Effects of bone-specific physical activity, gender and maturity on tibial cross-sectional bone material distribution; a cross-sectional pQCT comparison of children and young adults aged 5-29 years

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Abstract

Growth is the opportune time to modify bone accrual. While bone adaptation is known to be dependent on local loading and consequent deformations (strain) of bone, little is known about the effects of sex, and bone-specific physical activity on location-specific cross-sectional bone geometry during growth. To provide more insight we examined bone traits at different locations around tibial cross sections, and along the tibia between individuals who vary in terms of physical activity exposure, sex, and pubertal status. Data from 304 individuals aged 5-29 years (172 male, 132 female) were examined. Peripheral quantitative computed tomography (pQCT) was applied at 4%, 14%, 38%, and 66% of tibial length. Maturity was established by estimating age at peak height velocity (APHV). Loading history was quantified with the bone-specific physical activity questionnaire (BPAQ). Comparisons, adjusted for height, weight and age were made between sex, maturity, and BPAQ tertile groups. Few to no differences were observed between sexes or BPAQ tertiles prior to APHV, whereas marked sexual dimorphism and differences between BPAQ tertiles were observed after APHV. Cross-sectional location-specific differences between BPAQ tertiles were not evident prior to APHV, whereas clear location-specificity was observed after APHV. In conclusion, the skeletal benefits of physical activity are location-specific in the tibia. The present results indicate that the peri- or post-pubertal period is likely a more favourable window of opportunity for enhancing cross-sectional bone geometry than pre puberty. Increased loading during the peri-pubertal period may enhance the bone of both sexes.

Keywords: Bone QCT; Exercise; Bone-muscle interactions; Ontogeny; Puberty

Abbreviations

Age at peak height velocity.....APHV.

Analysis of variance..... ANOVA.

Bone mineral content .....BMC.

Bone-specific physical activity questionnaire ..... BPAQ.

Endocortical radii.....EndoR.

Multivariate analysis of covariance ..... MANCOVA.

Peak height velocity.....PHV.

Peak total body bone mineral content accrual velocity .....PBMCV.

Pericortical radii.....PeriR.

Peripheral quantitative computed tomography .....pQCT.

Physical activity.....PA.

Standard deviation .....SD.

Volumetric bone mineral density.....vBMD.

1. Introduction

Animal experiments have established that bones adapt mass and geometry to the prevalent loading environment[1–5]. Lower than normal loading leads to bone loss and higher than normal loading leads to bone gains[1,3]. Data from humans mirror observations from animal studies; with disuse (bed rest, immobilization, paralysis) leading to relatively rapid and marked bone loss[6], and increased loading (e.g. exercise intervention) leading to bone gains[7–9]. Moreover, animal experiments, in which the bone has been loaded in bending, have suggested that the adaptation is locally driven by the location-specific strains (deformation caused by the loading) [1,3]. Similarly, location-specific bone accrual has been reported at the tibial shaft in response to exercise interventions in pre- to peri pubescent boys[10] and in post-menopausal women[11]. Further, bed rest leads to location-specific bone loss at the tibial shaft [12]. In the aforementioned studies bone was primarily added or lost from the anterior and posterior surfaces of the tibia, which corresponds to the dominant pattern of sagittal plane bending at the tibial shaft during typical weight bearing loading [13–17].

It appears that the skeleton is more sensitive to loading during growth than after it[18,19], and consequently it has been suggested that growth is the opportune time for exercise interventions[19–25]. Examination of growth is encumbered by differences in the timing of puberty between individuals and between sexes. However, when age is expressed with respect to puberty (identified by peak height velocity [PHV][26] or menarche), a rather more consistent picture of skeletal growth during the peri pubertal period emerges[27–31]. PHV is followed by peak total body bone mineral content accrual velocity (PBMCV) with only a 0.7

year lag, and in girls PBMCV all but coincides with menarche[27], making age at PHV (APHV) a convenient marker of maturity. Around a quarter of the adult skeletal mass is accrued in the two-year period around PBMCV [27].

Sexual dimorphism of the skeleton emerges during puberty when boys gain more bone than girls[32–35]. In addition to the amount of bone gained during puberty, relative endosteal and periosteal surface deposition differs between boys and girls; girls accumulating more endosteal bone than boys[32,35,36]. While animal studies suggest the bones of females are less sensitive to loading than those of males due to the effects of oestrogen[36], location-specificity of tibial shaft adaptation appears to be similar between the sexes[18,37]. However, little is known about the effects of sex on the association between physical activity and diaphyseal location-specific cross-sectional bone geometry during growth.

Therefore, the purpose of the present study was to examine whether bone material distribution is dependent on bone-relevant physical activity (PA) exposure when sex and maturational status are controlled. It was hypothesized that a difference would be observed in bone material distribution between bone-relevant PA groups. Further, it was hypothesized that there would be no difference in location-specific differences between bone-relevant PA groups prior to, and after PHV. And finally, due to the sexual dimorphism in skeletal ontogeny over puberty[32,35,36], we hypothesised that there would be a sex – maturity effect in the association between bone-relevant PA and bone material.

2. Materials and Methods

The present study is a re-examination of the intersection of estimated bone strength from peripheral quantitative computed tomography (pQCT) and exposure to osteogenic physical activity estimated from the bone-specific physical activity questionnaire (BPAQ)[38] data from participants of previous studies conducted at Griffith University, Gold Coast, Australia aged 5 to 29 years-of-age. Some of the data has been published previously in support of exercise or validation studies[39–43]. The inclusion criteria common for the pooled studies included sound general health, and being fully ambulatory. Exclusion criteria included medications known to affect bone, medical conditions that restrict physical activity participation, and recovering from a lower limb fracture or other immobilized injury. Strategies used to recruit the participants included contacting local schools, advertising in the local community with flyers, and messages to e-mail posting lists. The projects in which the data were originally acquired were approved by the Griffith University Human Research Ethics Committee (PES/12/05/HREC, PES/09/09/HREC, PES/25/11/HREC). Written informed consent was acquired from all participants and/or their legal guardians prior to the assessments.

2.1. Anthropometry

Participants were weighed to the nearest 0.1 kg with electronic scales (Soehnle Co., Switzerland). Height and sitting height were determined to the nearest millimetre with a portable stadiometer (HART Sport & Leisure, Australia). Leg length was calculated by subtracting the sitting height from total height, which yields sub-ischial leg length.

2.2. Maturity assessment

Maturity was determined from age at peak height velocity (APHV) as the marker of puberty[26]. APHV was derived from age, height, sitting height and leg length using the sex-specific regression equations from Mirwald et al. 2002[26];

$$M = \begin{cases} -9.236 + 2.708 * L_L * H_S - 0.1663 * A * L_L + 0.7216 * Age * H_S + 0.022952 * {}^{W}/_{H}\,; Boys \\ -9.376 + 1.882 * L_L * H_S + 0.22 * A * L_L + 0.5841 * A * H_S - 0.002658 * A * W + 0.07693 * {}^{W}/_{H}\,; Girls \end{cases}$$

Where M = maturity offset in years, L_l = leg length in metres, H_s = sitting height in metres, H = height in metres, A = age in years, and W = weight in kg. Note that the coefficients are different to Mirwald et al. to account for expressing the lengths in metres instead of centimetres. Also, the W/H ratio coefficients have not been adjusted, as the coefficients reported in Mirwald et al. [26] were too low by a factor of 100, which is accounted for by expressing height in metres. An estimate of APHV was obtained by subtracting maturity offset (M) from age. In the Canadian population the regression equation was developed with the maturity offset estimate error was 0.24 (SD 0.65) years for boys, and 0.001 (0.68) years for girls, while the coefficients of determination were between 0.91 and 0.92 for boys and girls, respectively [26].

2.3. Bone-specific Physical Activity Questionnaire (BPAQ)

Participants were asked to complete a bone-specific physical activity questionnaire (BPAQ) as previously described[38]. Briefly, the BPAQ is a questionnaire designed to capture bone-relevant weight-bearing exercise history. The data is then analysed using a purpose-built on-line calculator (http://www.fithdysign.com/BPAQ/) developed from algorithms based on force platform testing of a wide range of typical physical activities to

derive a relative load rating index [38]. We have previously reported that the BPAQ score is positively associated with dual-energy x-ray absorptiometry-derived areal bone mineral density with the coefficients of determination varying from 0.36 to 0.68 depending on bone site [38]. Although the calculator produces past (whole of life), current (previous 12 months) and total BPAQ score (tBPAQ), only tBPAQ was used in the present study. We have reported that BPAQ measures exhibit excellent inter-tester (ICC 0.93-0.97) and intra-tester reliability (ICC 0.86-0.93) for male and female participants from 5-83 years of age [41].

2.4. Bone assessments

Peripheral quantitative computed tomography (pQCT) was used to evaluate the cross-section of the tibia at 4%, 14%, 38% and 66% of tibial length from the distal endplate (in-plane pixel size 0.5 x 0.5 mm, slice thickness 2.3 mm, XCT 3000, Stratec Medizintechnik GmbH, Pforzheim, Germany). The pQCT scans were taken from the non-dominant limb (non-kicking leg for lower limb).

2.5. pQCT analysis

All pQCT analyses were conducted using the BoneJ [44] ImageJ-plugin (rsbweb.nih.gov/ij). A threshold value of 280 mg/cm^3 was used to analyse tibial shaft. Polar cortical volumetric bone mineral density (vBMD) distribution, cortical bone mineral mass (BMC) distribution, and endo- (EndoR, mm) and pericortical radii (PeriR, mm) were calculated for shaft slices as previously described [45]. In brief, the centre of the medullary cavity was defined and a radius was incremented by 0.1 mm from the centre until the endocortical border was detected. Thereafter, the vBMD of each pixel was noted by appending the latest value to a vector (empty at first) with further increments of the radius until reaching the pericortical border. Thereafter the direction of the radius was incremented by one degree and the radius

incrementing process repeated. The acquired 360 vBMD vectors were aligned by defining the angle between the initial direction of radius incrementation in the image and the line going from the centre of tibia to the centre of fibula and selecting the first vBMD vector in such a way that it corresponded to 5° counter clockwise from the tibia to fibula line. Starting from that vector, the values of ten consecutive vectors were averaged to represent the vBMD of a 10° sector, resulting in 36 10° polar sectors in total (Figure 1). A similar approach was used for BMC and for endo- and pericortical radii.

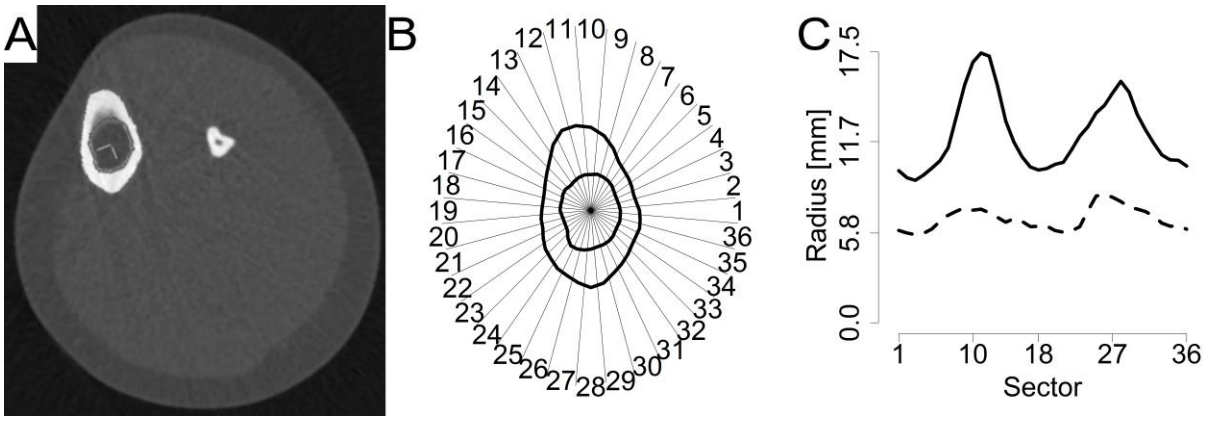

Figure 1. Example of dividing tibial cross-section into thirty-six ten-degree sectors in the polar radii distribution analysis. A) the slice from 66% of tibial length rotated to align the line connecting the tibial, and fibular marrow centres with the horizon. B) the endo- and pericortical circumferences extracted from tibia, and divided into 36 polar sectors. C) Endo- (dashed line), and pericortical (solid line) radii in the 36 polar sectors.

For distal bone sites, a threshold of 180 mg/ cm³ was used to differentiate bone from soft-tissues. Polar BMC distribution and PeriR were calculated similarly to the approach used for shaft images, but the origin of the radii was the centre of the bone area rather than the

medullary cavity. The coefficient of variation for different pQCT measurements ranges from 0.6 to 6.0%[45,46].

2.6. Group Divisions and Statistical Analysis

Unless otherwise noted, all results are reported as means and standard deviations (SD). Statistical analyses were conducted with SPSS software version 21 (IBM corporation) and the significance level was set at $P \leq 0.05$.

Analysis of variance (ANOVA) was used to evaluate between-group differences and interactions in anthropometric variables and total BPAQ. No adjustments were applied on the post-hoc comparisons. To examine sex and maturation effects on the association between bone-relevant physical activity location-specific bone traits the data was divided into 12 different groups according to sex, maturity (pre-pubescent > 1 year prior to their predicted APHV; post-pubescent > 2 years past their predicted APHV), and BPAQ for location-specific analyses; that is, boys/men vs girls/women, pre-pubertal vs post-pubertal, and three BPAQ divisions based on within-group BPAQ tertiles. The groups divisions (sex [0 = boys, 1 = girls], maturity [0 = pre-pubescent, 1 = post-pubescent], and BPAQ tertile [1 = lowest tertile, 2 = mid tertile, 3 = highest tertile]) were used as the between-subject factors in subsequent statistical analyses. Multivariate analysis of covariance (MANCOVA) with sex, maturity and BPAQ tertiles as between-subject factors, polar sector as a within-subject factor and age, height and weight as co-variates was used to evaluate between-group differences and interactions in the location-specific bone trait distributions (EndoR, PeriR, polar BMC, and polar vBMD distribution). No adjustments were applied on the post-hoc comparisons. Where percent differences between groups are reported they have been calculated from MANCOVA

adjusted estimates with either girls, pre-pubescent, or lowest BPAQ tertile values applied as the denominator.

3. Results

A total of 172 boys/men (aged 5-29 years, mean age = 14.4(6.8) years, height = 154(22) cm, weight = 52.4(27.1) kg) and 132 girls/women (aged 5-29 years, mean age = 13.7(5.8) years, height = 150(20) cm, weight = 44.4(16.6) kg) with both pQCT and BPAQ data were identified from studies conducted between years 2009 and 2012, and their data extracted. The anthropometric data according to sex, maturity and total BPAQ is presented in Table 1. Analysis of variance indicated that the BPAQ tertile groups differed from each other in terms of height, weight, age ($P < 0.001$ to $P = 0.04$), and, expectedly, total BPAQ ($P < 0.001$).

Table 1. Descriptive characteristics (mean(SD)) according to sex, maturity and level of bone-specific physical activity.

		BPAQ [tertile]	N	Age [years]	Height [m]	Weight [kg]	BPAQ [index]	APHV [years]
Boys/ men	Pre pubertal	Lowest	33	8.3 (2.0)[bc]	1.31 (0.11)[bc]	28.5 (6.5)[bc]	10.0 (3.9)[bc]	12.6 (0.9)[bc]
		Mid	37	10.2 (1.3)[a]	1.43 (0.10)[a]	36.9 (10.1)[a]	20.5 (2.6)[ac]	13.2 (0.5)[a]
		Highest	37	10.6 (1.9)[a]	1.43 (0.11)[a]	35.5 (9.2)[a]	37.9 (10.7)[ab]	13.4 (0.9)[a]
	Post pubertal	Lowest	24	20.8 (4.1)[bc]	1.79 (0.06)	82.4 (16.9)	21.2 (7.1)[bc]	13.9 (0.8)[b]
		Mid	21	22.9 (4.4)[a]	1.80 (0.07)	82.7 (17.1)	35.2 (3.1)[ac]	14.7 (0.5)[a]
		Highest	20	22.9 (4.4)[a]	1.79 (0.06)	83.9 (17.3)	54.7 (11.7)[ab]	14.2 (0.7)
Girls/ women	Pre pubertal	Lowest	22	8.0 (2.0)	1.29 (0.15)[b]	28.4 (7.4)	7.23 (4.47)[bc]	11.2 (0.6)[b]
		Mid	22	9.4 (1.4)	1.36 (0.10)[a]	30.7 (5.9)	23.8 (7.9)[ac]	11.7 (0.4)[a]
		Highest	23	8.9 (1.7)	1.33 (0.11)	31.4 (9.3)	63.2 (26.6)[ab]	11.5 (0.5)
	Post pubertal	Lowest	25	17.2 (1.5)[bc]	1.66 (0.05)	57.7 (8.0)	12.1 (6.3)[bc]	12.7 (0.5)
		Mid	21	19.1 (4.6)[a]	1.68 (0.06)	61.6 (10.4)	31.0 (6.5)[ac]	12.7 (0.6)
		Highest	19	20.3 (4.1)[a]	1.67 (0.06)	57.8 (6.9)	89.4 (39.3)[ab]	13.1 (0.5)

[a] $P \leq 0.05$ compared to lowest BPAQ tertile of the same sex and maturity-group

[b] $P \leq 0.05$ compared to middle BPAQ tertile of the same sex and maturity-group

[c] $P \leq 0.05$ compared to highest BPAQ tertile of the same sex and maturity-group

3.1. Comparisons between sexes, maturity groups, and BPAQ tertiles

Multivariate analysis of co-variance adjusted for height, weight and age, and bone sector as a within-subject factor indicated that the sexes differed from each other in BMC at all measurement sites ($P < 0.001$) (Table 2), boys/men having 8.4% to 19.8% higher values than girls/women. Endocortical radii differed at the 38%, and 14% measurement sites ($P < 0.001$ to $P = 0.001$), males having 6.0% to 6.5% shorter endocortical radii than females. The pericortical radii at the 66% and 4% measurement sites ($P = 0.001$ to $P = 0.026$) were 1.6% to 2.9% longer in men than in women. The vBMD at the 14% and 66% measurement sites ($P = 0.007$ to $P = 0.045$) was 1.4% to 2.5% lower in males than in females (Table 2).

Maturity groups differed from each other at all shaft measurement sites (66%, 38%, and 14%) in all of the measured variables apart from BMC at the 38%, and the 4% measurement sites ($P < 0.001$ to $P = 0.042$), and in pericortical radii ($P = 0.018$) at the distal measurement site. The vBMDs were 5.7% to 9.9% higher post puberty than pre-puberty, whereas, the endo- and pericortical radii were 3.5% to 5.5% shorter, respectively. The BMCs were 3.4% to 8.4% higher post puberty compared to pre puberty (Table 2).

BPAQ tertiles differed from each other in BMC at the 38%, 14%, and 4% measurement sites ($P = 0.005$ to $P = 0.031$) with the middle and highest BPAQ tertiles having 3.1% to 5.1% higher values than the lowest tertile (Table 2).

Table 2. Tibial parameters (mean(SD)) at the 4%, 14%, 38% and 66% measurement sites according to sex, maturity and level of bone-specific physical activity. Please see text for post-hoc comparisons.

				Tib 4			*Tib 14*			*Tib 38*				*Tib 66*			
		BPAQ	N	PeriR [mm]	BMC [mg]	EndoR [mm]	PeriR [mm]	BMC [mg]	vBMD [mg/cm³]	EndoR [mm]	PeriR [mm]	BMC [mg]	vBMD [mg/cm³]	EndoR [mm]	PeriR [mm]	BMC [mg]	vBMD [mg/cm³]
Boys/ men	Pre pubertal	Lowest	33	15.4 (1.4)	6.62 (1.55)	6.48 (0.83)	9.65 (0.93)	3.60 (0.79)	834 (67)	3.86 (0.65)	8.64 (1.02)	4.87 (1.10)	1010 (50)	6.48 (0.90)	10.7 (1.1)	5.38 (1.30)	927 (45)
		Mid	37	16.7 (1.5)	7.51 (1.33)	7.09 (1.06)	10.6 (1.1)	4.40 (0.85)	861 (58)	4.29 (0.70)	9.59 (1.00)	6.04 (1.19)	1010 (50)	7.29 (1.21)	11.9 (1.4)	6.56 (1.22)	934 (59)
		Highest	37	17.3 (1.6)	8.36 (1.64)	7.02 (1.30)	10.6 (1.4)	4.49 (1.05)	842 (78)	4.16 (0.95)	9.64 (1.26)	6.21 (1.49)	1010 (50)	7.12 (1.14)	11.8 (1.4)	6.80 (1.44)	931 (57)
	Post pubertal	Lowest	24	20.6 (1.7)	12.5 (2.3)	8.12 (1.20)	13.3 (1.3)	8.71 (1.67)	939 (73)	5.01 (0.69)	12.5 (1.1)	12.3 (2.2)	1100 (50)	8.93 (1.40)	15.4 (1.4)	13.3 (2.3)	995 (54)
		Mid	21	20.6 (1.5)	13.4 (2.5)	7.77 (1.01)	13.3 (1.1)	9.45 (1.75)	948 (61)	4.82 (0.79)	12.7 (1.2)	12.9 (2.5)	1110 (40)	8.38 (1.12)	15.3 (1.5)	14.1 (2.5)	1020 (60)
		Highest	20	20.8 (1.5)	14.0 (2.8)	7.72 (0.91)	13.4 (1.0)	9.52 (1.71)	931 (72)	4.65 (0.75)	12.8 (0.9)	13.1 (2.2)	1090 (50)	8.68 (1.04)	15.6 (1.2)	14.1 (2.1)	997 (58)
Girls/ women	Pre pubertal	Lowest	22	14.8 (1.3)	5.97 (1.14)	6.21 (0.94)	9.25 (1.00)	3.28 (0.81)	832 (64)	3.89 (0.69)	8.43 (1.10)	4.56 (1.18)	1020 (50)	6.26 (1.12)	10.3 (1.3)	4.99 (1.26)	924 (47)
		Mid	22	15.6 (1.3)	6.32 (1.23)	6.94 (0.80)	9.96 (0.78)	3.73 (0.58)	866 (53)	4.15 (0.55)	9.00 (0.84)	5.30 (0.96)	1030 (30)	6.81 (0.88)	11.1 (1.0)	5.86 (0.97)	949 (40)
		Highest	23	15.5 (1.5)	6.57 (1.95)	6.74 (0.78)	9.77 (0.95)	3.63 (0.83)	849 (63)	4.16 (0.52)	9.01 (0.92)	5.23 (1.16)	1010 (50)	6.67 (0.72)	10.9 (1.0)	5.67 (1.26)	933 (49)
	Post pubertal	Lowest	25	18.0 (1.1)	8.16 (1.11)	8.05 (1.02)	11.8 (0.8)	6.05 (0.71)	974 (63)	4.73 (0.54)	10.6 (0.6)	8.22 (1.09)	1120 (40)	7.46 (1.05)	12.9 (0.9)	9.41 (1.02)	1040 (50)
		Mid	21	18.5 (1.3)	9.28 (1.45)	7.93 (0.91)	12.1 (0.7)	6.80 (0.82)	966 (62)	4.54 (0.66)	11.1 (0.7)	9.50 (1.27)	1110 (50)	7.92 (1.08)	13.6 (1.0)	10.5 (1.4)	1030 (60)
		Highest	19	18.1 (1.2)	8.79 (1.14)	7.58 (0.75)	11.8 (0.7)	6.72 (0.83)	980 (58)	4.35 (0.55)	10.9 (0.6)	9.40 (1.15)	1120 (40)	7.39 (1.19)	13.2 (1.0)	10.3 (1.1)	1040 (40)
MANCOVA main effects p-value	Sex			**0.001**	**< 0.001**	**< 0.001**	0.649	**< 0.001**	**0.007**	**0.001**	0.077	**< 0.001**	0.192	0.811	**0.026**	**< 0.001**	**0.045**
	Maturity			**0.018**	0.809	**0.019**	**0.042**	**0.034**	**0.006**	**0.002**	**< 0.001**	0.368	**< 0.001**	**0.002**	**0.004**	**0.043**	**< 0.001**
	BPAQTertile			0.192	**0.005**	0.715	0.521	**0.031**	0.625	0.466	0.096	**0.029**	0.26	0.869	0.206	0.061	0.379
	Sex x Maturity			0.636	**< 0.001**	**< 0.001**	0.084	**< 0.001**	0.165	0.271	0.055	**< 0.001**	0.6	0.685	0.227	**< 0.001**	0.065
	Sex x BPAQ tertile			0.111	0.052	0.53	0.437	0.683	0.673	0.518	0.349	0.412	0.72	0.078	0.078	0.587	0.737
	Maturity x BPAQ tertile			0.172	0.237	**0.04**	0.512	0.17	0.422	0.41	0.725	0.231	0.183	0.818	0.81	0.385	0.152
	Sex x Maturity x BPAQ tertile			0.987	0.928	0.739	0.727	0.778	0.76	0.848	0.572	0.99	0.301	0.128	0.326	0.776	0.26

MANCOVA adjusted with weight, height, age, and using sex, maturity (pre- or post-pubertal), and BPAQ tertile as between-subjects factors. EndoR = endocortical radius, PeriR = pericortical radius, BMC = bone mineral content for a 1 mm thick slice, vBMD = volumetric cortical bone mineral density

A sex × maturity interaction was observed in BMC at all measurement sites ($P < 0.001$). Post-pubertal males had 9.1% to 14.6% higher values than the pre-pubertal, whereas the post-pubertal girls had 4.9% to 7.6% lower BMC at the 38% and 4% measurement sites than pre-pubertal girls. When comparing the sexes, no difference was observed in BMC prior to puberty at the 66%, and 38% measurement sites, but boys had 4.8% to 10.3% higher values than girls at the 14%, and 4% measurement sites. After puberty, boys/men had 15.1% to 30.2% higher BMC than girls/women at all measurement sites. No sex × BPAQ tertile, maturity × BPAQ tertile, or sex × maturity × BPAQ tertile interaction was observed at any of the measured bone sites ($P = 0.052$ to 0.99) apart from maturity × BPAQ tertile interaction in endocortical radius at the 14% measurement site ($P = 0.040$). Comparisons between BPAQ tertiles before, or after puberty did not reveal any significant differences of the endocortical radius at the 14% measurement site ($P = 0.09$ to 0.62) (Table 2).

3.2. Bone sector interactions for sexes, maturity groups and BPAQ tertiles

A bone sector × sex interaction was observed in all bone variables at all measurement sites ($P = 0.001$ to $P = 0.035$) apart from the 38% and 14% measurement site endocortical radii, and the 38% measurement site vBMD distribution. A bone sector × maturity-group interaction was observed for all bone variables at all bone sites ($P < 0.001$ to $P = 0.043$) with the exceptions of BMC at the 38% and 4% measurement sites. A bone sector × BPAQ tertile interaction in BMC was observed at all tibial shaft sites (66%, 38%, and 14%) ($P = 0.008$ to $P = 0.014$), and the same interaction was observed for pericortical radius at the distal tibia (4% measurement site) ($P = 0.002$).

A sector × sex × maturity-group interaction was observed for BMC at all tibial sites (P = 0.005 to P = 0.019), and for pericortical radius at the distal tibia (P = 0.026). A sector × sex × BPAQ tertile interaction was observed for BMC at all tibial sites (P = 0.030 to P = 0.003), and for endocortical radius (P = 0.030) and BMD (P = 0.050) at the 66% measurement site. A sector × maturity × BPAQ tertile interaction was observed at all tibial shaft measurement sites for BMC (P = 0.006 to P = 0.017), at the 66% and 38% measurement sites for endocortical radius (P < 0.001) and at the 66% site for pericortical radius (P = 0.011) .

A sector × sex × maturity-group × BPAQ tertile interaction was observed at all tibial shaft measurement sites (14%, 38% and 66%) for BMC (P = 0.006 to P = 0.009), and for pericortical radius (P = 0.020) and BMD (P = 0.031) at the 14% measurement site (Figure 2 & Figure 3).

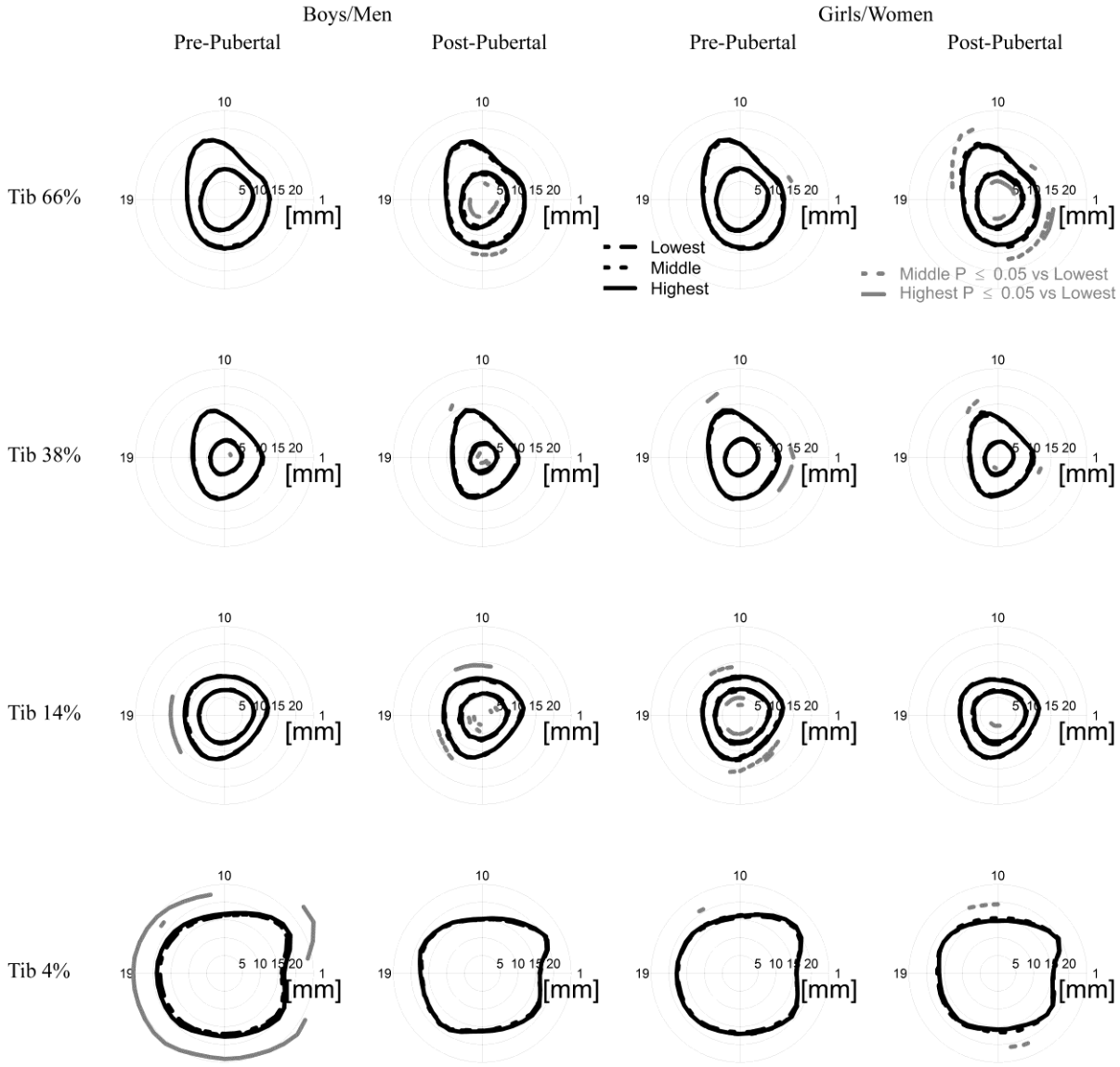

Figure 2. Illustration of the polar endo- and pericortical radii distribution based on the repeated measures analysis of covariance (adjusted for height, weight, and age using polar sector as the within-subject factor) of the different sexes in the two different maturity groups divided into three tertiles (lowest = dash-dot line, middle = dot-line, highest = solid line) based on total bone-specific physical activity questionnaire (BPAQ) score. Sector 1 (top) opens towards the fibula, sector 12 – 13 is anterior, sector 21-22 is medial, and sector 31-32 is posterior. Sectors, with statistically significant sector-specific post-hoc comparisons against the lowest BPAQ tertile are indicated with gray lines.

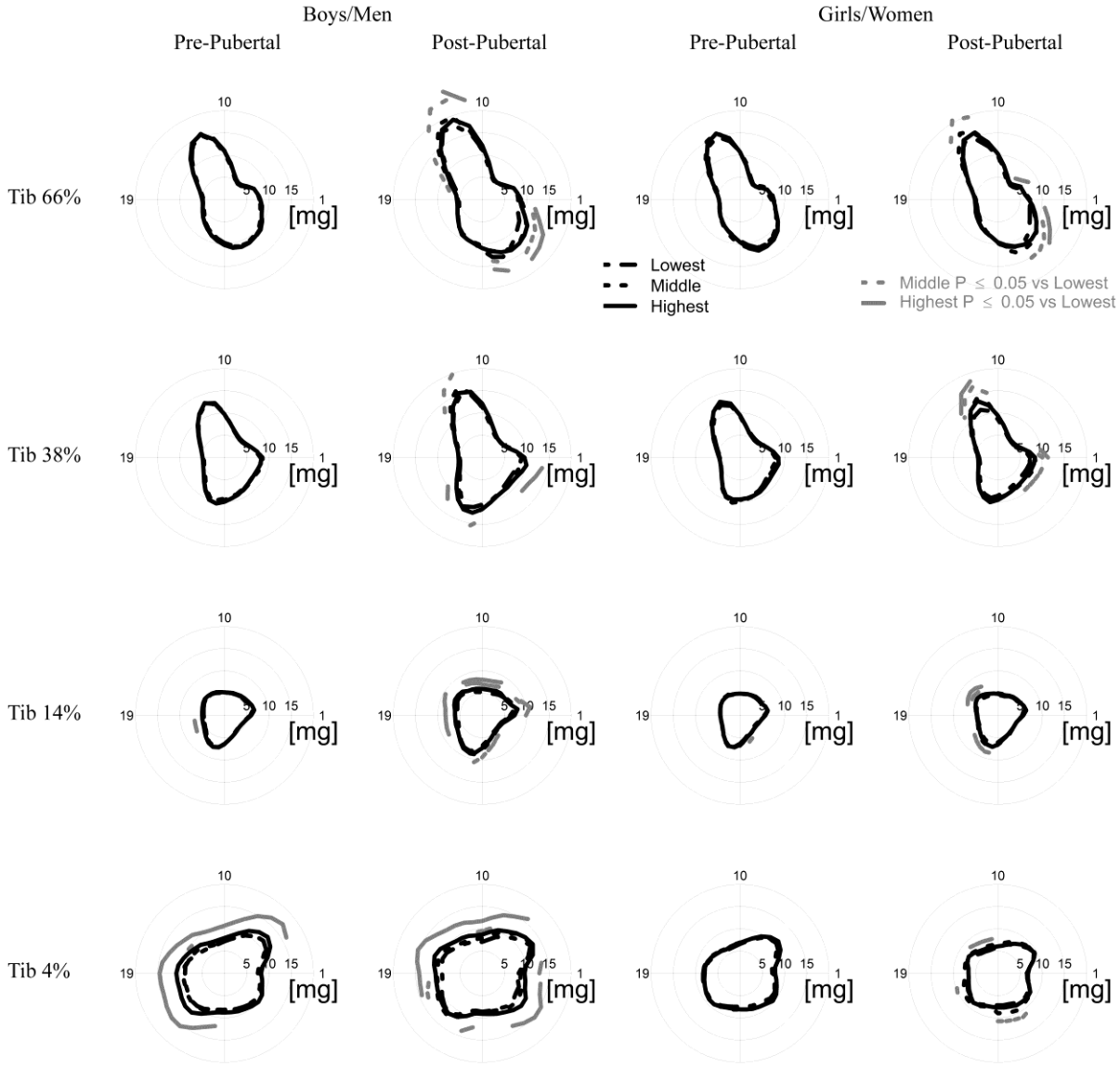

Figure 3. Illustration of the polar bone mineral content distribution based on the repeated measures analysis of covariance (adjusted for height, weight, and age using polar sector as the within-subject factor) of the different sexes in the two different maturity groups divided into three tertiles (lowest = dash-dot line, middle = dot-line, highest = solid line) based on total bone-specific physical activity questionnaire (BPAQ) score. Sector 1 (top) opens towards the fibula, sector 12 – 13 is anterior, sector 21-22 is medial, and sector 31-32 is posterior. Sectors, with statistically significant sector-specific post-hoc comparisons against the lowest BPAQ tertile are indicated with gray lines.

Discussion

The hypotheses examined were 1) that a difference would be observed in bone material distribution between bone-relevant PA groups, 2) that there would be no difference in location-specific differences between bone-relevant PA groups prior to, and after PHV, and 3) that there would be a sex – maturity effect in the association between bone-relevant PA and bone with respect to PHV between sexes. With regards to hypothesis 1, we found that bone parameters differed between the least and most active individuals, the more active individuals having more bone mineral/larger tibial cross-section. The differences between bone-relevant PA groups become more marked after PHV and are mostly evident on the anterior and posterior aspects of the tibial shaft (Figure 2 & Figure 3). For hypothesis 2, we found that location-specific differences between bone-relevant PA groups can be observed both prior to, and after PHV, however the differences are more marked after PHV (Figure 2 & Figure 3). In reference to hypothesis 3, no sex × maturity × BPAQ tertile interaction was seen, whereas a sector × sex × maturity × BPAQ tertile interaction was observed in BMC distribution indicating that, with maturation, there may be a sex difference in change in the localization of the BMC adaptation to bone-relevant PA.

The location-specific analysis indicated that individuals with more historical bone-relevant PA had more bone mass, and a more robust bone geometry compared to those with less bone-relevant PA. The results are in accord with previous DXA-based studies, which have indicated that more physically active children accrue more bone over the pubertal period than their less physically active peers[27,47].

There is a limited body of literature on the growth of the cross-sectional shape of the tibia and the effects of bone-specific physical activity on that shape. Our physical activity-related location-specific findings are in line with results of the lone exercise intervention in prepubertal boys, where MacDonald et al. reported anterior-posterior increase in bone mass at tibial shaft following a jumping intervention[10]. Interestingly in the present study, location-specific differences were observed more markedly in the post-pubertal groups (Figure 2 & Figure 3). Moreover, while the differences were location-specific at the shaft, the differences in mineral mass were rather more uniformly distributed at the distal tibia. The findings align with the response of the tibia to loads during walking (and likely other forms of locomotion). During walking the proximal tibia is loaded in bending, but the loading mode changes to compression distally[15–17].

We found that sex differences in bone traits emerged after PHV, while few differences were observed prior to puberty. These findings are in accord with previous reports; it is well-accepted that dimorphism in body composition, including skeletal mass[32–35,48], emerges over the pubertal period[49,50]. More marked positive differences in tibial bone traits between pre and post PHV were observed in males than in females. Curiously, females had lower values relative to body size after PHV than before. It is well-established that the ratio of bone mass to muscle mass changes in females over puberty result in more bone per unit of muscle after puberty than prior to it, whereas the ratio remains relatively constant in males[33,34,49]. However, this did not appear to modify the association between puberty and bone in a sex-specific manner (apart from the localization of the adaptation indicated by the sector × sex × maturity × BPAQ tertile interaction in BMC in the absence of sex x maturity x BPAQ tertile interaction) in the present data, which suggests that the female skeleton is as responsive to loading interventions as male.

Oestrogen is associated with reduced periosteal expansion in females compared to males during the pubertal period[51,52]. It has been suggested that oestrogen facilitates endosteal apposition, and thus is responsible for greater endosteal constriction in girls than boys during the pubertal period[53]. Some cross-sectional studies have reported that higher levels of participation in bone-specific physical activity (tennis[54], gymnastics[55], and physical activity in general[56]) are also related to endocortical constriction [54–56]. The present findings are somewhat at odds with those observations, as no sex × maturity-group × BPAQ tertile interaction was observed for EndoR. Notwithstanding the negative interaction finding, Figure 2 indicates that there may have been a tendency towards shorter endocortical radii in the two highest BPAQ tertiles compared to the lowest BPAQ tertile in both sexes. Keeping in mind that one of the few prospective studies that has examined bone geometry over the pubertal period found no evidence of endocortical constriction[52], we postulate that since a similar trend towards shortened endocortical radii was observed in both sexes, the apparent endocortical constriction observed in previous cross-sectional studies may be more a function of reduced endocortical resorption rather than increased endosteal apposition.

There is considerable heterogeneity in the literature as to whether the pre or peripubertal skeleton is most responsive to loading[22,24] . We observed few to no differences in bone parameters between high and low activity groups prior to puberty. While the differences in bone traits in the post-pubertal group between high and low activity groups were more marked in males than in females, higher values were also observed in more active female groups post-puberty. With the caveat that ongoing growth-related bone modelling may have masked bone-specific PA-related bone differences in the pre-pubertal group, the present

findings suggest that the peri-, and postpubertal period is, at the very least, a period of altered mechanosensitivity and therefore potentially an opportune time for exercise interventions in both sexes. Considering the important contribution of muscles to the mechanical loading milieu, it is possible that the capacity of the prepubertal system to provide progressively increasing muscle overload, and thereby stimulate bone adaptation is limited. While prepubertal muscles are not amenable to resistance training induced hypertrophy[57], muscular force production may be increased to some extent in the absence of hypertrophy[58]. Nevertheless, there is inevitably a point, where further strength gains would require hypertrophy, and thus targeting the peripubertal period, when muscles are capable of responding by marked hypertrophy, could be considered prudent, when designing osteogenic exercise interventions.

There were a number of study limitations. Our cross-sectional design is hypothesis generating, and does not permit inferring causal relationships. Cross-sectional data is also susceptible to selection bias. That is, it has been speculated that physically stronger individuals (with correspondingly stronger bones) may be more likely to engage in physical activities[24]. In addition, the BPAQ tertiles differed in terms of body size and age, and although corresponding statistical adjustments were used when comparisons were made, it is possible that the results may have been affected by the between-group body size and age differences. Furthermore, maturity was assessed from a single time-point based on published regression equations. Obviously, such an approach will have an error associated with the estimate of the timing of PHV. An effort was made to minimize the effect of the PHV estimate error by excluding a relatively wide age-span of participants around the estimated age of PHV in order to dichotomise the comparison groups. Moreover, a relatively large sample of children, adolescents and young adults was examined, which resulted in sufficient

numbers of individuals in each sub-group, enabling the tertile-based analysis approach. The location-specific distribution analysis utilized in the present study may be seen as both a strength and a limitation. Due to the paediatric sample, relatively low density thresholds were used to segment the cortical bone, such that the results may be affected by partial volume effect [45]. The strength of the location-specific distribution analysis is in revealing the shape of the tibial cross-section and in the improved sensitivity to detect the location-specific growth of the tibia.

In conclusion, the present results suggest the peri-, and post-pubertal rather than pre-pubertal period is the most favourable window of opportunity for positively modifying skeletal mass and geometry. We also found that greater loading over the peri- and post-pubertal period may be expected to be anabolic in both sexes. Finally, we observed that the skeletal benefits of physical activity are most marked at the locations in a bone cross section that experience the largest strains when loaded in normal locomotion. The findings should be taken into account when designing exercise interventions.

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