

Magnetic Resonance Imaging in Rheumatoid Arthritis: Summary of OMERACT Activities, Current Status, and Plans

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ABSTRACT. Complementing the 3 papers that precede it, this paper explains the rationale for the activities of an OMERACT working party on magnetic resonance imaging (MRI) evaluation of rheumatoid arthritis (RA), sets out provisional recommendations for the acquisition and scoring of MRI of the hand and wrist in RA, and delineates some of the many residual problems that need to be addressed. (J Rheumatol 2001;28:1158–61)

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The ability to quantify synovitis and damage in rheumatoid arthritis (RA) and to measure with speed and accuracy the

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changes in these aspects of the disease is critical to efficient evaluation of the therapies and strategies becoming available to the clinical community. The “measurement” of synovitis, based on a mixture of poorly reproduced clinical features such as swollen and tender joint counts and laboratory tests of acute phase reactants, has never been secure. Damage assessment, in the form of cartilage loss and bone erosion, has used radiography, and its “measurement” has employed scoring systems, such as the Sharp¹ and Larsen² scores and their modifications^{3,4}. Although these methods are at least as reliable as other clinical measures⁵, the scoring systems raise a number of conceptual and methodological issues: the system's interval properties, and floor and ceiling effects; the intra- and interreader reliability, and the influence of reading order. Some of these have already been the focus of OMERACT scrutiny^{6,7}.

As it became evident that magnetic resonance imaging (MRI) was capable of imaging both synovitis and damage in RA and of detecting change in damage rather more quickly than radiography⁸⁻¹⁰, it seemed especially important to establish communication between experts in MRI technology, clinicians interested in quantifying rheumatoid damage and synovitis, and metrologists with expertise in developing scores and scales, so that, in conjunction, they could work towards an optimal system of capturing and measuring the rheumatoid pathology of interest. An initial meeting was convened at the American College of Rheumatology (ACR) meeting in San Diego in 1998 and from that emerged a working party that met subsequently at the EULAR Congress in Glasgow in 1999. An initial multicenter MRI scoring exercise was completed for the ACR meeting in Boston towards the end of 1999, and the scoring method was modified for a second international multicenter exercise completed for discussion at OMERACT 5 in

Toulouse. The results of both of these multicenter image scoring exercises are reported by Østergaard, *et al*¹¹.

Although the group is working towards a sensitive, reliable, and accessible MRI based method to detect and measure rheumatoid pathology, it would be inappropriate for the current status of our working recommendations to be interpreted as a definitive, OMERACT endorsed MRI scoring system for RA suitable for international adoption. The aim of work to date has been to develop, at least among the 5 participating centers, enough agreement on MRI detected rheumatoid pathology to provide a common reference point of communication, a common language from which ongoing studies can build an optimal system for measuring the rheumatoid lesions of interest.

As discussed by Østergaard, *et al*¹¹, the less than satisfactory agreement of scores between centers for reading exercises 1 and 2 is readily explained by a number of factors, particularly poorly defined lesion descriptors, variability in image acquisition methods, and lack of reader training and calibration. The OMERACT meeting was used to overcome some of these deficiencies and to draw up a “core set” of MRI acquisition specifications, to better define the lesion descriptors and to redraft the scoring system. These working recommendations, which refer only to the evaluation of the hand and wrist, are set out below. They are provisional but are set out simply to indicate the progress made by the working party. The suitability of these propositions is yet to be tested and they may be further modified if, in the next reading exercise, they are still considered unsatisfactory.

RECOMMENDATIONS FOR MRI EVALUATION OF THE HAND AND WRIST IN RHEUMATOID ARTHRITIS

1. Image acquisition specifications

For specific types of data or patient requirements, a variety of sequences and projections may be considered useful. However, for the purpose of scoring images on patients with RA, it was agreed that the following specifications should be adopted:

Sequences: T1 weighted images pre and post gadolinium; T2 with fat suppression or STIR.

Slice thickness: a maximum of 3 mm with zero gaps.

Projections: coronal and axial.

Field of view: 10 cm or smaller (for the wrist).

Matrix 256 × 192

2. Definitions of lesions to be scored

Erosion: a bone defect with sharp margins, visible in 2 planes (when 2 planes are available) with a cortical break seen in at least one plane.

Defect: a sharply marginated area of trabecular loss without a visible cortical break.

Bone edema: a lesion, which may occur alone or surround a

“defect” or “erosion,” with ill defined margins and high signal intensity on T2 weighted sequences. It is recognized that these edematous or edema-like lesions, in which the signal behavior is consistent with the presence of tissue water, may also represent inflammation.

Synovitis: the area in the synovial compartment that shows enhancement of a thickness greater than the width of the joint capsule after gadolinium.

Cartilage: will not be scored because the demarcation of this tissue in the small joints of the wrist and hand is too unreliable to allow useful scoring.

3. Scoring system

Erosion: 0 to 10 by the *volume of the defect* as a proportion of the “assessed bone volume” by 10% increments judged on all available images; for the carpal bones, the “assessed bone volume” will be the whole bone. For long bones, the “assessed bone volume” will be from the cortex of the articular surface (or its best estimated position if absent) to a depth of 1 cm.

Defect: 0 to 10 by the volume of the defect, as for erosion.

Bone edema: 0 to 10 by the volume of edema, as for erosion and defect.

Synovitis: CMC 1 and MCP 1 will not be scored; MCP 2–5 will be scored by 2 methods:

Method 1: A global score 0–3. Score 0 is normal, with no enhancement or enhancement that is no thicker than the normal synovium, i.e., the thickness of the joint capsule. Score 1–3: is by thirds of the presumed maximum volume of enhancing tissue in the synovial compartment, as per reference films.

Method 2: The measure, in mm, of the maximum thickness of enhancing tissue on the axial scan in the slice showing the most thickening.

Carpus will also be scored by 2 methods:

Method 1: A global score 0–3; score 0 is normal with no enhancement or enhancement thicker than the normal synovium, i.e., the thickness of the joint capsule. Score 1–3: is by thirds of the presumed maximum volume of enhancing tissue in the synovial compartment, as per reference films, in 3 areas: the radioulnar joint, the radiocarpal joint, and the intercarpal-CMC joints.

Method 2: The measure, in mm, of the maximum thickness of enhancing tissue perpendicular to the cortical surface, as follows:

In the coronal scan: from the scaphoid; from the triquetrum.

In the axial scan: at the radioulnar joint; along the curved dorsal surface of the 1st and 2nd carpal rows.

SHORT TERM PLANS

To test these new recommendations in a further round of multicenter readings, a set of reference films will be circulated to participants to provide examples of the different scores for synovitis at both the metacarpophalangeal joint

and the carpus. New films fulfilling the acquisition specifications will be generated for scoring carpal synovitis and these, with the films used in the earlier exercises, will be rescored using the Toulouse recommendations. The results have been analyzed in time for review and discussion at the ACR meeting in Philadelphia in October and November 2000.

FURTHER ISSUES AND PLANS

The OMERACT discussion groups provided the opportunity to gain input from a broad cross section of opinion into some of the issues of concern to the working party.

Most of the suggestions related to methods of improving the scoring system had been foreshadowed by the working group, notably the generation of reference films, improved training and calibration of readers, and better standardization of acquisition specifications. One important issue is whether it will be more profitable in the long term to invest time, effort, and money in better scoring methods or in techniques of measuring lesions, presumably using computer technology.

Validation studies are needed to determine the significance of the many different types of lesions seen on MRI. Is bone edema, for example, always followed by erosion or does it sometimes resolve spontaneously; and is it possible to distinguish which will progress and which resolve? Is synovitis, defined as an area within the synovial compartment that shows enhancement following gadolinium, a prerequisite for erosion? How much does evaluation of tenosynovitis contribute to an understanding of "functional impairment" and "damage"? A number of validation approaches is possible, for example, MRI changes can be set against changes evident on other imaging modalities, such as radiography and ultrasound, or against histological lesions in bone, cartilage, and synovium.

It was a disappointment to the group to be forced to abandon the assessment of cartilage in the wrist and hand, particularly since there is emerging evidence that different pathophysiological processes may be responsible for bone erosion and cartilage loss. Ultra-high resolution MRI can detect cartilage well and is of research interest but is not currently useful for scoring since it is applicable only to one or 2 small joints. This raises the question of priorities in selecting tissues for assessment by MRI. Clearly, the research question is the principal determinant of this choice, but from the viewpoint of what the MRI does best, assessment of synovium, tenosynovitis, and bone erosion takes precedence. It follows that a comprehensive evaluation of the tissues of interest in RA may require the combined use of different imaging techniques — MRI (for synovium and erosion) with computerized tomography or radiography (for joint space narrowing). Such formal assessment combinations would generate their own requirements for validation, reliability, and feasibility.

To use resources of patient involvement, time, and money most efficiently, it will also be important to determine just how many joints need to be studied to obtain a representative sampling of a patient's synovitis and joint damage. Data bearing on this question could be derived from the results of radiological scoring studies of hands and feet in some of the large therapeutic trials.

Once we have established a basic scoring system with an acceptable level of agreement between the readers, it will be possible to begin to assess inter- and intra-reader reliability, to derive a measurement error, and to establish an estimate of the "smallest detectable difference"¹². With this more secure basis for communication and comparison it will then be easier to initiate a research agenda that addresses some of the issues raised. Clearly, a similar exercise is required for the use of MRI as an outcome or process measurement tool in other arthropathies, particularly osteoarthritis.

The activities of this working group are not exclusive. OMERACT, with its measurement and epidemiological expertise, and its confirmed interest in the accuracy and reliability of imaging as an outcome, provides a good forum for work of this kind. But clinicians and researchers from many fields are interested in having an accurate grasp on the anatomy and physiology of the tissues in their system of interest, and the new and developing imaging technologies offer immense potential to allow this. Harnessing this power is a big project and should engage a wide range of interested groups. Accordingly, the (very) provisional image acquisition and scoring recommendations of the working party outlined in this paper must not be interpreted as a premature closure on the subject but as a start to the collaborative, ordered process necessary to make the best scientific use of these wonderful, evolving new ways of studying the pathology of the diseases that interest us.

REFERENCES

1. Sharp JT, Lidsky MD, Collins LC, Moreland J. Methods of scoring the progression of radiologic changes in rheumatoid arthritis. Correlation of radiologic, clinical and laboratory abnormalities. *Arthritis Rheum* 1971;14:706-20.
2. Larsen A, Dale K, Eek M. Radiographic evaluation of rheumatoid arthritis and related conditions by standard reference films. *Acta Radiol Diagn* 1977;18:481-91.
3. van der Heijde D. How to read radiographs according to the Sharp/van der Heijde method. *J Rheumatol* 1999;26:743-5.
4. Scott D, Houssien D, Laasonen L. Proposed modification to Larsen's scoring method for hand and wrist radiographs. *Br J Rheumatol* 1995;34:56.
5. Lassere M, van der Heijde 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.
6. Kirwan J. Conceptual issues in scoring radiographic progression in rheumatoid arthritis. *J Rheumatol* 1999;26:720-5.
7. van der Heijde D, Boers M, Lassere M. Methodological issues in radiographic scoring methods in rheumatoid arthritis. *J Rheumatol*

- 1999;26:726-30.
8. Østergaard M, Hansen M, Stoltenberg M, Lorenzen I. Quantitative assessment of the synovial membrane in the rheumatoid wrist: an easily obtained MRI score reflects the synovial volume. *Br J Rheumatol* 1996;35:965-71.
 9. McGonagle D, Conaghan P, O'Connor P, et al. The relationship between synovitis and bone changes in early untreated rheumatoid arthritis. A controlled magnetic resonance imaging study. *Arthritis Rheum* 1999;42:1706-11.
 10. McQueen F, 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.
 11. Østergaard M, Klarlund M, Lassere M, et al. Inter-reader agreement in the assessment of magnetic resonance imaging of rheumatoid arthritis wrist and finger joints. *J Rheumatol* 2001;28:1143-50.
 12. Lassere M, Boers M, van der Heijde D, et al. Smallest detectable difference in radiological progression. *J Rheumatol* 1999;26:731-9.