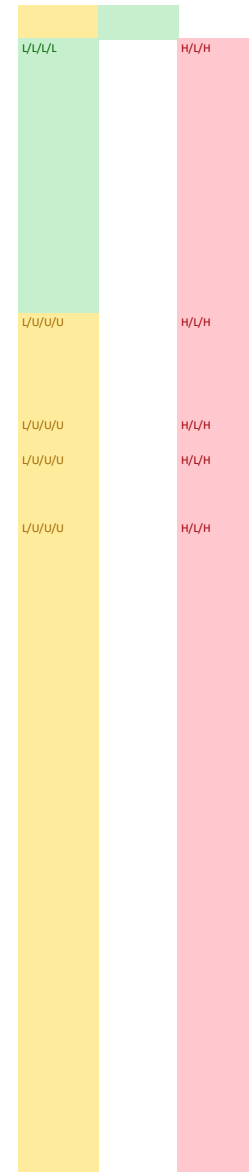


Supplementary table 3. Summary of studies on the assessment of inflammatory activity at patient level

Studies	Study design	Study population (n)	Disease activity (mean)	Disease duration (mean)	Diagnostic test Description	Cut-off (if applicable)	Reference standard Description	Cut-off (if applicable)	Time interval	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	OR (95%CI, p value)	Correlation coefficient (95% CI, p-)	Other	Risk of bias ⁴¹	Risk of bias of individual studies	Concerns regarding applicability ⁴³
Biomarker vs composite index																			
Algergawy, 2013	Case control	Patients suspected of and diagnosed with RA (n=40)	NR	NR	Cartilage oligomeric matrix protein	Positive	DAS	Moderate to high	Same time point	71.0	88.9	95.7	47.1				H/H/H/L		H/L/H
					ACPA	Positive	DAS categories	Low vs moderate vs high	Same time point							p<0.001			
Andres Cerezo, 2017	Cross-sectional	Patients with active RA (n=40)	DAS28 4.39 (1.19)	6.72Y	Synovial fluid S100A11	NA	DAS28	NA	NR					r=0.350, p=0.027; r=0.414, p=0.011, adjusted by age, BMI, ACPA		H/H/U/H		H/L/H	
Avouac, 2014	Cross-sectional	RA patients (n=236)	DAS28 57 (24-87), median (range)	NR	High-sensitivity cardiac troponin (HS-cTnT)	>14ng/L	DAS28-CRP	>5.1	Same time point	0.11 (1.6-35.5, -)		21.2	94.6	r=0.2; p=0.020; Adjusted by all variables with a p value ≤0.1 as covariates		L/U/U/L		H/L/H	
Bae, 2018	SLR: 14 (quantitative analysis: 8)	RA patients (n=638)	NR	NR	miR-146a	NA	DAS28	NA	NR					r=0.434 (95%CI 0.163-0.798, p=0.148)	Circulating and synovial tissue/fluid miR-146a levels are high in patients with RA, and circulating miR-146a levels positively correlate with ESR.	High	NR	-	
Bustos Rivera-Bahena, 2016	Cross-sectional	RA patients (n=121)	DAS28 4.7	7.25Y	Leptin	NA	DAS28	NA	Same day					r=0.513, p<0.0001		L/U/L/L		H/L/H	
					Resistin	NA	DAS28	NA	Same day					r=0.403, p<0.0001					
					Adiponectin	NA	DAS28	NA	Same day					r=-0.151, p>0.05					
					IL-6	NA	DAS28	NA	Same day					r=0.313, p<0.005					
					IL-17	NA	DAS28	NA	Same day					r=0.373, p<0.0001					
					TNFα	NA	DAS28	NA	Same day					r=0.213, p<0.05					
do Prado, 2016	Cross-sectional	RA patients (n=64)	DAS28-ESR 4.02	5Y	IL-2	NA	DAS28-ESR	NA	Same day					r=-0.08 (-0.33-0.17), ns		L/L/L/L		H/L/L	
					IL-4	NA	DAS28-ESR	NA	Same day					r=-0.004 (-0.26-0.25), ns					
					IL-6	NA	DAS28-ESR	NA	Same day					r=0.31 (0.07-0.52), p<0.01					
					IL-10	NA	DAS28-ESR	NA	Same day					r=-0.11 (-0.37-0.14), ns					
					TNF	NA	DAS28-ESR	NA	Same day					r=-0.01 (-0.27-0.23), ns					
					IFN	NA	DAS28-ESR	NA	Same day					r=-0.09 (-0.34-0.17), ns					
					VEGF	NA	DAS28-ESR	NA	Same day					r=0.18 (-0.77-0.41), ns					
Gunaydin, 2006	Cross-sectional	RA patients (n=50)	DAS28 5.4 (1.17)	10Y	Serum leptin level	NA	DAS28	NA	Same day					r=-0.111, p=0.442		L/U/U/L		H/L/H	
Ha, 2014	Cross-sectional	RA patients (n=69)	DAS28 3.04 (1.58)	5.3Y	Leukine-rich alpha-2 glycoprotein (LRG) serum level	NA	DAS28	NA	Same day					r=0.671, p<0.001		L/U/L/L		H/L/H	
Johnson, 2018	SLR: 22 (quantitative analysis: 8)	RA patients (n=3879)	DAS28 3.2-6.0, except for one study of patients in remission (range)	NR	MBDA score	NA	DAS28-CRP	NA	NR					r=0.41 (95%CI 0.36-0.46)	The MBDA demonstrates moderate convergent validity with DAS28-CRP and DAS28-ESR, but weaker correlations with SDAI, CDAI, and RAPID3. While it appears to complement existing RA disease activity measures, further assessment of the MBDA's performance	Moderate	Low	-	
					MBDA score	NA	DAS28-ESR	NA	NR					r=0.48 (95%CI 0.38-0.58)					
					MBDA score	NA	SDAI	NA	NR					r=0.35 (95%CI 0.26-0.43)					

Author	Study Design	Population	Primary Outcome	Secondary Outcome	Marker	Comparison	Result	Significance	Notes		
Kawashiri, 2011	Cross-sectional	RA patients (n=22)	DAS28 5.69; SDAI 30.6; CDAI 28.3	2.3Y	MBDA score	NA	CDAI	NA	NR	r=0.26 (95%CI 0.19-0.33)	characteristics warranted.
					VEGF	NA	DAS28	NA	Same day	r=0.59, p<0.01	
					VEGF	NA	SDAI	NA	Same day	r=0.54, p<0.05	
					VEGF	NA	CDAI	NA	Same day	r=0.51, p<0.05	
					MMP-3	NA	DAS28	NA	Same day	r=0.61, p<0.01	
					MMP-3	NA	SDAI	NA	Same day	r=0.58, p<0.01	
					MMP-3	NA	CDAI	NA	Same day	r=0.55, p<0.05	
					MMP-9	NA	DAS28	NA	Same day	r=0.27, ns	
					MMP-9	NA	SDAI	NA	Same day	r=0.23, ns	
					MMP-9	NA	CDAI	NA	Same day	r=0.18, ns	
Kurosaka, 2010	Cross-sectional	RA patients (n=70)	DAS28-CRP 3.324	4.43Y	TIMP-1	NA	DAS28	NA	Same day	r=0.39, ns	
					TIMP-1	NA	SDAI	NA	Same day	r=0.42, ns	
					TIMP-1	NA	CDAI	NA	Same day	r=0.37, ns	
					VEGF serum level	NA	DAS28-CRP	NA	NR	r=0.6527, p<0.0001	
					ANG-1 serum level	NA	DAS28-CRP	NA	NR	r=0.2435, p=0.0489	
					ANG-2 serum level	NA	DAS28-CRP	NA	NR	r=0.2147, p=0.0743	
Lee, 2007	Cross-sectional	RA patients (n=50)	DAS28 3.69	15.5M	Leptin	NA	DAS28	NA	NR	r=0.363, p<0.05	
					Serum IL-17A	NA	DAS28	NA	NR	r=0.556, p=0.001	
Metawi, 2011	Cross-sectional	RA patients with knee effusion (n=30)	DAS28 4.8	9.5Y	Synovial IL-17A	NA	DAS28	NA	NR	r=0.392, p=0.032	
					IL-2	NA	DAS28-ESR	NA	Same day	r=-0.005, ns	
Milman, 2010	Cross-sectional	RA patients (n=47)	DAS28-ESR 4.3; DAS28-CRP 4.4; SDAI 27.9; CDAI 27.1	13.7Y	IL-2	NA	DAS28-ESR	NA	Same day	r=0.021, ns	
					IL-2	NA	DAS28-CRP	NA	Same day	r=0.003, ns	
					IL-2	NA	SDAI	NA	Same day	r=0.024, ns	
					IL-4	NA	DAS28-ESR	NA	Same day	r=0.191, ns	
					IL-4	NA	DAS28-CRP	NA	Same day	r=0.256, ns	
					IL-4	NA	CDAI	NA	Same day	r=0.175, ns	
					IL-4	NA	SDAI	NA	Same day	r=0.222, ns	
					IL-6	NA	DAS28-ESR	NA	Same day	r=0.409, p=0.005	
					IL-6	NA	DAS28-CRP	NA	Same day	r=0.378, p=0.011	
					IL-6	NA	CDAI	NA	Same day	r=0.312, p=0.033	
					IL-6	NA	SDAI	NA	Same day	r=0.310, p=0.039	
					IL-8	NA	DAS28-ESR	NA	Same day	r=0.234, ns	
					IL-8	NA	DAS28-CRP	NA	Same day	r=0.276, ns	
					IL-8	NA	CDAI	NA	Same day	r=0.250, ns	
					IL-8	NA	SDAI	NA	Same day	r=0.257, ns	
					IL-10	NA	DAS28-ESR	NA	Same day	r=0.226, ns	
					IL-10	NA	DAS28-CRP	NA	Same day	r=0.256, ns	
					IL-10	NA	CDAI	NA	Same day	r=0.212, ns	
					IL-10	NA	SDAI	NA	Same day	r=0.219, ns	
					VEGF	NA	DAS28-ESR	NA	Same day	r=0.142, ns	
VEGF	NA	DAS28-CRP	NA	Same day	r=0.241, ns						
VEGF	NA	CDAI	NA	Same day	r=0.228, ns						
VEGF	NA	SDAI	NA	Same day	r=0.275, ns						
INF-Y	NA	DAS28-ESR	NA	Same day	r=0.252, ns						
INF-Y	NA	DAS28-CRP	NA	Same day	r=0.309, p=0.039						
INF-Y	NA	CDAI	NA	Same day	r=0.269, ns						
INF-Y	NA	SDAI	NA	Same day	r=0.301, p=0.045						
INF-A	NA	DAS28-ESR	NA	Same day	r=-0.009, ns						
INF-A	NA	DAS28-CRP	NA	Same day	r=0.018, ns						
INF-A	NA	CDAI	NA	Same day	r=0.034, ns						



Shah, 2014	Cross-sectional	RA patients (n=58)	DAS28 5.3	5Y, median	Serum ACPA	NA	DAS28	NA	NR			r=-0.126, p=0.348	L/U/U/U	H/L/H
Skacelova, 2017	Cross-sectional	RA patients (n=92)	DAS28 3.74	15.66Y	MMP-3	NA	DAS28	NA	NR			r=0.301, p<0.05	L/U/U/U	H/L/H
Sockaling, 2009	Cross-sectional	RA patients (n=51)	DAS28 4.11, median	NR	Serum ACPA	NA	DAS28	NA	NR			No correlation	L/U/U/U	H/L/H
Targońska-Stepniak, 2008	Cross-sectional	RA patients (n=37)	DAS28 4.8	136.5M	Serum leptin (all patients)	NA	DAS28	NA	NR			No correlation	L/U/U/U	H/L/H
					Serum leptin (RA duration >10Y)	NA	DAS28	NA	NR			r=0.68, p=0.002		
					Serum leptin (RA duration <10Y)	NA	DAS28	NA	NR			r=0.97, p=0.34		
Tekeoğlu, 2016	Cross-sectional	RA patients (n=102)	DAS28 3.50	40.85M	Platelet count	NA	DAS28	NA	NR			r=0.299, p<0.001	L/U/U/L	H/L/H
					Neutrophil lymphocyte ratio (NLR)	NA	DAS28	NA	NR			r=0.192, p=0.05		
					Mean platelet volume (MPV)	NA	DAS28	NA	NR			r=-0.316, p=0.055, p=0.124		
					Platelet distribution width (PDW)	NA	DAS28	NA	NR			r=-0.055, p=0.124		
Tuncer, 2019	Cross-sectional	RA patients (n=59)	DAS28 3.94	9.0Y	MMP-3	18.73 ng/ml	DAS28	3.2	NR	93.2	82.8	r=0.674, p<0.001	L/U/U/U	H/L/H
Uslu, 2015	Cross-sectional	RA patients (n=104)	NR	NR	Neutrophil-lymphocyte ratio	NA	DAS28	NA	NR			r=0.345, p<0.0001	L/U/U/U	H/L/H
					Platelet-lymphocyte ratio	NA	DAS28	NA	NR			r=0.352, p<0.0001		
Valle, 2009	Cross-sectional	RA patients (n=41)	DAS28 5.87	9.6Y	soluble TNF α receptor type I (sTNFRI) level	NA	DAS28	NA	NR			r=0.219, ns	L/U/U/L	H/L/H
					soluble TNF α receptor type II (sTNFRII) level	NA	DAS28	NA	NR			r=0.375, p=0.017		
Vanichapuntu, 2010	Cross-sectional	RA patients (n=125)	DAS28 3.95	38.2M	ACPA	25 units/ml	DAS28	>2.6	NR			r=0.121, p=0.180	L/U/U/U	H/L/H
					RF	15 IU/ml	DAS28	>2.6	NR			r=0.265, p=0.003		
Yildirim, 2004	Cross-sectional	RA patients (n=47)	DAS28 5.2	10.8Y	Haptoglobin	NA	DAS28	NA	NR			r=0.331, p<0.05	L/U/U/U	H/L/H
					Ferritin	NA	DAS28	NA	NR			r=0.299, p<0.05		
					Fibrinogen	NA	DAS28	NA	NR			r=0.373, p<0.01		
Yuan, 2019	Cross-sectional	RA patients (n=230)	NR	NR	mRNA levels of IL-37	NA	DAS28-ESR	NA	NR			r=0.641, p<0.001	L/U/U/U	H/L/H
Zengin, 2018	Cross-sectional	RA patients (n=317)	NR	NR	Neutrophil to lymphocyte ratio (NLR)	NA	DAS28	NA	NR			r=0.33, p<0.001	L/U/U/U	H/L/H
					Platelet to lymphocyte ratio (PLR)	NA	DAS28	NA	NR			r=0.22, p<0.001		
Zhang, 2019	SLR: 7 studies (quantitative analysis: 7)	RA patients (n=NR)	NR	NR	IL-17	NA	DAS28	NA	NR			Pooled r=0.335 (0.173-0.496), p<0.001	Moderate	Low
Imaging vs composite index														
Besselink, 2018	Cross-sectional	RA patients (n=50)	DAS28-ESR 3.9 (1.20)	NR	Optical spectral transmission (OST) model (both hands)	NA	DAS28	NA	NR			r=0.06 (95CI-0.26-0.36, p=0.71)	L/H/L/L	H/L/L

Conclusion: Circulating IL-17 level is significantly elevated in inflammatory arthritis and is related to the disease activity of AS and RA, suggesting that it plays an important role in the pathogenesis and progression of inflammatory arthritis (especially in AS and RA).

Author	Study Design	Population	Age	Gender	Measures	NA	CDAI	NA	NR	Correlation	Color 1	Color 2
Ceponis, 2014	Cross-sectional	Established RA patients (n=46)	CDAI 15.9	16.6Y	US: total Synovial Hypertrophy score (tSH), range 0-135: Synovial hypertrophy (B-mode examination) was scored on a semiquantitative scale (where 0=absence, 1=mild, 2=moderate, and 3=severe. orsal and palmar joint regions and ulnar and radial aspects of the interphalangeal and second through fifth PIP joints; dorsaland palmar joint regions of the first through fifth and ulnar and radial aspects of the second and fifth MCP joints; and dorsal and volar joint regions and radial and ulnar aspects of the wrist (distal radioulnar, midcarpal, radiocarpal, and ulnar-carpal) joints were examined in long (sagittal plane) and short (axial plane) axes.	NA	CDAI	NA	NR	r=0.4612, p<0.005	L/U/L/U	H/L/H
					US: total Synovial PD score (tSPD)	NA	CDAI	NA	NR	r=0.5043, p<0.005		
					US: Sonographic effusion	NA	CDAI	NA	NR	r=0.3627, p<0.01		
Ciurtin, 2017 ^a	Cross-sectional	RA patients who were referred for examination of hands and feet (n=46)	NR	NR	US: PD scores of hands and feet joints	NA	DAS28	NA	NR	r=0.14, p=0.02	L/U/L/U	L/L/L
Filer, 2017 ^a	Cross-sectional	RA patients with at least 1 joint amenable to biopsy (n=15)	NR	NR	US: PD score of MTP joints	NA	DAS28	NA	NR	r=0.03, p=0.09		
					GS US (12 joint indices for MCP and wrist joints), score 0-3	NA	DAS28	NA	NR	r=0.70, p<0.05	L/U/L/L	H/L/L
					PD US (12 joint indices for MCP and wrist joints), score 0-3	NA	DAS28	NA	NR	r=0.66, p<0.05		
Kawashiri, 2011	Cross-sectional	RA patients (n=22)	DAS28 5.69; SDAI 30.6; CDAI 28.3	2.3Y	US: PD in 12 joints, sum score (bilateral elbows (anterior and posterior recess), wrists (dorsal and carpal recess), second and third MCP joints (dorsal and palmar recess), knees (suprapatellar and lateral parapatellar recess) and ankles (anterior tibiotalar recess, medial tendon sheaths and lateral tendon sheaths))	NA	SDAI	NA	Same day	r=0.72, p<0.001	L/U/L/L	H/L/H
					US: PD in 12 joints, sum score (bilateral elbows (anterior and posterior recess), wrists (dorsal and carpal recess), second and third MCP joints (dorsal and palmar recess), knees (suprapatellar and lateral parapatellar recess) and ankles (anterior tibiotalar recess, medial tendon sheaths and lateral tendon sheaths))	NA	SDAI	NA	Same day	r=0.6, p=0.006		
					US: PD in 12 joints, sum score (bilateral elbows (anterior and posterior recess), wrists (dorsal and carpal recess), second and third MCP joints (dorsal and palmar recess), knees (suprapatellar and lateral parapatellar recess) and ankles (anterior tibiotalar recess, medial tendon sheaths and lateral tendon sheaths))	NA	CDAI	NA	Same day	r=0.6, p=0.006		

					US: PD in 6 joints, sum score (bilateral wrists (dorsal recess) and second and third MCP joints (dorsal recess))	NA	DAS28	NA	Same day	r=0.67, p<0.01		
					US: PD in 6 joints, sum score (bilateral wrists (dorsal recess) and second and third MCP joints (dorsal recess))	NA	SDAI	NA	Same day	r=0.55, p<0.05		
					US: PD in 6 joints, sum score (bilateral wrists (dorsal recess) and second and third MCP joints (dorsal recess))	NA	CDAI	NA	Same day	r=0.54, p<0.05		
Krabbe, 2016 ^a	Cross-sectional	RA patients (n=62)	DAS28 3.6, median	NR	Optical spectral transmission imaging of wrists, MCP1-5, (PIP)1-5 of both hands, at patient level	NA	DAS28	NA	NR	r=0.31, p=0.02	L/U/L/U	H/L/L
Mandl, 2011	SLR: 14 (quantitative analysis: 0)	RA patients (n=1307)	NR	NR	US to assess synovitis using GS (n=1), PD (n=1) or GS+PD (n=12) using different scoring systems (binary (n=8), semiquantitative (n=14), quantitative (n=2), cumulative score of individual joint scores (n=14))	NR	Clinical (n=13), laboratory (n=13), X-ray (n=3), US (n=1) or MRI (n=6)	NR	NR		Moderate	Moderate
												US can be regarded as a valuable tool for globally examining the extent of synovitis in RA. However, it is presently difficult to determine a minimal number of joints to be included in a global US score. Further validation of proposed scores is needed.
Ngai ng, 2019 ^a	Cross-sectional	RA patients (n=19)	DAS28-CRP 4.66, median	5.5Y, median	Whole body magnetic resonance imaging: sum-score of 26 joints (28 conventional joints minus elbows), joint inflammation was defined in two ways; 1) as presence of synovitis and/or osteitis, 2) as the presence of synovitis only (28 conventional joints, bilateral ankles, MTP1-5)	NA	DAS28-CRP	NA	NR	r=0.20, p=0.47	L/H/L/L	H/L/H
					Ultrasound: sum-score of 28 joints (conventional joints; US was graded 0-3 on both B-mode and colour Doppler(CD), and subsequently converted to +/- by defining US synovitis as B mode ≥2 or CD ≥1)	NA	DAS28-CRP	NA	NR	r=-0.26, p=0.28		
Van Onna, 2016	Case control	RA patients in different categories of disease activity: DAS28<2.6, 2.6-5.1, >5.1 (n=59)	DAS28 3.6	1-9Y (range of medians)	Optical spectral transmission (OST) in 7 joints, at patient level	NA	DAS28	NA	Same day (within window of 4h)	r=0.42, p=0.001	L/H/L/L	H/L/L
Vlad, 2011	Cross-sectional	RA patients with at least one painful or clinically swollen joint (n=42)	DAS28 6.15; CDAI 33.90; SDAI 64.23	64.64M	US: Echographic Score, sum of GS scores (0-3) of 10 joints (MCP2-5 dorsal and volar, PIP2-5 dorsal and volar, radiocarpal dorsal and intercarpal joint dorsal) of both hands	NA	CDAI	NA	Same day	r=0.591, p<0.001; r=0.628, p<0.001 (different in text and table)	L/L/L/L	H/L/H
					US: Echographic Score, sum of GS scores (0-3) of 10 joints (MCP2-5 dorsal and volar, PIP2-5 dorsal and volar, radiocarpal dorsal and intercarpal joint dorsal) of both hands	NA	SDAI	NA	Same day	r=0.351, p<0.001; r=0.403, p<0.01 (different in text and table)		
					US: Echographic Score, sum of GS scores (0-3) of 10 joints (MCP2-5 dorsal and volar, PIP2-5 dorsal and volar, radiocarpal dorsal and intercarpal joint dorsal) of both hands	NA	DAS28	NA	Same day	r=0.394, p=0.010		
					US: Volar echographic Score, sum of GS scores (0-3) of 8 joints (MCP2-5 volar, PIP2-5 volar) of both hands	NA	CDAI	NA	Same day	r=0.471, p=0.002; r=0.470, p<0.01 (different in text and table)		

					US: Volar echographic Score, sum of GS scores (0-3) of 8 joints (MCP2-5 volar, PIP2-5 volar) of both hands	NA	SDAI	NA	Same day	r=0.379, p=0.013; r=0.468, p<0.01 (different in text and table)		
					US: Volar echographic Score, sum of GS scores (0-3) of 8 joints (MCP2-5 volar, PIP2-5 volar) of both hands	NA	DAS28	NA	Same day	r=0.374, p=0.015; r=0.407, p<0.01 (different in text and table)		
					US: Dorsal echographic Score, sum of GS scores (0-3) of 10 joints (MCP2-5 dorsal, PIP2-5 dorsal, radiocarpal dorsal and intercarpal joint dorsal) of both hands	NA	CDAI	NA	Same day	r=0.625, p<0.001; r=0.690, p<0.01 (different in text and table)		
					US: Dorsal echographic Score, sum of GS scores (0-3) of 10 joints (MCP2-5 dorsal, PIP2-5 dorsal, radiocarpal dorsal and intercarpal joint dorsal) of both hands	NA	SDAI	NA	Same day	r=0.251, p<0.001; r=0.274, p=0.08 (different in text and table)		
					US: Dorsal echographic Score, sum of GS scores (0-3) of 10 joints (MCP2-5 dorsal, PIP2-5 dorsal, radiocarpal dorsal and intercarpal joint dorsal) of both hands	NA	DAS28	NA	Same day	r=0.345, p=0.025; r=0.407, p<0.01 (different in text and table)		
					US: Number of echographically Positive Joints for synovitis of 10 joints (MCP2-5 dorsal and volar, PIP2-5 dorsal and volar, radiocarpal dorsal and intercarpal joint dorsal) of both hands	NA	DAS28	NA	Same day	r=0.390, p=0.011		
					US: Number of volar echographically Positive Joints for synovitis of 8 joints (MCP2-5 volar, PIP2-5 volar) of both hands	NA	DAS28	NA	Same day	r=0.373, p=0.015		
					US: Number of dorsal echographically Positive Joints for synovitis of 10 joints (MCP2-5 dorsal, PIP2-5 dorsal, radiocarpal dorsal and intercarpal joint dorsal) of both hands	NA	DAS28	NA	Same day	r=0.341, p=0.027		
Witt, 2016	Cross-sectional	RA patients (n=45)	DAS28 4.1; CDAI 21.2; SDAI 22.5	NR	Automated breast volume scanner (The dorsal and palmar sides of each hand and the dorsal aspect of the toes were scanned)	NA	CDAI	NA	NR	r=0.41	L/U/U/U	H/L/L
					Automated breast volume scanner (The dorsal and palmar sides of each hand and the dorsal aspect of the toes were scanned)	NA	SDAI	NA	NR	r=0.45		
Yokota, 2018	Cross-sectional	RA patients with musculoskeletal symptoms (n=27)	DAS28-CRP 3.5 9.4Y		Superb microvascular imaging score (in the joints of both hands (MCP, PIP, and IP joints), the wrists, elbows, and knees (total 26 joints))	NA	DAS28-CRP	NA	Same day	r=0.74, p<0.001	L/L/L/L	H/L/H

					Conventional PD imaging (cPDI) (in the joints of bothhands (MCP, PIP, and IP joints), the wrists,elbows, and knees (total 26 joints))	NA	DAS28-CRP	NA	Same day	r=0.57, p=0.002		
Zufferey, 2014	Cross-sectional	RA patients (n=536)	DAS28-ESR 3.4 (1.4)	6.5Y, median	US: SONAR B-mode score (0-3) of 22 joints (MCP2-5 joints, PIP2-5 joints, wrist, elbows, knees)	NA	DAS28-ESR	NA	Within 15 days	r=0.40 (0.32-0.47, p<0.0001)	L/H/H/L	H/L/H
					US: PD score (0-3) of 22 joints (MCP2-5 joints, PIP2-5 joints, wrist, elbows, knees)	NA	DAS28-ESR	NA	Within 15 days	r=0.40 (0.32-0.48, p<0.0001)		
Histology vs composite index												
Ostendorf, 2001	Cross-sectional	RA patients (n=22)	DAS 4.15	6.42Y	Miniarthroscopy: Macroscopic hyperaemia (2nd MCP joint of dominant hand)	NA	DAS	NA	NR	p=0.004	L/L/L/L	H/L/L
					Miniarthroscopy: Villus proliferation (2nd MCP joint of dominant hand)	NA	DAS	NA	NR	p=0.0035		
Biomarker vs clinical assessment												
do Prado, 2016	Cross-sectional	RA patients (n=64)	DAS28-ESR 4.02	5Y	IL-2	NA	TJC28	NA	Same day	r=-0.03 (-0.29-0.23), ns	L/U/H/L	H/L/L
					IL-2	NA	SJC28	NA	Same day	r=0.06 (-0.18-2.71), ns		
					IL-4	NA	TJC28	NA	Same day	r=0.02 (-0.25-0.28), ns		
					IL-4	NA	SJC28	NA	Same day	r=0.17 (-0.74-0.39), ns		
					IL-6	NA	TJC28	NA	Same day	r=0.09 (-0.17-0.32), ns		
					IL-6	NA	SJC28	NA	Same day	r=0.39 (0.15-0.59), p<0.01		
					IL-10	NA	TJC28	NA	Same day	r=-0.12 (-0.37-0.14), ns		
					IL-10	NA	SJC28	NA	Same day	r=0.09 (-0.14-0.31), ns		
					IL-17	NA	TJC28	NA	Same day	r=0.12 (-0.15-0.35), ns		
					IL-17	NA	SJC28	NA	Same day	r=0.17 (-0.91-0.40), ns		
					TNF	NA	TJC28	NA	Same day	r=0.03 (-0.24-0.30), ns		
					TNF	NA	SJC28	NA	Same day	r=0.07 (-0.15-0.32), ns		
					IFN	NA	TJC28	NA	Same day	r=0.05 (-0.19-0.32), ns		
					IFN	NA	SJC28	NA	Same day	r=-0.04 (-0.29-0.19), ns		
					VEGF	NA	TJC28	NA	Same day	r=0.15 (-0.12-0.40), ns		
					VEGF	NA	SJC28	NA	Same day	r=0.14 (-0.13-0.41), ns		
Gunaydin, 2006	Cross-sectional	RA patients (n=50)	DAS28 5.4 (1.17)	10Y	Serum leptin level	NA	SJC28	NA	Same day	r=0.046, p=0.749	L/U/H/L	H/L/H
					Serum leptin level	NA	TJC28	NA	Same day	r=0.072, p=0.619		
Ha, 2014	Cross-sectional	RA patients (n=69)	DAS28 3.04 (1.58)	5.3Y	Leukine-rich alpha-2 glycoprotein (LRG) serum level	NA	SJC28	NA	Same day	r=0.671, p<0.001	L/U/H/L	H/L/H
					Leukine-rich alpha-2 glycoprotein (LRG) serum level	NA	TJC28	NA	Same day	r=0.514, p<0.001		
Metawi, 2011	Cross-sectional	RA patients with knee effusion (n=30)	DAS28 4.8	9.5Y	Serum IL-17A	NA	TJC	NA	NR	r=0.495, p=0.005	L/U/H/U	H/L/H
					Synovial IL-17A	NA	TJC	NA	NR	r=0.403, p=0.027		
					Serum IL-17A	NA	SJC	NA	NR	r=0.573, p=0.001		

					Synovial IL-17A	NA	SJC	NA	NR	r=0.223, p=0.236		
Myngbay, 2019	Cross-sectional	RA patients (n=57)	DAS28-CRP 3.79	8.04Y	Collagen triple helix repeat containing 1 (CTHRC1) protein	NA	SJC28	NA	Same time point	r=0.307, p=0.02	L/U/H/L	H/L/H
					Collagen triple helix repeat containing 1 (CTHRC1) protein	NA	TJC28	NA	Same time point	No correlation		
Nordal, 2017	Cross-sectional	RA patients (n=141)	DAS28-ESR 4.4	6.8Y	Calprotectin	NA	SJC32	NA	Same time point	r=0.47, p<0.05	L/U/H/L	H/L/L
					Calprotectin	NA	TJC32	NA	Same time point	r=0.17, p<0.001		
					S100A12	NA	SJC32	NA	Same time point	r=0.35, p<0.05		
					S100A12	NA	TJC32	NA	Same time point	r=0.14, ns		
					IL-6	NA	SJC32	NA	Same time point	r=0.41, p<0.05		
					IL-6	NA	TJC32	NA	Same time point	r=0.09, ns		
					VEGF	NA	SJC32	NA	Same time point	r=0.13, ns		
					VEGF	NA	TJC32	NA	Same time point	r=-0.03, ns		
Papadopoulos, 2008	Cross-sectional	ACPA positive RA patients (n=72)	DAS28 6.52	NR	ACPA	NA	TJC	NA	Same day	No correlation	L/U/H/L	H/L/H
Rooney, 2011	Cross-sectional	RA patients (n=105)	DAS28-ESR 3.7 (2.6-4.5); CDAI 11.1 (5.7-18.4); SDAI 11.9 (6.1-19.1).	6.1Y, median	Plasma fibrinogen	NA	SJC28	NA	Same day Within 2W from clinical visit	No correlation r=0.30, p=0.0021	L/U/H/L	H/L/H
					Plasma fibrinogen	NA	SJC28	NA	Within 2W from clinical visit	r=0.26, p=0.0091		
Shah, 2014	Cross-sectional	RA patients (n=58)	DAS28 5.3	5Y, median	Serum ACPA	NA	TJC28	NA	NR	r=-0.144, p=0.282	L/U/H/U	H/L/H
					Serum ACPA	NA	SJC28	NA	NR	r=-0.051, p=0.705		
Sockaling, 2009	Cross-sectional	RA patients (n=51)	DAS28 4.11, median	NR	Serum ACPA	NA	TJC	NA	NR	No correlation (p=0.478)	L/U/H/U	H/L/H
					Serum ACPA	NA	SJC	NA	NR	No correlation (p=0.417)		
Targońska-Stepniak, 2008	Cross-sectional	RA patients (n=37)	DAS28 4.8	136.5M	Serum leptin (RA duration >10Y)	NA	TJC	NA	NR	r=0.59, p=0.01	L/U/H/U	H/L/H
					Serum leptin (RA duration <10Y)	NA	TJC	NA	NR	r=0.41, p=0.69		
Imaging vs clinical assessment												
Axelsen, 2014	Cross-sectional	RA patients (n=20)	DAS28-CRP 4.30 (1.91-7.32), median (range)	6Y, median	MRI assessment of synovitis in 76 joints (lateral sternoclavicular, acromioclavicular, glenohumeral, elbow, wrist, first CMC, first/fifth MCP, first IP, second/fifth PIP, second/fifth DIP, hip, knee, ankle, first tarsometatarsal (TMT), first/fifth MTP, first/fifth PIP and second/fifth DIP joints of the feet)	NA	SJC66	NA	Within 1W	k=0.04 (not specified: -0.29-1.00)	L/U/H/L	H/L/H
					MRI bone marrow oedema (a lesion within the trabecular bone, with ill-defined margins and signal characteristics consistent with increased water content, i.e. high signal intensity on STIR images and low signal intensity on T1-weighted images)	NA	SJC66	NA	Within 1W	k=0 (not specified: -0.98-1)		

					MRI assessment of synovitis in 76 joints (lateral sternoclavicular, acromioclavicular, glenohumeral, elbow, wrist, first CMC, first through fifth MCP, first IP, second through fifth PIP, second through fifth DIP, hip, knee, ankle, first tarsometatarsal (TMT), first through fifth MTP, first through fifth PIP and second through fifth DIP joints of the feet)	NA	TJC68	NA	Within 1W	k=0.12 (not specified: -0.36-0.59)		
					MRI bone marrow oedema (a lesion within the trabecular bone, with ill-defined margins and signal characteristics consistent with increased water content, i.e. high signal intensity on STIR images and low signal intensity on T1-weighted images)	NA	TJC68	NA	Within 1W	k=0.00 (not specified: -0.35-0.35)		
Besselink, 2018	Cross-sectional	RA patients (n=50)	DAS28-ESR 3.9 (1.20)	NR	Optical spectral transmission (OST) model (sum of affected joints)	NA	Clinical swollen joints	NA	Same day	r=0.30 (95%CI 0.11-0.46, p<0.01)	L/H/H/L	H/L/L
					Optical spectral transmission (OST) model (sum of affected joints)	NA	Clinical tender joints	NA	Same day	r=-0.02 (95%CI -0.21-0.17, p=0.84)		
Ceponis, 2014	Cross-sectional	Established RA patients (n=46)	CDAI 15.9; HAQ 0.64	16.6Y	US: total Synovial Hypertrophy score (tSH), range 0-135: Synovial hypertrophy (B-mode examination) was scored on a semiquantitative scale (where 0=absence, 1=mild, 2=moderate, and 3=severe. dorsal and palmar joint regions and ulnar and radial aspects of the interphalangeal and second through fifth PIP joints; dorsal and palmar joint regions of the first through fifth and ulnar and radial aspects of the second and fifth MCP joints; and dorsal and volar joint regions and radial and ulnar aspects of the wrist (distal radioulnar, midcarpal, radiocarpal, and ulnar-carpal) joints were examined in long (sagittal plane) and short (axial plane) axes.	NA	SJC28	NA	NR	r=0.4804, p<0.005	L/L/H/U	H/L/H

Author	Study Design	Population	Follow-up	Outcome	Measure	Score	Scale	Time	Statistical Results	Direction	Direction	
Filer, 2017 ^a	Cross-sectional	RA patients with at least 1 joint amenable to biopsy (n=15)	NR	NR	US: total Synovial Hypertrophy score (tSH), range 0-135: Synovial hypertrophy (B-mode examination) was scored on a semiquantitative scale (where 0=absence, 1=mild, 2=moderate, and 3=severe. orsal and palmar joint regions and ulnar and radial aspects of the interphalangeal and second through fifth PIP joints; dorsal and palmar joint regions of the first through fifth and ulnar and radial aspects of the second and fifth MCP joints; and dorsal and volar joint regions and radial and ulnar aspects of the wrist (distal radioulnar, midcarpal, radiocarpal, and ulnar-carpal) joints were examined in long (sagittal plane) and short (axial plane) axes.	NA	TJC28	NA	NR	r=0.4314, p<0.005	L/U/H/L	H/L/L
					US: total Synovial PD score (tSPD)	NA	SJC28	NA	NR	r=0.6546, p<0.005		
					US: total Synovial PD score (tSPD)	NA	TJC28	NA	NR	r=0.3559, p<0.01		
					US: Sonographic effusion	NA	SJC28	NA	NR	r=0.3270, p<0.05		
					US: Sonographic effusion	NA	TJC28	NA	NR	r=0.3449, p<0.01		
Hammer, 2018 ^a	Cross-sectional	RA patients (n=174)	NR	10Y	GS US (12 joint indices for MCP and wrist joints), score 0-3	NA	SJC28	NA	NR	r=0.78, p<0.01	L/U/H/L	H/L/L
					GS US (12 joint indices for MCP and wrist joints), score 0-3	NA	TJC28	NA	NR	r=0.65, p<0.05		
					PD US (12 joint indices for MCP and wrist joints), score 0-3	NA	SJC28	NA	NR	r=0.76, p<0.05		
					PD US (12 joint indices for MCP and wrist joints), score 0-3	NA	TJC28	NA	NR	ns		
					TJC32 (wrist, MCP1-5, PIP2-3, elbow, knee, ankle and MTP1-5 bilaterally)	Presence/absence	US: GS	0-3	Same day	k 0.21		
TJC32 (wrist, MCP1-5, PIP2-3, elbow, knee, ankle and MTP1-5 bilaterally)	Presence/absence	US: PD	0-3	Same day	k 0.20							
SJC32 (wrist, MCP1-5, PIP2-3, elbow, knee, ankle and MTP1-5 bilaterally)	Presence/absence	US: PD	0-3	Same day	k 0.57							
SJC32 (wrist, MCP1-5, PIP2-3, elbow, knee, ankle and MTP1-5 bilaterally)	Presence/absence	US: PD	0-3	Same day	k 0.56							
Kawashiri, 2011	Cross-sectional	RA patients (n=22)	DAS28 5.69; SDAI 30.6; CDAI 28.3	2.3Y	US: PD in 12 joints, sum score (bilateral elbows (anterior and posterior recess), wrists (dorsal and carpal recess), second and third MCP joints (dorsal and palmar recess), knees (suprapatellar and lateral parapatellar recess) and ankles (anterior tibiotalar recess, medial tendon sheaths and lateral tendon sheaths))	NA	TJC	NA	Same day	r=0.52, p=0.017	L/U/H/L	H/L/H

					US: PD in 12 joints, sum score (bilateral elbows (anterior and posterior recess), wrists (dorsal and carpal recess), second and third MCP joints (dorsal and palmar recess), knees (suprapatellar and lateral parapatellar recess) and ankles (anterior tibiotalar recess, medial tendon sheaths and lateral tendon sheaths))	NA	SJC	NA	Same day	r=0.48, p=0.028			
					US: PD in 6 joints, sum score (bilateral wrists (dorsal recess) and second and third MCP joints (dorsal recess))	NA	TJC	NA	Same day	r=0.50, p<0.05			
					US: PD in 6 joints, sum score (bilateral wrists (dorsal recess) and second and third MCP joints (dorsal recess))	NA	SJC	NA	Same day	r=0.44, p<0.05			
Van Omma, 2016	Case control	RA patients in different categories of disease activity: DAS28<2.6, 2.6-5.1, >5.1 (n=59)	DAS28 3.6	1-9Y (range of medians)	Optical spectral transmission (OST) in ? joints, at patient level	NA	SJC28	NA	Same day (within window of 4h)	r=0.50, p<0.0001	AUC-ROC 0.79 (95%CI 0.72-0.86, p<0.0001)	L/H/H/L	H/L/L
					Optical spectral transmission (OST) in ? joints, at patient level	NA	TJC28	NA	Same day (within window of 4h)	r=0.25, p=0.037	AUC-ROC 0.78 (95%CI 0.71-0.83, p<0.0001)		
Vlad, 2011	Cross-sectional	RA patients with at least one painful or clinically swollen joint (n=42)	DAS28 6.15; CDAI 33.90; SDAI 64.23	64.64M	US: Echographic Score, sum of GS scores (0-3) of 10 joints (MCP2-5 dorsal and volar, PIP2-5 dorsal and volar, radiocarpal dorsal and intercarpal joint dorsal) of both hands	NA	SJC	-	Same day	r=0.432, p=0.004		L/L/H/L	H/L/H
					US: Echographic Score, sum of GS scores (0-3) of 10 joints (MCP2-5 dorsal and volar, PIP2-5 dorsal and volar, radiocarpal dorsal and intercarpal joint dorsal) of both hands	NA	TJC	-	Same day	r=0.430, p=0.004			
					US: Volar echographic Score, sum of GS scores (0-3) of 8 joints (MCP2-5 volar, PIP2-5 volar) of both hands	NA	SJC	NA	Same day	r=0.385, p=0.012			
					US: Volar echographic Score, sum of GS scores (0-3) of 8 joints (MCP2-5 volar, PIP2-5 volar) of both hands	NA	TJC	NA	Same day	r=0.325, p=0.036			
					US: Dorsal echographic Score, sum of GS scores (0-3) of 10 joints (MCP2-5 dorsal, PIP2-5 dorsal, radiocarpal dorsal and intercarpal joint dorsal) of both hands	NA	SJC	NA	Same day	r=0.406, p=0.008			
					US: Dorsal echographic Score, sum of GS scores (0-3) of 10 joints (MCP2-5 dorsal, PIP2-5 dorsal, radiocarpal dorsal and intercarpal joint dorsal) of both hands	NA	TJC	NA	Same day	r=0.476, p=0.001			
Witt, 2016	Cross-sectional	RA patients (n=45)	DAS28 4.1; CDAI 21.2; SDAI 22.5	NR	Automated breast volume scanner (The dorsal and palmar sides of each hand and the dorsal aspect of the toes were scanned)	NA	SJC	NA	NR	r=0.46		L/U/H/U	H/L/L
Biomarker vs imaging													
do Prado, 2016	Cross-sectional	RA patients (n=64)	DAS28-ESR 4.02	5Y	IL-2	NA	US: 10-joint PD score (wrist, MCP2-3, PIP2-3 of both hands)	NA	Same day	r=-0.04 (-0.29-0.22, ns)		L/L/H/L	H/L/L
					IL-2	NA	US: 10-joint GS score (wrist, MCP2-3, PIP2-3 of both hands)	NA	Same day	r=-0.12 (-0.37-0.15, ns)			

					IL-4	NA	US: 10-joint PD score (wrist, MCP2-3, PIP2-3 of both hands)	NA	Same day	r=0.03 (-0.21-0.29), ns		
					IL-4	NA	US: 10-joint GS score (wrist, MCP2-3, PIP2-3 of both hands)	NA	Same day	r=-0.04 (-0.29-0.21), ns		
					IL-6	NA	US: 10-joint PD score (wrist, MCP2-3, PIP2-3 of both hands)	NA	Same day	r=0.33 (0.07-0.56), p<0.01		
					IL-6	NA	US: 10-joint GS score (wrist, MCP2-3, PIP2-3 of both hands)	NA	Same day	r=0.23 (-0.03-0.46), ns		
					IL-10	NA	US: 10-joint PD score (wrist, MCP2-3, PIP2-3 of both hands)	NA	Same day	r=0.04 (-0.21-0.30), ns		
					IL-10	NA	US: 10-joint GS score (wrist, MCP2-3, PIP2-3 of both hands)	NA	Same day	r=-0.08 (-0.34-0.18), ns		
					IL-17	NA	US: 10-joint PD score (wrist, MCP2-3, PIP2-3 of both hands)	NA	Same day	r=0.02 (-0.24-0.27), ns		
					IL-17	NA	US: 10-joint GS score (wrist, MCP2-3, PIP2-3 of both hands)	NA	Same day	r=-0.08 (-0.35-0.17), ns		
					TNF	NA	US: 10-joint PD score (wrist, MCP2-3, PIP2-3 of both hands)	NA	Same day	r=-0.11 (-0.36-0.16), ns		
					TNF	NA	US: 10-joint GS score (wrist, MCP2-3, PIP2-3 of both hands)	NA	Same day	r=-0.15 (-0.39-0.10), ns		
					IFN	NA	US: 10-joint PD score (wrist, MCP2-3, PIP2-3 of both hands)	NA	Same day	r=-0.20 (-0.45-0.09), ns		
					IFN	NA	US: 10-joint GS score (wrist, MCP2-3, PIP2-3 of both hands)	NA	Same day	r=-0.25 (-0.47-0.02), ns		
					VEGF	NA	US: 10-joint PD score (wrist, MCP2-3, PIP2-3 of both hands)	NA	Same day	r=-0.10 (-0.35-0.15), ns		
					VEGF	NA	US: 10-joint GS score (wrist, MCP2-3, PIP2-3 of both hands)	NA	Same day	r=-0.009 (-0.27-0.23), ns		
Kawashiri, 2011	Cross-sectional	RA patients (n=22)	DAS28 5.69; SDAI 30.6; CDAI 28.3	2.3Y	VEGF	NA	US: PD in 12 joints, sum score (bilateral elbows (anterior and posterior recess), wrists (dorsal and carpal recess), second and third MCP joints (dorsal and palmar recess), knees (suprapatellar and lateral parapatellar recess) and ankles (anterior tibiotalar recess, medial tendon sheaths and lateral tendon sheaths))	NA	Same day	r=0.62, p=0.005	L/L/H/L	H/L/H
					MMP-3	NA	US: PD in 12 joints, sum score (bilateral elbows (anterior and posterior recess), wrists (dorsal and carpal recess), second and third MCP joints (dorsal and palmar recess), knees (suprapatellar and lateral parapatellar recess) and ankles (anterior tibiotalar recess, medial tendon sheaths and lateral tendon sheaths))	NA	Same day	r=0.47, p=0.03		
					MMP-9	NA	US: PD in 12 joints, sum score (bilateral elbows (anterior and posterior recess), wrists (dorsal and carpal recess), second and third MCP joints (dorsal and palmar recess), knees (suprapatellar and lateral parapatellar recess) and ankles (anterior tibiotalar recess, medial tendon sheaths and lateral tendon sheaths))	NA	Same day	r=0.38, p=0.08		

Kawashiri, 2011	Cross-sectional	RA patients (n=22)	DAS28 5.69; SDAI 30.6; CDAI 28.3	2.3Y	US: PD in 6 joints, sum score (bilateral wrists (dorsal recess) and second and third MCP joints (dorsal recess))	NA	US: PD in 12 joints, sum score (bilateral elbows (anterior and posterior recess), wrists (dorsal and carpal recess), second and third MCP joints (dorsal and palmar recess), knees (suprapatellar and lateral parapatellar recess) and ankles (anterior tibiotalar recess, medial tendon sheaths and lateral tendon sheaths))	NA	Same day	r=0.92, p<0.0001		L/U/H/L	H/L/H	
Mandl, 2011	SLR: 14 (quantitative analysis: 0)	RA patients (n=1307)	NR	NR	US to assess synovitis using GS (n=1), PD (n=1) or GS+PD (n=12) using different scoring systems (binary (n=8), semiquantitative (n=14), quantitative (n=2), cumulative score of individual joint scores (n=14))	NR	Clinical (n=13), laboratory (n=13), X-ray (n=3), US (n=1) or MRI (n=6)	NR	NR		US can be regarded as a valuable tool for globally examining the extent of synovitis in RA. However, it is presently difficult to determine a minimal number of joints to be included in a global US score. Further validation of proposed scores is needed.	Moderate	Moderate	-
Ngai ng, 2019*	Cross-sectional	RA patients (n=19)	DAS28-CRP 4.66, median	5.5Y, median	Whole body magnetic resonance imaging: sum-score of 26 joints (28 conventional joints minus elbows), joint inflammation was defined in two ways; 1) as presence of synovitis and/or osteitis, 2) as the presence of synovitis only (28 conventional joints, bilateral ankles, MTP1-5)	NA	Ultrasound: sum-score of 28 joints (conventional joints; US was graded 0-3 on both B-mode and colour Doppler(CD), and subsequently converted to +/- by defining US synovitis as B mode ≥2 or CD ≥1)	NA	NR	r=0.72, p=0.003		L/U/H/U	H/L/H	
					Whole body magnetic resonance imaging: sum-score of 26 joints (28 conventional joints minus elbows), joint inflammation was defined as the presence of synovitis (28 conventional joints, bilateral ankles, MTP1-5)	NA	Ultrasound: sum-score of 28 joints (conventional joints; US was graded 0-3 on both B-mode and colour Doppler(CD), and subsequently converted to +/- by defining US synovitis as B mode ≥2 or CD ≥1)	NA	NR	r=0.07, p=0.78				
Schäfer, 2013	Cross-sectional	RA patient (n=18)	DAS28 4.6 (1.6)	4.9Y	Fluorescence optical imaging (FOI): Fluorescence readout of indocyanine green in phase 1 (1-120 seconds) of five joints (wrist, MCP2-3, PIP2-3), at patient level	>1.2	MRI of carpal, MCP and PIP joints of dominant hand, at patient level	Presence/absence (RAMRIS)	Within 2D	66 (48-80)	AUC-ROC 0.58	L/H/H/L	H/L/L	
					Fluorescence optical imaging (FOI): Fluorescence readout of indocyanine green in phase 2 (121-240 seconds) of five joints (wrist, MCP2-3, PIP2-3), at patient level	>1.2	MRI of carpal, MCP and PIP joints of dominant hand, at patient level	Presence/absence (RAMRIS)	Within 2D	71 (36-92)	AUC-ROC 0.65			
					Fluorescence optical imaging (FOI): Fluorescence readout of indocyanine green in phase 3 (241-360 seconds) of five joints (wrist, MCP2-3, PIP2-3), at patient level	>1.2	MRI of carpal, MCP and PIP joints of dominant hand, at patient level	Presence/absence (RAMRIS)	Within 2D	67 (51-79) 77 (62-88)	AUC-ROC 0.67			
Vlad, 2011	Cross-sectional	RA patients with at least one painful or clinically swollen joint (n=42)	DAS28 6.15; CDAI 33.90; SDAI 64.23	64.64M	US: Echographic Score, sum of GS scores (0-3) of 10 joints (MCP2-5 dorsal and volar, PIP2-5 dorsal and volar, radiocarpal dorsal and intercarpal joint dorsal) of both hands	NA	US: Number of echographically Positive Joints for synovitis of 10 joints (MCP2-5 dorsal and volar, PIP2-5 dorsal and volar, radiocarpal dorsal and intercarpal joint dorsal) of both hands	>0.5 mm	Same day	r=0.935, p<0.001		L/U/H/L	H/L/H	
					US: Echographic Score, sum of GS scores (0-3) of 10 joints (MCP2-5 dorsal and volar, PIP2-5 dorsal and volar, radiocarpal dorsal and intercarpal joint dorsal) of both hands	NA	US: Number of volar echographically Positive Joints for synovitis of 8 joints (MCP2-5 volar, PIP2-5 volar) of both hands	>0.5 mm	Same day	r=0.868, p<0.001				

					US: Echographic Score, sum of GS scores (0-3) of 10 joints (MCP2-5 dorsal and volar, PIP2-5 dorsal and volar, radiocarpal dorsal and intercarpal joint dorsal) of both hands	NA	US: Number of dorsal echographically Positive Joints for synovitis of 10 joints (MCP2-5 dorsal, PIP2-5 dorsal, radiocarpal dorsal and intercarpal joint dorsal) of both hands	>0.5 mm	Same day	r=0.848, p<0.001		
					US: Volar echographic Score, sum of GS scores (0-3) of 8 joints (MCP2-5 volar, PIP2-5 volar) of both hands	NA	US: Number of echographically Positive Joints for synovitis of 10 joints (MCP2-5 dorsal and volar, PIP2-5 dorsal and volar, radiocarpal dorsal and intercarpal joint dorsal) of both hands	>0.5 mm	Same day	r=0.851, p<0.001		
					US: Volar echographic Score, sum of GS scores (0-3) of 8 joints (MCP2-5 volar, PIP2-5 volar) of both hands	NA	US: Number of volar echographically Positive Joints for synovitis of 8 joints (MCP2-5 volar, PIP2-5 volar) of both hands	>0.5 mm	Same day	r=0.917, p<0.001		
					US: Volar echographic Score, sum of GS scores (0-3) of 8 joints (MCP2-5 volar, PIP2-5 volar) of both hands	NA	US: Number of dorsal echographically Positive Joints for synovitis of 10 joints (MCP2-5 dorsal, PIP2-5 dorsal, radiocarpal dorsal and intercarpal joint dorsal) of both hands	>0.5 mm	Same day	r=0.653, p<0.001		
					US: Dorsal echographic Score, sum of GS scores (0-3) of 10 joints (MCP2-5 dorsal, PIP2-5 dorsal, radiocarpal dorsal and intercarpal joint dorsal) of both hands	NA	US: Number of echographically Positive Joints for synovitis of 10 joints (MCP2-5 dorsal and volar, PIP2-5 dorsal and volar, radiocarpal dorsal and intercarpal joint dorsal) of both hands	>0.5 mm	Same day	r=0.859, p<0.001		
					US: Dorsal echographic Score, sum of GS scores (0-3) of 10 joints (MCP2-5 dorsal, PIP2-5 dorsal, radiocarpal dorsal and intercarpal joint dorsal) of both hands	NA	US: Number of volar echographically Positive Joints for synovitis of 8 joints (MCP2-5 volar, PIP2-5 volar) of both hands	>0.5 mm	Same day	r=0.647, p<0.001		
					US: Dorsal echographic Score, sum of GS scores (0-3) of 10 joints (MCP2-5 dorsal, PIP2-5 dorsal, radiocarpal dorsal and intercarpal joint dorsal) of both hands	NA	US: Number of dorsal echographically Positive Joints for synovitis of 10 joints (MCP2-5 dorsal, PIP2-5 dorsal, radiocarpal dorsal and intercarpal joint dorsal) of both hands	>0.5 mm	Same day	r=0.923, p<0.001		
Van Onna, 2016	Case control	RA patients in different categories of disease activity: DAS28<2.6, 2.6-5.1, >5.1 (n=59)	DAS28 3.6	1-9Y (range of medians)	Optical spectral transmission (OST) in PIP, MCP and wrist joints, at patient level	NA	US: GS and PD in MCP, PIP and wrist joints, at patient level	US inflammation: GS>1 and/or PD>0	Same day (within window of 4h)	r=0.64, p<0.0001	AUC-ROC 0.81 (95%CI 0.77-0.84, p<0.0001)	L/H/H/L
					Optical spectral transmission (OST) in PIP, MCP and wrist joints, at patient level	NA	US: GS in MCP, PIP and wrist joints, at patient level	US inflammation: GS>1 and/or PD>0	Same day (within window of 4h)	r=0.61, p<0.0001		
					Optical spectral transmission (OST) in PIP, MCP and wrist joints, at patient level	NA	US: PD in MCP, PIP and wrist joints, at patient level	US inflammation: GS>1 and/or PD>0	Same day (within window of 4h)	r=0.62, p<0.0001		
					Optical spectral transmission (OST) in PIP, MCP and wrist joints, at patient level	NA	US: GS and PD in MCP, PIP and wrist joints, semi-quantitative score (0-3 per joint), at patient level	NA	Same day (within window of 4h)	r=0.60, p<0.0001		
					Optical spectral transmission (OST) in PIP, MCP and wrist joints, at patient level	NA	US: GS in MCP, PIP and wrist joints, semi-quantitative score (0-3 per joint), at patient level	NA	Same day (within window of 4h)	r=0.57, p<0.0001		

Witt, 2016	Cross-sectional	RA patients (n=45)	DAS28 4.1; CDAI 21.2; SDAI 22.5	NR	Optical spectral transmission (OST) in PIP, MCP and wrist joints, at patient level	NA	US: PD in MCP, PIP and wrist joints, semi-quantitative score (0-3 per joint), at patient level	NA	Same day (within window of 4h)	r=0.63, p<0.0001	L/U/H/U	H/L/L
					Automated breast volume scanner (The dorsal and palmar sides of each hand and the dorsal aspect of the toes were scanned)	NA	US (wrists, MCP, PIP and MTP joints)	NA	Same day	r=0.79		
Imaging vs histology												
Ostendorf, 2001	Cross-sectional	RA patients (n=22)	DAS 4.15	6.42Y	Miniarthroscopy: Extent of synovitis (2nd MCP joint of dominant hand)	NA	MRI: Synovial proliferation (MCP2-5 of dominant hand), sum of score 0-3 per joint	NA	Miniarthroscopy y 24h after MRI	p=0.001	L/L/H/L	H/L/L
					Miniarthroscopy: Extent of hyperaemia (2nd MCP joint of dominant hand)	NA	MRI: Synovial proliferation (MCP2-5 of dominant hand), sum of score 0-3 per joint	NA	Miniarthroscopy y 24h after MRI	p=0.0038		
					Miniarthroscopy: Vascularity (2nd MCP joint of dominant hand)	NA	MRI: Synovial proliferation (MCP2-5 of dominant hand), sum of score 0-3 per joint	NA	Miniarthroscopy y 24h after MRI	p=0.0058		
					Miniarthroscopy: Synovial thickening (2nd MCP joint of dominant hand)	NA	MRI: Synovial proliferation (MCP2-5 of dominant hand), sum of score 0-3 per joint	NA	Miniarthroscopy y 24h after MRI	p=0.0063		

ACPA: anti-citrullinated protein antibody; AUC-ROC: area under the curve - receiver operating characteristic; BL: baseline; BMI: body mass index; CDAI: clinical disease activity index; CI: confidence interval; CMC: carpometacarpal; CRP: C-reactive protein; D: days; DAS28: disease activity score assessing 28 joints; DIP: distal interphalangeal; ESR: erythrocyte sedimentation rate; GS: Gray scale; h: hours; H: high; IFN: interferon; IL: interleukin; IP: interphalangeal; IQR: interquartile range; k: kappa agreement; l: liter; L: low; M: months; MBDA: multi-biomarker disease activity score; MCP: metacarpophalangeal; mm: millimeter; MMP: matrix metalloproteinase; MRI: magnetic resonance imaging; MTP: metatarsophalangeal; n: number of patients; NA: not applicable; ng: nanogram; NPV: negative predictive value; NR: not reported; ns: not significant; OR: odds ratio; PD: power doppler; PIP: proximal interphalangeal; PPV: positive predictive value; RA: rheumatoid arthritis; RAPID3: routine assessment of patient index data 3; RAMRIS: rheumatoid arthritis MRI scoring system; RF: rheumatoid factor; s: significant; RoB: risk of bias; SDAI: simplified disease activity index; SIC: swollen joint count; SLR: systematic literature review; STIR: short tau inversion recovery; TIMP: tissue inhibitor of metalloproteinase; TJC: tender joint count; TMT: tarsometatarsal; TNF: tumor necrosis factor; U: unclear; US: ultrasonography; VEGF: vascular endothelial growth factor; W: weeks; Y: years; ^: abstract.

1. Risk of Bias according to QUADAS-2 for individual studies: Patient selection/Index test/Reference standard/Flow and timing; According to AMSTAR2 tool for SLRs: Low=zero or one non-critical weakness; Moderate=more than one non-critical weakness; High=one critical flaw with or without non-critical weaknesses; Critically high=more than one critical flaw with or without non-critical weaknesses; 2. Only applicable for SLRs: Summary of RoB of individual studies, as assessed in SLR Highest risk of bias as found (of individual studies). 3. Concerns regarding applicability for individual studies: Patient selection/Index test/Reference standard.