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Bone micro-architecture, estimated bone strength, and the muscle-bone interaction in elite athletes: An HR-pQCT study

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ABSTRACT

Athletes participating in sports characterized by specific loading modalities have exhibited different levels of augmentation of bone properties; however, the extent to which these loading environments affect bone micro-architecture and estimated bone strength (i.e. bone quality) remains unclear. Furthermore, the relative role of impact loading versus loading due to muscle forces in determining bone properties is confounded. The objectives of this study were 1) to examine the role of impact loading on bone quality of the distal radius and distal tibia in elite athletes, as determined by high resolution peripheral quantitative computed tomography (HR-pQCT) and finite element analysis (FEA), and 2) to investigate the relationship between bone quality and muscle strength in elite athletes. Ninety-five females ($n = 59$) and males ($n = 36$) between the ages of 16–30 years participated in the study. Participants included alpine skiers (high-impact), soccer players (moderate impact), swimmers (low-impact), and non-athletic controls.

All group comparisons were made after accounting for age, height, and body mass. As expected, minimal differences in HR-pQCT parameters across groups were observed at the non weight-bearing distal radius. At the weight-bearing distal tibia, female alpine skiers and soccer players had significantly higher bone density, cortical thickness, and failure load (i.e. bone strength (N) in compression estimated by FEA) than swimmers ($p < 0.05$). Female alpine skiers also had lower trabecular separation than swimmers and controls. Male alpine skiers had 20% higher trabecular bone mineral density than swimmers, and male soccer players exhibited 22% higher trabecular number than swimmers at the distal tibia ($p < 0.05$). Male alpine skiers and soccer players had 28–38% higher failure load at the distal tibia than swimmers. No differences in bone parameters were observed between swimmers and controls for either sex at either site. Both muscle strength and sporting activity were predictors of failure load at the distal tibia in the female cohort. Sporting activity, but not muscle strength, was a significant predictor of failure load in the male cohort at both the radius and tibia. This data suggests that impact loading in sporting activity is highly associated with bone quality. Longitudinal and interventional studies are required to further clarify the muscle–bone interaction.

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Introduction

Mechanostat theory suggests that bone remodeling is highly dependent on bone strain [1], a result of mechanical loading, which can include external impact forces and internal muscle forces [2]. This theory is well illustrated in elite athletes as they are often exposed to extreme loading environments, which is a rare occurrence in the general population. For example, athletes involved in high-impact sports such as volleyball and hurdling that are characterized by both high strain magnitude and strain rate have approximately 19–25% higher bone mineral content (BMC) and 37–44% higher polar section modulus (a surrogate for bone strength) at the distal tibia after adjusting for body size, when compared with those in low-impact sports, such as swimming [3].

Although previous studies investigating bone properties in athletes have provided insight into mechanisms of bone adaptation, most are limited by the imaging technology used to measure bone parameters. Dual energy X-ray absorptiometry (DXA) is commonly used to measure areal bone mineral density (aBMD, g/cm^2) and has also

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been used in conjunction with hip structural analysis, which when applied to DXA images can estimate structural parameters at the femur such as cross-sectional area (cm^2), section modulus (cm^3), and buckling ratio [4,5]. For example, this technique has revealed that male gymnasts and runners aged 18–35 have higher cross-sectional area of the proximal femur when compared with controls [6]. Although this technique has proven beneficial for our understanding of how bone can adapt to mechanical stimuli, the two-dimensional nature of this modality makes the measurement of true volumetric bone mineral density (BMD, g/cm^3) of the cortical and trabecular compartments impossible [7–10]. More recent studies addressed this issue using three-dimensional peripheral quantitative computed tomography (pQCT) [3,11–17]. These studies provided further insight into how loading may affect bone mass, BMD, bone geometry, and estimated bone strength in the upper and lower extremities. However, it remains unclear how impact loading influences detailed aspects of bone micro-architecture, a key determinant of bone strength [18–20]. As opposed to pQCT which provides single-slice data, high-resolution pQCT (HR-pQCT) provides 110 sections at a higher resolution than pQCT, which forms the basis for a 3D volumetric analysis of bone microarchitecture, and when coupled with the finite element method, a non-invasive estimate of bone strength [21].

Previous studies have indicated that in addition to impact loading, muscle strength might also influence bone properties. For example, it has been shown that trunk flexion isokinetic peak torque was strongly related to total body and femur aBMD ($r = 0.70–0.86$, $p < 0.05$) in elite female triathletes 21–37 years old [22]. Conversely, leg extensor strength has been shown to account for minimal variance in femoral neck cross-sectional area ($\beta = 0.196$, $p < 0.05$) and femoral neck section modulus ($\beta = 1.205$, $p < 0.05$) [23]. Similarly, female powerlifters aged 27.5 ± 6.3 years exhibited similar BSI at the distal tibia and tibial shaft compared with non-athletic controls, despite the maximally applied muscle forces present in their sport, a result the authors attributed to the low strain rate present in powerlifting [17]. Overall, previous data suggests that muscle strength and bone properties are related in athletes; however, how strongly these parameters are associated remains unclear [24–26]. Therefore, the purpose of this study was two-fold: (1) to investigate the relationship between impact loading and BMD, bone size and shape (macro-architecture), bone micro-architecture, and estimated bone strength in elite athletes; and, (2) to investigate the relative contribution of body composition, impact loading, and indicators of muscle strength to bone micro-architecture and estimated bone strength in elite athletes.

Methods

Participants

A total of 95 adolescents and young adults aged 16 to 30 years volunteered to participate in this study. We recruited athletes from the Canadian National Alpine Ski Team ($n = 24$; 10 women, 14 men) and the varsity men's and women's soccer ($n = 28$; 21 women, 7 men) and swimming ($n = 20$; 13 women, 7 men) teams at the University of Calgary, Canada. Non-athletic controls were recruited ($n = 23$; 15 women, 8 men) from the student population at the University of Calgary. The non-athletic controls had no history of participation in competitive sport or organized training programs. None of the participants had diseases or took medications known to affect bone metabolism, and all participants provided informed consent. The Conjoint Health Research Ethics Board at the University of Calgary approved all study procedures.

Each of the three sporting groups included in this study represented a specific loading modality, or "impact type", based primarily on the magnitude of ground reaction forces experienced in the sporting activity. The alpine skiers represented the high-impact group, as ground reaction forces during slalom events are estimated to exceed 3–4 times body weight [15,27–29] and time to peak force is approximately 400 ms [30]. Soccer players represented the moderate-impact group, as typical ground reaction forces during running and instep kicking are within the range of 1–3 times body weight [31–33]. Swimmers represented the low-impact group, as ground reaction forces are absent in the majority of swim training.

Health and training history, physical activity and dietary calcium

Each participant completed four questionnaires under the supervision of the study coordinator. A health history questionnaire addressed each participant's medical history, current health conditions, previous and current medication use, fracture history, and for women, any previous or current instances of amenorrhea. The validated International Physical Activity Questionnaire [34] was used to determine general physical activity in the form of metabolic equivalents (METs). A training history questionnaire was administered to the athletes to gain information on previous (age that the participant started to compete and training volume over the year prior) and current training regimes. A validated food frequency questionnaire [35,36] was used to determine dietary calcium intake (mg/day).

Anthropometrics

Standing height was measured to the nearest millimeter using a wall-mounted stadiometer (Seca model 222; Seca, Hamburg, Germany). Body mass was measured to the nearest 0.1 kg with an electronic scale (Seca model 876, Seca, Hamburg, Germany). Dual energy X-ray absorptiometry (DXA, Discovery A, Hologic Inc., USA) was used to obtain measurements of bone mineral free lean mass (kg) from a whole-body scan. Three trained technicians acquired and analyzed all DXA scans according to standard Hologic protocols, and also performed daily quality control procedures.

High-resolution peripheral quantitative computed tomography

High-resolution peripheral quantitative computed tomography (HR-pQCT, XtremeCT, Scanco Medical, Brüttisellen, Switzerland) was used to obtain measurements of bone mineral density (BMD, g/cm^3), and bone macro- and micro-architecture of the dominant distal radius and dominant distal tibia for each participant. We scanned the non-dominant radius in five participants (one female control, one male control, two female soccer players, and one male soccer player) who reported a previous fracture to their dominant radius.

A detailed description of scan acquisition is provided elsewhere [37]. Briefly, the HR-pQCT scans provided high-resolution images of a 9.02 mm section of the distal radius and distal tibia (Fig. 1). This system used a nominal isotropic voxel size of 82 μm, with an equal in-plane and between-plane voxel size. The first of 110 slices was acquired 9.5 mm proximal to the endplate of the radius and 22.5 mm proximal to the endplate of the tibia. A single trained operator acquired all scans and performed daily quality control procedures.

All HR-pQCT scans were analyzed according to the manufacturer's recommended protocol [38] to produce standard morphological outcomes including total BMD (Tt.BMD, mg HA/cm^3), trabecular BMD (Tb.BMD, mg HA/cm^3), trabecular number (Tb.N, mm^{-1}), trabecular thickness (Tb.Th, mm), and trabecular separation (Tb.Sp, mm) [39]. These measurements were validated against micro-computed tomography [40,41] and in our lab, the in vivo short-term reproducibility is <4.5% for all outcomes [41]. In addition to the standard morphological analysis, we applied a customized segmentation algorithm [37,42,43] to the HR-pQCT scans to assess cortical BMD (Ct.BMD, mm HA/cm^3), total cross-sectional area (Tt.Ar, mm^2), cortical thickness (Ct.Th, mm) [44], and cortical porosity (Ct.Po, %) [37,42,43]. This technique can reduce variation in Ct.Th measures caused by differences in

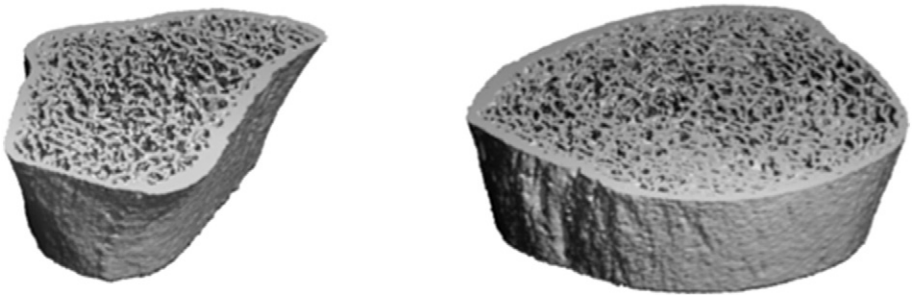

Fig. 1. HR-pQCT (XtremeCT, Scanco Medical, Brüttisellen, Switzerland) images of the distal radius (left) and distal tibia (right). For the radius, the most distal of 110 slices was acquired 9.5 mm proximal to the endplate of the radius, and the most distal slice of the distal tibia was acquired 22.5 mm proximal to the endplate.

degree of bone mineralization, which can be present when obtaining Ct.Th by dividing cortical bone volume by the periosteal surface. In vivo reproducibility for these cortical measures is <2.9%, with the exception of Ct.Po, which has a reported least significant change of 0.58% for the radius and 0.84% for the tibia [42]. One trained technician analyzed all HR-pQCT scans.

Finite element analysis

To obtain accurate estimates of bone strength, we used custom finite element analysis (FEA) software to analyze each HR-pQCT scan based on a linear, homogenous model with a mesh generated using the voxel conversion approach. This method incorporates the three-dimensional micro-architecture and local BMD of the scanned region of interest [45,46]. The models were solved using custom large-scale FEA software (Numerics88 Solutions, Calgary, Canada) [47] on a desktop workstation (Mac, OS X v10.5; 2 × 2.8 GHz Quad-Core Intel Xeon; 32 GB 800 MHz DDR2 FB-DIMM). Using this custom software, the radius and tibia models required an average of 60 min each to solve. The primary outcome was failure load (N), based on simulating axial compressive loading of the bone to 1% strain [48].

Biodex muscle testing and grip strength

A Biodex isokinetic dynamometer (Biodex®, System 3, New York, USA) was used to measure maximal isokinetic knee extension and flexion torque (Nm) of the dominant leg. The Biodex seat was adjusted until the popliteal crease was at the edge of the chair and the axis of rotation was at the level of the femoral condyle. The leg pad was placed just above the malleoli. Participants began each test with their leg in a flexed position and commenced with knee extension at 90°/s. Once the participant reached the point of maximum extension they immediately reverted to knee flexion also at 90°/s. The combination of extension and flexion consisted of one practice trial followed by three experimental trials with no rest. A digital low-pass filter with a cut-off frequency of 5 Hz reduced noise. This test is highly reliable [49] and targets large muscle groups such as the quadriceps and hamstrings that insert on the proximal tibia.

A grip strength dynamometer (Almedic, Quebec, Canada) was used to determine overall isometric strength (kg) of the hand and forearm muscles of the dominant arm (or non-dominant for those participants with previous forearm fractures) using the Canadian Physical Activity, Fitness, and Lifestyle Approach protocol [50]. Participants were instructed to hold the dynamometer firmly in their palm with the grip placed on the middle knuckles. The dynamometer was held approximately 45° away from the body with the elbow joint fully extended. Participants were then instructed to squeeze with maximal effort for 5 s while exhaling and the maximum value of three trials was recorded. This test has shown good reliability in women aged 56–90 years (CV 4.2–4.6%) [51].

Statistical analysis

All statistical analyses were performed using SPSS (PASW Statistics v19.0). A Kolmogorov–Smirnov test was used to ensure all HR-pQCT data was normally distributed. Means and standard deviations were used as descriptive statistics. To address our primary aim, descriptive characteristics (e.g. height, body mass, lean mass) were first compared across groups for men and women separately using analysis of variance (ANOVA), with a Tukey post-hoc test used to identify any significant group differences. Analysis of covariance was used to compare HR-pQCT outcomes across groups adjusting for body size and body composition, which included the covariates age, height, and body mass. A Bonferroni correction was used to adjust for multiple comparisons. To address our secondary aim we fit a hierarchical multivariable linear regression model. Predictors selected were those most likely to influence variance in bone parameters [3,52], and were entered into the model in the following order: (1) age, height, and body mass, (2) grip strength (radius only) and knee extension torque (tibia only), and (3) sporting activity. Three dummy variables were created for sporting activity (alpine skiing, soccer, swimming) with the control group serving as a reference category. An α-level of 0.05 was used for all analyses.

Results

Unless stated otherwise, in the next section all discussed differences are statistically significant at the $p < 0.05$ level. For HR-pQCT parameters, unadjusted data is reported, while statistical significance is flagged after adjusting for age, height, and body mass. Adjustment for lean mass has the potential to mask differences in bone outcomes across groups when used in supplementation to age, height, and body mass [53], and in our cohort, lean mass correlated highly with body mass ($r = 0.768$ in women, $r = 0.927$ in men, $p < 0.001$). Therefore, lean mass was not selected as a covariate. Furthermore, lean mass that was excluded from the regression model is correlated with grip strength ($r = 0.423$ for women, $r = 0.561$ for men, $p < 0.001$) and knee extension torque ($r = 0.430$ for women, $r = 0.649$ for men, $p < 0.001$).

Descriptive characteristics and muscle strength

Descriptive characteristics of the participants are provided in Table 1. For both men and women, age was similar across groups. Female swimmers were taller and leaner than soccer players and controls, and also tended to be heavier than soccer players and alpine skiers. All female athletes began training at a similar age (6.5 years–8.2 years); however, overall training volume and weight-training volume was higher in alpine skiers compared with soccer players and swimmers. Alpine skiers also had higher grip strength than controls, and higher knee extension torque compared with all other groups.

Table 1
Subject characteristics of the female cohort and the male cohort, expressed as mean ± standard deviation. This table includes data regarding body size, body composition, training history, nutritional intake, and health history.

Females (N = 59)	Skiers (n = 10)		Soccer (n = 21)		Swimmers (n = 13)		Controls (n = 15)	
Subject characteristics	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (yrs)	22.7	3.9	20.2	1.5	21.5	1.8	22.6	3.9
Height (cm)	168.8	4.5	165.1	6.6	174.9[b,d]	5.5	165.0	6.0
Body mass (kg)	66.3	4.2	62.6	8.9	68.6	5.6	68.6	16.6
Lean mass (kg)	51.4[d]	3.1	46.7	5.7	52.3[b,d]	3.2	45.3	6.4
Grip strength (kg)	45.3[d]	3.2	39.8	3.9	40.3	6.3	35.9	6.3
KET (Nm)	159.2[b,c,d]	22.0	129.5[c]	25.8	115.4	21.7	118.9	23.7
Age when started to compete (yrs)	8.1	2.2	6.5	3.1	8.2	1.5	–	–
Average training volume (h/wk)	26.4[b,c]	9.8	12.9	4.1	20.5[b]	2.5	–	–
Weight-training volume (h/wk)	7.8[b,c]	2.8	2.9	2.1	3.1	0.4	–	–
IPAQ (MET/wk)	–	–	6425	2929	10,549[b,d]	2554	4544	3262
TDCI (mg/day)	846	366	894	536	948	575	857	604
Age of menarche (yrs)	13.3	1.3	13.4	1.5	13.2	0.9	12.6	1.7
% taking oral contraceptive	60.0	–	60.0	–	30.0	–	20.0	–
Males (N = 36)	**Skiers (n = 14)**		**Soccer (n = 7)**		**Swimmers (n = 7)**		**Controls (n = 8)**	
Subject characteristics	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (yrs)	24.8	3.5	21.3	2.0	21.8	2.0	23.7	3.7
Height (cm)	182.2	6.9	176.1	5.4	185.3	5.1	176.8	7.8
Body mass (kg)	87.0[d]	9.6	76.7	8.2	81.4	8.2	73.7	8.8
Lean mass (kg)	72.5[b,d]	6.1	64.0	5.9	70.7[d]	6.0	57.4	5.1
Grip strength (kg)	67.8[b,c,d]	8.1	55.3	4.8	49.4	8.9	45.8	7.5
KET (Nm)	224.7[d]	50.9	200.2	53.9	184.1	56.7	157.5	33.9
Age when started competing (yrs)	8.0[b]	4.1	7.9	2.8	9.0[b]	3.1	–	–
Average training volume (h/wk)	23.8	10.2	9.0	2.2	24.0	5.1	–	–
Weight-training volume (h/wk)	9.5[b,c]	4.7	2.1	1.8	4.1	1.4	–	–
IPAQ (MET/wk)	–	–	4352	1737	12,556[b,d]	3628	2520	1301
TDCI (mg/day)	879	272	945	550	2197[a,b,d]	1526	1069	559

KET = Knee extension torque.
IPAQ = International Physical Activity Questionnaire.
TDCI — Total Daily Calcium Intake.
[a] Significantly higher than alpine skiers ($p < 0.05$).
[b] Significantly higher than soccer players ($p < 0.05$).
[c] Significantly higher than swimmers ($p < 0.05$).
[d] Significantly higher than controls ($p < 0.05$).

Male alpine skiers had significantly higher body mass than controls, and also had greater lean mass than the other athletes and the controls. All male athletes began training at a similar age (7.9 years–9.0 years), but alpine skiers and swimmers had significantly higher total training volume than soccer players and alpine skiers spent more time weight training than both soccer players and swimmers. Alpine skiers had significantly higher grip strength than all other groups and significantly higher knee extension torque than controls.

HR-pQCT — radius

In the female cohort, alpine skiers had 28% (75.1 mm^2) higher Tt.Ar than controls after adjusting for height, body mass, and lean mass. In the male cohort, alpine skiers had 24% (42 mg HA/cm^3) higher Tb.BMD and 14% (57.3 mm^2) higher Tt.Ar compared with swimmers. Tb.N was 14% (0.28 mm^{-1}) and 18% (0.35 mm^{-1}) higher in the soccer players compared with swimmers and controls, respectively. Tb.Sp was 20% (0.070 mm to −0.073 mm) higher in both swimmers and controls compared with soccer players. Alpine skiers had 60%, 75%, and 44% (1477 N, 1685 N, and 1205 N) higher failure load indicating stronger bones than soccer players, swimmers, and controls, respectively (Table 2).

HR-pQCT — tibia

Results of the HR-pQCT tibia scans for each sex and group are presented in Table 3. In the female cohort, Tt.BMD was approximately 24% higher (68.0 mg HA/cm^3 and 65.7 mg HA/cm^3) in alpine skiers and soccer players, respectively, compared with swimmers. A similar result was observed for Tb.BMD, as alpine skiers and soccer players had 25% and 17% higher Tb.BMD (45.2 mg HA/cm^3 and 30.7 mg HA/cm^3), respectively, than swimmers. Conversely, swimmers had 1% higher Ct.BMD (6.7 mg HA/cm^3) compared with soccer players. Ct.Th was 23.8%–29.5% higher (0.25 mm–0.31 mm) in alpine skiers and soccer players compared with swimmers. Regarding bone micro-architecture, controls and swimmers had 16%–23% (0.06 mm–0.091 mm) higher Tb.Sp, respectively, than alpine skiers. The general trend for augmented bone parameters in alpine skiers and soccer players compared with swimmers was also observed with failure load, as soccer players and alpine skiers had 15%–26% (942 N–1634 N) greater failure load than swimmers.

Tb.BMD was 20% (38.7 mg HA/cm^3) higher in alpine skiers compared with swimmers. Tb.N was 22% (0.38 mm^{-1}) higher in male soccer players compared with swimmers, and Tb.Sp was 22% (0.105 mm) lower in male soccer players compared with swimmers. Male alpine skiers and soccer players had 28%–38% higher failure load (718 N–2654 N) than swimmers.

Predictors of HR-pQCT parameters at the distal radius

Any predictors discussed in this section are those with an F-value change that is statistically significant at the $p < 0.05$ level, unless otherwise stated. All results pertaining to the regression analysis can be found in Table 4.

In females, age, height, and body mass accounted for 43% of the variance in Ct.BMD. The variation in Tt.Ar was most strongly predicted by age, height, and body mass (25%) and the addition of grip strength to the model accounted for an additional 19% of the variance

Table 2
HR-pQCT parameters of the distal radius for the female and male cohorts. Data presented is expressed as mean ± standard deviation. Significant differences flagged across groups are after adjusting for age, height, and body mass.

Outcome measure	Skiers		Soccer		Swimmers		Controls	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Female								
Tt.BMD (mg HA/cm^3)	320.7	60.9	307.6	42.1	294.4	53.5	315.4	50.3
Ct.BMD (mg HA/cm^3)	928.3	41.4	917.3	26.3	930.1	45.9	949.3	37.5
Tb.BMD (mg HA/cm^3)	192.4	33.7	168.0	32.6	158.7	35.0	154.9	30.2
Tt.Ar (mm^2)	338.7[c]	52.8	291.7	41.6	327.4	48.4	263.6	36.5
Ct.Th (mm)	0.89	0.19	0.89	0.12	0.86	0.17	0.92	0.18
Ct.Po (%)	1.2	0.6	1.3	0.4	1.5	0.8	1.1	0.4
Tb.N (1/mm)	2.13	0.17	2.0	0.3	2.04	0.33	2.03	0.24
Tb.Th (mm)	0.075	0.014	0.07	0.01	0.065	0.011	0.064	0.011
Tb.Sp (mm)	0.396	0.037	0.442	0.079	0.44	0.096	0.436	0.063
Failure load (N)	2920.0	710.0	2327.0	460.0	2531.0	545.0	2586.0	722.0
Male								
Tt.BMD (mg HA/cm^3)	336.1	42.6	335.5	46.3	291.0	44.3	340.8	50.5
Ct.BMD (mg HA/cm^3)	864.1	45.5	863.6	29.6	846.5	38.5	873.6	73.3
Tb.BMD (mg HA/cm^3)	218.1 c	20.4	215.6	36.8	176.1	26.4	200.2	29.5
Tt.Ar (mm^2)	459.7[b]	67.3	381.2	41.1	402.4	54.0	353.9	73.7
Ct.Th (mm)	1.05	0.22	1.0	0.13	0.91	0.13	1.02	0.13
Ct.Po (%)	2.7	1.0	3.0	1.4	3.0	0.5	2.9	2.3
Tb.N (1/mm)	2.17	0.2	2.3[b,c]	0.18	2.02	0.21	1.95	0.2
Tb.Th (mm)	0.084	0.011	0.078	0.01	0.073	0.011	0.086	0.013
Tb.Sp (mm)	0.38	0.035	0.358	0.038	0.428[a]	0.05	0.431[a]	0.052
Failure load (N)	3925.0[a,b,c]	773.0	2448.0	453.0	2240.0	189.0	2720.0	568.0

Tt.BMD = total bone mineral density, Ct.BMD = cortical bone mineral density, Tb.BMD = trabecular bone mineral density, Tt.Ar = total cross-sectional area, Ct.Th = cortical thickness, Ct.Po = cortical porosity, Tb.N = trabecular number, Tb.Th = trabecular thickness, Tb.Sp = trabecular separation.
[a] Significantly higher than soccer players ($p < 0.05$), after adjusting for age, height, body mass.
[b] Significantly higher than swimmers ($p < 0.05$), after adjusting for age, height, body mass.
[c] Significantly higher than controls ($p < 0.05$), after adjusting for age, height, body mass.

in Tt.Ar. Age, height, and body mass were the only significant predictors of Ct.Po accounting for 20% of the variance in this parameter.

For the male cohort, sporting activity was the only significant predictor of Tt.BMD and Tb.BMD at the distal radius, accounting for 20% and 29% of the variance in these parameters, respectively. Conversely, age, height, and body mass explained 54% of the variance in Ct.BMD, grip strength accounted for an additional 6.4% of the variance, and sporting activity had a negligible effect. Sporting activity was the

Table 3
HR-pQCT parameters of the distal tibia for the female and male cohorts. Data presented is expressed as mean ± standard deviation. Significant differences flagged across groups are after adjusting for age, height, and body mass.

Outcome measure	Skiers		Soccer		Swimmers		Controls	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Female								
Tt.BMD (mg HA/cm^3)	348.0[c]	38.8	345.7[c]	32.4	280.0	38.7	326.2	32.7
Ct.BMD (mg HA/cm^3)	961.3	18.5	944.4	35.0	951.1[b]	27.1	956.4	38.8
Tb.BMD (m HA/cm^3)	223.6[c,d]	25.2	209.1[c]	24.6	178.4	24.0	184.9	27.3
Tt.Ar (mm^2)	776.1[d]	86.3	718.5	86.2	797.9	114.7	659.3	86.2
Ct.Th (mm)	1.30[c]	0.22	1.36[c]	0.15	1.05	0.15	1.33	0.14
Ct.Po (%)	2.1	0.8	2.7[a]	1.1	2.7	0.9	2.3	1.2
Tb.N (1/mm)	2.03	0.18	1.95	0.21	1.77	0.28	1.83	0.23
Tb.Th (mm)	0.092	0.012	0.09	0.011	0.085	0.013	0.085	0.013
Tb.Sp (mm)	0.403	0.037	0.429	0.05	0.494[a]	0.091	0.469[a]	0.07
Failure load (N)	7844.0[c,d]	834.0	7152.0[c,d]	839.0	6210.0	660.0	6044.0	879.0
Male								
Tt.BMD (mg HA/cm^3)	339.4	37.8	353.1	34.8	291.0	20.4	350.0	40.9
Ct.BMD (mg HA/cm^3)	892.6	33.2	896.4	27.9	902.0	28.4	914.6	44.9
Tb.BMD (mc HA/cm^3)	232.3[c]	23.7	233.0	30.7	193.6	16.3	216.4	22.1
Tt.Ar (mm^2)	1012.9	131.6	886.2	98.5	913.9	109.9	794.6	144.4
Ct.Th (mm)	1.38	0.2	1.47	0.17	1.13	0.15	1.44	0.19
Ct.Po (%)	4.1	1.1	3.5	0.9	3.5	0.8	3.8	1.3
Tb.N (1/mm)	2.03	0.28	2.13[c]	0.18	1.75	0.23	1.8	0.32
Tb.Th (mm)	0.096	0.01	0.092	0.011	0.093	0.012	0.103	0.018
Tb.SD (mm)	0.403	0.058	0.382	0.041	0.487[b]	0.063	0.469	0.087
Failure load (N)	9624.0[c]	1069.0	8920.0 c	789.0	6970.0	1225.0	7688.0	1015.0

Tt.BMD = total bone mineral density, Ct.BMD = cortical bone mineral density, Tb.BMD = trabecular bone mineral density, Tt.Ar = total cross-sectional area, Ct.Th = cortical thickness, Ct.Po = cortical porosity, Tb.N = trabecular number, Tb.Th = trabecular thickness, Tb.Sp = trabecular separation.
[a] Significantly higher than alpine skiers ($p < 0.05$), after adjusting for age, height, body mass.
[b] Significantly higher than soccer players ($p < 0.05$), after adjusting for age, height, body mass.
[c] Significantly higher than swimmers ($p < 0.05$), after adjusting for age, height, body mass.
[d] Significantly higher than controls ($p < 0.05$), after adjusting for age, height, body mass.

Table 4
Summarized results from the hierarchical multivariable linear regression analysis.

		Female				Male			
		Radius		Tibia		Radius		Tibia	
Parameter	Predictors	R^2	ΔR^2	R^2	ΔR^2	R^2	ΔR^2	R^2	ΔR^2
Tt.BMD	1	0.035	0.035	0.432[a]	0.432[a]	0.196	0.196	0.234[b]	0.234[b]
	2	0.071	0.036	0.512[a]	0.080[a]	0.264	0.068	0.239	0.005
	3	0.089	0.018	0.581	0.069	0.463[b]	0.199[b]	0.390	0.151
Ct.BMD	1	0.426[a]	0.426[a]	0.278[a]	0.278[a]	0.540[a]	0.540[a]	0.177	0.177
	2	0.460	0.034	0.280	0.002	0.604[b]	0.604[b]	0.177	0.000
	3	0.491	0.031	0.417[b]	0.137[b]	0.665	0.061	0.226	0.049
Tb.BMD	1	0.048	0.048	0.156[b]	0.156[b]	0.174	0.174	0.144	0.144
	2	0.062	0.014	0.332[a]	0.176[a]	0.175	0.001	0.192	0.048
	3	0.126	0.064	0.457[b]	0.125[b]	0.461[a]	0.286[a]	0.348	0.156
Tt.Ar	1	0.246[a]	0.246[a]	0.507[a]	0.507[a]	0.482[a]	0.482[a]	0.587[a]	0.587[a]
	2	0.436[a]	0.190[a]	0.561[b]	0.054[b]	0.655[a]	0.173[a]	0.605	0.018
	3	0.519	0.083	0.644[b]	0.083[b]	0.666	0.011	0.668	0.063
Ct.Th	1	0.072	0.072	0.431[a]	0.431[a]	0.188	0.188	0.149	0.149
	2	0.111	0.039	0.469	0.038	0.192	0.004	0.177	0.028
	3	0.143	0.032	0.578[b]	0.109[b]	0.459[a]	0.267[a]	0.358	0.181
Ct.Po	1	0.199[a]	0.199[a]	0.254[a]	0.254[a]	0.274[b]	0.274[b]	0.190	0.190
	2	0.201	0.002	0.255	0.001	0.285	0.011	0.190	0.000
	3	0.255	0.054	0.410[a]	0.155[a]	0.355	0.070	0.218	0.028
Tb.N	1	0.038	0.038	0.064	0.064	0.029	0.029	0.196	0.196
	2	0.047	0.009	0.092	0.028	0.103	0.074	0.256	0.060
	3	0.087	0.040	0.220	0.128	0.366[b]	0.263[b]	0.409	0.153
Tb.Th	1	0.046	0.046	0.053	0.053	0.115	0.115	0.113	0.113
	2	0.097	0.051	0.138[b]	0.085[b]	0.180	0.065	0.120	0.007
	3	0.131	0.033	0.151	0.013	0.396[b]	0.216	0.182	0.062
Tb.Sp	1	0.052	0.052	0.123	0.123	0.047	0.047	0.220	0.220
	2	0.056	0.004	0.177	0.054	0.102	0.055	0.281	0.061
	3	0.109	0.053	0.305[b]	0.128[b]	0.388[b]	0.286[b]	0.445	0.164
Failure load	1	0.074	0.074	0.168[b]	0.168[b]	0.286[b]	0.286[b]	0.299[b]	0.299[b]
	2	0.076	0.002	0.470[a]	0.302[a]	0.352	0.066	0.363	0.064
	3	0.112	0.036	0.638[a]	0.168[a]	0.642[a]	0.290[a]	0.659[a]	0.296[a]

Tt.BMD = total bone mineral density, Ct.BMD = cortical bone mineral density, Tb.BMD = trabecular bone mineral density, Tt.Ar = total cross-sectional area, Ct.Th = cortical thickness, Ct.Po = cortical porosity, Tb.N = trabecular number, Tb.Th = trabecular thickness, Tb.Sp = trabecular separation.
Predictors 1 = age, height, body mass.
Predictors 2 = age, height, body mass, grip strength (radius only) or knee extension torque (tibia only).
Predictors 3 = age, height, body mass, grip strength (radius only) or knee extension torque (tibia only), alpine skiing, soccer, swimming.
[a] Indicates F-value change statistically significant at $p < 0.01$.
[b] Indicates F-value change statistically significant at $p < 0.05$.

only significant predictor of micro-architectural parameters, accounting for 26%, 22%, and 29% of the variance in Tb.N, Tb.Th, and Tb.Sp, respectively. For bone strength, age, height, and body mass accounted for 29% of the variance in failure load. The addition of grip strength to the model had no effect, while sporting activity accounted for an additional 29% of the variance in failure load.

Predictors of HR-pQCT parameters at the distal tibia

For the female cohort, age, height, and body mass accounted for approximately 43%, 28%, and 16% of the variance in Tt.BMD, Ct.BMD, and Tb.BMD, respectively. Knee extension torque did not explain any of the variance in Ct.BMD, but did explain 8% of the variance in Tt.BMD and 18% of the variance in Tb.BMD. Sporting activity was a predictor of Ct.BMD and Tb.BMD, accounting for approximately 13% of the variability in these parameters; however, sporting activity was not a significant predictor of Tt.BMD. Knee extension torque was the only predictor of Tb.Th, and accounted for 8% of the variance. Tb.Sp was only predicted by sporting activity, explaining 13% of the variance. In terms of bone strength, age, height, and body mass explained 17% of the variance in failure load, knee extension torque explained 30% of the variance, and sporting activity accounted for 17% of the variance in failure load.

For the male cohort, age, height, and body mass accounted for 23% of the variance in Tt.BMD, 59% of the variance in Tt.Ar, and 30% of the variance in failure load. Knee extension torque was not a significant predictor of any HR-pQCT parameters at the distal tibia in the male cohort. Failure load was the only parameter predicted by sporting activity, which accounted for an additional 30% of the variance in bone strength.

Discussion

This study investigated the relationship between loading modalities present in three sporting activities and BMD, bone macro- and micro-architecture, and estimated bone strength through the use of three-dimensional imaging technology (HR-pQCT) and applied non-invasive mechanical testing techniques (FEA). Additionally, we investigated the relative contribution of age and body size, muscle strength, and sporting activity to HR-pQCT derived bone parameters. Although several bone parameters were not significantly different between athlete groups and controls, a trend emerged showing that high- and moderate-impact groups (alpine skiers and soccer players) have significantly augmented bone parameters when compared with the low-impact group (swimmers), who were never significantly different from controls. Our findings suggest that muscle strength and sport-specific impact loading each play a role in determining bone quality; however, the relative contribution of these predictors remains in question and may vary depending on the specific bone property under examination.

In the female cohort, bone size (Tt.Ar) at the distal radius was higher in alpine skiers than controls after adjusting for age, height, and body mass. Similarly, average bone size of the male alpine skiers was significantly larger than the male swimmers (swimmers were

not different from controls). Given that impact loading is assumed to be absent in the upper extremities in these sports, a possible explanation for this is that female alpine skiers had higher grip strength than controls, and male alpine skiers had significantly higher grip strength than all other groups. Additionally, female and male alpine skiers spent more time weight training than their respective athletic counterparts. This suggests that muscle strength is a predictor of bone size, which agrees with recent literature [54]. This result is further supported by our regression analysis, as grip strength was a predictor of Tt.Ar of the radius in both cohorts, while sporting activity was not a significant predictor.

At the tibia in the female cohort, there was a general trend for alpine skiers and soccer players to have augmented bone parameters when compared with swimmers and controls, albeit less frequently for controls, after adjusting for age, height, and body mass. This finding suggests a positive relationship between impact loading and bone quality. The regression analysis supports this, and in this female cohort, an interesting pattern emerged. All cortical parameters (Ct.BMD, Ct.Th, and Ct.Po — cortical bone mineral density, cortical thickness, and cortical porosity, respectively) were predicted by sporting activity, but none were predicted by muscle strength (knee extension torque). This may suggest that impact loading has potential to enhance cortical bone well beyond the capabilities of muscle forces. This agrees with Nikander et al. [3], who showed that in elite female athletes representing a variety of sports, loading modality account for 25% of the variance in Ct.Th at the distal tibia, as measured by pQCT, while muscle strength only accounted for approximately 4% of the variance. It is possible that muscle forces do not generate high levels of bone strain rate to the same extent as impact loading, which may infer a weaker association between cortical bone parameters and muscle strength. For instance, it has been suggested that thick cortical walls are necessary to cope with the demands of impact loading, and high bone strains in unusual directions are highly beneficial for the augmentation of bone properties [22,55]. Therefore, in our cohort, sporting activity may have played a substantially larger role in the determination of cortical bone parameters when compared to muscle strength, suggesting that impact loading is a stronger predictor of cortical parameters, while muscle strength may be a stronger predictor of trabecular outcomes (e.g. Tb.BMD, Tb.Th — trabecular bone mineral density and trabecular thickness, respectively).

Both muscle strength and sporting activity were significant predictors of failure load at the distal tibia in the female cohort, but muscle strength accounted for approximately 13% more of the variance in failure load than sporting activity. When investigating the distal tibia of the male cohort, sporting activity accounted for 30% of the variance in failure load, while muscle strength accounted for none. These seemingly opposite results may have arisen due to sex differences in the variability of muscle strength parameters. Specifically, the variability in knee extension torque was substantially higher in men than women, which may have influenced our ability to detect a relationship between muscle strength and bone quality in men. This data is in contrast with Nikander et al. [3] who showed that loading modality, but not muscle power or muscle strength, was a predictor of bone strength index at the distal tibia in female athletes (male athletes were not investigated). A possible explanation for the discrepancy is that the bone strength index used by Nikander et al. (density-weighted polar section modulus) is an indicator of bone's resistance to torsion and bending, while the failure load that we estimated is purely a compressive property. Thus, it is difficult to directly compare the results of the two studies.

As stated previously, our results generally indicate that sporting activity involving impact loading is associated with augmented bone quality in both female and male athletes. One single, but perhaps major discrepancy found in this study was that of female swimmers having significantly higher Ct.BMD at the distal tibia than soccer players after adjusting for age, height, and body mass. We observed a similar trend in males, but the difference across groups was not statistically significant. This finding may suggest that the lack of impact loading in swimming is associated with lower intracortical remodeling, which agrees with previous work [12,56] that showed both young and old female athletes have lower Ct.BMD at the tibial shaft than non-athletic controls. Furthermore, Rantalainen et al. [56] showed the trend that young high-impact and odd-impact female athletes exhibit lower Ct.BMD by pQCT than swimmers (not statistically significant), and Ct.BMD of swimmers is not different from controls. Additionally, our findings in conjunction with the result that female swimmers had thinner cortices than both other athlete groups could suggest an adaptational response to swimming. In contrast to alpine skiing and soccer, the nonweight-bearing environment of swimming may have elucidated an adaptational response necessary to increase the strength to weight ratio of the skeleton. This could allow for the optimization of the skeleton that is beneficial for a swimmer, where the skeleton can withstand applied forces in their sport and training, while simultaneously limiting the weight of the skeleton.

Although it is possible that optimization of the skeleton has occurred in swimmers due to their loading environment, it is also possible that swimmers are naturally equipped with this type of bone structure, and are therefore more likely to continue in their sport. It has previously been shown that genetics account for approximately 60–80% of the variance in bone structure [57–59], and it seems very likely that self-selection bias exists for bone parameters on a larger scale that correlate highly with body size and shape, for example total cross-sectional area of a bone. However, regarding other parameters such as Ct.BMD in this sample, particularly after adjusting for body size, it seems more plausible that an adaptational response has occurred, and any other self-selection bias would not depend on specific bone traits, but instead neuromuscular and fitness traits. For example, it seems more likely a child who has better coordination, easier access to sporting activity, gains enjoyment from the sport, and has particular advantages pertaining to large-scale structure (e.g. height), may be directed into particular sports, but not solely because of inherited bone traits. Nevertheless, we cannot disregard the possibility of self-selection bias, and therefore must consider it as a potential reason for observable differences in bone traits across sporting activities.

We note important limitations of this study. First, the cross-sectional design does not allow for evaluation of causal relationships between loading occurring during sporting activity and bone quality, and this data may also be affected by selection bias. Due to this possibility, our findings should be considered hypothesis generating, and as such, they provide a foundation for future prospective studies. Second, our health history questionnaire revealed a history of menstrual cycle disturbances in four female subjects (one alpine skier, three controls) and these may have lead to alterations in bone metabolism in these participants. However, we did not adjust for history of amenorrhea/oligomenorrhea in our analysis, as these subjects were not identified as outliers for bone parameters. Third, we did not measure vitamin D intake nor did we obtain serum samples of serum 25(OH)D. Thus, we cannot rule out the possibility that seasonal variation in vitamin D levels may have influenced our findings. Fourth, HR-pQCT scanning is limited to the distal radius and distal tibia, sites of minimal or no muscle insertion points. Furthermore, type of resistance training should also be considered in future studies. High bone strain rates in unusual directions could be an important factor for enhancing the loading effect on bone quality [55].

Conclusion

To our knowledge, this is the first study to use HR-pQCT to measure BMD, bone macro-architecture and micro-architecture in athletes across multiple sports. In addition, finite element analysis was used to obtain non-invasive estimates of bone strength. This study provides evidence that impact loading is positively associated with bone quality, which is consistent with previous studies, providing

further knowledge into the relationship between mechanical loading and bone adaptation at the micro-architectural level. Specifically, it was shown that bone micro-architecture, a significant determinant of bone strength, was augmented in elite athletes that participated in impact-loading sports. Additionally, muscle strength was a predictor of bone properties contributing to bone strength, particularly bone size; however, the relative role of impact loading versus muscle strength in determining bone quality remains in question. Longitudinal and interventional studies would potentially resolve questions surrounding the influence of impact loading on bone quality and the complex muscle-bone interaction.

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