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Laterality and grip strength influence hand bone micro-architecture in modern humans, an HRpQCT study

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Abstract

It is widely hypothesized that mechanical loading, specifically repetitive low-intensity tasks, influences the inner structure of cancellous bone. As such, there is likely a relationship between handedness and bone morphology. The aim of this study is to determine patterns in trabecular bone between dominant and non-dominant hands in modern humans. Seventeen healthy patients between 22 and 32 years old were included in the study. Radial carpal bones (lunate, capitate, scaphoid, trapezium, trapezoid, 1st, 2nd and 3rd metacarpals) were analyzed with high-resolution micro-computed tomography. Additionally, crush and pinch grip were recorded. Factorial analysis indicated that bone volume ratio, trabeculae number (Tb.N), bone surface to volume ratio (BS.BV), body weight, stature and crush grip were all positively correlated with principal components 1 and 2 explaining 78.7% of the variance. Volumetric and trabecular endostructural parameters (BV/TV, BS/BV or Tb.Th, Tb.N) explain the observed inter-individual variability better than anthropometric or clinical parameters. Factors analysis regressions showed correlations between these parameters and the dominant side for crush strength for the lunate ($r^2 = 0.640$, $P < 0.0001$), trapezium ($r^2 = 0.836$, $P < 0.0001$) and third metacarpal ($r^2 = 0.763$). However, despite a significant lateralization in grip strength for all patients, the endostructural variability between dominant and non-dominant sides was limited in perspective to inter-individual differences. In conclusion, handedness is unlikely to generate trabecular patterns of asymmetry. It appears, however, that crush strength can be considered for endostructural analysis in the modern human wrist.

Key words: grip strength; human; laterality; trabecular bone; wrist.

Introduction

Background

Frost's mechanostat theory first established the ability of bone to remodel in response to mechanical loading (Frost, 1987). Knowing that intrinsic factors such as bone mineral content, material properties, hormonal changes, age and sex all impact hand skeletal morphology – the effect of unique biomechanical signatures on bone architecture has been well documented (Tocheri et al. 2005; Skinner et al. 2015).

The potential effects of asymmetrical behaviors on the skeletal structure have long been documented. In particular, the tendency to preferentially use one hand in a variety of actions (laterality or 'handedness') has been argued to cause bone structural asymmetry (Shaw, 2011). An important task is to determine whether the inner structure of bone reflects this behavior as suggested by endostructural patterns. Indeed, to investigate the origin of handedness in past populations, many researchers have relied on the inner bone morphology that can be traced in skeletal remains (Macchiarelli et al. 1999; Lazenby et al. 2008b; Ubelaker & Zarenko, 2012; Barak et al. 2013). The effect of handedness on bone morphology in humans, however, remains uncertain. Further, most modern activities involve highly lateralized, repetitive, low-intensity mechanical loading. However, the effect of these behaviors on bone morphology is not well understood.

The lateralization of grip strength (GS) represents an important factor characterizing handedness, often

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considered as a reflection of human adaptation to tool-related behavior. GS lateralization has been described at a population level (Mitsionis et al. 2009). Even though several factors may influence GS, a curvilinear relationship with age has been described with a peak between 25 and 50 years of age (Mathiowetz et al. 1985). In adults, GS is significantly higher (~10%) in men than in women, and this difference increases with age (Kamide et al. 2015). However, this trend was reported only in right-handed individuals, whereas no GS asymmetry between genders was shown in left-handed people.

Few studies have examined the effects of these variations on bone architecture – knowledge that would be useful in examining the reaction of trabecular bone to the infraliminar constraints of daily life. However, reference data for standard behaviors are missing. The present study uses high-resolution peripheral quantitative computed tomography (HRpQCT) in a sample of living individuals to identify endostructural features of the human wrist that correlate to anthropometric and clinical measurements of GS and handedness.

Objectives

This study assessed bone morphological factors influenced by lateralized activities of daily life in healthy, young, modern humans.

Methods

Ethical statement

The local Institutional Review Board approved the protocol. All participants received a verbal and written description of the protocol prior to participation. Following this, each participant provided written informed consent.

Study design

Criteria for inclusion were age between 20 and 40 years. Participants with a medical history of bone disease or wrist fracture were excluded. Twenty participants were included initially. Two with previous wrist fracture were excluded, and one with no self-reported handedness was excluded.

Our final study cohort included 17 patients (six female and 11 male). Sample size was decided after computing data from previous studies (Tsegai et al. 2013).

Anthropometric and clinical measurements

Each participant completed a questionnaire to record their medical history, biometric data (height, weight and age), handedness and athletic activities (graded by UCLA score defined in Table 1). GS was recorded with a Jamar grip dynamometer (Jamar Plus+; Sammons Preston, Rolyon, Bolingbrook, IL, USA) for crush grip (fingers flexed on palm) and pinch grip (thumb and index finger). Each measurement was repeated three times, with averages reported. Patients had a standard posture, and three out of 17 were left-handed (Table 2). None had a lateralized occupation at work or in athletic activity, but they all had a self-reported handedness. Despite some patients having UCLA scores of 9 or 10, none practiced at competition level or could be considered as intensive practice. Only one patient was identified as a manual worker.

Micro-CT measurements and processing

Both the left and right wrists were analyzed. Patients sat during CT scan with their forearms placed in a rigid splint. A focus on the radial side of the hand is based on the assertion that the thumb column is the most likely to be impacted by prehensile and fine manipulation tasks (Marzke & Marzke, 2000). Moreover, muscles involved in prehension such as extensor carpi radialis longus and brevis are attached to the base of the 2nd and 3rd metacarpals. Thus, each participant had four carpal bones (lunate, scaphoid, capitate and trapezium) and three metacarpals (1st, 2nd and 3rd) analyzed on each side measured using an XtremeCT microCT (Scanco Medical, Switzerland). This machine produces isometric voxel size of 61 μm. Additionally, three-dimensional (3D) data analyses were performed using Amira 4.1 software (VSG, France). A 3D reconstruction of each bone (Fig. 1) was made initially, and volumes of interest (VOI) were placed. This technique was preferred to XtremeCt scan software in order to avoid any flaw due to potential motion during the exam on such small bones. Further, performing HRpQCT *in vivo* might generate images for which CT scan software would not assess precisely during acquisition. Our use of 3D reconstruction allowed for the verification of each slice, and to adjust gray-scales or correct artifacts. Finally, attenuation histograms were used to determine bone/soft tissue segmentation threshold in order to create 3D stacks of data in a DICOM format.

Endostructural parameters

Morphometric analyses were conducted with the CTAn software (SkyScan, www.bruker-microct.com). The following endostructural parameters were assessed using the VOI method: bone volume ratio (BV/TV), specific bone volume (BS/BV), trabecular pattern factor (Tb.Pf), trabecular thickness (Tb.Th), trabecular number (Tb.N), trabecular separation (Tb.Sp), degree of anisotropy (DA) and total

Table 1 UCLA activity score.

1: Wholly inactive, dependent on others, and cannot leave residence
2: Mostly inactive or restricted to minimum activities of daily living
3: Sometimes participates in mild activities, such as walking, limited housework and limited shopping
4: Regularly participates in mild activities
5: Sometimes participates in moderate activities such as swimming or could do unlimited housework or shopping
6: Regularly participates in moderate activities
7: Regularly participates in active events such as bicycling
8: Regularly participates in active events, such as golf or bowling
9: Sometimes participates in impact sports such as jogging, tennis, skiing, acrobatics, ballet, heavy labor or backpacking
10: Regularly participates in impact sports

Table 2 Sample investigated in this study with individual parameters.

	Weight	Height	BMI	Sex	Laterality	UCLA
1	67	172	22.6	M	Right	8
2	48	162	18.3	F	Right	8
3	62	167	22.2	F	Left	6
4	68	176	22.0	M	Right	10
5	75	169	26.3	M	Left	9
6	60	157	24.3	F	Right	4
7	63	183	18.8	M	Right	9
8	60	174	19.8	M	Right	3
9	60	169	21.0	F	Right	8
10	66	180	20.4	M	Right	7
11	75	179	23.4	M	Right	6
12	74	182	22.3	M	Right	8
13	74	183	22.1	M	Right	9
14	67	168	23.7	F	Right	5
15	81	180	25.0	M	Right	5
16	67	182	20.2	M	Left	10
17	60	169	21.0	F	Right	6
Mean	66.3	173.6	22.0			
Min	48.0	157.0	18.3			3
Max	81.0	183.0	26.3			10
SD	8.0	7.8	2.2			

BMI, body mass index.

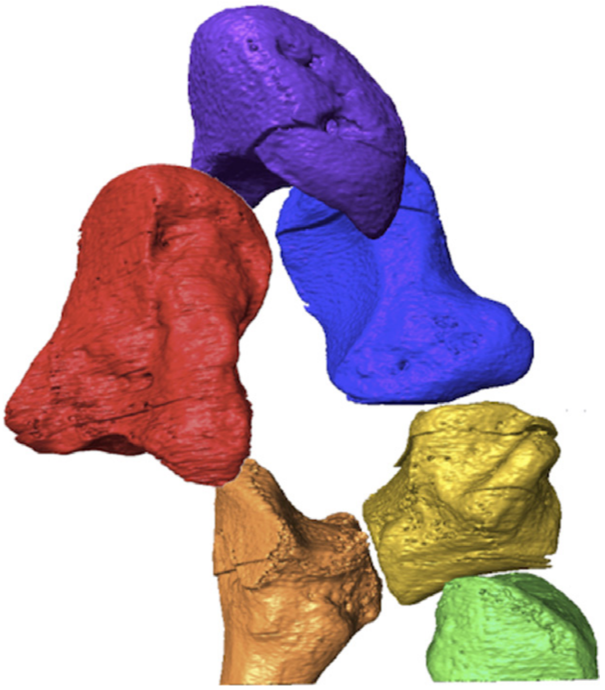

Fig. 1 Three-dimensional (3D) segmentation of wrist bones prior to volume of interest (VOI) analysis.

porosity (Po.tot). For each bone (except the capitate), the VOI was placed centrally in the bone volume, using three orthoslices planes scaled at 50% of the largest diameter. For the capitate, due to its particular shape, a 50% scaled VOI was placed and centered in the head proximally. For metacarpals 1, 2 and 3, the VOIs were scaled at 50% of the largest diameter of the proximal epiphysis.

Statistical analyses

Data were analyzed using the R software (www.R-project.org). Values were normally distributed in the global sample, and subgroups were also examined.

Principal component analyses (PCA) were performed to investigate the relationships between variables. A factor map was used to identify the anthropometric and clinical measurements and the endostructural features that most influenced the variation in our cohort. The PCA highlighted the discriminating parameters for each bone taken separately or considered together. The influence of intrinsic patient-related variables [sex, body weight, stature, body mass index (BMI)] and extrinsic variables (UCLA activity level) on bone endostructure was assessed for each patient. Regressions were performed considering laterality and bone microstructure patterns as independent and dependent variables, respectively. The strongest statistical models were applied to GS and handedness. *P*-value significance was set at < 0.05.

Results

Parameters explaining the observed variation among our sample

Looking at all the bones from each patient, the factorial analysis indicated that bone volume ratio, number of trabeculae and bone surface per bone volume were positively correlated with principal component (PC)1 and accounted for 58.7% of total variance (Fig. 3). PC2 (20.0% of variance) was positively correlated with porosity and negatively with bone volume ratio, number of trabeculae, trabecular pattern factor and bone surface per bone volume. Therefore, some endostructural parameters appear to explain better the variation among our sample than anthropometric and clinical measurements. No sex effects were found ($P = 0.488$) in any bone. A clear separation appeared between each bone on PCA, and PC1 and PC2 were significant for bone specificity ($P < 0.0001$). However, on both principal components, overlapping was shown for lunate–scaphoid and trapezium–MC-3. Figure 3 highlights how the positive end of PC1 reflects a compact and dense trabecular architecture, with low porosity subsequently. The positive end of PC2 showed a more porous trabecular bone and less robustly built architecture. The PCA results for each bone after statistical rotation and extraction are summarized in Table 3. The highest percentages of variances explained by the two-first components were obtained for the capitate (97.5%) and the first metacarpal (96.5%). For both the capitate and the first metacarpal, the first PC was explained mainly by the bone volume ratio (BV/TV; Fig. 2) and Po.tot (Table 3). Overall correlations of significant patterns (i.e. estimation on PC1 or PC2 > 0.750) are presented in Fig. 3 for each bone. Capitate, MC-1 and MC-2 were the most consistent groups of bones within the sample. Capitate was found with a robust and specific architecture, while MC-1 and MC-2 showed higher porosity and thinner trabeculae.

GS

Although no extreme lateralized occupation (e.g. intensive lateralized sport or asymmetrical work) was recorded, we observed significant differences between dominant and non-dominant crush grip (36.0 ± 9.6 N; $P = 0.002$) and pinch grip (6.0 ± 2.1 N; $P = 0.012$). The differences observed for crush grip were in favor of the dominant side in all but one patient (Table 4). The average difference was 7% (−15% to 15%) between both sides. Pinch grip had a different distribution with no statistical relation to sex or occupation. Four patients had a pinch grip in favor of the non-dominant side. The average difference was 6% (−9% to 23%). The UCLA score was not correlated to the lateralization of pinch or crush strength, respectively, $r^2 = 0.305$, $P = 0.769$ and $r^2 = 0.366$, $P = 0.646$.

The endostructural parameters for each bone were considered separately. Additionally, multiple regression analyses of GS indicated a highly significant correlation ($P < 0.0001$) between these parameters (PC1 and PC2) and the dominant side for the lunate ($r^2 = 0.640$), the trapezium ($r^2 = 0.836$, $P < 0.0001$) and the third metacarpal ($r^2 = 0.763$).

Laterality

We investigated whether handedness had an influence on the observed variability in endostructural values. It appeared that distribution is more related to bone than to side (Fig. 4). When considering each bone individually, we observed the distribution of dominant and non-dominant sides in PC1 vs. PC2 plots. As a general trend, we observed that the differences between dominant and non-dominant sides were limited and relatively less substantial than inter-individual variability. Figure 4 shows the PCA analysis per side. PC1 was found not to be significant for laterality ($P = 0.176$) as well as PC2 ($P = 0.796$). The dominant and non-dominant sides representing the same individual generally indicated similar endostructural values. For example, when we consider the endostructural values obtained for the lunate and the first metacarpal, patient number 15 appears relatively distinct from all the other individuals for both dominant and non-dominant sides. At the same time, lunate endostructural values obtained for dominant and non-dominant sides within several individuals are almost superimposed (e.g. patients 9 and 11). Importantly, no inter-individual difference due to sex, activity or GS explains the variability observed in this dataset. Further, these same trends are observed when examining the endostructural parameters of all bones together. Specifically for the capitate, the parameters BV/TV, BS/TV and Tb.N were higher in the dominant side whether Tb.Pf and Tb.Sp were lower. For

Table 3 Endostructural and anthropometric variables representation for each bone on principal component (PC 1 and 2).

Bone	All		Scaphoid		Lunate		Trapezium		Capitate		MC-1		MC-2		MC-3	
PC	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2
% Var	58.7	20.0	47.9	27.2	41.1	32.3	60.0	20.2	58.5	39.0	74.2	22.3	67.7	19.0	56.2	22.3
BMI																
Height														0.785		
Weight			−0.410											0.905		0.383
BS/BV	−0.933						0.853	0.365							0.949	
BV/TV	0.917	−0.322			−0.939		−0.993		0.965		−0.986		−0.976		−0.880	0.384
Tb.N	0.818	−0.328					−0.945						0.977			
Tb.Pf	−0.890		0.943		0.850	−0.338	0.985								0.845	−0.416
Tb.Sp					0.380	−0.837							−0.905			
Tb.Th	0.870										−0.953				−0.826	
DA														0.839		
Po.tot	−0.916	0.330	0.980		0.942		0.994		−0.966		0.986		0.976		0.903	−0.404

BMI, body mass index; PC, principal component.

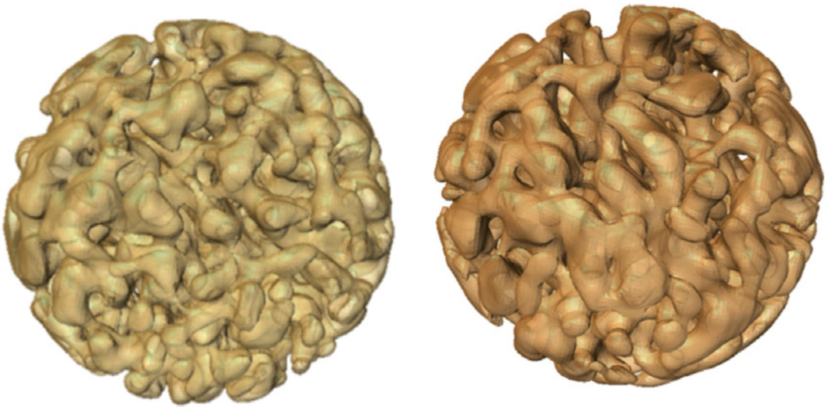

Fig. 2 Volume of interest (VOI) in capitate (non-dominant side on left, dominant side in right) on patient 2. Trabeculae are thicker (Tb.Th 0.35 mm vs. 0.31 mm) on the right sample, and bone volume fraction BV/TV is higher (37.3% vs. 30.9%).

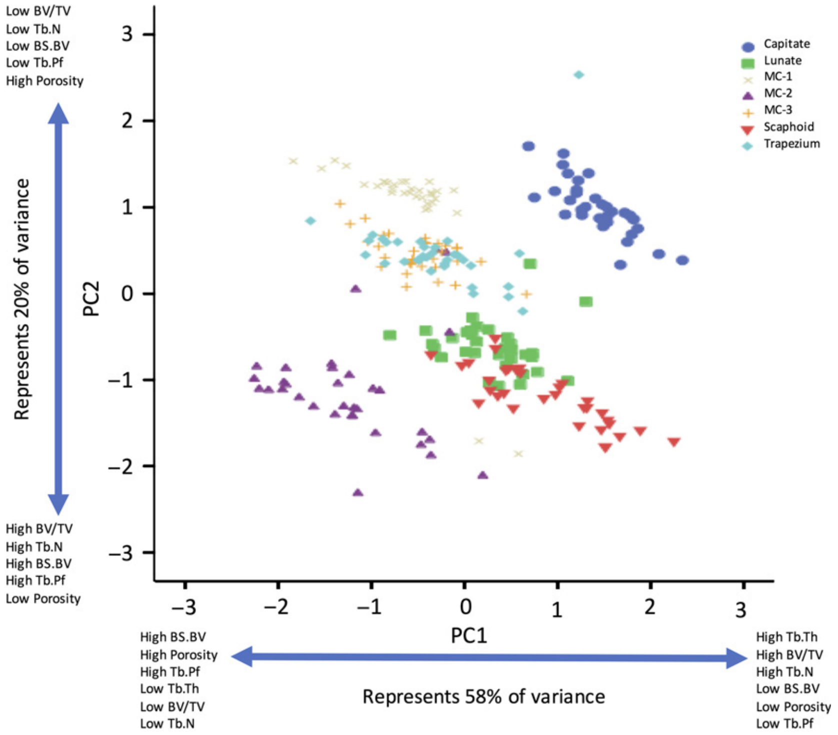

Fig. 3 Variables correlations on principal component analysis (PCA) on PC1 (*x*-axis) and PC2 (*y*-axis) per bone studied. The explanation of the variance per PC (58% for PC1 and 20% for PC2) is meant for all the bones studied.

the scaphoid, porosity was slightly higher in the dominant side but all the other parameters were comparable. For the lunate, BS/BV, Tb.Pf, Tb.Sp and porosity were higher in the dominant side whether BV/TV, BS/TV, Tb.N were lower. The trapezium, MC-1 and MC-2 had the same patterns, BV/TV, BS/TV, Tb.N were higher in the dominant side whether BS.BV, Tb.Pf, Tb.Sp and porosity were lower.

Discussion and conclusions

We sought to define the pattern of laterality *in vivo* on the carpal skeleton of the human hand. Specifically, we found bone volume ratio (BV/TV) as a specific parameter explaining variability in each bone. The number of trabeculae and the specific bone surface (BS/BV) appeared also recurrent indicators for variability. We observed a relationship between GS and trabeculae patterns for the lunate, MC-3 and trapezium. Conversely, pinch grip was inconsistent with hand preference and was not related to any specific variable. Despite these findings, the results of this study suggest that usual tasks (e.g. writing, eating) with a preferred hand do not stimulate sufficient asymmetric mechanostat biofeedback to influence bone modeling in the wrist. Indeed, a multifactorial analysis did not show any robust pattern. Further, endostructural parameters did not appear to be correlated with any anthropometric (body weight or stature), sex or clinical measurements. BMI was not involved in the variability in any bone. This is likely due to the fact that forelimbs are not used for locomotion (Marzke, 2009). As such, the modern behaviors sampled in this study may

Table 4 Patients strength for crush and pinch grips (N).

Patients #	Crush grip dominant	Crush grip non-dominant	Delta crush (%)	Pinch grip dominant	Pinch grip non-dominant	Delta pinch (%)
1	618.0	529.7	14	106.3	101.4	5
2	255.1	215.8	15	93.2	78.5	16
3	480.7	470.9	2	83.4	89.3	−7
4	640.9	608.2	5	107.9	99.7	8
5	506.9	582.1	−15	104.6	80.1	23
6	320.5	294.3	8	81.8	85.0	−4
7	608.2	542.8	11	139.0	147.2	−6
8	539.6	519.9	4	99.7	99.7	0
9	323.7	307.4	5	83.4	75.2	10
10	503.6	500.3	1	75.2	81.8	−9
11	670.4	572.5	15	106.3	101.4	5
12	595.1	529.7	11	106.3	96.5	9
13	565.7	497.0	12	103.0	93.2	10
14	255.1	235.4	8	89.9	75.2	16
15	588.6	526.5	11	106.3	103.0	3
16	621.3	588.6	5	107.9	96.5	11
17	467.6	425.1	9	91.6	80.1	13

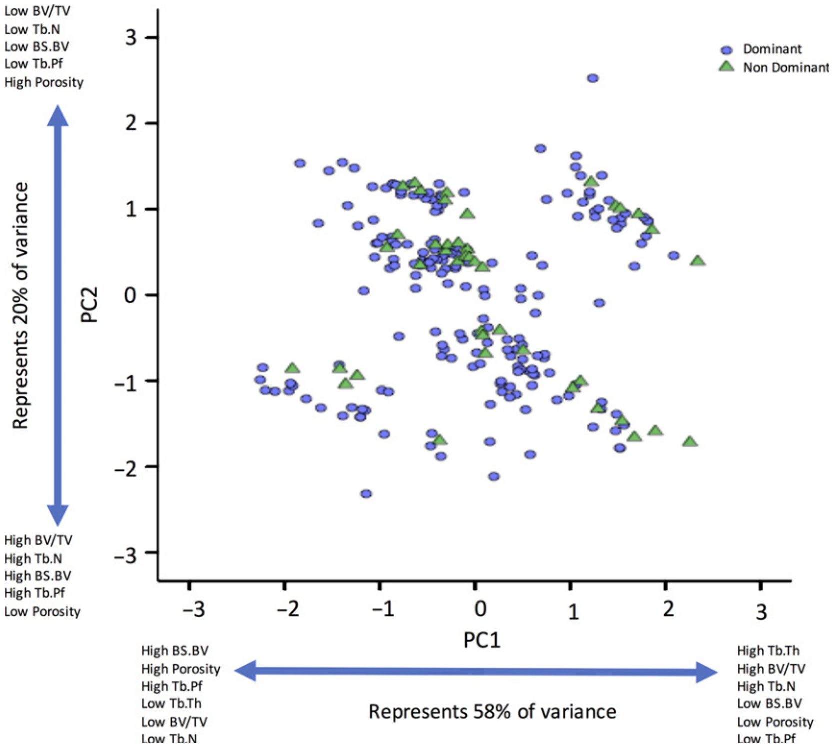

Fig. 4 Variables correlations on principal component analysis (PCA) on PC1 (*x*-axis) and PC2 (*y*-axis) for dominant and non-dominant sides. Dots indicate dominant and triangles indicate non-dominant. The explanation of the variance per PC (58% for PC1 and 20% for PC2) is meant for all the bones studied.

not create sufficient strains on the hand skeleton to influence bone modeling.

To our knowledge, this is the first study to assess the relationship between endostructure and strength in a living patient with standard activities. Unfortunately, the current literature is focused on athletes and extreme handedness (Ozener, 2012). Yet, we believe an investigation into the impact of handedness on bone in non-athletic individuals is necessary to fully understand the relationship between mechanostat biofeedback and bone modeling. Additionally, this study builds upon other studies that have reported the effect of age and sex on bone characteristics, but failed to investigate laterality (Hasegawa et al. 2001; Edwards et al. 2013; Szulc et al. 2013; Crockett et al. 2015). Finally, our use of pQCT to analyze cross-sectional bone provides more detailed data than similar studies only focusing on bone mass density.

Limitations

This study has several limitations. First, the sample size is small. Though other well-designed studies using identical segmentation methods have been published with comparable sample sizes (Stephens et al. 2016), we believe that further studies should be conducted using larger sample sizes to confirm the relationship between lateralized low-intensity activities on human bone morphology. Second, there are well-documented technical limitations with the collection of VOI data. Specifically, Kivell et al. (2011) expressed concerns about technical difficulties in collecting VOI data on wrist bones. Indeed, trabeculae distribution in such small bones is heterogeneous and choice of VOIs position is essential. As a consequence, assessments of handedness in fossil samples should be cautious, even in the case of observed side differences at the micro-architectural level. We used 61 μm voxels to limit time of acquisition, which can be considered a low resolution to assess endostructure on non-weight-bearing bones. The values reported, particularly the trabeculae thickness, appear to be higher than previously published data. That might be a limitation of our segmentation technique and the resolution used. Finally, we must consider some inaccuracy in determining the edges of the trabeculae due to marrow and fat content of the interstitial space, considering this is an *in vivo* study. Kivell (2016) detailed the difficulty of such an analysis in living samples and emphasized that current literature is focused only in high-activity athletes. Mice models have been developed with poor reliability and translational issues to human models. For these reasons, *in vivo* data must be considered with caution. As such, we reported all data as trends.

There are many data supporting the ability of high biomechanical loading to effect human bone structure. Erlandson et al. (2012) used dual-energy X-rays absorptiometry analysis to show that premenarchal elite gymnasts had a higher bone mass in the femoral neck, when compared with non-gymnasts. Further, such a difference was proven to remain unchanged 14 years later when the loading stimulus had decreased. These results highlight the ability of bone modifications from repetitive biomechanical loading to persist long after the termination of the loading behavior. Similarly, Sone et al. (2006) observed asymmetry in the tibia of individuals with a dominant leg for mobility and manipulation, and Sylvester et al. (2006) used radiographs to show differences in bone morphology and pathology (e.g. osteoarthritis) based on human activity (specifically rock climbing). Therefore, there is little doubt that mechanical behavior affects bone structure. Yet, important questions regarding the relationship between mechanical behavior and bone morphology remain – specifically, the effect of repetitive biomechanical loads on cancellous and cortical bone. In this context, the impact of handedness on bone clearly represents one of the most challenging questions to address. This study sought to better understand the impact of handedness on bone modeling by investigating endostructural parameters in modern human carpal bones. Carpal modeling represents a hallmark of adaptation to tool manipulation (Marzke, 2009). Our findings highlight that a level of activity or strength might be determined as a threshold to stimulate aptation to environment.

Lazenby et al. (2008a) suggest that volumetric variables such as BV/TV and Tb.N are sensitive to mechanical regulation and handedness. Further, they found that the influence of age is felt more on the left rather than the right metacarpal given the human propensity for right-handedness. This remains not obvious in our results. Our data suggest that usual tasks (e.g. writing, eating) with a preferred hand may be important inter-individual differences in endostructural parameters (i.e. as trabecular thickness and bone volume ratio). These tasks, however, did not produce strong morphological differences between the two sides. It should be noted that contrary findings have been described in the literature. Stephens et al. (2016) assessed the laterality in *Homo sapiens* and *Pan troglodytes* and *paniscus* by micro-CT scan*,* identifying specific and significant patterns of laterality (BV/TV, degree of anisotropy and elastic modulus in the base of the first metacarpal). Our results suggest similar patterns for MC-1 and MC-2 bases and trapezium (BV/TV = 11/17 on MC-1, 9/17 on MC-2 and 11/17 on trapezium), but remain unclear for the rest of the thumb column. We did not find anisotropy as a significant factor. In that same study, however, despite a flawless method, the lateralization could not be reported as the bone analyzed came from individuals from the 1st and 3rd centuries. The authors assumed that asymmetry of the bone is explained by laterality, but this fact is not invariable. In our sample, one individual showed a higher crush grip in the right hand when he reported himself as left-handed. In a society where right-handed preference reported is over 90%, usual tasks are taught and tools are made to facilitate this lateralization. This is an interesting fact that should not be underestimated when analyzing fossils. Earlier studies have illustrated the effect of lateralized sport activity and bone morphology. Notably, Shaw (2011) documented an effect on humeral, ulnar and tibial shaft morphology based on specific lateralized biomechanical loading patterns in cricket and hockey players. However, no significant asymmetry was observed in their control groups with a non-lateralized activity. This finding based on pQCT of 0.5 mm slices (μ-CT) suggested that bone modeling was not sufficient to produce a significant asymmetry in both non-professional athletes and runners and swimmers with no ‘habitual, highly intense or repetitive, unilateral upper limb activities in the loading histories of these groups’. Shaw concluded that laterality can produce a significant asymmetry only in the case of a marked biomechanical contrast between right and left sides – as in the high repetitive biomechanical loading experienced by cricket and hockey players. It should be noted that Shaw's finding reports an estimate of the torsional and average bending rigidity of the diaphysis and cortical area, an indicator of a bone's mechanical performance under biomechanical loading (Ruff et al. 2006). This method is limited in that it only concerns the diaphysis, and deemphasizes trabecular bone patterning. Moreover, no indication about patients' morphology, height, weight or BMI was analyzed as influencing factors. In our study, we assessed correlations between anthropometric variables and endostructure. As such, our study reinforces Shaw's finding that unilateral and repetitive stresses are required in low-intensity activities to mark bone structure in upper limb and carpal bones morphology.

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Author contributions

NR and JB designed the study and collected data. EC and JML contributed to statistical analysis and data collection. TK, WT and NR participated in writing discussion and revised the manuscript.

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