

# Imaging diagnosis of early rheumatoid arthritis

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## ABSTRACT

Early diagnosis of rheumatoid arthritis is essential for its proper management. Currently, the initial phase of rheumatoid arthritis is known to provide a window of therapeutic opportunity. Although the diagnosis is primarily clinical, the development and improvement of laboratory and imaging methods have contributed to earlier diagnosis and determination of procedures in early rheumatoid arthritis. In this article, the authors review the role of the major imaging methods used for assessing early rheumatoid arthritis, especially conventional radiography, ultrasonography, and magnetic resonance imaging.

**Keywords:** early rheumatoid arthritis, conventional radiography, ultrasonography, magnetic resonance imaging.

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## INTRODUCTION

Rheumatoid arthritis (RA) is a progressive systemic chronic inflammatory disease that affects primarily the synovial membrane and can lead to bone and cartilaginous destruction.<sup>1</sup> It is a frequent condition (1%–2% of the world population) that affects all ethnical groups.<sup>2</sup>

In the past years, the generalization of the concept of “initial” or “early” RA and the existence of a window of therapeutic opportunity – time during which the institution of adequate therapy for the disease would result in marked clinical improvement – have strengthened the notion that early diagnosis and treatment can modify the course of disease.<sup>3</sup>

Concomitantly, laboratory and imaging tests have been developed or refined, contributing to the earlier diagnosis and prognostication of initial RA; in addition, changes in the therapeutic approach of RA have been instituted, with the use of new classes of drugs.<sup>4</sup>

The diagnosis of RA is established considering the association of clinical findings, and neither a laboratory test, nor a histological finding, nor an imaging test alone can confirm it. When RA is fully

expressed with all its classic features, its recognition is simple. Its diagnosis in its early stage, however, is particularly difficult, because serological and radiological characteristics often lack.<sup>5</sup>

Although the identification of initial RA is primarily clinical, several complementary tests can be used to establish the diagnosis, make the differential diagnosis, determine prognosis, and follow disease up. This study is a brief review about the major imaging tests used for diagnosing and managing initial RA, especially conventional radiography, ultrasonography (US), and magnetic resonance imaging (MRI).

## IMAGING TESTS

Several imaging tests are used to assess RA, such as conventional radiology, US, bone scan, computed tomography (CT), MRI, and bone densitometry.<sup>6</sup>

Bone scan, despite having high sensitivity to detect conditions leading to increased metabolic activity, such as joint inflammation, has low specificity and spatial resolution. Although CT has high spatial resolution, its limited contrast resolution restricts its use for soft tissue assessment and does

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not allow the detection of medullary bone edema, reducing its use in early RA. Bone densitometry is the best method to detect bone mass loss, which is unspecific, but provides little additional information other than that; in addition, bone densitometry still lacks standardization for the specific finality of assessing disease activity.<sup>7</sup>

More recently, molecular imaging methods, such as positron emission tomography (PET/CT) and single photon emission computed tomography (SPECT), have been used to diagnose, characterize, and monitor the activity of inflammatory diseases, such as RA.<sup>7-9</sup> For example, (19)F-fluorodeoxyglucose PET/CT accurately detects inflammatory activity in large joints of patients with RA, and may be helpful for the early assessment of RA extent.<sup>7</sup> Although the real role of those new techniques in the investigation of RA has not been established, they hold great promise, and, in the future, may play a more critical role in the diagnosis and assessment of disease activity.<sup>8</sup>

Currently, the three imaging methods most used to assess RA, because of the longer time of use and the experience accumulated, are as follows: conventional radiography; US; and MRI.

### Radiography

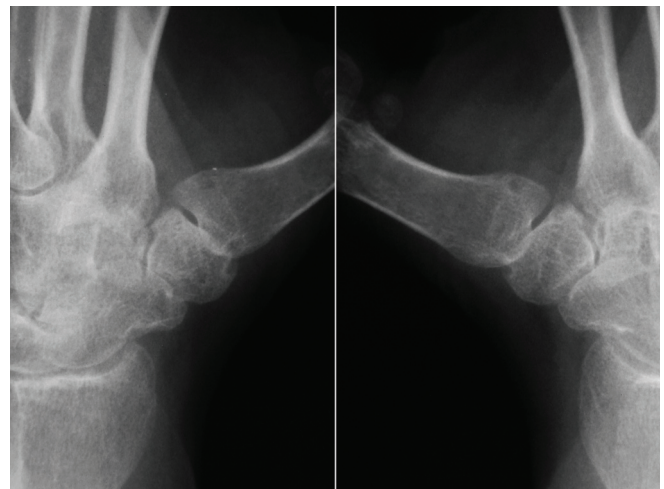
Conventional radiography (both in its analogical and digital forms) is still the imaging modality of choice in assessing RA, being indispensable for all patients already at their first medical consultation, because radiographic changes are part of the diagnostic criteria for RA.<sup>10</sup> In addition, the test is relatively inexpensive and almost universally available. However, the method is not sensitive to demonstrate the earliest changes of disease, mainly bone erosions; edema of the soft tissues and juxta-articular osteoporosis are some of the first radiographic findings (Figure 1). On radiography, the first sites affected are usually metacarpophalangeal joints (especially the second and third ones), metatarsophalangeal joints (especially the fifth), proximal interphalangeal joints, and ulnar and radial styloid processes.<sup>11</sup>

The most characteristic lesions appear later on radiography, and include narrowing of the joint space (due to cartilage destruction) and bone erosions (Figure 2). Patients with RA assessed with conventional radiography at an early stage of disease showed erosions as follows: on the first assessment, only 13%; after 12 months, 28%; after 24 months, 75%; and after 60 months of follow-up, 90%.<sup>12,13</sup>

In late stages, sequelae such as deformities, subluxations, and ankylosis can be observed. None of those changes is pathognomonic, but their presence, especially if symmetrical, in association with clinical findings strongly suggests disease. All patients should undergo a baseline initial radiography that



**Figure 1** Early rheumatoid arthritis (disease duration shorter than six months): radiograph, anteroposterior view, of the proximal portion of the right hand and wrist, revealing periarticular. Thickening of the soft tissues of the wrist is evident. Erosive joint disease still not identified.



**Figure 2** The patient is a 28-year-old female with symptoms compatible with rheumatoid arthritis for eight months. Plain radiograph, anteroposterior view, of the left hand and wrist showing characteristics of erosive rheumatoid arthritis in its early stage: small erosions in the carpometacarpal joints; minute erosions in the joint between the scaphoid and trapezium (left image); small erosion in the distal pole of the scaphoid (right image). The joint spaces are preserved, and neither deformities nor changes in bone alignment are observed.

allows radiographic follow-up, aiming at assessing disease progression and response to treatment.<sup>11</sup>

### Ultrasonography

US is an inexpensive exam that allows good assessment of soft tissues. The technique detects synovial thickening; presence of fluid in joints, bursae, and tendon sheaths; structural abnormalities of tendons, ligaments, and entheses; and superficial erosions.<sup>14,15</sup> However, it is examiner dependent, has low reproducibility, and has not been completely standardized to assess initial RA.<sup>16</sup> It does not allow assessing changes deeply located in the joints. In addition, the ultrasound beam does not penetrate bone, and, thus, bone assessment is restricted to the cortical surface and available acoustic windows. Techniques such Doppler can be useful in assessing disease activity, differentiating between active (*pannus*) and inactive inflammatory tissue. US may be useful to quantify disease progression and may monitor response to treatment in RA.<sup>17</sup> However, the quantification of inflammatory activity on US is yet to be standardized.<sup>15</sup>

### Magnetic resonance

Of the imaging techniques currently available, MRI is undoubtedly the most sensitive for detecting the changes of RA. It allows assessing all structures affected, such as soft tissues, bones and cartilages, and detecting early erosions (up to three years before conventional radiography). The pattern and site of the changes might have a prognostic implication.<sup>16</sup> The use of paramagnetic contrast agents (gadolinium compounds) is formally indicated in patients with RA, potentiating the detection of synovial thickening and anomalously enhanced areas, indicative of inflammatory activity in both soft tissues and bone; enhanced areas in medullary bone are seen even prior to the appearance of erosions and indicate increased risk for their development.<sup>16</sup>

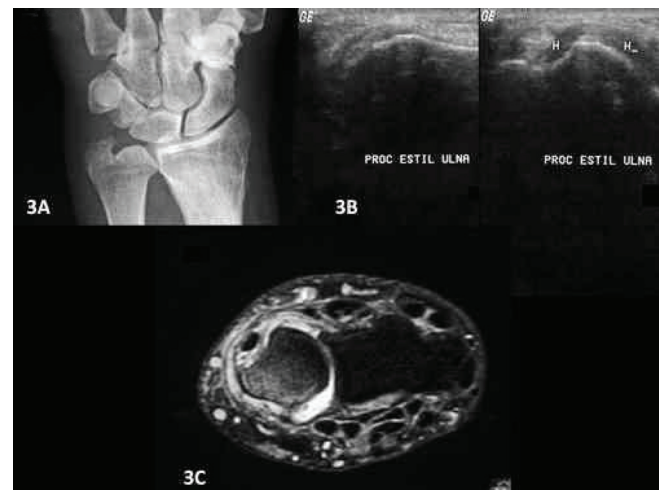
Erosions and the tenosynovial component of RA are also properly demonstrated on MRI, even with virtually normal radiographies. The CIMESTRA study has shown that the detection of bone edema on MRI in initial RA is the best predictor of radiographic progression of bone erosion after a two-year follow-up.<sup>18</sup> That result has been confirmed by a recent systematic review, which has suggested that performing MRI at an early stage of disease can be useful to increase its predictive value.<sup>19</sup>

In addition to its high cost and limited availability,<sup>20</sup> the disadvantages of MRI comprise the lack of method standardization and of a cutoff point for lesion definition (changes similar to erosions and synovitis have already been described in healthy individuals with no clinical evidence of RA). Moreover, sedation might be required for claustrophobic

patients; the position and the time required for the test might not be tolerated by elderly and/or debilitated patients, and some contraindications such as cardiac pacemaker holders or patients with ferromagnetic aneurysm clips still persist.<sup>21</sup>

Attempts to reduce the costs of MR include the use of new techniques. The isolated assessment of the fist of the dominant hand seems adequate to evaluate patients with initial RA, showing good sensitivity and specificity for the early detection of the typical changes of the disease.<sup>22</sup> A new technique proposed (modified “praying hands”) has proved to be, as compared with the traditional technique, equally sensitive to detect changes compatible with the early stage of disease, with a great advantage regarding the duration of the test. This would allow cost reduction and an increase in the number of exams performed in a certain time period.<sup>23</sup>

Figures 3 and 4 exemplify different imaging exams and their findings in patients with symptoms compatible with RA



**Figure 3**

(A) Radiograph of the right wrist showing gross erosions in the tip of the ulnar styloid process, marked osteoporosis in the neighboring medullary bone, and thickening of adjacent soft tissues. (B) Ultrasonography of the same wrist showing cortical irregularity of the tip of the ulnar styloid process, corresponding to the erosions seen on plain radiographs, and hypoechoogenicity (H) around the 5th and 6th extensor tendon compartments, due to rheumatoid tenosynovitis, which cannot be directly demonstrated on radiography. (C) Fat suppression T2-weighted axial view of the same patient. The erosions of the ulnar styloid process are due to severe extensor carpi ulnaris tenosynovitis, and synovial fluid and thickening are identified (darker linear structures amidst the fluid) distending its sheath; those findings, at a milder intensity, are also seen in other extensor compartments and alongside the flexor tendons. Fluid in the distal radioulnar joint and medullary bone edema of the ulnar epiphysis are also seen.



**Figure 4**

Plain radiograph (A) and fat suppression T2-weighted magnetic resonance imaging (B), coronal view, of the right wrist of a patient with a 10-month disease. The radiographic findings are still very subtle, consisting in regional soft tissue thickening, mild osteoporosis, and poorly defined radiolucency in carpal bones. The magnetic resonance imaging, however, is clearly abnormal, with significant joint effusion, extensive medullary bone edema (both showing as clearer areas on the dark background) and cortical bone erosions in the proximal and distal carpal rows (solutions of continuity filled with fluid and surrounded by bone edema).

for up to 12 months. Table 1 compares advantages and disadvantages of the major imaging tests used to assess initial RA.<sup>24</sup>

## CONCLUSIONS

The diagnosis of initial RA is primarily clinical, but several complementary tests can be used, such as imaging exams. Of the recent advances, MRI has gained increasing importance, showing high sensitivity at very early stages. In addition, methods, such as PET/CT and SPECT, have been used to diagnose, characterize and monitor the activity of inflammatory diseases such as RA.

On conventional radiography, erosions remain as the key measure for the structural outcome in initial RA, and their use has been recommended by a European committee of rheumatologists after a detailed review of all evidence available.<sup>25</sup>

Although plain radiographs remain essential for the initial assessment of patients with RA, several studies have suggested the use of ultrasonography and MRI as the imaging exams of choice for assessing early RA.<sup>26</sup> Enhanced MRI, in particular, is extremely sensitive, allowing the detection of areas of intraosseous inflammation before overt erosions develop. Technical refining of those methods is being studied and shows promising results. However, standardizing those methods in the context of rheumatoid disease, in addition to defining their real role in prognostication and assessment of response to treatment, are still required.

**Table 1**

Radiographic methods most frequently used for assessing early rheumatoid arthritis

Radiographic methods	Advantages	Disadvantages
<b>Conventional radiography</b>	<ul style="list-style-type: none"> <li>- Low cost</li> <li>- Wide availability and easy access</li> <li>- Standardization available</li> <li>- Easy reproducibility</li> <li>- Valid assessment methods</li> <li>- ACR criteria</li> <li>- Allows some differential diagnoses</li> </ul>	<ul style="list-style-type: none"> <li>- Two-dimensional representation of a three-dimensional lesion</li> <li>- Ionizing radiation</li> <li>- Relative insensitivity to early bone damage</li> <li>- Insufficient to assess soft tissues</li> </ul>
<b>Ultrasonography</b>	<ul style="list-style-type: none"> <li>- Non-invasive method</li> <li>- Relatively low cost</li> <li>- No ionizing radiation</li> <li>- Detection of inflammatory and destructive changes</li> <li>- Allows assessing several joints</li> <li>- Can guide diagnostic interventions, such as biopsies</li> <li>- Allows therapeutic procedures, such as infiltrations</li> <li>- In association with Doppler allows detecting synovitis</li> </ul>	<ul style="list-style-type: none"> <li>- Depends on the examiner</li> <li>- Difficult objective documentation</li> <li>- Low reproducibility</li> <li>- No standardization</li> <li>- Difficult visualization of some joints (wrists)</li> <li>- Questionable prognostic value</li> </ul>
<b>Magnetic resonance imaging</b>	<ul style="list-style-type: none"> <li>- Safe method</li> <li>- No ionizing radiation</li> <li>- High sensitivity</li> <li>- Assessment of all structures affected</li> <li>- Differential diagnosis of undifferentiated polyarthritis</li> <li>- Monitoring of therapeutic response</li> <li>- Complementation with contrast media and use of dynamic techniques</li> <li>- Detection of bone edema is an independent predictor of bone erosion</li> </ul>	<ul style="list-style-type: none"> <li>- High costs</li> <li>- Limited availability of the equipment</li> <li>- MRI exams require extended periods of time</li> <li>- Limited to one joint per exam</li> <li>- Correlation with clinical prognosis is still questionable</li> </ul>

ACR: American College of Rheumatology.



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