



POCUS Conference

Use of Ultrasound to aid the diagnosis of gout
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+ Case



- 90 y/o Chinese man with PMH of HTN, T2DM, CKD3, gout and dementia presents with right knee and right wrist pain and swelling. The pain limits ambulation and ROM.
 - Family reports that pts likes to drink beer and eat seafood.
 - Home Meds include: colchicine, amlodipine, metformin and januvia.

+ Physical Exam:

- VS: T: 36, HR:85, BP: 142/86, SpO2 97%.
- Gen: elderly Chinese man lying in bed in mild distress due to pain
- HEENT: unremarkable, no JVD
- CVS: RRR, no M/R/G
- Resp: CTAB
- Abdomen: soft, NT/ND, NABS
- Ext: **R knee and R wrist swelling, warm and tender to touch, with decreased ROM due to pain. Tophi are noted around the wrist.**

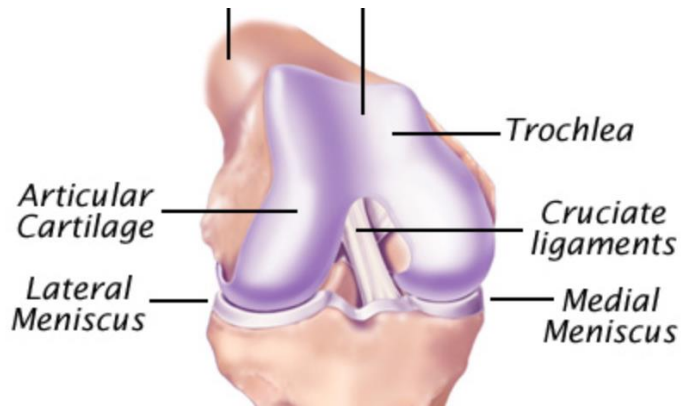
+ Labs

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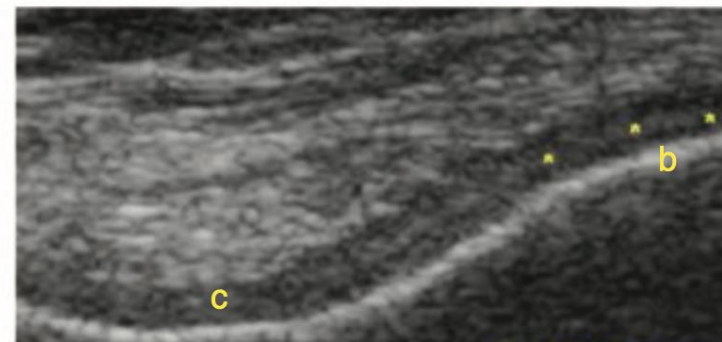
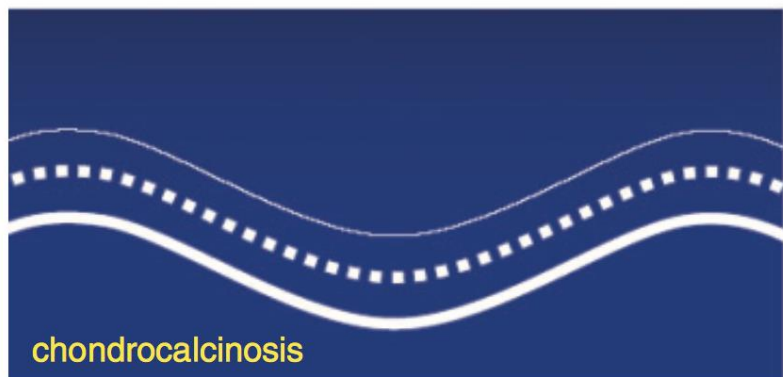
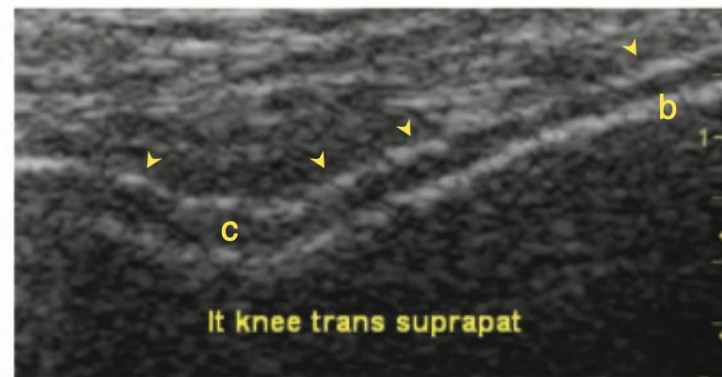
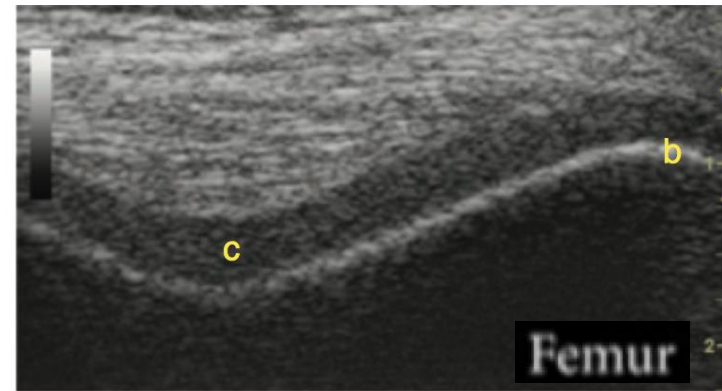
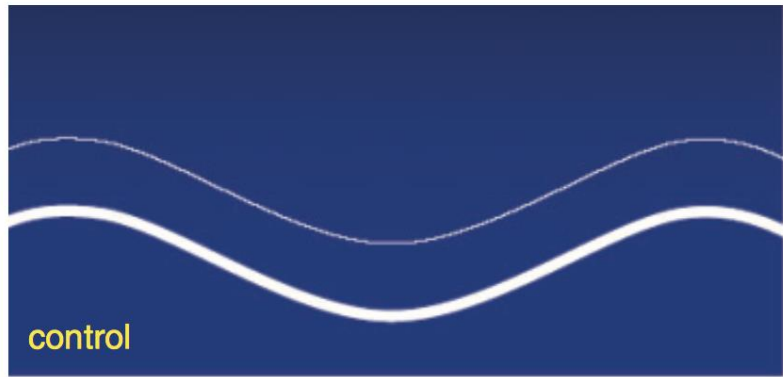
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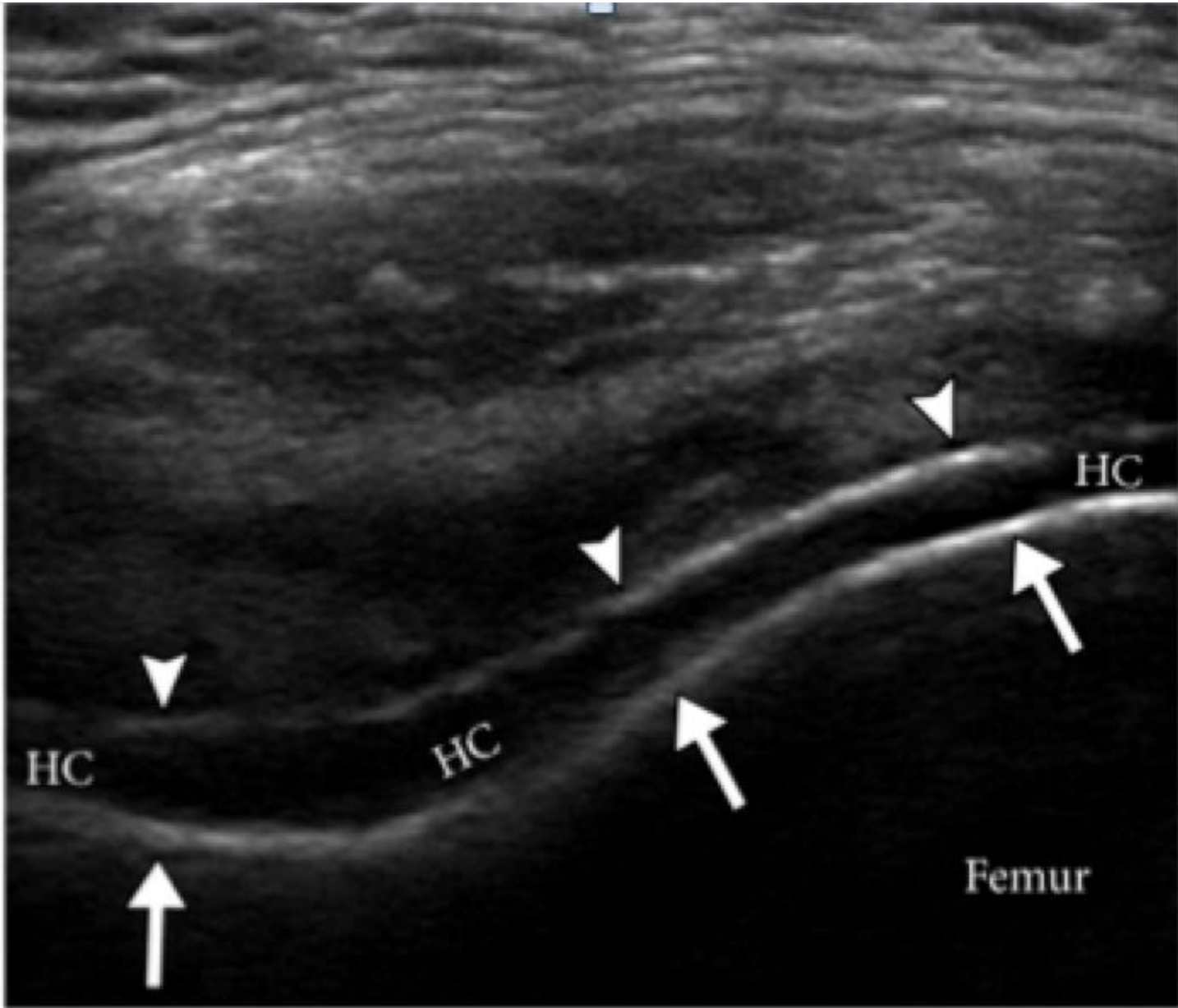
- Uric acid 6.4
- ESR 34
- CRP 16

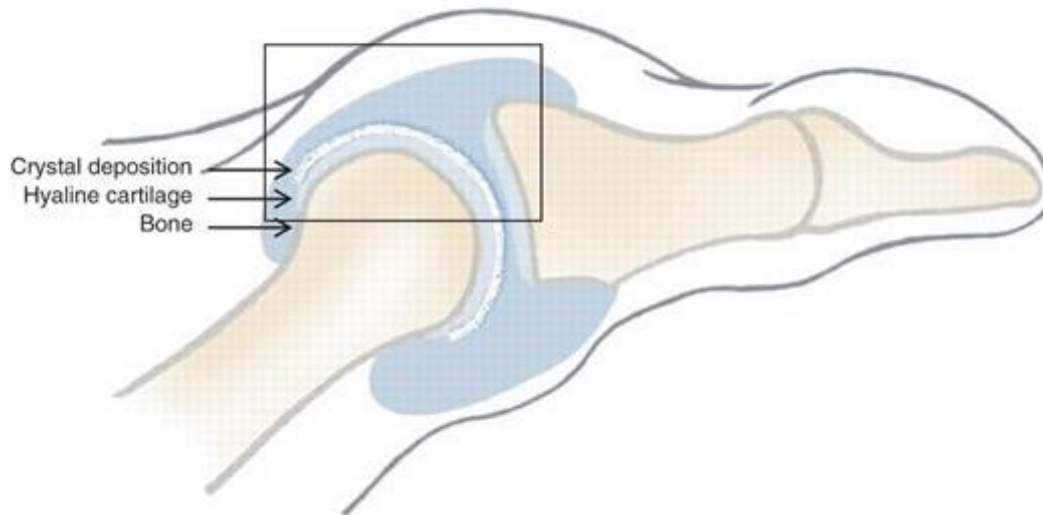
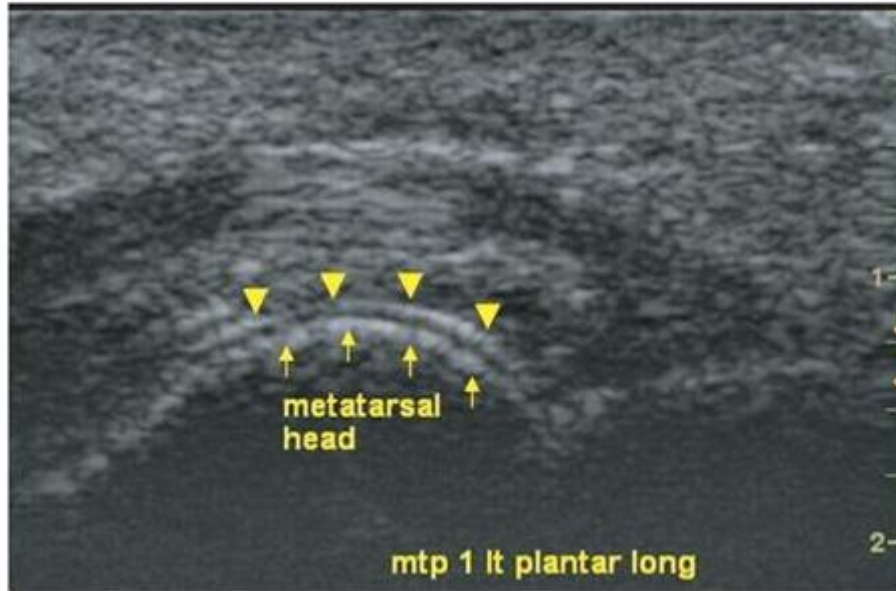
+ Knee US in gout



- High-frequency, linear transducer.
- Suprapatellar, transverse view with knee in maximal flexion.

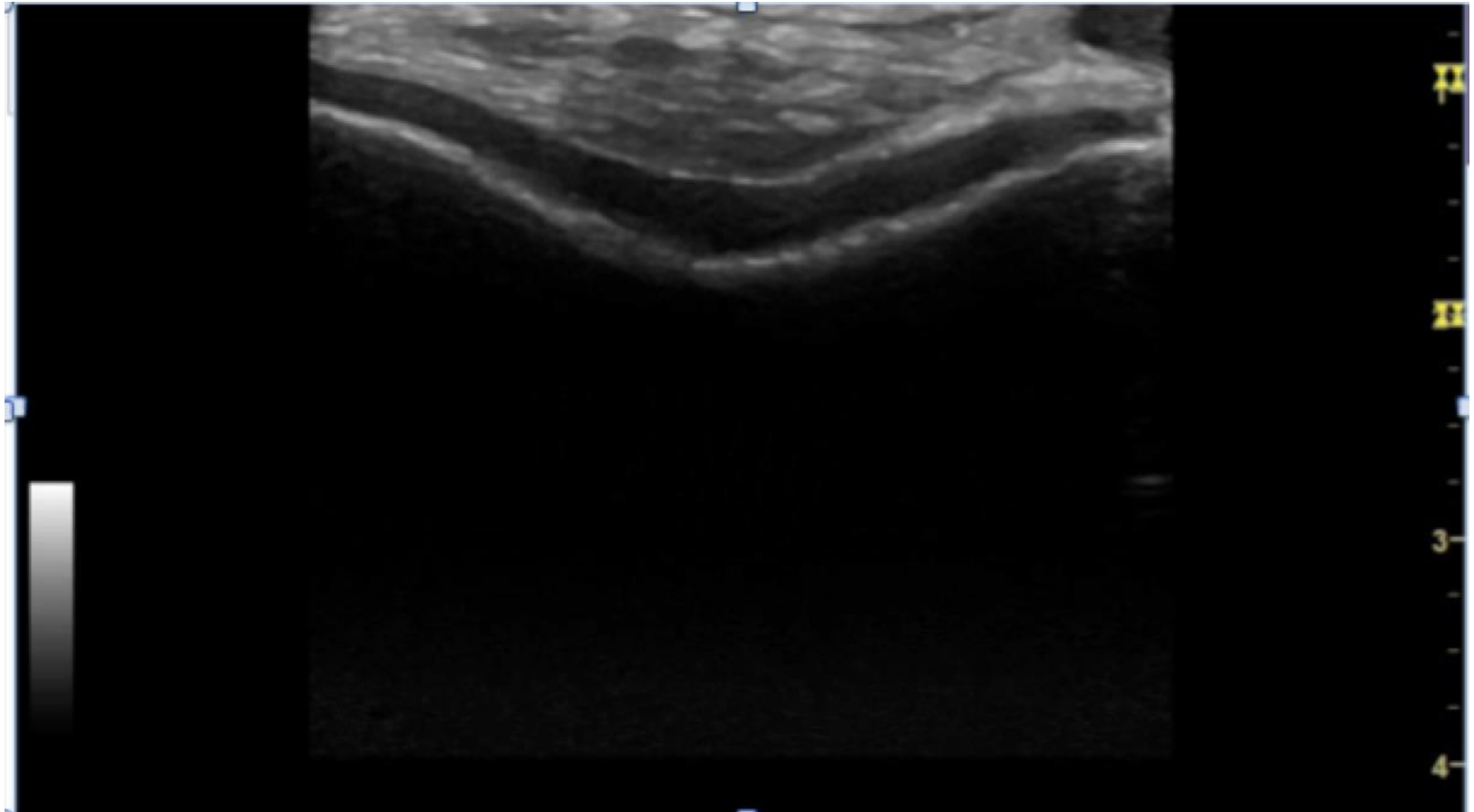






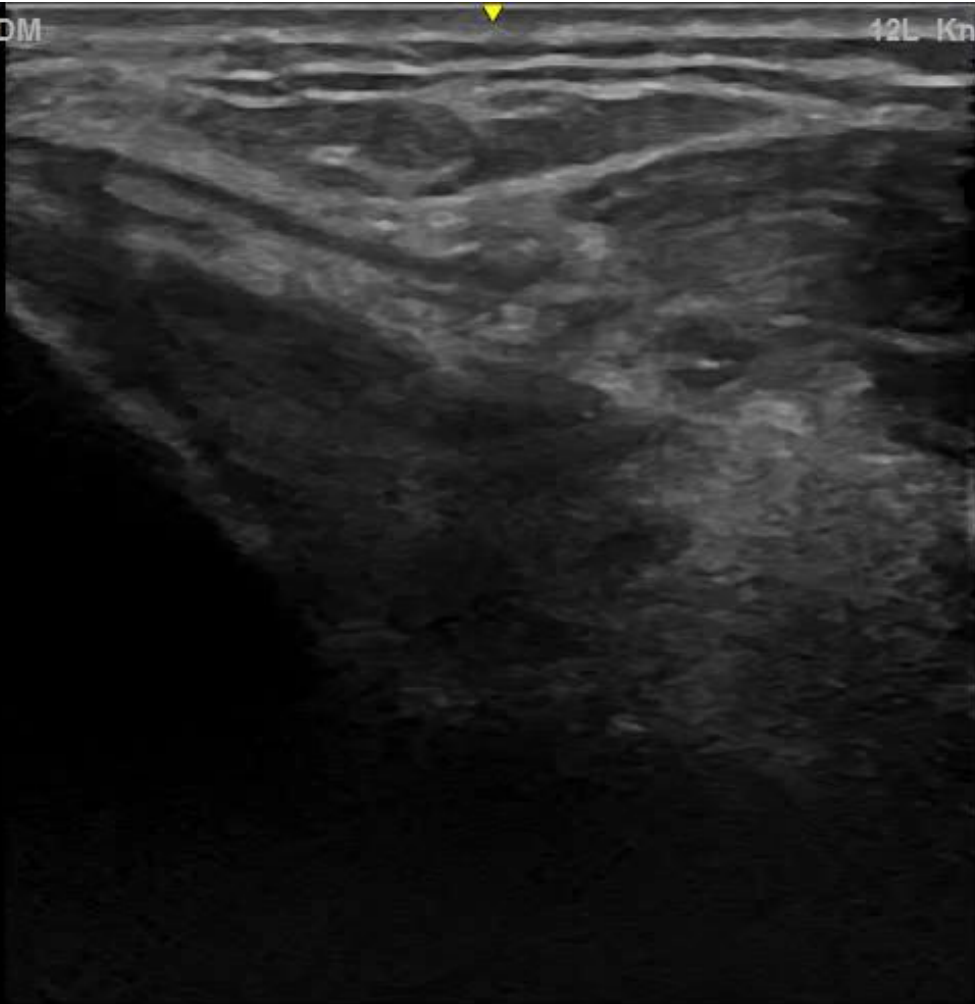
US finding in longstanding hyperuricemia: DC sign

Knee US



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12L Knee MI 1.2 TIs 0.4



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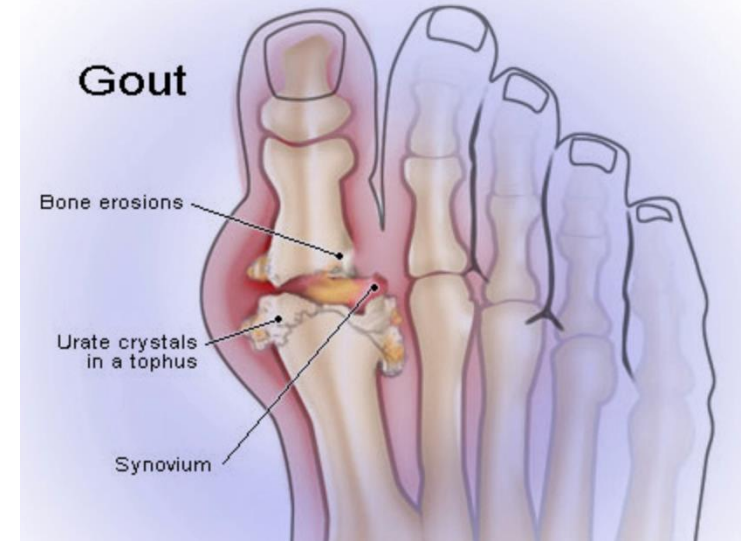
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+ Imaging Modalities in Gout



- X-ray: typical well-defined, punched out (rat bite), periarticular erosions with overhanging edges are not seen radiographically until 6–12 yrs after the initial acute attack.
- MRI is sensitive in showing synovial, soft tissue inflammation and osseous abnormalities of gout, although the imaging findings are not specific
- Dual-energy CT has good diagnostic accuracy for detection of monosodium urate (MSU) deposits and is able to identify even small occult tophaceous deposits. However, sensitivity is lower in patients with recent-onset disease.
- Ultrasound is used increasingly for diagnosing gout.
 - Double contour sign (DC)
 - Tophus: hyperechoic aggregates
 - Intra-articular aggregates: “snowstorm” appearance of floating hyperechoic foci representing MSU aggregates.
- The most reliable method of diagnosis is arthrocentesis and identification of crystals on polarizing microscopy

Diagnosis of gout by ultrasound

R. G. Thiele and N. Schlesinger¹

Objectives. To establish the usefulness of ultrasonography (US) for diagnosing gout and to determine whether there are sonographic features that are characteristic for gout but not for other arthropathies.

Methods. We retrospectively compared joint images of gout patients with matching images from patients with other rheumatic conditions. Images of 37 joints of 23 patients with monosodium urate (MSU) crystal-proven gout were reviewed. MSU crystals were identified in at least one joint in each patient. Our control group had 23 randomly selected patients with 33 examined joints with rheumatic conditions other than gout.

Results. Specific diagnostic features included a hyperechoic, irregular band over the superficial margin of the articular cartilage described as a double contour sign in 92% of gouty joints and in none of the controls ($P < 0.001$); hypoechoic to hyperechoic, inhomogeneous material surrounded by a small anechoic rim, representing tophaceous material, was seen in all gouty metatarsophalangeal (MTP) joints, in all metacarpophalangeal (MCP) joints and in none of the controls ($P < 0.001$); erosions adjacent to tophaceous material were seen in 65% of MTP joints and in 25% of MCP joints. One erosion was seen in a MTP joint in a control patient with psoriatic arthritis.

Conclusions. US can detect deposition of MSU crystals on cartilaginous surfaces ($P < 0.001$) as well as tophaceous material and typical erosions. US may serve as a non-invasive means to diagnose gout.

Key words: Gout, Gouty arthritis, Tophi, Ultrasonography, Diagnostic imaging.



+ Value of Ultrasonography in the diagnosis of gout in patients presenting with acute arthritis

Pattamapasong, N., Vuthiwong, W., Kahthawang, T. et al. *Skeletal Radiol* (2017).

+ Material and Methods

- 89 enrolled patients with acute arthritis
- 2 radiologist independently review US images
- A third radiologist consensus was achieved when interpretations of US features differed
- All patients underwent aspiration to confirm the diagnosis of acute gout by detecting MSU crystals



+ Results



- 53 (60%) of patients had gout
- 36 (40%) of patients had non-gout arthritis
- Mean serum acid level was 7.1 mg/dL in pts with gout and 4.7 mg/dL in non-gout arthritis

+ US features in gout

Ultrasound features	Description
Double contour sign	The irregular hyperechoic band over the superficial margin of the articular hyaline cartilage independent of the angle of ultrasound beam. The band can be either continuous or intermittent (Fig. 1)
Intra-articular aggregates	Thickened synovium containing multiple hyperechoic spots. Thickened synovial membranes were either smooth or nodular. This feature was also described as hyperechoic spots in the synovium (Fig. 2)
Tophus	Circumscribed heterogeneous hyper- or hypoechoic lesions surrounded by a complete or partial hypoechoic rim, which may or may not generate a posterior acoustic shadow (Fig. 3)
Intra-tendinous aggregates	Heterogeneous hyperechoic foci or cloud-like hyperechoic lesions confined to the tendons, which may generate a shadow (Fig. 4)

+ Double Contour Sign

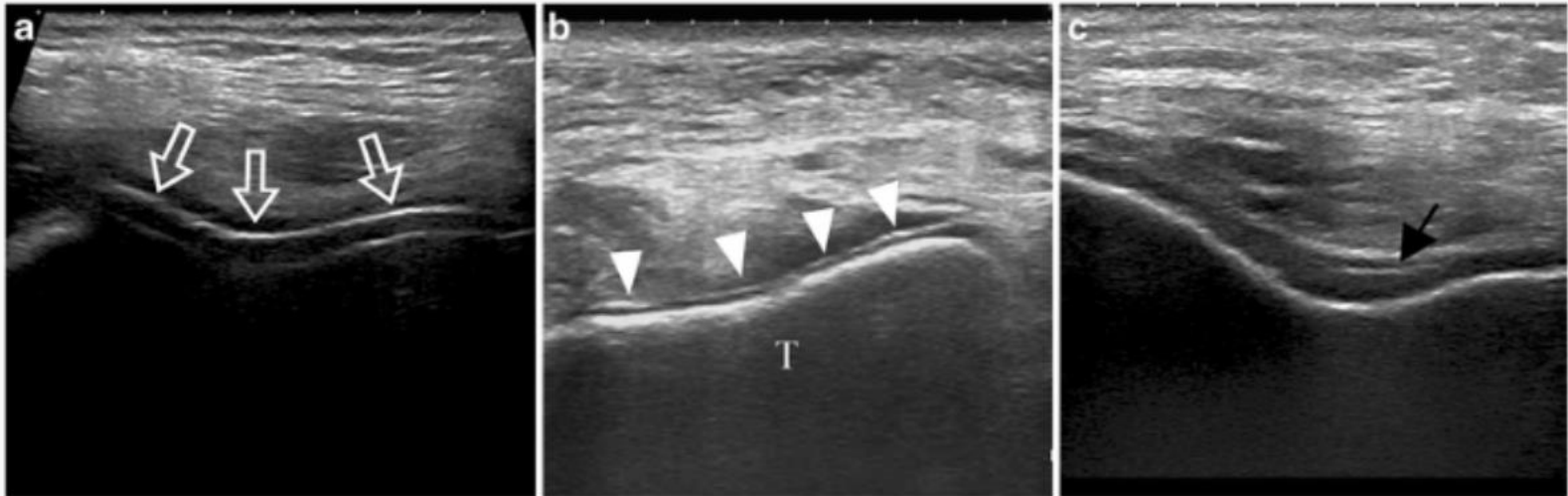


Fig. 1

Double contour sign. **a** Transverse scan of the femoral trochlea of a 57-year-old man with gout shows a continuous irregular echogenic line overlaying the cartilage surface (*open arrows*). **b** Transverse scan of the ankle of a 67-year-old man with gout shows an interrupted irregular echogenic line (*arrowheads*) (*T* talar dome). **c** False-positive double contour sign in a patient with non-gout arthritis. A transverse scan of the femoral trochlea shows a thin echogenic line between an effusion and normal articular cartilage, which is directly exposed to the sound beam (*arrow*)

+ Intra-articular Aggregates

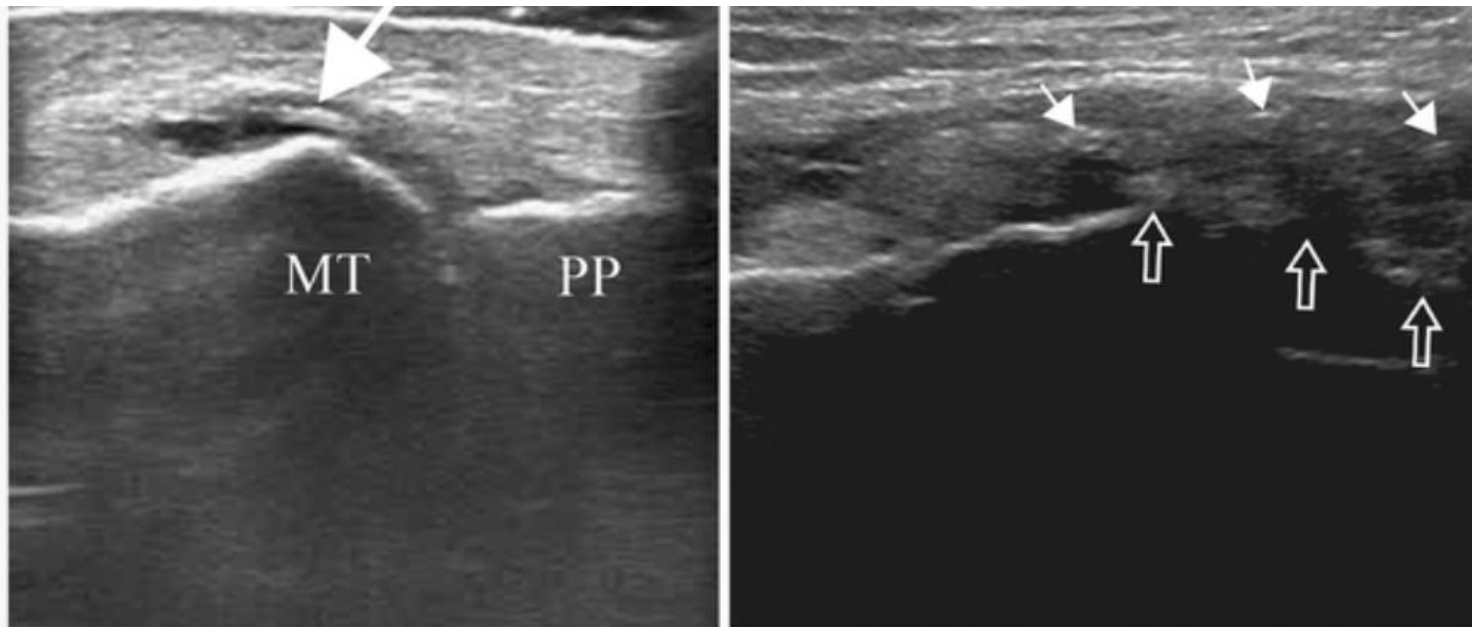


Fig. 2

Intra-articular aggregates. **a** Longitudinal scan of the first metatarsophalangeal joint of a 69-year-old man with gout shows hyperechoic aggregates (*arrow*) in the thickened synovium with a smooth surface (*MT* metatarsal head; *PP* proximal phalanx). **b** Transverse scan of the knee of a 57-year-old man with gout shows hyperechoic spots (*arrows*) in the thickened synovium with a nodular surface (*open arrows*)

+ Tophi

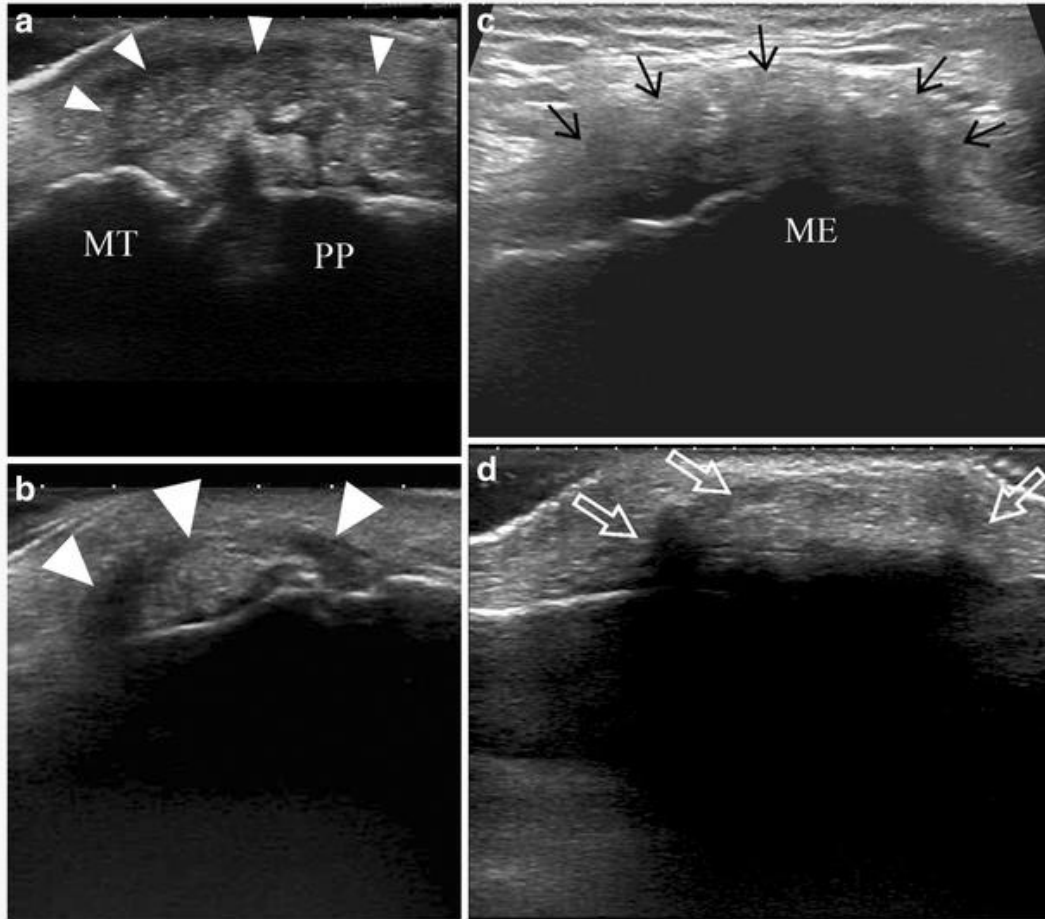


Fig. 3

Tophi (a-d). **a** Longitudinal scan of the first metatarsophalangeal joint of a 63-year-old man with gout shows a *soft tophus* presenting as an inhomogeneous hyperechoic lesion surrounded by a partial hypoechoic rim (*arrowheads*) with a weak posterior acoustic shadow (*MT* metatarsal head; *PP* proximal phalanx). **b** Longitudinal scan of the first metatarsophalangeal joint of a 71-year-old man with gout shows a hyperechoic tophus surrounded by a hypoechoic rim (*arrowheads*) without acoustic shadow. **c** Transverse scan of the medial femoral condyle of the knee of a 57-year-old man with gout shows a mixed echogenic tophus with an intermediate acoustic shadow (*black arrows*) (*ME* medial epicondyle). **d** Longitudinal scan of the medial aspect of knee of a 69-year-old man with gout shows a *hard tophus* presenting as a hyperechoic tophus with a strong acoustic shadow (*open arrows*)

+ Intra-tendinous Aggregates

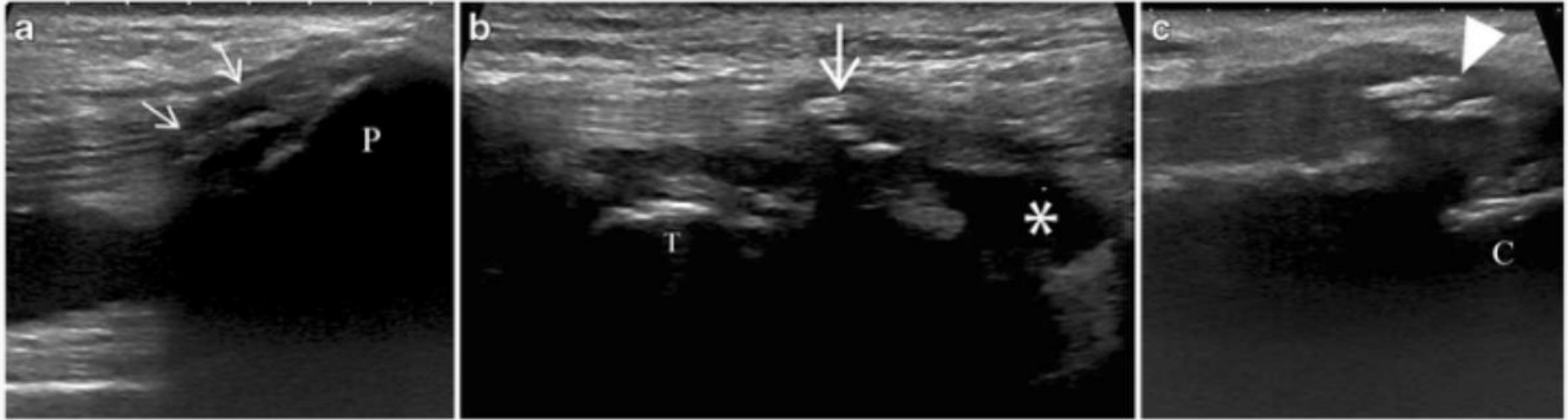


Fig. 4
Intra-tendinous aggregates. US findings in patients with gout (**a–b**) and a patient with CPPD arthropathy (**c**). **a** Longitudinal scan of the knee of a 78-year-old man with gout shows linear hyperechoic foci (*arrows*) in the quadriceps tendon with a posterior acoustic shadow. (*P* patella). **b** US image of the lateral aspect of ankle in the long axis of peroneus longus tendon of a 69-year-old man with gout shows hyperechoic bands with a posterior acoustic shadow. Note the joint effusion (*). (*T* talus). **c** Longitudinal scan of the Achilles tendon of an 84-year-old man with CPPD arthropathy shows hyperechoic bands (*arrowheads*). (*C* calcaneus)

+ US features

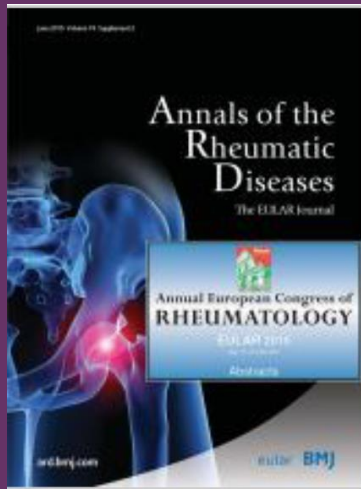


- 3 US features differed significantly ($p < 0.001$) between pts with gout vs. non-gout arthritis.
 - The double contour sign (42% vs 8% respectively)
 - Sensitivity: 42% **+LR: 5.25**
 - Specificity: 92% **-LR: 0.63**
 - Intra-articular aggregates (58% vs 8%)
 - sensitivity: 58%
 - specificity: 92%
 - Tophi (40% vs 0%)
 - Sensitivity: 40%
 - Specificity: 100%
 - Intra-tendinous aggregates (32% vs 17%, $p = 0.14$)
 - No statistical significance differences

+ Conclusion



- When the prevalence is high, these three ultrasound features may be a useful adjunct in the diagnosis of acute gout.



Imaging modalities for the + classification of gout systematic literature review and meta- analysis

Ogdie A, Taylor WJ, Weatherall M, et al. *Annals of the Rheumatic Diseases* 2015;74:1868-1874

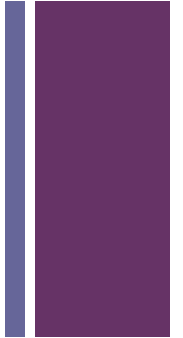


EXTENDED REPORT

Imaging modalities for the classification of gout: systematic literature review and meta-analysis

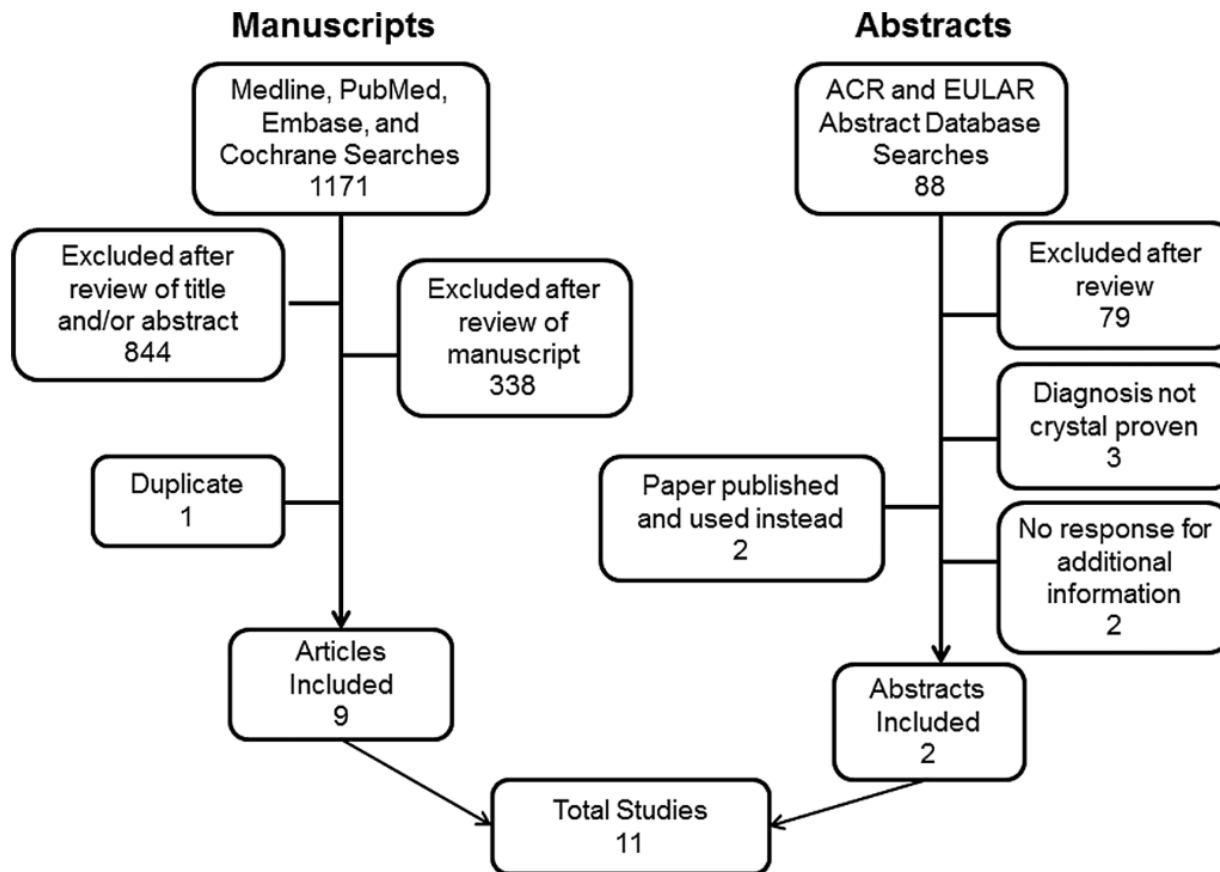
Alexis Ogdie,¹ William J Taylor,² Mark Weatherall,² Jaap Fransen,³ Tim L Jansen,³
Tuhina Neogi,⁴ H Ralph Schumacher,¹ Nicola Dalbeth⁵

- Objective of the study:
 - to examine the usefulness of imaging modalities in the classification of symptomatic gout when compared to MSU crystal confirmation as the gold standard.





- Systematic Literature Search by Medical librarian
- Sources:
 - Databases: Ovid Medline, PubMed, Embase and Cochrane from January 1946 to March 2014.
 - Abstracts: Relevant abstracts from American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) meetings from 2007 to 2013.
 - References from reviewed articles
- Exact Search terms reported: yes
- Search strategy previously validated: no



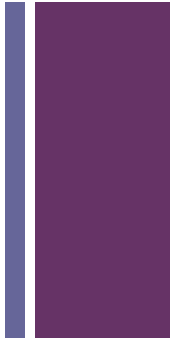


Inclusion Criteria



- Studies examining the diagnostic performance of an imaging modality (X-ray, MRI, US, CT or DECT) in gout.
- Inclusion of at least two groups of patients where one group had gout.
- Gout was confirmed by the presence of MSU crystals in joint fluid.
- The article or abstract also had to include either the raw results (positive vs negative imaging features for each group), or specificity and sensitivity.

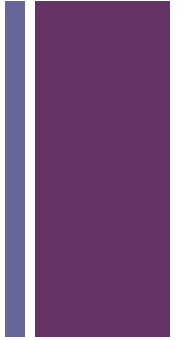
+ Exclusion criteria



- Article in a language other than English
- Studies not involving human subjects
- Case reports
- Use of clinical criteria or physician- or patient-report for classification of gout instead of MSU crystal confirmation
- Lack of a control or comparison group
- Cases with asymptomatic hyperuricemia
- Insufficient information provided to calculate sensitivity and specificity
- Fate of each excluded study clearly stated: no



Data extraction and quality assessment



- **Standardized data abstraction tool used: yes**
- Authors contacted for additional info if required: yes
- Likelihood of bias specifically explicitly assessed: no
- Quality of studies assessed: yes
- **Standardized study quality tool used: yes. QUADAS**
- Quality assessed independently by more than 1 author: yes

+ Meta-analysis



- **Point estimates:** sensitivity and specificity (co-dependently)
- **Methodology:** hierarchical summary receiver operating characteristic (HSROC) curve model of Rutter and Gatsonis.



Table 1 Patient characteristics

Study	Design	Population	Dates	Gout patients			Comparator patients			
				N	Disease duration, years (mean)	Age, years (mean)	N	Age, years (mean)	Arthrocentesis	Conditions
Ultrasound										
Ottaviani <i>et al</i> ¹⁵	Prospective case-control	Hospital outpatients with rheumatic disease	11/2008–10/2010	53	9.2	59.7	50	59.5	Yes	CPPD, RA, OA, PsA
Lamers-Karnebeek <i>et al</i> ¹⁸	Prospective cross-sectional	Patients presenting with mono- or oligoarthritis	NR	26	NR	63.5	28	NR	Yes	CPPD, ReA, PsA, OA, PMR, UA, Lofgren syndrome, gout with neg MSU (2 patients)
Thiele <i>et al</i> ¹⁷	Retrospective case-control	Rheumatology clinic patients with unclear diagnosis	11/2003–12/2004	23	NR	58.6	23	NR	No	CPPD, RA, sarcoidosis, OA, FMS, PsA, bursitis, tendinitis, inflammatory oligoarthritis NOS, lateral epicondylitis, muscle fibre tear
Naredo <i>et al</i> ¹⁴	Prospective case-control	Rheumatology and general practice clinics	NR	91	7	56.4	42	56.6	NR	RA, SpA, healthy
Nalbant <i>et al</i> ¹³	Prospective case-control	Patients with subcutaneous nodules and rheumatic disease attending rheumatology clinics	5/2001–10/2001	10	10.7	61.3	13	56.5	NR	RA
Ponce <i>et al</i> ^{21*}	Prospective cross-sectional	Patients with joint effusion	NR	13	NR	NR	88	NR	Yes	OA, RA, SpA, UIA, CTD, CPPD, bursitis, AVN, haemorrhagic joint
Bergner <i>et al</i> ^{20*}	Cross-sectional	Patients undergoing arthrocentesis	NR	39	NR	NR	74	NR	Yes	CPPD, non-crystal arthropathy
Dual energy computed tomography										
Glazebrook <i>et al</i> ¹²	Retrospective cross-sectional	Patients with arthralgia and potential gout	4/2008–2/2010	12†	NR	NR	19	NR	Yes	CPPD, possible diagnoses of RA, seronegative IA, and CTS
Bongartz <i>et al</i> ¹⁹	Prospective case-control	Patients with joint pain or swelling in rheumatology procedure clinic	10/2010–9/2012	40	NR‡	62.1	41	58.7	Yes	OA, RA, septic arthritis, CTD, CPPD, unknown
Choi <i>et al</i> ¹¹	Prospective case-control	Clinic patients with arthritis	12/2009–6/2011	40	13	62	40	53	NR	RA, PsA, OA, UIA, AS
Plain radiography										
Parker <i>et al</i> ¹⁶	Retrospective cross-sectional	Patients undergoing routine lateral CXR	1978–1980	20	NR	60.8	Healthy: 69 Arthritis: 88	Healthy: 52.6 Arthritis: 58	NR	Among those with arthritis: RA, ReA, AS, PsA, CPPD, PMR, DISH

*Refers to an abstract.

†43 patients included in study initially but only 12 were found to have MSU crystals.

‡20 patients had symptom duration <6 weeks.

AS, ankylosing spondylitis; AVN, avascular necrosis; CPPD, calcium pyrophosphate disease; CTD, connective tissue disease; CXR, chest radiograph; DISH, diffuse idiopathic skeletal hyperostosis; NR, not reported; OA, osteoarthritis; PMR, polymyalgia rheumatica; PsA, psoriatic arthritis; RA, rheumatoid arthritis; ReA, reactive arthritis; SpA, spondyloarthropathy; UIA, undifferentiated inflammatory arthritis.

+ Studies Characteristics



- Most studies were single center (with exception of Naredo et al.) cross sectional or case-control studies comparing gout to other arthritis.
- The mean duration of gout ranged from 7-13 years however half of the pts in one study had symptoms duration of <6 weeks.
- In most studies both active and inactive joints were included in the analysis.
- Arthrocentesis was performed in all pts with gout. Only half of the studies reported performing arthrocentesis in the control group.



Table 2 Study characteristics

Study	Training	Blinded	Features examined	Joints included	Active joints only	Arthrocentesis of all imaged joints
Ultrasound						
Ottaviani <i>et al</i> ¹⁵	Rheumatologists trained in MSK US	Reader 1: no Reader 2: yes	Double contour sign and tophus at MTP, knee, MCP	Bilateral MTP1, MTP2, knees, MCP2, MCP3 (10 joints total)	No	No
Lamers-Karnebeek <i>et al</i> ¹⁸	Rheumatologists (2 trainees, 2 established)	Yes	Double contour sign and tophus at MTP1, knee, wrist, ankle, MCP, elbow	Knee, MTP1, wrist, ankle	No	No
Thiele <i>et al</i> ¹⁷	Rheumatologist trained in MSK US Second rheumatologist with limited training	Yes	Double contour sign MTP effusion Power Doppler of synovium	Humeral head, humero-radial joint, MCP joints, knee, MTP1	Yes	No
Naredo <i>et al</i> ¹⁴	Rheumatologists trained in MSK US	Yes	Double contour sign intra-articular, intra-bursal, or tendon/ligament hyperechoic aggregates or hyperechoic linear band	Bilateral elbow, radiocarpal, midcarpal, ulnar-carpal, first through fifth MCP, knee, tibiotalar, talonavicular, and first MTP, wrist extensor and flexor tendons, quadriceps tendon, patellar tendon, ankle retromalleolar medial and lateral tendons, ankle extensor tendons, Achilles tendon, and medial and lateral collateral ligaments of the knee, deep infrapatellar bursa, retrocalcaneal bursa and gastrocnemius, semimembranosus bursae	No	No
Nalbant <i>et al</i> ¹³	Rheumatologist trained in MSK US	NR	Nodule characteristics: density (homogenous or heterogenous), hypoechoic, hyperechoic, post acoustic shadow, adjacent cortical bone irregularity, adjacent bursitis	Sites of nodule involvement	Yes	No
Ponce <i>et al</i> ^{21*}	Not reported	Yes	Fluid characteristics: cloudy, anechoic, cloudy, mixed, dotted, corpuscular, granular	Knees, shoulders, elbows, ankles, MCPs, Baker cysts	Yes	Yes
Bergner <i>et al</i> ^{20*}	NR	NR	Double contour sign, synovitis, hypervascularisation	Knees, small finger or toe joints, elbows, ankles, shoulders, wrists	Yes	Yes
Dual energy computed tomography						
Glazebrook <i>et al</i> ¹²	2 MSK radiologists	Yes	MSU crystal deposition	Affected joint	Yes	No
Bongartz <i>et al</i> ¹⁹	2 MSK radiologists	Yes	MSU crystal deposition	Affected joint†	Yes	Yes
Choi <i>et al</i> ¹¹	MSK radiologist	Yes	MSU crystal deposition	All peripheral joints (elbows, wrists, hands, knees, ankles and feet)	No	No
Plain radiography						
Parker <i>et al</i> ¹⁶	Rheumatologist and radiologist	Yes	Inflammatory bone changes Proliferative bone changes	Sternomanubrial joints	No	No



+ Studies Characteristics



- Most of the sonographers were rheumatologist with training in MSK US
- Four out of seven US studies utilized sonographers blinded to the pts diagnosis, one study had one unblinded and one blinded sonographer.

+ DISCUSSION



- Average gout diagnosis time was 7 years and this imaging modalities might perform differently in pts with early gout.
- Pt with asymptomatic hyperuricemia were excluded
- All pts were recruited from secondary care setting – this pts might have more severe disease compared to those in primary care settings.
- The studies to date have been small and have primarily involved people with longstanding, establish disease.

+ DISCUSSION

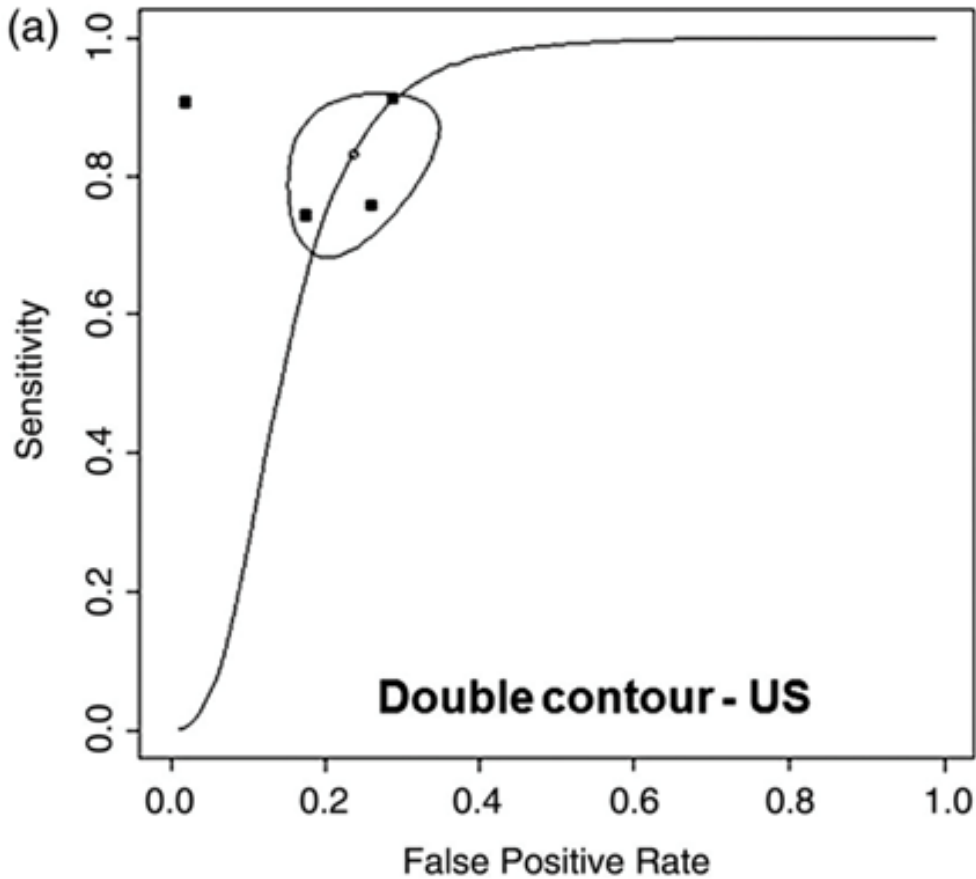
Table 3 Meta-analysis results

	Individual study parameters								AUC
	True positive	False positive	False negative	True negative	Sensitivity	Specificity	Sensitivity	Specificity	
Ultrasound: double contour sign									
Ottaviani <i>et al</i> ¹⁵	NR	NR	NR	NR	0.67	0.98	0.83 (0.72–0.91)	0.76 (0.68–0.83)	0.84
Lamers-Karnebeek <i>et al</i> ¹⁸	20	7	6	21	0.77	0.75			
Thiele <i>et al</i> ¹⁷	34	0	3	26	0.92	1.00			
Naredo <i>et al</i> ¹⁴	68	7	23	35	0.75	0.83			
Bergner <i>et al</i> ²⁰	36	21	3	53	0.92	0.72			
Ultrasound: tophus									
Ottaviani <i>et al</i> ¹⁵	NR	NR	NR	NR	0.74	1.00	0.65 (0.34–0.87)	0.80 (0.38–0.96)	0.75
Lamers-Karnebeek <i>et al</i> ¹⁸	5	2	21	26	0.19	0.93			
Thiele <i>et al</i> ¹⁷	27	0	10	26	0.73	1.00			
Naredo <i>et al</i> ¹⁴	78	11	13	31	0.86	0.74			
Nalbant <i>et al</i> ¹³	15	3	5	17	0.75	0.85			
Dual energy computed tomography: MSU crystal deposition									
Glazebrook <i>et al</i> ¹²	12	4	0	15	1	0.79	0.87 (0.79–0.93)	0.84 (0.75–0.90)	0.90
Bongartz <i>et al</i> ¹⁹	36	7	4	34	0.90	0.83			
Choi z <i>et al</i> ¹⁹	34	3	6	37	0.78	0.93			

AUC, area under the curve; MSU, monosodium urate, NR, not reported.

+LR: 3.46
- LR: 0.22

+ Double contour sign



The pooled (95% CI)
sensitivity 0.83 (0.72 to 0.91)
Specificity 0.76 (0.68 to 0.83)

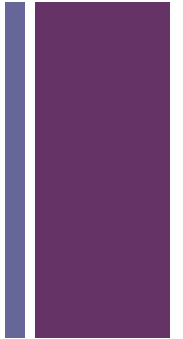
+LR: 3.46

- LR: 0.22



Is the Double Contour Sign Specific for Gout? Or Only for Crystal Arthritis?

Singh J and Dalbeth N. The Journal of Rheumatology March 2015, 42 (3) 353-354

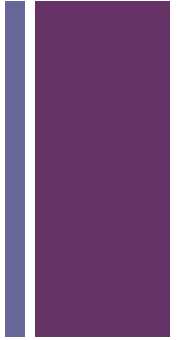


- 225 acutely inflamed joints were examined
- All patients underwent synovial fluid analysis to make the diagnosis of gout or CPPD or other arthritis
- The sensitivity of the DC sign for crystal arthritis was 85% and specificity was 80%.
- **Specificity for gout was 64%, and for CPPD 52%.**
- The combination of DC sign with hypervascularization in Doppler studies and elevated SUA levels increased specificity for gout to 90% ($p < 0.01$)
- The authors suggest that one reason their results differ from those of other reports is that previous studies have had very few control subjects with CPPD
- The DC sign has also been described in up to 29% of individuals with asymptomatic hyperuricemia



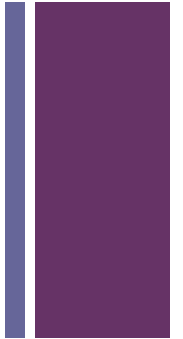
In conclusion...

- Synovial fluid analysis remains the preferred approach to diagnosing gout. Nevertheless, ultrasound might be helpful particularly in patients with high clinical suspicion of gout despite negative or technically difficult arthrocentesis.





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In the matter of Ms. M's pregnancy... Mr. Peanut... you ARE the father

