

Is power Doppler sonography the new frontier in therapy monitoring?

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Therapy monitoring is a veritable obsession for rheumatologists. Hundreds of researchers have dedicated an immense amount of time producing a great number of studies focusing on the critical question: How does the therapy work?

Several recent studies on musculoskeletal sonography support the hypothesis that this imaging technique could challenge the supremacy of conventional X-ray for the detection of bone erosions and disease progression in patients with rheumatoid arthritis (RA) (1-9). Sonography continues to evolve rapidly and new or updated, more cost-effective equipment seems to hold out great potential as reliable tools for the diagnosis of early aggressive arthritis and for the monitoring of therapy (9-14).

Power Doppler sonography (PDS) in particular seems to have very exciting possibilities because it could provide the solution to the still unsolved problem of combining high quality morphologic information with blood flow imaging (11-28). Present PDS technology has improved to the point that even marginally increased levels of vascularity can be detected quite early both around and inside joints and tendons. Although any predictions regarding the

future role of PDS in the monitoring of RA can only be based on extrapolation at the present time, it seems likely that this topic will develop into an important area of clinical research over the next few years. Up to now, to the best of our knowledge only a few studies focusing on the role of PDS in the monitoring of therapy in the rheumatic diseases have been published (Table I). A major challenge in PDS will be to assess its potential predictive value with respect to radiographic changes.

Probably only the handful of rheumatologists directly engaged in this exciting area of research and aware of the results that can be obtained with PDS have fully grasped the potential of this technique to become the gold standard for the assessment of soft tissue changes induced by acute and chronic inflammation. The widespread reluctance to accept the idea of an imminent sonographic revolution in therapy monitoring may be explained by the lack of strong evidence supporting the diagnostic potential of PDS and complex problems regarding the standardization of the procedure.

Standardisation must be a key target in PDS for it is perhaps the most equipment- and operator-dependent imaging technique currently in use. While evi-

Table I. Literature on power Doppler sonography in the monitoring of therapy in the rheumatic diseases.

Authors	No .of patients	Clinical diagnosis	Treatment	Follow-up	Reduction of synovial perfusion
Newman <i>et al.</i> 1996 (11)	7	5 RA 1 PA 1 CPPD	IA injection of 40 mg (1 ml) of triamcinolone hexacetonide and 2 ml of 1% lidocaine hydrochloride	1-2 weeks	7/7
Stone <i>et al.</i> 2001 (12)	12	12 RA	IV methylprednisolone (125 mg) for 3 consecutive days, then 20 mg oral prednisolone	1 week	10/10
Hau <i>et al.</i> 2002 (13)	5	5 RA	Etanercept (2 x 25 mg/week subcutaneously)	1 month	5/5
D'Agostino <i>et al.</i> 2002 (14)	2	2 SpA	IV infliximab (3 mg/kg) at weeks 0, 2 and 6	14 weeks	2/2

IA:intra-articular; IV: intravenous; RA: rheumatoid arthritis; PA: psoriatic arthritis; CPPD: calcium pyrophosphate-deposition disease; SpA: seronegative spondylarthropathy.

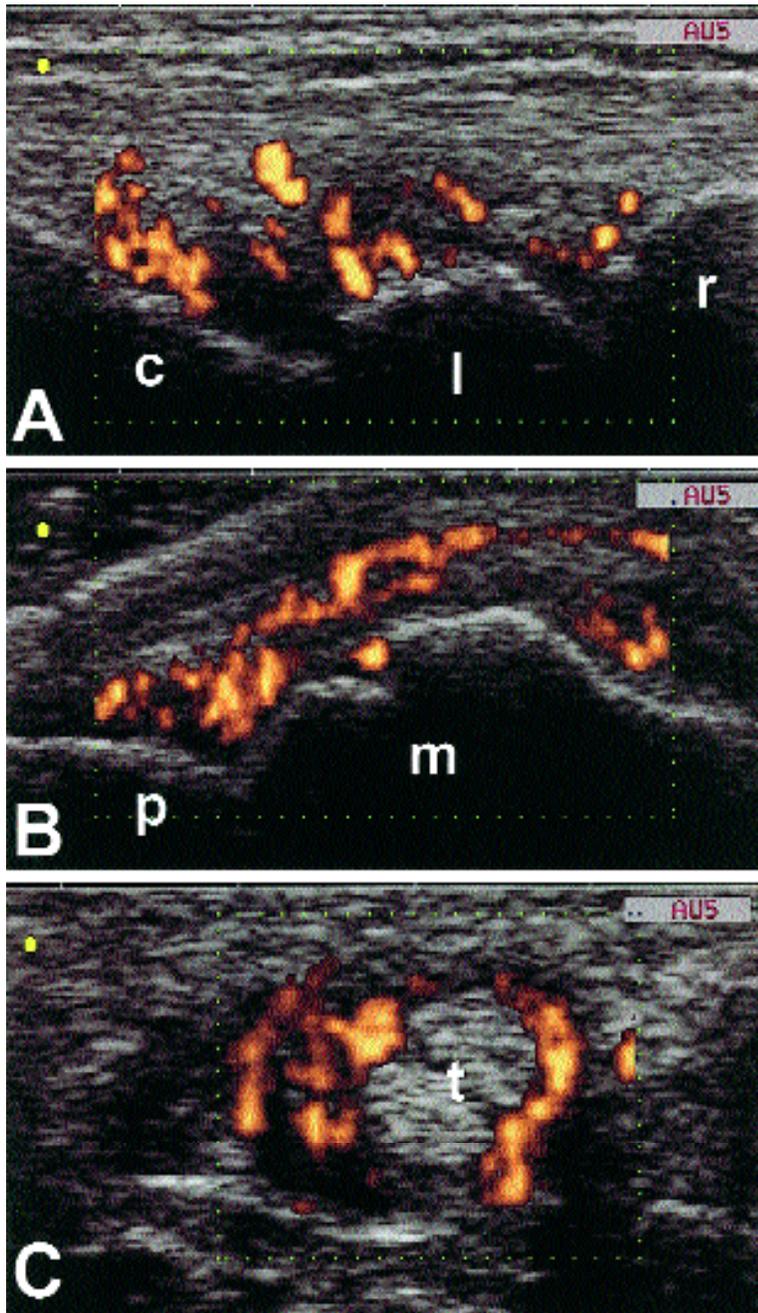


Fig. 1. Representative examples of PDS pictures showing active synovitis in patients with rheumatoid arthritis. PDS signals (coloured spots) correspond to areas of increased blood flow both around joints and tendons, and inside the rheumatoid pannus: (A) wrist joint; (B) metacarpophalangeal joint; (C) finger flexor tendons. c = capitate bone; l = lunate bone; r = radius; p = proximal phalanx; m = metacarpal head; t = finger flexor tendons.

dence is being gathered of the clinical efficacy and reliability of PDS in daily rheumatological practice, an "awareness-raising" process aimed at rheumatologists should be launched. If they have the opportunity to regularly see PDS images, it should open their minds to the provocative idea that "a picture is worth a thousand experiments" (29). From a pictorial point of view, images

of active synovitis are quite impressive, all the more so because no PDS signal can be detected in healthy subjects. Active synovitis is characterised by a marked increase of joint and tendon perfusion (Fig. 1). The raised blood volume in the target tissues can be clearly depicted by PDS using high resolution linear probes. PDS imaging of synovitis combines functional informa-

tion (blood flow imaging) and highly accurate morpho-structural details.

The high sensitivity of PDS in the detection of active synovitis has significant potential in therapy monitoring. Representative examples of the short-term changes in the PDS signal that follow the intra-articular injection of triamcinolone acetonide are shown in Figures 2 and 3. The loss of signal was clearly linked to the marked clinical improvement experienced after the injection. Figures 4 and 5 show PDS changes after 3 months of treatment with disease modifying anti-rheumatic drugs in patients with chronic arthritis. All of these images were obtained using an AU5-Harmonic Doppler sonograph (Esaote Biomedica, Genoa, Italy) equipped with a linear probe (B mode frequency 10-13 MHz and colour mode frequency 7 MHz). The PDS settings were standardised using a pulse repetition frequency of 1000 Hz and low wall filters. Colour gain was initially set at a level just below the disappearance of colour noise deep in the cortical bone. Our instrument did not detect any PDS signal inside the joints of asymptomatic healthy subjects at the reported setting. Clinical assessment of pain at baseline and during the follow-up study was carried out by the patient using a visual analogue scale (VAS) (ranging from 0 to 10).

Sonography has been defined as the "art of artefacts" since inter- and intra-operator variability can be significant. The main factors that can impinge on PDS findings, resulting in artefacts and misinterpretations include: the quality of the sonographic equipment, the machine settings, the scanning technique, and the methods used to score the images (30). At present this makes it difficult to compare data or evaluate the findings of PDS examinations performed at other institutions. However, standardisation of the PDS procedure would not be an impossible undertaking.

The future impact of PDS on the assessment of disease activity, disease progression, and the monitoring of therapy in patients with RA cannot yet be determined. Up to now PDS in rheumatology has been no more than a

Fig. 2. A 32-year-old woman with a 3-year history of rheumatoid arthritis presented with severe pain in her right wrist (VAS score: 8) and was treated with an intra-articular (IA) injection of triamcinolone acetonide (20 mg). Two weeks after the injection, joint pain was markedly decreased (VAS score: 2) and a reduction in the PDS signal was clearly evident in the sonographic image. Grey scale evaluation did not reveal significant morphological changes. **c** = capitate bone; **l** = lunate bone; **r** = radius; **t** = extensor tendons of the fingers.

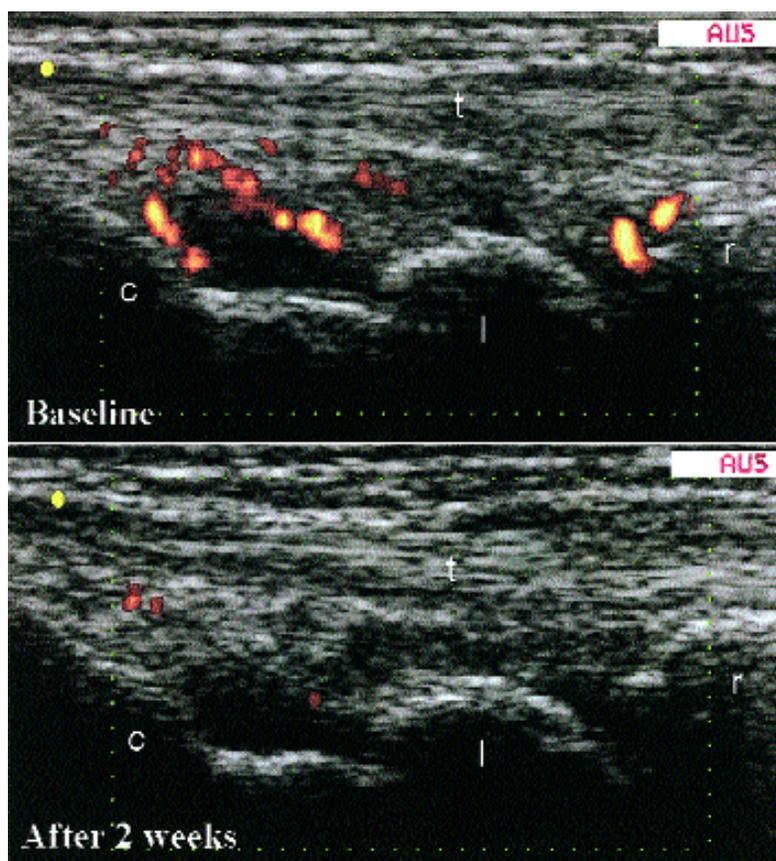
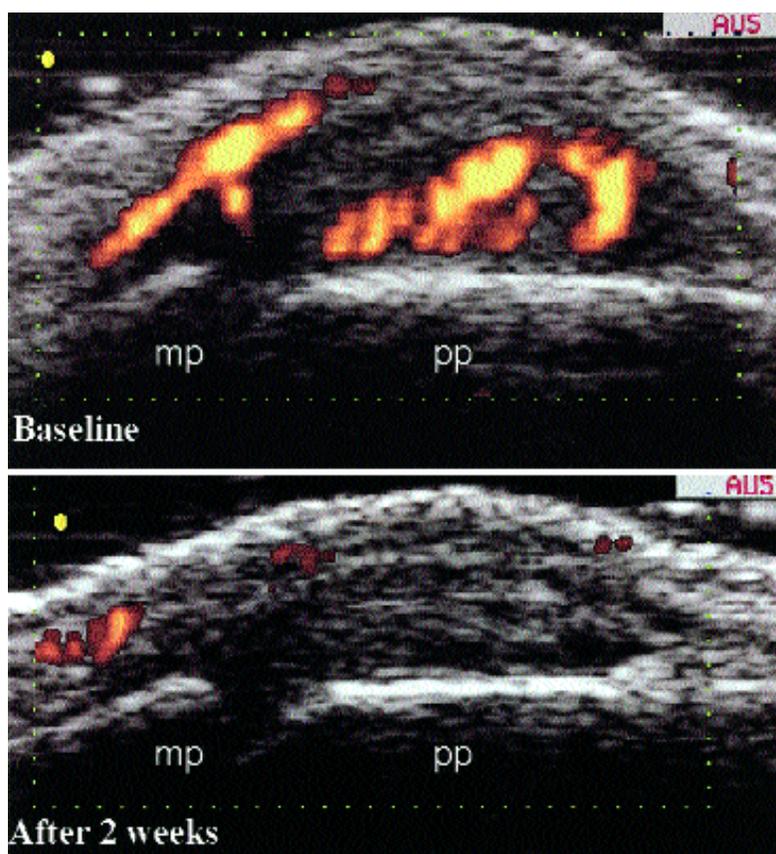


Fig. 3. A 37-year-old woman with psoriatic arthritis presented with acute onset of pain and swelling of the proximal interphalangeal joint of the third finger of her dominant hand. Baseline ultrasound examination showed the presence of the typical findings of very active synovitis: massive synovial proliferation with areas of high intensity indicating perfusion. The patient was treated with an IA injection of triamcinolone acetonide (10 mg). Two weeks after the injection, there was a dramatic reduction of pain (VAS score decreased from 8 to 3). Sonography showed decreased soft tissue thickening and a dramatic reduction in the PDS signals. **mp**: middle phalanx; **pp**: proximal phalanx.



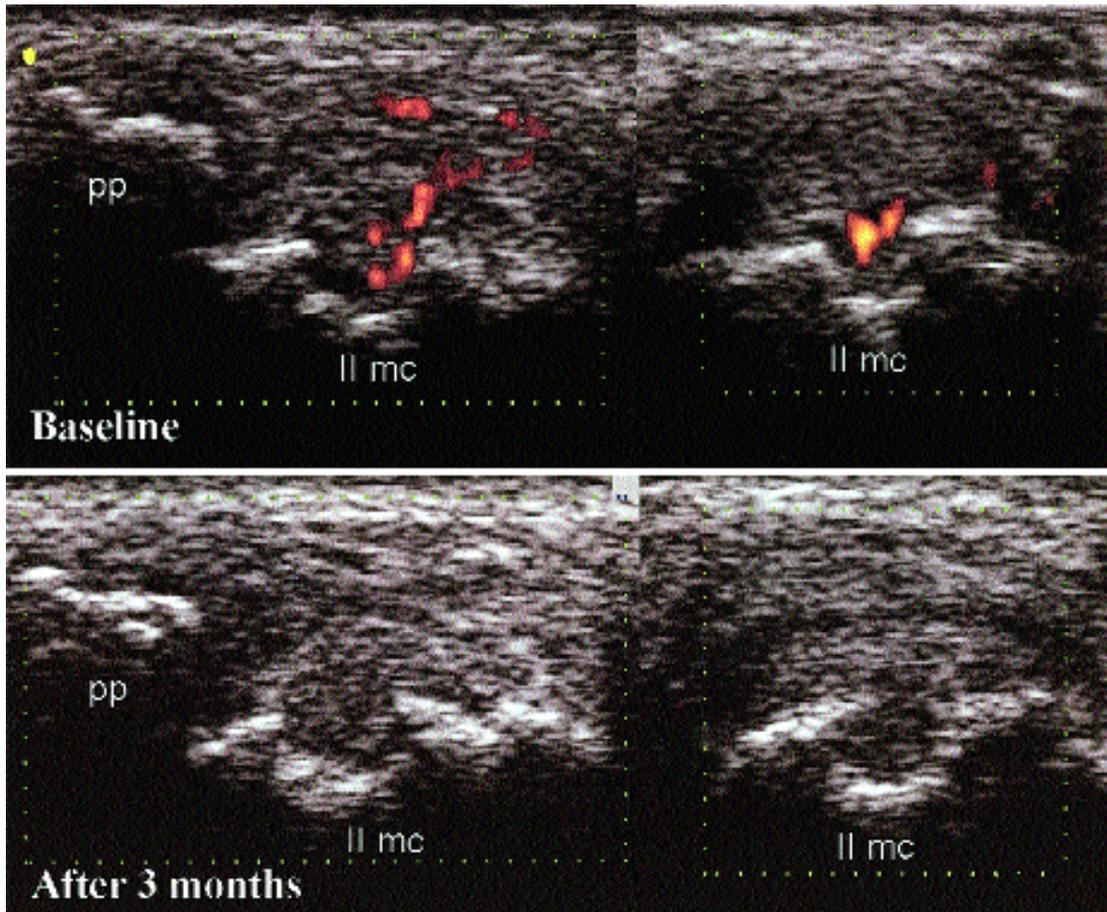


Fig. 4. A 57-year-old man presented with psoriatic arthritis and active synovitis of the second metacarpophalangeal joint of the left hand. Baseline sonographic examination revealed increased IA perfusion with synovial proliferation mainly localised around and inside an area of eroded bone at the metacarpal head. After 3 months of treatment with oral methotrexate (10 mg per week), pain improved (VAS score reduced from 6 to 0) and the intra-articular PDS signals disappeared. **II mc**: metacarpal head of the second metacarpophalangeal joint; **pp**: proximal phalanx.

fascinating and exciting tool for a few enthusiastic pioneers. However, even if conducting outcome research in this field may be labourious, we believe that the “power” of PDS is so important to justify immediate and intensive efforts to explore its potential benefits and to transform an intriguing “toy” into a powerful tool for daily clinical decision making. Evidence-based guidelines for PDS imaging in rheumatology are urgently needed, as well as clinical trials to assess the benefits of PDS for specific clinical problems.

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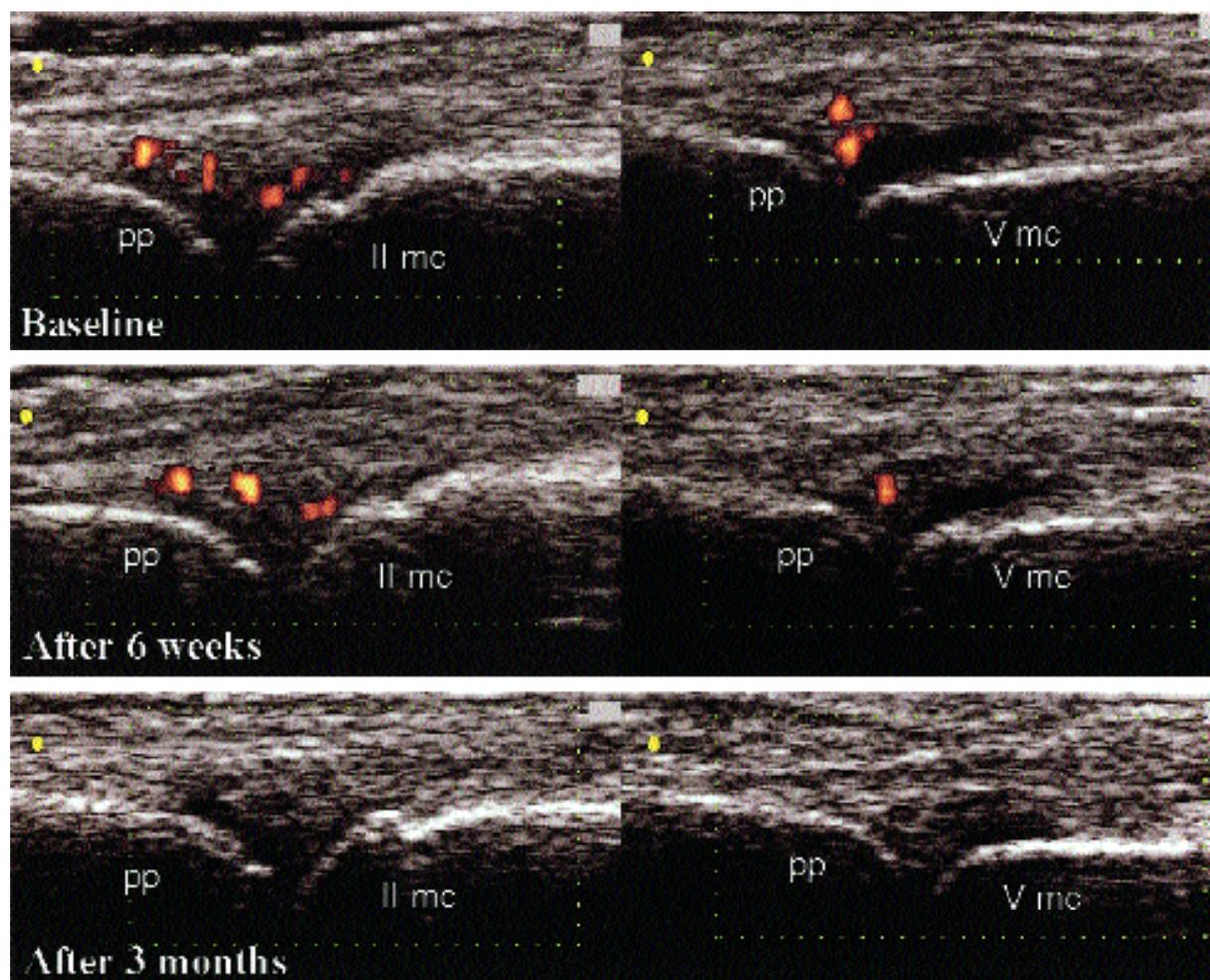


Fig. 5. Representative sonographic images at baseline and at follow-up sonographic examinations of the right hand of a 55-year-old woman with rheumatoid arthritis. Baseline sonographic examination showed mild joint cavity widening with intra-articular PDS signals. After 6 weeks of therapy with leflunomide 20 mg/day, although the VAS score fell from 8 to 4 there was no significant change in the PDS signals. After 3 months there was further clinical improvement (VAS score:0) and sonography showed no signs of increased perfusion. **II mc**: metacarpal head of the second metacarpophalangeal joint; **V mc**: metacarpal head of the fifth metacarpophalangeal joint; **pp**: proximal phalanx.

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