Ultrasound imaging for the rheumatologist XIX. Imaging modalities in rheumatoid arthritis

G. Meenagh¹, E. Filippucci², A. Delle Sedie³, L. Riente³, A. Iagnocco⁴, C.A. Scirè⁵, C. Montecucco⁵, S. Bombardieri³, G. Valesini⁴, W. Grassi²

¹Antrim Hospital, Antrim, United Kingdom; ²Cattedra di Reumatologia, Università Politecnica delle Marche, Jesi, Italy; ³Unità Operativa di Reumatologia, Università di Pisa, Pisa, Italy; ⁴Cattedra di Reumatologia, Sapienza -Università di Roma, Roma, Italy; ⁵Cattedra di Reumatologia, IRCCS Policlinico S. Matteo, Università di Pavia, Pavia, Italy.

Please address correspondence to: Prof. Walter Grassi, Cattedra di Reumatologia, Università Politecnica delle Marche, Ospedale "A. Murri", Via dei Colli 52,

60035 Jesi (AN), Italy. E-mail: walter.grassi@univpm.it

Received and accepted on February 4, 2009.

Clin Exp Rheumatol 2009; 27: 3-6. © Copyright CLINICAL AND EXPERIMENTAL RHEUMATOLOGY 2009.

Key words: Rheumatoid arthritis, x-ray, computerised tomography, ultrasonography, magnetic resonance imaging.

Competing interests: none declared.

Abstract

The field of inflammatory arthritis owes much to the advances in imaging technology which have enlightened not only clinical specialists but also researchers worldwide. The most exciting developments in recent decades have centred upon rheumatoid arthritis (RA) and more specifically the ultrasound (US) and magnetic resonance imaging (MRI) findings at various stages of the natural history of this condition. Investigation of RA using the standard techniques of plain radiography (x-ray) and more sophisticated computerised tomography (CT) have now been superseded by the exponential growth of use of US and MRI and this has been born out by the profusion of scientific papers published on these subjects.

This paper aims to review the array of imaging modalities available as investigative tools to the rheumatologist when presented with various clinical scenarios by patients with RA.

Introduction

The field of inflammatory arthritis owes much to the advances in imaging technology which have enlightened not only clinical specialists but also researchers worldwide. The most exciting developments in recent decades have centred upon rheumatoid arthritis (RA) and more specifically the ultrasound (US) and magnetic resonance imaging (MRI) findings at various stages of the natural history of this condition. Investigation of RA using the standard techniques of plain radiography (x-ray) and more sophisticated computerised tomography (CT) have now been superseded by the exponential growth of use of US and MRI and this has been born out by the profusion of scientific papers published on these subjects.

The necessary elements which any imaging tool must possess to be considered a robust method of investigation in RA include: low cost, minimal risk to patient safety, reproducibility and sensitivity to change longitudinally. This paper aims to review the array of imaging modalities available as investigative tools to the rheumatologist when presented with various clinical

Plain radiography

scenarios by patients with RA.

X-ray investigation in RA can document a wide range of changes according to the stage of the illness and the degree of severity. In the hands the pattern of involvement includes the metacarpo-phalangeal (MCP), proximal inter-phalangeal (PIP) and carpal joints. In the early stages, the plain xray findings can be subtle and include soft tissue shadowing around inflamed joints particularly in the hands and feet. Juxta-articular osteopenia may be seen as the inflammatory process progresses, indicative of a hypermetabolic state in the region joint inflammation (1, 2). Often this is followed by loss of joint space linked with focal eburnation of articular cartilage. One of the hallmark features of RA, bone erosion, is a pathognomonic radiographic feature which heralds a poorer prognosis for the patient and functional impairment (3, 4). The presence of joint erosion in early RA is a strong indicator of persistence of an active inflammatory process and is a useful guide to the rheumatologist when treatment options are being considered. It has been demonstrated by several researchers that compared to other imaging modalities, e.g. US and MRI, x-ray is an insensitive tool for detection of erosion in the early stages of RA (5-8).

Imaging modalities in rheumatoid arthritis / G. Meenagh et al.

The advance of RA in any one patient may vary between joints and is often non-linear in any single joint (9). The condition also has well documented soft tissue involvement which is not well visualised by x-ray and contributes significantly to the clinical presentation at all stages of the disease (10). Whilst x-rays are standardly performed in all patients with newly diagnosed RA it would appear that the findings are unable to predict overall functional status (11). In later disease, however, the degree of bony involvement is more intimately linked with functional level and degree of disability.

To many clinicians, plain x-ray remains the sole method of charting progression of RA (12). X-ray has several advantages including relatively low cost, widespread availability and reproducibility. There are caveats to this imaging doctrine including the insensitivity to identification of erosion and the paucity of information gathered about soft tissue pathology. The majority of clinical trials in RA employ validated scoring methods all of which concentrate on the characteristic features of RA (13-15). These methods are predominantly used within the research arena as they tend to be impractical for everyday use in clinical practice.

Computerised tomography

Computerised tomography (CT) scanning is rarely used in clinical practice to image patients with RA. Its capabilities do extend however to the accurate detection of bony erosions in RA and it has been shown to be more sensitive than MRI by some investigators (16-20). Some studies in RA have used CT as a gold standard reference tool for bone erosion quantification when compared with other imaging modalities. It is not a sensitive method for demonstrating changes in soft tissues and is therefore inferior to both US and MRI (21). Currently the relatively limited access to musculoskeletal CT coupled with its inherent limitations relating to soft tissue pathology, renders this particular mode of imaging an improbable candidate for further clinical use in RA.

Magnetic resonance imaging

The merits of using magnetic resonance imaging (MRI) in RA have been widely documented in the literature. It not only clearly demonstrates soft tissue changes within synovium and surrounding tissue but also erosive bony changes. There is excellent correlation between histomorphic changes within inflamed joints in RA and the MRI findings (22, 23). In addition MRI can detect oedematous change within bone marrow which appears to herald incipient bone erosion and therefore it is an impressive modality for predicting outcome in RA (24).

MRI scanning in RA requires enhancement with intravenous gadolinium to demonstrate synovitis and therefore standardly a pre- and post- gadolinium enhancement T-weighted scan is performed together with a T2-weighted fat saturated sequence to permit accurate description of bone oedema and erosive change, if present. The Outcome Measures in Rheumatology (OMERACT) group have adopted MRI for an internationally validated semi-quantitative scoring system for bone changes in RA (RAMRIS) (25). This system has been shown to be sensitive to change at all stages of the disease particularly in relation to progression of erosive changes when compared to plain x-ray (26, 27). Several studies have investigated the prognostic potential of MRI in early RA. Whilst the earliest changes seen with MRI such as bone oedema and synovitis may not be specific to RA when compared to other inflammatory arthritides. Baseline findings on MRI appear to correlate well with the prevalence of erosions in both short term and longer term follow-up in RA (28-30). The field of MRI development is certainly not a static environment and

tainly not a static environment and several innovations have recently been suggested which will impact favourably on patients with RA including newer contrast agents which will concentrate within the synovium for longer periods to allow multiple joint assessment to be performed in the same session and the use of total body MRI as a tool for targeting investigation at the most biologically active joints in RA (31, 32). In spite of the impressive qualities of MRI in imaging RA the method does have certain important drawbacks. These include limited access to scanners in some centres together with the cost and impracticalities of using it to be a feasible follow-up imaging tool in RA.

Ultrasound

Much has been written about the use of ultrasound (US) in RA in recent decades (33-35). Interest has gathered in momentum as rheumatologists have increasingly been introducing this modality into their daily routine clinical practice as a tool to diagnose, aid therapeutic intervention and monitor disease progression (36, 37). High frequency US provides many of the desirable qualities for an imaging tool in RA including accurate depiction of both soft tissue and bony changes at all stages of the disease process, dynamic capabilities, lack of radiation exposure, reproducibility and relatively low cost. Opponents to the diffusion of US in the hands of rheumatologists themselves have made much of the steep ascent of the US skills learning curve and the anatomical barriers which exist within some joints limiting its use.

US is able to detect a panoply of morphostructural changes in RA. These include inflammation of synovial tissue within joints and adjacent peri-articular structures using both grey scale and power Doppler modes (38-40). Bone erosion in RA is well visualised, even at microscopic level (<1mm diameter). US performs better than plain x-ray in its yield of erosions but appears to be slightly less sensitive than MRI in this respect (41-43). No currently validated system for assessing joints in RA exists although several have been suggested by various investigators. A systematic approach is most often adopted and tailored to the examination of the joints which are symptomatic and those which are most commonly targeted by RA.

Currently, there are limited longitudinal data available concerning the link between baseline US findings in patients with RA and subsequent functional outcomes. In short term follow-up studies, however, there would appear

Imaging modalities in rheumatoid arthritis / G. Meenagh et al.

IMAGING

to be a correlation between the degree of synovial inflammation as documented by grey scale/ power Doppler and subsequent disease activity and radiographic change (44, 45, 48, 49). It has been reported that low grade, subclinical synovitis can be detected in RA patients whose disease activity score (DAS) indicates clinical remission.

Several investigators have employed US as a therapeutic monitoring tool in RA (46-48). These studies have concentrated both on local joint injection therapies and more latterly with systemic immunosuppressive therapy including biologic agents. Results have been variable but do suggest that US may become a valuable method of monitoring RA. Its role in influencing management decisions by the rheumatologist has yet to be investigated.

The role of US in RA is now well embedded in routine rheumatological practice and likely to benefit further from the advances which are continually emerging within the realms of US technology. The advent of three-dimensional (3D) US promises to deliver solutions to the lengthy practical skills acquisition process necessary to perform conventional US (50). The most recent development in US is termed 'Fusion Imaging' (combining US imagery with MRI or CT contemporaneously) which improves diagnostic accuracy by generating imagery which expands on the individual accuracy of each modality (32).

The future of imaging in RA appears bright and likely to continue to guide rheumatological management of this debilitating form of arthritis.

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.
- WATT I: Basic differential diagnosis of arthritis. European Radiology 1997; 7: 344-51
- KAARELA K: Prognostic factors and diagnostic criteria in early rheumatoid arthritis. *Scand J Rheumatol Supp* 1985; 14: 1-54.
- 4. ØDEGÅRD S, LANDEWE R, VAN DER HEIJDE D *et al.*: Association of early radiographic damage with impaired physical function in rheumatoid arthritis: a ten-year, longitudinal observational study in 238 patients. *Arthritis Rheum* 2006; 54: 68-75.
- BACKHAUS M, KAMRADT T, SANDROCK D et al.: Arthritis of the finger joints. A comprehensive approach comparing conventional

radiography, scintigraphy, ultrasound, and contrast-enhanced magnetic resonance imaging. *Arthritis Rheum* 1999; 42: 1232-45.

- 6. SCHEEL AK, HERMANN KG, OHRNDORF S *et al.*: Prospective 7 year follow up imaging study comparing radiography, ultrasonography, and magnetic resonance imaging in rheumatoid arthritis finger joints. *Ann Rheum Dis* 2006; 65: 595-600.
- SZDUDLAREK M, KLARLUND M, NARVES-TAD E et al.: Ultrasonography of the metacarpophalangeal and proximal interphalangeal joints in rheumatoid arthritis: a comparison with magnetic resonance imaging, conventional radiography and clinical examination. *Arthritis Res Ther* 2006; 8: R52.
- GRASSI W, FILIPPUCCI E, FARINAA, SALAFFI F, CERVINI C: Ultrasonography in the evaluation of bone erosions. *Ann Rheum Dis* 2001; 60: 98-103.
- SOMMER OJ, KLADOSEK A, WEILER V, CZEMBIREK H, BOECK M, STISKAL M: Rheumatoid arthritis: a practical guide to state-of-the-art imaging, image interpretation, and clinical implications. *Radiographics* 2005; 25:381-98.
- FILIPPUCCI E, IAGNOCCO A, MEENAGH G et al.: Ultrasound imaging for the rheumatologist VII. Ultrasound imaging in rheumatoid arthritis. Clin Exp Rheumatol 2007; 25: 5-10.
- PAULUS HE, OH M, SHARP JT *et al.*: Correlation of single time-point damage scores with observed progression of radiographic damage during the first 6 years of rheumatoid arthritis. *J Rheumatol* 2003; 30: 705-13.
- 12. ØSTERGAARD M, PEDERSEN SJ, DØHN UM: Imaging in rheumatoid arthritis-status and recent advances for magnetic resonance imaging, ultrasonography, computed tomography and conventional radiography. *Best Pract Res Clin Rheumatol* 2008; 22: 1019-44.
- 13. SHARP JT, YOUNG DY, BLUHM GB et al.: How many joints in the hands and wrists should be included in a score of radiologic abnormalities used to assess rheumatoid arthritis? Arthritis Rheum 1985; 28: 1326-35.
- LARSEN A, DALE K & EEK M: Radiographic evaluation of rheumatoid arthritis and related conditions by standard reference films. *Acta Radiol: Diagnosis* 1977; 18: 481-91.
- 15. VAN DER HEIJDE D: Quantification of radiological damage in inflammatory arthritis: rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis. *Best Pract Res Clin Rheumatol* 2004; 18: 847-60.
- 16. DØHN UM, EJBJERG BJ, COURT-PAYEN et al.: Are bone erosions detected by magnetic resonance imaging and ultrasonography true erosions? A comparison with computed tomography in rheumatoid arthritis metacarpophalangeal joints. Arthritis Res Ther 2006; 8: R110.
- 17. 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.
- YAO L, MAGALNICK M, WILSON M et al.: Periarticular bone findings in rheumatoid arthritis: T2-weighted versus contrast-enhanced T1-weighted MRI. AJR 2006; 187: 358-63.

- DØHN UM, EJBJERG BJ, HASSELQUIST M et al.: Rheumatoid arthritis bone erosion volumes on CT and MRI: reliability and correlations with erosion scores on CT, MRI and radiography. Ann Rheum Dis 2007; 66: 1388-92.
- 20. DØHN UM, EJBJERG BJ, HASSELQUIST M et al.: Detection of bone erosions in rheumatoid arthritis wrist joints with magnetic resonance imaging, computed tomography and radiography. Arthritis Res Ther 2008; 10: R25.
- 21. ALASAARELA E, SURAMO I, TERVONEN O et al.: Evaluation of humoral head erosions in rheumatoid arthitis: a comparison of ultrasonography, magnetic resonance imaging, computed tomography and plain radiography. Br J Rheumatol 1998; 37: 1152-6.
- 22. KONIG H, SIEPER J, WOLF KJ: Rheumatoid arthritis: evaluation of hypervascular and fibrous pannus with dynamic MR imaging enhanced with gd-DTPA. *Radiology* 1990; 176: 473-7.
- 23. ØSTERGAARD M, STOLTENBERG M, LØV-GREEN-NIELSEN P et al.: Magnetic resonance imaging-determined synovial membrane and joint effusion volumes in rheumatoid arthritis and osteoarthritis: comparison with the macroscopic and microscopic appearance of the synovium. Arthritis Rheum 1997; 40: 1856-67.
- 24. JIMENEZ-BOJ E, NOBAUER-HUHMANN I, HANSLIK-SCHNABEL B et al.: Bone erosions and bone marrow edema as defined by magnetic resonance imaging reflect true bone marrow inflammation in rheumatoid arthritis. Arthritis Rheum 2007; 56: 1118-24.
- 25. ØSTERGAARD M, PETERFY C, CONAGHAN P et al.: OMERACT Rheumatoid Arthritis Magnetic Resonance Imaging Studies. Core set of MRI acquisitions, joint pathology definitions, and the OMERACT RAMRI scoring system. J Rheumatol 2003; 30: 1385-6.
- 26. DØHN UM, SKJØDT H, HETLAND ML et al.: No erosive progression revealed by MRI in rheumatoid arthritis patients treated with etanercept, even in patients with persistent MRI and clinical signs of joint inflammation. *Clin Rheumatol* 2007; 26: 1857-61.
- 27. LISBONA MP, MAYMO J, PERICH J et al.: Etanercept reduces synovitis as measured by magnetic resonance imaging in patients with active rheumatoid arthritis after only 6 weeks. J Rheumatol 2008; 35: 394-7.
- 28. QUINN MA, CONAGHAN PG, O'CONNOR PJ et al.: Very early treatment with infliximab in addition to methotrexate in early, poor-prognosis rheumatoid arthritis reduces magnetic resonance imaging evidence of synovitis and damage, with sustained benefit after infliximab withdrawal: results from a twelvemonth randomized, double-blind, placebocontrolled trial. Arthritis Rheum 2005; 52: 27-35.
- 29. JARRETT SJ, CONAGHAN PG, SLOAN VS *et al.*: Preliminary evidence for a structural benefit of the new bisphosphonate zoledronic acid in early rheumatoid arthritis. *Arthritis Rheum* 2006; 54: 1410-4.
- 30. DUREZ P, MALGHEM J, NZEUSSEU TA et al.: Treatment of early rheumatoid arthritis: a randomized magnetic resonance imaging study comparing the effects of methotrex-

IMAGING

ate alone, methotrexate in combination with infliximab, and methotrexate in combination with intravenous pulse methylprednisolone. *Arthritis Rheum* 2007; 56: 3919-27.

- CIMMINO MA, GRASSI W, CUTOLO M: Modern imaging techniques: a revolution for rheumatology practice. *Best Pract Res Clin Rheumatol* 2008; 22: 951-9.
- 32. CIMMINO MA, GRASSI W: What is new in ultrasound and magnetic resonance imaging for musculoskeletal disorders? *Best Pract Res Clin Rheumatol* 2008; 22: 1141-8.
- 33. EMERY P: Treatment of rheumatoid arthritis. *BMJ* 2006; 332: 152-5.
- 34. SMOLEN JS, ALETAHA D: Challenges of predicting treatment response in patients with rheumatoid arthritis. *Nat Clin Pract Rheumatol* 2005: 1: 62-3.
- WELLS G, BOERS M, TUGWELL P: Low disease activity state in rheumatoid arthritis: concepts and derivation of minimal disease activity. *Clin Exp Rheumatol* 2006; 24: S052-9.
- TAGGART A, FILIPPUCCI E, WRIGHT G et al.: Musculoskeletal ultrasound training in rheumatology: the Belfast experience. *Rheuma*tology 2006; 45: 102-5.
- MEENAGH G, FILIPPUCCI E, KANE D, TAG-GART A, GRASSI W: Ultrasonography in rheumatology: developing its potential in clinical practice and research. *Rheumatology* 2007: 6: 3-5.
- 38. GRASSI W, CERVINI C: Ultrasonography in rheumatology: an evolving technique. Ann

Imaging modalities in rheumatoid arthritis / G. Meenagh et al.

Rheum Dis 1998; 57: 268-71.

- NEWMAN JS, LAING TJ, MCCARTHY TJ et al.: Power Doppler sonography of synovitis: assessment of therapeutic response – preliminary observations. *Radiology* 1996; 198: 582-4.
- 40. SZKUDLAREK M, COURT-PAYEN, STRAND-BERG C et al.: 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: 2018-23.
- 41. WAKEFIELD RJ, GIBBON WW, CONAGHAN PG *et al.*: The value of sonography in the detection of bone erosions in patients with rheumatoid arthritis. *Arthritis Rheum* 2000; 43: 2762-70.
- 42. ALARCON GS, LOPEZ-BEN R, MORELAND LW: High-resolution ultrasound for the study of target joints in rheumatoid arthritis. *Arthritis Rheum* 2002; 46: 1969-70.
- 43. HOVING JL, BUCHBINDER R, HALL S et al.: A comparison of magnetic resonance imaging, sonography, and radiography of the hand in patients with early rheumatoid arthritis. *J Rheumatol* 2004; 31: 663-75.
- 44. BACKHAUS M, BURMESTER GR, SANDROCK D et al.: Prospective two year follow up study comparing novel and conventional imaging procedures in patients with arthritic finger joints. Ann Rheum Dis 2002; 61: 895-904.
- 45. SCHEEL AK, HERMANN KG, OHRNDORF S

et al.: Prospective 7 year follow up imaging study comparing radiography, ultrasonography, and magnetic resonance imaging in rheumatoid arthritis finger joints. *Ann Rheum Dis* 2006; 65: 595-600.

- 46. IAGNOCCO A, PERELLA C, NAREDO E et al.: Etanercept in the treatment of rheumatoid arthritis: clinical follow-up over one year by ultrasonography. *Clin Rheumatol* 2008; 27: 491-6.
- IAGNOCCO A, FILIPPUCCI E, PERELLA C et al.: Clinical and ultrasonographic monitoring of response to adalimumab treatment in rheumatoid arthritis. J Rheumatol 2008; 35: 35-40.
- 48. NAREDO E, COLLADO P, CRUZ A et al.: Longitudinal power Doppler ultrasonographic assessment of joint inflammatory activity in early rheumatoid arthritis: predictive value in disease activity and radiologic progression. Arthritis Rheum 2007; 57: 116-24.
- 49. TAYLOR PC, STEUER A, GRUBER J et al.: Comparison of ultrasonographic assessment of synovitis and joint vascularity with radiographic evaluation in a randomized, placebo-controlled study of infliximab therapy in early rheumatoid arthritis. Arthritis Rheum 2004; 50: 1107-16.
- 50. MEENAGH G, FILIPPUCCI E, ABBATTISTA T, BUSILACCHI P, GRASSI W: Three-dimensional power Doppler sonography in short-term therapy monitoring of rheumatoid synovitis. *Rheumatology* 2007; 46: 1736.