
PROCEEDINGS of OMERACT 6

Introduction**OMERACT Rheumatoid Arthritis MRI Studies Module**

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ABSTRACT. The rationale for an OMERACT Module on the use of magnetic resonance imaging (MRI) in the assessment of rheumatoid arthritis (RA) is outlined. This article also details the way in which the RA MRI Working Group developed and undertook a series of structured exercises to evaluate the reliability and sensitivity to change of the RA-MRI score (RAMRIS). (J Rheumatol 2003;30:1364-5)

Key Indexing Terms:

MAGNETIC RESONANCE IMAGING SCORING SYSTEMS RHEUMATOID ARTHRITIS

OMERACT is concerned with the adequacy of outcome measures used in rheumatology clinical trials. Damage, a major outcome in rheumatoid arthritis (RA), has been measured traditionally by scoring methods applied to radiographic images. OMERACT 4¹ and OMERACT 5² both addressed measurement issues arising from radiographic scores, and OMERACT 6 returned to this topic³. Clearly, it has been a challenge to capture and quantify RA damage on radiographic images by means of scoring systems of appro-

priate validity, discrimination, and feasibility — the elements of the OMERACT filter⁴.

Magnetic resonance imaging (MRI) is now in widespread clinical use. In articular disease, MRI is able to image synovitis and bone edema/inflammation as well as damage to cartilage and bone, and it can detect erosive change with greater sensitivity than radiography^{5,6}, particularly in early disease. MRI is also capable of detecting tendon pathology and evaluating ligament integrity. Despite its greater cost and relative inaccessibility, MRI has already gained a place as an attractive outcome method in RA clinical trials⁷. That being the case, the critical issue is how best to use MRI images as an outcome measure. The complexity and the amount of information produced by MRI poses a difficulty. Given the metrological problems of radiographic scoring systems, it seemed important, early in the development of attempts to quantify lesions on MRI, to establish communication between some of the leaders in MRI assessment of RA and experts in measurement and clinical trial outcome measures, so that, together, they could work towards a system of MRI use in RA with acceptable measurement standards. OMERACT proved a good forum for the project.

The purpose of the MRI Module at OMERACT 6 was to allow participants the opportunity to review the work to date of the MRI-RA Working Group and to decide whether and to what extent the RA-MRI Score (RAMRIS) complies with the standards of the OMERACT filter.

Development of the OMERACT RA-MRI Working Group

From initial meetings at the 1998 American College of Rheumatology meeting in San Diego and later at the EULAR Congress in Glasgow in 1999, there emerged a group of people willing to work together on this task. These included people with a strong track record in the use of MRI in RA: Charles Peterfy and Harry Genant from San

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Francisco; Mikkel Østergaard and Mette Klarlund from Copenhagen; Fiona McQueen and Neal Stewart from Auckland; Philip Conaghan, Dennis McGonagle, Paul Emery, and their radiological colleagues Wayne Gibbon and Phillip O'Connor from Leeds; and from Sydney, people with expertise in outcome assessment, MRI use in RA, and contact with OMERACT: Marissa Lassere, Ron Shnier, and John Edmonds. Later Bo Ejbjerg from Copenhagen and Paul Bird from Sydney joined the group as rheumatologist PhD students whose subject is MRI use in RA assessment.

Group Aims and Objectives

The group aimed to devise a method with acceptable standards of validity, discrimination, and feasibility to quantify RA pathology imaged by MRI. Our group did not aspire to create a system that captured as much information as may be possible when dedicated specialists explore the limits of this technology, nor did we expect to achieve the level of reader precision that may be possible in the most experienced hands. Because intra-reader reliability is generally greater than inter-reader reliability, it is likely that in the setting of a clinical trial, centralized readings will improve consistency. However, the purpose of the OMERACT MRI work was to develop a measurement method that would be generally applicable by investigators familiar with MRI techniques and image interpretation; we wanted then to test the reliability of the method so that users would know the level of inter-reader agreement to be expected.

Group Exercises

The initial activities of the Group were described by Østergaard, *et al*⁸. Briefly, a simple scoring system for RA changes in the wrist and metacarpophalangeal joints on MRI was devised and tested for inter-reader agreement among the 5 international centers. The first exercise led to specifications for image acquisition and improvements in the scoring system. A second inter-reader exercise was undertaken and both were reported at OMERACT 5 in Toulouse, France (Exercises 1 and 2)⁸. The experience gained from those 2 exercises led to further modifications in hand/wrist image acquisition and scoring, summarized by Conaghan, *et al*⁹. This iterative process produced modest agreement among readers for bone lesions, erosions, and synovitis, but scoring of joint space narrowing proved too unreliable for inclusion in the scoring system.

Using the "Toulouse OMERACT-MRI Score," a third cross-sectional reliability study (Exercise 3) was carried out and reported at OMERACT 6¹⁰, together with a longitudinal study (Exercise 4) to evaluate sensitivity to change¹¹.

The group had started with a scoring system because scoring change has been traditional in radiological assessment and because some had started their own scoring

systems. But they acknowledged alternative approaches to capturing the complexities of RA pathology on MRI and recognized the Toulouse RA-MRI score (RAMRIS) as a simple beginning rather than a definitive conclusion to this venture. Measurement rather than scoring of articular pathology is difficult, but with time and technology, this approach will likely provide the real benefit of MRI over radiography¹². To initiate the process, a preliminary inter-reader study measuring erosion volumes (rather than scoring them) was also undertaken (Exercise 5) and reported to OMERACT 6¹³.

John Edmonds and Marissa Lassere were the leaders of the MRI Module and edited the proceedings reported in the articles that follow.

REFERENCES

1. Molenaar ETH, Boers M, van der Heijde DMFM, et al. Imaging in rheumatoid arthritis: results of group discussions. *J Rheumatol* 1999;26:749-51.
2. Van der Heijde D, Lassere M, Edmonds J, et al. Minimal clinically important difference in plain films in RA: group discussions, conclusions and recommendations. *J Rheumatol* 2001;28:914-7.
3. Van der Heijde D, Sharp JT, Rau R, Strand CV. OMERACT Workshop: Repair of structural damage in rheumatoid arthritis. *J Rheumatol* 2003;30:1108-9.
4. Tugwell P, Bombardier C. A methodologic framework for developing and selecting endpoints in clinical trials. *J Rheumatol* 1982;9:758-62.
5. McQueen FM. MRI in early inflammatory arthritis: what is its role? *Rheumatology* 2000;39:700-6.
6. Peterfy CG. MRI in rheumatoid arthritis: current status and future directions. *J Rheumatol* 2001;28:1134-42.
7. Reece R, Kraan M, Radjenovic A, et al. Comparative assessment of leflunomide and methotrexate for the treatment of rheumatoid arthritis by dynamic enhanced magnetic resonance imaging. *Arthritis Rheum* 2002;46:366-72.
8. Ostergaard M, Klarlund M, Lassere M, et al. Inter-reader agreement in the assessment of MRI images of rheumatoid arthritis wrist and finger joints — an international multicenter study. *J Rheumatol* 2001;28:1143-50.
9. Conaghan P, Edmonds J, Emery P, et al. MRI in RA: summary of OMERACT activities, current status and plans. *J Rheumatol* 2001;28:1158-61.
10. Lassere M, McQueen F, Østergaard M, et al. OMERACT rheumatoid arthritis magnetic resonance imaging studies. Exercise 3: an international multicenter reliability study using the RA-MRI Score (RAMRIS). *J Rheumatol* 2003;30:1366-75.
11. Conaghan P, Lassere M, Østergaard M, et al. OMERACT rheumatoid arthritis magnetic resonance imaging studies. Exercise 4: an international multicenter longitudinal study using the RA-MRI Score (RAMRIS). *J Rheumatol* 2003;30:1376-9.
12. Edmonds J, Lassere M. Imaging damage: scoring versus measuring [editorial]. *J Rheumatol* 2001;28:1749-51.
13. Bird P, Ejbjerg B, McQueen F, Ostergard M, Lassere MND, Edmonds JP. OMERACT rheumatoid arthritis magnetic resonance imaging studies. Exercise 5: an international multicenter reliability study using computerized MRI erosion volume measurements. *J Rheumatol* 2003;30:1380-4.