ASSOCIATION BETWEEN BINDEX® ULTRASOUND AND DXA BONE PARAMETERS

by

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Abstract

Study Design. Observational analytic cohort study

The Bindex® device is a quantitative ultrasound device that calculates cortical thickness of the tibia and provides a density index (DI), which is an estimate of hip bone mineral density (BMD). This study assessed intra- and inter-session reliability of the Bindex® cortical thickness and DI measures at the proximal, mid, and distal tibia in young, physically active women at risk of bone stress injury. Our results indicate within session and between session agreement was good to excellent for tibia cortical thickness and DI measures, with ICC values ranging from .77 to .990. Associations between the Bindex® DI measures and BMD measures by dual-energy x-ray absorptiometry (DXA) were assessed, as well as associations between Bindex® cortical thickness measures and hip structural characteristic measured by DXA. Moderate correlations were found between the DI and whole-body BMD, femoral neck BMD, and total BMD, with ICC values ranging from .504 to .685. Associations between Bindex® derived measures and DXA measures were strongest at the proximal tibia with ICC values from .547 to .713. The results show that the Bindex® device is reliable within and across measurement sessions. With further study, the Bindex® device may be used in a young, physically active female population as s screening tool of bone health characteristics.

Contents

Introduction

Bone mineral density (BMD) and geometry have been established as key indicators of bone health across the lifespan [1,2]. Low BMD increases risk of bone stress injury and fracture in both older adults [3] and young, active adults [1,4–7]. Bone mass, which is commonly measured by volumetric BMD, typically reaches its peak during the third decade of life[2]. Bone geometry is another important factor for bone health and is linked to bone stress injury and fracture risk in both older and young, active adults[8–10]. Bone geometry is closely related to bone strength and has been shown to predict fractures independent of BMD[11,12]. Specifically, decreased cortical thickness contributes to lower bone strength and higher risk for fracture [11,13]. Smaller bone geometry has also been linked with bone stress injury in young adults[9,10,14,15].

Bone stress injuries are common in young active adults and servicemembers[4,16]. Females who participate in high-impact, vigorous physical activities have 1.5-3x increased risk of bone stress injury compared to males[4]. Bone stress injuries in female athletes and military personnel, which are most common in adolescence and young adulthood, are linked with lower BMD, smaller bone geometry and reduced bone strength, among other factors [4,5,10]. Knowledge of bone strength and risk factors for bone injury and disease at a young age has the potential to identify the need for early intervention to prevent bone stress injuries in an at-risk population and to improve bone health long term. Thus, low-cost and easy to administer tools to screen for bone health in young adults are needed.

Dual-energy x-ray absorptiometry (DXA) scanning is widely used as a screening and diagnostic tool for bone health across the lifespan[2]. While it is considered the gold standard measure of BMD, computed tomography can also be used to determine BMD and bone geometry[2,12]. DXA and CT are accurate measures, but are timely, costly, and involve radiation exposure. Quantitative ultrasound (QUS) has been introduced as an alternate screening tool. Quantitative ultrasound devices can provide multiple bone health measures, such as cortical thickness and BMD indices[17–20]. They are cost-effective, portable, free of radiation, and less time consuming than gold standard measures. QUS devices have been shown to be accurate and precise in measuring cortical thickness and have shown promising results for being accepted as a screening tool for bone health risk factors[18,21,22]with significant positive correlations to DXA [20,22–25].

The Bindex® is a relatively new QUS device that uses pulse ultrasound techniques to measure apparent proximal tibia cortical thickness and reports a Density Index (DI) that is an estimate of hip BMD measured with gold standard axial DXA [26]. The Bindex® calculates apparent cortical bone thickness by measuring the time difference between the echoes from periosteum and endosteum and the estimated constant speed of sound [26]. Because the speed of sound in bone varies with bone tissue and structure, the reported cortical bone thickness is an estimate[26]. The current model approved for use in the United States [27] outputs both cortical thickness and a proximal femur Density Index (DI), which is based on age, weight, height and cortical thickness measurements[25,26,28,29].

The Bindex® device has been primarily studied in older populations[25,28–31]. Data on the association of intra- and inter-session Bindex® measures and the associations of the Bindex® device measures relative to the reference standard DXA measurements in young active populations, including those at risk for bone stress injury during critical periods of bone development, are limited. One study did examine the reliability of Bindex® cortical thickness and DI and their associations with BMD measurements from DXA of the wrist, lumbar spine and proximal femur in a mixed sex population aged 20-35 years; the device was found to reliably measure cortical thickness and modest correlations between Bindex® measures (cortical thickness and DI) and DXA derived bone densities were reported[20]. However, the relationships between Bindex® cortical thickness and cortical thickness derived from DXA images were not examined. Moreover, only 9 of the 28 subjects were female.

Rationale

Bone geometry and density are known risk factors for bone stress injury and key inputs to musculoskeletal models of bone stress during activity. Cost-effective and efficient tools are needed to quantify bone characteristics in young adults at risk for bone stress injury. For Bindex® to be a valuable screening tool for female athletes or as a substitute for musculoskeletal model inputs, it is critical to determine the strength of the relationships between Bindex® estimates of female bone characteristics and the more invasive but widely accepted DXA bone measures. To our knowledge, neither intra- and inter-session associations of the Bindex® measures, nor the relationships with reference standard devices, like DXA, have been examined in our population of interest.

The knowledge gained from this preliminary study has the potential to lay the groundwork for future large-scale studies examining the efficacy of the Bindex® as a screening tool for poor bone quality and structure in at-risk athletes and servicemembers. The results from this study are also expected to provide valuable knowledge on the utility of Bindex® to inform subject-specific bone modeling inputs minimizing the need to radiation exposure in future biomechanical studies.

Objectives

The purpose of this study was two-fold. First, we investigated the association of intra- (within day) and inter-session (between day) Bindex® bone measures. Second, we investigated the associations between Bindex® and DXA bone measures in young, active females at risk of bone stress injury. Specifically, we:

1. examined the associations of intra-session and inter-session measures of tibial cortical thickness obtained from Bindex®
2. examined the associations of intra-session and inter-session DI measures obtained from Bindex®
3. quantified the associations between the proximal femur DI obtained from Bindex® and total hip BMD and femoral neck BMD obtained from proximal femur DXA
4. quantified the associations between the proximal femur DI obtained from Bindex® and whole BMD obtained from whole body DXA, and

5. quantified the associations between tibia cortical thickness obtained from Bindex® and hip structural analysis measures obtained from proximal femur DXA.

Methods

Sample Size

Based on previously reported correlations between femoral neck BMD from DXA and the Bindex® DI of the hip (r = 0.59-0.62)[20], a sample size of 15-17 was needed for a bivariate correlation model assuming a two-tailed test with an error probability of .05 and a power of .80 (GPower 3.1). In athletic populations, DXA BMD Z scores of less than -1.0 SD warrant further medical attention[32] and are associated with bone stress injury[33]. In a prior study, the Bindex® DI underestimates total hip BMD nearly 10%[20] and has 94% sensitivity and 82% specificity for the diagnosis of osteoporosis (Z score of -2.5 SD)[29]. Thus, greater accuracy may be needed to identify young active adults at risk of injury. Because of this, we powered our study to detect at least a 5% difference in BMD measures of the proximal hip between devices. A 5% difference between the Bindex® DI and the DXA femoral neck BMD that was reported by Behrens et al. (1.202 ± 0.115 g/cm^2)[20] corresponds to 0.060 g/cm^2. The average standard deviation reported by Behrens et. al.[20]during their second session across instruments was 0.108 g/cm^2; thus, a 5% difference between instruments appears to be associated with a modest effect size (0.56). Using this effect size in a GPower 3.1 sample size estimation, we estimated that a sample size of 28 will be needed to detect a 5% difference in BMD parameters with a two-tailed, paired t-test, a Type I error probability of .05 and a power of .80 (GPower 3.1). To account for attrition, we aimed for a sample size of 30 for this preliminary study.

Participants

Ten young, physically active female adults aged 18-30 years and two pilot participants were recruited for this preliminary study analysis. Recruitment methods included local advertising, email campaigns, web site postings, phone solicitations, pre-existing relationships with participants and social media.

Inclusion criteria. Females, 18-30 years of age, at risk for bone stress injury and fracture by nature of their sex and participation in high impact/vigorous activity. Vigorous activities were defined as activities that expend 6 times (≥ 6 METS) or more the amount of oxygen consumed while sitting at rest (1 MET)[34]. Examples included running, swimming, ball sports, court sports, and carrying heavy loads. High impact activities included weight-bearing activities like jumping, running, and cutting that impart a high strain magnitude or strain rate to the skeleton [35]. Other inclusion criteria included: no known cardiovascular problems, neuromuscular, musculoskeletal, or rheumatoid disorders exacerbated by exercise, uncontrolled metabolic disease, chronic infectious disease, or mental or physical impairment that restricts the ability to exercise. All volunteers needed to report a Physical Activity Rating (PAR) of ≥ 6/10. The Physical Activity Rating scale asked participants to describe their overall physical activity level on a scale of 0-10 [36]. A minimum requirement for this study was a PAR rating of 6/10 which is described as "Vigorous activity: runs 5 miles to less than 10 miles per week or spends 1 hour to less than 3 hours per week in comparable activity." A 10/10 was described as "Vigorous activity: runs over

25 miles per week or spends over 8 hours per week in comparable physical activity". Comparable physical activity was previously defined in the 4/10 rating on the tool as "running or jogging, lap swimming, cycling, rowing, aerobics, skipping rope, running in place, or engaging in vigorous aerobic-type activity such as soccer, basketball, tennis, racquetball, or handball."

Exclusion criteria. Subjects were excluded if they reported an injury that would have limited their ability to be physically active in 3 months prior to study participation, are pregnant, or did not pass the DXA safety questionnaire (which screened for pregnancy, the following procedures: iodine, barium, nuclear medicine isotope study, and the following devices: a prosthetic device, pacemaker leads, radioactive seeds, metal implants, surgical staples, or foreign bodies e.g. shrapnel and radio-opaque catheters or tubes.)

Screening

Prior to enrollment, participants completed an online self-administered health, injury, and activity history screening for inclusion and exclusion criteria via REDCap. Participants were also screened for radiation safety prior to study enrollment via this REDCap survey. Following completion of the online REDCap survey, study personnel reviewed the REDCap screening survey and contacted potential participants. Participants who met study inclusion and exclusion criteria were invited to participate.

Study participation consisted of 2 sessions at least one week apart. Upon arrival at the study location for the first session, informed consent was obtained according to ECU's University and Medical Center IRB standard operation procedures at the first session and verbally reviewed on the second session.

Data Acquisition

Session I (QUS Session). All study procedures for the QUS session occurred in the ECU Physical Therapy Department Movement Biomechanics Lab, part of the Human Movement Analysis Laboratories, within the Health Sciences Building (room 1425). Participants completed an online musculoskeletal injury history survey modified from the Oslo Sports Trauma Research Centre Overuse Injury Survey[37], female athlete triad screening[38] and a cumulative bone stress injury risk factor assessment[5] via REDCap. Next, height and mass were obtained using standard laboratory weight scale with stadiometer for input to the Bindex® (Bindex® Index Finland Ltd) software. Additionally, tibia length of the study limb was measured to identify the proximal 1/3, mid and distal 1/3 tibia locations which were then marked with a skin marker. Tibia length was measured from the upper head of the tibia (the medial knee joint line) to the distal head of the tibia (on the medial malleolus) using a tape measure. Participants underwent two trials of Bindex® testing at each location of the study leg in accordance with manufacturer instructions[26]. For each site, the participant was positioned with the study limb extended (Figure 1a), supported at ankle, and externally rotated about 45°. Demographic and anthropometric data was input to the Bindex® software. Following a demonstration, ultrasound gel was applied over measurement location. As the transducer head was slowly moved over the

measurement locations, echo spikes were shown by the Bindex® software during measurement. The software automatically captured a measurement when two peaks were shown with minimal noise; thus, five successful measurements comprise each Bindex® trial (Figure 1b). Individual measurements were repeated if the peaks lack uniformity is distance between peaks, location of signal peaks, or the shape of the signal[26]. After obtaining 5 successful measurements, the software output the apparent cortical thickness (mm) and proximal femur DI (g/cm^2) (based on age, weight, height and cortical thickness) of Bindex® software (Figure 1c); these outcomes were recorded for both trials at each site (proximal, distal, and mid tibia).

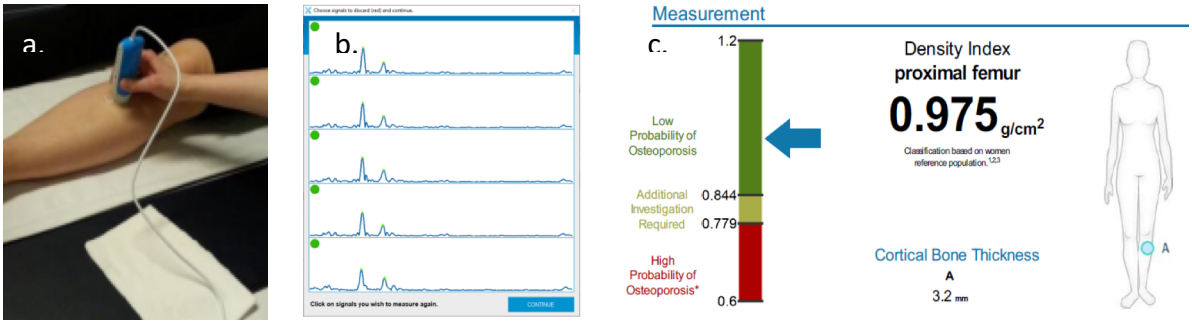

Figure 1a. Participant setup for using the Bindex® device; **b.** Five peaks of ultrasounds measurements for one Bindex® measurement to; **c.** Bindex® measurement output.

Session II (QUS/DXA Session). Study procedures for the QUS/DXA session, occurred at the Human Performance Laboratory in the ECU Ward Sports Sciences building (room 363). Participants were screened for radiation safety using ECU Human Performance Lab's radiation safety survey. Following successful screening, height, mass, and tibial length were obtained using QUS session procedures described above. Because two different scales were used, investigators calibrated scales with known masses to quantify differences and adjusted recorded mass as needed prior to Bindex® input. Participants underwent two trials of Bindex® testing of the study leg at each site (proximal, distal, mid) as described above and cortical thickness and proximal femur DI (g/cm^2) were recorded for both trials.

Participants also underwent one whole body DXA and one study limb proximal femur DXA scan in accordance with manufacturer instructions. If a scan was unusable (e.g., movement artifact or positioning errors), investigators repeated the scan, no more than one time, with participant verbal agreement. A Hologic Horizon A Dual Energy X-Ray Absorptiometer with APEX software was used for body composition and BMD measurements. Participants were advised to maintain their normal hydration level and refrain from heavy exercise at least 12 hours prior to the scan. They were also asked to refrain from heavy consumption of alcohol, nicotine, caffeinated beverages, and heavy meals at least 4 hours prior to the scan. Whole body BMD (g/cm^2) was extracted from the whole-body scan (Figure 2b). All scans were auto analyzed by the DXA software and reviewed and adjusted manually as needed. The region of interest for hip structural analysis was found using standards set by the manufacturer. The femoral head,

greater trochanter, and lesser trochanter were the anatomical landmarks used for determining region of interest (Figure 2b). Femoral neck BMD (g/cm^2) and total hip BMD (g/cm^2), were extracted from the proximal femur DXA report for analysis. Femoral neck cross section area (CSA), cross sectional moment of inertia (CSMI), and bending strength indicator (Z) were also reported from the hip structural analysis.

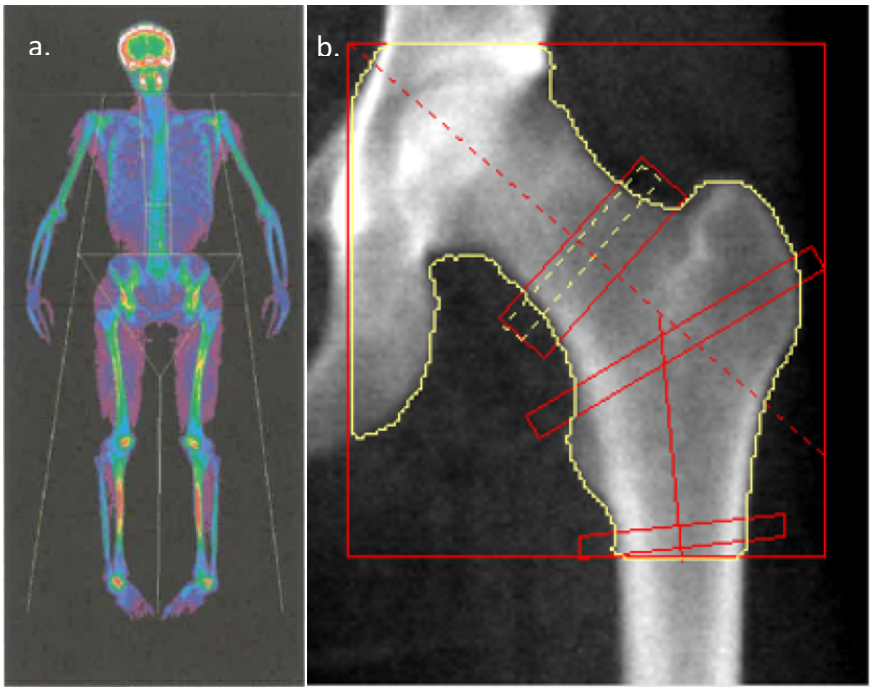

Figure 2a. Whole body DXA scan analysis; **b.** Structural analysis of DXA unilateral hip scan.

Statistics

Anthropometric, survey, cortical thickness in centimeters from both instruments, Bindex® DI (g/cm^2) and DXA BMD (g/cm^2) data was compiled for descriptive purposes. Cortical thickness and DI are both continuous variables. All planned statistics were performed using IBM SPSS Statistics Version 29.01.0. The same investigator performed all Bindex® device measurements, so no inter-tester reliability was considered. Having the same investigator ensured consistency in technique during measurements to promote reproducibility of measurements during Session I and Session II.

Intra-session (within day) absolute agreement of tibia cortical thickness (cm) for each site and DI (g/cm^2) were assessed using intraclass correlations (ICC (3,1)). QUS session and QUS/DXA session values were examined separately to provide insight into practice effects associated with Bindex® testing. Outcomes included means, mean differences with 95% confidence interval (CI), standard error of the difference (SD_{diff}), and ICC coefficients with 95% CI. ICC values below 0.5 were interpreted as poor agreement, between 0.5 and 0.75 moderate agreement, between 0.75 and 0.9 good agreement, and any value above 0.9 was considered excellent agreement[39].

Inter-session (between day) absolute agreement of tibia cortical thickness (cm) for each site and DI (g/cm^2) were assessed using average measures (ICC (3,2)). Trial and session differences were quantified using repeated measures ANOVA. In the absence of interaction or trial effects, trials were averaged within sessions for analysis ($\alpha = .05$). Outcomes included means, mean differences with 95% CI, SE_{diff}, ICC coefficients with 95% CI.

Using data from the same session (i.e., Session II), the Bindex® proximal femur DI (g/cm^2) associations with total hip BMD (g/cm^2) and whole-body BMD (g/cm^2) from the proximal femur and whole body DXA scans, respectively, were examined using Pearson's correlation coefficients. Bindex® data from Session II were screened for trial differences using paired t-tests. In the absence of trial differences, trial data were averaged for analysis ($\alpha = .05$). Outcomes included Pearson's correlation coefficients and coefficients of determination. Because of the preliminary and non-invasive nature of this study as well as the small sample size, we adopted a .10 level of significance such that we had a 10% probability of committing a type I error (rejecting the null hypothesis when it is actually true and concluding that an association exists when there is no actual association). Using a similar approach, the associations between the Bindex® apparent cortical thickness at the proximal, mid and distal tibia and the hip structural analysis measures obtained from the proximal femur DXA scan were examined with Pearson's correlation coefficients.

Results

Subjects. Table 1 displays mean values for subject height, weight, tibia length, PFA, PA-R, and history of a bone stress injury. Height and weight were entered into the Bindex ® software for estimating DI.

Table 1. Subject Characteristics

	Mean
Height (cm)	167.2
Weight (kg)	65.9
Tibia length (cm)	36.5
PFA	17
PA-R	7
Bone stress injuries*	3 (23%)

PFA: Perceived Functional Ability; PA-R: Physical Activity Rating

*Value represents N (%). Percent of participants with a history of a bone stress injury

Intrasession reliability. Intrasession data for Bindex® derived measures are shown in Table 2. Within-session absolute agreement for trial data was excellent (ICC values ≥0.9). Additionally,

no significant interaction or trial effects were observed for proximal, mid, or distal tibia cortical thickness measurements or density index measurements ($p > .05$).

Table 2. Intrasession results for Bindex® measures

	Trial 1	Trial 2	Mean Difference (95% CI)	SE_{Diff}	ICC (95% CI)
Session I					
Cortical Thickness (mm)					
Proximal Tibia	2.92	2.97	-.050 (-.406 to .306)	0.16	.908 (.695 to .972)
Mid Tibia	3.70	3.67	.033 (-.076 to .143)	0.05	.992 (.976 to .998)
Distal Tibia	3.77	3.70	0.067 (-.345 to .479)	0.187	.926 (.756 to .978)
Density Index (g/cm^2)					
Proximal Tibia	0.96	0.97	-.005 (-.035 to .026)	0.014	.926 (.754 to .977)
Mid Tibia	1.03	1.03	.003 (-.008 to .013)	0.005	.990 (.967 to .997)
Distal Tibia	1.03	1.03	-.003 (-.032 to .027)	0.013	.953 (.848 to .986)
Session II					
Cortical Thickness (mm)					
Proximal Tibia	3.00	2.93	.075 (-.086 to .236)	0.073	.970 (.901 to .991)
Mid Tibia	3.89	3.78	.108 (-.026 to .242)	0.061	.985 (.944 to .996)
Distal Tibia	4.09	4.20	-.108 (-.281 to .064)	0.078	.891 (.639 to .968)
Density Index (g/cm^2)					
Proximal Tibia	0.97	0.96	.007 (-.007 to .021)	0.006	.974 (.915 to .993)
Mid Tibia	1.05	1.04	.009 (-.001 to .020)	0.005	.989 (.956 to .997)
Distal Tibia	1.07	1.07	-.007 (-.022 to .008)	0.007	.937 (.789 to .981)

CI: confidence interval; SE_{Diff}: standard error for the difference; ICC: intraclass correlation coefficient

Intersession reliability. Intersession results for within-session averaged Bindex® measures are shown in Table 3. Two data points were excluded due to equipment malfunction, which is reflected in the sample size reported in Table 3. No significant interaction, session or trial effects were observed for proximal, mid, or distal tibia cortical thickness measurements or DI measurements ($p > .05$ for all); thus, trials were averaged with session for between session analysis. Between session reliability was good (ICC values ≥0.75).

Table 3. Intersession results for Bindex® measures

	Session I mean	Session II mean	$Mean_{Diff}$ (95% CI)	SE_{Diff}	N*	SD_{Diff}	ICC (95% CI)
Cortical Thickness (mm)							
Proximal Tibia	2.94	2.93	.021 (-.431 to .473)	0.21	12	0.71	.78 (.205 to .938)
Mid Tibia	3.69	3.84	.154 (-.281 to .589)	0.20	12	0.69	.89 (.613 to .967)
Distal Tibia	4.19	4.11	.080 (-.342 to .182	0.12	10	0.37	.83 (.316 to .957)
Density Index (g/cm^2)							
Proximal Tibia	0.967	0.969	.001 (-.038 to .041)	0.02	12	0.06	.83 (.401 to .953)
Mid Tibia	1.03	1.04	.014 (-.023 to .051)	0.02	12	0.06	.89 (.642 to .969)
Distal Tibia	1.07	1.06	.008 (-.015 to .031)	0.01	10	0.03	.77 (.111 to .944)

CI: confidence interval; SE_{Diff}: standard error for the difference; N: number of subjects taken into analysis; SD_{Diff}: standard deviation of the difference; ICC: interclass correlation coefficient

*Outliers were removed for intersession analysis

BMD Associations. Relationships between DXA derived BMD values and Bindex® derived DI values are shown in Table 4. Statistically significant (✔<.10) relationships were observed between the Bindex® DI measured at the proximal and distal tibia and whole-body BMD, the proximal and mid tibia and femoral neck BMD, the proximal and mid tibia and total hip BMD. The proximal tibia site displayed the strongest relationship with two of the three DXA based BMD measures; scatterplots of proximal tibia cortical thickness and whole-body and total hip BMD, two commonly reported DXA values, are displayed in Figure 3.

Table 4. Pearson's correlations (r) between DXA derived BMD values and Bindex® derived DI

	Mean (g/cm^2)	r	p value
Whole Body BMD and DI			
Whole body BMD	1.155	--	--
Proximal Tibia DI	0.969	0.609	0.061
Mid Tibia DI	1.041	0.504	0.138
Distal Tibia DI	1.072	0.685	0.029
Femoral Neck BMD and DI			
Whole body BMD	0.913	--	--
Proximal Tibia DI	0.969	0.622	0.055
Mid Tibia DI	1.041	0.609	0.062
Distal Tibia DI	1.072	0.493	0.147
Total Hip BMD and DI			
Whole body BMD	1.026	--	--
Proximal Tibia DI	0.969	0.626	0.053
Mid Tibia DI	1.041	0.57	0.085
Distal Tibia DI	1.072	0.515	0.127

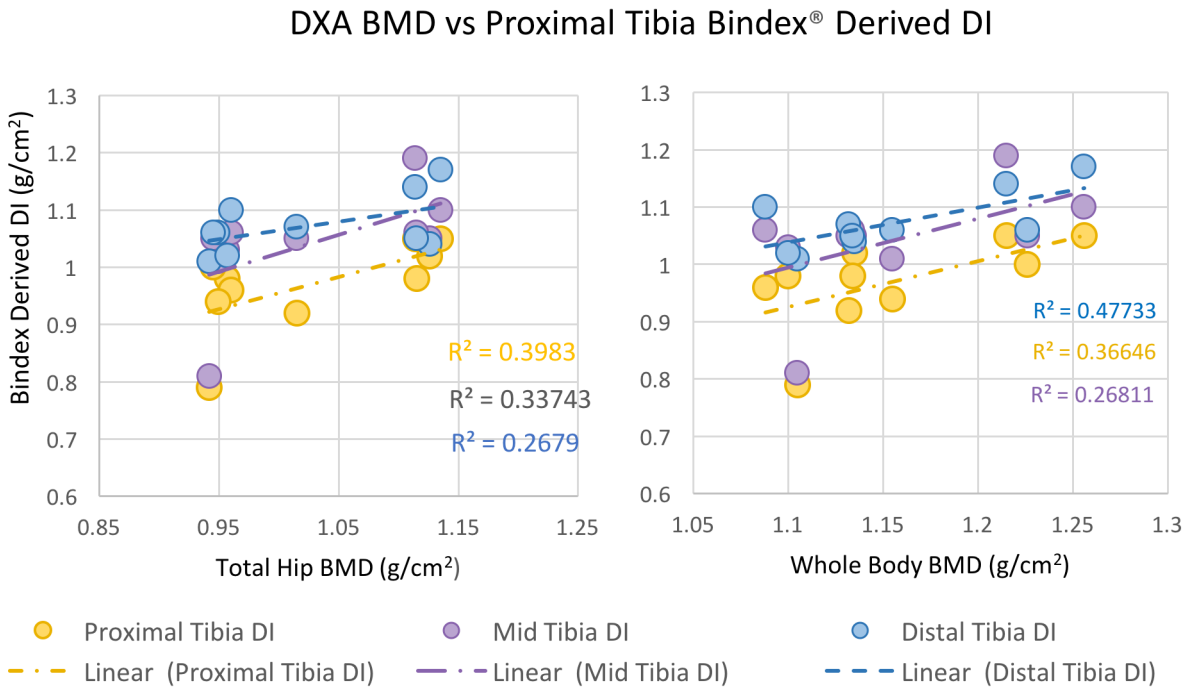

Figure 3. Relationships between DXA BMD (x-axis) and Bindex® DI measures (y-axis) at proximal (yellow), mid (purple), and distal tibia (blue).

Structural Analysis Associations. Correlations of cortical thickness measurements from the Bindex® device and measurements of the femoral shaft were not statistically significant. However, several correlations of Bindex® derived cortical thickness measures and DXA hip structural analysis measures were statistically significant (scatter plots displayed in Figure 4). Specifically, proximal tibia cortical thickness displayed moderate correlations with femoral neck CSA (r = .71, p = .02) and Z (r = 0.58, p = .08). Likewise, mid tibia cortical thickness displayed a moderate correlation with femoral neck CSA (r = .60, p = .07).

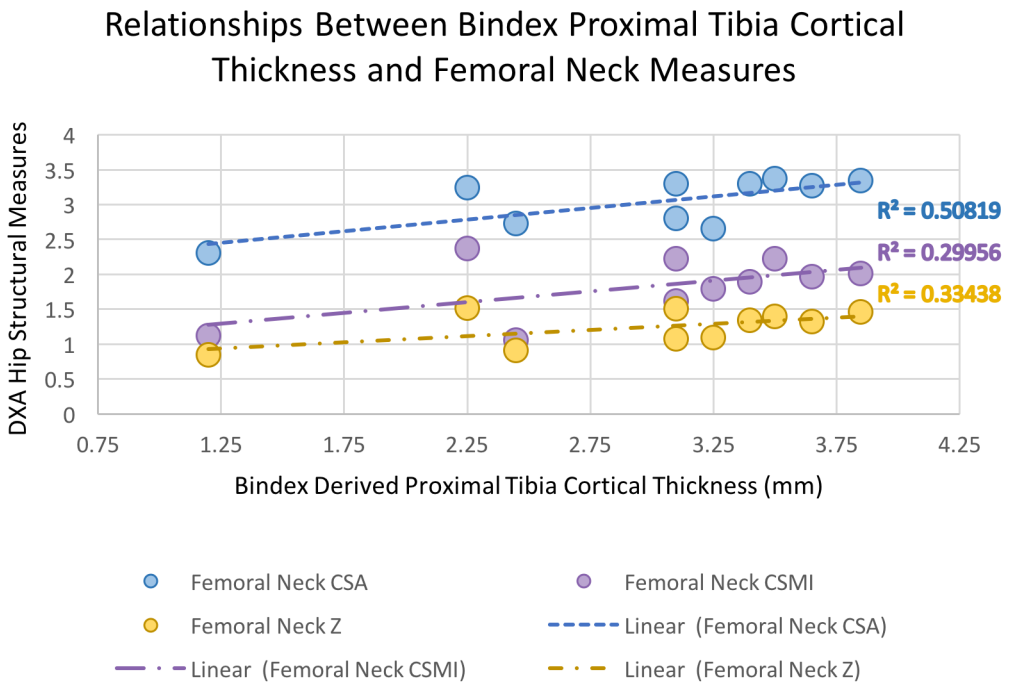

Figure 4. Relationships between Bindex® derived proximal tibia cortical thickness and DXA derived femoral neck CSA (cm^2), CSMI (cm^4), and Z (cm^3). CSA: cross sectional area; CSMI: cross sectional moment of inertia; Z: indicator of bending strength.

Discussion

This study sought to assess intra- and inter-session reliability of the Bindex® device, as well as establish relationships between Bindex® and DXA derived measurements of bone geometry and density.

Reliability of Bindex® bone measurements.

Data quantifying the intra- and inter-session associations and associations of the Bindex® device with reference standards in a young female population is limited. In early work, cortical thickness measured by ultrasound was found to accurately reflect cortical thickness measured with peripheral quantitative computed tomography in a group of males and females (r =. 91-.93, coefficients of variation = 7.5-7.9%)[40]. In another study of adults aged 20-35 (25.0 ± 3.6 years), the Bindex® device was reported to be a reliable measurement tool of cortical thickness both within (ICC = 0.98, CV = 1.5%) and between days (ICC = 0.98, CV = 1.4%)[20]. Our results, especially within session reliability, are comparable to these findings.

We found that within session and between session agreement was generally excellent for tibia cortical thickness and DI measures within days and good between days. As expected, inter-session ICC values were lower than intra-session ICC values, showing that the Bindex® device measurements are more consistent within the same measurement session. This may be attributed to slight variances in participant set up between collection sessions, day to day

variation in participant characteristics (time of day influence, hydration, etc.) as well as site-specific differences in environmental electromagnetic field radiation[26]. Unlike previous studies[20, 29] we performed our study in two different locations. In a similar two session study, Behrens et. al. reported a learning effect evidenced by higher ICC values in session II[20]. However, no significant trial or session effects were observed for cortical thickness measures or DI in our study; ICC values for session I ranged from .908 to .992, and ICC values for session II ranged from .891 to .985. These results suggest that no statistically significant learning effects were seen for the investigator performing the Bindex® measurements. Our research technician underwent training with a trained investigator and sent videos of her technique to the manufacturer support team for feedback and verification. Additionally, she performed two trials on four different participants at three locations of the tibia on two different days, for a total of 48 trials, prior to data acquisition. Thus, the investigator performing measurements with the Bindex® device should undergo sufficient training and be comfortable with the device usage to avoid inaccurate results caused by user error.

Manufacturer manual instructs measurements be taken at the proximal tibia, but interestingly our intra- and inter-session ICC values were highest at the mid tibia site for both cortical thickness and DI. Our results and existing literature indicate significant correlations between ultrasound measurement at the proximal tibia[25], however measurements as the distal tibia may have higher day-to-day reliability. Continued research is warranted.

In summary, excellent within session reliability and good between session reliability suggests the Bindex® device produced reasonable consistency both within similar measurement conditions as well across measurement conditions. Our results, in combination with prior work, suggest that the Bindex® device is reliable in measuring cortical thickness and estimating proximal femur BMD in young, active females at risk of bone stress injury.

Associations between Bindex® and DXA bone measurements.

BMD. Intra- and inter-session associations of the Bindex® DI and associations with criterion measures have been studied in older populations[25,29–31]. Much of the research has focused on diagnostic accuracy of the Bindex® in screening for osteoporosis. For example, one study done with 1091 Caucasian females aged 50-80 years found the sensitivity of the Bindex® in osteoporosis diagnostics ranged from 85-94%, and specificity from 82-92%, depending on the number of sites measured[29]. However, fewer studies have examined the direct relationships between the Bindex® device and the reference standards of cortical thickness and hip BMD. Karjalainen et al. reported significant correlations (r=.86) between a preliminary DI (based on age, weight, and tibia cortical thicknesses from 30 older female adults) and BMD derived from DXA [28]. In another study of 448 women aged 50-91, the DI provided by the Bindex® has a significant correlation to proximal femur BMD [25].

Behrens et. al reported moderate positive correlations between DXA-derived BMD of the femoral neck and the Bindex® DI (r =.59-.62; R^2= .35-.38) in young and healthy subjects. Relative to DXA, the Bindex® underestimated femoral bone mineral density 9.25% (mean difference = 0.111 g*cm^2). However, female representation (n=9) in this study was low. In our study, the DI values given by the Bindex® device were compared to DXA derived measurements for whole body BMD, femoral neck BMD, and total hip BMD. DI was measured with the Bindex® device at the proximal, mid, and distal tibia. Similar to prior findings, only moderate correlations between the DI at all three tibia sites of interest and whole-body BMD, femoral neck BMD, and total BMD. For two of the three BMD measures, the proximal tibia displayed strongest association with BMD (r = .62 to .63). However, the strongest association was seen with whole body BMD and the distal tibia Bindex® DI (r= 0.69). The proximal tibia cortical thickness is currently the recommended site for obtaining a DI measurement, however our results suggest that the distal tibia could potentially be incorporated into the DI estimation calculation. Our study differs from existing literature in that our subjects were young, physically active women who are at a higher risk of bone stress injury. On average, our subjects scored a 7 on the PAR scale, meaning they run over 10 miles a week or spend more than 3 hours a week in comparable activity, and our subjects were at or above population means for BMD. Based on our preliminary results, the Bindex® device has the potential to be a useful reliable, screening tool in assessing BMD measures for young, physically active women, but further study is needed.

Structural Analysis Associations. Bindex® derived cortical thickness measurements were compared to DXA hip structural analysis measurements of the femoral neck and femoral shaft, with statistically significant associations observed in the femoral neck. Associations between Bindex® derived measures and DXA measures were strongest at the proximal tibia, indicating that the cortical thickness of the proximal tibia measured by the Bindex® device may be more closely related to bone geometry of the femoral neck than cortical thickness of the mid or distal tibia. The Bindex® user manual advises cortical thickness measurements to be taken at the proximal tibia, so these results support the recommendation.

Prior studies have not examined associations between Bindex® based cortical thickness measures and hip structure measurements. Despite its utility for characterizing bone strength, a rapid review of PubMed indicated only two articles have examined DXA based hip structural analysis outcomes in young populations. Results of this literature suggest that amenorrheic athletes who are at greater risk of bone stress injury than eumenorrheic athletes are reported to have lower hip structural analysis bone strength characteristics[41]. Additionally, individuals with anorexia nervosa who are also at greater risk of bone stress injuries had reduced BMD of the proximal femur, as well as lower QUS measurements when compared to healthy individuals[24]. Implications for femoral stress injuries are seemingly implicit, however relationships between femur structural characteristics and structural characteristics of other long bones susceptible to BSI are unknown. Thus, the relevance of hip structural characteristics and bone stress injury has not been fully established.

Limitations.

The small sample size is the primary limitation of this preliminary ongoing study. Based off sample size estimate, the goal sample size for this study was 30 participants. Our small sample size limits power needed for statistical analysis and minimizes the likelihood of statistically significant results. Additionally, visual inspection of or preliminary data suggests that data normality should be monitored due to clustering of BMD values above and below 1.0. A larger sample size is expected to increase the statistical power, improve distribution normality and strengthen the preliminary results observed and provide further evidence of the reliability of the Bindex® device.

Another limitation of this study was the outliers caused by equipment malfunction of the Bindex® device. Distal tibia cortical thickness measurements for two subjects differed by greater than 2 millimeters between measurement days and deemed inaccurate. These cortical thickness measurements were also dramatically low compared to the mean of each measurement day. These outliers may have been caused by a malfunction of the Bindex® device or excessive signal noise; trial acquisition was notably difficult and marked variability in echo peaks were noted by the technician. As part of the troubleshooting process for remaining participants, researchers monitored environmental electromagnetic radiation frequency used a commercial smart phone app, ensured that measurement location was not near University wireless access points and made efforts to place nearby digital devices in airplane mode.

More data is required to have a comprehensive understanding of the relationships between Bindex® derived measurements and DXA derived measurements in young, active females. Participant enrollment and data collection will be continued for this study.

Conclusion.

Unlike a DXA or CT scan, the Bindex® device may be useful in providing estimates of BMD and proximal femur structural characteristics without exposing individuals to radiation. The results of this preliminary study suggest that the Bindex® ultrasound device is reliable in measurements across same-day trials and multi-day trials in young, active females. Cortical thickness and DI measurements derived from the Bindex® device shows some promising relationships with criterion measures that may be refined with future study, but more data is needed to conclude if the device can be used with confidence in a young, active female population as an indicator of bone health.

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