RELIABILITY AND VALIDITY OF BODY COMPOSITION AND BONE MINERAL DENSITY MEASUREMENTS BY DXA

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Reliability and Validity of Body Composition and Bone Mineral Density Measurements by DXA (Under the direction of **SHARON M. NICKOLS-RICHARDSON**)

Dual energy X-ray absorptiometry (DXA) has been well established in both clinical and research settings for measurement of bone mineral density (BMD), and is becoming more widely utilized for assessment of body composition. Reliability and validity are essential factors in both applications of this technique; however, neither have been confirmed for the QDR-4500A DXA at Virginia Tech. Therefore, measurements of the whole body (WB), lumbar spine (LS), total proximal femur (TPF) and total forearm (TF) were made in a group of young-adult males and females at two time-points, 5-7 days apart. Significant differences were not found in BMD (g/cm^2) at these body sites with repeated measurements by DXA. Furthermore, measures of percent body fat (%BF), lean body mass (LBM), and fat mass (FM) by DXA were reliable. Validity of %BF by DXA was assessed from comparison to single-frequency bioelectrical impedance analysis (BIA). Significant differences were not found in measures of %BF by DXA and BIA. A second study investigated the reliability and validity of the QDR-4500A DXA in measurements of distal tibia (DT) BMD. Significant differences were not found between repeated measurements. Validity was established by a significant correlation between WB BMD and DT BMD. A third study examined the influence of navel jewelry on the accuracy of LS DXA measurements. Repeated measurements with a spine phantom revealed that both a navel ring and a barbell produced significantly greater measures of LS BMD compared to the spine phantom alone. Manual correction of navel jewelry did not eliminate BMD inaccuracies. Data from these studies confirmed that the QDR-4500A DXA at Virginia Tech was a reliable and valid device in measurement of WB, LS, TPF, TF and DT BMD, as well as %BF, LBM, and FM. In addition, effects of navel jewelry on LS BMD have been recognized. Further studies

investigating the reliability and validity of DT BMD measures as well as effects of different types, gauges, and shapes of body jewelry on BMD measures in human subjects are warranted.

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CHAPTER I

INTRODUCTION

Dual energy X-ray absorptiometry (DXA) is the most widely accepted method for the quantitative assessment of bone mineral status *in vivo* (Gluer, 2000; Jergas et al., 1995; Lochmuller et al., 2001; Miller et al., 1999). DXA has also been regarded as a safe, convenient, and non-invasive method of measuring soft-tissue composition (Haarbo et al., 1991; Hansen et al., 1993; Lukaski, 1987; Pritchard et al., 1993). However, concern and uncertainty persist that both *in vivo* bone mineral density (BMD) measurements and estimation of DXA percent body fat are subject to sizable systematic inaccuracies (Bolotin, 1998, 2001; Pocock et al., 1997; Tataranni et al., 1996; Tothill & Avenell, 1998). Accuracy and reproducibility are key issues in both clinical and research applications of BMD and body composition measurements (Gluer et al. 1995; Madsen et al., 1997; Orwoll & Oviatt, 1991; Wells & Ryan, 2000). Therefore, establishing the validity of measures from the Hologic QDR-4500A DXA machine in the Bone metabolism, Osteoporosis and Nutrition Evaluation (BONE) Laboratory at Virginia Tech is imperative to research and applications related to bone health.

Osteoporosis is a clinically measurable deficit in BMD affecting approximately 24 million Americans (Ott, 1998). Osteoporosis and osteoporotic bone fractures represent a significant health problem, and result in substantial morbidity and mortality. Approximately one-half of individuals who are able to walk unaided before incurring a hip fracture cannot walk unassisted afterward (Ott, 1998). Hip fractures, the most serious osteoporosis-related fractures, are associated with reduced expected survival rates of 12% or more, with the greatest risk for mortality occurring 3 to 4 months after the fractures (Ott, 1998). In the United States, more than 1.5 million osteoporotic fractures occur each year (Ott, 1998). Health care expenditures

attributable to osteoporotic fractures in 1995 were estimated at $13.8 billion (Ray et al., 1997), a figure that is expected to rise to between $30 and $40 billion by the year 2020 (Fogelman & Blake, 2000).

Bone densitometry is a practical tool in the clinical setting for use in diagnosing osteoporosis and for monitoring BMD (Alhava, 1991; Miller et al., 1999). It also has potential for use in body composition assessment, which is fundamental to the study of biological processes in animals and humans (Pietrobelli et al., 1996; Pritchard et al., 1993). Nonetheless, gaps exist in current knowledge concerning both of these applications (Bolotin et al., 2001; Roubenoff et al., 1993). Both short- and long-term precision of *in vivo* and *in vitro* DXA BMD have been established. Results for long-term precision of lumbar spine, femoral neck, and total hip BMD have been confirmed at 1.12%; 2.21%; and 1.32%, respectively (Patel et al., 2000). However, these long-term precision studies have not yet confirmed the reliability of the DXA at Virginia Tech in either BMD or body composition studies. There is also a paucity of data regarding the reliability and validity of regional measures of tibial BMD by DXA, as well as the effect of jewelry and other metal artifacts on BMD readings and the ability of the operator to manually correct for these potential errors.

Therefore, the purpose of this proposed research was to: (1) establish the reliability and validity of the Hologic QDR-4500A DXA at Virginia Tech to measure body composition; (2) establish the reliability and validity of regional tibial DXA measures, and (3) determine measurement errors represented by metal artifacts, specifically navel jewelry, on lumbar spine BMD measures and the ability to accurately correct for these errors. The first study showed that the Hologic QDR-4500A DXA in the BONE Laboratory at Virginia Tech was reliable for BMD at the whole body, lumbar spine, nondominant total proximal femur, and nondominant total

forearm. Additionally, percent body fat (%BF), lean body mass (LBM), and fat mass (FM) measures by DXA were reliable. Compared to BIA, %BF measures by DXA were valid (Chapter III). Tibial BMD measures by DXA were reliable and valid when compared to whole body BMD measures (Chapter IV). The QDR-4500A DXA was not able to fully correct for errors in BMD measurements of the lumbar spine due to the presence of navel jewelry in the DXA scan (Chapter V). Lastly, future research and directions are presented in Chapter VI.

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CHAPTER II

REVIEW OF LITERATURE

Assessment of bone mineral density (BMD) has become the essential diagnostic procedure for evaluation of patients at risk for osteoporosis. Although various BMD technologies exist in clinical practice, dual energy X-ray absorptiometry (DXA) is currently the leading bone density technique. Interest has also been increasing in the use of DXA for the measurement of soft tissue composition, but with questions arising as to its accuracy and reliability in comparison with other methods, such as bioelectrical impedance analysis (BIA). In response to this increase in demand, DXA instruments have continuously undergone technological development. With each upgrade, issues arise regarding the compatibility with older-generation instruments and reference values established for older DXA instruments. Aside from these developmental issues, there still remain fundamental questions pertaining to the reliability and validity of DXA measurements. Researchers are now expressing concerns regarding systematic inaccuracies inherent in the technique, as well as other factors of variability.

Bone densitometry and osteoporosis

Bone densitometry has four major applications in clinical practice: quantification of bone mass or density; assessment of fracture risk; skeletal changes, and body-composition analysis (Ott, 1998). Measuring bone mass or density can be performed for four general reasons: to confirm suspected bone loss visible on a standard radiograph; to diagnose osteoporosis; to record effects of disease progression that alter bone mineral content (BMC) or density; and to monitor effects of disease process or response to therapy over time (Ott, 1998). Bone densitometry techniques measure the mineral content of bone either as areal density (g/cm^2) or as true volumetric density (g/cm^3) (Ott, 1998). Although bone mass is not the sole component of bone

strength, it is an important predictor of fracture risk. Just as blood pressure and cholesterol determinations are predictors of stroke and cardiovascular disease, so bone density predicts fracture risk (Miller et al., 1999).

A large variety of bone densitometry and quantitative ultrasound techniques can be used for the assessment of osteoporosis. Any method used for measuring BMD should be accurate, precise, sensitive, inexpensive, and involve a minimal exposure to ionizing radiation. Accuracy expresses how close the measured BMD is to the actual value. Precision assesses the reproducibility of the measuring technique, a high precision (low coefficient of variation) being essential in longitudinal studies of bone mass. Sensitivity is the aptitude of the technique to separate an abnormal (fracture) population from a normal (nonfracture population), or to easily detect changes in BMD with time and therapy. Excluding ultrasound, bone densitometry techniques are based on attenuation principles. Bone attenuates, or absorbs, ionizing radiation. A greater amount of bone will result in more absorption of the ionizing radiation, and therefore less radiation will be measured by the detection device (Ott, 1998).

In the early 1990s, a Consensus Development Conference convened and produced the definition of osteoporosis as "a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture" (Blake & Fogelman, 2001, p. 69; Smith & Shoukri, 2000, p.23). In 1994, a World Health Organization (WHO) report recommended a clinical definition of osteoporosis based on expression of BMD measurements in standard deviation (SD) units called T-scores. The T-score is calculated by taking the difference between a patient's measured BMD and the mean BMD of healthy, young-adults matched for gender and ethnic group, and expressing the difference relative to the young-adult population SD. A T-score, therefore,

indicates the difference between the patient's BMD and the ideal peak bone mass achieved by a young-adult. Osteoporosis in postmenopausal Caucasian women is defined as a value for BMD or BMC of more than 2.5 SD below the young average value (T-score ≤ -2.5) for the whole body, spine, hip, or forearm. An intermediate state of low bone mass (osteopenia) is defined by a T-score between – 2.5 and –1. A T-score ≥ -1 is considered normal. Severe osteoporosis uses the same threshold as previously defined, (T-score [-2.5), but in the presence of one or more fragility fractures. The rationale for these definitions arise from statistics indicating that when measurements are made at bone sites most vulnerable to fracture (hip, spine, and wrist), approximately 30% of postmenopausal women would have osteoporosis, according to the WHO definition. This figure approximates the average lifetime risk of fracture for a 50-year-old woman (Blake & Fogelman, 2001; Gluer, 2000; Kanis & Gluer, 2000).

Another useful way of expressing BMD measurements is in Z-score units. A Z-score represents the number of SDs above or below the bone density value for an age-, weight-, gender-, and ethnicity-matched adult population. The Z-score is a valuable concept because it expresses the patient's risk of sustaining an osteoporotic fracture relative to peers. Generally, every reduction of 1 SD in BMD is associated with an approximately twofold increase in the likelihood of fracture (Fogelman & Blake, 2000; Gluer, 2000; Ott, 1998; Ryan, 1997; Smith & Shoukri, 2000).

The reliability of diagnostic criteria for osteoporosis in other patient groups (e.g. non-whites, premenopausal women, and men) is not well established. Furthermore, the application of the WHO criteria using data from bone density measurement methods other than DXA may also be misleading. Reference data for the mean and the SD for each measurement technique are developed by the manufacturer of each method, or in the case of DXA by large population

screening – from the National Health and Nutrition Examination Survey (NHANES III) – data. Newer methods of BMD testing have not yet established extensive normative values. In addition, the detected amount of change in bone density as a result of age, gender, ethnicity, and disease state will vary with different methods used. Therefore, standardization and cross-comparison of the T- and Z-scores from various bone density techniques are challenging. Controversy exists regarding continued strict application of WHO diagnostic criteria or whether diagnostic criteria based on each technique should be developed.

History of dual energy X-ray absorptiometry (DXA)

Early methods of bone mass measurement (cortical index, radiographic densitometry) were rather unrefined and imprecise. The first valid technique of BMD measurement, introduced in 1963, was single photon absorptiometry (SPA) of the forearm (Adams, 1992; Maricic & Chen, 2000). A limitation of SPA was its applicability to only peripheral skeletal sites; hence, dual photon absorptiometry (DPA) was developed for BMD measurements in the axial body. This technique has now been replaced by DXA. From its clinical introduction in 1987, DXA has become the gold standard for bone densitometry (Ott, 1998) because of its high image quality, accuracy and precision, fast scanning times, and low radiation exposure (Ott, 1998). According to a 1997 National Osteoporosis Foundation (NOF) survey, 89% of bone density tests performed in the United States in one year used DXA (Smith & Shoukri, 2000).

There are three commercial manufacturers of DXA instruments: Hologic, Lunar, and Norland. The fundamental principle behind DXA is the measurement of the transmission through the body of X-rays of 2 different photon energy levels, which are absorbed differently by mineral and soft tissue. By combining data, DXA can accurately measure bone within soft

tissue. Results of DXA represent a composite measure of both cortical and trabecular bone, and are reported as an areal density in g/cm^2.

The first DXA system (Hologic QDR-1000) was introduced in 1990, and contained three main components. An X-ray generator and tube, located beneath the patient, produced a highly collimated pencil beam, with two energies produced by alternate pulse voltage at 70 kVp and 140 kVp. A cadmium tungstate crystal detector, attached to a mobile support above the patient, detected the transmitted X-rays. An internal calibration system was supplied by the manufacturer (Hologic, Waltham, MA). The X-ray pencil beam swept in rectilinear directions with a velocity of 60 mm/s for transverse scanning, which resulted in a scan time of about 10 minutes for an image of the lumbar spine. The program software allowed measurement of: posteroanterior (AP) lumbar spine, femur, wrist, complete spinal column in pediatric patients, femoral prosthesis, and bones of small animals (Barthe et al., 1997).

A newer Hologic DXA system, the QDR-4500A, was introduced in 1995. This second generation DXA scanner uses multidetector DXA and functions in the same way as the QDR 1000, except that X-rays are produced by accelerating voltages of 100 kVp and 140 kVp. Radiation in the form of a fan beam, as opposed to a pencil beam, is detected with 216 solid state detectors aligned along a C-shaped holder, whose motion is under computer control, and which rotates so that the source always faces this holder. The software allows for measurement of not only the most common sites (lumbar spine, femur, and wrist), but also of whole body bone density, lean body mass and fat mass. Lateral lumbar spine images can also be combined with AP images to calculate BMD in g/cm^3. A primary advantage of this second generation of scanners over the first generation is the decrease in scanning times. Times are 10s, 30s, 1 min, 2 min, 3 min, and 5 min in the “turbo”, “fast array”, “array” (most commonly used), “high

definition", "whole body", and "lateral image" modes, respectively (Barthe et al., 1997). Some disadvantages to this newer DXA system are a higher radiation exposure to both patient and operator, as well as questionable accuracy of BMC and total body composition measurements due to the geometric design of the fan-beam scan.

Measurement issues of BMD by DXA

When using bone densitometry for research and/or clinical practice, it is essential to understand concepts of accuracy and precision when choosing a specific device to answer a specific clinical question, and in interpretation of results. The accuracy of a test reflects how the measured result deviates from the true value. However, none of the absorptiometric techniques measure true bone density, but rather an areal bone density. Errors can be caused by factors such as variable soft tissue composition, fat content of bone, and errors in measurement of projected bone area, among various others. Accuracy errors, well known by DXA users, can to a certain extent be compensated for by using valid reference materials. However, care is to be taken when comparing results from different densitometers in longitudinal studies.

Precision is the reproducibility error between tests. Changes in BMD are generally very small and gradual; therefore, precision of measurements is extremely important. Precision is known to worsen with increase in age, increase in weight (for the femur), and with a reduction in density values (Lilley et al., 1991). A traditional index for precision error is the coefficient of variation (CV%), which is the function of the SD divided by the mean. The precision error of current DXA systems is 1.0% for whole body, ~0.5-1% for the spine, 2.0-5.0% for the femoral neck, depending on anatomic site analyzed (femoral neck, Ward's triangle, trochanteric region, shaft) (Adams, 1992; Alhava, 1991; Gluer et al., 1995), and ~0.6-1.6% for the forearm, again dependent on the anatomic site (proximal third, mid-distal, ultra-distal) (Nieves et al., 1992).

There is very little current literature available regarding the precision of tibial BMD measures by DXA; however, one group of authors has reported the precision of their measures of the diaphysis and distal epiphysis of the tibia to be 2.1% and 1.9%, respectively (Casez et al., 1994).

The accuracy of bone mineral measurements is slightly less than the precision, and depends on soft tissue mass and composition. Referred to as a "two component limitation", DXA methodology does not extend to bone sites consisting of more than two absorptiometrically different components. The technique assumes that there are only two tissue components with known attenuation coefficients. Regarding bone material as one component, it is then necessary to presume that the composition and distribution of all extra- and intra-osseous soft tissues and other body constituents present within the scan area represent an absorptiometrically homogenous second "component." It is clear that this assumption is not valid in the human body, since fat is a third component with very different attenuation characteristics than those of other soft tissues. Therefore DXA *in vivo* BMD measurements must be inaccurate to some degree, either underestimating or overestimating the true BMD to some extent in any given person. Estimates of accuracy errors range from 2% for measurements at the forearm, ~6% for AP spine, ~7% for the total hip, and ~10% for the lateral spine (Kanis & Gluer, 2000; Nielsen, 2000). The correction for fat assumes, among other things, that the distribution of fat in the body is homogenous. Therefore, when measuring BMD at the lumbar spine or hip, variable soft tissue densities and non-uniform distribution of fat in the abdomen present a problem, as the attenuation coefficients of the tissues involved lead to fat appearing as negative bone. This is of particular concern in osteoporotic and elderly persons with low BMD. The estimated random accuracy error due to fat inhomogeneity is ~3-4% for an AP spine scan, and 9-14% for a lateral spine scan (Svendsen et al., 1995). These limitations in accuracy created by non-uniform fat

distribution will most likely affect longitudinal studies if there are considerable changes of fat in a subject. However, the possibility of errors resulting from fat distribution should be kept in mind when classifying an individual's BMD.

Another systematic inaccuracy inherent in DXA systems is intraunit variation between devices, which can be as high as 20% (Nielsen, 2000). An example of this disparity is the finding that the Lunar DPX machine measures consistently higher BMD values (approximately 12-15%) than the Hologic QDR-1000 (Cawte et al., 1999; Mazess et al., 1991). Bone density results from different manufacturers' equipment cannot be interchanged when studying individual patients without careful allowance for the systematic differences. This is shown to be especially true for femur measurements, due to differences in manufacturers' databases (Laskey et al., 1992). Other possible causes of this disparity include variations in approach to dual-energy production, calibration procedures, edge detection algorithms, and assumptions regarding fat distribution, as well as differences in the dependency of measurement on the thickness of the subject and operator-dependent variables such as patient repositioning and scan analysis.

Not only is there variability between different brands, but also significant intermachine variability existing for the same brands. This is particularly true when upgrading from first to second generation systems, as a result of magnification and other differences inherent in fan beam geometry. Due to the magnification effect of fan beam geometry, BMC and bone area measurements show an apparent dependency on the bone-to-radiation-source distance (Dunn & Wahner, 1992). When upgrading from a Hologic QDR-1000W to the QDR-4500A, the latter produces a small systematic overestimate of BMD at low BMD and an underestimate at high BMD compared with the former. This is most apparent at the spine and femoral neck (Bouyoucef & Cullum, 1996). The use of the manufacturer's phantom is important in cross-

calibration to calculate differences between the two devices. Using the manufacturer's routine calibration procedures when upgrading DXA systems will not produce a significant error when diagnosing osteoporosis; however, it may affect the ability to detect changes in BMD in longitudinal studies (Finkelstein et al., 1994a).

The accurate diagnostic classification of an individual depends on various factors. These include the precise derivation of the reference population mean and SD used to calculate the T-score, and the comparability of bone mass measurements across different manufacturers. Discrepancies between patients classified according to the WHO criteria using different densitometers have been documented (Faulkner et al., 1996; Formica, 1998; Genant et al., 1994). Problems arise when a single T-score criterion is used for BMD measurements from different sites. This is due to the fact that T-scores depend on body size, and they vary greatly when measuring different sites. There is also a challenge when utilizing manufacturers' reference ranges. Several authors suggest that the normal reference database may not be appropriate, and propose that individual populations should use their own reference range T-scores to avoid misdiagnoses based on another populations' reference range T-scores (Ahmed et al., 1997; Gurlek et al., 2000; Maricic & Chen, 2000; Nielsen, 2000; Patel et al., 1998).

It is evident then that the WHO definition of osteoporosis cannot be applied to all sites of DXA BMD measurements. Correlations between BMD measurements performed at central and peripheral sites are poor (Delmas, 2000). Correlations are also poor between technologies at the same site, indicating that BMD at one site cannot be predicted from BMD measured at another site in an individual, and are thus of very low predictive value (Kanis & Gluer, 2000). Bone is biologically inhomogenous, and there are variable rates of bone loss at different sites with advancing age. Individuals deemed osteoporotic at one skeletal site may not be found to be

osteoporotic at another. So questions arise as to which measurement site is best. In the premenopausal and early postmenopausal years (up to age 65), vertebral fractures are the immediate concern, as age-related bone loss occurs most rapidly in the spine at this time. Therefore, spinal measurements typically provide the most accurate measure of skeletal state and response to aging and/or therapy. After the age of 65, hip fractures become the primary concern, and there are strong indications that hip BMD measurements are best for predicting hip fracture (Blake et al., 1998; Cummings et al., 1993). However, the degree to which spine BMD best predicts vertebral fracture, or a radius BMD forearm fracture is much weaker. Recent studies have confirmed that AP lumbar spine DXA remains the optimum technique for measuring longitudinal changes (Baran et al., 1997; Faulkner, 1998). Although in the elderly, degenerative stages will sometimes falsely elevate BMD if measured in the AP direction. If significant osteophytes, sclerosis, vertebral fracture, aortic calcification, and/or scoliosis is suspected in the spine, then either lateral spine, spinal quantitative computed tomography (QCT), or alternative skeletal sites should be evaluated to avoid an overestimation of BMD, and therefore, an underestimation of fracture risk. Another cause for inaccuracy of spinal BMD measures is due to the extremely labile state of vertebral marrow. Its red/yellow content changes with various situations such as altered physical activity, general health conditions, medicinal drug dosages, and aging. Therefore, DXA BMD inaccuracies can occur as a result of changes in marrow type, without any actual changes in bone material having taken place (Bolotin et al., 2001).

Lateral scanning of the spine evaluates primarily the vertebral body, which contains predominantly trabecular bone. This avoids some measurement errors that can occur with AP testing, which measures the mostly cortical posterior elements of the vertebrae. Because osteoporosis is usually characterized by a greater relative loss of trabecular than cortical bone,

lateral DXA measurements typically identify patients with osteopenia more often than AP DXA measurements (Adams, 1992; Finkelstein et al., 1994b; Peel & Eastell, 1994). However, the technique has poorer precision (2-5%) than AP scanning (Adams, 1992), making monitoring of change more difficult.

Investigations have shown that BMD based on projected two-dimensional area of the bone tends to overestimate the bone density of larger bones. Hence, another approach to estimating the true volumetric BMD, bone mineral apparent density (BMAD), has been proposed (Carter et al., 1992; Cummings et al., 1994). It is now possible to combine the AP and lateral spine data to infer a volumetric bone density value, which is an estimate of true physical density, measured in g/cm^3. This new measure appears to minimize the confounding effects of variation in bone size resulting from differences in age, height, weight, and changes in vertebral geometry with age. Although BMAD appears to provide insights in addition to those of areal density measures, and may prove useful in cross-sectional studies of various sized subjects and in extended longitudinal studies of individuals with changing skeletal dimensions, several authors have shown no improvement in diagnostic accuracy when using BMAD (Duan et al., 1999; Peel & Eastell, 1994; Tabensky et al., 1996).

Although DXA technology has been well established in the measurement of hip and lumbar spine BMD, the reliability of other regional measures has not been confirmed. Degenerative diseases among the elderly may compromise the ability to interpret spine and/or hip BMD values; therefore an alternate site, such as the distal tibia (DT) may provide information pertaining to mineral distribution, specifically the trabecular to cortical ratio, in a weight-bearing bone (Casez et al., 1994). In addition, military recruits and individuals engaging in athletics in which there is repetitive stress or strain to the lower leg are at a higher risk of incurring stress

fractures of the DT (Beck et al., 2000; Bennell et al., 1996; Bergman & Miller, 2001; Jones & Knapik, 1999; Korpelainen et al., 2001; Monteleone, 1995). Numerous factors have been proposed as potential risk factors for stress fractures, and although data are inconclusive at present, several authors have found lower BMD to be associated with risk of stress fractures, particularly in females (Bennell et al., 1996; Dugowson et al., 1991; Lauder et al., 2000; Pouilles et al., 1989). However, the reliability and validity of DT BMD measurements by the Hologic QDR-4500A DXA has not been well established in the literature or by the manufacturer of one type of DXA (Hologic Inc.).

Subjects undergoing DXA measurement are asked to remove all metal from their bodies or clothing, including items such as jewelry and body piercings. The presence of any metal on a person may interfere with the accuracy of the DXA scan, although the extent of this error is unknown. For example, a navel ring may be detected by the DXA as additional bone in the lumbar spine region; therefore, BMD results will be inaccurate. Studies have not tested whether it is possible for the operator to manually remove this affected area of the scan while maintaining accurate BMD results.

Body composition by DXA

Measurement of body composition is valuable in a number of clinical and research situations. Most methods of assessing body composition have shortcomings or are indirect in the sense that they rely on physical properties or chemical constants of the body (Svendsen et al., 1993). DXA was originally developed to measure BMC; however, it can also be used to estimate soft tissue composition (lean and fat content) from the soft tissue attenuation ratio (Rst), which is defined as the ratio of beam attenuation at the lower energy relative to the higher energy. Previous studies

have shown that Rst and percent fat (% fat) are inversely and linearly related (Svendsen et al., 1993). Based on this relationship, the % fat of soft tissues can be estimated from Rst.

DXA is becoming one of the most frequently used techniques for body composition assessment. This is due, in part, to the fact that it is affordable, practical, has a low radiation dose, is non-invasive, suitable for elderly and very sick patients, and permits quantification of multiple whole body and regional components including bone, fat, and lean soft tissue masses. The precision of DXA body composition measures (CV%) has been reported in several studies for fat mass, lean mass, and % fat as 1.7-2.7%, 0.6-1.4%, and 1.9-2.7%, respectively (Lukaski, 1993; Madsen et al., 1997; Pritchard et al., 1993; Tothill et al., 1994a).

Measurement issues of body composition by DXA

A principal assumption of DXA refers to the "two component limitation." DXA can accurately analyze only two components of tissue with sufficiently different attenuation coefficients – bone and non-bone tissue. However, there are four main components in the human body: bone mineral, fat-free soft tissue, fat, and water. DXA can legitimately be applied to determine fat and lean tissue in areas of the body where there is no bone. In whole body scanning, the fat and lean proportions can be determined in non-bone pixels, which comprise approximately 60% of the body (Tothill et al., 1994a, 1994b). However, in regions such as the thorax, arm, and head, the percentage of bone-free pixels will be much lower and may be insufficient for accurate soft-tissue determinations. It is then necessary to estimate the fat proportion in the remaining 40% of pixels overlying bone, both to calculate total body fat and to determine BMC, because fat appears as negative bone in these calculations. This requires assumptions about fat distribution. Manufacturers use different fat distribution models, and do not reveal what these are; however, all DXA measurements assume that the amount of fat over

bone is the same as that in the adjacent soft-tissue background. Despite this, the non-uniform distribution of adipose tissue in the abdomen, in particular, is known to cause error (Tothill & Nord, 1995b).

Different assumptions about fat distribution, including variations in calibration procedures or standards, probably contribute significantly to the inconsistency in results obtained from different DXA systems. Very large systematic differences in soft tissue values determined by the three DXA systems (Hologic, Lunar, and Norland) have been reported (Laskey, 1996; Tothill et al., 1995a). These differences vary with the region considered, such that precision and accuracy are lower for measurements of the trunk, where there is much less bone-free soft tissue, than for the legs (Roubenoff et al., 1993; Tothill et al., 1994a). Several other explanations for the inter-machine variability include different approaches to edge detection and dual-energy production. Additionally, differing system sensitivities to AP thickness of the body may exist (Haarbo et al., 1991; Roubenoff et al., 1993). X-ray beam hardening errors can occur, which cause the measured Rst value to decrease, and thus % fat to increase, with increasing tissue thickness (Goodsitt, 1992). At high tissue depths > 20-25 cm, the amount of fat and bone mineral were overestimated by Lunar and Hologic systems (Laskey, 1996). Finally, manufacturers use different sources of external calibration, and there is a lack of cross-validation of instruments from different manufacturers using a standard phantom.

When upgrading DXA systems from first to second generation by the same manufacturer, errors may occur due to fan-beam magnification. In one study (Ellis & Shypailo, 1998), fan-beam measurement gave higher lean values and lower fat values when compared with pencil beam values. Although speculation is made as to the possibility that the manufacturer may have changed their reference values or cutoff points for the attenuation coefficients used to define the

relative lean and fat fractions of the total soft tissue mass, reasons for these differences are unknown (Ellis & Shypailo, 1998).

Another underexplored area of DXA technology when assessing body composition is the influence of hydration on soft tissue component estimates. DXA assumes that the hydration of lean body mass is uniform and fixed at 0.73 mL/g, or 73% (Roubenoff et al., 1993). However, hydration can vary from 67% to 85%. If a subject contains more than the average amount of water, DXA will overestimate the fat content. Evidence suggests that DXA is prone to fat estimation errors related to variation in soft tissue hydration. However, under normal or even most clinical conditions, this error is expected to be so small as to not pose any substantial limitations to the accuracy of DXA measurements (Ellis, 2000; Pietrobelli et al., 1998; Tothill et al., 1994a).

Bioelectrical Impedance Analysis (BIA)

Bioelectrical impedance analysis is a simple, reproducible technique for the assessment of body composition and has been validated indirectly in normal human subjects (Heitmann, 1994; Lukaski et al., 1985). The ability of tissues to conduct an electric current has been recognized for more than 100 years. The aqueous tissues of the body, due to their dissolved electrolytes, are the major conductors of an electrical current, whereas body fat and bone are relatively poor conductors (Ellis, 2000). Bioelectrical impedance analysis is based upon the relationship between the volume of the conductor (i.e., the human body), the conductor's length (i.e., the subject's height), the components of the conductor (i.e., fat or fat-free mass), and its impedance (Z). Impedance is the pure resistance of a biological conductor to the flow of an alternating current. It is composed of the sum of two components, resistance (R) and reactance (Xc), measured at a particular frequency, and is defined by the equation, $Z = R^2 + Xc^2$ (Brodie et al.,

1998). Resistance is defined as the pure opposition of the body to the flow of an alternating current. Reactance is produced by the additional opposition to the current from the capacitant (storage) effects of cell membranes, tissue interfaces, and structural features (Chumlea & Guo, 1997). Both R and Xc are found in the body, although Xc is typically very small relative to Z at lower frequencies; therefore, R and Z are often considered interchangeable.

Bioelectrical impedance analysis measurements are performed using four adhesive surface electrodes. They are typically placed on the dorsal surfaces of the right hand and foot, at the distal metacarpals and metatarsals respectively, and between the distal prominences of the radius and the ulna at the wrist, and the medial and lateral malleoli at the ankle, while the subject lies flat on a non-conducting surface with legs abducted. For the single-frequency measurement, which is typically at 50 kHz, (multifrequency machines are in the order of 5 kHz to 1 mHz), a weak alternating current is passed through the outer pair of electrodes, while the voltage drop across the body is measured using the inner pair of electrodes from which the body's impedance is derived.

In addition to being a safe, noninvasive, and reliable approach for estimating human body composition, BIA offers advantages of a relatively inexpensive cost, rapid measurements, portability, and little operator skill or subject involvement required. Prediction errors of calculating body fat are estimated to be 3-5% (Brodie et al., 1998). However, even if precision of measuring current body composition is high and measurement error is acceptable, the precision of measuring individual changes over time will depend on the accuracy of the initial and later measurements. In general, BIA is not considered a good predictor of changes in body composition associated with physical training and weight loss (Lukaski et al., 1985).

There are assumptions and limitations for almost all body composition methods. The theory behind BIA assumes that the conductor is a perfect cylinder with a uniform cross-sectional area, which does not hold true in the human body. Each cylinder (arms, legs, trunk) has a different cross-sectional area, and therefore contributes a different resistance. Another consideration is that the differences in cross-sectional area are not proportional to the differences in percentage body mass. For example, the trunk may comprise 45% of body mass, but only about 10% of whole body resistance, while the arm, which contributes only about 4% of body weight, accounts for about 45% of whole body resistance (Elia, 1993). Therefore changes in the size and composition of the trunk have little effect on whole body resistance. In this way, variations in body proportions may enhance the error associated with percentage body fat predictions. Measurements taken of subjects at the extremes of body fatness will yield less accurate fat-free mass predictions, tending to overestimate fat mass in the lean and underestimate fat mass in the obese (Brodie et al., 1998; Chumlea & Guo, 1997; Okasora et al., 1999).

Worldwide, there are many different manufacturers of BIA machines, which often use different equations for converting the raw measurements of impedance or resistance to estimates of body composition. This results in the same measurements being translated to greatly different estimates of body composition in both lean and obese subjects. Estimations of body fat varying by more than 10% of body weight have been reported (Elia, 1993). There are several reasons for this disagreement in results.

One major concern relates to the equations incorporated into the software by manufacturers. The populations used to establish these equations are apparently comprised of a combination of lean and obese individuals, and have involved different ethnic groups. Gender, age, and weight are included in some equations, but not in others. Errors will occur when impedance is used to

assess body composition in patients with abnormal or changeable water status and/or electrolyte balance (Gudivaka et al., 1999; Kyle et al., 2001; Lukaski et al., 1985; Montagnani et al., 1998). Healthy subjects may also experience disturbances in fluid distribution under normal circumstances. Differences in gender, age, muscle mass, physical activity, menstrual cycle, drug intake, diet, etc., can be expected to influence impedance readings (Brodie et al., 1998). Therefore, it is necessary to use different predictive equations for different groups of subjects.

Another source of error pertains to the reference method from which the bioimpedance equation was established, usually densitometry or water dilution techniques, which make different assumptions. Any error or drawback in the reference method will be transmitted to the BIA equation.

Other factors that may influence the impedance measurement, thereby decreasing reliability include: skin temperature; strenuous exercise before measurement (exercise-induced dehydration); different body positions; ingestion of a meal before measurements; and incorrect positioning of electrodes (Brodie et al., 1998). Higher impedance values when taken on the left side compared to the right side have been reported (Heitmann, 1994; Lukaski et al., 1985). Several systematic errors of impedance instruments include: measured changes being less than measurement errors, and different resistance readings on the same subjects measured with different machines, due to differences in voltage drop and/or current between various instruments (Brodie et al., 1998).

Summary

Despite existing systematic inaccuracies, DXA has proven to be a valuable and efficient method for assessing BMD as well as body composition. Because DXA technology yields such high evaluation and diagnostic potential, there is a need to continue with studies in which

accuracy, as well as reliability and validity of DXA are established. Bone densitometry measurements have typically focused on regions of the lumbar spine and hip because of their ability to assess risk of fracture and osteoporosis. However, BMD measurements of other regional areas may prove beneficial, as DT BMD is suggestive of stress fracture risk. The accuracy of BMD measurements is highest when subjects have no metal on their bodies or clothing. However, irremovable jewelry such as navel rings must be considered when assessing BMD results. There is a need to determine measurement errors presented by metal artifacts and the ability to manually correct for these errors. The purpose of the current research, therefore, was threefold: (1) to establish the reliability and validity of the Hologic QDR-4500A DXA at Virginia Tech to measure body composition; (2) to establish the reliability and validity of regional tibial DXA measures, and (3) to determine measurement errors represented by metal artifacts on BMD measures at the lumbar spine and ability to correct for these errors. It was hypothesized that body composition measurements and BMD measurements for the whole body, lumbar spine, total proximal femur, and total forearm with the Hologic QDR-4500A DXA at Virginia Tech would be reliable and valid, with precision errors matching those found in the literature. It was further hypothesized that DT BMD measurements would produce reliable and valid results. Lastly, it was hypothesized that the DXA operator would be able to manually correct for any measurement error that body jewelry would have on lumbar spine BMD measurements.

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CHAPTER III

RELIABILITY AND VALIDITY OF BONE MINERAL DENSTIY AND BODY COMPOSITION MEASURES BY DXA

Abstract

Reproducibility of measurements by dual-energy X-ray absorptiometry (DXA) is an important factor in both clinical and research applications using this technique. The reliability and validity of bone mineral density (BMD) and body composition measures by the QDR-4500A DXA (Hologic, Inc., Bedford, MA) at Virginia Tech were investigated in this study. A group of 24 young-adult (age=22.7±2.0 years) males (n=14) and females (n=10) completed DXA scans of the whole body (WB), lumbar spine (LS), total proximal femur (TPF), and total forearm (TF) at two timepoints. Correlation coefficients and coefficients of variation (CV%) were calculated for BMD at each region to assess reliability. Significant differences were not found ($p>0.05$) between repeat measurements at any site. Correlations ranged from 0.993 to 0.996 ($p<0.01$), and CV% for WB, LS, TPF, and TF measures were 0.73%, 0.92%, 0.69%, and 1.09%, respectively. Body composition values were determined from WB scans to assess the reliability of DXA to measure percent body fat (%BF), lean body mass (LBM), and fat mass (FM). Significant differences were not found ($p>0.05$) between repeat measurements of %BF, LBM, or FM. Correlations were 0.998 for all measures ($p<0.01$), and CV% were 1.79%, 1.07%, and 1.75% for %BF, LBM, and FM, respectively. Validity of %BF by DXA was tested by comparison to single frequency bioelectrical impedance analysis (BIA). Significant differences in %BF were not observed between methods. The QDR-4500A DXA at Virginia Tech is reliable and valid for BMD and body composition measures.

KEY WORDS: BODY COMPOSITION, BONE MINERAL DENSITY, DUAL ENERGY X-RAY ABSORPTIOMETRY, QDR-4500A DXA, RELIABILITY, VALIDITY

Introduction

Dual energy X-ray absorptiometry (DXA) technology has become well established in both clinical and research settings because of its advantages of high precision, short scan times, and stable calibration (Fogelman & Blake, 2000; Orwoll & Oviatt, 1991). It is used primarily for diagnosing the costly and debilitating disease of osteoporosis, as well as for monitoring changes in bone mineral density (BMD) over time or with therapy. DXA has also been shown to provide safe and convenient measurements of soft-tissue composition for the assessment of percent body fat (%BF), lean body mass (LBM), and fat mass (FM) (Pietrobelli et al., 1996; Pritchard et al., 1993; Wagner & Heyward, 1999).

A key issue in the clinical and/or research application of DXA is reproducibility. Because changes in BMD are small and gradual, typically 0.5-5.0% per year in a postmenopausal woman (Davey, 1998; Heilmann et al., 1998), precision of the measurement technique is crucial. A second issue in application of DXA is validity. As various methods exist to calculate %BF, it is necessary to validate different tools against one another for cross-comparison of results.

Short-term reproducibility of DXA is excellent both *in vitro* (assessment of standards or phantoms), as well as *in vivo* (Orwoll & Oviatt, 1991). *In vitro* precision errors, expressed as coefficients of variation (CV%) typically range from ~0.40-0.55% for spine phantoms, and from ~0.60-1.70% for hip phantoms, depending on the region analyzed (Lilley et al., 1991). *In vivo* precision is ~0.5-1.0% for the spine and 2.0-5.0% for the femoral neck, again dependent on the site analyzed (Adams, 1992).

Body composition has been linked to a number of health conditions, such as cardiovascular disease, diabetes, certain types of cancers, osteoporosis, and osteoarthritis. Therefore, there is a clinical need to consistently and precisely measure %BF, distribution of BF, muscle mass, and

bone mass (Wagner & Heyward, 1999). Previous studies indicate good reproducibility of body composition measurements by DXA: a CV% of 0.3-3.9% has been reported for %BF (Tataranni et al., 1996), 0.6-1.4% for LBM (Chilibeck et al., 1994; Madsen et al., 1997; Pritchard et al., 1993), and 1.7-2.7% for FM (Chilibeck et al., 1994; Lukaski, 1993; Madsen et al., 1997; Pritchard et al., 1993).

Although a number of body composition methods are available, such as isotope dilution, potassium counting, neutron activation analysis, and magnetic resonance imaging, only a few are sufficiently accurate for quantifying components in the research laboratory. In addition, many of these methods are costly, time-consuming, inconvenient, require high radiation doses, or lack precision and/or accuracy, which all compromise their value as instruments in the clinical or research setting (Haarbo et al., 1991). DXA systems, on the other hand, are practical, require no active subject involvement, impose minimal risk, and allow for quantification of multiple whole body and regional components, including bone mineral, fat, and LBM (Pietrobelli et al., 1998). Many other composition techniques simply measure one phase and extrapolate to the others. Choice of methodology in a particular clinical setting is often a matter of weighing advantages and disadvantages; however, it is critical to know that the method of choice is valid and suitable.

Precision studies have not yet established the reproducibility of the QDR-4500A DXA at Virginia Tech in studies of BMD, nor have they determined the reliability and validity of the DXA for measures of body composition. Therefore, the purpose of this study was to confirm both the reliability and validity of BMD and body composition measures by the QDR-4500A DXA housed in Virginia Tech's Bone metabolism, Osteoporosis, and Nutrition Evaluation (BONE) Laboratory.

Materials and Methods

Reliability study participants

Fourteen males and ten females (N=24), aged 18 years and older were recruited from the Virginia Tech campus (Blacksburg, VA, U.S.A.) and surrounding communities to participate in this study testing the reliability of the QDR-4500A DXA (Hologic Inc., Bedford, MA, U.S.A.) housed in the BONE Laboratory. Electronic-mail announcements and word-of-mouth were used as recruitment tools.

This research project was approved by the Institutional Review Board for Research Involving Human Subjects at Virginia Tech. At least 24 hours in advance, each volunteer was given an Informed Consent Form and a Health Screening Questionnaire for review. Prior to participating in any procedure, participants signed an Informed Consent Form (Appendix A) and a Health Screening Questionnaire (Appendix B). Female subjects were excluded if pregnant, unsure of pregnancy, or if experiencing irregular menstrual cycles. There were no other exclusion criteria for males or females.

Procedures for reliability study

On the first day of testing (time 1), all subjects had their heights and weights measured using a wall-mounted stadiometer, and a digital scale, respectively. Each participant had one whole body (WB) DXA scan completed, as well as one lumbar spine (LS), one nondominant total proximal femur (TPF), and one nondominant total forearm (TF) (version 8.25a, 2000, Whole Body Analysis software, QDR-4500A, Hologic Inc., Bedford, MA, U.S.A.). All DXA scans were conducted by a Licensed Radiologic Technologist- Limited in the Commonwealth of Virginia. All scans required each participant to lie on the DXA table in the supine position or, for the radius scan, to place the forearm flat on the DXA table. All four scans required ~15

minutes of time from each participant. Five to seven days later (time 2), each participant had these same DXA scans (WB, LS, TPF, and TF) repeated, again requiring ~15 minutes of time from each participant. All DXA scans were completed in the BONE Laboratory (Room 229, Wallace Hall) on the Virginia Tech campus.

Validity study participants

The same 24 subjects (14 males, 10 females, aged 18 and older) from the DXA reliability study also participated in a study assessing the validity of body composition measurements by DXA when compared to single-frequency bioelectrical impedance analysis (BIA). At least 24 hours in advance, each participant was provided with two separate Informed Consent Forms to review. Prior to participating in any procedure, participants signed both Informed Consent Forms (Appendices C and D).

Procedures for validity testing

Each participant had one WB DXA scan completed (the same one conducted for the DXA reliability study). From this scan, LBM, FM, and %BF were calculated. Each participant then completed single-frequency (50 kHz) BIA assessment (Valhalla, 1990B Fitness Analyzer, San Diego, CA, U.S.A.). Approximately one week in advance, each participant was given a set of guidelines to follow in the 24 hours prior to his/her testing session, including: no food for 2-4 hours, no exercise for 8 hours, no caffeine for 12 hours, no caffeine-containing medications for 12 hours, no alcohol for 24 hours, and maintenance of adequate hydration the previous 24 hours. If a participant believed he/she may have trouble following any of these guidelines, the participant was asked to expound, and possible solutions (i.e. adjusting appointment time) were discussed. On the day of testing, each participant was asked to lie flat, without movement, for ~10 minutes. A trained Research Assistant placed four electrodes on each subject, one each on

the right wrist, hand, ankle, and foot. Wire leads were then clipped to each electrode. Participant's weight, height, gender, and age were entered into the Valhalla BIA device. After 5 minutes, 3 successive measurements for %BF were taken and recorded. After a total of 10 minutes, 3 additional successive measurements for %BF were taken and recorded. The total time required from each participant for the BIA testing was approximately ~20 minutes.

Statistical analyses

Means and standard deviations (SD) were computed for each variable of interest. Paired samples *t*-tests (*t*), Pearson correlation coefficients (*r*), coefficients of variation (CV%), and Bland-Altman analyses were computed to examine the reliability of repeated measurements of BMD and body composition by DXA. Pearson correlation coefficients, CV%, and Bland-Altman analyses were used to determine the validity of DXA. Statistical analyses were completed using the Statistical Package for Social Sciences (SPSS, version 10.0 for windows, 1999, SPSS Inc., Chicago, IL, U.S.A.).

Results

Reliability

Subject characteristics are displayed in Table I. Table II presents BMD values (g/cm^2) for all sites measured at time 1 and time 2. BMD measurements were not statistically significantly different ($p>0.05$) at time 1 compared to time 2 (Table III). Correlation coefficients ranged from 0.993 to 0.996 ($p<0.01$) (Table III and Figures 1, 3, 5, 7), and CV% ranged from 0.692% to 1.094% (Table III). Bland-Altman plots in Figures 2, 4, 6, and 8 illustrate the bias of BMD measurement at time 2 compared with measurement at time 1 for all sites (WB, LS, TPF, TF), the 95% confidence interval (95%CI) for the bias, as well as the 95% limits of agreement

(95%LofA) between repeat measures (broken red lines), indicating that 95% of the differences will fall within this range.

Table IV presents data for body composition measurements (%BF, LBM, FM) by DXA at time 1 and time 2. Differences were not statistically significant ($p>0.05$) between repeat measurements (Table V) and CV% ranged from 1.067% to 1.785% (Table V). Correlation coefficients were 0.998 ($p<0.01$) for all three components (Figures 9, 11, 13) and Bland-Altman plots in figures 10, 12, and 14 present the bias of body composition measurement at time 2 compared with measurement at time 1 for %BF, LBM, and FM, respectively, the 95%CI for the bias, and the 95% LofA between repeat measures.

Validity

Values for %BF by DXA and BIA are presented in Table VI. DXA measurements at time 1 or time 2 were not significantly different from BIA measures (t=0.888 for time 1, t=0.919 for time 2, both $p>0.05$). The correlation coefficient between mean %BF by DXA and BIA was 0.937 ($p<0.01$) (Figure 15). CV% at time 1 and time 2 were 9.86% and 10.10%, respectively. The Bland-Altman plot in figure 16 depicts the bias of DXA compared with BIA for %BF, the 95%CI for the bias, and the 95% LofA between methods.

Sensitivity

These 24 subjects were divided into 3 subgroups for further analysis: 1) male cyclists (MC), 2) male non-cyclists (MNC), and 3) female non-cyclists (FNC). Tables VII, VIII, and IX present subject characteristics, as well as all BMD and body composition data for these three subgroups. Analysis of variance (ANOVA) (Appendix H) and post hoc Scheffe's tests indicated that significant differences between groups in age, BMI, LS or TPF BMD did not exist for time 1 ($p>0.05$) or time 2 ($p>0.05$). Significant differences ($p<0.05$) existed between groups in height

and weight at time 1, and in WB and TF BMD, %BF, LBM and FM for both time 1 and time 2 as evaluated by Scheffe's post-hoc tests. FNC were shorter ($p<0.01$), had higher %BF ($p<0.01$) , and FM ($p<0.01$), but lower LBM ($p<0.01$) compared to MC and MNC at time 1 and time 2. FNC had significantly lower weight ($p<0.01$), WB ($p<0.01$), and TF BMD ($p<0.01$) compared to MNC, but not compared to MC at time 1 and time 2. Although not statistically significant, trends were observed among several comparisons. When LS BMD was compared between MC and MNC, *p* values were 0.090 and 0.075 for time 1 and time 2, respectively. When TPF BMD was compared between MNC and FNC, *p*-values were 0.065 and 0.073 for time 1 and time 2, respectively. Finally, when TF BMD at time 2 was compared between MC and MNC, the *p*-value was 0.090.

Table I. Subject characteristics*

Variable	Mean	±SD	Range
Age (y)	22.7	1.9	18.0-27.0
Height (in)	68.5	4.3	61.0-75.0
Weight (lbs)	157.8	35.4	116.0-256.0
BMI[a]	23.6	3.3	19.7-32.6

* N=24

[a] Body Mass Index, [weight (lbs) x 705 + height $(in)^2$]

Table II. Mean bone mineral density (BMD) values (g/cm^2) for all sites at time 1 and time 2

BMD site	Mean	±SD	Range
WB[a]1	1.205	0.101	1.010-1.433
WB2	1.207	0.104	1.013-1.455
LS[b]1	1.057	0.148	0.850-1.451
LS2	1.059	0.153	0.838-1.482
TPF[c]1	1.028	0.121	0.814-1.281
TPF2	1.031	0.126	0.770-1.300
TF[d]1	0.622	0.080	0.508-0.789
TF2	0.622	0.080	0.517-0.800

N=24

[a] Whole body

[b] Lumbar spine

[c] Total proximal femur

[d] Total forearm

Table III. Correlations and coefficients of variation for repeated measurements of bone mineral density (BMD) by dual energy X-ray absorptiometry

BMD site (g/cm^2)	*t*-value[a]	Correlation Coefficient[b]	Coefficient of Variation, CV%
WB[c]	0.474	0.993	0.734
LS[d]	0.677	0.996	0.922
TPF[e]	0.380	0.995	0.692
TF[f]	0.902	0.993	1.094

N=24
[a] $p>0.05$
[b] Pearson Correlation, $p<0.01$
[c] Whole body
[d] Lumbar spine
[e] Total proximal femur
[f] Total forearm

Table IV. Mean percent body fat and soft tissue measurements (kg) by dual energy X-ray absorptiometry at time 1 and time 2

Variable	Mean	± SD	Range
%BF[a]1	19.1	7.4	10.7-31.8
%BF2	19.1	7.5	10.2-31.7
LBM[b]1	56.4	14.7	37.5-95.5
LBM2	56.2	14.7	37.0-95.6
FM[c]1	13.6	5.4	6.7-27.0
FM2	13.6	5.3	6.4-26.0

N=24
[a] Percent body fat
[b] Lean body mass
[c] Fat mass

Table V. Correlations and coefficients of variation for repeated measurements by dual energy X-ray absorptiometry of percent body fat and soft tissue mass

Variable	*t*-value[a]	Correlation Coefficient[b]	Coefficient of Variation, CV%
%BF[c]	0.838	0.998	1.785
LBM[d]	0.312	0.998	1.067
FM[e]	0.292	0.998	1.748

N=24
[a] $p>0.05$
[b] Pearson correlation, $p<0.01$
[c] Percent body fat
[d] Lean body mass
[e] Fat mass

Table VI. Mean percent body fat (%BF) of repeated dual energy X-ray absorptiometry measurements and %BF by bioelectrical impedance analysis

Variable	Mean	± SD	Range
%BF[a]1	19.1	7.4	10.7-31.8
%BF2	19.1	7.5	10.2-31.7
BIA[b], %BF	19.0	6.1	8.7-30.0

N=24
[a] Percent body fat
[b] Bioelectrical impedance analysis

Table VII. Subject characteristics, mean bone mineral density (BMD) values (g/cm^2), percent body fat (%BF), and soft tissue measurements (kg) by dual energy X-ray absorptiometry at time 1 and time 2, for male cyclists*

Variable	Mean	±SD	Range
Age (y)	22.1	3.1	18.0-27.0
Height (in)	70.7	2.8	67.0-75.0
Weight (lbs)	159.4	18.3	137.0-192.0
BMI[a]	22.5	2.0	19.7-25.4
WB[b]1	1.211	0.067	1.078-1.281
WB2	1.208	0.062	1.079-1.270
LS[c]1	0.991	0.097	0.889-1.172
LS2	0.984	0.089	0.895-1.135
TPF[d]1	1.010	0.122	0.814-1.160
TPF2	1.010	0.123	0.805-1.150
TF[e]1	0.628	0.045	0.570-0.685
TF2	0.621	0.043	0.570-0.691
%BF[f]1	13.3	2.2	10.7-17.0
%BF2	13.2	2.2	10.2-16.8
LBM[g]1	60.8	6.8	53.5-72.5
LBM2	60.9	7.2	52.6-73.2
FM[h]1	9.8	2.2	6.7-13.1
FM2	9.7	2.2	6.4-12.7
BIA[i] %BF	13.5	3.3	8.7-16.6

* n=7
[a] BMI=Body Mass Index
[b] Whole body
[c] Lumbar spine
[d] Total proximal femur
[e] Total forearm
[f] Percent body fat
[g] Lean body mass
[h] Fat mass
[i] Bioelectrical impedance analysis

Table VIII. Subject characteristics, mean bone mineral density (BMD) values (g/cm^2), percent body fat (%BF), and soft tissue measurements (kg) by dual energy X-ray absorptiometry at time 1 and time 2, for male non-cyclists*

Variable	Mean	±SD	Range
Age (y)	23.3	0.5	23.0-24.0
Height (in)	71.9	2.4	69.0-75.0
Weight (lbs)	188.3	47.9	148.0-256.0
BMI[a]	25.3	5.1	20.6-32.6
WB[b]1	1.284	0.101	1.130-1.430
WB2	1.291	0.108	1.140-1.460
LS[c]1	1.164	0.189	0.880-1.450
LS2	1.169	0.198	0.890-1.480
TPF[d]1	1.123	0.108	1.020-1.280
TPF2	1.127	0.111	1.030-1.300
TF[e]1	0.694	0.093	0.520-0.790
TF2	0.699	0.093	0.530-0.800
%BF[f]1	14.3	4.4	10.7-22.8
%BF2	14.1	4.3	10.2-22.3
LBM[g]1	70.3	15.7	56.5-95.5
LBM2	69.5	16.0	54.9-95.6
FM[h]1	13.0	7.3	7.1-27.0
FM2	12.7	7.0	7.2-26.0
BIA[i] %BF	16.1	3.5	12.2-21.8

* n=7
[a] BMI=Body Mass Index
[b] Whole body
[c] Lumbar spine
[d] Total proximal femur
[e] Total forearm
[f] Percent body fat
[g] Lean body mass
[h] Fat mass
[i] Bioelectrical impedance analysis

Table IX. Subject characteristics, mean bone mineral density (BMD) values (g/cm^2), percent body fat (%BF), and soft tissue measurements (kg) by dual energy X-ray absorptiometry at time 1 and time 2, for female non-cyclists*

Variable	Mean	±SD	Range
Age (y)	22.8	1.6	21.0-26.0
Height (in)	64.0	2.6	61.0-69.0
Weight (lbs)	135.0	14.0	116.0-162.0
BMI[a]	23.2	2.1	20.6-27.0
WB[b]1	1.144	0.092	1.010-1.337
WB2	1.144	0.092	1.013-1.327
LS[c]1	1.030	0.119	0.850-1.172
LS2	1.034	0.125	0.838-1.181
TPF[d]1	0.984	0.102	0.816-1.145
TPF2	0.985	0.111	0.770-1.148
TF[e]1	0.566	0.048	0.508-0.651
TF2	0.568	0.042	0.517-0.644
%BF[f]1	26.7	4.3	18.0-31.8
%BF2	26.7	4.3	17.5-31.7
LBM[g]1	43.3	4.2	37.5-51.2
LBM2	43.4	4.4	37.0-51.2
FM[h]1	16.7	3.7	10.9-22.1
FM2	16.8	3.7	10.7-22.2
BIA[i] %BF	24.8	3.5	18.5-30.0

* n=9
[a] BMI=Body Mass Index
[b] Whole body
[c] Lumbar spine
[d] Total proximal femur
[e] Total forearm
[f] Percent body fat
[g] Lean body mass
[h] Fat mass
[i] Bioelectrical impedance analysis

Figure 1. Correlation between repeated whole body (WB) bone mineral density (BMD) measures (g/cm^2) (N=24)

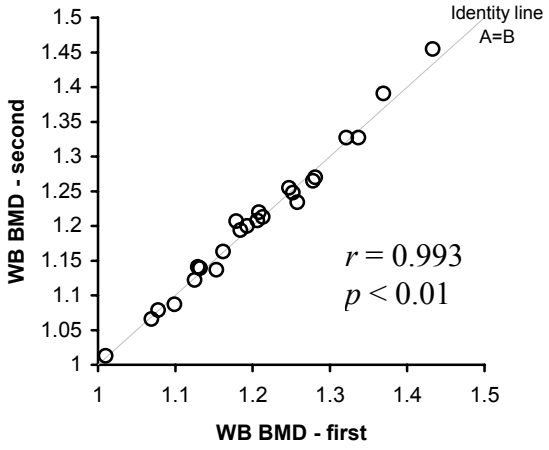
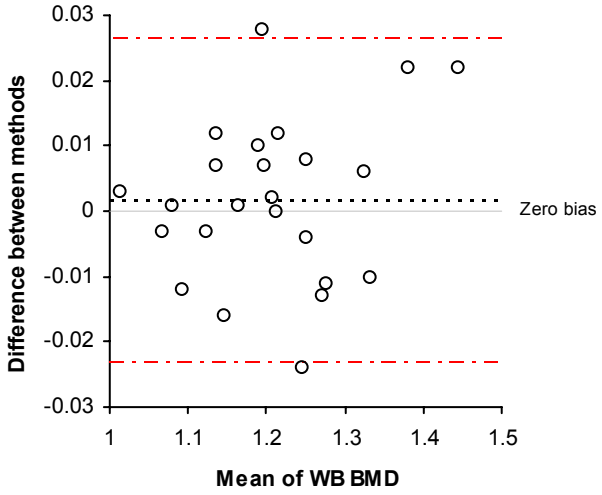


Figure 2. Bland-Altman bias plot for whole body (WB) bone mineral density (BMD)



Bias = 0.0019
95%CI = -0.0035 to 0.0072
95%LofA = -0.0229 to 0.0266

Figure 3. Correlation between lumbar spine (LS) bone mineral density (BMD) measures (g/cm^2) (N=24)

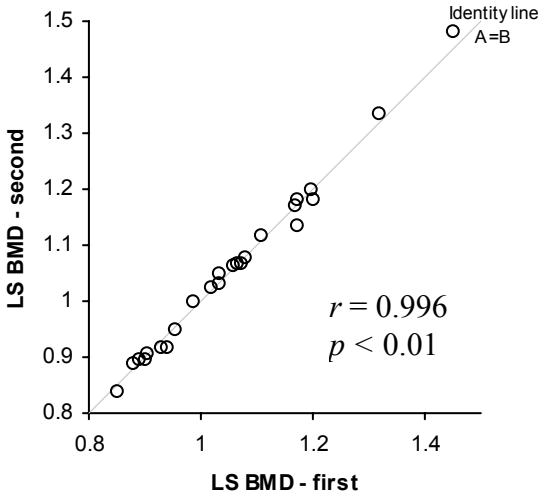
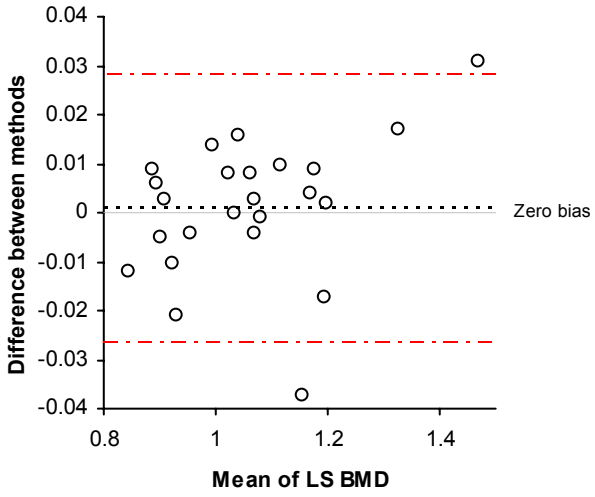


Figure 4. Bland-Altman bias plot for lumbar spine (LS) bone mineral density (BMD)



Bias = 0.0012
95%CI = -0.0047 to 0.0071
95%LofA = -0.0263 to 0.0287

Figure 5. Correlation between repeated total proximal femur (TPF) bone mineral density (BMD) measures (g/cm^2) (N=24)

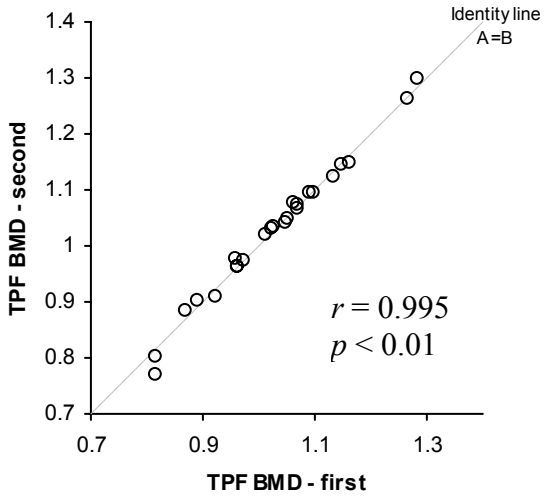
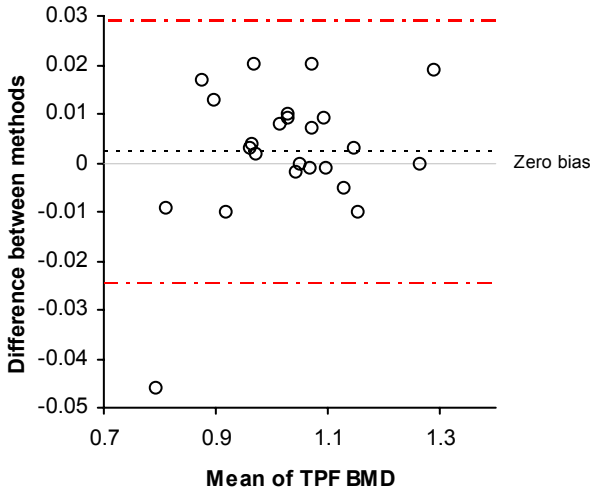


Figure 6. Bland-Altman bias plot for total proximal femur (TPF) bone mineral density (BMD)



Bias = 0.0025
95%CI = -0.0033 to 0.0083
95%LofA = -0.0243 to 0.0293

Figure 7. Correlation between repeated total forearm (TF) bone mineral density (BMD) measures (g/cm^2) (N=24)

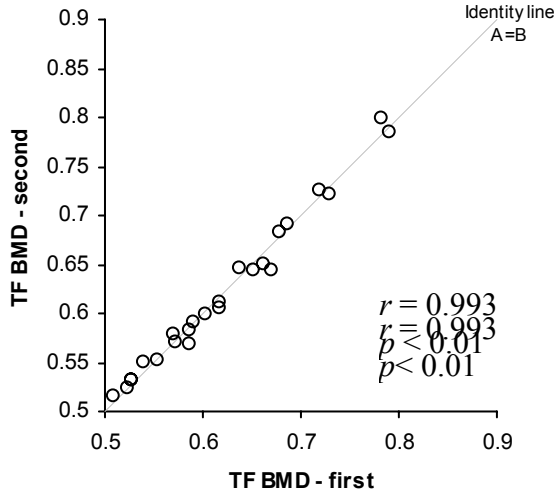
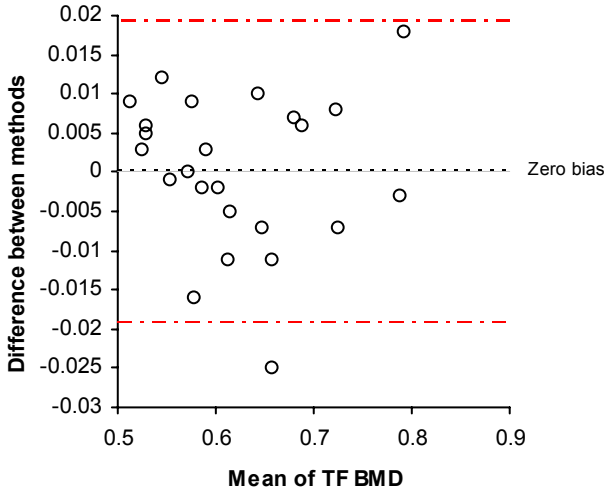


Figure 8. Bland-Altman bias plot for total forearm (TF) bone mineral density (BMD)



Bias = 0.0003
95%CI = -0.0039 to 0.0044
95%LofA= -0.0190 to 0.0195

Figure 9. Correlation between repeated % body fat measures by dual energy X-ray absorptiometry (N=24)

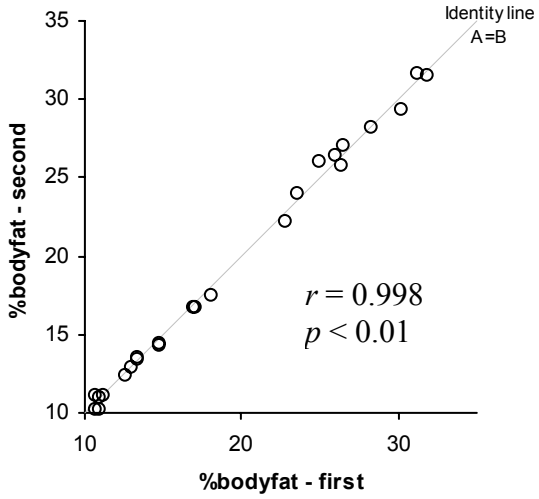
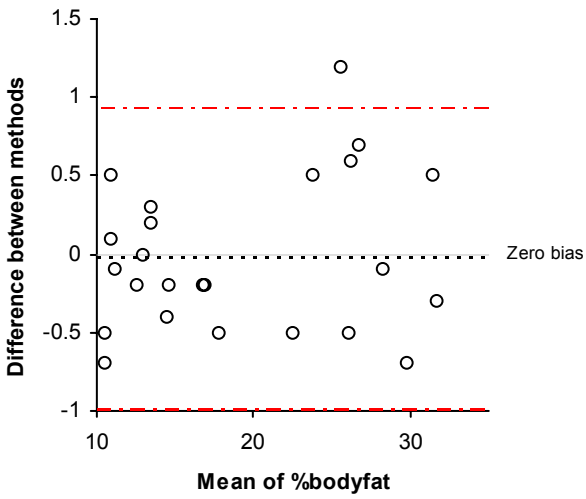


Figure 10. Bland-Altman bias plot for % body fat by dual energy X-ray absorptiometry



Bias = -0.021
95%CI = -0.229 to 0.187
95%LofA = -0.986 to 0.945

Figure 11. Correlation between repeated lean body mass (LBM) measures by dual energy X-ray absorptiometry (DXA) (N=24)

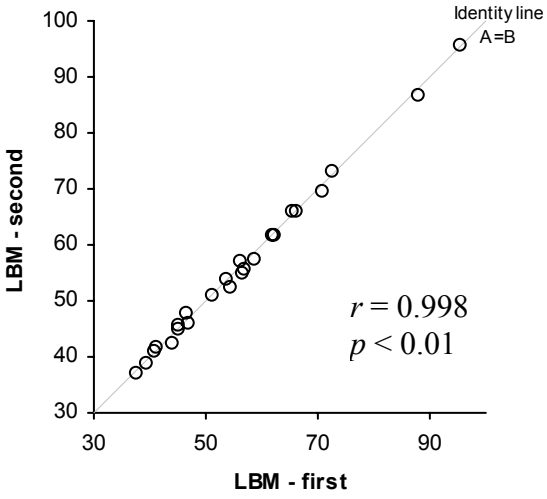
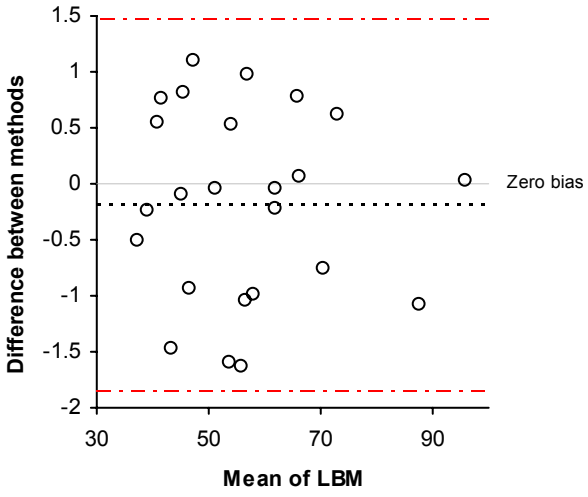


Figure 12. Bland-Altman bias plot for lean body mass (LBM) by dual energy X-ray absorptiometry (DXA)



Bias = -0.180
95%CI = -0.538 to 0.178
95%LofA = -1.842 to 1.483

Figure 13. Correlation between repeated fat mass (FM) measures by dual energy X-ray absorptiometry (DXA) (N=24)

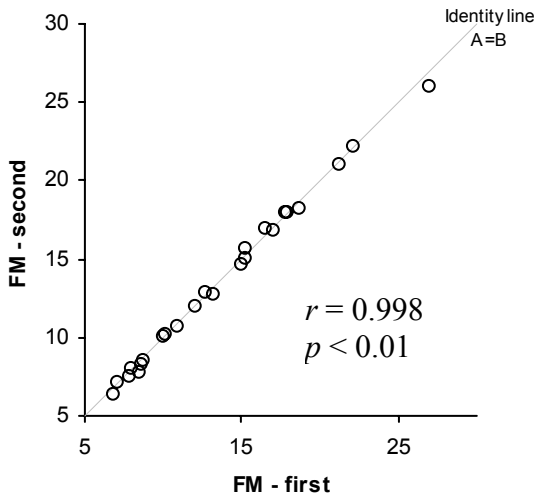
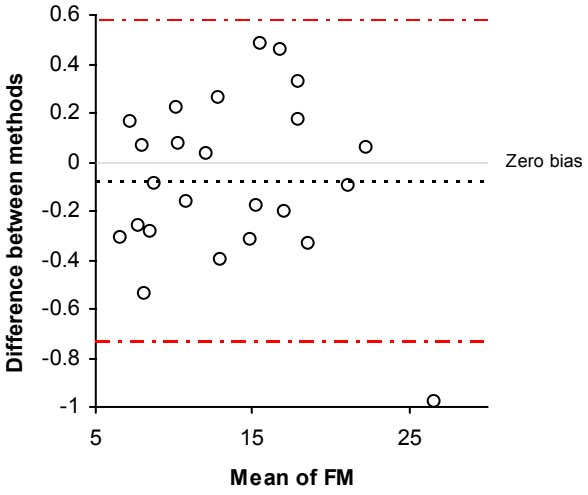


Figure 14. Bland-Altman bias plot for fat mass (FM) by dual energy X-ray absorptiometry (DXA)



Bias = -0.0738
95%CI = -0.2151 to 0.0676
95%LofA = -0.7300 to 0.5825

Figure 15. Correlation between % body fat measures by dual energy X-ray absorptiometry and bioelectrical impedance analysis (BIA) (N=24)

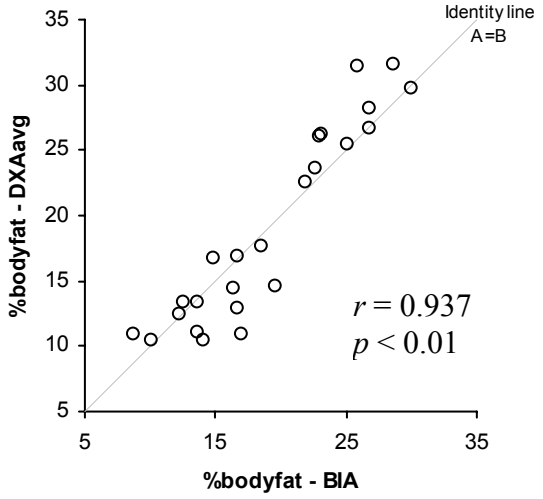
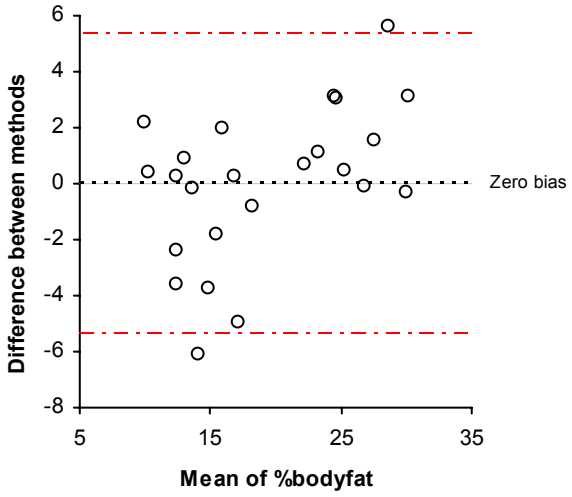


Figure 16. Bland-Altman bias plot for % body fat by dual energy X-ray absorptiometry and bioelectrical impedance analysis



Bias= 0.069
95%CI= -1.087 to 1.225
95%LofA = -5.297 to 5.434

Discussion

Reproducibility of BMD and body composition measurements by DXA is crucial in any clinical or research application of the technique. DXA has been previously shown to have good precision for both procedures (Fogelman & Blake, 2000; Wagner & Heyward, 1999). The reliability values for repeat measures over 5-7 days obtained from the QDR-4500A DXA at Virginia Tech are consistent with data reported in the literature.

The anthropomorphic spine phantom (#7316; Hologic, Inc., Bedford, MA, U.S.A.) used for *in vitro* calibration procedures in the BONE Laboratory and for this study has a CV% of 0.36% (N=295 scans). Correlation coefficients for repeat measurements of BMD were high, ranging from 0.993 to 0.996 ($p<0.01$) for the various sites analyzed. CV% of 0.73%, 0.92%, 0.69%, and 1.09% for WB, LS, TPF, and TF BMD, respectively, are similar to results obtained by others. Several authors have reported a CV% for WB BMD of 0.60-1.40% (Herd et al., 1993; Franck & Munz, 2000). The CV% for LS BMD values is typically <0.50% for *in vitro* measures (Laskey et al., 1991), and 1.00-1.10% for *in vivo* measures (Laskey et al., 1991; Orwoll & Oviatt, 1991). CV% for TPF BMD range from 1.60-4.70%, depending on the anatomic site analyzed (femoral neck, trochanteric region, Ward's triangle); however, a CV% of ~1.50% has been documented for the TPF (Svendsen et al., 1992). Precision of forearm measures also varies depending on the region analyzed (ultradistal, mid-distal, or proximal one-third). CV% ranging from 0.55-2.43% have been reported for these different regions (Hagiwara et al., 1994; Heilmann et al., 1998; Nieves et al., 1992; Overton & Wheeler, 1992; Ryan et al., 1992); however, a value of 1.50% has been cited for measures of the TF (Larcos & Wahner, 1991).

High correlations (r=0.998, $p < 0.01$) were obtained for all repeat measurements of body composition variables by DXA. Gutin et al. (1996) also reported the reliability of repeat

measurements of %BF by DXA to be 0.998 ($p \leq 0.01$). CV% of 1.79%, 1.07%, and 1.75% for %BF, LBM, and FM, respectively found in this study are consistent with values documented in the literature for body composition assessment by DXA. Typical CV% for %BF measures reported in the literature are 1.40-1.90% (Pritchard et al., 1993; Tothill et al., 1994; Wagner & Heyward, 1999). Values for LBM vary to a greater degree, ranging from 0.60-1.47% (Lees & Stevenson, 1992; Pritchard et al., 1992; Tothill et al., 1994). CV% cited for FM are ~1.80-2.73% (Chilibeck et al., 1994; Lees & Stevenson, 1992).

Numerous techniques are available for the assessment of body composition; however, there has been an increasing interest in utilizing DXA for this purpose because of its ability to measure regional composition. The validity of the QDR-4500A DXA at Virginia Tech for measuring %BF was established against a single-frequency BIA device. Although not without its own drawbacks, BIA has been confirmed by others to be a reliable and valid method for evaluation of human body composition (Heitmann, 1994; Kitano et al., 2001; Lukaski et al., 1985; Lukaski et al., 1986; Roubenoff, 1996). CV% for %BF between two separate DXA scans and a single BIA reading were 9.86% and 10.10%, respectively. The correlation between measurements of DXA and BIA for all subjects was 0.937 ($p<0.01$). All correlation values between DXA and BIA found in this study are similar to values reported by others, which are in the range of 0.57-0.987 (p[0.05) (Kitano et al., 2000; Kyle et al., 2001; Levenhagen et al., 1999; Okasora et al., 1999; Roubenoff, 1996; Sardinha et al., 1998).

To serendipitously examine data of cyclists, non-cyclists, and females, subjects were divided into three subgroups (MC, MNC, FNC) and differences between them were identified by analysis of variance (ANOVA). These groups did not differ significantly ($p>0.05$) in age, BMI, LS, or TPF BMD at either time 1 or time 2; however, significant differences ($p<0.05$) were

found for height and weight at time 1, and for WB and TF BMD, %BF, LBM, and FM measures at time 1 and time 2. FNC were significantly shorter and possessed less LBM, but had greater %BF and FM compared to MC and MNC. FNC were also significantly lower in weight, WB, and TF BMD than MNC, but not MC. Several comparisons did not reach the *a priori* level of statistical significance ($p<0.05$); however, trends tended to appear among some results. In comparisons of TPF BMD of MNC and FNC, resulting *p*-values were 0.065 and 0.073 for time 1 and time 2, respectively. This trend suggests that if a larger sample of males and females were included, BMD values for the TPF may have been significantly higher among MNC compared to FNC. When comparisons were made between MC and MNC for values of TF BMD, there were marked differences in level of significance between time 1 and time 2 ($p=0.181$, $p=0.090$, respectively). Although the value for testing at time 2 may indicate a trend toward MC having lower TF BMD than MNC, it also suggests that it may be more difficult to attain accuracy in repeat measurements of the forearm. Comparisons between LS BMD of MC and MNC produced a *p* value of 0.090 and 0.075 for time 1 and time 2, respectively. With a larger sample size and additional repeated measures, this value may have possibly reached statistical significance, with MC having a lower LS BMD than MNC. To support this notion, several studies have shown that male cyclists have lower BMD, particularly of the LS, when compared to controls (Fiore et al., 1996; Rico et al., 1993; Sabo et al., 1996; Stewart & Hannan, 2000). Thus, data from this study show that in general, FNC and MC appear to have similar BMD values.

Based on findings from the present study, the QDR-4500A DXA at Virginia Tech is a reliable and valid device for measuring BMD and body composition in the young-adult population. Principal advantages of this technique include its independence from assumptions regarding

relationships among body components and its use of radiologic principles for the direct determination of bone and soft tissue composition.

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CHAPTER IV

RELIABILITY AND VALIDITY OF DISTAL TIBIA MEASURES BY DXA

Abstract

Regional measurements of bone mineral density (BMD) by dual energy X-ray absorptiometry (DXA) have not been well established, although measures of the distal tibia (DT), specifically, may be beneficial for identifying individuals at risk for stress fractures of the lower leg. The reliability and validity of the QDR-4500A DXA (Hologic Inc., Bedford, MA) at Virginia Tech in measuring BMD of the DT were investigated in this study. Twenty-three young-adult (age=22.5±1.8 years) males (n=13) and females (n=10) had DXA scans of the DT completed at two time-points, 5-7 days apart. Correlation coefficients and coefficients of variation (CV%) were calculated to assess the reliability of measures. Significant differences were not found (p>0.05) between repeat measurements. The correlation was 0.804 (p<0.01) and the CV% was 4.63%. Subjects with >5% variability between measurements were excluded as outliers (n=6), and statistical analyses were re-calculated. The correlation without outliers was 0.971 (p<0.01) and CV% was 4.29%. The validity of DXA to perform DT measures was also assessed by comparing whole body (WB) BMD with DT BMD, as subjects with higher WB BMD should also have higher DT BMD. In two repeated measurements of DT BMD and WB BMD the correlations were 0.597 and 0.584 (p<0.01). When outliers were excluded, correlations were 0.689 and 0.715 (p<0.01). In conclusion, the QDR-4500A DXA is a reliable and valid technique for measuring DT BMD in the young-adult population, and may prove useful as an alternative measurement site in cases of degenerative disease as well as for identifying individuals at risk for stress fractures.

KEY WORDS: BONE MINERAL DENSITY, DISTAL TIBIA, DUAL ENERGY X-RAY ABSORPTIOMETRY, RELIABILITY, VALIDITY

Introduction

Dual energy X-ray absorptiometry (DXA) technology has been well established for bone mineral density (BMD) measures of the whole body (WB), lumbar spine, and hip; however, the reliability of other regional measures, such as the distal tibia (DT), has not been confirmed. Such measurements may be of interest when BMD and content values are not interpretable at the spine because of osteoarthritis, scoliosis, or aortic calcification, or at the femur because of osteoarthritis or hip prostheses. Evaluation of DT BMD could provide information on the cortical/trabecular ratio in a single weight-bearing bone (Casez et al., 1994).

In addition, there is a body of literature regarding stress fractures of the lower leg among athletes and military recruits and the potential risk factors that may predispose an individual to this type of injury. Reliable and valid measures of DT BMD by DXA may prove useful in helping to identify individuals at risk. Stress fractures are indeed a common overuse injury in the athletic population, particularly among runners (Bennell et al., 1996; Crossley et al., 1999; Korpelainen et al., 2001; Monteleone, 1995), and also a costly problem among military recruits (Beck et al., 2000; Gemmell, 2002; Pester et al., 1992). There are many causes of stress fractures, including both intrinsic and extrinsic factors (Korpelainen et al., 2001). A multitude of potential risk factors have been proposed, including: bone geometry, biomechanical variants, limb length, smaller, weaker muscles (Beck et al., 2000), age, gender, race, hormonal factors, footwear, arch structure (Korpelainen et al., 2001), excessive training (Bennell et al., 1996), fitness level (Monteleone, 1995), and low bone density (Bennell et al., 1996; Dugowson et al., 1991; Lauder et al., 2000; Pouilles et al., 1989).

When comparing groups of males with and without stress fractures, differentiating risk factors between these groups are typically nonexistent (Bennell et al., 1996; Crossley et al., 1999);

therefore, occurrence is difficult to predict. This may imply that other contributory factors not included in these studies are more important in men. However, several risk factors have been identified as positive predictors of stress fractures in women, including: later age of menarche, fewer menses per year since menarche, less lean mass in the lower limb, lower fat diet, discrepancy in leg length (Bennell et al., 1996; Korpelainen et al., 2001), lower lumbar spine and foot bone density (Korpelainen et al., 2001), less total body bone mineral content, and lower total bone density (Bennell et al., 1996; Dugowson et al., 1991; Lauder et al., 2000; Pouilles et al., 1989).

Although bone density values did not predict stress fracture occurrence in men, (which may be due to higher regional bone density in men compared with women), the possibility that lower bone density is a risk factor in male athletes cannot be excluded (Bennell et al., 1996). Moreover, because low BMD has been cited by several authors as a risk factor for stress fractures among women (Bennell et al., 1996; Dugowson et al., 1991; Korpelainen et al., 2001; Lauder et al., 2000; Pouilles et al., 1989), it is essential to establish the reliability and validity of DXA technology to measure DT BMD. Therefore, the purpose of this study was to investigate the capabilities of the Hologic QDR-4500A DXA at Virginia Tech for measurement of DT BMD.

Materials and Methods

Reliability study participants

Thirteen males and ten females (N=23), aged 18 to 26 were recruited from the Virginia Tech campus (Blacksburg, VA, U.S.A.) and surrounding communities to participate in this study testing the reliability of DT BMD measures by the QDR-4500A DXA (Hologic Inc., Bedford,

MA, U.S.A.) housed in the Bone metabolism, Osteoporosis, and Nutrition Evaluation (BONE) Laboratory. Electronic-mail announcements and word-of-mouth were used as recruitment tools.

This research project was approved by the Institutional Review Board for Research Involving Human Subjects at Virginia Tech. Each participant was given an Informed Consent Form and a Medical History Form (Appendices E and F) to review at least 24 hours in advance of the first testing session (time 1). Prior to participating in any procedure, participants signed the Informed Consent Form and completed the Medical History Form. Through this medical history, female participants who reported pregnancy, were unsure of pregnancy, or had irregular menstrual cycles were excluded. No other exclusion criteria for males or females existed.

Procedures

All procedures were completed in the BONE Laboratory, Room 229 Wallace Hall. Testing sessions were conducted at two timepoints: (1) baseline and (2) follow-up (approximately 5 to 7 days after the baseline session). Each testing session required ~15 minutes for completion. Each testing session involved measurement of body height and weight, using a wall-mounted stadiometer, and digital scale, respectively. Participants were then appropriately positioned on the DXA table for completion of one WB DXA scan and one DT DXA scan of the non-dominant leg (version 8.25a, 2000, Whole Body Analysis software, Hologic, Inc., Bedford, MA, U.S.A). All procedures were conducted by a Licensed Radiographic Technologist- Limited in the Commonwealth of Virginia

Statistical analyses

Means and standard deviations (SD) were computed for each variable of interest. Paired samples *t*-tests (*t*), Pearson correlation coefficients (*r*), coefficients of variation (CV%), and Bland-Altman analyses were computed to examine the reliability of repeated measurements of

DT BMD by DXA. Pearson correlation coefficients were calculated to determine the validity of DXA by comparison of WB BMD to DT BMD. Statistical analyses were completed using the Statistical Package for Social Sciences (SPSS, version 10.0 for windows, 1999, SPSS Inc., Chicago, IL, U.S.A.).

Results

Subject characteristics are displayed in Table I. Table II presents BMD values (g/cm^2) for DT BMD measurements of all subjects at time 1 and time 2. Differences between repeat measurements were not statistically significantly different (t=0.072, p>0.05). The correlation coefficient was 0.804 (p<0.01), and the CV% was 4.63%. Several subjects showed >5% variability between repeat measurements. These outliers (n=6) were excluded, and statistical analyses for reliability were repeated (Table III). With outliers excluded, differences between repeat measurements were not significantly different (t=0.091, p>0.05). The correlation coefficient was 0.971 (p<0.01), and the CV% was 4.29%. Figures 1 and 3 illustrate the correlation between DXA measurements of the DT at time 1 and time 2, with all subjects included and with outliers excluded, respectively. Bland-Altman plots in Figures 2 and 4 display the bias of measurement two (time 2) compared with measurement one (time 1), the 95% confidence interval (95%CI) of the bias, and the 95% limits of agreement (95%LofA) between repeat measures (broken red lines noting that 95% of the differences will fall within this range), for all subjects and with outliers excluded, respectively.

Validity of DXA was assessed by comparing two repeated measures of WB BMD with DT BMD, as those with higher measures of WB BMD should correlate with those having higher DT BMD (Table IV). The relationship between DT and WB BMD for all subjects at time 1 and time 2 was statistically significant (r=0.597, 0.584, respectively, both p<0.01). When repeating these

calculations with outliers of the group excluded (see Table V), the relationship was stronger (r=0.689, 0.715, for time 1 and time 2, respectively, both p<0.01).

Table I. Subject characteristics*

Variable	Mean	±SD	Range
Age (y)	22.5	1.8	18.0-26.0
Height (in)	68.4	4.4	61.0-75.0
Weight (lbs)	158.5	36.1	116.0-256.0
BMI[a]	23.7	3.3	19.7-32.6

*N=23

[a] Body Mass Index, [weight (lbs) % 705 + height $(in)^2$]

Table II. Mean distal tibia bone mineral density (BMD) values (g/cm^2) for all subjects* at time 1 and time 2

Variable	Mean	± SD	Range
DT[a1]	1.111	0.114	0.893-1.345
DT2	1.084	0.097	0.850-1.252

* N=23

[a] Distal tibia

Table III. Mean distal tibia bone mineral density (BMD) values (g/cm^2) with outliers excluded* at time 1 and time 2

Variable	Mean	±SD	Range
DT[a1]	1.072	0.088	0.893-1.238
DT2	1.081	0.079	0.888-1.210

* n=17

[a] Distal tibia

Table IV. Mean distal tibia (DT) and whole body (WB) bone mineral density (BMD) values (g/cm^2) for all subjects* at time 1 and time 2

Variable	Mean	± SD	Range
DT[a]1	1.111	0.114	0.893-1.345
WB[b]1	1.205	0.103	1.010-1.433
DT2	1.084	0.097	0.850-1.252
WB2	1.206	0.106	1.013-1.455

* N=23
[a] Distal tibia
[b] Whole body

Table V. Mean distal tibia (DT) and whole body (WB) bone mineral density (BMD) measures (g/cm^2) with outliers excluded* at time 1 and time 2

Variable	Mean	± SD	Range
DT[a]1	1.072	0.088	0.893-1.238
WB[b]1	1.195	0.114	1.010-1.433
DT2	1.081	0.079	0.888-1.210
WB2	1.196	0.118	1.013-1.455

* n=17
[a] Distal tibia
[b] Whole body

Figure 1. Correlation between repeated distal tibia (TIB) bone mineral density (BMD) measures (g/cm^2) (N=23)

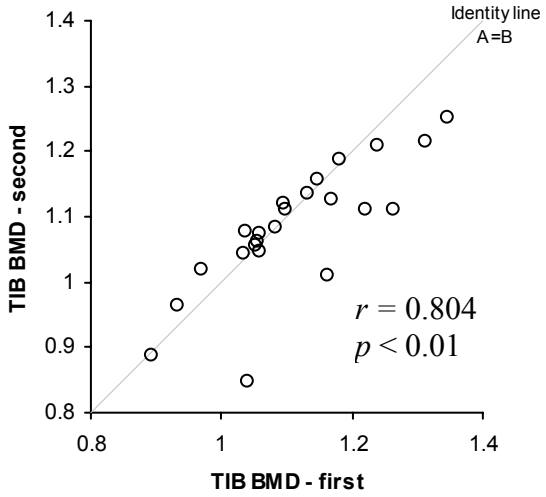
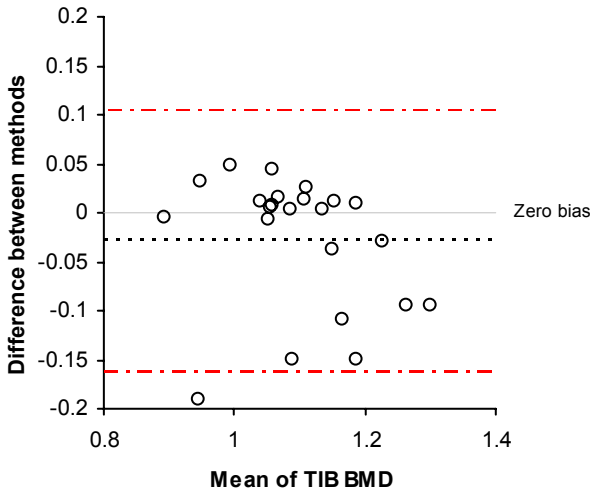


Figure 2. Bland-Altman bias plot for distal tibia (TIB) bone mineral density (BMD) (N=23)



Bias= -0.0269
95%CI= -0.0563 to 0.0026
95%LofA = -0.1605 to 0.1067

Figure 3. Correlation between repeated distal tibia (TIB) bone mineral density (BMD) measures (g/cm^2) (n=17)

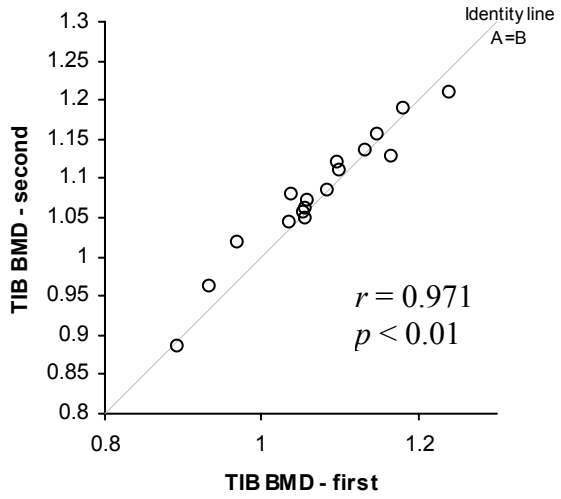
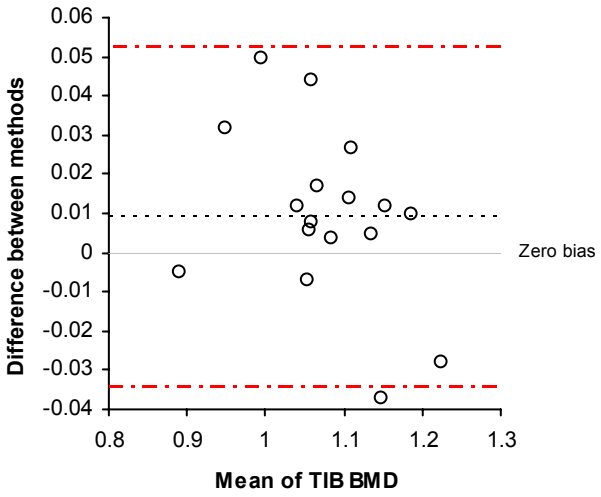


Figure 4. Bland-Altman bias plot for distal tibia (TIB) bone mineral density (BMD) (n=17)



Bias= 0.0096
95%CI= -0.0017 to 0.0210
95%LofA = -0.0338 to 0.0531

Discussion

Measures of reliability and validity of tibial BMD by DXA have not been well established; however, evaluation of DT BMD measures may be beneficial in a number of situations. The tibial diaphysis is comprised of nearly all cortical bone, while the epiphysis contains substantial amounts of highly active trabecular bone. When BMD values of the spine or hip are not easily interpreted due to disease or degenerative changes, measurements of DT BMD may provide valuable information regarding mineral distribution and the ratio of cortical to trabecular bone in a weight-bearing bone. Measurement of DT BMD may also be helpful in the prediction of stress fracture among high-risk populations, as low BMD may play a causative role in this overuse injury.

The statistical analyses performed on the repeated measures by the QDR-4500A DXA in this study demonstrate the reliability of this device for measurement of DT BMD. There were no significant differences between repeat measurements ($p>0.05$), and the correlation was 0.804 ($p<0.01$), with a CV% of 4.628%. There is a paucity of published data regarding precision of tibial BMD measurements. Only one report of mineral distribution along the distal third of the tibia exists in which CV% of 1.9% for measures of the distal epiphysis, and 2.1% for the diaphysis are reported (Casez et al., 1994).

After further analysis of data, >5% variability among some DT BMD measurements between time 1 and time 2 existed; therefore, these subjects were excluded as outliers (n=6), and statistical analyses for reliability were performed again. This new data set, with outliers excluded, produced a higher correlation between repeat measures ($r= 0.971$, $p<0.01$), and a slightly lower CV%. This suggests that obtaining accurate measures of DT BMD may be more difficult than for other regions.

One explanation for slightly less accurate analysis of DT BMD by the QDR-4500A DXA compared to WB measures, for example, is the use of forearm software for the analysis of DT BMD scans. CV% for repeated measures of the QDR-4500A DXA at Virginia Tech for analysis of forearm measures was 1.094% (Chapter III). Other published data has reported the CV% of forearm measures by DXA, as ranging from 0.55-2.43% for various regions of the forearm (ultradistal, mid-distal, proximal one-third) (Eckert et al., 1996; Hagiwara et al., 1994; Heilmann et al., 1998; Larcos & Wahner, 1991; Lefobb et al., 1992; Nieves et al., 1992; Ryan et al., 1992; Weinstein et al., 1991). Therefore, use of forearm software for analysis of DT BMD scans may produce slightly less accurate results compared to BMD measures of the forearm.

The validity of DT BMD measures by DXA was also assessed by comparing repeated measures of WB with DT BMD, as those with a higher WB BMD should also have higher DT BMD. Correlations between these two repeated measures in all subjects established a significant relationship (r=0.597, 0.584, both p<0.01), which was found to be somewhat stronger when outliers of the group were excluded from the analysis (r=0.689, 0.715, both, p<0.01).

Results from this study have provided novel information regarding the utility of DXA in regional BMD measurement. It can be concluded that the QDR-4500A DXA at Virginia Tech is a reliable and valid device for the measurement of DT BMD. DXA measures of the tibia may be beneficial in determining skeletal state in the presence of degenerative disease, as well as in predicting stress fractures of the lower extremities in athletes, military recruits, and other high-risk populations.

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CHAPTER V

INFLUENCE OF NAVEL JEWELRY ON BONE MINERAL DENSITY MEASURES OF THE LUMBAR SPINE

Abstract

Metallic jewelry inserted at the navel has the potential to interfere with bone mineral density (BMD) scans of the lumbar spine (LS). The purpose of this study was to examine the influence of navel jewelry on analyses of LS BMD measurements conducted by dual energy X-ray absorptiometry (DXA; QDR-4500A, Hologic, Inc.). DXA scans of the anthropomorphic phantom spine (PS) were completed with jewelry placements of: (1) PS alone (no jewelry); (2) PS with navel ring over L_4; (3) PS with ring over L_3/L_4; (4) PS with navel barbell over L_4; (5) PS with barbell over L_3/L_4. Eleven scans were completed for each placement. One ring and one barbell, each comprised of titanium plated surgical steel, were used in these scans. Analysis of variance indicated that the mean LS BMD (g/cm^2) values were statistically significantly greater ($p < 0.0001$) with the navel ring, despite placement (+4.36% and +4.11% for placements 2 and 3, respectively) and despite manual adjustment to remove the metal artifact (+1.03% and +0.60% for placements 2 and 3, respectively) compared to the PS alone. Mean LS BMD values were statistically significantly greater ($p < 0.0001$) with the barbell, despite placement (+3.40% and +3.23% for placements 4 and 5, respectively) and only despite manual adjustment for placement 4 (+0.67%) compared to the PS alone. Navel jewelry interferes with measurement of LS BMD. Ability to manually adjust analyses for such metal artifacts may depend on the jewelry shape and placement.

KEY WORDS: BODY PIERCING, BONE MINERAL DENSITY, DUAL ENERGY X-RAY ABSORPTIOMETRY, METAL ARTIFACTS, NAVEL JEWELRY

Introduction

Orthopedic metal prostheses affect measures of body composition including bone mass (Body Art 1994 Reader Survey). In humans, a titanium femoral implant increased bone mineral density (BMD) by nearly 27% when placed on the femoral area (Madsen et al., 1999). Among dogs, BMD was increased by >5% with the addition of a titanium implant on bone specimens (Markel et al., 1992). Although the addition of these implants did not impact the reliability of BMD measurements (Markel et al., 1992), absolute BMD values were erroneously altered. Because the use of orthopedic implants are reserved for individuals with established bone complications, the likelihood of misinterpretation of BMD scans due to these metal implants is minimal. However, another type of metal artifact – body piercing – has become more prevalent among Americans (Hadfield-Law L, 2001), and has the potential to influence BMD results.

Millner and Eichold found that body piercing was prevalent among individuals aged 19 to 55 years (2001). Among respondents to a survey conducted by *Body Art* magazine, 79% of individuals with a body piercing were ≥29 years of age (Body Art 1994 Reader Survey). At a northeastern university, 51% of male and female students who completed surveys had at least one body piercing (Mayers et al., 2002). Moreover, the prevalence of body piercing among these young-adult women was higher compared to these men (Mayers et al., 2002). Despite an individual's age or gender, metal artifacts from body piercing have the potential to interfere with accurate measurement of BMD. While a single set of pierced earrings, for example, has little impact on total body BMD measurements (Hologic, Inc., 1998), a navel ring or barbell spans a wide area of the lumbar spine (LS) relative to the total amount of bone captured by the scan. Thus, the purpose of this study was to examine the impact of navel jewelry on analyses of LS BMD measurements conducted by dual energy X-ray absorptiometry (DXA). It was

hypothesized that the presence of navel jewelry in a DXA scan of the LS would interfere with accurate measurement of BMD at this body site.

Materials and Methods

Materials

Previously completed LS BMD scans by DXA (QDR-4500A, Hologic, Inc., Bedford, MA, U.S.A.) of individuals with pierced navels were evaluated to locate the most common position of navel rings and barbells. Pierced navel jewelry appeared solely over the fourth lumbar vertebrae (L_4) in some of these scans and spanned portions of the third lumbar vertebrae (L_3) and L_4 in the remaining scans. Thus, two positions for jewelry placement for the current study were established.

Two common shapes of jewelry used in navel piercing were selected, including a ring (or loop) and a barbell. These items were purchased at a local novelty store (Spencer Gifts, Christiansburg, VA, U.S.A.). Both the ring (~½") and barbell (~¾") were 14 gauge (14G) in thickness and comprised of titanium plated surgical steel (Made in China and Korea, respectively).

The anthropomorphic spine phantom (#7316, Hologic, Inc., Bedford, MA, U.S.A.) was used for all measurements. The bone area, bone mineral content, and BMD of this phantom spine (PS) are 52.3 cm^2, 51.7 g, and 0.989 g/cm^2, respectively, when used with this fan-beam DXA model.

Procedures

All procedures were carried out in the Bone metabolism, Osteoporosis, and Nutrition Evaluation (BONE) Laboratory, Virginia Polytechnic Institute and State University (Blacksburg, VA, U.S.A.). Scans were completed on February 1, 2002. In sequence, five DXA scans of the

PS were conducted, including (1) PS alone; (2) PS with ring over L_4; (3) PS with ring over L_3 and L_4; (4) PS with barbell over L_4; (5) PS with barbell over L_3 and L_4 (please see Figure for jewelry placements). Each of these five scans (1 set) was repeated 11 times for a total of 55 scans. The PS was repositioned 11 times or between each set of scans. Scans were completed using the AP LS scan selection in "fast array" mode as recommended for human testing in a clinical setting (7). Standard quality control procedures were completed on the testing day. The PS has been previously scanned 296 times, producing a coefficient of variation (CV) of 0.36%.

All scans were analyzed using the standard spine protocol (version 8.26f:3, Hologic, Inc., Bedford, MA, U.S.A.). For the PS alone scans, no manual adjustments were made during these analyses. For all remaining scans (placements 2-5 with jewelry), manual editing as recommended by the QDR-4500A manufacturer (Hologic, Inc., 1998) was completed to remove the overlying jewelry shape. Scans were completed and analyzed by the same investigator.

Statistical analyses

Means ± standard deviations (SD) were computed for the 11 scans within each of the five placement groups. In addition, means ± SD were calculated for the manually adjusted scans (from placements 2-5). Analysis of variance (ANOVA) was conducted to identify differences in mean BMD (g/cm^2) between the two ring placements, two manually adjusted results, and the PS alone as well as between the two barbell placements, two manually adjusted results, and the PS alone. Post-hoc tests were completed to further explore statistically significant differences between groups for each ANOVA. Statistical analyses were completed using the Statistical Package for Social Sciences (SPSS, version 10.0 for windows, 1999, SPSS Inc., Chicago, IL, U.S.A.).

Results

Tables 1 and 2 present ANOVA results from evaluation of the ring placements and manual adjustments and from examination of the barbell placements and manual adjustments, respectively. Means ± SD and confidence intervals for each of the five placements as well as for the four manually adjusted scan results are included in these tables.

Placement of the ring (over L_4 or spanning L_3/L_4) made no difference in BMD measurements. Manual adjustment for the ring artifact, despite placement, produced the same BMD values. Although manual adjustment of the scans produced significantly different results from the scans with the unadjusted ring artifacts, these adjusted BMD values were still significantly different from the PS alone. Ring placement over the L_4 and spanning L_3/L_4 produced BMD values that were 4.36% and 4.11% greater compared to the PS alone. After manual adjustment of these scans, BMD values were 1.03% and 0.60% greater compared to the PS alone (L_4 and L_3/L_4 placements, respectively).

For the barbell, inclusion of the metal in the scan, regardless of placement, produced similar results. Manual adjustment for the barbell also yielded similar results, despite placement. While inclusion of the barbell in the DXA scans produced significantly greater BMD values compared to the PS alone (+3.40% for L_4 placement and +3.23% for L_3/L_4 placement), manual adjustment for these BMD values varied by placement compared to the PS alone. Manual adjustment of the barbell in the L_4 placement produced a significantly different mean BMD value (+0.67%) compared to PS alone, whereas manual adjustment of the barbell in the L_3/L_4 placement did not (+0.19%).

Discussion

Navel jewelry interferes with measurement of BMD at the LS. Because many individuals, potentially even persons with compromised BMD status, have pierced navels, these metal artifacts should be considered when completing BMD scans. Although repeatability of LS DXA scans were not influenced by navel jewelry, a navel ring or barbell may interfere with a DXA scan to the degree that LS BMD may be incorrectly interpreted as "normal" when, in fact, it is not. Even when the scan is manually adjusted to correct for navel jewelry, the adjustment may still produce inaccurate results, depending on the shape of the jewelry and placement of the jewelry over the LS area.

While some metal artifacts cannot be removed (Madsen et al., 1999) and some likely do not interfere with the overall results (Hologic, Inc., 1998), body jewelry at the navel should be removed before the completion of an AP DXA scan at the LS. Because such jewelry is radio-opaque, failure to take jewelry out of the scan field may result in inaccurate BMD measures. Such inaccuracies have implication for clinical and research applications involving DXA scans.

In the clinical or research arenas, the individual with a body piercing, such as a navel ring or barbell, may be unaware of how to remove this jewelry. The clinician or researcher may also be unfamiliar with body piercing removal. Rather than reschedule a patient or exclude a research participant with a pierced navel, practitioners may consider becoming educated or skilled at body piercing removal.

Limitations to this study existed. Only 14G jewelry comprised of titanium plated surgical steel in loop and barbell shapes was used. Finer gauges, other metals, and varied jewelry shapes may have produced different results. The PS was used to ensure uniformity in procedures and to avoid unnecessary radiation exposure in humans; thus, navel jewelry was analyzed only for its

influence on LS BMD. Further research is necessary to determine effects of navel jewelry on total body BMD and in humans. In the current study, only one piece of jewelry was examined; the influence of metal from multiple pierced body sites on total body BMD is also unknown. In conclusion, navel jewelry interferes with measurement of LS BMD. Ability to manually adjust analyses for such metal artifacts may depend on the jewelry shape and placement.

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Table 1. Analysis of variance for navel ring comparisons.

Navel jewelry placements and adjustments[§]	Bone mineral density (g/cm^2) mean ± SD	95% confidence interval for mean
Phantom spine (PS)	0.9958 ± 0.0046 (A)	0.9927 – 0.9989
PS with ring over L_4[†]	1.0392 ± 0.0035 (B)	1.0368 – 1.0415
PS with ring split between L_3[‡] and L_4	1.0367 ± 0.0029 (B)	1.0348 – 1.0387
Adjusted PS with ring over L_4	1.0061 ± 0.0031 (C)	1.0040 – 1.0082
Adjusted PS with ring split between L_3 and L_4	1.0018 ± 0.0039 (C)	0.9992 – 1.0044

[§]N = 11 scans per placement.

[†] $L_4 = 4^{th}$ lumbar vertebrae.

[‡]$L_3 = 3^{rd}$ lumbar vertebrae.

Means with different letters are statistically significantly different at $p < 0.0001$ (Scheffe's post-hoc test).

Table 2. Analysis of variance for navel barbell comparisons.

Navel jewelry placements and adjustments[§]	Bone mineral density (g/cm^2) mean ± SD	95% confidence interval for mean
Phantom spine (PS)	0.9958 ± 0.0046 (A)	0.9927 – 0.9989
PS with barbell over L_4[†]	1.0297 ± 0.0031 (B)	1.0276 – 1.0318
PS with barbell split between L_3[‡] and L_4	1.0280 ± 0.0043 (B)	1.0251 – 1.0309
Adjusted PS with barbell over L_4	1.0025 ± 0.0042 (C)	0.9996 – 1.0053
Adjusted PS with barbell split between L_3 and L_4	0.9977 ± 0.0040 (A,C)	0.9951 –1.0150

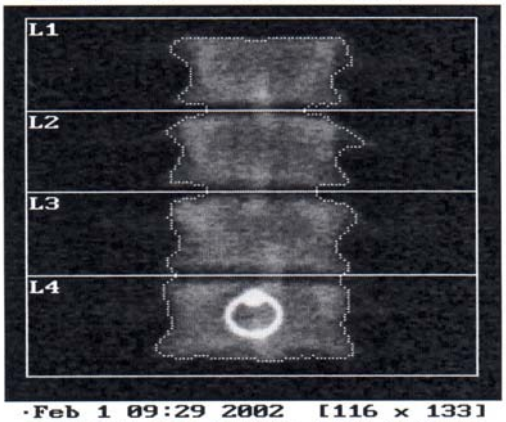
[§]N = 11 scans per placement.

[†] $L_4 = 4^{th}$ lumbar vertebrae.

[‡]$L_3 = 3^{rd}$ lumbar vertebrae.

Means with different letters are statistically significantly different at $p < 0.0001$ (Scheffe's post-hoc test).

k = 1.148 d0 = 52.6(1.000H) 6.790



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A

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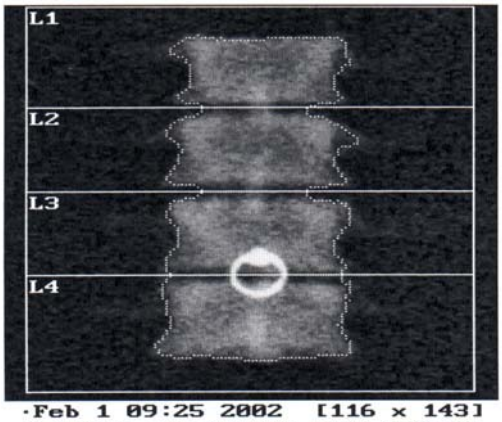

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B

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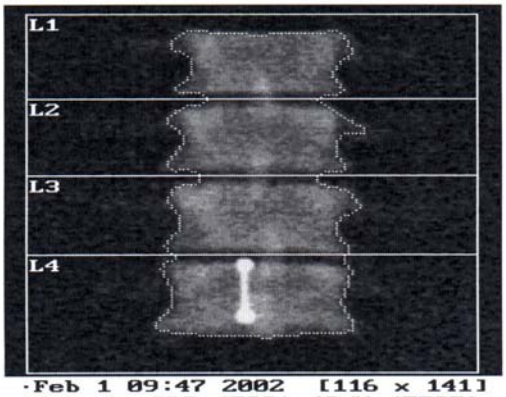

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C

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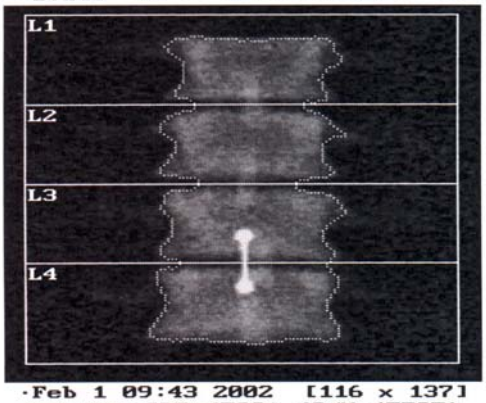

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Lumbar Spine V8.26f:3

D

Figure. Placement of navel jewelry in phantom spine scan field. Placements 2, 3, 4, and 5 are presented in A, B, C, and D, respectively.

CHAPTER VI

SUMMARY AND FUTURE DIRECTIONS

Reliability and validity of bone mineral density (BMD) and body composition measurements by the QDR-4500A dual energy X-ray absorptiometer (DXA, Hologic Inc., Bedford, MA) at Virginia Tech were examined in a group of young-adult males and females (N=24; Chapter III). Scans of the whole body (WB), lumbar spine (LS), total proximal femur (TPF) and total forearm (TF) were performed twice, without significant differences between repeated measures. Percent body fat (%BF), lean body mass (LBM), and fat mass (FM) were determined from whole body scans and assessed for reliability, while validity for DXA %BF was investigated by comparison with single frequency bioelectrical impedance analysis (BIA). Significant differences were not found between repeated body composition measures by DXA. In addition, the validity of DXA was confirmed as significant differences were not found between %BF measures by DXA and BIA. A sub-group of male cyclists participating in the study were found to have BMD values that were generally more similar to female non-cyclists compared to male non-cyclists. This agrees with other data reporting lower BMD in cyclists and suggests that the mechanical nature of cycling does not promote gains in BMD.

Reliability and validity of distal tibia (DT) BMD measures by the QDR-4500A DXA at Virginia Tech were also investigated in a group of 23 young-adult males and females (Chapter IV). Scans of the DT were performed twice, and significant differences were not found between repeated measurements. Participants in which >5% variability between DT BMD measures were observed were excluded (n=6). Statistical analyses were repeated, producing stronger correlations. In these procedures for DT BMD measurements, forearm software was used, and although CV% for total forearm measures was <1.1%, the use of such software may have

affected the accuracy of DT BMD measures. Validity of DXA in DT measures was established by comparing WB BMD with DT BMD, as those with higher WB BMD should have higher DT BMD. Correlations between measures were significant, confirming that the QDR-4500A DXA is a valid device for measurement of DT BMD.

The influence of navel jewelry on the accuracy of lumbar spine (LS) BMD measures by DXA, as well as the ability of the operator to correct for errors in LS BMD were analyzed (Chapter V). The presence of navel jewelry, ring- or bar-shaped, on a spine phantom artificially and significantly increased BMD of the LS. Manual correction of the scan region by the operator did not restore LS BMD back to original values in three of four navel jewelry placements in the LS scan field.

Several overall conclusions may be drawn from these studies. The reliability and validity of the QDR-4500A DXA at Virginia Tech has been confirmed for the measurement of WB, LS, TPF, TF, and DT BMD, as well as body composition variables. The accuracy of TF scans was slightly less than that of other regions. Thus, because DXA uses forearm software for analysis of DT scans, accuracy of DT BMD measures may also be slightly, but not significantly, impacted. Development of software for scanning and analyzing DT BMD must be considered. A novel finding of this study was the effect of metal artifacts on the accuracy of DXA. Specifically, a navel ring placed on a spine phantom will significantly raise LS BMD, without the possibility of complete manual correction by the operator. Future studies investigating this matter in human subjects may provide additional information regarding effects on whole body BMD results. Furthermore, effects of different gauges or types of metal were not examined in this study and may have different effects on BMD results. Therefore, future studies are warranted to continue the investigation of effects of body jewelry on BMD and the possibility of corrections or

modifications to DXA software which may correct for errors in BMD measures resulting from body jewelry.

APPENDIX

APPENDIX A

"DXA Reliability study"

Informed Consent Form

VIRGINIA POLYTECHNIC INSTITUTE AND STATE UNIVERSITY
Informed Consent for Participants of Investigative Projects

Title of Project: Validity and Reliability of Dual Energy X-ray Absorptiometry in Determining Body Composition Components – RELIABILITY STUDY

Investigator: Sharon M. (Shelly) Nickols-Richardson, Ph.D., R.D., L.D.

I. Purpose: The purpose of this research project is to determine the reliability of the QDR 4500A Dual Energy X-ray Absorptiometer (DXA) in determining bone mineral density and body composition. I understand that I may voluntarily participate in this study regardless of my body shape or size. When participating in this study, I will have a total of two whole body, two lumbar spine, two total proximal femur, and two radius DXA scans performed. I understand that a group of 20 adult males and females (aged 18 years and older) will participate in this study.

II. Procedures: For this research project, I will complete the following in sequence:

Test Session 1:

(1) arrive in Room 229, Wallace Hall on the Virginia Tech campus at my scheduled appointment day/time;
(2) sign the consent form (10 minutes); NOTE: **If I am pregnant or think that I may be pregnant, I should not undergo DXA scans.**
(3) lie on the DXA table as directed by an investigator for positioning (1 minute) for the whole body DXA scan (3 minutes; to determine lean body mass, body fat mass, bone mineral density, and percent body fat of the whole body);
(4) lie on the DXA table as directed by an investigator for positioning (1 minute) for the lumbar spine DXA scan (10 seconds; to determine bone mineral density of the lumbar spine);
(5) lie on the DXA table as directed by an investigator for positioning (1 minute) for the total proximal femur DXA scan (10 seconds; to determine bone mineral density of the femur);
(6) sit next to the DXA table as directed by an investigator for positioning (1 minute) for the radius DXA scan (30 seconds; to determine bone mineral density of the radius).

Test Session 2: (5 to 7 days after Test Session 1)
Repeat 1, 3, 4, 5 and 6 as in Test Session 1.

I understand that I should wear comfortable clothes (preferably shorts and a T-shirt) that do not contain metal (such as a metal zipper) during the DXA scan. I also understand that I should not wear any jewelry (with the exception of a wedding ring) including body piercing as this metal will interfere with the accuracy of my DXA scan. I will be asked to remove all metal from my body prior to the DXA scan if I arrive with any jewelry or metals on my body or clothes. A pair of shorts and a T-shirt will be available for use if I do not wear appropriate clothing. I understand that I may require more or less time than estimated to complete each procedure. I further understand that I will be given ample opportunity to complete all procedures in an unhurried manner.

III. Risks: I understand that exposure to radiation will occur during my DXA scan. The total amount of exposure of 20 mR during Test Session 1 and 20 mR during Test Session 2 for a total of 40 mR. This represents 4.0% of the estimated exposure expected to increase cancer risk in only 0.03% of the population. I understand that this dose is very small, as radiation doses from dental bite-wing film are 334 mR, environmental background is 4 mR per week and chest x-ray films are 40 mR for 2 standards

films. Thus, exposure is slight. I have been informed of this risk and may choose to not complete this DXA scans. If in the event that any scan is unreadable or unusable, a replacement scan will not be conducted to avoid further exposure. **I further understand that if I am pregnant or think that I may be pregnant that I should not undergo a DXA scan.** My DXA scan will be conducted in the BONE Laboratory, Room 229 Wallace Hall, on the Virginia Tech campus by the Principal Investigator or a Research Assistant who both hold Certification for Limited Licensure in Radiography from the Commonwealth of Virginia.

IV. Benefits of this Project: It is likely that I will benefit from participation in this research by having body composition components of lean body mass, body fat mass, bone mineral density, and percent body fat measured. I will be provided with my individual results from every procedure. I will be referred to an appropriate health care professional, if necessary, based on my individual results. Any and all costs related to such referral will be borne by me and not by Virginia Tech. My individual results will be provided to my Primary Care Physician (PCP) if I so request in writing and by initiating and completing a release of information form from my Primary Care Physician's office. The general public will benefit from my participation in this research as the reliability of the QDR 4500A DXA housed in the BONE Laboratory will established and utilized in all future studies related to body composition and bone mineral density conducted by the Principal Investigator. I understand that my participation in this research study is voluntary. I have not been promised or guaranteed benefits to encourage my participation in this study. I further understand that there is no promise that I will benefit from this research project.

V. Extension of Anonymity and Confidentiality: Due to the inability to assure anonymity, I understand that confidentiality of my results will be preserved. I understand that this means that all of my DXA scan results will be kept confidential. A three-digit code number will be assigned to me. I understand that a master list of participants' code numbers will be kept in a locked filing cabinet separate from completed data that will also be maintained in a locked filing cabinet. I further understand that only the investigator of this study or students of this investigator will be allowed access to any data. However, if I so choose, my individual results will be provided to my Primary Care Physician if I so request in writing by initiating and completing a release of information form from my Primary Care Physician's office. My individual results released results released to my Primary Care Physician will be identified by my name and not by my code number.

VI. Compensation: I will not be compensated or paid to be in this research project. However, I will receive my individual results from each procedure that I complete.

VII. Freedom to Withdraw: I understand that I can withdraw from this study at any time without penalty. I am free to not participate in any procedure included in this study without penalty. I understand that there may be circumstances under which the investigator may determine that I should not continue to participate in this project.

VIII. Approval of Research: This research project has been approved, as required, by the Institutional Review Board for Research Involving Human Subjects at Virginia Polytechnic Institute and State University and by the Department of Human Nutrition, Foods and Exercise.

IX. Subject's Responsibilities: I voluntarily agree to participate in this study which will involve the following responsibilities during Test Session 1 and 2: arrive in Room 229, Wallace Hall at my scheduled appointment date and time; read and sign this consent form (in Test Session 1 only);

complete a whole body DXA scan; complete a lumbar spine DXA scan; complete a total proximal femur DXA scan; complete a radius DXA scan; wear recommended and appropriate attire; and follow all directions of the investigator as related to this project.

X. Subject's Permission: I have read and understand the Informed Consent and conditions of this project. I have had all my questions answered. I hereby acknowledge the above and give my voluntary consent for participation in this project. If I participate, I may withdraw at any time without penalty. I agree to abide by the rules of this project.

Participant's Signature	Date
Investigator's Signature	Date

Should you have any questions about this research or its conduct, you may contact:

Sharon M. (Shelly) Nickols-Richardson, PhD, RD, Principal Investigator: (540) 231-5104
OR
H. T. Hurd, Chair, IRB, Research Division: (540) 231-5281

APPENDIX B

"DXA Reliability study"

Health Screening Questionnaire

Health Screening Questionnaire

Participant Code # _____

1. Date of Birth _____(mo)_____(day)_____(yr) 2. Age _____(yrs)

3. Height (cm)_____ 4. Weight (kg) _____ 5. BMI _____
#3 and #4 measured by investigator, NOT self-reported #5 calculated by investigator

6. Are you: MALE or FEMALE (Circle one) (If male, skip to question #8)

7. If female, please answer the following:
   a. When was the first day of your last menstrual cycle? _____(mo)_____(day)_____(yr)
   b. Are you pregnant or is there any possibility that you may be pregnant? YES NO
      - **If yes or unsure, provide card with Women's Clinic phone number and address and instruct participant to immediately contact the Women's Clinic or her Primary Care Physician for pregnancy testing and care. If yes or unsure, suspend research protocol.**
   c. Are you lactating? YES NO
   d. Are you taking an oral contraceptive? YES NO
      i. If yes, what type?_____
   e. Are you receiving estrogen replacement therapy or do you use hormone replacement therapy? YES NO
      i. If yes, what type?_____
   f. At what age did you begin your menstrual cycles? _____(age in yrs)
   g. Are you currently having regular menstrual cycles (i.e., at least 11 cycles over the last 12 months)? YES NO
      i. If **no** to question 14:
         a. Has a physician confirmed that you have gone through menopause? YES NO
         b. If no, do you believe that you have begun the menopause? YES NO
         c. When was your last regular, monthly menstrual cycle? _____(mo)_____(yr)
      ii. If **yes** to question 14:
         a. Do you menstruate:
            i. 12-14 times per year
            ii. 9-11 times per year
            iii. 6-8 times per year
            iv. 3-5 times per year
            v. <3 times per year
         b. Has a physician indicated that you have signs of menopause? YES NO
         c. Do you believe that you have begun the menopause? YES NO

8. Do you currently take any medications? YES NO
   a. If yes, please list name and amounts:_____
   _____
   _____

9. Please list any known medical condition:_____
   _____
   _____

10. Do you have a family history of osteoporosis? YES NO

11. Have you broken any bones? YES NO
    a. If yes, please list:_____

12. Are you taking a calcium supplement or other supplements or do you use any alternative therapies? YES NO
    a. If yes, please list brand name, amount, and number of pills: _____

APPENDIX C

"DXA Validity study"

Informed Consent Form

VIRGINIA POLYTECHNIC INSTITUTE AND STATE UNIVERSITY
Informed Consent for Participants of Investigative Projects

Title of Project: Validity and Reliability of Dual Energy X-ray Absorptiometry in Determining Body Composition Components – VALIDATION STUDY

Investigator: Sharon M. (Shelly) Nickols-Richardson, Ph.D., R.D., L.D.

I. Purpose: The purpose of this research project is to determine the validity of the QDR 4500A Dual Energy X-ray Absorptiometer (DXA) against Underwater Weighing in determining lean body mass and body fat mass. I understand that I may voluntarily participate in this study regardless of my body shape or size but that I may be excluded from participation in this study if I have a disability that prohibits my ability to independently submerge in water or if I am unwilling to submerge in water. When participating in this study, I will complete a Health Screening Questionnaire, have one whole body DXA scan performed, participate in Underwater Weighing, have my height and weight measured, and provide my date of birth. I understand that a group of 30 adult males and females (aged 18 years and older) will participate in this study.

II. Procedures: You will complete the listed procedures on two separate days:

(1) arrive in Room 229, Wallace Hall on the Virginia Tech campus at your scheduled appointment day/time;
(2) sign the consent form (10 minutes);
(3) answer questions included on the Health Screening Questionnaire to determine menstrual, pregnancy, and lactation status (if I am a female) and general health status regardless of gender (5 minutes);
NOTE: **If I am pregnant or think that I may be pregnant, I should not undergo DXA scans.**
(4) have my height and weight measured by an investigator and provide my date of birth (5 minutes; for the DXA database);
(5) lie on the DXA table as directed by an investigator for positioning (1 minute) for the whole body DXA scan (3 minutes; to determine lean body mass, body fat mass, bone mineral density, and percent body fat of the whole body);
(6) be escorted, by an investigator, to the Exercise Performance Laboratory in War Memorial, Room 230 (5 minutes);
(7) complete Underwater Weighing by sitting in a suspended chair in water, going under water to be immersed in water, blowing out as much air from my lungs as possible while under water, and remaining still for two seconds while by body weight is measured (repeat 8 times; 20 to 30 minutes; to determine lean body mass and body fat mass) and breathe five times into a rubber bag filled with oxygen while seated outside the water tank (10 minutes).

I understand that I should wear comfortable clothes (preferably shorts and a T-shirt) that do not contain metal such as a metal zipper) during the DXA scan. I also understand that I should not wear any jewelry (with the exception of a wedding ring) including body piercing as this metal will interfere with the accuracy of my DXA scan. I will be asked to remove all metal from my body prior to the DXA scan if I arrive with any jewelry or metals on my body or clothes. A pair of shorts and a T-shirt will be available for use if I do not wear appropriate clothing. During Underwater Weighing, I understand that I should wear my own swimming suit. If I do not have appropriate attire for Underwater Weighing, I will

be rescheduled and complete Underwater Weighing at another time. I understand that I may require more or less time than estimated to complete each procedure. I further understand that I will be given ample opportunity to complete all procedures in an unhurried manner.

III. **Risks:** I understand that there are two potential risks from my participation in this study. Exposure to radiation will occur during by DXA scan. The total amount of exposure of 1 mR. This represents 0.1% of the estimated exposure expected to increase cancer risk in only 0.03% of the population. I understand that this dose is very small, as radiation doses from dental bite-wing film are 334 mR, environmental background is 4 mR per week and chest x-ray films are 40 mR for 2 standards films. Thus, exposure is slight. I have been informed of this risk and may choose to not complete this DXA scan. If in the event that any scan is unreadable or unusable, a replacement scan will not be conducted to avoid further exposure. **I further understand that if I am pregnant or think that I may be pregnant that I should not undergo a DXA scan.** My DXA scan will be conducted in the BONE Laboratory, Room 229 Wallace Hall, on the Virginia Tech campus by the Principal Investigator or a Research Assistant who both hold Certification for Limited Licensure in Radiography from the Commonwealth of Virginia. Anxiety may occur prior to the Underwater Weighing procedure. I understand that a Research Assistant will fully explain this procedure to me before my first of eight trials. I will also have privacy during Underwater Weighing and during changing into and out of my swimming suit. I may choose to not complete Underwater Weighing if desired.

IV. **Benefits of this Project:** It is likely that I will benefit from participation in this research by having body composition components of lean body mass, body fat mass, bone mineral density, and percent body fat measured. I will be provided with my individual results from every procedure. I will be referred to an appropriate health care professional, if necessary, based on my individual results. Any and all costs related to such referral will be borne by me and not by Virginia Tech. My individual results will be provided to my Primary Care Physician (PCP) if I so request in writing and by initiating and completing a release of information form from your Primary Care Physician's office. The general public will benefit from my participation in this research as the validity of the QDR 4500A DXA housed in the BONE Laboratory will established and utilized in all future studies related to body composition and bone mineral density conducted by the Principal Investigator. I understand that my participation in this research study is voluntary. I have not been promised or guaranteed benefits to encourage my participation in this study. I further understand that there is no promise that I will benefit from this research project.

V. **Extension of Anonymity and Confidentialty:** Due to the inability to assure anonymity, I understand that confidentiality of my results will be preserved. I understand that this means that all of my data, including height, weight, date of birth, DXA scan and Underwater Weighing results, will be kept confidential. A three-digit code number will be assigned to me. All data recording sheets will be identified by code number only and not by my name. I understand that a master list of participants' code numbers will be kept in a locked filing cabinet separate from completed data that will also be maintained in a locked filing cabinet. I further understand that only the investigator of this study or students of this investigator will be allowed access to any data. However, if I so choose, my individual results will be provided to my Primary Care Physician if I so request in writing by initiating and completing a release of information form from my Primary Care Physician's office. My individual results released results released to my PCP will be identified by my name and not by my code number.

VI. Compensation: I will not be compensated or paid to be in this research project. However, I will receive my individual results from each procedure that I complete.

VII. Freedom to Withdraw: I understand that I can withdraw from this study at any time without penalty. I am free to not participate in any procedure included in this study without penalty. I understand that there may be circumstances under which the investigator may determine that I should not continue to participate in this project.

VIII. Approval of Research: This research project has been approved, as required, by the Institutional Review Board for Research Involving Human Subjects at Virginia Polytechnic Institute and State University and by the Department of Human Nutrition, Foods and Exercise.

IX. Subject's Responsibilities: I voluntarily agree to participate in this study which will involve the following activities: arrive in Room 229, Wallace Hall at my scheduled appointment date and time; read and sign this consent form; truthfully answer questions for the "Health Screening Questionnaire;" have body weight and height measured; complete a whole body DXA scan; be escorted to War Memorial; complete Underwater Weighing; wear recommended and appropriate attire; and follow all directions of the investigator as related to this project.

X. Subject's Permission: I have read and understand the Informed Consent and conditions of this project. I have had all my questions answered. I hereby acknowledge the above and give my voluntary consent for participation in this project. If I participate, I may withdraw at any time without penalty. I agree to abide by the rules of this project.

_____

Participant's Signature Date

_____

Investigator's Signature Date

Should you have any questions about this research or its conduct, you may contact:

Sharon M. (Shelly) Nickols-Richardson, PhD, RD, Principal Investigator: (540) 231-5104
OR
H. T. Hurd, Chair, IRB, Research Division: (540) 231-5281

APPENDIX D

"DXA Validity study"

BIA Informed Consent Form, Instructions for testing, Data Sheet

VIRGINIA POLYTECHNIC INSTITUTE AND STATE UNIVERSITY
Informed Consent Form

Project Title: Body Composition Assessment of Adults by the Bioelectrical Impedance Analysis Method
Investigator: Carrie P. Earthman, Ph.D., R.D.

I. The Purpose of this Project

The two primary aims of this project are: 1) to assess body composition in individuals across the spectrum of age, gender, ethnicity, and health using the non-invasive bioelectrical impedance analysis (BIA) method and 2) to compare three BIA devices (two single-frequency and one multi-frequency BIA devices) for inter-method agreement. Approximately 800 individuals will participate. If I have a pacemaker or other internally placed electrical medical device, I must not participate in this study.

II. Procedures

If I agree to participate in this study, I will be asked to complete the following:

1. Have my weight and height measured (5 minutes).
2. Have by body composition evaluated by three different bioelectrical impedance analysis devices over a 10 minute. period. Measurements will be taken by three different devices consecutively. I will remove my right sock and shoe, all jewelry and any metal objects on my person, then I will have my hand and foot gently cleaned with an alcohol pad, after which four small wires will be attached to my hand and foot by a sticky pad called an electrode. A small, undetectable electrical signal will be sent through these wires through my body by the bioelectrical impedance analyzer. The resistance of my body to this signal will provide an estimate of my body water, lean mass, and percent body fat. The measurement by each device will last less than 10 seconds in duration, and measurement by all three devices will take approximately 5-10 minutes.
3. Answer brief questions regarding my medical history and current health (5 minutes).
4. Meet the standard protocol conditions for body composition testing, including:
    a. Avoiding exercise 8 hours before testing.
    b. Avoiding alcohol 24 hours before and no caffeine consumption 12 hours before testing.
    c. Avoiding food intake 2-4 hours before testing.
    c. Urinating within 30 minutes of testing.
    e. Avoiding excessive fluid intake within 30 minutes of testing, but being sure to be adequately hydrated during the 12 hours before testing.
    f. Informing the technician if I feel I am retaining fluid as a result of menstruation (if I am a female subject).

III. Risks

There are no risks foreseen with participation in this study. The small bioelectrical signal I will be exposed to during bioelectrical impedance analysis measurements is minimal and there is no known risk associated with it.

IV. Benefits of this Project

I have not been promised or guaranteed benefits to encourage my participation in this study. While direct benefits to me cannot be guaranteed, I understand that I will be informed of the results from the measurement of my body composition.

V. Extent of Anonymity and Confidentiality

All information concerning my participation and any results of the various tests done in the study will be kept strictly confidential. I will be assigned a code number which will be recorded on the consent form, as well as any data collection forms used for the study. I understand that my Consent Form and a master list of participants' names and code numbers will be kept in a locked filing cabinet separate from my data which will also be stored

in a locked filing cabinet. Only investigators involved in this study or students of the investigators will be allowed access to the data collected in this study. Should results of this study be reported or published, no individual subjects' names will be used. All data will be filed according to the number identification coding system.

VI. Compensation

I will not be paid or compensated in any way for participating in this study.

VII. Freedom to Withdraw

I am free to withdraw from participation in this study without penalty at any time by simply telling the technician or principal investigator, or by contacting the Chair of the Virginia Tech IRB (listed below).

VIII. Approval of Research

This research project has been approved, as required, by the Institutional Review Board for Research Involving Human Subjects at Virginia Tech, and by the Department of Human Nutrition, Foods and Exercise.

IX. Subject's Responsibilities

I voluntarily agree to participate in this study. I have the following responsibilities:

1. Report for testing having meet the standard protocol conditions, as outlined under Procedures.
2. Remove my right sock and shoe, jewelry, and metal objects from my person; and then, lie down on a padded table to have my body composition evaluated by bioelectrical impedance analysis.
3. Answer brief questions regarding my medical history and current health, including questions about any medications I might be taking, any health problems I currently have, and general health habits.
4. Have my body weight and height measured.

X. Subject's Permission

I have read and I understand the Informed Consent and conditions of this project. I have had all my questions answered. I hereby acknowledge the above and give my voluntary consent for participation in this project.

If I participate, I may withdraw at any time without penalty. I agree to abide by the rules of this project.

Printed Name of Participant	Signature of Participant	Date
Identification Number (will be assigned)	Signature of Investigator	Date

Should I have any questions about this research or its conduct, I may contact any of the following individuals:

Carrie P. Earthman, Ph.D., R.D. Phone: 231-7421
Principle Investigator

David Moore, Ph.D. Phone: 231-4991
Chair, Institutional Review Board
Office of Research Compliance
Research & Graduate Studies

Instructions for Subjects to Follow Before Reporting to the BCM Laboratory (229 Wallace Hall) for Testing

You are scheduled to come to the BCM Laboratory (229 Wallace Hall) on

_____ at _____ AM/PM

On _____ (the day before you come to the BCM Laboratory)

- No exercise 8 hours before testing.
- No alcohol 24 hours before and no caffeine or nicotine consumption 12 hours before testing.
- No food intake 2-4 hours before testing.
- Urinate within 30 minutes of testing.
- Avoid excessive fluid intake within 30 minutes of testing, but be sure to be adequately hydrated during the 12 hours before testing (i.e., urine should be pale in color).
- Please do not take any medications 12 hours before testing (i.e. caffeine-containing medications).
- Please do not apply any lotions, oils, or creams to the skin.

On _____ (the day you come to the BCM Laboratory)

- Wear, light-weight, comfortable clothing with no buttons zippers, or other metal/hard plastic. (For ex. Wearing sweat pants, t-shirt, and sweat shirt would be a good choice).
- You will be asked to remove all jewelry, coins, keys, etc. from your person for testing.

What to expect while you're in the BCM Laboratory:

1. You will be requested to go to the restroom to void urine upon arrival to the lab.
2. Your height and weight will be measured.
3. You can expect to be in the BCM Laboratory for approximately 30 minutes.

BODY COMPOSITION STUDY
(BCM Laboratory)
SF-BIA – Valhalla

Initials	_____	Date:	_____
		TIME: 5 min	10 min
Subject ID #:	_____		

WEIGHT without shoes (kg) _____ _____ _____ . _____ _____

HEIGHT without shoes (cm) _____ _____ _____ . _____ _____

AGE (years) _____ _____

TRIAL 1			
RESISTANCE (ohms)	____ ____ ____	FAT MASS (kg)	____ ____ . ____
REACTANCE (ohms)	____ ____ ____	PERCENT FAT (%)	____ ____ . ____
IMPEDANCE	____ ____ ____	LEAN BODY MASS (kg)	____ ____ . ____
PHASE ANGLE	____ ____ ____	TOTAL BODY WATER (L)	____ ____ . ____
		TOTAL BODY WATER (%)	____ ____ . ____
TRIAL 2			
RESISTANCE (ohms)	____ ____ ____	FAT MASS (kg)	____ ____ . ____
REACTANCE (ohms)	____ ____ ____	PERCENT FAT (%)	____ ____ . ____
IMPEDANCE	____ ____ ____	LEAN BODY MASS (kg)	____ ____ . ____
PHASE ANGLE	____ ____ ____	TOTAL BODY WATER (L)	____ ____ . ____
		TOTAL BODY WATER (%)	____ ____ . ____
TRIAL 3			
RESISTANCE (ohms)	____ ____ ____	FAT MASS (kg)	____ ____ . ____
REACTANCE (ohms)	____ ____ ____	PERCENT FAT (%)	____ ____ . ____
IMPEDANCE	____ ____ ____	LEAN BODY MASS (kg)	____ ____ . ____
PHASE ANGLE	____ ____ ____	TOTAL BODY WATER (L)	____ ____ . ____
		TOTAL BODY WATER (%)	____ ____ . ____

APPENDIX E

"Tibial Reliability study"

Informed Consent Form

VIRGINIA POLYTECHNIC INSTITUTE AND STATE UNIVERSITY
Informed Consent for Participants of Investigative Projects

Title of Project: Reliability of Dual Energy X-Ray Absorptiometry in Measuring Tibial Bone Mineral Density

Investigator: Sharon M. (Shelly) Nickols-Richardson, PhD, RD

I. Purpose: The purpose of this research project is to test the reliability of the Hologic QDR 4500A Dual Energy X-ray Absorptiometer in measuring bone mineral density of the distal tibia, a bone that is in your lower leg. The tibia is also known as the "shin bone" and is the bone that runs down the front of your lower leg. The Dual Energy X-ray Absorptiometer is a piece of equipment that uses x-ray technology to measure the amount of mineral in a specific area of bone. For this study, the amount of mineral in one of the bones of your lower leg (near the ankle) will be measured at two different times. Approximately 20 individuals (18 to 26 years of age) will participate in this short study.

II. Procedures: You will complete the listed procedures on two separate days:

(1) arrive in Room 229, Wallace Hall on the Virginia Tech campus at your scheduled appointment day/time;
(2) sign the consent form (at baseline testing only; 10 minutes);
(3) stand next to a stadiometer to have your body height measured and stand on a digital scale to have your body weight measured (5 minutes);
(4) answer questions regarding menstruation (if female) and health (5 minutes);
(5) be positioned on the Dual Energy X-ray Absorptiometer as directed by a Licensed Radiologic Technologist – Limited who will conduct one scan of your non-dominant lower leg (the leg that you would not use to kick a ball in soccer, for example) for bone mineral density testing (5 minutes);
NOTE: If you are pregnant or think that you may be pregnant, you should not undergo Dual Energy X-ray Absorptiometry scans and should withdraw from this study <u>because radiation exposure from Dual Energy X-ray Absorptiometry scans may cause harm to your unborn fetus</u>.
(6) after the baseline testing session, be scheduled to return in 3 to 5 days to complete the exact same procedures.

You understand that participation in this study will require approximately 30 minutes of your time at each testing session. You also understand that you may require more or less time than estimated to complete each procedure and that you will be given ample opportunity to complete all procedures in an unhurried manner.

III. Risks: You understand that exposure to radiation will occur during Dual Energy X-ray Absorptiometry scans for measurement of your bone mineral density. Radiation exposure will occur from the Dual Energy X-ray Absorptiometry scans because the Dual Energy X-ray Absorptiometer machine uses x-ray technology. Radioation exposure is measured in milliards (or mR). Your total amount of exposure is 5 mR (non-dominant lower leg = 5 mR) during each testing time and your cumulative total exposure is 10 mR if you complete both Dual Energy X-ray Absorptiometry Scans. Because your combined total exposure for the entire study represents 0.5% of the estimated exposure expected to increase cancer risk in only 0.03% of the population, you understand that this dose is very small, and poses minimal

risk compared to radiation doses fro dental bite-wing films (334 mR) and environmental background exposure (100 to 400 mR per year) expected to occur in one 12-month period. The following table lists the radiation limits for an adult research participant according to the National Institutes of Health, Office for Protection from Research Risks (NIH-OPRR), compared to your exposure during this study.

NIH-OPRR Radiation Limits for an Adult Research Participant	**Your Exposure During Participation in this Research Study**
Lower leg (single dose) = 5,000 mR	Distal tibia (single dose) = 5 mR
Lower leg (annual cumulative dose) = 15,000 mR	Distal tibia (annual cumulative dose) = 10 mR
	ANNUAL CUMULATIVE EXPOSURE = 10 mR during 12 months

You have been informed of this risk and may choose to not complete these scans. If in the event that any scan is unreadable or unusable, a replacement scan will not be conducted to avoid further exposure. **You further understand that if you are pregnant or think that you may be pregnant that you should not undergo Dual Energy X-ray Absorptiometry scans and should withdraw from this study <u>because radiation exposure from Dual Energy X-ray Absorptiometry scans may cause harm to your unborn fetus</u>.** These Dual Energy X-ray Absorptiometry scans will be conducted in t he BONE Laboratory, Room 229 Wallace Hall, on the Virginia Tech campus by the Principal Investigator who is a Licensed Radiologic Technologist – Limited in the Commonwealth of Virginia.

IV. Benefits of this Project: You will be provided with your individual results from your Dual Energy X-ray Absorptiometry scans. You will be referred to an appropriate health care professional, if necessary, based on your individual results. Any and all costs related to such referral will be borne by you and not by Virginia Tech. Your individual results will be provided to your Primary Care Physician (PCP) if you so request in writing and by initiating and completing a release of information form from your PCP's office. The general public will benefit from your participation in this study as the reliability of the Hologic QDR 4500A Dual Energy X-ray Absorptiometer in measuring bone mineral density of the distal tibia will be established. You understand that your participation in this research study is voluntary. You have not been promised or guaranteed benefits to encourage your participation in this study. You further understand that there is no promise that you will benefit from this research project.

V. Extent of Anonymity and Confidentiality: Due to the inability to assure anonymity, you understand that confidentiality of your results will be preserved. You understand that this means that all of your data will be kept confidential. A three-digit code number will be assigned to you. All data recording sheets will be identified by code number only and not by your name. You understand that a master list of participants' code numbers will be kept in a locked filing cabinet separate from completed data that will also be maintained in a locked filing cabinet. You further understand that only the investigator of this study or students of this investigator will be allowed access to any data. However, if you so choose, your individual results will be provided to you PCP if you so request in writing by initiating and completing a release of information form from your PCP's office. Your individual results released results released to your PCP will be identified by your name and not by your code number.

VI. Compensation: You will not be compensated or paid to be in this research project. However, you will receive your individual results from each Dual Energy X-ray Absorptiometry scan that you complete.

VII. Freedom to Withdraw: You understand that you can withdraw from this study at any time without penalty. You are free to not participate in any procedure included in this study without penalty. You understand that there may be circumstances under which the investigator may determine that you should not continue to participate in this project.

VII. Review of Protocols Involving Human Subjects: This research protocol has been reviewed, as required, by the Institutional Review Board for Research Involving Human Subjects, by the Department of Human Nutrition, Foods and Exercise, and by the Radiation Safety Committee at Virginia Polytechnic Institute and State University for compliance with federal guidelines related to the safety and protection of human subjects, and has found it to be in compliance. However, while the Institutional Review Board has indicated that the procedures are in compliance with federal requirements, it is still necessary for you to decide for yourself whether you are willing to assume risk(s) associated with participation in the study.

IX. Subject's Responsibilities: You voluntarily agree to participate in this study which will involve the following activities:

- arrive in Room 229, Wallace Hall at your scheduled appointment dates and times;
- read and sign the consent form;
- have your body height and weight measured;
- answer questions regarding menstruation (if female) and medical status;
- complete Dual Energy X-ray Absorptiometry scans for bone mineral density testing.

You will truthfully answer all questions of the investigator including questions regarding your pregnancy status (if female). During the study, you will follow all directions of the investigator as related to this project.

X. Subject's Permission: You have read and understand the Informed Consent and conditions of this project. You have had all your questions answered. You hereby acknowledge the above and give your voluntary consent for participation in this project. If you participate, you may withdraw at any time without penalty. You agree to abide by the rules of this project.

_____

Participant's Signature Date

_____

Investigator's Signature Date

Should you have any questions about this research or its conduct, you may contact:

Sharon M. (Shelly) Nickols-Richardson, PhD, RD, Co-Investigator: (540) 231-5104
OR
David M. Moore, PhD, IRB Chair, Assistant Vice Provost for Research Compliance: (540) 231-4991

APPENDIX F

"Tibial Reliability study"

Medical History Questionnaire

Medical History Form – Male Participants

Investigator: Complete this data sheet in an interview format with the participant by asking the participant the following questions.

Date of Birth:_____

Are you currently taking any medications? YES NO
If yes, please list names and dosages (if known):_____
_____

Have you previously been exposed to X-ray procedures? YES NO
If yes, please list and describe including
DATE OF LAST EXPOSURE TYPE OF EXPOSURE NUMBER OF EXPOSURES
_____
_____
_____
_____

Have you had surgery or medical treatment involving any of the following? Check any that apply and list date(s).

[ ] tonsils_____
[ ] nose_____
[ ] thyroid_____
[ ] lungs_____
[ ] heart_____
[ ] eyes_____
[ ] ears _____
[ ] adenoids_____
[ ] wisdom teeth_____
[ ] other dental_____
[ ] gastrointestinal tract_____
[ ] reproductive organs_____
[ ] other _____(describe) _____

*These medical/surgical procedures may have included exposure to X-rays and are being listed to assess your prior exposure to radiation.

Have you ever broken your tibia or shin bone? YES NO
If yes, when: _____

Investigator: Measure the following and/or record and/or calculate the following information.

Age: _____(years)_____(months)

Height: _____(cm)_____(feet)_____(inches)

Weight: _____(kg)_____(pounds)

Non-Dominant Arm/Leg: Right Left

Medical History Form – Female Participants

Investigator: Complete this data sheet in an interview format with the participant by asking the participant the following questions.

Date of Birth: _____

When was the first day of your last menstrual cycle? _____(date)_____(month)_____(year)

Are you pregnant or is there any possibility that you may be pregnant? YES NO UNSURE
Note: If "yes" or "unsure", provide card with Women's Clinic phone number and address and instruct participant to immediately contact the Women's Clinic or her Primary Care Physician for pregnancy testing and care. **If yes or unsure, suspend research protocol.**

Are you taking an oral contraceptive? YES NO
If yes, what is the brand and dosage (if known):_____
If yes, for how long have you been taking this oral contraceptive?_____

Are you currently having regular menstrual cycles (i.e., at least 11 cycles over the last 12 months)? YES NO
If no, please describe and indicate why your menstrual cycles have been rregular:_____
_____
_____

If yes, do you menstruate:
a. 12-14 times per year
b. 9-11 times per year
c. 6-8 times per year
d. 3-5 times per year
e. <3 times per year

Are you currently taking any medications? YES NO
If yes, please list names and dosages (if known): _____
_____

Have you previously been exposed to X-ray procedures? YES NO
If yes, please list and describe including
DATE OF LAST EXPOSURE TYPE OF EXPOSURE NUMBER OF EXPOSURES
_____
_____
_____
_____

Have you had surgery or medical treatment involving any of the following? Check any that apply and list date(s).

[ ] tonsils_____ [ ] adenoids_____
[ ] nose_____ [ ] wisdom teeth_____
[ ] thyroid_____ [ ] other dental_____
[ ] lungs_____ [ ] gastrointestinal tract_____
[ ] heart_____ [ ] reproductive organs_____
[ ] eyes_____ [ ] other_____(describe) _____
[ ] ears _____

*These medical/surgical procedures may have included exposure to X-rays and are being listed to assess your prior exposure to radiation.

Have you ever broken your tibia or shin bone? YES NO
If yes, when: _____

Investigator: Measure the following and/or record and/or calculate the following information.

Age: _____(years)_____(months)

Height: _____(cm)_____(feet)_____(inches)

Weight: _____(kg)_____(pounds)

Non-Dominant Arm/Leg: Right Left

APPENDIX G

Data Sets

Final Data for DXA Study

Subject	Group	Gender	Age	Height	Weight	BMI
7701	NC	FEMALE	23	64	126	21.69
7702	C	FEMALE	21	69	146	21.62
7703	NC	FEMALE	21	61	134	25.39
7704	NC	MALE	23	75	256	32.09
7705	NC	FEMALE	22	63	116	20.61
7706	C	MALE	22	73	157	20.77
7707	NC	FEMALE	23	65	131	21.86
7708	NC	MALE	24	74	193	24.85
7709	NC	FEMALE	21	62	125	22.93
7710	C	MALE	22	72	171	23.26
7711	C	MALE	25	67	162	25.44
7712	NC	MALE	23	70	150	21.58
7713	NC	FEMALE	22	65	162	27.03
7714	NC	MALE	23	70	143	20.57
7715	NC	FEMALE	26	66	138	22.34
7716	NC	FEMALE	24	61	132	25.01
7717	C	MALE	18	75	192	24.06
7718	NC	MALE	23	71	148	20.70
7719	NC	FEMALE	23	69	151	22.36
7720	NC	MALE	23	74	253	32.57
7721	C	MALE	19	70	137	19.71
7722	C	MALE	22	69	154	22.80
7723	NC	MALE	24	69	168	24.88
7724	C	MALE	27	69	143	21.18

Whole Body			Lumbar Spine		TPF		TF	
first	second	avg BMD	first	second	first	second	first	second
1.153	1.137	1.145	1.080	1.079	0.958	0.978	0.539	0.551
1.162	1.163	1.163	1.017	1.025	0.922	0.912	0.571	0.571
1.129	1.141	1.135	1.172	1.181	1.025	1.034	0.617	0.606
1.433	1.455	1.444	1.451	1.482	1.264	1.264	0.782	0.800
1.069	1.066	1.068	0.850	0.838	0.868	0.885	0.554	0.553
1.252	1.248	1.250	1.172	1.135	1.068	1.067	0.670	0.645
1.337	1.327	1.332	1.167	1.171	1.145	1.148	0.651	0.644
1.247	1.255	1.251	1.071	1.067	1.023	1.033	0.729	0.722
1.010	1.013	1.012	0.905	0.908	0.816	0.770	0.527	0.532
1.208	1.220	1.214	0.987	1.001	1.060	1.080	0.685	0.691
1.281	1.270	1.276	1.066	1.069	1.088	1.097	0.617	0.612
1.206	1.208	1.207	1.197	1.199	1.045	1.043	0.677	0.684
1.179	1.207	1.193	1.033	1.049	1.096	1.095	0.586	0.584
1.132	1.139	1.136	0.880	0.889	1.049	1.049	0.522	0.525
1.193	1.200	1.197	1.108	1.118	1.012	1.020	0.508	0.517
1.099	1.087	1.093	0.901	0.896	0.972	0.974	0.526	0.532
1.258	1.234	1.246	0.955	0.951	1.160	1.150	0.603	0.601
1.321	1.327	1.324	1.317	1.334	1.131	1.126	0.637	0.647
1.125	1.122	1.124	1.057	1.065	0.961	0.965	0.589	0.592
1.369	1.391	1.380	1.200	1.183	1.281	1.300	0.789	0.786
1.184	1.194	1.189	0.889	0.895	0.890	0.903	0.662	0.651
1.078	1.079	1.079	0.928	0.918	0.960	0.963	0.586	0.570
1.278	1.265	1.272	1.031	1.031	1.067	1.074	0.719	0.727
1.213	1.213	1.213	0.940	0.919	0.814	0.805	0.570	0.579

DT		%bodyfat				
first	second	first	second	avg.bf	BIA	avDXABIA
1.056	1.049	26.30	25.80	26.05	22.90	25.00
0.932	0.964	26.40	27.10	26.75	26.80	26.77
1.039	0.850	30.10	29.40	29.75	30.00	29.83
1.180	1.190	22.80	22.30	22.55	21.80	22.30
1.054	1.062	23.50	24.00	23.75	22.60	23.37
1.166	1.129	10.90	11.00	10.95	8.70	10.20
1.131	1.136	18.00	17.50	17.75	18.50	18.00
1.161	1.012	16.90	16.70	16.80	14.80	16.10
0.893	0.888	31.20	31.70	31.45	25.80	29.57
1.261	1.111	12.90	12.90	12.90	16.60	14.13
1.082	1.086	13.30	13.60	13.45	13.60	13.50
1.310	1.217	11.20	11.10	11.15	13.50	11.93
1.146	1.158	28.30	28.20	28.25	26.70	27.73
0.969	1.019	10.70	11.20	10.95	17.00	12.97
1.034	1.046	25.90	26.50	26.20	23.10	25.17
1.052	1.058	24.90	26.10	25.50	25.00	25.33
1.036	1.080	14.70	14.30	14.50	16.30	15.10
1.219	1.111	12.60	12.40	12.50	12.20	12.40
1.098	1.112	31.80	31.50	31.65	28.50	30.60
1.238	1.210	14.70	14.50	14.60	19.50	16.23
1.057	1.074	10.70	10.20	10.45	10.00	10.30
1.095	1.122	17.00	16.80	16.90	16.60	16.80
1.345	1.252	10.90	10.20	10.55	14.10	11.73
.	.	13.30	13.50	13.40	12.50	13.10

LBM		FM	
first	second	first	second
40.54	41.09	15.262	15.087
46.95	46.01	17.709	18.039
41.19	41.95	18.652	18.324
87.86	86.79	26.995	26.016
39.14	38.91	12.602	12.868
61.70	61.66	7.933	7.999
46.58	47.68	10.872	10.712
70.57	69.82	14.956	14.639
37.50	36.99	17.839	18.013
65.29	66.07	10.129	10.208
61.98	61.77	9.931	10.152
58.53	57.54	7.749	7.493
51.18	51.15	21.153	21.061
56.48	54.85	7.058	7.229
44.94	44.84	16.527	16.986
43.99	42.53	15.211	15.698
72.54	73.16	13.129	12.736
56.81	55.77	8.599	8.319
45.04	45.87	22.136	22.194
95.53	95.56	17.029	16.825
53.50	54.03	6.735	6.428
56.12	57.10	11.953	11.986
66.01	66.09	8.385	7.851
54.24	52.64	8.681	8.592

Key 1. Units of Measure

Variable	Units
Height	Inches
Weight	Pounds
BMD	g/cm^2

Key 2. Abbreviations

Abbreviation	Meaning
NC	Non-cyclist
C	Cyclist
BMI	Body Mass Index
TPF	Total proximal femur
TF	Total forearm
DT	Distal tibia
BIA	Bioelectrical impedance analysis
avDXABIA	Average of DXA&BIA
LBM	Lean body mass
FM	Fat mass

APPENDIX H

Statistics

ANOVA Data for 3 Subgroups

ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
AGE	Between Groups	4.594	2	2.297	.575	.572
	Within Groups	79.841	20	3.992		
	Total	84.435	22			
HEIGHT	Between Groups	295.366	2	147.683	21.995	.000
	Within Groups	134.286	20	6.714		
	Total	429.652	22			
WEIGHT	Between Groups	11186.075	2	5593.037	6.454	.007
	Within Groups	17333.143	20	866.657		
	Total	28519.217	22			
BMI	Between Groups	30.896	2	15.448	1.430	.263
	Within Groups	215.981	20	10.799		
	Total	246.877	22			
WBBMD1	Between Groups	7.726E-02	2	3.863E-02	4.960	.018
	Within Groups	.156	20	7.788E-03		
	Total	.233	22			
WBBMD2	Between Groups	8.507E-02	2	4.253E-02	5.287	.014
	Within Groups	.161	20	8.045E-03		
	Total	.246	22			
LSBMD1	Between Groups	.117	2	5.836E-02	3.034	.071
	Within Groups	.385	20	1.924E-02		
	Total	.501	22			
LSBMD2	Between Groups	.130	2	6.509E-02	3.206	.062
	Within Groups	.406	20	2.030E-02		
	Total	.536	22			
TPFBMD1	Between Groups	8.363E-02	2	4.182E-02	3.439	.052
	Within Groups	.243	20	1.216E-02		
	Total	.327	22			
TPFBMD2	Between Groups	8.596E-02	2	4.298E-02	3.262	.059
	Within Groups	.264	20	1.318E-02		
	Total	.350	22			
TFBMD1	Between Groups	6.390E-02	2	3.195E-02	7.803	.003
	Within Groups	8.189E-02	20	4.095E-03		
	Total	.146	22			
TFBMD2	Between Groups	6.746E-02	2	3.373E-02	8.731	.002
	Within Groups	7.727E-02	20	3.863E-03		
	Total	.145	22			
BF1	Between Groups	916.484	2	458.242	31.085	.000
	Within Groups	294.834	20	14.742		
	Total	1211.318	22			
BF2	Between Groups	946.089	2	473.044	32.770	.000
	Within Groups	288.708	20	14.435		
	Total	1234.797	22			
BIA	Between Groups	571.321	2	285.660	24.596	.000
	Within Groups	232.277	20	11.614		
	Total	803.598	22			
LBM1	Between Groups	3006.886	2	1503.443	15.864	.000
	Within Groups	1895.464	20	94.773		
	Total	4902.350	22			
LBM2	Between Groups	2850.528	2	1425.264	14.251	.000
	Within Groups	2000.188	20	100.009		
	Total	4850.715	22			
FTMASS1	Between Groups	190.440	2	95.220	4.149	.031
	Within Groups	458.999	20	22.950		
	Total	649.439	22			
FTMASS2	Between Groups	199.786	2	99.893	4.661	.022
	Within Groups	428.671	20	21.434		
	Total	628.457	22			

APPENDIX I

Navel Jewelry Data

Group	scan #	BMD
Normal	1	0.989
Normal	2	0.995
Normal	3	0.997
Normal	4	0.993
Normal	5	0.991
Normal	6	0.998
Normal	7	0.996
normal	8	0.993
normal	9	1.004
normal	10	1.003
normal	11	0.995
ring 1	1	1.038
ring 1	2	1.04
ring 1	3	1.04
ring 1	4	1.039
ring 1	5	1.041
ring 1	6	1.046
ring 1	7	1.042
ring 1	8	1.039
ring 1	9	1.037
ring 1	10	1.037
ring 1	11	1.032
cor.rg* 1	1	1.001
cor.rg 1	2	1.008
cor.rg 1	3	1.007
cor.rg 1	4	1.008
cor.rg 1	5	1.006
cor.rg 1	6	1.011
cor.rg 1	7	1.007
cor.rg 1	8	1.006
cor.rg 1	9	1.006
cor.rg 1	10	1.007
cor.rg 1	11	1
ring 2	1	1.034
ring 2	2	1.035
ring 2	3	1.041
ring 2	4	1.036
ring 2	5	1.039
ring 2	6	1.036
ring 2	7	1.031
ring 2	8	1.04
ring 2	9	1.036
ring 2	10	1.039

ring 2	11	1.037
cor.rg** 2	1	0.995
cor.rg 2	2	1.002
cor.rg 2	3	1.008
cor.rg 2	4	0.997
cor.rg 2	5	1.003
cor.rg 2	6	1.001
cor.rg 2	7	1
cor.rg 2	8	1.006
cor.rg 2	9	1
cor.rg 2	10	1.006
cor.rg 2	11	1.002
bar 1	1	1.037
bar 1	2	1.029
bar 1	3	1.03
bar 1	4	1.031
bar 1	5	1.03
bar 1	6	1.029
bar 1	7	1.03
bar 1	8	1.027
bar 1	9	1.026
bar 1	10	1.026
bar 1	11	1.032
cor.bar† 1	1	1.01
cor.bar 1	2	1.008
cor.bar 1	3	0.999
cor.bar 1	4	0.999
cor.bar 1	5	1.002
cor.bar 1	6	0.997
cor.bar 1	7	1.003
cor.bar 1	8	1.001
cor.bar 1	9	1.007
cor.bar 1	10	0.999
cor.bar 1	11	1.002
bar 2	1	1.03
bar 2	2	1.029
bar 2	3	1.031
bar 2	4	1.033
bar 2	5	1.028
bar 2	6	1.028
bar 2	7	1.026
bar 2	8	1.026
bar 2	9	1.028
bar 2	10	1.017
bar 2	11	1.032
cor.bar‡ 2	1	0.999
cor.bar 2	2	1
cor.bar 2	3	0.997
cor.bar 2	4	1.005

cor.bar 2	5	0.999
cor.bar 2	6	1
cor.bar 2	7	0.995
cor.bar 2	8	0.996
cor.bar 2	9	0.994
cor.bar 2	10	0.99
cor.bar 2	11	1

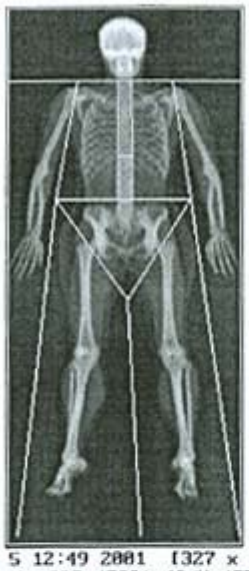
* corrected ring, L_4
** corrected ring, L_3/L_4
† corrected barbell, L_4
‡ corrected barbell, L_3/L_4

APPENDIX J

Sample DXA Scans

(Whole body, Lumbar spine, Total proximal femur, Total forearm, Distal tibia)

VPI & SU BONE LAB



A0921010E Fri Sep 21 10:23 2001
Name:
Comment: MZ study
I.D.: 7781 Sex: F
S.S.#: - - Ethnic: C
ZIP Code: Height:5' 4"
Operator: SNR Weight: 126
BirthDate: Age: 23
Physician:
Image not for diagnostic use

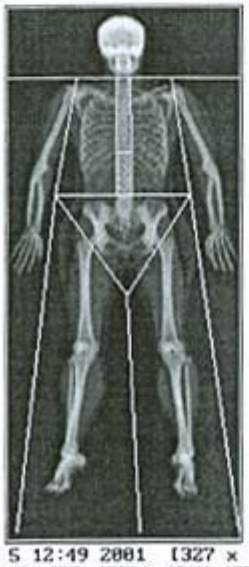
TOTAL BMC and BMD CV is < 1.0%
C.F. 1.829 1.884 1.888

Region	Area (cm2)	BMC (grams)	BMD (gms/cm2)
L Arm	182.23	131.45	0.721
R Arm	184.24	138.05	0.749
L Ribs	115.75	71.96	0.622
R Ribs	138.97	81.34	0.621
T Spine	92.92	82.17	0.884
L Spine	57.27	61.38	1.072
Pelvis	231.50	287.82	1.240
L Leg	348.45	405.38	1.163
R Leg	358.85	428.23	1.198
SubTot	1694.18	1678.97	0.991
Head	231.50	541.64	2.340
TOTAL	1925.68	2220.61	1.153

HOLOGIC

oOct 5 12:49 2001 [327 x 158]
Hologic QDR-4500A (S/N 45727)
Whole Body Fan Beam V8.26a:3*

VPI & SU BONE LAB



A0921010E Fri Sep 21 10:23 2001
Name:
Comment: MZ study
I.D.: 7781 Sex: F
S.S.#: - - Ethnic: C
ZIP Code: Height:5' 4"
Operator: SNR Weight: 126
BirthDate: Age: 23
Physician:
Image not for diagnostic use

TBAR1668 - 1
F.S. 68.88% 0(10.88)%
Head assumes 17.0% brain fat
LBM 73.2% water

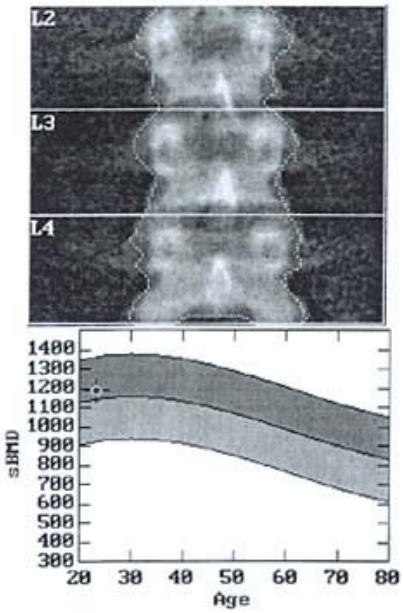
Region	Fat (grams)	Lean+BMC (grams)	% Fat (%)
L Arm	748.5	2835.5	26.7
R Arm	817.0	2862.1	28.4
Trunk	6857.9	21223.5	22.2
L Leg	3357.5	6776.1	33.1
R Leg	3386.0	6994.6	32.6
SubTot	14359.7	39891.7	26.9
Head	902.5	3668.3	19.7
TOTAL	15262.2	42759.9	26.3

HOLOGIC

oOct 5 12:49 2001 [327 x 158]
Hologic QDR-4500A (S/N 45727)
Whole Body Fan Beam V8.26a:3*

VPI & SU BONE LAB

A0921010F



A0921010F Fri Sep 21 10:28 2001
Name:
Comment: MZ study
I.D.: 7701 Sex: F
S.S.#: - - Ethnic: C
ZIP Code: Height:5' 4"
Operator: SNR Weight: 126
BirthDate: Age: 23
Physician:

Hologic QDR-4500A (S/N 45727)
Analyze Version 8.26f:3
·Dec 24 08:34 2001
sBMD CV 1.0%
Image not for diagnostic use

AP Lumbar Spine (L2-L4) Results

sBMD* (mg/cm²) = 1193
Z-Score (age matched sBMD) = 0.39

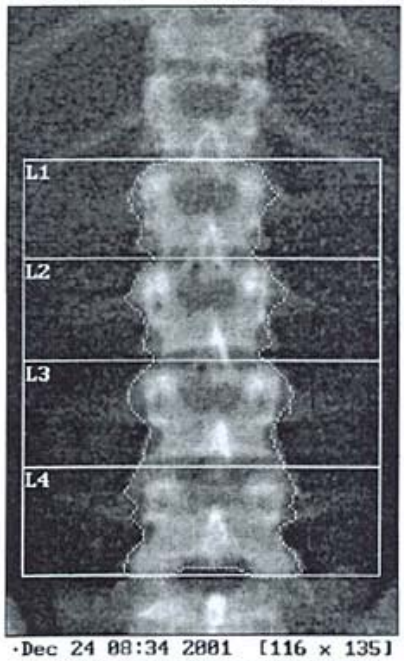
T-Score (relative to peak sBMD) = 0.27

* sBMD = Standardized Bone Mineral Density

HOLOGIC

k = 1.135 d0 = 49.7(1.000H) 5.938

BONE LAB



·Dec 24 08:34 2001 [116 x 135]
Hologic QDR-4500A (S/N 45727)
Lumbar Spine V8.26f:3

A0921010F Fri Sep 21 10:28 2001
Name:
Comment: MZ study
I.D.: 7701 Sex: F
S.S.#: - - Ethnic: C
ZIP Code: Height:5' 4"
Operator: SNR Weight: 126
BirthDate: Age: 23
Physician:
Image not for diagnostic use

TOTAL BMD CV FOR L1 - L4 1.0%

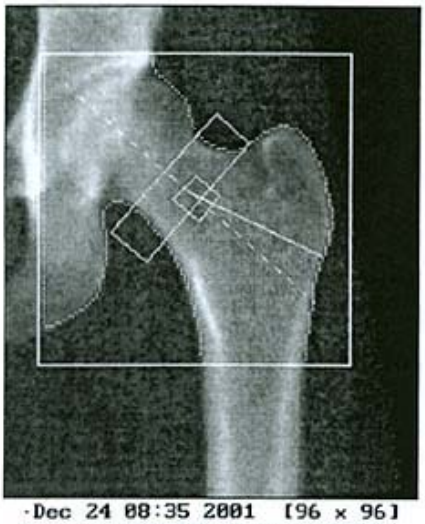
C.F. 1.029 1.004 1.000

Region	Est.Area (cm²)	Est.BMC (grams)	BMD (gms/cm²)
L1	13.12	12.79	0.976
L2	14.36	15.43	1.074
L3	15.88	18.10	1.140
L4	18.24	20.23	1.109
TOTAL	61.60	66.55	1.080

HOLOGIC

VPI & SU BONE LAB

k = 1.136 d0 = 51.6(1.000H) 5.576



·Dec 24 08:35 2001 [96 x 96]
Hologic QDR-4500A (S/N 45727)
Left Hip V8.26f:3

A0921010G Fri Sep 21 10:30 2001
Name:
Comment: MZ study
I.D.: 7701 Sex: F
S.S.#: - - Ethnic: C
ZIP Code: Height:5' 4"
Operator: SNR Weight: 126
BirthDate: Age: 23
Physician:
Image not for diagnostic use

TOTAL BMD CV 1.0%

C.F.	1.029	1.004	1.000

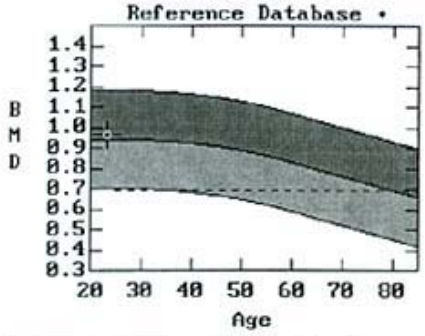
Region	Est.Area (cm^2)	Est.BMC (grams)	BMD (gms/cm^2)
Neck	4.73	4.36	0.922
Troch	10.36	7.59	0.732
Inter	16.12	17.94	1.113
TOTAL	31.21	29.89	0.958
Ward's	1.12	0.87	0.780

Midline (92,104)-(168, 38)
Neck -49 x 15 at [24, 10]
Troch 14 x 44 at [0, 0]
Ward's -11 x 11 at [6, 2]

HOLOGIC

VPI & SU BONE LAB

f Left Hip
Reference Database •



BMD(Total[L]) = 0.958 g/cm^2

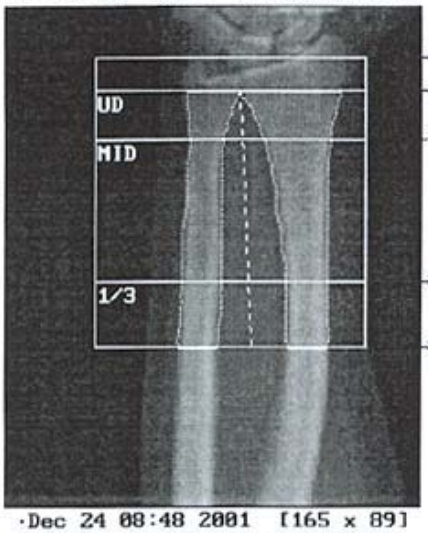
Region	BMD	T	Z
Neck	0.922	+0.65 109% (25.0)	+0.65 109%
Troch	0.732	+0.29 104% (25.0)	+0.29 104%
Inter	1.113	+0.08 101% (35.0)	+0.17 102%
TOTAL	0.958	+0.13 102% (25.0)	+0.13 102%
Ward's	0.780	+0.39 106% (25.0)	+0.39 106%

• Age and sex matched
T = peak BMD matched
Z = age matched NHA 02/01/97

A0921010G Fri Sep 21 10:30 2001
Name:
Comment: MZ study - repeat
I.D.: 7701 Sex: F
S.S.#: - - Ethnic: C
ZIP Code: Height:5' 4"
Operator: SNR Weight: 126
BirthDate: Age: 23
Physician:

HOLOGIC

VPI & SU BONE LAB



·Dec 24 08:48 2001 [165 x 89]
Hologic QDR-4500A (S/N 45727)
Left Forearm V8.26a:3

A0921010H Fri Sep 21 10:32 2001
Name:
Comment: MZ study
I.D.: 7701 Sex: F
S.S.#: - - Ethnic: C
ZIP Code: Height:5' 4"
Operator: SNR Weight: 126
BirthDate: Age: 23
Physician:
Forearm Length: 23.6 cm
Image not for diagnostic use

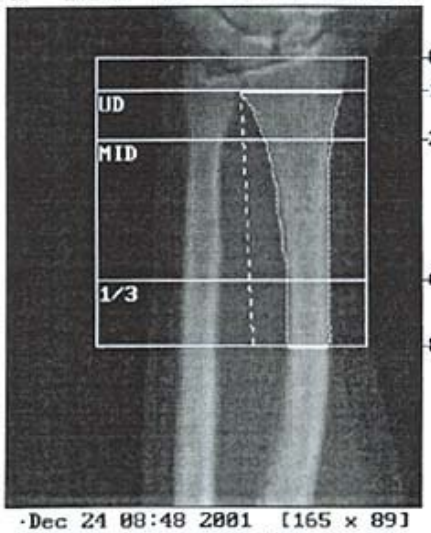
TOTAL BMD CV IS LESS THAN 1.0%

C.F.	1.029	1.004	1.000

RADIUS + ULNA	Area (cm2)	BMC (grams)	BMD (gms/cm2)
UD	5.26	2.10	0.400
MID	9.86	5.47	0.554
1/3	4.61	3.07	0.666
TOTAL	19.74	10.64	0.539

HOLOGIC

VPI & SU BONE LAB



·Dec 24 08:48 2001 [165 x 89]
Hologic QDR-4500A (S/N 45727)
Left Forearm V8.26a:3

A0921010H Fri Sep 21 10:32 2001
Name:
Comment: MZ study
I.D.: 7701 Sex: F
S.S.#: - - Ethnic: C
ZIP Code: Height:5' 4"
Operator: SNR Weight: 126
BirthDate: Age: 23
Physician:
Forearm Length: 23.6 cm
Image not for diagnostic use

TOTAL BMD CV IS LESS THAN 1.0%

C.F.	1.029	1.004	1.000

RADIUS	Area (cm2)	BMC (grams)	BMD (gms/cm2)
UD	3.45	1.52	0.441
MID	5.68	3.44	0.606
1/3	2.35	1.70	0.723
TOTAL	11.47	6.66	0.580

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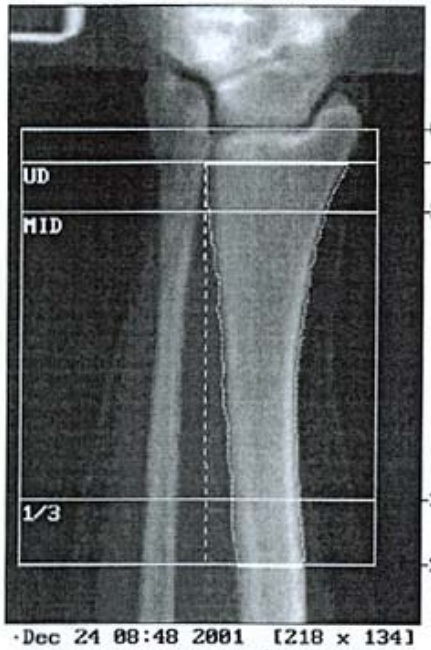
VPI & SU BONE LAB

k = 1.236 d0 = 64.3(1.000)[4]



0mm
10.1
25.2
113.9
134.1

·Dec 24 08:48 2001 [218 x 134]
Hologic QDR-4500A (S/N 45727)
Left Forearm V8.26a:3

A0921010I Fri Sep 21 10:33 2001
Name:
Comment: MZ study
I.D.: 7701 Sex: F
S.S.#: - - Ethnic: C
ZIP Code: Height:5' 4"
Operator: SNR Weight: 126
BirthDate: Age: 23
Physician:
Forearm Length: 37.2 cm
Image not for diagnostic use

TOTAL BMD CV IS LESS THAN 1.0%
C.F. 1.029 1.004 1.000

RADIUS	Area (cm2)	BMC (grams)	BMD (gms/cm2)
UD	5.47	4.52	0.825
MID	18.85	19.69	1.044
1/3	3.80	5.49	1.446
TOTAL	28.12	29.70	1.056

HOLOGIC

VITA

Melissa Kareen Zack, daughter of Russell and Bonnie Wood, was born on July 19, 1977 in Camp Hill, Pennsylvania. Melissa received a Bachelor of Art degree in Sport and Exercise Science from Messiah College, Grantham, Pa. in May 1999. During her time at Virginia Polytechnic Institute and State University, she has been funded by a grant from the United States Army Medical Research and Materiel Command (DAMD17-00-1-0114). After Melissa receives her Master's degree in Sports Nutrition and Chronic Disease from VPI&SU, she and her husband plan to return to Pa., where she will continue with coursework and apply for a Dietetic Internship.