EULAR recommendations for the use of imaging in the diagnosis and management of spondyloarthritis in clinical practice

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Handling editor Tore K Kvien

▶ Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/annrheumdis-2014-206971).

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Received 11 November 2014
Revised 23 February 2015
Accepted 7 March 2015
Published Online First 2 April 2015

ABSTRACT

A taskforce comprised of an expert group of 21 rheumatologists, radiologists and methodologists from 11 countries developed evidence-based recommendations on the use of imaging in the clinical management of both axial and peripheral spondyloarthritis (SpA). Twelve key questions on the role of imaging in SpA were generated using a process of discussion and consensus. Imaging modalities included conventional radiography, ultrasound, magnetic resonance imaging, computed tomography (CT), positron emission tomography, single photon emission CT, dual-emission x-ray absorptiometry and scintigraphy. Experts applied research evidence obtained from systematic literature reviews using MEDLINE and EMBASE to develop a set of 10 recommendations. The strength of recommendations (SOR) was assessed by taskforce members using a visual analogue scale. A total of 7550 references were identified in the search process, from which 158 studies were included in the systematic review. Ten recommendations were produced using research-based evidence and expert opinion encompassing the role of imaging in making a diagnosis of axial SpA or peripheral SpA, monitoring inflammation and damage, predicting outcome, response to treatment, and detecting spinal fractures and osteoporosis. The SOR for each recommendation was generally very high (range 8.9–9.5). These are the first recommendations which encompass the entire spectrum of SpA and evaluate the full role of all commonly used imaging modalities. We aimed to produce recommendations that are practical and valuable in daily practice for rheumatologists, radiologists and general practitioners.

The group of spondyloarthritides comprises a number of closely related rheumatic diseases with common clinical features,[1] including ankylosing spondylitis (AS), psoriatic arthritis (PsA), arthritis/spondylitis related to inflammatory bowel disease and reactive arthritis (ReA).[2–6]

In addition to these subtypes, patients with spondyloarthritis (SpA) can also be grouped into two categories based on their predominant clinical presentation: axial and peripheral.[1 2] This division was reflected in the Assessment of Spondyloarthritis International Society (ASAS) classification criteria, which separated axial and peripheral SpA (axSpA and pSpA).[7 8] Imaging is a key component of classification criteria for SpA, primarily due to the lack of specific clinical symptoms as well as varying disease activity over time. For example, radiographic sacroiliitis is an essential part of the internationally accepted modified New York criteria for AS.[4] Significant advances have been made within the field of imaging in SpA over the past decade. Several imaging modalities are now available that may aid in the diagnosis and monitoring of both axSpA and pSpA as well as in predicting structural damage and treatment response. However, conventional radiography (radiography) only visualises the late structural consequences of the inflammatory process, while the early inflammatory changes can be detected by MRI, often several years before the appearance of sacroiliitis on radiography.[9] Accordingly, MRI was incorporated in the ASAS classification criteria for axSpA as well as pSpA.[7 8]

Reflecting the perceived need for developing evidence-based recommendations on the use of musculoskeletal imaging in the clinical management of SpA, a European League Against Rheumatism (EULAR) taskforce was convened to develop evidence-based recommendations on the use of musculoskeletal imaging in the clinical management of SpA, for rheumatologists, radiologists and general practitioners.

METHODS

An expert group of 21 rheumatologists, radiologists and methodologists representing 11 countries formed the taskforce. The objectives were to formulate key clinical questions relating to the role of imaging in SpA, to identify and critically appraise the available evidence, and to generate recommendations based on both evidence and expert opinion.

At the initial taskforce meeting, members proposed clinically relevant questions related to key aspects of the use of imaging in SpA. Twelve final research questions (Q1–12) were formulated and agreed upon by consensus, encompassing the full spectrum of the role of imaging in diagnosing axSpA or pSpA, monitoring inflammation and damage, predicting outcome and response to treatment, as well as detecting spinal fractures and

To cite: Mandl P, Navarro-Compán V, Terslev L, *et al*. *Ann Rheum Dis* 2015;**74**:1327–1339.

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osteoporosis (see online supplementary material S1: research questions).

Three systematic literature searches were performed using MEDLINE and EMBASE databases. The first search summarised research questions 1–10 (Q1–10) (questions on the diagnostic, monitoring and predictive role of imaging), while the research question on the detection of spinal fractures (Q11) and that on the detection of osteoporosis (Q12) were covered by independent searches. Specific medical subject headings and additional keywords were used to identify all relevant studies (see online supplementary material S2: search strategy). In addition, abstract archives of relevant international rheumatology and radiology meetings (2011, 2012) as well as the bibliographies of included papers were hand searched for evidence of other studies for inclusion. Titles and abstracts of all citations identified were screened, and potentially relevant articles were reviewed in full text using predetermined inclusion and exclusion criteria.

Studies published in English up to January 2013, on the use of imaging in adults (≥18 years) with a suspected or established clinical diagnosis of SpA (including inflammatory and low back pain for the research question on the diagnostic role of imaging in axSpA), axSpA or pSpA (and suspicion of spinal (vertebral) fracture with regard to Q11), were included. Imaging modalities included radiography, ultrasound (US), MRI, CT, positron emission tomography, single-photon emission CT (SPECT), quantitative sacroiliac (SI) joint scintigraphy (QSS) and dual-energy X-ray absorptiometry (DXA). Study types included randomised controlled trials (RCTs), systematic reviews, controlled clinical trials, cohort, case–control and diagnostic studies.

Studies not in English language, those including patients ≤18 years of age and those reporting data acquired from <20 patients with suspected or established disease (and/or <20 control patients for questions 1–2 on the diagnostic role of imaging) were excluded. Quality assessment of all included studies was done using the QUADAS-2 tool[10] and presented graphically for each research question.[11]

Data from the literature reviews were categorised and presented at the second taskforce meeting according to study design using a hierarchy of evidence in descending order according to quality.[12] The literature review was conducted by PM, VNC and PB. Data extraction for each research question was reviewed by at least two of the above-mentioned taskforce members. Greater emphasis was given to the best available evidence, although all data were collected and reviewed. Expert evidence was cited only when available research evidence was lacking. The experts finally formulated 10 recommendations based on the 12 clinical questions through a process of discussion and consensus, followed by final wording adjustments by email exchange. The finally perceived strength of recommendation (SOR) for each proposition was scored by the experts using a 0–10 visual analogue scale (VAS; 0=not recommended at all, 10=fully recommended) with data from the quality assessment. Scores reflected both research evidence and clinical expertise.[13]

A research agenda was agreed upon by consensus following the presentation of the literature reviews.

RESULTS

The combined search for Q1–12 resulted in a total of 7550 records, of which a total of 158 articles were finally selected for inclusion in the systematic literature review. Articles that were relevant to >1 research question were included in the review more than once. The flow charts showing the detailed results of all three searches are shown in online supplementary figure S3. The number of articles included for each research question is shown in online supplementary table S4. Taskforce members produced 10 recommendations based on a process of discussion. The recommendations, SOR (mean VAS and 95% CI) and level of evidence are presented in table 1. A full reference list for articles included in each recommendation is shown in online supplementary material S5.

Recommendations

Recommendation 1: diagnosing axial SpA

A. In general, conventional radiography of the SI joints is recommended as the first imaging method to diagnose sacroiliitis as part of axial SpA. In certain cases, such as young patients and those with short symptom duration, MRI of the SI joints is an alternative first imaging method.

B. If the diagnosis of axial SpA cannot be established based on clinical features and conventional radiography, and axial SpA is still suspected, MRI of the SI joints is recommended. On MRI, both active inflammatory lesions (primarily bone marrow oedema (BME)) and structural lesions (such as bone erosion, new bone formation, sclerosis and fat infiltration) should be considered. MRI of the spine is not generally recommended to diagnose axial SpA.

C. Imaging modalities other than conventional radiography and MRI are not generally recommended in the diagnosis of axial SpA*.

*CT may provide additional information on structural damage if conventional radiography is negative and MRI cannot be performed. Scintigraphy and US are not recommended for diagnosis of sacroiliitis as part of axial SpA.

Strength of recommendation: 9.5 (95% CI 9.2 to 9.8).

Twenty-five studies evaluated the diagnostic utility of various imaging modalities in axSpA.[14–38] Five studies reported on the diagnostic utility of radiography.[14–18] They demonstrated varying sensitivity (SE) and specificity (SP) of radiography in diagnosing sacroiliitis in inflammatory back pain (IBP)/suspicion of SpA, while one observational study reported an SE of 0.84 and an SP of 0.75 in diagnosing sacroiliitis in AS.[14–18] A single study reported only fair agreement between radiography and CT in suspected sacroiliitis and many false positive results using radiography.[18] Two studies reported higher SE for CT than radiography for diagnosing sacroiliitis (1 in AS, 1 in suspected SpA).[15 17]

Thirteen studies evaluated the diagnostic utility of MRI demonstrating varying SE and overall higher SP in patients with IBP or those with suspicion of SpA (table 2).[19–31] Three studies reported SE (0.73–0.9) and SP (0.9–0.97) for SI joint BME on MRI in established AS.[22 23 25] Wick *et al*[26] reported an SE of 0.11 and an SP of 0.93 for MRI SI joint erosions for diagnosis of AS, while Weber *et al*[25] reported that the combined features of SI joint erosion and/or BME increased SE to 0.98–0.96 compared with BME alone (0.91–0.83) without reducing SP and the area under the curve for diagnosis of AS. Heuft-Dorenborsch *et al* found that initial assessment of structural changes by radiography followed by MRI assessment of inflammation with negative radiography gives the highest returns for detecting involvement of the SI joint in patients with recent IBP.[27] Finally, two studies found MRI of the SI joint superior to QSS or radiography for diagnosing sacroiliitis in IBP and SpA.[14 33]

With regard to MRI of the spine, three studies reported SE of and SP for corner fat lesions and corner inflammatory lesions (CILs) in patients suspected for axSpA,[29 30 31] while two studies reported SE and SP in established AS.[31 32] Finally, Weber *et al*[32] have demonstrated that spinal MRI adds little incremental value

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Table 1 EULAR recommendations for the use of imaging in the diagnosis and management of spondyloarthritis in clinical practice

		SOR	LOE
1	*Axial SpA: diagnosis* A. In general, conventional radiography of the SI joints is recommended as the first imaging method to diagnose sacroiliitis as part of axial SpA. In certain cases, such as young patients and those with short symptom duration, MRI of the SI joints is an alternative first imaging method. B. If the diagnosis of axial SpA cannot be established based on clinical features and conventional radiography, and axial SpA is still suspected, MRI of the SI joints is recommended. On MRI, both active inflammatory lesions (primarily bone marrow oedema) and structural lesions (such as bone erosion, new bone formation, sclerosis and fat infiltration) should be considered. MRI of the spine is not generally recommended to diagnose axial SpA. C. Imaging modalities, other than conventional radiography and MRI are generally not recommended in the diagnosis of axial SpA*.	9.5 (9.2–9.8)	III
2	*Peripheral SpA: diagnosis* When peripheral SpA is suspected, US or MRI may be used to detect peripheral enthesitis, which may support the diagnosis of SpA. Furthermore, US or MRI might be used to detect peripheral arthritis, tenosynovitis and bursitis.	9.4 (9.0–9.8)	III
3	*Axial SpA: monitoring activity* MRI of the SI joints and/or the spine may be used to assess and monitor disease activity in axial SpA, providing additional information on top of clinical and biochemical assessments. The decision on when to repeat MRI depends on the clinical circumstances. In general, STIR sequences are sufficient to detect inflammation and the use of contrast medium is not needed.	9.2 (8.8–9.6)	Ib
4	*Axial SpA: monitoring structural changes* Conventional radiography of the SI joints and/or spine may be used for long-term monitoring of structural damage, particularly new bone formation, in axial SpA. If performed, it should not be repeated more frequently than every second year. MRI may provide additional information.	9.3 (8.8–9.8)	Ib
5	*Peripheral SpA: monitoring activity* US and MRI may be used to monitor disease activity (particularly synovitis and enthesitis) in peripheral SpA, providing additional information on top of clinical and biochemical assessments. The decision on when to repeat US/MRI depends on the clinical circumstances. US with high-frequency colour or power Doppler is sufficient to detect inflammation and the use of US contrast medium is not needed.	9.3 (8.9–9.7)	Ib
6	*Peripheral SpA: monitoring structural changes* In peripheral SpA, if the clinical scenario requires monitoring of structural damage, then conventional radiography is recommended. MRI and/or US might provide additional information.	8.9 (8.4–9.4)	III
7	*Axial SpA: predicting outcome/severity* In patients with ankylosing spondylitis† (not non-radiographic axial SpA), initial conventional radiography of the lumbar and cervical spine is recommended to detect syndesmophytes, which are predictive of development of new syndesmophytes. MRI (vertebral corner inflammatory or fatty lesions) may also be used to predict development of new radiographic syndesmophytes.	9.0 (8.5–9.5)	Ib
8	*Axial SpA: predicting treatment effect* Extensive MRI inflammatory activity (bone marrow oedema), particularly in the spine in patients with ankylosing spondylitis, might be used as a predictor of good clinical response to anti-TNF-alpha treatment in axial SpA. Thus, MRI might aid in the decision of initiating anti-TNF-alpha therapy, in addition to clinical examination and CRP.	8.9 (8.3–9.5)	Ib
9	*Spinal fracture* When spinal fracture in axial SpA is suspected, conventional radiography is the recommended initial imaging method. If conventional radiography is negative, CT should be performed. MRI is an additional imaging method to CT, which can also provide information on soft tissue lesions.	9.3 (8.9–9.7)	IV
10	*Osteoporosis* In patients with axial SpA without syndesmophytes in the lumbar spine on conventional radiography, osteoporosis should be assessed by hip DXA and AP-spine DXA. In patients with syndesmophytes in the lumbar spine on conventional radiography, osteoporosis should be assessed by hip DXA, supplemented by either spine DXA in lateral projection or possibly QCT of the spine.	9.4 (9.0–9.8)	III

*CT may provide additional information on structural damage if conventional radiography is negative and MRI cannot be performed. Scintigraphy and US are not recommended for diagnosis of sacroiliitis as part of axial SpA.
†That is, radiographic axial spondyloarthritis.
Level of evidence (LOE): Ia, evidence for meta-analysis of randomised controlled trials; Ib, evidence from at least one randomised controlled trial; IIa, evidence from at least one controlled study without randomisation; IIb, evidence from at least one other type of quasi-experimental study; III, evidence from non-experimental descriptive studies, such as comparative studies, correlation studies and case–control studies; IV, evidence from expert committee reports or opinions or clinical experience of respected authorities, or both.
AP, anterior–posterior; CRP, C-reactive protein; DXA, dual-energy X-ray absorptiometry; EULAR, European League Against Rheumatism; nr-axSpA, non-radiographic axial spondyloarthritis; QCT, quantitative CT; SI, sacroiliac; SIJ, sacroiliac joints; SOR, strength of recommendation; SpA, spondyloarthritis; STIR, short tau inversion recovery; TNF-alpha, tumour necrosis factor alpha; US, ultrasonography.

compared with MRI of the SI joint alone in terms of lesion detection and classification of patients with early SpA. Four studies reported that QSS has low SE for diagnosis of sacroiliitis in patients with IBP.[14 33–35] Klauser *et al*[36 37] reported that contrast-enhanced US is a sensitive and specific tool for diagnosing active sacroiliitis in patients with IBP and AS. One study reported that pulsatile monophasic colour Doppler US detects sacroiliitis in patients with AS.[38] Quality assessment is reported in online supplementary figure S6.1; of note risk of patient selection bias and applicability concerns with regard to patient selection were high in 52% and 36% of the included manuscripts, respectively.

Recommendation 2: diagnosing peripheral SpA

When peripheral SpA is suspected, US or MRI may be used to detect peripheral enthesitis, which may support the diagnosis of SpA. Furthermore, US or MRI might be used to detect peripheral arthritis, tenosynovitis and bursitis.

Strength of recommendation: 9.4 (95% CI 9.0 to 9.8)

Nine studies evaluated grey-scale and/or power Doppler US (GSUS/PDUS, respectively) for assessment of entheses in patients with established pSpA[39–47] using clinical examination as gold standard. Eight studies evaluated multiple entheses,[39–46] while one study evaluated only the Achilles tendon.[47] One study reported that PDUS has an SE of 0.76 and an SP of 0.81 in suspected SpA,[41] while four studies reported varying SE and overall higher SP in established PsA.[39 45–47] Four studies reported an SE of 0.83–0.98 and an SP of 0.48–0.9 for PDUS assessment in established pSpA.[40–43] Finally, Feydy *et al*[44] reported that MRI of the heel had an SP of 0.94 but SE of 0.22 for discriminating between patients with SpA and controls.

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Table 2 Recommendation 1: summary of studies on the use of MRI in diagnosing axial spondyloarthritis

Studies	No.	Study population	Gold standard	SIJ/spine	MRI lesion	SE	SP	+LR	−LR
Longitudinal/RCT									
Bennett *et al*[19]	50	SpA	X-ray	SIJ	Grade 3 SI+HLAB27 27B27	0.62	0.92	7.7	0.41
Marzo-Ortega *et al*[20]	76	IBP (NSBP, HC)	Clinical diagnosis	SIJ	Grade 1 SI	0.82	0.43	1.4	0.41
					Grade 2 SI	0.73	1.0	∞	0.73
Oostveen *et al*[21]	25	IBP	X-ray	SIJ	Grade ≥2 SI	0.85	0.47	1.6	0.31
Cross-sectional/case-control									
Weber *et al*[22 23]	187	AS, IBP (NSBP, HC)	Clinical diagnosis	SIJ	BME (AS)	0.9	0.97	44.6	0.92
					BME (IBP)	0.51	0.97	26	0.50
					BME+ERO	0.81	0.97	27	0.19
Weber *et al*[24 25]	157	AS, IBP (NSBP, HC)	Clinical diagnosis	SIJ	BME	0.73	0.9	7.3	0.3
					BME and/or ERO	0.82	0.9	8.2	0.2
					FI	0.21	0.97	8.3	0.81
					FI with BME or ERO	0.24	0.97	9.2	0.78
Heuft-Dorenbosch *et al*[27]	68	IBP	X-ray	SIJ	chronic changes	0.49	0.97	16.3	0.52
Weber *et al*[30]	95	AS, IBP, (HC)	Clinical diagnosis	Spine	>2 CIL (AS)	0.69	0.94	12	0.32
					>2 CIL (IBP)	0.32	0.96	8	0.70
					LIL	0.97	0.31	1.4	0.09
Kim *et al*[31]	104	AS (HC)	Clinical diagnosis	Spine	MRI corner sign	0.44	0.96	11	0.58
Retrospective									
Wick *et al*[26]	179	AS (various)	Clinical diagnosis	SIJ	ERO	0.11	0.93	1.57	0.95
					BME	0.35	0.78	1.59	0.83
Bennett *et al*[28 29]	185	SpA (DA, IBP, HC)	Clinical diagnosis	SIJ and spine	>3 RLs	0.33	0.97	12.4	0.69
					Posterior BME lesion	0.13	0.99	14.5	0.87
					≥5 FRLs	0.22	0.98	12.6	0.79

The terms of the individual original publications have been used in the table.
AS, ankylosing spondylitis; BME, bone marrow oedema; CIL, corner inflammatory lesion; DA, degenerative arthropathy; ERO, erosion; FI, fatty infiltration; FRL, 'fatty Romanus' lesion; HC, healthy control; HLA27, human leucocyte antigen B27; IBP, inflammatory back pain; LIL, lateral segment inflammatory lesion; +LR, positive likelihood ratio; −LR, negative likelihood ratio; No., number of individuals included in the study; NSBP, non-specific back pain; RCT, randomised controlled trial; RL, 'Romanus' lesion; SE, sensitivity; SP, specificity; SI, sacroiliitis, SIJ, sacroiliac joints; SpA, spondyloarthritis.

Quality assessment is reported in online supplementary figure S6.2; of note risk of patient selection bias and applicability concerns with regard to the index test were high in 55% and 33% of included manuscripts, respectively.

Recommendation 3: monitoring disease activity in axial SpA

MRI of the SI joints and/or the spine may be used to assess and monitor disease activity in axial SpA, providing additional information on top of clinical and biochemical assessments. The decision on when to repeat MRI depends on the clinical circumstances. In general, short tau inversion recovery (STIR) sequences are sufficient to detect inflammation and the use of contrast medium is not needed.

Strength of recommendation: 9.2 (95% CI 8.8 to 9.6)

Thirty-four studies evaluated the utility of MRI in monitoring disease activity in axSpA.[20 21 48–79] Table 3 summarises and presents the results of longitudinal[20 21 50 52–54 61 63 64 66–69 71 73 74 76] as well as cross-sectional[51 59 60 70 79] studies evaluating correlation with accepted disease activity parameters (Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score (ASDAS), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)) or pain.

In addition, seven studies compared the utility of different MRI sequences (contrast-enhanced T1-weigthed (T1Gd) and STIR), for monitoring disease activity in axial SpA,[48 49 53 56 57 65 72] six of which reported high levels of agreement or correlation between the two sequences.[48 49 53 56 57 65] A single longitudinal and two cross-sectional studies reported higher SE of STIR,[49 53 65] while a single longitudinal and two cross-sectional studies reported higher diagnostic confidence/reliability of the T1Gd-DPTA sequence.[48 49 53]

Regarding frequency of spinal MRI examination, two longitudinal studies reported significant changes detected already at 6 or 12 weeks[50 72] with similar results for both STIR and T1Gd sequences.[72] There is currently no evidence for how frequently MRI should be repeated for monitoring disease activity in axial SpA. Quality assessment is reported in online supplementary figure S6.3.

Recommendation 4: monitoring structural changes in axial SpA

Conventional radiography of the SI joints and/or spine may be used for long-term monitoring of structural damage, particularly new bone formation, in axial SpA. If performed, it should not be repeated more frequently than every second year. MRI may provide additional information.

Strength of recommendation: 9.3 (95% CI 8.8 to 9.8)

Twenty-three studies evaluated the utility of various imaging modalities in monitoring structural damage in axSpA.[50 63 70–72 80–97] Of 13 radiography studies, 10 reported correlation between radiographic changes and accepted measures of function (Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Metrology Index (BASMI), metrological measures (chest expansion, occiput-to-wall distance, finger-to-floor distance, tragus-wall distance, Schober's test, spinal flexion, cervical rotation)) (table 4).[63 81–83 85–87 93 94 96]

Six studies compared various spine radiography scoring methods (Bath Ankylosing Spondylitis Radiology Index (BASRI), Stoke Ankylosing Spondylitis Spinal Score (SASSS), modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS), Berlin X-ray score, Radiographic Ankylosing Spondylitis Spinal Score (RASSS)),[83 84 87 92 93 96] of which two reported mSASSS being superior to BASRI and SASSS.[93 96] Baraliakos *et al*[83] reported the RASSS method, which includes the thoracic segment, superior to mSASSS, while Ramiro *et al*[92] reported no advantage of RASSS over mSASSS. Taylor *et al*[95] reported correlation between CT changes and QSS in the SI joint.

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Table 3 Recommendation 3: summary of studies on the use of MRI in monitoring disease activity in axial spondyloarthritis

Studies	No.	Region	MRI scoring method	Correlation				
				ASDAS	BASDAI	CRP	ESR	Pain
Longitudinal/RCT								
Marzo-Ortega *et al*[20]	76	Spine	LEEDS	–	NS	NS	–	NS
Oostveen *et al*[21]	25	SIJ	mNY			OR 2.1	OR 2.1	OR 1.2
Baraliakos *et al*[50]	40	Spine	ASspiMRI-a	–	NS	NS	NS	–
Bonel *et al*[52]	28	Spine	ASspiMRI-a	–	0.41	–	–	–
Braun *et al*[53]	20	Spine	ASspiMRI-a/c	–	0.49–0.6	–	–	–
Braun *et al*[54]	98	Spine	ASspiMRI-a	0.35	NS	0.4	–	NS
Lambert 2007[61]	82	Spine/SIJ	SPARCC	–	NS	p=0.018	–	NS
Machado *et al*[63]	221	Spine	ASspiMRI-a	0.14	NS	–	–	–
Machado *et al*[64]	221	Spine	ASspiMRI-a	0.23	NS	0.32	–	–
Maksymowych *et al*[66]	68	Spine	SPARCC	–	NS	0.65–0.68	–	NS
Maksymowych *et al*[67]	36	Spine	SPARCC	–	NS	0.45	0.44	–
Marzo-Ortega *et al*[68]	42	Spine/SIJ	LEEDS	–	p=0.04	–	–	–
Pedersen *et al*[69]	82	Spine/SIJ	Berlin	0.46/0.31	−0.41/−0.31	NS	–	–
Puhakka *et al*[71]	34	SIJ	BME	–	NS	–	–	–
Rudwaleit *et al*[73]	62	Spine/SIJ	Berlin	–	NS	NS	NS	NS
Sieper *et al*[74]	20	Spine	ASspiMRI-a	–	0.5	NS	NS	–
Song *et al*[76]	76	Spine/SIJ	ASspiMRI-a/Berlin	p=0.04	–	NS	–	–
Visvanathan *et al*[77]	279	Spine	ASspiMRI-a	–	–	p<0.001	–	–
Cross-sectional/case-control								
Blachier 2013[51]	648	Spine/SIJ	Dichotomous	–	–	–	–	aOR 1.71–2.86
Goh *et al*[55]	34	Spine	ASspiMRI-a	–	NS	NS	NS	–
Kiltz *et al*[59]	100	Spine/SIJ	Berlin	NS	NS	0.22	–	–
Konca *et al*[60]	50	Spine	ASspiMRI-a	0.37	NS	0.33	0.39	–
Puhakka *et al*[70]	41	SIJ	BME enhancement	–	NS	–	–	–
Weber *et al*[79]	197	ACW	Dichotomous	–	–	–	–	κ 0.21–0.33

The Spearman test for rank correlation is used for test of correlation, values are correlation coefficients (rho), if not otherwise indicated. p Values indicate the level of statistical significance.
aOR, adjusted odd ratio; ACW, anterior chest wall; AS, ankylosing spondylitis; ASDAS, Ankylosing Spondylitis Disease Activity Score; ASspiMRI-a/c, ankylosing spondylitis spine MRI score for activity; BASDAI, Bath Ankylosing Spondylitis Disease Activity Score; BME, bone marrow oedema; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LEEDS, Leeds MRI scoring system; mNY, modified New York; MRI, magnetic resonance imaging; No., number of individuals included in the study; NS, not statistically significant; OR, odds ratio; RCT, randomised controlled trial; SIJ, sacroiliac joints; SPARCC, Spondyloarthritis Research Consortium of Canada Scoring System; –, not done.

Five studies reported correlation between changes over time in MRI and radiography and/or CT parameters of structural damage,[71 84 88–90] while Puhakka *et al*[91] found MRI and CT are superior to radiography. A single study reported correlation between spinal MRI and metrological measures,[97] while two reported no correlation.[70 91] One study reported correlation between MRI changes and BASMI,[88] whereas two studies reported no correlation with BASFI.[70 97] Akgul *et al*[80] reported that fatty infiltration of the paraspinal muscles on MRI correlates with metrological measures. Regarding the frequency of MRI examinations for the monitoring of structural changes under treatment with a tumour necrosis factor (TNF) inhibitor, Rudwaleit *et al*[72] reported no significant spinal or SI joint changes after 24 weeks, while Baraliakos *et al* reported significant deterioration in the mean Ankylosing Spondylitis spinal MRI chronicity score (ASspiMRI-c) in the placebo group at 48 weeks.[50] There is currently no evidence whether and if so how frequently MRI should be repeated for the monitoring of structural changes in axial SpA. Quality assessment is reported in online supplementary figure S6.4; of note risk of patient selection bias and applicability concerns with regard to patient selection were high in 43% and 30% of included manuscripts, respectively.

Recommendation 5: monitoring disease activity in peripheral SpA

US and MRI may be used to monitor disease activity (particularly synovitis and enthesitis) in peripheral SpA, providing additional information on top of clinical and biochemical assessments. The decision on when to repeat US/MRI depends on the clinical circumstances. US with high-sensitivity colour or power Doppler is sufficient to detect inflammation and the use of US contrast medium is not needed.

Strength of recommendation: 9.3 (95% CI 8.9 to 9.7)

Fifteen studies evaluated the utility of various imaging modalities in monitoring disease activity in pSpA,[39 40 98–110] of which 10 investigated GSUS/PDUS for the assessment of entheses (8 on multiple entheses, 2 on the Achilles tendon). Out of the 10 studies investigating GSUS/PDUS, only a single study was longitudinal,[98] while the remaining 9 were cross-sectional.[39 40 99–105] A single study reported correlation with BASDAI,[99] while four reported no correlation.[98 100–102] Aydin *et al*[100] reported correlation between grey-scale entheseal changes of the Achilles tendon and CRP, while five studies reported no correlation with CRP and/or ESR.[98 101–104] Hamdi *et al*[99] reported correlation between pain and power Doppler entheseal changes of the lower limb entheses, while Kiris *et al*[102] reported no correlation between PD and axial entheses.

Two studies reported correlation with swollen or tender joint count,[39 104] while a single study reported no correlation.[40] Hamdi *et al*[99] reported correlation with clinical enthesis indices (Maastricht Ankylosing Spondylitis Score, Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index), while two studies reported no correlation.[39 98] Two studies reported discrepancies in abnormal entheses detected by US versus clinical examination.[40 105]

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Table 4 Recommendation 4: summary of studies on the use of radiography in monitoring structural changes in axial spondyloarthritis

Studies	No.	Region	X-ray scoring method	Correlation			
				BASFI	BASMI	Metrological measures	CT
Longitudinal/RCT							
Machado *et al*[63]	214	Spine	mSASSS	0.18; p=0.008	0.59; p<0.001	–	–
Averns *et al*[81]	53	Spine	SASSS	–	–	−0.396, p<0.01 (CE) 0.503, p<0.001 (OWD) 0.351, p<0.02 (FFD) −0.690, p<0.0001 (Schober) −0.717, p<0.0001 (total spinal movement)	–
Baraliakos *et al*[82]	82	Spine	mSASSS	NS	0.49–0.59; p=0.01	–	–
Baraliakos *et al*[83]	80	Spine	mSASSS	–	0.49	NS	–
Creemers *et al*[85]	50	Spine	mSASSS	–	–	p=0.05–0.0005 (CE, OWD, SF)	–
Salaffi *et al*[93]	95	Spine	mSASSS	p=0.02	p=0.01	–	–
Taylor *et al*[94]	70	Spine/SIJ	Semi-quantitative	–	–	−0.40; p<0.05 (SF)	0.52; p<0.01 (spine) 0.75; p<0.001 (SIJ)
Wanders *et al*[96]	133	Spine/SIJ	mSASSS SASSS BASRI	0.41	–	−0.77 (SF) 0.65 (OWD) −0.76 (mSchober)	–
Cross-sectional/case–control							
Lee *et al*[86]	39	Spine	BASRI	–	–	–	0.53–0.73 (p<0.001)
Lubrano *et al*[87]	77	Spine	BASRI mSASSS	NS	0.47; p<0.001	0.49, p<0.001 (CR) 0.34, p<0.01 (TWD) 0.49, p<0.001 (OWD) −0.24, p<0.05 (mSchober) 0.37, p<0.01 (FFD)	–

The Spearman test for rank correlation is used for test of correlation, values are correlation coefficients (rho), if not otherwise indicated. p Values indicate the level of statistical significance.
BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; BASRI, Bath Ankylosing Spondylitis Functional Radiology Index; CE, chest expansion; CR, cervical rotation; FFD, finger-to-floor distance; mSASSS, modified Stoke Ankylosing Spondylitis Score; mSchober, modified Schober's test; No., number of individuals included in the study; NS, not statistically significant; OWD, occiput-wall distance; RCT, randomised controlled trial; SASSS, Stoke Ankylosing Spondylitis Score; SF, spinal flexion; SIJ, sacroiliac joints; TWD, tragus-to-wall distance; –, not done.

Four longitudinal[106–109] and a single cross-sectional[110] study evaluated the utility of MRI in monitoring disease activity in pSpA with three longitudinal studies reporting the psoriatic arthritis MRI score (PsAMRIS) and rheumatoid arthritis MRI score performing well regarding SE to change.[106–108] Tan *et al* found no correlation between BME (as scored by PsAMRIS) and clinical disease activity measures in a cross-sectional study.[110] There is currently no evidence whether and if so how frequently US and/or MRI should be repeated for the monitoring of disease activity in peripheral SpA. Quality assessment is reported in online supplementary figure S6.5; of note patient selection bias was high in 47% of included manuscripts.

Recommendation 6: monitoring structural changes in peripheral SpA

In peripheral SpA, if the clinical scenario requires monitoring of structural damage, then conventional radiography is recommended. MRI and/or US might provide additional information.

Strength of recommendation: 8.9 (95% CI 8.4 to 9.4)

Seven studies evaluated the utility of conventional radiography (CR) to monitor structural changes in pSpA,[101 102 111–115] with one study also evaluating PDUS[102] and an additional study evaluating MRI.[110] Among the studies assessing the utility of radiography, two reported correlation with the functional indices Health Assessment Questionnaire and/or Arthritis Impact Measurement Scales.[114 115] A longitudinal study on 74 patients with PsA reported correlation between clinical joint deformity, typical radiographic changes in PsA and the PsA-modified Sharp score.[114] A case–control study on 98 patients with ReA reported correlation between radiographic condylar erosions of the temporomandibular joint and patient-reported outcomes.[112] A cross-sectional study on 60 patients with AS reported correlation between BASFI and both radiographic and sonographic signs of enthesitis,[102] while a cross-sectional study on 44 patients with SpA reported correlation between the SpA tarsal radiographic index and the Glasgow Ultrasound Enthesitis Score, but no correlation between the radiographic index and BASMI or BASRI.[101] Finally, Tan *et al*[110] reported correlation between MRI erosions/BME and CR erosions/joint space narrowing in 28 patients with PsA. Quality assessment is reported in online supplementary figure S6.6; of note risk of patient selection bias was high in 50% of included manuscripts. There is currently no evidence whether and if so how frequently US and/or MRI should be repeated for the monitoring of structural changes in peripheral SpA.

Recommendation 7: predicting outcome/severity in axial SpA

In patients with AS* (not non-radiographic axial SpA), initial conventional radiography of the lumbar and cervical spine is recommended to detect syndesmophytes, which are predictive of development of new syndesmophytes. MRI (vertebral corner inflammatory or fatty lesions) may also be used to predict development of new radiographic syndesmophytes.

*That is, radiographic axial spondyloarthritis.

Strength of recommendation: 9.0 (95% CI 8.5 to 9.5)

Seventeen publications were included.[19 81 82 116–129] All studies evaluating radiography reported that baseline radiographic change (syndesmophytes) predicts radiographic progression in AS.[82 116 118 122 126 129] Baraliakos *et al* reported that syndesmophytes/ankylosis, rather than erosion or sclerosis, were the features most frequently showing progression in AS.[116] Maksymowych *et al*[122] found that high baseline mSASSS (cut-off of 10 units; OR 18.6) was an independent predictor of 2-year progression in AS.

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Six studies reported correlation between CILs or vertebral edge inflammation on MRI and subsequent radiographic syndesmophyte formation in patients with AS.[117 119 120 123 124 128] Madsen *et al*[121] reported correlation of baseline inflammation and subchondral fatty marrow deposition on MRI with radiographic progression in the SI joint of patients with AS.

In a 2-year longitudinal study, Pedersen *et al*[124] found that new syndesmophytes develop more frequently from vertebral corners where a CIL had completely resolved on follow-up, and that no single vertebral corner evolved into a new syndesmophyte where a CIL was persistently observed on both baseline and follow-up MRI. Along the same line, a 2-year longitudinal study of patients with axSpA/AS revealed an association between decreasing inflammation in the SI joint and the concomitant development of new syndesmophytes (OR 12.48).[125] In a 1-year longitudinal study, Song *et al*[127] presented a significant relationship between the disappearance of inflammation and the appearance of fatty lesions in the spine of patients with axSpA. Moreover, Baraliakos *et al*[119] showed that both spinal inflammation and fatty degeneration were associated with later syndesmophyte development but fatty degeneration showed the highest risk in AS. In contrast, a retrospective analysis of 100 patients with AS, inflammation (OR 5.8) emerged as a more significant predictor of new syndesmophytes than did fat infiltration (OR 1.9).[120] Finally, Bennett *et al*[19] reported no association between baseline BME on lumbar spine MRI and mSASSS progression after 8 years in patients with AS.

Averns *et al*[81] reported correlation between baseline QSS values and radiographic progression in the spine at follow-up (median: 9 years) in patients with AS. Quality assessment is reported in online supplementary figure S6.7.

Recommendation 8: predicting treatment effect in axial SpA

Extensive MRI inflammatory activity (BME), particularly in the spine in patients with AS, might be used as a predictor of good clinical response to anti-TNF-alpha treatment in axial SpA. Thus, MRI might aid in the decision of initiating anti-TNF-alpha therapy, in addition to clinical examination and CRP.

Strength of recommendation: 8.9 (95% CI 8.3 to 9.5)

A total of three studies were included. A longitudinal study of 62 patients with AS under treatment anti-TNF-alpha biologics reported a positive likelihood ratio of 6.7 for achieving BASDAI50 response in patients with a Berlin MRI spine score >11, while the absence of active inflammatory lesions in the spine was highly predictive of not achieving BASDAI50. Only a trend was found for the MRI SI joint score.[73] An RCT of 185 patients with non-radiographic axial SpA reported that a baseline SPARCC MRI score ≥2 for either the SI joint or the spine was associated with better response after 12 weeks of adalimumab.[75] An RCT including 40 human leucocyte antigen B27 (HLAB27)-positive patients with MRI sacroiliitis found no significant difference in BASDAI changes between patients with mild versus moderate/severe MRI SI joint BME at baseline.[130] Quality assessment is reported in online supplementary figure S6.8; of note risk of patient selection bias, as well as of flow and timing and applicability concerns, was each high in 33% of included manuscripts.

Recommendation 9: spinal fracture

When spinal fracture in axial SpA is suspected, conventional radiography is the recommended initial imaging method. If conventional radiography is negative, CT should be performed. MRI is an additional imaging method to CT, which can also provide information on soft tissue lesions.

Strength of recommendation: 9.3 (95% CI 8.9 to 9.7)

Although no study met the inclusion criteria for this recommendation, two studies selected for full-text review were presented to the taskforce as they could provide some evidence (quality assessment however was not performed). The first study included 11 patients with AS and neurological symptoms after trauma to the neck region. CT and MRI detected all fractures while radiography detected 82% of them. Soft tissue injuries were detected in four patients, only by MRI.[131] The second study included 199 patients from the general population with suspected cervical spine injury. Twenty-one acute fractures were detected in 14 patients. Weighted average SE to detect acute fractures for MRI and radiography were 0.43 (95% CI 0.21 to 0.66) and 0.48 (95% CI 0.30 to 0.65), respectively. In contrast, weighted average SE to detect soft tissue injuries for MRI and radiography were 0.55 (95% CI 0.39 to 0.70) and 0.07 (95% CI 0.02 to 0.13), respectively.[132] In addition to its utility in imaging soft tissue, MRI allows the direct visualisation of the spinal cord and thus direct evaluation of spinal cord injuries.

Recommendation 10: osteoporosis

In patients with axial SpA without syndesmophytes in the lumbar spine on conventional radiography, osteoporosis should be assessed by hip DXA and anterior–posterior (AP)-spine DXA. In patients with syndesmophytes in the lumbar spine on conventional radiography, osteoporosis should be assessed by hip DXA, supplemented by either spine DXA in lateral projection or possibly quantitative CT (QCT) of the spine.

Strength of recommendation: 9.4 (95% CI 9.0 to 9.8)

A total of 42 studies were included,[133–174] while one additional study that did not meet the inclusion criteria but provided some evidence was also shown to the taskforce.[175] Only one study compared the diagnostic utility between two different techniques for detecting osteoporosis in SpA. This reported moderate SE (0.50–0.75) and SP (0.67–0.75) for quantitative US compared with DXA.[133] Three studies reported no additional value of quantitative US compared with DXA[134–136] while three studies compared QCT to DXA and reported that in patients with advanced AS osteoporosis is more frequently detected by QCT of the spine than using DXA of the spine[137 175] or the hip region.[138]

Moreover, 37 studies (32 in axSpA and 6 in PsA) provided data on the site for performing DXA.[139–173] In axSpA, 20 studies compared DXA at different sites for distinguishing between patients with AS and controls. Fifteen of these studies compared the AP/posterior–anterior (PA) projection at the spine versus the hip region but the results were inconsistent: six studies observed no differences,[136 139–143] eight reported results in favour of the hip[135 144–150] and one in favour of the spine.[151] Three studies compared the AP/PA versus the lateral projection at the spine and all reported that the lateral projection differentiated better between AS and controls.[145 146 149] Only four studies compared forearm DXA with other regions, all of them reporting data in favour of spine or hip[137 142 152 153] regions.

Furthermore, some studies also evaluated the possible influence of radiographic change, disease duration or disease activity in bone mineral density (BMD) determination at different regions (table 5). Most of the studies found the hip region being less influenced by radiographic change than the AP/PA projection of the spine.[137 138 142 145 147 148 154 155 156] Two studies reported the lateral spine projection being less influenced by radiographic change than the AP/PA projection.[145 157] Moreover, the majority of the studies found a positive correlation between BMD and disease duration with AP/PA projection of the spine while no correlation was found with the lateral projection or at hip. However, most of the studies did not observe

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Table 5 Recommendation 10: summary of studies evaluating different localisations to perform dual-energy X-ray absorptiometry in patients with axial spondyloarthritis

(A)		Radiographic damage (syndesmophytes/BASRI spine) Results in favour of	
Study N=11	No.	AP/PA spine	Hip
Devogelaer *et al*[137]	70		X
Karberg 2005[138]	103		X
Jun 2006[140]	68	ND	ND
Mullaji 1994[142]	33		X
Gilgil 2005[145]	20		X
Muntean 2011[147]	44		X
Taylan 2012[148]	55		X
Vasdev 2001[151]	80	ND	ND
Baek 2005[154]	76		X
Capaci 2003[155]	73		X
Donelly 1994[156]	87		X
N=2		**AP/PA spine**	**Lateral spine**
Gilgil 2005[145]	20		X
Klingberg 2012[157]	204		X

(B)		Disease duration Correlation between BMD and disease duration	
Study N=12	No.	AP/PA spine	Hip
Arends 2011[170]	198	r=0.34	NS
El Magahroui 1999[173]	80	r=0.23	NS
Gilgil 2005[145]	20	r=0.52	NS
Grazio 2012[158]	80	r=0.05	r=−0.361
Jansen *et al*[133]	50	No	r=0.35
Meirelles 1999[141]	30	r=0.65	NS
Mermerci 2010[146]	100	r=0.25	r=−0.20
Muntean 2011[147]	44	NS	NS
Speden *et al*[135]	66	NS	NS
Taylan 2012[148]	55	r=0.30	NS
van der Weijden 2011[160]	130	NS	NS
Vasdev 2011[151]	80	NS	NS
N=2		**AP/PA spine**	**Lateral spine**
Gilgil 2005[145]	20	r=0.52	NS
Memerci 2010[146]	100	r=0.25	NS

(C)		Disease activity Correlation between BMD and disease activity parameters (ASDAS, BASDAI, CRP, ESR)	
Study N=9	No.	AP/PA spine	Hip
Frediani *et al*[134]	186	NS	NS
Grazio 2012[158]	80	r=−0.30	r=−0.22
Mermerci 2010[146]	100	r=−0.24	r=−0.24
Mullaji 1994[142]	33	NS	NS
Muntean 2011[147]	44	NS	NS
Park 2008[159]	35	NS	r=−0.49
Taylan 2012[148]	55	NS	NS
van der Weijden 2011[160]	130	NS	NS
Vasdev 2011[151]	80	NS	NS
N=1		**AP/PA spine**	**Lateral spine**
Mermerci 2010[146]	100	r=−0.24	r=−0.30

The Pearson test for rank correlation is used for test of correlation, values are correlation coefficients (r).
AP, anterior–posterior; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Score; BASRI, Bath Ankylosing Spondylitis Radiology Index; BMD, bone mineral density; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; ND, no statistically significant differences; NS, not statistically significant; PA, posterior–anterior.

correlation with AP/PA projection of the spine or at hip.[135 141 146–148 151 158–160] In patients with PsA, published data are scarce. Three studies compared the ability of AP/PA DXA of the spine with DXA of the hip to distinguish between patients with PsA and controls but the results were not consistent.[134 161 162] In patients with PsA, no correlation was observed between BMD detected by AP/PA DXA of the spine or the hip with disease duration[134 163] or with disease activity.[134 164]

Box 1 Future research agenda

1. To further investigate which imaging findings (imaging modality, anatomical location and type of pathology) provides the best clinical utility for early and accurate diagnosis of SpA.
2. To further investigate which imaging findings (imaging modality, anatomical location and type of pathology) are best for monitoring peripheral and axial disease activity and structural damage in SpA in clinical practice.
3. To further investigate which imaging findings (imaging modality, anatomical location and type of pathology) best predict the disease course (structural progression, pain, functional ability, health-related quality of life) and treatment response in SpA.
4. To further investigate which imaging approaches best identify and monitor specific SpA-related features (such as enthesitis, dactylitis, synovitis and tenosynovitis, at different locations) in clinical practice.
5. To further investigate the spatial and temporal relation between different imaging findings (imaging modality, anatomical location and type of pathology) providing further insight into the disease process of SpA, which may inform future clinical management of SpA.
6. To investigate the importance of subclinical (detected only on imaging) axial and peripheral inflammation (including bone marrow oedema, synovitis, tenosynovitis and/or enthesitis), and if possible to identify thresholds to guide intervention. Subsequently to investigate the benefits (eg, on functional ability and quality of life) of incorporating such thresholds into treat-to-target strategies.
7. To investigate new and/or alternative technical options to existing imaging technologies (US: eg, 3D/4D-transducers, Doppler quantification, elastosonography; MRI: eg, whole-body MRI, diffusion-weighted MRI and dynamic contrast-enhanced MRI with automated reading) as well as new imaging modalities (eg, optical imaging, new nuclear medicine techniques) of potential use in SpA in clinical practice.
8. To further evaluate specific areas/joints to be assessed, timing of assessment(s) and the evaluation system to be employed in order to optimise the role of modern imaging modalities in the diagnosis, prognosis and outcome measurement of SpA.
9. To investigate which imaging approach provides the best clinical utility for diagnosing spinal fractures, and the consequences thereof.
10. To investigate which imaging approach provides the best clinical utility for diagnosis and monitoring of osteoporosis in SpA.

SpA, spondyloarthritis; US, ultrasound; 3D, three-dimensional; 4D, four-dimensional.

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Finally, only four longitudinal studies assessed BMD over time to monitor osteoporosis in patients with SpA.[165–168] In these studies, changes in BMD were observed after 1–2 years, especially in patients with active disease. Quality assessment is reported in online supplementary figure S6.9; of note risk of index test and reference standard bias were high in 86% and 88% of included manuscripts, respectively.

DISCUSSION

These are the first recommendations produced by a EULAR taskforce on the use of imaging in SpA clinical practice. The group combined research-based evidence and expert opinion through a translational process among the experts from the presented literature-derived evidence to the final wording. Recommendations were primarily based on available research evidence with the exception of recommendation 9, which, lacking available data, was reliant on expert opinion. Finally, experts scored the SOR for each recommendation using data from the quality assessment.

We acknowledge that there is still a large amount of research required to optimise the use of imaging tools in the routine clinical practice of SpA.[176] We have summarised the most important topics for future research according to currently available evidence and clinical practice in box 1. These recommendations will likely need to be revisited in the future when important new evidence becomes available.[12]

In summary, we have developed 10 recommendations on various aspects of imaging in SpA. These are based on the best available evidence and clinical expertise supported by an international panel of experts. We aimed to produce recommendations that are practical and valuable in daily practice for rheumatologists, radiologists and general practitioners.

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Competing interests PM: consultancy/speaker fees: AbbVie, BMS, GE, Janssen, MSD, Pfizer, Roche, UCB; VN-C: consultancy/research grants: AbbVie, BMS, MSD, Novartis, Pfizer, Roche, UCB; LT: consultancy/speaker fees: AbbVie, GE, MSD, Roche, UCB; PA: none; DvdH: consultancy/research grants: AbbVie, Amgen, AstraZeneca, Augurex, BMS, Boehringer Ingelheim, Celgene, Centocor, Chugai, Covagen, Daiichi, Eli-Lilly, Galapagos, GSK, Janssen Biologics, Merck, Novartis, Novo-Nordisk, Otsuka, Pfizer, Roche, Sanofi-Aventis, UCB, Vertex, Director of Imaging Rheumatology International; MAD'A: consultancy/speaker fees: AbbVie, BMS, MSD, Novartis, Pfizer, UCB; XB: consultancy/speaker fees: AbbVie, Amgen, Boehringer Ingelheim, BMS, Celgene, Centocor, Chugai, Janssen, MSD, Novatis, Pfizer, Sandoz, UCB; SJP: consultancy/speaker fees: AbbVie, MSD, Pfizer, Roche, UCB, Wyeth; research grants: AbbVie, MSD; AGJ: none; EN: research grants: MSD, Spanish Foundation of Rheumatology; speaker fees: Abbvie, BMS, ESAOTE, GE, Pfizer, Roche, UCB; CS-W: speaker fees: AbbVie, Eli-Lilly, Roche; UW: speaker fees: AbbVie, MSD; MCW: none; PACB: none; EF: speaker fees: Abbvie, BMS, MSD, UCB; PGC: consultancy/speaker fees: Abbvie, BMS, Janssen, Merck, Novartis, Pfizer, Roche; MR: consultancy: AbbVie, BMS; speaker fees: Chugai, MSD, Novartis, Pfizer, Roche, UCB; GS: none; JS: consultancy/speaker fees: Abbott, Janssen, Merck, Lilly, Novartis, Roche; research grants: Abbott, Merck, Pfizer; ST: speaker fees: AstraZeneca, Norpharma, Pfizer; research grants paid to institute: AbbVie, BMS, Mundipharma, Roche; HM-O: speaker fees/research grants: AbbVie, Celgene, Janssen, MSD, Novartis, Pfizer, UCB; MØ: research grant: Abbvie, Janssen, Merck; consultancy/speaker fees: Abbvie, BMS, Boehringer Ingelheim, Celgene, Centocor, Eli-Lilly, GSK, Hospira, Janssen, Merck, Mundipharma, Novartis, Orion, Pfizer, Roche, Takeda, UCB.

Provenance and peer review Not commissioned; externally peer reviewed.

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