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Horizon Scanning Technology Prioritising Summary

MRI for diagnosis of rheumatoid arthritis

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AHTA

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PRIORITISING SUMMARY (UPDATE 2009)

REGISTER ID:	**000356**
NAME OF TECHNOLOGY:	**MRI FOR DIAGNOSIS OF RHEUMATOID ARTHRITIS**
PURPOSE AND TARGET GROUP:	**PATIENTS WITH EARLY RHEUMATOID ARTHRITIS**

2009 SAFETY AND EFFECTIVENESS ISSUES

Since the original prioritising summary was published, there have been seven studies investigating magnetic resonance imaging (MRI) for diagnosis of rheumatoid arthritis (RA).

Two studies were identified which compared MRI against conventional radiography (CR), using computed tomography (CT) as the reference standard. One study assessed the performance of MRI and CR for detection of wrist joint bone erosions in a total of 315 wrist bones from 17 RA patients and four controls. Erosions were measured independently by CT, MRI and CR through medical imaging software and were scored according to the Outcome Measure in Rheumatology (OMERACT) Rheumatoid Arthritis MRI Scoring System (RAMRIS)[1] (for CT and MRI images) or Sharp/van der Heijde scoring method[2] (for CR images). It was reported that MRI offered superior sensitivity and accuracy in identifying bone erosions, when compared with CR (sensitivity: 61% vs 24%; accuracy: 77% vs 63%); whilst the specificity of MRI was not as good as that of CR (93% vs 99%). The intra-modality agreements of erosion volume measurements were high for both CT (CT reading A vs CT reading B: ρ=0.92, p<0.01) and MRI (MRI reading A vs MRI reading B: ρ=0.90, p<0.01). The volumes and OMERACT-RAMRIS scores of individual erosions were correlated for both MRI (ρ= 0.99, p<0.01) and CT (ρ= 0.96, p<0.01); and the correlations between persons' total erosion volume and total erosion score for MRI and CT were 0.80 and 0.83, respectively. The author also reported that participants' total Sharp/van der Heijde erosion score on CR was associated with total OMERACT-RAMRIS score on MRI (ρ= 0.66, p<0.01). However, the CR erosion scores of individual bones and their corresponding MRI scores were not correlated (ρ=0.10, p=0.11) (Døhn et al (2008) (level III-2 diagnostic evidence).

[1] The Outcome Measure in Rheumatology Rheumatoid Arthritis MRI Scoring System is a semi-quantitative scoring system where each bone erosion is assigned a score ranging from 0 to 10, based on the percentage (in increments of 10%) of the bone volume eroded: 0: 0%; 1: 1-10%; 2: 11-20%, etc. (Østergaard et al 2003).

[2] According to the Sharp/van der Heijde score method, erosions are scored as follows: 0: no erosion; 1: discrete erosion; 2: large erosion not extending over the mid-line of the bone; 3: large erosion extending over the mid-line; and the sum of above scores (with a maximum of 5), if more than one erosion in a bone (van der Heijde 2000).

The study by Duer-Jensen assessed two MRI machines, the Esaote Artoscan 0.2 T (Artoscan) and the MagneVu MV 1000 0.2 T (MagneVu), for identifying bone erosions in RA metacarpophalangeal and wrist joints. CT was used as standard reference method. A total of 550 bones from 20 RA patients and 5 controls were examined. For both metacarpophalangeal and wrist joints, Artoscan had better sensitivity in detection of bone erosions than CR, with sensitivities of 68 per cent vs 57 per cent for metacarpophalangeal joint erosions and 50 per cent vs 29 per cent for wrist joint erosions; whereas MagneVu was not as sensitive as CR for revealing metacarpohalangeal joint erosions (54%) and wrist joint erosions (23%). Both Artoscan and MagneVu demonstrated good specificity for bone erosions (≥92%); however, neither of these two MRI units had superior specificity than CR. The overall accuracies for detecting metacarpohalangeal joint erosions were 90 per cent for Artoscan, 88 per cent for MagneVu, and 93 per cent for CR; the corresponding accuracies for wrist joint erosions were 75 per cent, 70 per cent, and 71 per cent, respectively (Duer-Jensen et al 2008) (level III-1 diagnostic evidence).

Another study evaluated MRI, CR and ultrasonography (US) in detection of bone erosions in 26 children with juvenile RA or juvenile idiopathic arthritis (JIA). Two independent readers assigned MRI scores (0-4), using a devised MRI scoring system[1]. Images from CR were scored according to the Sharp/van der Heijde scoring system as described previously. Of the three imaging examinations, MRI was the most sensitive method for identifying bone erosions. MRI identified erosive changes in 96 per cent of 26 JIA patients while both CR and US had sensitivities of 50 per cent. The ability of MRI in detecting bone erosions was significantly better than that of CR or US in the group of children with a JIA history of less than 3 years (p=0.002 for MRI vs CR; p=0.0002 for MRI vs US). It was reported that MRI scores and CR erosion scores were closely correlated (r=0.82). Good inter-observer agreement and intra-observer agreement were also observed, with inter-observer interclass correlation coefficient (ICC) of 0.97 and intra-observer ICCs of 0.97 and 0.79 for the two readers (Malattia et al 2008) (level III-2 diagnostic evidence).

MRI was compared to US in three studies. In the study by Weiss et al, the detection of temporomandibular joint arthritis was compared between MRI and US in a total of 32 children who were newly diagnosed with JIA. MRI was better than US for detecting temporomandibular joint arthritis in JIA patients. Acute temporomandibular joint arthritis was identified in 75 per cent and 0 per cent of JIA patients by MRI and US, respectively. Seventy-one per cent of those diagnosed as acute temporomandibular joint arthritis were asymptomatic. In addition, MRI detected more chronic temporomandibular joint arthritis than US in patients with new-diagnosed JIA (69%

[1] In the devised MRI scoring system, erosions are scored as follows: 0: no erosion; 1: 1-25% of bone eroded; 2: 26-50% of bone eroded; 3: 51-75% of bone eroded; 4: 76-100% of bone eroded (Malattia et al 2008).

vs 28%). More than half (53%) of JIA children had both acute and chronic temporomandibular joint arthritis revealed by MRI (Weiss et al 2008) (level III-2 diagnostic evidence).

In a study involving 32 RA patients, both synovitis diagnosed by MRI and synovitis detected by power Doppler US were graded (0-3) according to the RAMRIS semi-quantitative scale[1]. Power Doppler US was used as the reference standard. Grades 0-1 and 2-3 were grouped in calculating the percentage exact agreement (PEA) between MRI and US as well as the sensitivity and specificity of MRI. A moderate correlation was observed between MRI and Power Doppler US for detecting synovitis in RA patients, with PEA scores ranging from 52.9 to 72.6 per cent across different extremity joints. MRI was not a sensitive method for diagnosis of synovitis (sensitivity: 21.4-57.7%). However, the specificity of MRI was relatively high (71.4-83.3%) (Freeston et al 2008) (level III-2 diagnostic evidence).

MRI was used as the reference standard in Bruyn et al's study which assessed US in detecting shoulder pathology in five RA patients. Good overall agreement was reported between MRI and US for the presence/absence of humeral head erosions and complete cuff tear, with overall agreement of 79 per cent and 84 per cent, respectively. Agreement between MRI and US with regard to posterior recess synovitis (64%) and bicepts tenosynovitis (50%) was moderate. MRI did not correlate with US for identification of anterior recess synovitis (overall agreement: 31%) (Bruyn et al 2009) (level III-2 diagnostic evidence).

A recent study investigated the performance of MRI in differentiating metacarpophalangeal joint involvement between RA and psoriatic arthritis in a total of 20 patients (10 with RA and 10 with psoriatic arthritis). There were no significant differences in the total numbers (p=0.315) and the sizes (p=0.165) of erosions between RA group and psoriatic arthritis group on MRI. However, more synovitis and tenosyovitis were observed in patients with RA than those in psoriatic arthritis patients (both p<0.0001). Entheseal-related features, such as extracapsular soft tissue enhancement, on MRI were not significantly different between RA and psoriatic arthritis (p=1.000). The authors concluded that MRI might be of limited diagnostic utility for differentiating RA from psoriatic arthritis on the basis of metacarpophalangeal joint diseases (Marzo-Ortega et al 2009) (level III-3 diagnostic evidence).

None of the studies identified for this update reported any adverse or safety related events.

[1] According to the RAMRIS semi-quantitative scale, grade 0: no bone involvement; 1: grade 1: 1-33% of the original bone eroded; grade 2: 34-66% of the original bone eroded; grade 3: 67-100% of the original bone eroded (Østergaard 2005)

Five studies were included in the original prioritising summary.

2009 COST IMPACT

No cost information was found during update preparation.

2009 HEALTHPACT ACTION:

The use of MRI for the diagnosis of rheumatoid arthritis appears to be waning in the hospital environment. Although the monitoring of bone erosion may assess a patient's response to treatment, other clinical measures may be used. Therefore HealthPACT has recommended that further assessment of this technology is no longer warranted.

2009 NUMBER OF INCLUDED STUDIES

Total number of studies	
Level III-1 diagnostic evidence	1
Level III-2 diagnostic evidence	5
Level III-3 diagnostic evidence	1

2009 REFERENCES:

Bruyn, G. A., Naredo, E., et al. (2009). 'Reliability of ultrasonography in detecting shoulder disease in patients with rheumatoid arthritis', *Ann Rheum Dis,* 68 (3)**,** 357-61.

Døhn, U. M., Ejbjerg, B. J., et al. (2008). 'Detection of bone erosions in rheumatoid arthritis wrist joints with magnetic resonance imaging, computed tomography and radiography', *Arthritis Res Ther,* 10 (1)**,** R25.

Duer-Jensen, A., Ejbjerg, B., et al. (2008). 'Does low-field dedicated extremity MRI (E-MRI) reliably detect RA bone erosions? A comparison of two different E-MRI units and conventional radiography with high resolution CT', *Ann Rheum Dis*, in press.

Freeston, J. E., Brown, A. K., et al. (2008). 'Extremity magnetic resonance imaging assessment of synovitis (without contrast) in rheumatoid arthritis may be less accurate than power Doppler ultrasound', *Ann Rheum Dis,* 67 (9)**,** 1351.

Malattia, C., Damasio, M. B., et al. (2008). 'Magnetic resonance imaging, ultrasonography, and conventional radiography in the assessment of bone erosions in juvenile idiopathic arthritis', *Arthritis Rheum,* 59 (12)**,** 1764-72.

Marzo-Ortega, H., Tanner, S. F., et al. (2009). 'Magnetic resonance imaging in the assessment of metacarpophalangeal joint disease in early psoriatic and rheumatoid arthritis', *Scand J Rheumatol***,** 1-5.

Østergaard, M., Edmonds, J., et al. (2005). 'An introduction to the EULAR-OMERACT rheumatoid arthritis MRI reference image atlas ', *Ann Rheum Dis,* 64 (Suppl 1)**,** i3-7.

Østergaard, M., Peterfy, C., et al. (2003). 'OMERACT Rheumatoid Arthritis Magnetic Resonance Imaging Studies. Core set of MRI acquisitions, joint pathology definitions, and the OMERACT RA-MRI scoring system', *J Rheumatol,* 30 (6)**,** 1385-6.

van der Heijde, D. (2000). 'How to read radiographs according to the Sharp/van der Heijde method', *J Rheumatol,* 27 (1)**,** 261-3.

Weiss, P. F., Arabshahi, B., et al. (2008). 'High prevalence of temporomandibular joint arthritis at disease onset in children with juvenile idiopathic arthritis, as detected by magnetic resonance imaging but not by ultrasound', *Arthritis Rheum,* 58 (4)**,** 1189-96.

REGISTER ID: **000356**

NAME OF TECHNOLOGY: **MRI FOR THE DIAGNOSIS OF RHEUMATOID ARTHRITIS (2008)**

PURPOSE AND TARGET GROUP: **PATIENTS WITH EARLY RHEUMATOID ARTHRITIS**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

☒	Yet to emerge	☐	Established
☐	Experimental	☐	Established *but* changed indication or modification of technique
☐	Investigational	☐	Should be taken out of use
☐	Nearly established		

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

☒	Yes	Many MRI scanners are approved by the TGA. These could be used for RA diagnosis.
☐	No	
☐	Not applicable	

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
Denmark		✓	
New Zealand	✓		
Germany	✓		
USA		✓	
UK		✓	

IMPACT SUMMARY:

Clinics and hospitals equipped with MRI capabilities would provide early diagnosis of rheumatoid arthritis (RA). The advent of small office based MRI machines may provide a more accessible and cheaper mode of diagnosis and monitoring of RA patients. Diagnosis at an early stage may allow RA to be treated earlier and therefore minimise the degenerative effects of the disease. As the degenerative effects are often not reversible and cumulative, early detection of RA is a priority. Wider access to MRI would allow the monitoring of patients undergoing therapy. Based on this monitoring better clinical decisions could be made to maximise the delay before RA induced disability occurs.

BACKGROUND

Rheumatoid arthritis (RA) is a systemic inflammatory disease caused by the immune system inappropriately attacking the host tissue. The immune attack on joint tissue leads to the characteristic swollen, inflamed and painful joints. This eventually leads to degradation of the joints and hence lessened mobility and deformation of the joints. RA also affects other organs such as blood vessels, the skin, lungs, muscles and heart. There is evidence that major damage to the joints occurs in the early stage of the disease and, as this damage is irreversible and cumulative, its prevention should be a priority. Hence diagnosis at an early stage is important so that patients can be treated with existing therapies. Several drugs have been shown to be effective in preventing or reducing joint damage therefore limiting downstream symptoms such as loss of mobility and joint function. The long term effects of these drugs have not been fully elucidated and patient monitoring is necessary to determine the drug's effectiveness or adverse events caused by them. MRI is emerging as a tool to both diagnose patients who may have RA and monitor those who are diagnosed and placed on therapy.

CLINICAL NEED AND BURDEN OF DISEASE

Rheumatoid arthritis is a major disease burden in Australia. The prevalence of RA in Australia has been calculated to be 2.5 per cent of the population in 2007 based on (AE 2007). RA is Australia's most prevalent autoimmune disease and affects women more than men with an estimated 57.1 per cent of RA sufferers being women. The onset of RA generally occurs between 25-50 years of age and given the debilitating effects of RA, the loss of QALYs[1] and productivity is significant. There is a significant impact on the work ability of more than half of RA patients after 10 years of disease, this can be either reduction of working time or complete cessation of work due to disability (AE 2007). In 2007 an estimated $ 405 million was allocated to expenditure on RA in the Australian health care system. Of expenditure for all arthritic conditions, 3.5 and 16.1 per cent of hospital inpatient and outpatient expenditure, respectively, is attributable to RA.

DIFFUSION

No evidence of MRI being used in early diagnosis of RA was found in literature searches conducted for this summary.

COMPARATORS

The diagnosis of RA in its early stages is difficult due to the non-specific and variable symptoms. RA is diagnosed using several clinical and test based markers. For a definitive diagnosis of RA at least four of the seven conditions must be met from the following table (AIHW 2005).

[1] QALY = quality adjusted life year

Table 1 American College of Rheumatology rheumatoid arthritis diagnostic criteria

	Criteria	Comment
1	Morning stiffness	Duration > 1 hour; lasting > 6 weeks
2	Arthritis of at least 3 areas	Soft tissue swelling or exudation lasting > 6 weeks
3	Arthritis of hand joints	Wrist, metacarpophalangeal joints or proximal interphalangeal joints lasting > 6 weeks
4	Symmetrical arthritis	At least one area, lasting > 6 weeks
5	Rheumatoid nodules	As observed by a physician
6	Serum rheumatoid factor	As assessed by a method positive in less than 5% of control subjects
7	Radiographic changes	As seen on anteroposterior films of wrists and hands

Source: (AIHW 2005)

SAFETY AND EFFECTIVENESS ISSUES

MRI can be used to measure the extent of synovitis and bone erosion within the examined joint of the RA patient. The advantage of MRI over conventional X-ray based imaging is its ability to identify damage in the soft tissue, which is not easily visible in X-ray radiographs. The first study describing the use of MRI compared to conventional radiography (CR) reported erosions in 45 per cent of early RA patients, whereas CR was only sensitive enough to detect bone erosions in 15 per cent of patients. In this study 42 consecutively recruited patients were examined with both CR and MRI. All patients were in the early stages of RA with symptoms present for less than six months. A 1.5 Tesla scanner was used for the MRI diagnoses (McQueen, Stewart 1998) (Level III-2 diagnostic evidence).

Using computed tomography (CT) as the reference standard a small study involving 17 RA patients and 4 controls compared MRI, US and CR. The aim of the study was to investigate whether bone erosions visualised in MRI and US but not on CR were true erosions. For erosions detected by CT, MRI showed sensitivity, specificity and accuracy of 68, 96 and 98 per cent. The joints which did not show erosion in CR but did show erosion in MRI were found by CT to be truly eroded in 96 per cent of cases. As CT was the reference standard, soft tissue damage could not be compared (Dohn, Ejbjerg 2006) (Level III-2 diagnostic evidence).

Most MRI studies have used either 1.5 or 3.0 T MRI scanners. The availability, cost and size of these machines limits the applicability of MRI diagnosis of early RA. Consequently, several small, office based 0.2 T MRI scanners are now available and can be used for RA diagnosis. In a study of 17 RA patients the diagnostic capability of conventional 1.5 T MRI scanning was compared to 0.2 T analysis. A good to excellent (kappa 0.74 to 0.94) correlation for synovitis and erosions, was obtained

with both MRI scanners, while the agreement for tenosynovitis was moderate (kappa 0.51 to 0.65). While overall there was good agreement between the two MRI modalities the study was small in size and as such the results should be interpreted with caution (Schirmer, Scheel 2007) (Level III-2 diagnostic evidence).

Different strategies for MRI diagnosis of disease progression were investigated in a study which recruited 35 RA patients (median age 55 years: RA disease duration 5 years) and nine healthy controls. Two MRI approaches were used, one which evaluated many joints and the other which evaluated few joints. The results from these two strategies were compared to conventional radiography. Patients were given baseline tests and re-examined one year later. Both MRI approaches were found to be significantly better (25 patients with progression detected, $p < 0.001$) at detecting progression over one year compared to CR (9 patients with progression detected) (Ejbjerg, Vestergaard 2005) (Level III-2 diagnostic evidence).

A recent study compared conventional radiography (CR) and ultrasound (US) using MRI as the reference standard. The population consisted of 40 RA and 20 control patients (5 years median RA disease duration; median age 58). For the assessment of bone erosion, ultrasound had sensitivity, specificity and accuracy[1] of 59, 98, and 96 per cent respectively when compared to MRI. In the same comparison CR showed sensitivity, specificity and accuracy of 42, 99 and 95 per cent versus MRI. Soft tissue involvement was most accurately detected by MRI with the relative sensitivity, specificity and accuracy of US being 70, 78 and 76 per cent respectively. CR sensitivity, specificity and accuracy relative to MRI was 40, 85 and 72 per cent, respectively (Szkudlarek, Klarlund 2006) (Level III-2 diagnostic evidence).While this is not a direct measure of the effectiveness of MRI, the results clearly show that both CR and US are not as sensitive as MRI . Additionally, MRI was more effective at visualising soft tissue involvement.

None of the reports examined for this prioritising summary reported any adverse or safety related incidents.

In summary, most of the MRI diagnostic studies for RA have small patient populations, often lack any form of blinding or control groups, and long term follow up and patient outcomes are not investigated nor reported. Despite this, the evidence which is available shows that MRI appears to be the best available diagnostic technique for RA. Additionally MRI can be used to monitor patient disease progression. MRI has the advantage over X-ray based imaging in that it allows the visualisation of both bone and soft tissue, both of which are extensively involved in RA. Further large scale assessments of MRI are needed before definitive conclusions about its effectiveness can be drawn.

[1] Accuracy is the overall agreement in diagnosis when compared to MRI

COST IMPACT

No cost information was reported in the studies examined.

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified/raised in the sources examined.

OTHER ISSUES

No issues were identified/raised in the sources examined.

SUMMARY OF FINDINGS

Based on the limited evidence available MRI appears to be the best diagnostic test for diagnosis and progression monitoring of RA, especially in early stage RA patients where interventions stand the best chance of producing cost-effective outcomes. Other imaging techniques do not provide the same resolution (ultrasound) or do not image all of the appropriate tissues (CT and X-ray radiography).

HEALTHPACT ACTION:

With the increased use of TNFα inhibitors for the early treatment of rheumatoid arthritis, early diagnosis of this disease is desirable. Therefore HealthPACT have recommended that this technology be monitored in 12 months time. There is also considerable interest in the use of office-based 0.2-0.5 tesla MRI units for the diagnosis of bone and joint disease. Therefore HealthPACT have recommended that a Prioritising Summary be commissioned on this subject.

NUMBER OF INCLUDED STUDIES

Total number of studies	
Level III-2 diagnostic evidence	5

REFERENCES:

AE (2007). *Painful Realities: The economic impact of arthritis in Australia in 2007,* Access Economics for Arthritis Australia.

AIHW (2005). *Arthritis and musculoskeletal conditions in Australia 2005,* Australian Institute of Health and Welfare.

Dohn, U. M., Ejbjerg, B. J., et al. (2006). '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,* 8 (4)**,** R110.

Ejbjerg, B. J., Vestergaard, A., et al. (2005). 'The smallest detectable difference and sensitivity to change of magnetic resonance imaging and radiographic scoring of structural joint damage in rheumatoid arthritis finger, wrist, and toe joints: a comparison of the OMERACT rheumatoid arthritis magnetic resonance imaging score applied to different joint combinations and the Sharp/van der Heijde radiographic score', *Arthritis Rheum,* 52 (8)**,** 2300-6.

McQueen, F. M., Stewart, N., et al. (1998). '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,* 57 (6)**,** 350-6.

Schirmer, C., Scheel, A. K., et al. (2007). 'Diagnostic quality and scoring of synovitis, tenosynovitis and erosions in low-field MRI of patients with rheumatoid arthritis: a comparison with conventional MRI', *Ann Rheum Dis,* 66 (4)**,** 522-9.

Szkudlarek, M., Klarlund, M., et al. (2006). '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,* 8 (2)**,** R52.

SEARCH CRITERIA TO BE USED:

Arthritis, Rheumatoid/ diagnosis
Magnetic Resonance Imaging/standards