



Older asymptomatic women exhibit patterns of thumb carpometacarpal joint space narrowing that precede changes associated with early osteoarthritis

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ABSTRACT

In small joints, where cartilage is difficult to image and quantify directly, three-dimensional joint space measures can be used to gain insight into potential joint pathomechanics. Since the female sex and older age are risk factors for carpometacarpal (CMC) joint osteoarthritis (OA), the purpose of this in vivo computed tomography (CT) study was to determine if there are any differences with sex, age, and early OA in the CMC joint space. The thumbs of 66 healthy subjects and 81 patients with early stage CMC OA were scanned in four range-of-motion, three functional-task, and one neutral positions. Subchondral bone-to-bone distances across the trapezial and metacarpal articular surfaces were computed for all the positions. The joint space area, defined as the articular surface that is less than 1.5 mm from the mating bone, was used to assess joint space. A larger joint space area typically corresponds to closer articular surfaces, and therefore a narrower joint space. *We found that the joint space areas are not significantly different between healthy young men and women. Trends indicated that patients with early stage OA have larger CMC joint space areas than healthy subjects of the same age group and that older healthy women have larger joint space areas than younger healthy women.* This study suggests that aging in women may lead to joint space narrowing patterns that precede early OA, which is a compelling new insight into the pathological processes that make CMC OA endemic to women.

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1. Introduction

Osteoarthritis (OA) is thought to emerge and progress under the influence of abnormal mechanical loading (Griffin and Guilak, 2005). While acute injury can give rise to posttraumatic arthritis as soon as six months post injury, due to abnormal impact that triggers necrotic, apoptotic, and inflammatory activity, or due to ligamentous destabilization that shifts the centers of pressure in the joint to areas of cartilage that are not prepared to bear load (Lotz, 2010), the role of joint biomechanics on the slower and natural progression of idiopathic OA in joints such as the thumb carpometacarpal (CMC) joint remains unknown. Although aging plays a role in reducing the proliferative activity of chondrocytes

(Loeser, 2009), OA is no longer considered simply a process of aging, but rather a multifactorial disease, likely linked to systemic—metabolic, genetic, hormonal—or local, i.e. mechanical, susceptibility. Advanced stage OA is characterized by both abnormal cartilage health and abnormal joint biomechanics, but in order to understand the sequence of events that lead to the simultaneous manifestation of these outcomes, the disease should be studied at the early stage and from both aspects—cartilage biology and joint mechanics.

Findings from studies of contact areas in cadaveric thumb CMC joints of varying arthritic stages are not in agreement (Ateshian et al., 1995; Eaton and Glickel, 1987; Eaton and Littler, 1969; Kuczyński, 1974; Napier, 1955; Pellegrini et al., 1993; Pieron, 1973), and a comparative analysis between the contact mechanics of healthy and arthritic-prone joints, which would provide insight into the potential etiology of CMC OA, is missing. Previous cadaver studies are limited by simulated positions and intervention with pressure-sensitive film within the joint space. More recently, joint space measurements from computed tomography images have emerged

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as a reliable and elegant alternative for studying articular-surface interactions in vivo (Anderst and Tashman, 2003; Marai et al., 2004). This method involves the computation of minimum bone-to-bone distance maps on the articular surfaces of bone models in different positions. The area on an articular surface that is within a specified distance from the mating articular surface is defined as the joint space area, such that an increase in joint space area is an indicator of joint space narrowing, because it signifies closer proximity between the mating articular surfaces. The center of pressure on the joint surface is estimated by computing the weighted center of the joint space area and is referenced as the joint space centroid.

The purpose of this study was to determine if the size of the CMC joint space area and the location of the CMC joint space centroid across different physiological positions differ with sex, age, and OA onset by using the aforementioned computational estimates. As part of a larger study that aims to track in vivo CMC joint biomechanics longitudinally, this investigation should provide baseline evidence against which future findings can be evaluated. We hypothesized that patients with early stage CMC OA would not have significantly larger joint space areas when compared to healthy controls, since at this stage there is usually little or no radiographic evidence of joint space narrowing (Eaton and Glickel, 1987). We also hypothesized that the joint space centroid would be located more volarly in arthritic patients than in healthy controls, potentially due greater dorsal subluxation, which is associated with CMC OA.

2. Materials and methods

2.1. Subjects

Following approval from our Institutional Review Board, completion of informed consents, and initial screenings for eligibility, 147 subjects—66 asymptomatic men and women of two age groups and 81 patients with early stage OA (Table 1)—were recruited as part of a broader study on CMC joint biomechanics (Halilaj et al., 2014a, 2014b, 2014c, 2014d, 2014e, 2013). Exclusion criteria for the study included pre-existing conditions that could have altered CMC joint morphology or kinematics, such as traumatic injury, hand or thumb surgery, inflammatory arthritis, systemic conditions, e.g. connective tissue disease, metabolic bone disease, other non-OA diseases of the thumb, or pregnancy. Posterior-anterior (PA), lateral, Robert's (Ladd, 2014; Robert, 1936), and bilateral stress X-ray views were taken for each subject and reviewed by a hand surgeon. Early stage OA subjects, who presented with localized pain at the base of the thumb and had one or more positive clinical signs of CMC OA (e.g., positive grind test), were screened and staged according to a modified Eaton staging system (Eaton and Glickel, 1987). The modified staging system classifies as stage 0 patients who have no radiographic evidence of any arthritis and as stage 1 those who have minimal evidence, including minimal or no joint space narrowing, minimal contour changes, no debris, as well as minimal or no subluxation. Only patients in stages 0 and 1 were included (Fig. 1).

2.2. Imaging protocol

The dominant hands of the asymptomatic subjects and the affected hands of the symptomatic subjects were imaged with a 16-slice clinical computed tomography (CT) scanner (GE LightSpeed 16, General Electric, Milwaukee, WI) at tube settings of 80 kVp and 80 mA, slice thickness of 0.625 mm, and in-plane resolution of at least $0.4 \text{ mm} \times 0.4 \text{ mm}$. The positions included a splinted neutral position, three functional positions—lateral key pinch, jar grasp, and jar twist—and four thumb range-of-motion positions: flexion, extension, abduction, adduction. For the neutral scan, wrist and thumb positions were standardized with a modified Rolyan® Original adjustable wrist and thumb spica-splint brace (Patterson Medical, Bolingbrook, Illinois). Custom-made mechanical fixtures were used to standardize wrist and thumb posture in the other positions (Fig. 2). Subjects were advised not to apply any load during the functional positions included in this study.

2.3. Joint space measurements

The outer cortical surfaces of the trapezium and first metacarpal were segmented from the neutral CT volumes with commercial software (Mimics v.13.1,

Table 1

Mean (\pm SD) ages of the participating subjects divided by group.

Group	Age (yrs.)
Young men ($n=16$)	24.7 ± 4.5
Young women ($n=16$)	24.9 ± 3.3
Older men ($n=16$)	53.8 ± 8.7
Older women ($n=18$)	56.0 ± 6.7
Early OA men ($n=34$)	60.6 ± 7.1
Early OA women ($n=47$)	53.3 ± 6.2

Materialise, Leuven, Belgium) and exported as meshed surfaces. Six-degree-of-freedom bone kinematics from the neutral position to each of the remaining seven positions were determined automatically with a markerless bone registration algorithm that utilizes the bone models from the neutral scan and tissue-classified image volumes from all the scans (Marai et al., 2006). The articular surface area (ASA) on each bone was manually selected by following the visible lining of cartilage on the subchondral surface. Bone-to-bone distance maps on the metacarpal and trapezium were computed by using a combined distance-field and meshed-surface representation of the bone models for each of the scanned positions (Marai et al., 2004) (Fig. 3). The areas on the trapezium and metacarpal within a threshold of 1.5 mm from the mating bone were computed and defined as the joint space area (JSA). The 1.5 mm threshold was chosen because it resulted in a JSA that in the neutral position was equal to or smaller than the ASA. Since the trapezium and metacarpal JSAs for a given joint position were not significantly different, only the trapezium JSA was considered for the analysis presented here. To address the effect of joint size, the JSA was expressed as a percentage of the ASA. The centroid of the JSA weighted linearly by the bone-to-bone distance, which is an approximation of the center of pressure in the joint, was computed and its location was expressed in terms of the dorsal-volar (DV) and radial-ulnar (UR) components of both the trapezium and metacarpal segment coordinate systems. These coordinate systems were centered at the saddle points of the articular surfaces and aligned with the principal directions of curvature, or the concavities and convexities, of the saddle-shaped articular surfaces (Halilaj et al., 2013). DV and UR were normalized by the square root of the articular surface area to account for bone-size differences.

2.4. Statistical analysis

A correlated error general linear model was used to determine the effects of sex, age, and OA on the JSA, as well as on the trapezium and metacarpal DV and UR components of the joint space centroid. The Holm test was used to determine statistical significance, which, after adjusting for multiplicity, was set at $p=.05$. Based on inspection of model residuals, a normal distribution was selected for all the variables. Results are presented as means with 95% confidence intervals in the figures and means with standard deviations in the text.

3. Results

Overall, trends indicated that JSA differences between age and health groups were not similar in men and women (Fig. 4). The JSAs of healthy young and older men were not different in any of the positions ($p > .645$) (Fig. 4a). The JSAs of arthritic men, however, were approximately 28% larger in the neutral position ($p=.008$), 33% larger in jar grasp ($p=.001$), and 31% larger in jar twist ($p=.046$) than the JSAs of healthy older men (Fig. 4a). Healthy older women had significantly larger JSAs than healthy young women only in extension ($p=.028$), but there were clear trends of higher JSAs when moving from younger to older to arthritic women, in every position (Fig. 4b). Despite the dissimilar effects of age group in the JSAs of men and women, there were no significant differences with sex in the JSAs of young healthy subjects in any of the positions ($p > .178$) (Fig. 4).

The metacarpal joint space centroid was located on the volar half of the metacarpal articular surface and its location was not affected by sex ($p > .171$) or age ($p > .139$), but in 4 of the 8 positions it was located more volarly—closer to the beak—in arthritic women than in healthy women (Fig. 5). Across all the subjects, the metacarpal joint space centroid was located $1.2 \pm 1.3 \text{ mm}$ volarly and $1.3 \pm 1.6 \text{ mm}$ ulnarly in key pinch, $1.5 \pm 1.2 \text{ mm}$ volarly and $2.5 \pm 1.0 \text{ mm}$ ulnarly

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