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Dimorphism in axial and appendicular dimensions, cortical and trabecular microstructure and matrix mineral density in Chinese and Caucasian women

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ABSTRACT

Introduction: Appendicular fractures are less common in Chinese than Caucasian women. Bone mineral density (BMD) is lower, not higher than in Caucasians because Chinese have smaller appendicular dimensions than Caucasians. However, smaller bones may offset the liability to fracture by being assembled with a more robust microstructure. We hypothesized that Chinese assemble an appendicular skeleton with a thicker, less porous and more mineralized cortex that is less deteriorated in advanced age than in Caucasians.
Methods: We compared anthropometry in 477 Chinese and 278 Caucasian women and compared bone microstructure using high-resolution peripheral quantitative computed tomography in another cohort of 186 Chinese and 381 Caucasian women aged 18 to 86 years, all living in Melbourne, Australia. Trabecular plate (p) and rod (r) bone volume/total volume (BV/TV) were quantified using individual trabecula segmentation (ITS). Bone strength was estimated using micro-finite element analysis (μFEA).
Results: Premenopausal Chinese were shorter than Caucasian women, mainly due to shorter leg length. Distal radial total cross sectional area (CSA) was 14.8% smaller ($p < 0.001$). After adjusting for age and total CSA, Chinese had similar cortical and medullary areas but 0.30 SD lower cortical porosity and 0.27 SD higher matrix mineral density (both $p < 0.05$). Trabecular plate-to-rod ratio was 0.55 SD higher due to a 0.41 SD higher pBV/TV and 0.36 SD lower rBV/TV (p ranging 0.001 to 0.023). Chinese also had 0.36 SD greater whole bone stiffness and 0.36 SD greater failure load than Caucasians (both $p < 0.05$). After adjusting for age and total CSA, postmenopausal Chinese had 3.3% smaller cortical area, medullary area was 2.1% larger, cortical porosity was no lower, matrix mineral density and pBV/TV were no higher compared with Caucasians at the distal radius. Whole bone stiffness was 0.39 SD lower and failure load was 0.40 SD lower in Chinese (both $p < 0.05$).
Conclusion: Chinese build a more robust skeleton than Caucasians during growth, an advantage not observed in advanced age due to greater bone loss or race-specific secular trends in bone morphology.

1. Introduction

The incidence of appendicular fractures is lower in Chinese than Caucasians [1–3]. This is not explained by the racial differences in bone mineral density (BMD). Indeed, BMD is lower, not higher than in Caucasians because Chinese have smaller appendicular dimensions than Caucasians [4]. However, resistance to fracturing of a smaller skeleton may be achieved by assembling it more robustly during growth; forming thicker cortices relative to the total cross-sectional area with lower porosity and thicker more connected trabeculae of the metaphyseal region in Chinese [5]. Shorter stature or leg length in Chinese may also be associated with better balance and a lower impact following a fall [6].

Quantification of racial differences in bone microstructure is challenging because meticulous attention is needed in choosing the region of interest (ROI) [7]. In an individual, adjacent cross sections of a long bone are assembled using similar amounts of mineralized bone matrix [7,8]. What differs is how that mineralized matrix is fashioned as cortical and trabecular bone along the length of the bone. Distally the constant amount of material is mainly trabecular with a thin cortical shell whereas proximally in the metaphyseal-diaphyseal region and especially the midshaft more of the constant amount of mineralized

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matrix is assembled as cortical bone.

For racial comparisons to be valid, the same position of a ROI relative to the length of the bone must be compared. Chinese have a shorter appendicular skeleton than Caucasians. When a ROI of the distal radius or distal tibia is chosen using a fixed distance from the midpoint of the radio-carpal joint space, the ROI is positioned more proximally in Chinese [7]. The more proximal positioning exaggerates the racial difference described above; Chinese will have thicker less porous cortices, the matrix mineral density will be higher and trabecular density will be lower [7]. Several approaches can be taken to correct for this positioning error. The recommended approach is to use a percentage of the radial or tibial bone length (~4–6%). If this is not available, correcting for racial differences in bone length by racial differences in the total bone cross-sectional area (CSA) achieves similar accuracy as using the 4–6% of the bone length [7].

In addition, secular drifts in sitting and standing height are race specific. Height generally increases in more recently born individuals forming the young cohort in a cross sectional sample, but this may differ by race, body segment and sex [9,10]. If the secular increase in height is associated with secular trends towards an earlier puberty then the taller stature, irrespective of race, is likely to be due to greater trunk length (because leg length should be shorter if puberty occurs earlier in life in more recently born women).

We hypothesized that, (i) relative to Caucasians, Chinese are shorter mainly due to their shorter leg length, (ii) more recently born women of each race are taller than earlier born women, (iii) Chinese have an earlier menarche and so will have shorter leg length but comparable trunk length, (iv) across age, the taller stature in younger women is due to trunk length not leg length, irrespective of race, and (v) Chinese have lower cortical porosity, higher matrix mineral density, and higher trabecular plate to rod ratio than Caucasians after adjusted for total bone CSA.

2. Methods

2.1. Subjects

We studied anthropometry on 477 healthy Chinese and 278 Caucasians women and quantified bone microstructure in an additional 186 Chinese and 381 Caucasian women aged 18 to 86 years using high-resolution peripheral quantitative computed tomography (HR-pQCT). All women were ambulatory and recruited from the local community in Melbourne, Australia. They had no illness and received no medication known to affect bone mass or size, and had no history of fractures. About 70% of the Chinese were immigrants who arrived in Australia after aged 18 years with a mean stay of 13.4 years (range 1 month to 41 years) while 7% were born in Australia with parents from China. Approximately 90% were from Southern China and South-east Asia. Recalled age of menarche was recorded on the questionnaire. All participants gave informed consent. The study was approved by the Human Research Ethics Committee of the Austin Health.

2.2. Anthropometry

Standing and sitting heights were measured in the morning using a Holtain stadiometer. Sitting height was measured with the women sitting on a stool with the legs at right angles to the trunk [11]. Leg length was calculated by subtracting sitting from standing height. Arm span was measured by the method of Steele and Mattox [12]. Subjects stood straight with shoulder and heels against the wall. The arms were outstretched horizontally with the palms facing forwards. A calibrated extended ruler was used to measure the two points from the middle finger of the right hand to the middle finger of the left hand along the wall. Measurements were recorded to the nearest 0.1 cm.

Body mass was measured by an electronic scale and was recorded to the nearest 0.1 kg. Femur and tibia lengths were measured by using the ruler function in the total body images from DXA (DPX-L, Lunar Corp., Madison, WI, version 4.6). Femur length was the length of the central long axis of left femur from the junction of the upper rim of the femoral neck and the greater trochanter to the distal end of the intercondylar notch [13]. Tibia length was the distance between the medial condyle and the medial malleolus. The coefficient of variation was 1.5% based on three repeated scans in 10 subjects within three weeks.

2.3. Microstructure

The non-dominant distal radius and distal tibia were scanned using HR-pQCT (Xtreme CT, Scanco Medical AG, Switzerland). The default manufacturer protocol was used and the resolution was 82 μm isotropic voxel size [14]. The 110 slices were obtained at a fixed distance of 9.5 and 22.5 mm from the reference line that was manually placed at the middle point of the endplate of the distal radius and tibia, respectively. Of the 567 subjects had HRpQCT measurements, 8 had motion artefact at the radius and 14 had motion artefact at the tibia and were excluded. There were 559 radius scans and 542 tibia scans included in the analysis. Differing sample size in the radius and tibia was also the result of 11 subjects having only distal radial measurements.

Bone was segmented from background and into its compartments using StrAx1.0, a non-threshold-based segmentation algorithm [15,16]. The method automatically and reproducibly segments bone into the compact-appearing cortex, the outer and inner transitional zones, and trabecular bone. In each cortical compartment, porosity was quantified by estimating the void volume fraction of each voxel. Matrix mineral density is quantified by determining the mean density of voxels with attenuation between 80 and 100% of fully mineralized bone. The precision error was 0.8 to 4.0% [15]. The proximal 49 slices were included in the StrAx1.0 analysis for cortical assessment. Total, cortical and trabecular CSA, and cortical thickness were also quantified.

Individual trabecula segmentation (ITS) methods were applied to quantify trabecular plate and rod microarchitecture from HR-pQCT images of the distal radius and distal tibia. Trabecular elements were classified as a surface or curve that was then classified as a plate or rod [17,18]. Axial bone volume fraction (aBV/TV) along the longitudinal axis, plate and rod bone volume fraction (pBV/TV, rBV/TV), plate-to-rod (P-R) ratio, plate and rod number (pTb.N and rTb.N, 1/mm) and the average thickness of plates and rods (pTb.Th, rTb.Th, mm) were assessed [19,20].

2.4. Bone mechanical properties

Bone stiffness and failure load were estimated using micro-finite element analysis (μFEA) for each image. This was applied to the whole bone to determine axial stiffness. Each voxel was converted to an 8-node elastic brick voxel-based element (82 μm^3). For μFEA, bone tissue was modeled as an isotropic, linear elastic material with a Young's modulus (E_s) of 15 GPa and a Poisson's ratio of 0.3 [21].

2.5. Statistical analysis

Summary statistics were expressed as mean ± standard deviation (SD). Unpaired two-sample *t*-tests were used to determine the significance of trait differences between groups. Differences in standardized terms were calculated by dividing the mean difference between groups by the pooled SD for anthropometry, bone microstructural and mechanical parameters. Analyses were performed initially for each covariate to quantify any association with microstructure. The covariates selected for this study were age, height, body mass, total CSA. Those significant univariate relationships (age, height and total CSA) were then examined in a multivariable analysis. Height was then removed from the model due to its collinearity with total CSA. Analysis of Covariance (ANCOVA) was used to adjust for age and total CSA in cortical and trabecular parameters. T score defined as the number of

Table 1

Age, weight, and anthropometry measurements in pre- (18–45 years) and postmenopausal (55–86 years) Chinese and Caucasian women.

Variables	Premenopausal		Postmenopausal	
	Chinese (n = 146)	Caucasians (n = 153)	Chinese (n = 173)	Caucasians (n = 76)
Age (years)	35.4 ± 8.2	34.5 ± 7.8	64.5 ± 6.3[a]	65.9 ± 7.4[a]
Body mass (kg)	55.7 ± 9.1**	65.5 ± 12.9	56.7 ± 8.2**	68.4 ± 15.1
Height (cm)	158.2 ± 5.6**	164.0 ± 5.8	154.5 ± 5.2**[a]	159.7 ± 5.9[a]
Arm span (cm)	157.3 ± 6.7**	165.3 ± 6.6	154.1 ± 5.8**[a]	162.7 ± 6.3[a]
Arm span — height (cm)	−0.95 ± 3.35**	1.26 ± 3.31	−0.39 ± 3.33**	3.15 ± 3.46[a]
Sitting height (cm)	86.3 ± 3.1*	87.1 ± 2.9	83.6 ± 3.0[a]	84.0 ± 3.8[a]
Leg length (cm)	71.9 ± 3.6**	76.9 ± 3.9	71.0 ± 3.1**[a]	75.8 ± 3.7
Femur length (cm)	37.8 ± 1.9**	40.8 ± 2.2	37.6 ± 1.6**	40.6 ± 2.0
Tibia length (cm)	30.3 ± 1.7**	32.5 ± 2.0	29.6 ± 1.4**[a]	31.9 ± 1.9[a]

Mean ± standard deviation (SD). *$p < 0.05$, **$p < 0.001$ compared with Caucasians.

[a] $p < 0.05$ compared with premenopausal women.

SDs from the mean of premenopausal women of the same race. Associations between cortical porosity and matrix mineral density, trabecular BV/TV was analysed using Pearson's correlation. STATA 14.2 (StataCorp. 2015. Stata Statistical Software. College Station, TX: StataCorp LP.) was used for all statistical analyses and $p < 0.05$ (two tailed) was considered as significant.

3. Results

3.1. Racial dimorphism in premenopausal women

The age of menarche did not differ by race (Chinese 12.8 ± 1.3, Caucasians 13.0 ± 1.5 years). Chinese had 0.27 SD shorter sitting height, 1.31 SD shorter leg length (Table 1, Fig. 1), 14.8% smaller distal radial CSA, 7.9% smaller cortical area and 19.3% smaller medullary area. After adjusting for age and total CSA, Chinese and Caucasians had similar cortical and medullary areas but cortical vBMD was higher in Chinese because they had a 0.30 SD lower total cortical porosity and 0.27 SD higher matrix mineral density (Table 2, Fig. 2). Trabecular BV/TV did not differ by race but in Chinese, pBV/TV was 0.41 SD higher, rBV/TV was 0.36 SD lower producing a favorable P-R ratio ($p = 0.001$) (Fig. 2). Chinese had 0.36 SD greater whole bone stiffness and 0.36 SD greater failure load than Caucasians (both $p < 0.05$).

Findings were similar at the distal tibia (Table 3). Chinese had a 8.9% smaller total CSA, 6.5% smaller cortical area and 10.0% smaller medullary area. After adjusting for age and total CSA, Chinese had a

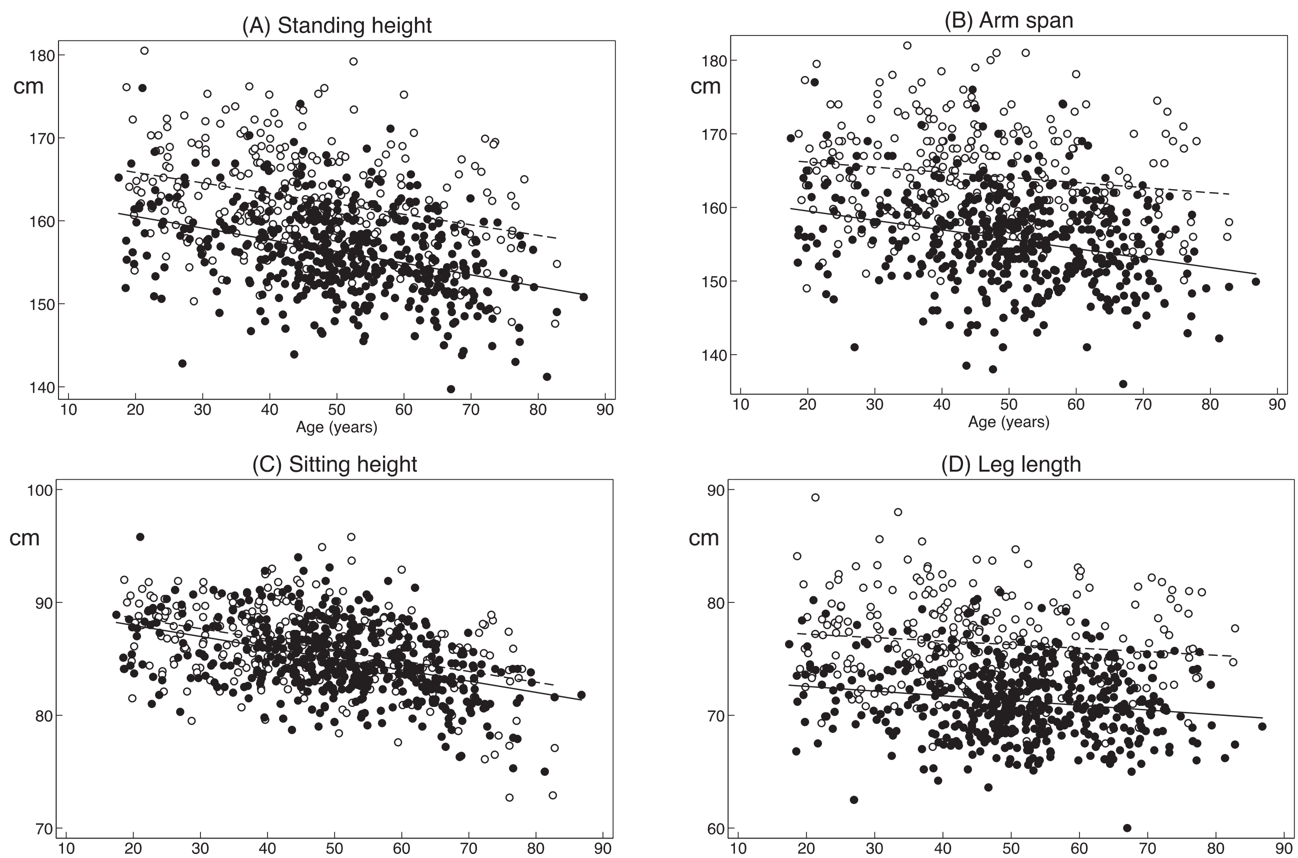

Fig. 1. The age-related differences in (A) standing height, (B) arm span, (C) sitting height and (D) leg length in Chinese (filled circles, solid line) and Caucasian (open circles, dashed line) women.

Table 2
Distal radius microstructure in pre- and postmenopausal Chinese and Caucasian women.

	Premenopausal				Postmenopausal			
	Chinese (n = 67)	Caucasian (n = 155)	*p*	Adj. *p*	Chinese (n = 51)	Caucasian (n = 131)	*p*	Adj. *p*
Age (years)	37.8 ± 8.3	35.6 ± 7.3	0.053		65.0 ± 7.9	64.1 ± 7.2	0.449	
Age at menarche (years)	12.8 ± 1.3	13.0 ± 1.5	0.344		13.7 ± 2.1	13.2 ± 1.3	0.054	
Distal radial CSA								
Total (mm^2)	189.3 ± 32.0	222.1 ± 38.5	< 0.001		198.2 ± 38.2	214.7 ± 37.1	0.009	
Cortical area (mm^2)	80.5 ± 8.7	87.4 ± 9.9	< 0.001	0.325	77.2 ± 8.0	83.2 ± 11.0	< 0.001	0.031
Cortical/total CSA	0.43 ± 0.05	0.40 ± 0.05	< 0.001	0.787	0.40 ± 0.06	0.39 ± 0.05	0.507	0.127
Medullary (mm^2)	108.7 ± 26.8	134.7 ± 32.2	< 0.001	0.325	121.1 ± 33.2	131.5 ± 30.7	0.046	0.031
C.Th (mm)	1.80 ± 0.18	1.81 ± 0.21	0.758	0.129	1.68 ± 0.17	1.76 ± 0.19	0.012	0.003
Cortical porosity (%)								
TC	48.2 ± 4.9	53.0 ± 5.4	< 0.001	0.011	56.5 ± 7.2	56.4 ± 6.2	0.980	0.276
CC	32.4 ± 3.4	35.5 ± 4.0	< 0.001	0.030	40.1 ± 6.1	40.3 ± 6.2	0.789	0.590
Outer TZ	36.8 ± 2.9	39.0 ± 3.2	< 0.001	0.110	45.1 ± 5.6	44.2 ± 5.4	0.292	0.100
Inner TZ	84.4 ± 2.8	85.0 ± 2.8	0.106	0.608	87.6 ± 3.0	86.1 ± 2.9	0.002	< 0.001
MMD (%)	67.3 ± 1.5	66.2 ± 1.5	< 0.001	0.044	65.6 ± 1.8	65.8 ± 1.7	0.348	0.084
Trabecular bone								
BV/TV	0.257 ± 0.046	0.248 ± 0.054	0.195	0.453	0.192 ± 0.058	0.231 ± 0.058	< 0.001	< 0.001
aBV/TV	0.113 ± 0.035	0.096 ± 0.033	0.001	0.009	0.074 ± 0.027	0.085 ± 0.028	0.021	0.012
pBV/TV	0.109 ± 0.045	0.086 ± 0.040	< 0.001	0.008	0.070 ± 0.031	0.077 ± 0.034	0.213	0.098
rBV/TV	0.148 ± 0.029	0.161 ± 0.031	0.004	0.023	0.121 ± 0.038	0.154 ± 0.035	< 0.001	< 0.001
P-R ratio	0.78 ± 0.43	0.55 ± 0.30	< 0.001	0.001	0.60 ± 0.23	0.51 ± 0.22	0.010	0.057
pTb.N (1/mm)	1.42 ± 0.16	1.36 ± 0.18	0.014	0.057	1.24 ± 0.17	1.31 ± 0.18	0.019	0.010
rTb.N (1/mm)	1.77 ± 0.15	1.84 ± 0.15	0.003	0.026	1.65 ± 0.22	1.82 ± 0.17	< 0.001	< 0.001
pTb.Th (mm)	0.214 ± 0.009	0.206 ± 0.008	< 0.001	< 0.001	0.211 ± 0.009	0.208 ± 0.008	0.049	0.176
rTb.Th (mm)	0.215 ± 0.008	0.213 ± 0.006	0.083	0.176	0.209 ± 0.005	0.210 ± 0.006	0.172	0.268
Mechanical properties								
Whole stiffness (N/mm)	86,633 ± 16,011	83,321 ± 18,822	0.210	0.019	60,609 ± 14,947	69,001 ± 17,605	0.003	0.016
Failure load (N)	4115 ± 726	3998 ± 847	0.325	0.020	2880 ± 691	3294 ± 810	0.002	0.011

Mean ± standard deviation (SD). Adj. *p*: adjusted *p* values for racial comparisons were all adjusted for age and total CSA (Premenopausal: at age = 36.3 and total CSA = 212.2; Postmenopausal: at age = 64.3 and total CSA = 210.1). C.Th: cortical thickness; TC: total cortex; CC: compact-appearing cortex; TZ: transitional zone; BV/TV: bone volume/total volume; Tb. Th: trabecular thickness; Tb. N: trabecular number.

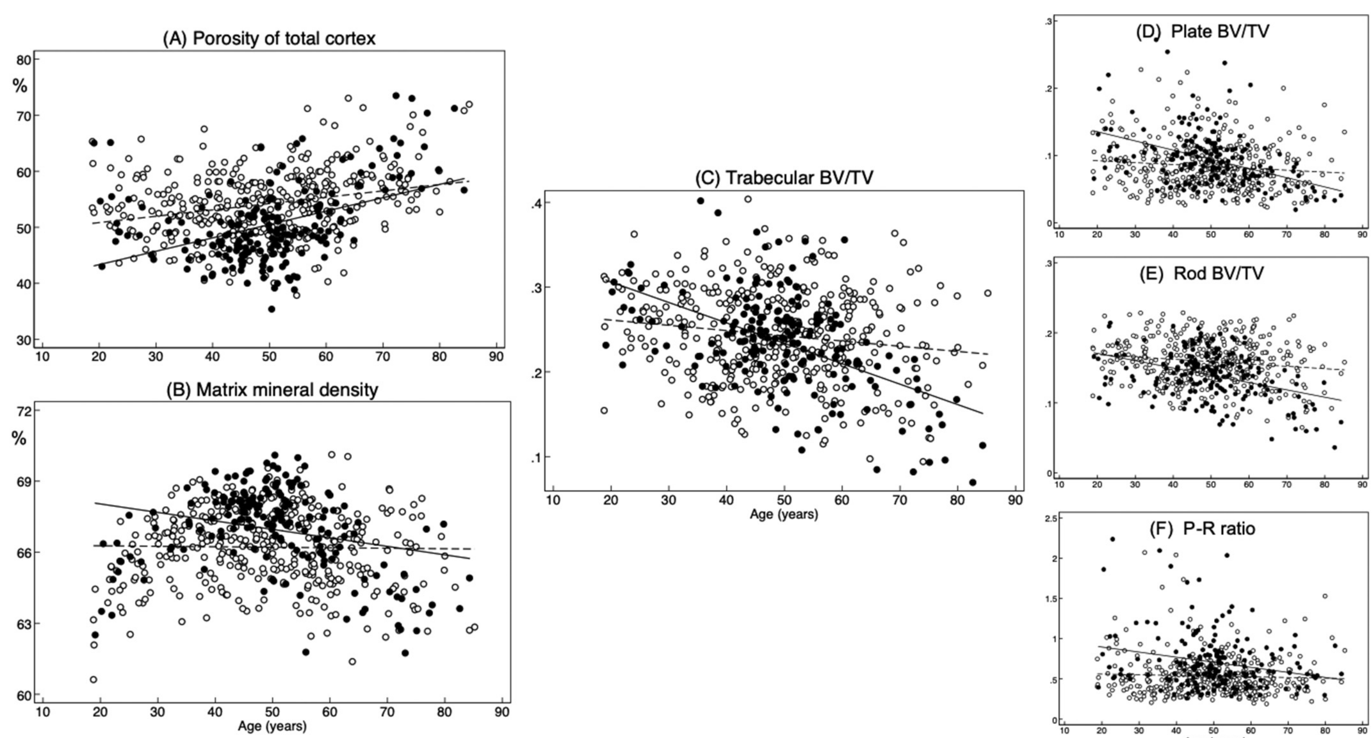

Fig. 2. The age-related differences in (A) porosity of the total cortex and (B) matrix mineral density at the distal radius in Chinese women (filled circles, solid line) and Caucasians (open circles, dashed line). The age-related differences in (C) trabecular BV/TV, (D) plate BV/TV, (E) rod BV/TV and (F) P-R ratio at the distal radius in Chinese women (filled circles, solid line) and Caucasians (open circles, dashed line).

Table 3
Distal tibia microstructure in pre- and postmenopausal Chinese and Caucasian women.

	Premenopausal				Postmenopausal			
	Chinese (n = 65)	Caucasian (n = 151)	*p*	Adj. *p*	Chinese (n = 49)	Caucasian (n = 125)	*p*	Adj. *p*
Age (years)	37.8 ± 8.4	35.8 ± 7.3	0.082		65.2 ± 7.9	64.1 ± 7.3	0.364	
Distal tibial CSA								
Total (mm^2)	568.3 ± 89.4	623.7 ± 118.2	0.001		597.8 ± 110.1	634.5 ± 103.8	0.041	
Cortical area (mm^2)	188.4 ± 20.2	201.6 ± 23.8	< 0.001	0.020	188.8 ± 20.7	194.9 ± 25.0	0.136	0.612
Cortical/total CSA	0.34 ± 0.05	0.33 ± 0.05	0.387	0.015	0.32 ± 0.05	0.31 ± 0.05	0.218	0.824
Medullary (mm^2)	379.8 ± 82.6	422.1 ± 104.7	0.004	0.020	409.0 ± 101.3	439.6 ± 96.7	0.066	0.612
C.Th (mm)	2.27 ± 0.27	2.32 ± 0.26	0.209	0.014	2.22 ± 0.26	2.21 ± 0.30	0.891	0.652
Cortical porosity (%)								
TC	55.1 ± 4.0	58.0 ± 4.6	< 0.001	0.003	65.9 ± 6.1	65.2 ± 6.3	0.533	0.130
CC	35.8 ± 3.4	38.8 ± 4.2	< 0.001	< 0.001	48.6 ± 6.2	49.4 ± 8.2	0.472	0.911
Outer TZ	37.8 ± 2.7	40.3 ± 3.2	< 0.001	< 0.001	50.9 ± 6.3	49.8 ± 7.2	0.345	0.136
Inner TZ	83.7 ± 2.9	84.3 ± 3.1	0.191	0.286	87.7 ± 2.9	86.4 ± 2.8	0.010	0.003
MMD (%)	66.6 ± 1.1	65.7 ± 1.3	< 0.001	0.001	63.7 ± 1.6	64.1 ± 1.6	0.098	0.052
Trabecular bone								
BV/TV	0.267 ± 0.048	0.274 ± 0.054	0.324	0.818	0.220 ± 0.059	0.264 ± 0.049	< 0.001	< 0.001
pBV/TV	0.151 ± 0.048	0.122 ± 0.044	< 0.001	< 0.001	0.118 ± 0.043	0.113 ± 0.038	0.451	0.577
rBV/TV	0.116 ± 0.032	0.152 ± 0.038	< 0.001	< 0.001	0.101 ± 0.032	0.151 ± 0.039	< 0.001	< 0.001
aBV/TV	0.139 ± 0.036	0.116 ± 0.032	< 0.001	< 0.001	0.109 ± 0.035	0.110 ± 0.027	0.899	0.794
P-R ratio	1.44 ± 0.75	0.87 ± 0.49	< 0.001	< 0.001	1.27 ± 0.64	0.82 ± 0.39	< 0.001	< 0.001
pTb.N (1/mm)	1.49 ± 0.12	1.46 ± 0.15	0.204	0.050	1.38 ± 0.17	1.44 ± 0.14	0.013	0.015
rTb.N (1/mm)	1.63 ± 0.18	1.81 ± 0.19	< 0.001	< 0.001	1.54 ± 0.21	1.81 ± 0.20	< 0.001	< 0.001
pTb.Th (mm)	0.229 ± 0.014	0.222 ± 0.012	< 0.001	0.001	0.228 ± 0.011	0.220 ± 0.012	< 0.001	< 0.001
rTb.Th (mm)	0.213 ± 0.007	0.213 ± 0.007	0.950	0.938	0.214 ± 0.007	0.212 ± 0.007	0.198	0.196
Mechanical properties								
Whole stiffness (N/mm)	242,687 ± 46,335	239,671 ± 55,657	0.702	0.030	188,570 ± 57,085	205,462 ± 44,706	0.040	0.156
Failure load (N)	11,258 ± 2129	11,160 ± 2499	0.784	0.033	8770 ± 2575	9626 ± 1999	0.021	0.100

Mean ± standard deviation (SD). Adj. *p*: adjusted p values for racial comparisons were all adjusted for age and total CSA (premenopausal: at age = 36.4 and total CSA = 607.0; postmenopausal: at age = 64.4 and total CSA = 624.2). C.Th: cortocal thickness; TC: total cortex; CC: compact-appearing cortex; TZ: transitional zone; BV/TV: bone volume/total volume; Tb. Th: trabecular thickness; Tb. N: trabecular number.

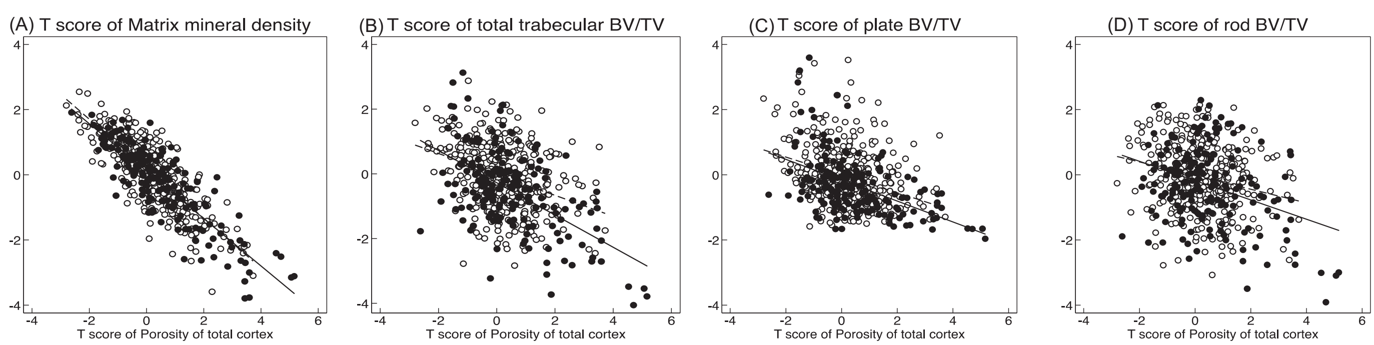

Fig. 3. The scatterplot of T scores of (A) matrix mineral density, (B) total trabecular BV/TV, (C) plate BV/TV, (D) rod BV/TV against T score of porosity of the total cortex in Chinese women (filled circles, solid line) and Caucasians (open circles, dashed line).

3.3% smaller cortical area, a 1.6% larger medullary area, cortical vBMD was higher because porosity was 0.36 SD lower and matrix mineral density was 0.48 SD higher than in Caucasians. Trabecular BV/TV did not differ by race but in Chinese, pBV/TV was 0.64 SD higher, rBV/TV was 0.85 SD lower producing a favorable P-R ratio ($p = 0.001$). Chinese had 0.30 SD greater whole bone stiffness and 0.29 SD greater failure load at the tibia.

3.2. Racial dimorphism in postmenopausal women

Postmenopausal Chinese had later menache than postmenopausal Caucasian women (13.7 ± 2.1 vs 13.2 ± 1.3 years, $p = 0.054$), leg length was 1.46 SD shorter, sitting height was similar, distal radial total CSA was 7.7% smaller, cortical area was 7.2% smaller and medullary area was 6.6% smaller than in Caucasians (Table 1, Fig. 1). After adjusting for age and total CSA, Chinese had a 3.3% smaller cortical area, 2.1% larger medullary area, 5.1% thinner cortices. Total cortical porosity was no longer lower, and matrix mineral density was no longer higher, than in Caucasians (Table 2, Fig. 2). Trabecular BV/TV was lower by 0.69 SD, pBV/TV was similar and rBV/TV was 0.86 SD lower in Chinese so the higher P-R ratio was maintained (after adjustment 0.58 vs. 0.51, $p = 0.057$) (Fig. 2). Chinese had 0.39 SD lower whole bone stiffness and 0.40 SD lower failure load than Caucasians at the distal radius (both $p < 0.05$, Table 2).

Chinese had a 5.8% smaller distal tibial total CSA ($p = 0.041$), 3.1% smaller cortical area ($p = 0.136$) and 7.0% smaller medullary area ($p = 0.066$). After adjusting for age and total CSA, Chinese had similar cortical and medullary areas, similar cortical thickness, total cortical porosity was no lower, and matrix mineral density was no higher than Caucasians (Table 3). Trabecular BV/TV was lower, pBV/TV was similar and rBV/TV was 1.24 SD lower in Chinese so the higher P-R ratio was maintained (after adjustment: 1.24 vs. 0.83, $p < 0.001$). Chinese had similar whole bone stiffness and failure load compared to Caucasians at the distal tibia (Table 3).

In both pre- and post-menopausal Chinese and Caucasian women, there was an inverse correlation between T scores of cortical porosity and matrix mineral density at both sites (r: −0.71 to −0.87, all $p < 0.001$) (Fig. 3). Inverse correlations were present between T scores of cortical porosity and total trabecular BV/TV, plate and rod BV/TV (r: −0.23 to −0.57, all $p < 0.001$) (Fig. 3).

3.3. Secular trends

Menarche occurred earlier in pre- than post-menopausal Chinese women (12.8 ± 1.3 vs 13.7 ± 2.1 yrs, $p = 0.005$), but did not differ in pre- and post-menopausal Caucasians (Table 2). Premenopausal women were taller than postmenopausal women (Chinese: 0.68 SD; Caucasians: 0.74 SD, NS) due to greater sitting height and leg length in both races. Of the secular difference in height, 74% was truncal and 26% was leg length in both races. Arm span was greater in pre- than post-menopausal women in both races (Chinese: 0.51 SD; Caucasians: 0.40 SD, NS).

4. Discussion

We confirm that growth assembles a smaller but more robust skeleton in Chinese than Caucasians. The shorter stature was mainly due to shorter leg length, an effect that may be partly the result of an earlier menarche. However, we did not detect the earlier age of menarche in Chinese than Caucasians. The shorter appendicular skeleton was associated with smaller total and medullary CSAs. The cortices were less porous with a higher matrix mineral density, trabeculae were more plate- than rod-like and estimated bone strength was higher in premenopausal Chinese than premenopausal Caucasians.

The findings in postmenopausal women were different. Chinese were shorter than Caucasians, but contrary to our hypothesis, the racial dimorphism in bone microstructure was not observed. Distal radial cortices were not relatively thicker, cortical porosity was no lower, matrix mineral density was no higher, and trabecular plate BV/TV was no higher than in postmenopausal Caucasians. However, plate to rod ratio remained higher than postmenopausal Caucasians because postmenopausal Chinese had fewer trabecular rods. Estimated bone strength was lower at the distal radius and no different at the distal tibia compared to postmenopausal Caucasians.

Axial and appendicular dimensions are the result of the differing tempo of growth prior and during puberty [22]. Appendicular growth is more rapid than axial growth before puberty and decelerates at puberty as axial growth accelerates. Consequently, an early puberty produces a longer trunk relative to the legs. Thus, the shorter leg length but similar trunk length in Chinese compared with Caucasians may be partly the result of a shorter period of rapid pre-pubertal linear appendicular growth and an earlier and high peak velocity of truncal growth. Whether shorter leg length is associated with better balance and reduced propensity for falls and less severe falls in Chinese is uncertain [23].

Periosteal apposition ceases around the time of puberty. Closure of the epiphyses results in a smaller total CSA while endocortical apposition thickens the cortex. Trabeculae emerging from the growth plate thicken and coalesce contributing to cortical thickness and a reduction in cortical porosity [24,25]. More plate-like trabecular morphology in premenopausal Chinese women is consistent with the notion that the earlier puberty contributes to trabecular bone formation producing 'corticalization' of trabeculae thickening the cortex and forming thicker more highly connected trabeculae. For a fixed bone volume fraction, plate-like trabeculae contribute to mechanical strength [26,27]. Secondary mineralization increases matrix mineral density. Each of these morphological features distinguished appendicular bone in Chinese from Caucasians.

We observed an inverse association with cortical porosity and matrix mineral density in Chinese and Caucasian women. In premenopausal women, remodelling is balanced and slow. Bone multicellular units (BMUs) excavate a transient cavities (porosity) that refill during 3 months with the same volume of bone that is transiently undermineralized until primary and secondary mineralization is complete. Hence, the inverse association between higher porosity and lower matrix mineral density. After menopause, remodelling becomes unbalanced and rapid, now porosity becomes permanent due to less bone being deposited than resorbed. Porosity increases as years since menopause increase and matrix mineral density decreases due to persistent high remodelling replacing more mineralized bone with younger less mineralized bone [28].

After menopause, the racial differences in cortical porosity and matrix mineral density were no longer detected, confirming this observation reported by Boutroy et al. [5]. Whether Chinese lose bone more rapidly after menopause than Caucasians remains uncertain. Some studies support more rapid bone loss in Chinese than Caucasians [29,30], others do not [27]. The lack of consistency may be partly the result of errors introduced by the challenges in the positioning of the ROI. Lower cortical porosity and higher matrix mineral density in Chinese may be partly due to positioning the ROI more proximally, a location of thicker and less porous cortices with higher matrix mineral density [7]. We adjusted for this source of error by correcting for total CSA, an approach shown to largely rectify this potential source of error [7]. We also addressed this by examining a group of Chinese and Caucasian premenopausal women matched by leg length (data not shown) and the racial differences in bone microstructure remained the same. Prospective studies are needed with attention to positioning the ROI within and between individuals to examine this question.

The study has limitations other than the challenges of positioning the ROI. It is cross-sectional. Age of menarche was self-reported so its validity cannot be assured [31]. Chinese living in Australia might have diverse origins and inferences based on the results of this study may not be valid in other cohorts. About 90% of the women were from Southern China and South-east Asian and they arrived in Australia after aged 18 years so the genetic and local environmental factors operative in China may have influenced morphology and remain undefined. FEA models the behaviour of bone under constraints imposed by the model [32]. While the estimated stiffness and peak strength have been tested ex vivo, whether these models describe the mechanical behaviour of the bone in vivo is uncertain. Another limitation is the challenge in segmenting cortical from trabecular bone in advanced age when cortical fragments produced by intracortical remodelling may result in these fragments being 'seen' as trabeculae leading to an over estimate of 'trabecular' density and an underestimate in cortical porosity (which is 'seen' as being part of the medullary canal) [16].

In summary, Chinese assemble a more robust appendicular skeleton with less porous cortices with a higher matrix mineral density and more plate-like than rod-like trabeculae occupying the smaller medullary canal. While this structure may be less accessible to being remodelled, these features were not observed in postmenopausal women; cortices were thinner, porosity and matrix mineral density were no different to Caucasians and trabecular BV/TV was less suggesting the benefits may be lost during advancing age and so may contribute to bone fragility.

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