

# The OMERACT MRI in Arthritis Working Group — Update on Status and Future Research Priorities

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

**ABSTRACT.** *Objective.* To provide an update on the status and future research priorities of the Outcome Measures in Rheumatology (OMERACT) magnetic resonance imaging (MRI) in arthritis working group.

*Methods.* A summary is provided of the activities of the group within rheumatoid arthritis (RA), psoriatic arthritis (PsA), and osteoarthritis (OA), and its research priorities.

*Results.* The OMERACT RA MRI score (RAMRIS) evaluating bone erosion, bone edema (osteitis), and synovitis is now the standard method of quantifying articular pathology in RA trials. Cartilage loss is another important part of joint damage, and at the OMERACT 12 conference, we provided longitudinal data demonstrating reliability and sensitivity to change of the RAMRIS JSN component score, supporting its use in future clinical trials. The MRI group has previously developed a PsA MRI score (PsAMRIS). At OMERACT 12, PsAMRIS was evaluated in a randomized placebo-controlled trial of patients with PsA, demonstrating the responsiveness and discriminatory ability of applying the PsAMRIS to hands and feet. A hand OA MRI score (HOAMRIS) was introduced at OMERACT 11, and has subsequently been further validated. At OMERACT 12, good cross-sectional interreader reliability, but variable reliability of change scores, were reported. Potential future research areas were identified at the MRI session at OMERACT 12 including assessment of tenosynovitis in RA and enthesitis in PsA and focusing on alternative MRI techniques.

*Conclusion.* MRI has been further developed and validated as an outcome measure in RA, PsA, and OA. The group will continue its efforts to optimize the value of MRI as a robust biomarker in rheumatology clinical trials. (First Release Feb 15, 2015; J Rheumatol 2015;42:2470–2; doi:10.3899/jrheum.141248)

## Key Indexing Terms:

OMERACT                      MAGNETIC RESONANCE IMAGING                      RHEUMATOID ARTHRITIS  
PSORIATIC ARTHRITIS                      OSTEOARTHRITIS                      JOINT SPACE NARROWING

From the Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Glostrup Hospital, Copenhagen, Denmark; Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark; University of New South Wales, Sydney, Australia; Department of Rheumatology, Pitié-Salpêtrière Hospital, APHP, Université Paris 6-UPMC, Paris, France; Sheba Medical Center, Tel Aviv University, Tel Aviv, Israel; Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway; Spire Sciences, Boca Raton, Florida, USA; Department of Rheumatology, Slagelse Hospital, Slagelse, Denmark; Division of Rheumatology Research, Swedish Medical Center, University of Washington School of Medicine; and Seattle Rheumatology Associates, Seattle, Washington, USA; Department of Radiology, Charité University Hospital, Berlin, Germany; Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds; National Institute for Health Research (NIHR) Leeds Musculoskeletal Biomedical Research Unit, Leeds, UK; University of California, San Francisco, and Synarc Inc., San Francisco, California, USA. M. Østergaard, MD, PhD, DMSc, Professor of Rheumatology, Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Glostrup Hospital and Department of Clinical Medicine, University of Copenhagen; P. Bird, BMed (Hons), FRACP, PhD, Grad Dip MRI, Senior Lecturer, University of NSW; F. Gandjbakhch, MD, Practicing Rheumatologist, Department of Rheumatology, Pitié-Salpêtrière, APHP, Université Paris 6-UPMC; I. Eshed, MD, Professor of Radiology, Sheba Medical Center, Tel Aviv University; I.K. Haugen, MD, PhD, Postdoctoral Researcher, Department of Rheumatology, Diakonhjemmet Hospital; E.A. Haavardsholm, MD, PhD, Postdoctoral Researcher, Department of Rheumatology,

Diakonhjemmet Hospital; S. Lillegraven, MD, PhD, Postdoctoral Researcher, Department of Rheumatology, Diakonhjemmet Hospital, University of Oslo; V. Foltz, MD, Practicing Rheumatologist, Department of Rheumatology, Pitié-Salpêtrière Hospital, APHP, Université Paris 6-UPMC; D. Glinatsi, MD, Research Fellow, Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Glostrup Hospital, University of Copenhagen; C. Peterfy, MD, PhD, FRCP, Chief Executive Officer, Spire Sciences; B. Ejbjerg, MD, PhD, Consultant Rheumatologist, Department of Rheumatology, Slagelse Hospital; P. Bøyesen, MD, PhD, Department of Rheumatology, Diakonhjemmet Hospital; P.J. Mease, MD, Division of Rheumatology Research, Swedish Medical Center, University of Washington School of Medicine, and Seattle Rheumatology Associates; K.G. Hermann, MD, PhD, Consultant Radiologist, Department of Radiology, Charité University Hospital; P. Emery, MA, MD, FRCP, ARC Professor in Rheumatology, Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, and NIHR Leeds Musculoskeletal Biomedical Research Unit; H.K. Genant, MD, FACR, FRCP, 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 Musculoskeletal Biomedical Research Unit.

Address correspondence to Prof. M. Østergaard, Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Copenhagen University Hospital Glostrup, Nordre Ringvej 57, DK-2600 Glostrup, Denmark. E-mail: mo@dadlnet.dk

Magnetic resonance imaging (MRI) allows sensitive assessment of disease activity and damage in inflammatory arthritides and is now frequently used as an outcome measure in rheumatology clinical trials, providing new insights into disease pathogenesis and treatment response. The Outcome Measures in Rheumatology (OMERACT) magnetic resonance imaging (MRI) working group has been instrumental in this pursuit, and the OMERACT rheumatoid arthritis (RA) MRI score (RAMRIS)<sup>1,2,3,4,5,6</sup>, evaluating bone erosion, bone marrow edema (osteitis), and synovitis, is now the standard MRI method used in RA trials. More recently, the MRI working group has developed an OMERACT method for assessment of cartilage loss/joint space narrowing (JSN) as a potential addition to the original RAMRIS system. Further, the group has developed and validated a psoriatic arthritis (PsA) MRI scoring method (PsAMRIS)<sup>7,8</sup>, and most recently a Hand Osteoarthritis MRI Scoring System (HOAMRIS)<sup>9</sup>.

At the OMERACT 12 conference in Budapest, Hungary, in May 2014, the group presented further work within RA, PsA, and hand OA, in line with what had been planned following OMERACT 11<sup>10</sup>.

#### **Validation of the OMERACT RA MRI Joint Space Narrowing Score (RAMRIS-JSN)**

Improved outcome measures of structural joint damage in RA are still needed. The OMERACT RAMRIS has gained acceptance as outcome measure of joint inflammation and bone erosion in RA<sup>1,2,3,4,5,6</sup>. However, cartilage damage is an important part of the disease process in RA, and studies assessing JSN on conventional radiography have shown that JSN is independently associated with functional impairment and decreased work ability<sup>11</sup>. Consequently, incorporating a JSN assessment into RAMRIS will broaden its assessment of structural joint damage, and may also improve the regulatory view of the usefulness of MRI in RA.

Evaluation of cartilage/JSN was left out in the early phase of developing the RAMRIS (late 1990s) because image quality at that time was insufficient. At OMERACT 10 the assessment of joint cartilage/JSN by MRI was reconsidered, based on the fact that image quality has increased, and a preliminary RAMRIS JSN scoring system was subsequently developed based on cross-sectional studies, including comparison with computed tomography<sup>12,13</sup>. Before OMERACT 12, validation was performed in a longitudinal study. The RAMRIS-JSN score showed high overall intrareader and interreader reliability, and moderate sensitivity to change<sup>14</sup> supporting its validity as a tool for assessing JSN in RA clinical trials.

#### **Validation of the OMERACT PsA MRI Scoring System (PsAMRIS)**

Sensitive outcome measures in PsA, capturing the diverse inflammatory and damage pathologies, are warranted. At

OMERACT 9 and OMERACT 10, a PsA MRI scoring system (PsAMRIS, assessing synovitis, tenosynovitis, osteitis, bone erosions, and proliferations and periarticular inflammation), including validation data for hand PsA, was presented<sup>7,8,15</sup>. However, further validation was hindered by lack of appropriate datasets given a paucity of MRI outcome studies in PsA. Recently, data from a randomized placebo-controlled trial of patients with PsA<sup>16</sup> were made available to our MRI group, and a validation exercise of the PsAMRIS, based on this material, was undertaken. PsAMRIS showed good intrareader and interreader reliability for most variables in the hand and foot, and the scores of inflammatory features were responsive to change<sup>17</sup>. This suggests that PsAMRIS is a valid tool for MRI assessment of hands and feet in PsA clinical trials.

#### **Validation of the OMERACT Hand OA MRI Scoring System (HOAMRIS)**

Structure and symptomatology relationships in OA are still poorly understood, and structure modification has been difficult to achieve, in part because of poor outcome measures. Sensitive outcome measures in hand OA are therefore needed, and MRI provides assessment of appropriate pathologies. At an imaging level, established hand OA demonstrates many pathologies in common with hand PsA, and it has been a logical step to extend the OMERACT MRI group's activities into developing and validating an MRI scoring system for hand OA, given the group's extensive knowledge and experience in developing definitions and scoring systems for other peripheral joint diseases. Consequently, the OMERACT HOAMRIS was developed and presented at OMERACT 11<sup>9</sup>. However, further validation was needed, including validation of the score in a longitudinal dataset. At OMERACT 12, the responsiveness and longitudinal reliability of the HOAMRIS were tested. Good cross-sectional interreader reliability was found on status scores, whereas the reliability of change scores was variable<sup>18</sup>. Results suggest that MRI is sensitive to change in hand OA, but that further validation of MRI measurements is needed before MRI can be recommended as a primary outcome measure in clinical hand OA trials.

#### **Future Research**

At OMERACT 12 potential future research areas were discussed during the MRI special interest group session. In RA, further knowledge of the performance of the RAMRIS-JSN component score in randomized controlled trials and in comparison with conventional radiography is important. Focus on which particular sites show more responsiveness to change, so that the scoring system can be potentially reduced in terms of number of anatomical sites evaluated, is also relevant because this could improve its feasibility.

Several approaches to further developing the RAMRIS

may also be considered, including validation in the first finger, the interphalangeal joints, and the feet. Further, tenosynovitis is a frequent finding in RA, and the participants at OMERACT strongly suggested investigation of the potential value of MRI assessment of tenosynovitis as an addition to the RAMRIS, with testing of reliability, responsiveness, and discriminatory ability of any putative tenosynovitis score. Peripheral enthesitis, which is a common pathology in spondyloarthritides, was also suggested as an area of future research.

Regarding HOAMRIS, further testing in longitudinal exercises using images from higher field strengths was suggested. With respect to PsAMRIS, gathering data from other randomized controlled trials in PsA is crucial to fully clarify the utility of PsAMRIS. Participants at OMERACT 12 also felt that the development and provision of a PsAMRIS atlas, either electronically or Web-based, would further improve the utility of the tool. It was also suggested that development of educational tools, such as online training modules to allow knowledge transfer regarding both RAMRIS and PsAMRIS, would be helpful. Finally, investigations of alternative MRI methodologies such as whole-body MRI, dynamic contrast-enhanced MRI, and diffusion-weighted MRI, were also suggested as potential areas for future focus for the group.

Important new data on MRI in RA, PsA, and hand OA validating the RAMRIS-JSN, the PsAMRIS, and the HOAMRIS methods, were presented at OMERACT 12, as was a series of exciting potential future research priorities. The group will continue its efforts to optimize the value of MRI as a useful tool in rheumatology clinical trials.

## REFERENCES

1. Østergaard M, Peterfy C, Conaghan P, McQueen F, Bird P, Ejbjerg B, et al. OMERACT rheumatoid arthritis magnetic resonance imaging studies. Core set of MRI acquisitions, joint pathology definitions, and the OMERACT RA-MRI scoring system. *J Rheumatol* 2003;30:1385-6.
2. Østergaard M, Edmonds J, McQueen F, Peterfy C, Lassere M, Ejbjerg B, et al. An introduction to the EULAR-OMERACT rheumatoid arthritis MRI reference image atlas. *Ann Rheum Dis* 2005;64 Suppl 1:i3-i7.
3. Bird P, Conaghan P, Ejbjerg B, McQueen F, Lassere M, Peterfy C, et al. The development of the EULAR-OMERACT rheumatoid arthritis MRI reference image atlas. *Ann Rheum Dis* 2005;64 Suppl 1:i8-i10.
4. Conaghan P, Bird P, Ejbjerg B, O'Connor P, Peterfy C, McQueen F, et al. The EULAR-OMERACT rheumatoid arthritis MRI reference image atlas: the metacarpophalangeal joints. *Ann Rheum Dis* 2005;64 Suppl 1:i11-i21.
5. Ejbjerg B, McQueen F, Lassere M, Haavardsholm E, Conaghan P, O'Connor P, et al. The EULAR-OMERACT rheumatoid arthritis MRI reference image atlas: the wrist joint. *Ann Rheum Dis* 2005;64 Suppl 1:i23-i47.

6. McQueen F, Ostergaard M, Peterfy C, Lassere M, Ejbjerg B, Bird P, et al. Pitfalls in scoring MR images of rheumatoid arthritis wrist and metacarpophalangeal joints. *Ann Rheum Dis* 2005;64 Suppl 1:i48-i55.
7. Østergaard M, McQueen F, Wiell C, Bird P, Boyesen P, Ejbjerg B, et al. The OMERACT psoriatic arthritis magnetic resonance imaging scoring system (PsAMRIS): definitions of key pathologies, suggested MRI sequences, and preliminary scoring system for PsA Hands. *J Rheumatol* 2009;36:1816-24.
8. Bøyesen P, McQueen FM, Gandjbakhch F, Lillegraven S, Coates L, Wiell C, et al. The OMERACT Psoriatic Arthritis Magnetic Resonance Imaging Score (PsAMRIS) is reliable and sensitive to change: results from an OMERACT workshop. *J Rheumatol* 2011;38:2034-8.
9. Haugen IK, Østergaard M, Eshed I, McQueen FM, Bird P, Gandjbakhch F, et al. Iterative development and reliability of the OMERACT Hand Osteoarthritis MRI Scoring System. *J Rheumatol* 2014;41:386-91.
10. Conaghan PG, McQueen FM, Bird P, Peterfy C, Haavardsholm E, Gandjbakhch F, et al. Update on the OMERACT magnetic resonance imaging task force: research and future directions. *J Rheumatol* 2014;41:383-5.
11. Smolen JS, van der Heijde DM, Keystone EC, van Vollenhoven RF, Goldring MB, Guerette B, et al. Association of joint space narrowing with impairment of physical function and work ability in patients with early rheumatoid arthritis: protection beyond disease control by adalimumab plus methotrexate. *Ann Rheum Dis* 2013;72:1156-62.
12. Østergaard M, Bøyesen P, Eshed I, Gandjbakhch F, Lillegraven S, Bird P, et al. Development and preliminary validation of a magnetic resonance imaging joint space narrowing score for use in rheumatoid arthritis: potential adjunct to the OMERACT RA MRI scoring system. *J Rheumatol* 2011;38:2045-50.
13. Døhn UM, Conaghan PG, Eshed I, Boonen A, Bøyesen P, Peterfy CG, et al. The OMERACT-RAMRIS rheumatoid arthritis magnetic resonance imaging joint space narrowing score: intrareader and interreader reliability and agreement with computed tomography and conventional radiography. *J Rheumatol* 2014;41:392-7.
14. Glinatsi D, Lillegraven S, Haavardsholm E, Eshed I, Conaghan PG, Peterfy C, et al. Validation of the OMERACT Magnetic Resonance Imaging Joint Space Narrowing score (RAMRIS-JSN) for the wrist in a multireader longitudinal trial. *J Rheumatol* 2015;42:2480-5.
15. McQueen F, Lassere M, Duer-Jensen A, Wiell C, Conaghan PG, Gandjbakhch F, et al. Testing an OMERACT MRI scoring system for peripheral psoriatic arthritis in cross-sectional and longitudinal settings. *J Rheumatol* 2009;36:1811-5.
16. Mease P, Genovese MC, Gladstein G, Kivitz AJ, Ritchlin C, Tak PP, et al. Abatacept in the treatment of patients with psoriatic arthritis: results of a six-month, multicenter, randomized, double-blind, placebo-controlled, phase II trial. *Arthritis Rheum* 2011;63:939-48.
17. Glinatsi D, Bird P, Gandjbakhch F, Mease P, Bøyesen P, Peterfy C, et al. Validation of the OMERACT Psoriatic Arthritis Magnetic Resonance Imaging Score (PsAMRIS) for the hand and foot in a randomized placebo-controlled trial. *J Rheumatol* 2015;42:2473-9.
18. Haugen IK, Eshed I, Gandjbakhch F, Foltz V, Østergaard M, Bøyesen P, et al. The longitudinal reliability and responsiveness of the OMERACT Hand Osteoarthritis MRI Scoring system (HOAMRIS). *J Rheumatol* 2015;42:2486-91.