The sonographic identification of cortical bone interruptions in rheumatoid arthritis: a morphological approach

Edoardo Cipolletta* ⓘD, Gianluca Smerilli*, Andrea Di Matteo, Jacopo Di Battista, Marco Di Carlo, Walter Grassi and Emilio Filippucci

Abstract: Bone erosions are the hallmark of structural damage in rheumatoid arthritis (RA). Among imaging techniques, ultrasonography (US) has emerged as an accurate, reliable, repeatable, low-cost and non-invasive imaging modality to detect erosive changes in RA. However, small interruptions of the cortical bone detectable by last generation US equipment do not necessarily represent bone erosions. According to the available data, in addition to cortical bone interruption itself, only a few morphological US findings have been proposed to define RA bone erosions. However, other additional features may be considered to facilitate the interpretation of US cortical bone interruptions in RA. These could be summarised using the following four domains: size, site, shape and scenery. This hypothesis article provides a critical literature review of US features characteristic of RA bone erosions and pictorial evidence supporting the potential role of a morphological analysis in the US identification of bone erosions in RA patients.

Keywords: bone erosions, OMERACT, rheumatoid arthritis, structural damage, ultrasonography

Plain language summary

The ultrasonographic morphology of cortical interruptions is helpful for the identification of bone erosions in rheumatoid arthritis: the "four Ss" approach

- Bone erosions are characteristic features of rheumatoid arthritis. They are associated with a more aggressive disease and with irreversible physical disability.
- In recent years, ultrasonography has emerged as an accurate and reliable technique for the detection of bone erosions, that appear as interruptions of the cortical bone with variable size. However, cortical bone interruptions do not necessarily represent bone erosions. Since bone erosions represent the earliest evidence of the destructive behaviour of RA, their identification is crucial.
- Besides the cortical interruption itself, only a few morphological ultrasonographic features were proposed to characterise bone erosions in rheumatoid arthritis.
- We believe that a morphological approach, including size, site, shape and scenery, may be considered to facilitate the interpretation of ultrasonographic cortical bone interruptions in rheumatoid arthritis.
- In this hypothesis article we carried out a critical review of the scientific literature and provided extensive pictorial evidence of the ultrasonographic spectrum of cortical interruptions supporting the potential role of considering the "four Ss" for the ultrasonographic identification of bone erosions in rheumatoid arthritis.

Correspondence to:
Edoardo Cipolletta
Rheumatology Unit, Department of Clinical and Molecular Sciences, Polytechnic University of Marche, "Carlo Urbani" Hospital, Via Aldo Moro 25, Jesi, Ancona, 60035, Italy
edoardocipolletta@gmail. com

Gianluca Smerilli
Andrea Di Matteo
Jacopo Di Battista
Marco Di Carlo
Walter Grassi
Emilio Filippucci
Rheumatology Unit, Department of Clinical and Molecular Sciences, Polytechnic University of Marche, 'Carlo Urbani' Hospital, Jesi (Ancona), Italy

*These authors contributed equally

The relevance of bone erosions in rheumatoid arthritis

In patients with rheumatoid arthritis (RA), chronic synovitis leads to joint damage and irreversible physical disability.[1] Structural joint damage in RA affects both bone and cartilage, resulting in bone erosions and cartilage thinning.[2–5] Bone erosions are the hallmark of structural damage in RA and they can occur in the very early stage of the disease, affecting approximately half of untreated patients within 6 months after disease onset.[6–13] Since their first description, more than 60 years ago,[14] bone erosions have become a key feature in the diagnosis and prognosis of RA patients.[15,16] In fact, the European League Against Rheumatism (EULAR) allows the diagnosis of RA (erosive criterion)[15] when at least three separate joints show typical bone erosions on conventional radiography (CR) even without the fulfilment of the 2010 American College of Rheumatology (ACR)/EULAR classification criteria. Moreover, the updated 2019 EULAR recommendations for the management of RA suggest to add a biologic or a targeted-synthetic disease modifying anti-rheumatic drug (DMARD) when the treatment target is not achieved with the first-line conventional DMARD and in the presence of poor prognostic factors, such as bone erosions.[16] Furthermore, preventing the development and progression of bone erosions is one of the most important endpoints in randomised clinical trials in RA.[17]

Imaging techniques in the detection of bone erosions in RA

Currently, CR remains the reference imaging tool for the detection of joint damage in RA.[18,19] In fact, according to the EULAR recommendations for the use of imaging of the joints in the clinical management of RA, CR should be used as the first-line imaging tool for the identification of joint damage (i.e. bone erosions and joint space narrowing).[20] However, the sensitivity of CR in the identification of bone erosions is lower compared with other imaging techniques such as magnetic resonance imaging (MRI),[21–23] ultrasonography (US)[24–29] and computed tomography (CT),[22,23,28,30] especially in the early phase of the disease. These techniques have generated new opportunities and challenges in the interpretation of cortical bone discontinuities. In particular, US has emerged as an accurate, reliable, repeatable and low-cost imaging modality to detect erosive changes in RA, widely accepted by patients due to its safety and non-invasive profile.[31–33] The US identification of bone erosions is noteworthy. In fact, US-detected bone erosions predict the development of RA in both undifferentiated arthritis and anti-cyclic citrullinated peptide (CCP) positive at-risk individuals,[8,11,34] and the radiographic progression of structural damage in RA patients.[21,35] In contrast, a recent study has demonstrated that CR-detected bone erosions are uncommon and do not predict the development of RA in 'at-risk' individuals with positive anti-CCP antibodies.[36] The results of these studies suggest that US may represent the optimal imaging technique in the assessment of bone erosions in RA.

Limits of the current sonographic definition of bone erosion

Small interruptions of the cortical bone detectable by last generation US equipment, which would fulfil the Outcome Measure in Rheumatology (OMERACT) definition (intra-articular discontinuity of the bone surface that is visible in two perpendicular planes),[37] do not necessarily represent bone erosions. In fact, several imaging studies have documented different mimickers of bone erosions (pseudo-erosions) including physiological cortical vascular channels and cortical irregularities (osteophytes, cortical bone notches and subcortical bone cysts).[26,28,29,37–41] Pseudo-erosions may satisfy the OMERACT US definition of bone erosion, reducing the specificity of US in the assessment of bone erosions,[25,26,28,29] particularly when cortical defects are smaller than 2 mm. In fact, the prevalence of the OMERACT-defined bone erosions at metacarpophalangeal (MCP) and metatarsophalangeal (MTP) joints ranges from 0% to 18% of healthy subjects,[42–44] and increases with age.[45]

Since bone erosions represent the earliest evidence of the destructive behaviour of RA, the differentiation between bone erosions and pseudo-erosions has relevant implications, because false-positive results would lead to an overestimation of structural damage in RA, whereas false-negative results to a delay in the identification of an aggressive disease.

In a considerable number of RA patients, the US diagnosis of bone erosions is achievable using only the current OMERACT definition. However, in doubtful cases, other additional US features may be useful to distinguish between bone erosions and pseudo-erosions. In fact, the OMERACT US

Table 1. Morphological US features reported in previous studies for the identification of RA bone erosions.

Authors	Morphological domains			
	Size	**Site (at joint level)**	**Shape**	**Scenery**
Wakefield *et al.*[24]	Any size	/	Irregular floor	/
Bajaj *et al.*[46]	BE with its largest diameter ≥2 mm	/	Irregular floor	/
Finzel *et al.*[28]	Any size	Palmar region of MHs and PBs are rich of cortical vascular channels	/	Osteophytes can mimic BE, especially when these lesions form forceps-like structures
Tamas *et al.*[31]	BE with its largest diameter ≥1 mm	/	/	/
Zayat *et al.*[50]	BE of any size in the MTP5 or a BE with its largest diameter ≥2.5 mm in the DU, MCP2, MCP5	BE were more frequent at the proximal dorso-radial quadrant of MCP2, proximal dorso-ulnar quadrant of MCP5 and dorso-ulnar side of the DU. In the MTP5, BE were more frequent in the proximal dorso-lateral and plantar-lateral quadrants	/	/
Roux *et al.*[49]	Single BE with its largest diameter ≥2 mm or multiple BE	/	/	/
Finzel *et al.*[48]	Cortical vascular channels were generally smaller than BE (e.g. mean width 0.68 *versus* 1.56 mm)	RA BE clearly predominated at the radial and to a lesser extent ulnar sites of the bare areas of MCP and PIP, whereas cortical vascular channels were found mainly in the palmar regions of these joints	/	In cortical vascular channels, the PD signal is rather low and may be synchronous with heart rhythm. In contrast, BE usually showed an overall more intensive PD signal than cortical vascular channels

BE, bone erosion; DU, distal ulna; MCP, metacarpophalangeal joint; MH, metacarpal head; MT, metatarsal head; MTP, metatarsophalangeal joint; PB, phalangeal base; PD, power Doppler; PIP, proximal interphalangeal joint; RA, rheumatoid arthritis; US, ultrasonography.

definition of bone erosion may not encompass the entire morphological spectrum of erosive changes in RA, being anchored solely to the concept of cortical break.

Morphological analysis of bone erosions in RA: current concepts

According to literature data, only a few morphological US features have been proposed to define RA bone erosions: the irregular floor, the presence of an intense power Doppler signal inside the cortical break, the anatomical site and the size of the cortical defect greater than 1 or 2 mm.[24,28,31,46–50] A recently published systematic literature review on US and bone erosions in RA was used as the starting point.[47] Since the research question for the present article aimed to identify the morphological appearance of RA bone erosions, we extracted studies on this topic from the original systematic literature review,[47] and using the same search strategy we added relevant articles from an updated search in PubMed (from May 2014 to May 2020). The references of the included studies were then screened for additional studies that may have been missed. Table 1 provides a schematic representation of the morphological US features adopted by previous studies in the identification of RA bone erosions.

Morphological analysis of bone erosions in RA. The 'four Ss': size, site, shape and scenery

A morphological approach may facilitate the interpretation of US cortical bone interruptions
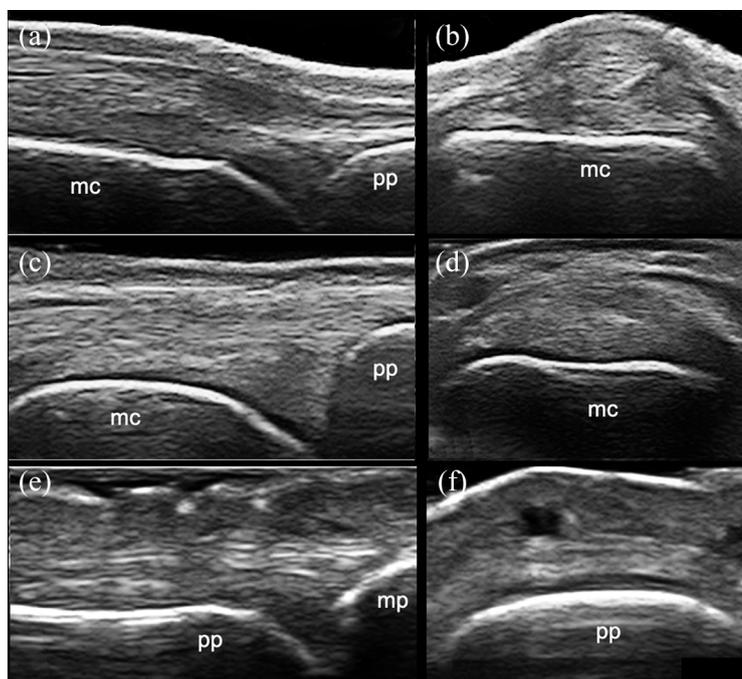
Figure 1. (a–f) Normal cortical bone in healthy subjects. Metacarpophalangeal joint. Longitudinal (a, c) and transverse (b, d) scans obtained at the dorsal (a, b) and the radial (c, d) aspects using a 18 MHz probe. Proximal interphalangeal joint. Longitudinal (e) and transverse (f) scans obtained at the dorsal aspect using a 22 MHz probe. When perpendicularly insonated, normal cortical bone appears as a sharp, regular, continuous and highly hyperechoic line with a posterior acoustic shadowing.

mc, metacarpal bone; mp, middle phalanx; pp, proximal phalanx.

in RA patients and may broaden the current OMERACT definition. In fact, our hypothesis is not in contrast with the OMERACT definition, which is the 'conditio sine qua non'. In fact, it consists of an extension of the OMERACT definition to include further morphological features that may increase the ability of US in the identification of RA bone erosions.

In our opinion, when assessing an US picture showing an interruption of the cortical bone visible in at least two perpendicular planes the following additional US features, which we call the 'four Ss', should be considered:

- Size (measured in the largest diameter of the cortical bone interruption after a multiplanar assessment)
- Site (in the dorsal, volar or lateral aspect of the joint; in the bare area or in the subchondral bone)
- Shape (linear or irregular delineation of the cortical bone interruption)
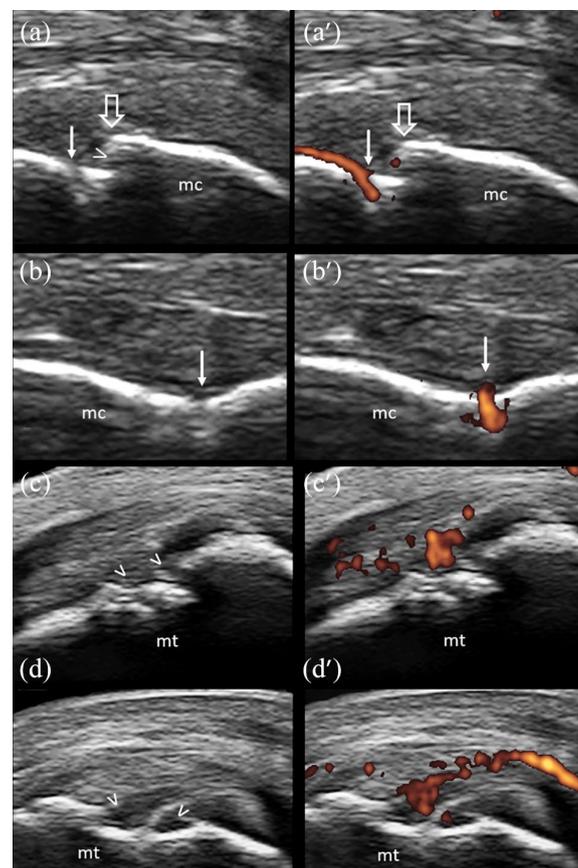
Figure 2. (a–d) Pseudo-erosions. Metacarpophalangeal joint. Longitudinal (a, a') and transverse (b, b') scans obtained at the dorsal aspect using a 22 MHz probe with (a', b') and without (a, b) power Doppler. Physiological cortical vascular channels (arrows) are characterised by an interruption of the bony cortex with sharp, parallel and straight margins, submillimetric size and the absence of any sign of synovial inflammation, with or without the presence of a linear Doppler signal that appears as a curved or straight line crossing the bony cortex. Note the step-up appearance of the osteophyte (open arrows) generating a posterior acoustic shadowing and an erosion-like feature (arrowhead) at the metacarpal bone level. Metatarsophalangeal joint. Longitudinal (c, c') and transverse (d, d') scans obtained at the medial aspect of the first metatarsal head using a 18 MHz probe with (c', d') and without (c, d) power Doppler. Note the presence of a cortical interruption (arrowheads) in a patient with hallux valgus.

mc, metacarpal bone; mt, metatarsal bone.

- Scenery (presence or absence of surrounding soft tissues abnormalities such as synovial hypertrophy and/or power Doppler signal and/or osteophytes).

To support our hypotheses, we provided pictorial evidence and a literature review describing how

morphological analysis of the US images could facilitate the interpretation of cortical bone interruptions. To do that, we selected representative US images of normal bone surface (Figure 1) and of pseudo-erosions (Figure 2) in healthy subjects and in patients with osteoarthritis. Moreover, we selected US images showing examples of bone erosions and pre-erosive changes in RA patients (Figures 3–6).
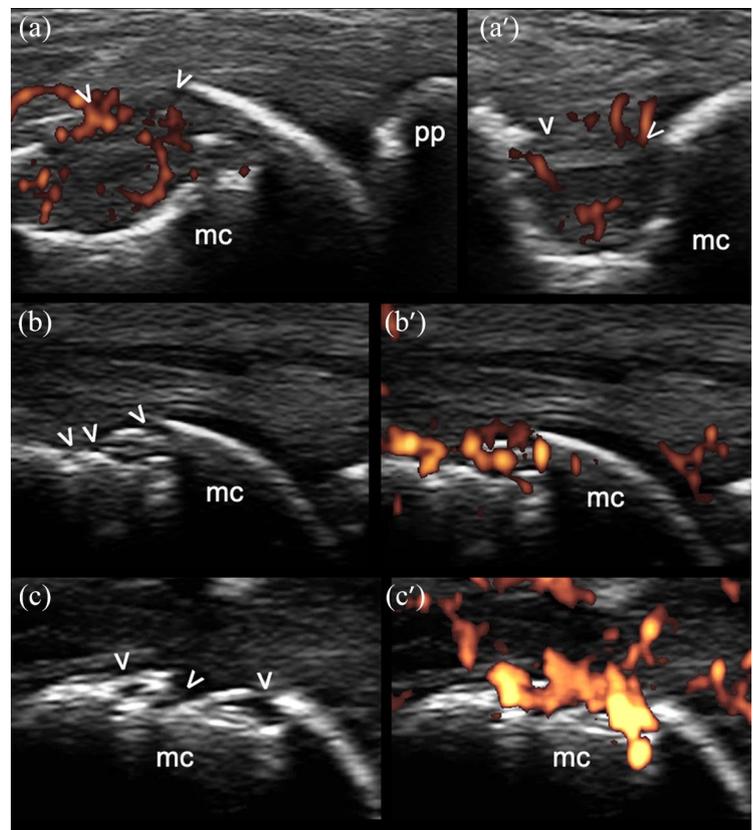
Size

The size of an US bone erosion is one of the key features determining its specificity. In fact, Roux *et al.* reported that the US detection of a single bone erosion >2 mm or of multiple bone erosions <2 mm was accurate in the discrimination between RA and other disease controls with a sensitivity of 72.1% and a specificity of 89.1%.[49] Similar results were obtained by Zayat *et al.*,[50] who reported that the identification of a bone erosion with its maximum diameter ⩾2.5 mm yielded to a sensitivity of 58.6% and a specificity of 90.0%. In both these studies, the inclusion of small (<1 mm) bone erosions in the analysis led to a higher sensitivity and a lower specificity.[49,50]

The size of the cortical break can also discriminate between a RA bone erosion and a physiological vascular channel, the former being significantly larger and deeper than the latter (cf. Figures 2 and 3). [48] In fact, several authors defined RA bone erosion as an interruption of the bony cortex >1 mm or >2 mm in its largest diameter.[31,46,51–57]

Nevertheless, we think that the adoption of a cut-off value could strongly impair the diagnostic potential of US in the early identification of a bone erosion in RA patients. In fact, as shown in Figures 4 and 6, definite microerosive changes and Ω-shaped bone erosions may appear as interruptions of the cortical bone <1 mm.

However, an association between bone erosions and age was reported in both healthy subjects and RA patients,[45,50] with a progressive increase in the number of bone erosions above the age of 50 years. This suggests that the threshold between normality and pathology changes with increasing age.[45]

To summarise, the size of a cortical break is an important issue to consider in its interpretation: the greater the size, the higher the chance that a cortical break is a bone erosion. However, to maximise the
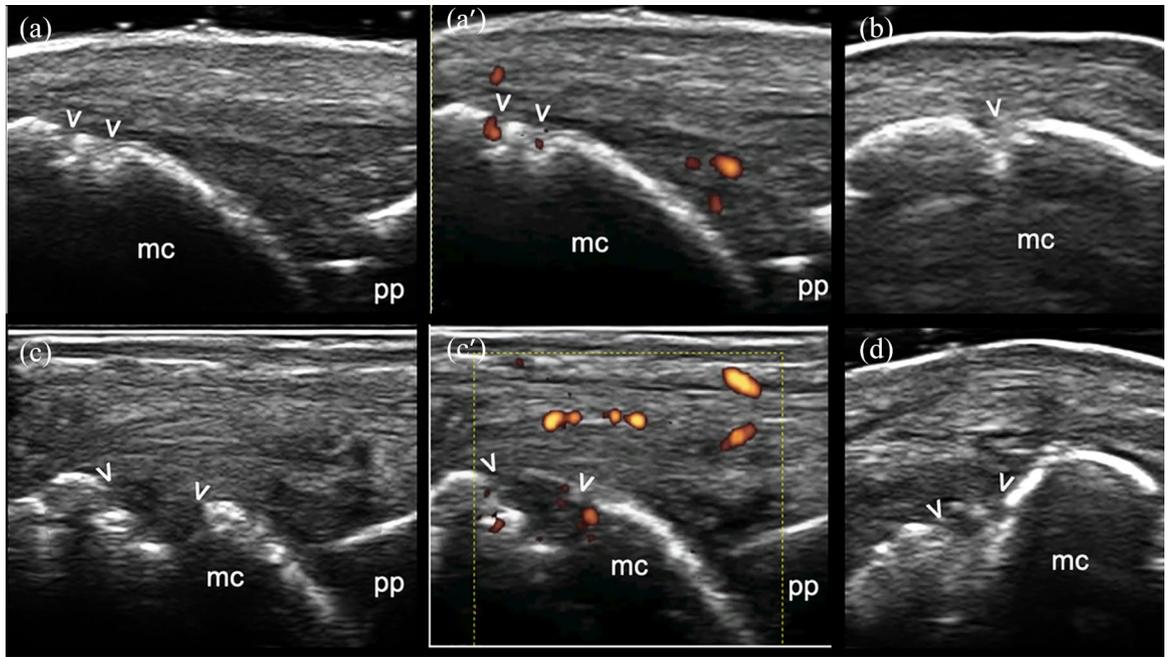

Figure 3. (a–c) Size and shape. Metacarpophalangeal joint. Longitudinal (a) and transverse (a′) scans obtained at the lateral aspect of the metacarpal head using a 18 MHz probe. Note the presence of a 'hot' bone erosion (arrowheads) characterised by a large diameter (3.4 mm) and power Doppler within the crater. Metacarpophalangeal joint. Longitudinal (b, b′) and transverse (c, c′) scans obtained at the dorsal side of the metacarpal head using a 18 MHz probe, showing smaller (ranging from 0.5 to 1.2 mm), multiple 'hot' bone erosions with inflamed synovial tissue within the erosive crater. Note the irregular margins of the bone erosions.
mc, metacarpal bone; pp, proximal phalanx.

sensitivity of US, the definition of US bone erosion should not include any size threshold.

Site

Although US allows for a multi-site and multi-tissue assessment, the ideal scanning protocol for the detection of bone erosions in RA should include all the relevant anatomical areas without being time-consuming. According to current evidence, the most specific sites for the detection of bone erosions in RA are MCP joints (especially the second and the fifth), fifth MTP joints and ulnar styloids.[31,47,50,58] Zayat *et al.* found that the identification of bone erosions of any size in the fifth MTP joint was accurate for RA (sensitivity 68.6% and specificity 85.4%).[50] Conversely, the first MTP joint and the humeral head are not

Figure 4. (a–d) Site. Metacarpophalangeal joint. Longitudinal (a, a', c, c') and transverse (b, d) scans obtained at the dorsal side of the metacarpal head using a 22 MHz probe with (a', c') and without (a, b, c, d) power Doppler, revealing active submillimetric [0.4 mm (a, b); 1.1 mm (c, d)] subchondral cortical breaks (arrowheads), indicative of bone erosions.
mc, metacarpal bone; pp, proximal phalanx.
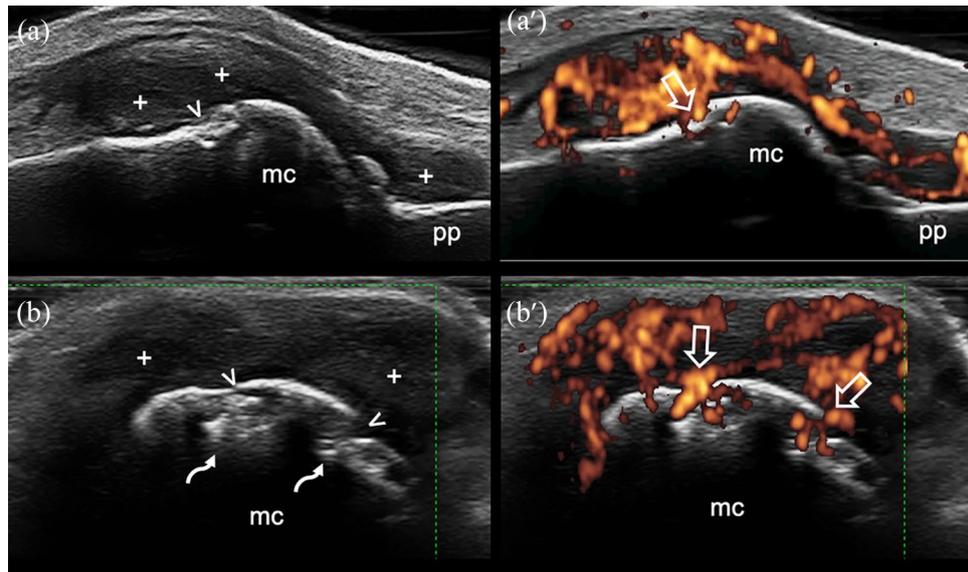
Figure 5. Scenery.
(a, b) Metacarpophalangeal joint. Longitudinal (a, a') and transverse (b, b') scans obtained at the dorsal aspect using a 18 MHz probe with (a', b') and without (a, b) power Doppler. Note a cortical break (arrowheads) in the area of the metacarpal depression, which is a common site for pseudo-erosions. The surrounding scenery, characterised by florid synovial hypertrophy (+) showing power Doppler signal in contact with, and invading into, the cortical break (open arrows), provides additional information supporting the diagnosis of bone erosion. The deep echoes (curved arrows) in b and b' suggest the presence of bone erosions despite submillimetric small cortical interruptions (0.2 and 0.6 mm) (arrowheads).
mc, metacarpal bone; pp, proximal phalanx.

specific targets due to the high prevalence of bone erosions in patients with other rheumatic diseases and healthy controls.[31,47,59–61]

At joint level, the site of a cortical break might be specific enough to define it as a bone erosion. In fact, given a clinical suspicion of RA, a subchondral cortical break of any size is highly indicative of a bone erosion (Figure 4). However, subchondral bone erosions are a late and relatively infrequent US finding in RA. Thus, a careful evaluation of the whole joint should always be performed. Among the other areas of the MCP and MTP joints, the lateral aspect was found to be the most specific site to be assessed,[24,26,28,31,48] whereas, in the proximal interphalangeal (PIP) joints, the dorsal side was the most frequently affected.[48] In fact, in both MCP and PIP joints of RA patients, physiological vascular channels predominated in the palmar aspect (78.8% of MCP joints and 100% of PIP joints).[48] As documented by Finzel *et al.* in a comparative study with high-resolution peripheral quantitative CT,[28] false-positive results in the identification of US bone erosions were related mainly to the misinterpretation of vascular channels in the volar side of the MCP joint. On the other hand, false-negative results were linked mainly to the underestimation of US bone erosions in the dorsal metacarpal depression.[28] At that level, pseudo-erosions correspond to the physiological depression of the dorsal aspect of the metacarpal bone, located just proximal to the hyaline cartilage. Using US, Falkowski *et al.* evaluated the MCP joints of 100 healthy subjects.[39] The authors found that every subject had pseudo-erosions in at least one MCP joint, 99% of them had a bilateral involvement and 81.5% had at least three or more MCP joints with pseudo-erosions on the metacarpal depression. The shape and the size of the cortical break and the surrounding scenery may provide further evidence to distinguish pseudo-erosions from RA bone erosions at that level (cf. Figures 2 and 5).

To summarise, the site of the cortical break has a relevant impact on its interpretation, both with regard to which joint (e.g. fifth *versus* first MTP joints) or which area of a joint (e.g. subchondral *versus* palmar aspect of a MCP joint) is under examination.

Shape

The shape is not included in the OMERACT US definition of bone erosion. Conversely, the
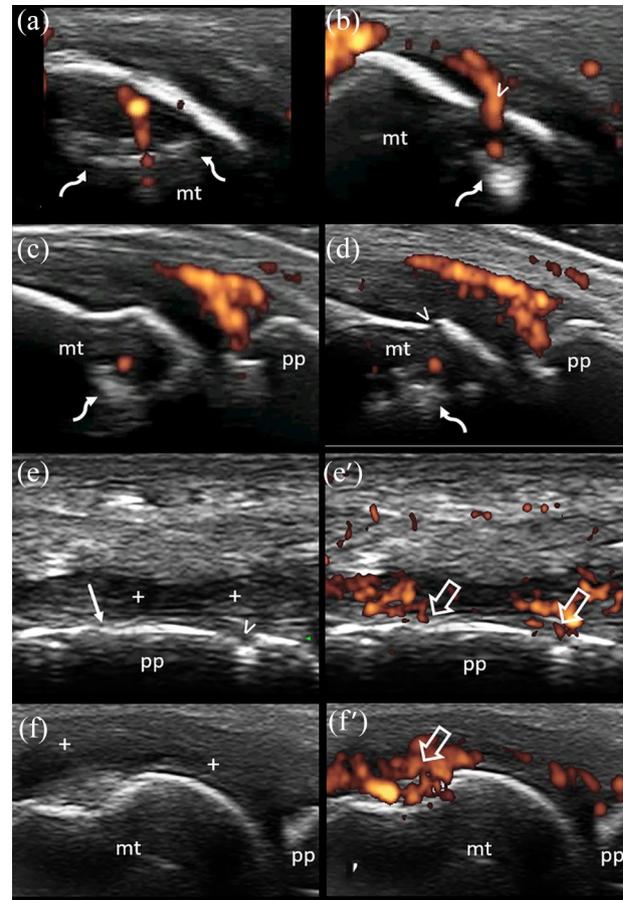
Figure 6. (a–f) Microerosions and other atypical cortical interruptions. Metatarsophalangeal joint. Transverse (a, b) and longitudinal (c, d) scans obtained at the lateral aspect of the metatarsal head of the 5th digit using a 18 MHz probe showing a Ω-shaped bone erosion characterised by Doppler signal and deep echoes (curved arrows) with a small cortical break (0.24 mm) (arrowheads). Proximal interphalangeal join. Transverse (e, e') scans obtained at the dorsal aspect with (e') and without (e) power Doppler using a 22 MHz probe revealing a loss of sharpness of the bony cortex suggestive for a pre-erosive change (white arrow) and a definite cortical break indicative of a microerosion (arrowhead). Note the presence of highly vascularised synovial hypertrophy contacting the bone surface (open arrows). Metatarsophalangeal joint. Longitudinal (f and f') scans obtained at the lateral aspect of the metatarsal head of the 5th digit with (f') and without (f) power Doppler using a 18 MHz probe showing both a cortical defect without a definite cortical interruption and a loss of sharpness of the bone surface. The presence of Doppler signal contacting the bony cortex (open arrows) and the absence of this notch in the contralateral 5th metatarsal head are highly indicative of an atypical bone erosion. mt, metatarsal bone; pp, proximal phalanx.

high-resolution peripheral quantitative CT definition of bone erosion includes the nonlinear shape of the cortical break to differentiate it from vascular channels penetrating the cortex.[62] Accordingly, the irregular floor and the ill-defined borders of the erosive crater have been reported as US features of RA bone erosions.[46,63] In our experience, as shown in Figures 3–6, the

irregular lining of the cortical breaks is a distinctive US feature of RA bone erosions. In addition, the identification of other US abnormalities, such as the focal loss of sharpness of the bony cortex under orthogonal insonation and/or atypical deep echoes under the cortical surface may help in the detection of Ω-shaped bone erosions characterised by a very small interruption of the cortical bone and a larger defect of the trabecular bone as documented by high resolution CT studies (Figure 6).[26,28]

Scenery

Unlike CR and CT, US is able not only to assess cortical bone interruptions but also to reveal even minimal morpho-structural and vascular changes of the surrounding soft tissues. Thus, the presence of an inflamed synovial tissue in or around an interruption of the cortical bone can help to discriminate between bone erosions and physiological vascular channels.[19,48,64] In fact, nonlinear or multifocal power Doppler signal within the cortical defect is highly indicative of active bone erosion regardless of its size, whereas a single and thin linear vessel crossing the cortical line is indicative of a feeding vessel. Moreover, pathological Doppler signal is usually wider and more intense than the physiological vascular signal.[48] In addition, the identification of synovial hypertrophy in close contact with a cortical defect is highly suggestive of a bone erosion rather than pseudo-erosion as shown in Figures 5 and 6.

Conclusions

The representative images presented in this report provide pictorial evidence supporting the hypothesis that inclusion of the 'four S' domains (size, site, shape and scenery) to the simple assessment of a cortical discontinuity may improve the interpretation of US cortical bone interruptions. Besides the cortical break itself, other additional features may be considered to facilitate the interpretation of US cortical bone interruptions in RA patients, especially in the early phases of the erosive disease. However, given the high variability of scenarios that may be encountered in daily practice, we decided not to adopt a hierarchical approach with regard to the 'four Ss'. In fact, one single morphological characteristic (e.g. a very large cortical break or a subchondral cortical interruption) may be sufficient in some cases to define a cortical break as a bone erosion; on the other hand, a combination of suggestive features may be needed, especially in the early phases of disease.

This hypothesis needs to be further corroborated through the application of the OMERACT methodology in order to develop, test and validate an updated definition of US bone erosion.

ORCID iD

Edoardo Cipolletta (iD) https://orcid.org/0000-0002-6881-8197

Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

References

1. McInnes IB and Schett G. The pathogenesis of rheumatoid arthritis. *N Engl J Med* 2011; 365: 2205–2219.

2. Cipolletta E, Hurnakova J, Di Matteo A, *et al*. Prevalence and distribution of cartilage and bone damage at metacarpal head in healthy subjects. *Clin Exp Rheumatol*, Epub ahead of print 2 March 2021.

3. Hurnakova J, Filippucci E, Cipolletta E, *et al*. Prevalence and distribution of cartilage damage at the metacarpal head level in rheumatoid arthritis and osteoarthritis: an ultrasound study. *Rheumatology (Oxford)* 2019; 58: 1206–1213.

4. Cipolletta E, Filippucci E, Di Matteo A, *et al*. The reliability of ultrasound in the assessment of hyaline cartilage in rheumatoid arthritis and healthy metacarpal heads. *Ultraschall Med.* Epub ahead of print 30 October 2020. DOI: 10.1055/a-1285-4602.

5. Aletaha D, Funovits J and Smolen JS. Physical disability in rheumatoid arthritis is associated

with cartilage damage rather than bone destruction [published correction appears in *Ann Rheum Dis* 2011; 70: 1880]. *Ann Rheum Dis* 2011; 70: 733–739.

6. Filippucci E, Cipolletta E, Mashadi Mirza R, *et al*. Ultrasound imaging in rheumatoid arthritis. *Radiol Med* 2019; 124: 1087–1100.

7. Kleyer A, Finzel S, Rech J, *et al*. Bone loss before the clinical onset of rheumatoid arthritis in subjects with anticitrullinated protein antibodies. *Ann Rheum Dis* 2014; 73: 854–860.

8. Di Matteo A, Mankia K, Duquenne L, *et al*. Ultrasound erosions in the feet best predict progression to inflammatory arthritis in anti-CCP positive at-risk individuals without clinical synovitis. *Ann Rheum Dis* 2020; 79: 901–907.

9. Thabet MM, Huizinga TWJ, Van der Heijde DM, *et al*. The prognostic value of baseline erosions in undifferentiated arthritis. *Arthritis Res Ther* 2009; 11: R155.

10. Zabotti A, Finzel S, Baraliakos X, *et al*. Imaging in the preclinical phases of rheumatoid arthritis. *Clin Exp Rheumatol* 2020; 38: 536–542.

11. Nam JL, Hensor EMA, Hunt L, *et al*. Ultrasound findings predict progression to inflammatory arthritis in anti-CCP antibody-positive patients without clinical synovitis. *Ann Rheum Dis* 2016; 75: 2060–2067.

12. Rakieh C, Nam JL, Hunt L, *et al*. Predicting the development of clinical arthritis in anti-CCP positive individuals with non-specific musculoskeletal symptoms: a prospective observational cohort study. *Ann Rheum Dis* 2015; 74: 1659–1666.

13. van der Heijde DM. Joint erosions and patients with early rheumatoid arthritis. *Br J Rheumatol* 1995; 34(Suppl. 2): 74–78.

14. Fletcher DE and Rowley KA. The radiological features of rheumatoid arthritis. *Br J Radiol* 1952; 25: 282–295.

15. van der Heijde D, van der Helm-van Mil AHM, Aletaha D, *et al*. EULAR definition of erosive disease in light of the 2010 ACR/EULAR rheumatoid arthritis classification criteria. *Ann Rheum Dis* 2013; 72: 479–481.

16. Smolen JS, Landewé RBM, Bijlsma JWJ, *et al*. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. *Ann Rheum Dis* 2020; 79: 685–699.

17. Lillegraven S, van der Heijde D, Uhlig T, *et al*. What is the clinical relevance of erosions and joint space narrowing in RA? *Nat Rev Rheumatol* 2012; 8: 117–120.

18. Tan YK and Conaghan PG. Imaging in rheumatoid arthritis. *Best Pract Res Clin Rheumatol* 2011; 25: 569–584.

19. Grassi W, Okano T, Di Geso L, *et al*. Imaging in rheumatoid arthritis: options, uses and optimization. *Expert Rev Clin Immunol* 2015; 11: 1131–1146.

20. Colebatch AN, Edwards CJ, Østergaard M, *et al*. EULAR recommendations for the use of imaging of the joints in the clinical management of rheumatoid arthritis. *Ann Rheum Dis* 2013; 72: 804–814.

21. Funck-Brentano T, Gandjbakhch F, Etchepare F, *et al*. Prediction of radiographic damage in early arthritis by sonographic erosions and power doppler signal: a longitudinal observational study. *Arthritis Care Res* 2013; 65: 896–902.

22. 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.

23. 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: 1388–1392.

24. 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: 2762–2770.

25. Ellegaard K, Bliddal H, Moller Dohn U, *et al*. Validity and reliability of 3D US for the detection of erosions in patients with rheumatoid arthritis using MRI as the gold standard. *Ultraschall Der Medizin* 2014; 35: 137–141.

26. Døhn UM, Ejbjerg BJ, Court-Payen M, *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.

27. Rahmani M, Chegini H, Najafizadeh SR, *et al*. Detection of bone erosion in early rheumatoid arthritis: ultrasonography and conventional radiography versus non-contrast magnetic resonance imaging. *Clin Rheumatol* 2010; 29: 883–891.

28. Finzel S, Ohrndorf S, Englbrecht M, *et al*. A detailed comparative study of high-resolution

ultrasound and micro-computed tomography for detection of arthritic bone erosions. *Arthritis Rheum* 2011; 63: 1231–1236.

29. Døhn UM, Terslev L, Szkudlarek M, *et al*. Detection, scoring and volume assessment of bone erosions by ultrasonography in rheumatoid arthritis: comparison with CT. *Ann Rheum Dis* 2013; 72: 530–534.

30. Peters M, van Tubergen A, Scharmga A, *et al*. Assessment of cortical interruptions in the finger joints of patients with rheumatoid arthritis using HR-pQCT, radiography, and MRI. *J Bone Miner Res* 2018; 33: 1676–1685.

31. Tămaș MM, Filippucci E, Becciolini A, *et al*. Bone erosions in rheumatoid arthritis: ultrasound findings in the early stage of the disease. *Rheumatology (Oxford)* 2014; 53: 1100–1107.

32. Baillet A, Gaujoux-Viala C, Mouterde G, *et al*. Comparison of the efficacy of sonography, magnetic resonance imaging and conventional radiography for the detection of bone erosions in rheumatoid arthritis patients: a systematic review and meta-analysis. *Rheumatology (Oxford)* 2011; 50: 1137–1147.

33. Di Matteo A, Mankia K, Azukizawa M, *et al*. The role of musculoskeletal ultrasound in the rheumatoid arthritis continuum. *Curr Rheumatol Rep* 2020; 22: 41.

34. Filer A, de Pablo P, Allen G, *et al*. Utility of ultrasound joint counts in the prediction of rheumatoid arthritis in patients with very early synovitis. *Ann Rheum Dis* 2011; 70: 500–507.

35. Foltz V, Gandjbakhch F, Etchepare F, *et al*. Power doppler ultrasound, but not low-field magnetic resonance imaging, predicts relapse and radiographic disease progression in rheumatoid arthritis patients with low levels of disease activity. *Arthritis Rheum* 2012; 64: 67–76.

36. Di Matteo A, Mankia K, Nam J, *et al*. In anti-CCP+ at-risk individuals, radiographic bone erosions are uncommon and are not associated with the development of clinical arthritis. *Rheumatology (Oxford)*. Epub ahead of print 13 December 2020. DOI: 10.1093/rheumatology/keaa761.

37. Bruyn GA, Iagnocco A, Naredo E, *et al*. OMERACT definitions for ultrasonographic pathologies and elementary lesions of rheumatic disorders 15 years on. *J Rheumatol* 2019; 46: 1388–1393.

38. Hirtler L, Rath C, Platzgummer H, *et al*. Pseudoerosions of hands and feet in rheumatoid arthritis: anatomic concepts and redefinition. *J Clin Med* 2019; 8: 2174.

39. Falkowski AL, Jacobson JA, Kalia V, *et al*. Ultrasound characterization of pseudoerosions and dorsal joint recess morphology of the hand and wrist in 100 asymptomatic subjects. *Eur J Radiol* 2020; 124: 108842.

40. Peluso G, Bosello SL, Gremese E, *et al*. Detection of bone erosions in early rheumatoid arthritis: 3D ultrasonography versus computed tomography. *Clin Rheumatol* 2015; 34: 1181–1186.

41. Boutry N, Lardé A, Demondion X, *et al*. Metacarpophalangeal joints at US in asymptomatic volunteers and cadaveric specimens. *Radiology* 2004; 232: 716–724.

42. Millot F, Clavel G, Etchepare F, *et al*. Musculoskeletal ultrasonography in healthy subjects and ultrasound criteria for early arthritis (the ESPOIR cohort). *J Rheumatol* 2011; 38: 613–620.

43. Fodor D, Felea I, Popescu D, *et al*. Ultrasonography of the metacarpophalangeal joints in healthy subjects using an 18 MHz transducer. *Med Ultrason* 2015; 17: 185–191.

44. Padovano I, Costantino F, Breban M, *et al*. Prevalence of ultrasound synovial inflammatory findings in healthy subjects. *Ann Rheum Dis* 2016; 75: 1819–1823.

45. Berlin A, Simon D, Tascilar K, *et al*. The ageing joint-standard age- and sex-related values of bone erosions and osteophytes in the hand joints of healthy individuals. *Osteoarthr Cartil* 2019; 27: 1043–1047.

46. Bajaj S, Lopez-Ben R, Oster R, *et al*. Ultrasound detects rapid progression of erosive disease in early rheumatoid arthritis: a prospective longitudinal study. *Skeletal Radiol* 2007; 36: 123–128.

47. Szkudlarek M, Terslev L, Wakefield RJ, *et al*. Summary findings of a systematic literature review of the ultrasound assessment of bone erosions in rheumatoid arthritis. *J Rheumatol* 2016; 43: 12–21.

48. Finzel S, Aegerter P, Schett G, *et al*. Identification, localization and differentiation of erosions and physiological bone channels by ultrasound in rheumatoid arthritis patients. *Rheumatology (Oxford)*. Epub ahead of print 17 May 2020. DOI: 10.1093/rheumatology/keaa183.

49. Roux C, Gandjbakhch F, Pierreisnard A, *et al*. Ultrasonographic criteria for the diagnosis of erosive rheumatoid arthritis using osteoarthritic patients as controls compared to validated

radiographic criteria. *Joint Bone Spine* 2019; 86: 467–474.

50. Zayat AS, Ellegaard K, Conaghan PG, *et al*. The specificity of ultrasound-detected bone erosions for rheumatoid arthritis. *Ann Rheum Dis* 2015; 74: 897–903.

51. Schmidt WA, Schicke B, Ostendorf B, *et al*. Low-field MRI versus ultrasound: which is more sensitive in detecting inflammation and bone damage in MCP and MTP joints in mild or moderate rheumatoid arthritis? *Clin Exp Rheumatol* 2013; 31: 91–96.

52. Magnani M, Salizzoni E, Mulè R, *et al*. Ultrasonography detection of early bone erosions in the metacarpophalangeal joints of patients with rheumatoid arthritis. *Clin Exp Rheumatol* 2004; 22: 743–748.

53. McGonagle 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: 329–331.

54. Chaiamnuay S, Lopez-Ben R and Alarcón GS. Ultrasound of target joints for the evaluation of possible inflammatory arthropathy: associated clinical factors and diagnostic accuracy. *Clin Exp Rheumatol* 2008; 26: 875–880.

55. Lerch K, Borisch N, Paetzel C, *et al*. Sonographic evaluation of the elbow in rheumatoid arthritis: a classification of joint destruction. *Ultrasound Med Biol* 2003; 29: 1131–1135.

56. Lopez-Ben R, Bernreuter WK, Moreland LW, *et al*. Ultrasound detection of bone erosions in rheumatoid arthritis: a comparison to routine radiographs of the hands and feet. *Skeletal Radiol* 2004; 33: 80–84.

57. Reynolds PPM, Heron C, Pilcher J, *et al*. Prediction of erosion progression using ultrasound in established rheumatoid arthritis: a 2-year follow-up study. *Skeletal Radiol* 2009; 38: 473–478.

58. Hammer HB, Haavardsholm EA, Bøyesen P, *et al*. Bone erosions at the distal ulna detected by ultrasonography are associated with structural damage assessed by conventional radiography and MRI: a study of patients with recent onset rheumatoid arthritis. *Rheumatology (Oxford)* 2009; 48: 1530–1532.

59. 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: 1152–1156.

60. Schmidt WA, Schmidt H, Schicke B, *et al*. Standard reference values for musculoskeletal ultrasonography. *Ann Rheum Dis* 2004; 63: 988–994.

61. Wright SA, Filippucci E, McVeigh C, *et al*. High-resolution ultrasonography of the first metatarsal phalangeal joint in gout: a controlled study. *Ann Rheum Dis* 2007; 66: 859–864.

62. Barnabe C, Toepfer D, Marotte H, *et al*. Definition for rheumatoid arthritis erosions imaged with high resolution peripheral quantitative computed tomography and interreader reliability for detection and measurement. *J Rheumatol* 2016; 43: 1935–1940.

63. Ventura-Ríos L, Hernández-Díaz C, Sanchez-Bringas G, *et al*. A descriptive, cross-sectional study characterizing bone erosions in rheumatoid arthritis and gout by ultrasound. *Clin Rheumatol* 2016; 35: 2269–2276.

64. Kawashiri SY, Fujikawa K, Nishino A, *et al*. Ultrasound-detected bone erosion is a relapse risk factor after discontinuation of biologic disease-modifying antirheumatic drugs in patients with rheumatoid arthritis whose ultrasound power Doppler synovitis activity and clinical disease activity are well controlled. *Arthritis Res Ther* 2017; 19: 108.

Visit SAGE journals online
journals.sagepub.com/
home/tab

$SAGE journals