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**Adaptations in tibial cortical thickness and total volumetric bone density in
postmenopausal South Asian women with small bone size**

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Abstract

There is some evidence that South Asian women may have an increased risk of osteoporosis compared with Caucasian women, although whether South Asians are at increased risk of fracture is not clear. It is unknown whether older South Asian women differ from Caucasian women in bone geometry. This is the first study, to the authors' knowledge, to use peripheral Quantitative Computed Tomography (pQCT) to measure radial and tibial bone geometry in postmenopausal South Asian women. In comparison to Caucasian women, Asian women had smaller bone size at the 4% (-18% $p<0.001$) and 66% radius (-15% $p=0.04$) as well as increased total density at the 4% (+13% $p=0.01$) radius. For the tibia, they had a smaller bone size at the 4% (-16% $p=0.005$) and 14% (-38% $p=0.002$) sites. Also, Asians had increased cortical thickness (-17% $p=0.04$) at the 38% tibia, (in proportion to bone size (-30% $p=0.003$)). Furthermore, at the 4% and 14% tibia there were increased total densities (+12% to +29% $p<0.01$) and at the 14% tibia there was increased cortical density (+5% $p=0.005$) in Asians. These differences at the 14% and 38% (but not 4%) remained statistically significant after adjustment for Body Mass Index (BMI). These adaptations are similar to those seen previously in Chinese women. Asian women had reduced strength at the radius and tibia, evidenced by the 20-40% reduction in both polar Strength Strain Index (SSIp) and fracture load (under bending). Overall, the smaller bone size in South Asians is likely to be detrimental to bone strength, despite some adaptations in tibial cortical thickness and tibial and radial density which may partially compensate for this.

Keywords South Asians, postmenopausal women, pQCT, bone, ethnicity

1.0 Introduction

There is some concern that migrant Asians to western societies may have poorer musculoskeletal health than the indigenous population. For example, a recent U.S. study found that South Asian women had a higher prevalence than Caucasian women of femoral neck osteoporosis [1]. South Asian women have also been found to have a higher incidence of wrist fracture than Chinese women, although South Asians did not differ from White Caucasian women on these measures [1, 2]. To investigate these epidemiological findings of increased osteoporosis incidence, but similar fracture rates, it is important to examine the differences in bone geometry between South Asians and White Caucasians.

Measures of bone geometry have been associated with prediction of fracture risk [3-5], leading to considerable research assessing bone geometry in different population groups [6-9]. However, this has been limited within the female South Asian population, with most studies only assessing areal Bone Mineral Density, using dual-x ray absorptiometry (DXA). These studies suggest a lower areal bone mineral density (aBMD) in South Asian compared with Caucasian women [10, 11]. However, aBMD measures do not assess true volumetric density (vBMD), as they are influenced by actual bone size. The smaller bone size of South Asian populations has been found to explain the apparent lower aBMD in this ethnic group as compared with Caucasians [12].

Furthermore, research suggests that osteoporosis diagnosis varies when western dwelling individuals of South Asian descent are classified using aBMD according to Caucasian as opposed to Indian reference ranges [13], suggesting this underestimation of bone density may have clinical implications.

Therefore to confirm if South Asians do have a lower bone density than Caucasians, it is important that their volumetric bone mineral densities (vBMD) are investigated in addition to

bone structure (e.g. cortical and trabecular density) and size . The known small bone size in South Asians suggests a biomechanical detriment that is likely to lead to increased risk of fracture.

It is possible to measure bone size, vBMD and other aspects of bone architecture using pQCT although to date very few studies have assessed a South Asian sample by this method. The study by Ward et al (2007)[14] assessed the radius by pQCT in premenopausal UK South Asian women and showed a smaller cross sectional area, lower bone mineral content (BMC) and vBMD, smaller cortical thickness and cortical area in South Asians compared to Caucasians [14]. Interestingly, ethnic differences in body size in this study did not explain these differences, and there was no difference in stress-strain index by ethnicity despite the observed differences in bone geometry [14]. The only other study to assess pQCT measures in adult South Asian populations found similar vBMD at the radius in young UK South Asian women compared to Caucasian women[12]. Recently, bone geometry in Chinese women has been examined in detail using HR-pQCT, and it has been found that an increased vBMD and cortical thickness, when compared to Caucasians, may lead to increased bone strength, despite a smaller bone size [9, 15-17].

It must be emphasised that the above findings only relate to premenopausal women, and to the radius. To the authors' knowledge there has been no research using pQCT to examine bone geometry of either the radius or tibia in postmenopausal South Asian women, either dwelling in the UK or in South Asia. Therefore, bone geometry data are urgently needed in this group. It would be clinically relevant to assess whether similar bone adaptations are present in South Asian women as have been seen in Chinese women.

Hence, in this study we assessed bone geometry at the radius and tibia, using pQCT, in postmenopausal South Asian women and compared them with postmenopausal Caucasian

women. Based on previous research comparing South Asian and White Caucasian populations[12], we hypothesised that for all sites of the radius, total vBMD would be similar between the two ethnic groups, but with South Asians having a smaller bone size. It is known that postmenopausal women of South Asian origin living in the UK have a higher BMI than their Caucasian counterparts, due to their reduced standing height and increased relative body weight for height. Therefore, it was hypothesised that there would be increased tibial vBMD in South Asians compared to Caucasians, as a result of the increased weight bearing load of a larger BMI on a smaller bone size.

2.0 Materials and Methods

2.1 Subjects

Subjects had been enrolled previously in the D-FINES study (Diet, Food Intake, Nutrition, and Exposure to the Sun in Southern England) at the University of Surrey, UK. This was a longitudinal cohort study conducted from June 2006-June 2007. A random sample of healthy Caucasian participants had been recruited via the databases of General Practitioner surgeries in Surrey, Hampshire, Berkshire and outer London. Healthy South Asian women fulfilling the same inclusion criteria had been recruited via local Asian Women's networks. Ethnic origin was self-reported. All the South Asian women were born in South Asia, and were mainly of Pakistani and Indian origin. It was not possible to match the Asian and Caucasian women for height and BMI as the populations have widely different anthropometric characteristics. In terms of exclusion criteria, potential participants were excluded from the study if they had a diagnosis of calcium homeostasis disorders, including liver or renal disease. They were also excluded if they were currently taking steroids or any other prescribed medication likely to affect bone, calcium or vitamin D metabolism. Participants were screened for abnormalities in liver, thyroid and renal function. Any women showing an abnormality on any of these tests was excluded and her doctor notified of the abnormal result. The inclusion criteria were women who were aged 19–70 years, of Caucasian or South Asian origin, of any BMI category, who were premenopausal or postmenopausal and who had not suffered from any condition or taken any prescribed medication likely to affect their bone metabolism. Women needed to be willing to attend the University of Surrey Clinical Investigations Unit for key measurements over a period of 12 months and must not have been frequent fliers abroad during that time. Occasional holiday trips were acceptable. If subjects were users of a vitamin D supplement, they were allowed to partake in the study as long as

they were willing to refrain from using the supplement 2–3 months before the data collection period and did not use the supplement during the 12 month data collection period (June 2006–May 2007).

In D-FINES 2006, n=375 subjects undertook a DXA scan. In June to September 2010, the entire original cohort of n=375 postmenopausal and premenopausal women were contacted and invited to return to the University of Surrey for pQCT, anthropometric and biochemical measurements. One hundred and twenty women (32% of original cohort) returned. Of these women, n=82 (n=21 South Asian; n=61 Caucasian) were postmenopausal, their results are reported here. All of the n=82 postmenopausal women had a pQCT scan of the radius undertaken. Due to time constraints, n=76 also had the tibia scanned (n=19 South Asian; n=57 Caucasian). Some of the women, as a result of the DXA scan obtained during the original study in 2006, had subsequently been diagnosed with osteoporosis or osteopenia and were now on anti-resorptive medications (mainly bisphosphonates). These women on bone medications (n=14; n=3 South Asian; n=11 Caucasian) had pQCT scans undertaken but were excluded from the current data analysis. This left n=68 (n=50 Caucasian and n=18 South Asian) radius measurements and n=65 (n=48 Caucasian and n=17 South Asian) tibia measurements for use in this analysis. Of these n=18 South Asian women, n=8 (44%) had been born in India, n=5 (28%) in Pakistan and n=5 (28%) in other South Asian countries. Anthropometric information (height, weight, hip and waist circumference) were collected using standard weighing scales and a standard stadiometer. Data were also collected on health and lifestyle by questionnaire. Written, informed consent was given by all participants, and the research was approved by the Local Research Ethics Committee (National Health Service 10/H1109/25) and the University of Surrey Research Ethics Committee (EC/2010/53/FHMS). All research was conducted in accordance with the Declaration of Helsinki.

2.2 Bone densitometry

Bone geometry was measured at the radius and tibia using a Stratec X2000L (Stratec Medizintechnik, GmbH, Pforzheim, Germany; software version 6.20) pQCT scanner. The radius in the non-dominant arm and the equivalent tibia were scanned. Radius slices (2.2mm) were taken at the distal end and at the mid shaft of the radius (4% and 66% sites). Tibia slices (2.2mm) were taken at the distal end of the tibia shaft (4%) and also further up the tibial shaft (14% and 38% sites). Figure 1 illustrates these scan positions, with the parameters measured or calculated at each site. The distal radius (4%) was examined due to the clinical significance of this site. One diaphysial radius site (66%) and two diaphysial sites of the tibia (14% and 38%) were also measured due to the potential importance of considering the morphology of the whole bone for fracture risk.

Equal numbers of South Asian and Caucasian subjects were scanned by each of the two operators of the machine (ALD and OAH). Scanning procedure for both the South Asian and Caucasian women was also identical, using the same pQCT machine and software with standardised instructions. Particularly, the procedure for measuring the length of radius and tibia was standardised and undertaken as per manufacturer's guidelines. Hence, radial object length was assessed as the distance (in mm) from the processus styloideus to the olecranon. Tibial object length was assessed as the distance from the middle of the inner ankle to the tibial plateau. A scout view of 30 lines, at 40mm/sec was run for each participant for each scan. The reference line was placed at the cortical end plate of the radius or distal end of the tibia, as appropriate. The CT scan was run at 20mm/sec for the tibia and 30mm/s for the radius, both with a voxel size of 0.50mm. For analysis, the threshold for cortical bone was set automatically by the software at 711mg/cm^3 . All standard parameters (vBMD, bone mineral content (BMC), bone area, bone density of trabecular and cortical areas, cortical

thickness and periosteal/endosteal circumferences) were reported. Fracture load (under bending) was calculated by the software using a bending test length of 180mm and bone ultimate bending strength of 180Mpa. The formula used by the Stratec software for calculation of bending fracture load is:

$$F_B = \frac{4\sigma_B * SSI}{l}$$

FB= Fracture load [N]; σ_B = Ultimate load = 180 Mpa; l = distance between supports

The ratio of cortical thickness in relation to total bone area was calculated (cortical thickness / total area; abbreviated to CT:ToA). The SSIp is a measure of the bone's ability to resist torsional forces, and was calculated automatically by the software using the formula

$$SSI = \sum_{(i=1,n)} ((r_i^2 * a * CD) / r_{max} * ND).$$

CD= measured cortical density (mg/cm²) and ND=normal physiological density (1200mg/cm³) (source: Stratec manual 6/11/9 Man62e.doc)

2.3 Statistical Analysis

For unadjusted analyses, independent T-tests were performed to assess ethnic differences in each available pQCT parameter at each site. Analysis of Covariance (ANCOVA) was then used to adjust for age, height and BMI in separate analyses. These confounders were not assessed together due to the high degree of correlation between them. All variables not showing a normal distribution were log transformed prior to statistical analysis, and normality re-checked by Kolmogorov-Smirnov test. PASW (v.18.0) (Chicago, US) was used for the t-test statistical analyses, and GraphPad Prism (v.5.04) (San Diego, US) was used for the linear regression analyses and production of figures. Statistical significance was assessed using the conventional $p < 0.05$.

3.0 Results

3.1 Participant Characteristics

Participant characteristics are given in table 1. South Asian women had a significantly higher BMI compared to the Caucasian women ($p=0.007$), with the Asians on average being classified as borderline overweight-obese (mean= 29.6, SD=4.2), and the Caucasians on average being considered borderline normal-overweight (mean= 25.9, SD=5.0). There was a small but significant difference in age between the two groups, with Caucasians on average two years older than Asians (66 (4.8) vs. 64 (3.6) years respectively, $p=0.05$) but no significant difference in years since onset of menopause. Ethnic differences for all pQCT parameters are summarised in table 2 and 3. Values for Asian parameters, as a percentage of Caucasian parameters, are illustrated in figures 2 and 3. In the text, for brevity, unadjusted data is reported, with the adjustments also reported if deemed to be significant to the interpretation of the results.

3.2 Distal radius- 4%

There was no significant difference in total BMC by ethnicity, even after adjustment for confounders. However, Asians had a significantly smaller area than Caucasians (-18%, ($p<0.001$)) and a significantly greater total density (+13%, ($p=0.014$)). Trabecular area was significantly smaller in Asians than Caucasians (-18%, ($p<0.001$)), but trabecular density was not significantly different.

3.3 Radial Shaft-66%

Total area (-15% $p=0.039$) and age adjusted total BMC (-12% $p=0.029$) were significantly smaller in the Asians. Cortical area was also smaller in Asians (-10%, $p=0.042$), but there

was no significant ethnic difference in cortical density. In Asians,, the CT:ToA ratio was 108% of that of the Caucasians ($p=0.329$). This suggests the Asians had a non-statistically significant trend for a thicker cortex in relation to their overall bone size.. In terms of bone strength, SSIP ($p=0.023$) and fracture load (x axis; $p=0.03$ and y axis; $p=0.02$) were significantly higher by around 20% in Caucasians. These differences were not statistically significant when height was controlled for, suggesting they were due to the smaller skeletal size of the Asians.

3.4 Distal Tibia- 4%

There was no significant ethnic difference in total BMC, but total area was significantly smaller in Asians (-16%, $p=0.005$). Accordingly, total density was significantly larger (+12%, $p=0.003$). The increased total density did not remain significant when BMI was controlled for, suggesting this might be influenced by the increased weight for height in the Asians. Trabecular area was larger in Caucasians (+16%, $p=0.005$); however, there was no significant ethnic difference in trabecular density.

3.5 Tibia Shaft-14%

BMC was significantly lower in the Asians (-24%, $p=0.013$), with total area smaller by 27% ($p=0.002$) and total density higher by 29% ($p<0.001$). Also, cortical area was significantly smaller by 19% in Asians ($p=0.051$), with cortical density 5% higher ($p=0.001$). The increased cortical density was still significant after adjusting for the confounders, suggesting this was not due to increased BMI. In Asians, the CT:ToA ratio was 174% of that of the Caucasians ($p<0.001$), suggesting a significantly thicker cortex in the Asians, in relation to their overall bone size. For measures of bone strength, SSIP was significantly reduced in

Asians by 37% ($p=0.006$) This difference remained significant, even after adjusting for age, height and BMI ($p<0.01$).

3.6 Tibia Shaft-38%

Total bone area was smaller in Asians (-30%, $p=0.003$) with a smaller BMC (-27%, $p=0.004$). There was no significant difference in total density, or cortical density by ethnicity. Cortical area was significantly smaller by 28% ($p=0.004$) and cortical thickness was significantly smaller by 17% ($p=0.035$). The CT:ToA ratio in the Asians was 117% of that of the Caucasians ($p<0.001$). However, In Asians, SSIP was significantly reduced by 38% ($p<0.001$). Fracture load was also reduced in Asians by 30% (y axis; $p=0.02$) to 40% (x axis; $p<0.001$)

3.7 BMI relationships with tibia measurements

The associations between BMI and the tibial adaptations (tibial total density and tibial cortical thickness) seen in the Asians were examined for both ethnic groups by linear regression. In Caucasians, there were weak, but statistically significant, positive relationships between BMI and total density at the 4% ($R^2=0.177$, $p=0.003$) and 14% ($R^2=0.099$ $p=0.030$) sites but not the 38% ($R^2=0.029$ $p=0.245$) site. Similar results were found for BMI and cortical thickness at the 14% ($R^2=0.138$ $p=0.009$) site but not the 38% ($R^2=0.035$ $p=0.206$) site. For Asians there were no significant associations between BMI and total density at the 4% ($R^2=0.006$ $p=0.761$), 14% ($R^2=0.165$ $p=0.106$) and 38% ($R^2=0.047$ $p=0.405$) sites. There were also no significant associations between BMI and cortical thickness at the 14% ($R^2=0.004$ $p=0.810$) and 38% ($R^2=0.091$ $p=0.240$) sites. The above relationships are illustrated in Figure 4.

4.0 Discussion

4.1 Radius

At the distal (4%) radius, we found smaller bone size and a similar BMC between Caucasians and Asians, with the smaller bone size in the Asians leading to increased total density. In contrast, for the mid shaft (66%) radius, although we found a smaller area, we also found less BMC, and thus similar bone density to that of Caucasians. Interestingly, cortical thickness at the 66% radius was also proportionately thicker (for overall bone size) in the Asians.

These findings suggest an ethnic difference in radial bone geometry at the distal radius, which, due to smaller bone size, are predicted to translate into poorer bone strength in Asians. Indeed, much lower radial bone strength (strength strain indexes) was predicted in Asians than Caucasians. This difference did not persist when height was controlled for, which suggests that lower bone strength in the Asians was mainly explained by their smaller bone size. As SSI and fracture load calculations do not consider the thickness of the cortex, further modelling or mechanical testing would be required of the bone properties to assess whether a thicker cortex in Asian women at the diaphysial radius increases bone strength. Also, SSI and fracture load calculations were only assessed at the mid shaft radius, so this estimate did not consider the increased total density seen at the distal site. Despite the limitations of using the SSI and the fracture load as measures of bone strength, the existence of such poor estimated radial bone strength in Asians is a matter of concern, considering the increased risk of fracture this would predict. It is particularly of concern that slender bones may also contain more damageable bone material [18].

In terms of previous research, our finding of a smaller radial bone size in Asians concurs with findings in younger South Asian women [12, 14] and in other Asian groups (e.g. Chinese [9], Vietnamese [19]). However, some of our findings are in contradiction to previous research. Islam et al, (2011) [20] found that premenopausal women of Bangladeshi origin had no

differences at the distal (4%) radius in total BMC, total area or trabecular density when compared to Finnish Caucasians. This supports our finding of no ethnic differences in BMC and trabecular density but contrasts with our results where we found smaller bone area at this site in South Asians. At the mid shaft radius, Islam et al, (2011) [20] found that the Bangladeshi women had smaller total BMC, total area, cortical area, and cortical density, but a similar SSI to the Caucasians [20]. This is again similar to our results, except that we found equivalent cortical density and BMC at this site, a thicker cortex (in proportion to bone size) and a lower SSI. Ward et al (2007)[14] found no differences in trabecular vBMD, total vBMD or total area at the distal radius in their premenopausal South Asian women. These results are in discordance to our older South Asian cohort who showed a smaller total area at both the distal and mid shaft radius, as compared to Caucasians, as well as increased total density at the distal radius. The most likely explanation for the differences between our study results and that of previous research is the postmenopausal status of our participants. Indeed, age and oestrogen status are important determinants of bone structure, so it is difficult to compare the results of our postmenopausal South Asian women with that of studies of premenopausal women, as all of our postmenopausal women grew up on the South Asian continent. Therefore, their childhood nutrition and lifestyle factors (e.g. exercise) are likely to be different from that of South Asian premenopausal women, who are usually born in the UK, or enter the UK at a very young age. This is likely to have affected their bone development, including that of peak bone mass.

4.2 Tibia

For the distal tibia, we found that bone in Asians is similar in structure to Caucasians, with all parts in proportion but on a smaller scale. However, we also found increased total density at this site in Asians. This increased total density did not remain significant when BMI was

controlled for. This suggests that the total density at this bone site was influenced by the increased weight for height in the Asians, which perhaps causes increased compression strain at this tibia area. However, the finding of no relationship between BMI and total density at the 4% site in Asians did not support this conclusion.

At the 14% tibia, as at the distal tibia, we found a higher total density and higher cortical density in Asians than Caucasians, due to increased bone mineral relative to smaller bone size. Again, we could speculate that this may be an adaptation to offset the detrimental effect of increased body weight for height, but this was not supported by the data on relationships between BMI and tibial total density in Asians. Bone strength (SSI) in our South Asian women at the 14% site was also consistently and substantially (30-40%) lower than in the Caucasians. This was despite an increased cortical density which suggests the strength detriment was due to smaller bone size. Last, for the 38% tibia in Asians, our findings again suggested a bone that is smaller, but proportionately similar in structure to Caucasians. However, interestingly, there was an increased cortical thickness in relation to overall bone size (i.e. the same cortical thickness as that of Caucasians, but in a smaller bone) and also reduced SSI and fracture load. Despite this, there was no increased bone density at this site. This is likely due to the priority for offsetting torsion and bending forces at the more mid shaft section of the tibia, rather than compressive strength.

In terms of comparing our tibia data with previous research, unfortunately there are no known South Asian data at the tibia to compare with our older South Asian sample. However, tibial bone geometry has been studied in Chinese women. It is well established that Chinese women have both a thicker cortex and thicker trabeculae inside a smaller bone size [21]. These adaptations may be beneficial in improving bone strength as more bone mineral within a smaller bone size will reduce the amount of bone remodelling. This is due to a lower surface area (with the denser bone), for remodelling to take place, which is especially

important during ageing [21]. We saw this adaptation in our older South Asian women, with all sites having a smaller bone size with either equivalent mineral mass, or proportionately more mass for size than Caucasians.

Interestingly, the ethnic difference in overall bone size seen in our present study was even larger than that previously reported for older Chinese and Caucasian women by Walker et al (2011)[9]. Our study showed a 15-20% smaller total area at the radius and 16-38% smaller total area at the tibia in the Asians as compared with the Caucasians. This is in comparison to 10% smaller area at the distal radius and 8% smaller area at the distal tibia seen in the Chinese women [9]. As described above, we found a higher cortical thickness (in relation to size) in Asians at the 38% tibia as compared to Caucasians. An increased cortical thickness has also been seen in other groups of East Asian women at the radius and tibia, and femoral neck [6, 9]. Walker et al (2011)[9] found a significantly higher cortical thickness (+10% tibia, +18% distal radius) in older Chinese women compared to older Caucasian women. These differences could be partly explained by differences in anthropometry between South Asian and Chinese women. A recent study found that 50-69 year old South Asian women had a significantly higher BMI than Chinese women [1]. In agreement with this, our South Asian women were of a similar height, but heavier body weight, as compared with the Chinese women in the study by Walker et al [9]. Therefore, it appears that South Asians have an increased weight for height, as compared with Chinese women. This means they are likely to have an even greater need for adaptations at the tibia to withstand increased loading.

However, we did not find the increased trabecular density at the distal sites that has been seen in some [9, 16] but not all studies [9, 19] of East Asian women. The differences in resolution in the two different types of pQCT and site positioning used in our study as compared with other studies may explain some of this variation, as well as the different ethnic groups studied.

4.3 Relationships between BMI and geometry of the tibia

As mentioned above, it would be thought that some of the tibial adaptations may be due to increased BMI in the Asian women. However, the lack of statistical significance for the relationship between tibial total density and cortical thickness and BMI in the Asians does not support this hypothesis. Nonetheless, it is possible that this analysis was underpowered, due to small numbers of Asian participants. Indeed, there was a weak, but statistically significant relationship between BMI and total density, and between BMI and cortical thickness in the Caucasian women, for whom a larger sample existed. Also, in some cases (e.g. 14% total density), the Asians had a larger correlation coefficient than the Caucasians, although this was not statistically significant. This suggests that at least for some bone parameters, the small sample size is affecting the significance of the results. Alternatively, we can speculate that the ethnic differences seen in this study are due to adaptations to improve strength in a smaller bone. This seems very likely due to the adaptive ability of bone to change its structure in response to an increased weight for height. In addition, it is not known whether there are other ethnic differences in the growth or ageing process which could also underpin these differences. In terms of ageing, there is some research which suggests there is a very fast rate of bone loss after the menopause in South Asian women [22].

4.4 Limitations

There are some limitations to this work that should be considered. It is likely that there are bone architectural differences between South Asians and Caucasians which are not measurable without the use of HR-pQCT (e.g. connectivity, number and thickness of individual trabeculae). Also, the scope of our study was restricted to a small number of younger elderly, postmenopausal women. Our Asian women were of relatively high socio-

economic status and reasonably good health, so are likely to be an optimistic description of the true bone health of the wider population group.

5.0 Conclusion

To conclude, we found that older South Asian women have smaller bone size, and heavier body weight for skeletal size, but have some structural adaptations to improve strength.

These include increased total density at the distal radius and distal tibia, as well as a higher total density and higher cortical density at the 14% tibia. There was a proportionately thicker cortical thickness in relation to bone size at the 66% radius and 38% tibia. However, despite these adaptations, the wider implications are that South Asian women are still likely to be of higher fracture risk than same-age Caucasians, because of the substantial negative contribution to strength of a smaller bone size.

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Dedication

This paper is dedicated to Mr John Pheasant, Practice Manager at Thornton Heath Medical Centre, London who helped with the study recruitment for the D-FINES study and who sadly died in 2008.

Authors' roles

Authors' roles: Study design: SLN, KHH, ALD and OAH. Study conduct: SLN, ALD, KHH and OAH. Data collection: SLN, OAH, ALD and KHH. Data analysis: ALD, SLN, KHH. Data interpretation ALD, SLN, KHH, KH, JLB, MAG, LC. Drafting manuscript: ALD, SLN, KHH, KH, JLB, MAG, LC. Revising manuscript content: ALD, SLN, KHH, KH, JLB, MAG, LC. Approving final version of manuscript: ALD, SLN, KHH, KH, JLB, MAG, LC. SLN takes responsibility for the integrity of the data analysis.

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Tables and Figures

Table 1 Participant characteristics

	CAUCASIAN n=50		ASIAN n=18		T-test
	Mean	SD	Mean	SD	p
Height (cm)	161.8	6.8	154.6	4.8	<0.001
Weight (Kg)	67.9	12.0	69.6	9.2	0.594
BMI (Kg/m ²)	25.9	5.0	29.6	4.2	0.007
Age ^a	65.9	4.8	63.5	3.6	0.052
Time since menopause onset(years)	16.3	6.7	16.8	2.9	0.861

a Age ranges: Asians=58-71 years; Caucasians 59-75 years

Table 2 Radial bone geometry outcomes by ethnic group- raw data and adjusted for age/BMI

Parameter	CAUCASIAN (C) n=50		ASIAN (A) n=18			Independent T-test/ANCOVA			
Radius	Mean	SD	Mean	SD	A as % C	P ^a unadj.	P ^b age	P ^c height	P ^d BMI
4% Radius									
BMC g/cm	1.03	0.20	0.96	0.18	93.2	0.203	0.176	0.997	0.075
ToA mm²	384	63	314	45	81.8	<0.001	0.000	0.043	<0.001
ToD mg/cm³	272	54	306	35	112.8	0.014	0.027	0.089	0.100
Trab A mm²	173	28	141	20	81.8	<0.001	0.000	0.043	<0.001
Trab D mg/cm³	168	44	183	33	108.6	0.209	0.193	0.314	0.524
66% Radius									
BMC g/cm	0.99	0.20	0.88	0.15	88.9	0.059	0.029	0.152	0.001
ToA ≠ mm²	154	38	130	26	84.6	0.039	0.038	0.068	0.002
ToD mg/cm³	655	99	688	82	105.1	0.209	0.396	0.084	0.178
SSIp ≠ mm³	245	79	196	57	79.9	0.027	0.022	0.185	0.002
CoA mm²	68	16	61	11	89.7	0.042	0.024	0.415	0.007
CoD ≠ mg/cm³	1070	51	1088	40	101.7	0.179	0.533	0.004	0.113
CT mm	1.8	0.4	1.8	0.4	97.8	0.73	0.359	0.468	0.512
CT:ToA	0.013	0.010	0.014	0.004	108	0.329	0.472	0.208	0.180
Fracture Load x(N)	500	166	398	130	79.5	0.034	0.031	0.105	0.002
Fracture Load y (N)	564	162	458	135	81.1	0.021	0.011	0.142	0.001

Radius site 4% (distal) 66% (mid shaft) BMC= bone mineral content SSIp=polar strength strain index, ToA= total area,

ToD=total density, CoA=cortical area, TrabA=trabecular area, TrabD=trabecular density ^aRaw data; ^badjusted for age ^cadjusted for height

^dadjusted for BMI ; ≠log transformed for statistical analysis

Table 3 Tibial bone geometry outcomes by ethnic group- raw data and adjusted for age/BMI

	CAUCASIAN (C) n=48		ASIAN (A) n=17			Independent T-test/ANCOVA			
	Mean	SD	Mean	SD	A as a % C	P ^a unadj.	P ^b age	P ^c height	P ^d BMI
4% Tibia									
BMC g/cm	3.02	0.76	2.87	0.55	95.0	0.456	0.340	0.835	0.114
ToA mm ²	1116	238	940	121	84.2	0.005	0.003	0.136	0.005
ToD mg/cm ³	272	49	304	31	111.9	0.003	0.020	0.092	0.105
TrabA mm ²	502	107	423	54	84.2	0.005	0.003	0.137	0.005
TrabD mg/cm ³	226	48	237	43	104.6	0.436	0.393	0.859	0.954
14% Tibia									
BMC g/cm ³	2.26	0.35	1.71	0.77	75.7	0.013	<0.001	0.003	<0.001
SSI _p mm ³	1366	291	860	532	62.9	0.006	<0.001	0.001	<0.001
ToA mm ²	505	84	316	162	62.7	0.002	<0.001	<0.001	<0.001
ToD mg/cm ³	457	84	587	123	128.5	<0.001	<0.001	0.001	<0.001
CoA mm ²	140	27	116	49	82.8	0.051	<0.001	0.047	<0.001
CoD mg/cm ³	1033	52	1084	50	105.0	0.001	0.004	0.001	0.005
CT mm	1.9	0.4	2.1	0.4	107.2	0.241	0.571	0.320	0.690
CT:ToA	0.004	0.001	0.010	0.008	200	<0.001	<0.001	<0.001	<0.001
38% Tibia									
BMC g/cm	3.21	0.40	2.34	1.08	72.9	0.004	<0.001	0.002	<0.001
SSI _p mm ³	1462	283	905	522	61.9	<0.001	<0.001	0.002	<0.001
ToA mm ²	391	49	272	116	69.7	0.003	<0.001	<0.001	<0.001
ToD mg/cm ³	828	91	840	80	101.6	0.607	0.854	0.717	0.955
CoA mm ²	254	36	183	88	72.1	0.004	<0.001	0.003	<0.001
CoD mg/cm ³	1135	35	1151	33	101.5	0.095	0.235	0.053	0.287
CT mm	4.6	0.7	3.8	1.4	83.1	0.035	0.001	0.048	0.001
CT:ToA	0.012	0.002	0.015	0.003	125	<0.001	<0.001	0.005	<0.001
Fracture Load x(N)	3370	661	2017	1147	59.8	<0.001	<0.001	<0.001	<0.001
Fracture Load y (N)	2718	470	1921	1127	70.7	0.015	<0.001	0.003	<0.001

Tibia site 4% (distal) 14%(shaft) 38% (shaft) BMC= bone mineral content, SSI_p=polar strength strain index, ToA= total area,

ToD=total density, CoA=cortical area, , TrabA=trabecular area, TrabD=trabecular density ^aRaw data; ^badjusted for age ^cadjusted for height

^dadjusted for BMI ; ≠log transformed for statistical analysis

Figure Legends

Figure 1- Scan sites used for Tibia and Radius

Figure 2- Radial bone geometry, unadjusted data Asian as a percent of Caucasian values

BMC= bone mineral content, SSIP=polar strength strain index, ToA= total area, ToD=total density, CoA=cortical area, CoD=cortical density, CT=cortical thickness, PC=periosteal circumference, EC=endosteal circumference, TrabA=trabecular area, TrabD=trabecular density, Figures 3A-J Tibial total density and cortical thickness in relation to BMI in Caucasians and Asians

Figure 3- Tibial bone geometry, unadjusted data Asian as a percent of Caucasian values

BMC= bone mineral content, SSIP=polar strength strain index, ToA= total area, ToD=total density, CoA=cortical area, CoD=cortical density, CT=cortical thickness, PC=periosteal circumference, EC=endosteal circumference, TrabA=trabecular area, TrabD=trabecular density, Figures 3A-J Tibial total density and cortical thickness in relation to BMI in Caucasians and Asians

Figure 4 Tibial total density and cortical thickness in relation to BMI

Figures

Figure 1

Figure 2

Figure 3

Figure 4

Cortical Thickness 38% Tibia- Caucasians

Cortical Thickness 38% Tibia- Asians