Seronegative Inflammatory arthropathy: Exploring beyond Rheumatoid Arthritis

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Consultant sonographer

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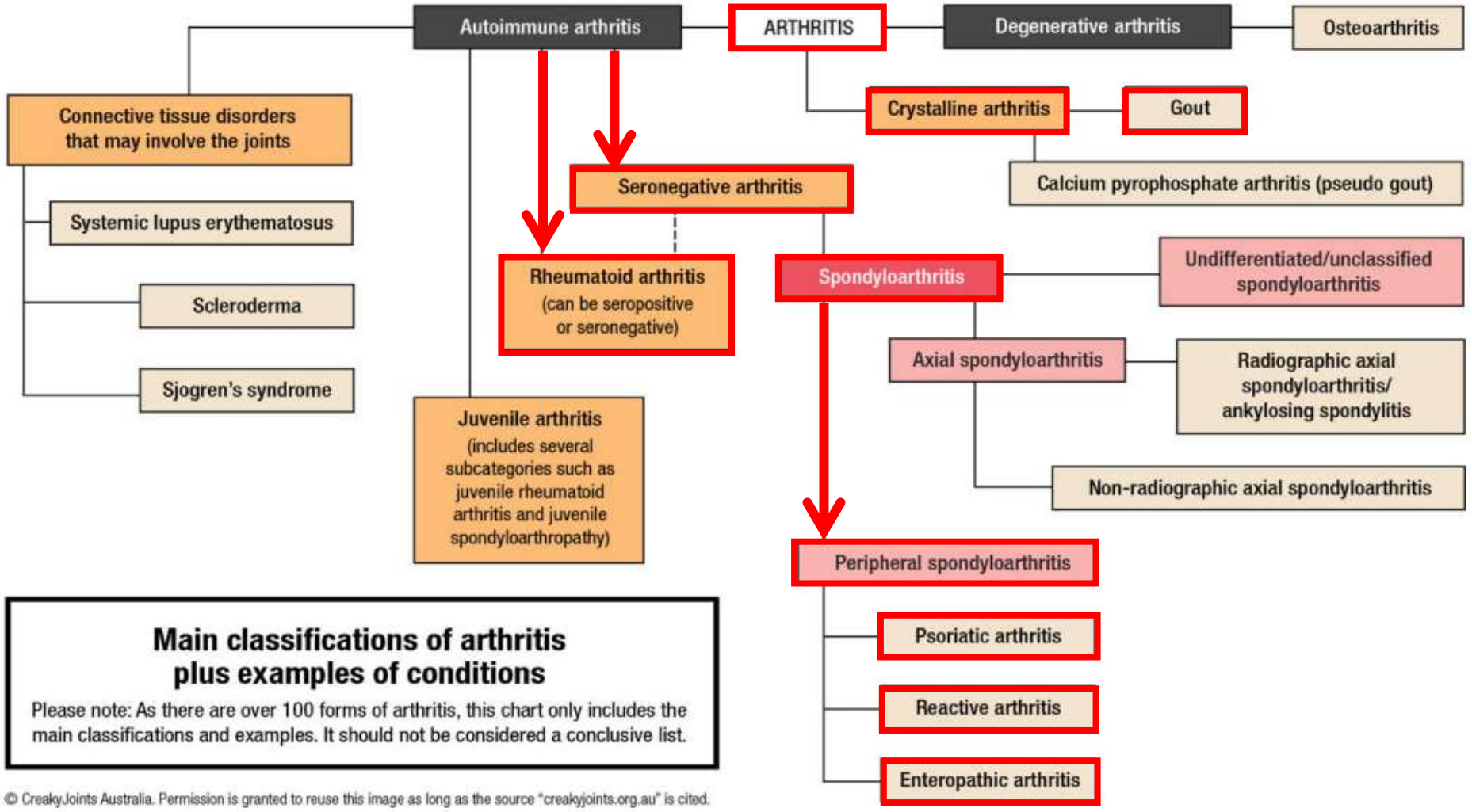
Arthritis classifications



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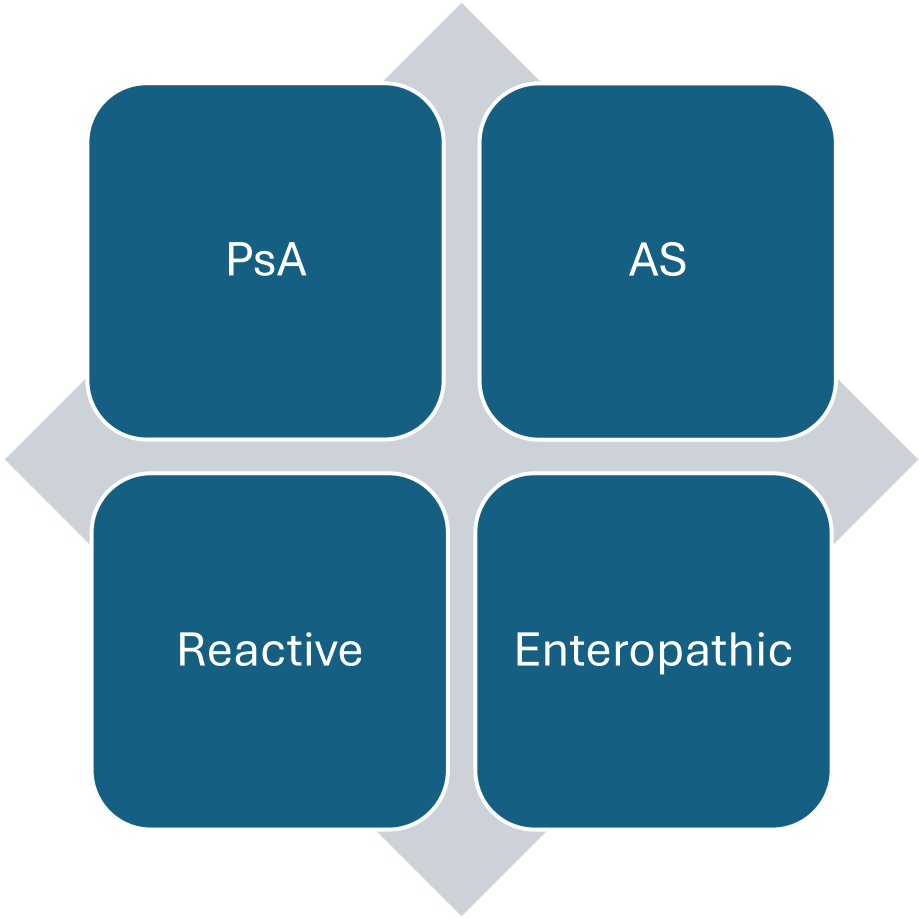
Seronegative arthritis



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Seronegative arthritis

- Negative for the presence of Rheumatoid factor or CCP antibodies, often present with normal inflammatory markers.
- Inflammatory arthritis typically affects a combination of small/large peripheral joints.
- Can also affect the spine.
- Can be mono (1 joint) to polyarticular (>5 joints)
- Approximately 3/10 RA cases are seronegative

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Reactive arthritis

- Reactive arthritis is a condition that causes redness and swelling (inflammation) in various joints in the body, especially the knees, feet, toes, hips and ankles.
- Reactive arthritis can occur 2 – 6 weeks post-infection usually STI (chlamydia), eye infection (conjunctivitis), urine infection or gastroenteritis.

"can't see, can't pee, can't climb a tree!"

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Reactive arthritis

- Usually affects mono (1 joint) to oligoarticular (<5 joints), typically affects larger joints.
- In most cases, it clears up within a few months and causes no long-term problems.
- Men and women of any age can get it, but it's more common in men, aged 20-40.
- Can have similar ultrasound appearances as PsA, affects lower limb more (asymmetric initially).

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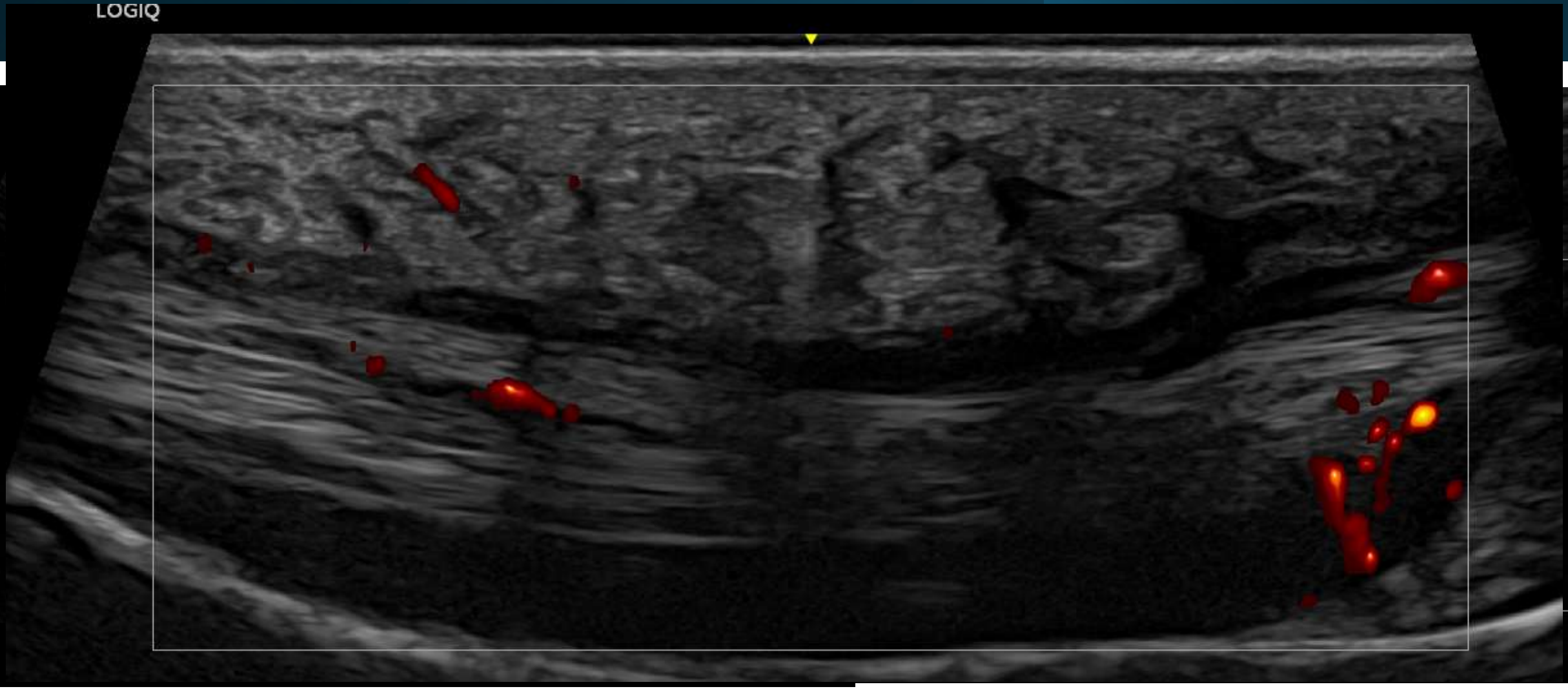
Reactive arthritis



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Psoriatic arthritis

Presents in patients aged 20-40 year-olds

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RA vs PsA

- Can be difficult to differentiate as features overlap.
- CASPAR criteria (next slide).
- Joint involvement is typically, but not always, asymmetric in PsA, while it is predominantly symmetrical in RA.
- Bone erosions, without new bone growth, and cervical spine involvement are distinctive of RA, while axial spine involvement, psoriasis and nail dystrophy are distinctive of PsA.
- Patients with PsA typically have seronegative test findings for rheumatoid factor (RF) and cyclic citrullinated peptide (CCP) antibodies, while approximately 80% of patients with RA have positive findings for RF and CCP antibodies.

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CASPAR Criteria (2006)

Psoriatic arthritis is considered present in patients with inflammatory arthritis who have at least 3 points; this has a specificity of 98.7% and a sensitivity of 91.4%

Clinical Features/Characteristics/Points

- Skin psoriasis: present - 2
- Psoriasis previously or family history but patient not affected - 1
- Nail lesions: onycholysis, pitting, hyperkeratosis - 1
- Dactylitis: present or past, documented by a rheumatologist - 1
- Rheumatoid factor: negative by any method except for latex - 1
- Juxta-articular bone formation: distinct from osteophytes - 1

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RA vs PsA

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Table 1

Clinical, serological and radiographic characteristics of PsA and RA

Characteristic	PsA	RA
Clinical		
Psoriasis	+++	–
Symmetric joint involvement	+	+++
Asymmetric joint involvement	++	+
Polyarthritis	++	+++
Oligoarthritis/monarthritis	+	+
Distal interphalangeal joint involvement	+++	–
Metacarpophalangeal and wrist involvement	+++	+++
Metatarsophalangeal joint involvement	+++	+++
Axial spine involvement	+++	–
Cervical spine involvement	+	+++
Imaging		
Pencil-in-cup deformity	++	–
Ankylosis	++	–
Subluxation	++	++
Bone proliferation	+++	–
Number of erosions	+	+++
Bone erosion	+	+++
Synovitis	++	+++
Tenosynovitis	++	+++
Distal interphalangeal joint involvement	+++	–
Enthesitis	+++	–
Dactylitis	+++	+
Synovitis	++	+++
Tenosynovitis	++	+++
Nail dystrophy	+++	–
Arthritis mutilans	+	–
Interstitial lung disease	–	++

(Merola et al. 2018)

Enthesitis

- Inflammation of insertions of tendons, ligaments and capsules into the bone.
- Entheses are predominantly extra-articular structures that represent a key target of musculoskeletal inflammation in diseases such as psoriatic arthritis (PsA) and spondyloarthritis (SpA).
- Enthesitis arises from robust activation of prostaglandin E2 and the IL-23–IL-17 axis, leading to the influx of innate immune cells and homing of inflammation into the entheses, which is followed by mesenchymal tissue responses and new bone formation.
- Enthesitis often mimics symptoms associated with mechanical injury. Symptoms include tenderness/soreness/pain at entheses (which may be elicited via palpation) and potential visible signs, such as redness and swelling at insertion sites .
- The disease can occur at one or more sites simultaneously, and occurs more often in lower than upper extremities. The plantar fascia and Achilles tendon insertion sites are commonly affected.

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Signs to look for at the enthesis

In 2014, the Outcome Measures in Rheumatology (OMERACT) Ultrasound Task Force proposed the below appearances as ‘core elementary lesions’ of US-detected enthesitis.

- Hypoechogenicity
- Tendon thickening
- Calcification / enthesophyte
- Erosions
- Increased Doppler signal

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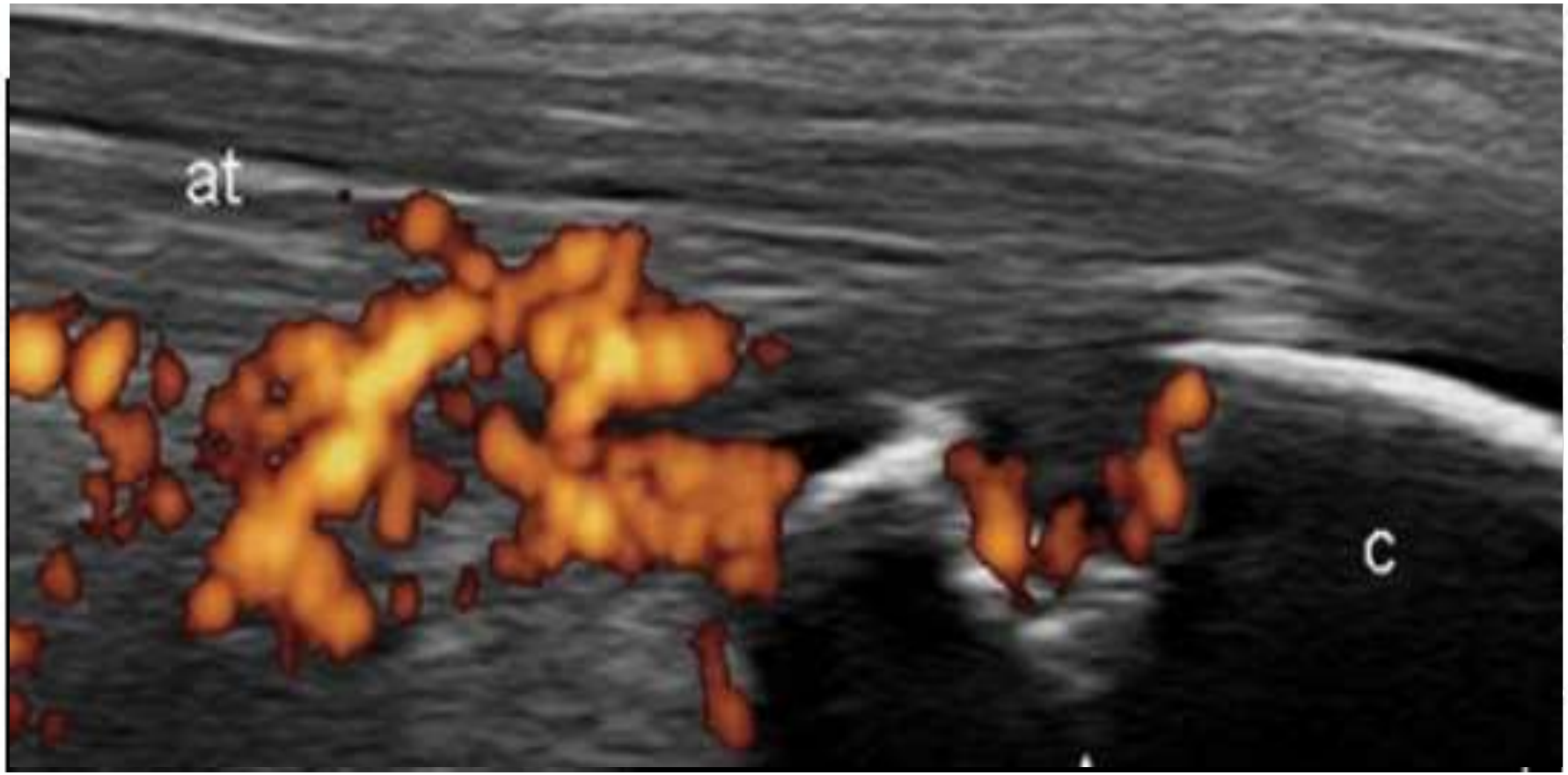
Enthesitis



(Schett et al. 2017, Tang et al. 2020, Gutierrez et al. 2010)

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Dactylitis

- In 1998, Rothschild et al. defined dactylitis, or ‘sausage-shaped digits,’ as “uniform swelling such that the soft tissues between the metacarpophalangeal and proximal interphalangeal, proximal and DIP, and/or DIP and digital tuft are diffusely swollen to the extent that the actual joint swelling could no longer be independently recognised.” **Clinically, dactylitis is recognised by swelling of an entire digit that is different from adjacent digits.** Swelling of the synovial sheaths often prevents flexion (Bagel & Schwartman, 2018).

- Key US components of dactylitis include - **Soft tissue thickening, soft tissue oedema, flexor tendon tenosynovitis, paratenonitis and joint synovitis**.

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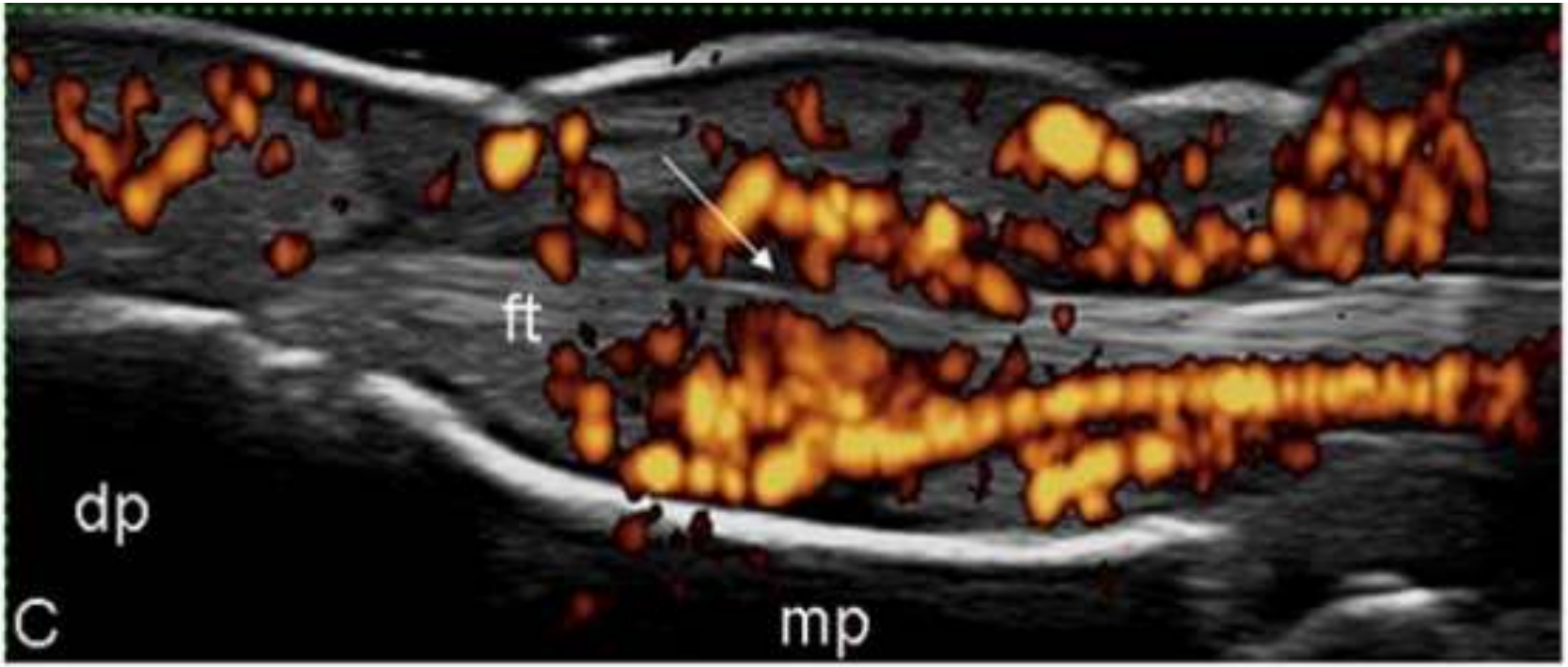
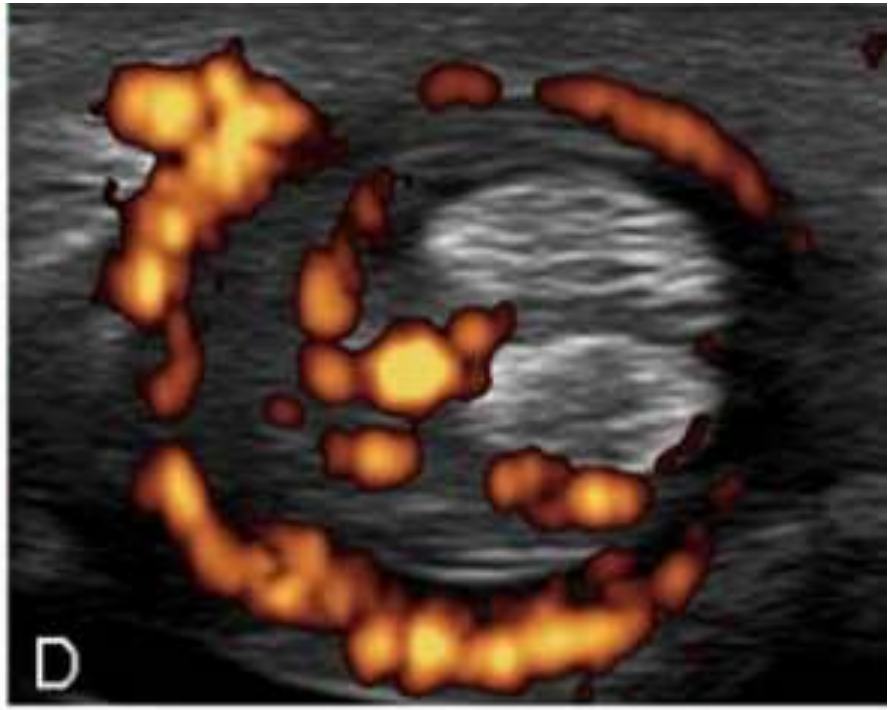
Dactylitis





Gutierrez et al. (2010)

PsA findings

Inflammatory entheseal changes are commonly found in people who have psoriasis or arthralgia, preceding clinical onset of PsA.
Zabotti et al (2019).

Mechanical strain, triggers the inflammatory process of the synovial entheseal complex (SEC).
McGonagle et al. (2008).

The presence of nail psoriasis has shown increased tendon enthesitis and increased enthesitis at remote sites.
Ash et al, (2012).

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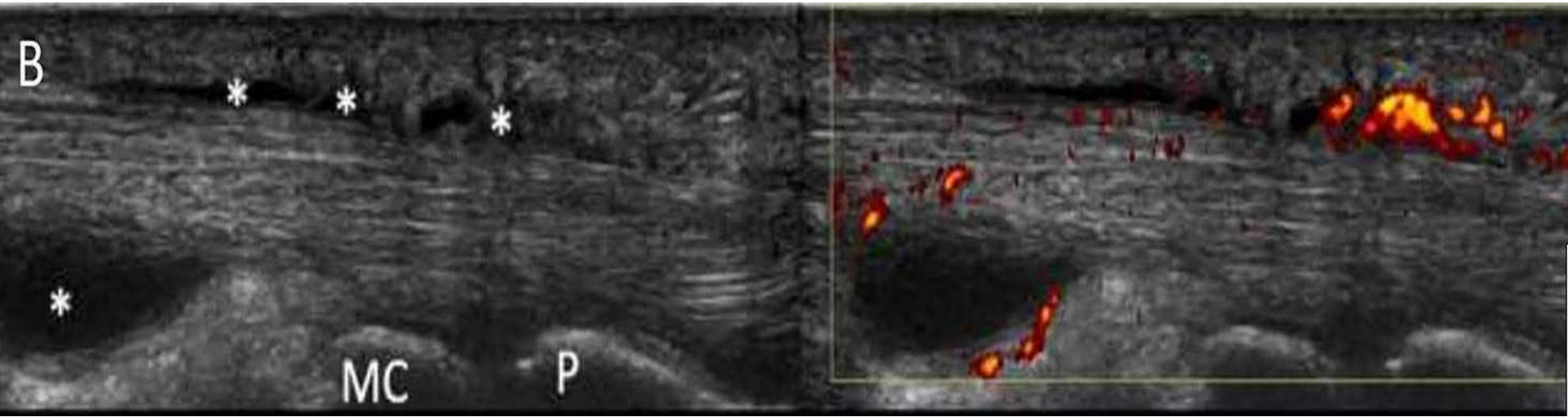
Tenosynovitis



(Dubash et al, 2020)

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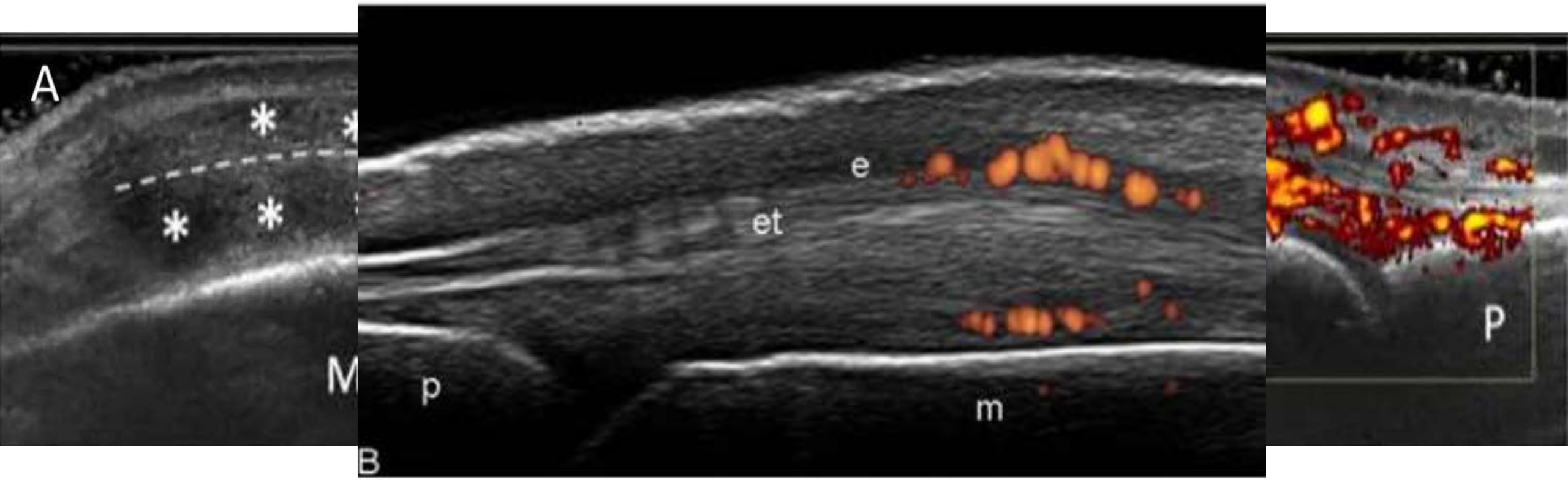
Paratenonitis



(Zabotti et al. 2016, Kaeley et al. 2018)

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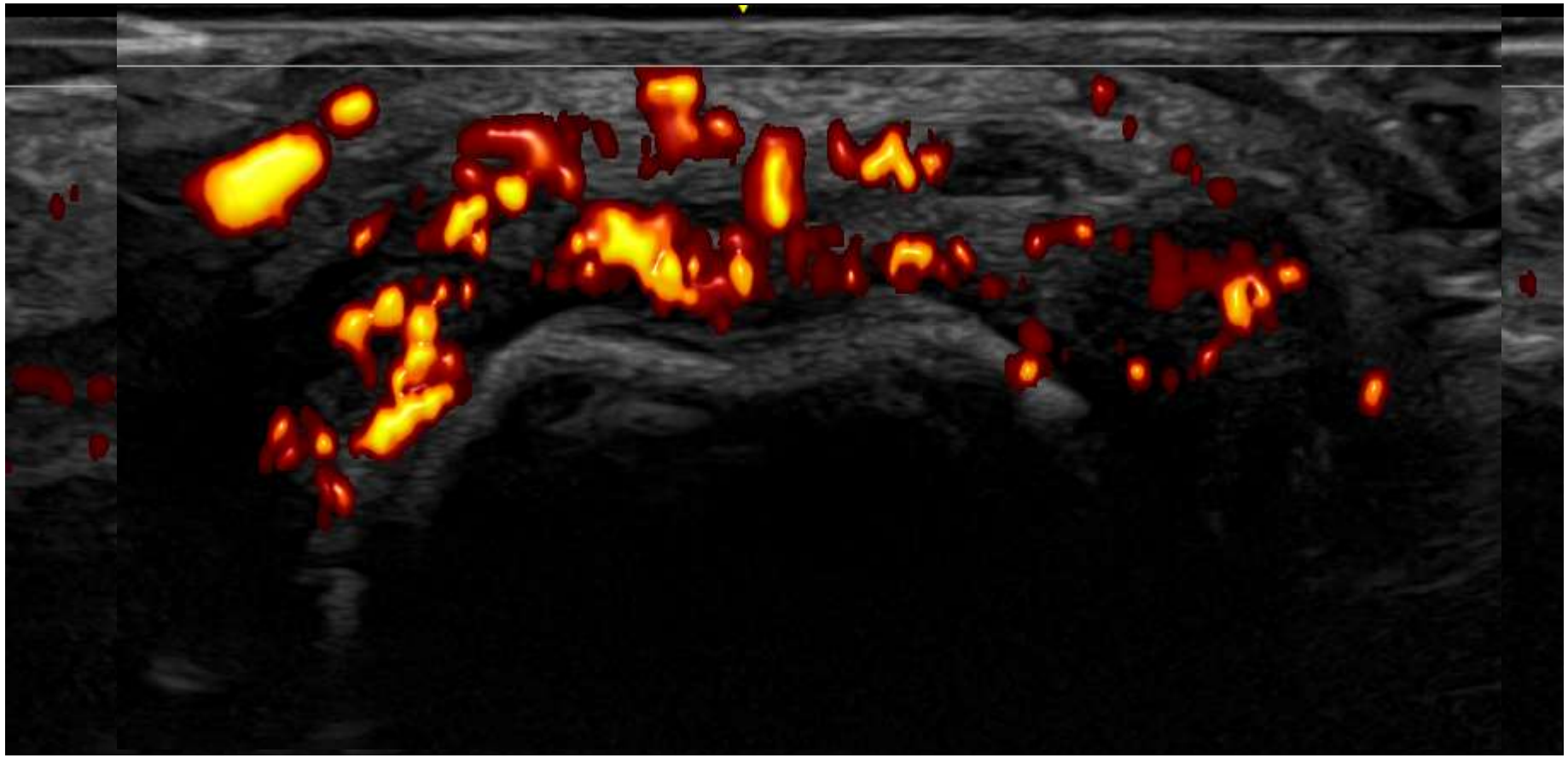
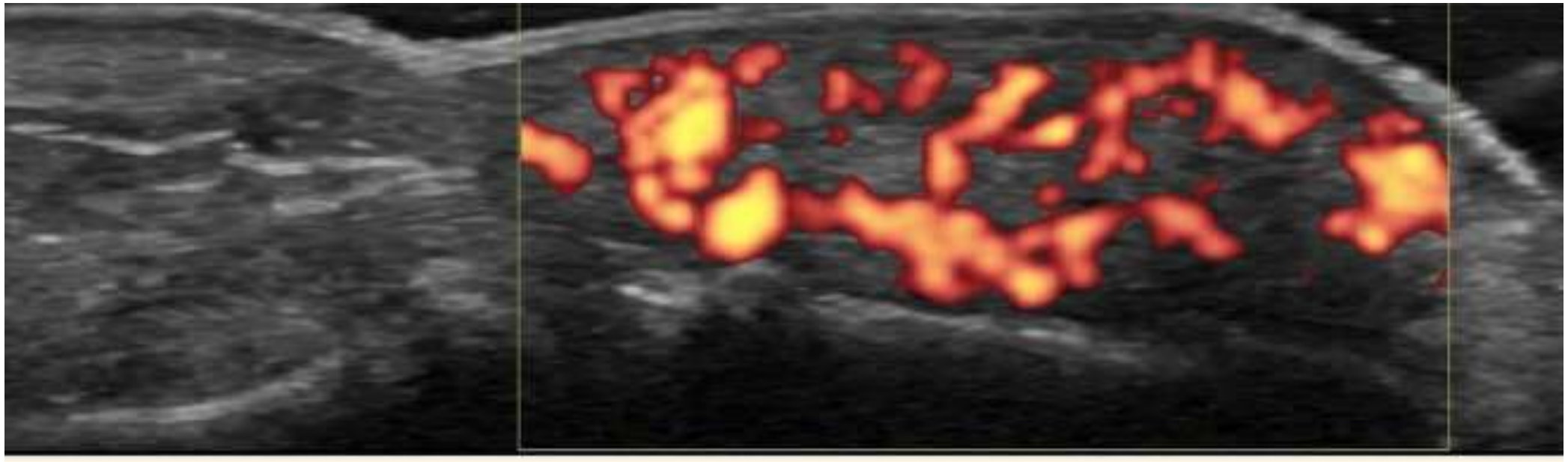
Paratenonitis / synovitis / enthesitis



(Authors images with permission)

Pulp vascularity



(Kaeley et al.2020)

Doctoral study

- Cross-sectional, observation study assessing PsO patients (PEST score<3) with ultrasound, scanning multiple joints, tendons, enthesis and tendons.
- Find the most common sites for inflammation.
- Create a protocol for patients who do not meet the NICE referral guidelines.

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Thank you for listening

Any questions?

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