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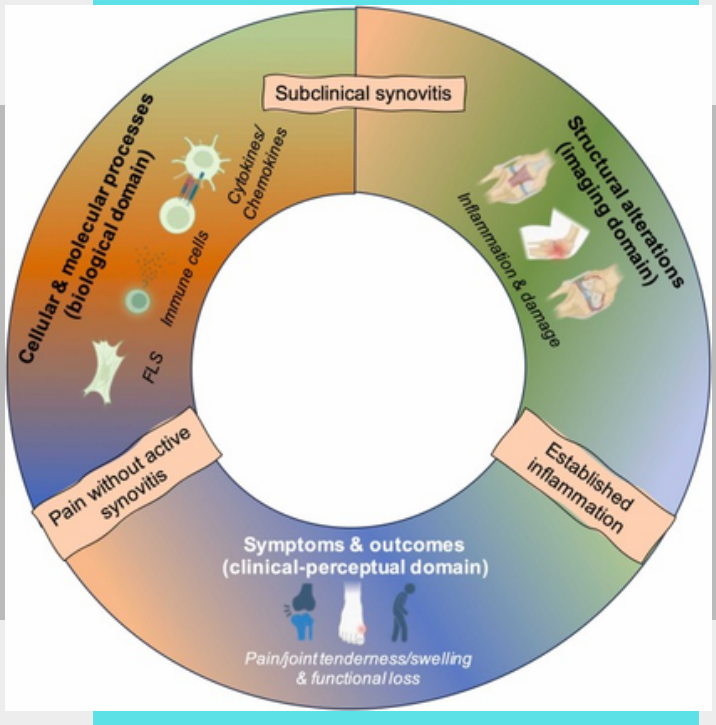
NEWSLETTER

The synovial interface: At the intersection from cells to humans

presented by
Peter Mandl

Further readings:

Article link



The synovium is increasingly recognized as a dynamic interface that integrates immunological, mechanical, sensory, and anatomical signals within the joint. In inflammatory rheumatic and musculoskeletal diseases, synovial inflammation represents not only a biological process driven by immune-synovial stromal interactions, but also a clinical construct shaped by the perception of both the patient and the health care professional (HCP), both in terms of physical findings and patient- and HCP reported outcomes, as well as laboratory- or imaging-based interpretation. Despite major advances in understanding the cellular and molecular mechanisms of synovitis, the reliable detection and monitoring of synovial inflammation in clinical practice remains challenging. Clinical joint assessment shows only moderate reliability and limited agreement with patient-reported findings, while pain and tenderness frequently reflect factors beyond active inflammation, including existing structural damage, central sensitization and comorbidities. Imaging modalities such as ultrasound and magnetic resonance imaging have substantially improved the visualization of synovitis and joint damage, increasing measurement reliability and construct validity. However, imaging-guided treat-to-target strategies have not consistently translated into superior clinical outcomes, highlighting a persistent gap between improved detection and effective therapeutic decision-making. This perspective frames the synovium as a multidimensional interface at the intersection of biology, anatomy, perception, and technology. By integrating evidence from cellular models, clinical examination, imaging studies, and emerging monitoring strategies, we propose that future progress in inflammatory arthritis will depend on hybrid approaches that move beyond single modalities toward interface-based assessment of disease activity.

Interview with
Peter Mandl

Peter Mandl
Assoc. Professor and Director of Clinical and Epidemiological Research, Division of Rheumatology
Medical University of Vienna

MSUS Academy: You recently published an article about the synovial interface. Can you briefly summarize what this means for the future of rheumatology? [https://pubmed.ncbi.nlm.nih.gov/41093632/#full-view-affiliation-4]

PM: Despite significant advances in understanding the cellular and molecular basis of synovitis, reliably detecting and monitoring synovial inflammation remains difficult both in routine clinical practice and within the framwork of observational studies and trials. Clinical joint assessment demonstrates only moderate reliability in all major forms of arthritis and often limited concordance with patient-reported outcomes. Pain and tenderness frequently reflect factors beyond active inflammation, such as structural damage, central sensitization, and comorbid conditions. Imaging techniques, including ultrasound and magnetic resonance imaging, have markedly enhanced the visualization of synovitis and joint damage, improving both measurement reliability and construct validity. However, imaging-guided treat-to-target approaches have not consistently resulted in better clinical outcomes, underscoring a persistent disconnect between improved detection and effective therapeutic decision-making. In this perspective article I attempted to conceptualize the synovium as a multidimensional interface spanning biology, anatomy, perception, and technology.

MSUS Academy: Patients with psoriatic arthritis present differently both clinically and on ultrasound. What's the idea behind clusters based on ultrasound-detected inflammation? [https://pmc.ncbi.nlm.nih.gov/articles/PMC12874723/pdf/12891_2025_Article_9434.pdf]

PM: The ULTIMATE trial, in which I was honoured to participate is a pivotal study in that it featured ultrasound-assessed synovitis as primary outcome. Psoriatic arthritis is characterized by heterogeneous musculoskeletal manifestations. One of the aims of ULTIMATE was to use power-Doppler (PD) ultrasound to identify homogeneous groups of patients based on the level of severity of ultrasound-detected synovitis and then to determine the longitudinal trajectory of response with secukinumab vs. placebo for each cluster up to week 12. Using machine-learning based methods 3 clusters were identified, with clusters 2 and 3 showing higher global EULAR OMERACT synovitis score(GLOESS) scores than cluster 1, with cluster 2 exhibiting the highest PD signal and greater clinical joint counts, while enthesitis scores were similar across groups. Synovitis in clusters 2 and 3 more frequently involved both small and large joints, particularly MCP, MTP, and wrists, with cluster 3 showing relatively greater involvement of elbows, knees, and ankles. Treatment responses favored secukinumab across clusters but were most pronounced in cluster 2, whereas clusters 1 and 3 demonstrated more modest or variable improvements.

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MSUS Academy: In everyday clinical practice, ultrasound examinations of the foot are often not performed in sufficient detail. What should rheumatologists pay particular attention to? [https://link.springer.com/article/10.1007/s10067-025-07503-y]

PM: We have long known that the foot is often ignored during physical assessment of patients with RMDs, including those with arthritis. Rheumatologists should pay particular attention to systematically assessing the forefoot—especially the metatarsophalangeal (MTP) joints—using both grey-scale and power Doppler ultrasound, as these sites are among the most frequently affected, and such affection is often poorly reflected by routine clinical examination or composite scores, which typically exclude the feet and may therefore underestimate disease activity. To make things even worse, recent studies have drawn attention to the presence of, commonly mild degrees of synovitis, in particular effusion but also synovial hypertrophy in the toes of healthy subjects, which underline the importance of careful sonographic evaluation and the exclusion of synovial effusion from the sonographic definition of synovitis according to the global OMERACT- EULAR ultrasound synovitis score (GLOESS). A careful, structured evaluation should also include entheses and tendon compartments (e.g., Achilles insertion), as foot involvement is multifactorial and contributes significantly to functional impairment, making comprehensive ultrasound assessment essential for accurate disease characterization and treatment decisions.

MSUS Academy: Finally, do you have any advice for young colleagues in training using musculoskeletal ultrasound?

PM: For colleagues in training, the most important step after completing their first basic musculoskeletal ultrasound course is to integrate scanning into daily clinical practice. Many people sit back and give themselves a few weeks to let the knowledge "settle in" after such training, but that’s the worst thing they can do! The best advice I can give is to choose one large and one small joint that you’ll examine with ultrasound on at least three patients each day (regardless of diagnosis), so you can get used to the standard scans, and once you’ve got that down, you can gradually add the next joints to your routine, until you become an well-rounded musculoskeletal sonographer! Once you achieve this state, start paying even more attention to anatomy, adding new structures to your armamentarium.

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Publication of the month

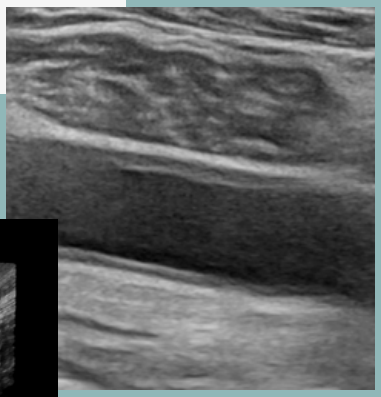
Link

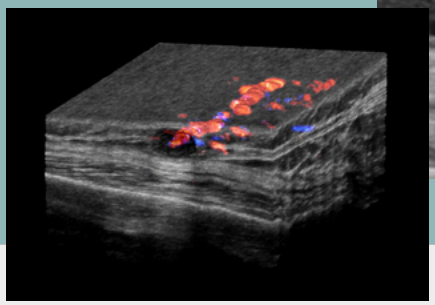
> Semin Arthritis Rheum. 2026 Apr:77:152927. doi: 10.1016/j.semarthrit.2026.152927. Epub 2026 Jan 25.

Definitions and online reliability assessment of elementary ultrasound lesions in Takayasu arteritis: a study from the OMERACT Ultrasound Working Group

Highlights

- Consensus definitions for ultrasound lesions in Takayasu arteritis were developed.
- Seven arterial sites for ultrasound monitoring of Takayasu arteritis were selected.
- Image-based scoring showed good inter- and intra-reader agreement.
- The ‘macaroni sign’ had the highest reliability among ultrasound findings.
- This study provides a basis for a standardized ultrasound score in Takayasu arteritis.





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