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MR. ALEXANDER MATHIESSEN (Orcid ID : 0000-0002-9696-2081)
PROF. HILDE BERNER HAMMER (Orcid ID : 0000-0001-7317-8991)
DR. LENE TERSLEV (Orcid ID : 0000-0001-8193-9471)
DR. MARIA-ANTONIETTA D'AGOSTINO (Orcid ID : 0000-0002-5347-0060)
DR. IDA KRISTIN K. HAUGEN (Orcid ID : 0000-0001-7810-2216)
DR. GEORGE AW BRUYN (Orcid ID : 0000-0001-7020-5798)
DR. MARGREET KLOPPENBURG (Orcid ID : 0000-0002-9294-2307)
DR. PETER MANDL (Orcid ID : 0000-0003-1526-4052)
MRS. KAREN ELLEGAARD (Orcid ID : 0000-0002-5009-3597)

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Title: Ultrasonography of Inflammatory and Structural Lesions in Hand Osteoarthritis: An OMERACT Agreement and Reliability Study

Running title: Ultrasonography of inflammatory and structural lesions in hand OA

Authors: Alexander Mathiessen (MD, PhD)[1,2], Hilde B. Hammer (MD, PhD)[1,2], Lene Terslev (MD, PhD)[3], Marion C. Kortekaas (MD, PhD)[4], Maria A. D'Agostino (MD, PhD)[5], Ida K. Haugen (MD, PhD)[1], George A. Bruyn (MD, PhD)[6], Georgios Filippou (MD, PhD)[7], Emilio Filippucci (MD, PhD)[8], Margreet Kloppenburg (MD, PhD)[4,9], Luana Mancarella (MD)[10], Peter Mandl (MD, PhD)[11], Ingrid Möller (MD, PhD)[12], Mohamed A. Mortada (MD, PhD)[13], Esperanza Naredo (MD, PhD)[14], Andrea Delle Sedie (MD, PhD)[15], Joseph Sexton (PhD)[1], Ruth Wittoek (MD, PhD)[16], Annamaria Iagnocco (MD, PhD)[17], and Karen Ellegaard (MSc, PhD)[18]

on behalf of the OMERACT Ultrasound working Group

[1] Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway.

[2] Institute of Clinical Medicine, University of Oslo, Oslo, Norway.

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[3] Center for Rheumatology and Spine Disease, Rigshospitalet, Copenhagen, Denmark.
[4] Department of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands.
[5] Department of Rheumatology, APHP, Hôpital Ambroise Paré, Boulogne-Billancourt, France.
[6] Department of Rheumatology, MC Groep Hospitals, Lelystad, Netherlands.
[7] Department of Rheumatology, Luigi Sacco University Hospital, Milan, Italy
[8] Rheumatology Clinic, Università Politecnica delle Marche, Jesi (Ancona), Italy.
[9] Department of Clinical Epidemiology, Leiden University Medical Center, Leiden, The Netherlands.
[10] Medicine & Rheumatology Unit, IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy
[11] Division of Rheumatology, Medical University of Vienna, Vienna, Austria.
[12] Instituto Poal, University of Barcelona, Barcelona, Spain.
[13] Rheumatology and Rehabilitation Department, Zagazig University, Zagazig, Egypt.
[14] Department of Rheumatology, Joint and Bone Research Unit, Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain.
[15] Rheumatology Unit, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy.
[16] Department of Rheumatology, Ghent University Hospital, Ghent University, Ghent, Belgium.
[17] Academic Rheumatology Centre - Dipartimento Scienze Cliniche e Biologiche, Università degli Studi di Torino, Turin, Italy.
[18] The Parker Institute, Copenhagen University Hospital Bispebjerg-Frederiksberg, Frederiksberg, Denmark

Corresponding author:

Alexander Mathiessen, alexander_mathiessen@hotmail.com, phone +47-97501889, fax +47-22451778.

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Abstract

Objective: To standardize and assess the reliability of ultrasonographic assessment of inflammatory and structural lesions in patients with hand osteoarthritis (OA).

Methods: The Outcome Measures in Rheumatology (OMERACT) Ultrasound Working Group selected synovial hypertrophy (SH), joint effusion (JE), and power Doppler (PD) signals as the main inflammatory lesions in hand OA, and suggested osteophytes in the scapho-trapezio-trapezoid (STT) and cartilage defects in the proximal interphalangeal (PIP) joints as novel additions to previous structural scoring systems. A complementary imaging atlas provided detailed examples of the scores. A reliability exercise of static images was performed for the inflammatory features, followed by a patient-based exercise with six sonographers testing inflammatory and structural features in twelve hand OA patients. We used Cohen's kappa (κ) for intra-reader and Light's κ for inter-reader reliability for all features except PD, in which Prevalence-Adjusted Bias-Adjusted Kappa (PABAK) was applied. Percentage agreement was also assessed.

Results: The web-based reliability exercise demonstrated substantial intra- and inter-reader reliability for all inflammatory features (κ>0.64). In the patient-based exercise, intra- and inter-reader reliability varied: SH κ=0.73 and 0.45; JE κ=0.70 and 0.55; PD PABAK=0.90 and 0.88; PIP cartilage κ=0.56 and 0.45; STT osteophytes κ=0.62 and 0.36. Percentage close agreement was high for all features (>85%).

Conclusion: With ultrasound, substantial to excellent intra-reader reliability was found for inflammatory features of hand OA. Inter-reader reliability was moderate, but overall high close agreement between readers suggest that better reliability is achievable after further training. Assessment of osteophytes in the STT joint and cartilage in the PIP joints achieved less good reliability and the latter is not endorsed.

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Significance and Innovations

- Based on previous work and definitions on ultrasonographic lesions in hand OA, we present data from a real-life reliability exercise on synovial hypertrophy, effusion, and power Doppler signals, a new scoring system for cartilage and exploration of osteophyte assessment of the thumb base joint.
- In this exercise, reliability for inflammation was shown to be moderate to excellent, for both intra- and inter-reader reliability, whereas for US structural damage scoring systems intra- and inter-reader reliability was fair to moderate.
- The complementary ultrasonographic imaging atlas is expected to enhance unified interpretations of the grading scales between sonographers, departments and countries.

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Introduction

Hand osteoarthritis (OA) is a common musculoskeletal disorder causing considerable pain and disability, with still largely unknown etiology (1, 2). It is recognized that inflammation is frequently present in hand OA (3-5), and that inflammatory features, as detected by Magnetic Resonance Imaging (MRI) and ultrasound, are associated with clinical features and progression of structural abnormalities (6-11). It has been suggested that some OA patients may benefit structurally and clinically from anti-inflammatory interventions (12). Moreover, a recent proof-of-concept study showed that six weeks of prednisolone treatment improved pain and function in hand OA patients with concurrent joint inflammation (13).

Due to these developments, it is anticipated that numerous randomized controlled trials on disease modifying OA drugs and other treatment strategies for OA will be performed or are already in the pipeline. Ultrasound is feasible, readily available, non-invasive and inexpensive, and therefore inflammatory and structural ultrasonographic scoring systems could be suitable instruments for such trials (14).

Unfortunately, there is no consensus yet on ultrasonographic scoring systems of most elementary lesions in hand OA. In 2008, a preliminary scoring system was developed and included semiquantitative assessments of the elementary lesions *synovitis* (greyscale synovial hypertrophy (SH) and joint effusion (JE) combined), *power Doppler (PD) signals* and *osteophytes* (15). However, this scoring system was not further developed, and since then, various modifications and other scoring systems have been used for hand OA research (16, 17), making it difficult to compare research outcomes.

The Outcome Measures in Rheumatology (OMERACT) ultrasound working group, subgroup OA, has therefore started developing ultrasonographic scoring systems for structural and inflammatory abnormalities in hand OA. This resulted in the definition of the ultrasonographic scoring system for structural damage, comprising the elementary lesions osteophytes and cartilage, as well as the

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development of an ultrasonography atlas as a reference (18). Subsequent reliability testing showed good reliability of osteophyte semiquantitative scoring, but the reliability of the cartilage semiquantitative scoring system in the MCP-joints was disappointing and only a dichotomous scoring could therefore be endorsed. Furthermore, the scapho-trapezio-trapezoid (STT) joint was not included. The STT joint is, however, often affected by OA on radiographs and was therefore included in the recent OMERACT thumb base OA MRI scoring system (19). An association between radiographic OA damage and pain in the thumb base was recently demonstrated, and in contrast to finger OA studies, this association seemed more important in predicting thumb base pain than inflammatory features (20).

The aim of the current study by the OMERACT ultrasound working group was 1) to develop an ultrasonographic scoring system for the *inflammatory* lesions SH, JE and PD signals in hand OA, 2) to introduce a novel scoring system for *cartilage* in the palmar aspect of the proximal interphalangeal (PIP) joints and 3) to extend the *osteophyte* scoring system (that has already been defined and found reliable) to also include the STT joint. Finally, the scoring systems were tested in a web-based and patient-based exercise.

Patients and Methods

Based on the literature and already existing ultrasound definitions of OA pathologies a Delphi survey was carried out to develop scoring systems. These were subsequently tested in web-based and patient-based exercises.

Delphi survey

A Delphi survey was performed to agree on which elementary lesions to include in the scoring systems and which joints and scans were relevant when examining hand OA with ultrasound. An initial round of questionnaire for level of agreement according to a Likert scale (1='strongly disagree' to 5='strongly agree') was distributed to 22 OMERACT participants (subgroup hand OA; participants listed in the Online Supplementary File S1) through a web-portal (www.wufoo.com). Based on the results and comments, a steering group prepared and distributed a second survey. Each survey was

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considered valid when ten or more experts responded, and consensus on each statement was achieved when ≥75% agreed to a score of 4 ('agree') or 5 ('strongly agree').

Ultrasound imaging atlas

Based on the Delphi, a preliminary ultrasound atlas was developed and made available for the web-based exercise, and later edited according to feedback from the experts and used in the patient-based exercise. Anonymized images were collected of hand OA patients in the rheumatological outpatient clinic at Diakonhjemmet Hospital (Oslo, Norway) and participants of hand OA studies from the Parker Institute (Copenhagen, Denmark) and Leiden University Medical Hospital (The Netherlands).

Web-based exercise

A web-based reliability exercise was performed on the inflammatory features SH, JE and PD signals using the developed ultrasound atlas. A pool of 99 static and anonymized ultrasound images was selected by AM to represent all degrees of pathology. These were distributed to the expert panel and scored semiquantitatively (0-3) for inter-reader reliability. For intra-reader reliability, 40 images were randomly chosen and redistributed two weeks after the first round.

Patient-based exercise

A training session for the sonographers was held before the patient-based reliability exercise. Six sonographers and three facilitators met in Copenhagen (Denmark) as well as three experts who participated through a videoconference. It was agreed to assess SH and JE separately in addition to PD signals – all on semiquantitative scale (0-3; Table 1). Osteophytes in the STT joint was deemed feasible to score on a 0-3 scale (Table 1). Finally, it was decided to also include an assessment of cartilage. However, compared to previous work with dorsal and longitudinal scan of the metacarpophalangeal (MCP) joints (18), the group instead suggested a transverse scan of the palmar aspect of the PIP joints (Table 1). Due to many joints and lesions, we limited the number of joints in the patient-based exercise to the following:

a) Inflammation in the 2nd–5th PIP and distal interphalangeal (DIP) joints of the dominant hand, assessing SH and JE separately in both dorsal and palmar aspect of the joints (grade 0-3) but PD activity on the dorsal side only (grade 0-3).

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b) Osteophytes in the STT joint bilaterally (grade 0-3), since good reliability was previously demonstrated in the other finger joints (18).
c) Cartilage defects (partial or complete loss of cartilage, or loss of interphase sharpness) on the palmar side of the 2nd–5th PIP joints bilaterally (grade 0-2), with the fingers fully extended and the probe in a transverse view.

Six experienced sonographers from 5 European countries performed the ultrasound exam on twelve hand OA patients (11 females; mean age 73.8 (SD 7.8) years) recruited from the Parker institute (Bispebjerg-Frederiksberg Hospital, Copenhagen, Denmark). The participants fulfilled the American College of Rheumatology clinical criteria of hand OA (21) and inflammatory joint diseases were excluded. Written consent was obtained before the exercise.

Six high-end ultrasound machines (GE Logiq E9) were used – all equipped with two multifrequency linear probes operating at a frequency of 15 MHz (for inflammation and osteophytes) and 18 MHz (for cartilage). The same settings (15 MHz probe: GS frequency 15 MHz, GS gain 51, Doppler frequency 7.5 MHz, pulse repetition frequency 0.4 kHz, Doppler gain 18.5; 18 MHz probe: GS frequency 15 MHz, GS gain 45) were used on all units and each sonographer was allowed to modify only the depth and focus. The patients were positioned in separate rooms with their hands resting on a small table close to the ultrasound machines. The assessments were performed on fully extended fingers, but when in doubt during the scoring of synovial thickening and effusion in the PIP joints, the joint could be slightly flexed to identify the extensor complex correctly. The sonographers rotated between the rooms and were given 20 minutes to complete each evaluation. They examined each patient twice with at least a two-hour interval.

Statistical analysis

Intra-reader reliability was calculated by Cohen's kappa (κ) with quadratic weighting (22). Inter-reader reliability was calculated as the average of all possible n(n-1)/2 two-rater Cohen's κ, i.e. Light's κ (23). The 95% confidence intervals (CI) were based on patient resampling by bootstrapping. To account for bias through low prevalence (relative probability) and difference in reported frequencies between raters (marginal distribution), we instead calculated Prevalence-Adjusted Bias-

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Adjusted Kappa (PABAK) for power Doppler signals (24). All of the kappa coefficients were evaluated using the guideline outlined by Landis and Koch (25), with the following strength of the kappa coefficients: 0.01-0.20 poor; 0.21-0.40 fair; 0.41-0.60 moderate; 0.61-0.80 substantial; and 0.81-1.00 excellent. Percentage of exact agreement (PEA, i.e. percentage of observations that obtained the same score) and percentage of close agreement (PCA; i.e. a score difference of +/–1) between all possible pairs of raters, as well as prevalence of the observed lesions, were also calculated. Analyses were performed using R: A Language and Environment for Statistical Computing version 3.4.4 (R Foundation for Statistical Computing, Vienna, Austria).

Results

The Delphi survey was completed by 20 (round 1) and 18 (round 2) of in total 22 invited experts. The first survey included 15 statements for voting (Online Supplementary File S1), of which 10 items reached consensus. The remaining statements were revised and modified according to the expert's comments and suggestions and proposed again in the second round with 7 new statements for voting (Online Supplementary File S1), of which 6 items reached consensus. Three inflammatory features (SH, JE and PD signals) and two structural features (osteophytes and cartilage) were selected as core elements for ultrasound assessment of hand OA. The ultrasound characteristics of these features, except for cartilage defects, were based on previous definitions (26-29). Final ultrasound methodology, morphologic description and scoring systems of these lesions are summarized in Table 1.

Ultrasound imaging atlas

An ultrasonographic imaging atlas of elementary lesions was developed, with a comprehensive version available for the reliability exercise (Online Supplementary File S4) and an extended version for publication (Online Supplementary File S2).

Web-based reliability exercise

In total 13 experts completed the first round and 11 the second round of the web-based reliability exercise of the scoring systems. SH and PD severity were evenly distributed across grade 0 to 3,

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whereas few joints were assessed as having JE grade 3 (1.5%; Table 2). The intra- and inter-reader κ coefficients were excellent for scoring PD activity (Table 2), and substantial to excellent agreement was demonstrated for SH and JE scoring on 0-3 semiquantitative scales (Table 2).

Patient-based reliability exercise

All ultrasound features were present across the whole spectrum of severity (Table 3). However, for all features except cartilage, there was a low prevalence of the highest score.

Greyscale synovial hypertrophy and joint effusion

SH and JE was frequently observed in the interphalangeal joints (Table 3), but both features were slightly more prevalent in the dorsal (~45% and ~40% respectively) than the palmar (~34% and ~30%, respectively) aspects of the PIP and DIP joints.

The mean κ coefficients for intra-reader reproducibility were 'substantial' for both SH (0.73) and JE (0.70) on the dorsal side of the interphalangeal joints (Table 4), whereas intra-reader agreement on the palmar side was only 'moderate' (0.56 and 0.54, respectively). All six readers achieved 'substantial' or 'excellent' intra-reader agreement on dorsal SH assessment, and four readers achieved the same for dorsal JE (Online Supplementary File S3).

The inter-reader agreement was more variable. PCA between all possible reader pairs was very high for both features (>92%), but PEA was lower (52-64%). The κ coefficients were better on the dorsal than the palmar side for both SH and JE, but inter-reader agreement was 'moderate' at best, with κ=0.45-0.55 on dorsal scans (Table 4).

Doppler signals

In contrast to the more common greyscale inflammatory features, PD signals were only reported in 6% of the interphalangeal joints (Table 3). This explains the striking improvement in reliability, from low κ coefficients to high PABAK that was only seen for PD signals and not the other features: intra- and inter-reader agreement was 'excellent' (0.88-0.90) in the prevalence-adjusted PABAK analyses (Table 4). PEA between readers was noticeably higher for PD (91%) than the other features.

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Cartilage defects

Morphological cartilage abnormalities were found in 82% of the palmar aspect of the PIP joints according to the newly proposed 0-2 scoring system (Table 3). Both intra- and inter-reader agreement was 'moderate' according to κ coefficients (Table 4), but two readers achieved 'substantial' and 'excellent' intra-reader reproducibility (Online Supplementary File S3).

Osteophytes

The largest discrepancy between the first and second reading amongst all the features was observed for the lower spectrum of osteophytes in the STT joints, in which many readers shifted their assessment from grade 0 to grade 1 (Table 3). Still, intra-reader reproducibility was fairly good, with a mean κ coefficient of 0.62. However, inter-reader reliability was quite low, with κ coefficients of 0.36 and PEA of 44% at best (Table 4), but PCAs between all reader pairs were satisfactory (85-87%).

Discussion

This study has developed and assessed the first consensus-based scoring systems for inflammatory and structural lesions with ultrasonography of hand OA using the OMERACT methodology (30). Based on previous ultrasonographic definitions of elementary lesions, we scored the inflammatory abnormalities SH and JE separately in addition to PD signals. We also introduced a novel scoring system of cartilage in the PIP-joints, and added the STT joint to the osteophyte scoring system that has already been defined and found reliable (18). Semiquantitative ultrasonographic assessment of hand OA as an outcome measure is a target area for OMERACT, as numerous trials on potential structure-modifying or cartilage-protective treatments and other management strategies for OA are anticipated. Our scoring systems can be instruments for domains determined by the OMERACT hand OA working group to be assessed in clinical trials of hand OA (14, 31). Finally, the complementary ultrasonographic imaging atlas is expected to enhance unified interpretations of the grading scales between sonographers, departments, and countries.

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The inflammatory lesions were tested in a web-based exercise with substantial to excellent agreement. This may be because images selected for web-based exercises are of high quality and do not include acquisition (32). In contrast to a preliminary ultrasonographic scoring system for hand OA that combined SH and JE into one greyscale synovitis score (15), we demonstrated that SH and JE can be scored *separately* on 0-3 scales. This is similar to recent OMERACT studies of rheumatoid arthritis (RA) of the hand (33) and OA of the foot (34), except they scored JE as absent/present (0–1). In our study, both features were tested in the patient-based exercise and reached substantial intra-reader agreement in dorsal scans of the interphalangeal joints, and moderate agreement between readers. PEA ranged 52-64% and were higher than previously demonstrated for other inflammatory features in the Oslo Hand OA MRI score: synovitis (46%) and flexor tenosynovitis (36%) (35). The benefit of an ultrasonographic semiquantitative JE score in contrast to a binary score needs further exploration, but all grades were present in the current exercise and evidently possible to score. The role of effusion in hand OA is yet not clear, and one could imagine that it might not be the same as in RA where it has been shown to have little relevance for the disease (36). There is also a high prevalence of joint effusion in healthy subjects (37). The current semiquantitative score may be more helpful in elucidating this role in hand OA and other diseases compared to binary scores alone.

In general, some variation in intra-reader reliability and a significant discrepancy between intra- and inter-reader reliability is probably due to the initial difficulty applying new definitions in a 'real life' scanning. We applied a free longitudinal scan for more accurate detection of the real amount of inflammation, although standardized alignment of the probe in the midline has been found to improve reliability when assessing small joints (38, 39) and may be applied in future studies for reliability purposes. Furthermore, better reliability and higher frequency of SH and JE was demonstrated for dorsal scans of the interphalangeal joints compared to palmar scans. This, and the additional time required of a palmar scan, favors a dorsal ultrasound approach to finger joints in OA, similar to RA (38). However, large osteophytes may dominate the dorsal joint aspect, and future study protocols may opt for a palmar scan of SH and JE if in doubt, and only report the highest dorsal or palmar score.

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Similar to previous studies on hand and foot OA (9, 34), we demonstrated excellent reliability for assessment of PD activity on still images and we reproduced this in the patient-based exercise after adjusting for low prevalence and bias. PABAK was used since PD activity was rarely seen and a low prevalence may give misleadingly low Cohen's kappa values (34, 40). At the same time, the high PEA and PCA should be interpreted with caution due to high number of joints with absent PD signals.

A previous attempt to develop a semiquantitative 0-3 scoring system for cartilage in hand OA found moderate intra-reader and only fair inter-reader agreement (18), and it was suggested that the proposed definitions could not help to sufficiently discriminate between intermediary grades, pointing in the direction that a 0-2 score is more suitable. Another recent study on cartilage in RA patients simplified the scoring to a 0-2 scale and found moderate to excellent reliability in the MCP-joints, but only poor reliability for the PIP-joints (41). We opted for a 0-2 semiquantitative scoring system based on the morphological integrity of the superficial interphase of the cartilage and the cartilage thickness. We also changed to a palmar scan of cartilage since osteophytes may cover the dorsal joint space and chose the PIP instead of the MCP joints due to higher prevalence and incidence of OA (42). With this approach, moderate to excellent intra-reader reliability but only moderate inter-reader reliability was found. As with previous attempts, the current study suggests there are technical and interpretational pitfalls of a semiquantitative cartilage assessment that we have yet not overcome, and the current scoring system is not endorsed.

In the current study, we explored assessment of osteophytes in the STT joint as a supplement to the OMERACT osteophyte scoring system for hand OA that has already been defined and found reliable (18). Encouragingly, we found substantial intra-reader reproducibility, although with a larger variation than previously found for other hand joints (18), and only fair to moderate inter-reader agreement. The divergent prevalence between the first and second round for grade 0 and 1 indicate the difficulty in assessing this joint, and the group recon both probe position and image interpretation as areas of improvement.

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To complete the current real-life reliability study, relevant joints were omitted from the exercise, especially inflammatory features of the carpometacarpal, MCP and DIP joints. These joints should be examined for domains reflecting structural change and inflammation in future studies (15). Bone erosions were also omitted. Imaging studies applying MRI and ultrasound have found erosive changes in the majority of patients with hand OA, including those without signs of erosions at conventional radiographs (9, 43-46). However, scoring of centrally located erosions in hand OA with ultrasound is difficult due to osteophytes that limit the acoustic window (15). The only proposed scoring system for ultrasound-detected bone erosions demonstrated erosions more frequently – but not specifically – for RA compared to OA, psoriatic arthritis, gout, or healthy controls (47). We propose a systematic literature review on ultrasonography of erosions in OA and then to discuss whether this should be a focus area for future work.

In conclusion, OMERACT consensus-based semiquantitative scoring systems for SH, JE and PD activity in hand OA were developed using a complementary ultrasonographic imaging atlas with detailed examples of all scores. We found moderate to substantial agreement for SH and JE as well as excellent PABAK for PD activity, supporting scoring of inflammatory pathologies with US in hand OA. Osteophyte assessment in the STT joints achieved fair to substantial agreement, whereas cartilage assessment of the palmar PIP joints was only moderately reproducible and is therefore not endorsed.

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Tables

Table 1. Ultrasonographic assessment of the elementary lesions in hand osteoarthritis included in the current work.

Ultrasonographic lesion	Joint (projection)*	Morphologic description	Scoring
Joint effusion (JE)	CMC 1 (radiopalmar) MCP 1-5 (dorsal) IP 1 (dorsal + palmar) **PIP 2-5 (dorsal + palmar)** **DIP 2-5 (dorsal + palmar)**	Abnormal hypoechoic or anechoic (relative to subdermal fat, but sometimes may be isoechoic or hyperechoic) intraarticular material that is displaceable and compressible, but does not exhibit Doppler signal (28).	0-3, scored relative to the maximal size of effusion that can be seen in the respective joint group (Online Supplementary File S2 and S4): 0 = none 1 = minimal 2 = moderate 3 = severe
Synovial hypertrophy (SH)	CMC 1 (radiopalmar) MCP 1-5 (dorsal) IP 1 (dorsal + palmar) **PIP 2-5 (dorsal + palmar)** **DIP 2-5 (dorsal + palmar)**	Abnormal hypoechoic (relative to subdermal fat, but sometimes may be isoechoic or hyperechoic) intraarticular tissue that is non-displaceable and poorly compressible and which may exhibit Doppler signal (28).	0-3: 0 = none 1 = minimal (up to the level of the horizontal line connecting bone surfaces of the joint) 2 = moderate (extending beyond joint line but with upper surface concave or flat) 3 = severe (extending beyond joint line but with upper surface convex)
Doppler signals	CMC 1 (radiopalmar) MCP 1-5 (dorsal) IP 1 (dorsal) **PIP 2-5 (dorsal)** **DIP 2-5 (dorsal)**	Flow signal in the synovium; must be detected within synovial hypertrophy to be considered as a sign of synovitis (26, 27).	0-3: 0 = no flow in the synovium 1 = minor (single vessel signals, one or more) 2 = moderate (confluent vessel signals in less than half of the area of the synovium) 3 = major (vessel signals in more than half of the area of the synovium)
Osteophytes	**STT (radiopalmar)** CMC 1 (radiopalmar) MCP 1-5 (dorsal) IP 1 (dorsal)	A clear, step-up cortical prominence at the bony margin that is visible in 2 perpendicular planes (29).	0-3, severity scored relative to the respective joint group (Online Supplementary File S2 and S4); proximal and distal margin assessed together, and

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	PIP 2-5 (dorsal) DIP 2-5 (dorsal)		the largest osteophyte is scored: 0 = none 1 = minor 2 = moderate 3 = major
Cartilage defects	**PIP 2-5 (palmar)**	Normal cartilage has a sharp interphase (white band) on its margins perpendicular to the probe. Loss of sharpness occurs when cartilage interphase is not visible. Complete loss when cartilage cannot be visualized.	0-2: 0 = normal cartilage (anechoic structure with visible cartilage interface) 1 = focal or complete thinning of cartilage, or loss of sharpness of at least one cartilage margin 2 = focal or complete loss of cartilage

***** Joints and projections in **bold** were included in the patient-based reliability exercise.

CMC=carpometacarpal joint; DIP=distal interphalangeal joint; MCP=metacarpophalangeal joint; PIP= proximal interphalangeal joint; STT=scaphotrapeziotrapezoid joint.

Table 2. Reader agreement in the web-based reliability exercise of inflammatory ultrasound features: 1) Mean prevalence (%) of observed lesions; 2) Intra-reader agreement according to mean (range) Cohen's kappa with quadratic weighting; 3) Inter-reader agreement according to Light's kappa (95% confidence interval; CI), i.e. mean Cohen's kappa with quadratic weighting between all pairs of readers.

	Mean prevalence (%)				Intra-reader	Inter-reader
	Gr. 0	Gr. 1	Gr. 2	Gr. 3	mean kappa (range)	kappa (95%CI)
Synovial hypertrophy	28.7	28.5	26.3	16.5	0.78 (0.46–0.95)	0.83 (0.77–0.89)
Joint effusion	47.4	35.0	16.1	1.5	0.79 (0.54–0.97)	0.64 (0.50–0.78)
Power Doppler signals	30.2	25.0	25.0	19.8	0.94 (0.85–1.00)	0.86 (0.72–1.00)

Table 3. Mean prevalence of observed lesions (% joints) between the six sonographers in the patient-based reliability exercise, including 12 patients.

Feature	**Joints (projection)**	**n joints**	**First scan, mean prevalence (%)**	**Second scan, mean prevalence (%)**

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			Gr. 0	Gr. 1	Gr. 2	Gr. 3	Gr. 0	Gr. 1	Gr. 2	Gr. 3
SH	PIP+DIP (dorsal)	576	54.9	31.6	10.6	3.0	56.1	30.6	10.9	2.4
	PIP+DIP (palmar)	576	66.8	23.3	8.7	1.2	65.0	26.8	6.8	1.4
JE	PIP+DIP (dorsal)	576	59.5	30.9	8.0	1.6	61.4	28.3	8.5	1.7
	PIP+DIP (palmar)	576	69.7	20.2	8.3	1.7	68.9	22.7	6.8	1.6
PD	PIP+DIP (dorsal)	576	94.1	3.8	1.9	0.2	93.6	4.9	1.4	0.2
Cartilage defects	PIP (palmar)	288	18.8	43.9	37.2	NA	17.8	43.0	39.2	NA
Osteophytes	STT (palmar)	144	38.9	35.4	18.8	6.9	29.2	45.1	19.4	6.3

DIP=distal interphalangeal joint; JE=joint effusion; NA=not (methodologically) applicable; PD=power Doppler; PIP=proximal interphalangeal joint; SH=synovial hypertrophy; STT=scaphotrapeziotrapezoid joint.

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Table 4. Reader agreement in the patient-based reliability exercise: 1) Intra-reader agreement according to mean (range) Cohen's kappa (with quadratic weighting) or PABAK*; 2) Inter-reader agreement according to Light's kappa (95% confidence interval; CI), i.e. mean Cohen's kappa (with quadratic weighting) or PABAK* between all pairs of readers and percentage exact and close (+/–1 grade) agreement between all readers.

Feature	Joints (projection)	Intra-reader agreement	Inter-reader agreement, first scan			Inter-reader agreement, second scan		
		Kappa mean (range)	Kappa (95%CI)	PEA	PCA	Kappa (95%CI)	PEA	PCA
SH	PIP+DIP (dorsal)	**0.73 (0.64–0.83)**	0.45 (0.33–0.57)	53%	94%	0.45 (0.33–0.57)	52%	94%
	PIP+DIP (palmar)	0.56 (0.48–0.69)	0.31 (0.17–0.45)	59%	92%	0.35 (0.23–0.47)	57%	94%
JE	PIP+DIP (dorsal)	**0.70 (0.55–0.81)**	0.52 (0.40–0.64)	63%	96%	0.55 (0.43–0.67)	64%	96%
	PIP+DIP (palmar)	0.54 (0.36–0.76)	0.33 (0.23–0.43)	63%	92%	0.31 (0.21–0.41)	62%	93%
PD	PIP+DIP (dorsal)	**0.90 (0.75–0.96)***	**0.88 (0.82–0.94)***	91%	98%	**0.88 (0.80–0.96)***	91%	99%
Cartilage defects	PIP (palmar)	0.56 (0.42–0.81)	0.44 (0.34–0.54)	53%	NA	0.45 (0.35–0.55)	56%	NA
OP	STT (palmar)	**0.62 (0.37–0.80)**	0.36 (0.20–0.52)	44%	85%	0.27 (0.09–0.45)	36%	87%

* PD kappa reported as Prevalence-Adjusted Bias-Adjusted Kappa (PABAK).

DIP=distal interphalangeal joint; JE=joint effusion; NA=not (methodologically) applicable; OP=osteophytes; PABAK=Prevalence-Adjusted Bias-Adjusted Kappa; PCA=percentage close agreement, i.e. +/–1 grade; PEA=percentage exact agreement; PD=power Doppler; PIP=proximal interphalangeal joint; SH=synovial hypertrophy; STT=scaphotrapeziotrapezoid joint.

Bold=substantial to excellent agreement.

Online Supplementary Files

Online Supplementary File S1: OMERACT Delphi exercise results

Online Supplementary File S2: Ultrasound Hand OA atlas, extended version

Online Supplementary File S3: Intra-reader agreement for each reader in the patient-based reliability exercise

Online Supplementary File S4: Ultrasound Hand OA atlas, comprised for the patient-based reliability exercise

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Declarations

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Author contribution: Conceived and designed the analysis: AM, HBH, LT, MCK, MADA, IA, KE. Collected the data: all authors.

Contributed data or analysis tools: all authors. Performed the analysis: AM, JS. Wrote the paper: all authors.

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Ethical Approval and Consent to participate: The study was approved by the local ethical committee, and all subjects provided written informed consent to participate in the study.

Availability of supporting data: Please contact the authors for data requests.

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