

An Automatic Model-based System for Joint Space Measurements on Hand Radiographs: Initial Experience¹

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This ethics committee–approved pilot study was performed with informed consent. A Web-based service that was developed for automated measurement of joint space and automatic analysis of radiographs was tested prospectively. A total of 160 metacarpophalangeal joint spaces were measured in 20 patients (average age, 48 years; age range, 18–89 years; 16 women) suspected of having rheumatoid arthritis or osteoarthritis. The technical success rate was 93%. The smallest detectable difference in repeated automatic joint space width measurements varied from 0.08 to 0.31 mm, and the coefficient of variation was 2%–7%. Compared with the reference standard (interactive segmentation of the joint space widths) measurements, results were within a mean error of 0.19–0.40 mm. The proposed Web-based service enables reproducible joint space measurements to be obtained in metacarpophalangeal joints with moderate erosive and osteophytic disease.

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Radiography is the standard technique used to monitor the long-term progression of cartilaginous degradation and bone erosions in patients with rheumatoid arthritis. Long-term assessment of joint space narrowing is limited by inter- and intrareader variations and by the fact that the correct delineation of the joint space is not always possible owing to overlapping or destroyed joint borders (1,2). Published scoring systems are affected by substantial interreader variation and their use requires specialized training that is not readily available to many radiologists. This lack of training results in a shortage of qualified readers (3,4).

One way to address these issues was to introduce computer-based measurement methods. The first generation of computer-based methods used to measure the joint space of the knees, hips, and finger joints was based on direct manual annotations on digitized images. Techniques in the second generation of computer-based measurement methods were referred to as computer-assisted techniques because user input was combined with a limited degree of automation (5–11). To our knowledge, all of these methods included manual interaction with the joint as part of the

measurement procedure and were limited to the facility where images were acquired. To overcome these constraints, we developed a method that could be accessed from different geographic locations by multiple users via the Internet and that did not require manual interaction with the measured joints, such as manually identifying or marking joint contours. Thus, the purpose of our study was to prospectively test the Web-based service that we developed for automatic joint space measurement.

Materials and Methods

The software (RAQuantify, www.raquantify.org) used in this study was developed by one of the authors (G.L.) within the research project AAMIR number ~P17083-N04 (funded by the Austrian Funds for Scientific Research) and was provided free of charge. All other authors had full control over the inclusion of any data or information that might have presented a conflict of interest for this author.

Patients

The protocol for our pilot study was approved by the ethics committee of the Medical University of Vienna. According to this protocol, all included hand radiographs were acquired for routine clinical purposes, no radiation was administered for study purposes, and data safety and patient anonymity were guaranteed. In accordance with the quality management system at the Medical University of Vienna, informed consent was obtained from all patients. Before patients gave their consent, they were informed of the nature and potential risks of the protocol and of their right to refuse to participate. Images were acquired from January to July 2005. Pa-

tient inclusion, training of the active shape model (ASM) algorithm, and automatic joint space measurement were performed after images were acquired.

Patients referred from the rheumatologic outpatient clinic were included if they had rheumatoid arthritis according to the 1987 criteria for the classification of rheumatoid arthritis (12) or osteoarthritis according to the 1990 classification criteria for osteoarthritis of the hand (13) and if they underwent standard dorsopalmar radiography (high-spatial-resolution film, 40 kV, 8 mAs, 104-cm focus-film distance, 90° elevated shoulder, 90° flexed elbow, x-ray beam centered on the third metacarpal head) of both hands.

Patients were excluded if they had advanced erosive disease of the metacarpophalangeal (MCP) joints, defined as a modified Sharp erosion score of three or higher (4), or advanced osteoarthritis of the MCP joints, defined as a Kellgren-Lawrence score higher than three (14). Patients were also excluded if they had a subluxation or had undergone surgery of the MCP joints or if image quality was inappropriate owing to a nonstandardized projection technique or truncated finger tips.

Twenty consecutive patients (average age, 48 years; age range, 18–89 years; 16 women) who met these criteria were included. One author (F.K., 20 years of experience in musculoskeletal imaging) selected patients and classified radiographs before he was informed of

Advances in Knowledge

- The proposed Web-based service allows reproducible (2%–7% coefficient of variation) joint space width measurements, with a technical success rate of 93%, in metacarpophalangeal joints with moderate erosive and osteophytic disease.
- Joint space width measurements are performed in an observer-independent manner, as no manual measurements on the images are needed; hence, this method can be used by nonmedical staff.
- The mean absolute error of automatic measurement results compared with the standard of reference was significantly ($P = .006$) increased in joints with overlapping contours and signs of joint disease.

Implication for Patient Care

- Fully automated computer-based joint space measurements may help demonstrate the benefit of new treatments in therapeutic trials and thus facilitate the earlier approval of new treatments.

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Abbreviations:

ASM = active shape model
MCP = metacarpophalangeal

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Guarantor of integrity of entire study, P.P.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; manuscript final version approval, all authors; literature research, G.L.; clinical studies, P.P., J.S., M.R., F.K.; statistical analysis, M.W.; and manuscript editing, M.W., H.I., H.B., F.K.

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the study protocol. The original images were cropped such that the displayed final image was restricted to the joint being investigated to avoid confounding of classification. Thus, we performed joint-per-joint classification. No patient information was displayed in these details. The MCP joints were classified according to the damage attributable to rheumatoid arthritis or osteoarthritis, as described according to the modified Sharp and Kellgren-Lawrence scores (4,14). Thus, 29 (18%) of the 160 MCP joints had definite osteophytes (Kellgren-Lawrence score of 2 or 3) and 26 (16%) had erosive disease (modified Sharp erosion score of 1 or 2) (4,14). Fifty-three (33%) of the 160 joints showed changes within the previously defined ranges. Radiographs were then digitized by using a laser tabletop scanner (Lumiscan 75; Lumisys, Sunnyvale, Calif) with a 12-bit gray-scale resolution and a 300-dpi spatial resolution (0.085-mm pixel size) (15). The joint space of the thumb was excluded because it was not required to obtain a modified Sharp score and because it was a hinge joint where a clear-cut definition of the joint space was harder to obtain.

Definition of Joint Space Margins

The joint space is confined by the cortex of the metacarpal bones and a surrogate joint border at the base of the proximal phalanx where the cortex is not directly visible. We determined the concave highest gray-level gradient at the base of the proximal phalanx to be a reproducible substitute for the true distal joint margin (Fig 1). This surrogate was chosen because of its reproducibility and clearness, although it may be affected by the changes associated with subchondral sclerosis. To our knowledge, no data about intraindividual changes in the thickness of the subchondral cortical plate at the base of the proximal phalanx are available in the literature. According to published reports, there are no variations in the thickness of the subchondral cortical plate in knees within a time frame of 18–24 months; therefore, an artificial widening of the MCP joint space is unlikely to be found

at annual follow-up (16). The measurements were confined to the central part of the joint, which was defined by excluding its peripheral (ie, radial and ulnar) convex parts. The software automatically accomplished this task. The proximal phalanx joint region served as a reference contour, from which the minimum distance to the metacarpal bone from at least 82 points (mean, 102 points; maximum, 145 points) on a dense interpolation was used to obtain the final measurements (Fig 2).

Training of Algorithms and Definition of Reference Standard

During training, bone shapes were segmented with a computer application that enabled semiautomatic segmentation of bones with an algorithm (livewire algorithm) on the 40 included dorsoplantar radiographs (17). This method enables interactive segmentation of the metacarpal bones and proximal phalanges. Segmentation was conducted by a 4th-year radiology resident (P.P., 9 months of musculoskeletal subspecialty training) who was trained to handle the software before the study was initiated by evaluating a training set of 10 additional patients with a total of 40 MCP joints that were not included in the final data analysis. The resulting numeric data were then used to train the shape-aware local linear mappings and ASMs, both of which will be described in detail. Joint space width measured by using this interactive delineation with the livewire algorithm served as the reference standard, as histopathologic proof was not available (Fig 3).

User Interface for Joint Space Width Measurement

After images in Digital Imaging and Communications in Medicine, or DICOM, format were loaded into a structured database and the hand was framed with two mouse clicks (ie, initialization) to clip the borders of the radiographs, the joint space widths were quantified autonomously with the algorithm, and measurement results were provided in a printable report. The software did not require definition of the lateral extent or center of the joints, nor did joints have

to be cropped, rotated, or centered for the measurement procedure. Thus, the user interface tested in our study could be used by a research assistant without

Figure 1

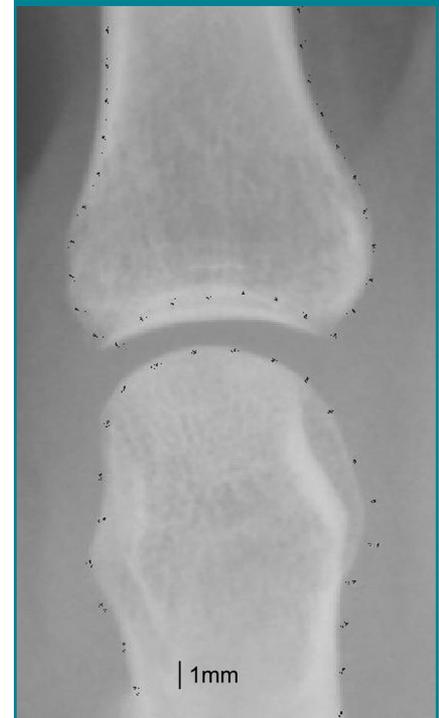


Figure 1: Automatically detected landmarks (●) on the bone contour of a dorsopalmar hand radiograph in the left fourth MCP joint region. Results from 10 repeated runs. The MCP joint is formed by the reception of the rounded heads of the metacarpal bones into shallow cavities on the proximal ends of the first phalanges. For this reason, the distal margin of the joint space is always obscured by overlying bone structures, and radiologic anatomy is variable. The distal joint margin could be defined as one line of peak radiographic density or, as in the actual example, as several ridges of increased density at the base of the proximal phalanx (2,7). In this MCP joint, the cortex is not continuously visible. We suggest that the highest gray-level gradient in the base of the proximal phalanx should be used as the unequivocal and reproducible substitute for the true distal joint margin. The proximal joint margin can be easily delineated as a line of maximum slope in radiographic density in most joints. The visible inaccuracies at the central part of the joint where measurements are obtained are within a range of 0.1 mm. The slightly inaccurate contour detection on the adjoining shaft does not interfere with the measurement results. The spatial resolution of images was 300 dpi with a pixel size of 0.085 mm.

the need for detailed instructions. RAQuantify software supports batchwise measurements, and many radiographs can be uploaded prior to measurement.

Image Analysis Concept of RAQuantify Software

The joint space width measurement algorithm was used to assess each joint in four steps (Fig 4). First, the joint was located by using shape-aware local linear mappings. These are neural networks that exploit the dependencies be-

tween local image content (eg, gray scale) and anatomic landmark positions. Second, on the basis of the results of shape-aware local linear mappings, bone contours, defined by the highest gray-level gradient of the metacarpals and proximal phalanges, are segmented autonomously with ASMs. ASMs feature a statistical model of the shape and signal intensity values for each bone. This model is derived from numeric data extracted by segmentations performed by a radiologist on a training set of radiographs. ASMs enable automatic

segmentation of bones with application of this statistical model and enable the algorithm to constrain the search to plausible shapes of anatomic structures. The MCP joints are defined by using 20 landmarks arranged with the method based on the minimum description length principle; this method allows the automatic definition of a region of interest, independent of individual anatomic variability (18). Third, image analysis is completed with an ASM-driven snake algorithm that fits the bone contour in the joint region while gradually decreasing the influence of the model constraint. Fourth, printable reports of the measurement results are generated.

Statistical Analysis

All statistical analyses were performed with a personal computer by using a

Figure 2

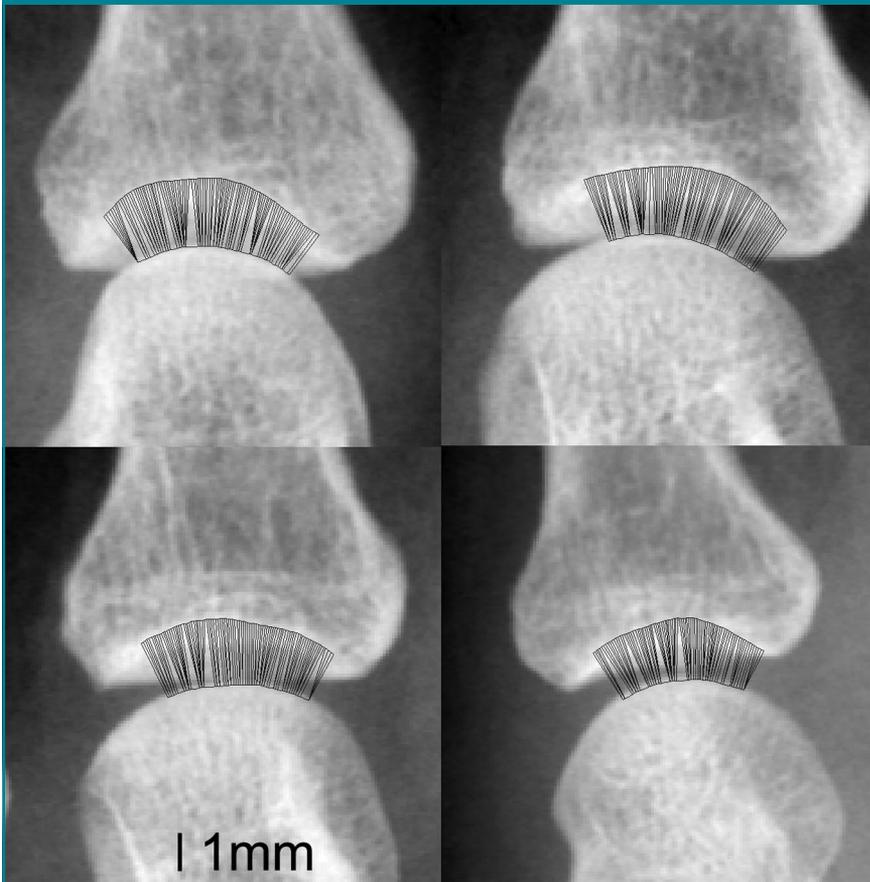


Figure 2: Measurement regions for the second through fifth MCP joints on a left dorsopalmar hand radiograph. The reference region on the proximal phalanx is defined by ASM landmarks, while the corresponding measurement points on the metacarpal bones are chosen to be the closest points on the metacarpal bone contour for each proximal phalanx reference contour point. The exact number of measurement points depends on the size of the joint. The minor inaccuracies on the metacarpal heads on the two bottom images are examples of the dimension of measurement errors caused by the RAQuantify algorithm. The contour detection of the algorithm does not always coincide with a clearly depictable line because it defines the joint space border as the highest gray-level gradient in a circumscribed area. The spatial resolution of images was 300 dpi with a pixel size of 0.085 mm.

Figure 3



Figure 3: Example of output images after 10 repeated measurements on a left dorsopalmar hand radiograph by RAQuantify software (dark gray lines) compared with the interactively delineated contour (pale gray line). This joint has erosive changes (two discrete erosions on the ulnar MCP head) and overlapping joint contours. As joint space contour identification is guided by using the highest gray-level gradient, it can differ from the contour visible with the naked eye. The spatial resolution of images was 300 dpi with a pixel size of 0.085 mm.

commercially available software package (SPSS Windows, version 11.5.1; SPSS, Chicago, Ill). Metrical data were expressed as mean, minimum, and maximum values. For statistical tests, $P \leq .05$ was considered to indicate a significant difference. All measurement experiments were performed with a leave-one-out procedure: 39 images (training set) were used to train the ASMs and local linear mappings, and the remaining image (test image) that was not included in the training procedure was used to test the algorithm against the reference standard. Joints were grouped into the following three subgroups on the basis of their radiographic appearance: (a) normal joints, (b) normal joints with overlapping contours, and (c) diseased joints, as classified with the modified Sharp score and the Kellgren-Lawrence score (see "Patients" section) (4,14).

To exclude potential correlations between the joints in the hand, scoring and training of the algorithm was performed on a joint-per-joint basis. For this purpose, the original images were cropped such that the displayed final image was restricted to the joint being investigated to avoid confounding of results. Despite the fact that the algorithm analyzes the image as a whole, it measures each joint independently (ie, in a joint-per-joint fashion).

We evaluated the joint space width measurement algorithm in the following manner. First, we calculated the technical success rate, which was expressed as the percentage of joints successfully measured in all of the 10-fold repeated measurements of the same 160 joints (resulting in 1600 measurements) with different regions of interest (ie, different operator input). Thus, success was defined as the absence of apparent malfunction (ie, out-of-range joint space width) of the algorithm in all of 10 independent runs per joint. The reasons for algorithm malfunction were recorded.

Second, one of the authors (M.R.) documented the time (in seconds) required to perform the entire procedure (including patient administration, file management, measurement initialization, review, and storage of results)

Figure 4

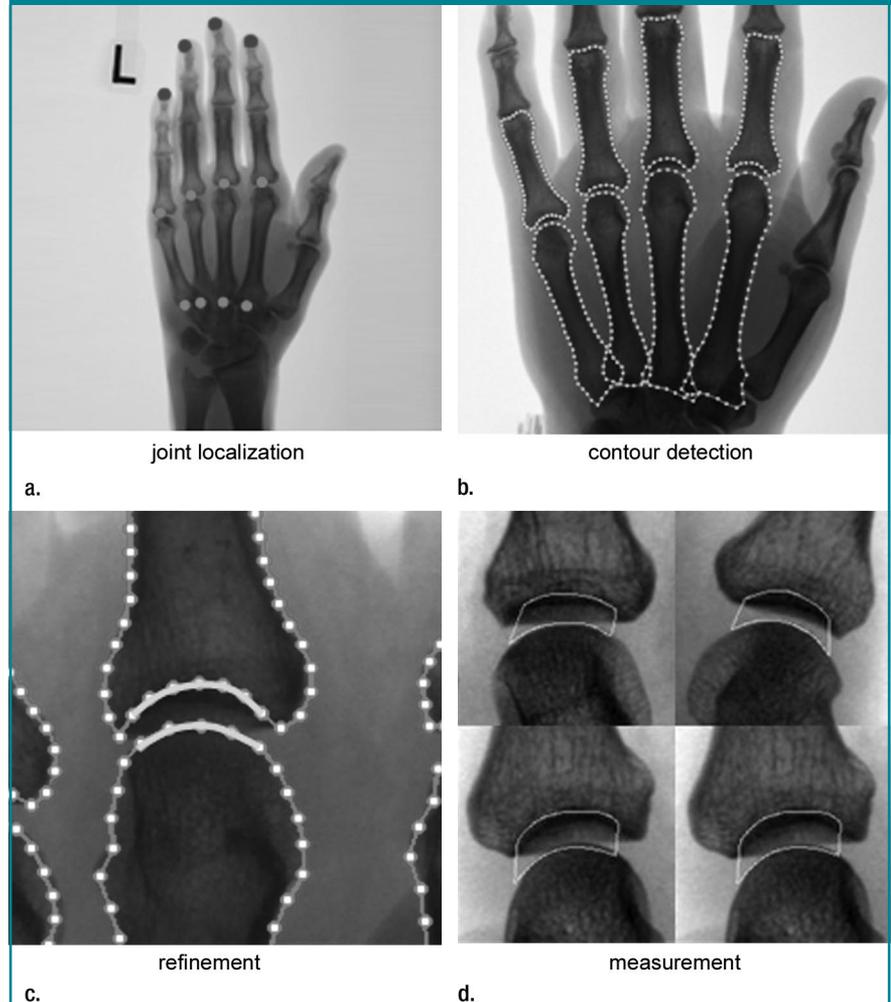


Figure 4: Image analysis concept of RAQuantify software. (a) First, joints are located with shape-aware local linear mappings. The positions of 12 reference joints (circles) are visible. (b) Then, bone contours are segmented with ASMs. The ASM landmarks (circles) define the bone contour. For better visibility, they are connected by lines. (c) Image analysis is completed with an ASM-driven snake algorithm to perform fine adjustment of the bone contour. (d) The measurement results are displayed for review. Lines indicate the detected contours within the measurement region.

with an electronic stopwatch. Third, computation time (in seconds) was measured by calculating the time differences between the batchwise procedures performed, as given in the data files. Fourth, agreement of the automatic measurement results with the reference standard was expressed as the mean absolute error of automatic joint space width (in millimeters).

Fifth, we calculated the reproducibility of the results in a stepwise fashion after 10-fold repeated measure-

ment with altered initialization was performed on each of the 160 joints. The automatic contour detection in the joint region was evaluated by calculating the absolute standard deviation of results from the mean position over 10 contour-detection procedures. The smallest detectable difference of 10 repeated automatic joint space width measurements was assessed. The smallest detectable difference is the smallest difference between two measurements that does not stem from measurement error

but instead stems from a real change with significant probability (4,19). The coefficient of variation for 10 repeated measurements was calculated with the standard deviation of the repeated measurement sessions.

Sixth, dependency between the absolute measurement errors, compared with the reference standard and after repeated measurements, and the three subgroups was calculated with analysis of variance with repeated measures given the repetitive and dependent character of the measurements. Seventh, the mean, minimum, and maximum joint space widths for all MCP joints were calculated.

Results

Technical Success and Time

No system crashes or data loss occurred. The technical success rate was 93% (149 of 160 joint spaces) because an apparent malfunction of the algorithm occurred for 11 joints in at least

one of the 10 repeated measurements. These joints were excluded from analysis. Reasons for algorithm malfunction were low contrast at the carpo-metacarpal junction, a narrow region of interest, and anatomic variability not contained within the training data.

The mean time needed to perform the whole measurement procedure was 398 seconds (minimum, 216 seconds; maximum, 660 seconds). Mean computation time alone was 70 seconds (minimum, 66 seconds; maximum, 75 seconds).

Statistical Analysis

The mean absolute error of the automatic measurement results compared with the reference standard was 0.19–0.40 mm (Table 1). The standard deviation of the automatic measurements for 10 repeated measurements ranged from 0.04 to 0.13 mm (Table 1, Fig 3). The smallest detectable difference of 10 repeated automatic joint space width measurements ranged from 0.08 to 0.31 mm (Table 2).

The coefficient of variation for 10

repeated measurements was 2%–7% (Table 3). The mean absolute error of automatic measurement results compared with the reference standard significantly increased in joints with overlapping contours and signs of joint disease ($P = .006$), as demonstrated at analysis of variance with repeated measures.

The absolute standard deviation of the automatic measurements for 10 repeated measurements significantly increased in joints with overlapping joint contours ($P = .017$) but was not altered by the existence of osteophytes or erosions ($P = .41$), as demonstrated at analysis of variance with repeated measures. The mean, minimum, and maximum MCP joint space width values from 40 radiographs are shown in Table 4.

Discussion

RAQuantify, the Web-based software tested in our study, provides an observer-

Table 1

Mean Absolute Error and Standard Deviation for MCP Joints

MCP Joint	Mean Absolute Error of Automatic Joint Space Width Measurement (mm)		Standard Deviation for 10 Repeated Measures (mm)	
	Overlap	Nonoverlap	Overlap	Nonoverlap
Second	0.29	0.25	0.13	0.08
Third	0.40	0.33	0.13	0.05
Fourth	0.30	0.28	0.07	0.04
Fifth	0.22	0.19	0.09	0.04

Note.—Spatial resolution of images was 300 dpi with a pixel size of 0.085 mm.

Table 2

Smallest Detectable Difference of Mean Joint Space Width

MCP Joint	Diseased (mm)	Healthy (mm)	Overlap (mm)	Nonoverlap (mm)
Second	0.31	0.18	0.24	0.16
Third	0.18	0.20	0.25	0.09
Fourth	0.16	0.17	0.13	0.08
Fifth	0.22	0.17	0.18	0.08

Note.—Spatial resolution of images was 300 dpi with a pixel size of 0.085 mm.

Table 3

Coefficient of Variation of Mean Joint Space Width

MCP Joint	Overlap (%)	Nonoverlap (%)
Second	7	4
Third	6	3
Fourth	4	3
Fifth	5	2

Table 4

Results of Automated Joint Space Width Measurements

MCP Joint	Mean JSW (mm)	Minimum JSW (mm)	Maximum JSW (mm)
Second	1.88	1.55	2.11
Third	1.76	1.45	1.94
Fourth	1.64	1.35	1.80
Fifth	1.74	1.31	1.95

Note.—As spatial resolution of images was 300 dpi, a joint space width (JSW) of 1.7 mm approximates 20 pixels. Measurements were performed without device calibration.

independent joint space width measurement method that, because the software is embedded in a Web service, allows shared use by several users in different geographic locations.

Model-based image analysis applies information about the visual appearance of the anatomic structure of interest. A radiologist extracts the data necessary for algorithm training from radiographs. In our study, the shapes of metacarpal bones and proximal phalanges on 40 radiographs were segmented interactively. The resulting ASM incorporates shape and texture information and is used to detect the bone contour (ie, the highest gray-level gradient) on newly obtained radiographs. In addition, the landmark-based character of ASMs enables consistent identification of certain anatomic landmarks on various bone contours, which is important for the definition of circumscribed regions. This is in contrast to other contour-based segmentation algorithms that do not enable identification of anatomic landmarks (6,8,20–22). The findings of recent studies have shown that a certain amount of user interaction with the images was required to perform computer-assisted MCP joint space width measurements (23). Our technical success rate of 93% can be partly attributed to the limited number of training cases. Thus, ongoing research must be focused on efficient training procedures. For the short term, operator-dependent steps (eg, manual identification of joint surfaces) can improve the overall success rate but should be implemented only if the observer independency of the measurements is not sacrificed.

The time required to perform an examination was not mentioned in previous reports (6,8,21,22). In our study, the mean time required for the entire measurement procedure was 398 seconds, whereas computation time alone was, on average, 70 seconds. Thus, the time required to perform an examination was, in large part, a consequence of manual patient data input. For this reason, measurements can be initiated batchwise and performed independently afterward (eg, overnight).

Despite different pathomechanisms, rheumatoid arthritis and osteoarthritis

both lead to joint space narrowing. Angwin et al (6) described a joint space measurement method used to assess rheumatoid arthritis of the finger joints; this method was highly reproducible (smallest detectable difference, 0.09–0.106 mm), and results were consistent with those achieved with the traditional scoring technique. Remarkably, the measurement method increased the study power compared with the traditional joint space narrowing scoring method (6). In another interactive approach, in which points had to be placed manually in the MCP joint, a considerably high reproducibility rating was achieved (smallest detectable difference, 0.07–0.31 mm) (8,24). The smallest detectable difference achievable with RAQuantify software and use of a training set of 39 radiographs was 0.08–0.31 mm.

The coefficients of variation of 2%–7% that are obtainable with RAQuantify software without specific user interaction (ie, fully automatic) are comparable to published coefficients of variation of 3.8%–8.3% for semiautomatic measurements (7,24–26). Notably, our results were achieved with no manual annotation on the measured joints.

The higher deviation from the reference standard (0.19–0.4 mm) compared with the reproducibility of measurement results after repeated measurements (0.04–0.13 mm) reflects the limitations of a small training set. There was a significant increase in the deviation from the reference standard in joints with overlapping contours and signs of joint disease ($P = .006$). Joint disease did not interact with the absolute standard deviation of the repeated automatic measurements ($P = .41$), which increased significantly in joints with overlapping joint contours ($P = .017$). As the visible joint space is a surrogate measure, reproducibility remains the major goal of computerized joint space measurement. Considering the 300-dpi spatial resolution and 0.085-mm pixel size, a 0.35-mm error approximates 4 pixels of a 1.7-mm joint space width containing approximately 20 pixels. This emphasizes the performance of our method and the need for a spatial resolution of at least 300 dpi for computerized quantitative analysis of radiographs.

To our knowledge, this is the first published report of a joint space width measurement method that can be accessed by multiple users in different geographic locations via the Internet and that does not require manual interaction with the measured joints or costly investments in hardware.

There were several limitations to our study. First, the joint space measurement results were not correlated with the clinical history and the time series were not measured. It was not a goal of our study to evaluate the clinical relevance or discriminative power of radiographic joint space measurements. These issues, as well as the influence of positioning on measurement results, have been and will continue to be investigated in other studies (1,4,27,28). A second limitation is the lack of histologic verification. Joint space segmentation with an interactive segmentation method, namely the livewire method, was used as a reference standard, allowing detailed and reproducible definition of anatomic structures (17).

The third limitation of our study was that upload times were not recorded. However, we believe that upload time was strongly dependent on technical factors, primarily the type of Internet connection. This cannot be simulated; therefore, we did not address this issue. The values (in millimeters) cannot be taken as absolute values, as they are based on imager spatial resolution information. We performed experiments without device calibration, and we did not compensate for distortion owing to beam geometry because the main issue was the reproducibility of measurements.

A fourth limitation was that the number of images in the training set was small ($n = 39$) and thus limited the amount of anatomic adaptability of the model. Model adaptability can be improved by a larger training set size. The training set size will be enlarged if ongoing studies suggest an increase of algorithm performance. However, the small size of the training set in our study demonstrates the expandability of the method to other joints.

Severe cases of deformation pose

special demands for computer-assisted model-based measurements, as their appearance differs substantially from that of the training set. An interactive user interface is projected to allow the expert to edit measurements in mutilated joints with the livewire method. Subsequently, more diseased joints will be gradually included to assess the adaptability of the ASMs on severely diseased joints.

Current work is focused on the automatic quantification of erosive changes to complete the quantitative assessment of joint destruction in patients with rheumatoid arthritis.

In conclusion, the results of our pilot study show that joint space width can be measured efficiently with a Web-based technique, with a technical success rate of 93%. The measurement results obtained in normal and moderately diseased MCP joints are reproducible and consistent with the reference standard. Fully automated measurement systems could become a part of multiobserver clinical imaging studies, notably when both the agreement and the reproducibility of results are important.

Measurement of more severely diseased joints and quantitative assessment of erosive changes pose future challenges for advanced medical imaging research on model-based image analysis in patients with rheumatoid arthritis.

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