Commentary

The value of sensitive imaging modalities in rheumatoid arthritis

Peter C Taylor

The Kennedy Institute of Rheumatology Division, Faculty of Medicine, Imperial College London, UK

Correspondence: Peter C Taylor (e-mail: peter.c.taylor@imperial.ac.uk))

Received: 22 May 2003 Accepted: 2 Jul 2003 Published: 16 Jul 2003

Arthritis Res Ther 2003, **5**:210-213 (DOI 10.1186/ar794)

Abstract

X-ray evaluation of rheumatoid joints is relatively inexpensive, is widely available and has standardised methods for interpretation. It also has limitations, including the inability to reliably determine structural change in less than 6–12 months, the need for experienced readers to interpret images and the limited acceptance of this technique in routine clinical practice. High-frequency ultrasound, with or without power Doppler, and magnetic resonance imaging of rheumatoid joints permit an increasingly refined analysis of anatomic detail. However, further research using these sensitive imaging technologies is required to delineate pathophysiological correlates of imaging abnormalities and to standardise methods for assessment.

Keywords: magnetic resonance imaging, power Doppler, radiography, rheumatoid arthritis, ultrasonography

Introduction

Evaluation of disease activity and structural damage to joints in rheumatoid arthritis (RA) is essential in both routine clinical management and clinical trials. But does conventional radiography (CR) remain the gold-standard methodology for assessment of joint damage in RA?

The assessment of structural damage by CR relates poorly to function in early RA, although in disease of 5 years' duration or longer there is a weak but significant correlation [1]. Although CR evaluation of joint structure is relatively inexpensive, is widely available and has standardised methods for interpretation, it also has many limitations. These limitations include the use of ionising radiation and projectional superimposition, which can obscure erosions and mimic cartilage loss as an inevitable consequence of representing a three-dimensional structure in only two planes. Furthermore, in the context of clinical trials, experienced readers are required to interpret the films, often using time-consuming methods [2], and structural change cannot be reliably determined in less than 6–12 months. CR offers only late signs of preceding disease activity and the resulting cartilage and bone destruction. In comparison, images obtained using newer magnetic resonance and ultrasonographic technologies emphasise the inadequacy of CR for soft tissue assessment in RA.

Ultrasonography

Recent studies addressing the use of conventional grey-scale (B-mode) ultrasonography (US) in the evaluation of RA synovial inflammation and joint damage indicate that clinical joint examination and CR are comparatively insensitive tools [3–5]. The most important technical requirement for joint US is a high-quality imaging system. Optimal ultrasound equipment for musculoskeletal work should be equipped with standard 7.5–10 MHz transducers for conventional examination. Higher frequency transducers (13, 15, 20, 22 and 30 MHz) are necessary to depict the fine details of superficial tissues. The 20 MHz transducers have an axial resolution power of 0.038 mm. However, the 20 MHz transducers have a limited image field of view, have poor beam penetration and do not allow the evaluation of structures deeper than 1.5 cm below the surface. Recent developments in US technology have allowed the realisation of high-resolution broadband transducers (5–10, 8–16 and 10–22 MHz).

Recent years have witnessed the emergence of a new paradigm in the treatment strategy for RA, involving early

CR = conventional radiography; MRI = magnetic resonance imaging; PD = power Doppler; RA = rheumatoid arthritis; US = ultrasonography.

and aggressive suppression of synovitis by means of pharmacological intervention with drugs proven to modify the rate of progression of structural damage to joints. Preservation of joint integrity is closely associated with maintenance of functional capability. However, many patients with early RA are excluded from clinical studies because radiology does not detect erosions. Furthermore, the introduction of disease-modifying antirheumatic drugs may be delayed because of the absence of radiological erosions. In this circumstance, when the diagnosis of early RA is suspected but the patient has yet to fulfil the necessary number of classification criteria, imaging technologies such as high-frequency US, particularly of the second and third metacarpophalangeal joints and the fifth metatarsophalangeal joint, may be very valuable to confirm the presence of erosive disease.

While high-frequency (grey-scale) US measurements of joint space are robust, showing reproducible delineation of synovial thickening in small joints of the hands in patients with active RA, the analysis of such images does not necessarily demonstrate a clear relationship with clinical assessments of disease activity [6]. This observation probably reflects the fact that high-frequency US identifies synovial thickening without differentiating actively inflamed or fibrous tissue.

The additional use of Doppler techniques, in which a signal generated by moving blood cells permits assessment of vascularised synovium [3,7,8], might be predicted to better reflect the presence of active synovitis. Large-vessel blood flow is at high velocity and is readily detected by conventional colour Doppler sonography that encodes the mean Doppler frequency shift. However, blood flow at the microvascular level, which is of interest with respect to rheumatoid synovitis, is at a lower velocity and is less readily detectable by this means.

In contrast, power Doppler (PD) sonography encodes the amplitude of the power spectral density of the Doppler signal and is a sensitive method for demonstrating the presence of blood flow in small vessels. The PD signal is actually a measure of the density of moving reflectors at a particular level, and thus of the fractional vascular volume [9,10]. PD is insensitive to flow in submillimetre vessels, in common with most other ultrasound methods, and is thus only an indirect surrogate for measurement of capillary flow. Several recent studies have, however, demonstrated that PD ultrasound is capable of detecting synovial hyperaemia in the inflamed RA joint [3,7,11,12] and that signal intensity correlates well with histological assessment of synovial membrane microvascular density [11]. Quantitative PD assessment of vascularised synovium in the metacarpophalangeal joints of patients with RA has been reported to correlate with erythrocyte sedimentation rate [6].

The close relationship between findings on PD and those on gadolinium-enhanced magnetic resonance imaging (MRI) are an encouraging indication that a synovial vascular signal on PD is associated with inflammatory processes [8]. Three small, uncontrolled studies have reported a reduction in the PD signal following therapeutic intervention in RA [7,13,14]. The use of intravenous microbubble echo-contrast agents may enhance the sensitivity of a PD signal in RA joints [15], but with the disadvantages of cost, time and invasiveness.

The main advantages of US as compared with other imaging techniques include the absence of radiation, good visualisation of tendons and joint space, low running costs, multiplanar imaging capability, and easy comparison with the contralateral side. US can be performed at the bedside and is readily acceptable to patients. However, the image acquisition procedure for high-frequency US and PD has yet to be standardised, and the quality of the examination is highly dependent upon the skill of the operator and the use of optimal equipment. Furthermore, there are potential problems with reproducibility based on intra-observer and inter-observer variability and the use of different machines.

Computed tomography

The tomographic perspective permitted by computed tomography overcomes some of the limitations of CR and permits particularly good definition of bony change. However, it entails greater exposure to ionising radiation and has an inferior sensitivity to changes in RA soft tissues in comparison with US and MRI [16].

Magnetic resonance imaging

MRI has the capability to image all components of the joint simultaneously and is more sensitive than clinical assessment and CR for the detection of joint inflammation and destruction [17,18]. The ability to distinguish between RA joint effusion and synovial proliferation by MRI has been greatly improved by the introduction of paramagnetic contrast agents. The early post-gadolinium synovial membrane enhancement in RA joints, determined by dynamic MRI, is considered to reflect synovial perfusion and permeability. However, the image quality, and therefore interpretation, will depend on a number of technical factors including the magnet strength, the use of dedicated coils and the choice of MRI sequences.

Attempts to standardise image acquisition, terminology and quantification have been made by an international panel of experts at Outcome Measures in Rheumatoid Arthritis consensus conferences [19]. However, further clarification of nomenclature for image abnormalities is required where pathophysiological correlates are uncertain. For example, MRI signs of increased water content in the bone marrow compartment, generally termed ‘bone oedema’, are

reversible but often associated with subsequent erosive damage [18,20]. Difficulties may arise when it is assumed that there is identity in the pathological basis of lesions labelled as 'erosions' by different imaging modalities. For example, only one in four lesions identified as 'erosions' on MRI progress to CR erosions at the same site [21], and progression of CR hand scores may not be associated with change in 'erosions' as determined by MRI at the metacarpophalangeal joints [22]. Mineralised bone does not generate a signal on MRI, but is detected as the gap between adjacent tissues containing mobile protons. Most MRI 'erosions' appearing to be larger in volume than corresponding lesions detected by CT may occur because MRI depicts abnormalities in bone marrow around, as well as filling, bone defects [23].

Much work yet remains to reduce the high inter-rater variability reported when various scoring methods are used in the assessment of magnetic resonance images obtained at different centres using slightly different means of image acquisition [24]. One potential approach to this difficulty is to develop quantitative techniques for measuring MRI synovial volumes and erosion volumes using image analysis software [25]. Very low intra-observer variability is reported for this methodology, but inter-rater variation, a crucial issue if wider, reliable application in the context of clinical trials is to be useful, remains to be tested.

Conclusions

It is evident that technological advances in imaging permit an increasingly refined analysis of fine anatomic detail. However, there is much work to be carried out in standardising new imaging technologies in the assessment of RA and in determining the pathophysiological correlates of certain image abnormalities. It would therefore be premature to regard MRI or US as usurping the status of CR as the recommended 'gold standard' for assessment of structural damage to joints in the context of clinical trials. Even so, we can conclude that these rapidly advancing imaging technologies hold much promise as sensitive clinical tools, with the potential to detect early changes in inflammatory processes and joint destruction that may ultimately permit reduced clinical trial size and duration, and may permit better informed management decisions in a bid to optimally suppress synovitis and improve treatment outcomes.

Competing interests

None declared.

References

1. Scott DL, Pugner K, Kaarela K, Doyle DV, Woolf A, Holmes J, Hieke K: **The links between joint damage and disability in rheumatoid arthritis.** *Rheumatology (Oxford)* 2000, **39:**122-132.
2. van der Heijde DM: **Plain X-rays in rheumatoid arthritis: overview of scoring methods, their reliability and applicability.** *Baillieres Clin Rheumatol* 1996, **10:**435-453.
3. Hau M, Schultz H, Tony HP, Keberle M, Jahns R, Haerten R, Jenett M: **Evaluation of pannus and vascularization of the metacarpophalangeal and proximal interphalangeal joints in rheumatoid arthritis by high-resolution ultrasound (multidimensional linear array).** *Arthritis Rheum* 1999, **42:**2303-2308.
4. Wakefield RJ, Gibbon WW, Conaghan PG, O'Connor P, McGonagle D, Pease C, Green MJ, Veale DJ, Isaacs JD, Emery P: **The value of sonography in the detection of bone erosions in patients with rheumatoid arthritis.** *Arthritis Rheum* 2000, **43:** 2762-2770.
5. Grassi W, Filippucci E, Farina A, Salaffi F, Cervini C: **Ultrasonography in the evaluation of bone erosions.** *Ann Rheum Dis* 2001, **60:**98-103.
6. Qvistgaard E, Rogind H, Torp-Pedersen S, Terslev L, Danneskiold-Samsoe B, Bliddal H: **Quantitative ultrasonography in rheumatoid arthritis: evaluation of inflammation by Doppler technique.** *Ann Rheum Dis* 2001, **60:**690-693.
7. Newman JS, Laing TJ, McCarthy CJ, Adler RS: **Power Doppler sonography of synovitis: assessment of therapeutic response — preliminary observations.** *Radiology* 1996, **198:** 582-584.
8. Szkudlarek M, Court-Payen M, Strandberg C, Klarlund M, Klausen T, Ostergaard M: **Power Doppler ultrasonography for assessment of synovitis in the metacarpophalangeal joints of patients with rheumatoid arthritis: a comparison with dynamic magnetic resonance imaging.** *Arthritis Rheum* 2001, **44:**2018-2023.
9. Rubin JM, Adler RS, Fowlkes JB, Spratt S, Pallister JE, Chen JF, Carson PL: **Fractional moving blood volume: estimation with power Doppler US.** *Radiology* 1995, **197:**183-190.
10. Bude RO, Rubin JM: **Power Doppler sonography.** *Radiology* 1996, **200:**21-23.
11. Walther M, Harms H, Krenn V, Radke S, Faehndrich TP, Gohlke F: **Correlation of power Doppler sonography with vascularity of the synovial tissue of the knee joint in patients with osteoarthritis and rheumatoid arthritis.** *Arthritis Rheum* 2001, **44:**331-338.
12. Carotti M, Salaffi F, Manganelli P, Salera D, Simonetti B, Grassi W: **Power Doppler sonography in the assessmentof synovial tissue of the knee joint in rheumatoid arthritis: a preliminary experience.** *Ann Rheum Dis* 2002, **61:**877-882.
13. Hau M, Kneitz C, Tony H-P, Keberle M, Jahns R, Jenett M: **High resolution ultrasound detects a decrease in pannus vascularisation of small finger joints in patients with rheumatoid arthritis receiving treatment with soluble tumour necrosis factor α receptor (etanercept).** *Ann Rheum Dis* 2002, **61:**55-58.
14. Terslev L, Torp-Pedersen S, Qvisgaard E, Kristoffersen H, Rogind H, Danneskiold-Samsoe B, Bliddal H: **Effects of treatment with etanercept (Enbrel, TNFR:Fc) on rheumatoid arthritis evaluated by Doppler ultrasonography.** *Ann Rheum Dis* 2003; **62:** 178-181.
15. Klauser A, Frauscher F, Schirmer M, Halpern E, Pallwein L, Herold M, Helweg G, ZurNedden D: **The value of contrast-enhanced color Doppler ultrasound in the detection of vascularisation of finger joints in patients with rheumatoid arthritis.** *Arthritis Rheum* 2002, **46:**647-653.
16. Alasaarela E, Suramo I, Tervonen O, Lahde S, Takalo R, Hakala M: **Evaluation of humeral head erosions in rheumatoid arthritis: a comparison of ultrasonography, magnetic resonance imaging, computed tomography and plain radiography.** *Br J Rheumatol* 1998, **37:**1152-1156.
17. McQueen FM, Stewart N, Crabbe J, Robinson E, Yeoman S, Tan PLJ, McClean L: **Magnetic resonance imaging of the wrist in early rheumatoid arthritis reveals a high prevalence of erosion at four months after symptom onset.** *Ann Rheum Dis* 1998, **57:**350-356.
18. McGonagle D, Conaghan P, O'Connor, Gibbon W, Green M, Wakefield RJ, Ridgway J, Emery P: **The relationship between synovitis and bone changes in early untreated rheumatoid arthritis. A controlled magnetic resonance imaging study.** *Arthritis Rheum* 1999, **42:**1706-1711.
19. Conaghan P, Edmonds J, Emery P, Genant H, Gibbon W, Klarlund M, Lassere M, McGonagle D, McQueen F, O'Connor P, Peterfy C, Shnier R, Stewart N, Ostergaard M: **Magnetic resonance in rheumatoid arthritis: summary of OMERACT activities, current status, and plans.** *J Rheumatol* 2001, **28:** 1158-1162.

20. McQueen FM, Stewart N, Crabbe J, Robinson E, Yeoman S, Tan PJL, McLean L: **Magnetic resonance imaging of the wrist in early rheumatoid arthritis reveals progression of erosions despite clinical improvement.** *Ann Rheum Dis* 1999, **58:**156-163.
21. McQueen FM, Benton N, Crabbe J, Robinson E, Yeoman S, McLean L, Stewart N: **What is the fate of erosions in early rheumatoid arthritis? Tracking individual lesions using X rays and magnetic resonance imaging over the first two years of disease.** *Ann Rheum Dis* 2001, **60:**859-868.
22. Klarlund M, Ostergaard M, Jensen KE, Madsen JL, Skjodt H, Lorenzen I, the 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:** 521-528.
23. Goldbach-Mansky R, Woodburn J, Yao L, Lipsky P: **Magnetic resonance imaging in the evaluation of bone damage in rheumatoid arthritis: a more precise image or just a more expensive one?** *Arthritis Rheum* 2003, **48:**585-589.
24. Ostergaard M, Klarlund M, Lassere M, Conaghan P, Peterfy C, McQueen F, O'Connor P, Shnier R, Stewart N, McGonagle D, Emery P, Genant H, Edmonds J: **Interreader agreement in the assessment of magnetic resonance images of rheumatoid arthritis wrist and finger joints — an international multicenter study.** *J Rheumatol* 2001, **28:**1143-1150.
25. Bird P, Lassere M, Shnier R, Edmonds J: **Computerized measurement of magnetic resonance imaging erosion volumes in patients with rheumatoid arthritis: a comparison with existing magnetic imaging scoring systems and standard clinical outcome measures.** *Arthritis Rheum* 2003, **48:**614-624.

Correspondence

Peter C Taylor, Senior Lecturer and Honorary Consultant Rheumatologist, The Kennedy Institute of Rheumatology Division, Faculty of Medicine, Imperial College London, 1 Aspenlea Road, London W6 8LH, UK. Tel: +44 20 8383 4494; fax: +44 20 8748 3293; e-mail: peter.c.taylor@imperial.ac.uk