Determining Metacarpophalangeal Flexion Angle Tolerance for Reliable Volumetric Joint Space Measurements by High-resolution Peripheral Quantitative Computed Tomography

Stephanie Tom, Mark Frayne, Sarah L. Manske, Andrew J. Burghardt, Kathryn S. Stok, Steven K. Boyd, and Cheryl Barnabe

ABSTRACT. ***Objective.*** The position-dependence of a method to measure the joint space of metacarpophalangeal (MCP) joints using high-resolution peripheral quantitative computed tomography (HR-pQCT) was studied.

Methods. Cadaveric MCP were imaged at 7 flexion angles between 0 and 30 degrees. The variability in reproducibility for mean, minimum, and maximum joint space widths and volume measurements was calculated for increasing degrees of flexion.

Results. Root mean square coefficient of variance values were < 5% under 20 degrees of flexion for mean, maximum, and volumetric joint spaces. Values for minimum joint space width were optimized under 10 degrees of flexion.

Conclusion. MCP joint space measurements should be acquired at < 10 degrees of flexion in longitudinal studies. (J Rheumatol 2016;43:1941-4; doi:10.3899/jrheum.160649)

Key Indexing Terms:
HIGH-RESOLUTION PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY
JOINT SPACE NARROWING RHEUMATOID ARTHRITIS OSTEOARTHRITIS

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Impaired physical function is the principal adverse outcome of inflammation-related bone destruction in rheumatoid arthritis (RA) and joint degeneration in osteoarthritis (OA), with cartilage loss being common to both diseases and appearing as joint space narrowing by medical imaging. Semiquantitative scoring scales have been developed that assign a grade of severity to joint space narrowing in both RA[1,2] and OA[3,4,5] with plain radiography, and with magnetic resonance imaging (MRI) for RA[6]. Methods that are reliable, automated, and sensitive at detecting changes over time are desired in the longitudinal assessment of joint space. The ability to extract quantitative measurements and account for the 3-D nature of the joint would also contribute greatly to current methods used in imaging assessment.

Our groups have proposed methods to provide precise measurements of joint space using high-resolution peripheral quantitative computed tomography (HR-pQCT; Scanco Medical AG)[7,8]. HR-pQCT accurately and reproducibly generates images of bone microstructure at a nominal isotropic voxel dimension of 82 micrometers (μm). Further, 3-D imaging derived using HR-pQCT provides a more direct representation of joint morphology. Although reproducibility of measurements *in vivo* with repositioning at a single timepoint has been demonstrated, there is a knowledge gap pertaining to the variability of joint space measurements obtained at increasing degrees of flexion. In this study, the second and third metacarpophalangeal (MCP) joints of cadaver hands were scanned at 7 flexion angles between 0 and 30 degrees to elucidate the effect of degree of flexion on joint space measurement.

MATERIALS AND METHODS

Specimens. Six whole cadaveric hands were obtained through the University of Calgary human anatomy laboratory following approval from the Conjoint Health Research Ethics Board. No identifying information was obtained for the study. The specimens had initially been frozen but were thawed to room temperature for the study.

Positioning. A positioning platform was built to be placed in the standard HR-pQCT holder, which could be precisely set at varying degrees of flexion between 0 and 30 degrees (maximum possible flexion allowed by the holder) in 5-degree increments. All specimens were imaged at the same angle in sequence.

HR-pQCT imaging. A region of interest measuring 1.8 cm around the second and third MCP joints was imaged with HR-pQCT using standard acquisition measures (60 kVp, 1000 μA, 100 ms integration time, 1536 × 1536 reconstruction matrix). Reference landmarks were selected to ensure that there was no artifact across the joint space[9]. Scans were acquired for 7 positions for each of the MCP (0, 5, 10, 15, 20, 25, and 30 degrees flexion).

Volumetric joint space analysis. First, an approximate contour is manually drawn around the cortical bone surface of each joint, and the manufacturer's processing software (μCT Evaluation Program V6.0, Scanco Medical AG) uses an edge detection process to snap precise contours to the periosteal surfaces of both the proximal and distal bones. For quality control, each slice contour is verified. We then applied a custom automated image analysis process (Image Processing Language v5.48b, Scanco Medical) to determine the volumetric joint space width[8]. In summary, grayscale data obtained from HR-pQCT is binarized using the standard patient analysis method[10] to extract the bones from the surrounding soft tissue. The contours are used to create masks of the metacarpal and proximal phalange bones that are then dilated until they become connected, then eroded until the bone is returned back to the original size. For this study, a dilation and erosion of 40 voxels was found to be optimal. The original masks of the bones are subtracted from this image to yield a mask of the joint space (Figure 1). The joint space masks were visually verified. The 3-D joint space volume (mm^3) is calculated by voxel-counting all voxels in the joint space mask. The joint space morphology is calculated directly on the joint space mask using the distance transform, or "fitting maximal spheres"[11]. Specifically, the joint space at a given point was defined by the diameter of the largest sphere that could be fitted between the bony surfaces. The distribution of joint space thickness was characterized as the Euclidian mean, minimum, maximum (all in millimeters).

Statistical analysis. The root mean square coefficient of variance (RMSCV)[12] was used to determine the effects of joint position on mean, minimum, and maximum joint space widths and joint space volume measurements. We calculated the RMSCV for changes in position between the following degrees of flexion: (1) 5 degrees (i.e., 0–5, 5–10, 10–15, 15–20, 20–25, 25–30 degrees); (2) 10 degrees (i.e., 0–10, 5–15, 10–20, 15–25, 20–30); (3) 15 degrees (i.e., 0–15, 5–20, 10–25, 15–30); (4) 20 degrees (i.e., 0–20, 5–25, 10–30); (5) 25 degrees (i.e., 0–25, 5–30), and (6) 30 degrees (i.e., 0–30). Although there is no literature standard for an acceptable coefficient of variation, we predetermined that a value of about 5% would indicate reliability for these assessments.

RESULTS

Range of estimates. Mean values and SD for mean, maximum, and minimum joint space width, and joint space volume, are shown in Figure 2. There was no evidence for nonlinear relationship across increasing degrees of flexion.

Variability in joint space width and volume measurements (Table 1): With the exception of the 5–15 degrees of flexion position, RMSCV values for mean and maximum joint space and joint space volume were < 5% when repositioned under 20 degrees of flexion. RMSCV values for minimum joint space width were poor, but were optimized under 10 degrees of flexion.

DISCUSSION

Our study evaluated the effect of joint flexion on width and volume assessment of the joint space, necessary for informing image acquisition standards in arthritis studies where HR-pQCT is used for outcome determination. We have done this by calculating the variation in joint space width and volume measurements obtained when the degree of flexion at the MCP joints is varied. Acceptable reproducibility values for mean and maximum joint space as well as joint space volume were obtained up to 20 degrees of flexion. A position of < 10 degrees afforded the optimal value for minimum joint space width determination, which exhibited large variability at all degrees of flexion.

Our study has direct relevance to advancing image acquisition in arthritis conditions. In OA, joint space narrowing is the hallmark of disease, along with associated bony changes including sclerosis, cysts, and osteophytes. The key structural features associated with physical disability in patients with RA are joint space narrowing, which represents cartilage loss,

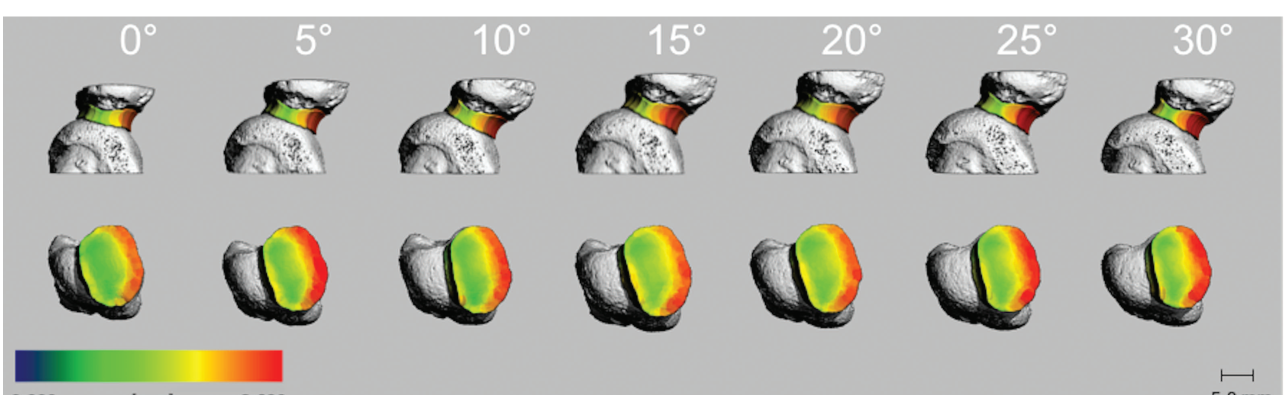

Figure 1. Masks of the joint space at increasing angles of flexion.

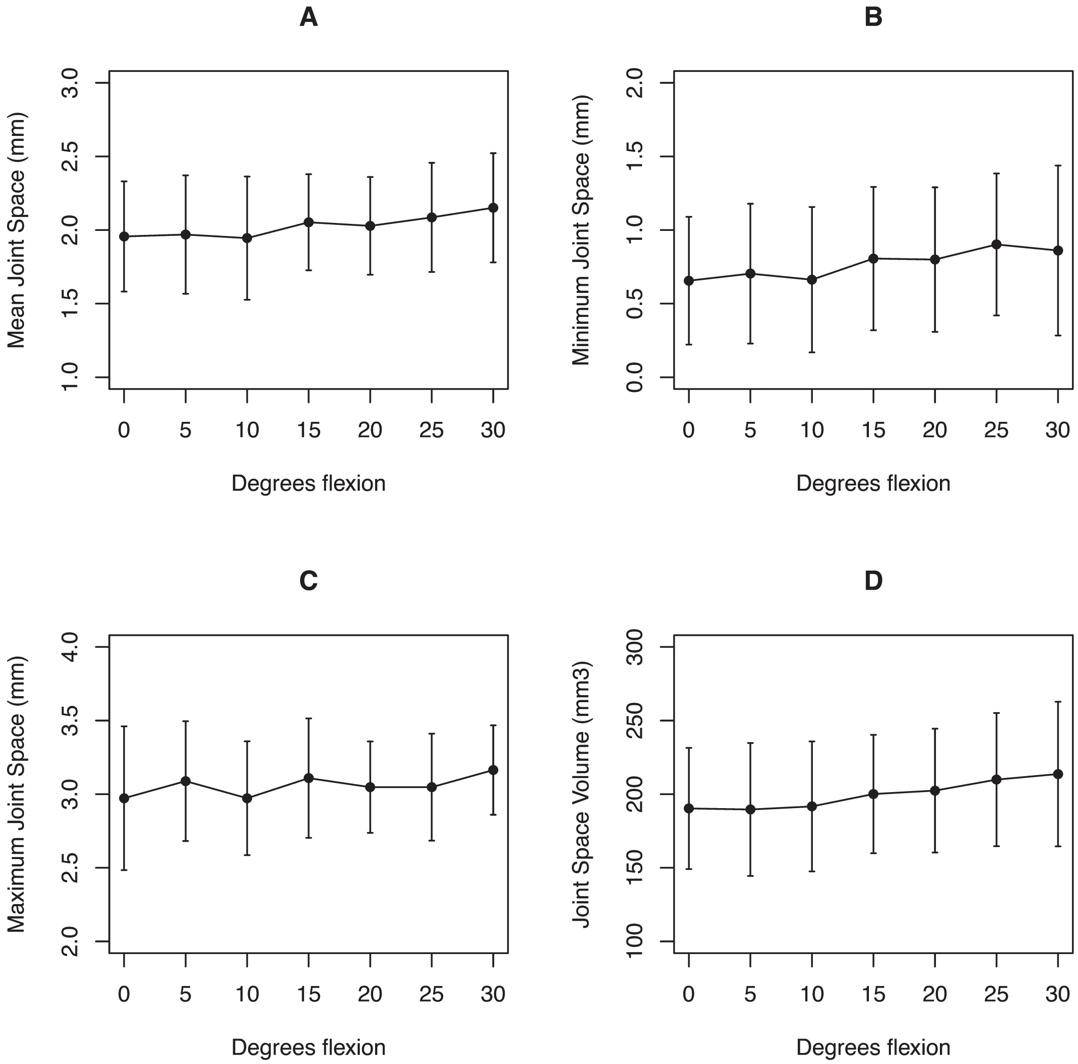

Figure 2. Mean values for mean, minimum, and maximum joint space width and volume at increasing degrees of flexion of the metacarpophalangeal joints.

and erosions, which distort joint anatomy. It has been hypothesized for RA that joint space narrowing may be a more significant factor affecting physical function than erosive changes[13], although with potential limitations that require further exploration[14]. In a recent study, joint space narrowing at the wrist was significantly related to grip strength as a measure of physical function[15]. However, the measurement of joint space has been a challenge to the bone imaging community. Plain radiography, widely used and available, is limited in sensitivity to sufficiently distinguish changes in joint damage over time[16] and is additionally limited by technical factors in measurement including the effect of joint positioning, 2-dimensional interpretation, and properties of ordinal scoring scales[17]. Only recently has MRI been reliably applied in the assessment of joint space[6]; the Outcome Measures in Rheumatology (OMERACT) consensus group has developed a scoring system to identify the smallest detectable change of joint space narrowing of the wrist in RA, which has demonstrated good intrareader and interreader reliability[6]. We and others have described the use of HR-pQCT to assess bony damage in inflammatory arthritis, as summarized in the review by Nagaraj, *et al*[18]. The advantage of HR-pQCT is in its ability to map the bone segments in a 3-D orientation, and allow for proper discrimination of bone and soft tissue. HR-pQCT additionally provides quantitative measurement of bone density and microarchitecture.

Our study's limitation was in the use of cadaveric specimens. Because the extensive repeat imaging would require significant radiation exposure for patients, we could not do an *in vivo* study. Ideally, additional studies evaluating the effect of different sources of variation in joint space measurements should be performed, for example, to assess for diurnal variation in joint space width, or the effect of antiinflammatory or disease-modifying therapy administration, on measurements obtained.

Table 1. Variation in measurements (root mean square coefficient of variance) by degrees of flexion of the metacarpophalangeal joints.

Degrees of Flexion	Angles	Mean, %	Minimum, %	Maximum, %	Volume, %
5	0–5	1.6	3.8	2.1	1.5
	5–10	2.3	4.4	2.3	1.0
	10–15	3.0	14.0	2.8	2.1
	15–20	1.9	8.5	2.2	1.6
	20–25	1.5	11.5	2.6	1.7
	25–30	1.3	12.7	1.9	1.3
10	0–10	3.8	8.0	4.4	2.2
	5–15	5.6	38.9	5.4	5.1
	10–20	4.0	18.6	4.0	3.4
	15–25	4.9	27.6	4.9	4.4
	20–30	4.1	29.4	4.0	4.0
15	0–15	4.4	19.5	4.9	3.2
	5–20	4.2	19.1	4.4	3.8
	10–25	4.4	29.3	4.7	4.2
	15–30	3.9	23.0	4.3	3.7
20	0–20	4.6	20.8	5.1	3.9
	5–25	4.8	30.9	4.8	4.6
	10–30	4.9	28.8	4.6	4.7
25	0–25	5.1	33.1	5.4	4.8
	5–30	5.2	30.2	4.7	5.3
30	0–30	5.6	32.3	5.4	5.4

Our study has applied a technique to quantify joint space width and volume to demonstrate it is a position-independent method based on testing cadaveric control specimens. We advise that HR-pQCT images be acquired with < 10 degrees of flexion at the MCP for optimal distance measurements, or that volumetric measures be applied that are robust to positioning angle.

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Correction

Determining Metacarpophalangeal Flexion Angle Tolerance for Reliable Volumetric Joint Space Measurements by High-resolution Peripheral Quantitative Computed Tomography

Tom S, Frayne M, Manske SL, Burghardt AJ, Stok KS, Boyd SK, Barnabe C. Determining metacarpophalangeal flexion angle tolerance for reliable volumetric joint space measurements by high-resolution peripheral quantitative computed tomography. J Rheumatol 2016;43:1941-4. The first statement in paragraph 2 of the Results section of the text has been revised as follows: "Variability in joint space width and volume measurements (Table 1): Root mean square coefficient of variation values for mean and maximum joint space and joint space volume were < 5% when repositioned under 20 degrees of flexion." An error in a denominator in the output spreadsheet altered some of the values given in Table 1, which should read as shown below. The findings overall are unaffected.

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Table 1. Variation in measurements (root mean square coefficient of variation) by degrees of flexion of the metacarpophalangeal joints.

	Angles	Mean, %	Minimum, %	Maximum, %	Volume, %
5-degree increments	0–5	1.9	4.7	2.6	1.8
	5–10	2.8	5.4	2.8	1.2
	10–15	3.7	17.2	3.4	2.6
	15–20	2.3	10.4	2.6	1.9
	20–25	1.8	14.1	3.2	2.0
	25–30	1.7	15.5	2.4	1.6
10-degree increments	0–10	3.8	8.0	4.4	2.2
	5–15	4.1	17.6	3.9	3.0
	10–20	4.0	18.6	4.0	3.4
	15–25	3.3	21.2	4.4	3.1
	20–30	2.7	18.6	3.3	3.0
15-degree increments	0–15	4.4	19.5	4.9	3.2
	5–20	4.2	19.1	4.4	3.8
	10–25	4.4	29.3	4.7	4.2
	15–30	3.9	23.0	4.3	3.7
20-degree increments	0–20	4.6	20.8	5.1	3.9
	5–25	4.8	30.9	4.8	4.6
	10–30	4.9	28.8	4.6	4.7
25-degree increments	0–25	5.1	33.1	5.4	4.8
	5–30	5.2	30.2	4.7	5.3
30-degree increments	0–30	5.6	32.3	5.4	5.4