The OMERACT Rheumatoid Arthritis Magnetic Resonance Imaging (MRI) Scoring System: Updated Recommendations by the OMERACT MRI in Arthritis Working Group

Mikkel Østergaard, Charles G. Peterfy, Paul Bird, Frédérique Gandjbakhch, Daniel Glinatsi, Iris Eshed, Espen A. Haavardsholm, Siri Lillegraven, Pernille Bøyesen, Bo Ejbjerg, Violaine Foltz, Paul Emery, Harry K. Genant, and Philip G. Conaghan

ABSTRACT. ***Objective.*** The Outcome Measures in Rheumatology (OMERACT) Rheumatoid Arthritis (RA) Magnetic Resonance Imaging (MRI) scoring system (RAMRIS), evaluating bone erosion, bone marrow edema/osteitis, and synovitis, was introduced in 2002, and is now the standard method of objectively quantifying inflammation and damage by MRI in RA trials. The objective of this paper was to identify subsequent advances and based on them, to provide updated recommendations for the RAMRIS.

Methods. MRI studies relevant for RAMRIS and technical and scientific advances were analyzed by the OMERACT MRI in Arthritis Working Group, which used these data to provide updated considerations on image acquisition, RAMRIS definitions, and scoring systems for the original and new RA pathologies. Further, a research agenda was outlined.

Results. Since 2002, longitudinal studies and clinical trials have documented RAMRIS variables to have face, construct, and criterion validity; high reliability and sensitivity to change; and the ability to discriminate between therapies. This has enabled RAMRIS to demonstrate inhibition of structural damage progression with fewer patients and shorter followup times than has been possible with conventional radiography. Technical improvements, including higher field strengths and improved pulse sequences, allow higher image resolution and contrast-to-noise ratio. These have facilitated development and validation of scoring methods of new pathologies: joint space narrowing and tenosynovitis. These have high reproducibility and moderate sensitivity to change, and can be added to RAMRIS. Combined scores of inflammation or joint damage may increase sensitivity to change and discriminative power. However, this requires further research.

Conclusion. Updated 2016 RAMRIS recommendations and a research agenda were developed. (First Release August 1 2017; J Rheumatol 2017;44:1706–12; doi:10.3899/jrheum.161433)

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From the Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup; Department of Clinical Medicine, University of Copenhagen, Copenhagen; Slagelse Hospital, Slagelse, Denmark; Spire Sciences Inc., Boca Raton, Florida; Medicine and Orthopedics, University of California; Synarc Inc., San Francisco, California, USA; University of New South Wales (NSW), Sydney, Australia; Hôpital Pitié-Salpétrière, APHP, Université Paris VI, Paris, France; Sheba Medical Center, Tel Aviv University, Tel Aviv, Israel; Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway; Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, and UK National Institute for Health Research (NIHR) Leeds Biomedical Research Centre, Leeds, UK.

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M. Østergaard, MD, PhD, DMSc, Professor, COPECARE, Center for Rheumatology and Spine Diseases, Rigshospitalet, and the Department of Clinical Medicine, University of Copenhagen; C.G. Peterfy, MD, PhD, FRCP, Chief Executive Officer, Spire Sciences Inc.; P. Bird, BMed (Hons), FRACP, PhD, Grad Dip MRI, Associate Professor, University of NSW; F. Gandjbakhch, MD, Practicing Rheumatologist, Hôpital Pitié-Salpétrière, APHP, Université Paris VI; D. Glinatsi, MD, Research Fellow, COPECARE, Center for Rheumatology and Spine Diseases, Rigshospitalet; I. Eshed, MD, Professor of Radiology, Sheba Medical Center, Tel Aviv University; E.A. Haavardsholm, MD, PhD, Professor, Department of Rheumatology, Diakonhjemmet Hospital; S. Lillegraven, MD, MPH, PhD, Postdoctoral Researcher, Department of Rheumatology, Diakonhjemmet Hospital; P. Bøyesen, MD, PhD, Department of Rheumatology, Diakonhjemmet Hospital; B. Ejbjerg, MD, PhD, Consultant Rheumatologist and Senior Lecturer, Slagelse Hospital, and Department of Clinical Medicine, University of Copenhagen; V. Foltz, MD, Practicing Rheumatologist, Hôpital Pitié-Salpétrière, APHP, Université Paris VI; P. Emery, MA, MD, FRCP, ARC Professor in Rheumatology, Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, and NIHR Leeds Biomedical Research Centre; H.K. Genant, MD, FACR, FRCR, Professor Emeritus of Radiology, Medicine and Orthopedics, University of California, San Francisco, and Synarc Inc.; P.G. Conaghan, MB, BS, PhD, FRACP, FRCP, Professor of Musculoskeletal Medicine, Leeds Institute of

Rheumatic and Musculoskeletal Medicine, University of Leeds, and NIHR Leeds Biomedical Research Centre.

Address correspondence to Professor M. Østergaard, Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Valdemar Hansens vej 17, DK-2600 Glostrup, Denmark. E-mail: mo@dadlnet.dk

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Magnetic resonance imaging (MRI) allows sensitive assessment of disease activity and structural damage in inflammatory arthritides, and MRI variables are now frequently used outcome measures in rheumatoid arthritis (RA) clinical trials, providing new insights into disease status and treatment response[1,2]. The Outcome Measures in Rheumatology (OMERACT) RA MRI Scoring system (RAMRIS) was developed and validated from 1998–2002 by the OMERACT MRI Working Group[3]. A core set of MRI acquisitions, joint pathology definitions, and a scoring system for semiquantitative evaluation of bone erosion, bone marrow edema (osteitis), and synovitis were provided[3], and this method is now the standard MRI method used in RA clinical trials[1,2].

Since 2002, new developments and increased knowledge have become available. These include development of an MRI atlas, new data from clinical trials, technical developments, and development and validation of MRI scoring methods for assessing additional pathologies that are important in RA. These improvements and their implication for the use of RAMRIS have never been systematically described, which is our intention here.

Thus, in our present article, the OMERACT MRI in Arthritis Working Group for the first time since the RAMRIS was published in 2003 describe the advances related to the RAMRIS, which include clinical trial data, MRI technical improvements, and development of assessment methods for new RA pathologies, and provide updated recommendations on how to use the OMERACT RAMRIS for different purposes in RA clinical trials and observational studies.

MATERIALS AND METHODS

Based on recent developments on MRI in RA in general and the OMERACT RAMRIS in particular, we summarize the important achievements of relevance for RAMRIS, including technical developments, new validated instruments[4], and acquired scientific knowledge. Updated recommendations by the OMERACT MRI in Arthritis Working Group, including an updated list of RAMRIS definitions (Table 1) and scoring systems (Table 2 and Figure 1) for RA pathologies are provided. Further, a research agenda is outlined (Table 3).

RESULTS

The performance of the original RAMRIS features. The superior sensitivity of MRI for assessing inflammation and structural damage, as compared to clinical examination and conventional radiography, has been documented in many randomized controlled trials (RCT) of patients with early and established RA[1,5,6,7], also documenting the feasibility of RAMRIS. Compared to radiography, MRI can document statistically significant structural damage inhibition in less than half the time and with fewer than half the patients[8,9]. The American College of Rheumatology RA Clinical Trials Task Force Imaging Group and the OMERACT MRI in Arthritis Working Group have, based on a systematic literature review, concluded that MRI best serves the purpose of achieving sensitive ascertainment of structural damage in RCT, and additionally provides objective measures of inflammatory predictors of damage[2]. An independent value of early MRI inflammatory changes (synovitis and osteitis) and changes therein for predicting subsequent structural damage progression has been documented[10,11,12].

MRI osteitis and synovitis have documented criterion validity, by comparison with histology, and MRI erosion has documented construct validity by comparisons with computed tomography[1,2,13,14,15,16]. Criterion validity of MRI of articular cartilage has also been demonstrated[17].

Recently, the relevance of MRI findings (synovitis, osteitis, erosion, tenosynovitis) for important patient-reported outcomes (PRO) of functional disability [Health Assessment Questionnaire (HAQ)] and pain has been documented[18,19]. Independent, statistically significant associations of RAMRIS synovitis, erosion, and tenosynovitis scores with pain and patient's global (synovitis only) and HAQ (all) have been found[18,19]. Further, improvements in synovitis and bone erosion were associated with improvements in PRO[18]. In contrast, radiographic change, assessed by the Sharp/van der Heijde method (SvDH), were not associated with PRO. A significant correlation between HAQ and radiographic joint damage (SvDH) has, however, been documented[20], but this required larger studies.

Considerations for technical improvements in MRI image acquisition. MRI is undergoing continuous technical innovations and refinements, and important developments have occurred since 2002. Improvements in hardware (magnets, gradients, and coils) and software (pulse sequences) have made it possible to acquire images with higher resolution and signal-to-noise ratios. These and other improvements allowed our group to develop the joint space narrowing (JSN) score, which was not originally included in 1998–2002 because of insufficient image quality at that time. Other technical developments that may in the future lead to alternative assessment methods to RAMRIS include dynamic contrast-enhanced MRI[6,21,22], automated volumetric quantification, e.g., using active appearance modeling (referred to as the Rheumatoid Arthritis Magnetic Resonance Imaging Quantitative assessment system)[6], and whole-body MRI[23,24]. These methods require further validation and testing.

It is still recommended to use postcontrast T1-weighted sequences for optimal assessment of synovitis, T1-weighted sequences that enable visualization in 2 planes for assessment of bone erosions, and T2-weighted fat-saturated (T2FS) or short-tau inversion recovery (STIR) images for assessment of bone marrow edema/osteitis, whereas tenosynovitis can

Table 1. OMERACT MRI in RA group's updated 2016 recommendations of a "core set" of basic MRI sequences and MRI definitions of important RA joint pathologies for use in the RA MRI scoring system (OMERACT 2016 RAMRIS).

"Core set" of basic MRI sequences:

It is suggested that future MRI studies, which intend to assess inflammatory and destructive changes in RA joints, should include at least the following:

- T1-weighted images before and after IV gadolinium-contrast injection* that enable visualization in 2 planes**
- T2-weighted fat-saturated or STIR images

Definitions of important RA joint pathologies:

- Synovitis: An area in the synovial compartment that shows above-normal postgadolinium enhancement (signal intensity increase) of a thickness greater than the width of the normal synovium
- MRI bone erosion: A sharply marginated bone lesion, with correct juxtaarticular localization and typical signal characteristics[†], which is visible in 2 planes with a cortical break seen in at least 1 plane[††]
- MRI osteitis/bone marrow edema: A lesion[‡] within the trabecular bone, with ill-defined margins and signal characteristics consistent with increased water content[‡‡]
- MRI joint space narrowing: Reduced joint space width compared to normal, as assessed in a slice perpendicular to the joint surface
- MRI tenosynovitis: Peritendinous effusion[#] and/or tenosynovial postcontrast enhancement[##], seen on axial sequences over ≥ 3 consecutive slices

*IV gadolinium injection is particularly important if assessment of synovitis is considered important. **Bi-planar imaging can be achieved by a 2-dimensional sequence in 2 planes or a single 3-D acquisition with isometric voxels allowing reconstruction in multiple planes. A dedicated cartilage sequence, e.g., a fat-suppressed 3-D gradient echo sequence, will improve cartilage assessment. [†]On T1-weighted images: discontinuity of the signal void of cortical bone and loss of normal high signal intensity of bone marrow fat. Rapid post-gadolinium enhancement suggests presence of active, hypervascularized pannus tissue in the erosion. [††]Other focal bone lesions and variations of normal anatomy must obviously be considered, but are generally distinguishable with associated imaging and clinical findings. [‡]May occur alone or surrounding an erosion. [‡‡]High signal intensity on T2-weigted fat-saturation or STIR images, and low signal intensity on T1-weighted images. [#]High signal intensity on T2-weigted fat-saturated/STIR images. [##]Enhancement (signal intensity increase) is judged by comparison of T1-weighted images obtained before and after IV gadolinium-contrast. OMERACT: Outcome Measures in Rheumatology; MRI: magnetic resonance imaging; RA: rheumatoid arthritis; RAMRIS: Rheumatoid Arthritis Magnetic Resonance Imaging Scoring system; IV: intravenous; STIR: short-tau inversion recovery.

Table 2. The OMERACT MRI in Arthritis Working Group's updated 2016 recommendations of the OMERACT RA MRI scoring system (OMERACT 2016 RAMRIS).

Bone erosion	• Each bone (wrists: distal radius, distal ulna, carpal bones, metacarpal bases; MCP joints: metacarpal heads, phalangeal bases) is scored separately • The scale is 0–10, based on the proportion of eroded bone compared to the "assessed bone volume," judged on all available images: 0 = no erosion; 1 = 1–10% of bone eroded; 2 = 11–20%, etc. For long bones, the "assessed bone volume" is from the articular surface (or its best estimated position if absent) to a depth of 1 cm, while in carpal bones it is the whole bone • In case a bone is fused with another bone, bone erosion is scored as 10 in the bone
Osteitis/bone marrow edema	• Each bone is scored separately (as for erosions) • The scale is 0–3 based on the proportion of bone with osteitis, as follows: 0 = no osteitis; 1 = 1–33% of bone with osteitis; 2 = 34–66%; 3 = 67–100%
Synovitis	• Synovitis is assessed in 3 wrist regions (1. the distal radioulnar joint; 2. the radiocarpal joint; 3. the intercarpal and carpometacarpal joints) and in each MCP joint. The first carpometacarpal joint is not scored • The scale is 0–3. Score 0 is normal, while 1– 3 (mild, moderate, severe) are by thirds of the presumed maximum volume of enhancing tissue in the synovial compartment
Joint space narrowing	• Joint space narrowing is assessed at 17 locations in the wrist, between distal radius and carpal bones (2 sites), between the carpal bones (except the pisiform; 10 sites), and between carpal bones and each metacarpal bone (5 sites), and in each MCP joint • The scale is 0–4, as follows: 0 = no narrowing; 1 = focal or mild (< 33%) narrowing; 2 = moderate (34–66%) narrowing; 3 = moderate to severe (67–99%) narrowing; 4 = ankylosis
Tenosynovitis	• In the wrist, tenosynovitis is assessed at 6 extensor tendon compartments and 3 flexor tendon compartments, between the radioulnar joint and the hook of hamate. At the level of the MCP joints, flexor tendons are assessed in an area from 1 cm proximal to 1 cm distal to each joint • Tenosynovitis is scored based on the maximum width of the effusion and/or tenosynovial enhancement measured perpendicularly to the tendon • The scale is 0–3, as follows: 0 = no; 1 = < 1.5 mm; 2 = ≥ 1.5 mm but < 3 mm; 3 = ≥ 3 mm peritendinous effusion and/or postcontrast tenosynovial enhancement

OMERACT: Outcome Measures in Rheumatology; MRI: magnetic resonance imaging; RA: rheumatoid arthritis; RAMRIS: Rheumatoid Arthritis Magnetic Resonance Imaging Scoring system; MCP: metacarpophalangeal.

Table 3. Research agenda.

List of proposed areas for investigation* by the OMERACT MRI in Arthritis Working Group:

- Combined scores of inflammation (synovitis, osteitis, and tenosynovitis) and of damage (bone erosion and cartilage damage/JSN)
- New sequences, e.g., MRI without intravenous contrast injection for assessment of synovitis, dedicated cartilage sequences, and diffusion-weighted MRI
- Validation of RAMRIS in other joints, such as proximal interphalangeal joints (hands), first interphalangeal joints, and metatarsophalangeal joints
- Whole-body MRI
- Quantitative methods, including dynamic contrast-enhanced MRI, automated volume quantification (e.g., RAMRIQ)
- Simplified RAMRIS, e.g., scoring of reduced amounts of anatomical areas, e.g., fewer sites for JSN assessment, first carpometacarpal joint, etc.
- Development of an updated tool for training and calibration.

*Including, but not limited to, assessment of reproducibility, sensitivity to change, and discriminatory ability. OMERACT: Outcome Measures in Rheumatology; MRI: magnetic resonance imaging; JSN: joint space narrowing; RAMRIS: Rheumatoid Arthritis Magnetic Resonance Imaging Scoring system; RAMRIQ: Rheumatoid Arthritis Magnetic Resonance Imaging Quantitative assessment system.

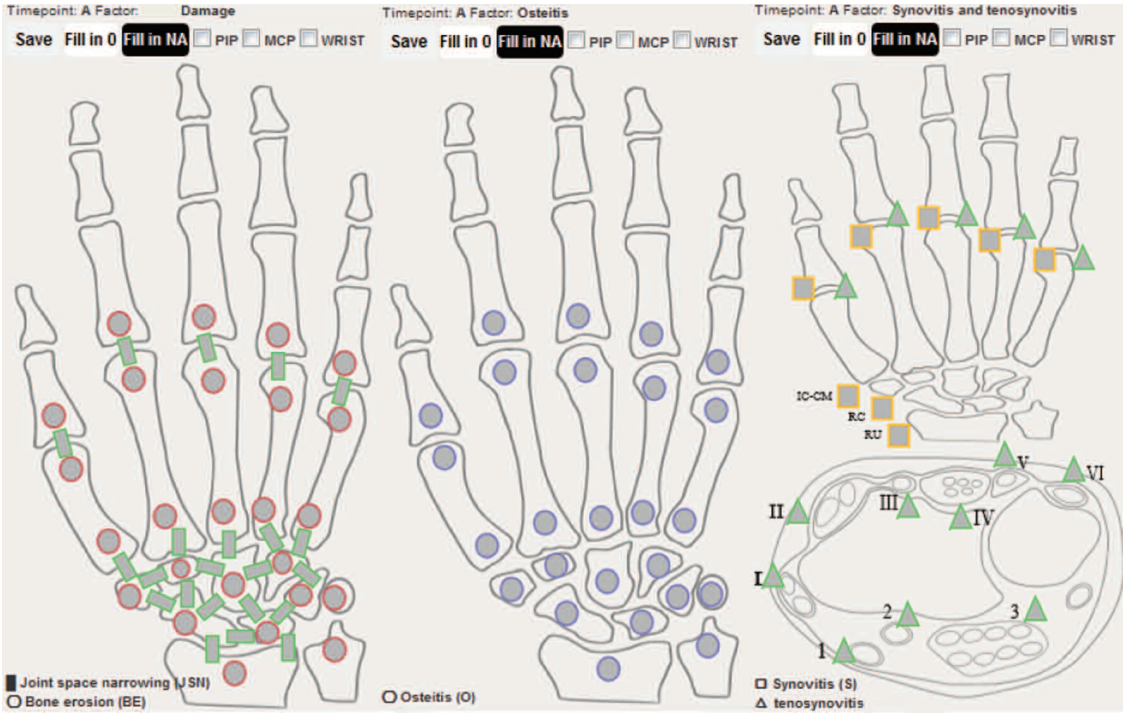

Figure 1. Pathologies and areas assessed by the 2016 updated Rheumatoid Arthritis Magnetic Resonance Imaging Scoring recommendations. Illustration of locations assessed for bone erosion and joint space narrowing (left), osteitis (center), and synovitis and tenosynovitis (right) of wrist and metacarpophalangeal joint. The drawing is an electronic case report form used for entering MRI scores on www.copecare.org. IC-CM: intercarpal-carpometacarpal joints; RC: radiocarpal joint; RU: distal radioulnar joint; I–VI and 1–3: extensor respectively flexor tendon compartments of the wrist; NA: not applicable; MCP: metacarpophalangeal joints; PIP: proximal interphalangeal joints.

be assessed by T2FS/STIR or by pre- and postcontrast T1-weighted images. Potentially new sequences may replace the need for intravenous contrast injection for synovitis assessment, but because studies so far have found a lower sensitivity and reproducibility of T2FS/STIR than postcontrast T1-weighted images[25,26], these cannot be generally recommended for synovitis assessment. For optimal assessment of cartilage/JSN, sequences specifically suited for cartilage assessment, such as fat-suppressed, T1-weighted 3-D– gradient echo sequences, provide the highest image quality[5,17,27]. Different MRI sequences for cartilage visualization have been extensively studied in knee osteoarthritis,

but studies of the relative sensitivity to change and reproducibility of different sequences for cartilage/JSN assessments in RA hands and wrists have not been performed. RAMRIS has been successfully applied in other joints, such as proximal interphalangeal joints (hands), first interphalangeal joints, and metatarsophalangeal joints. The validation of findings in these joints is, however, limited.

Based on the general current availability of high-quality MRI units, which allows such sequences, it is recommended to use thin slices (thicknesses of ≤ 2 mm), or 3-D sequences with isotropic (i.e., cubic) voxels, allowing reconstruction of the anatomy in 2 perpendicular imaging planes. It should be noted that even better spatial resolution can be achieved on certain MRI systems. However, the current OMERACT recommendations are not intended to be exclusive, but rather provide common standards/minimal requirements, which are feasible in most centers in which RA clinical trials are likely to be carried out. If of high quality, RAMRIS may be used even with low field strength units. If a change in methodology is introduced, it is important to compare its performance with the original method, for the specific scientific question asked[28].

Assessment of additional RA pathologies. The original OMERACT RAMRIS[3] evaluated bone erosion, bone marrow edema/osteitis, and synovitis. An atlas illustrating the scoring method, aimed at improving accessibility and standardization among investigators worldwide, was published in 2005[29]. Acknowledging that cartilage damage is an important part of the disease process in RA[20], from 2008 to 2014 we developed and validated an OMERACT method for assessing cartilage loss/JSN as a potential addition to the original RAMRIS system[30,31,32]. Similarly, because tenosynovitis is a frequent and early inflammatory feature that can cause tendon rupture and may be associated with subsequent bone erosion[33,34], a RAMRIS tenosynovitis scoring system has recently been developed and validated[35] (Table 1 and Table 2).

Thus, RAMRIS now covers a broader spectrum of pathologies seen in RA, which have all been shown to be assessable with high reproducibility and at least moderate sensitivity to change[31,32,35,36]. The recommendation to include the additional pathologies and joints is based on the reasons described above.

In an individual clinical study, all or just a subset of these variables can be applied. Some studies may aim only to assess the antiinflammatory efficacy, e.g., in a Phase 1 or 2 trial, and thus focus on synovitis, osteitis, and tenosynovitis, whereas studies testing other mechanisms of action, e.g., osteoclast inhibition[37], may focus only on bone erosion and JSN to assess structural damage progression. More commonly, all RAMRIS variables will be relevant because both inflammation and damage are integral parts of the RA disease process and this approach also allows assessing the spatial and temporal relation between them.

The first metacarpophalangeal joint (MCP1), which was not covered in the original RAMRIS because of technical limitations at the time, has since been successfully included in several clinical trials. Given the importance of the thumb to the functionality of the hand, including MCP1 is relevant.

Combined scores of inflammation (synovitis, osteitis, and tenosynovitis) or damage (bone erosion and JSN) may offer superior discrimination of treatment effects, but their use thus far has been limited, and thus they require further research (Table 3). However, preliminary data suggest that addition of tenosynovitis[38,39,40] may increase the sensitivity to change and provide additional information. A "total damage" score combining cartilage loss and bone erosion has also been shown to demonstrate significant progression over time and discrimination of treatment effects (active vs placebo treatment)[5,40]. Combining inflammatory and structural damage variables into a single score is not relevant, however, because they represent different constructs.

DISCUSSION

Our paper describes advances since the OMERACT RAMRIS was developed 15 years ago, and provides updated recommendations from the OMERACT MRI in Arthritis Working group regarding MRI assessment of patients with RA according to RAMRIS.

The advances include increased knowledge of the validity and utility of RAMRIS, further validating its fulfillment of the OMERACT filter[4]. Data have been provided regarding sensitivity to change, discrimination between therapies in clinical trials, and associations with patient-centered outcomes, such as functional ability and pain, improvements in MRI acquisition, and updated RAMRIS recommendations, including new definitions and scoring methods for the additional pathologies (tenosynovitis and JSN). These improvements are expected to further increase the utility of RAMRIS in RA clinical trials and clinical cohorts.

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