



Published in final edited form as:

J Racial Ethn Health Disparities. 2017 August ; 4(4): 587–598. doi:10.1007/s40615-016-0262-8.

Racial Differences in Bone Microarchitecture and Estimated Strength at the Distal Radius and Distal Tibia in Older Adolescent Girls: A Cross-Sectional Study

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Abstract

Background—Previous studies have demonstrated that an individual's race and ethnicity are important determinants of their areal bone mineral density (aBMD), assessed by dual-energy x-ray absorptiometry. However, there are few data assessing the impact of race on bone microarchitecture and strength estimates, particularly in older adolescent girls and young adults. We hypothesized that bone microarchitecture and strength estimates would be superior in Blacks compared to White and Asian American adolescent girls and young adults of similar age based on reports of higher aBMD in Blacks.

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Conflicts of Interest

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Disclosures: All authors state that they have no conflicts of interest.

Methods—We assessed BMD using DXA, bone microarchitecture at the distal radius and distal tibia using high resolution peripheral quantitative computed tomography (HRpQCT) and estimated measures of bone strength using micro-finite element analysis (FEA) in 35 White, 15 Asian-American and 10 Black girls 14–21 years.

Results—After controlling for height, most DXA measures of aBMD and aBMD Z-scores were higher in Black girls compared with Whites and Asian-Americans. HRpQCT and FEA showed that at the distal radius, Blacks had greater cortical perimeter, cortical area, trabecular thickness, trabecular BMD, estimated failure load and stiffness than the other two groups. For the distal tibia, trabecular number and BMD were higher in Blacks than Asian-Americans.

Conclusions—Particularly at the distal radius, adolescent and young adult White and Asian-American girls have less favourable bone microarchitecture and lower bone strength than Blacks, possibly explaining the lower risk of fracture seen in Blacks.

Level of Evidence—Level II

Keywords

Race; microarchitecture; finite element analysis; failure load

INTRODUCTION

Osteoporosis affects women and men of all races and remains under-diagnosed and under-treated. Particularly, the lifetime risk of an osteoporosis related fracture is as high as 40% in White women (1, 2). In order to develop strategies to optimize bone health in women and prevent osteoporosis, it is essential to study determinants of low bone density in the general population. This is particularly important in the adolescent and young adult years, a critical time for bone mineral acquisition, and a time when effective treatment for vulnerable groups with risk factors for low bone mineral density (BMD) may optimize acquisition of peak bone mass and reduce future fracture risk (3).

There are many determinants of BMD in any individual, including genetic factors such as height, lean mass, and menarchal age which account for up to 70% of the variability in peak BMD, nutritional status, exercise activity, calcium and vitamin D intake, and hormonal changes. In addition, race appears to be an important determinant, as adolescent and adult Whites tend to have lower BMD than Blacks (4–9) and are variably reported to have higher, no different, or lower BMD than Asians or Asian Americans (3, 10–12). Moreover, race may be a determinant of bone strength and therefore fracture risk, and the incidence of hip fractures is reported to be higher in White versus Black and Asian women (13, 14). Of note, most studies thus far have relied on dual-energy x-ray absorptiometry (DXA) to measure areal bone mineral density (aBMD), which does not adjust for body or bone size, and does not differentiate between cortical and trabecular bone compartments.

With advances in imaging technology and availability of high resolution peripheral quantitative computed tomography (HR-pQCT), it is now possible to obtain measures of volumetric bone density and microarchitecture of cortical and trabecular bone at peripheral skeletal sites with minimal radiation exposure (15). These high resolution images can also be

utilized to compute estimates of bone strength and assess the mechanical load distribution across the two compartments. HR-pQCT measurements have been used to show that adult women and men with a history of fractures have lower total and trabecular volumetric bone density (vBMD), cortical thickness, trabecular number and trabecular thickness, and higher trabecular separation compared to subjects with no history of fractures (16–20). Investigators are beginning to examine bone architecture (using peripheral QCT) (21, 22) and microarchitecture (using HRpQCT) (23–25) across racial groups, and have reported differences in Blacks versus Whites (21, 22, 25) and Asians versus Whites (23, 24). However, there are limited data regarding bone microarchitecture (assessed using HR-pQCT) and estimates of bone strength [assessed using micro-finite element analysis (μ -FEA)] in older adolescent girls, a time critical for bone accrual, across all three racial groups, namely Blacks, Asian Americans and Whites.

In this study, we sought to assess (i) whether bone microarchitecture, as assessed by HR-pQCT, and estimated bone strength, as assessed using μ -FEA, differ in White, Asian American, and Black adolescent girls, and (ii) determinants of differences in microarchitectural and estimated strength parameters. We hypothesized that bone microarchitecture and strength estimates would be superior in Black adolescent girls compared to White and Asian American adolescent girls.

MATERIALS AND METHODS

Subject Selection

We enrolled 60 adolescent girls and young women between the ages of 14–21 years old (35 self-identified as White, 15 as Asian-American and 10 as Black) between 2010–2014 from the control groups of two ongoing bone density studies in adolescent and young adult women. Subjects were recruited through medical clinics and advertising in local newspapers and colleges throughout greater Boston, MA. Inclusion criteria included a bone age of 14 years, a BMI between the 10th and 90th percentiles for age, and at least nine menses in the preceding year without a history of late menarche. Exclusion criteria included use of medications or underlying medical conditions that may affect bone metabolism. Twenty-six screened participants did not participate in the study: 19 did not meet weight criteria, four did not meet criteria for menses, and three lost interest in the study after the screen. To comply with ethical consideration denoted by the World Medical Association's Declaration of Helsinki, the study was approved by the Institutional Review Board of Partners Health Care. Informed consent was obtained from subjects 18 years of age, and from parents of subjects who were <18 years old. Informed assent was obtained from subjects < 18 years of age.

Experimental Protocol

We obtained a complete history from our subjects, including self-identification of race. Subjects who reported belonging to more than one race were classified as Black or Asian if either parent was from these respective races. No participant identified as belonging to both Black and Asian races. Height was measured using a wall-mounted stadiometer as the

average of three separate measurements. Weight was measured on an electronic scale. BMI was calculated as weight (in kilograms) divided by height (in meters)².

Bone age was assessed using the methods of Greulich and Pyle (26), and body composition, including fat mass, lean mass and percent body fat were assessed using dual-energy X-ray absorptiometry (DXA) (Hologic 4500A, Waltham, MA). Bone mineral density (BMD) of the spine, hip, and whole body was also assessed by DXA. In order to control for differences in height amongst groups, bone mineral apparent density (BMAD) of the lumbar spine was calculated using an established formula [bone mineral content of lumbar vertebrae 2–4/ (bone mineral area of lumbar vertebrae 2–4)^{1.5}](27). Bone density Z-scores were not race adjusted.

Participants completed a written 4-day food and supplement diary to assess dietary intake (three weekdays and one weekend day), validated for use in young women (28, 29). Description of portion sizes and preparation methods were recorded and dietary intake data (from food and supplements) were analyzed by the Bionutrition Core of the Clinical Research Center of our institution using Nutrient Data System for Research software version 2008 developed by the Nutrition Coordinating Center (NCC), University of Minnesota, Minneapolis, MN (30). In a comparison of various methods of dietary intake assessment, the 4-day food records had a higher correlation to estimates of food consumption than the 24 hour dietary recall and a detailed quantitative two month history. The analysis of the food record includes averages of total caloric intake, as well as intake of specific macronutrients and micronutrients. Supplement intake was also recorded and added to the corresponding nutrient totals from food intake. The food record was completed within two weeks of the study visit.

Areal Bone Mineral Density Assessment

DXA (Hologic QDR-Discovery A, Apex software version 13.3; Hologic Inc., Waltham, MA) was used to assess spine, total hip, femoral neck, and whole body areal BMD (aBMD), as well as body composition. The coefficients of variation for BMD, fat mass, and lean mass for this software are 0.8% to 1.1%, 2.1%, and 1.0%, respectively. The same scanner and software version were used for all participants.

Bone Microarchitecture

Trabecular and cortical bone density and microarchitecture at both the distal radius and tibia were assessed using HR-pQCT (XtremeCT, Scanco Medical AG, Basserdorf, Switzerland) in all participants. Scans were acquired at 82 μm isotropic voxel size. During scan acquisition, the non-dominant arm or leg of the patient (31) was immobilized in an anatomically formed carbon fibre shell. An antero-posterior scout view was used to manually place a reference line at the endplate of the radius or tibia. The first CT slice was acquired 9.5 mm proximal to the reference line of the distal radius and 22.5 mm proximal to the reference line of the distal tibia. At each skeletal site, 110 CT slices were acquired extending approximately 9 mm in the axial direction. The effective radiation dose was less than 5 μSv per measurement.

Using semi-automated software, total, trabecular and cortical volumetric bone density were determined as were multiple aspects of bone microarchitecture including total, cortical and trabecular cross-sectional area, cortical thickness and perimeter, trabecular thickness, trabecular number and trabecular separation. In addition, detailed cortical bone analysis was performed by a semi-automated segmentation technique as previously described (32–35) to determine cortical porosity, cortical pore volume, and cortical pore diameter. We also used the 3D HR-pQCT images to perform linear μ -FEA and calculate apparent biomechanical properties under uniaxial compression, as previously described (17, 19, 20, 35–37). We calculated estimates of stiffness and failure load, and the proportion of load carried by the cortical and trabecular compartments (%) at the distal and proximal ends of the region of interest. Short-term reproducibility, computed from repeat scans performed after repositioning on 19 healthy young subjects age 20 to 30 years recruited through a different protocol, ranged from 0.2% to 1.7% for density values and from 0.7% to 8.6% for microarchitecture variables, consistent with prior reports (16). Short term reproducibility ranged from 2.1 to 4.8% for variables derived from μ -FEA.

Biochemical Analysis

25-hydroxyvitamin D [25(OH)D] was determined with a chemiluminescent immunoassay (DiaSorin, Stillwater, MN; sensitivity 4 ng/ml; intraassay coefficient of variation 2.9–5.5%).

Statistical Methods

JMP Statistical Discoveries (version 5.01; SAS Institute, Inc., Cary, NC) was used for all statistical analyses. Data are reported as means \pm standard deviation (SD). P values of less than 0.05 were considered significant. We first conducted an ANOVA or the Kruskal-Wallis test to assess whether a significant difference existed among the three groups (depending on whether or not the data were normally distributed). If a significant difference was noted on the overall ANOVA, the Tukey-Kramer analysis was performed to determine which groups were significantly different, while controlling for multiple comparisons. We similarly controlled for multiple comparisons when the Kruskal-Wallis test was employed by using the Steel-Dwass test. Pearson's correlations were used to determine associations of height, BMI, lean mass, menarchal age and 25(OH)D status with bone microarchitectural parameters. Because height, lean mass and 25(OH)D levels are important determinants of BMD and microarchitectural parameters and differed among study groups, and because menarchal age is a very important determinant of bone density and microarchitecture (even though it did not differ across groups), we next used multivariate analysis to control first for (i) height alone (as height impacts bone size parameters), and then for (ii) height, lean mass, menarchal age and 25(OH)D levels, while assessing differences among groups for radial and tibial bone microarchitecture and estimated bone strength. We did not include BMI in this multivariate model because height and lean mass, which were included in the model, correlated strongly with BMI. We used stepwise regression analysis with race, height, lean mass, menarchal age and 25(OH)D levels entered into the model to determine the percent variability of specific microarchitectural and FEA parameters independently determined by combinations of these covariates. We had sufficient power to adjust for six variables in our analysis.

RESULTS

Subject Characteristics

No differences were noted among the groups for chronological age, bone age, age of menarche, weight, BMI and total fat mass (Table 1). Asian Americans were shorter than Whites and trended to be shorter than Blacks. Lean mass was lower, and percent trunk fat and trunk to extremity fat ratio higher in Asian Americans than the other two groups. Although reported calcium and vitamin D consumption did not differ among groups, 25(OH)D levels were highest in White girls, followed by Asian Americans, and lowest in Blacks.

Areal Bone Mineral Density

Lumbar spine, femoral neck and whole body aBMD and corresponding Z-scores, as well as spine BMAD were higher in Blacks compared to Asian Americans and Whites (Table 1). Femoral neck BMD and BMD Z-scores were also higher in Whites than in Asian Americans. Hip BMD Z-scores were higher in Blacks and Whites compared with Asian Americans. After controlling for height, Blacks had higher BMD and BMD Z-scores at the spine, femoral neck and whole body than Asian Americans and Whites, and higher hip BMD Z-scores than Asian Americans. After controlling for height, lean mass, menarchal age and 25(OH)D levels, compared with Black participants, (i) Asian Americans had lower spine BMAD, total hip and femoral neck BMD and BMD Z-scores, and whole body BMD Z-scores, and (ii) Whites had lower femoral neck BMD and BMD Z-scores and lower whole body BMD Z-scores (Table 1).

Bone Microarchitecture and Estimated Strength Parameters

A. Distal Radius—Figure 1 shows scans from Black, Asian American and White participants. Table 2 shows HRpQCT and FEA data for the distal radius (non-weight bearing bone) in Black, Asian American, and White participants.

Size parameters: Cortical perimeter was higher in Black than Asian American and White participants, and cortical thickness and area were higher in Blacks than Whites. After controlling for height, Blacks had greater cortical thickness and perimeter than Asian Americans and Whites, and greater cortical area than Whites. After controlling for height, lean mass, menarchal age and 25(OH)D levels, cortical thickness remained higher in Blacks than Whites.

Density parameters: Trabecular vBMD was higher in Blacks than in Asian Americans, with differences persisting after multivariate adjustment. Also, after controlling for height, Blacks had higher trabecular and total vBMD than Whites.

Microarchitectural parameters: At the radius, trabecular thickness was higher in Black participants than in Whites, even after adjusting for height. In addition, after controlling for height, trabecular thickness was higher in Blacks than Asian Americans. These differences were lost after also controlling for menarchal age, lean mass and 25(OH)D levels. The races did not differ for trabecular number or separation, or cortical porosity.

Estimated strength parameters: Estimated stiffness and failure load of the distal radius was higher in Black compared with White and Asian American participants, and these differences persisted after controlling for height, and trended to remain significant after also controlling for lean mass, menarchal age, and 25(OH)D levels.

B. Distal Tibia—Table 3 shows HRpQCT and FEA data for the distal tibia (non-weight bearing bone) in Blacks, Asian Americans, and White girls and young women.

Size parameters: In contrast to the radius, cortical perimeter, area and thickness were similar in Whites and Blacks at the distal tibia. Cortical perimeter was greater in Whites than Asian Americans, however, this difference was lost after controlling for covariates. Furthermore, cortical thickness and area did not differ between Whites and Asian Americans.

Density parameters: Trabecular vBMD was higher in Blacks compared with Asians after controlling for height, but not when we also controlled for lean mass, menarchal age and 25(OH)D levels. Cortical and total volumetric density did not differ among groups.

Microarchitectural parameters: Trabecular number was lower in Asian Americans compared with Whites in the unadjusted model, and lower in Asian Americans than in Blacks after controlling for height, but not when we also controlled for lean mass, menarchal age and 25(OH)D levels. Trabecular separation was higher in Asian Americans compared with Whites in the unadjusted model, but not after controlling for covariates. Trabecular thickness did not differ among groups. Cortical porosity and pore volume were higher in Whites compared with Asian Americans, but these differences did not persist after controlling for covariates.

Estimated strength parameters: Estimated stiffness and failure load trended highest in Blacks. Differences were no longer apparent after controlling for height and other covariates.

Associations of HRpQCT and FEA measures with Covariates

Distal Radius—Menarchal age, height and lean mass correlated with several bone parameters (Table 4). We found no association of **BMI** or **25(OH) D levels** with microarchitectural parameters, but a positive association was observed of BMI with strength estimates. In a stepwise regression model (with race, height, lean mass, menarchal age and 25(OH)D levels entered into the model), race and menarchal age accounted for 28.6%, 14.7%, and 22.8% of the variability in cortical thickness, area and percent cortical area. Race and lean mass explained 27.0% of the variability in cortical perimeter, and with height predicted 42.7% and 33.4% of the variability in trabecular vBMD and trabecular thickness. Race, menarchal age and lean mass explained 28.7% of the variability in stiffness, while menarchal age and lean mass explained 30.7% of the variability in failure load. Race was not a determinant of cortical porosity, pore volume, pore diameter, trabecular number and separation, and cortical and total vBMD. Menarchal age explained 11.1% of the variability in cortical vBMD, and with height explained 33.0% of the variability in total vBMD. Height

alone predicted 9.0%, 7.6%, 11.0% and 17.6% of the variability in trabecular number and separation, and cortical pore volume and percent porosity respectively.

Distal Tibia—Associations of **menarchal age, height, BMI, lean mass** and **25(OH)D** levels with bone parameters are shown in Table 5. In a stepwise regression model (with race, height, lean mass, menarchal age, and 25(OH)D levels entered into the model), race was the sole predictor of trabecular number and separation, accounting for 11.8% and 13.5% of the variability in these parameters. Race and lean mass predicted 24.7% of the variability in cortical percent porosity. Height and lean mass predicted cortical thickness, perimeter and area, percent cortical area, trabecular and total vBMD, and estimated stiffness and failure load (accounting for 38.7%, 59.8%, 39.7%, 42.0%, 28.1%, 42.7%, 40.3% and 40.3% of the variability in these parameters respectively). Menarchal age was an independent determinant of trabecular thickness, lean mass of cortical pore volume, and height of cortical vBMD (14.0%, 19.4% and 24.6% of the variability explained).

Discussion

We report significant differences in areal and volumetric BMD and bone microarchitecture in Black, White and Asian American girls and young women 14–21 years old. Compared with Asian Americans and Whites, Blacks had higher measures of areal BMD at the spine, femoral neck and whole body, higher measures of trabecular vBMD and greater estimated stiffness and failure load at the distal radius, even after controlling for height. However, at the weight-bearing distal tibia, there were no differences among races for estimates of bone strength.

Measures of areal BMD at the spine, femoral neck and whole body were higher in Black participants compared with Whites and Asian Americans, as was spine BMAD, while total hip BMD was higher in Blacks and Whites compared with Asian Americans. Although areal BMD is susceptible to artifactual lowering in shorter individuals (27) and Asian Americans were overall the shortest group in this study, differences among groups persisted after controlling for height. Lean mass, an important positive determinant of bone density, was lower in Asian Americans than in Blacks and Whites. Menarchal age, an important inverse determinant of bone density (38–40), did not differ among groups (and is thus unlikely to explain differences across groups). 25(OH)D levels positively predict bone density in some studies (41), and were higher in Whites than Blacks. In this study, after controlling for height, lean mass, menarchal age and 25(OH)D, differences among groups for lumbar spine BMD and BMD Z-scores were lost (though groups continued to differ for lumbar spine BMAD, a height adjusted measure of BMD). However, even after controlling for these covariates, compared with Asian Americans, Blacks had higher spine BMAD, and total hip BMD and BMD Z-scores, and compared with Asian Americans and Whites, had higher femoral neck BMD and femoral neck and whole body BMD Z-scores. Our data are consistent with reports of higher BMD in Blacks than Whites (4–9, 42), although few studies have compared adolescent girls and young women of all three racial groups in a single study. Higher aBMD in Whites than Asian Americans at the hip and femoral neck is consistent with published reports in adults and adolescent girls (24, 43).

Although bone density can predict fracture risk, bone microarchitecture and FEA strength estimates are associated with fragility fractures independent of aBMD (17, 18, 44). Compared to non-fracture subjects, adult fracture subjects have lower cortical density (16, 18, 44), cortical thickness (45), trabecular density (16–18), thickness (17, 45) and number (16, 18), and higher trabecular separation (16–18). A few studies have used HR-pQCT and FEA to assess differences in Chinese American versus White women, and a few have utilized pQCT or histomorphometry to assess differences in Black versus White prepubertal children or late adolescent girls. However, studies in adolescent girls have not utilized HRpQCT or FEA to assess differences in microarchitecture and bone strength in White, Asian American and Black girls.

In our study, at the non-weight bearing distal radius Blacks had greater estimated bone strength (stiffness and failure load) measured using FEA compared with Whites and Asian Americans, and these differences persisted after controlling for height, and trended to remain significant after also controlling for lean mass, menarchal age, and 25(OH)D levels. Another study in adolescent girls using pQCT reported higher bone strength at the distal radius in Blacks than Whites, however, these differences were no longer evident after controlling for bone size (21). It should be noted that pQCT does not measure bone microarchitecture, and the previous study did not use FEA to estimate bone strength. A study using pQCT in children also reported greater bone strength at the radius in Blacks versus Whites, attributable to greater vBMD (22), as did a study using HRpQCT in postmenopausal women (25).

Our data suggest that Black girls and young women are at a lower risk of forearm fractures, or conversely, that Whites and Asian Americans are at a higher risk of such fractures. Although data are limited, there is some evidence that White girls are at a higher risk for fractures than Black girls, particularly at the upper limb (46). Specific microarchitectural parameters that may explain this include differences in bone size (as indicated by greater cortical perimeter), and in cortical and trabecular thickness, all of which were higher in Blacks compared with Whites and Asian Americans after controlling for height. Our data are consistent with histomorphometry studies in children that reveal greater cortical thickness in Blacks compared with Whites at the iliac crest (47), and with an HR-pQCT study in adults showing more favorable cortical parameters in postmenopausal African American women compared to Caucasians (25). Additionally, histomorphometric studies have reported higher trabecular thickness in Black compared with White adults (48). However, unlike studies in adults, we did not find thicker cortices (23, 24, 49) and trabeculae (23, 49) in Asian Americans compared with Whites. It is possible that unlike Whites, Asian Americans continue to increase their cortical and trabecular thickness through the adult years. However, given that most bone acquisition occurs in the perimenarchal years, it is more likely that Whites have relatively greater bone loss than Asian Americans in adulthood.

Cortical porosity, trabecular number and separation did not differ among groups at the distal radius. In adult women, trabecular number has variably been reported to be lower (23, 24), no different (49) or higher (43) in Chinese Americans compared to Whites. Also, studies suggest lower total (23, 24, 49) and trabecular cross-sectional area in Asian American compared with Caucasian women (23). In our study of adolescent girls, although trends

were similar, differences between Asian Americans and Whites were not significant for bone size at the radius.

Cortical vBMD at the distal radius did not differ among groups, however, trabecular vBMD was higher in Blacks than in Asian Americans, even after controlling for covariates, and was higher in Blacks compared with Whites and Asian Americans after controlling for height alone. In adult women, some studies have reported lower cortical vBMD in Whites compared with Chinese Americans (23, 24), and either no differences (23), or lower trabecular vBMD in Whites compared with Chinese Americans (49). We found no differences between Asian Americans and Whites for any microarchitecture or strength parameter at the distal radius, suggesting that racial differences between Asians and Caucasians are not attributable to differences in bone acquisition, but perhaps to differences in age-related bone loss in adulthood.

Interestingly, differences among groups were less marked at the weight-bearing distal tibia. Although White participants had greater cortical perimeter and trabecular area than Asians, these differences were not significant after controlling for covariates. Our data are similar to a study in adults that reported higher tibial total and trabecular cross-sectional area in Whites compared with Chinese Americans, and a lack of differences after controlling for height and weight (23). White girls and young women in our study had higher cortical porosity than Asian Americans; however, this difference was no longer significant after controlling for covariates. We found inverse associations of height with cortical porosity, which may be related to older age being associated greater cortical porosity, pore volume and diameter (50), and older age being associated with taller heights in adolescents. There were no differences among groups for tibial trabecular thickness, in contrast to reports of lower trabecular thickness in Whites compared with Chinese Americans (23, 24). However, trabecular number was lower and separation greater in Asians than Whites, consistent with a study that reported similar findings in Chinese American compared with White women (23, 24). We found lower trabecular vBMD in Asian Americans than Blacks after controlling for height (but not all covariates). Total and cortical vBMD did not differ across groups, in contrast to reports of higher total vBMD in Chinese Americans than Whites (23), and higher cortical vBMD in Black compared with White adolescents (21).

Differences among groups for cortical porosity, and trabecular number, spacing and density at the distal tibia did not translate to differences in estimated bone strength in our study. Studies in adult women have similarly reported no differences in Chinese Americans and Whites for bone stiffness at the distal tibia (24). In children and also older adolescent girls, however, bone strength at the tibia using pQCT was reported to be higher in Blacks than Whites (21, 22). Similarly, higher strength estimates have been reported at the tibia in African American compared with White post-menopausal women using HRpQCT (25). Of note, adult Asian American women have lower fracture risk than White women (51). It is possible that even in the absence of marked differences in bone parameters in adolescent Asian Americans compared with Whites, there may be differences in the rate and pattern of age-related bone loss in early adulthood that contributes to variations in skeletal fragility. Furthermore, persistence of lower weight and shorter height in Asian Americans could result in lower impact during falls and lower fractures rates than in heavier and taller women.

Limitations of this study include its cross-sectional nature and inability to correlate strength parameters with fracture rates, as the latter requires a much larger sample size. Furthermore, the study had a relatively modest sample size that may have limited our ability to detect differences between groups for some variables. Nonetheless, our data do provide important and novel information regarding differences between races for bone structure and strength in older adolescent girls and young women.

In conclusion, our preliminary data suggest that Blacks are at an advantage over their White and Asian American peers with more favorable bone microarchitecture that may contribute to lower fracture risk at the forearm. Our data also suggest that some of the racial differences in BMD and microarchitecture seen in adults are well established during the adolescent years. Mechanisms underlying these differences remain to be elucidated. Future studies are necessary that examine bone density, structure and strength parameters in adolescents and young adults across the various races using a larger number of participants in the different racial groups, as well as the determinants of these differences. Studies of these bone parameters are also necessary in adolescent boys and young adult men.

Acknowledgments

All authors have made substantial contributions to the manuscript. MM worked on study conception and design, data acquisition, analysis and interpretation, and drafted the manuscript. KEA, AF and MLB worked on data acquisition and interpretation and revised the manuscript critically for intellectual content. KP, AN, GG, LP worked on data acquisition, analysis and interpretation and reviewed the manuscript. MM and MLB accept responsibility for the integrity of data analysis. All authors have approved the final version of the submitted manuscript.

Sources of support: NIH Grants UL1 RR025758; R01 HD060827; R01 DK062249; NIH/NCRR 1 S10 RR023405

ABBREVIATIONS

BMD	bone mineral density
aBMD	areal BMD
vBMD	volumetric BMD
BMAD	bone mineral apparent density
DXA	dual energy x-ray absorptiometry
HRpQCT	high resolution peripheral quantitative computed tomography
FEA	finite element analysis
25(OH)D	25-hydroxy vitamin D

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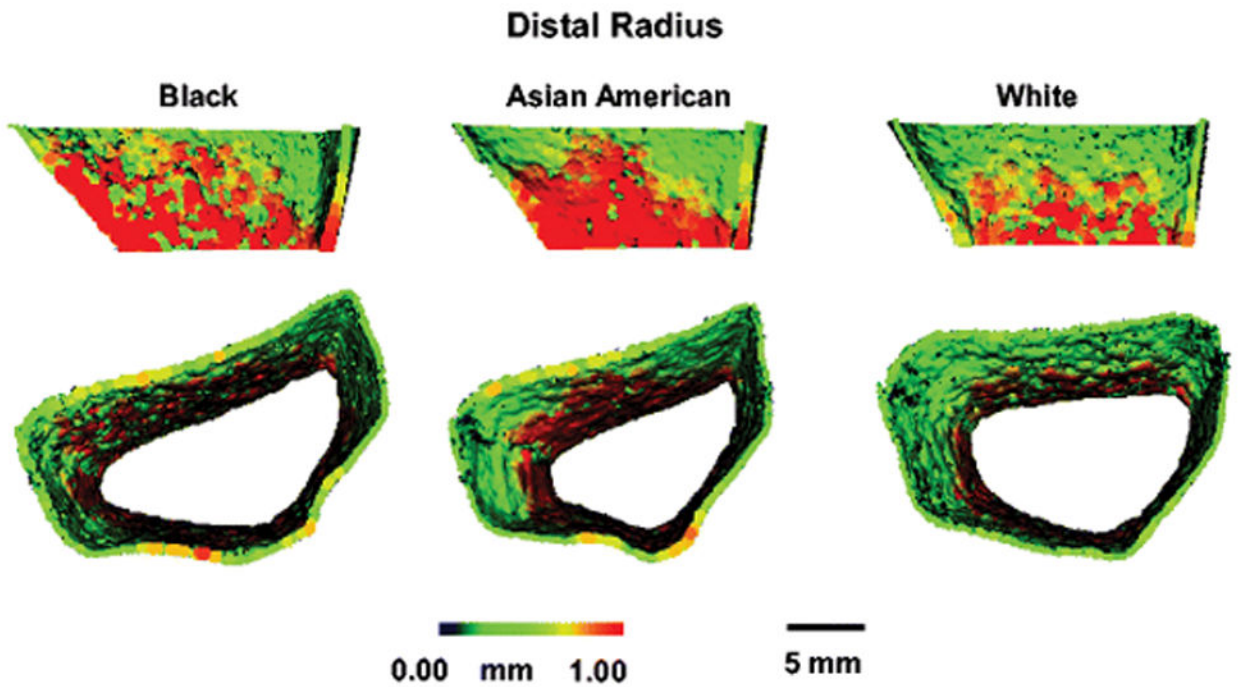


Figure 1. HRpQCT images of Black, Asian American and White girls at the distal radius, showing greater cortical thickness in the Black compared with the White girl, and greater cortical perimeter in the Black compared with the Asian American girl.

Table 1

Clinical Characteristics of Asian American, Black and White Adolescent Girls

	Asian American n = 15	Black n = 10	White n = 35	P	P*	P**
Age (years)	18.5 ± 0.5	19.3 ± 0.6	18.6 ± 0.3	0.5		
Bone age (years)	17.5 ± 0.3	17.8 ± 0.2	17.5 ± 0.2	0.7		
Menarchal age (years)	12.1 ± 0.4	12.1 ± 0.3	12.8 ± 0.2	0.2		
Tanner stage (3,4, 5)	2,0,13	0,2,8	1,3,31	0.2		
Height (cm)	158.8 ± 2.3	165.4 ± 2.6	165.1 ± 1.1	0.02^b		
Weight (kg)	55.1 ± 1.8	62.5 ± 3.7	61.0 ± 1.4	0.1		
BMI (kg/m ²)	21.8 ± 0.5	22.8 ± 0.9	22.3 ± 0.4	0.6		
Total fat mass (kg)	16.2 ± 1.1	15.7 ± 1.9	15.9 ± 0.8	0.9		
Total lean mass (kg)	38.8 ± 1.3	45.3 ± 2.4	44.0 ± 1.0	0.02^{bc}		
Percent Body Fat	28.3 ± 1.2	24.4 ± 2.0	25.4 ± 0.8	0.07		
Caloric Intake (cals)	1893 ± 128	1879 ± 205	1835 ± 121	0.9		
Vitamin D Intake (IU)	164.5 ± 23.5	177.0 ± 35.8	197.9 ± 24.5	0.7		
Calcium Intake (mg/d)	818 ± 78	719 ± 123	1053 ± 91	0.07		
25(OH)D (ng/mL)	22.5 ± 2.4	14.6 ± 2.0	31.6 ± 2.3	0.002^a		
Calcium (mg/dL)	9.1 ± 0.1	9.0 ± 0.2	9.0 ± 0.1	0.6		
Spine BMD (g/cm ²)	0.943 ± 0.03	1.112 ± 0.04	0.992 ± 0.02	0.0007^{ac}	0.002^{ac}	0.07
Spine BMD Z-score	-0.54 ± 0.25	1.1 ± 0.38	-0.07 ± 0.15	0.0005^{ac}	0.002^{ac}	0.06
Spine BMAD (g/cm ³)	0.13 ± 0.004	0.14 ± 0.004	0.13 ± 0.002	0.004^{ac}	0.002^{ac}	0.03^c
Hip BMD (g/cm ²)	0.913 ± 0.03	1.065 ± 0.03	1.009 ± 0.02	0.001^{bc}	0.008^{bc}	0.03^c
Hip BMD Z-score	-0.58 ± 0.27	0.77 ± 0.27	0.29 ± 0.17	0.003^{bc}	0.01^c	0.04^c
FN BMD (g/cm ²)	0.784 ± 0.03	0.968 ± 0.03	0.869 ± 0.02	0.0002^{abc}	0.001^{ac}	0.002^{ac}
FN BMD Z-score	-0.95 ± 0.31	0.75 ± 0.30	-0.17 ± 0.16	0.0005^{ac}	0.002^{ac}	0.003^{ac}
WB BMD (g/cm ²)	1.037 ± 0.02	1.158 ± 0.03	1.063 ± 0.01	0.004^{ac}	0.002^{ac}	0.06
WB BMD Z-score	-0.97 ± 0.29	0.69 ± 0.39	-0.62 ± 0.17	0.001^{ac}	0.002^{ac}	0.04^{ac}

^aWhite vs. Black p<0.05,

^bWhite vs. Asian p<0.05,

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^cBlack vs. Asian $p < 0.05$;

* Controlled for height;

** Controlled for height, lean mass, menarchal age, 25(OH)D;

FN: femoral neck, WB: whole body

Table 2
HRpQCT and FEA data for the distal radius (non-weight bearing bone) in Blacks, Asian Americans and Whites

Radius	Black (n=10)	Asian (n=15)	White (n=35)	P	P*	P**
Size Parameters						
Cortical Thickness (mm)	0.97 ± 0.10	0.78 ± 0.06	0.73 ± 0.03	0.01^a	0.01^{ac}	0.02^a
Cortical Perimeter (mm)	74.5 ± 3.6	65.0 ± 1.5	68.7 ± 0.9	0.005^c	0.02^{ac}	0.06
Cortical Area (mm ²)	59.4 ± 3.9	50.1 ± 3.7	49.4 ± 1.6	0.05^a	0.05^a	0.16
% Cortical Area	22.8 ± 1.8	21.5 ± 2.0	18.5 ± 0.8	0.07	0.10	0.15
Microarchitecture Parameters						
Cortical Pore Volume (mm ³) [†]	3.91 ± 0.71	2.95 ± 0.38	4.10 ± 0.42	0.23	0.63	0.26
Cortical Porosity (%) [†]	0.75 ± 0.11	0.68 ± 0.11	0.90 ± 0.10	0.37	0.54	0.22
Cortical Pore Diameter (mm) [†]	0.143 ± 0.004	0.138 ± 0.004	0.139 ± 0.001	0.40	0.57	0.94
Trabecular Thickness (mm)	0.082 ± 0.003	0.072 ± 0.004	0.072 ± 0.002	0.05^a	0.008^{ac}	0.15
Trabecular Number (mm ⁻¹)	2.07 ± 0.08	1.94 ± 0.07	2.03 ± 0.04	0.37	0.20	0.50
Trabecular Separation (mm) [†]	0.409 ± 0.016	0.456 ± 0.023	0.427 ± 0.011	0.44	0.14	0.38
Density Parameters						
Cortical Density (g/mm ³) [†]	841.9 ± 13.4	832.3 ± 23.1	819.0 ± 10.2	0.46	0.59	0.85
Trabecular Density (g/mm ³)	202.1 ± 6.2	165.6 ± 8.2	176.6 ± 6.0	0.03^c	0.001^{ac}	0.04^c
Total Density (g/mm ³) [†]	355.1 ± 14.5	325.6 ± 18.8	308.7 ± 8.9	0.08	0.04^a	0.17
Estimated Strength Parameters						
Stiffness (kN/m)	90.8 ± 4.7	73.4 ± 4.1	78.3 ± 1.8	0.006^{ac}	0.01^{ac}	0.10
Failure load (kN)	4.59 ± 0.23	3.66 ± 0.19	3.98 ± 0.09	0.008^{ac}	0.005^{ac}	0.07
Apparent modulus [†]	2319 ± 119	2025 ± 124	1946 ± 55	0.02^a	0.01^{ac}	0.14

^aWhite vs. Black p<0.05,

^bWhite vs. Asian p<0.05,

^cBlack vs. Asian p<0.05;

* Controlled for height;

** Controlled for height, lean mass, menarcheal age and 25(OH)D;

[†] Kruskal Wallis test

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HRpQCT and FEA data for the distal tibia (weight bearing bone) in Blacks, Asian Americans and Whites

Table 3

Tibia	Black (n=10)	Asian (n=15)	White (n=35)	P	P*	P**
Size Parameters						
Cortical Thickness (mm)	1.33 ± 0.07	1.29 ± 0.05	1.23 ± 0.04	0.4	0.3	0.6
Cortical Perimeter (mm)	99.8 ± 3.0	93.9 ± 2.4	101.1 ± 1.3	0.02^b	0.5	0.4
Cortical Area (mm ²)	131.9 ± 6.5	120.0 ± 4.6	123.5 ± 3.5	0.3	0.3	0.8
% Cortical Area	20.5 ± 1.4	21.1 ± 1.3	18.6 ± 0.7	0.2	0.3	0.6
Microarchitecture Parameters						
Cortical Pore Volume (mm ³) [‡]	12.78 ± 2.59	11.80 ± 2.43	18.36 ± 1.94	0.02^b	0.2	0.3
Cortical Porosity (%) [‡]	1.3 ± 0.2	1.2 ± 0.2	1.8 ± 0.2	0.02^b	0.1	0.2
Cortical Pore Diameter (mm) [‡]	0.143 ± 0.004	0.151 ± 0.005	0.152 ± 0.003	0.08	0.2	0.3
Trabecular Thickness (mm) [‡]	0.087 ± 0.003	0.088 ± 0.004	0.084 ± 0.002	0.6	0.7	0.8
Trabecular Number (mm ⁻¹) [‡]	2.09 ± 0.10	1.79 ± 0.08	2.00 ± 0.03	0.005^b	0.03^c	0.06
Trabecular Separation (mm) [‡]	0.40 ± 0.02	0.49 ± 0.04	0.42 ± 0.01	0.007^b	0.09	0.06
Density Parameters						
Cortical Density (g/mm ³) [‡]	896.1 ± 12.5	892.8 ± 11.5	874.9 ± 6.1	0.1	0.2	0.5
Trabecular Density (g/mm ³) [‡]	217.2 ± 5.3	185.3 ± 9.9	200.1 ± 5.3	0.05	0.03^c	0.3
Total Density (g/mm ³)	358.8 ± 12.8	337.2 ± 14.7	326.7 ± 8.8	0.2	0.06	0.4
Estimated Strength Parameters						
Stiffness (kN/m)	243.1 ± 11.8	209.2 ± 9.9	228.1 ± 5.9	0.07	0.2	0.6
Failure load (kN)	12.2 ± 0.6	10.5 ± 0.5	11.4 ± 0.3	0.05	0.2	0.6
Apparent modulus	2958 ± 402	2860 ± 136	2657 ± 78	0.1	0.08	0.3

^aWhite vs. Black p<0.05,

^bWhite vs. Asian p<0.05,

^cBlack vs. Asian p<0.05;

* Controlled for height;

** Controlled for height, lean mass, menarcheal age and 25(OH)D;

[†]Kruskal Wallis test

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Table 4
Distal Radius: Correlations of microarchitecture and FEA parameters with covariates

	Menarchal Age		Height		BMI		Lean mass		25(OH) vitamin D	
	r	p	r	p	r	p	r	p	r	p
Size Parameters										
Cortical Thickness (mm)	-0.36	0.005	-0.18	-	0.09	-	-0.05	-	-0.15	-
Cortical Perimeter (mm)	0.13	-	0.43	0.0006	0.19	-	0.44	0.0005	-0.09	-
Cortical Area (mm ²)	-0.28	0.03	0.06	-	0.17	-	0.18	-	-0.03	-
% Cortical Area	-0.39	0.002	-0.30	0.02	0.05	-	-0.17	-	-0.11	-
Microarchitecture Parameters										
Cortical Pore Volume (mm ³)	0.08	-	0.29	0.02	0.20	-	0.26	0.04	-0.01	-
Cortical Porosity (%)	0.15	-	0.26	0.05	0.18	-	0.21	-	-0.01	-
Cortical Pore Diameter (mm)	-0.20	-	0.05	-	0.06	-	0.07	-	-0.17	-
Trabecular Thickness (mm)	-0.41	0.001	-0.30	0.02	0.18	-	0.007	-	-0.10	-
Trabecular Number (mm ⁻¹)	-0.05	-	-0.10	-	0.12	-	-0.05	-	0.12	-
Trabecular Separation (mm)	0.09	-	0.05	-	-0.14	-	-0.01	-	-0.09	-
Density Parameters										
Cortical Density (g/mm ³)	-0.32	0.01	-0.23	0.08	0.03	-	-0.10	-	0.005	-
Trabecular Density (g/mm ³)	-0.35	0.007	-0.29	0.03	0.22	0.09	-0.01	-	0.002	-
Total Density (g/mm ³)	-0.46	0.0003	-0.37	0.004	0.14	-	-0.14	-	-0.08	-
Estimated Strength Parameters										
Stiffness (kN/m)	-0.30	0.02	0.21	-	0.27	0.04	0.40	0.002	0.09	-
Failure load (kN)	-0.29	0.03	0.24	0.06	0.26	0.05	0.42	0.0008	0.06	-

Only p values of <0.1 are reported

Table 5
Distal Tibia: Correlations of microarchitecture and FE/ parameters with covariates

	Menarchal Age		Height		BMI		Lean mass		25(OH) vitamin D	
	r	p	r	p	r	p	r	p	r	p
Size Parameters										
Cortical Thickness (mm)	-0.31	0.02	-0.42	0.0009	0.39	0.002	-0.02	-	0.02	-
Cortical Perimeter (mm)	0.40	0.001	0.78	<.0001	0.31	0.02	0.74	<.00001	0.26	0.06
Cortical Area (mm ²)	-0.10	-	-0.01	-	0.60	<.0001	0.40	0.002	0.17	-
% Cortical Area	-0.39	0.002	-0.61	<.0001	0.18	-	-0.29	0.03	-0.10	-
Microarchitecture Parameters										
Cortical Pore Volume (mm ³)	0.19	-	0.41	0.001	0.40	0.001	0.49	<.00001	0.24	0.09
Cortical Porosity (%)	0.22	0.08	0.47	0.0002	0.31	0.02	0.49	<.00001	0.21	-
Cortical Pore Diameter (mm)	0.10	-	0.10	-	0.08	-	0.11	-	0.10	-
Trabecular Thickness (mm)	-0.39	0.002	-0.38	0.003	0.03	-	-0.08	-	-0.02	-
Trabecular Number (mm ⁻¹)	0.16	-	0.32	0.01	0.26	0.05	0.35	0.006	0.19	-
Trabecular Separation (mm)	-0.13	-	-0.38	0.003	-0.21	-	-0.36	0.005	-0.23	-
Density Parameters										
Cortical Density (g/mm ³)	-0.31	0.01	-0.48	0.0001	0.09	-	-0.26	0.04	-0.06	-
Trabecular Density (g/mm ³)	-0.24	0.06	-0.05	-	0.23	0.08	0.24	0.07	0.12	-
Total Density (g/mm ³)	-0.40	0.002	-0.47	0.0002	0.23	0.08	-0.11	-	-0.02	-
Estimated Strength Parameters										
Stiffness (kN/m)	-0.05	-	0.26	0.04	0.51	<.0001	0.60	<.00001	0.32	0.02
Failure load (kN)	-0.03	-	0.29	0.03	0.53	<.0001	0.62	<.00001	0.29	0.04

Only p values of <.1 are reported