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Dual-energy X-ray absorptiometry of human metatarsals: Precision, least significant change and association to *ex vivo* fracture force

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Abstract

Background—Fractures are common in foot bones, but clinicians lack adequate indices of bone strength.

Objectives—We used dual-energy X-ray absorptiometry (DXA) to measure bone mineral density (BMD) and content (BMC) of excised human metatarsals, determined intra- and inter-rater measurement precision, and assessed associations between BMD/BMC and *ex vivo* bone fracture strength.

Methods—Two raters each made two measurements of whole-bone and sub-regional BMD and BMC in both second and third metatarsals from 10 cadavers. Variance components analysis was used to assess variability attributable to repeat measurements, raters, sub-regions, bones, sides, and cadavers. Rootmean-square standard deviation (RMS-SD) and least-significant change (LSC) were used to assess rater precision and ultimate forces during 3-point bending were tested for correlations with BMD and BMC.

Results—Variation due to repeat measurements and rater was low (<1% combined) for BMD and BMC. RMS-SD for whole metatarsal BMD of both metatarsals ranged from 0.004 to 0.010 g/cm² and 0.062 to 0.086 g for BMC. Whole metatarsal and sub-region BMD and BMC were strongly correlated to *ex vivo* fracture force ($r^2 = 0.67$ – 0.93).

Conclusions—DXA measurements of BMD and BMC have high intra- and inter-rater precision and are strongly correlated to *ex vivo* bone strength.

Keywords

Metatarsal bone density; DXA; Rater precision; Metatarsal fracture

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1. Introduction

The metatarsals are common sites of foot fractures, particularly stress fractures and fragility fractures. Stress fractures of the metatarsals occur with or without acute traumatic events [1]. In athletes, roughly 20% of metatarsal stress fractures occur in either the second (Met2) or third (Met3) metatarsal [2,3]. In individuals with diabetes mellitus and peripheral neuropathy, metatarsal stress fractures have been linked to focal osteopenia, thus these fractures are considered neuropathic fragility fractures [4]. In neuropathic individuals, metatarsal fractures often go unrecognized as ‘silent’ bone stress injuries that can persist for months [5,6] and if left untreated may result in delayed fracture healing and progressive foot deformities [7,8].

With the high prevalence of metatarsal fractures, there has been much interest in pedal bone health and particularly the role of bone mineral density (BMD) and mineral content (BMC) in metatarsal-stress and neuropathic-fragility fractures, yet there have been few studies of dual energy X-ray absorptiometry (DXA) of human metatarsals either *in vivo* or *ex vivo* and no previous report of the intra- and inter-rater BMD/BMC precision of whole human metatarsals and sub-regions of metatarsals. In one study, the coefficient of variation was reported for repeated DXA measurements of the central 1 cm of excised human 4 metatarsals (metatarsals 2 and 3) that were scanned 10 times each without repositioning the bones between scans [9]. In addition, one metatarsal was scanned 10 times with repositioning between each scan. Measurement variance estimates were determined for a single rater with unspecified experience. The coefficient of variation for BMD with repeated scans without repositioning was 1.8% and with repositioning was 2.3%. In a subsequent study, DXA scans were performed on 12.5-mm regions of the central shafts of excised cadaver second metatarsals, with the scanned regions corresponding to regions scanned with peripheral quantitative computed tomography scanning [10]. Utilizing small animal model software, one metatarsal was scanned six times with re-positioning; the reported coefficient of variation was 1.2%.

In the only *in vivo* study, DXA was used to assess changes in BMD in the feet of 11 subjects who had acute Charcot neuroarthropathy and who had undergone 6 months of treatment with oral bisphosphonate (Alendronate®) therapy to reduce bone loss [11]. As part of this randomized controlled trial, the DXA BMD measurement reproducibility (precision) was described for whole feet (metatarsal bones not specified) and distal phalanges. The sizes and locations of the regions of interest (phalanx, tarsus or metatarsus) were determined manually, though the software reported the bone density of a single region of interest. Ten repeat measurements of each foot were made, with repositioning between measurements. Information was not provided for the numbers of feet and individuals scanned, the number of raters (who made measurements), nor the resulting precision of the BMD measurements. After 6 months of alendronate therapy, the authors reported a 33% increase in whole foot BMD and a 25% increase in the distal phalanx BMD [11]; however, which bones gained densities were not reported, nor was it reported whether or not these increases exceeded measurement error (as determined from measurement precision). To date, no study has reported intra- and inter-rater precision for DXA measurements of whole metatarsals and sub-regions of metatarsals.

There were three purposes for our study: (1) to perform variance components analyses to determine the percentage of BMD and BMC measurement variation within and between raters making DXA measurements of whole bone and sub-regions of cadaver metatarsals; (2) to determine the intra- and inter-rater measurement precision and least-significant change (LSC) for BMD and BMC measurements; and (3) to determine the associations between DXA measurements of BMD and BMC and *ex vivo* fracture forces. We hypothesized that:

(1) intra- and inter-rater measurement variation would be low (each <2%); (2) intra- and inter-rater measurement precision would be high (that is, low root mean square standard deviations); and (3) BMD and BMC would be positively associated with *ex vivo* ultimate fracture force.

2. Materials and methods

This study was conducted under the rules and protocol assurances in accordance with the requirements of the Institutional Review Board and the Human Body Donor Program at Washington University School of Medicine, St Louis, MO. Our protocol was exempted from Human Subjects approval since it used cadaver specimens.

The right and left feet from 10 fresh cadavers were used in this study. After the Human Body Donor Program was notified regarding the study needs, the cadavers were obtained in a sequential order. Other than requesting specimens with both feet intact (*e.g.*, no partial or complete foot amputations) no pre-selection criteria were used. There were seven females and three males. Age ranged from 56 to 99 years (mean age = 83 ± 13 , standard deviation). The second (Met2) and third (Met3) metatarsals were excised from each foot. While denuding the bones of surrounding soft tissue, care was taken not to damage the periosteum. The bones were wrapped in saline-soaked gauze, placed in 75-mL specimen tubes and kept frozen at -20°C . On the day of testing prior to performing DXA scans, the metatarsals ($n = 40$ – that is, 10 cadavers $\times$ 2 feet $\times$ 2 metatarsals) were thawed to room temperature (~ 4 – 6 h).

2.1. Dual-energy X-ray absorptiometry (DXA)

All DXA scans were performed by a single certified clinical bone densitometry technician (KLB) using a Hologic Discovery W QDR Series bone densitometer (Bedford, MA, USA). Prior to scanning the metatarsals, a daily quality control calibration was performed according to the manufacturer's specifications, which required the use of an anthropomorphic spine phantom. With regular preventive maintenance, the phantom's BMD has remained stable over time. The excised metatarsals were individually scanned from the proximal (base) to distal (head) with the dorsal side up. To ensure that the metatarsals did not shift during the scans, they were placed in a plastic container filled with small plastic beads. Prior to scanning the metatarsals, a preliminary scan was performed on the container with beads only. The results indicated that the container with beads was radiolucent. After scanning, metatarsals were refrozen until mechanical testing.

Two raters individually made DXA measurements. Each scan was analyzed utilizing the Hologic lumbar spine analysis software. The whole metatarsal region of interest (ROI) was set to include the container's edges. To determine the area (cm^2) of each metatarsal, each rater utilized the bone mapping software to manually create an outline of the bone, and the software filled in the outline to complete the bone's boundary on the image. Bone mineral content (BMC in grams, g) of each metatarsal was determined based on the internal DXA calibration filter and the completed bone image. Bone mineral density (BMD) (g/cm^2) was determined by DXA software by dividing BMC by area. The metatarsals were divided unequally into three sub-regions (proximal, shaft and distal). Each rater placed two lines on the DICOM image displayed on the computer's monitor based on their knowledge of metatarsal anatomy. The raters varied the contrast of the image to aid in determining the transitional regions of the shaft to the proximal base and distal head sub-regions. The sub-regions of a metatarsal were determined by placing horizontal lines to separate the proximal base from the diaphyseal shaft and another horizontal line to separate the shaft from the distal head. By varying the image contrast, the rater was able to visualize the widening of the intramedullary canal and the cortical thinning of the shaft near the ends of the metatarsal.

This resulted in three separate unequal sub-regions of interest (sROI) for area, BMC and BMD measurements (Fig. 1A).

2.2. Raters and repeat measurements

The two raters made measurements of 20 Met2 and 20 Met3 bones. Each rater performed measurements twice (original and repeat) with an average time of one week between original and repeat measurements. Rater 1 (KLB) is certified by the International Society of Clinical Densitometry (ISCD) as a clinical bone densitometry technician (CBDT) and has 10 years of experience in performing and analyzing DXA scans. Rater 2 (DJG) has some experience in performing and analyzing DXA scans but does not have ISCD certification. Each rater was masked (blinded) to the other rater's measurements and did not share information regarding results.

2.3. Mechanical fracture testing

Only the right metatarsals were used in mechanical testing. Prior to the day of mechanical testing, the right Met2 and Met3 metatarsals ($n = 20$ bones) were removed from the freezer and thawed to room temperature. After the saline-soaked gauze was removed from a metatarsal, it was blotted dry and mounted for the bending test. Details of the bending test are reported elsewhere [12]. In brief, each metatarsal is loaded monotonically to failure (ultimate fracture) in 3-point bending in an Instron 8841 materials testing machine (Instron, Canton, MA, USA) (Fig. 1B). The span length is held constant at 33 mm for all metatarsals. The span length of 33 mm was chosen because it is the longest distance that ensured the vertical loading posts would be located within the metatarsal shaft for all bones even the shortest metatarsals tested. Fixture posts for 3-point bending were machined with 3-mm-diameter rounded tips to minimize the effect of local cortical buckling at the fixture sites and help ensuring that bone failure would occur due to bending forces rather than local contact stress. The central compressive load is applied at the span midpoint to the dorsal side of the metatarsal (inverted) (Fig. 1B). The two other forces are applied at equal distances from the mid point on the plantar sides of the metatarsal to mimic the predominant *in vivo* loading mode during the push-off phase of walking or running [13,14]. A pre-load equal to 10 N and a displacement rate equal to 0.1 mm/s is used, and the force-displacement data are sampled at 60 Hz. The ultimate fracture force (UFF) (in N) was defined as the maximum force registered between the onset of loading and metatarsal fracture [12] (Fig. 1C).

2.4. Statistical analysis

Each rater made 320 measurements (bones from 2 sides [left and right] $\times$ 2 bones [Met2 and Met3] $\times$ 2 time points [original and repeat] $\times$ 4 sites [whole metatarsal and 3 sROI] $\times$ 10 cadavers). The BMD and BMC values of each whole metatarsal and 3 sROI were entered into a variance components analysis to determine the percentages of the total variance attributable to the following random and nested factors: (1) side – metatarsals from the left and right feet; (2) bone – Met2 and Met3; (3) sROI – proximal, shaft and distal sub-regions of interest; (4) rater – Rater 1 and Rater 2; (5) time points – original and repeat measurements. The nesting of variables is indicated in Table 1. Because the investigators selected the cadavers based on sequential order of availability, cadaver was a fixed effect with the residual (within) variance component (not accounted for by the random effects) considered to be the variance attributable to cadaver. For the variance components analyses, we used the Bayesian method because negative variance components resulted with use of the restricted maximum likelihood (REML) method. The Bayesian method forces variance components to be positive and non-zero. Variance component analyses were performed with the Variability Platform available with JMP Statistical Software Release 10.0.0 (SAS Institute, Inc., Cary, NC).

To determine measurement precision, the original and repeat measurements were used to calculate root mean square standard deviation (RMS-SD) for BMD and BMC for the whole metatarsals and the 3 sROI [15–17]. In turn, the RMS-SD was used to calculate the least significant change (LSC) as follows:

$$\text{LSC} = \text{RMS} - \text{SD} \times 2.77$$

This formula uses the 95% statistical confidence level to calculate LSC. LSCs represent the magnitude of changes in measurement units needed to indicate that true biological changes have occurred and that the changes are not attributable to measurement errors (i.e., the inability to reproduce measurements) [17]. Separate calculations of RMS-SDs and LSCs were made for each rater for BMC and BMD. In addition, these calculations were made for the pooled measurements from both raters. An assumption in reporting DXA measurement precision for pooled data is that variances are equal for the data that is to be pooled [18,19]. To test for equality of variances, the O'Brien, Brown–Forsythe, Levene and Bartlett tests were used. To test for biases (that is, differences in means), multivariate analysis of variance (MANOVA) was used. For equality-of-variances testing, all *p* values were 0.72, and for MANOVA testing, all *p* values were 0.09, thus assumptions were met for data pooling.

To assess the associations between *ex vivo* 3-point bending and DXA measurements of the whole metatarsals and the 3 sROI, linear product-moment correlation coefficients (*r*) and coefficients of determination (*r*²) were calculated between UFF measurements and BMD and BMC measurements determined by Rater 1. An assumption for these determinations is that residuals are normally distributed. Plots of residuals were examined and no violation of normality was detected. The same calculations were performed for Rater 2 but the results for Rater 2 are not reported here (results are available from the authors upon request). Backward stepwise multiple regression analyses, were used to determine which of the following variables best predicted UFF for each metatarsal: (1) whole bone BMD, (2) shaft BMD, (3) whole bone BMC and (4) shaft BMC. Minimum corrected Akaike information criterion was used to choose the best model. With regard to our regression and correlation analyses, with alpha level set at 0.05, a 2-tailed test, and a sample size of 10, our study had a power of 80% to yield a statistically significant result. All statistical analyses were performed with Statistica Release 10 (StatSoft, Inc., Tulsa, OK), JMP Statistical Software Release 10.0.0 (SAS Institute, Inc., Cary, NC), and MedCalc Statistics for Biomedical Research Version 12.4.0.0 (MedCalc Software, Mariakerke, Belgium).

3. Results

3.1. Variance components, precision and least significant change

Table 1 contains the variance components and the percentages of variance that each component contributed to the total variances of BMD and BMC measurements. The between (inter-) rater variation represented 0.4% of the total variance and the intra-rater variation (that is the ability to repeat measurements by the same rater) represented 0.03% of the total variance. Most of the variance in DXA measurements of metatarsal BMD or BMC was due to the differences among cadavers (54.4% for BMD and 42.3% for BMC) and sub-region of the metatarsal (35.5% for BMD and 45.5% for BMC). Variance due to side (left and right) and variance due to bone (Met2 and Met3) contributed 6% of measurement variance.

Fig. 2A and B shows variability plots for BMD and BMC measurements. Table 2 contains the precision estimates as RMS-SD and LSC values for Rater 1 and both raters pooled for BMD and BMC for the whole metatarsal and sROI for the right Met2 and Met3. For the right Met2 shaft BMD measurements made by Rater 1, the RMS-SD was 0.011 g/cm² with a

LSC of 0.030 g/cm^2 . For the right Met3 shaft BMD measurements made by Rater 1, RMS SD was 0.006 g/cm^2 with a LSC of 0.016 g/cm^2 , thus (based on LSC values for Rater 1) to be 95% certain that real biological changes have occurred in shaft BMD of Met2 and Met3, the changes must be 0.03 g/cm^2 and 0.016 g/cm^2 respectively.

Table 3 shows the means and standard deviations for ultimate fracture forces (UFFs) and the means and standard deviations for BMD and BMC measurements for right Met2 and Met3 for Rater 1. The correlation coefficients (r) and coefficient of determination (r^2) for the associations of UFF with BMD and BMC are also shown in Table 3. Fig. 3A–D is regressions of UFF on BMD (these correspond to the correlations listed in Table 3. For Met2, a backward multiple stepwise regression analysis determined that shaft BMC was the best predictor of UFF. A similar analysis for Met3, determined that shaft BMD was the best predictor of UFF. In the two backward multiple stepwise regression analyses, no other variable was retained.

4. Discussion

DXA measurements of human metatarsal BMD and BMC have high intra- and inter-rater precision and are strongly correlated to *ex vivo* bone strength. This is the first study of human metatarsals to demonstrate the amounts of measurement variation attributable to within- and between-rater variability. The variance components analyses for metatarsals 2 and 3 demonstrated that less than 1% of measurement variation is attributable to rater variability, with most of the measurement variation (88%) being attributable to cadaver (subject) plus sub-regions of the metatarsals. Similarly, this is the first study to report the intra-rater and inter-rater measurement precision (RMS-SD) for DXA measurements of metatarsals.

Measurement precision and LSC of BMD and BMC vary by subregion of interest, bone and side with little variation attributable to rater or repeat measurement. Measurement precision is the extent to which a numerical result can be reproduced when no biological change has taken place [17a]. The advantage of expressing precision as the RMS-SD is the measurement variation (error) is expressed in the units of measurement instead of a percent of the variation. Measurement precision is used to calculate LSC, which is commonly used to make diagnostic and therapeutic decisions. For our study we chose 95% statistical confidence for LSC; thus LSC represents how large of a change in BMD or BMC must occur for it to be considered (with 95% confidence) a true (real) biological change and not change due to error (*e.g.*, equipment or rater error) [17b]. Methods for determining RMS-SD and LSC have been previously outlined in position papers [20] and a white paper [21]. The ISCD recommendations are to perform separate precision studies for each rater and each skeletal site; with the same single rater making all measurements for a study; and with each subject being measured serially using the same equipment (*e.g.*, for a given subject, serial scans must be made with the same equipment from the same manufacturer under the same measurement conditions). For determining clinical precision, the ISCD recommends 30 degrees of freedom [17a]. This can be achieved by performing two repeat scans and measurements on 30 subjects or by performing three repeat scans and measurements on 15 subjects. In our study, we used 40 bones from 10 pairs of cadaver feet, and each of our two raters made 320 measurements independently of one another. We used these measurements to demonstrate measurement variance and to calculate intra-rater and inter-rater precision. Although our sample size is smaller than recommended by the ISCD for determining clinical precision, our sample size is adequate for determining precision of DXA measurements of metatarsals. The ISCD requirement of 30 degrees of freedom prevents the upper 95% confidence limit of the RMS-SD from being 34% greater than the calculated value of precision [22]. To calculate the upper 95% confidence limit for RMS-SD, the asymmetric

chi-square distribution is used [15,16]. We provide an example for this calculation elsewhere [23]. The calculation of the upper 95% confidence limit for RMS-SD does not affect the calculation of RMS-SD, and to the extent that the cadavers that we used are representative of a larger sample of similar cadaver subjects, assessing a larger sample would not meaningfully change the values we calculated for RMS-SD and LSC although a larger sample would result in a tighter upper 95% confidence limits. The upper 95% confidence limits for the values of RMS-SD are available from the authors upon request.

We demonstrated that for metatarsal scans using the lumbar spine software there was little measurement variation between two independent raters with different levels of experience with DXA densitometry measurement. Prior studies assessing foot-bone density have been mostly limited to calcaneus measurements using dual X-ray and laser (DXL) [24,25] or quantitative ultrasonometry [26,27]. The calcaneus, however, is largely comprised of trabecular bone with only a thin surrounding cortical shell; therefore, any bone loss (or gain) of the calcaneus is presumably in the trabecular component of the bone and not in the cortical component of the bone. By contrast, the metatarsals are largely comprised of cortical bone throughout the shaft sub-region, so if cortical bone loss or gain is anticipated, metatarsals are more appropriate bones to assess.

Few studies have reported BMD measurements of human metatarsals. In previous studies using DXA to measure BMD of the metatarsals, only the middle 1–1.25 cm of excised metatarsals was assessed [9,10]. These studies reported coefficients of variation from repeated measurements ranging from 1.2% to 2.3% with repositioning and 1.8% without repositioning. In both studies, BMD measurements were reliably reproduced indicating that it is feasible to use DXA for precise BMD measurements of sites other than those for which the manufacturer had originally intended measurements to be made.

In our study, for both Met2 and Met3, lower bone density and content in the metatarsal shaft region resulted in lower fracture forces. Multiple stepwise regression analyses demonstrated that for metatarsal 2, shaft BMC was the best predictor of ultimate fracture force, whereas for metatarsal 3, shaft BMD was the best predictor of ultimate fracture force. Our results are in agreement with those previously published for the central 1 cm of the shafts of metatarsals 2 and 3 [9]. Our results extend the findings of another study that used the 4-point bending test to determine ultimate fracture force whereas we used the 3-point bending test [9]. In the study that used the 4-point bending test, the sample consisted of 11 cadavers (with a mean age of 63 years) whereas our sample of 10 cadavers (with a mean age of 83 years) was 20 years older. Nevertheless, the r^2 values of 0.83 and 0.81 for Met2 and Met3 determined in the published study are similar to the r^2 values that we determined. The results of our study and previous studies help to validate DXA for BMD and BMC metatarsal measurements as predictors of fracture strength. Previous studies [9,10] were limited to the middle 1–1.25 cm of the shaft for their DXA measurements and our study utilized the entire metatarsal including sub-regions for the DXA measurements and analyses. Our results expand the knowledge of the metatarsal subregions that are prone to fracture and trauma including Freiberg's infraction of the metatarsal head [28].

A methodological limitation is the metatarsals used for this study were thawed and refrozen prior to the fracture testing. While previous studies reported freezing of human femora at -20°C for 20 days caused no change in bending properties [29] and specimens frozen at -20°C or -70°C for 14 days had no adverse effects on bone stiffness [30], we did not investigate the impact of thawing and re-freezing on biomechanical properties of the metatarsals. Another limitation is that we did not perform repeat scans after repositioning as recommended by the ISCD for clinical densitometry. The focus of our study was to assess two raters' (with different levels of experience) variation in measurements of whole

metatarsals and sub-regions of interest of metatarsals. Though our study did not follow strict clinical recommendations, our study's methods simulated DXA analysis of metatarsal BMD and BMC and is similar to protocols that would be employed in randomized, controlled, clinical trials (RCT) that would use metatarsal BMD or BMC as either a primary or secondary outcome [26,31]. Most clinical densitometry protocols of either the hip or lumbar spine perform serial scans to assess changes in measurements in response to disease progression or pharmacological therapies [16]. When performing repeat serial clinical DXA scans, the densitometry technician typically has access to and reviews the measurements obtained from a previous scan [32].

A thorough assessment of measurement precision of DXA measurements of metatarsal BMD and BMC of the feet of living subjects requires further study. Obtaining measurements similar to ours for the whole metatarsal and sub-region BMD and BMC may present difficult challenges to even the most skilled densitometry technician; this is because *in vivo*, the proximal bases of the metatarsals overlap with each other or articulate closely to the cuneiform bones.

Future studies using DXA and analysis with the lumbar spine software will be conducted using *in vivo* scans of intact feet. The major advantage of using DXA compared with quantitative computed tomography [33] is that DXA produces a low amount of radiation exposure and has quick scan and analysis times. DXA analyses of feet could assist in identifying patients who have low metatarsal BMD or BMC and may be at risk of having stress or neuropathic fragility fractures.

5. Conclusions

DXA measurements of human metatarsal BMD and BMC have high intra- and inter-rater precision and are strongly correlated to *ex vivo* bone strength. Least significant changes of whole metatarsal and shaft can be used to detect changes over time that exceed measurement error and reflect true biological changes. DXA measurements of metatarsal BMD and BMC are well suited for use in clinical practice and randomized clinical trials to assess the impact of disease progression, therapeutic interventions and pharmacological agents on pedal bone health.

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Fig. 1. (A) Metatarsal subregion analysis using DXA. (B) Human metatarsal mounted in an Instron for 3-point bending to fracture. (C) Force-displacement curve for human metatarsal. $F_{ultimate\ fx}$ is ultimate fracture force.

Fig. 2. Variability plots for bone mineral density (BMD) (A) and bone mineral content (BMC) (B). The points of the diamonds are the 95% confidence intervals. The lines in the middle of the diamonds are mean values. Time is 1st original and 2nd repeat measures; Rater is Rater 1 and Rater 2; Sub-region is distal, proximal and shaft; Bone is metatarsal 2 (Met2) and 3 (Met3); Side is left or right.

Fig. 3.

Regression plots of ultimate fracture force with whole metatarsal BMD (A); shaft BMD (B); distal (head) BMD (C); and proximal (base) BMD (D).

Table 1

Bayesian variance component estimates for DXA measurements of human metatarsal bone mineral density (BMD) and bone mineral content (BMC).

Component	BMD		BMC	
	Variance component	Percent of total	Variance component	Percent of total
Side	0.00047644	5.1	0.01774098	6.3
Bone [side]*	0.00042456	4.5	0.01570191	5.5
Sub-region [side, bone]	0.00331630	35.5	0.12925519	45.5
Rater [side, bone, sub-region]	0.00003840	0.411	0.00091229	0.3214
Time [side, bone, sub-region, rater]	0.00000264	0.0283	0.00006311	0.0222
Subject (cadaver)	0.00508458	54.4	0.12018074	42.3
Total	0.00934291	100	0.28385423	100

Side is left or right; bone is Met2 or Met3; Sub-region is distal, proximal or shaft; Rater is Rater 1 or Rater 2; Subject is cadaver sample. [*] indicates nesting – e.g., bone nested within side.

Table 2

Mean, root mean square- standard deviation (RMS-SD) and least significant change (LSC) estimates for human-metatarsal, DXA measurements of bone mineral density (BMD) and bone mineral content (BMC) for Rater 1 and for Pooled Raters. Units of measurement are g/cm² and g.

BMD (g/cm ²)	Right metatarsal 2				Right metatarsal 3			
	Whole bone	Distal	Shaft	Proximal	Whole bone	Distal	Shaft	Proximal
Rater 1								
Mean	0.310	0.209	0.378	0.313	0.288	0.192	0.334	0.304
RMS-SD	0.010	0.006	0.011	0.018	0.004	0.009	0.006	0.008
LSC	0.027	0.017	0.030	0.049	0.012	0.025	0.016	0.021
Pooled raters								
Mean	0.312	0.211	0.375	0.316	0.289	0.195	0.332	0.305
RMS-SD	0.005	0.008	0.012	0.009	0.007	0.007	0.011	0.017
LSC	0.013	0.023	0.032	0.026	0.020	0.020	0.029	0.048

BMC (g)	Right metatarsal 2				Right metatarsal 3			
	Whole bone	Distal	Shaft	Proximal	Whole bone	Distal	Shaft	Proximal
Rater 1								
Mean	3.03	0.55	1.54	0.94	2.61	0.44	1.28	0.89
RMS-SD	0.086	0.036	0.062	0.072	0.062	0.025	0.088	0.097
LSC	0.238	0.100	0.171	0.201	0.172	0.068	0.245	0.268
Pooled raters								
Mean	3.06	0.55	1.55	0.95	2.63	0.43	1.32	0.88
RMS-SD	0.078	0.023	0.093	0.045	0.066	0.029	0.116	0.070
LSC	0.216	0.063	0.257	0.125	0.182	0.080	0.323	0.194

Table 3

Mean $\pm$ SD, correlation coefficients (r) and coefficients of determination (r^2) of 2nd and 3rd metatarsal bone mineral density (BMD) and bone mineral content (BMC) with ultimate fracture force (UFF).

	Right metatarsal 2				Right metatarsal 3			
	Mean $\pm$ SD	r (95% CI)	r^2	p	Mean $\pm$ SD	r (95% CI)	r^2	p
UFF (N)	572 $\pm$ 299				406 $\pm$ 244			
Whole BMD (g/cm ²)	0.308 $\pm$ 0.075	0.90 (0.63–0.98)	0.81	<0.01	0.288 $\pm$ 0.080	0.92 (0.69–0.98)	0.84	<0.01
Whole BMC (g)	3.02 $\pm$ 0.94	0.89 (0.59–0.97)	0.79	<0.01	2.60 $\pm$ 0.95	0.94 (0.77–0.99)	0.89	<0.01
Shaft BMD (g/cm ²)	0.376 $\pm$ 0.111	0.82 (0.39–0.96)	0.67	<0.01	0.333 $\pm$ 0.104	0.97 (0.86–0.99)	0.93	<0.01
Shaft BMC (g)	1.56 $\pm$ 0.63	0.93 (0.72–0.98)	0.86	<0.01	1.32 $\pm$ 0.51	0.87(0.54–0.97)	0.76	<0.01
Distal BMD (g/cm ²)	0.207 $\pm$ 0.04	0.76 (0.25–0.94)	0.58	0.01	0.191 $\pm$ 0.045	0.86 (0.49–0.97)	0.73	<0.01
Distal BMC (g)	0.56 $\pm$ 0.17	0.63 (0.01–0.90)	0.40	0.05	0.43 $\pm$ 0.18	0.89 (0.60–0.97)	0.79	<0.01
Proximal BMD (g/cm ²)	0.307 $\pm$ 0.07	0.82 (0.39–0.96)	0.67	<0.01	0.302 $\pm$ 0.09	0.80 (0.33–0.95)	0.63	0.01
Proximal BMC (g)	0.91 $\pm$ 0.26	0.54 (–0.13–0.87)	0.29	0.10	0.85 $\pm$ 0.34	0.84 (0.44–0.96)	0.70	<0.01