Spring 2010

Comparison of Two Bone Mineral Density Pre-Screening Tools: Qus and Ra, to the Dxa

Rachel Beth Newcomer

Comparison of Two Bone Mineral Density Pre-screening Tools: QUS and RA, to the DXA

by

Rachel Newcomer

(Under the Direction of Jim McMillan)

ABSTRACT

Osteoporosis is a health issue that is becoming more prominent in today's society. Bone mineral density (BMD) tests have the ability to: detect low bone density before a fracture occurs and predict the chances of future fractures occurring and determine an individual's rate of bone loss. Purpose: (1) Determine the relationship between BMD t-scores measured by the QUS and RA devices, compared to the DXA measurement, the gold standard. (2) Examine the agreement between osteoporosis classifications produced by the QUS and RA devices, compared to those produced by the DXA, the gold standard. Methods: 132 subjects reported to the Human Performance lab in Hanner Field house to complete a university approved informed consent, a short questionnaire and data collection. The subjects were volunteers from the Georgia Southern Community. All subjects were 18 years of age or older and were not pregnant. The Metriscan applied radiographic absorptiometry to estimate an individual's relative phalangeal bone density of the three middle fingers. The GE Lunar DEXA device provided a total body non-invasive and precise method of measuring BMD. The device used x-ray densitometry techniques to obtain these measurements. The Hologic Sahara UBA575 applied ultrasound to obtain BMD at the heel. Results: The only significant agreement between T-scores was seen with the DXA and RA ($r=.624$, $p\leq.001$). The only significant correlation between kappa classification agreement was found with the DXA and QUS($k=.214$, $p=.01$). Conclusion: The QUS device has the ability to

be used as a BMD pre screening tools at health fair.

Index words: Osteoporosis, Bone Mineral Density, Bone, Fractures, T-scores, QUS, DXA, RA

Comparison of Two Bone Mineral Density Pre-screening Tools: *QUS and RA*, to the DXA

by

Rachel Newcomer

B.S., Georgia Southern University, 2008

A Thesis Submitted to the Graduate Faculty of Georgia Southern University in Partial Fulfillment of the Requirements for the Degree

MASTER OF SCIENCE

STATESBORO, GEORGIA

2010

Comparison of Two Bone Mineral Density Pre-screening Tools: QUS and RA, to the DXA

by

Rachel Newcomer

Major Professor: Jim McMillan
Committee: Barry Joyner
Stephen Rossi
Kathy Thornton

Electronic Version Approved:
May 2010

Dedication

I would like to dedicate this to my brother Joel. He passed away on January 11, 2008 from AML Leukemia. He was my best friend and only sibling. He is my hero and throughout his fight he taught me to appreciate life and the small things involved, as well as patience and determination.

Acknowledgements

I would like to acknowledge and thank, first and foremost, my thesis committee for your support and guidance during the thesis process. Dr. McMillan, Dr. Rossi and Dr. Joyner: I have had the privilege to work with you for seven years and you have guided me to where I am today; for this I will always be grateful. I would also like to thank the faculty and staff of Health and Kinesiology for your help along the way, as well as my colleagues.

TABLE OF CONTENTS

Page

LIST OF TABLES

Page

CHAPTER I

INTRODUCTION

Purpose of study

Bone is living, growing tissue. It is primarily made of collagen, a protein that supplies the soft framework, and calcium phosphate, a mineral that provides strength and hardens the framework of the bone. The combination of these two items makes the bone strong as well as flexible, which assists the bone in withstanding stress. More than 99 percent of the body's store of calcium is found in the teeth and bones. The additional 1 percent is located in the blood. During an individual's lifetime bone resorption and formation occur. Resorption is the removal of old bone and formation is the addition of new bone. Many separate factors' can influence this processes including many hormones, growth factors and vitamins. Inadequate calcium intake or low levels of calcium regulating hormone can lead to a withdrawal of calcium stores from bone. Throughout the childhood and teenage years the addition of new bone outpaces the removal of bone. During this time the bones become larger, heavier and denser. This outpacing occurs until peak bone mass is reached, which normally occurs around the age of 30. Peak bone mass is termed as the period when an individual has maximum bone density and strength. After peak bone mass is reached, the removal of bone starts to occur at a faster rate than the addition of new bone.[14]

Osteoporosis develops when bone resorption occurs too quickly or when replacement occurs too slowly. It mainly affects women but may also affect men. For women, bone loss is fastest in the year's immediately following menopause and continues at a slower rate into

postmenopausal years. Individuals can also be classified at a higher risked to be diagnosed with osteoporosis if they're of an ethnicity that is predisposed to weaker bones. Osteoporosis is more likely to develop if an individual does not reach optimal peak bone mass during the bone building years. Several risk factors are traced to the development of the disease and add to an individual's chances of developing the disease. The risk factors are grouped by the ability to prevent them. Unpreventable risk factors include: gender, age, body size, ethnicity and family history. Preventable risk factors include: sex hormones, anorexia nervosa, calcium and vitamin D intake, medication use, lifestyle, smoking and alcohol intake. Prevention of the disease can occur by taking action to assure reaching peak bone mass and continuing to build bone tissue during the aging process. This can occur by: the adequate intake of calcium and vitamin D, proper exercise, abstaining from smoking and alcohol, avoiding medication known to cause bone loss and taking preventative medications.[14]

Bone mineral density (BMD) testing is the most effective way to determine an individual's bone health. BMD tests have the ability to: detect low bone density before a fracture occurs, confirm a diagnosis of osteoporosis if an individual has already experienced one or more fractures, predict the chances of future fractures occurring, and track an individual's rate of bone loss.[14] The determination of bone mineral content and bone mineral density is essential in the investigation of an individual's calcium metabolism and associated diseases.[9] The density of each individual's bones is dependent upon the amount of stress placed on the bone, as well as the nutritional intake of the individual. The most widely used method of measuring BMD is a DXA test, dual-energy x-ray absorptiometry. The DXA test can obtain the BMD of the hip and spine, and the total body. Quantitative computed tomography is the only current method that provides an actual measurement of volumetric bone density. [14] BMD tests provide a BMD score,

a T score based on the age group, which is shown in standard deviations and indicates a classification of how much an individual's bone density is above or below normal, and a classification based on the T score. Many tests also provide a Z score, which compares an individual to what is normal in an individual of their same age and gender.[19]

BMD via DXA

The most accurate method used to determine BMD is dual x-ray absorptiometery (DXA). This device is most often used at the posterior-anterior and lateral lumbar spine, proximal femur and forearm. [3] The DXA is an accurate and reproducible method of measuring bone mineral content. [1] It is non-invasive and can be safely repeated, as the radiation dose is small. [1] The device has its popular notoriety because the absorption of x-rays is very sensitive to calcium content present in the tissue .[5]

The DXA can provide information on bone mineral content of the whole skeleton and individual bones, including those most vulnerable to fracture. In addition, the device is used to visualize lateral images of the spine from T4 to L4 to detect deformities of the vertebral bodies.[5]

BMD via Ultrasound

Although the DXA has been termed the preferred method for BMD analysis, the quantitative ultrasound instruments (QUS) have now been accepted as an alternative method for the DXA in diagnosing osteoporosis.[1] The performance characteristics of ultrasound are similar to those of the DXA. Several corporations now have their own QUS instruments that can measure broadband ultrasound attenuation (BUA) and speed of sound (SOS) .[14] Many experts suggest that broadband ultrasound attenuation (BUA) or speed of sound (SOS) at the heel are linked with a 1.5 to 2 fold increase in detecting risk for each deviation decrease in BMD.[1]

Advantages of QUS methods of measuring BMD include: a radiation-free measure, portability of the device and cost effectiveness. It also does not require a registered x-ray technologist to operate it. The Sahara does not require water like other similar units that utilize QUS; therefore there is no variability in results due to fluctuations in water temperature. The device price point is less than half of the DXA bone densitometer.[1]

BMD via Radiation

Radiographic absorptiometry (RA) is another method also available to measure BMD. This device applies storage phosphor technology that replaces the use of x-ray film as a radiation detection sensor. The scanning process takes no longer than a second and does not require any gels or other preparation. This occurs at the phalanges and metacarpals. The measurement takes a single, low-dose x-ray image of the fingers with the accumulated radiation at less than 5 percent of a typical dental x-ray. The methods of this device have been proven to be both accurate, as well as predictive of future hip fractures. It has also been said to be a reliable method for assessing total body BMD status.[4]

The new radiographic and ultrasound methods are being examined in comparison to the gold standard, the DXA. The radiographic and ultrasound devices provide sub-regional measurements, meaning they use a particular part of the body and do not provide a total body measure, as does the DXA unit. It is essential to test these sub-regional devices against the DXA to determine if portable devices can be used at health fairs. The development of the disease is steadily increasing; therefore, it is essential that cost-effective easily available measures of BMD are found. These ultrasound and radiation devices have the ability to fit these needs. Therefore the first purpose of the study was to determine the relationship between t-scores measured by the

QUS and RA as compared to the DXA. The second purpose was to examine the agreement between osteoporosis classifications produced by the QUS and RA devices, compared to the classifications provided by the DXA.

Delimitations:

Subjects were included in the studied under the following qualifications

1. Must be at least 18 years of age
2. Must not be pregnant at the time of testing

Limitations:

The research may have been limited by the following

1. Non random selection (volunteer based study)
2. Small sample size
3. Malfunctioning of devices
4. Lack of diseased individual's

Assumptions:

The study was run under the following assumptions

1. Participants followed all pre-test instructions for tests
2. Truthful answers were given on questionnaires
3. All measurement's on devices by tester's are performed properly and recorded accurately
4. Consistent use of non-dominant limbs between devices

CHAPTER II

REVIEW OF LITERATURE

Introduction of bone

The basic structure of the bone consists of: an outer cortical or compact zone, an inner trabecular or spongy zone, a periosteum and an endosteum. The major functions of the bone include: providing structural support to the body, providing protection to the vital organs, providing an environment for marrow and acting as a mineral reservoir for calcium homeostasis in the body.[6]

Bone is made up of support cells, which are osteoblasts and osteoclasts. Osteoclasts are remodeling cells composed of a non mineral matrix of collagen and non collagenous proteins, osteoids, and inorganic mineral salts deposited within the matrix. Osteoblasts are responsible for the matrix synthesis and its mineralization. Osteocytes are responsible for begin resorption or formation in response to physical forces brought to the bone and to transducer messages to the osteoblasts on the bones surface. Osteoclasts are responsible for resorption of mineralized tissue and are found attached to the surface of the bone at sites of active bone resorption. The hardness and rigidity of the bones matrix is due to the presence of mineral salt in the osteoid portion of the bone. Bone development and growth or osteogenesis occurs via two processes. The first process includes intramembranous ossification, at which point the replacement of connective tissue membrane portions with bone tissue occurs and this ends in the building of flat bones. The second process involves endochondral ossification, which includes the replacement of hyaline cartilage with bone tissue, such as in the femur and tibia.[6]

Bone maintenance is vital and includes several vital components. Resorption is the daily removal of small amounts of bone mineral and this process must be balanced in combination with the deposition of new mineral if bone strength is to be preserved. The balance between resorption and deposition is dependent on the osteoblasts and osteoclasts. This balance controls how much bone is made, maintained or lost. These cells are also vital in the bone remodeling cycle. Osteoclasts are first activated which leads to bone resorption and next a reversal phase occurs at which point a resorption pit is accompanied by osteoblast precursor cells. Bone formation begins to occur as continual waves of osteoblasts form and compile new bone matrix. Bone formation tends to outpace bone resorption therefore a sudden increase in remodeling often leads to an increased net loss of bone.[6]

Peak Bone Mass

Bone mass at the closing of the growth period is termed as peak bone mass (PBM). Several factors determine the accumulation of bone mass during growth: heredity, Vitamin D, bone tropic nutrients (calcium, proteins), end factors (sex steroids), mechanical forces (physical activity, body weight).[1] The most vital determinant of PBM has been shown to be genetically related.[1]

Osteoporosis

Osteoporosis is a disease of the bones. It is termed as a systemic skeletal disease characterized by low bone mass and deterioration of bone tissue, with an increase in fracture risk. People with osteoporosis have weaker bones than the average person and this increases their chances of a bone fracture. Common sites for osteoporotic fracture

include: the proximal humerus, distal forearm, hip and spine, also called vertebrae. In 2000, approximately 620,000 new fractures at the hip, 574,000 at the forearm, 250,000 at the proximal humerus and 620,000 clinical spine fractures occurred in women and men over the age of 50. [9] Osteoporotic fractures are a significant cause of morbidity.[9] There are several risk factors that increases an individual's chances of developing osteoporosis, these risk factors are grouped by those that are controllable and those that are not. Risk factors that an individual can not control include: having a small or thin body frame (under 127 lbs), having a family history of osteoporosis, being over 65 years old and not getting an appropriate amount of physical activity due to a disability.[22] Risk factors for osteoporosis that can be controlled include: smoking, drinking an excessive amount of alcohol, consuming a diet low in dairy products and not getting enough exercise.[22] Long term uses of medications such as: glucocorticoids, some antiseizure medications, gonadotropin releasing hormone, antacids with aluminum, some cancer treatments and an excessive amount of replacement thyroid hormone can also have a negative effect on bone health.[22] In addition, an individual should contact their healthcare provider if they develop other symptoms of osteoporosis such as: loss in height, developing a slumped or hunched posture, onset of sudden unexplained back pain, an individual is over age 45, post menopausal and breaks a bone.[22]

Prevention of Osteoporosis

There are several ways to prevent the occurrence of bone density diseases such as osteoporosis. Building strong bones during childhood and the teenage years is one of the

best ways to prevent the future occurrence of osteoporosis. As an individual ages bone loss occurs at a more rapid pace and it is important to take the proper steps to prevent additional losses in bone that occur naturally in the aging process. One vital step is to consume the proper amount of calcium.[22] An individual can consume calcium through diet or by taking a calcium supplement. Individuals between 19-50 should consume a minimum of 1000 milligrams (mgs) of calcium per day.[22] Individuals older than 51 yrs old should consume a minimum 1200 mgs of calcium per day.[22] Other important prevention methods include: taking the proper amount of vitamin D, consuming a healthy diet, participating in physical activity including weight bearing activity, not smoking, moderate consumption of alcohol if one chooses to drink and making the home safe from potential falls.[22] It is important for an individual to have their bone health checked on a regular basis as the aging process takes a toll on the body. Bone mineral density testing is the easiest and the most prevalently used method for determining BMD.[22]

Bone Mineral Density

Bone mineral density (BMD) is the amount of bone mass per unit volume per unit area. [22] It is an important determinant that can indicate the presence of health risks, as well as disease. The common diagnosis of diseases related to bone health such as osteoporosis lies within the testing of bone mineral density (BMD). The testing of BMD may be an indication of bone health and has a high correlation with bone strength. [3] There are several objectives for obtaining BMD measurement, which are to provide diagnostic criteria, prognostic information or chance of future fractures and a baseline on which to monitor the natural history of the treated or untreated patient. [9] If an individual is 65 or

older they should have their bone mineral density checked on an annual basis. If an individual is between 40 and 60 they should discuss with their health care provider, the possible risk factors that may exist for low bone mass to prevent possible future occurrences of bone health issues. [22]

Variations in BMD between genders

BMD in females

Unfortunately, just the act of being a female itself increases an individual's chances of developing osteoporosis.[22]Among the approximately10 million Americans approximated to be diagnosed with osteoporosis eight million are women. [15] Osteoporosis can cause women serious problems, particularly if it occurs in the vertebrae. Vertebral fractures are common in older and menopausal women. [22] In women, after menopause occurs, the probability of a fracture at any of these sites is 12%. [9] A verterbal fracture occurs in women from normal activities such as climbing stairs, lifting objects or bending forward. Indicators of osteoporosis in this region include: sloping shoulders, curve in the back, height loss, back pain, hunched posture and a protruding abdomen. Women who are older than 60 with risk factors for osteoporosis should obtain BMD testing.[22] In addition, women older than 45 who have had past bone breaks should obtain testing prior to 60 to monitor bone health.[22]

Young female athletes are a specific group of individuals that are predisposed to being diagnosed with osteoporosis. Nattiv et al performed a study analyzing the female athlete triad. The triad describes the intertwining relationships between energy

availability, menstrual function and bone mineral density, which have the ability to have clinical manifestations including eating disorders, amenorrhea, and osteoporosis. Low energy intake in the diet and a lack of regular menstrual activity are the main determinants that have a negative effect on the skeletal health of these female athletes. Research has shown the importance of coaches and trainers in monitoring the habits of their athletes. It is recommended that preventive measures and early interventions be implemented with coaches, trainers, parents and administrators so have the ability to educate those below them on the early stages of the triad and the potential harms that may occur such as osteoporosis.[14]

BMD in males

Although osteoporosis is mostly known to affect women, it still has the potential to be an issue for men. In the United States over two million men have been diagnosed with osteoporosis with men over the age of 50 at a greater risk.[22] The National Osteoporosis Foundation has found that 20% of those affected by osteoporosis are men.[15]

Research done by the American College of physicians has established "Clinical Guidelines" for screening osteoporosis.[16] Guideline one states that clinicians should periodically do individualized assessments of risk factors for osteoporosis in older men over 50 or those who have experienced bone fractures at a younger age. Guideline two states that clinicians perform DXA scans for men who are predetermined to be at risk for osteoporosis and are potential candidates for drug therapy. Guideline three states that further research needs to be performed in the potential need for osteoporosis screening tests in men. These guidelines are based on the premise that osteoporosis in men is

substantially under diagnosed, under treated, underreported and inadequately researched. Studies have shown that osteoporotic fractures increase morbidity, mortality, and financial issues to the male population. Due to the aging of our current population, rates of osteoporosis in males are predicted to increase by approximately 50% in the next 15 years and the occurrence of fractures at the hip are also predicted to double or triple by the year 2040.[16]

Variations in BMD between ethnicities

The National Osteoporosis foundation has found that significant risk for being diagnosed with osteoporosis has been reported in people of all ethnic backgrounds. Twenty percent of non-Hispanic Caucasian and Asian females who are 50 and older are estimated to have osteoporosis and 52% of these individuals are predicted to be osteopenic, which means they have a low bone mass and are at risk for being diagnosed with osteoporosis in the future. Seven percent of non-Hispanic Caucasian and Asian men who are 50 and older are estimated to currently have osteoporosis and 35% are predicted to be osteopenic, which means they have a low bone mass and are at risk for being diagnosed with osteoporosis in the future. Five percent of non-Hispanic African American women ages 50 or older are estimated to have osteoporosis and around 35% currently have low bone mass, which puts them at risk for acquiring osteoporosis in the future. Four percent of non-Hispanic African American men are estimated to currently have osteoporosis and 19% are estimated to be in the osteopenic range. Ten percent of Hispanic women ages 50 or older are estimated to currently have osteoporosis and 49% are estimated to be in the low bone mass ranges. Three percent of Hispanic men age 50

and older are estimated to currently have osteoporosis and 23% are estimated to currently have a low bone mass. When comparisons in research have been made between other ethnic backgrounds risk for being diagnosed with osteoporosis is climbing most rapidly among Hispanic Women. Experts have predicted that costs tied to fractures produced by osteoporosis among Hispanics will go from approximately $754 million in 2005 to around $2 billion per year by 2025.[15]

Testing devices for BMD

BMD via DXA

Lewiecki et al in 2006 performed research to assess the options for bone mineral density (BMD) testing in the clinical practice setting. They found that the DXA, or dual x-ray absorptiometry, measurements at the spine, hip and forearm are the gold standard in monitoring and testing BMD. Biomechanical research is cited to support a strong correlation between mechanical strength and BMD measured by the DXA.[10] Accuracy and precision of the DXA were shown to be highly sufficient and radiation exposure was shown to be low. The World Health Organization (WHO) is mentioned as setting the BMD classifications shown by the DXA as a reference for all types of BMD testing devices.[10]

Shepherd et al in 2006 performed a research study comparing the short-term precision error of two dual x-ray absportiometry devices: the GE Lunar Prodigy and the Delphi Hologic scanner. Eighty seven women were included in the study were measured multiple times on both devices. Precision error was calculated using a root mean square standard deviation and coefficient of variation was calculated for the repeated

measurements. The right and left femur of each subject were analyzed separately and as a combined dual femur precision. The precision errors of the two devices were compared using an ANOVA which determined significance of any differences seen. Precision errors for both devices were found to be low; however the Prodigy DXA precision errors were significantly lower than the Hologic DXA at the spine (1% vs. 1.2%), total femur (0.9% vs. 1.3%), and femoral neck (1.5% vs. 1.9%), and dual total femur (0.6% vs. 0.9%). Overall, the DXA shows high reproducibility rates and the Prodigy DXA was favored over the Hologic device.[17]

BMD via RA

Thorpe at al performed a study in 2008 to evaluate the Alara Metriscan as useful Radiographic Absorptiometry (RA) device. One hundred and seventy white female subjects participated who were between the ages of 55 and 70. Seventy of the females were osteoporotic and 100 were non-osteoporotic as termed by a hip and spinal scan. All subjects had two scans performed on the non dominant hand and one performed on the dominant hand. Radiation exposure for the participants was mentioned as being < 0.1 microSv per scan, which is less than a routine dental scan. An area of safety of 1 meter was established around the testing device. In Vitro precision was 0.17% for the dominant hand and 0.22% for the re-positioned non-dominant hand. Long term in vitro precision was 0.31% measured over a six-month span. The study concluded that the Metriscan is a suitable device for BMD testing for postmenopausal women in combination with a total body scan.[20]

BMD via QUS

Kaufman et al in 2007 performed a study to develop an ultrasound device, which can estimate BMD at the calcaneus or heel. The device was reported as being portable and self contained. The device utilizes real time evaluation of the BMD from the heel by computing a parameter termed net time delay (NTD). NTD is termed as the difference from the transit time through the heel of a given ultrasound wave and the transit time through an object of equal thickness but only containing tissue that is soft in nature (to the heel). Thirty six 'sample' subjects were utilized as a pilot guide for the study with BMD's ranging from 0.25 t0 1.83 g/cm2. The NTD and BMD were found to have a high correlation (r=0.99), which demonstrated the devices high sensitivity to BMD in the heel. The IRB then approved the use of 85 adult women as subjects for the study. A correlation of 0.86 was found between the NTD and BMD, which a significant finding but not nearly as high as that is found in the pilot study. These differences from the pilot study to the actual study were attributed to errors in reproducibility and positioning of the area of interest. A conclusion was reached that QUS was a good way to test BMD but more research needs to be performed on error precision between trials.[8]

Malavolta et al in 2004 performed a review of literature on the quantitative ultrasound (QUS) of bone. It is stated that QUS provides additional information in regards to structure of the bone, trabecular orientation and micro-architecture. Ultrasound utilizes a vibration that is mechanical in nature which propagates in a fluid or solid medium. The scattering of waves and absorption of ultrasound waves in the bone produces the BMD measurement of the heel. With the calcaneal systems for testing BMD, the heel is positioned between two ultrasound transducers, one of the transducers

transmits a US signal and the other transducer is receives it after it passes through the heel. Two parameters are reported at the conclusion of the scan: BUA and SOS. Bua is broadband ultrasound attenuation and SOS is speed of sound. Two other indexes reported by more advanced systems include: a heel stiffness index and a quantitative ultrasound index (QUI). The study concluded with BUA and SOS aspects of the QUS device as being able to predict the potential for osteoporotic fractures as well as the DXA can at the hip and spine, although more research needs to be done on QUS testing. Advantages of QUS include: no patient or tester exposure to radiation, low cost and portability. [12]

Comparisons of non-invasive bone mineral measurements

There have been several studies that have examined the commonly used available methods of measuring an individual's bone mineral status. The studies utilize various populations to examine these methods. Grampp et al in 1997 examined the newer methods of radiographic absorptiometry and ultrasound technologies ability to noninvasively assess bone mineral status across three female populations. The three populations included healthy premenopausal, healthy postmenopausal and osteoporotic postmenopausal women. The study examined the interrelationships, comparing their respective abilities to reflect age and menopause related bone loss, discriminate women with osteoporotic vertebral fractures and classified women diagnostically as osteopenic or osteoporotic. There were a total of 47 subjects who were postmenopausal and 36 who were osteoporotic postmenopausal. All women were examined with the following techniques: (1) quantitative computed tomography; (2) dual x-ray absorptiometry; (3) peripheral QCT; (4) two radiographic absorptiometry techniques of the carpal and

metacarpal; (5) two quantitative ultrasound devices of the calcaneus for speed of sound and broadband ultrasound attenuation (BUA). To compare the techniques for their diagnostic ability, a kappa score analysis was performed on the classifications of postmenopausal women and osteoporotic postmenopausal women. Every woman from the postmenopausal group was categorized as osteopenic if their T score with respect to the pre score (reference group) was less than – 2.0. Every subject from the osteoporotic group was classified as osteoporotic if their T score compared with the reference group was less than – 2.5. The strongest correlation (r= 0.87) was between the QCT and DXA. For each anatomic site, the methods providing the best results were: (1) spine, QCT; (2) hip, DXA; (3) Radius, DXA; (4) hand, RA and (5) calcaneus, SOS and BUA. Kappa score analysis showed that as a whole the diagnostic agreement among these measurements in classifying women as osteopenic or osteoporotic was poor, with scores averaging at about 0.4.[3]

Madsen et al in 2001 examined the relationship of bone quality and bone mass utilizing quantitative ultrasound (QUS) and dual X ray absorptiometry (DXA) in women with rheumatoid arthritis (RA). They used these 2 differing forms of assessment to assess quadriceps strength in the provided population. The subjects included 67 women with RA with a mean age of 62 years and average disease duration of 15 years. QUS provided the calcaneal bone quality expressed given as speed of sound (SOS), broadband ultrasound attenuation (BUA) and stiffness. The DXA unit measured BMD of the femoral neck, spine and distal forearm. A multiple regression analysis was utilized. Quadriceps strength predicted SOS, BUA, stiffness, and femoral neck independently of height, age, disease duration, and weight. After the adjustments were made for covariates

women with subnormal BMD of the femoral neck had a 20% smaller QS score than those with a normal BMD. The researchers concluded that the bone quality of the calcaneus and femoral neck BMD were indeed associated with QS in women with RA. They also stated that the utilization of QUS has the ability to predict osteoporotic fractures at the calcaneus as well as the DXA can at the hip and spine. [7]

Laabes et al in 2008 produced a cross sectional study examining the bone quality of black male athletes by use of calcaneal ultrasound. They aimed to describe the bone characteristics of competitive top ranked Nigerian male athletes using the calcaneal ultrasound. Then to establish whether intensive training leads to higher bone density in an environment that is reported as having low calcium intake, and to analyze the correlation of stiffness index (SI) in relation to activity level. Energy expenditure is said to correlate with length of training and by extension also magnitude of skeletal loading. One hundred and two male athletes were recruited as subjects and the sports included were: football (n=68), running (n=15), handball (n=7), taekwondo (n=6), cycling (n=2), judo (n=1), badminton (n=1), and high jump (n=1). Bone density was established using lunar Achilles calcaneal ultrasonometer. The mean age of the athletes was 25 +/ - 6 years. Football was a significant determinant of speed of sound independent of age, height, weight and BMI. The average SI was 127 +/ - 16 and the median T score was 0.82. The mean SI differed significantly between sports. Multivariate analysis showed that football and running were significant determinants of SI independent from BMI and age. The median T score of footballers 0.94 was higher than that of the other sports included. Laabes at al concluded from this study that repetitive skeletal loading at the calcaneus has the ability to produce gains in bone density in black male athletes. They

stated that although the DXA is the gold standard and shows a high correlation with bone strength, around 25-30% of the variance seen in this strength results from the effects of microstructure, architecture and remodeling. They therefore chose to utilize the ultrasound technique because it has the ability to provide additional information on the biomechanical properties of bone, which cannot be obtained from the DXA.[6]

Hansen et al in 2009 performed a study to determine the ability of radiographic absorptiometry (RA) to indentify male patients with osteoporosis. They utilized the RA device instead of the DXA stating that it was not chosen due to accessibility issues and cost. The RA and quantitative ultrasound (QUS) devices were developed due to their portability and user-friendly screening methods. RA is available as a self-contained portable device, providing BMD measures of the phalangeal bones of the hand. They stated that the method is rapid, reproducible and utilizes a very low radiation exposure. The cost is also about a fifth of that of the DXA unit. BMD was taken of the intermediate phalanges of the second to fourth finger, lumbar spine and total hip in 218 men aged from 60-74 years utilizing RA and the DXA. A Metriscan device was utilized to measure RA. Osteopenia and osteoporotic classifications were obtained for each individual. The BMD of the phalanges (RA) correlated significantly ($R=0.47$, $P< 0.001$) with the BMD of the hip and lumbar spine (DXA) ($R=0.46$, $P< 0.001$). They concluded that RA has the ability to be applied as a pre screening tool.[4]

Associations of sub regional measurements of BMD

Although the DXA, which is the gold standard in BMD testing, provided a total body measure other devices don't supply this same feedback. The RA and QUS devices

provide sub regional measures in relation to total body BMD. It is important to establish how these sub regional tests relate to total body measures.[10]

Taal et al in 1999 examined the usefulness of quantitative heel ultrasound (a sub regional area) with the DXA in determining BMD in chronic haemodialysis patients. It is states that although the DXA is a standard non-invasive method to assess BMD; the QUS is mobile, inexpensive and can predict fractures to the same extent in a sub regional area. The DXA was utilized to measure BMD at the hip and spine. QUS was utilized to obtain BMD at the left heel measuring BUA and velocity of sound (VOS). Correlations between DXA and QUS parameters were calculated. Patients were classified by BMD scores as osteopenic (t>-2.5 and < -1) or osteoporotic (t< -2.5) by WHO criteria. Eighty eight patients (45.5% women), mean age 58 +/ - 17 years were utilized for the study. A total of 19% and 49% showed femoral neck BMD's in the osteoporosis and osteopenic ranges. There were solid correlations between hip BMD and QUS parameters (r= 0.68-0.79, p< 0.001). Therefore the DXA and QUS parameters were significantly correlated. The QUS was found to be a valid pre-screening sub regional tool for BMD.[10]

Franck et al in 2008 utilized patients with rheumatoid arthritis (RA) to project associations with sub regional measurements of BMD. They evaluated sub regional BMD of the hand and the correlation of BMD to other regional bone losses, parameters of inflammation or bone resorption in 421 patients with RA, as well as a control group. The RA patients showed significantly lower BMD values in the carpal joints as compared to the controls. There was no significant difference seen in BMD at the lumbar spine and hip. There were significant correlations seen between BMD total of the hand, its sub

regions, the forearm and hip. Therefore, they found the hand as a sub regional area of BMD measurement to be a valid measure of BMD.[2]

Bone Health among the American population

Bone health is an issue that has the ability to affect the lives of all Americans regardless of age, gender or race. It is a factor that takes into account the overall health of an individual and can hinder an individual's quality of life. The maintenance of healthy bones allows the skeleton for an individual to be readily mobile and to protect against potential injuries. Research funded by the Office of the Surgeon General has shown that the bone health of Americans appears to be in jeopardy and if an individual chooses to leave their bone health unchecked bone health status will get worse with the aging process. Large improvements can be made in the prevention, assessment, detection, diagnosis and treatment of bone health status if American's take advantage of the available testing and use information available. Research has shown that a large gap is present between what has been seen in research and what is applied by American consumers and healthcare providers. An area of specific concern exists in serving ethnic and racial minorities and other deprived populations; this includes the uninsured, underinsured and those who reside in rural areas. Closing these existing gaps will not take place without research that includes specific strategies and programs geared towards positive changes in bone health all of these existing populations. The Office of the Surgeon General has stated that the topic of bone health is connected to the area of public health's approach to promoting health. The Surgeon General is calling for Federal, State and local governments to come together with the private sector and community

organizations in a joint effort to promote bone health. This concern states the importance of establishing portable bone mineral density testing devices that all areas of the American of the population can gain access to. Validating these devices will raise the prevalence of their use in health fairs and other possible health promotion events, and this in turn will slowly raise the awareness and prevention of Osteoporosis. [21]

CHAPTER III

METHODOLOGY

Subjects

The study was open to all individuals at Georgia Southern University; this included faculty, staff, students, as well as the surrounding community. Pregnant woman were excluded from the study. This was done in hopes of recruiting subjects with a wide range of ages, gender, and ethnicities. Subjects were solicited via flyers around the University's campus, by word of mouth, and by referral. Approval from the individual building supervisors around campus was received before the flyers were posted. All testing on the subjects was done in the human performance lab located in Hanner 2310. All subjects signed a University IRB approved informed consent form before testing. After signing the consent form each subject was assigned an identification number to maintain subject confidentiality. A questionnaire (refer to appendix B) was given to determine: age, gender, menstrual status (if female), race, height, weight, disease, medications and treatments known to effect bone metabolism. All subjects completed all three BMD tests: RA, DXA and QUS. Due to malfunctions in the devices several subjects completed the testing of the three devices on two separate days. All subjects's performed the testing procedures in the same order with the exception of those who had to return due to malfunctioning of one of the devices. Before being tested on each device all participants were provided with proper pre-test instructions. Each subject was provided with a copy of the feedback from the three devices, as well as a copy of their informed consent and a short handout with further BMD information.

Instrumentation and procedures

The Metriscan device is a portable device utilized radiographic absorptiometry to estimate an individual's relative phalangeal bone density of the three middle fingers. Prior to the use of the device a self-calibration was performed. [7] The scan process took about one second and total time from start to printing of results was about one minute. The printout included the subject's average T-score, which is the estimated relative bone density in comparison to that of a healthy young female Caucasian population of the 3 fingers measured and a classification based on their t-score. It also offered a z score, which compared their BMD to that of an age-matched population of the subject's same gender and ethnicity. It has a precision error of +/- 1%. Due to the radiation produced by the device the subject was offered a lead vest and a thyroid protector to wear prior to beginning each test. The subject's non-dominant hand was placed on the device and the three middle fingers were properly aligned in the unit. After alignment was verified by the tester, the subject was told to extend their arm and the tester held down the exposure button. [7] Two copies of the form were printed, one for analysis and one for the subject.

The Hologic Sahara UBA575 utilized quantitative ultrasound (QUS) to obtain BMD. The device provided a T score; a classification based on the T score, as well as an estimated heel BMD, which was found by measuring an individual's heel, or calcaneus, thickness. The process took less than two minutes and only required the subject to place their bare foot, after being cleaned, within the set parameters of the unit after the heel was cleaned on both sides. The same trained testers performed all scans. During the test the individual was seated in a stable back supporting chair. A clean paper towel was placed

below the non-dominant foot in the Sahara device for sanitation purposes. Two silicone nodules were gelled prior to beginning the test and placing of the foot. The subject's foot was aligned with the back of the heel against the back of the device with the leg angled and two nodules compress against the calcaneus to obtain the individual's BMD. The device then provided a printout with each individual's BMD score of the heel and a standardized T-score. [6]

The GE Lunar DEXA device provided a non-invasive and precise method of measuring BMD and areal density. The device used x-ray densitometry techniques to obtain these measurements. The same trained testers performed all scans. Only those individuals with the proper training operated the device. Before each day of testing was begun the DEXA passed a quality control check calibration. Each subject was weighed on a calibrated scale in the lab before the DXA scan was performed and then the subject's data was entered in the computer. The subject was instructed on how to properly position his/her body and how the test procedures were going to occur. The subject was then positioned his/her head approximately two inches from the top parameter outlined on the device with his/her body aligned down the middle. The tester then made sure the subject remained inside the outlined parameters. The subject's knees and ankles were secured with velcro straps to ensure the hips were rotated inward. [7] The subject was instructed to remain still while the scan was performed. The scan took about 6-11 minutes to complete varying based on the size of the subject. A print out was provided with their T score, classification based on T score, and BMD total body measurement based on pre-established norms. [7]

Design and Analysis

SPSS version 17.0 was utilized to analyze the data. The relationship between T-scores of the three devices was examined utilizing Pearson's *r*. The disease classification provided by the QUS and RA devices was compared to that provided by the DXA. The disease classifications of the QUS and RA units will also be compared again one another. Cohen's kappa coefficient was utilized, which provided an index of agreement between ratings of two variables when the same scale is utilized for both. This measure corrected the observed percentage agreement for chance. It also had the ability to normalize the resulting value; therefore the coefficient provided consistently ranges from -1 to +1. A product of 1 showed perfect agreement while -1 indicates perfect disagreement. A value of 0 proves that the relationship between the two variables is the same as one would expect by chance.[4] Sensitivity and specificity were determined. Sensitivity was found, which is the probability that the clinical test declares those person's positive, which have the disease. Specificity was also found which notes the probability that the clinical test declares the individual negative that do not have the disease. Alpha was set at .05.

CHAPTER IV

RESULTS

Subjects

Participants in the study included 132 individual are who were from the southeast region of Georgia. They were pooled from the Georgia Southern University community, which included faculty, staff, students as well as individuals from the surrounding areas. The subject's (n= average) height (170.2 +/- 16.8 cm), weight (71.4+/- 17.3 kg), and age (37 +/- 37 years).

DXA vs. RA

The correlations of t-scores were analyzed via Pearson correlations (see in **Table 1)**. These results showed that the comparison between the t scores of the DXA and RA was significant. This relationship was positive and moderate when assessing its strength and direction. Proportion of agreement between the two devices was found to be 70.4%. The following kappa and corresponding confidence interval was found: .122= 95% CI (.008, .236). Kappa was found to be significant (k=.019). Sensitivity, which assesses the proportion of the time that a positive diagnosis of the disease is found correctly, was found to be 77.7%. Specificity, which assesses the proportion of the time that a negative diagnosis of the disease is found correctly, was found to be 69.9%. **Table 2** provides the data used to collect proportion of agreement, sensitivity and specificity.

Table 1: Pearson's correlation between t-scores

DXA	1	–	–
QUS	r=.223 p=.015	1	–
RA	r=.638 p≤.001	r=.123 p=.159	1
	DXA	QUS	RA

Table 2: Kappa classification agreements between DXA and RA

	Diseased	Not Diseased
Diseased	A=7	B=37
Not diseased	C=2	D=86

DXA vs. QUS

The correlations of t-scores were analyzed via Pearson correlations and can be found in **Table 1**. These results showed that the comparison between the DXA and QUS was significant. This relationship was positive. Proportion of agreement between the two devices was found to be 76.3%. The following kappa and corresponding confidence interval was found: 0.128= 95% CI (-.042, .298). Kappa was found to be significant (0.128). **Table 3** provides the data used to collect proportion of agreement, sensitivity and specificity.

Table 3: Kappa classification agreements between DXA and QUS

	Diseased	Not Diseased
Diseased	A=4	B=27
Not Diseased	C=4	D= 96

RA and QUS

The correlations of t-scores were analyzed via Pearson correlations and can be found in **Table 1**. These results showed that the comparison between the RA and QUS was not significant. Proportion of agreement between the two devices was found to be 64%. The following kappa and corresponding confidence interval was found: .163= 95% CI (.084, .242). Kappa was found to be significant.

Discussion

The present study was designed to establish portable bone mineral density prescreening tools by comparing them to the gold standard. The RA and QUS devices were compared against the DXA, which is the gold standard, to establish the reliability for these instruments for use in events such as health fairs. Pre screening devices have the ability to cut down on the high number of fractures seen in the elderly population. Educating the elderly and even younger populations on the risks of osteoporosis at an earlier age and the possibility of the existence of the disease has the ability to increase their awareness on the disease. Bone mineral density testing can also increase their awareness on fractures and falling. Bone mineral density

instruments such as the QUS and RA have been found in past research to be valid pre-screening tools for assessing an individual's risk of being diagnosed with osteoporosis.

The DXA has been found to be the gold standard in testing due to its reproducibility of testing results and the use of the total body for testing. The DXA however is quite complex and requires a higher level of training than the pre screening tools, as well as being more costly and non portable. The QUS and RA tools are portable and easy to use. The pre screening methods of QUS and RA have been evaluated in limited combinations in past studies when assessing various combinations of gender's and ethnicities utilized in the present study. Past research has shown that populations used and definition of osteoporosis vary between studies, comparisons are hard to make.

The key findings of the present study in regards to the correlations between t-scores established that the relationship between the DXA and RA, as well as DXA and QUS were both significant; however, the relationship between the DXA and RA was much more meaningful when comparing t-scores. When assessing the classification agreements via kappa, the relationship between the DXA and QUS was much stronger than that between the DXA and RA.

When assessing the findings between the DXA and RA devices a significant relationship was seen between t-scores. This relationship was seen to be positive and moderate in nature. There was however lower kappa scores seen with this comparison than the others analyzed. Previous research has stated that specific t- scores and classifications are effective in use when the reference group applied was selected from the same population as the individual's being analyzed. However, when differences exist between the reference groups used for varying devices t-scores may also vary.

The internal calculations used by the QUS and RA devices vary based on the reference groups utilized therefore this has the potential to explain the lack of significance in the correlation. Similar past research has assessed the differences between reference curves for BMD between Chinese, Japanese and American Caucasian women. World Health Organization's (WHO) reference based T-scores were assessed to establish comparisons. The DXA was utilized for analysis at the lumbar spine, hip and forearm. The prevalence of osteoporosis in various regions for Chinese women was found to be between 10.1%-19.8%, for Japanese women 11.6%-16.8%, and for Caucasian women 13%-20%. The study concluded with the fact that racial differences in BMD references curves, prevalence and risks of being diagnosed with osteoporosis exists amount ethnicities.[11]

When assessing the results between the DXA and QUS there was higher significance found between the osteoporosis classification agreement of the DXA and QUS . Compared to past research the kappa seen was found to be slight (.01-.20) and not as as high as desired. The scale ranges from 0-1 therefore this slight agreement is not strong. A similar study was performed on 3 groups of women: healthy premenopausal, healthy postmenopausal and osteoporotic postmenopausal.[4] This study differs in that it only used women as subjects however; the same three devices were used to analyze the agreement between classifications provided. The study also differs from the present one in that DXA scans of specific sites were used as opposed to a total body scan which was utilized in the present study. There was no significant agreement seen in classifications when assessing all comparisons between devices in the study. The lack of significance can be attributed to many factors. The lack of a varied population was mentioned as being the main issue, as only women were used. The use of a reference t-score for all populations was also a strong indicator of the lack of significance seen. The point of all BMD

anatomical measurement sites using the same T-score was mentioned as not being advisable for comparisons between varying devices, techniques and populations. Future research is necessary comparing individuals of the same gender with varying health statuses, as well as research with varied populations to establish reliable portable BMD devices.

CHAPTER V

CONCLUSION

Past research has suggested that the RA and QUS devices both have the ability to be utilized as BMD pre screening tools due to their lower cost and portability. The results from the present study however suggest that the QUS is a more valid and reliable tool to utilize at events such as health fairs where a large, diverse group of people may be found. The differences seen in comparison to past research are due to the variation in gender and ethnicities utilized in the present study. Most of the available past research doesn't make comparisons between portable devices, instead only compares one device against the DXA, the gold standard. There are also limited variations in the populations utilized in past research, as many studies concentrate on a specific group such as postmenopausal women. The use of referenced WHO t-scores between devices has also been questioned, as it used for all populations and all sub-regional testing devices. Future studies are necessary to address the internal calculations between devices as well as the referenced t-scores utilized by the devices. This future research is vital to help combat the growing bone health issues seen in our society to date.

References

1. Bonjour, Jean-Philippe, Thierry Chevalley, Serge Ferrari, and Rene Rizzoli. "The importance and relevance of peak bone mass in the prevalence of osteoporosis." Salud Publica Mex 51.1 (2009): 1-21. Web. 2 Feb 2010.

2. Deodhar, AA, J Brabyn, PW Jones, MJ Davis, and AD Woolf. "Measurement of hand bone mineral content by dual energy x-ray absorptiometry." Annals of the Rheumatic Diseases 53. (1994): 685-690. Web. 20 Sept 2009.

3. Franck, H, and J Gottwalt. "Associations with sub regional BMD-measurements in patients with rheumatoid arthritis." Rheumatol Int. 29.1 (2008): 47-51. Web. 1 Nov 2009.

4. Grampp, S, HK Genant, A Mathur, P Lang, and M Jergas. "Comparisons of Noninvasive Bone Mineral Measurements in Assessing Age-Related Loss, Fracture discrimination, and Diagnostic Classification." Journal of Bone and Mineral Research 12. (1997): 697-711. Web. 28 Sept 2009.

5. Hansen, SJ, MM Nielsen, J Ryg, K Wraae, and K Brixen. "Radiographic absorptiometry as a screening tool in male osteoporosis: results from the Odense Androgen Study." Acta Radiol. 50.6 (2009): 658-663. Web. 2 Oct 2009.

6. “International Osteoporosis Foundation.” IOF Bone Health. International Osteoporosis Foundation, 2010. Web. 20 Feb 2010. <http://www.iofbonehealth.org/patients-public/about-osteoporosis/what-is-osteoporosis.html>.

7. Kanis, JA, N Burlet, C Cooper, PD Delmas, and JY Reginster. “European guidance for the diagnosis and management of osteoporosis in postmenopausal women.” Osteoporosis Int. 19.4 (2008): 399-428. Web. 28 Oct 2009.

8. Kaufman, Jonathon, gangming Luo, and Robert Siffert. “A portable real time ultrasonic bone densitometer.” Ultrasound Med. Biol. 33.9 (2007): 1445-1452. Web. 29 Mar 2010.

9. Laabes EP, Vanderjagt DJ, Obadofin MO, Sendeht AJ & Glew RH. “Assessment of the bone quality of black male athletes using calcaneal ultrasound; a cross sectional-study.” Nutrition & Metabolism 5.13 (2008): 1-8. Web. 25 Sept 2009.

10. Lewiecki, Michael, and Joah Borges. “Bone density testing in clinical practice.” Arq Bras Endocrinol Metab 50.4 (2006): 1-12. Web. 5 Feb 2010.

11. Madsen, OR, OH Sorensen, and C Egsmose. “Bone Quality and bone mass as assessed by quantitative ultrasound and dual energy x ray absorptiometry in women with rheumatoid arthritis: relationship with quadriceps strength.” Annual Rheumatoid Disease 61. (2001): 325-329. Web. 1 Oct 2009.

12. Malavolta, N, R Mule, and M Frigato. “Quantitative ultrasound assessment of bone.” Aging Clin Exp Res 16.3 (2004): 23-28. Web. 29 Mar 2010.

13. Nattiv, A, AB Loucks, MM Manore, CF Sanborn, and J Sundogt-Borgen. “American College of Sports Medicine Position stand. The female athlete triad.” Medicine Science Sports Exercise 39.10 (2007): 1867-1882. Web. 12 Jan 2010.

14. http://www.niams.nih.gov/Health_info/Bone/Osteoporosis/default.asp

; Accessed 8/25/2009

15. http://www.nof.org/osteoporosis/diseasefacts.htm; accessed 9/25/2009

16. Qaseem, Amir, Vincenza Snow, Paul Shekelle, Robert Hopkins, and Mary Ann Forciea. “Screening for Osteoporosis in Men: A clinical Practice Guideline from the American College of Physicians.” Annals of Internal Medicine 148.9 2008. 680-685. Web.

17. Shepherd, JA, B Fan, Y Lu, EM Lewiecki, and P Miller. “Comparison of BMD precision for Prodigy and Delphi spine and femur scans.” Osteoporosis Int. 17.9 (2006): 1303-1308. Web. 10 Feb 2010.

18. Sim, J, and C Wright. “The kappa statistic in Reliability studies: use, interpretation, and same size requirements.” Physical Therapy 85.3 (2005): 257-268. Web. 25 Feb 2010.

19. Taal, MW, MJD Cassidy, D Pearson, D Green, and T Masud. “Usefulness of quantitative heel ultrasound compared with dual-energy X-ray absorptiometry in determining bone mineral density in chr.” Nephrol Dial Transplant 14. (1999): 1917-1921. Web. 30 Oct 2009

20. Thorpe, JA, and SA Steel. “The Alara Metriscan phalangeal densitometer: evaluation and triage thresholds..” Br J Radiol. 81.970 (2008): 778-783. Web. 29 Jan 2010.

21. U.S. Department of Health and Human Services. The 2004 Surgeon General's Report on Bone Health and Osteoporosis: What it Mean to You. U.S Department of Health and Human Services, office of Surgeon General, 2004.

22. U.S. WomensHealth.gov. Washington D.C: Office of Women, 2009. Web. 29 Mar 2010.

23. Wu, XP, EY Liao, G Huang, RC Dai, and H Zhang. "A comparison study of reference curves of bone mineral density at different skeletal sites in native Chinese, Japanese, and American Caucasian women.." Calcification Tissue International 73.2 (2003): 122-132. Web. 29 Mar 2010.

24. Yang, Nan-Ping, Ian Jen, Shao-Yuan Chuang, Shui-Hu Chen, and Pesus Chou. "Screening for low bone mass with quantitative ultrasonography in a community without dual-energy X-ray absorptiometry: population-based survey." BMC Musculoskeletal Disorders 7.24 (2006): 1-9. Web. 29 Mar 2010.

APPENDICES

APPENDIX A

INFORMED CONSENT

COLLEGE OF HEALTH AND HUMAN SCIENCES

DEPARTMENT OF HEALTH AND KINESIOLOGY

Informed Consent

The purpose of this study "The Comparison of Two Bone Mineral Density Pre-screening Tools, QUS and RA, to the DXA, the Gold Standard." Is to determine the relationship between bone mineral density measurements by QUS and RA, compared to the DXA measurement (gold standard). Participation in this research will include completion three separate tests of bone mineral density on Georgia Southern University's campus that includes a dual x-ray total body scan, a radiographic scan of the hand and an ultrasound scan of the foot. In total the process will take about 45 minutes. The benefits to the participant include obtaining three free bone mineral density scans. The benefits to society include establishing a cost effective method of diagnosing osteoporosis. The DXA and RA devices emit radiation and the QUS utilizes ultrasound. However, the amount of x-ray absorbed by the subject during the DXA scan is about $1/10^{th}$ of that received during a chest x-ray and that received during the Metriscan is less than 5% of that received during a dental x-ray. Only the researchers' will have access to results and it will be kept in a locked room within a locked filing cabinet. It will be destroyed at the conclusion of three years. Participants have the right to ask questions and have those questions answered. If you have questions about this study, please contact the researcher Jim McMillan (912-478-1926, jmcmillan@georgiasouthern.edu). For questions concerning your rights as a research participant, contact Georgia Southern University Office of Research Services and Sponsored Programs at 912-478-0843. Compensation includes the free compiled results of the three bone mineral density scans. This study is based on voluntary participation and subjects are not required to participate in this research and may end participation at any time by telling the researcher. No questions on the questionnaire have to be answered if the participant is not comfortable releasing that information. There is no penalty for deciding not to participate in the study; an individual may decide at any time they don't want to participate further and may withdraw without penalty or retribution. You must be 18 years of age or older to consent to participate in this research study. The individual must not be pregnant in order to participate in testing. If you consent to participate in this research study and to the terms above, please sign your name and indicate the date below.

You will be given a copy of this consent form to keep for your records.

Title of Project: The Comparison of Two Bone Mineral Density Pre-screening Tools, QUS and RA, to the DXA, the Gold Standard." Is to determine the relationship between bone mineral density measurements by QUS and RA, compared to the DXA measurement (gold standard).

Principal Investigator: Dr. Jim McMillan, 912-478-1926, jmcmillan@georgiasouthern.edu
Other Investigator(s): Rachel Newcomer, 770-605-4504, rnewcome@georgiasouthern.edu
Dr. Stephen Rossi, 912-478-0775, srossi@georgiasouthern.edu
Dr. Kathy Thornton, 912-478-0888, kthorn@georgiasouthern.edu

_____ _____

Participant Signature Date

I, the undersigned, verify that the above informed consent procedure has been followed.

_____ _____Investigator

Signature Date

APPENDIX B

QUESTIONNAIRE

Questionnaire

Name (Please print) _____
Date of birth (month/day/year) _____
Gender (circle one) Male Female
If female, please indicate menstrual status: (Circle one)
Regular Irregular Absent Post- menopause
Race _____
Weight (In pounds) _____
Height (In inches) _____
Supplements (example: calcium 500mg/day)
_____
_____
_____
Current prescription medications
_____
_____
_____
Treatments past or present known to affect your bones
_____
_____
Past or present bone fractures and when these occurred
_____**Date: _____**
_____ **Date:**_____
_____ **Date**:_____
Dominant hand used to write (circle one) Right Left
Dominant foot used to kick a ball (circle one) Right Left
Status (circle one) Student Faculty Staff Other
If other please explain _____

APPENDIX C

IRB NARRATIVE

Personnel.
Please list any individuals who will be participating in the research beyond the PI and advisor. Also please detail the experience, level of involvement in the process and the access to information that each may have.

Individuals that will be participating in the study include: Dr. Stephen Rossi, Dr. Kathy Thornton, and Ms. Rachel Newcomer. Dr. Stephen Rossi has experience in utilizing the DXA device as well as analyzing results from it. **Dr. Rossi and Dr. Thornton have been trained on all three devices. Ms. Newcomer has been trained on the QUS and RA devices and will assist on the DXA tests. All researchers will have access to data collected. The data will be kept in Hanner 2310, a locked room, within a locked file cabinet. Limited access will occur as described above and the data will be shredded after three years.**

Purpose. *1. Briefly describe in one or two sentences the purpose of your research. 2. What questions are you trying to answer in this experiment? Please include your hypothesis in this section. The jurisdiction of the IRB requires that we ensure the appropriateness of research. It is unethical to put participants at risk without the possibility of sound scientific result. For this reason, you should be very clear on how participants and others will benefit from knowledge gained in this project. 3. What current literature have you reviewed regarding this topic of research? How does it help you to frame the hypothesis and research you will be doing? Include citations in the description.*

The purpose of this study is to:
(1) Determine the relationship between BMD measured by the QUS and RA devices, compared to the DXA measurement, the gold standard.
(2) Examine the agreement between osteoporosis classifications produced by the QUS and RA devices, compared to those produced by the DXA, the gold standard.
Hypotheses include the following:

(1) The correlation between the BMD score provided by the DXA and RA, DXA and QUS, and RA and QUS will all be greater than 0 (Positive).
(2) There will be positive classification agreement between the classifications provided by the DXA and RA, DXA and QUS, and RA and QUS.

Osteoporosis is a prominent disease.[4] Dual x-ray absorptiometry (DXA) is the most common method and the gold standard for BMD testing because of it sensitivity to bone quality and its use of the total body bone mineral density measuring ability.[6] Uultrasound (QUS) Has been compared to DXA and both were found to be a valid and reliable measure in a population of women with Rheumatoid Arthritis.[9] Radiographic absorptiometry (RA) is an additional osteoporosis screening tool and when compared to the DXA was found to produce reliable BMD scores in a population of males with osteoporosis.[5] Much of the previous research with these machines used subject populations that had a disease or were at greater risk for a disease that warranted bone density measurement. Thus there is a gap in research

with subjects without these related diseases and a need to establish normal measures of BMD for reference.

Outcome. *Please state what results you expect to achieve? Who will benefit from this study? How will the participants benefit (if at all). Remember that the participants do not necessarily have to benefit directly. The results of your study may have broadly stated outcomes for a large number of people or society in general.*

We hope to find strong correlations between both portable devices and the gold standard for BMD scores and bone health classifications. This would suggest that the RA and QUS devices would be appropriate tools for pre-screening for BMD. **Since both devices are portable, and provide results quickly, they could be used to provide access to a larger segment of the population, for example people attending health fair at a local mall.** The subjects' in this study will benefit in that they will obtain a free set of BMD screenings that are normally very costly. They can take the results to their health care provider if they have further questions regarding the outcomes of the tests. **Subjects who cannot successfully complete the DXA scan due to body size limitations will be allowed, if they choose, to complete the other two tests but will be excluded from the statistical data pool.**

A cost-effective method for diagnosing osteoporosis is needed in our society. **Since it has been established osteoporosis can occur at a young age and the awareness in these individuals is minimal it is necessary that pre-screening, portable BMD tools be identified and utilized to increase awareness about bone health.**[2,6,7]

Describe your subjects. *Give number of participants, approximate ages, and gender requirements (if any).*
Describe how they will be recruited, how data will be collected (i.e., will names or social security numbers be collected, or will there be any other identification process used that might jeopardize confidentiality?), and/or describe any inducement (payment, etc.) that will be used to recruit subjects. Please use this section to justify how limits and inclusions to the population are going to be used and how they might affect the result (in general).

The study will be open to all individuals at Georgia Southern University; this includes faculty, staff, students, as well as the surrounding community. Inclusion criteria include **non pregnant females**, and males and females between the ages of 18 and 65. **The target sample size will be 80-200 subjects based on past research.** [2,7,10,11,12] **Past research has shown that osteoporosis can occur in all populations, including males, young females, athletes of all ages and various races and genders.** [2,7,10,11,12] **A diverse population between the ages of 18-65 will be recruited to be included because a gap in research does exist when it comes to assessing these populations.** Recruitment of subjects will occur through a publication in the George Anne, the on campus newspaper, as well as through flyers hung, with prior approval, in various buildings around campus. All testing on the subjects will be done in the Human Performance Lab located in Hanner 2310. All subjects will sign an IRB approved informed consent before testing and be assigned an identification number to maintain

subject confidentiality. **A questionnaire will be given to determine: age, gender, if female, menstrual status, race, height, weight, medications and treatments/conditions known to affect bone metabolism.** All subjects should complete all three BMD tests: DXA, QUS and RA. Before being tested on each device all participants will be provided with proper pre-test instructions. In lieu of payment, subjects will receive free copies of their test results.

Methodology (Procedures). *Enumerate specifically what will you be doing in this study, what kind of experimental manipulations you will use, what kinds of questions or recording of behavior you will use. If appropriate, attach a questionnaire to each submitted copy of this proposal. Describe in detail any physical procedures you may be performing.*

All three devices will be located in Hanner 2310. The Metriscan utilizes radiographic absorptiometry to estimate an individual's relative phalangeal bone density of the three middle fingers. **The amount of radiation received is about 5% of that received during a dental x-ray. The subject will wear a lead apron for protection during the testing process**. **The researcher will initiate the test and quickly move one meter away from the device, thus minimizing the radiation dose. Prior to each use the device will be thoroughly cleaned and a self calibration will be performed**. The subject's non dominant hand is placed in the device and the three middle fingers are properly aligned in the unit. The scan process takes about one second and total time from start to printing of results is about one minute. The device offers a printout with the subject's average T-score of the 3 finger's measured, which is the estimated relative bone density in comparison to that of a healthy young female Caucasian population. It also offers a z-score, which compares' their BMD to that of an age-matched population of the subject's same gender and ethnicity. The device requires no routine maintenance. It has a precision error of +/- 1%. [1]

The Hologic Sahara UBA575 utilizes ultrasound to obtain BMD. **Since this device utilizes ultrasound no radiation is emitted. Prior to each use the device will be thoroughly cleaned and a self calibration will be performed**. If the device does not calibrate properly the test cannot take place. The device provides a T score, a classification based on the T score, as well as an estimated heel BMD utilizing an individual's heel, or calcaneus, thickness. The process takes less than two minutes and only requires the subject to remove their shoe and place their foot within the set parameters of the unit. During the test the individual is seated in a stable back supporting chair. A paper towel is placed below the non dominant foot in the Sahara device. Two silicone nodules are gelled prior to beginning the test and foot placement. The subject's foot is aligned and two nodules compress against the calcaneus. The device then provides a printout with each individual's BMD score of the heel and a standardized T-score. [8]

The GE Lunar DEXA device provides a non-invasive and precise method of measuring BMD. The device uses x-ray densitometry techniques to obtain these measurements. **The amount of x-ray received during a DXA scan is about 1/10th of that received during a chest x-ray. The operator will stand outside the three foot area, which is clearly marked on the floor, while test is performed. An area monitor radiation badge is also present at the three foot mark from the device. The device is evaluated each quarter. Results from previous area monitor radiation badge**

evaluations suggest minimal radiation exposure at this three foot distance. Before each test is begun a calibration check is performed. There is also an annual calibration from a manufacturer technician done on site. Subject's data is entered in the computer before the scan. The subject's knees and ankles are secured with Velcro straps to ensure the hips are rotated inward. The subject is instructed to remain still while the scan is performed. The scan takes about 7-10 minutes. A print out is provided with their T score, classification based on T score, and BMD total body measurement based on pre established norms. [3]

See Back Page for References

Special Conditions:

Risk. *Is there greater than minimal risk from physical, mental or social discomfort? Describe the risks and the steps taken to minimize them. Justify the risk undertaken by outlining any benefits that might result from the study, both on a Participant and societal level. Even minor discomfort in answering questions on a survey may pose some risk to subjects. Carefully consider how the subjects will react and address ANY potential risks. Do not simply state that no risk exists. Carefully examine possible subject reactions. If risk is no greater than risk associated with daily life experiences state risk in these terms.*

There is a relatively small radiation exposure during two of the tests. For the DXA, each subject will only be scanned once. The amount of x-ray absorbed by the subject during the DEXA scan is about 1/10th of that received during a chest x-ray.[3] The tester will remain at least 3 feet from the device to minimize his/her exposure. For the RA test on the Metriscan the subject will wear a lead apron and have his/her arm extended away from the body. The amount of x-ray absorbed from the Metriscan device is less than 5% of a dental x-ray.[1] The tester will initiate the test and quickly move away from the test to minimize his/her exposure. The ultra-sound device is radiation free.[8]

Cover page checklist. *Please provide additional information concerning risk elements checked on the cover page and not yet addressed in the narrative. If none, please state "none of the items listed on the cover page checklist apply." The cover page can be accessed from the IRB forms page. (Note – if a student, make sure your advisor has read your application and signed your cover page. (Your advisor is responsible for the research you undertake in the name of GSU.)*

None of the items listed on the cover page checklist apply

Reminder: No research can be undertaken until your proposal has been approved by the IRB.

References

1. Alara, INC. “Screening for osteoporosis in your hands.” (2007)

2. Bonis , M, M Loftin, R Speaker, and A Kontos. "Body Composition of elite, eumenorrheic and amenorrheic, adolescent cross-country runners.." *Pediatr. Exerc. Sci.* 21.3 (2009): 318-328. Web. 10 Jan 2010.

3. GE Lunar Prodigy Operation Manual.

4. Grampp, S, HK Genant, A Mathur, P Lang, and M Jergas. "Comparisons of Noninvasive Bone Mineral Measurements in Assessing Age-Related Loss, Fracture discrimination, and Diagnostic Classification." *Journal of Bone and Mineral Research* 12. (1997): 697-711. Web. 28 Sept 2009

5. Hansen, SJ, MM Nielsen, J Ryg, K Wraae, and K Brixen. "Radiographic absorptiometry as a screening tool in male osteoporosis: results from the Odense Androgen Study.." *Acta Radiol.* 50.6 (2009): 658-663. Web. 2 Oct 2009

6. Laabes EP, Vanderjagt DJ, Obadofin MO, Sendeht AJ & Glew RH. "Assessment of the bone quality of black male athletes using calcaneal ultrasound; a cross sectional-study." *Nutrition & Metabolism* 5.13 (2008): 1-8. Web. 25 Sept 2009.

7. Liang, MT, S Bassin , D Dutto, W Braun, and N Wong. "Bone mineral density and leg muscle strength in young Caucasian, Hispanic, and Asian women.." *J Clin Densitom.* 10.2 (2007): 157-164. Web. 9 Jan 2010.

8. Hologic, INC. “Hologic Sahara Clinical Bone Sonometer Operation Manual.” (1997)

9. Madsen, OR, OH Sorensen, and C Egsmose. "Bone Quality and bone mass as assessed by quanitative ultrasound and dual energy x ray absorptiometry in women with rheumatoid arthritis: relationship with quadriceps strength." *Annual Rheumatoid Disease* 61. (2001): 325-329. Web. 1 Oct 2009.

10. Nattiv , A, AB Loucks, MM Manore, CF Sanborn, and J Sundgot-Borgen. "American College of Sports Medicine position stand. The female athlete triad." *Med Sci Sports Exerc.* 39.10 (2007): 1867-1882. Web. 11 Jan 2010.

11. Rocchietti, March M, D Pisani , and G Aliberti. "Male Osteoporosis." *Minerva Endrocrinology* 34.4 (2009): 325-332. Web. 11Jan2010.

12. Wiksten-Almstromer, M, AL Hirschberg, and K Hagenfeldt. "Reduced bone mineral density in adult women diagnosed with menstrual disorders during adolescence." *Acta*