Contrast enhanced ultrasound in Rheumatology

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High-resolution ultrasound (US): more sensitive than clinical assessment in detecting joint synovitis and enthesitis in inflammatory arthritis.

Gray scale and power Doppler imaging: evaluate the neovascularization of synovium – allow grading and follow up post treatment.

Ultrasound contrast agents significantly enhance the signal in vessels are expected to increase the diagnostic value of ultrasound in inflammatory arthritis.
The contrast-enhanced ultrasonography (CEUS) of joints is performed with linear probes, with a mechanical index less than 0.1.

The mean frequency used by these probes, corresponding to the resonance frequency of microbubbles, does not allow obtaining perfect resolution images.

**Levovist**: obsolete  
**Sonovue**: 4.8 ml or 2.4 ml in bolus (rapid one minute perfusion) or Slow (15-20 minute perfusion)

Bolus administration: the examination window is of 3-5 minutes. The slow 15-20 minutes intravenous perfusion allows the examination of the joints throughout this time period.
Technique

High variability of the time interval from injection to the appearance of microbubbles in the joints

In normal articular and periarticular structures in the hand and the foot, the contrast agent frequently appears later, after up to 30 seconds, due to the very small caliber of the vessels at this level.

In the inflamed synovium of the large joints the presence of microbubbles is frequently detected 15 seconds after contrast agent administration.

In old, largely fibroserd synovial pannus, vessels can be visualized in gray scale, sometimes only 1-2 minutes after the contrast injection.

Rednic et al, Med Ultrason 2011
Remember

Normal joints may show minor or scattered vessels

The detection of vascularization in normal joints depends on:
• the quality of the ultrasound machine
• optimal setting
• the accuracy of the image acquisition technique
• the examined joint

Two studies reported no color signal before or after contrast administration in the small hand joints of healthy subjects

Further studies are required in order to establish the threshold between normal and pathological findings in various joints, using standard equipment and examination techniques
Contrast-enhanced ultrasound findings in arthritis

a) Longitudinal dorsal gray-scale ultrasound of the second MTP joint, showing a hump (arrow) of hypertrofic synovitis in a patient with rheumatoid arthritis
b) unenhanced Power Doppler demonstrates pathologic color signal
c) power Doppler signal enhances after intravenous contrast agent injection, at least one grade. Note new vessels visible in the middle of the pannus

Rednic et al, Med Ultrason, 2011
Contrast-enhanced ultrasound findings in arthritis

a) Residual pannus (arrow) in the elbow of a treated rheumatoid arthritis patient. The absence of power Doppler signal suggests inactivity.
b) 20 seconds after contrast agent injection a rim of enhancement (arrows) is detected proving still active disease.
c) Two minutes after injection a new vessels (arrow) is detected in the middle of fibrotic pannus.

Rednic et al, Med Ultrason, 2011
Longitudinal scan of the lateral epicondyle enthesis in a 31-year-old patient

A: Active enthesitis (grade 3) with vascularization adjacent to the cortical bone and large confluent marked vessel covering >50% of the examined area.

B: Contrast-enhanced ultrasound examination using the dedicated Contrast Tuned Imaging technology (LA522 probe) confirms abnormal vascularization arising from periosteal artery (arrow), and shows movement of bubbles in capillaries (asterisks) 20 seconds after the injection of the contrast agent.

Mouterde et al Arthritis Care and Research 2014
Transverse plane at the wrist through extensor carpi ulnaris tendon. (a) CEUS examination with hypoechoic peritendinous space before contrast medium washin. (b) Hyperechoic peritendinous space and intratendinous enhancement after contrast medium washin. (c) PDUS examination. Grade 2 in every scoring system. Arrows, border of tendon sheath; cross, synovial thickening; ECU, extensor carpi ulnaris tendon

Klauser et al, Arthritis Res Ther. 2010
A 21-year-old male patient with clinically bilateral active sacroiliitis. Bony landmarks are marked as the following: is located at the median sacral crest; ▲ points toward the bony contour of the sacrum. The thin arrow shows enhancement in the first sacral foramen. Thick arrows show bilateral enhancement in the dorsocaudal parts of the sacroiliac (SI) joints.

Klauser et al, Arthritis Rheum 2009
Grayscale, power Doppler and contrast-enhanced US are accurate tools for the detection and follow-up of synovitis in RA wrist and finger joints, with contrast-enhanced US being most sensitive compared to MRI

Ohrndorf et al Ultraschall Med 2011

When the synovitis in painful knee osteoarthritis was evaluated a higher sensitivity of contrast enhanced power Doppler compared to MRI in the characterization of inflammatory changes of the suprapatellar recess was demonstrated

Song et al, Annals Rheum Dis 2008
Controversies

The differences in the results of the studies regarding contrast enhanced power Doppler sensitivity can be explained by the small number of examinations, the quality of the equipment used, the technical image acquisition accuracy, the normal-pathological differentiation criteria, the examined joint, or the joint disease.
An important contribution to the contrast agent in the arthritis management is the possibility of evaluation of the thickness of the inflamed synovium.

The amount of synovitis is correlated with its aggressive, erosive behavior. The exact measurement of the thickened synovium is also important in therapy monitoring (b).
Analyzing the time-intensity curves in a region of interest offers an opportunity for quantitative quantification of the inflammation, a permanent goal in rheumatology.

Area under the curve, the slope of the ascending and descending curve, the possibility to calculate the flow rate, vascular volume and mean velocity are promising tools to quantify inflammation.

**Reproducibility is not verified**
Aim

The purpose of this study is the sonographic investigation of active synovitis in small hand joints in patients with early psoriatic arthritis by the use of contrast enhanced ultrasound (CEUS)
Methods and Materials I

We recruited 43 patients (15 men, 28 women, ages 17-44 years) with established psoriasis and strong clinical suspicion of psoriatic arthritis. All patients were evaluated according the Psoriasis Area Severity Index (PASI) score.

Each patient underwent gray scale and power Doppler US scan in transverse and longitudinal section in all small metacarpophalangeal and interphalangeal joints between the second and the fifth digit of the most affected hand. The machine used was a Logiq 9 (GE Medical Systems Ultrasound) with linear array transducers (10 MHz and hockey-stick).

The software for contrast agent was activated for the linear 10 MHz transducer. Subsequently the most suspicious joint was selected and was rescanned after bolus injection of intravenous contrast agent (Sonovue, Bracco). Five normal volunteers were also included in the study as controls.
The bolus administration of contrast agent (Sonovue, 1 fl, linear transducer 10 MHz, Mechanical Index=0.12) was followed by scanning of the selected joint for a maximum of 3.5-4 minutes. None of the patients had any allergic reaction to the contrast agent. The total scanning time for each patient was ~30 minutes.
Results

All 43 patients had skin psoriasis, 2 had dactylitis and 3 nail involvement. The mean time with skin disease was 12.7 years (2-34 years) and mean PASI score was 7.8

A total of 516 small hand joints were scanned in patients with psoriasis and 60 normal joints in controls

Thickening of the synovium was evident in 27/516 joints and normal found to be 489/516 (94.8%) small hand joints. The PDUS scan was positive for neovascularity in 8/516 (1.6%) whereas CEUS was positive for neovascularity in 15/516 (2.9%) (p<0.05)
Technical considerations - limitations

1. Time limit for microbubbles - a maximum of two joints were examined in a couple of patients

2. A visual classification of pathology was performed - no curve was recorded.

3. The CEUS software was not activated in the hockey-stick transducer.
CEUS seems to enhance the presence of abnormal synovial vessels in small joints of the hand and it may be used as a supplementary imaging tool in the detection of active synovitis in patients with psoriasis and early psoriatic arthritis. The evolution of sonographic equipment could aid in the clinical application of this sophisticated technique.

Larger studies need to be conducted in order to evaluate the precise role of CEUS in diagnosis and follow up of patients with various types of inflammatory arthritis.
Thank you for your attention