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Regional variation of bone density, microarchitectural parameters, and elastic moduli in the ultradistal tibia of young black and white men and women

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ABSTRACT

Whole-bone analyses can obscure regional heterogeneities in bone characteristics. Quantifying these heterogeneities might improve our understanding of the etiology of injuries, such as lower-extremity stress fractures. Here, we performed regional analyses of high-resolution peripheral quantitative computed tomography images of the ultradistal tibia in young, healthy subjects (age range, 18 to 30 years). We quantified bone characteristics across four regional sectors of the tibia for the following datasets: white women ($n = 50$), black women ($n = 51$), white men ($n = 50$), black men ($n = 34$), and all subjects ($n = 185$). After controlling for potentially confounding variables, we observed statistically significant variations in most of the characteristics across sectors ($p < 0.05$). Most of the bone characteristics followed a similar trend for all datasets but with different magnitudes. Regardless of race or sex, the anterior sector had the lowest trabecular and total volumetric bone mineral density and highest trabecular separation ($p < 0.001$), while cortical thickness was lowest in the medial sector ($p < 0.05$). Accordingly, the anterior sector also had the lowest elastic modulus in the anterior-posterior and superior-inferior directions ($p < 0.001$). In all sectors, the mean anisotropy was ~3, suggesting cross-sector similarity in the ratios of loading in these directions. In addition, the bone characteristics from regional and whole-bone analyses differed in all datasets ($p < 0.05$). Our findings on the heterogeneous nature of bone microarchitecture in the ultradistal tibia may reflect an adaptation of the bone to habitual loading conditions.

1. Introduction

Lower-extremity stress fractures, caused by repeated loading to the bone, are common overuse injuries among Service members and athletes [1–4]. Military recruits who participate in basic combat training are at particularly high risk of this injury because of the sudden increase in physical activities, such as marching, running, and repetitive jumping [1]. Risk factors for stress fracture include, among others, race, sex, age, and body mass index [5–7]. In military recruits, whites compared to blacks, and women compared to men, are at higher risk of this injury [5,7]. Our recent study of the ultradistal tibia in young, healthy subjects, using whole-bone analyses of high-resolution peripheral

Abbreviations: μCT, Micro-computed tomography; μFE, Micro-finite element; Ct.Po, Cortical porosity; Ct.Th, Cortical thickness; Ct.vBMD, Cortical volumetric bone mineral density; E_1, Medial-lateral elastic modulus; E_2, Anterior-posterior elastic modulus; E_3, Superior-inferior elastic modulus; HR-pQCT, High-resolution peripheral quantitative computed tomography; SD, Standard deviation; Tb.N, Trabecular number; Tb.Sp, Trabecular separation; Tb.Th, Trabecular thickness; Tb.vBMD, Trabecular volumetric bone mineral density; Tt.vBMD, Total volumetric bone mineral density

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quantitative computed tomography (HR-pQCT) images, showed that whites compared to blacks, and women compared to men, have inferior bone-health related characteristics, which might explain the higher risk of fractures in these groups [8].

Conventional whole-bone analyses of the HR-pQCT images, which averages bone characteristics over the entire cross section, while important in the field of bone biomechanics, can obscure regional variation in these characteristics [9–11]. For example, although whole-bone values of density and microarchitecture of cortical and trabecular bones between stress-fractured and non-stress-fractured women athletes (n = 19; age range, 18 to 45 years) showed no significant differences, regional analyses revealed a significant difference between the two groups in the posterior sector [10].

Few studies have investigated regional variation of density and microarchitectural parameters of the tibia, especially for subjects with an age range similar to that of military recruits [9,11–14]. Using pQCT images of the ultradistal tibia, Evans et al. reported regional variation in cortical and trabecular bone mineral density of young military recruits (n = 128; 108 women and 20 men; age range, 18 to 21 years) [12]. However, owing to the limited resolution of the pQCT images, the authors were not able to evaluate the microarchitectural parameters at the tibia. Regional variations of both density and microarchitectural parameters of ultradistal trabecular bone were quantified by Sode et al. using HR-pQCT images of healthy men and women (n = 146; 93 women and 53 men; age range, 20 to 78 years; 46% Asians and 46% whites) [11]. However, this study recruited only 30 subjects (17 women and 13 men) younger than 29 years, and the analyses were not stratified based on race.

In this study, we performed regional analyses of HR-pQCT images of the ultradistal tibia collected from a larger cohort of young, healthy subjects with an age range similar to that of military recruits. We also stratified the subjects based on race and sex to identify differences in bone characteristics that might be correlated with the reported differences in the risk of stress fracture between blacks and whites as well as between men and women. Specifically, we quantified the variation in density measurements, microarchitectural parameters, and mechanical properties for the following datasets: white women, black women, white men, black men, and all subjects. We hypothesized that for each of the four stratified datasets, we would observe significant regional variation in bone characteristics.

2. Materials and methods

2.1. Subjects and imaging protocol

Briefly, as previously reported [8], we enrolled 185 young, healthy subjects: 50 white women, 51 black women, 50 white men, and 34 black men, all between the ages of 18 to 30 years and having a body mass index between 18 and 30 kg/m^2 (Table 1). To determine the sample size, we conducted a power analysis using the method of Chow et al. [15], under the assumption that racial/ethnic differences in bone characteristics of young, healthy women are equal to those in post-menopausal women [16]. We calculated that between 25 and 52 women subjects in the black and white groups would be needed to achieve 75% power to detect differences in group means ranging between 10% and 7%, respectively, with a significance level of 15%.

All subjects completed a questionnaire, which surveyed, among other items, socio-economic status, health, bone fracture history, and recent physical activity [e.g., type, frequency (hours-per-week), duration (months-per-year and years-per-life)]. For each subject, we measured height using a wall-mounted stadiometer, body mass using a calibrated electronic scale, and tibial length, defined as the distance from the medial tibial plateau to the distal edge of the medial malleolus, using an anthropometric tape. Further details on subject enrollment, exclusion criteria, and imaging protocols are described in our earlier study [8]. We received approval for the study from the Human Research Protection Office at the U.S. Army Medical Research and Materiel Command (Ft. Detrick, Maryland) and the Institutional Review Board of Partners Health Care (Boston, Massachusetts). Prior to study participation, we obtained written consent from each subject.

We obtained HR-pQCT images (XtremeCT; Scanco Medical AG, Brüttisellen, Switzerland) of the tibia of the non-dominant leg of each subject. We scanned the contralateral leg for subjects with a history of leg or ankle fracture. Using an isotropic voxel resolution of 82 µm, we collected 110 image slices (corresponding to 9.02 mm) at an ultradistal tibial site (i.e., 4% of the tibial length proximal to the distal end of the tibia). The short-term precision for HR-pQCT measurements, due to repositioning of the tibia, ranged from 0.2 to 1.7% for density parameters, from 0.7 to 8.6% for microarchitectural parameters, and from 2.1 to 4.8% for stiffness obtained by micro-finite element (µFE) analyses.

2.2. Regional analyses of bone density and microarchitectural parameters

We performed regional analyses of bone density and microarchitectural parameters in three steps. In the first step, we used a semi-automated segmentation procedure in Image Processing Language (IPL v5.08b; Scanco Medical AG) to identify the periosteal and endocortical surface contours. We inspected the periosteal and endocortical surfaces for accuracy, and modified the surfaces whenever necessary. We then determined whole-bone and cortical-bone volumes from the periosteal and endocortical surface contours, respectively, and subtracted the cortical-bone volume from the whole-bone volume to obtain the trabecular-bone volume.

In the second step, we divided the whole bone into four sectors, similar to previously published studies on regional analyses of tibial bone [9–11]. First, we extracted an image at the center of the HR-pQCT scan of each subject and identified the centroids of the tibia and fibula, using image-processing tools in MATLAB (The MathWorks, Inc., Natick, MA). Then, with a line connecting the centroids as a reference, we divided the whole-bone volume into lateral, posterior, medial, and anterior sectors, using a customized script in IPL (Fig. 1a).

In the third and final step, we determined bone density and microarchitectural parameters for the whole bone and each sector, using

Table 1
Characteristics of 185 young, healthy subjects (101 women and 84 men) considered for the study [8]. Subjects ranged from 18 to 30 years of age, with a body mass index between 18 and 30 kg/m^2. The data are presented as mean ± one standard deviation.

	White women	Black women	White men	Black men	Total
	(n = 50)	(n = 51)	(n = 50)	(n = 34)	(n = 185)
Age (years)	24.5 ± 2.9	22.2 ± 3.2	24.9 ± 3.2	24.3 ± 3.6	24.4 ± 3.4
Height (m)	1.65 ± 0.11	1.66 ± 0.08	1.80 ± 0.08	1.78 ± 0.07	1.72 ± 0.10
Mass (kg)	63.4 ± 9.6	64.4 ± 10.2	78.5 ± 11.5	78.2 ± 11.4	70.5 ± 12.7
Body mass index (kg/m^2)	23.3 ± 3.2	23.3 ± 2.5	24.2 ± 2.9	24.9 ± 3.4	23.9 ± 3.0
Tibial length (cm)	36.8 ± 2.4	37.8 ± 2.9	40.8 ± 2.9	41.3 ± 3.1	39.0 ± 3.4
Physical activity (h/wk)	4.9 ± 4.3	2.3 ± 2.8	5.9 ± 5.4	5.1 ± 8.6	4.5 ± 5.5