

# Ultrasound of the hand in systemic sclerosis

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## ABSTRACT

Systemic sclerosis is a chronic connective tissue disease characterized by multi-organ involvement but the main clinical changes occur in the hands, secondary to skin, joint and microvascular damage. Therefore the hand received a special attention for imaging and especially for ultrasound evaluation. In rheumatology US become an extension of the clinical examination and particularly in systemic sclerosis it has been proven to help with a better assessment of the skin, blood vessels, joints and tendons involvement. This evolution was allowed by permanent improvement of technology along with expanding the range of ultrasound applications which happened especially in past decade.

**Keywords:** systemic sclerosis, ultrasound, hand, musculoskeletal

## BACKGROUND

Systemic sclerosis (SSc) is a chronic connective tissue disease characterized by multi-organ involvement and may affect the skin, vessels, the heart, joints, kidneys and lungs (1). Ultrasound (US) is a cost-effective, noninvasive, accessible imaging modality that clinicians use at the point of care to assess disease activity, morphostructural changes, and therapeutic efficacy regarding different rheumatic conditions. Therefore, US is available for assessment of different organ targets involved in SSc (2).

## MUSCULOSKELETAL

In rheumatology and especially in rheumatology related-US, it is obvious that the musculoskeletal (MSK) system receives the most attention and SSc is a connective tissue disease with frequent MSK involvement, reported between 46 and 97% (3,4). MSK involvement could include stiffness, arthritis, tendon sheath involvement, joint contractures, and proximal muscle weakness, but hands (particularly the metacarpophalangeal [MCP] and proximal inter-

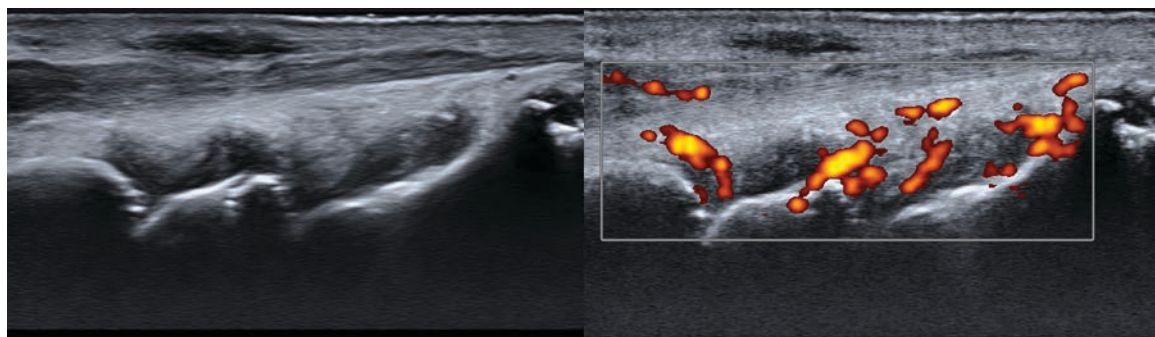
phalangeal [PIP] joints), and wrists are the most commonly affected joints (5). Data from the European League Against Rheumatism Scleroderma Trial and Research Group (European Scleroderma and Trials and Research group) database indicate point prevalences of 16% for synovitis, 11% for tendon friction rubs, and 31% for joint contractures (6). It is well known that US is superior to clinical examination in detecting wrist and hand synovitis and tenosynovitis in SSc (7,8). Very recently, a new study reconfirmed the previous published data (9).

## Joints

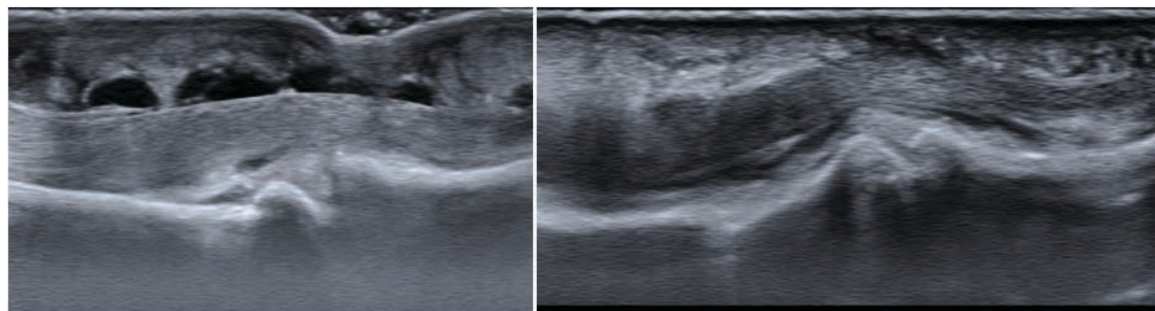
In order of frequency, the main changes detected by US of the hands and wrists joints in SSc patients are: joint effusion, synovial proliferation associated or not with power doppler (PD) signal, periarticular calcinosis and joint space narrowing. Joint effusion and synovial proliferation are found in half of cases with significantly higher and more complex involvement of the wrist (7,10). A high prevalence of synovial hypertrophy and joint effusion was demonstrated in SSc patients with arthralgia, with an 11-49% rate

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**FIGURE 1.** Dorsal longitudinal scan of the wrist with evidence of synovial hipertrophy with intense PD signal



**FIGURE 2.** Palmar longitudinal scan of the 3rd and 4th finger showing tenosynovitis of the flexor tendon

of PD positivity at the wrists (11). Interestingly, there was a similar prevalence of joint effusion in rheumatoid arthritis (RA) patients, however, the presence of PD signal and synovial hypertrophy were more frequent in RA patients, especially PD grade 2 or 3 (7,8).

## Tendons

Tendon involvement is another common manifestation in SSc patients. Tenosynovitis of the hand was found in 27% of SSc patients, showing a double pattern, inflammatory and sclerosing type (8). The sclerosing pattern is defined as an iso- or hyperechoic hypertrophy of the tendon sheath with concentric alternating iso-and/or hyperechoic layers and it has been described as a specific characteristic of the disease (8,12). An important thing is that sclerosing tenosynovitis is clinically characterized by palpable tendon friction rubs (13). Tendon friction rubs and also sclerosing tenosynovitis in the hand, has been demonstrated to be associated with diffuse cutaneous involvement and interstitial lung disease (12,14). This specific pattern is more frequently detected at the extensor tendons of the hand (8). Another frequent manifestation in SSc patients detected by US in hands is A1 pulley thickening (15). This feature is not specific to SSc but it is correlated with hand disability and disease duration (16).

US enthesopathy are frequently found in SSc patients. Furthermore, common extensor tendons en-

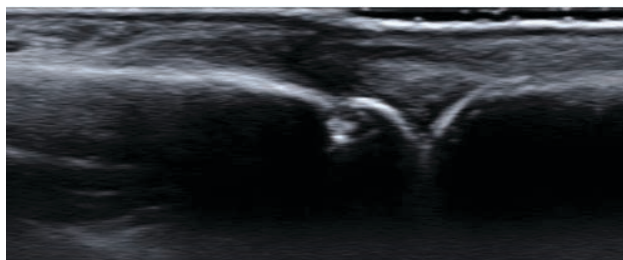
thesopathy was correlated with synovio-entheseal complex inflammation, suggesting that enthesal inflammation in SSc may share the same micro-anatomical targets as found in SpA (17).

## Bones

Distinctive abnormalities detected by US include bone erosions, cortical irregularities, acroosteolysis and osteophytes. Erosions are small, discrete, and less invasive than those of RA (5). There are much less common than in RA patients being found in up to 11% of SSc cases (7). Cortical irregularities are described as loss of continuity of cortical bone without any clear evidence of erosion/osteophyte/fracture. In some studies the prevalence of bone erosions and cortical irregularities was not significantly higher in patients than in healthy controls (10).

The normal distal phalanx, when assessed with US via a dorsal approach, showed either a straight or slightly concave cortical hyperechoic line at its waist that ends with small elevation at the tuft. Disappearance of this outline was defined as a sign of acroosteolysis, as well as an abrupt ending of the dorsal cortex. The most of the patients present PD signal in the area of resorption. (18). This represent a characteristic feature of the disease and it was found in 20% of cases with a 90% sensitivity (18).

According to Keen et al. US osteophytes are defined as cortical protrusions seen in two planes



**FIGURE 3.** Lateral longitudinal scan of the 2<sup>nd</sup> metacarpophalangeal joint showing a small erosion of 2<sup>nd</sup> metacarpal head bone

(19,20). This is a nonspecific finding and it appears in the context of degenerative lesions of the joint (15). US showed a significantly higher number of joints with osteophytes than X-rays (59 vs 27%) (7).

## CALCINOSIS

Calcinosis represent another specific characteristic of the disease and it is defined as hyperechoic foci with or without acoustic shadowing. In order of frequency it can be located in different sites - soft tissue (71%), peritendinous (47%), periarticular (35%) and tendon (12%) (18). Sensitivity of US in calcinosis detection was demonstrated to be up to 89% (18) but was discovered in varying percentages 27% - 40% (7,8,18). An interesting correlation between ulnar artery occlusion, a marker of decreased peripheral perfusion which will be discussed below, and X-ray identified calcinosis was recently found, claiming an association between vascular disease in SSc and the pathogenesis of calcinosis (21).

Calcinosis can determine the appearance of twinkling artifact (15). The twinkling artifact represent the presence of colour or power Doppler signal immediately behind a high echogenic area, such as urinary tract stones, soft tissue calcific deposits or bones, acquiring a false appearance of blood flow (22).

## NERVE

Neurological complications occur between 1 and 40 % of SSc patients (23). Ultrasonography is an easy method to detect different types of nerve lesions, such as nerve entrapments, nerve tumors, and traumatic nerve injuries. To identify carpal tunnel syndrome is very easy to evaluate the median nerve at carpal tunnel level by measuring the nerve cross-sectional area. Median nerve area and also transverse diameter are increased in all phases of asymptomatic SSc patients, independently to clinical variables (24). Another study shown that median nerve area was significantly different between the 3 phases of skin in-

volvement, being higher in patients in the edematous phase (25).

US can be used for a quantitative evaluation of nerve density that can separate normal nerves from pathologic nerves (26). An automated software analyzes nerve images to calculates the density. In limited cutaneous SSc patients, median nerve density was reduced, especially in the symptomatic group, compared to control subjects. The nerve was evaluated outside carpal tunnel to avoid overlapping results with compressive neuropathies (27). The possible etiology of peripheral nerve damage in SSc patients could be a vascular or autoimmune dependent neuropathy with primary involvement of the vasa nervorum (28).

## VASCULARIZATION

Raynaud phenomenon (RP) and vascular manifestations in SSc may be the primary events, even preceding skin involvement. Vascular involvement in SSc is characterized by two main mechanisms. The first is an early destructive vasculopathy with progressive loss of capillaries. The second is an obliterative vasculopathy due to intimal hyperplasia with proliferation of vascular cells and intimal fibrosis (29). US can be used in assessment and monitoring both of microvascular and macrovascular damages.

Regarding microvascular involvement Doppler US proved to be useful in distinguishing primary by secondary RP. The nail bed vascularity was analyzed before and after a cold and warm challenge. Patients with primary RP had normal vascularity at ambient temperature but differed from healthy controls in the response to a dynamic temperature challenge with a more pronounced decrease of signal after the cold test. In contrast to healthy controls and primary RP patients, secondary RP patients showed a lower vascularity also at ambient temperature and even a more pronounced difference was observed after the cold challenge. US was able to distinguish primary RP from secondary RP in up to 90 % of the cases (30,31). A good level of correlation was found between nail-fold capillaroscopy and Power Doppler US findings both in primary and secondary RP (31).

At the hand level macrovascular involvement can be assessed by investigating hand and finger arteries using color Doppler. The US image of finger arteries in systemic sclerosis is entirely different from that in vasculitis. They appear very small with decreased pulsation and frequently with stenoses which lead to increased blood flow velocities and turbulent flow.



Artery walls are thickened and slightly hyperechoic (32). Schmit et al. (33) evaluated the superficial palmar arch, and the radial and ulnar arteries at the wrists after an induced vasodilatation with hot water. Three different types of vascular pathology was described in this study: “type 1” showing narrowing or chronic occlusion of some proper digital arteries; “type 2” characterized by the same finding affecting all proper digital arteries; and “type 3” including acute occlusions. SSc patients mainly have vascular type 1 or 2 (33).

Ulnar artery occlusion (UAO) is considered as a frequent and specific vascular feature of SSc (8,34,35). On the other hand, radial artery is rarely involved (36). UAO has been shown to associate with digital ulcers (DUs), pitting scars, calcinosis, and acroosteolysis (29) and it has proven to represent an important risk factor for the development of DUs in patients with SSc (37). Another recent multicenter study demonstrate that UAO can be a severity marker of vasculopathy in SSc and has shown an association of UAO with key severity markers of vasculopathy such as the late capillaroscopic pattern according to Cutolo’s classification, the presence of skin telangiectasia, altered DLCO measures and the history of fingertip ischemic DUs (38). UAO and pathological finger pulp blood flow (FPBF) assessed by power doppler ultrasonography are associated with a severe capillary loss on capillaroscopic evaluation (29,39) and also with a history of multiple episodes of ischemic DUs. Even more the association between UAO and pathological FPBF in the same patient is an independent predictor of new ischemic DUs (40). A pathological FPBF was defined as a significant decrease of the doppler signal on the peripheral part of the finger pulp or on the entire finger pulp recorded at least on one of the two evaluated fingers (40). DUs are also associated with digital artery resistivity index (39). The resistivity index, defined as the difference between the peak systolic and end diastolic flow velocities divided by the peak systolic velocity, was calculated at radial and ulnar proper palmar digital arteries at the level of the proximal phalanx of third and fourth fingers.

## SKIN

The progressive skin fibrosis represent the clinical hallmark of the SSc and also a marker for disease classification and activity. Clinically it is used the modified Rodnan skin score (mRSS) to evaluate the severity of skin thickening (41). The mRSS has some disadvantages, as it is unable to detect small degrees of skin thickness, difficulty to differentiate between

oedematous and fibrotic phase and a high variability among different examiners (42,43). In recent years, high-frequency US has become a useful method in skin assessment by capacity to measure skin thickness and to depict accurately different layers of the skin providing a detailed image of the morphostructural changes. It has been shown to be a valid measurement of skin thickening with a high correlation to RSS (44). Cross sectional studies have shown excellent inter- and intraobserver variability for dermal thickness (45-47). High-frequency US can separate epidermis, dermis and subcutaneous layers, can identify oedematous phase, which may precede palpable skin involvement and may thus be useful to early diagnosis and to identify patients with diffuse form very early in the disease process (44,46). Subclinical dermal involvement may be also detectable by US even in skin areas with a normal mRSS (48). Further, dermal finger thickness proved to be associated with nailfold microangiopathy severity assessed by capillaroscopy (49).

A relatively new US technology to analyze elastic properties of tissues is US elastography (UE) and mainly includes strain elastography and shear wave elastography. The strain elastography examines the deformability of a given tissue during its controlled compression with an ultrasonographic transducer. The result is expressed on a semiquantitative color scale or as a strain ratio obtained by dividing the deformability of the tissue of interest by the deformability of a prespecified reference area (50). However, this technique is qualitative rather than quantitative because of its operator dependence (51). On the other hand shear wave elastography examines the speed at which the transducer-generated wave is propagated across the examined tissue and it were been proven to be more accurate and reproducible than those obtained during strain elastography (50).

The first study using UE in SSc patients was made in 2010, after other studies demonstrated that UE can improve the measurement of dermal thickness and also the assessment of fibrotic skin (52). The studies using either strain elastography or shear wave elastography showed that the elastographic strain of the skin in SSc patients is higher than those of healthy controls and that elastographic parameters are characterized by a high repeatability and reproducibility (52-54). In last years shear wave elastography was much more studied in SSc and it proved to reflect the degree of skin involvement and to have a higher sensitivity in detecting subtle skin changes than US (55) and also than RSS, especially in cases with non-detectable

changes at physical evaluation (56). This non-invasive, real-time and operator-independent imaging technique could be an ideal tool for the assessment of SSc disease (51).

## CONCLUSIONS

Permanent improvement of US technology allowed new research in the field which led to multiple and more important applications of US in SSc. In rheumatology US become an extension of the clinical examination and particularly in SSc it helps to a bet-

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ter evaluate of the skin, blood vessels, joints and tendons involvement. It also allows the differentiation between primary and secondary RP, between limited and diffuse form of the disease bringing new elements for a better understanding of SSc pathogenesis. All this making US to become an important tool in disease assessment.

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