OMERACT Rheumatoid Arthritis Magnetic Resonance Imaging Studies. Summary of OMERACT 6 MR Imaging Module

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ABSTRACT. Magnetic resonance image (MRI) scanning is a new method for imaging and quantifying joint inflammation and damage in rheumatoid arthritis (RA). Over the past 4 years, the OMERACT MR Imaging Group has been developing and testing the RA-MRI scoring system (RAMRIS) for use in RA. The OMERACT filter demands that an ideal outcome measure satisfy the elements of truth, discrimination, and feasibility. The RAMRIS as it currently stands incorporates measures of joint inflammation and damage including bone erosion, edema, and synovitis. Tendonitis has not been scored because of feasibility issues; joint space narrowing, reflecting cartilage damage, has also been excluded as reliability was low at the small joints of the hands. Anatomical coverage of the score is currently restricted to the wrists and hands but can provide a basis for a more comprehensive score. The MR measurement of synovitis correlates closely with histological evidence and work continues on validating MR erosions with reference to radiographic techniques. The RAMRIS has demonstrated good reliability for bone erosion and synovitis at the wrists and metacarpophalangeal joints subject to reader training, with slightly lower levels of reader agreement for bone edema. Reliability was less satisfactory in discriminating between 2 time points, and further work is required if the score is to be used to monitor change. Feasibility also needs to be considered for the practical application of the score, including the time taken for scanning and scoring, as well as cost and safety issues. The OMERACT RAMRIS provides a framework for scoring inflammation and damage in RA upon which further modifications can be built. It has been endorsed by the MRI working group and OMERACT 6 participants as useful for inclusion as an outcome measure in clinical trials. (J Rheumatol 2003;30:1387–92)

Key Indexing Terms:
MAGNETIC RESONANCE IMAGING SCORING SYSTEMS RHEUMATOID ARTHRITIS

Rheumatologists can no longer afford to ignore magnetic resonance imaging (MRI) as a means to measure disease activity and joint damage in rheumatoid arthritis (RA). Due to its unparalleled ability to image soft tissues of varying water content, MRI can reveal synovitis, tenosynovitis, and joint effusions in a format that allows inflammation to be quantified; something that was previously only approximated using crude clinical tools such as joint tenderness and swelling scores. The early detection of bony erosions is

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possibly an even more important role for MRI, given the implication of joint damage and potential future clinical disability. This technique has 7 to 9-fold the sensitivity of plain radiography for detecting erosions in early disease[1,2] and the ability to "see" lesions 6 to 12 months before they appear on plain radiograph[3,4]. Thus, it is the obvious imaging modality for measurement of joint damage in clinical trials of drugs and biologicals that might alter the course of early disease and potentially prevent erosions. Indeed, MRI has already been applied in this context[5,6], making the development of a standardized scoring system for quantifying MRI changes all the more urgent and important.

BACKGROUND — THE OMERACT PROCESS

The OMERACT MRI group was formed in 1998, as an offshoot of the OMERACT radiographic imaging group, in response to the emergence of MR as an important new imaging modality in RA. A provisional MRI-RA scoring system (RAMRIS) was devised and tested in 2 exercises[7] presented at OMERACT 5 in Toulouse (May 2000).

Decisions arising from that meeting were that a standardized series of sequences should be used to image RA joints. T1-weighted images in axial and coronal planes, before and after intravenous gadolinium, were optimal for detection of erosions and synovitis, while T2-weighted images (or equivalent STIR sequences) showed bone marrow edema to best effect. A further recommendation was that scoring of joint space narrowing be omitted because of difficulty in assessing this accurately at the small joints of the hand using standard equipment and sequences[8].

Over the last 2 years, the group has attempted to refine the scoring system into a more reliable and useful tool, completing 3 additional exercises. Exercise 3 involved scoring further sets of wrists and metacarpophalangeal (MCP) joints from early RA patients and analyzing results to assess reliability in scoring synovitis, erosion, and bone edema on a cross-sectional basis[9]. As an extension of this exercise, data on intrareader reliability were generated when scans were scored on 2 separate occasions by one reader. Exercise 4 attempted longitudinal scoring of MR scans taken one year apart in a similar group of patients, and the change in score over time was compared between readers[10]. Additional work has also been undertaken by various subgroups including a separate longitudinal analysis of MCP and wrists by the EULAR-MRI group using the OMERACT system[11], a study of erosion volume measurement using a computerized imaging program[12], and a study examining the importance of gadolinium in scoring MR scans[13]. These studies will be presented elsewhere.

THE OMERACT FILTER

A major aim in the development of an MRI scoring system under the auspices of OMERACT is that it satisfies the elements of the OMERACT filter in terms of truth, discrimination, and feasibility[14].

Truth

Does the measurement in question (in this case the MRI scoring system) measure what is intended? Does it conform with notions of face, content, construct, and criterion validity contained within the concept of truth?

Face and Content Validity

Face validity requires that the measure be credible, that it make sense. Since MR provides unparalleled imaging potential, particularly with regard to soft tissues, any conscientious attempt to capture this information must have a degree of face validity.

Content validity asks whether the measure is comprehensive, whether it includes all the areas of relevance. In that field, the OMERACT 2002 RAMRIS raises more issues of concern, both in the assessment of disease activity (inflammation) and damage.

Disease activity is reflected by synovitis, bone edema, and tendonitis/tenosynovitis, but the RAMRIS includes assessment of only synovitis and bone edema. Issues of feasibility were felt to preclude the scoring of tendonitis and tenosynovitis at this stage. Detailed knowledge of relevant 3 dimensional anatomy, at a level likely to be achieved only by dedicated musculoskeletal radiologists, is required to accurately identify these structures in the hand and wrist. As the RAMRIS is being devised to be suitable for general use by radiologists or rheumatologists, this requirement was felt to be too restrictive, and the assessment of tendonitis has, for the present, been sacrificed to practicality. However, comparative studies with other MRI scoring systems that include these elements[3] are required to determine whether disease activity is being adequately measured.

Joint damage is reflected by bone erosion and cartilage change. In the RAMRIS, only bone erosion is measured. Joint space narrowing, reflecting cartilage loss, was dropped from the initial Toulouse version because of lack of reliability in terms of reader agreement, reflecting difficulty in measuring the joint space in the small joints of the hands and wrists. Appropriate studies could be designed to assess cartilage thickness and viability using specialized MR sequences[15] and highly trained readers, but again this would restrict application of the score to dedicated specialists exploring the limits of this technology. Interestingly, plain radiography remains superior to conventional MRI sequences in the assessment of joint space narrowing in the hand, largely because it clearly images the cortical plates of adjacent bones and allows measurement of the intervening distance. Thus, recommendations for grading joint damage using the RAMRIS as it stands may include its addition to, rather than replacement of, a standard radiographic score.

An aspect of content validity that needs to be addressed is whether the anatomical coverage represented in the score (wrist and/or MCP of the dominant hand) is representative

of overall disease. The RAMRIS has been developed for use with databases available to members of the MRI group; the databases consist of images of MCP joints and wrists. While this material has been useful to start development of a scoring system, coverage of both hands and both feet would provide more complete information. Currently, we are constrained by technical factors including the reduction of resolution, which tends to accompany an increased field of view, but rapid advances in the field of imaging technology are likely to surmount such obstacles within the next few years. Thus, while the area of coverage is limited at present, it can be viewed as a framework upon which a more anatomically comprehensive score can be built.

Construct and Criterion Validity

Construct validity is whether the measure makes biological sense, and whether it is consistent with other measures, while criterion validity is the degree to which the measure truly reflects a gold standard, i.e., the clinical status. These standards cut to the core of rheumatologists' reluctance to welcome MRI. Can we really be sure that MR evidence of synovitis or erosions are the same as the "real thing"? For synovitis, the most convincing comparator, or gold standard, is histological evidence of synovial inflammation. Quite extensive data are now available comparing MR synovitis with histological evidence from synovial tissue obtained at arthroscopy. Comparisons in early and late RA show high correlations between MR synovial membrane thickening and enhancement post-gadolinium, and histological inflammatory changes[16-19].

For MR erosions the answer is less clear. For many years, the gold standard for bony erosions has been plain radiography. However, numerous studies have now been published revealing MRI to be much more sensitive than plain radiography in the detection of early rheumatoid erosions[1,3,20,21]. This is almost certainly because MR is a multiplanar modality that can see erosions at sites obscured on radiography (because of superimposition of shadows). A study tracking MR erosions at the wrist in RA patients revealed that only 1 in 4 progressed to radiographic erosions after 1 and 2 years[4], but radiographic identification of erosions at the wrist is notoriously difficult in early RA[22], to the extent that many sites have been excluded from the van der Heidje modification of the Sharp score[23]. Thus, although historically the gold standard, radiography is inadequate for defining erosions in this context and is not suitable for comparison with MR. Histology is not available because of a lack of candidates willing to sacrifice a finger or hand to science. A study using miniarthroscopy of MCP joints has reported macroscopic evidence of bony disease (as seen through the arthroscope) that correlated with MR erosions, but only surface areas of the lesions were visible[19]. Computerized tomography (CT) does provide multiplanar imaging with the radiographic advantages of good definition of bony anatomy, but preliminary observations suggest there is also considerable interobserver variability in the detection of erosions by CT[24]. Further studies are in progress comparing MR and CT erosions in RA. Ultrasound has also been compared with MR for the detection of erosions, and it is reassuring that the same lesions were observed using both modalities[25].

It is worth remembering that histological gold standards do not underpin many other outcome measures that are in frequent clinical use. For example, the patient and physician global assessments of disease activity have not been exhaustively compared with evidence of joint inflammation and damage at a histological level, but remain key outcome measures in many clinical trials. MRI is rapidly becoming regarded as a gold standard against which traditional measures are being compared, giving rise to concepts such as subclinical synovitis, which is detectable only on MR[26]. In addition, at present, features such as bone edema can be identified only by MRI, making the question of a gold standard irrelevant. Only longitudinal studies comparing MR and radiographic features with clinical progress will elucidate the true significance of these changes.

Discrimination (reliability and sensitivity to change)

Reliability. The OMERACT MRI group have analyzed the reliability of the RAMRIS using 2 statistical tools: the intraclass correlation coefficient (ICC), a relative measure of reader agreement, and the smallest detectable difference (SDD), an absolute measure of agreement. Results from Exercises 3 and 4 suggest reasonable reliability in scoring bone erosions using the RAMRIS with fixed effects single measure ICC ranging from 0.46 to 0.85 and SDD from 24% to 42%. Reliability was generally lower at the wrist compared with MCP joints, which may reflect greater potential for error in scoring anatomically complex regions. Reader training also appeared to influence reliability, probably accounting for the drop in ICC values from Exercise 3 to Exercise 4, when a group of less experienced readers was used. The term "bone defects" was introduced to cover bony abnormalities that did not meet criteria for erosions, but low ICC and high SDD values suggest reader dissatisfaction with this term, and it will be excluded from the score in future.

Inter-reader reliability was also high for scoring synovitis with ICC at wrists and MCP joints ranging from 0.56 to 0.77 for Exercise 3 and 0.68 to 0.89 for Exercise 4. Interestingly, global assessment of synovitis was more reliable than direct measurement of synovial membrane thickness, probably because the intensity of synovitis on MR is reflected both by synovial thickness and the degree of enhancement post-gadolinium. The global score would capture both aspects, but direct measurement, only the first. Bone edema generally had slightly lower reliability levels than synovitis and erosion. Again, this was most obvious in Exercise 4, and may reflect the influence of less trained readers. However,

the quantitation of bone edema can be difficult: it is dependent on suitable T2-weighted or STIR sequences being available with appropriate fat saturation, and technical deficiencies in some of the scans included in these exercises could account for lower reader agreement.

Intrareader reliability was tested for one trained reader (musculoskeletal radiologist) and was found to be high for all variables (ICC 0.78 for synovitis, 0.92 for bone erosion, and 0.93 for bone edema). Similar values were obtained for another "new reader" from the Sydney group (PB). This finding is reassuring in that individual readers have been shown to be internally consistent; it also supports the proposition that inter-reader reliability should be amenable to improvement by training.

How does reliability of the RAMRIS compare with other clinical outcome measures in regular use? Reliability of the joint swelling score and patient global assessment is of a similar order (ICC 0.15–0.52 for joint swelling and 0.75 for patient global assessment)[27]. Reliability of radiographic scoring is higher when this has been tested in both early and established disease (Sharp score ICC 0.41–0.97)[27]. Delegates at OMERACT 6 were asked to grade their perceptions of the score's reliability in the context of randomized clinical trials (RCT) and observational studies of RA progression. Results are presented in Table 1 and suggest that reliability was considered adequate (> 5/10) for all measures except bone edema.

Sensitivity to change. Analysis of the longitudinal study in Exercise 4 revealed disappointingly low reliability for discrimination between 2 time points, one year apart, with ICC approximately one-half those achieved when scans were assessed cross-sectionally. Why should this be? First and most important, small degrees of change were being assessed, increasing the impact of reader variability. Second, the introduction of new readers in Exercise 4 may have resulted in reduced reliability overall, as alluded to above. Third, the score may not have sufficient sensitivity in the lower part of the range to capture a small increase in bone erosion occurring over one year, as volume was assessed by increments of 10%. Consideration may need to be given to modifying the system according to the clinical setting in which it is being applied. For example, in studies of early disease, increments of 1% or 5% might be necessary.

Feasibility

The practical application of a scoring system demands feasibility, and several factors are of importance when MR imaging is considered.

Time. The MR examination can be quite time-consuming and arduous for the patient. The addition of post-gadolinium and T2 sequences increases the duration of the scan to 35–45 minutes. Further work is being done to determine whether MR sequences can be limited (for example to exclude contrast use) to shorten examination time without compromising reliability[13]. The time taken to score an MRI scan is also relevant. This is influenced by the complexity of the site being imaged (wrists take longer to score than MCP joints), the number of sequences being used, and experience of the reader.

Cost. This has been a major barrier to the acceptance of MR as a means of scoring joint damage in RA. The cost of a scan of the dominant wrist with all sequences described above is about 3 times the cost of plain radiographs of both hands and feet. Use of gadolinium increases the cost. However, cost is coming down (by almost one-half in Australasia over the past 6 years) and low cost, dedicated systems for extremity MRI are being developed[2]. In a clinical trial setting, the use of MRI to measure erosion development may allow meaningful results to be achieved in 6 months rather than 2 years, greatly reducing the overall cost. There is also evidence that synovitis, bone edema, and erosions detected using MR in early RA can help differentiate those with aggressive disease, allowing targeting of expensive therapies to those most in need[4]. The downstream effect would be to reduce the overall cost of care for RA patients.

Safety. MR does not involve exposure to ionizing radiation and therefore poses no risk of teratogenicity or future malignancy as far as we are aware. The contrast agent, gadolinium, is a small non-immunogenic molecule and

Table 1. Median (range) group scores for impressions of reliability*.

	Reliability for:			
	RCT		Observational Studies	
	Interobserver	Intraobserver	Interobserver	Intraobserver
MCP				
Synovitis	6 (2–9)	6 (2–10)	7 (2–8)	8 (3–10)
Bone erosion	5 (2–9)	6 (2–10)	6 (4–8)	8 (4–10)
Bone edema	4 (1–8)	6 (1–10)	6 (1–8)	7 (2–9)
Wrists				
Synovitis	5 (2–9)	5 (2–10)	6 (2–9)	7 (2–10)
Bone erosion	5 (2–7)	7 (2–10)	6 (3–8)	8 (4–10)
Bone edema	4 (1–8)	6 (1–10)	5 (1–8)	8 (2–10)

* A score of 0 indicates no reliability, while 10 indicates maximum possible reliability.

Table 2. Overall voting results of OMERACT delegates (70 participants).

Question 1	Do you consider that the OMERACT MRI scoring system is a useful framework for further development of MR assessment of RA?		
Answer	Yes 89%	No 4%	Don't know 7%
Question 2	Is it reasonable to suggest that the OMERACT MRI scoring system be used as a standard comparator for new/alternative MRI methods for RA assessment?		
Answer	Yes 63%	No 16%	Don't know 21%
Question 3	Do you agree that it is now appropriate to trial the OMERACT scoring system in observational studies and RCT to obtain further data re sensitivity to change, construct validity, etc?		
Answer	Yes 86%	No 9%	Don't know 5%

allergic reactions are extremely uncommon. Internal metal clips can be dislodged by the powerful magnetic field and scans cannot be performed in patients with pacemakers, but as long as precautions are taken, MR is very safe.

SUMMARY

The OMERACT RAMRIS has now been tested in a number of multicenter exercises and reasonable reliability has been demonstrated for most variables, with the expectation that this may improve with training. Weaknesses of the current system include inability to accurately score cartilage thinning or damage and exclusion of tendonitis and tenosynovitis for reasons of feasibility. More data are needed on the score's sensitivity to change, its operating characteristics in different clinical settings including established disease, and the adequacy of sampling for representation of whole body change. It should be recalled that the equivalent radiographic score, the Sharp score, was first described in 1971[28], and modifications continued until 1992[29], suggesting that MR scoring is in its infancy. The MRI working group agrees with OMERACT participants that further data are required to bring the system to the standard required by the OMERACT filter. Equally, both groups agree that enough has now been done to endorse trials of the OMERACT 2002 RAMRIS in observational studies and RCT in order to obtain these data (Table 2). It is exciting to reflect that with the advent of MR, rheumatologists will be able to image and measure rheumatoid activity and damage in an entirely new way. Harnessing this knowledge should allow clinicians to better pursue the clinical goal of improving patient care and disease outcome.

REFERENCES

1. Klarlund M, Østergaard M, Jensen KE, Lysgard JM, Skjodt H, Lorenzen I, TIRA group. Magnetic resonance imaging, radiography and scintigraphy of the finger joints: one year follow up of patients with early arthritis. Ann Rheum Dis 2000;59:521-8.
2. Lindegaard H, Vallo J, Horslov Petersen K, Junker P, Østergaard M. Low field dedicated magnetic resonance imaging in untreated rheumatoid arthritis of recent onset. Ann Rheum Dis 2001; 60:770-6.
3. McQueen FM, Stewart N, Crabbe J, et al. Magnetic resonance imaging of the wrist in early rheumatoid arthritis reveals a high prevalence of erosions at four months after symptom onset. Ann Rheum Dis 1998;57:350-6.
4. McQueen FM, Benton N, Crabbe J, et al. What is the fate of erosions in early RA? Tracking individual lesions using MR and XR over the first 2 years of disease. Ann Rheum Dis 2001; 60;859-68.
5. Veale DJ, Reece RJ, Radjenovic A, et al. Intra-articular primatised anti CD4: efficacy in resistant rheumatoid knees. A study of combined arthroscopy, magnetic resonance imaging and histology. Ann Rheum Dis 1999;58:342-9.
6. 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.
7. Ostergaard M, Klarlund M, Lassere M, et al. Interreader agreement in the assessment of magnetic resonance images of rheumatoid arthritis wrist and finger joints: an international multicenter study. J Rheumatol 2001;28:1143-50.
8. Conaghan P, Edmonds J, Emery P, et al. Magnetic resonance imaging in rheumatoid arthritis: Summary of OMERACT activities, current status and plans. J Rheumatol 2001;28:1158-61.
9. 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.
10. 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.
11. O'Connor P, Østergaard M, Klarlund M, et al. Longitudinal evaluation of MRI scoring in rheumatoid arthritis B an international multicenter study of interreader agreement [abstract]. Arthritis Rheum 2001;44 Suppl:S315.
12. Bird P, Ejbjerg B, McQueen F, Østergaard M, Lassere M, Edmonds J. 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.
13. Ostergaard M, Conaghan P, Ejbjerg B, et al. Reducing costs, duration and invasiveness of MRI in RA by omitting intravenous gadolinium injection B. Does it affect assessments of synovitis, bone erosions and bone edema? Arthritis Rheum 2002:(submitted).
14. Boers M, Brooks P, Strand CV, Tugwell P. The OMERACT filter for outcome measures in rheumatology. J Rheumatol 1998; 25:198-9.
15. Peterfy C. MR imaging. Baillieres Clin Rheumatol 1996;10:635-78.
16. Konig H, Sieper J, Wolf KJ. Rheumatoid arthritis: evaluation of hypervascular and fibrous pannus with dynamic magnetic resonance imaging enhanced with Gd DTPA. Radiology 1990;176:473-7.
17. Gaffney K, Cookson J, Blake D, Coumbe A, Blades S. Quantification of rheumatoid synovitis by magnetic resonance

imaging. Arthritis Rheum 1995;38:1610-7.
18. Ostergaard M, Stoltenberg M, Lovgreen Nielsen P, Volck B, Jensen C, Lorenzen I. Magnetic resonance imaging determined synovial membrane and joint effusion volumes in rheumatoid arthritis and osteoarthritis. Arthritis Rheum 1997;40:1856-67.
19. Ostendorf B, Peters R, Dann P, et al. Magnetic resonance imaging and miniarthroscopy of metacarpophalangeal joints. Arthritis Rheum 2001;44:2492-502.
20. Foley Nolan D, Stack JP, Ryan M, et al. Magnetic resonance imaging in the assessment of rheumatoid arthritis a comparison with plain film radiographs. Br J Rheumatol 1999;30:101-6.
21. Jorgensen C, Cyteval C, Anaya JM, Baron MP, Lamarque JL, Sany J. Sensitivity of magnetic resonance imaging of the wrist in very early rheumatoid arthritis. Clin Exp Rheumatol 1993;11:163-8.
22. Scott DL, Coulton BL, Popert AJ. Long term progression of joint damage in rheumatoid arthritis. Ann Rheum Dis 1986;45:373-8.
23. Sharp JT, Young DY, Bluhm GB, et al. How many joints in the hand and wrist need to be included in a score of radiologic abnormalities? Arthritis Rheum 1985;28:1326-35.
24. Bedair H, Murphy M, Fleming D, et al. A comparison of MRI and CT in detecting carpal bone erosions in early rheumatoid arthritis [abstract]. Arthritis Rheum 2001;44 Suppl:S222.
25. Wakefield RJ, Gibbon W, Conaghan P, et al. The value of sonography in the detection of bone erosions in patients with rheumatoid arthritis. A comparison with conventional radiography. Arthritis Rheum 2000;43:2762-70.
26. Goupille P, Roulot B, Akoka S, et al. Magnetic resonance imaging: a valuable method for the detection of synovial inflammation in rheumatoid arthritis. J Rheumatol 2001;28:35-40.
27. Lassere M, van der Heidje D, Johnson K, Boers M, Edmonds J. The reliability of measures of disease activity and disease damage in rheumatoid arthritis: implications for the smallest detectable difference, the minimal clinically important difference, and the analysis of treatment effects in randomized controlled trials. J Rheumatol 2001;28:892-903.
28. Sharp JT, Lidsky MD, Collins LC, Moreland J. Methods of scoring the progression of radiologic changes in rheumatoid arthritis. Arthritis Rheum 1971;14:206-20.
29. van der Heijde D, van Leeuwen MA, van Riel PL, et al. Biannual radiographic assessments of hands and feet in a three year prospective followup of patients with early rheumatoid arthritis. Arthritis Rheum 1992;35:26-34.