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The role of whole-body MRI in musculoskeletal inflammation detection and treatment response evaluation in inflammatory arthritis across age: A systematic review

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ABSTRACT

Objective: To evaluate the relation between whole-body MRI (WBMRI) outcomes and disease activity measures, including clinical examination, composite scores, and other imaging outcomes, and the ability of WBMRI to detect treatment response in patients with inflammatory arthritis (IA) across age.
Methods: Human studies published as full text or abstract in the PubMed and MEDLINE and Cochrane databases from inception to 11th April 2021 were systematically and independently searched by two reviewers. Studies including patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), spondyloarthritis (SpA), juvenile idiopathic arthritis (JIA) or unclassified inflammatory arthritis (UA) who underwent WBMRI and which reported on disease outcomes were included.
Results: Nineteen full-text studies were eligible for inclusion: 2 interventional, 7 retrospective and 10 prospective observational studies, comprising 540 participants (SpA 38.7%, RA 24.8%, JIA 17.8%, PsA 11.5%, healthy controls 5.9%, UA 1.3%). Abstracts of 6 conference papers were reported separately. Five studies in PsA and SpA and 4 in RA measured the frequency of WBMRI-detected and clinically-detected synovitis, and all found the former to be more frequent. Less enthesitis was detected by WBMRI than clinical examination in 5/8 studies. After biologic treatment, the WBMRI inflammation scores declined in 3 studies in SpA and 2 in RA, whilst in 3 studies the results were equivocal.
Conclusion: The ability of WBMRI to assess disease activity and treatment response in IA was adequate overall. Further studies are needed to corroborate WBMRI findings with IA outcomes and investigate the clinical value of subclinical inflammation.

Introduction

Imaging has become an integral part of the management of inflammatory arthritis (IA), not only for diagnostic purposes but increasingly for the monitoring of disease activity. There is evidence that definitions of clinical remission in rheumatoid arthritis (RA) might not be sufficient to rule out ongoing subclinical disease activity which leads to structural damage [1–3] and that subclinical synovitis predicts development of RA [4]. On the other hand, there is also a risk of overestimating disease activity in patients with coexistent fibromyalgia clinically, which is a prevalent comorbidity in inflammatory arthritis [5].

Therefore, there have been many initiatives to develop and validate disease-specific imaging outcomes that can be used in clinical trials to assess reliably the effectiveness of pharmacological treatments for the different types of IA. These proposals often originated from an international initiative aiming to establish Outcome Measures in Rheumatology, known as OMERACT. Magnetic Resonance Imaging (MRI) is a sensitive imaging technique for detecting synovitis, as well as soft tissue inflammation, and is the preferred method for detecting bone marrow oedema (BMO) or osteitis, which is a cardinal feature of enthesitis, sacroiliitis and spinal inflammation, and part of the inflammatory process in joints. Examples of MRI outcomes include the OMERACT RA MRI score (RAMRIS) [6] and Psoriatic Arthritis MRI score (PsAMRIS) [7], which derive from MRI hand examinations, whereas in axSpA there are various semi-quantitative methods to measure the burden of acute inflammation and damage

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in the spine and sacroiliac joints (SIJ) [8–12] from dedicated MRI scans.

However, these scores might lead to an under- or over-estimation of the overall disease activity, as IA (depending on the clinical phenotype) have a varying musculoskeletal distribution. Whole-body MRI (WBMRI) is a relatively new technique which offers the opportunity to evaluate the entheses, peripheral joints and the axial skeleton within one examination. OMERACT has proposed protocol sequences and a scoring methodology based on the evaluation of BMO, soft tissue inflammation and synovitis in the peripheral joints and entheses on WBMRI [13]. It remains unclear however, how WBMRI-detected inflammation compares to clinical and conventional imaging outcomes, as well as whether WBMRI can detect changes in the disease activity.

The purpose of this systematic review is to assess the performance of WBMRI in assessing musculoskeletal inflammation and structural changes in IA across age, in comparison with clinical outcomes and other imaging methods (where available), as well as investigate the ability of WBMRI to detect treatment response.

Methods

The protocol for the systematic review was registered in PROSPERO (CRD42019116783).

Search strategy

We designed a comprehensive search for the databases MEDLINE, EMBASE and Cochrane Library from their inception to 11th April 2021 without imposing any language restrictions. Conference abstracts were included if the reported results were not otherwise available in full-text publications.

The search terms for each database are described in Supplementary Data S1, but in summary they consisted of a variety of different terms for (a) whole-body MRI and (b) types of IA across age, or synovitis, or enthesitis. We also searched manually for clinical trials, theses and dissertations, conference papers and citations of the included manuscripts and relevant reviews (details available in the supplementary material).

Eligibility criteria for study inclusion

We included studies of any design but excluded case reports. Studies were eligible if they included patients with inflammatory arthritis (IA): RA, spondyloarthritis (SpA), psoriatic arthritis (PsA), JIA and unclassified inflammatory arthritis (irrespective of including or not healthy controls) who underwent at least one WBMRI scan, and provided information on either of the following domains:

(1) Any type of disease activity outcome measures (validated or not): e.g. patient-reported outcomes, such as the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), physician-reported outcomes, such as swollen joint count (SJC), or composite scores such as the Disease Activity Score-28 (DAS-28)

(2) Imaging outcomes of any type, in addition to WBMRI, such as radiography, MRI of specific body areas, ultrasound and nuclear medicine scans.

We excluded studies that did not provide information on any of our outcomes of interest described below. The abstracts and full texts were screened independently by two reviewers (VC, AVM). In cases of disagreement, a third senior reviewer (CC) decided on the inclusion of studies.

Outcomes of interest, data collection, and synthesis

Data were collected independently by two reviewers (VC and AVM) using the same data extraction sheet (available upon request from the authors). The outcomes of interest were: (1) the relation between WBMRI and clinical disease activity measures, (2) the relation between WBMRI and conventional imaging findings where available, and (3) the assessment of treatment response by WBMRI, and its relationship with clinical response; we applied no restrictions on treatment type. Other data items collected comprised of study characteristics (study design, number of patients and controls, inclusion criteria, number and timing of scans, other imaging for comparison), patient characteristics (age, type of IA, baseline disease activity measures, medications), WBMRI protocol parameters (sequences, planes, scan duration, gadolinium administration, field strength, coverage of joints, spine and entheses), reporting methodology (number of readers, independent or consensus reading, blinding, inflammatory and structural lesions, scoring methodology), WBMRI findings (enthesitis, synovitis, spinal inflammation, damage) in patients and controls. The heterogeneity between studies was assessed with regards to the participants' characteristics, selected clinical and WBMRI measures, statistical analysis, and study quality. The data synthesis was qualitative due to the great heterogeneity of clinical and WBMRI outcomes, which did not make a meta-analysis feasible. A descriptive analysis per type of IA for the outcomes 1 and 3 was performed, where possible.

Bias and quality assessment

We selected the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool to assess the quality of studies [14,15]. Two reviewers (VC and AVM) performed the quality assessment independently for all studies and a consensus decision for each rating was reached in cases of disagreement. In terms of sensitivity analysis, the quality assessment for each study was taken into consideration for the synthesis of the results and for the identification of research gaps that need to be addressed.

Results

Selected studies and patients' characteristics

Nineteen studies were included in the final systematic review. Fig. 1 details the number of studies included and excluded, with reasons for exclusions. These 19 studies, including one sub-study [16] of a main study [17], correspond to 25 individual publications, as non-overlapping results from four studies were reported in 10 different papers, none of which could be excluded as duplicate. Of the 25 publications, 17 were peer-reviewed manuscripts, 7 were conference papers [18–23], one was a letter to the editor [24],

Only two additional conference abstracts were identified manually, as these were already identified via Embase, or because a full-text manuscript was included from the same study. Some studies [25–29,30–33] were excluded as the protocol or the analysis focused only on one region.

The study and patient characteristics are summarised in Table 1. In terms of design, two studies were interventional, seven retrospective and 10 prospective observational studies. In total, 540 participants were included in the systematic review. Seven studies involved patients with a diagnosis of RA and six studies with adult-onset SpA, albeit with a total number of 209 SpA and 134 RA patients. Other IA types were as follows: JIA in five studies (96 patients), adult-onset PsA in three studies (62 patients), and undifferentiated arthritis in one study (7 patients). Three studies recruited 32 healthy controls (HCs) in addition to patients. Most of the studies (10/19) involved patients with a mean/median disease duration of less than 5 years. In

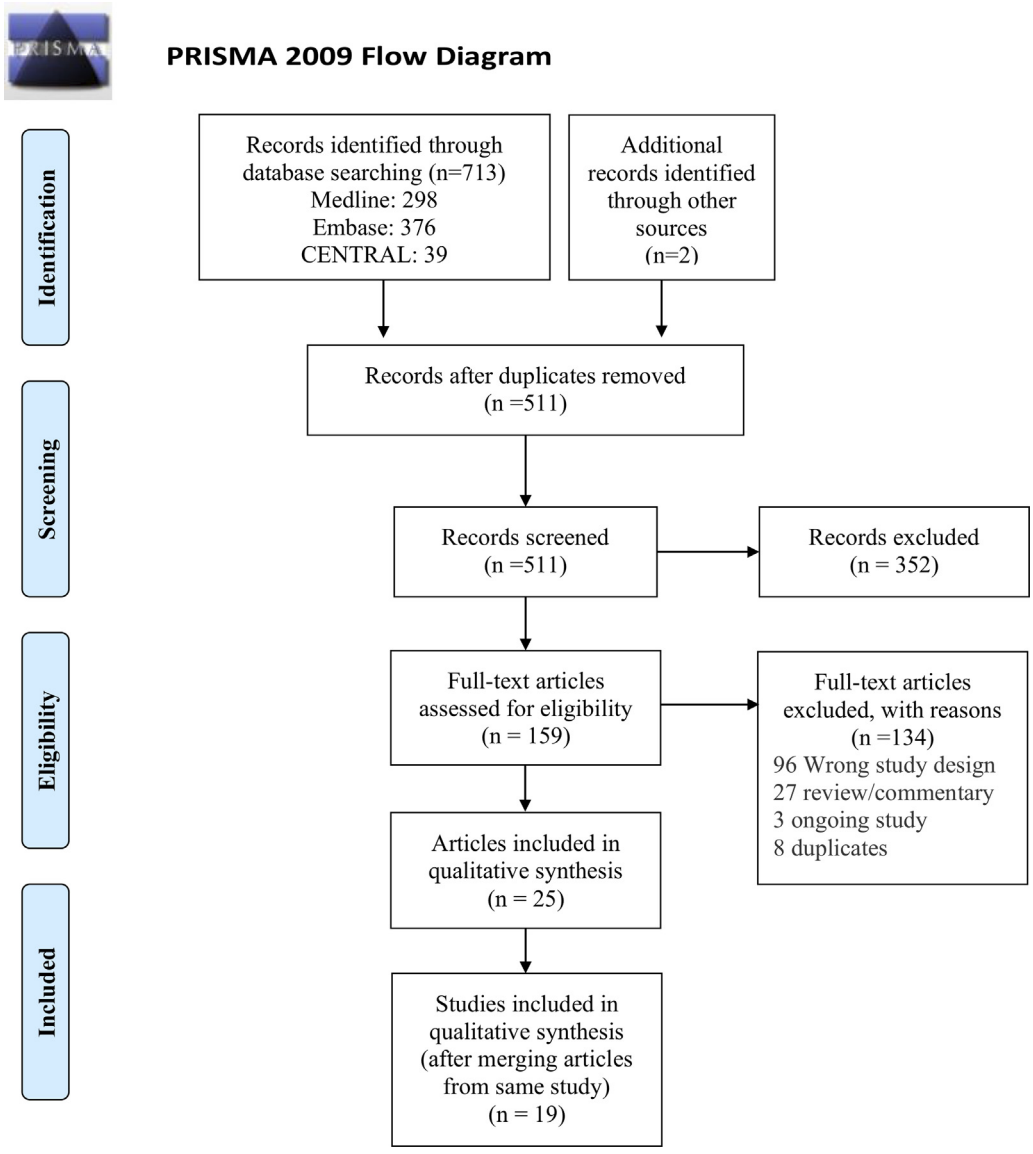

Fig. 1. PRISMA flow diagram of selected records for systematic review.

six studies of RA patients, the baseline mean/median DAS28-ESR or DAS28-CRP was recorded and corresponded to moderate or high disease activity. Similarly, the mean/median BASDAI was available in five studies with SpA patients and indicated active disease. All five studies including JIA patients were only published as conference papers. In six observational and two interventional studies, patients with different types of IA underwent WBMRI before and after starting various biologic treatments.

Whole-body MRI protocols

Seventeen studies provided at least a partial description of the WBMRI protocol used, which accounted for 13 protocols, listed in Table 2. Post-contrast images were acquired according to nine protocols, along with short tau inversion recovery (STIR) sequences in five of them, and fat suppressed T2-weighted (T2W) imaging in one protocol. In the remaining non-contrast protocols, STIR sequences were used for the detection of inflammation, as well as diffusion weighted imaging (DWI) in one study. The scan duration ranged from less than 30 to 65 min. The elbows, followed by the toes were frequently not in the field of view, whereas the temporomandibular joints (TMJs) were not covered in most protocols.

Quality assessment

The QUADAS-2 assessment is summarised in Supplementary Table S1, along with the key issues identified. The quality assessment of the abstracts was restricted by the limited information available.

Relationship with clinical findings

Seventeen of 25 articles (16 studies) included information about the relation between clinical and WBMRI examination findings; of those five recruited RA, five SpA, one PsA, three JIA, one SpA and PsA and one JIA and SpA patients. A summary of the findings is presented in Table 3.

In RA, three studies presented results on the frequency of MRI synovitis and clinical swelling. Two studies [17,34] reported a numerically higher (mean or median) number of synovitic joints on MRI per patient than SJC and a third study found a higher frequency of synovitis per joint detected by MRI than due to swelling, for most joints

TABLE 1
Characteristics of studies evaluating the use of whole-body MRI in IA across age

Author, year, reference	Disease	Study design	WBMRI timepoints	Number of participants	Age, years	Male sex, N (%)	Disease duration, years (unless otherwise indicated)	Disease activity (baseline)	Treatment at baseline and/or started during the study
Axelsen, 2014 (35)	RA	Cross-sectional	one	20	median (range): 54 (21-76)	6 (30)	median (range): 6 (1-20)	DAS28-CRP, median (range): 4.3 (1.91-7.32)	MTX n=9, HCQ n=1, MTX and SSZ n=2, TNFi monotherapy n=1, TNFi+DMARDs n=5, rituximab n=1. Prednis- olone 2.5-5 mg/day, n=3.
Axelsen, 2017 (17)	RA	Multi-centre, prospective	0, 6, 16, and 52 weeks	37	median (range): 53 (26-77)	5 (14)	median (range): 4.5 (0-32)	DAS28-CRP, median (range): 4.8 (3.5 – 7.3)	ADA started
Freeston, 2012[a] (21)	RA, UA	Prospective	one	15 (8 RA, 7 UA)	N.A.	N.A.	N.A (new patients early arthritis clinic)	N.A.	N.A.
Kamishima, 2010 (34)	Unclassified arthritis, diagnosed with RA within 2 years	Single centre, retrospective	one	17	median (range): 65 (38–77)	5 (29)	median (range), 3 (1–6) months	DAS28-CRP, median (range): 3.55 (1.82-	N.A.
Kamishima, 2013 (24)	RA	Retrospective	baseline and follow-up (unclear interval)	12	median (range), 60 (35–73)	2 (16.7)	Median (range) symptom duration 55 (7–276) months	N.A.	IFX n=10, ETN n=4, all on MTX
Kono, 2017, Kono, 2014[a] (45)	RA	Single-centre, retrospective	0, 1 year	30	mean (SD) 57.1 (17.9)	2 (6.6)	median (range): 3.1 (0.9–11.0)	DAS28-ESR, mean (SD): 5.31 (1.29)	77% bDMARDs-naïve, 73% MTX at baseline. Started TCZ (n=21), ETN (N=5), IFX (N=4)
Ng, 2020 (16)	RA	Substudy (Axelsen, 2017)	0 and week 16	18	median (range) 54.5 (26–73)	2 (11)	median (range): 4.5 (1–28)	median (range) DAS28-CRP 4.52 (3.48–6.66)	ADA started
Poulsen, 2021 (43)	RA, PsA, HC	Two clinics, prospective	0 and week 1	40 (14 PsA, 10 RA, 16 HC)	median (range) PsA 48 (31-68), RA 49 (26-58), HC (23-54	PsA: 4(29), RA: 2 (20), HC: 7(44)	symptoms duration, median (range) PsA: 10 (0-24), RA: 7 (3-24)	SJC 0-76/TJC (0-78)/ entheses (0-33), median (range) PsA:5 (2-12)/ 11 (3-24)/ 10 (0-21), RA: 6(3-15), 8(3-31), 4(0-14), HC: 0 (0-0), 0 (0-1), 0(0-3)	N.A.
Karpitshka, 2013 (40)	AS	Single centre, prospective	0, 26 and 52 weeks	10	mean ± SEM (range): 40 ± 11 (26.9-62.5)	4 (40)	Less than 5 years	BASDAI, mean ± SEM (range): 5.5±0.5 (3.3–8.0)	ETN started
Krabbe, 2018 (44) Krabbe 2020 (39)	AxSpA	Randomised, double-blind, placebo-controlled, investigator-initiated trial (NCT01029847)	0,6,24,48 weeks	49 (25 ADA, 24 placebo)	mean (SD): ADA: 39.9 (10.8), Placebo35.1 (7.8)	ADA: 15 (60), placebo: 10 (42)	symptom duration, mean (SD) ADA 13.8 (13.4), placebo 10.4 (7.1)	BASDAI, mean: 6.3 (ADA), 6.4 (placebo)	ADA or placebo started
Krabbe, 2020 (41)	AxSpA	Investigator-initiated cohort study (NCT02011386)	0,4,16,52 weeks	53	mean (median, IQR): 37.5 (35, 28–44)	28 (53)	symptom duration, mean (median, IQR): 8.1 (5.1, 2.6–12.8)	Mean (median, IQR) BASDAI: 6.2 (6.2, 5.1–7.1)	SSZ n=2, MTX n=1, LEF=1, no csDMARD n=49 at baseline, GOL started

(*continued on next page*)

TABLE 1 (*Continued*)

Author, year, reference	Disease	Study design	WBMRI timepoints	Number of participants	Age, years	Male sex, N (%)	Disease duration, years (unless otherwise indicated)	Disease activity (baseline)	Treatment at baseline and/or started during the study
Poggenborg, 2015 (38) (42)	PsA, SpA, HC	Pilot	one	48 (18 PsA, 18 SpA, 12 HC)	median (IQR) PsA: 49 (37-58), SpA: 42 (32-52), HC: 32 (27-47)	PsA: 7 (39), SpA: 10 (56), HC: 4 (33)	symptom duration, median (IQR) PsA: 4 (2-14), SpA: 16 (8-27)	BASDAI (0-100 mm)/ SJC (0-76)/TJC (0-78), median: PsA: 44/5/13 SpA: 56/1/4 HS: 2/0/0	N.A.
Song, 2011 (46) Althoff, 2013 (77) Althoff, 2016 (37) Song, 2015 (78)	SpA (AS and nr-axSpA)	Multi-centre, randomised open label trial (NCT00844142)	0,24 and 48 weeks, year 2, year 3	76 (40 ETN, 36 SSZ)	mean (SD): 33.7 (8.5)	44 (57.9)	mean (SD): 2.9 (1.7)	BASDAI, mean (SD): 5.5 (1.3) ETN, 6.0 (1.2) SSZ	ETN or SSZ started
Weckbach, 2011 (36)	PsA	Single centre, prospective	one or two (follow-up scan in 3 patients)	30	Mean (range): 47 (25-78)	17 (56.7)	N.A.	N.A.	N.A.
Arcuri, 2016*[a](20)	JIA	Retrospective	one	24	median 11.7	N.A.	N.A.	N.A.	N.A.
Choida, 2021[a] (23)	JIA	One clinic, prospective	one	32	Mean (SD): 18.7 (2.5)	15 (46.9)	Mean (SD): 10.3 (6.2)	Mean (SD) JADAS10-CRP: 6.7 (6.1)	csDMARDs only n=8 (25%), bDMARDs only n=9 (28.1%), combination n=9 (28.1%), neither n=6 (18.8%)
Rachils 2011[a] (19)	Retrospective	one	23	Mean (SD) 12.6 (2.1)	19 (83)	mean (SD):18.2 (19.1) months	65% had arthritis and 52% enthesitis	78% NSAIDs, 52% DMARDs, 9% TNFi	
Srinivasalu 2012[a] (18)	Retrospective (patients selected from cohort study)	one	13 patients, 4 HC	N.A.	66%	median (IQR): 36 (17.5-108) months	All patients had at least one tender enthesis on exam; 77% had more than 4 tender entheses.	N.A.	
Yutong 2019[a] (22)	Retrospective	one to four	7	Medina (range) 11 (3-16)	N.A.	N.A.	N.A.	N.A.	

ADA,: adalimumab, axSpA: axial SpA, AS:: ankylosking spondylitis, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, bDMARD: biologic DMARD, CRP: c-reactive protein, csDMARD: conventional synthetic DMARD, CRP: c-reactive protein DAS28-CRP disease activity score 28 joints-CRP, DAS28-ESR: disease activity score 28- erythrocyte sediment ratio, DMARD: disease modifying antirheumatic drug, ERA: enthesitis related arthritis, ETN: etanercept, GOL: golimumab, HC: healthy control, HCQ: hydroxychloroquine, IFX: infliximab, IQR: interquartile range, JADAS10-CRP: juvenile arthritis disease activity score 10 joints-CRP, JIA: juvenile idiopathic arthritis, MTX: methotrexate, n: number, N.A: not available, nr-axSpA: non-radiographic axSpA, NCT: National Clinical Trial (registration number), NSAIDs: non-steroidal anti-inflammatory drugs, PsA: psoriatic arthritis, RA: rheumatoid arthritis, SD: standard deviation, SEM: standard error of mean, SJC: swollen joint count, SpA: spondyloarthritis, SSZ: sulfasalazine, TCZ: tocilizumab, TJC: tender joint count, TNFi: tumour necrosis factor alpha inhibitors, UA: undifferentiated arthritis, USpA: undifferentiated SpA

[a] Conference abstracts

Table 2
Whole-body MRI protocols used across various eligible IA studies.

Author, ref	Disease	Field strength	Sequences	Planes	Time	Coverage/stations	Gd
Song, 2011 [46] **Althoff, 2013 [77]** **Althoff, 2016 [37]** **Song, 2015 [78]**	SpA	1.5T	T1W fast SE, STIR	coronal (whole-body), sagittal (whole spine), oblique coronal (SIJ), oblique sagittal (hindfoot) (79)	65 mins	Head, neck, chest and chest wall, abdomen, pelvis lower extremities (excluding elbows, hands and toes)	No
Axelsen, 2014 [35]	RA	3T	Pre and post contrast T1W, STIR	axial (feet), sagittal (cervical, upper thoracic) and coronal (thoracic spine/shoulders, lumbar spine, pelvis/ hands, knees). Hands positioned under pelvis	60 min	1.feet, 2. knees, 3. pelvis/ hips/SIJ/hands, 4. lumbar spine, 5. thoracic spine and shoulders and 6. cervical /upper thoracic spine.	Yes
Axelsen, 2017 (17) Poggenborg, 2015 [38,42] **Ng, 2020 (16)**	RA RA, PsA RA	3T	Pre and post contrast T1W SE. Post contrast only for hips, hands, knees, feet	coronal (spine, elbows, hips/hands, knees, ankles), sagittal (neck) and axial (feet)	60–61 min	1.cervical, 2. thoracic, 3. lumbar spine, 4. hips/ hands, 5. knees, and 6. feet	Yes
Kamishima, 2010 [34] **Kamishima, 2013 (24)** **Kono 2017 [45]**	RA	1.5T	Post-contrast, fat suppressed T1W SE, additional GRE sequences for feet	axial (AA joint, shoulder, feet), coronal (hands, hips, knees). Hands on a stand over pelvis	Less than 30 mins	AA joint, shoulders, wrists, metacarpal and proximal IP joints, hips, knees, and MTP joints (13 body regions)	Yes
Karpitshka, 2013 (40)	AS	1.5T	Pre and post contrast T1W turbo SE, STIR	sagittal (spine and sacrum), coronal (shoulder girdle, pelvis, hips, knees, ankles), sagittal and coronal (post-contrast images)	N.A.	Spine and SIJ, shoulder girdle, pelvis, hips, knees, ankles	Yes
Weckbach, 2011 [36]	PsA	1.5T	STIR, pre and post contrast GRE VIBE, dynamic sequence of most painful region	coronal (shoulder girdle, pelvis, knees, ankles/ feet and hands), sagittal (spine) Hands upon pelvis	45 min	Shoulders/STJs/ ACJs, hips/ symphysis pubis/SIJ, knees, ankles/feet and hands, spine	Yes
Krabbe, 2018 [44], **Krabbe 2020 [39]**	AxSpA	3T	Pre and post contrast T1W SE without fat saturation and STIR	coronal (shoulders/c-spine, thoracic, lumbar/ SIJ, hips/hands, knees, feet), sagittal (shoulders/c-spine), axial (feet)	N.A.	1.C-spine/shoulders, 2. thoracic, 3. lumbar, SIJ, pelvis, 4. hips and hands, 5. knees, 6. ankles and feet	Yes
Krabbe, 2020 [41,80]	AxSpA	3T	T1W SE, STIR	coronal (shoulders, chest wall, hands, pelvis, feet) and sagittal (knees, ankles), sagittal spine/semi-coronal SIJ Hands under pelvis	52 min 11 s.	shoulders and chest wall, hands, pelvis, knees, ankles, feet	No
Poulsen, 2021 [43]	RA, PsA	3T	STIR and pre and post contrast T1W SE	coronal (shoulders, anterior chest wall, pelvis, hips, hands), sagittal (cervical, thoracic, lumbar spine, knees, ankles), axial (ankles, feet). Hands positioned behind the buttocks	N.A.	shoulders and anterior chest wall, thoracic and lumbar spine, pelvis and hips, hands, knees, ankles, feet.	Yes
Arcuri, 2016[a] [20]	JIA	1.5T	T1W, STIR, DWI	N.A.	N.A.	N.A.	No
Freeston, 2012[a] **[21]**	RA	3 T	T2W FS (spine, SIJ), post-contrast VIBE Dixon (peripheral joints, entheses)	N.A.	N.A.	shoulder, STC, wrist, MCP, PIP, hip, knee, ankle, mid/hind foot, MTP, IP joints, spine and sacroiliac joints	Yes
Choida, 2021[a] [23]	JIA	N.A.	Post-contrast mDixon	N.A.	N.A.	81 joints	Yes

AA: atlantoaxial, ACJ: acromioclavicular joints, DWI: diffusion weighted imaging, FS: fat suppressed, Gd: gadolinium, GRE: gradient echo, IP: interphalangeal, mDixon: modified Dixon, mmol/kg: millimole per kilogram, MTP: metatarsophalangeal, N.A.: not available, Ref: reference, SE: spin echo, SIJ: sacroiliac joints, STJ: sternoclavicular joints, STIR: short tau inversion recovery, T: Tesla, T1W: T1-weighted, T2W: T2-weighted, VIBE: volumetric interpolated breath-hold examination

[a] Conference abstracts

Table 3
Frequency of whole-body MRI versus clinical synovitis and/or enthesitis, agreement, and correlation with other disease activity measures.

Diagnosis Reference	Frequency of MRI vs CE findings in joints	Frequency of MRI vs CE findings in entheses	Agreement and/or correlation between MRI and CE findings in joints or entheses	Correlation between MRI and other measures of disease activity
RA Axelsen, 2014 [35]	MRI synovitis more frequent than swelling (for all sites other than STC and DIP joints), and more frequent than tenderness (apart from STC, finger PIP2−5, knee and MTP1−5 joints)	N.A.	Low agreement at joint level between clinical tenderness and MRI synovitis, κ= 0.12 (−0.36−0.59) and between clinical swelling and MRI synovitis κ=0.04 (−0.29−1.00).	N.A.
RA Axelsen, 2017 [17]	Mean (SD) 58-joint MRI synovitis: 14.3 (6.6) vs 66-SJC: 8.7 (5.5) and 68-TJC:16.8 (10)	Mean (SD) 19-entheses MRI BMO: 1.1 (1.3) and MRI soft tissue inflammation: 2.5 (1.8) vs entheseal tenderness (0−19): 4.2 (3.3)	N.A.	N.A.
RA, UA Freeston, 2012[a] [21]	MRI pathology (osteitis, synovitis, erosion, enthesitis) at more sites per pt than CE (10 vs. 6, $p < 0.05$), n = 15. CE: SJC and entheseal tenderness.	Joined results for entheses and joints as described	N.A.	N.A.
RA Kamishima, 2010 [34]	Median (range) joints with MRI synovitis: 11 (4−34) vs TJC:2 (0−18), SJC 3 (0−13)	N.A.	Joints with MRI synovitis related to tender hand joints, tender joints other than the hand joints, swollen hand joints and swollen joints other than the hand joints (chi-square test, $p < 0.0001$).	There was no correlation between number of MRI positive hand joints and DAS-28.
RA Ng, 2020 (16)	N.A.	N.A.	Agreement between MRI and TJC and SJC was fair-poor with $\kappa <$ 0.40 for all joints. Agreement between MRI and TJC was 52−67%, and with SJC 35−74% depending on site. WBMRI26 did not correlate with TJC28 (rho = −0.24, p = 0.34) or SJC (rho = 0.37, p = 0.13 at baseline, nor at week 16 (rho = 0.39, p = 0.19) and (rho = −0.07, p = 0.83).	WBMRI 26 did not correlate with DAS28-CRP at baseline (rho = 0.05, p = 0.86), and wk 16 (rho = 0.13, p = 0.67)
AS **Karpitshka, 2013 [40]**	MRI synovitis not detected by CE (ankle) in 1/10 pts. Synovitis (knee) in 1/10 detected by both methods.	WBMRI enthesitis not detected by CE at pubic symphysis in 3/10 pts, at the right ischium in 1/10, bilateral bursitis of the hip in 3/10. Dactylitis not detected by WBMRI in 1/10.	WBMRI detected areas of synovitis and enthesitis with a sensitivity of 90% compared to a sensitivity of clinical examination alone of 20%.	There was no significant correlation between MRI enthesitis and clinical parameters (BASDAI, BASFI and CRP).
AxSpA **Krabbe 2020 [39]**	114/2174 (5%) MRI- positive (osteitis and/or synovitis) joints vs 131/3430 (4%) tender, and 8 (0.2%) swollen. 35 (71%) pts with ≥1 MRI-positive joint (0−56) vs 5/49 (10%) pts with ≥1 swollen joint (0−68) and 26 (53%) with ≥1 tender joint (0−70)	59/597 (10%) entheses were MRI-positive (osteitis and/or soft tissue inflammation) vs 327/1617 (20%) were tender. 28 (57%) pts had ≥1 MRI-positive enthesis (0−15) vs 40 (82%) pts had ≥1 tender (0−33) enthesis	Joints: 17 and 1965 of 2139 concordantly positive and negative (tenderness and MRI), 60/2139 tender but not MRI positive 97 MRI-positive but not tender (κ=0.14). Entheses: 19 and 388 of 597 concordantly positive and negative (tenderness and MRI),	N.A.

(*continued*)

Table 3 (*Continued*)

Diagnosis Reference	Frequency of MRI vs CE findings in joints	Frequency of MRI vs CE findings in entheses	Agreement and/or correlation between MRI and CE findings in joints or entheses	Correlation between MRI and other measures of disease activity
			104 tender but MRI negative and 37 MRI positive but not tender (κ=0.08). Poor agreement (κ <0.4) site-by-site for most entheses and joints	
AxSpA **Krabbe 2020 [41]**	47/53 (89%) pts with ≥1 MRI positive joint (osteitis or synovitis), vs 6/53 (11%) with ≥1 swollen joint (0–66) and 26/53 (49%) with ≥1 tender joint (0–68).	49/53 (92%) patients had≥1 peripheral enthesis with MRI inflammation (0–30) vs 41/53 (77%) patients ≥1 tender enthesis (0–35)	N.A.	N.A.
PsA, SpA Poggenborg, 2015 [38]	N.A.	WBMRI enthesitis: 148/888 (17%) sites, clinical enthesitis: 193 (22%) of corresponding entheseal sites. PsA: 57 WBMRI positive, and 95 clinically positive entheseal sites. AxSpA: 57 WBMRI positive and 75 clinically positive entheseal sites	Agreement between WBMRI and clinical enthesitis was 68–100% for all entheseal sites, except for medial femoral condyle (64%), Achilles' tendon (52%) and greater trochanter (49%). All κ values <40% or could not be calculated due to zero-only values on MRI.	Significant correlations between WBMRI Index 3 (supraspinatus, PSIS and Achilles entheses) and BASDAI item 4 (tenderness in relation to entheses) (rho=0.31, p = 0.04), BASDAI (r = 0.30, p = 0.04) and pt global (r = 0.29, p = 0.04).
PsA, SpA Poggenborg, 2015 [42]	Median (IQR) 76-joint MRI synovitis PSA: 12 (7–14), SpA: 10 (3–17), vs SJC PsA: 5 (3–11), SpA:1 (0–2)	N.A.	28-SJC correlated significantly with BMO on MRI in same 28 joints (all pts: r = 0.31; P = 0.04; PsA-only: r = 0.54; P = 0.03). MRI synovitis was not significantly correlated with SJC or TJC.	WBMRI global structural damage (joints and spine/SIJ) correlated with BASMI (rho=0.37, p = 0.016). No correlations between WBMRI scores for peripheral joints and clinical measures of disease activity were found.
SpA **Althoff, 2016 [37]**	N.A.	MRI enthesitis: 22/861 sites in 9 (21%) patients vs clinical enthesitis: 85/697 sites in 24 (57%) patients	Significant correlation between WBMRI and CE at chest wall and pelvis, but not at the foot and knee, at baseline. No correlation between WBMRI and CE at all regions in year 2 and 3.	No correlation between BASDAI or ASDAS-CRP and whole-body MRI at all timepoints
PsA **Weckbach, 2011 [36]**	N synovitic joints/pt by MRI significantly higher compared to CE (Mann- Whitney-U-Test, $p < 0.001$)	N enthesitic areas/patient by MRI higher than CE (Mann- Whitney-U-Test, $p < 0.001$), CE: MASES	More enthesitic sites on MRI than CE in 24 (80%) pts, same n in 3 (10%) and more sites on CE in 3 (10%). More synovitic joints on MRI than CE (excluding hands and feet) in 17 (56.7%) and same n in 13 (43.3%) pts. More synovitis/dactylitis in finger and foot joints on CE than MRI in 10 (30%) pts.	N.A.
JIA **Arcuri, 2016[a] [20]**	18/24 (75%) pts had WBMRI lesions (osteitis or synovitis) not detected by CE. CE not described.	N.A.	N.A.	N.A.
JIA **Choida, 2021[a] [23]**	15 pts had≥1 active joint on CE, 7 of 15 had subclinical	N.A.	14 (43.8%) pts had ≥1 joint with MRI synovitis not detected by CE	N.A.

(*continued*)

Table 3 (*Continued*)

Diagnosis Reference	Frequency of MRI vs CE findings in joints	Frequency of MRI vs CE findings in entheses	Agreement and/or correlation between MRI and CE findings in joints or entheses	Correlation between MRI and other measures of disease activity
	synovitis. 17 pts had no active joint on CE, 7/17 had subclinical synovitis			
ERA **Rachils, 2011[a] [19]**	70% pts (out of 23) had MRI arthritis (most common in SIJ-48%) vs 65% pts on CE MRI arthritis: synovitis, effusion, or joint erosions CE not described	26% (hips 17%) patients had enthesitis on WB-MRI vs 52% pts on CE	More sites of enthesitis on WBMRI than CE in 5%, similar results in 82%, and less sites in 13%. More joints with arthritis on WBMRI in 7%, similar results in 79% and less in 14% pts compared to CE. Good agreement ($\kappa >$ 0.4) for knee, ankle and foot arthritis, and hip region enthesitis.	N.A.
ERA,juvenile PsA, SpA **Srinivasalu, 2012[a] [18]**	N.A.	2/13 pts had MRI enthesitis vs all pts had ≥1 clinical enthesitis	Poor agreement between MRI and CE for enthesitis at all sites (kappa=0).	N.A.
JIA **Yutong, 2019[a]** [22]	N.A.	N.A.	Clinical descriptions against MRI had sensitivity 31.7%, specificity 83.8%, accuracy 54.6%, positive predictive value 68.2%, negative predictive value 52.5% in detecting diseased joints in 13 regions	N.A.

AS: ankylosing spondylitis, ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score c-reactive protein, AxSpA: axial spondyloarthritis, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASMI: Bath Ankylosing Spondylitis Metrology Index, BASFI: Bath Ankylosing Spondylitis Functional Index, BMO: bone marrow oedema, CE: clinical examination, DIP: distal interphalangeal, ERA: enthesitis-related arthritis, HC: healthy controls, JIA: juvenile idiopathic arthritis, κ: Cohen's kappa coefficient, MASES: Maastricht Ankylosing Spondylitis Enthesitis Score, MRI: magnetic resonance imaging, MTP: metatarsophalangeal, N.A.: not available, n: number, p: p-value, PIP: proximal interphalangeal, PsA: psoriatic arthritis, PSIS: posterior superior iliac spine, pt: patient, RA: rheumatoid arthritis, rho: Spearman's rank correlation coefficient, SD: standard deviation, SJC: swollen joint count, SIJ: sacroiliac joints, SPARCC: Spondyloarthritis Research Consortium of Canada, TEC-33: tender enthesis count, TJC: tender joint count, UA: undifferentiated arthritis, USpA: undifferentiated spondyloarthritis, WBMRI: whole-body MRI,[a]Conference abstracts.

[35]. The results were contradictory for the numerical comparisons between MRI synovitis and TJC in two studies, where these were available [17,34]. Furthermore, there was no correlation between DAS-28 and MRI synovitis [16,34], and the agreement between MRI synovitis and clinical swelling or tenderness was low [35], or fair to poor [16] according to Cohen's kappa coefficient (κ).

Five studies included SpA and PsA patients and all of them documented a higher number of MRI synovitic joints per patient or number of patients with MRI synovitis, compared to those detected by clinical examination. Nonetheless, in one of these studies, clinical examination detected more synovitis/dactylitis in hands and feet than WBMRI [36].

As far as JIA is concerned, all four studies eligible reported WBMRI superiority in identifying arthritis, although one study also reported a higher number of joints per patient with clinical arthritis than WBMRI in 14% of patients [19].

Clinical and MRI-detected enthesitis was measured in eight studies involving patients with one or more of the following conditions: SpA (six studies), PsA (two studies) or JIA, mainly with enthesitis-related arthritis (ERA) (two studies). Enthesitis was found in fewer patients, or in fewer sites per patient by MRI than clinical examination in five of those studies [18,19,37–39]. Conversely, more enthesitis was demonstrated by MRI in three studies; two studies in SpA [40,41] and one in PsA [36], although in one of them trochanteric bursitis was a frequent finding and included as enthesitis [40]. The agreement between clinical and MRI enthesitis was reported as low or poor [18,39], although a positive correlation for some regions was reported in one study [37]. There was no correlation between BASDAI and WBMRI scores [37,40,42], with the exception of one MRI score based only on three entheses in one study [38].

Comparison with other imaging techniques

Five studies assessed the relation between WB-MRI findings and other imaging techniques, namely MRI of the hands [42,43], MRI spine and SIJ [42,44], joint ultrasound (42 joints) [16] and X-ray of the hands [45]. Further information on the imaging protocols, analysis and results is displayed in the Supplementary Table S2.

There was no significant correlation between hand synovitis detected by MRI hands vs. WBMRI in PsA patients [42], and low correlations (p-values not showed) were recorded for wrist and hand synovitis in another study of RA and PsA patients [43]. With regards to axial MRI, there was a moderate to high correlation for BMO in SIJ and spine between a dedicated MRI scan and WBMRI in SpA patients in one study [44], whereas another study showed similar results for the SIJ, but weaker or not significant correlations for spinal activity and damage [42].

The relation between WBMRI and ultrasound findings, before and after adalimumab treatment, was assessed in RA patients in a prospective study [16]. At the patient level, inflammation scores based on the 'DAS-28′ joints deriving from both imaging methods (WBMRI26 and US28) correlated at baseline (rho = 0.78; $p < 0.01$), but not after 16 weeks of treatment.

Assessment of treatment response by WBMRI

The changes in WBMRI findings after the initiation of biologic treatment were reported in eight studies. The results are summarised in Table 4; two papers [16,37] presented separately results from the main studies they originated from [17,46], as the patient groups did not completely overlap.

Four studies were focused on SpA. Two studies included a comparator group to the biologic treatment group, which received placebo [44] and sulfasalazine [46], respectively, and reported significant differences in the reduction of WBMRI activity between the groups. Three studies reported a significant decline with treatment in the total MRI inflammation score [40,41,44], whilst the fourth study [46] reported an improvement but is not clear if it was statistically significant. With regards to peripheral lesions (enthesitis and/or synovitis), there was a numerical reduction in sites after treatment in all studies [40,41,44]. There was a positive correlation between changes in BASDAI and total MRI inflammation (axial and peripheral) in two studies [40,41] but no correlation between the former and peripheral MRI inflammation in two studies [41,46].

Three RA studies reported WB-MRI changes with treatment response. One study showed a numerical improvement in the WBMRI 26-joint count [17], which was not statistically significant for the total number of patients at week 16 [47], whereas a different study demonstrated a statistically significant improvement in the MRI synovitis score after a year of treatment [45]. There was correlation between the change in DAS28-ESR and WBMRI synovitis score in one study [24], but not between the difference in DAS28-CRP and WBMRI26-joint count in another [16].

In PsA and JIA, the sensitivity to change after treatment of WBMRI-inflammation has not yet been reported, but results from three clinical trials are awaited [48–50].

Healthy controls

Three of the IA studies eligible for this systematic review also included WB-MRI findings in HCs. One observational study [43] reported overall fewer abnormal lesions in asymptomatic HCs compared to RA and PsA patients, with the highest frequency of synovitis per joint in HCs being noted at the metatarsophalangeal joints (20%), followed by the wrists (19%), ankles and tarsometatarsal joints (15%) and knees (13%). Moreover, comparison between WBMRI scores (synovitis in 76 joints, SIJ BMO, and spinal BMO) between HCs and PsA or HCs and SpA subjects showed no statistical difference, whilst there were detected differences in global BMO scores [42]. Finally, no enthesitis was detected on WBMRI in four healthy subjects according to a conference paper [18].

Discussion

This systematic review provides the best level of evidence for clinical use of WBMRI in the assessment of IA across age.

Although there is a previous systematic review focused on the technical aspects of WBMRI [51] and other reviews discussing the role of WBMRI in IA in adults and children [52,53], this is the first systematic review which offers information on two potential applications of WBMRI technique in IA, namely measuring disease activity and treatment response.

We found that WBMRI detected more synovitis than clinical examination in patients with RA, SpA, PsA and JIA. On the other hand, overall WBMRI detected less areas with enthesitis than entheseal tenderness in patients with SpA, PsA or ERA.

The lower detection of enthesitis on WBMRI with reference to examination could have several explanations. Firstly, tenderness at entheseal sites is not a specific finding as also seen in fibromyalgia or due to mechanical causes [54]. On the other hand, it is possible that WBMRI has reduced sensitivity for enthesitis detection due to reduced spatial resolution or predominantly distal distribution of lesions. Indeed, one study reported that only 53% of entheseal sites were readable [38].

This systematic review found that validated clinical activity scores, such as BASDAI and DAS-28 did not correlate with WBMRI findings. This lack of correlation has been previously demonstrated for dedicated images of the spine and SIJ and BASDAI [55], while RAMRIS score positively correlated with DAS-28 [56,57].

We identified a limited number of studies which evaluated WBMRI against other imaging methods with variable results based on arthritis phenotype and the type of imaging used as a comparator. Conventional sacroiliac MRI in SpA correlated better with WBMRI findings than hand MRI in RA and PsA. Better agreement on synovitis detection between ultrasound and WBMRI was found for the upper limb joints in RA. Although hand MRI (RAMRIS score) is known to correlate with the EULAR-OMERACT ultrasound combined score, and synovial biopsy scores in RA [58], this was not replicated by the WBMRI/hand MRI comparisons, possibly due to the lower resolution of WBMRI, as well as disparities in the methodology. In addition, the assessment for correlation is not as informative as sensitivity analysis or agreement at the joint or patient level.

Sensitivity to change is a required feature for any outcome potentially useful for clinical practice, according to the OMERACT filter [59]. A significant post-treatment improvement in WBMRI inflammation scores as well as numerical improvement of inflamed sites was demonstrated in SpA and RA studies, although changes in peripheral synovitis scores did not reach statistical significance in some studies, whilst the axial inflammation did, possibly due to lower prevalence of peripheral inflammation or WBMRI protocol variability. For example, the sensitivity for the diagnosis of synovitis is better on post-contrast images, compared to STIR [60].

Limitations

To comprehensively evaluate the literature, we included studies available as peer-reviewed abstracts, despite the inadequate information on methodology or statistical analysis, which is reflected by the quality assessment. The main weakness of this systematic review is that the high heterogeneity of the studies included precluded a meta-analysis. The number of joints and entheses clinically examined varied across studies, and they did not always fully correspond to the WBMRI sites, which complicated comparisons between outcomes within and across studies. There were also variations in the definitions of pathology on WBMRI, and the burden of synovitis and/or enthesitis was estimated differently (e.g. per patient or joint) preventing direct study comparisons. Finally, the QUADAS-2 tool is designed for diagnostic studies, but the judgement on the reference standard was problematic due to the lack of gold-standard for comparison. Despite this barrier, it remained the most suitable option for the evaluation of imaging studies, especially in the absence of a control group.

Importance of MRI-detected inflammation

There has been accumulating evidence supporting the use of MRI for the diagnosis and monitoring of IA, which has led to the development of EULAR recommendations for their use in RA and SpA [61,62]. Subclinical inflammation on MRI [63,64] has been shown to predict radiographic progression in RA. However, despite the evidence that patients in remission can have subclinical inflammation on MRI [65,66] and are thus at risk of developing silent damage [67], a treat-to-target approach based on MRI or ultrasound has not been proven to be more successful than using clinical parameters alone in RA [63,68–70]. There is limited evidence that assessing inflammation on hand MRI in patients with early RA at baseline could be valuable in

Table 4
Treatment response measured by clinical and WBMRI scores and their relation.

Diagnosis, Ref	WBMRI TP	Treatment, n	Change in clinical outcomes	Change in WBMRI findings	Relation between MRI and clinical response
RA Axelsen, 2017 [17]	Baseline, week 6, 16, 52	ADA, *n* = 30 week 16 (*n* = 19, week 52)	50% achieved good response, 47% moderate response, 3% no response at week 16, based on EULAR criteria (47)	Numerical but n.s. reduction in median WBMRI 26-joint count from baseline to week 16 or 52, same applies to 58-joint count at week 6, 16, 52	Median (range) 26-joint MRI count, reduced from 6 (0−17) to 4 (0−14) week 16 ($p = 0.04$) for pts with good response
RA Ng, 2020 [16] Substudy of [17]	Baseline, week 16	ADA, *n* = 18, (*n* = 13, week 16)	Median (range) DAS28-CRP reduced from 4.52 (3.48−6.66) to 3.26 (1.97−4.76), TJC from 6.5 (2−19) to 3 (0−11), SJC from 5.5 (1−13) to 1 (0−5)	Median (range) WBMRI26-joint count declined from 8 (0−26) to 5 (1−21)	WBMRI26 did not correlate with the change in DAS28-CRP (rho = −0.07, $p = 0.82$)
RA Kamishima, 2013 [24]	Baseline, follow-up (unknown interval)	IFX or ETN, *n* = 12	N.A.	N.A.	Moderate positive correlation (0.576, $p < 0.05$) between delta MRI synovitis score for total joints (hands and remaining joints) and delta DAS28-ESR; delta: difference between baseline and follow-up
RA Kono, 2017 [45] Kono, 2014[a] [81]	Baseline, year 1	TOC *n* = 21, ETN *n* = 5, IFX n = 4	Median DAS28 from 5.1 to 2.1	WBMRI synovitis from mean 31.2 to 23.2, $p = 0.02$ and BMO scores from median 11 to 3, $p = 0.03$. For TCZ (81), WBMRI synovitis and BMO at year 1 improved from baseline, ($p < 0.01$ for both)	N.A.
SpA Karpitshka, 2013 [40]	Baseline, week 26, 52	ETN, *n* = 10	The BASDAI decreased from 5.5 ± 0.5 at baseline to 1.7 ± 0.4 at week 26, $p < 0.05$) and to 1.7 ± 0.5 at week 52, $p < 0.05$	The total score for axial and peripheral lesions (mean± SEM) decreased from 38.9 ± 10.7 to 15.7 ± 6.0, $P = 0.053$ at week 26, and 2.2 ± 0.9, $p < 0.05$ at week 52. Peripheral inflammatory lesions (5 pts) decline from 3.3 ± 1.2 at baseline to 1.3 ± 0.7 at week 26 (60.6% reduction, n.s.) and 0.2 ± 0.2 at week 52 (93.9% reduction, $p < 0.05$)	Significant correlation between changes in BASDAI/BASFI and changes in WBMRI total lesions (spine, SIJ, joints, entheses), p-values 0.007 and 0.005, respectively
SpA Krabbe, 2018 [44] Krabbe 2020 [39]	Baseline, week 6, 24, 48	ADA, *n* = 25 placebo, *n* = 24 (0−6 weeks)	At week 6, reduction of BASDAI by ≥50% or ≥2.0 in 52% pts in the ADA group vs 13% in the placebo group ($p = 0.005$). Significant decrease in TJC70 and TEC33 at week 24 and 48 in ADA group but not for SJC.	At week 6, WBMRI total inflammation index decreased in 44% pts in the ADA group vs 13% in the placebo; risk difference was 32% (95% CI 4−59%, $p = 0.025$). Significant change of total inflammation score, enthesitis score and BMO axial score at week 6, 24, 48 in ADA group, but n.s. change for peripheral joint inflammation score.	62% (8/13) of joints with tenderness that resolved with ADA at 6 weeks were MRI positive at baseline compared to 26% (9/34) whose tenderness resolved but were MRI negative at baseline ($p = 0.041$).
SpA Krabbe, 2020 [41]	Baseline, week 4,16, 52	GOL, *n* = 53 (*n* = 48, week 52)	At week 52, 58% achieved BASDAI-50 (50% reduction), 38% achieved ASDAS inactive disease	At week 4,16 and 52, there was significant reduction in the mean score of MRI total inflammation index and axial	MRI-AXIAL-50 (50% reduction SIJ and spine score) and MRI-TOTAL-50 (50% reduction axial and peripheral score) were

(*continued*)

Table 4 (*Continued*)

Diagnosis, Ref	WBMRI TP	Treatment, n	Change in clinical outcomes	Change in WBMRI findings	Relation between MRI and clinical response
				inflammation index from baseline. At week 16 and 52 there was significant reduction in the MRI peripheral joints and entheses inflammation index from baseline.	associated with BASDAI50 and ASDAS-CII but MRI-PERIPH-50 (50% reduction peripheral score; entheses and joints) was not associated with BASDAI50 or ASDAS-CII at week 52 (Fisher's exact).
SpA Song, 2011 [46]	Baseline, week 48	ETN n = 40 (n = 35, week 48)	At week 48, mean BASDAI reduced from 5.5 to 2.5, enthesitis (0−17) reduced from 4.4 to 1.8.	Mean SIJ score declined from 7.8 to 2.4, spinal score 2.3 to 1.0, enthesitis 26 sites in 15 pts reduced to 11 sites in 11 pts at week 48.	Change in MRI SIJ score correlated with change in BASDAI, BASFI at week 48 (ANCOVA, p = 0.04 and p = 0.0069). No correlation between MRI spine score or MRI enthesitis and BASDAI, BASFI, enthesitis count.
SpA Althoff, 2016 [37] Song, 2015 [78]	Baseline, year 2, year 3	ETN, n = 41	Total enthesitis count reduced from 85 at baseline to 24 and 28, (57% to 19% and 16% pts) at year 2 and 3, respectively, (SRM:0.55 year 2, 0.47 year 3). BASDAI mean (SD) reduced from 5.5 (1.2) to 1.9 (1.6) and 1.9 (1.5)	MRI enthesitis 22 lesions in 9 (21%) pts reduced to 9 lesions in 13% pts at year 2, and to 8 lesions in 14% pts at year 3 (SRM: 0.34 year 2, SRM:0.28 year 3) Mean absolute change (95% CI) in MRI SIJ score was 5.10 (2.98, 7.21) at year 2, 4.91 (2.77, 7.06) at year 3, MRI spine score 1.00 (−0.14, 2.15) at year 2 and 0.77 (−0.43, 1.97) at year 3.	Mean absolute change in BASDAI of pts with resolved SIJ osteitis on MRI (n = 20) vs pts with persisting SIJ osteitis (n = 15) was higher at year 2, but not at year 3
PsA Weckbach, 2011 [36]	Average of 11 months	Unclear, n = 3	N.A.	Reduction of pathological findings in repeat scan from 6 to 2, 14 to 10 and 2 to 0 in 3 patients, respectively.	N.A.

ADA: adalimumab, ANCOVA: analysis of covariance, ASDAS: Ankylosing Spondylitis Disease Activity Score, ASDAS-CII: ASDAS clinically important improvement (reduction≥1.1), BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis, Functional Index, BMO: bone marrow oedema, CI: confidence interval, DAS28-ESR: disease activity score 28 joints erythrocyte sediment ratio, DAS28-CRP: disease activity score 28 joints c-reactive protein, ETN: etanercept, EULAR: European League Against Rheumatism, GOL: golimumab, IFX: infliximab, IQR: interquartile range, MRI: magnetic resonance imaging, n: number of patients, N.A.: not available, n.s.: not significant, p: p-value, pt: patient, RA: rheumatoid arthritis, Ref: reference, SD: standard deviation, SEM: standard error of mean, SIJ: sacroiliac joint, SJC: swollen joint count, SpA: spondyloarthritis, SRM: standard response of mean, TEC33: tender entheseal count 33, TJC: tender joint count, TOC: toclizumab, TP: time periods, WBMRI: whole-body MRI.

[a] Conference abstracts.

guiding treatment escalation [71], but it did not predict DMARD-free remission [72]. In addition, a retrospective study of JIA patients in remission who underwent MRI scans of previously affected joints revealed that 65.5% of patients had subclinical synovitis, and this was associated with an increased risk of flares, whilst high BMO scores increased the risk of radiographic damage progression [73].

Future research on WBMRI

Further research studies are needed to investigate the potential benefits of subclinical inflammation detection by WBMRI in different types of IA, as predictor for treatment response or damage. In addition, WBMRI-derived outcomes could be used as surrogate endpoints in clinical studies. In Fig. 2 we summarize potential research questions that could be addressed by future WBMRI studies. As our systematic review highlighted, greater consistency is needed in the definitions of pathology and selection of imaging and clinical outcomes to allow for cross-validation of results in independent studies. Moreover, there is a need for representability of real-life patient populations in future WBMRI studies, as patients in remission or with low disease activity, with longer disease duration, or with JIA or PsA have been underrepresented so far. The inclusion of healthy controls will also improve our understanding about other factors contributing to MRI-detected inflammation. Finally, there are barriers to the use of WBMRI, including restricted availability despite its increasing use in cancer [74,75], scan duration, which if reduced can improve the patient tolerability and cost of scans; prolonged reporting time because of comprehensive scores, which will require a more pragmatic approach and the potentially high frequency of incidental findings [76].

In conclusion, WBMRI shows promise as an assessment tool for disease activity and response to treatment in patients with IA across age, while future research is required to address the methodological limitations and assert its role in routine clinical practice.

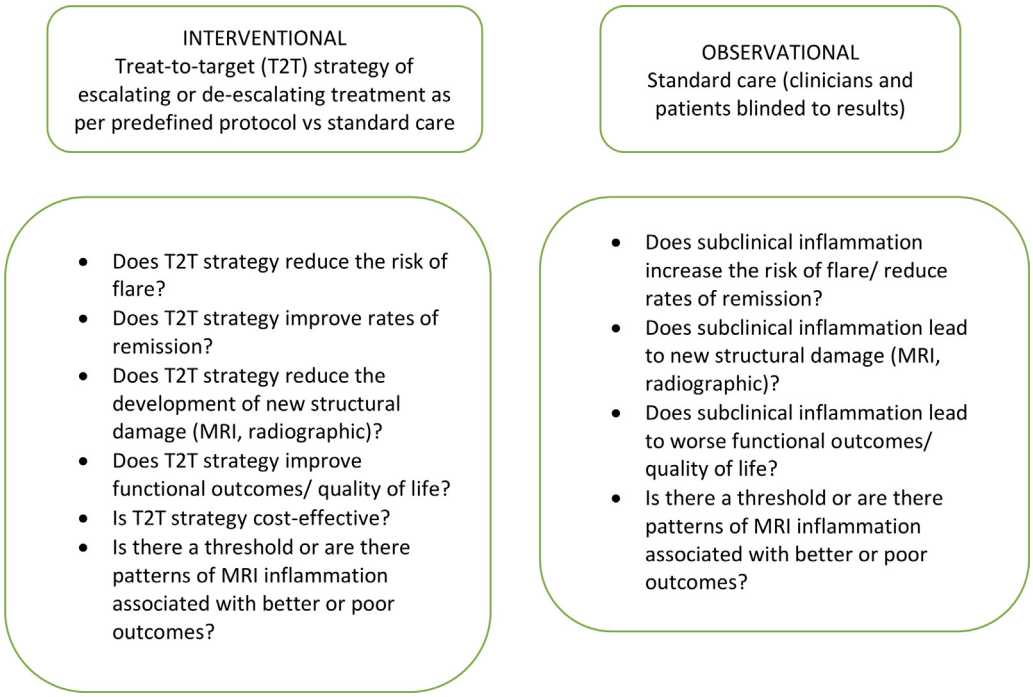

Fig. 2. Research agenda for studies investigating the use of whole-body MRI (WBMRI) for patient benefit in inflammatory arthritis.

Declaration of Competing Interest

None.

CRediT authorship contribution statement

Varvara Choida: Conceptualization, Methodology, Validation, Investigation, Formal analysis, Data curation, Writing – original draft, Visualization. **Anastasia-Vasiliki Madenidou:** Conceptualization, Methodology, Software, Validation, Investigation, Data curation, Writing – review & editing, Visualization. **Debajit Sen:** Conceptualization, Writing – review & editing, Visualization. **Margaret A. Hall-Craggs:** Conceptualization, Writing – review & editing, Visualization, Supervision. **Coziana Ciurtin:** Conceptualization, Methodology, Validation, Investigation, Writing – review & editing, Visualization, Supervision, Project administration.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.semarthrit.2022.151953.

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