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MEN AND WOMEN HAVE SIMILARLY SHAPED CARPOMETACARPAL JOINT BONES

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Abstract

Characterizing the morphology of the carpometacarpal (CMC) joint bones and how they vary across the population is important for understanding the functional anatomy and pathology of the thumb. The purpose of this paper was to develop a statistical shape model of the trapezium and first metacarpal bones to characterize the size and shape of the whole bones across a cohort of 50. We used this shape model to investigate the effects of sex and age on the size and shape of the CMC joint bones and the articulating surface area of the CMC joint. We hypothesized that women have similar shape trapezium and first metacarpal bones compared to men, following scaling for overall size. We also hypothesized that age would be a significant predictor variable for CMC joint bone changes. CT image data and segmented point clouds of 50 CMC bones from healthy adult men and women were obtained from an ongoing study and used to generate two statistical shape models. Statistical analysis of the principal component weights of both models was performed to investigate morphological sex and age differences. We observed sex differences, but were unable to detect any age differences. Between men and women the only difference in morphology of the trapezia and first metacarpal bones was size. These findings confirm our first hypothesis, and suggest that the women have similarly shaped trapezium and first metacarpal bones compared to men. Furthermore, our results reject our second hypothesis, indicating that age is a poor predictor of CMC joint morphology.

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6. Conflict of interest statement

We declare no conflict of interest.

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Keywords

Statistical shape model; SSM; Carpometacarpal; CMC; Sex differences

1. Introduction

Characterizing the morphology of the carpometacarpal (CMC) joint bones and how they vary across the population is important for understanding the functional anatomy and pathology of the thumb. Bone size and morphology influences the articulating contact area and shape of the joint (Halilaj et al., 2014b), the location and action of ligaments (Nanno et al., 2006), and the kinematics, moment arms, and lines of action of muscles crossing the joint (Arnold and Delp, 2001; Hollister et al., 1992). These factors are critical for estimating the forces and stresses placed on the joint tissues (Anderson et al., 2010; Van Nortwick et al., 2013; Xu et al., 1998), which are important considerations for surgical implant design and believed to play a role in the mechanical etiology of CMC osteoarthritis (Hunter and Wilson, 2009; Koff et al., 2003; Xu et al., 1998). A recent large scale study has found knee morphology, specifically tibial plate slope, was a predictor of osteoarthritis presentation and progression (Neogi et al., 2013). In order to incorporate representative CMC morphologies into biomechanical simulations to investigate the link between morphology and osteoarthritis, we must first understand the natural variations in CMC joint shape.

CMC joint osteoarthritis is common and two to six times more prevalent in women than in men (Acheson et al., 1970; Dias et al., 2007; Haara et al., 2004; Segal et al., 1998; Valdes and von der Heyde, 2012). The sexual dimorphism of the CMC joint bones is believed to play an important role in this discrepancy (Ateshian et al., 1992; Kovler et al., 2004; North and Rutledge, 1983; Xu et al., 1998). Prior studies investigating sex differences in morphology of the CMC joint bones have been focused on the articular surface morphology and range in complexity from simple descriptive classification (Van Nortwick et al., 2013), to measurement of curvature, through the use of dial indicators (North and Rutledge, 1983) and 3D models obtained through stereophotogrammetry (Ateshian et al., 1992; Xu et al., 1998), segmentation of CT images (Conconi et al., 2014; Halilaj et al., 2014b), and laser scanning (Kovler et al., 2004; Marzke et al., 2012). In contrast to previous findings, recent CT-imaging-based studies have found no sex differences in the articular shape of the CMC joint (Conconi et al., 2014; Halilaj et al., 2014b; Marzke et al., 2012). However, there are scarce data concerning the morphology of the entire CMC bones and their variation, in terms of how the bones change or scale across the population. This information has important implications for the scaling of musculoskeletal models, methods for which do not currently account for potential sex differences in morphology (Cooney and Chao, 1977; Giurintano et al., 1995; Goislar de Monsabert et al., 2014; Valero-Cuevas et al., 2003; Wohlman and Murray, 2013). Can we assume that a female bone is simply a scaled version of a male bone?

Age is also a factor that might alter the morphology and function of the CMC joint bones. The kinematics of the CMC joint seem to be influenced by age (Halilaj et al., 2014c), which might be due to changes in the morphology of the articular surface (Halilaj et al., 2014b).

However, it is not clear whether the entire morphology changes with age in CMC joint bones.

Statistical shape modeling is necessary to quantify the variation in shape across a population (Chan et al., 2013; Fitzpatrick et al., 2011; Van Haver et al., 2013; Zhang et al., 2014) and classify morphological variation by decomposing shapes into a set of statistically significant modes (commonly principal components) (Cootes et al., 1992; Dryden and Mardia, 1998). This is effective for understanding morphology (Bischoff et al., 2013; Vos et al., 2004) and for determining relationships between morphology and parameters of interest, such as sex and age (Anderson et al., 2010; Bischoff et al., 2013; Fitzpatrick et al., 2011). Furthermore, statistical shape models allow us to investigate specific anatomical regions and examine local shape changes, which can be correlated to parameters of interest or anatomical features, such as ligament or tendon attachment sites.

The purpose of this paper was to develop a statistical shape model of the trapezium and first metacarpal bones to characterize the size and shape of the whole bones across a cohort of 50. We used this shape model to investigate the effects of sex and age on the size and shape of the CMC joint bones and the articulating surface area of the CMC joint. We hypothesized that women have similar shape trapezium and first metacarpal bones compared to men, following scaling for overall size. We also hypothesized that age would be a significant predictor variable for CMC joint bone changes.

2. Methods

CT image data and segmented point clouds of 50 carpometacarpal (CMC) bones from healthy adult males and females were obtained from an on-going study (Halilaj et al., 2014a; Halilaj et al., 2014c). An iterative fitting process involving principal component analysis (PCA) was performed to generate two statistical shape models: one including size variations and one normalized for size. Statistical analysis of the principal component weights of both statistical shape models was performed to investigate morphological sex and age differences.

2.1. Subject information

After Institutional Review Board approval and informed consent, the dominant wrists and thumbs consisting of 40 right hands and 10 left hands of 50 healthy non-osteoarthritic (radiographic and asymptomatic) volunteers (23 men, age 35.6 ± 13.7 yrs and 27 women, age 42.9 ± 15.3 yrs) were imaged in a clinical neutral position (Figure 1 A) with a 16-slice clinical CT scanner (GE LightSpeed 16, General Electric, Milwaukee, WI).

2.2. Imaging protocol

The settings used on the scanner were: tube parameters at 80 kVp and 80 mA, slice thickness of 0.625 mm, and in-plane resolution of $0.4 \text{ mm} \times 0.4 \text{ mm}$. The trapezia and the first metacarpals were segmented semi-automatically by the Department of Orthopedics at Brown University using Mimics v12.11 (Materialise, Leuven, Belgium) and 3-D bone models were exported as meshed surfaces (Figure 1 B). The vertices of these surfaces were extracted to produce a training set of point clouds.

2.3. Statistical shape model generation

The technique implemented to generate the statistical shape model for this paper was based on the work by Zhang et al. (2014). In summary, a custom template cubic-Lagrange piece-wise parametric mesh (Nielsen, 1987) (Figure 1 C) was created and fitted to all data clouds in the training set via an iterative fitting process (Figure 1 D). The process involved a series of coarse to fine fits in which the template mesh was initially brought to within 4 mm RMS of the data clouds such that the meshes were close for fitting. Fitted meshes were then rigidly aligned to each other by minimizing the least squared distances of corresponding points and PCA (as in section 2.5) was carried out on mesh node coordinates to obtain a shape model. This process was repeated 5 times in which the shape model was used to first fit the mesh, thereby propagating fitting correspondence across the training set and finally achieving a RMS error of 0.4 mm. Thus, the shapes of each metacarpal and trapezium of the CMC joint training set were represented by maximally correspondent meshes (Zhang et al., 2014). A final PCA was performed on the nodal coordinates of the training set meshes to yield the statistical shape model (Figure 1 E) and determine the principal components of variation used in subsequent analysis.

2.4. Size-normalization

For statistical shape models involved in biological systems, size typically dominates the first principal component (Chan et al., 2013; Cootes et al., 1992; Fitzpatrick et al., 2011; Zhang et al., 2014). To investigate pure-shape differences in the trapezia and 1st metacarpal bones between men and women, a general Procrustes analysis (least-squares minimization of correspondent point differences) was performed on the fitted meshes to filter out scaling variations (Bischoff et al., 2013; Ross, 2004; Stegmann and Gomez, 2002) producing the size-normalized shape model.

2.5. Principal Component Analysis

Principal component analysis was used for dimensionality reduction and allowed any shape $\mathbf{x}$ in the training set to be approximated as a sum of the mean shape $\bar{\mathbf{x}}$ and the weighted sum of n principal components ϕ (Heimann and Meinzer, 2009; Zhang et al., 2014):

$$\mathbf{x} = \bar{\mathbf{x}} + \sum_{i=0}^n \omega_i \phi_i \quad (1)$$

where n was chosen to be 8 such that the accumulated variance explained by the components account for 90% of the total variation in the population. Thus, the shape of each bone in the training set was described by 8 weights, ω . These weights and the sex and age of the corresponding subjects were used for the following statistical analyses.

2.6. Statistical analysis

Principal component weights, which dictate the degree of variation along a principal component, were extracted for the bones of each subject from each shape model and used for t-test against sex, and linear regression was performed against age. For our purposes, it was important to characterize all morphological differences present in the population of CMC joint bones, including both size and shape variations.

2.6.1. Characterizing size differences—We expected the first principal component of our non size-normalized shape model to be dominated by size variation. Therefore, we extracted the weights of the first principal component (ϕ_1) for men and women. Q-Q plots and a Shapiro-Wilk test were used to determine normality and a Levene test was carried out to confirm equal variance to satisfy t-test assumptions. Finally, t-test was performed on the weights classified by sex in conjunction with a boxplot to test if women have significantly smaller trapezia and metacarpal bones compared to men. Linear regression was performed on the weights against age to test for relationships between morphology and age.

2.6.2. Characterizing pure-shape differences—PCA weights from the first five principal components of the size-normalized shape model were used to explore sex and age related pure-shape differences after uniform scale adjustment. After confirming normality and equal variance, t-tests with Bonferroni correction were performed on the weights of each principal component, classified by sex to explore if women exhibited significant shape differences to men along each principal component. Linear regression was used to test for relationships between age and morphology.

2.7. Articulating surface areas

The articulating surface landmark was identified during parametric template mesh design (Figure 1 C) where mesh elements were created to segregate the articulating surface and fitted to maximize correspondence.

We expected the articulating surface area to be dependent on both the size and shape. Both shape models were varied by the first principal component weights of the training set and the articulating surface landmark elements were extracted.

Articular surface area means and standard deviations were calculated for men and women. A t-test was also performed on the on the surface areas to confirm if the articulating surface areas between the two populations were different.

3. Results

3.1. shape model

The first seven principal components of the non size-normalized shape model accounted for over 90% of the variance in morphology present in the training set (Figure 2 A). The leave-one-out root-mean-squared (RMS) error for the non size-normalized shape model was 0.4 mm. The RMS error was smaller than the voxel dimensions, indicating a representative shape model with a sufficiently large training set. As expected, the first principal component was size and accounted for 71% of the variation. The size of the trapezium was linearly correlated ($p < 0.001$) to the size of the metacarpal.

3.2. Characterizing size differences

The trapezium and first metacarpal bones were smaller ($p < 0.001$) in women than in men (Figure 3). Correlation of the mode weights with age was poor ($R^2=0.4$)

The articulating surface areas of both the trapezium and first metacarpal bones were smaller in women ($p < 0.0001$) than in men (Table 1).

The mean first metacarpal bone volume in men was 6101 mm^3 and in women was 4570 mm^3 , and the mean trapezium in men and women were 2459 mm^3 and 1755 mm^3 , respectively.

3.3. Size-normalized shape model

The first seven principal components of the size-normalized shape model for the training set population accounted for approximately 60% of the variation (Figure 2 B). The first principal component alone accounted for 24% of the size-normalized variance present in the training set. For the first metacarpal, this was qualitatively observed as aspect ratio when varied from one extreme to the other (Figure 4), where the proximal and distal ends of the first metacarpal moved further apart as the principal component weights became more positive, and the diameter of the epiphysis became narrower. In the trapezium, the first principal component did not represent aspect ratio. Instead, as the weights became more positive, the radial ridge diminished and the ulnar ridge became more prominent. Changes observed in this mode were very small.

3.4. Characterizing pure-shape differences

Since there was a noticeable decrease in the gradient of the cumulative variation curve around the fifth principle component (Figure 2 B), subsequent principal components were not uniquely and consistently defined. Therefore, investigation of shape differences for these principal components was not performed.

We found a statistically significant difference ($p=0.01$ after Bonferroni correction) in the weights of the first principal component of the size-normalized shape model between men and women. In women, the first metacarpals had higher aspect ratios, meaning a longer and narrower bone, and the trapezia had a more prominent ulnar ridge (Figure 4). None of the first five principal components correlated to age ($R^2 = 0.43$) indicating no relationship between these variables. Though statistically significant, the differences between the men and women as a result of varying the first principal component of the size-normalized shape model were small (less than 1 voxel in magnitude), and indicated a small effect size. These effects were small and could only be distinguished at the extremes of the population (2–3 standard deviations away from the mean) (Figure 4).

The articulating surface area of the first metacarpal after size-normalization remained smaller in women ($p < 0.005$) than in men (Table 3). The articulating surface area of the trapezium was larger in women ($p < 0.008$). However, the standard deviations between men and women overlap indicating no difference in the population.

4. Discussion

The purpose of this study was to characterize the size and shape of the entire trapezium and first metacarpal bones in a cohort of 50 healthy CMC joints using a statistical shape model. We achieved this by characterizing morphological differences in the population of

carpometacarpal (CMC) joint bones, including both size and uniform scale adjusted shape variations using two shape models (non size-normalized shape model and size normalized shape model), and analyzing the principal component weights in the population. We compared the principal component weights between men and women, and performed regression of the principal component weights against age. Of the two parameters studied, sex was the only parameter that accounted for differences in principal component weights of morphological modes of variation. We found that the only difference in the morphology of the trapezia and first metacarpal bones between men and women was size, thus, confirming our first hypothesis that women and men have similarly shaped trapezium and first metacarpal bones compared to men. Furthermore, we found no correlation between morphology with age and rejected our second hypothesis.

Previous statistical shape models investigating morphological variation in bones have shown that size dominates the first principal component (Chan et al., 2013; Cootes et al., 1992; Fitzpatrick et al., 2011; Zhang et al., 2014). This was the case in our statistical shape model, where the first principal component accounted for 71% of the morphological variation in CMC joint bones, which was attributed to size (Figure 2). The large reduction in variation from 71% variation represented in the first principal component to the second principal component, which exhibited 10% of the morphological variation, suggested that the morphology of the CMC joint bones do not vary much in shape, but instead, mostly vary in size. Bone volumes observed in this study (Table 2) were similar to those reported previously (Crisco et al., 2005; Halilaj et al., 2014b; Moore et al., 2007). By varying the size and shape along the first principal component of the non size-normalized shape model, we observed that the size of the CMC joint bones dictated the size of the articulating surface area in both the first metacarpal and the trapezium ($p < 0.0001$). As expected, this means that a smaller bone exhibits a smaller articulating surface (Table 1). Despite the inclusion of only the first principal component of the non size-normalized shape model, we yielded articular surface areas similar to those reported by Ateshian et al. (1992). This was not surprising, since most of the variation in the CMC joint bones (71%) was accounted for by size.

These findings improve upon our current understanding of the CMC joint bones, and have various implications. Firstly, size accounts for the majority of the variation in the CMC joint bones with women having smaller bones on average than men by $\sim 2200 \text{ mm}^3$ (Table 2). Size is important when considering the forces, stresses and form-function relationship of the wrist and hand, since scaling of bones influences the action of the ligaments (Nanno et al., 2006), muscles, and the size of the moment arms at joints (Arnold and Delp, 2001). For example, if we consider that the moment arms of muscles crossing the joint would scale with bone size, the forces required to generate the same torques for a given task would be higher in a joint with smaller bones. It has been hypothesized that smaller joints would therefore experience higher stresses due to the smaller articulating surfaces (Kovler et al., 2004; Xu et al., 1998). From our findings, we expect that CMC joints of women with smaller bones would experience higher stresses than men since we expect the forces to be higher and the articular surface areas to be smaller by approximately 15% (Table 1). The effect of size might play an important role in the mechanical etiology of CMC joint pathology, such as osteoarthritis (OA). Recent studies have shown that the articular surface is no different between men and women after scaling for size (Conconi et al., 2014; Halilaj

et al., 2014b; Marzke et al., 2012). To the author's knowledge, this is the first report suggesting that the shape of the entire CMC joint bones between men and women are similar. The lack of sex difference in shape in the CMC joint suggests that the function of the CMC joint might also be similar between men and women, although further biomechanical analyses would be required to investigate this. A study of a larger cohort with higher imaging resolution would be beneficial to confirm these findings. The implications that men and women have similar shaped CMC joint bones that are simply scaled by size extends from implant design to the scaling of musculoskeletal models. It would seem appropriate to isotropically scale an implant or model of the CMC joint bones based on overall size, regardless of sex.

We hypothesized that age would be a significant predictor variable for CMC joint bone shape changes. However, since we were unable to find any correlation between age and any of the principal components through linear regression ($R^2 = 0.4$, and $R^2 = 0.43$), we must reject our hypothesis based on our methods. A scatter plot of the principal component weights indicated that the distribution was random, rather than dependent on age through a linear or non-linear relationship. Our findings suggest that age is a poor predictor of CMC joint morphology, which contrasts with the current literature, where the articular surfaces of the first metacarpal and trapezium bones have been shown to become flatter (lower curvature) and more conforming with age (Halilaj et al., 2014b; Xu et al., 1998). The discrepancies in the results may be due to poor sensitivity of our PCA based statistical shape model to subtle local shape differences. Since we investigated the entire morphology of the CMC joint bones, the ability of the model to capture small variations in articular shape may be compromised. However, the changes observed by Halilaj et al. (2014b) were localized and specific to sub-regions of the articular surface, and is possible to not have been captured in the primary principal components of our statistical shape model.

Although we found a statistically significant shape difference between men and women in our size normalized shape model ($p=0.01$), we believe this difference to be clinically insignificant in terms of biomechanics and pathology, since average point to point differences in the morphology of the CMC joint bones were small (within 1 voxel) and were only apparent at the extremes of the principal component (2–3 standard deviations from the mean) (Figure 4), indicating a small effect size. Also, at 2 standard deviations from the mean, we noted only a 2% difference in bone volume of the trapezium. Our statistical shape models represented the segmented data points well to ~0.4 mm RMS (Heimann and Meinzer, 2009). However, our models do not account for any errors arising from poor imaging resolution or segmentation resolution, which can be a significant source of error. Our higher order meshes should reduce these kinds of resolution-related error by smoothing across data points. Though smoothing may have removed potentially meaningful local detail, when considering the scale of detail which is meaningful, the purpose of our models, and our low RMS error, we believe our model remains valid for its purpose. The overlap of the standard deviation (Table 3) and the small effect size lead us to conclude that this finding though statistically significant is not clinically significant, and therefore further reinforces our previous finding that the morphology of the CMC joint bones does not vary in shape, but in size.

Our investigation of the entire morphology of the healthy CMC joint bones is not without its limitations. A high resolution data set would have provided more data points to allow for a more refined mesh such that the statistical shape model could capture more subtle differences in morphology. We assumed that the template mesh landmarks fit well to the anatomical landmarks. This was reasonable since we maximized mesh correspondence through iterative mesh fitting and no artifacts (such as changes in nodal position without changes in mesh geometry e.g. nodal “sliding”) were detected in the shape models. Our data consisted of only dominant hands from both left and right handed subjects. The left handed data sets were mirrored to generate consistent training set data. This was deemed as appropriate since we found no difference in morphology between the two groups. Therefore, our study is limited to the characterization of morphology CMC joint bones in dominant hands and does not characterize those in non-dominant hands. Furthermore, the statistical methods used (such as PCA and linear regression) were not able to discern local and non-linear variation. A local shape model or ICA may be used in the future to analyze local shape variations, while non-linear alternatives to PCA such as Linear Local Embedding could be used to analyze non-linear variation once a larger dataset becomes available.

We have characterized the morphology of the entire CMC joint bones across a cohort of 50 subjects and investigated the effects of sex and age on the morphology. Our findings confirm our first hypothesis, and suggest that the women have similarly shaped trapezium and first metacarpal bones compared to men, following scaling for overall size. Furthermore, our results reject our second hypothesis, indicating that age is a poor predictor of CMC joint morphology. The findings have important implications for the design of implants for the CMC joint, as well as scaling of musculoskeletal models to investigate function of the CMC joint.

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Figure 1.

Overview of the process for statistical shape model generation. A training set of CT images (A) were manually segmented to produce a triangulated mesh (B). Vertices of a representative triangulated mesh were extracted as a point clouds on which a parametric template mesh (C) was created. The template mesh was fitted to all point clouds in an iterative fitting process (D). The principal components of variation were determined (E).

Figure 2.

Variation and cumulative variation represented by principal component number for non size-normalized shape model (A) and size-normalized shape model (B).

Figure 3. Boxplots of mean metacarpal (A) and trapezium (B) bones showing a significant difference (one-way ANOVA $p < 0.001$) between men and women for first principal component.

Figure 4.

Overview of the shape variation exhibited in first principal component of the size-normalized metacarpal and trapezium bones showing the mean ($\bar{x}$) varied by 3 standard deviations (3σ) in the negative direction (men) and positive direction (women).

Mean articular surface areas of the CMC joint mean varied along the first principal component of the non size-normalized shape model by the weights of the training set.

Table 1

Metacarpal	n	Mean area (mm ²)	Trapezium	n	Mean area (mm ²)
Men	23	139.83 ± 13.92	Men	23	149.26 ± 14.54
Women	27	117.67 ± 13.05	Women	27	126.25 ± 13.50
Men vs. Women		<i>p</i> < 0.0001	Men vs. Women		<i>p</i> < 0.0001

Table 2

Mean bone volumes of the CMC joint bones stratified by sex.

Mean Bone Volume (mm ³)	n	Metacarpal	Trapezium	Total
Men	23	6101.0 ± 924.2	2458.8 ± 424.3	8559.8 ± 1286.4
Women	27	4569.7 ± 764.3	1755.3 ± 296.5	6325.0 ± 1010.6
Mean Difference		1531.3	703.5	2234.8

Table 3

Mean articular surface areas of the CMC joint mean varied along the first principal component of the size normalized model by the weights of the size normalized training set.

Metacarpal	n	Mean area (mm ²)	Trapezium	n	Mean area (mm ²)
Men	23	128.36 ± 3.02	Men	23	133.69 ± 0.96
Women	27	126.09 ± 1.75	Women	27	134.34 ± 0.59
Men vs. Women		$p < 0.005$	Men vs. Women		$p < 0.008$