REVIEW ARTICLE

Advanced imaging in rheumatoid arthritis

Part 2: Erosions

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Abstract Rheumatoid arthritis (RA) is a chronic and progressive inflammatory disorder primarily affecting the synovium. We now recognise that conventional radiographic images show changes of rhuematoid arthritis late after irreversible joint damage has occured. With the advent of powerful disease-modifying drugs there is a need for early demonstration of rheumatoid arthritis and to monitor progress of the disease and response to therapy. Advanced imaging techniques such as ultrasound and MRI have focussed on the demonstration and quanitification of synovitis and erosions and allow early diagnosis of RA. The technology to quantify synovitis and erosions is developing rapidly and now allows change in disease activity to be assessed. However, problems undoubtedly exist in quantification techniques and this review serves to highlight them. Much of the literature on advanced imaging in RA appears in rheumatological journals and may not be familiar to radiologists. This review article aims to increase the awareness of radiologists to this field and to encourage them to participate and contribute to the ongoing development of these modalities. Without this collaboration it is unlikely that these modalities will reach their full potential in the field of rheumatological imaging. This review is in two parts. This first part addresses synovitis imaging. The second part will look at advanced imaging of erosions in RA.

Part 1 of this article (Synovitis) can be found at: http://dx.doi.org/10.1007/s00256-006-0219-9.

In our previous article we described issues surrounding the advanced imaging of synovitis. This article addresses erosions in a similar manner.

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Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune multisystem disorder of unknown aetiology. It has an incidence in the community of approximately 1% and represents an important cause of morbidity and mortality. The defining pathological feature of RA is bone erosion. Erosions are important in RA diagnosis and their presence is a key indicator of prognosis [1]. Erosions are common in RA patients and have been found in up to 97% of patients [2]. The majority develop during the first 2 years of the disease [3]. Early erosive disease is a poor prognostic sign signalling potentially aggressive disease [4].

Recently introduced biologic disease-modifying anti-rheumatic drugs (DMARDS) have been extremely successful in suppressing disease activity. They work by inhibiting the inflammatory cascade reducing inflammatory change in and around joints. Their effect in preventing irreversible joint damage is most marked when treatment is initiated early in the disease process [5]. Accurate and early diagnosis of RA has become imperative, placing increased demands on imaging to identify the earliest sign of erosive joint damage and predict future structural and functional deterioration.

Our objective is to present the advanced imaging techniques in detection and monitoring of rheumatoid erosive disease and to review the current literature.

Pathophysiology

Synovial proliferation is often the earliest stage during the course of RA that patients become symptomatic with joint pain, swelling and morning stiffness. The natural history of the disease then progresses to pannus formation and periarticular bone demineralisation, cartilage destruction and subchondral bone erosions [6]. The speed of disease progression varies between patients and changes with time even in individual patients. Collagenase, produced at the interface of pannus and cartilage, is believed to be largely responsible for the bony erosions.

Several markers of the disease have been evaluated for correlation with erosion on MRI. For example serum levels of immunoglobulin A (IgA), IgG and IgM rheumatoid factor [7], C-reactive protein [8] and serum vascular endothelial growth factor (VEGF) [9] have been shown to correlate with erosion on MRI.

Controversy exists regarding the relationship of clinical symptoms, synovitis and erosions in RA. Several studies have demonstrated that joint swelling and pain are poor indicators of disease severity when compared with radiological changes of synovitis and erosions [10–13]. To the contrary local expression of early RA activity measured as swelling and pain in an individual joint at baseline and at the 1-year follow-up has been shown to be strongly related to progression of damage [14]. There are studies that have shown that the link between synovitis and erosions is weak and that they do not necessarily represent the same pathological process [10]. However the majority of studies have concluded that synovitis is preerosive and predictive for erosions in early RA [11, 15–18]. Furthermore randomised studies of RA patients during treatment show that the rate of erosive progression on MRI is highly correlated with baseline synovial volume scores and, particularly, with the area under the curve values of synovial membrane volume [18, 19].

Many studies show that bone oedema is strongly correlated with bone erosion [8, 11, 12, 17, 20, 21].

Imaging modalities

Imaging should be complimentary to the clinical examination, provide the clinician with a more confident diagnosis of RA, distinguish patients with early aggressive disease requiring DMARDS and monitor therapeutic response.

A study of 50 patients with polyarthralgia suspected of having early RA clinically and radiographically underwent gadolinium (Gd-DTPA)-enhanced MR imaging of the hands. Thirty percent more patients were correctly diagnosed using MRI than using the classification tree of the American Rheumatism Association [22].

Multiplanar imaging techniques such as ultrasound (US), computed tomography (CT) and MRI have been shown in several studies to demonstrate erosions with greater sensitivity than conventional radiography (CR), particularly in early RA [23, 24] (Fig. 1a–c).

In a comparison of US, MRI, CT and CR in detecting bone erosions in the humeral head in 26 patients with RA, MRI depicted erosions in 25 (96%), US in 24 (92%), CT in 20 (77%) and CR in 19 (73%) cases [24]. This study also showed CR was particularly insensitive to small erosions. Erosions generally only become visible on conventional radiography (CR) after a large proportion of the bone is destroyed [25].

Clinical trials and practice

To assess the literature effectively it is important to differentiate between clinical practice and clinical trials imaging papers. In general the literature is targeted at the use of imaging as an outcome measure for clinical trials work. The roles played by imaging in clinical trials are similar to those in clinical practice, such as disease diagnosis, severity assessment and prognostication, monitoring of disease progression and treatment response and evaluation of complications. However the priorities differ between these two contexts. Methods described in the literature to score erosions and determine disease progression may be impractical to implement in daily clinical practice that is geared towards individual patients rather than a study population. For example the Larsen and Sharp radiographic scores and their modifications are standard methods for determining joint damage and its progression in clinical trials but are rarely used in clinical practice to determine a management plan.

The role of clinical trials in validating precise methods for identifying patients that would benefit from DMARDS and for monitoring therapy is essential to establish the efficacy and safety of new drugs. In fact it is often during clinical testing of new therapies that imaging tools that will ultimately be used in clinical practice first get developed.

The use of advanced imaging such as MRI and US in clinical trials is of great financial advantage to drug companies as it allows study populations and study duration to be decreased with a subsequent large incentive to use expensive equipment in trials. Biologic agents are currently very expensive and clinicians are increasingly relying on advanced imaging modalities to identify a subset of patients with aggressive disease suitable for treatment. With these therapies being used with increasing frequency
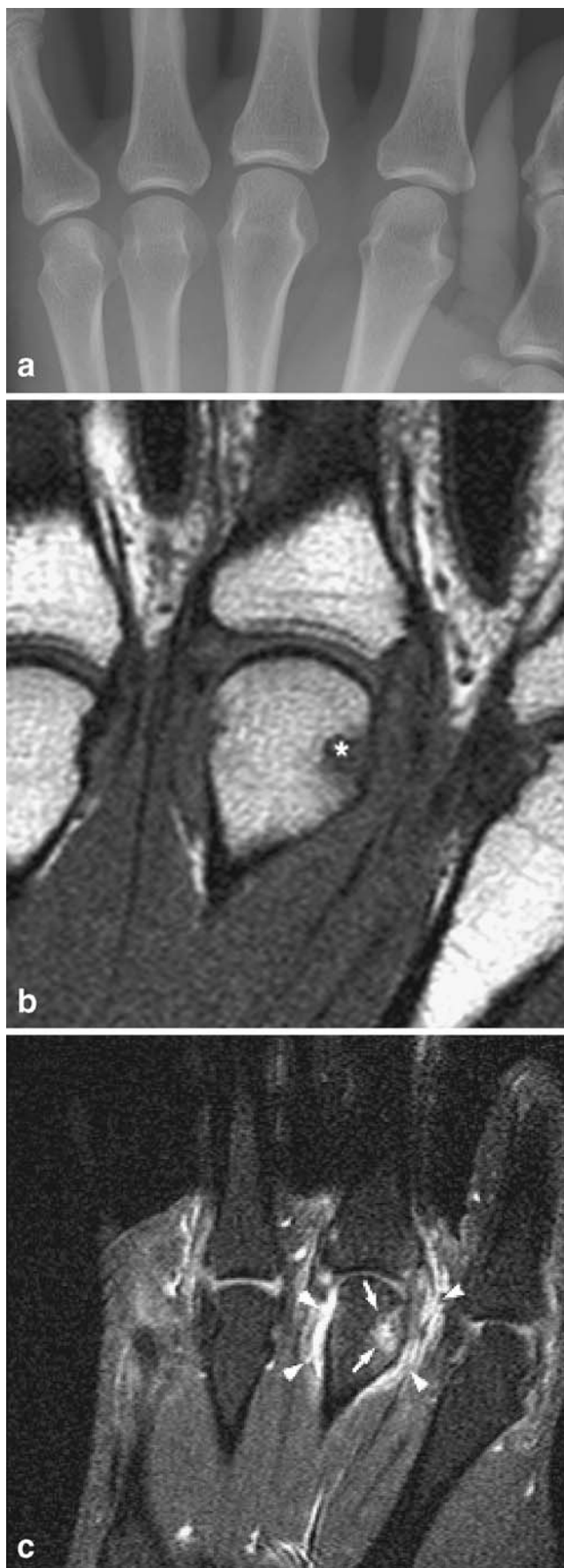
Fig. 1 a–c The left hand of a patient with early RA. Comparison of radiograph and MRI. **a** Plain PA radiograph of the 2nd–5th MCP joints demonstrating normal appearances of the metacarpal heads with no erosions. **b** T1-weighted coronal MRI shows erosion of the radial aspect of the 3rd metacarpal head (*). **c** T2 fat suppressed coronal MRI demostrates oedema (arrows) associated with periarticular inflammatory change (arrowheads)

it is likely that advanced imaging techniques will play an increasing role in the management of patients with early RA.

Enormous costs are incurred by drug companies in getting a drug to the market place. Drug companies must now achieve Food and Drug Administration (FDA) approval for phase-three trials. Neither MRI nor US have FDA approval as outcome measures in RA. The next major challenge for MRI will be consideration for approval as an outcome measure.

MRI

The Outcome Measures In Rheumatoid Arthritis Clinical Trials (OMERACT) definition of an erosion on MRI is a sharply marginated bone lesion, with correct juxtaarticular location and typical signal characteristics, which is visible in at least two planes with a cortical break seen in at least one plane [26]. On T1-weighted images there is loss of normal low signal intensity of cortical bone and loss of normal high signal intensity of trabecular bone as marrow fat is replaced. Rapid post-Gd-DTPA enhancement suggests the presence of active, hypervascularized pannus tissue in the erosion [26]. Erosions enhance with contrast and are thereby differentiated from intraosseous fluid-filled cystic lesions [25].

There are no pathological correlation data available for MRI erosions in rheumatoid. MRI cannot be compared to the previous gold standard for bone erosions, CR. CR is an ineffective gold standard as MRI has been found to be more sensitive in the detection of early rheumatoid erosions and long-term follow-up is ineffective as all patient cohorts are subject to disease-modifying therapy. A study using miniarthroscopy of MCP joints has reported macroscopic evidence of erosive disease that correlated with MR erosions, but only surface areas of the lesions were visible [27]. Some reassurance comes from the fact that ultrasound [23] and CT [28] reveal the same erosive lesions as MRI.

Studies show that there is 13% to 19% mismatch between MR erosion and lesions detected with CT [24, 28]. It is accepted that CT is a more reliable imaging modality to assess bone structure and CT is therefore more likely than MR to represent a gold standard in terms of assessing bone destruction in rheumatoid patients. These studies indicate that not all erosions seen at MR represent bone destruction. Either focal oedema in the cortex and

underlying bone, partial voluming, observer error or even normal variation are all possible explanations for these findings.

There are no pathological studies of MR-detected bone oedema in the literature with no imaging comparator available for concurrent validation. Only longitudinal studies comparing MR bone oedema and radiographic progression with clinical progress will elucidate the true significance of these changes [29].

Several studies have demonstrated superior sensitivity in depiction of erosions on MRI in early disease compared with CR [8, 19, 21, 30–34]. MRI has the ability to visualise lesions 6 to 12 months before they appear on CR [8, 35]. One study revealed carpal erosions on MRI in 45% of RA patients at 4 months from the onset of symptoms, whereas only 15% had erosions on CR [8], rising to 74% at 1 year on MRI and 28.6% on CR [11]. Occasionally erosions are detected on CR and not MRI [34]. This is unusual and is probably the result of technical factors relating to the MRI such as unfortunate slice selection or movement artefact.

There are conflicting data regarding the progression of MRI-detected erosions to erosions detected by CR. One study shows that only one in four of the MRI erosions progressed to radiographic erosion during the 1st year of the disease, possibly owing to healing or observer error [35]. This study also showed that patients with a high total MRI score, including erosion, bone oedema, synovitis and tendonitis scores, were more likely to develop erosions on CR at 2 years. Longitudinal studies demonstrate the persistence and progression of MRI erosions. These studies indicate that MRI erosions are not usually reversible and are present in 95% [11] to 100% [34] of those patients that had erosions at baseline.

OMERACT defines bone marrow oedema as a lesion within the trabecular bone, which may occur alone or surrounding an erosion or other bone abnormality, with ill-defined margins and signal characteristics consistent with increased water content [26]. It appears as low signal intensity on T1-weighted images and high signal on fat-saturated T2 and STIR images, resulting from an increased amount of water in the marrow, and may represent the internal bone response to external inflamed synovium [20] (Fig. 2).

Oedema cannot be appreciated on CR, US or CT.

Bone marrow oedema seems to be a stronger predictor of future erosion than synovial volume [8, 11, 12, 17, 20, 21]. One study showed that if bone oedema was present at a specific site at baseline it was associated with a six-fold increase in the chance of erosion occurrence at the same site after 1 year [11].

MRI has important implications for the diagnosis and correct management of patients with early unclassified

Fig. 2 T1-weighted fat-suppressed post Gd-DTPA coronal MRI shows diffuse oedema (black arrows) in the radial aspect of the 2nd metacarpal head with intact overlying cortex. Synovitis (arrowheads) and nonenhancing effusion (white arrows) are present in the 2nd and 3rd MCP joints

polyarthritis. MRI studies of four groups of patients (established RA, early RA, other arthritis and arthralgias) have shown bone marrow oedema was found in 68% of patients with established RA and the number of bones with oedema was significantly higher than in any of the other patient groups [16]. Twenty patients with recent onset knee effusion underwent MRI and prominent peri-entheseal bone marrow oedema was a feature in six out of ten spondyloarthropathy patients, but was not found in the RA patients studied [36].

MRI scans performed at the first presentation of RA can, by detecting the presence of bone marrow oedema or synovitis, be used to diagnose and predict future radiographic damage, allowing DMARDS to be targeted to patients with aggressive disease [8, 12, 19, 37].

Reliabilty and reproducibilty

The OMERACT 6 study, a multireader (five observers), multicentre study assessed the inter-reader reliability of the RA-MRI scoring system (RAMRIS) in the assessment of disease status and progression [38, 39]. Abnormalities were recorded according to proportion of bone volume involved (0–10 for erosions and defects and 0–3 for edema). Reasonable reliability in scoring bone erosions was found

with intraclass correlation coefficient (ICC) values ranging from 0.46 to 0.85 and smallest detectable difference (SDD) from 24% to 42%. The results were better for status scores than progression scores. Reliability was generally lower at the wrist compared with MCP joints, which may reflect greater potential for error in scoring anatomically complex regions [29].

Bird et al. developed a computerized technique for estimating erosion volumes that demonstrated excellent intraobserver and interscan agreement [40]. ICC values for intraobserver agreement of erosion volume were 0.93–0.96, and interscan ICC values were 0.92–0.99 [40]. These results were comparable with those obtained using the OMERACT erosion grading score.

MRI and CR both have reported interobserver agreement for erosion detection of around 90% [33]. Maximal variation in MRI detected erosions when intraobserver, interobserver and inter-MRI variations were combined was reported to be 26% [41].

The EULAR (European League Against Rheumatism)-OMERACT RA MRI reference imaging atlas is an international reference set of images for bone erosions, bone oedema and synovitis aiming to standardise assessment of the disease and allowing semiquantative scoring. Coronal and axial pre-contrast images were chosen to grade erosions from 0–10 according to the percentage of bone occupied by erosion. T2-weighted fat-saturated or STIR sequence images provided the most sensitive visualisation and scoring for bone oedema [42].

Pitfalls

There are several factors that can influence interpretation of MRI of the wrist and MCP joints. Artefacts related to the imaging process itself such as susceptibility, partial volume, chemical shift and movement artefacts can simulate erosive change if the observer is unaware of these pitfalls. Normal features can also cause confusion, for example, the interosseous ligaments at the wrist and the nutrient foramina of the carpal bones can simulate erosions [43]. Small erosive-like lesions occur in around 2% of metacarpal and wrist bones in normal subjects [44].

Articular ligaments attaching to the MCP joint recesses and carpal ligamentous attachments with adjacent synovial inflammation can mimic erosive change [43]. Erosions containing pannus can appear high signal on T2-weighted imaging, making differentiation from bone oedema difficult.

Slice thickness is another important consideration. A slice thickness of 3 mm or less is required to detect fine anatomical detail, but even then small erosions can be missed due to partial volume averaging. There is however a trade off as thinner slices makes reviewing the images more time consuming and the signal-to-noise ratio decreases [43].

Imaging of joints that have been altered anatomically by the disease process can be difficult to interpret. Subluxation at the MCP joints can make assessment of erosions at the metacarpal heads more difficult and gross deformity of the wrist can cause confusion in identifying the individual carpal bones.

A decreasing erosion count can be a potential pitfall when monitoring disease activity over time. For example a patient can have two erosions affecting a metacarpal head that enlarge and coalesce over the duration of a study. Despite disease progression the erosion count can decrease Fig. 3a and b.

Healing erosions is also problematic in erosion scoring. Erosion visualisation relies on increased signal in adjacent tissues on T2 or T1 post-gadolinium scans to highlight the eroded cortex or subchondral plate. Anti-inflammatory therapy can reduce synovitis and bone oedema and thus decrease erosion conspicuity. The erosion has not healed; it has just become harder to see.
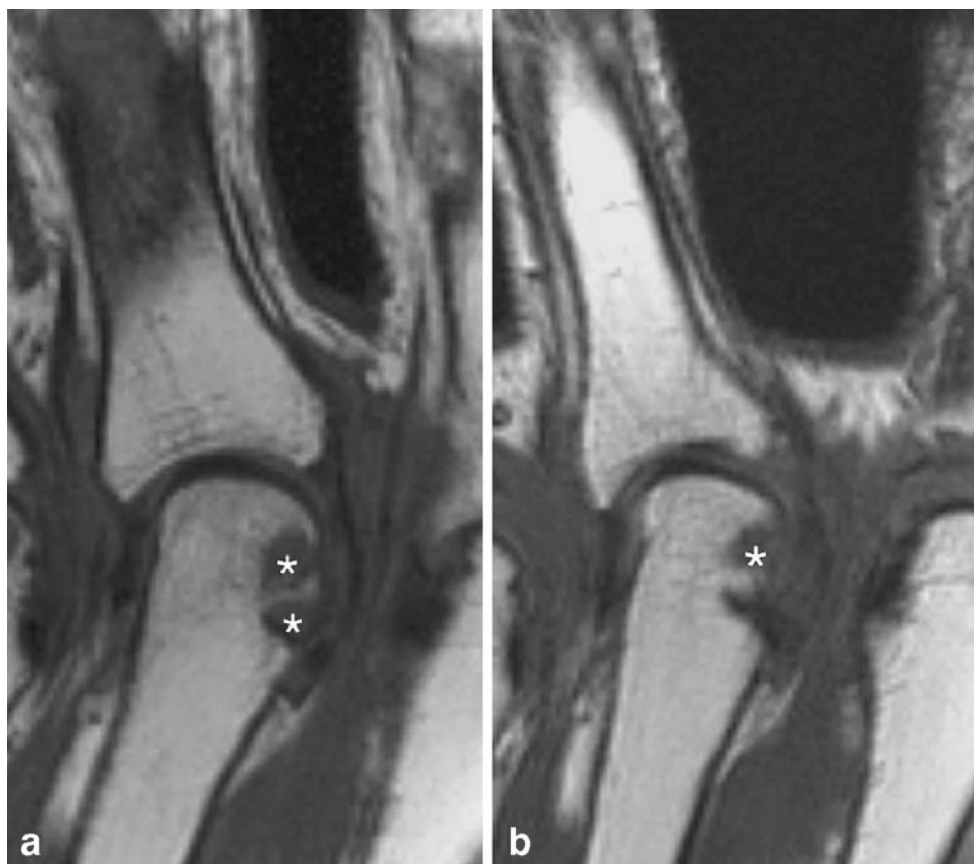
Ultrasound

The OMERACT definition of erosion on US is an intraarticular discontinuity of the bone surface that is visible in two perpendicular planes [45]. US scoring systems may be semiquantitative, representing the number and extent of erosions with a global score such as 0 to 3 or 4. Alternatively a quantative assessment allows grading of erosions according to size.

Ultrasound is at an earlier stage of development as an imaging outcome measure compared to MR. There is a paucity of validity data in terms of comparison with histology and MRI, although these data are increasing. There is one concurrent pathology validation [46] although this study was somewhat limited by the small numbers of patients examined. There are several concurrent validaton papers using MR as a comparator. The degree of validation conferred by MR varies widely between studies. A mixture of high- and low-field MR has been used, while the majority of studies have a single observer reading the MR. The proportion of ultrasounded joints scanned with MR also varies. The reader must be aware of the nature of the MR validation before accepting the quoted sensitivity and specificities. Reliability data are scarce particularly relating to intraobserver and intermachine reliability. Predictive evidence is also scarce with few longitudinal and blinded studies assessing responsiveness to therapies. There are few data available on the US appearance of normal joint structures [45].

US has been shown to be more sensitive than CR in detection of erosions [23, 47]. A comparison of US and CR in the detection of erosions in MCP joints found that US detected 6.6-fold more erosions than CR in early disease

and 3.4-fold more in late disease [23]. In this study MRI was used to validate the ultrasound diagnosis of an erosion, but only in a subset of the joints studied. The Cohen-kappa values for intra- and interobserver reliability of sonography were 0.75 and 0.76, respectively [23]. Another study that found that B-mode US detected 20% more lesions than did CR supports these findings and the lesions correlated with cumulative scores for clinical joint inflammation [47]. A further study of 150 small joints and 2 observers (muscu-loskeletal radiologist and rheumatologist with limited US experience) reports an interreader ICC value of 0.78 for erosion detection (grade 0–3), which was better than those for US detection of synovitis [48].

The ability of US and MRI to detect bone erosions has been compared [49]. US detected more MCP joint erosions although no significant difference was observed in wrist joints. Ten controls underwent examination of the same joints by US and none showed bone erosions at US examination. The authors suggest that US is at least as sensitive as MRI in detecting bone erosions in MCP and wrist joints and that it is a useful diagnostic tool for early arthritis and may be utilized in the follow-up of patients with an established diagnosis of RA Fig. 4.

Issues such as the validity, reliability and responsiveness to change of US must be addressed. Further data regarding

important methodological and measurement issues must be obtained before US gains wider acceptance. There needs to be more stringent application of concurrent validation in ultrasound with blinded twin observer MR comparator studies that exclude equivocal findings. Interscanner and interscan variation requires assessment in future studies.

Ultrasound has a particular advantage over MRI in that an experienced observer can rapidly screen several joints
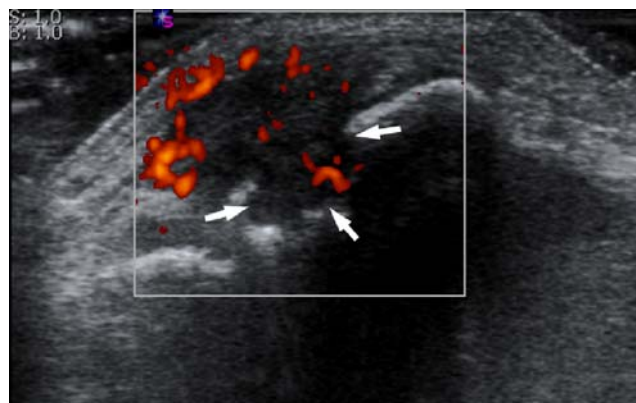
Fig. 4 Sagittal PD US of MCP joint demonstrates cortical break with erosion of the dosral aspect of the metacarpal head (arrows). Neovascular synovitis extends from the joint into the erosion

for erosions in a relatively short time frame. In our centre we would expect to use a 15-min appointment to review the wrist, MCP and PIP joints of the hand along with the MTP joints of the foot. The question of what experience is required to imply competence remains, and this is something that groups such as the British Society of Skeletal Radiology and the British Society of Rheumatology are currently addressing.

Computed tomography (CT)

CT provides multiplanar imaging with the radiographic advantages of good definition of bony anatomy especially with thin slice thickness; however fewer data are available regarding its sensitivity to determine erosions in RA.

Once again further studies assessing the validity, reliability and responsiveness of CT to change need to be undertaken.

A recent study compared CT with MR imaging of the wrist for detection of erosions in a group of 9 rheumatoid patients (135 sites) of similar disease duration [28]. Erosion scores derived from CT scans of the wrist were found to be significantly higher than erosion scores from MR scans of the same region. Lesions were identified by both modalities in 87% (117 sites) of cases, but there was a mismatch in the remaining 13%. Lesions were identified by CT and not MRI in 9%, mainly at the metacarpal bases, and by MRI and not CT in 4%. The authors suggest that partial volume artefacts on MR images and change in slice position account for most of the erosion mismatch. Interobserver reliability for CT and MR erosions was high (ICC 0.99 and 0.91, respectively).

Conclusion

Erosive rheumatoid disease occurs early, within the first 6 months of symptom onset, in patients with aggressive disease. This subgroup of patients needs to be targeted early with DMARDS to halt the progression of erosion, joint destruction and disability. Considering the available data on the increased sensitivity of bone erosion detection using MRI, CT and US in early disease it is inevitable that these modalities will play an increasingly important role in the routine clinical management of patients with diagnosed or suspected inflammatory joint diseases. MRI in particular has predictive value for future progressive damage and can help to tailor different therapeutic regimens.

This two part review has highlighted the role advanced imaging techniques are starting to play in imaging rheumatoid arthritis. However research validating their role needs to continue. To date many studies only utilise small numbers of subjects. Another common fault is the existence of observer bias with single observer studies being plentiful, and even where two observers are used, reading is often done by consensus. Reproducibility in terms of intraobserver and interobserver variation is often not addressed and when it is results are highly variable. Intermachine variability remains an unknown quantity. Studies have used a variety of ultrasound and MRI machines of different age and technical level. A particular example is the widespread use of both high and low field strength MRI scanners. While it may be clear in the original article that a low-field strength system has been used, it is not always clear from the ensuing review articles that then get accepted as dogma.

As can be seen from the bibliographies of this review, much of the literature, despite being radiological in nature, has appeared in the rheumatology journals. This means that papers with complex radiology may be peer reviewed by rheumatologists who despite an outstanding clinical knowledge may have a more limited understanding of issues relating to imaging. It is important that radiologists become more involved in this development process to ensure these modalities are able to reach their full potential in the field of rheumatological imaging.

References

1. Brower AC. Use of the radiograph to measure the course of rheumatoid arthritis. The gold standard versus fool's gold. Arthritis Rheum 1990;33:316–24.
2. Pierre-Jerome C, Bekkelund SI, Mellgren SI, et al. The rheumatoid wrist: bilateral MR analysis of the distribution of rheumatoid lesions in axial plan in a female population. Clin Rheumatol 1997;16:80–6.
3. van der Heijde DM. Joint erosions and patients with early rheumatoid arthritis. Br J Rheumatol 1995;34(Suppl 2):74–8.
4. van der Heijde DM, van Riel PL, van Leeuwen MA, et al. Prognostic factors for radiographic damage and physical disability in early rheumatoid arthritis. A prospective follow-up study of 147 patients. Br J Rheumatol 1992;31:519–25.
5. Korpela M, Laasonen L, Hannonen P, et al. Retardation of joint damage in patients with early rheumatoid arthritis by initial aggressive treatment with disease-modifying antirheumatic drugs: 5-year experience from the FIN-RACo study. Arthritis Rheum 2004;50:2072–81.
6. Tehranzadeh J, Ashikyan O, Dascalos J. Magnetic resonance imaging in early detection of rheumatoid arthritis. Semin Musculoskelet Radiol 2003;7:79–94.
7. Di Franco M, Spadaro A, Mauceri MT, et al. Relationship of rheumatoid factor isotype levels with joint lesions detected by magnetic resonance imaging in early rheumatoid arthritis. Rev Rhum Engl Ed 1999;66:251–5.
8. 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 4 months after symptom onset. Ann Rheum Dis 1998;57:350–6.
9. Taylor PC. VEGF and imaging of vessels in rheumatoid arthritis. Arthritis Res 2002;4(Suppl 3):S99–107.

10. Kirwan JR. The relationship between synovitis and erosions in rheumatoid arthritis. Br J Rheumatol 1997;36:225–8.

11. McQueen FM, Stewart N, Crabbe J, et al. Magnetic resonance imaging of the wrist in early rheumatoid arthritis reveals progression of erosions despite clinical improvement. Ann Rheum Dis 1999;58:156–63.

12. McQueen FM, Benton N, Perry D, et al. Bone edema scored on magnetic resonance imaging scans of the dominant carpus at presentation predicts radiographic joint damage of the hands and feet 6 years later in patients with rheumatoid arthritis. Arthritis Rheum 2003;48:1814–27.

13. Lipsky PE, van der Heijde DM, St Clair EW, et al. Infliximab and methotrexate in the treatment of rheumatoid arthritis. Anti-Tumor Necrosis Factor Trial in Rheumatoid Arthritis with Concomitant Therapy Study Group. N Engl J Med 2000;343:1594–602.

14. Boers M, Kostense PJ, Verhoeven AC, et al. Inflammation and damage in an individual joint predict further damage in that joint in patients with early rheumatoid arthritis. Arthritis Rheum 2001;44:2242–6.

15. McGonagle D, Conaghan PG, 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.

16. Savnik A, Malmskov H, Thomsen HS, et al. Magnetic resonance imaging of the wrist and finger joints in patients with inflammatory joint diseases. J Rheumatol 2001;28:2193–200.

17. Savnik A, Malmskov H, Thomsen HS, et al. MRI of the wrist and finger joints in inflammatory joint diseases at 1-year interval: MRI features to predict bone erosions. Eur Radiol 2002;12:1203–10.

18. Conaghan PG, O'Connor P, McGonagle D, et al. Elucidation of the relationship between synovitis and bone damage: a randomized magnetic resonance imaging study of individual joints in patients with early rheumatoid arthritis. Arthritis Rheum 2003;48:64–71.

19. Ostergaard M, Hansen M, Stoltenberg M, et al. Magnetic resonance imaging-determined synovial membrane volume as a marker of disease activity and a predictor of progressive joint destruction in the wrists of patients with rheumatoid arthritis. Arthritis Rheum 1999;42:918–29.

20. McQueen FM. Magnetic resonance imaging in early inflammatory arthritis: what is its role? Rheumatology (Oxford) 2000;39:700–6.

21. Lindegaard H, Vallo J, Horslev-Petersen K, et al. Low field dedicated magnetic resonance imaging in untreated rheumatoid arthritis of recent onset. Ann Rheum Dis 2001;60:770–6.

22. Sugimoto H, Takeda A, Hyodoh K. Early-stage rheumatoid arthritis: prospective study of the effectiveness of MR imaging for diagnosis. Radiology 2000;216:569–75.

23. Wakefield RJ, Gibbon WW, Conaghan PG, 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.

24. Alasaarela E, Suramo I, Tervonen O, et al. Evaluation of humeral head erosions in rheumatoid arthritis: a comparison of ultrasonography, magnetic resonance imaging, computed tomography and plain radiography. Br J Rheumatol 1998;37:1152–6.

25. Cimmino MA, Bountis C, Silvestri E, et al. An appraisal of magnetic resonance imaging of the wrist in rheumatoid arthritis. Semin Arthritis Rheum 2000;30:180–95.

26. Ostergaard M, Peterfy C, Conaghan P, et al. OMERACT rheumatoid arthritis magnetic resonance imaging studies. Core set of MRI acquisitions, joint pathology definitions, and the OMER-ACT RA-MRI scoring system. J Rheumatol 2003;30:1385–6.

27. Ostendorf B, Peters R, Dann P, et al. Magnetic resonance imaging and miniarthroscopy of metacarpophalangeal joints: sensitive detection of morphologic changes in rheumatoid arthritis. Arthritis Rheum 2001;44:2492–502.

28. Perry D, Stewart N, Benton N, et al. Detection of erosions in the rheumatoid hand; a comparative study of multidetector computerized tomography versus magnetic resonance scanning. J Rheumatol 2005;32:256–67.

29. McQueen F, Lassere M, Edmonds J, et al. OMERACT rheumatoid arthritis magnetic resonance imaging studies. Summary of OMERACT 6 MR Imaging Module. J Rheumatol 2003;30:1387–92.

30. 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 1991;30:101–6.

31. Jorgensen C, Cyteval C, Anaya JM, et al. Sensitivity of magnetic resonance imaging of the wrist in very early rheumatoid arthritis. Clin Exp Rheumatol 1993;11:163–8.

32. Ostergaard M, Gideon P, Sorensen K, et al. Scoring of synovial membrane hypertrophy and bone erosions by MR imaging in clinically active and inactive rheumatoid arthritis of the wrist. Scand J Rheumatol 1995;24:212–8.

33. Klarlund M, Ostergaard M, Gideon P, et al. Wrist and finger joint MR imaging in rheumatoid arthritis. Acta Radiol 1999;40:400–9.

34. Klarlund M, Ostergaard M, Jensen KE, et al. Magnetic resonance imaging, radiography, and scintigraphy of the finger joints: 1 year follow-up of patients with early arthritis. The TIRA Group. Ann Rheum Dis 2000;59:521–8.

35. McQueen FM, Benton N, Crabbe J, et al. What is the fate of erosions in early rheumatoid arthritis? Tracking individual lesions using x rays and magnetic resonance imaging over the first 2 years of disease. Ann Rheum Dis 2001;60:859–68.

36. McGonagle D, Gibbon W, O'Connor P, et al. Characteristic magnetic resonance imaging entheseal changes of knee synovitis in spondylarthropathy. Arthritis Rheum 1998;41:694–700.

37. Ostergaard M, Hansen M, Stoltenberg M, et al. New radiographic bone erosions in the wrists of patients with rheumatoid arthritis are detectable with magnetic resonance imaging a median of 2 years earlier. Arthritis Rheum 2003;48:2128–31.

38. Conaghan P, Lassere M, Ostergaard M, et al. OMERACT Rheumatoid Arthritis Magnetic Resonance Imaging Studies. Exercise 4: an international multicenter longitudinal study using the RA-MRI Score. J Rheumatol 2003;30:1376–9.

39. Lassere M, McQueen F, Ostergaard M, et al. OMERACT Rheumatoid Arthritis Magnetic Resonance Imaging Studies. Exercise 3: an international multicenter reliability study using the RA-MRI score. J Rheumatol 2003;30:1366–75.

40. Bird P, Lassere M, Shnier R, et al. Computerized measurement of magnetic resonance imaging erosion volumes in patients with rheumatoid arthritis: a comparison with existing magnetic resonance imaging scoring systems and standard clinical outcome measures. Arthritis Rheum 2003;48:614–24.

41. Ostergaard M, Stoltenberg M, Gideon P, et al. Changes in synovial membrane and joint effusion volumes after intraarticular methylprednisolone. Quantitative assessment of inflammatory and destructive changes in arthritis by MRI. J Rheumatol 1996;23:1151–61.

42. Bird P, Conaghan P, Ejbjerg B, et al. The development of the EULAR-OMERACT rheumatoid arthritis MRI reference image atlas. Ann Rheum Dis 2005;64(Suppl 1):i8–10.

43. McQueen F, Ostergaard M, Peterfy C, et al. Pitfalls in scoring MR images of rheumatoid arthritis wrist and metacarpophalangeal joints. Ann Rheum Dis 2005;64(Suppl 1):i48–55.

44. Ejbjerg B, Narvestad E, Rostrup E, et al. Magnetic resonance imaging of wrist and finger joints in healthy subjects occasionally shows changes resembling erosions and synovitis as seen in rheumatoid arthritis. Arthritis Rheum 2004;50:1097–106.

45. Wakefield RJ, Balint PV, Szkudlarek M, et al. Musculoskeletal ultrasound including definitions for ultrasonographic pathology. J Rheumatol 2005;32:2485–7.

46. Mc Gonagle D, Gibbon W, O'Connor P, et al. A preliminary study of ultrasound aspiration of bone erosion in early rheumatoid arthritis. Rheumatology (Oxford) 1999;38:329–31.

47. Weidekamm C, Koller M, Weber M, et al. Diagnostic value of high-resolution B-mode and Doppler sonography for imaging of hand and finger joints in rheumatoid arthritis. Arthritis Rheum 2003;48:325–33.

48. Szkudlarek M, Court-Payen M, Jacobsen S, et al. Interobserver agreement in ultrasonography of the finger and toe joints in rheumatoid arthritis. Arthritis Rheum 2003;48:955–62.

49. Magnani M, Salizzoni E, Mule R, et al. Ultrasonography detection of early bone erosions in the metacarpophalangeal joints of patients with rheumatoid arthritis. Clin Exp Rheumatol 2004;22:743–8.