or about the study, you can contact the Chair of the Biomedical Research Ethics Board, University of Saskatchewan at 306-966-4053. This number can be called collect if you are phoning long distance.

Consent to Participate:

I, _____,
(please print name)

- Have read or have had this read to me and understood the research subject information and consent form
- Have had sufficient time to consider the information provided and to ask for advice if necessary
- Have had the opportunity to ask questions and have had satisfactory responses to my questions
- Understand that all of the information collected will be kept confidential and that the result will only be used for scientific objectives
- Understand that my participation in this study is voluntary and that I am completely free to refuse to participate or to withdraw at any time without changing in any way the quality of care that I receive
- Understand that I am not waiving any of my legal rights as a result of signing this consent form
- Understand that there is no guarantee that this study will provide any benefits to me
- Have read this form and I freely consent to participate in this study
- Have been told that I will receive a dated and signed copy of this form for my records

Participant's Signature:_____ Date: _____

Researcher Signature:_____ Date: _____

APPENDIX C – PQCT MEASUREMENT PROTOCOL

pQCT Measurement Protocol

- Participants were seated in a chair with their non-dominant arm at shoulder height, extended through the gantry so that their elbow was within the clamp
- Hand was pronated through the gantry and was comfortably rested on the hand attachment
- A foam cushion was placed under the arm to ensure comfort and a tensor bandage was wrapped around the fingers to eliminate movement from the hand
- They were instructed to find a comfortable position and sit as still as possible during the scanning period
- Talking was not permitted during the scan to minimize any movement
- Scout scans were obtained prior to scanning and reference lines were placed at the medial tip of the distal radius endplate
- At each site we acquired a single 2.3 mm slice at a scan speed of 20 mm/s.
- The pQCT operator scanned the phantom daily to maintain quality assurance

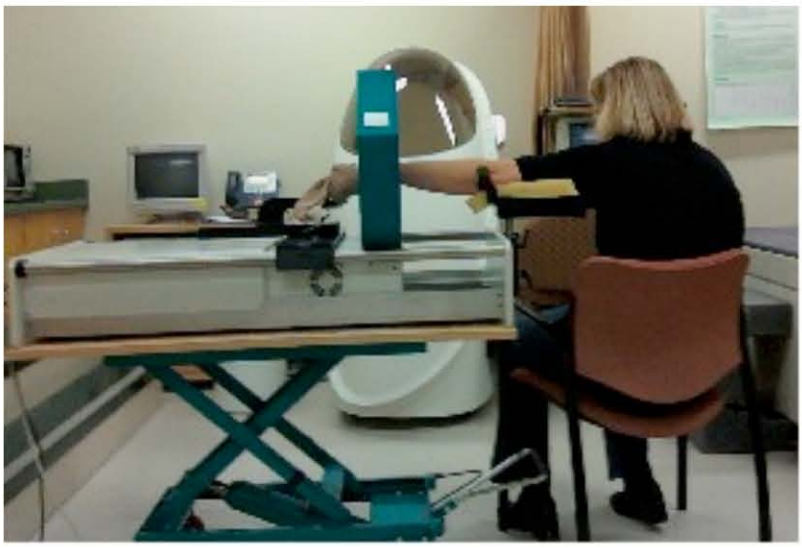

Figure G. A participant seated for pQCT scanning of the non-dominant radius. Arm extended and supinated through the gantry. Foam support for the upper arm and bandage wrap for the distal arm to maximize comfort and minimize movement, respectively.

APPENDIX D – TABLES OF HIERARCHICAL LINEAR REGRESSION ANALYSES

Table C.1.0 – Hierarchical Linear Regression on Dependent Variable BSI_c (Step 1)

Model Summary[b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.795[a]	.632	.601	1053.68025

a. Predictors: (Constant), Weight, Gender, Height

b. Dependent Variable: Rad_BSI

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	Correlations			Collinearity Statistics	
		B	Std. Error	Beta			Zero-order	Partial	Part	Tolerance	VIF
1	(Constant)	9687.323	4996.677		1.939	.060					
	Gender	-1699.999	497.977	-.510	-3.414	.002	-.668	-.495	-.345	.458	2.183
	Height	-48.335	30.986	-.282	-1.560	.128	.557	-.252	-.158	.312	3.204
	Weight	52.198	12.598	.627	4.143	.000	.715	.568	.419	.447	2.237

a. Dependent Variable: Rad_BSI

Table C.1.1 - Hierarchical Linear Regression on Dependent Variable BSI_c (Step 2)

Model Summary[b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.847[a]	.717	.685	936.50730

a. Predictors: (Constant), MCSA, Height, Weight, Gender

b. Dependent Variable: Rad_BSI

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	Correlations			Collinearity Statistics	
		B	Std. Error	Beta			Zero-order	Partial	Part	Tolerance	VIF
1	(Constant)	3891.640	4785.395		.813	.422					
	Gender	167.416	725.087	.050	.231	.819	-.668	.039	.021	.171	5.860
	Height	-27.663	28.264	-.162	-.979	.334	.557	-.163	-.088	.296	3.374
	Weight	9.316	17.301	.112	.538	.594	.715	.091	.048	.187	5.341
	MCSA	1.169	.360	.908	3.251	.003	.838	.482	.292	.104	9.645

a. Dependent Variable: Rad_BSI

Table C.1.2 - Hierarchical Linear Regression on Dependent Variable BSI_c (Step 3)

Model Summary[b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.815[a]	.664	.626	1020.77448

a. Predictors: (Constant), GripL, Weight, Gender, Height

b. Dependent Variable: Rad_BSI

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	Correlations			Collinearity Statistics	
		B	Std. Error	Beta			Zero-order	Partial	Part	Tolerance	VIF
1	(Constant)	10072.780	4845.202		2.079	.045					
	Gender	-1083.794	588.044	-.325	-1.843	.074	-.668	-.297	-.181	.308	3.244
	Height	-59.858	30.670	-.350	-1.952	.059	.557	-.313	-.191	.299	3.344
	Weight	48.087	12.409	.577	3.875	.000	.715	.548	.380	.432	2.313
	GripL	40.200	21.936	.328	1.833	.075	.698	.296	.180	.301	3.326

a. Dependent Variable: Rad_BSI

Table C.1.3 - Hierarchical Linear Regression on Dependent Variable BSI_c (Step 4)

Model Summary[b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.825[a]	.681	.645	994.55792

a. Predictors: (Constant), RTD, Height, Weight, Gender

b. Dependent Variable: Rad_BSI

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	Correlations			Collinearity Statistics	
		B	Std. Error	Beta			Zero-order	Partial	Part	Tolerance	VIF
1	(Constant)	11001.071	4750.030		2.316	.027					
	Gender	-2083.053	498.065	-.625	-4.182	.000	-.668	-.577	-.399	.408	2.451
	Height	-55.710	29.419	-.325	-1.894	.067	.557	-.305	-.181	.309	3.241
	Weight	59.686	12.320	.717	4.845	.000	.715	.634	.463	.416	2.401
	RFD	-37.620	16.178	-.267	-2.325	.026	.254	-.366	-.222	.690	1.450

a. Dependent Variable: Rad_BSI

Table C.2.0 - Hierarchical Linear Regression on Dependent Variable SSI_p (Step 1)

Model Summary[b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.852[a]	.725	.703	72.15245

a. Predictors: (Constant), Weight, Gender, Height

b. Dependent Variable: Rad_SSIp

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	Correlations			Collinearity Statistics	
		B	Std. Error	Beta			Zero-order	Partial	Part	Tolerance	VIF
1	(Constant)	-201.450	342.156		-.589	.560					
	Gender	-94.288	34.100	-.357	-2.765	.009	-.738	-.419	-.241	.458	2.183
	Height	2.508	2.122	.185	1.182	.245	.759	.193	.103	.312	3.204
	Weight	2.779	.863	.421	3.222	.003	.766	.473	.281	.447	2.237

a. Dependent Variable: Rad_SSIp

Table C.2.1 - Hierarchical Linear Regression on Dependent Variable SSI_p (Step 2)

Model Summary[b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.876[a]	.767	.741	67.36839

a. Predictors: (Constant), MCSA, Height, Weight, Gender

b. Dependent Variable: Rad_SSIp

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	Correlations			Collinearity Statistics	
		B	Std. Error	Beta			Zero-order	Partial	Part	Tolerance	VIF
1	(Constant)	-523.151	344.241		-1.520	.138					
	Gender	9.366	52.160	.035	.180	.859	-.738	.030	.015	.171	5.860
	Height	3.655	2.033	.269	1.798	.081	.759	.291	.147	.296	3.374
	Weight	.399	1.245	.060	.321	.750	.766	.054	.026	.187	5.341
	MCSA	.065	.026	.635	2.509	.017	.855	.390	.205	.104	9.645

a. Dependent Variable: Rad_SSIp

Table C.2.2 - Hierarchical Linear Regression on Dependent Variable SSI_p (Step 3)

Model Summary[b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.886[a]	.785	.761	64.72386

a. Predictors: (Constant), GripL, Weight, Gender, Height

b. Dependent Variable: Rad_SSIp

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	Correlations			Collinearity Statistics	
		B	Std. Error	Beta			Zero-order	Partial	Part	Tolerance	VIF
1	(Constant)	-159.832	307.218		-.520	.606					
	Gender	-27.757	37.286	-.105	-.744	.462	-.738	-.125	-.058	.308	3.244
	Height	1.264	1.945	.093	.650	.520	.759	.109	.051	.299	3.344
	Weight	2.335	.787	.354	2.968	.005	.766	.448	.232	.432	2.313
	GripL	4.340	1.391	.446	3.121	.004	.822	.467	.244	.301	3.326

a. Dependent Variable: Rad_SSIp

Table C.2.3 - Hierarchical Linear Regression on Dependent Variable SSI_p (Step 4)

Model Summary[b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.860[a]	.740	.710	71.24271

a. Predictors: (Constant), RTD, Height, Weight, Gender

b. Dependent Variable: Rad_SSIp

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	Correlations			Collinearity Statistics	
		B	Std. Error	Beta			Zero-order	Partial	Part	Tolerance	VIF
1	(Constant)	-257.603	340.257		-.757	.454					
	Gender	-77.916	35.678	-.295	-2.184	.036	-.738	-.346	-.188	.408	2.451
	Height	2.823	2.107	.208	1.340	.189	.759	.221	.116	.309	3.241
	Weight	2.459	.882	.372	2.787	.009	.766	.426	.240	.416	2.401
	RFD	1.608	1.159	.144	1.388	.174	.552	.228	.120	.690	1.450

a. Dependent Variable: Rad_SSIp

APPENDIX E – MUSCLE PROPERTY AND BONE STRENGTH CORRELATION MATRIX

Muscle property and bone strength correlation matrix

	MCSA	**Grip Force**	**RTD**	**BSI_c**	**SSI_p**
MCSA	1	0.854 *	0.528 *	0.838 *	0.855 *
Grip Force	-	1	0.448 *	0.698 *	0.822 *
RTD	-	-	1	0.254	0.552 *
BSI_c	-	-	-	1	0.712 *
SSI_p	-	-	-	-	1

* $p<0.01$

MCSA = muscle cross sectional area
RTD = rate of torque development
BSI_c = bone strength index in compression
SSI_p = polar strength strain index

APPENDIX F – CERTIFICATE OF ETHICAL APPROVAL

UNIVERSITY OF SASKATCHEWAN

Biomedical Research Ethics Board (Bio-REB)

Certificate of Approval

PRINCIPAL INVESTIGATOR	DEPARTMENT	Bio #
[illegible]	Kinesiology	09-74

INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT
College of Kinesiology
87 Campus Drive
Saskatoon SK S7N 5B2

STUDENT RESEARCHER(S)
Amanda Lorbergs

SPONSORING AGENCIES
UNFUNDED

TITLE: The Bone to Muscle Relationship in the Forearm at Midlife

ORIGINAL REVIEW DATE	APPROVED ON	APPROVAL OF	EXPIRY DATE
11-Mar-2009	13-Apr-2009	Researcher's summary (27-Mar-2009) Consent Form (09-Apr-2009) Appendix C Questionnaire (09-Apr-2009)	30-Mar-2010

Delegated Review: [X] Full Board Meeting: [ ]

CERTIFICATION
The study is acceptable on scientific and ethical grounds. The Bio-REB considered the requirements of section 29 under the Health Information Protection Act (HIPA) and is satisfied that this study meets the privacy considerations outlined therein. The principal investigator has the responsibility for any other administrative or regulatory approvals that may pertain to this research study, and for ensuring that the authorized research is carried out according to governing law. This approval is valid for the specified period provided there is no change to the approved protocol or consent process.

FIRST TIME REVIEW AND CONTINUING APPROVAL
The University of Saskatchewan Biomedical Research Ethics Board reviews above minimal studies at a full-board (face-to-face) meeting. Any research classified as minimal risk is reviewed through the delegated (subcommittee) review process. The initial Certificate of Approval includes the approval period the REB has assigned to a study. The Status Report form must be submitted within one month prior to the assigned expiry date. The researcher shall indicate to the REB any specific requirements of the sponsoring organizations (e.g. requirement for full-board review and approval) for the continuing review process deemed necessary for that project. For more information visit http://www.usask.ca/research/ethics_review/.

REB ATTESTATION
In respect to clinical trials, the University of Saskatchewan Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the Food and Drug Regulations and carries out its functions in a manner consistent with Good Clinical Practices. This approval and the views of this REB have been documented in writing. The University of Saskatchewan Biomedical Research Ethics Board has been approved by the Minister of Health, Province of Saskatchewan, to serve as a Research Ethics Board (REB) for research projects involving human subjects under section 29 of The Health Information Protection Act (HIPA).

Gordon McKay, Ph.D., Vice-Chair
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Biomedical Research Ethics Board

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