Review Article

# Ultrasound Utility in the Management of Morphea: A Comprehensive Review

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## Abstract

**Introduction:** Morphea, an autoimmune progressive disorder, can significantly impact patient well-being, yet therapeutic options, though expanding, exhibit limited efficacy. A persistent challenge in disease management revolves around monitoring disease activity and gauging treatment effectiveness. To address this, various clinical assessment tools have been devised, each with its inherent limitations. The realm of imaging in morphea has undergone noteworthy expansion, with ultrasonography (US) emerging as an efficacious and cost-effective avenue for quantifying disease activity and evaluating therapeutic outcomes. However, the evidential support for its application remains equivocal. Our aim was to explore and analyze the existing evidence concerning the utility of ultrasound in the management of morphea. **Materials and Methods:** We conducted a comprehensive literature review using PubMed Medline to assess evidence concerning US utility in morphea management. **Results:** Sixteen total studies were included in our review. **Discussion:** Although the studies presented carry their own limitations, cumulative findings indicate the potential of ultrasound, particularly when coupled with Doppler, in facilitating staging, assessing disease activity, and longitudinal assessment of therapeutic efficacy in patients with morphea.

**Keywords:** *High-frequency ultrasound, morphea, ultrasound*

## Introduction

Morphea, or localized scleroderma, is an autoimmune progressive disorder, beginning with erythematous patches with mild edema, followed by central hypopigmented sclerosis surrounded by a violaceous border, and atrophic plaques in later stages.[1] Histologically, the inflammatory phase of the lesion demonstrates interstitial and perivascular inflammatory cell infiltrates in the dermis, and sometimes in the subcutaneous tissue, along with tissue edema and dilated blood vessels. The sclerotic phase exhibits the homogenization of collagen bundles in the papillary dermis and sclerosis extending to the reticular dermis. In the fibrotic/inactive phase, minimal inflammation and atrophy of appendages are noted, resulting in a hardened and thin dermis.[2,3]

Incidence rates range from 0.4 to 2.7 per 100,000 with a higher susceptibility observed in women.[2] Morphea comprises five major distinct subtypes, which are plaque (circumscribed), generalized, linear, mixed, and pansclerotic. However, less common subtypes are also present, such as atrophoderma, eosinophilic fasciitis, keloidal, bullous, and guttate morphea. Each subtype displays varying clinical manifestations.[4] Treatment strategies hinge on the subtype, depth of involvement, and disease activity, with early intervention crucial to mitigate potential complications like contractures or limb deformities. However, treatment efficacy remains a challenge due to the absence of objective disease activity assessment methods.[5]

Various clinical scoring systems exist, including the Localized Scleroderma Cutaneous Assessment Tool (LoSCAT), incorporating modified localized scleroderma skin severity index (mLoSSI) and localized scleroderma skin damage index.[6] Despite its sensitivity to lesional changes, even this tool falls short in identifying subclinical activity. Among the tools available for imaging, ultrasonography (US) has emerged as a potentially valuable option for monitoring of morphea lesions by assessing thickness, echogenicity, and morphologic features in



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an easy-to-use, cost-effective manner that minimizes harm to the patient.[7] However, the evidence supporting its role in management of morphea is still uncertain.

In our comprehensive review, our aim was to explore the existing evidence concerning the utility of ultrasound in the management of morphea, thus contributing to a more profound understanding of its potential role in the field.

## Materials and Methods

A literature search was conducted on the PubMed Medline database. For this review, a single investigator conducted the initial search, title, abstract, and full-text screenings. The search strategy included the terms "ultrasound" and "morphea" or "localized scleroderma". All studies from inception to August 2023 were reviewed. Exclusion criteria included systemic sclerosis, case reports, and expert opinions. Our inclusion criteria included all subtypes of morphea in all stages of disease, utilization of ultrasound B-mode scan, and either clinically or histologically proven lesions.

For each study included, the following were recorded: author, year, type of study, ultrasound probe frequency, ultrasound scanning mode, use of color doppler, mean age of patients, age range of patients, number of patients, subtypes of morphea, number of lesions examined, basis of diagnosis, outcome measure, and study outcomes.

## Results

Sixteen studies met our criteria and were included in our review. Three out of those studies solely comprised of the pediatric population. Three studies were cross-sectional, ten were prospective cohorts, and three were retrospective cohort studies.

In our review, four studies utilized US probes with frequencies less than 15 MHz, nine studies utilized probes with frequencies between 15 and 30 MHz, and three studies utilized probes with frequencies higher than 30 MHz [Figure 1]. Six studies utilized color Doppler sonography in addition to B-mode scanning.

Two studies in our review particularly focused on the diagnostic features of morphea on US. Three studies focused on US features of the different stages of morphea. Three studies assessed the activity status of morphea lesions via US. Six studies assessed US as a tool to longitudinally assess therapeutic efficacy. Lastly, two studies evaluated both therapeutic efficacy longitudinally and activity assessment via US. All studies included in this review are summarized in Table 1.

## Discussion

The value of US in morphea lies within four major domains of patient management. These include the diagnostic evaluation of the lesion, staging, activity assessment of the lesion, and longitudinal assessment of therapeutic efficacy.

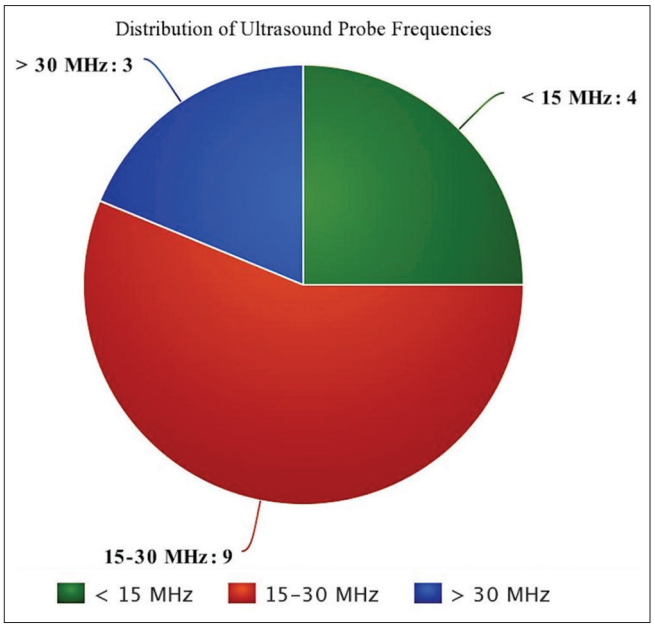


**Figure 1: Distribution of the ultrasound probe frequencies among studies included in our review**

### *Diagnostic evaluation*

Current literature evidence does not support ultrasound as a sole diagnostic tool. However, two studies in our review focused on diagnostic features of morphea on US. Hoffman *et al.*, 1991 evaluated sclerotic lesions of morphea against contralateral healthy skin controls and identified a significant increase in dermal thickness (DT) measurements on US at baseline. In addition, they noted that DT increased or decreased with progression or regression of the disease on treatment, respectively.[23] In addition, Cosnes *et al.*, 2003 conducted a prospective study that compared 16 skin plaques with morphea as a potential diagnosis to a healthy control group and a control group with different dermatological diagnoses using a 13 MHz US B-mode scan.[21] They established criteria based on US features that were 92% sensitive and 100% specific for morphea. The criteria included meeting four of the following five signs: undulations of the dermis, disorganization, loss of thickness, thickened hyperechoic bands in the hypodermis, and the "yo-yo" image. However, no additional prospective studies have been conducted to further assess the efficacy of this criteria as a diagnostic tool. In addition, this study did not categorize morphea lesions into subtypes or consider the stage of the disease, thereby limiting its generalizability.

### *Staging*

There may be evidence to support the utility of US in staging morphea lesions as either inflammatory, sclerotic, or atrophic. Three studies in our review evaluated this particular outcome. Nezafati *et al.*, 2011 found that dermal echogenicity correlated significantly with the clinical stage and amount of sclerosis present in histology.[19] On a 14 MHz US scan, inflammatory lesions appeared

isoechogenic, sclerotic lesions appeared hyperechogenic, and atrophic lesions appeared hypoechogenic when they were all evaluated against site-matched healthy skin. In addition, they did not find any relationship between modified Rodnan skin score (mRSS) and US measurements, which highlighted the inadequacy and subjectivity in the clinical scoring system.

However, Ranosz-Janicka *et al.*, 2019 found differing evidence regarding US measurements and stages of morphea. They evaluated 92 lesions in 40 patients with 20 MHz US for relative DT and relative echogenicity scores against site-matched unaffected skin and compared the difference to LoSCAT clinical scores. They found a significant relationship between an increase in DT and a decrease in the echogenicity of the dermis with the inflammatory phase of the disease, an increase in the DT as well as in the echogenicity of the dermis with the sclerotic phase, and a decrease in the DT and increase in the echogenicity of the dermis with the atrophic phase.[14]

Zhang *et al*., 2023 reported similar findings regarding the staging of the lesions in their cross-sectional study of 34 patients matched with histopathological examination. Inflammatory lesions showed hypoechogenicity around appendages in 85.7% of the lesions and 71.4% showed a hypoechogenic dermis. The sclerotic stage correlated with a hyperechogenic dermis in 85% of the cases and 70% of them had acoustic attenuation of the dermis. All atrophic lesions showed a hyperechogenic dermis; however, only 28.6% had an unclear boundary between the dermis and subcutaneous fat, whereas 71% of inflammatory and 85% of sclerotic lesions were noted to have an unclear boundary.[8]

Dermal echogenicity is positively correlated with the amount of collagen fibers present and negatively correlated with the interstitial matrix. Water influx in the dermis causes a decrease in the echogenicity, likely due to distension of the fiber network which creates more space for the sound waves to penetrate through instead of being reflected.[22]

Hypoechogenicity observed in the dermis of inflammatory morphea lesions corresponds to heightened swelling of collagen fibers and dermal edema during the early phase, also contributing to dermal thickening upon measurement via US. As the condition progresses, hyperechogenicity emerges in the dermis during the sclerotic stage, intensifying further in the atrophic stage marked by increased fibrosis. However, the concurrent atrophy characteristic of the atrophic stage imparts a thinner appearance to the dermis as visualized and measured through US.[8]

## *Activity assessment*

Evidence suggests that there may be the utility of US in detecting lesional activity. Five studies in our review evaluated this outcome. Wortsman *et al.*, 2011 defined the criteria for determining the activity of morphea lesions on US.[18] They defined an active morphea lesion on US as meeting two of the three following criteria: increased DT, decreased dermal echogenicity, and increased subcutaneous tissue. Or, any increased cutaneous blood flow in the dermis or subcutaneous tissue as seen on Doppler imaging would automatically classify a lesion as active. Inactive lesions were those that did not meet the active criteria. Lastly, atrophic lesions were defined as those that did not have increased blood flow and showed decreased dermal and subcutaneous thickness. Utilizing this criterion, they did not find any statistical difference between the activity of lesions on US versus histological grading. The US grading criteria were found to be 100% sensitive and 98.8% specific. Both increased subcutaneous tissue echogenicity and increased cutaneous blood flow are 100% sensitive and 100% specific for signs of activity in the lesion.

In addition, Marti-Marti *et al.*, 2022 found that all active lesions in their study met the US activity criteria as described above. The most sensitive sign was increased Doppler activity, which was present in all active lesions. None of the inactive lesions met the US activity criteria in their study.[11]

Building off of the activity criteria, Vera-Kellet *et al.*, 2021 devised an ultrasound morphea activity score (US-MAS).[12] This scoring system quantifies activity in morphea lesions based on increased subcutaneous echogenicity, loss of dermal-hypodermal border, increased subcutaneous vascularization, arterial or venous flow, number of body segments affected, increase in size of affected areas compared to previous exam, appearance of new areas, and decrease in maximum size or number of affected areas. This system was further modified by Wortsman *et al*., 2023, who proposed further subdividing corporal segments during US examinations for higher sensitivity and standardization.[24]

Similarly, in the pediatric population, Li *et al*., 2011 evaluated if ultrasound disease activity correlated with clinically active lesions. Although the clinical activity of lesions was determined retrospectively based on a chart review of the physical examination, they found that total echogenicity, hypodermis echogenicity, and deep tissue layer vascularity were significantly higher in active lesions when compared to inactive lesions.[17]

Not only lesional activity could be detected, but Parra-Cares *et al*., 2023 demonstrated that subclinical activity in morphea could be detected by color Doppler ultrasonography (CDU) utilizing the US-MAS grading criteria.[9] Subclinical Doppler activity was detected in 36.1% of the lesions in the study. The subclinical activity detected was directly adjacent to the clinically active lesion in 54% of the cases, 23% in nonadjacent regions, and 23% at the site of a clinically inactive lesion. Similarly, Marti-Marti *et al.*, 2022 also evaluated the discordance of US features with clinical activity as a secondary outcome of

their study.[11] Discordance in clinical evaluation of disease and US examination was found in 23.6% of cases with most being characterized as inactive on clinical evaluation but having signs of activity on US examination.

The evidence, therefore, suggests that determining lesional activity via CDU may be beneficial in the management of morphea. US-MAS grading may be a useful quantitative tool in following treatment responses and also determining subclinical activity for earlier interventions in patients.

## *Longitudinal assessment of therapeutic efficacy*

Lastly, eight of the studies included in our review presented evidence regarding the longitudinal evaluation of lesions with US to assess for therapeutic efficacy.

Szymańska *et al*., 2000 evaluated the evolution of morphea lesions via US compared to contralateral healthy skin. A significant reduction of DT was noted with the regression of the disease and an increase in DT was noted with progression of the disease.[22] They also found that echogenicity and thickness depended on the region on the body that was imaged along with the age of the patient. Therefore, it was recommended that measurements should always be compared to normal, contralateral skin in longitudinal evaluations.

In their prospective study, Arisi *et al*., 2018 evaluated responses of active morphea lesions to UVA1 therapy as measured on 50 MHz US and clinical scores. Quantitative measures on US, which included thickness and dermal density, did not show a significant difference pre- and post-treatment, whereas clinical scores were significantly decreased post-treatment. Morphologically, however, they noted a significant decrease in the presence of dermal undulations and "yo-yo" images post-treatment.[15] It is possible that no quantitative difference could be noted on a 50 MHz US due to the limited penetration at this frequency. In contrast, Sator *et al.*, 2009 found significantly decreased DT as measured by 20 MHz US after UVA1 therapy when compared to baseline thickness before therapy.[20]

Marti-Marti *et al.,* 2022 also evaluated the percentage of patients with morphea whose treatment changed as a result of US. Management change occurred in 19.4% of patients based on US evaluation over a period of 1.5 years with examinations every 6 months.[11] Management change was defined as a biopsy or a change in medication regimen and was based on activity assessments via US.

Vera-Kellet *et al*., 2021 evaluated the efficacy of methotrexate as a therapeutic option based on CDU evaluation and US-MAS scoring.[12] Using this US scoring method and comparing it to existing clinical evaluation models, the authors found methotrexate to be a treatment option with low effectiveness in morphea. Zhang *et al*., 2023 also assessed the efficacy of methotrexate therapy in a cohort of 10 patients. On longitudinal assessments with US, they found a significant decrease in DT with the average decrease being 69% [Figure 2].[10] Although no statistical difference existed between the clinical scoring systems and US measurements, the US measurements were more sensitive as the changes could be detected earlier in response to the treatment with the average first reaction time being 1.8 months. This provides further evidence for the utility of US as a tool to assess therapeutic efficacy.

Longitudinal assessment of therapeutic efficacy via US has also been assessed in the pediatric population. Porta *et al*., 2014 evaluated seven pediatric patients on treatment over a six-month period and found a significant decrease in DT over that period in six out of the seven patients with a mean difference of 1.7 mm.[16] On the contrary, Weibel *et al*., 2020 demonstrated that DT and dermal echogenicity did not show any significant difference over the treatment period. However, they hypothesized that the inclusion of atrophic plaques in their study was likely the confounding factor which affected US measurements.[13]

Evidence supports longitudinal assessments of morphea lesions to evaluate for treatment efficacy. Most studies utilized DT as a quantitative measure for longitudinal assessment. They noted a decrease in thickness with the regression of active disease and an increase in thickness with the progression of active disease when compared to normal skin control. However, US-MAS scoring based on CDU examinations may be more sensitive to determine subclinical activity in lesions and measure longitudinal therapeutic efficacy along with DT. However, further

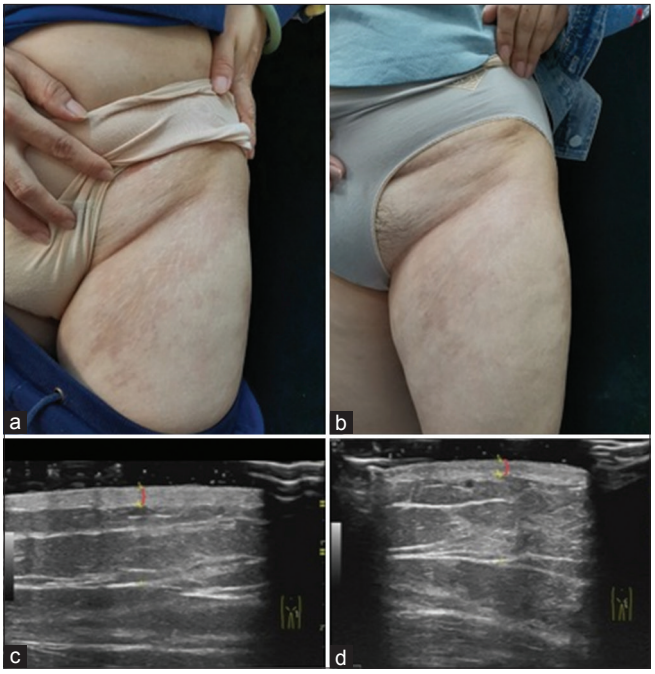


**Figure 2: (a and b) Localized morphea lesion in the groin with clinical improvement of the lesion during the six-month treatment period. (c and d) Changes in dermal thickness, as indicated by red arrow, on 15-MHz ultrasound before and after the treatment**

**Table 1: Summary of studies regarding utilization of ultrasound in the management of morphea**

| Paper | Study Type | Probe frequency | Color Doppler | Mean age of patients (Range) | Morphea subtype | No. of patients/No. of lesions | Diagnosis Basis | Outcome measure | Outcomes |
|---|---|---|---|---|---|---|---|---|---|
| Zhang *et al*., 2023[8] | Cross-sectional | 50 and 20 MHz | No | 30.18 years (6-58) | N/A | 34/Not reported | Histology | Staging | -Based on 50 MHz.<br>-71.4% inflammatory lesions showed a hypoechogenic dermis.<br>-85% of sclerotic lesions showed a hyperechogenic dermis and 85% had an unclear boundary between dermis and subcutaneous tissue.<br>-100% of atrophic lesions showed a hyperechogenic dermis and 28.6% had an unclear boundary between the dermis and subcutaneous tissue ($P$<0.05). |
| Parra-Cares *et al*., 2023[9] | Cross-sectional | 18 MHz | Yes | 29.5 years (10–66) | Plaque (50%)<br>Generalized (5%)<br>Pansclerotic (9%)<br>Deep (5%)<br>Linear extremities (9%)<br>En Coup De Sabre (20%)<br>Parry Romberg (2%) | 36/36 | Histology | Activity assessment | -Prevalence of subclinical activity (based on US-MAS) in 36.1% of patients.<br>-No difference in subclinical activity between subtypes ($P$>0.05).<br>-Weak positive correlation between US-MAS and mLoSSI score ($P$>0.05). |
| Zhang *et al*., 2023[10] | Prospective cohort | 15 MHz | No | 39.3 years (5–56) | Generalized (40%)<br>Linear (40%)<br>Plaque (20%) | 10/Not reported | Histology | Longitudinal assessment | -With methotrexate therapy, difference of dermal thickness between lesional and normal skin control on US decreased from 0.13 to 0.04 cm ($P$=0.009).<br>-No correlation between US measures and LoSCAT scores.<br>-US measures changed before clinical scores. |
| Marti-Marti *et al*., 2022[11] | Retrospective cohort | 15, 18, 22 MHz | Yes | 58 years (40.5–69) | Plaque (61.3%)<br>Generalized (25.8%)<br>Linear (6.5%)<br>Parry-Romberg (6.5%) | 31/31 | Histology | Longitudinal assessment and activity assessment | -Management change due to HFUS evaluation instituted in 19.4% of morphea cases<br>-Discordance between clinical evaluation and HFUS evaluation found in 23.6% of cases.<br>-100% of patients deemed to have active disease had increased doppler activity. |
| Vera-Kellet *et al*., 2021[12] | Retrospective cohort | 18 MHz | Yes | 20.5 years (4–59) | Linear (59.1%)<br>Circumscribed (18.2%)<br>Mixed (13.6%)<br>Generalized (9.1%) | 22/22 | Histology | Longitudinal assessment and activity assessment | -Significant negative correlation between methotrexate dose and change in US-MAS was found ($P$<0.035).<br>-In all cases, color doppler ultrasonography (CDU) showed signs of subclinical activity. |

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**Table 1: Contd...**

| Paper | Study Type | Probe frequency | Color Doppler | Mean age of patients (Range) | Morphea subtype | No. of patients/No. of lesions | Diagnosis Basis | Outcome measure | Outcomes |
|---|---|---|---|---|---|---|---|---|---|
| Weibel *et al*., 2020[13] | Prospective cohort | 20 MHz | No | 6.0 years (0.2–14.4) | Linear (95.5%)<br>Deep (4.5%) | 22/22 | Clinical | Longitudinal assessment | -No significant change in dermal thickness or echogenicity noted over the treatment period. |
| Ranosz-Janicka *et al*., 2019[14] | Prospective cohort | 20 MHz | No | 49 years (34–65) | Plaque (27.5%)<br>Generalized (25%)<br>Linear (10%)<br>Mixed (7.5%) | 40/92 | Clinical, but histology in difficult cases | Staging | -LoSCAT erythema scores correlated positively with dermal thickness and negatively with intensity scores (echogenicity) on US ($P$<0.01).<br>-LoSCAT skin thickness score correlated positively with dermal thickness and intensity score ($P$<0.01).<br>-LoSCAT atrophy scores correlated positively with intensity scores and negatively with skin thickness scores ($P$<0.01). |
| Arisi *et al*., 2018[15] | Prospective cohort | 50 MHz | No | 64.05 years (20–90) | Generalized (82.3%)<br>Deep (17.3%) | 14/14 | Histology | Longitudinal assessment | -No significant difference in US quantitative measures after UVA1 therapy.<br>-Significantly lower clinical scores after UVA1 therapy ($P$<0.05).<br>-Decrease in morphological features of dermal hyperechogenic bundles and disappearance of "yoyo" figures after therapy ($P$<0.05). |
| Porta *et al*., 2014[16] | Prospective cohort | 18 MHz | No | 8.49 years (2.9–13.9) | Linear (70%)<br>Circumscribed (30%) | 10/10 | N/A | Longitudinal assessment | -Six out of the seven patients on treatment demonstrated significant reduction in dermal thickness on US over six months when compared to healthy contralateral skin ($P$<0.05). |
| Li *et al*., 2011[17] | Retrospective cohort | 8–14 MHz | Yes | 12.2 years (4.6–18) | Linear (33.3%)<br>Circumscribed (28.6%)<br>Generalized (9.5%)<br>Pansclerotic (4.8%)<br>Mixed (23.8%) | 21/52 | Clinical | Activity assessment | -Total echogenicity, hypodermis echogenicity, and deep tissue layer vascularity differed significantly between active and inactive lesions ($P$<0.05).<br>-No significant differences between tissue thickness for any tissue layer between active and inactive lesions. |
| Wortsman *et al*., 2011[18] | Prospective cohort | 7–15 MHz | Yes | 28 years (4–68) | N/A | 51/104 | Histology | Activity assessment | -No significant difference between sonographic and histologic assessment of disease activity ($P$>0.05).<br>-Increased subcutaneous tissue echogenicity and increased cutaneous blood flow were 100% sensitive and 100% specific for disease activity. |

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**Table 1: Contd...**

| Paper | Study Type | Probe frequency | Color Doppler | Mean age of patients (Range) | Morphea subtype | No. of patients/No. of lesions | Diagnosis Basis | Outcome measure | Outcomes |
|---|---|---|---|---|---|---|---|---|---|
| Nezafati *et al*., 2011[19] | Cross-sectional | 14 MHz | No | 34 years (7–60) | Generalized (50%)<br>Plaque (25%)<br>Linear (25%) | 14/16 | Histology | Staging | -No significant relationship between mRSS clinical scoring and US measurements.<br>-Inflammatory lesions were isoechogenic ($P$<0.05).<br>-Sclerotic lesions were hyperechogenic ($P$<0.05).<br>-Atrophic lesions appeared hypoechogenic ($P$<0.05).<br>-Echogenicity was significantly positively correlated with grade of sclerosis on histology ($P$<0.05). |
| Sator *et al*., 2009[20] | Prospective cohort | 20 MHz | No | 49 years (15–69) | Plaque (100%) | 14/Not reported | Histology | Longitudinal assessment | -Statistically significant decrease in dermal thickness 3–6 months after medium and low-dose UVA1 therapy as measured on US ($P$<0.025). |
| Cosnes *et al*., 2003[21] | Prospective cohort | 13 MHz | Yes | 40 years (6–67 years) | N/A | 26/40 | Histology | Diagnostic features | -⅘ signs were 92% sensitive and 100% specific for diagnosing morphea.<br>These include:<br>-Undulations of dermis<br>-Loss of thickness of hypodermis<br>-Disorganization of hypodermis<br>-Thickened bands in hypodermis<br>-Yo-yo image |
| Szymańska *et al*., 2000[22] | Prospective cohort | 32 MHz | No | N/A | Plaque morphea (73.5%)<br>Linear morphea (26.5%) | 34/34 | N/A | Longitudinal assessment | -Reduction of dermal thickness noted with regression of disease ($P$<0.005).<br>-Increase in dermal thickness noted with progression ($P$<0.005). |
| Hoffmann *et al*., 1991[23] | Prospective cohort | 20 Hz | No | 49 years (9–74) | Plaque (85%)<br>Linear (6%<br>Eosinophilic Fascitis (6%)<br>Atrophoderma (3%) | 29/29 | Histology | Diagnostic features | -Sclerotic plaques showed an increase in dermal thickness ($P$<0.001).<br>-The relative increase in thickness was dependent on the area affected. Thinner areas like groin, showed the highest percentage of thickness gained.<br>-Decrease in dermal thickness was associated with regression and increase in thickness with progression of disease ($P$<0.001). |

Localized scleroderma cutaneous assessment tool (LoSCAT). Modified localized scleroderma skin severity index (mLoSSI). Modified Rodnan skin score (mRSS). Ultrasound (US). Ultrasound morphea activity score (US-MAS). High-frequency ultrasound (HFUS)

prospective studies are needed to thoroughly evaluate the efficacy of these criteria.

### *Limitations*

Due to the utilization of different ultrasound probe frequencies in studies included in our review, it cannot be concluded which probe frequency provided the most reliable results. In general, higher frequency probes (≥15 MHz ) provide greater resolution of the superficial structures and are better equipped to detect changes in echogenicity and morphological features, whereas lower frequency probes are able to penetrate deeper. Although the higher resolution via high-frequency ultrasound would be the most sensitive to morphological changes, visualization of the deeper structures, such as the subcutaneous tissue, is also important in a pathology like morphea. This trade-off could be seen in the studies assessing the efficacy of UVA1 therapy via 50 MHz and 20 MHz US, with 50 MHz US detecting morphological changes and 20 MHz US detecting changes in DT.[15,20] Nonetheless, generally a probe between 15 and 20 MHz is utilized for skin examinations.[25] However, further studies are required.

## Conclusions

Our review suggests the utility of US in the clinical management of morphea, more specifically in terms of staging, activity assessment of the lesions, and assessment of therapeutic efficacy. However, several limitations remain, such as current subjective scanning protocols, undefined US probe frequencies, and potential addition to the cost of care. Therefore, future studies are needed that focus on larger sample sizes and standardized protocols and measurements that would allow for more generalizable findings.

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### *Conflicts of interest*

There are no conflicts of interest.

## References

1. Sehgal VN, Srivastava G, Aggarwal AK, Behl PN, Choudhary M, Bajaj P. Localized scleroderma/morphea. Int J Dermatol 2002;41:467-75.
2. Knobler R, Moinzadeh P, Hunzelmann N, Kreuter A, Cozzio A, Mouthon L, *et al*. European Dermatology Forum S1-guideline on the diagnosis and treatment of sclerosing diseases of the skin, Part 1: Localized scleroderma, systemic sclerosis and overlap syndromes. J Eur Acad Dermatol Venereol 2017;31:1401-24.
3. Vasquez R, Sendejo C, Jacobe H. Morphea and other localized forms of scleroderma. Curr Opin Rheumatol 2012;24:685-93.
4. Peterson LS, Nelson AM, Su WP. Classification of morphea (localized scleroderma). Mayo Clin Proc 1995;70:1068-76.
5. Wenzel D, Haddadi NS, Afshari K, Richmond JM, Rashighi M. Upcoming treatments for morphea. Immun Inflamm Dis 2021;9:1101-45.
6. Skrzypek-Salamon A, Lis-Święty A, Ranosz-Janicka I, Brzezińska-Wcisło L. Localized scleroderma cutaneous assessment tool (LoSCAT) adapted for use in adult patients: Report from an initial validation study. Health Qual Life Outcomes 2018;16:185.
7. Abignano G, Del Galdo F. Quantitating skin fibrosis: Innovative strategies and their clinical implications. Curr Rheumatol Rep 2014;16:404.
8. Zhang S, Zhu QL, Xiao MS, Liu J. The value of dermoscopy and high-frequency ultrasound in staging morphea. J Dermatol 2023;50:511-17.
9. Parra-Cares J, Wortsman X, Alfaro-Sepúlveda D, Mellado-Francisco G, Ramírez-Cornejo C, Vera-Kellet C. Color doppler ultrasound assessment of subclinical activity with scoring of morphea. J Cutan Med Surg 2023;27:454-60.
10. Zhang F, Li J, Zhao Q, Liu H, Zhang F. Study about evaluation of efficacy of methotrexate in localized scleroderma using ultrasonography. Skin Res Technol 2023;29:e13300.
11. Marti-Marti I, Morgado-Carrasco D, Podlipnik S, Rizo-Potau D, Bosch-Amate X, Lledó GM, *et al*. Usefulness of high-frequency ultrasonography in the evaluation and monitoring of sclerosing dermatoses: A cohort study. Clin Exp Dermatol 2022;47:351-58.
12. Vera-Kellet C, Meza-Romero R, Moll-Manzur C, Ramírez-Cornejo C, Wortsman X. Low effectiveness of methotrexate in the management of localised scleroderma (morphea) based on an ultrasound activity score. Eur J Dermatol 2021;31:813-21.
13. Weibel L, Theiler M, Howell KJ, Denton CP, Waelchli R, Atherton D, *et al*. Prospective evaluation of treatment response and disease reversibility of paediatric localized scleroderma (morphoea) to steroids and methotrexate using multi-modal imaging. J Eur Acad Dermatol Venereol 2020;34:1609-16.
14. Ranosz-Janicka I, Lis-Święty A, Skrzypek-Salamon A, Brzezińska-Wcisło L. An extended high-frequency ultrasound protocol for assessing and quantifying of inflammation and fibrosis in localized scleroderma. Skin Res Technol 2019;25:359-66.
15. Arisi M, Lorenzi L, Incardona P, Fusano M, Zanca A, Rossi MT, *et al*. Clinical, histological and high-frequency ultrasonographic evaluation (50 MHz) of morphoea treated with ultraviolet A1 phototherapy. Clin Exp Dermatol 2019;44:270-76.
16. Porta F, Kaloudi O, Garzitto A, Prignano F, Nacci F, Falcini F, *et al*. High frequency ultrasound can detect improvement of lesions in juvenile localized scleroderma. Mod Rheumatol 2014;24:869-73.
17. Li SC, Liebling MS, Haines KA, Weiss JE, Prann A. Initial evaluation of an ultrasound measure for assessing the activity of skin lesions in juvenile localized scleroderma. Arthritis Care Res (Hoboken) 2011;63:735-42.
18. Wortsman X, Wortsman J, Sazunic I, Carreño L. Activity assessment in morphea using color Doppler ultrasound. J Am Acad Dermatol 2011;65:942-8.
19. Nezafati KA, Cayce RL, Susa JS, Setiawan AT, Tirkes T, Bendeck SE, *et al*. 14-MHz ultrasonography as an outcome measure in morphea (localized scleroderma). Arch Dermatol 2011;147:1112-5.
20. Sator PG, Radakovic S, Schulmeister K, Hönigsmann H, Tanew A. Medium-dose is more effective than low-dose ultraviolet A1 phototherapy for localized scleroderma as shown

by 20-MHz ultrasound assessment. J Am Acad Dermatol 2009;60:786-91.
21. Cosnes A, Anglade MC, Revuz J, Radier C. Thirteen-megahertz ultrasound probe: Its role in diagnosing localized scleroderma. Br J Dermatol 2003;148:724-9.
22. Szymańska E, Nowicki A, Mlosek K, Litniewski J, Lewandowski M, Secomski W, *et al*. Skin imaging with high frequency ultrasound-preliminary results. Eur J Ultrasound 2000;12:9-16.
23. Hoffmann K, Gerbaulet U, el-Gammal S, Altmeyer P. 20-MHz B-mode ultrasound in monitoring the course of localized scleroderma (morphea). Acta Derm Venereol Suppl (Stockh) 1991;164:3-16.
24. Wortsman X, Vera-Kellet C. Ultrasound Morphea Activity Scoring (US-MAS): Modified US-MAS. J Ultrasound Med 2023;42:2447-50.
25. Almuhanna N, Wortsman X, Wohlmuth-Wieser I, Kinoshita-Ise M, Alhusayen R. Overview of Ultrasound Imaging Applications in Dermatology [Formula: See text]. J Cutan Med Surg 2021;25:521-29.