4ο ΔΙΑΠΑΝΕΠΙΣΤΗΜΙΑΚΟ ΠΡΟΓΡΑΜΜΑ ΕΚΠΑΙΔΕΥΣΗΣ ΣΤΗ ΡΕΥΜΑΤΟΛΟΓΙΑ 2022-24

Απεικόνιση στην Ρευματοειδή Αρθρίτιδα

Νέστορας Αυγουστίδης

Ρευματολόγος, Επιμελητής Α’

Ρευματολογική Κλινική ΠΑΓΝΗ

EULAR Certified MSK sonographer

ΠΑΝΕΠΙΣΤΗΜΙΑΚΟ ΝΟΣΟΚΟΜΕΙΟ ΗΡΑΚΛΕΙΟΥ

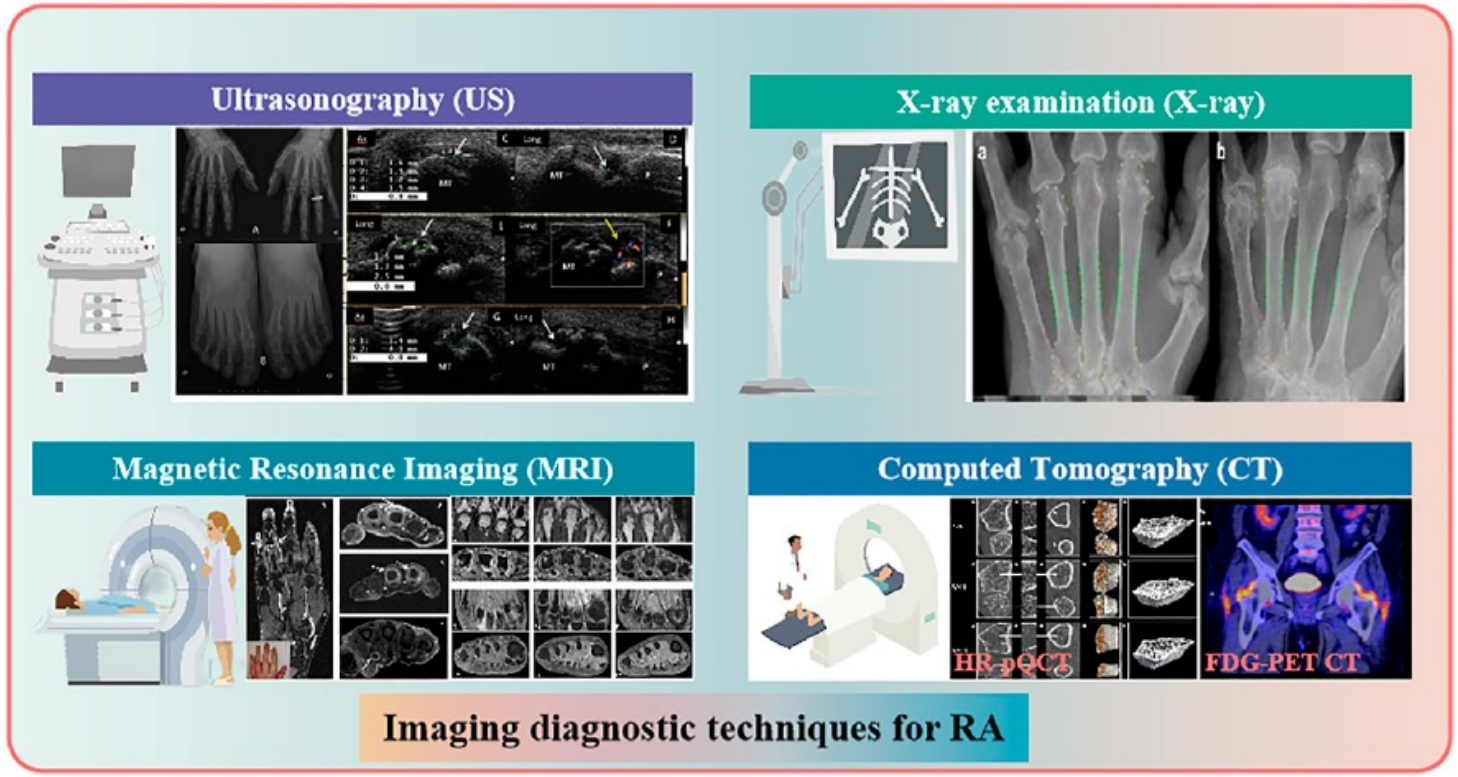


FIGURE 4 | Different imaging diagnostic techniques for RA.

Conventional imaging

- Radiographs still represent a useful technique despite its limitations, because of :

1. easy availability
2. reliability
3. experience
4. relative low cost.
5. baseline imaging for future comparisons and follow-ups .

A. Drosos et al. Rheumatology International (2019)

Scoring systems

- Many clinical trials still use radiographic progression as an outcome measure, with radiographic scoring methods well established and sensitive to change.

- Mostly used

1. Larsen score and it's modifications

2. van der Heijde modified Sharp score

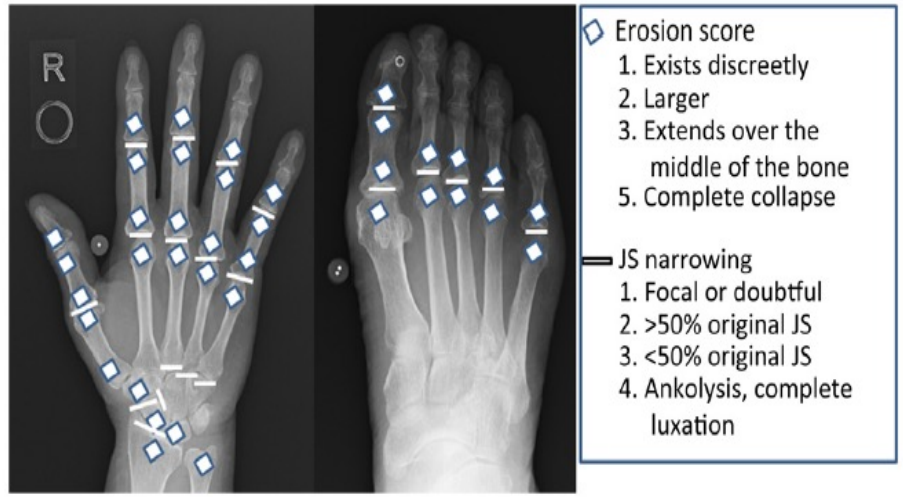


Figure 1. Sharp/van der Heijde score scoring system. JS, joint space.

M. Andersson et al. Clinical Rheumatology (2021)

Conventional imaging

- It can depict :

1. Periarticular osteopenia
2. Periarticular soft tissue swelling
3. Joint erosions
4. Joint space narrowing
5. Joint subluxations-luxations
6. Joint destruction
7. Calcifications(D/D from CPPD/HADD)- Systemic diseases: Sscl, DM

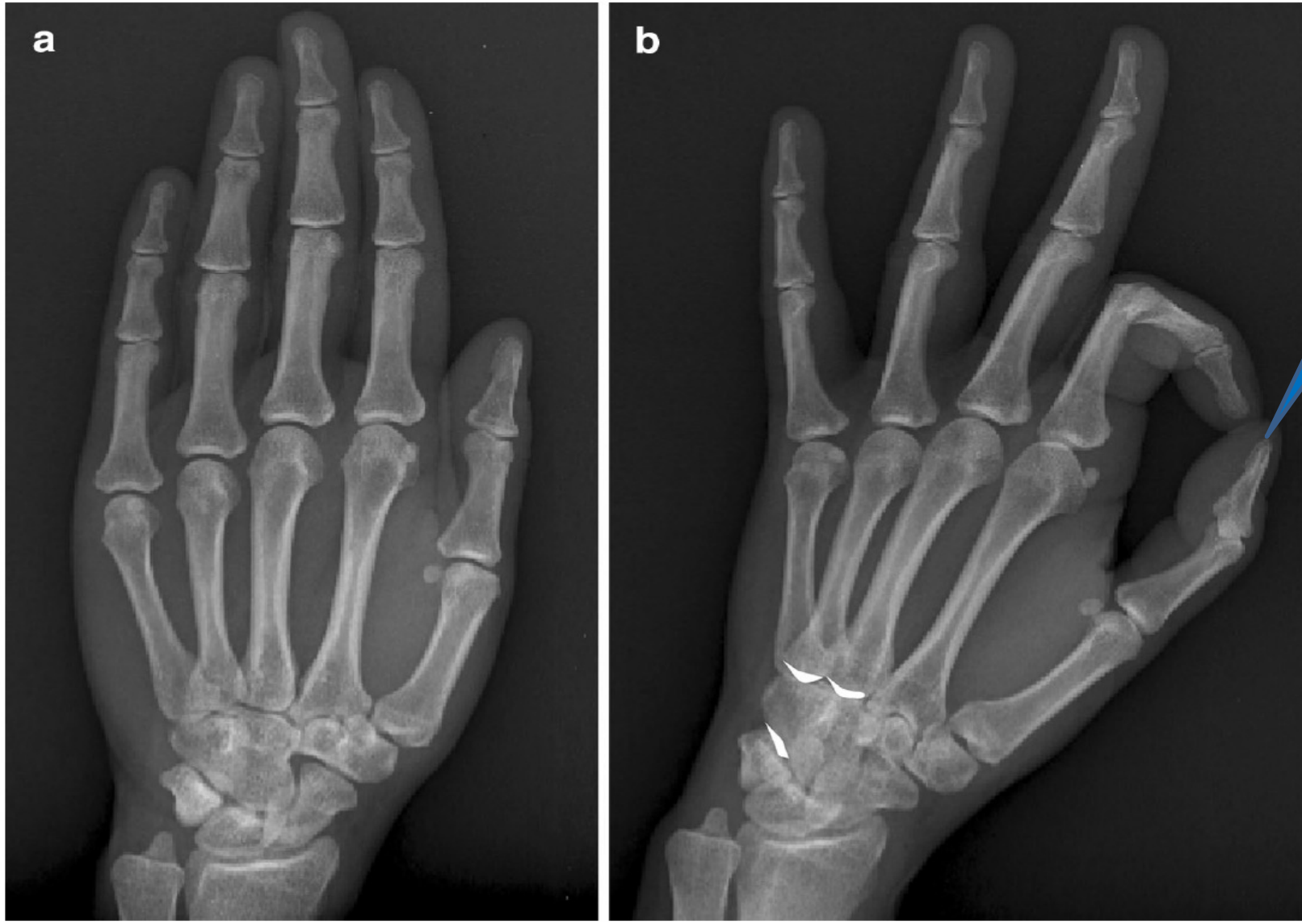
A. Drosos et al. Rheumatology International (2019)

Conventional imaging

- Disadvantages of radiographs include:

1. low sensitivity to detect early joint damage
2. three-dimensional structures are shown in two dimensions
3. ionising radiation is used.
4. It can not depict synovium and periarticular structures (bursae, tendons, synovial sheaths) and consequently it is not possible to assess inflammatory process (activity)

A. Drosos et al. Rheumatology International (2019)



ball-catcher view

1 **a** Posteroanterior and **b** Nørgaard view of a healthy individual. In the latter, the anatomic regions of early erosive changes of an inflamma-
arthropathy are marked in white

A. Drosos et al. Rheumatology International (2019)

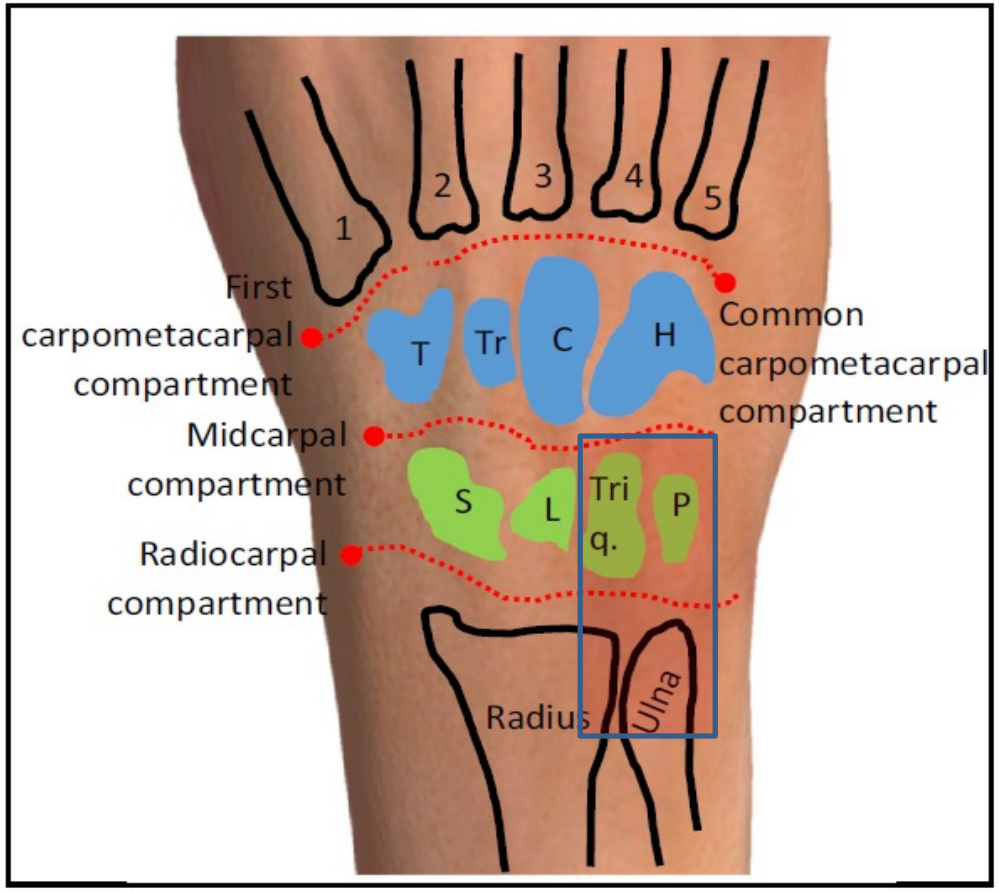


Fig. 2 Anatomical compartments of the wrist (schematic representation). Early erosions in inflammatory arthritides begin in the pisiform and triquetral bones. 1–5, metacarpal bones; T, trapezium; Tr, trapezoid; C, capitate; H, hamate; S, scaphoid; L, lunate; Triq., triquetral; P, pisiform

Rheumatology International (2019) 39:1331–1341

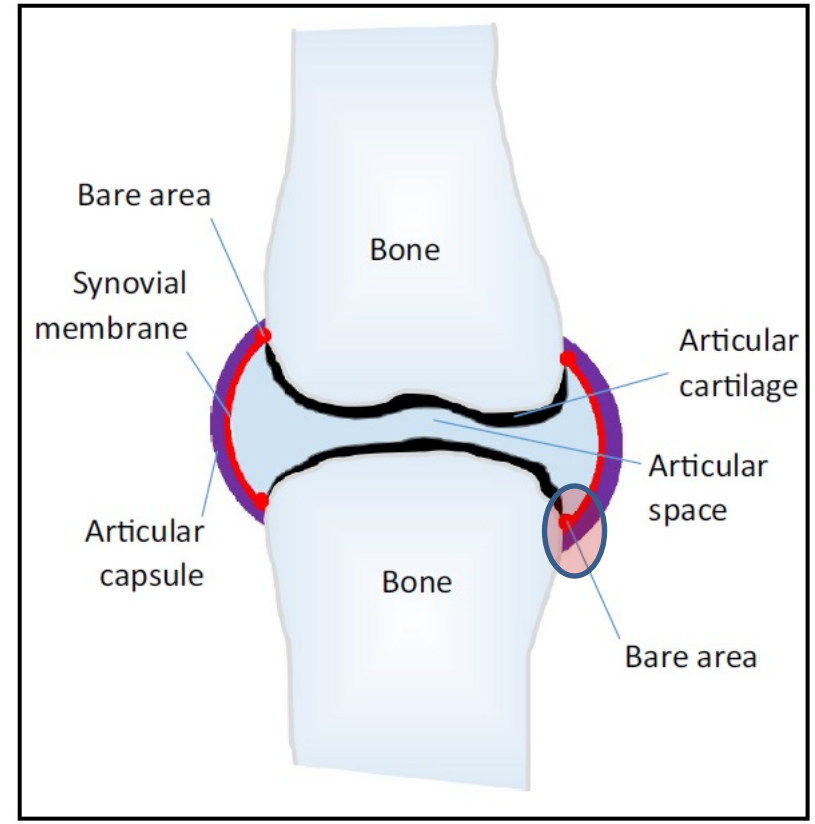


Fig. 6 Schematic representation of a diarthrodial joint in which the bare areas of the joint are shown. These areas are located between the edge of the articular cartilage and the attachment of the synovial membrane. Owing to the direct contact with the synovium, without any protecting layer of the cartilage these areas are very susceptible to inflammation, which leads to erosions and bone destruction

A. Drosos et al. Rheumatology International (2019)

Radiographic hallmarks of rheumatoid arthritis are :

1. marginal erosions, frequently in the radial side of the (MCP) joint

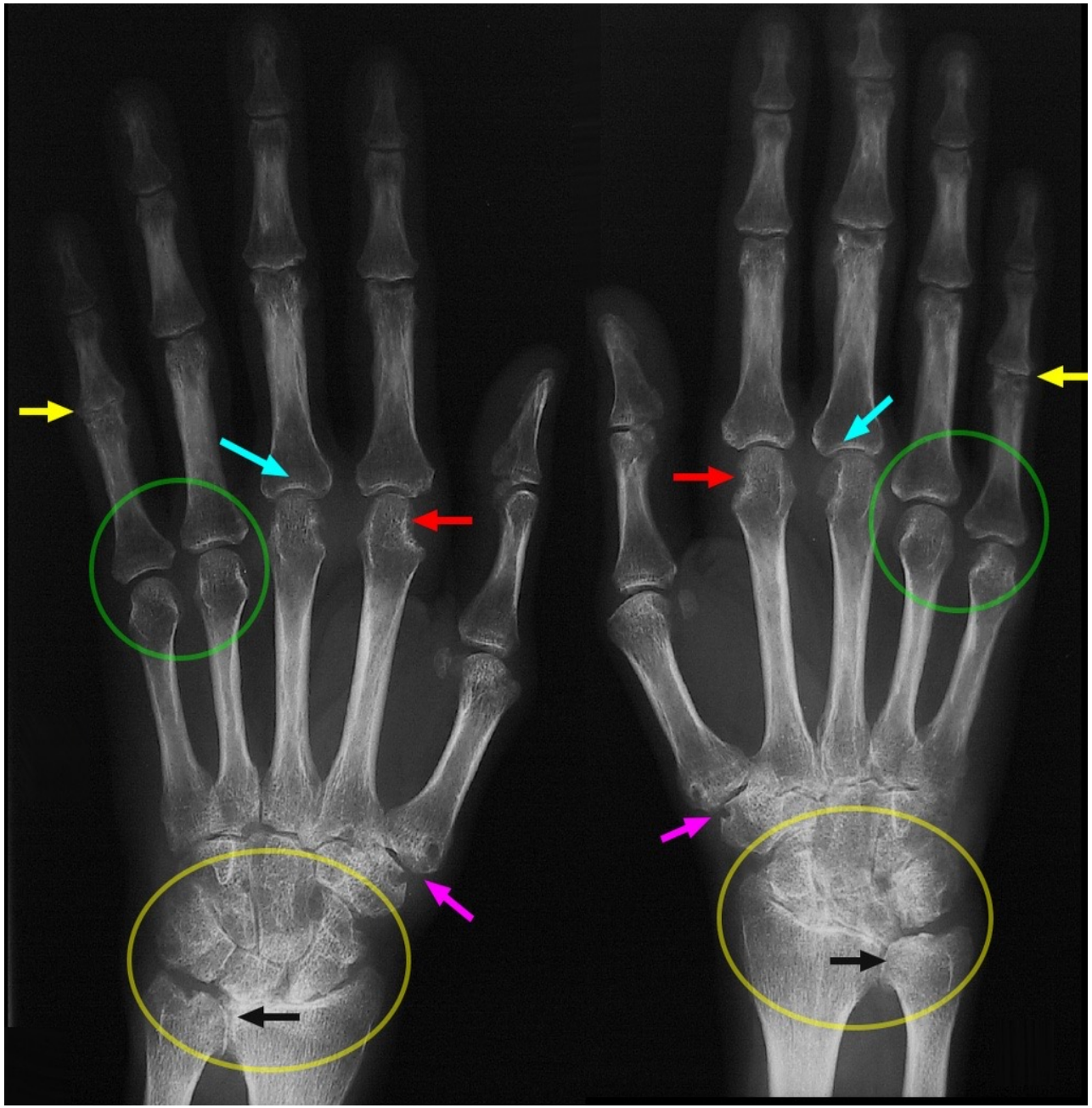
2. No bone production –periarticular osteopenia

3. PIP and MCP joints (especially 2nd and 3rd MCP), ulnar styloid , triquetrum, pisiform, distal radioulnar joint, while DIP joints are spared

4. similar to the hands, there is a predilection for the PIP and MTP joints (especially 4th and 5th MTP) involvement of subtalar joint & mid foot

5. Cervical spine : C1-C2 involvement : erosion of the dens, atlantoaxial subluxation

A. Drosos et al. Rheumatology International (2019)



1. bilateral and symmetrical involvement
2. proximal interphalangeal joint space narrowing (yellow arrows)
3. metacarpal heads erosions (red arrows)
4. metacarpophalangeal joint space narrowing (blue arrows)
5. metacarpophalangeal joint osteopenia (green circles)
6. pancarpal and radiocarpal involvement with erosions (yellow circles)
7. carpometacarpal erosion (purple arrows)
8. distal radioulnar joint loss of space (black arrows)
9. distal interphalangeal joints spared
10. soft tissue swelling

Fig. 4 Periarticular (or juxta-articular) osteoporosis of both wrists in an RA patient with more prominent findings on the right hand

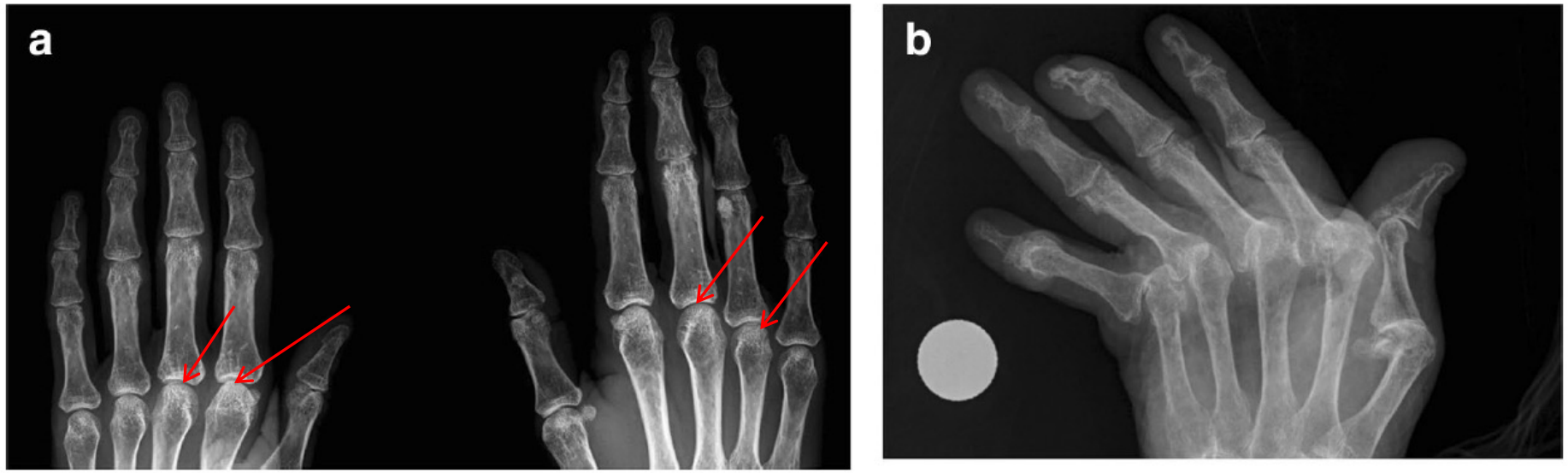
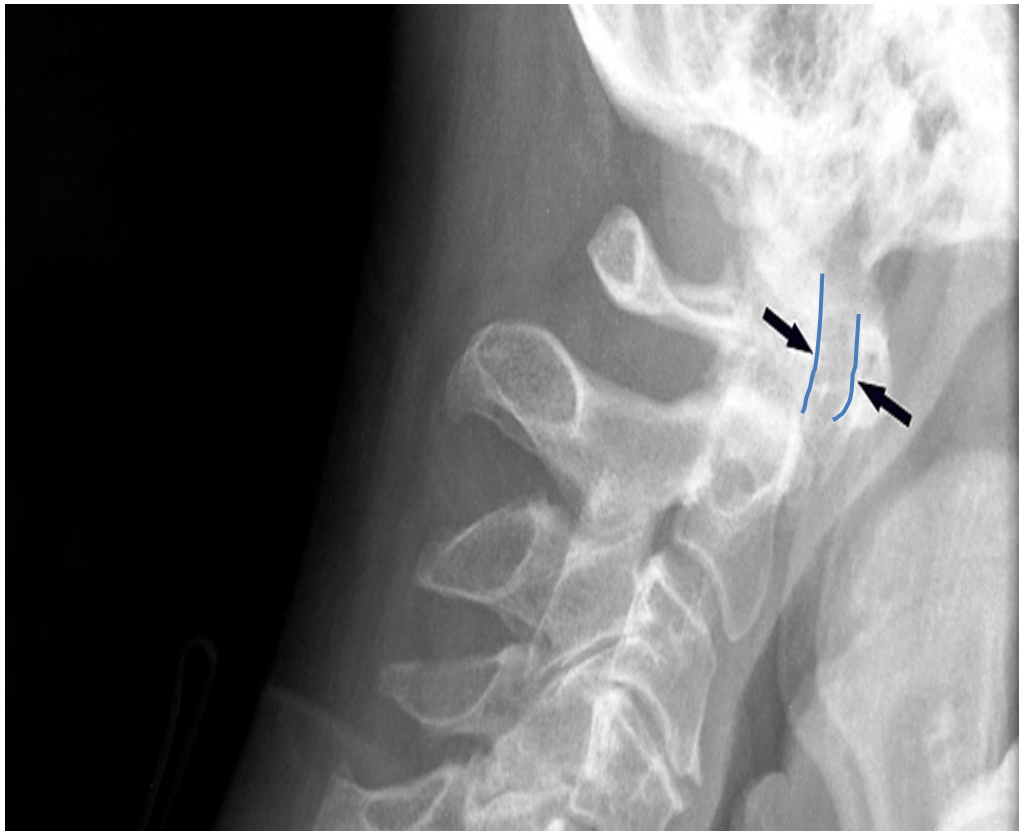


Fig. 5 **a** Early RA patient, uniform joint space narrowing affecting the second–fifth MCP joints bilaterally. **b** Subluxations in an RA patient. Note that proximal phalanges sublux in an ulnar direction in relation to the adjacent metacarpals. Also, diffuse osteopenia with cortical thinning of the metacarpals and all the phalanges are shown

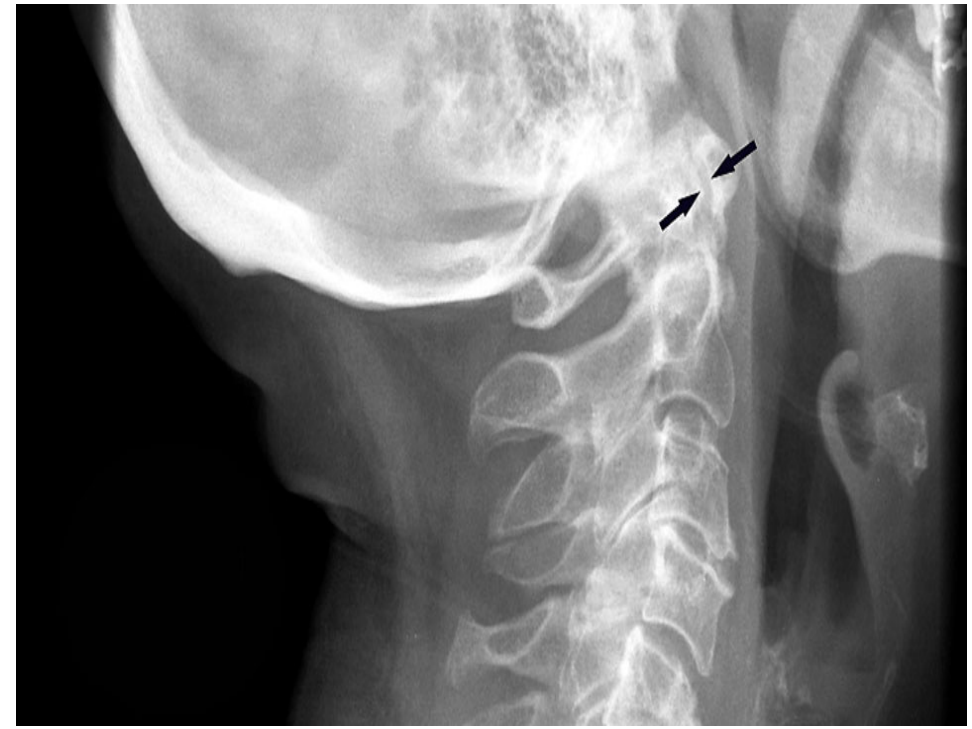
1. Studies have shown a correlation between joint damage seen on CR and disability in longstanding RA.

2. It has also been shown that the presence of radiographic changes is associated with worse outcomes and prognosis.

A. Drosos et al. Rheumatology International (2019)



Cervical spine instability flexion. Plain radiograph of the cervical spine showing 5 mm of anterior subluxation (arrowed) of C1 on C2, reflected in an increased anterior atlanto-dens interval (AADI) on flexion.



Cervical spine instability extension. While the anterior atlanto-dens interval (AADI) increases on flexion, it is reduced with cervical extension.

Table 1 Imaging changes occurring in hands and wrists in RA patients using conventional radiography

Imaging changes	Early RA	Advanced RA
Soft tissue changes	Symmetrical swelling around the PIPs and wrists	Atrophy
Mineralization	Juxta-articular osteoporosis	Diffuse osteoporosis
Subluxation	None	MCPs (proximal phalanges subluxed ulnarly and palmarly)
Joint space narrowing	Maintained	Uniform loss in PIPs, MCPs and carpal bones
Erosions	Mild, sometimes aggressive	Large, aggressive
Joint distribution	PIPs, MCPs, and pancarpal	PIPs, MCPs, and pancarpal

RA rheumatoid arthritis, *MCPs* metacarpophalangeals, *PIPs* proximal interphalangeals

A. Drosos et al. Rheumatology International (2019)

Can help us to differentiate RA from other inflammatory arthritides

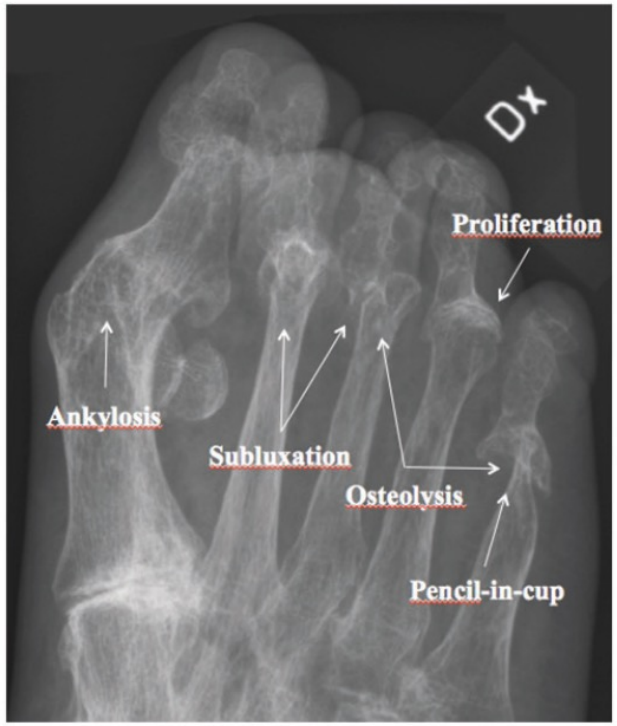


Fig. 1. Radiography of a 66-year-old female patient with psoriatic arthritis mutilans with a history psoriatic arthritis of 27 years with all the five classical sign of arthritis mutilans.

Radiopaedia

CPPD crystal deposition hand and wrist. Oblique radiograph of the hand shows chondrocalcinosis at the level of the triangular fibrocartilage (*black arrowheads)* as well as along the capsule of the metacarpophalangeal joints, particularly the second and third (*white arrows*). Note the “drooping” or “hooklike” osteophytes along the radial aspects of the heads of the second and third metacarpals (*white arrowheads*).

Figure 4. Tophaceous gout: X-ray shows soft tissue swelling, tophus and overhanging sign.

[Musculoskeletal Key]

MSK Ultrasound

- It can depict :

- Synovial hypertrophy-thickening
- Presence of fluid
- Tenosynovitis
- Bone erosions
- Bursitis
- Rheumatoid nodules
- Assessment of disease activity with use of (PD)
- Evaluation of treatment response
- Pathology of periarticular tissues (tendons, bursae, etc)
- Differential diagnosis from crystal induced arthropathies

Ultrasound guided injections (allow for increased accuracy)
Ultrasound guided synovial biopsies (patient stratification-treatment guidance)

V.K. Ranganath, et al. Best Practice & Research Clinical Rheumatology 2020

MSK Ultrasound

Disadvantages :

- Long learning curve
- High cost
- Time consuming especially in busy OPD
- Operator dependent
- It can’t depict bone marrow oedema
- It is not suited for deep joints

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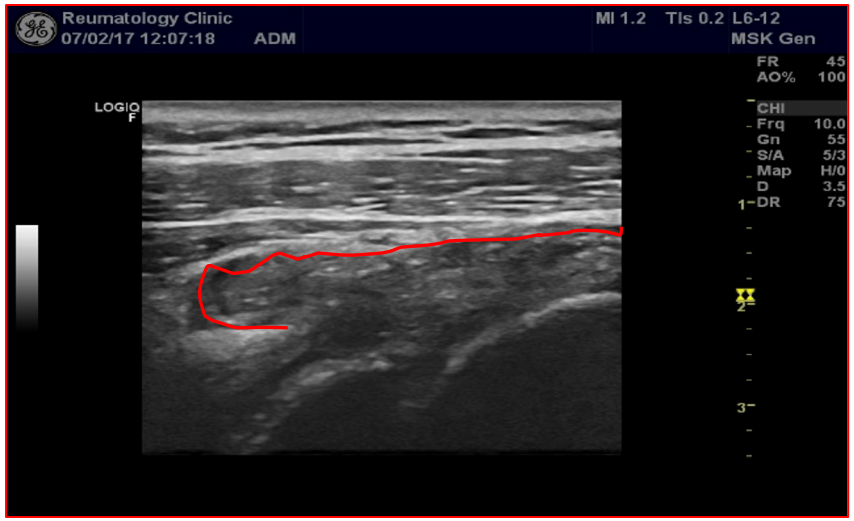
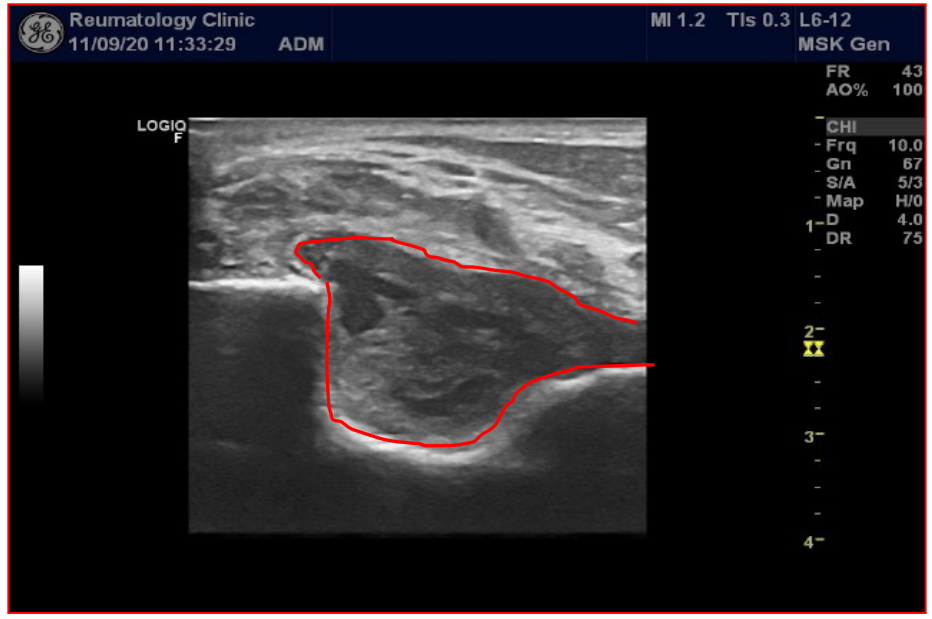
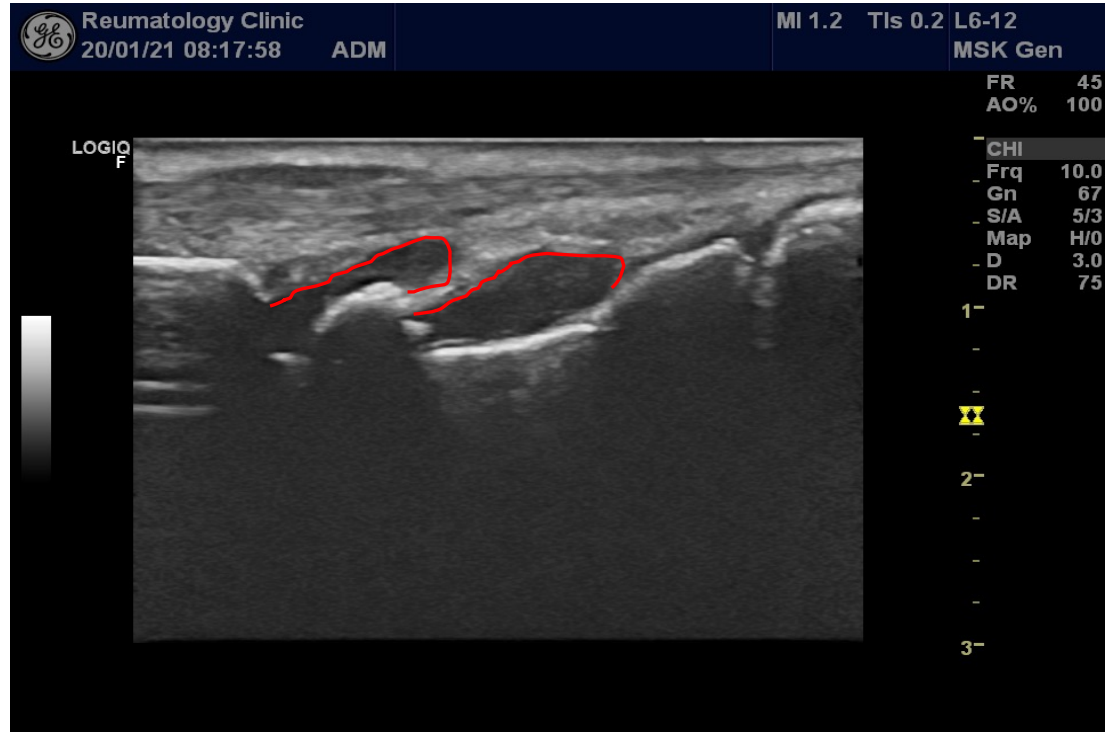
Synovial hypertrophy-thickening

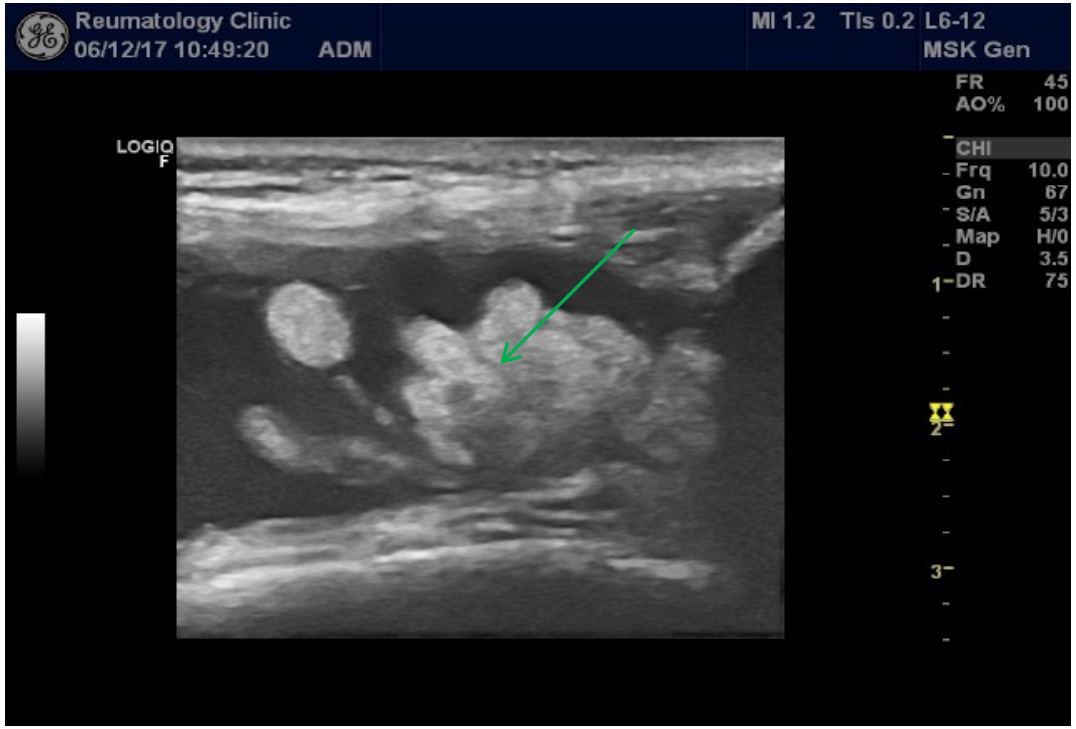


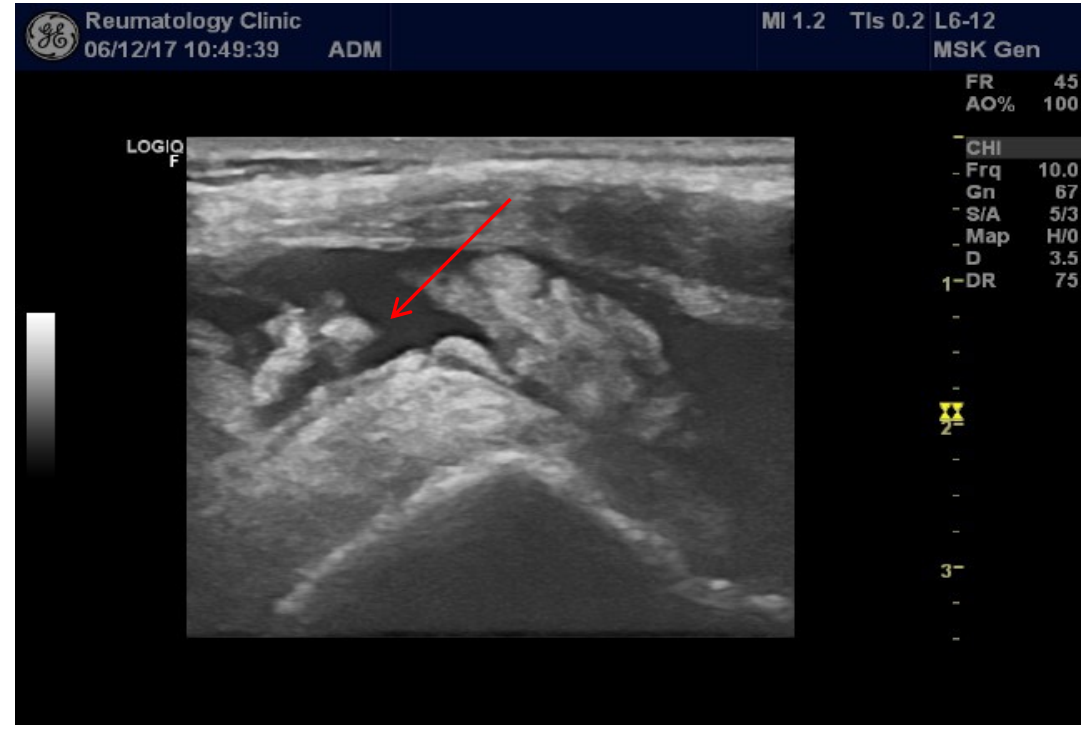


Synovial hypertrophy-thickening



Synovial hypertrophy-thickening





- Red arrow: fluid
- Green arrow: hypertrophic synovium

Bone erosions

Figure 2 Erosion in 5th metatarsophalangeal joint. (A) Erosion in longitudinal view and (B) transverse view. PL, plantar lateral; PM, plantar medial; MT, metatarsal; P, Phalanx; JS, joint space. This was scored 2.

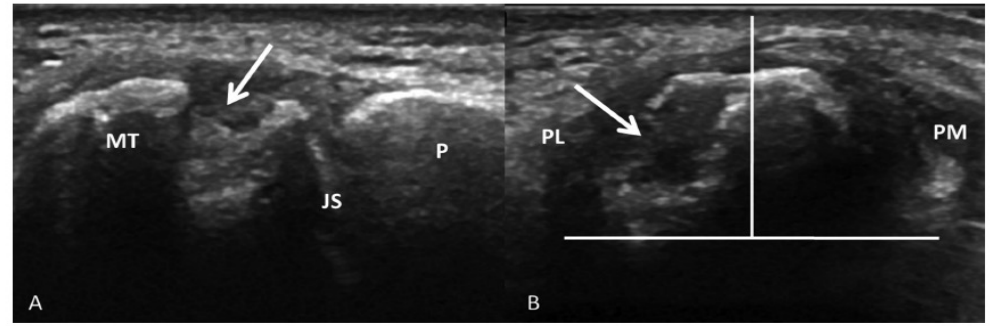


Fig. 1 RA. Second metacarpophalangeal joint on a longitudinal dorsal scan. Grey-scale US images showing bone erosions at the metacarpal head level (←). Maximal diameters of erosion are 0.9 mm (**A**), 1.9 mm (**B**), 3.8 mm (**C**) and 5.8 mm (**D**), corresponding to Grade 1, Grade 2, Grade 3 and Grade 4, respectively, according to the semiquantitative scoring system proposed by Kane *et al*. [19]. The white lines indicate where the calliper was located for the measurement of erosions. m: metacarpal bone; p: proximal phalanx.

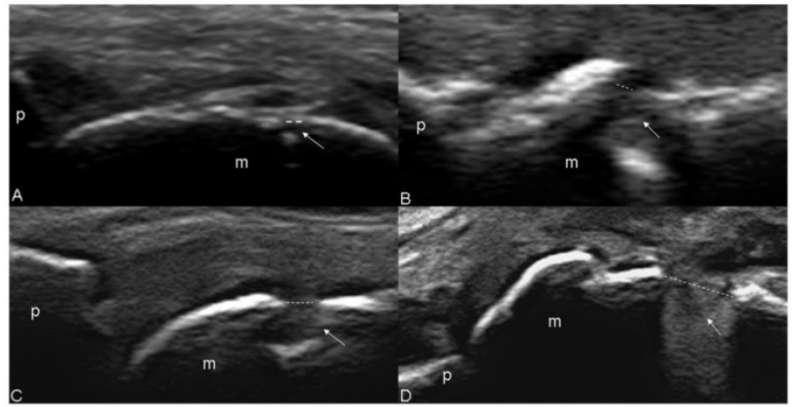
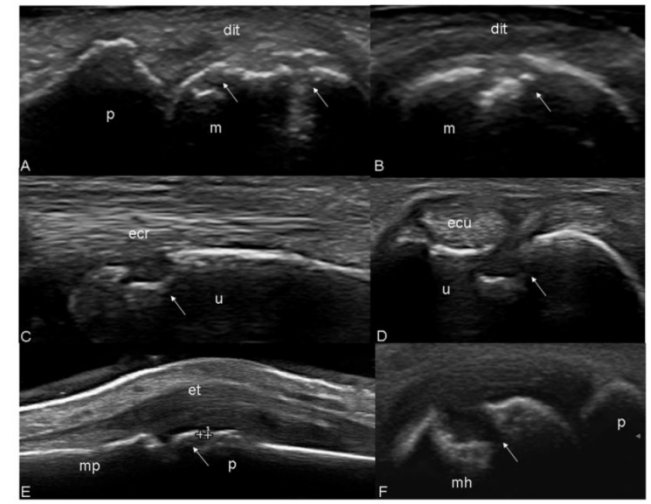


Fig. 4 RA. Grey-scale US features of bone erosions (←) of the second metacarpal head on longitudinal (**A**) and transverse (**B**) lateral scans; ulnar head on longitudinal (**C**) and transverse (**D**) lateral scans. m: metacarpal bone; p: proximal phalanx; u: ulnar bone; dit: first dorsal interosseous tendon; ecr: extensor carpi ulnaris tendon.



Marwin Gutierrez et al. Rheumatology 2011

Tenosynovitis

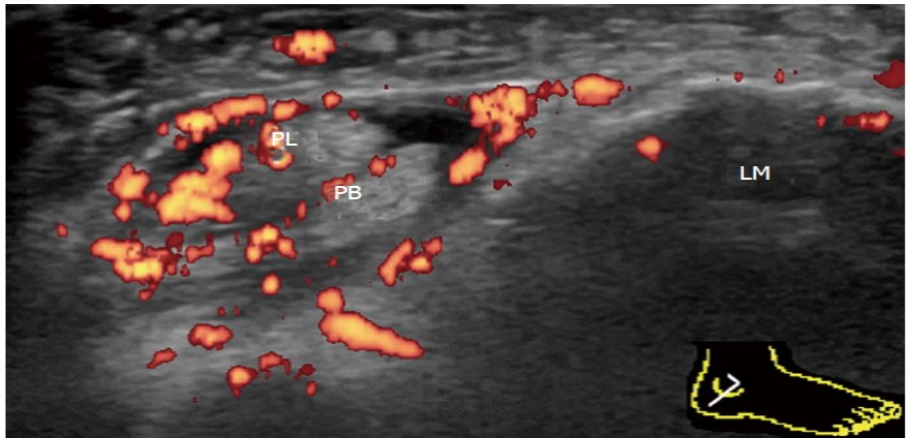


Figure 13 Proliferative tenosynovitis of the peroneus longus and brevis in rheumatoid arthritis. Transverse power Doppler sonogram through the lateral ankle at the level of the lateral malleolus shows thickening and marked hyperemia of the tenosynovium surrounding the peroneus longus and peroneus brevis. PL: Peroneus longus; PB: Peroneus brevis; LM: Lateral malleolus.

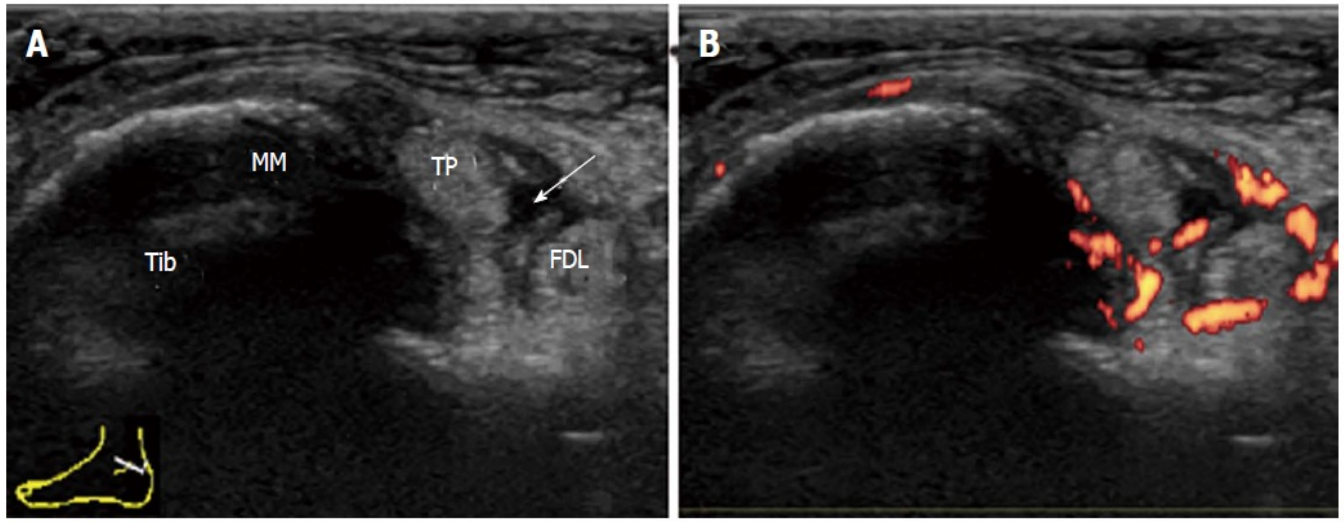
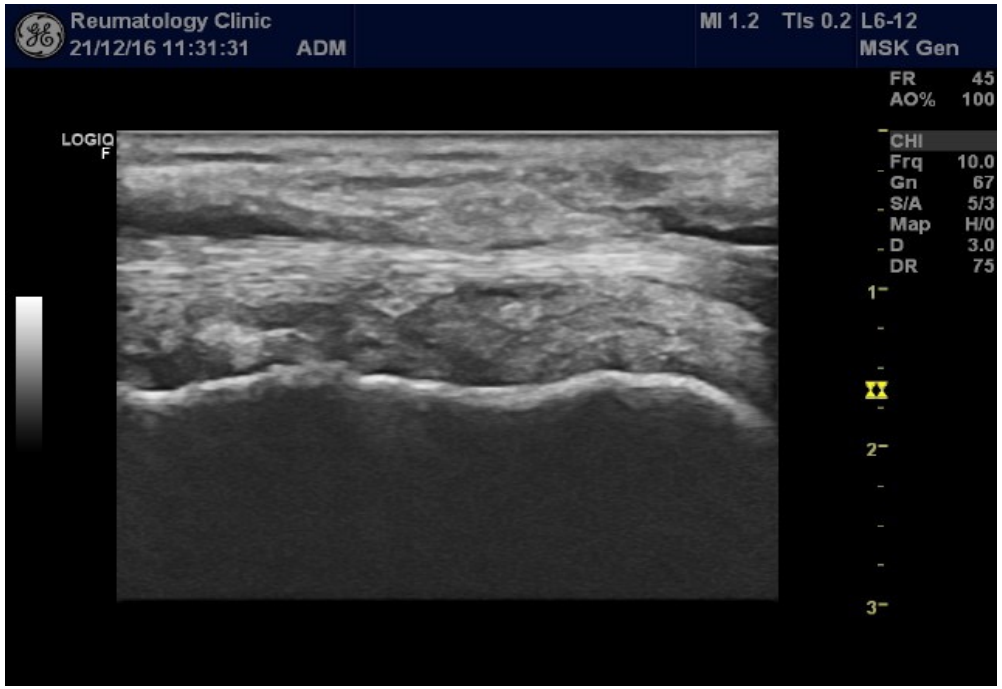
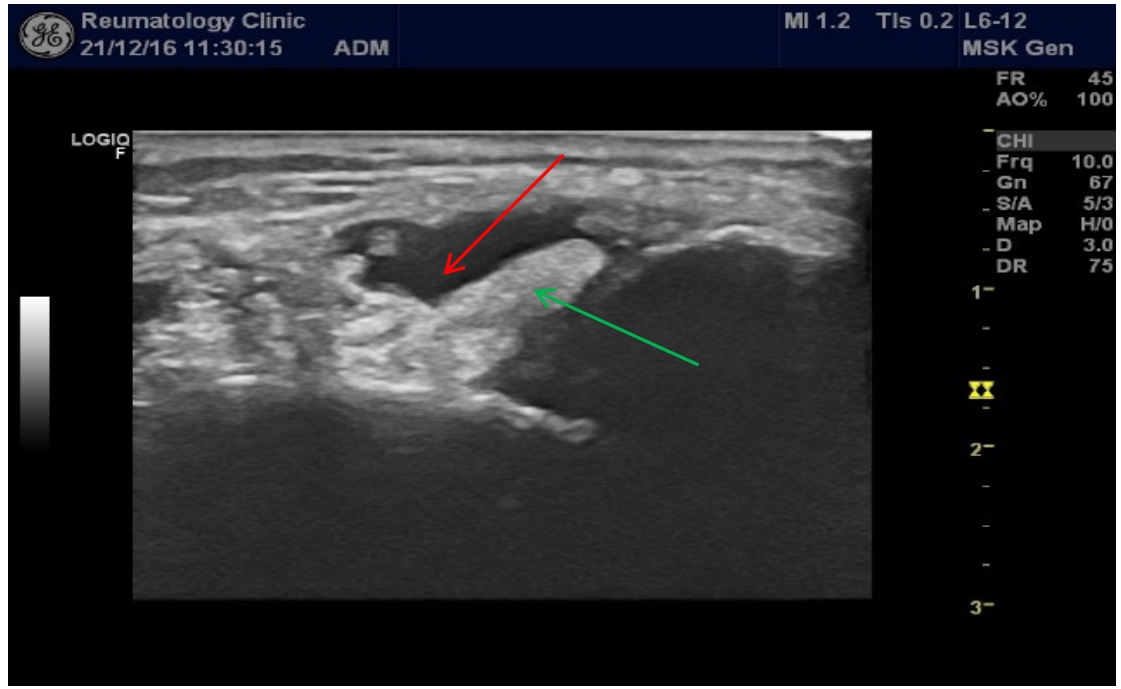


Figure 10 Proliferative tenosynovitis of the tibialis posterior in rheumatoid arthritis. A: Transverse grey-scale sonogram through the medial ankle at the level of the medial malleolus (MM). Hypoechoicthickened tenosynovium of the TP with anechoic effusion (arrow) within the sheath is depicted; B: Power Doppler sonogram shows hyperemia of the tenosynovium surrounding the TP and the FDL. Tib: Tibia; TP: Tibialis posterior; MM: Medial malleolus; FDL: Flexor digitorum longus.

Suzuki T et al. *World J Orthop 2014*

Presence of fluid within TB sheath in RA patient





- Red arrow: fluid
- Green arrow: tendon

Power Doppler activity

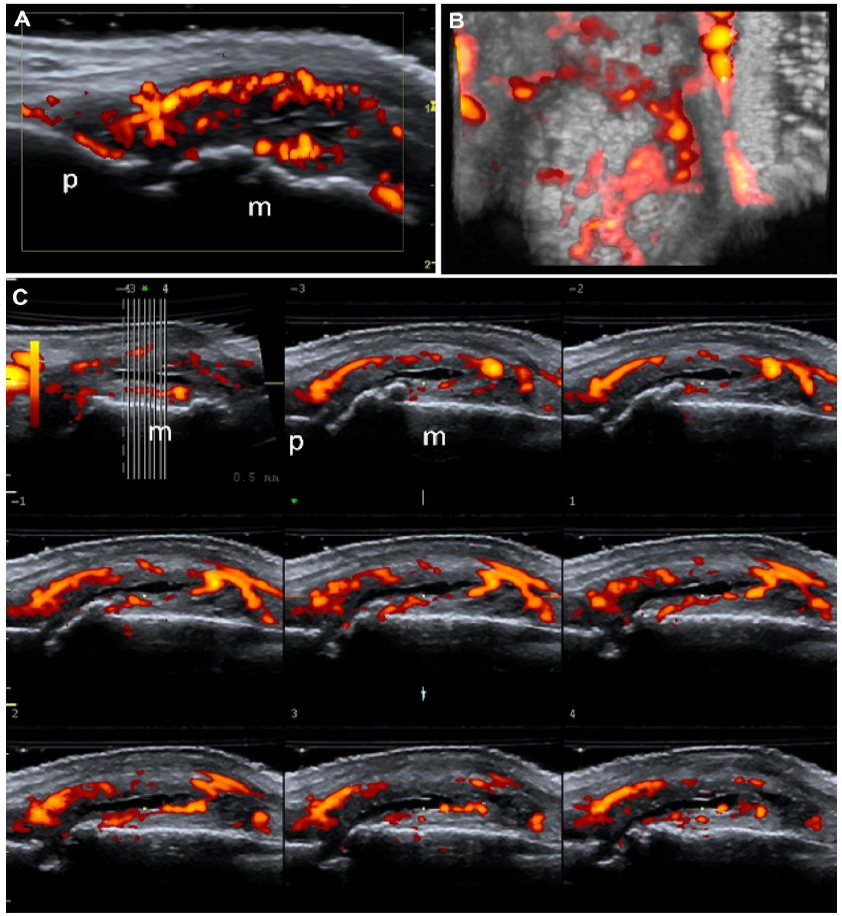
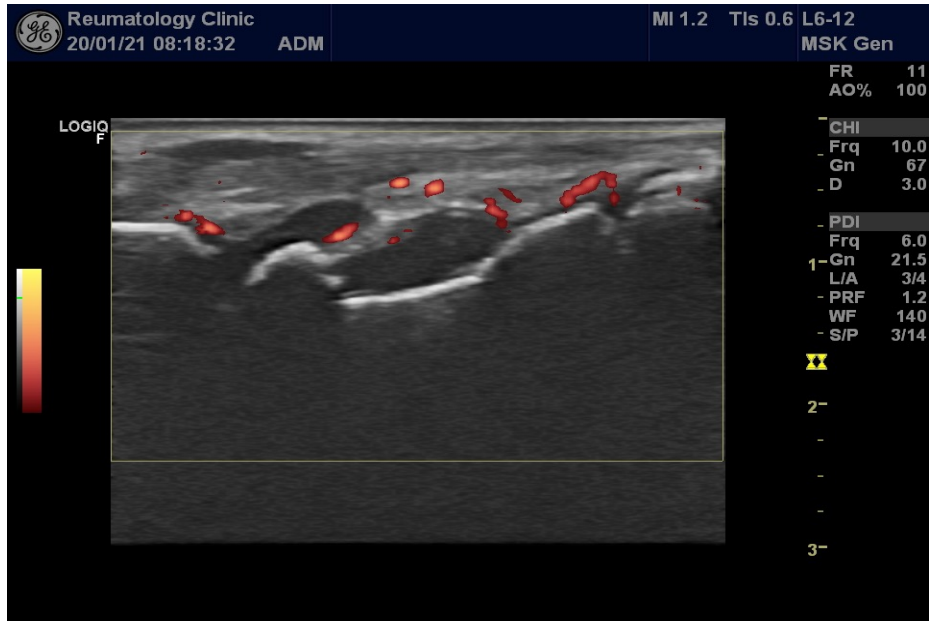


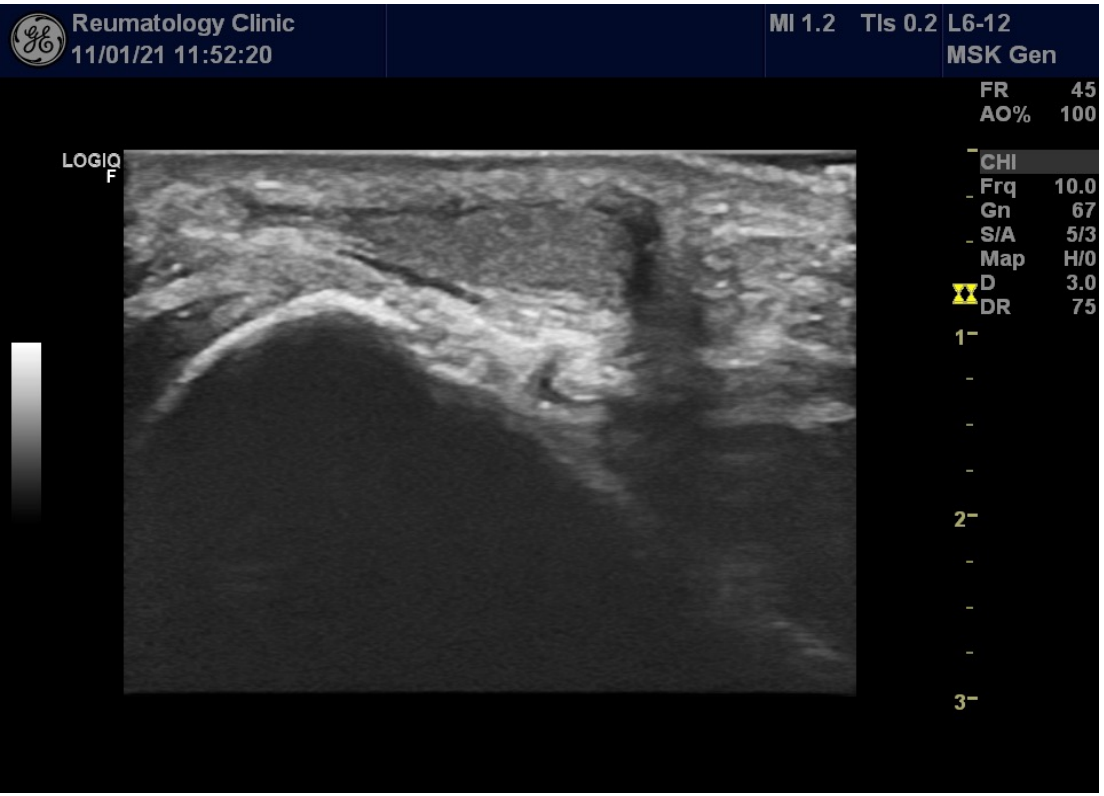
Figure 5 Rheumatoid arthritis. Power Doppler images of a second metacarpophalangeal joint. (**A**) Conventional two-dimensional ultrasound image acquired on a dorsal longitudinal scan. (**B**) Corresponding three-dimensional view. (**C**) Mosaic of pictures automatically displayed by tomographic ultrasound imaging software showing images obtained on adjacent scanning planes, 0.5 mm away from each other.
Abbreviations: m, metacarpal bone; p, proximal phalanx.

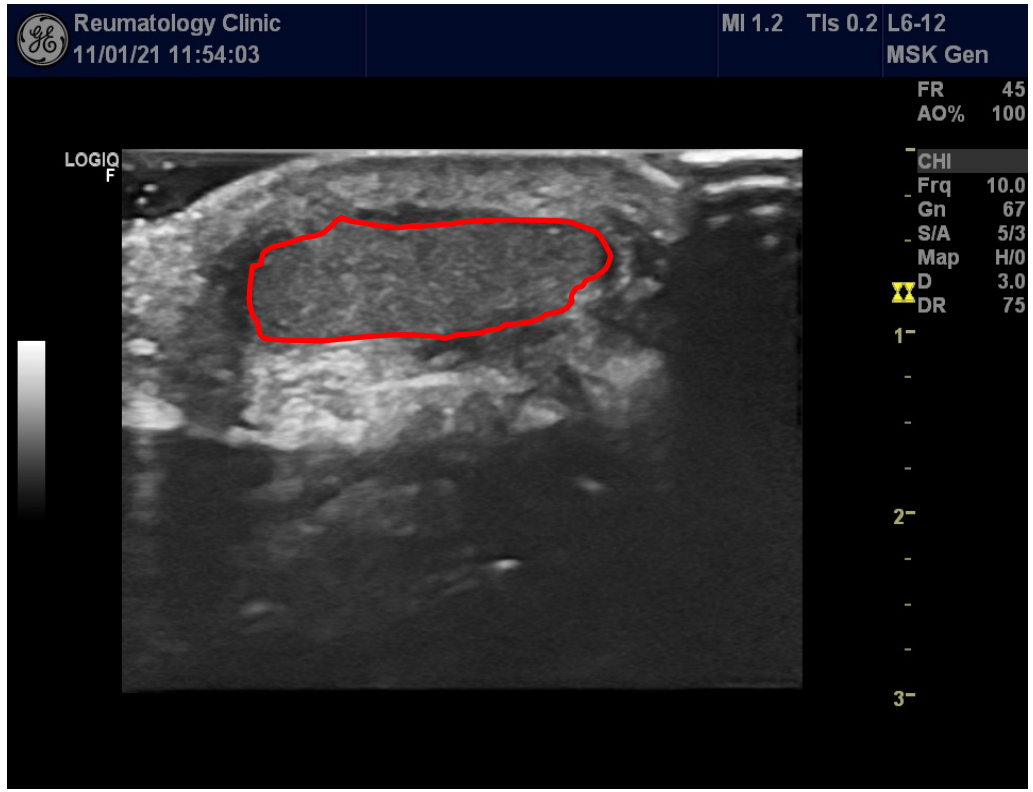


Filippucci et al. Reports in Medical Imaging 2013

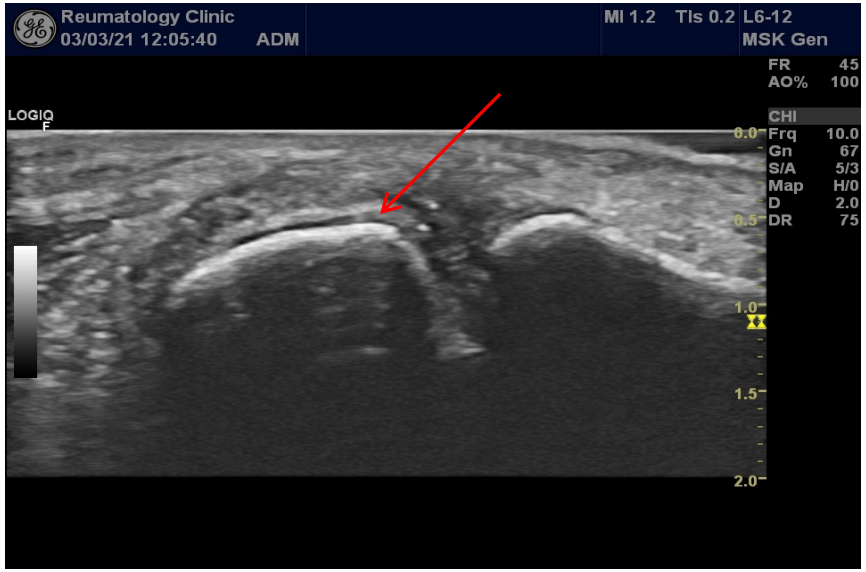
Subacromial- Subdeltoid bursitis with extensive synovial hypertrophy

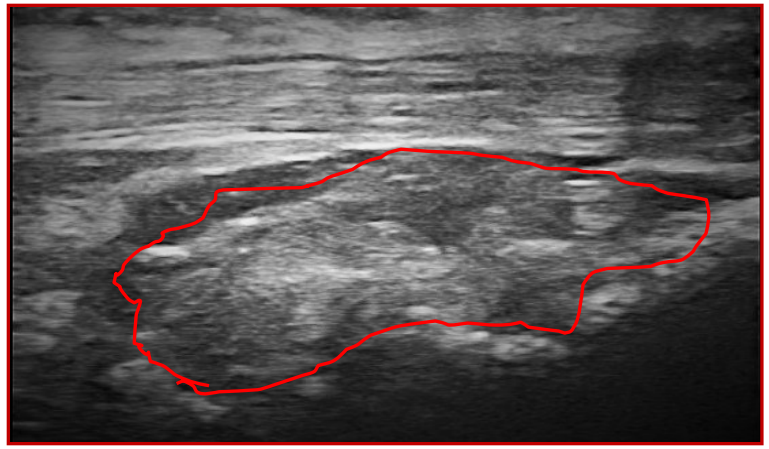
Rheumatoid nodule

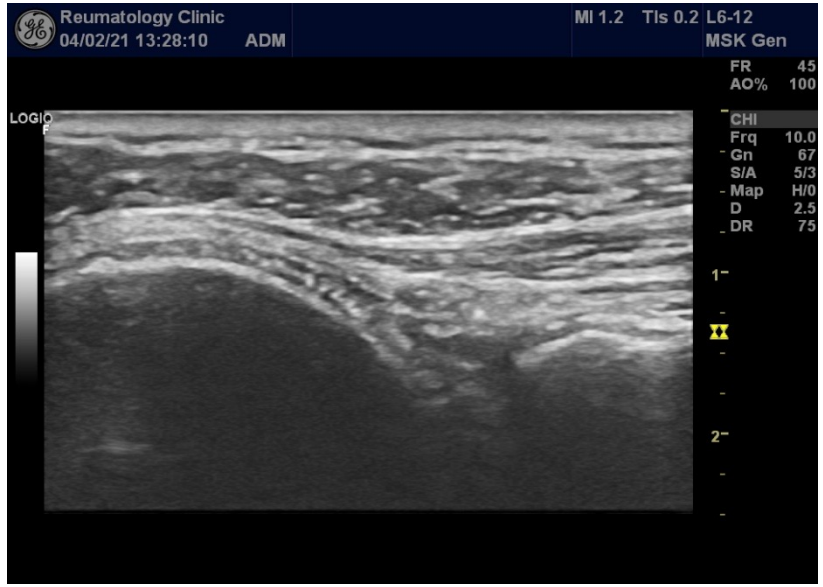


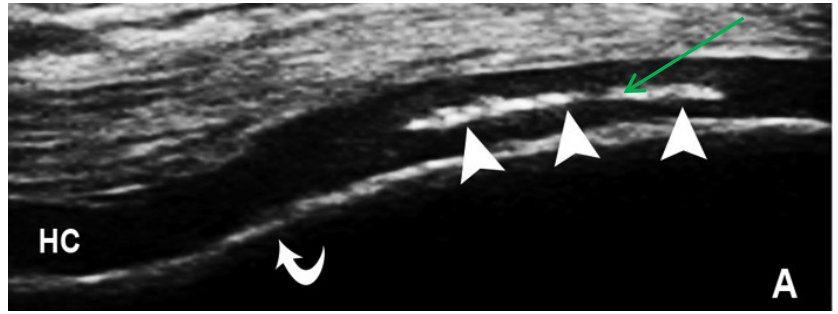


CPPD/GOUT









- Red arrow: Double contour sign
- Green arrow: CP crystals within HC

G. Filippou et al. Osteoarthritis and Cartilage (2016)

Treatment response

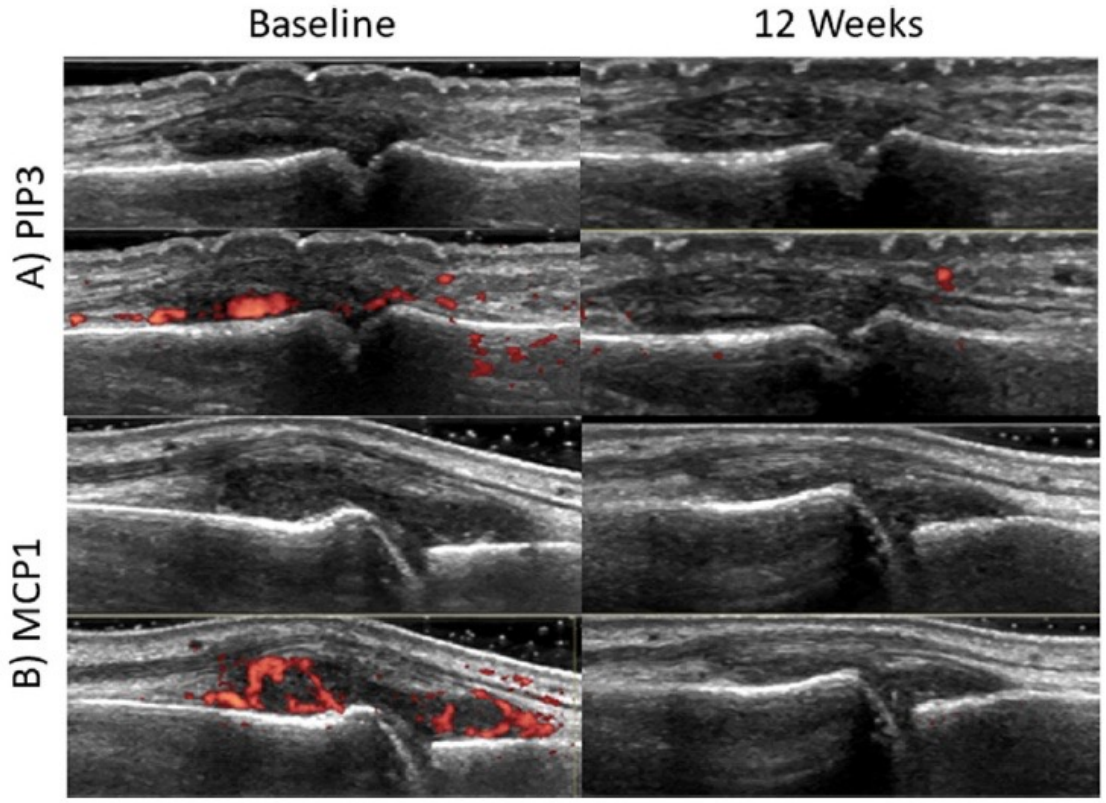


Fig. 1 Baseline and 12-Week MSUS images after treatment with tofacitinib (GSUS and PDUS). Panels **a** and **b** show images of PIP3 and MCP1 in both B-mode and power Doppler before and after treatment with tofacitinib

Razmjou et al. BMC Rheumatology (2020)

Ultrasound guided injections

- Using imaging guidance leads to better accuracy compared with palpation-guided interventions.

- Positioning a needle or another instrument in, rather than outside the target reduces the risk of adverse events

- It could also have beneficial effects on short-term and long-term pain, as well as on efficacy outcomes.

- Patient perception and satisfaction

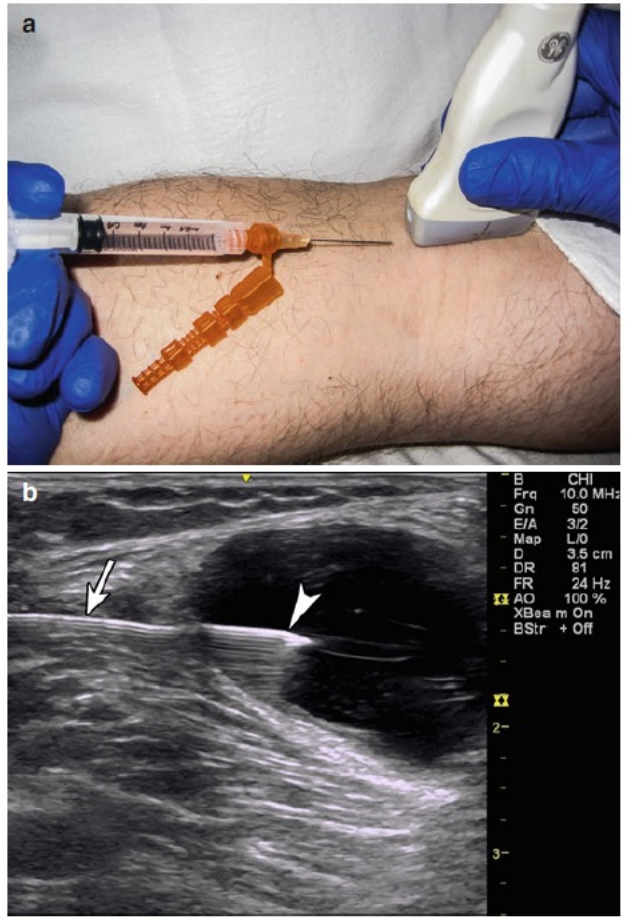


Fig. 6.14 (a) Example of sagittal probe position over posterior knee with in-plane injection technique. (b) *Arrow* indicates needle, *arrowhead* indicates needle tip within Baker's cyst

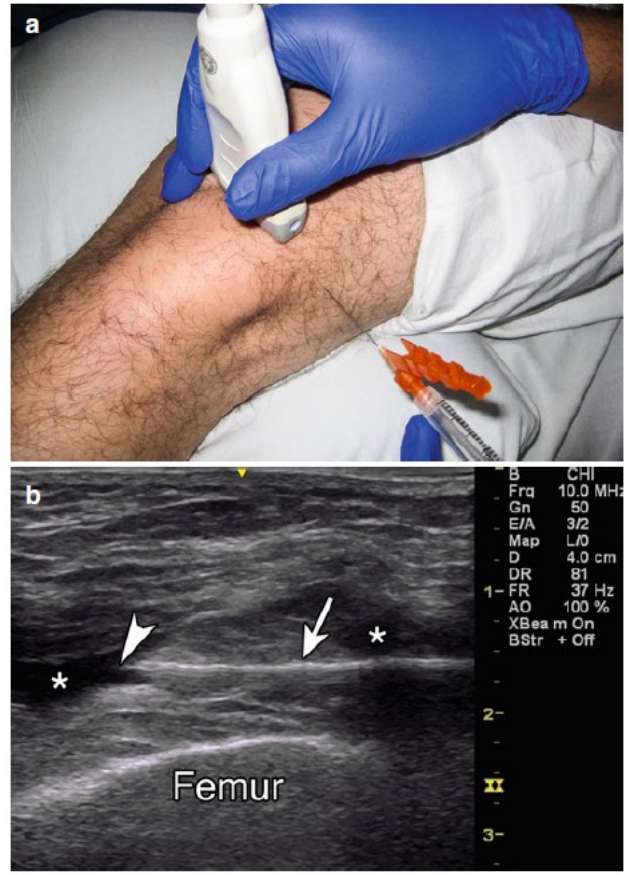


Fig. 6.2 (a) Example of probe position over suprapatellar joint recess with in-plane injection technique. (b) *Arrowhead* indicates needle tip within joint recess, *arrow* points to needle, *asterisk* indicates effusion, femur labeled

Bosch P, *et al. RMD Open 2021*

Ultrasound guided synovial biopsies

FIGURE 6 | Insertion of biopsy needle.

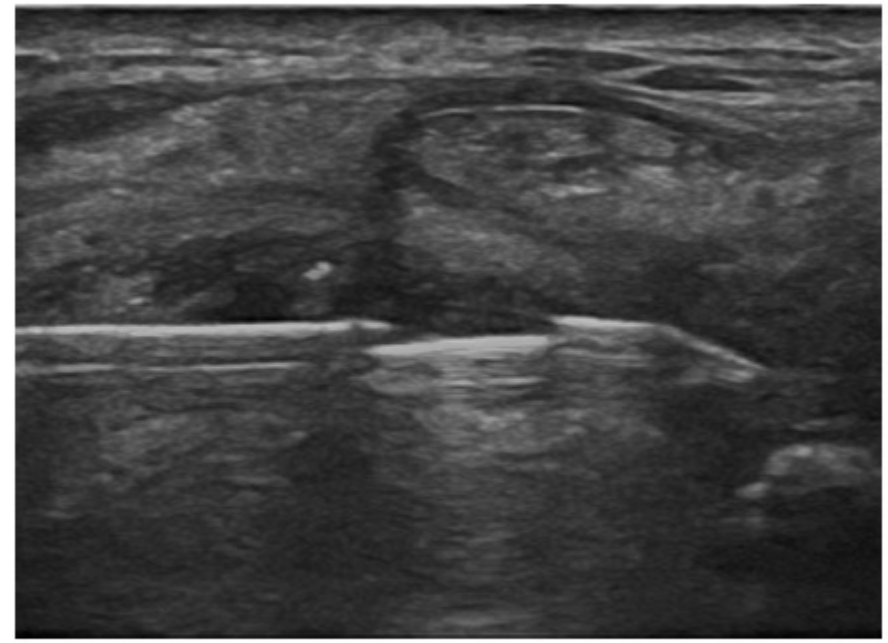


FIGURE 7 | Biopsy needle inside the joint.

F. Saraiva. Ultrasound-Guided Synovial Biopsy . Frontiers in Medicine. April 2021

MRI

- Magnetic resonance imaging can assess all the structures affected by RA.
- Very useful for imaging of deep joints and for differential diagnosis from other pathologies
- It can depict bone marrow oedema
- It can detect early and accurate synovitis, tenosynovitis and erosions (even in preclinical cases)
- The T1-weighted (T1W) sequence is used to detect anatomy . T2-weighted (T2W), proton density-weighted fat-saturated (PDW-FS) and short-tau inversion recovery (STIR) sequences are ideal modalities to detect free fluid and regions of inflammation.
- Gadolinium-contrasted T1W sequences allow further detection of active inflammation in areas of enhanced vascularity

V.K. Ranganath, et al. Best Practice & Research Clinical Rheumatology 2020

MRI

Disantvantages:

- Not real time examination
- High cost , limited availability
- Time consuming
- Contraindications (pacemaker, metallic implants etc)
- Claustrophobia, contrast allergy

V.K. Ranganath, et al. Best Practice & Research Clinical Rheumatology 2020

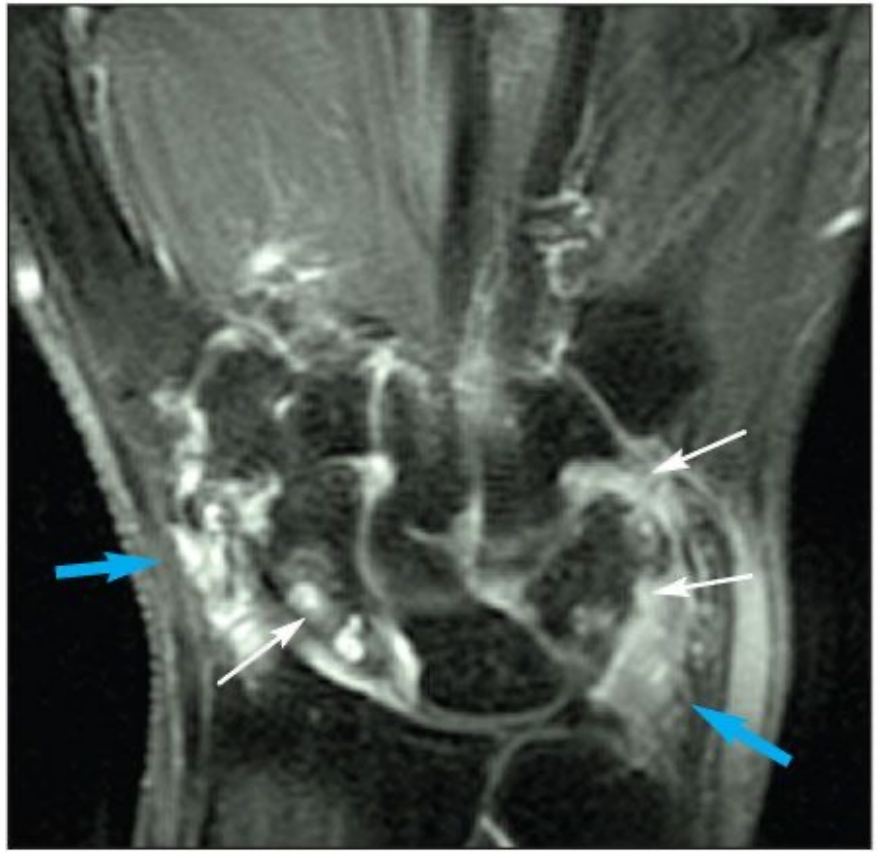


Figure 2 – A coronal postgadolinium-enhanced T1–fat-saturated image shows prominent areas of enhancement at the radioscaphoid and ulnocarpal articulations consistent with synovitis (blue arrows). Multiple erosions also are present (thin arrows)

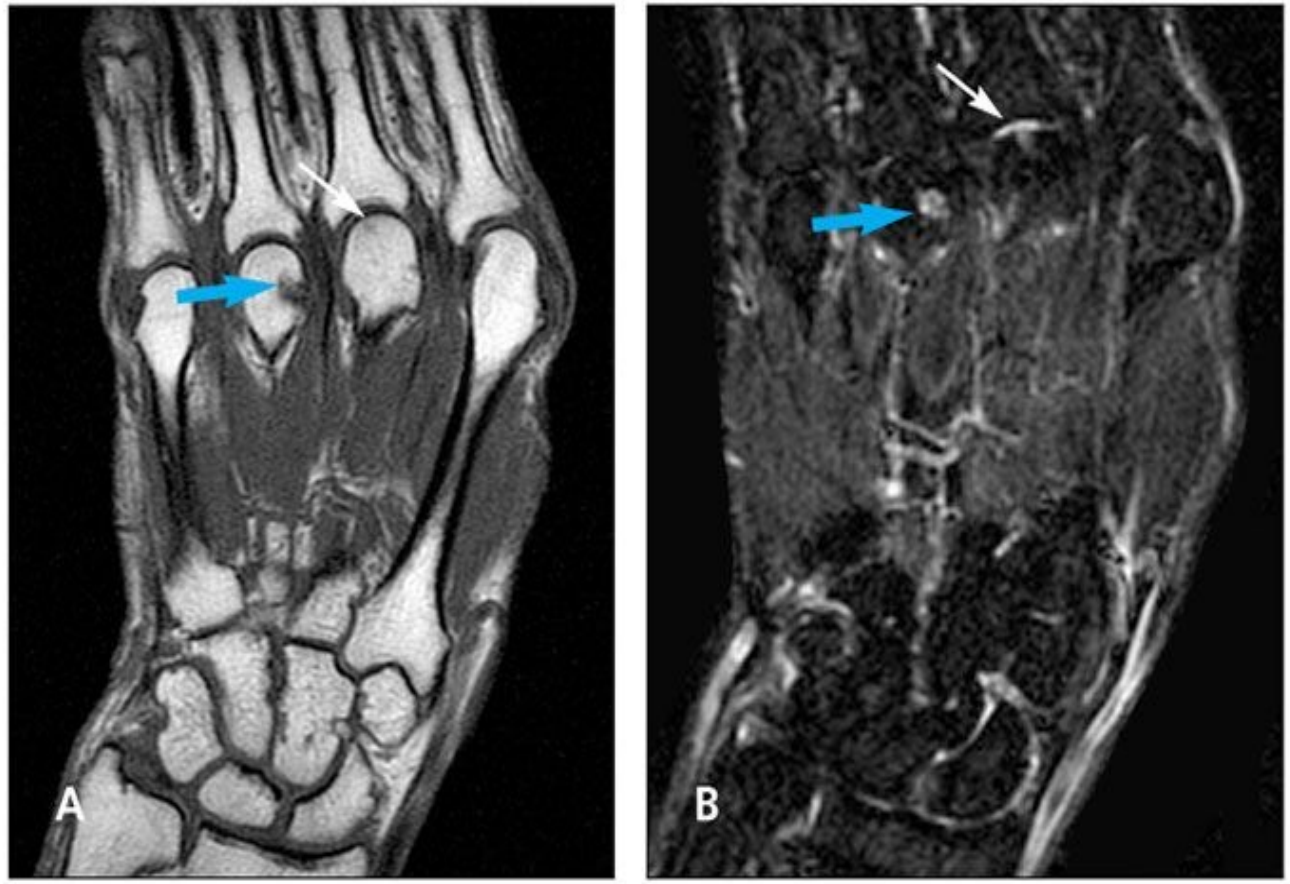


Figure 1 – A diagnosis of an erosion is made on MRI by identifying a sharply marginated bone lesion in a juxta-articular location typically seen in inflammatory arthritis. Coronal T1 (A) and inversion recovery (a T2-weighted sequence) (B) images show focal erosion in the fourth metacarpal head (blue arrows). A more subtle erosion is seen in the third metacarpal head (thin arrows).

M . Walter et al. The Journal of Musculoskeletal Medicine (2009)

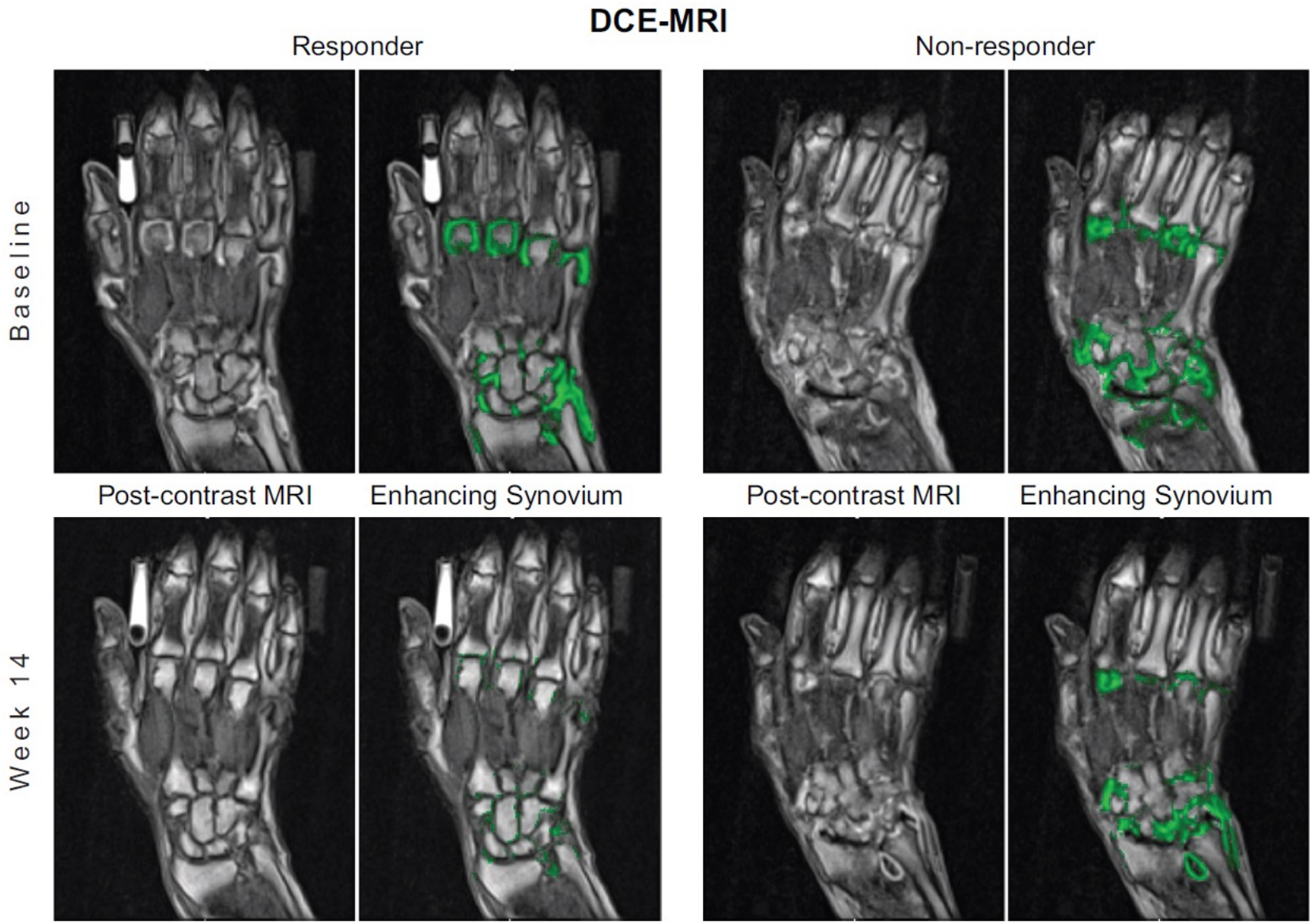


Fig 3. Baseline vs Week 14 DCE-MRI. Enhancing Synovium (green regions of interest) decreased dramatically from baseline to Week 14 in a clinical responder treated with infliximab (left), but was largely unchanged in a non-responder treated with placebo (right). Responder was defined as change from baseline in DAS28(CRP) >1.2 and non-responder as <0.6.

Chan Beals et al. MRI assessments in a randomized trial of infliximab. PLOS ONE 2017

ure 2 Imaging examples. (A) 51-year-old male patient with seronegative RA. No erosions are apparent in CT or in any of three MRI sequences. (B) 52-year-old female patient with seronegative RA during therapy with methotrexate. An erosion he head of metacarpal bone II and a pseudoerosion at the capitate bone are clearly visible in all modalities (arrowheads). wever, T1 and VIBE show a false-positive detection of another erosion in the head of the metacarpale bone II (arrow). 64-year-old male patient with seronegative RA treated with corticosteroids. VIBE and SWI show a cystic bone lesion in lunate bone (arrow), which is misinterpreted as an erosion in T1w imaging. A small erosion is detected in the head of tacarpal bone V in CT and SWI (arrowhead), whereby T1w and VIBE overestimated this lesion. SWI, susceptibility-weighted aging; T1w, T1-weighted; VIBE, volumetric interpolated breath-hold examination.

- Susceptibility-weighted imaging (SWI) improves the specificity of MRI for erosion detection and is superior to standard T1-weighted (T1w) imaging and 3D-gradient echo sequences.

- SWI provides additional information based on direct depiction of bone structures such as calcifications, which is limited with conventional MRI sequences.

Ulas ST, *et al. RMD Open* 2022;

Practice points

- MSUS and MRI can be helpful in making a diagnosis of RA as both modalities are more sensitive than clinical examination for the detection of joint synovitis, tenosynovitis, tendonitis, and bursitis.
- Inflammation detected by use of MSUS or MRI may influence decisions on when to start DMARDs.
- With strict use of T2T algorithms, three recent RCTs suggest that there was no benefit to the utilization of MSUS/MRI targets in treatment strategies.
- Subclinical inflammation detected by MSUS/MRI may be predictive of RA flares and radiographic progression.
- MSUS is a valuable tool for evaluation of the source of pain.

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CT

- Currently limited usefulness on every day clinical practise
- Modern techniques such are HR peripheral quantitative CT can give us 3D reconstruction images
- Early detection , morphometric and volumetric evaluation of bone erosions
- Other techniques such as DECT can help us to differentiate crystal induced arthropathy
- Problems: limited availability, radiation , no imaging of synovium and periarticular tissues & contraindicated in pregnancy

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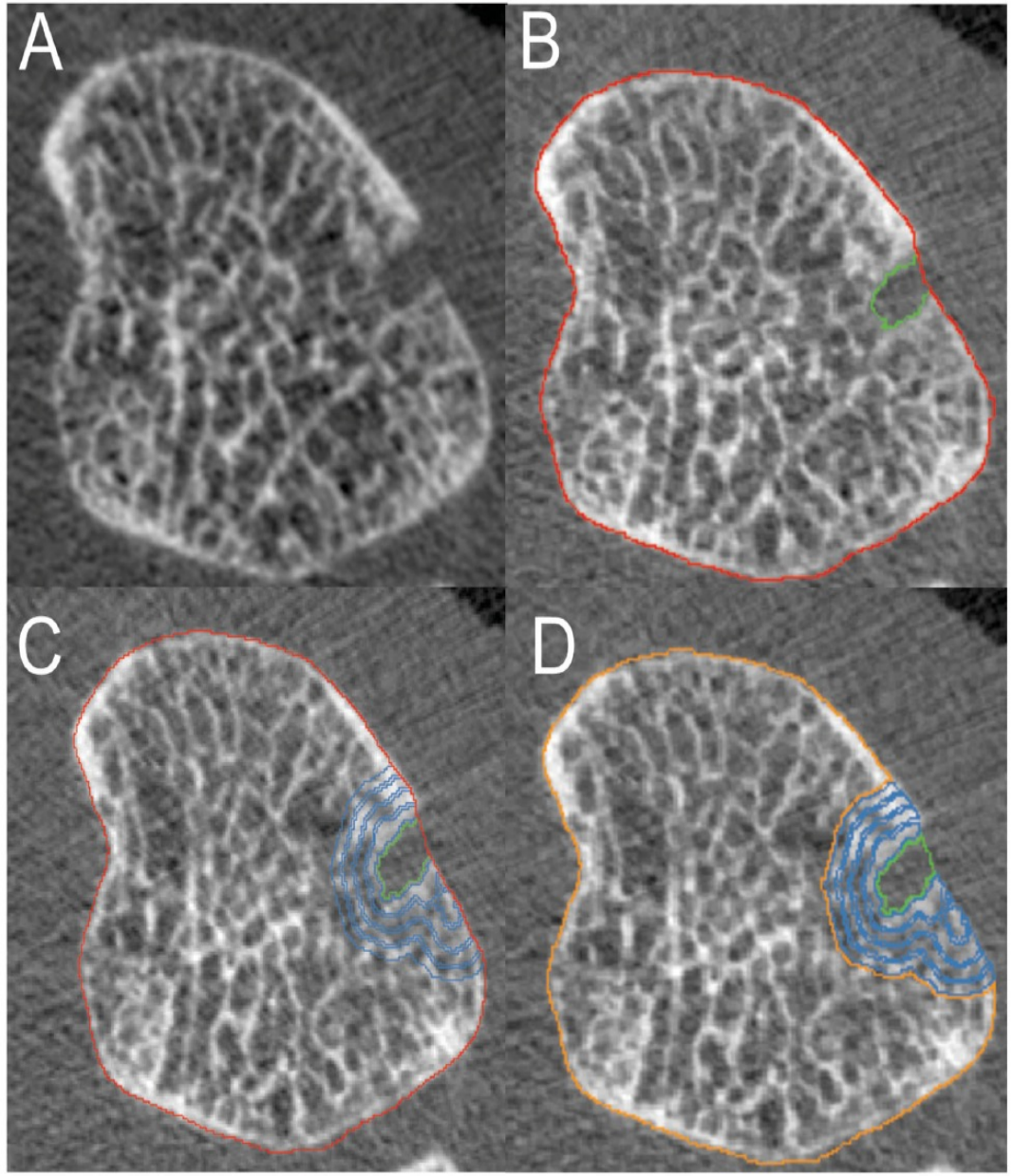

Figure 3. HR-pQCT scan of a 2nd metacarpal head of a patient with rheumatoid arthritis in an axial plane. (A) Erosion at quadrant IV; (B) MIAF bone segmentation as a continuous line around metacarpal head and erosion segmentation as a line inside metacarpal head; (C) Four different layers of bone mineral density (BMD) values around erosion (lines around bone erosion) provided by Medical Image Analysis Framework (MIAF); (D) BMD of total metacarpal head (MCP) analyzed by MIAF as a continuos line at the edge of metacarpal head and without the area around the bone erosion.

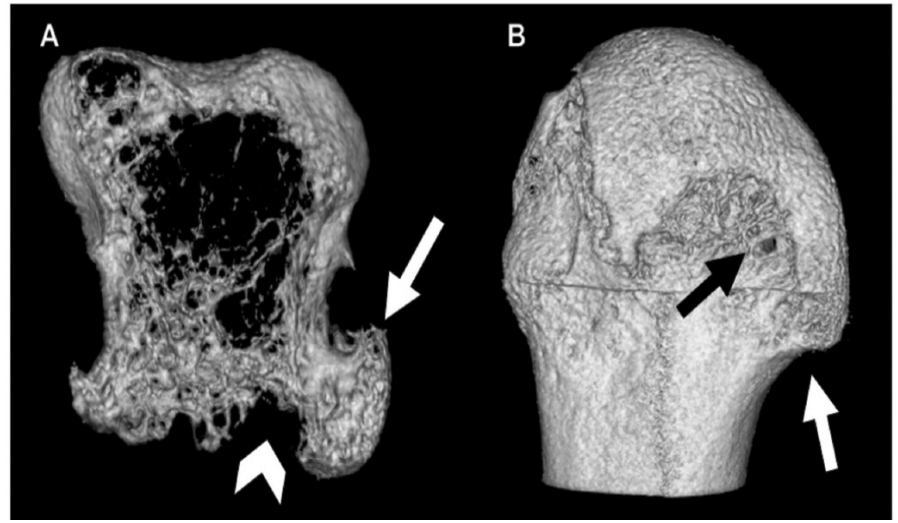

Figure 4. HR-pQCT scan of 2nd metacarpal heads. (A) and (B) - rheumatoid arthritis patient: in (A) axial slice showing close association between osteophyte (white arrow) and erosion (white head arrow). (B) the same bone lesions in a 3D reconstruction, erosion (black arrow) and osteophyte (white arrow) represented

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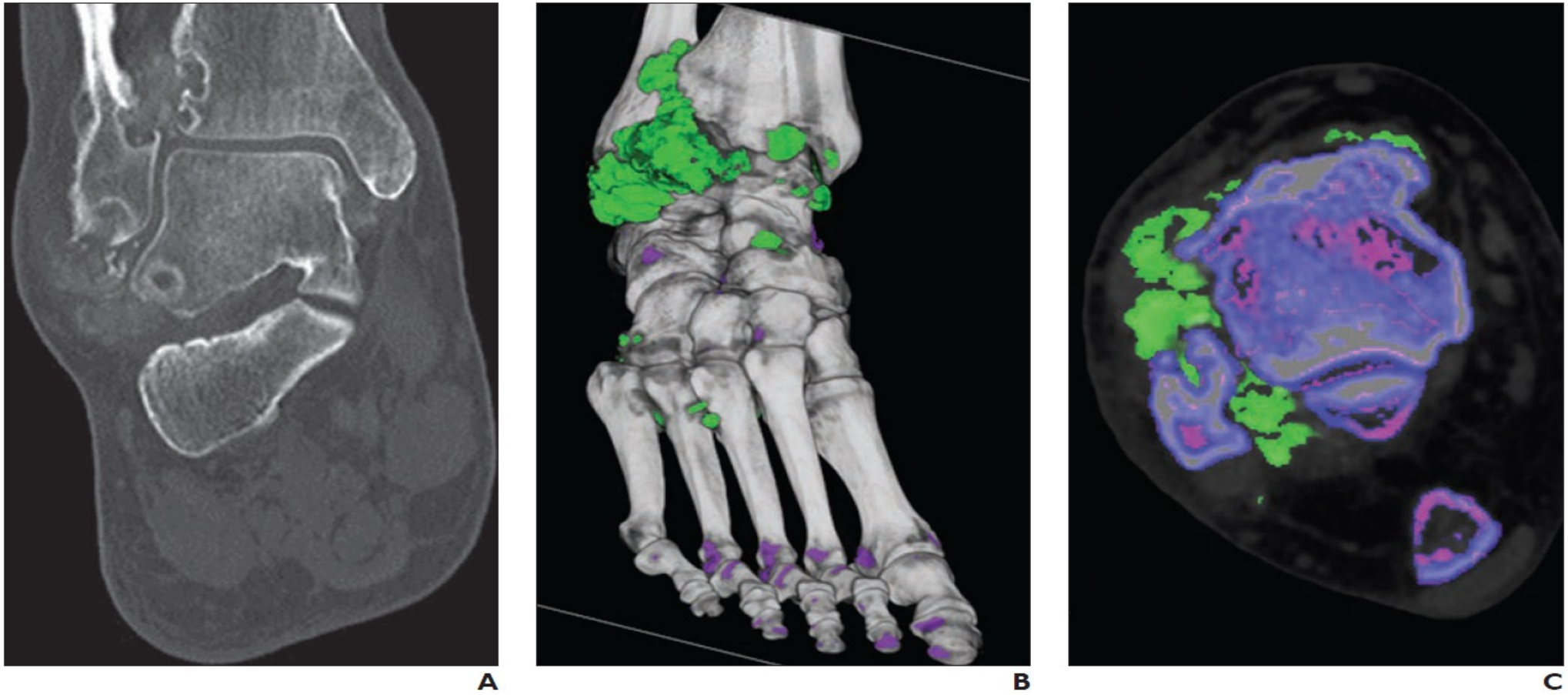

Fig. 7—42-year-old man with right ankle pain.
A, Coronal multiplanar reformmated 2D CT image of right ankle and foot shows high-attenuation tophi associated with erosions in distal tibia, fibula, and talus.
B, Axial 2D dual-energy CT (DECT) with color mapping shows uric acid deposits (*green*) in periarticular tissues of ankle, extending into erosion in anterior fibula.
C, Three-dimensional DECT with color mapping shows uric acid depositions (*green*) within ankle joint and midfoot.

Girish et al. *AJR 2013*

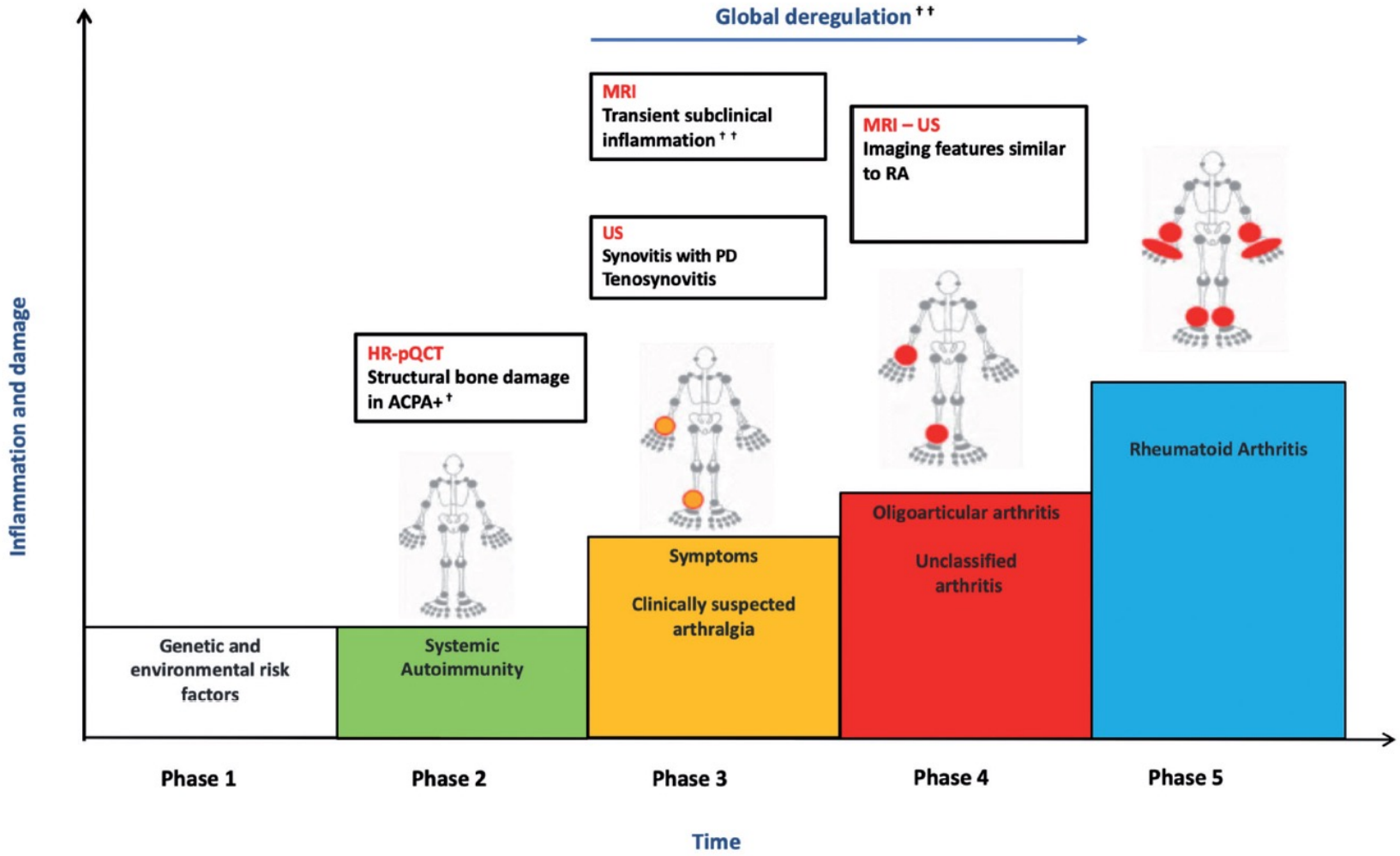

Fig. 1. The detection of inflammation and damage by imaging tools in the preclinical phases of RA.
†Kleyer *et al*. *Ann Rheum Dis* 2014; 73(5): 854-60; ††Ten Brick RM *et al*. *RMD Open* 2018; 4: e000748. Figure 1 adapted with permission from van Steenbergen HW *et al*. Arthritis Rheum 2013; 65: 2219-32.

A. Zabotti et al. Clinical and Experimental Rheumatology 2020

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Table 2. Comparison of ultrasound (US), magnetic resonance imaging (MRI) and high-resolution peripheral quantitative CT (HR-pQCT): advantages and disadvantages

	US	MRI	HR-pQCT
Advantages	*Can visualizes structures in real-time*	*Can visualizes bone marrow edema*	*Very high resolution (<142 µm)*
	No ionizing radiation	*No ionizing radiation*	*High sensitivity for bone changes*
	Relative accessible and inexpensive	*Can be used in pregnancy*	*Can assess bone density and micro-architectural changes*
	Patient friendly	*Comparison of sequential images relatively easy*	*Comparison of sequential images relatively easy*
	Can be used in pregnancy		*Short scan time (2.8 minutes to acquire an axial 9.02 mm section)*
	No contrast agent required		
Disadvantages	*Operator dependent*	*Long examination time*	*Radiation involved (up to 24µSv, which is 1/5 of a conventional chest X-ray)*
	Cannot penetrate bone	*Relatively higher cost and lower availability*	*Limited availability*
	Poor resolution for deep seated joints	*Potential adverse events when administration of contrast agent*	*Cannot visualize soft tissue structures*
		Presence of contra-indications, eg: claustrophobia, certain metallic implants, contrast agent allergy	*Cannot assess joints proximal to elbows and knees*
			Limited field of view (e.g. metacarpophalangeal joints 2-4 only)
			Contra-indicated in pregnancy

Extra-articular disease

- Don’t forget the role of HRCT and ultrasound in RA-ILD

- More advanced techniques such are MRA and PET-CT are used for vascular imaging

LUS in RA-ILD

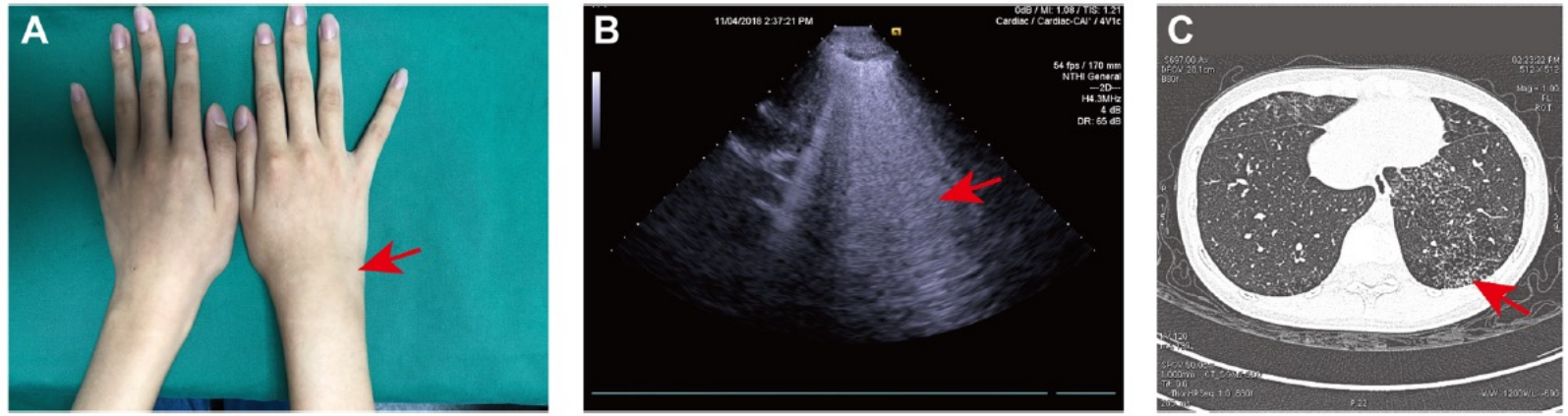

Fig. 2 Case 1. **A** Physical examination showed right wrist swelling (arrow). **B** Lung ultrasound revealed multiple B-lines (arrow). **C** HRCT demonstrated diffuse ground glass opacity, reticular abnormalities, and traction bronchiectasis (arrow)

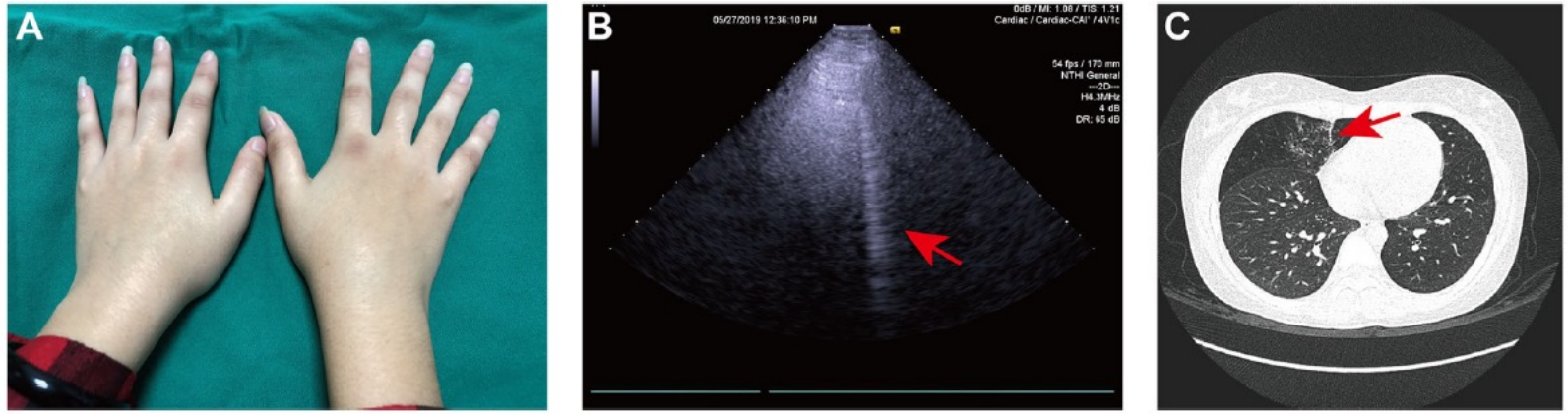

Fig. 3 Case 2. **A** Physical examination showed polyarthritis of the hand joint. **B** Lung ultrasound revealed B-lines (arrow). **C** HRCT demonstrated ground glass opacity and interlobular septal thickening pattern located at the anterior segment of the right upper lobe (arrow)

Wang et al. Arthritis Research & Therapy (2021)

Conclusions

- All patients with initial diagnosis of RA must have at base line conventional x-rays (hands and feet)
- Ultrasound is powerful but complementary tool in the hands of Rheumatologist
- Use MRI carefully and wisely.
- Don’t use imaging in place of clinical examination