Three-Dimensional Power Doppler Sonographic Visualization of Synovial Angiogenesis in Rheumatoid Arthritis

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In recent years musculoskeletal ultrasound has become an established imaging technique in the diagnosis of patients with rheumatic diseases[1]. Technological improvements such as high resolution ultrasound and power Doppler mode have made possible the assessment of synovial proliferation along with the detection of low-velocity blood flow at the microvascular level[2]. Joint damage in rheumatoid arthritis (RA) is caused by a tumor-like proliferation of synovial cells accompanied by an increase in vasculature (angiogenesis) to support the metabolic requirements.

Neovascularization is a complex process in which new blood vessels develop from the existing microvascular bed, involving endothelial cell division, selective degradation of vascular basement membranes and the surrounding extracellular matrix, and endothelial cell migration. Since 3D power Doppler sonography plays an important role in obstetrics and oncology for assessing the vascular system[3,4], we use it to visualize intraarticular synovial new blood vessel formation in painful and swollen joints of patients with RA.

Patients and methods. Inflamed wrist, knee, or finger joints (metacarpophalangeal joint, MCP, and proximal interphalangeal joint, PIP) were investigated by ultrasound in 21 patients with active RA. The group consisted of 16 women and 5 men, ranging from 30 to 82 years of age (mean age 57.8). In 15 (71%) patients rheumatoid factor was found and laboratory disease activity variables such as C-reactive protein (CRP; > 1 mg/dl) or erythrocyte sedimentation rate (ESR; > 20 mm/h) were elevated in 20 (95%) patients (Table 1).

Ultrasonography was carried out by a linear array transducer with variable frequency from 5 to 12 MHz (L12-5/38 mm, HDI 5000, ATL, Philips, Bothell, WA, USA). Standardized scans according to the Guidelines for Musculoskeletal Ultrasound in Rheumatology[5] were performed to investigate joint effusion. Vascularity near and inside the joint capsule was visualized by power Doppler mode. In a region with high Doppler signal intensity the transducer was mechanically moved in one direction (freehand technique) to obtain a sequence of 2D power Doppler images to provide the third dimension. The online 3D power Doppler function, provided by the ATL, HDI 5000 vascular software, was used to generate a 3-dimensional image of the peri- and intraarticular blood vessels in which grey-scale information of the surrounding tissue was already subtracted. The acquired data were digitally stored on hard disk as a cine loop in which the 3D blood vessel tree could be viewed as it rotates, which enhances depth perception and gives a true 3D perspective.

Table 1. Clinical characteristics of the 21 patients with rheumatoid arthritis.

Patient	Age/Sex	Joint	CRP, mg/dl	ESR, mm h	RF (Pos/Neg)
1	74 F	Wrist	4.3	50	Pos
2	30 F	Wrist	7.6	63	Pos
3	59 F*	Wrist	1.5	27	Pos
4	64 F	Wrist	1.9	41	Pos
5	61 F	Wrist	1.5	20	Pos
6	33 M*	Knee	1.3	25	Neg
7	42 F	Wrist	1.5	38	Pos
8	72 F	Wrist	1.8	57	Pos
9	63 M	Knee	2.4	13	Pos
10	71 F	Wrist	2.6	48	Pos
11	51 F	Wrist	0.5	41	Pos
12	55 M	MCP II	1.2	27	Pos
13	78 F	Wrist	3.8	96	Neg
14	72 F	Wrist	1.2	45	Pos
15	82 F*	MCP II	3.3	59	Neg
16	54 F	Knee	1.5	71	Pos
17	48 F	Wrist	2.7	44	Neg
18	51 F	Wrist	3.2	64	Pos
19	35 M	Wrist	0	25	Neg
20	58 M	Wrist	0	12	Pos
21	62 F	PIP III	1.1	24	Neg

CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, RF: rheumatoid factor. * Patient 3: Figure 2a & b; Patient 6: Figure 1a & b; Patient 15: Figure 3a & b.

Results. In 21 patients with RA who showed power Doppler signals in 2D mode, the 3D function revealed a blood vessel tree branching out from periarticular small blood vessels into the joint capsule. To date it was possible to obtain good 3D imaging of synovial vasculature in the wrist (15 patients, Figure 2), knee (3 patients Figure 1), and finger joints (MCP II and PIP III; 3 patients, Figure 3).

In all of these patients we found clinical evidence of arthritis in the examined joint, and in 95% of the patients

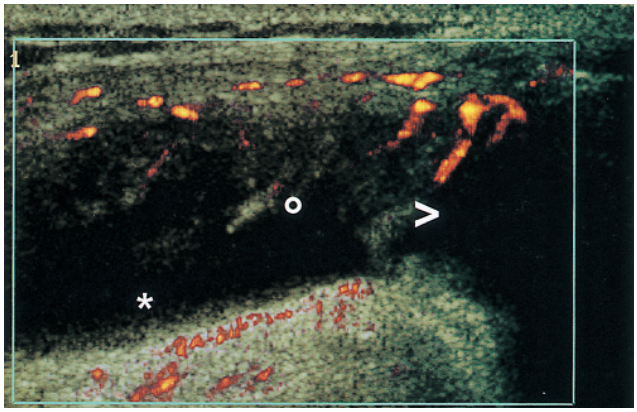

Figure 1A. Knee joint: Suprapatellar transverse scan in neutral position (standard scan[5]), lateral recessus; showing effusion (*), synovial proliferation (°), peri- and intraarticular blood vessels (>) .

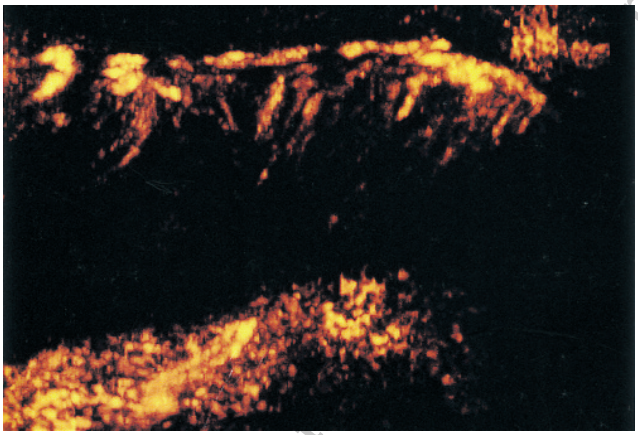

Figure 1B. 3D power Doppler image.

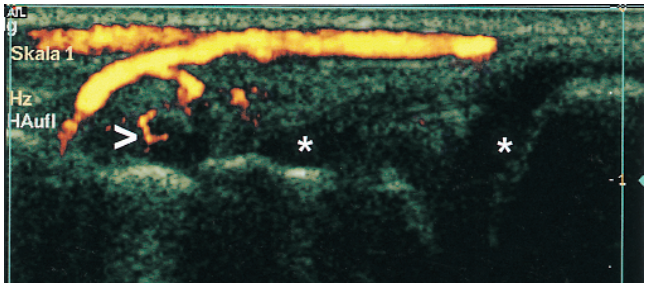

Figure 2A. Wrist: Dorsal longitudinal ulnar scan (standard scan[5]) showing effusion (*), peri- and intraarticular blood vessels (>).

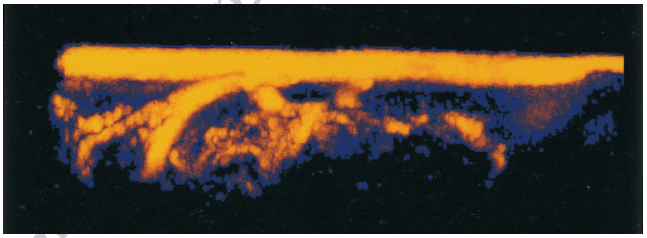

Figure 2B. 3D power Doppler image.

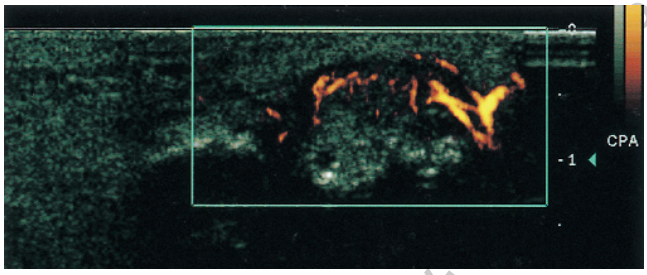

Figure 3A. Metacarpophalangeal II joint: Dorsal longitudinal scan (standard scan[5]) showing synovial proliferation and peri- and intraarticular blood vessels.

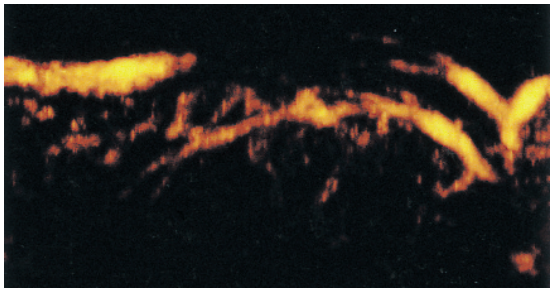

Figure 3B. 3D power Doppler image.

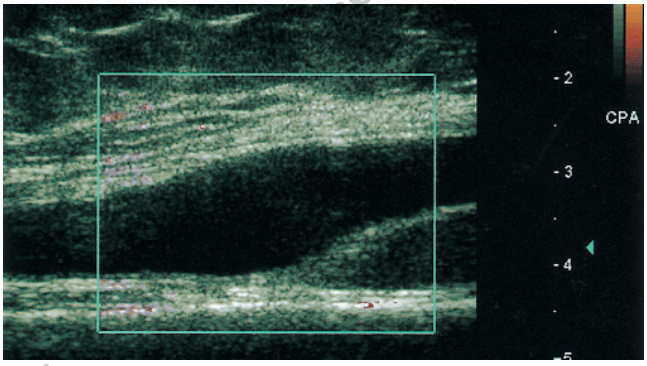

Figure 4A. Osteoarthrosis of knee joint (79-year-old woman): suprapatellar longitudinal scan (standard scan[5]) lateral recessus showing effusion with no power Doppler signal.

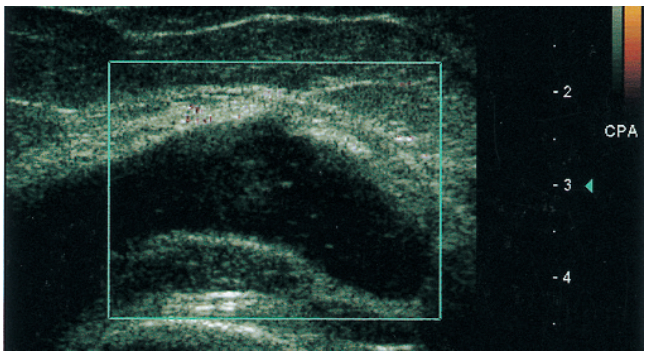

Figure 4B. Osteoarthrosis of knee joint (79-year-old woman): suprapatellar transverse scan (standard scan[5]) lateral recessus showing effusion with no power Doppler signal.

laboratory disease activity could be proven by elevated CRP values or an increased ESR.

Conclusion. This is the first report on 3D power Doppler imaging of synovial angiogenesis, confirming it as a marked improvement for the assessment of synovial vasculature and its morphologic structure. In comparison with 2D power Doppler, 3D mode reveals more, very small blood vessels in connection with the whole blood vessel tree, and provides a new opportunity to study the architecture and alterations of synovial vasculature in various joint disorders (Figure 4) and under different conditions.

Thus 3D power Doppler sonography is not only a valuable method for diagnosis and monitoring of disease activity in RA, it may also be used as an "*in vivo*" model to study the mechanisms between inflammation and angiogenesis in rheumatoid joint damage.

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