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Bone mass, microarchitecture and strength are influenced by race/ethnicity in young adult men and women

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ABSTRACT

Lower rates of fracture in both Blacks compared to Whites, and men compared to women are not completely explained by differences in bone mineral density (BMD). Prior evidence suggests that more favorable cortical bone microarchitecture may contribute to reduced fracture rates in older Black compared to White women, however it is not known whether these differences are established in young adulthood or develop during aging. Moreover, prior studies using high-resolution pQCT (HR-pQCT) have reported outcomes from a fixed-scan location, which may confound sex- and race/ethnicity-related differences in bone structure.

Purpose: We determined differences in bone mass, microarchitecture and strength between young adult Black and White men and women.

Methods: We enrolled 185 young adult (24.2 ± 3.4 yrs) women ($n = 51$ Black, $n = 50$ White) and men ($n = 34$ Black, $n = 50$ White) in this cross-sectional study. We used dual-energy X-ray absorptiometry (DXA) to determine areal BMD (aBMD) at the femoral neck (FN), total hip (TH) and lumbar spine (LS), as well as HR-pQCT to assess bone microarchitecture and failure load by micro-finite element analysis (μFEA) at the distal tibia (4% of tibial length). We used two-way ANOVA to compare bone outcomes, adjusted for age, height, weight and physical activity.

Results: The effect of race/ethnicity on bone outcomes did not differ by sex, and the effect of sex on bone outcomes did not differ by race/ethnicty. After adjusting for covariates, Blacks had significantly greater FN, TH and LS aBMD compared to Whites ($p < 0.05$ for all). Blacks also had greater cortical area, vBMD, and thickness, and lower cortical porosity, with greater trabecular thickness and total vBMD compared to Whites. μFEA-estimated FL was significantly higher among Blacks compared to Whites. Men had significantly greater total vBMD, trabecular thickness and cortical area and thickness, but greater cortical porosity than women, the net effects being a higher failure load in men than women.

Conclusion: These findings demonstrate that more favorable bone microarchitecture in Blacks compared to Whites and in men compared to women is established by young adulthood. Advantageous bone strength among Blacks and men likely contributes to their lower risk of fractures throughout life compared to their White and women counterparts.

Abbreviations: MrOS, Osteoporotic Fractures in Men Study; SWAN, Study of Women Across the Nation; FEA, finite element analysis; PA, posterior-anterior; FN, femoral neck; TH, total hip; Tt.Ar, total cross-sectional area; Tt.vBMD, total vBMD; Tb.vBMD, trabecular vBMD; Tb.N, trabecular number; Tb.Sp, trabecular separation; Tb.Th, Trabecular thickness; Ct.Ar, cortical area; Ct.Th, cortical thickness; Ct.vBMD, cortical vBMD; Ct.TMD, cortical tissue mineral density; Ct.Po, cortical porosity; Tb.Ar, trabecular area; Ct.Ar/Tt.Ar, cortical area fraction; μFEA, micro-finite-element-analysis; PTH, parathyroid hormone.

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1. Introduction

Worldwide, there are well-established differences in fracture rates by race and ethnic-origin [1–5]. In particular, Blacks/African-Americans have lower incidence of fractures in both youth and older adulthood than Whites/Caucasians residing in the US [3,6]. Black men and women also have a 2–3 fold lower incidence of stress fracture compared to their White counterparts [7,8]. Although Black individuals have higher areal bone mineral density (aBMD) than Whites/Caucasians at all ages [9–13], this higher aBMD does not entirely account for the lower fracture risk seen in Black compared to White individuals [14–16].

Therefore, it has been hypothesized that variation in bone morphology and microarchitecture due to racial background contributes to observed differences in fracture incidence [13,17–21]. Accordingly, as assessed by quantitative computed tomography (QCT), older Black men from the Osteoporotic Fractures in Men (MrOS) study had more favorable morphology at the proximal femur compared to White men [17]. Similarly, high-resolution peripheral quantitative computed tomography (HR-pQCT) scans of the distal radius and tibia revealed that postmenopausal Black women from the Study of Women Across the Nation (SWAN) cohort had greater trabecular volumetric BMD (vBMD), and cortical thickness compared to their White counterparts [13]. While studies comparing Asian compared to Caucasian women suggest that these differences in bone microarchitecture are evident in premenopausal women [18–20], there are few studies to indicate whether these race/ethnic advantages in bone microarchitecture among Black individuals are established during growth and development, or result from a different pattern of age-related changes in bone.

It is also well known that men have lower fracture risk than women at all ages. Many prior studies have reported higher aBMD and advantageous bone microarchitecture in adult men compared to women [22–25] [23,26]. However, to date, studies comparing bone microarchitecture by HR-pQCT in adults have used a fixed region-of-interest, starting 9.5 mm or 22.5 mm proximal to the distal endplate of the radius and tibia, respectively, regardless of body size. Therefore, results using this approach may be difficult to interpret in individuals of differing stature or limb length, as some bone microarchitecture outcomes vary significantly along the length of the limb in this metaphyseal region [27–29].

Thus, there is strong rationale to study the bone morphology and microstructural features that may explain race/ethnicity- and sex-based differences in both stress fracture risk in young adults and osteoporosis-related fracture risk later in life, particularly among young adult men and women of African ancestry. Therefore the, primary aim of this study was to determine differences in bone morphology, microarchitecture, and finite element analysis (FEA) derived bone strength of the distal tibia according to sex- and race/ethnic-origin in young Black and White adults. We located the region of interest relative to bone length to overcome potential confounding by differences in bone length and height among groups. We hypothesized that Black men and women will have more favorable bone microarchitecture parameters than White men and women, and that men of both races will have more favorable bone microarchitecture parameters than women.

2. Materials and methods

2.1. Subject characteristics

We enrolled young adult men and women between the ages of 18–30 yrs with a body mass index (BMI) between 18 and 30 kg/m^2. Subjects self-identified as White/Caucasian (50 women, 50 men) or Black/African-American (51 women, 34 men). For this study, we defined racial group identification as having at least three of four grandparents of the same race/ethnic background as the subjects' self-identified race/ethnicity. Women enrolled in this study were required to be currently eumenorrheic (>9 menses in the prior 12 months, including 1 menses in last 60 days). Exclusion criteria included underlying medical conditions or use of medications known to affect bone health, history of an eating disorder, and history of bilateral lower limb fractures. We screened 244 potential participants for this study: 59 screened subjects did not participate in the study, including 25 who did not meet BMI criteria, 15 who did not meet race criteria, 7 who were outside the age range, 2 who had a history of metabolic bone disorder, 2 who had an eating disorder, 2 who had a history of bilateral ankle fractures, 2 who were amenorrheic, 2 who had an endocrine disorder possibly affecting bone, 1 who was taking anti-seizure medication, and 1 who met more than one exclusion criteria. This study was approved by the Institutional Review Board of Partners Health Care and the Human Research Protection Office at the US Army Medical Research and Materiel Command. Informed written consent was obtained from each subject prior to participation in the study.

2.2. Clinical history and anthropometric measurements

We assessed socio-economic status, education, health history, fracture history, and physical activity history through questionnaires. For women, questionnaires also captured menstrual status and contraceptive use. Height (to the nearest millimeter) was obtained using a wall-mounted stadiometer. Body mass (to the nearest 0.1 kg) was measured on a calibrated electronic scale. BMI was calculated as mass (kg) divided by height squared (m^2). We measured tibia length from the medial tibial plateau to the distal edge of the medial malleolus to the nearest mm using an anthropometric tape. All measurements were taken twice, and the mean of two readings was used.

2.3. Areal bone mineral density

We used dual energy X-ray absorptiometry (DXA: QDR45000A; Hologic Inc., Bedford, MA, USA) to assess the posterior-anterior (PA) spine, femoral neck (FN), and total hip (TH) aBMD (g/cm^2). Quality control was maintained through daily measurements of a Hologic CXA anthropomorphic spine phantom and visual review of every scan image by an investigator experienced in bone densitometry.

2.4. Bone microarchitecture

We measured cortical and trabecular vBMD and microarchitecture at the distal tibia using HR-pQCT (XtremeCT, Scanco Medical AG, Basserdorf, Switzerland; isotropic voxel size of 82 μm). The scan region started at 4% of tibial length (distal) and extended proximally for 110 slices (9.02 mm). The non-dominant leg was scanned, unless there was a prior leg or ankle fracture, in which case the contralateral leg was scanned. Quality control was maintained with daily scanning of the manufacturer's phantom. All scans were reviewed immediately for motion artifact and were repeated up to two times if significant motion artifact was noted. Movement artifact was scored on a 5-point scale, with 1 = no movement and 5 = severe movement artifact [30].

Using Scanco analysis software version 5.11, total cross-sectional area (Tt.Ar mm^2), total and trabecular vBMD (Tt.vBMD, Tb.vBMD, mg HA/cm^3), and trabecular number (Tb.N, 1/mm) were measured directly. Trabecular separation (Tb.Sp, mm) and trabecular thickness (Tb.Th, mm) were then calculated from Tb.vBMD and Tb.N. We used a semiautomated technique [31,32] to measure cortical area (Ct.Ar, mm^2), cortical thickness (Ct.Th, mm), cortical vBMD (Ct.vBMD, mg HA/-cm^3), cortical tissue mineral density (Ct.TMD, mg HA/cm^3), cortical porosity (Ct.Po, %), and trabecular area (Tb.Ar, mm^2). Cortical area fraction (Ct.Ar/Tt.Ar,%) was then calculated. We also used 3D HR-pQCT images to perform linear micro-finite-element-analysis (μFEA) to estimate tibia metaphyseal stiffness and failure load under axial compression. In this method, each voxel in the HRpQCT image is converted to a linear

isotropic hexahedral element, assuming a Young's modulus of 10 GPa, and Poisson's ratio of 0.3 for all elements. The finite element model is then subjected to axial compression, with a compressive strain of 1% applied along the vertical axis with the top and bottom surfaces fully constrained. Following previous guidelines, failure load was defined as the load at which the equivalent strain exceeds 0.7% in at least 2% of the elements [33]. Short term reproducibility (with repositioning) for HR-pQCT measurements at the tibia in our laboratory ranged from 0.2 to 1.7% for density parameters, from 0.7 to 8.6% for microarchitecture parameters, and from 2.1 to 4.8% for μFEA parameters.

2.5. Statistical analysis

Data are reported as mean ± standard deviation (SD) unless otherwise noted. We performed a two-way ANOVA to assess between-group differences and assess race by sex interactions for subject demographics, covariates and bone outcomes. Univariate regression analyses were used to determine association of age, height, weight, fracture history, contraceptive use, age of menarche, recent physical activity, income, education, smoking history, and alcohol use with bone microarchitectural parameters. Because age, height, weight, and physical activity were significantly associated with BMD and microarchitectural parameters and differed among study groups, we next used an analysis of covariance (ANCOVA) to control for these variables while assessing differences by race and sex. We did not include BMI in this multivariate model because height and weight were already included in the model. Comparisons with a p-value of <0.05 are reported as statistically significant. We used Stata version 14.2 (StataCorp LP, College Station, TX) for all statistical analyses.

3. Results

3.1. Subject characteristics

We enrolled 185 subjects, including 100 White (50 women, 50 men) and 85 Black (51 women, 34 men) individuals. Subjects averaged 24.4 ± 3.4 years old, with a BMI of 23.9 ± 3.0 kg/m^2 (Table 1). Black women and men were slightly younger, participated in fewer hours of recent physical activity per week, had fewer prevalent fractures, less education and lower familial income, on average, than White women and men. Contraceptive use was lower among Black women compared to White women. As expected, women weighed less and were shorter than men, on average. Women also had a lower BMI, participated in fewer hours of recent weight-bearing physical activity per week, and had fewer prevalent fractures than men.

3.2. Areal bone mineral density

Blacks had higher aBMD of the PA spine, FN and TH compared to Whites ($p < 0.01$ for all, Table 2) before and after adjustment for age, height, weight, and physical activity (all $p < 0.01$). In unadjusted analyses, men had greater aBMD than women at the femoral neck and total hip ($p < 0.01$), but not the PA spine. Following multivariate adjustment, hip BMD did not differ between sexes, however, men had higher aBMD at the PA spine ($p < 0.01$).

3.3. vBMD and microarchitecture

In both unadjusted and adjusted analyses, bone morphology and microarchitecture were generally more favorable in Black than White adults, and also more favorable in men than women (Table 3, Figs. 1–4). The effect of race/ethnic-origin was independent of sex. Overall bone size was similar in Black and White subjects, as evidenced by no significant differences in Tt.Ar. However, Black men and women had greater Tt.vBMD and more favorable cortical microarchitecture, including greater Ct.Th (13%), Ct.Ar (10%), Ct.Ar/TtAr (16%), Ct.vBMD (5%), Ct.TMD (2.5%), and lower Ct.Po (25%) than their White counterparts (all $p < 0.01$). Tb.vBMD (9%) and Tb.Th (9%) were significantly higher, but Tb.N significantly lower (−5%) in Blacks compared to Whites in the unadjusted model. All differences remained significant after multivariate adjustment, except for Tb.vBMD ($p = 0.19$ after adjustment).

Most morphological and microarchitectural parameters were more favorable in men compared to women in unadjusted analyses, including greater Tt.Ar (21%), Ct.Ar (14%), Ct.Th (13%), and Ct.Ar/Tt.Ar (14%). Men also had greater Tt.vBMD (8%) and Tb.vBMD (11%), Tb.N (5%), and Tb.Th (7%) compared to women (all $p < 0.01$). However, Ct.vBMD (3%) was

Table 1
Demographic characteristics of study subjects. Values are Mean (SD) or n (%).

	White women $n = 50$	Black women $n = 51$	White men $n = 50$	Black men $n = 34$	p race/sex interaction	p race	p sex
Age (y)	24.5 (2.9)	22.2 (3.2)	24.9 (3.2)	24.3 (3.6)	0.02	<0.001	0.210
Height (cm)	164.9(10.8)	166.1 (7.9)	179.9 (8.0)	177.8 (7.4)	0.14	0.689	<0.001
Weight (kg)	63.4 (9.6)	64.4 (10.2)	78.5 (11.5)	78.2 (11.4)	0.69	0.848	<0.001
BMI (kg/m$^{2)}$	23.3 (3.2)	23.3 (2.5)	24.2 (2.9)	24.9 (3.4)	0.68	0.291	0.010
Tibia length (mm)	367.9 (24.1)	378.3 (29.2)	408.3 (28.8)	413.4 (30.7)	0.53	0.065	<0.001
Physical activity (h/week)	4.9 (4.3)	2.3 (2.8)	5.9 (5.4)	5.1 (8.6)	0.26	0.029	0.018
Age of menarche (y)	12.8 (1.6)	11.8 (1.3)			–	0.291	–
Fracture history (total)	18 (36%)	4 (8%)	24 (48%)	6 (18%)	0.74	<0.001	0.062
Education level					0.95	<0.001	0.661
High school	0 (0%)	3 (6%)	0 (0%)	6 (18%)			
Bachelors deg	44 (88%)	45 (88%)	39 (78%)	26 (75%)			
Graduate deg	6 (12%)	3 (6%)	11 (22%)	2 (6%)			
Family income					0.03	<0.001	0.440
Less than $20 K	0 (0%)	6 (12%)	0 (0%)	4 (12%)			
$20 K to $99 K	27 (54%)	27 (53%)	14 (28%)	22 (65%)			
$100 K or more	23 (46%)	18 (35%)	36 (72%)	8 (23%)			
Current smoking					0.50	0.508	0.499
Daily	0 (0%)	0 (0%)	0 (0%)	1 (3%)			
<Daily	1 (2%)	1 (2%)	1 (2%)	0 (0%)			
None	49 (98%)	50 (98%)	49 (98%)	33 (97%)			
Hormonal contraceptive use					–	<0.001	–
Current use	37 (74%)	13 (25%)					
Past use	7 (14%)	9 (18%)					
No use	6 (12%)	29 (57%)					

Table 2
Results from dual-energy x-ray absorptiometry at the femoral neck (FN), total hip (TH) and lumbar spine (LS). Values are Mean (SD).

	White women $n = 50$	Black women $n = 51$	White men $n = 50$	Black men $n = 34$	p race/sex interaction	p race	p sex	*p race	*p sex
FN aBMD (g/cm^2)	0.859 (0.134)	0.958 (0.141)	0.947 (0.124)	1.080 (0.186)	0.427	<**0.001**	<**0.001**	<**0.001**	0.359
TH aBMD (g/cm^2)	0.978 (0.121)	1.054 (0.153)	1.051 (0.138)	1.174 (0.168)	0.286	<**0.001**	<**0.001**	<**0.001**	0.380
PA Spine aBMD (g/cm^2)	1.032 (0.119)	1.116 (0.140)	1.046 (0.119)	1.153 (0.131)	0.547	<**0.001**	0.178	<**0.001**	**0.004**
FN *Z*-score	0.1 (1.2)	0.1 (1.0)	0.1 (0.9)	0.1 (1.2)	0.956	0.870	0.741	0.679	**0.007**
TH *Z*-score	0.3 (1.0)	0.2 (1.0)	0.1 (0.9)	0.0 (1.0)	0.905	0.393	0.293	0.212	<**0.001**
PA Spine Z-score	−0.1 (1.1)	−0.3 (1.3)	−0.4 (1.1)	0.5 (1.2)	0.361	0.097	0.200	0.142	<**0.001**

Bold = $p < 0.05$.
* Adjusted for height, weight, age, and physical activity.

significantly higher and Ct.Po significantly lower (−34%) in women than men. After adjusting for height, weight, age and physical activity most differences remained significant, however, there was no longer a significant difference in Tt.Ar, Ct.vBMD, or Tb.N.

3.4. μFEA

As predicted, given their more favorable bone microarchitecture, Blacks had significantly higher μFEA-derived bone stiffness (8%) and failure load (7%) than Whites, and men had significantly higher stiffness (28%) and failure load (27%) than women (Table 3). In both cases, these significant differences persisted after multivariate adjustment.

4. Discussion

In this study, we found that young adults of Black/African-American race have greater hip and spine aBMD, along with more favorable bone microarchitecture and higher μFEA-estimated failure load at the distal tibia than their White/Caucasian counterparts. Notably, these differences were seen in both men and women, and remained significant after adjusting for factors known to influence bone structure, including age, weight, height, and physical activity. Moreover, our findings of favorable bone traits in individuals of Black race/ethnicity are consistent with a lower self-reported history of fracture in Black compared to White subjects in our study.

Our findings of higher aBMD in young Black adults compared to White adults are consistent with many studies showing that Black individuals, from childhood to older adulthood, have higher aBMD by DXA than other racial groups [9–13,34–42]. Our results suggest that higher aBMD values in Black men and women are largely attributable to enhanced cortical bone properties, including greater Ct.Ar/Tt.Ar, Ct.Th, Ct.vBMD, and Ct.TMD. In contrast, we observed no difference in Tb.vBMD between Black and White subjects after multivariate adjustment, though Tb.Th was higher and Tb.N lower in Black compared to White subjects. This pattern of enhanced cortical, but not trabecular bone in young adults is consistent with a prior study in 18–19 year-old Black and White women that used pQCT measures of the tibia to show that Black women have significantly greater Ct.vBMD, Ct.Th and Ct.Ar, but lower Tb.vBMD than their White counterparts [43]. Favorable cortical bone structure appears to be established early in puberty, as 9–13 year old Black boys and girls have higher Ct.Th and Ct.vBMD by pQCT of the tibial diaphysis than corresponding White children [44]. Our and others' findings demonstrating similar or lower Tb.vBMD at the appendicular skeleton in Black compared to White individuals differ from a prior report of increased Tb.vBMD in Black compared to White subjects at the spine at the end of puberty [45] and at the femoral neck in older men [17]. These discrepancies suggest that effects of race/ethnicty on bone structure may vary by skeletal site.

Favorable bone structure in persons of Black race/ethnic background appears to be maintained throughout life in both men and women. For example, we previously used HR-pQCT measurements of the appendicular skeleton to show that postmenopausal Black women from the SWAN cohort have greater Ct.Ar and Ct.Th, and greater μFEA-estimated failure load than White women [13]. Consistent with the pattern of racial differences in bone structure seen in the current study and the SWAN cohort, Black men from the MrOS cohort (i.e., >65 yrs. of age) had a higher proportion of cortical bone and integral vBMD at the femoral neck, as assessed by QCT, than their White counterparts [17].

Mechanisms to explain differences in bone density, strength and microarchitecture by race/ethnic-origin are not well understood.

Table 3
Tibial bone microarchitecture (4% distal) in young adult men and women according to race/ethnic origin [Mean (SD)].

	White women $n = 50$	Black women $n = 51$	White men $n = 50$	Black men $n = 34$	p race/sex interaction	p race	p sex	*p race	*p sex
Size/morphology									
Tt.Ar (mm^2)	865 (115)	850 (129)	1098 (168)	1069 (151)	0.74	0.230	<**0.001**	0.634	0.173
Ct.Ar (mm^2)	90.6 (15.4)	103.5 (20.6)	120.6 (18.2)	136.8 (29.3)	0.60	<**0.001**	<**0.001**	<**0.001**	<**0.001**
Ct.Ar/Tt.Ar (%)	10.7 (2.3)	12.4 (11.6)	11.2 (2.4)	12.9 (2.7)	0.93	<**0.001**	0.147	<**0.001**	<**0.001**
Microarchitecture									
Ct.Th (mm)	0.80 (0.16)	0.94 (0.19)	0.94 (0.17)	1.09 (0.22)	0.82	<**0.001**	<**0.001**	<**0.001**	<**0.001**
Ct.Po (%)	4.29 (1.46)	3.22 (1.07)	6.05 (2.13)	4.91 (2.16)	0.89	<**0.001**	<**0.001**	**0.006**	**0.005**
Tb.Th (mm)	0.076 (0.011)	0.083 (0.0100)	0.081 (0.012)	0.090 (0.010)	0.72	<**0.001**	**0.001**	<**0.001**	<**0.001**
Tb.Sp (mm)	0.388 (0.052)	0.392 (0.062)	0.351 (0.060)	0.380 (0.070)	0.17	0.079	**0.006**	**0.028**	0.748
Tb.N(1/mm)	2.18 (0.26)	2.14 (0.28)	2.35 (0.29)	2.18 (0.34)	0.15	**0.014**	**0.015**	**0.005**	0.680
Density									
Tt.vBMD (mgHA/cm^3)	263 (40)	293 (46)	293 (51)	315 (51)	0.55	<**0.001**	<**0.001**	**0.002**	<**0.001**
Tb.vBMD(mgHA/cm^3)	198 (31)	213 (35)	229 (41)	234 (39)	0.32	0.069	<**0.001**	0.191	<**0.001**
Ct.vBMD (mmHA/cm^3)	873 (38)	908 (35)	847 (42)	889 (37)	0.56	<**0.001**	<**0.001**	<**0.001**	0.287
Ct.TMD (mgHA/cm^3)	930 (31)	950 (29)	921 (27)	948 (27)	0.38	<**0.001**	0.201	<**0.001**	0.881
μFEA									
Stiffness (kN/mm)	211.6 (39)	245.7 (53)	304 (53)	337 (68)	0.90	<**0.001**	<**0.001**	<**0.001**	<**0.001**
Failure Load (kN)	10.8 (1.9)	12.4 (2.6)	15.5 (2.5)	16.9 (3.4)	0.77	<**0.001**	<**0.001**	<**0.001**	<**0.001**

Bold = $p < 0.05$.
* Adjusted for height, weight, age, and physical activity.

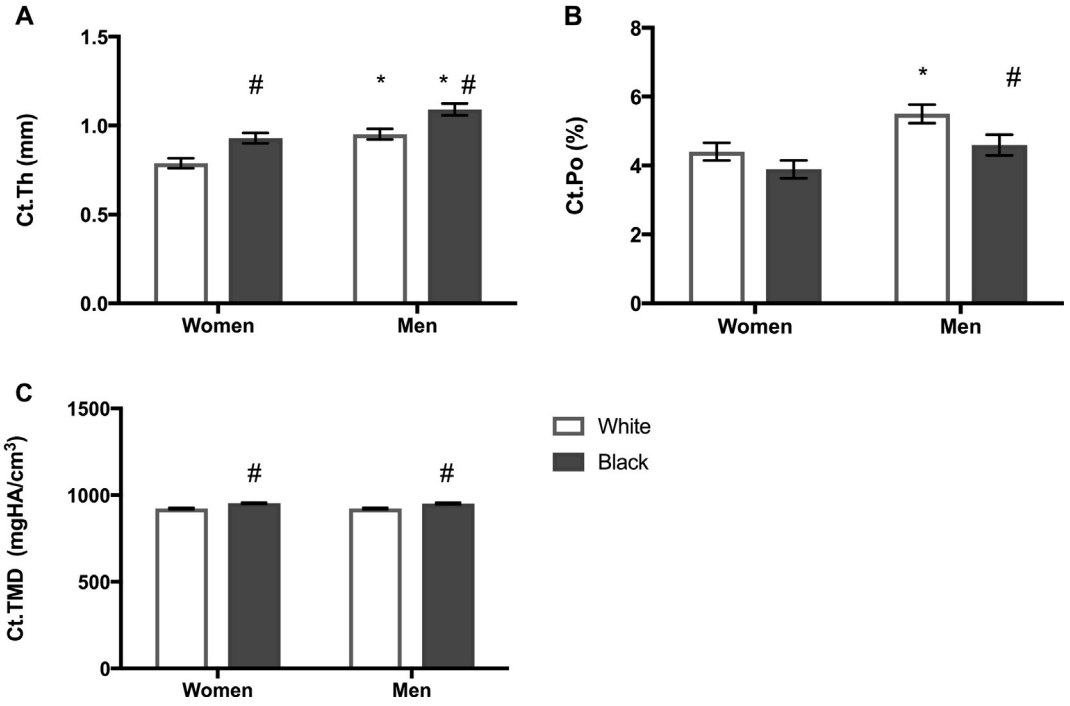

Fig. 1. Cortical bone microarchitecture at the distal tibia in White and Black men and women after multivariate adjustment (Mean ± SE). A) Cortical thickness (Ct.Th), B)cortical porosity (Ct.Po) and C) cortical tissue mineral density (Ct.TMD) for White and Black women and men. # $p < 0.05$ for Black vs. White within sex. *$p < 0.05$ for men vs. women within race. Multivariate model adjusted for height, weight, age, and physical activity.

While groups of the same race/ethnic-origin share genetic components that influence skeletal health [46], prior studies indicate that environment, income and education may also modulate skeletal differences associated with race/ethnicity [47,48]. We examined the role of several possible lifestyle factors, including contraceptive use, age of menarche, physical activity, income, education, smoking history, and alcohol use, and found that only physical activity was related to bone microarchitecture. This result, along with our observation of favorable bone microarchitecture and failure load in Black subjects after adjustment for age, height, weight and physical activity, suggest that factors

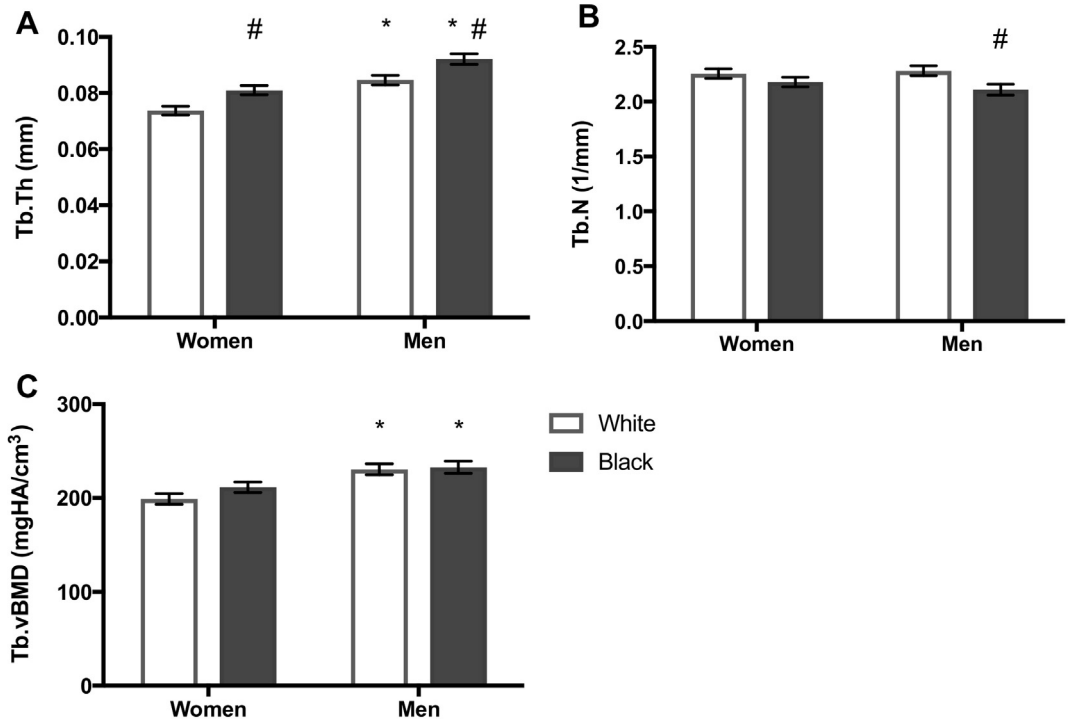

Fig. 2. Trabecular bone microarchitecture at the distal tibia in White and Black men and women after multivariate adjustment (Mean ± SE). A) Trabecular thickness (Tb.Th), B) trabecular number (Tb.N) and C) trabecular bone mineral density (Tb.vBMD) for White and Black women and men. # $p < 0.05$ for Black vs. White within sex. *$p < 0.05$ for men vs. women within race. Multivariate model adjusted for height, weight, age, and physical activity.

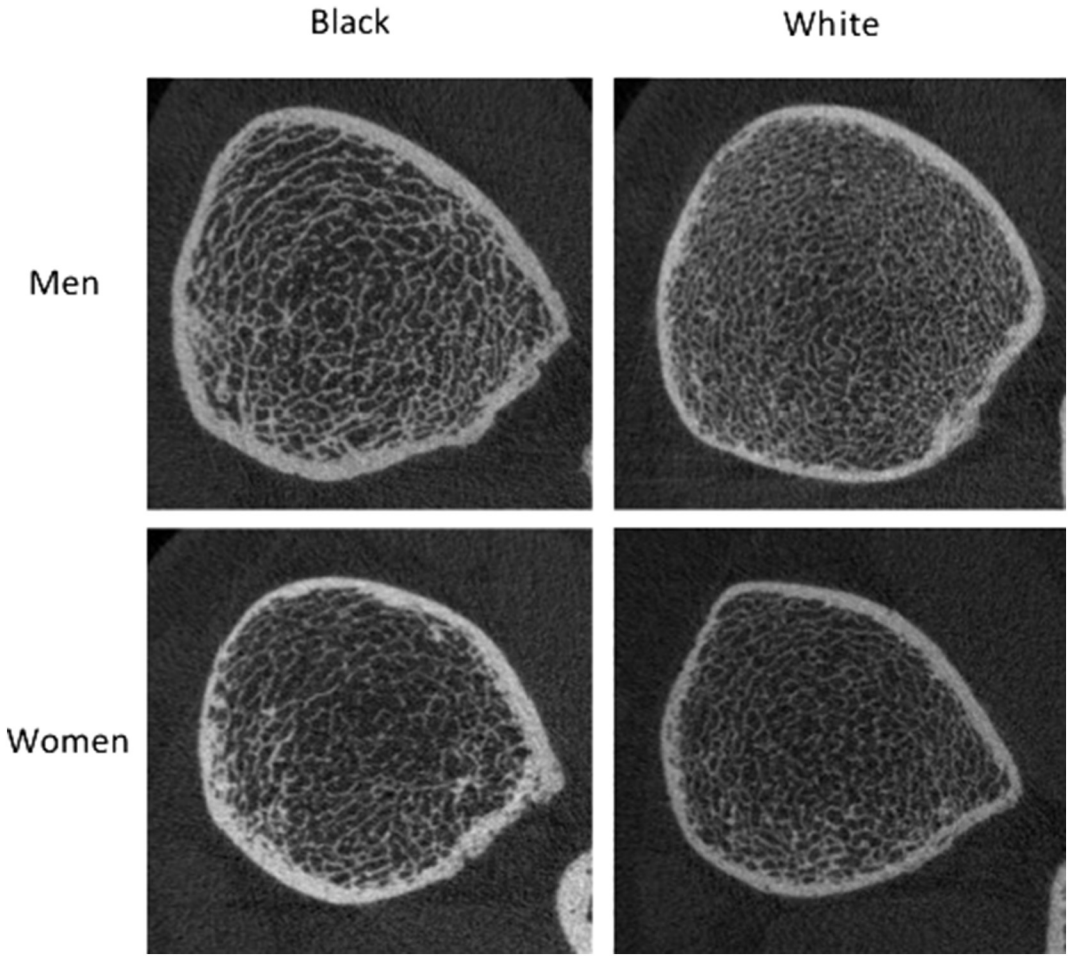

Fig. 3. Representative 2D HR-pQCT images of the distal tibia from Black and White men and women.

other than lifestyle contribute to variation in bone microarchitecture by race/ethnic-origin.

Different rates of bone metabolism are a plausible explanation for disparities in bone microarchitecture by race/ethnicity. Our HR-pQCT findings are supported by histomorphometric analyses of iliac crest biopsies in men and women (20–84 yrs), which showed that Blacks have greater Ct.Th and Tb.Th than Whites [49–51], potentially due to lower bone turnover among Blacks. In particular, after double-tetracycline labeling, biopsies showed that the bone formation rate among Black adults ranges from 35%–75% that of White adults [51,52]. In addition, serum markers of bone turnover are generally reported to be lower in Black than White children [53] and adults [10,54–57], though some studies report similar values in Black compared to White women [58–61].

Differences in bone metabolism by race/ethnicity may, in part, be driven by lower skeletal sensitivity to parathyroid hormone (PTH)

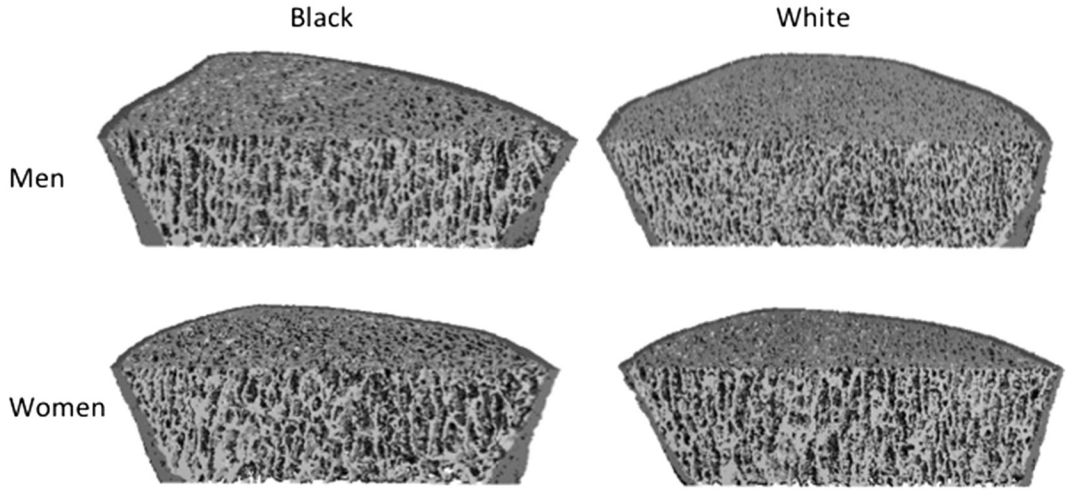

Fig. 4. Representative HR-pQCT images of the distal tibia from Black and White men and women; 3D visualization of the mineralized cortical bone and trabecular bone structure.

among Blacks compared to Whites [55,62]. Despite the observed lower bone turnover among Blacks, several studies have reported higher plasma PTH in Black adults compared to their White counterparts [58,63–65]. Accordingly, following PTH infusion, there was a smaller increase in bone resorption markers in Black premenopausal women compared to their White counterparts [56]. Moreover, there is evidence that Black individuals with similar calcium intakes and with similar concentrations of 25(OH) vitamin D, $1,25(OH)_2$ vitamin D, and PTH exhibit lower urinary calcium excretion compared to White individuals, indicating higher renal mineral conservation among Blacks [62]. This calcium conservation has been associated with greater aBMD and peak bone mass among Blacks compared to Whites [66,67], and likely contributes to their favorable cortical bone microarchitecture.

Osteocyte morphology may also contribute to more favorable bone microarchitecture in Black compared to White individuals [68]. Data from iliac crest biopsies show that Black women have greater osteocyte and lacunar density than White women [69]. Given the prominent role of osteocytes in orchestrating bone remodeling [70,71], it is plausible that a greater osteocyte density may contribute to more favorable bone microarchitecture. Notably, Dong et al. reported that regions of human cortical bone specimens with greater osteocyte lacunar number and density were less porous compared to regions with lower lacunar density [72]. Furthermore, decreased osteocyte lacunar number and density have been reported with age [73] and among adults with an osteoporotic fracture compared to healthy adults [74,75], suggesting that osteocytes play an important role in skeletal maintenance. Future studies should focus on elucidating the role of osteocyte density and differences in bone strength and microarchitecture by race/ethnic-origin.

Our observations of higher Tt.vBMD, Tb.vBMD, Ct.Th and Ct.Ar/Tt.Ar, as well as higher Ct.Po in men compared to women are largely similar to results from prior studies examining sex-related differences in bone microarchitecture [22,24,76–83]. Importantly, the current results are consistent with studies that utilized a fixed region of interest irrespective of limb length. The similarity of results across studies, despite different protocols, suggests that differences in the relative region of interest do not markedly confound sex-related differences in men compared to women. Our data support the notion that sex differences in bone microarchitecture and estimated bone strength are established by young adulthood and persist throughout the lifespan even after accounting for differences in body size by scanning at a region relative to limb length, suggesting sex-specific biological differences impact bone accrual and maintenance [84–90].

Our study has several important strengths. In contrast to prior studies, we measured bone microarchitecture at a location relative to limb length rather than one that was fixed. Nonetheless we found similar differences by sex and race/ethnicity as compared to prior reports [13,17,21,23,24,26,40,43,77,82,83]. This suggests that sex- and race/ethnicity-related differences in bone parameters are not confounded to a large extent by differences in limb length when using a fixed scan location. However, this observation applies only to studies with an approximate 10% difference in limb length that we observed here. While our results showing differences in aBMD and bone microarchitecture are similar to what has been reported between men and women and between older Black and White women, our findings confirm that these differences are also present in young adults. Limitations of this study include the cross-sectional design and lack of biomarkers, such that we can only speculate at the biological mechanisms contributing to the differences in bone mass and microarchitecture by sex- and race/ethnic-origin. In addition, we relied on self-reported physical activity history and other lifestyle variables, which are subject to recall bias.

5. Conclusion

In summary, our results confirm and extend prior observations of higher aBMD and more favorable bone microarchitecture in Black compared to White individuals, and suggest that these race-related differences are independent of sex and are established by early adulthood. Moreover, we confirm prior reports of favorable bone microarchitecture in young adult men compared to women. Advantageous bone strength among Blacks appears attributable to denser, less porous, and thicker cortices compared to Whites, and among men attributable to larger bones with denser and thicker cortices compared to women. This advantage in bone microarchitecture likely contributes to lower fracture, and stress fracture risk among Blacks and men compared to their White and women counterparts.

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Conflicts of interest

The authors have no conflicts of interest to disclose. The results of this study do not constitute endorsement by Bone.

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