Summary Findings of a Systematic Review of the Ultrasound Assessment of Synovitis

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ABSTRACT. This report presents the results of a recent systematic review performed by the OMERACT Ultrasound Group on the metric properties of ultrasound for the detection of synovitis in inflammatory arthritis. Reviews were conducted for the hand, wrist, elbow, shoulder, knee, ankle, and foot; most reports were related to the hand and knee, and the most common disease process was rheumatoid arthritis. The review highlights the current gaps in the literature, including a lack of reliability data with respect to intra-occasion and intra- and inter-reader reliability. Current work by our group is addressing these issues. (J Rheumatol 2007;34:839–47)

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Ultrasound (US) is increasingly being investigated as a tool for the assessment of synovitis. It is a noninvasive, nonionizing method of assessing joints through the use of reflected sound waves to provide an image. To enable its use in routine practice and clinical trials an assessment of its metric qualities is required.

Measurement applies scientific principles of design with selected statistical methods to describe and quantify. The reliability of a test result is its ability to be reproduced. In US this is a critical issue. US can be divided into the acquisition and the reading phases, as well as the reliability of one observer (intraobserver) and multiple observers (interobserver) to reproduce the result. Validity is the ability of US to accurately reveal what it is supposed to. Responsiveness is the ability of the tool to demonstrate change. These are all components of the OMERACT filter[1].

The OMERACT Ultrasound Special Interest Group (OUSIG), as part of its evaluation of US as a measurement tool of synovitis, needed to assess the gaps in current knowledge. To do this a systematic review of the literature was performed.

METHODS

The review process comprised 5 steps. (1) The objective of the review was defined. (2) A single joint was given to a small group for evaluation. (3) The literature was searched to locate all studies that incorporated US of the joint specified and inflammatory arthritis. (4) Data from the articles were extracted using a standardized template. (5) The results were sent to a single center and collated.

The OUSIG decided to evaluate the available literature on US assessment of synovitis in the hand, wrist, elbow, shoulder, knee, ankle and posterior foot, and forefoot. The data were extracted using a template that was specifically designed for the review. The data collected were descriptive and contained primarily information on the metric quality (reliability, validity, responsiveness) being studied in the article. Data were then put into an Excel spreadsheet and sent to one investigator for collation (FJ).

Aspects of reliability covered included the intra-occasion, inter-observer, and intra-observer. Reliability was further divided into acquisition and image-reading reliability. Criterion validity was considered when US was compared to histology or macroscopic appearance as this is the closest comparison to a "gold standard." Construct validity is achieved when measures agree with other measures that evaluate the same phenomenon. This was achieved when comparison was made between US with other imaging techniques and laboratory and clinical data. Responsiveness of US is its ability to change after an intervention.

RESULTS

Studies that evaluated US and the joint specified and synovitis were identified in PubMed from January 1966 to June 2005. The search was limited to English language articles and included only original articles. Reviews and letters were noted but not included.

Tables 1 to 7 summarize the data for each joint and disease and the performance characteristic studied.

Table 1. Hand OMERACT filter.

Study	Year	No.	Condition	Intra-occasion Reliability	Intra-observer Acquisition Reliability	Intra-observer Reading Reliability	Inter-observer Acquisition Reliability	Inter-observer Reading Reliability	Sensitivity to Change	Criterion Validity	Construct Validity	Comparator
De Flaviis[4]	1988	20	RA	—	—	—	—	—	—	—	Yes	Clinical, x-ray
Fornage[5]	1989	16	RA	—	—	—	—	—	—	Yes	Yes	Pathology, clinical
Grassi[6]	1993	20	RA	—	—	—	—	—	—	—	Yes	Clinical
Lund[7]	1995	29	RA	—	—	—	—	Yes	—	—	Yes	Clinical
Grassi[8]	1995	20	RA	—	—	—	—	—	—	—	Yes	Clinical, x-ray
Olivieri[9]	1996	10	SpA	—	—	—	—	—	—	—	Yes	Clinical, MRI
Hau[10]	1999	34	RA	—	—	—	—	—	—	—	Yes	Clinical
Backhaus[11]	1999	60	RA, SpA	—	—	Yes	—	—	—	—	Yes	Clinical, MRI, bone scan
Kane[12]	1999	17	SpA	—	—	—	—	—	—	—	Yes	Clinical, x-ray
Kotob[13]	1999	54	RA	—	—	—	—	—	—	Yes	Yes	Pathology, clinical
Wakefield[14]	2000	100	RA	—	—	Yes	Yes	Yes	—	—	Yes	X-ray, MRI
Swen[15]	2000	21	RA	—	—	—	—	—	—	Yes	Yes	Pathology, MRI
Magarelli[16]	2001	1	SpA	—	—	—	Yes	Yes	—	—	—	
Qvistgaard[17]	2001	18	RA	—	—	Yes	—	Yes	—	—	Yes	Clinical, laboratory
Stone[18]	2001	12	RA	—	—	—	—	—	Yes	—	Yes	Clinical, laboratory
Szkudlarek[19]	2001	15	RA	—	—	—	—	—	—	—	Yes	Clinical, laboratory
Ferrell[20]	2001	13	RA	—	—	—	—	—	—	—	Yes	Clinical, laser Doppler
Hau[21]	2002	5	RA	—	—	—	—	—	Yes	—	Yes	Clinical, laboratory
Klauser[22]	2002	46	RA	—	—	—	—	—	—	—	Yes	Clinical
Ribbens[23]	2003	11	RA	—	—	Yes	—	Yes	Yes	—	Yes	Clinical, laboratory
Szkudlarek[24]	2003	30	RA	—	—	—	Yes	—	—	—	Yes	Clinical
Szudlarek[25]	2003	18	RA	—	—	—	—	—	—	—	Yes	Clinical, MRI
Terslev[26]	2003	11	RA	—	—	—	—	—	Yes	—	Yes	Clinical
Terslev[27]	2003	29	RA	—	—	—	—	—	—	—	Yes	Clinical, MRI
Weidekamm[28]	2003	47	RA	—	—	—	—	—	—	—	Yes	Clinical, x-ray
Lopez[29]	2003	10	RA	—	—	—	—	—	—	—	Yes	X-ray
Raza[30]	2003	30	Inflammatory arthritis	—	—	—	—	—	—	Yes	—	Pathology
Czekajska-Chehab[31]	2003	7	RA	—	—	—	—	—	—	—	Yes	Clinical
D'Agostino[32]	2004	70	RA	—	—	—	Yes	Yes	—	—	—	
Hoving[33]	2004	46	RA	—	—	—	—	—	Yes	—	Yes	X-ray, MRI
Hielscher[34]	2004	2	RA	—	—	—	—	—	—	—	Yes	Clinical, laboratory, laser Doppler
Magnani[35]	2004	13	RA	—	—	—	—	—	—	—	Yes	Clinical, laboratory, MRI
Agarwal[36]	2005	10	RS_3PE	—	—	—	—	—	—	—	Yes	Clinical
Scheel[37]	2005	13	RA	—	—	—	—	—	—	—	Yes	Clinical, laser Doppler
Scheel[38]	2005	4	RA	—	—	—	Yes	Yes	—	—	Yes	Clinical, MRI
Scheel[39]	2005	46	RA	—	—	—	—	Yes	—	—	Yes	Clinical, x-ray, MRI
Varsamidis[40]	2005	32	RA	—	Yes	Yes	—	—	—	—	Yes	Clinical

PsA: psoriatic arthritis, SpA: spondyloarthropathy, HCV: hepatitis C virus, SS: Sjögren's syndrome, PMR: polymyalgia rheumatica, RS_3PE: remitting seronegative symmetrical synovitis with pitting edema, NS: nonsignificant.

Table 2. Wrist OMERACT filter.

Study	Year	No.	Condition	Intra-occasion Reliability	Intra-observer Acquisition Reliability	Intra-observer Reading Reliability	Inter-observer Acquisition Reliability	Inter-observer Reading Reliability	Sensitivity to Change	Criterion Validity	Construct Validity	Comparator
Speigel[41]	1987	6	RA	—	—	—	—	—	—	—	Yes	Clinical
De Flaviis[4]	1988	20	RA	—	—	—	—	—	—	—	Yes	Clinical
Fornage[5]	1989	31	RA	—	—	—	—	—	—	Yes	—	Pathology
Goldenstein[42]	1989	25	Wrist swelling	—	—	—	—	—	—	Yes	Yes	Pathology, clinical, CT, MRI
Koski[43]	1992	50	Inflammatory arthritis	Yes	—	—	—	—	—	—	Yes	Clinical, US after injection of saline
Lund[7]	1995	39	RA	—	—	—	—	Yes	—	Yes	Yes	Pathology, clinical
van Vugt[44]	1997	7	Inflammatory arthritis	—	—	—	—	—	—	Yes	—	Pathology
Koski[45]	2001	85	RA	—	—	—	—	—	Yes	—	Yes	Clinical
Frediani[46]	2002	178	RA, SpA, PMR	—	—	Yes	—	—	—	—	Yes	Clinical, laboratory
Ribbens[23]	2003	21	RA	—	—	—	Yes	Yes	—	—	Yes	Clinical, laboratory
Terslev[26]	2003	29	RA	—	—	—	—	—	—	—	Yes	Clinical, laboratory, MRI
Weidekamm[28]	2003	47	RA	—	—	—	—	—	—	—	Yes	Clinical, x-ray
Terslev[27]	2003	16	RA	—	—	—	—	—	Yes	—	Yes	Clinical
Hoving[33]	2004	46	RA	Yes	—	—	Yes	Yes	—	—	Yes	Clinical, laboratory, x-ray, MRI
Magnani[35]	2004	13	RA	—	—	—	—	—	—	—	Yes	MRI
Strunk[47]	2004	33	RA	—	—	—	—	Yes	—	—	Yes	Clinical, laboratory
Varsamidis[40]	2005	43	RA	—	Yes	—	—	—	—	—	Yes	Clinical

Table 3. Elbow OMERACT filter.

Study	Year	No.	Condition	Intra-occasion Reliability	Intra-observer Acquisition Reliability	Intra-observer Reading Reliability	Inter-observer Acquisition Reliability	Inter-observer Reading Reliability	Sensitivity to Change	Criterion Validity	Construct Validity	Comparator
Koski[48]	1990	65	RA	—	—	—	—	—	—	—	Yes	Clinical
Okamoto[49]	2000	32	RA	—	—	—	—	—	—	Yes	—	Pathology
Lerch[50]	2003	320	PMR	—	—	—	—	—	—	—	Yes	X-ray
Luukkainen[51]	2005	50	RA	—	—	—	—	—	—	—	Yes	Clinical

DISCUSSION

US has potential as a measurement tool in inflammatory arthritis and has been increasingly investigated. It is a safe, cheap, nonionizing, dynamic method of imaging, but for routine use the performance characteristics of reliability, validity, and responsiveness must be investigated. This review summarizes the findings of a systematic review of the literature assessing the use of US in the assessment of inflammatory arthritis.

The major inflammatory condition studied was rheumatoid arthritis, as expected, given the larger burden of disease of this condition. The major joints studied are the hand and knee, due to the ease of assessing these joints and the preponderance for inflammatory diseases to affect them.

The majority of studies were concerned with proving that US assessment is demonstrating what it is supposed to. The assessment was primarily in contrast to other constructs such as clinical assessments, laboratory markers, and other imaging techniques such as radiographs, bone scan, computerized tomography and magnetic resonance imaging. There was less information comparing US to standards such as histopathology or surgical macroscopic findings.

In US, reliability must be further divided into the acquisition and reading of images because of the subjective nature of image acquisition. The scanning technique for each joint needs to be standardized, and through consensus meetings, position statements have been developed[2]. Even with standard imaging protocols it is important to test the acquisition reliability of US because of the multiplanar capability of US scanning, and the choice of image is at the discretion of the sonographer. The next step is the reliability of image reading.

From our review there are major gaps in the reliability test-

Table 4. Shoulder OMERACT filter.

Study	Year	No.	Condition	Intra-occasion Reliability	Intra-observer Acquisition Reliability	Intra-observer Reading Reliability	Inter-observer Acquisition Reliability	Inter-observer Reading Reliability	Sensitivity to Change	Criterion Validity	Construct Validity	Comparator
Koski[52]	1989	56	RA	—	—	—	—	—	—	Yes	—	Pathology
Koski[53]	1991	99	RA	—	—	—	—	—	—	Yes	—	Pathology
Koski[54]	1992	19	PMR	—	—	—	—	—	—	—	Yes	Historical
Alasaarela[55]	1994	44	RA	—	—	—	—	—	—	—	Yes	Clinical, x-ray
Alasaarela[56]	1997	56	RA	—	—	—	—	—	—	—	Yes	MRI
Alasaarela[57]	1997	60	RA	—	—	—	—	—	—	—	Yes	MRI
Alasaarela[58]	1998	26	RA	—	—	—	—	—	—	—	Yes	X-ray, MRI, CT
Alasaarela[59]	1998	36	RA	—	—	—	—	—	—	Yes	—	Pathology
Coari[60]	1999	352	RA, PMR	—	—	—	—	—	—	—	Yes	Clinical
Cantini[61]	2001	171	PMR	—	—	—	—	—	—	—	Yes	MRI
Cantini[62]	2001	18	PMR	—	—	Yes	—	Yes	—	—	Yes	Laboratory
Naranjo[63]	2002	54	RA	—	—	—	—	—	—	—	Yes	Clinical, x-ray
Falsetti[64]	2002	450	RA, SpA, OA	—	—	—	—	—	—	—	Yes	Clinical, x-ray
Frediani[46]	2002	178	PMR	—	—	—	—	—	—	—	Yes	Clinical
Hermann[65]	2003	43	RA	—	—	—	—	—	—	—	Yes	X-ray, MRI
Strunk[66]	2003	41	RA	—	—	—	—	Yes	—	—	Yes	Clinical
Wamser[67]	2003	24	RA	—	—	—	—	—	—	—	Yes	MRI

ing of US. This is primarily in the assessment of acquisition reliability, although the reading reliability is also limited. This is an important deficiency, because if the reliability is poor it is very difficult to have confidence in test results. The recognition of this deficiency has led to studies through OUSIG and independent groups evaluating reliability[3].

There are studies looking at sensitivity to change, but again this is limited. This is expected, as other metrics need to be proven first.

The challenge in US is to confirm reliability results before moving on to prospective studies that will evaluate the relationship of US findings to disease progression to prove the utility of US above other imaging and clinical measures.

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Table 5. Knee OMERACT filter.

Study	Year	No.	Condition	Intra-occasion Reliability	Intra-observer Acquisition Reliability	Intra-observer Reading Reliability	Inter-observer Acquisition Reliability	Inter-observer Reading Reliability	Sensitivity to Change	Criterion Validity	Construct Validity	Comparator
Moore[80]	1975	14	RA	No	No	No	No	No	Yes	Yes	Yes	Surgery
Cooperberg[81]	1978	NS	RA	No	No	No	No	No	Yes	Yes	Yes	Clinical, arthrography
Hammer[82]	1986	NS	RA	No	No	No	No	No	Yes	Yes	Yes	MRI
van Holsbeeck[83]	1988	20	RA	No	No	No	No	No	Yes	Yes	Yes	Clinical, biology, therapy
Rubaltelli[84]	1994	25	RA, PsA	No	No	No	No	No	Yes	Yes	Yes	Histology
Lehitinen[85]	1994	20	SpA	No	No	No	No	No	Yes	Yes	Yes	Clinical
Ostergaard[86]	1995	20	RA, OA, healthy	No	No	No	No	No	Yes	Yes	Yes	MRI, clinical
Lehitinen[87]	1995	23	SpA	No	No	No	No	No	Yes	Yes	Yes	Clinical, laboratory
Newman[88]	1996	6	RA	No	No	No	No	No	No	No	No	NS
Fiocco[89]	1996	24	RA, PsA	No	No	No	No	No	Yes	Yes	Yes	Histology
McGonagle[90]	1998	20	RA, PsA	No	No	No	No	No	Yes	Yes	Yes	MRI
Schmidt[91]	2000	20	RA, OA	NS	NS	NS	NS	NS	Yes	Yes	No	Histology
Giovagnorio[92]	2001	17	RA, SpA OA	NS	NS	NS	NS	NS	Yes	NS	Yes	Clinical
Walther[93]	2001	23	RA, OA	NS	NS	NS	NS	NS	Yes	NS	Yes	Histology
Frediani[94]	2001	80	RA, PsA	No	No	No	No	No	Yes	No	No	NS
Magarelli[95]	2001	40	RA, PsA, others	No	No	No	No	Yes	Yes	Yes	Yes	MRI
Frediani[96]	2002	80	RA, PsA	NS	NS	NS	NS	NS	NS	NS	NS	NS
M Carotti[97]	2002	42	RA	NS	NS	NS	NS	NS	Yes	NS	Yes	Clinical, laboratory
Iagnocco[98]	2002	91	SS, RA + SS	No	No	No	No	No	Yes	No	No	NS
Balint[99]	2002	35	SpA	No	No	No	No	No	Yes	Yes	Yes	Clinical
Fiocco[100]	2003	17	RA, PsA	No	No	No	Yes	Yes	Yes	No	Yes	Arthritis
Tarhan[101]	2003	74	OA	No	No	No	No	No	Yes	No	Yes	MRI
Terslev[102]	2003	51	RA	No	No	No	No	No	No	Yes	No	Clinical
D'Agostino[103]	2003	224	SpA	NS	NS	NS	Yes	Yes	Yes	Yes	NS	Clinical
Kane[104]	2003	22	RA	No	No	No	No	No	Yes	Yes	No	Clinical
Kamel[105]	2003	32	SpA	No	No	No	No	Yes	Yes	Yes	Yes	MRI
Salaffi[106]	2004	18	RA	NS	NS	NS	NS	NS	Yes	Yes	No	Clinical, laboratory
Karim[107]	204	60	RA	No	No	No	Yes	Yes	Yes	No	Yes	Clinical, arthroscopy
Iagnocco[108]	2004	29	HCV	NS	Yes	Yes	Yes	Yes	NS	NS	NS	Clinical
Kamel[109]	2004	16	SpA	No	No	No	No	No	Yes	no	NS	MRI
Naredo[110]	2005	51	RA	NS	NS	NS	NS	NS	Yes	Yes	No	Clinical, laboratory
Naredo[111]	2005	11	RA	NS	NS	NS	NS	NS	Yes	Yes	No	Clinical, laboratory
D'Agostino[112]	2005	600	OA	NS	NS	NS	NS	NS	Yes	Yes	NS	Clinical, x-ray
Acebes[113]	2005	30	OA	NS	NS	NS	NS	NS	Yes	Yes	No	Clinical, x-ray
Beckers[114]	2005	16	RA	NS	NS	NS	NS	NS	Yes	Yes	Yes	Clinical, laboratory, MRI
Scheel[115]	2005	4	RA, SpA	NS	NS	Yes	NS	No	NS	NS	Yes	MRI
Fiocco[116]	2005	20	RA, PsA	NS	NS	NS	Yes	Yes	NS	NS	NS	Clinical, laboratory
Iagnocco[117]	2006	23	PsA, RA	NS	Yes	Yes	Yes	Yes	Yes	Yes	NS	Clinical, laboratory
Naredo[118]	2006	24	PMR, OA, SpA	NS	NS	Yes	NS	Yes	NS	NS	NS	No
Jan[119]	2006	30	OA	No	No	No	No	No	Yes	Yes	No	Clinical, x-ray

PsA: psoriatic arthritis, SpA: spondyloarthropathy, HCV: hepatitis C virus, SS: Sjögren's syndrome, PMR: polymyalgia rheumatica, NS: nonsignificant.

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Table 6. Ankle OMERACT filter.

Study	Year	No.	Condition	Intra-occasion Reliability	Intra-observer Acquisition Reliability	Intra-observer Reading Reliability	Inter-observer Acquisition Reliability	Inter-observer Reading Reliability	Sensitivity to Change	Criterion Validity	Construct Validity	Comparator
Koski[68]	1990	18	RA, SpA, gout	—	—	—	—	—	—	—	Yes	Clinical
Nazarian[69]	1995			—	—	—	—	—	—	—	Yes	Clinical
Lehtinen[70]	1996	17	RA	—	—	—	—	—	—	—	Yes	Clinical, MRI
Jacobson[71]	1998			—	—	—	—	—	Yes	Yes	Yes	Pathology, MRI
Luukkainen[72]	2003	20	RA	—	—	—	—	—	—	—	Yes	Clinical

Table 7. Foot OMERACT filter.

Study	Year	No.	Condition	Intra-occasion Reliability	Intra-observer Acquisition Reliability	Intra-observer Reading Reliability	Inter-observer Acquisition Reliability	Inter-observer Reading Reliability	Sensitivity to Change	Criterion Validity	Construct Validity	Comparator
Koski[68]	1990	18	+	—	—	—	—	—	—	—	Yes	Clinical
Koski[73]	1993	25	RA	—	—	—	—	—	—	—	Yes	Clinical
Coakley[74]	1994	28	RA, TEAR	—	—	—	—	—	—	—	Yes	Clinical
Koski[75]	1995	25	RA, SpA	—	—	—	—	—	—	—	Yes	Clinical
Koski[76]	1998	25	RA	—	—	—	—	—	—	—	Yes	Clinical
Kane[12]	1999	17	SpA	—	—	—	—	—	—	—	Yes	Clinical, x-ray
Klocke[77]	2001	15	RA	—	—	—	—	—	—	—	Yes	x-ray
Iagnocco[78]	2001	112	RA, OA, SpA	—	—	—	—	—	—	—	Yes	Clinical
Szkudlarek[24]	2003	30	RA	—	—	—	Yes	—	—	—	Yes	Clinical
Luukkainen[72]	2003	30	RA	—	—	—	—	—	—	—	Yes	Clinical
D'Agostino[79]	2005	68	RA, SpA	—	—	—	—	—	—	—	Yes	Clinical

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Articles presented at the OMERACT 8 Conference
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1. Biomarkers and Surrogate Endpoints
2. Imaging
3. Outcome Measures
4. Workshops and Special Interest Groups

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