

Overview of Ultrasound Imaging Applications in Dermatology

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Abstract

Complete visualization of lesions is critical for the accurate diagnosis and management of dermatological diseases. Currently, the most readily available technologies used by dermatologists include dermoscopy and photography. Nevertheless, ultrasound has emerged as a useful non-invasive modality in dermatology, which can be added to the clinical examination supporting an early and more accurate diagnosis. Moreover, there are significant technological advances in recent years, such as the development of handheld devices and ultra-high frequency probes that have expanded the integration of ultrasound into daily dermatology practice. In this article, we reviewed the most common applications of ultrasound in the field of dermatology.

Keywords

ultrasound, high-frequency ultrasound, skin sonography, imaging

Introduction

In recent years, the use of ultrasound (US) in dermatology has expanded and gained popularity. High-frequency ultrasound (HFUS), ≥ 15 megahertz (MHz) wavelength, allows a high-resolution visualization of the skin layers with sufficient depth to capture the full thickness of the skin.¹

US is a safe imaging modality that uses acoustic waves to travel through the skin; the echoes reflected by the different cutaneous tissues return to the transducer forming a visual image.² The echogenicity of each skin structure is determined by its density affecting the acoustic wave's speed passing through it.³ The primary sources of echogenicity in the skin layers are keratinocytes in the epidermis, collagen in the dermis, and fat in the subcutis.³

At 15-20 MHz, the normal skin layers of the non-glabrous skin appear as a hyperechoic epidermal line, then a hyperechoic dermal band, and a much larger hypoechoic subcutis layer.⁴ In the glabrous skin of the palms and soles, the epidermis presents as a hyperechoic bilaminar structure due to a thicker stratum corneum (Figure 1).⁴

Color Doppler US is an application of US that enables the real-time visualization of the blood flow, which is increased in neo-angiogenesis, tumors, and inflammation.⁵

Wortsman et al. proposed guidelines to standardize the performance of US examinations in dermatology.¹ They recommend a minimum frequency of 15 MHz, the performance of a minimum of 300 skin examinations per physician

annually to ensure competence, and the routine use of color Doppler US to assess vascularity.¹

US has the advantage of being non-invasive and inexpensive compared to other imaging techniques such as magnetic resonance imaging (MRI). It has a higher axial resolution than MRI and computerized tomography.³ The axial resolution of US can vary from 100 μm at 15 MHz to 30 μm , which is closer to the lower magnification of histology.²

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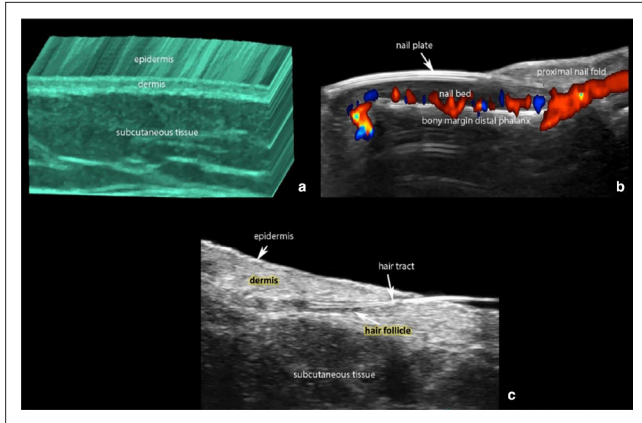


Figure 1. (a) Normal ultrasound anatomy of the skin (3D reconstruction of greyscale with color filter). (b) Nail (color Doppler longitudinal view of the nail of the index finger with the blood flow in colors). (c) Hair.

The main applications of US in dermatology are the study of benign and malignant tumors, nail pathology, inflammatory dermatoses, and to reduce complications of esthetic procedures. Moreover, it is radiation-free and can help avoid skin biopsy, which is especially useful in the pediatric population.^{6,7} Sonographic findings of common dermatological diseases are summarized in Table 1.

Table 1. Sonographic Findings of Common Dermatological Diseases.

Epidermal Cyst	Intact cysts show well defined round anechoic or hypoechoic structures in the dermis and subcutaneous layer, without blood flow.
Pilomatricoma	Target sign, with a hypoechoic rim and a calcium-rich hyperechoic center.
Hemangioma	In proliferative phase, they present as a hypoechoic solid and hypervascular mass with arterial, venous, and sometimes arteriovenous shunts.
Basal Cell Carcinoma	Hyperechoic spots within the lesion (pathognomonic sign).
Dermatofibrosarcoma Protuberans	Jellyfish-like sign, an oval-shaped hypoechoic body within the dermis with tentacle-like or pseudopods projections spreading through the subcutaneous tissue.
Hidradenitis Suppurativa	Widening of the hair follicles.
Morphea	Inflammatory phase lesions show increased thickness and decreased echogenicity of the dermis, increased echogenicity of the subcutaneous tissue, and increased dermal and subcutaneous blood flow.

The US limitations include the inability to detect lesions that measure <0.1 mm at 15 MHz and <0.03 mm at 70 MHz or intraepidermal macular lesions such as solar lentiginos and cafe-au-lait macules.⁶

With the increased interest in technology, especially in non-invasive bedside tools, we present an up-to-date review of the use of US in dermatology. We searched MEDLINE, EMBASE, and Cochrane Central Register from their respective conception dates to January 4, 2020. The search included keywords related to US and cutaneous diseases that usually need further investigation, such as skin biopsy or imaging.

In this review, dermatological conditions will be divided into benign tumors, followed by vascular lesions, malignant tumors, inflammatory conditions, hair diseases, nail diseases, and exogenous material.

Benign Tumors

Epidermal cyst. Distinguishing features on US depend on the phase of the cyst. Intact cysts show well defined round anechoic or hypoechoic structures in the dermis and subcutis (Supplemental Figure S1).⁸ Ruptured cysts present an ill-defined irregular or lobulated shape and increased blood flow at the periphery.^{9,10} Usually, within the cysts, there are anechoic bands that correspond to the cholesterol crystals. Underneath the cyst, it is frequent to see a posterior acoustic enhancement artifact.¹¹

Sometimes on the cyst's surface, an anechoic or hypoechoic band is detected, which correlates with the punctum seen on clinical examination.¹²

Pilomatricoma

For this common benign hair matrix tumor, the diagnostic accuracy of physical exam alone is only 16%.¹³ On US exam, it commonly presents as a target-like lesion, with a hypoechoic rim and a calcium-rich hyperechoic center.¹⁴ Solivetti et al. classified US findings of pilomatricoma into five types; type 1: fully calcified, type 2: partially calcified or target, type 3: complex lesion, type 4: pseudocysts, and type 5: pseudo-tumoral.¹⁵

Bandera et al. defined a characteristic sign, both hyperechoic dots, which represent calcification and echogenic dots that represent proteinaceous material, mostly keratin (Supplemental Figure S2).¹⁶

Vascular Lesions

Infantile hemangiomas. Infantile hemangiomas are the most common soft tissue tumors in the pediatric age. Although they are usually diagnosed clinically, the depth of involvement would be difficult to assess by clinical examination alone.

The US appearance of infantile hemangiomas varies according to the phase. In the proliferative phase, they

present as hypoechoic solid and hypervascular mass with arterial, venous, and sometimes arteriovenous shunts (Supplemental Figure S3).¹⁷ During the partial involuting phase, they present a mixed echogenicity with hyperechoic and hypoechoic areas and an intermediate degree of vascularity.¹⁸ In the involuted phase, the lesion appears hyperechoic, hypovascular, and fibrofatty tissue can be seen.¹⁹

Vascular Malformations

Vascular malformations are classified as either high-flow; including arterial and arteriovenous, or low flow; such as venous, capillary, and lymphatic.

In contrast with hemangiomas, vascular malformations are errors in morphogenesis and don't present a mass-effect.⁹ Arterial, venous, and lymphatic vascular malformations show anechoic tubules or lacunar areas. Capillary malformations usually demonstrate changes in the echogenicity of the cutaneous layers that can vary according to the location. Importantly, color Doppler allows for assessing the type and velocity of flow using the spectral curve analysis. Arterial flow typically demonstrates a systolic and diastolic morphology while the venous flow shows a monophasic curve. Conversely, the lymphatic and capillary malformations have no flow (Supplemental Figure S4).¹⁸

In arteriovenous malformations, a turbulent arterialized venous type of flow is usually found.¹⁸ Low flow venous malformation is prone to develop painful intralesional thrombosis; US can help detect these blood clots.²⁰ An important clue to differentiate deep infantile hemangiomas from venous malformation is the presence of acoustic shadow on US, indicative of phleboliths in venous lesions.²¹

Malignant Tumors

Melanoma. There is some evidence that US can assist in the clinical diagnosis and surgical management of melanoma. However, it is not incorporated into melanoma clinical practice guidelines and is not part of the standard of care.

Since the 1990s, investigators have shown that using US allows a precise preoperative assessment of tumor thickness that correlates with histology.²²⁻²⁴ Machet et al. used US to plan a one step surgical excision in 31 patients with lesions suspicious for melanoma. The authors demonstrated that Breslow thickness correlates well with the ultrasonographic thickness in 26 out of the 31 studied cases [74%, 95% CI 55-88], sparing these patients a second operation.²¹ The authors also retrieved data from 7 studies assessing a total of 1611 melanomas, where the ultrasonographic thickness was used to predict histologic thickness.²¹ Among these studies, the predictive value to determine the tumor thickness ranged from 72% (95% CI 65-79) to 89% (95% CI 80-94).^{25,26} In another prospective study evaluating 131 melanoma patients, HFUS correlated

well with histology and showed excellent inter-rater reproducibility, making HFUS a reliable in vivo assessment tool for melanoma thickness.²⁷ These findings have led to its implementation in the routine dermatology assessment at some institutions.²⁸ Supplemental Figure S5 shows color Doppler US findings in melanoma.

Satellite lesions are cutaneous or subcutaneous melanoma lesions occurring within 2 cm of the primary tumor, whereas in-transit metastases occur beyond 2 cm.²⁷ These metastatic lesions appear as hypoechoic and hypervascular subcutaneous nodules on HFUS.^{29,30} In a cohort study of 600 melanoma patients, US was able to detect in-transit or satellite metastases in 63 clinically negative patients.³¹ The same group showed that HFUS was superior to positron emission tomography-computed tomography and thermography for the diagnosis of in-transit metastases.³²

While HFUS can aid preoperative evaluation and early detection of clinically occult satellite or in-transit melanoma metastases, it is at present unreliable in differentiating benign from malignant melanocytic lesions. This is due to the limitation of US in detecting melanin and superficial, particularly epidermal lesions. However, in these cases, US can be used as a complementary tool along with standard dermoscopy to assess the thickness of the lesions.³³

Nonmelanoma Skin Cancers

Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are the most common forms of skin cancer.³⁴ Non-invasive detection of tumor thickness guided by HFUS was studied in 100 patients with either SCC or BCC before Mohs micrographic surgery to evaluate the ultrasonographic tumor thickness compared to histology.³⁴ In this study, the sensitivity of HFUS was low (32%); the specificity reached 88%.³⁴ However, it is not clear in this study if the US technicians who performed the US examinations were trained on skin examination. In contrast, Bobadilla et al. studied 25 patients with 29 suspicious lesions of BCC that were surgically removed, and histologic tumoral thickness was correlated with their US measurements, showing a very good correlation between US and histology.³⁵ The authors concluded, based on their results, that the application of HFUS was a useful technique for the preoperative planning of BCC.

Interestingly, US can help distinguish histological subtypes associated with high-risk or low-risk for recurrence in BCC. This discrimination is done by identifying hyperechoic spots within the lesions, which are almost pathognomonic signs of BCC (Supplemental Figure S6). A cut-off of 7 or more hyperechoic spots suggests a high-risk histological BCC subtype such as the micronodular, infiltrative, morphoform, sclerosing, and metatypical variants.^{36,37} Supplemental Figure S7 shows an US image of SCC.

Dermatofibrosarcoma Protuberans

Dermatofibrosarcoma protuberans is a rare and locally aggressive cutaneous malignancy that initially presents as an asymptomatic ill-defined flesh-colored plaque.

Early diagnosis and surgical intervention are crucial yet challenging due to its initial subtle presentation.³⁸

Dermatofibrosarcoma protuberans presents a “jellyfish-like” image on HFUS that was described as an oval-shaped hypoechoic body within the dermis with tentacle-like or pseudopods projections spreading through the subcutaneous tissue.³⁸ Other findings included hyperechoic areas within the tumor related to stromal infiltrate on histology and increased vascularity seen with color Doppler (Supplemental Figure S8).³⁸ These ultrasound findings support the implementation of HFUS in the diagnostic process and preoperative planning of this malignancy.

Inflammatory Conditions

Hidradenitis suppurativa. In the evaluation of hidradenitis suppurativa (HS), US has demonstrated utility in diagnosing, staging, and assessing disease activity. This helps select medical treatment, determining the extent of surgical excision, and monitoring response to treatment.^{39,40}

It is difficult to determine the extent of HS by relying only on physical examination. US has a value in recognizing these subclinical deeper findings such as fistulas or fluid collections.⁴¹

Currently, there are ultrasonographic signs for diagnosing HS that include the presence of dilated hair follicles, pseudocysts, fluid collections, and fistulas, which are called the main key lesions.^{40,42} 80% of HS patients present ectopic hair tract fragments within the fluid collections or fistulae.⁴³

Wortsman et al. developed sonographic diagnostic criteria shown in Table 2.⁴⁴ They found that US use led to modification of management in 82% of the patients, including a switch in 24% of the cases from medical to surgical management. Similarly, a recent study showed that 44.7% of HS

Table 2. Sonographic Criteria of Hidradenitis Suppurativa.⁴⁴

Criteria
Widening of the hair follicles
Thickening or abnormal echogenicity of the dermis
Dermal pseudocystic nodules (round or oval-shaped hypoechoic or anechoic nodular structures)
Fluid collections (anechoic or hypoechoic fluid deposits, in the dermis or hypodermis connected to the base of widened hair follicles)
Fistulous tracts (anechoic or hypoechoic band-like structures across skin layers in the dermis or hypodermis connected to the base of widened hair follicles)

^aTo diagnose HS, you need three or more of the above signs.

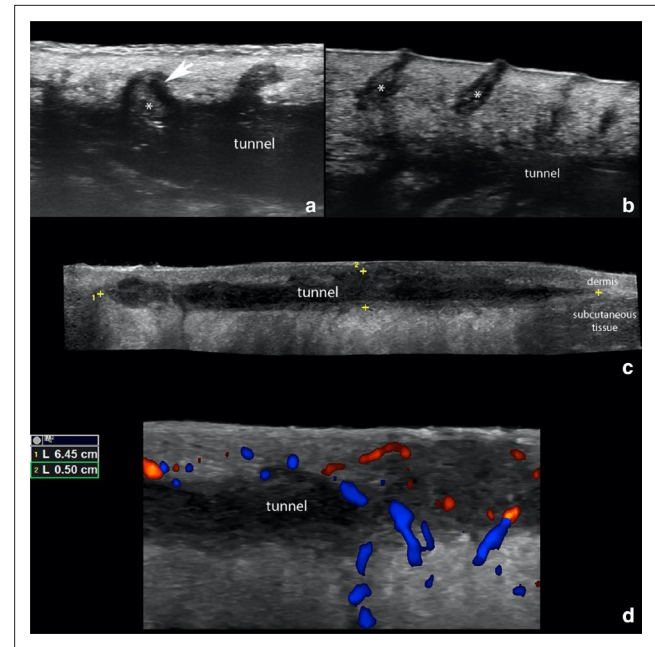


Figure 2. Hidradenitis Suppurativa. (a) shows ballooning of a hair follicle (*, arrow) that is protruding into the periphery of a tunnel (donor of keratin sign). (b) presents dilation of the regional hair follicles (*). (c) demonstrate a 6.45 cm (length) × 0.5 cm (thickness) hypoechoic band-like structure that corresponds to a tunnel that runs in the dermis and upper subcutaneous tissue. (d) Doppler ultrasounds demonstrate hypervascularity in the periphery of the tunnel.

patients diagnosed clinically as Hurley stage 1 were restaged to Hurley stage 2 or 3 after using US, which resulted in management modification.⁴⁵

US examination is also used in assessing disease activity; color and power Doppler can evaluate the degree of vascularization, which correlates with the degree of active inflammation and pain in the HS lesions (Figure 2).⁴⁶

On color Doppler US, the fistulous tracts have been classified according to their degree of edema and fibrosis into three types of severity.⁴⁷ Type 1: low fibrotic scar with high or low edema, type 2: high fibrotic scar with low edema, and Type 3: high fibrotic scar with high edema.⁴⁷

It has been reported that the presence of communicating sinuses is more frequent in type three (71%) and type two (29%), and these two types represent 63% of patients with multiple tracts, which correlate with the severity of the disease.⁴⁷

Martorell et al. described 4 different fistulae patterns: Type A; dermal fistula, Type B; dermo-epidermal fistula, Type C; complex fistula, and Type D; subcutaneous fistula. After 6 months of medical therapies, a complete resolution has been described in type A (95%) and type B (65%). Conversely, types C and D showed no significant response after medical management.⁴⁸

A standardized technique for reporting US findings in HS has been proposed and includes documenting the type and extent of the pseudocysts, fluid collections, and fistulas, besides the locoregional vascularity.⁴⁹ Online supplemental video 1 showing US-guided needle insertion into a sinus tract (available online supplemental video 1).

Systemic Sclerosis and Morphea

Color Doppler US is usually used to assess the activity in systemic sclerosis and morphea.^{50,51} Furthermore, US examination can distinguish between the inflammatory and atrophic stages of the disease, which is essential for prognosis and management.⁵²

Wortsman et al. found that the sensitivity of the US in determining the active phase of morphea was 100% (95% CI 84% to 100%) and specificity was 98.8% (95% CI 93% to 99%) when compared to the gold standard histologic examination.⁵³

They found the most accurate signs of morphea activity are increased echogenicity of subcutaneous tissue and increased blood flow.⁵³ The inflammatory phase lesions show increased thickness and decreased echogenicity of the dermis, increased echogenicity of the subcutaneous tissue, and increased dermal and subcutaneous blood flow (Supplemental Figure S9).⁵³ Conversely, the lesions in the atrophic phase present decreased dermal and subcutaneous thickness with a lack of blood flow.^{54,55}

Calcinosis in systemic sclerosis manifests on US examination as a hyperechoic subcutaneous focal deposit that commonly generates a posterior acoustic shadowing artifact.⁵⁶

US can also be used in defining the pathology and extent of skin ulcers in Systemic sclerosis.⁵⁷ A study by Sulli et al. showed that US examination was superior to clinical assessment using the modified Rodnan skin score in assessing the extent and degree of skin sclerosis.⁵⁸

Panniculitis

US can help in differentiating septal from lobular panniculitis. In a study of 64 patients, the sensitivity and specificity of US examination in distinguishing mostly lobular from mostly septal panniculitis was 85% and 88%, respectively.⁵⁹ Lobular panniculitis shows diffuse hyperechogenicity of the fatty lobules, while septal panniculitis presents a hypoechoic thickening of the septa between the hyperechoic fatty lobules (Supplemental Figure S10).⁶⁰

Hair Diseases

The evaluation of hair diseases is performed mainly by clinical assessment supported by trichoscopic examination while scalp biopsy is reserved for challenging cases. Despite the development in trichoscopy techniques, the findings obtained are limited to the skin surface, and direct assessment in the dermis and subcutaneous tissue is not feasible. Therefore,

other non-invasive modalities facilitating the evaluation of the deeper skin tissues are still in demand and US might potentially replace or support the currently-available diagnostic tools. In addition, the detection of fibrosis and inflammation around hair follicles, which is not directly observable by trichoscopy, might be possible by US serving as an effective tool to evaluate severity and activity of hair diseases. On US examination, the normal hair presents 2 distinct morphologies. The first is terminal hair which is common in the scalp displays a trilaminar hyperechoic appearance with an inner hyperechoic medulla and an outer cortex-cuticle complex. The corporal hair, also called villus hair, presents as a bilaminar hyperechoic structure without a medulla.^{61,62}

Given the tiny size of the hair shaft/follicle ranging from 1.2 to 3.1 mm² on average, conventional US is of limited value in assessing hair disorders at frequencies of 15-18 MHz.⁶³⁻⁶⁵ However, newly developed ultra-high-frequency (UHF) transducers of up to 70 MHz allowing excellent visualization of the hair and surrounding tissues.⁶⁶ Figure 3 a and b demonstrate a comparison between conventional US with 5-18 mHz transducer and UHF-US with 50-71 mHz transducer (VevoMD; VisualSonics, Toronto, Ontario, Canada). As evident in the images, conventional US fails to capture individual hair shaft/follicle and skin appendages, whereas UHF-US successfully detects each hair follicle.

Figure 3 (c) shows the scalp of a patient with androgenetic alopecia (AGA), while (b) is taken from a healthy control. AGA is characterized by a diversity of hair shaft diameters whereas the normal scalp demonstrates homogeneously arranged hair shafts with similar diameters. Another difference exists in telogen/anagen ratios. All the hairs depicted in the normal scalp (3b) are anagen hairs as they end in subcutaneous tissue illustrating the “bottom-heavy” pattern. Conversely, AGA scalp (3 c) contains small ovoid and relatively hyperechoic structures in keeping with telogen hair follicles. Further assessment, such as the calculation of hair density, average hair shaft/follicle diameter, telogen/anagen hair ratio, is possible by combining these sequential vertical images with specialized image processing software.

Nail Diseases

The use of US can help avoid nail biopsy which is peculiarly painful and associated with the risk of permanent nail destruction. The main applications include tumoral conditions, inflammatory entities, and growth abnormalities.

Glomus Tumor

Glomus tumor is a lesion derived from the neuromyoarterial plexus and on US shows as an oval-shaped hypoechoic nodule in the nail bed that generates scalloping of the bony margin of the distal phalanx (Supplemental

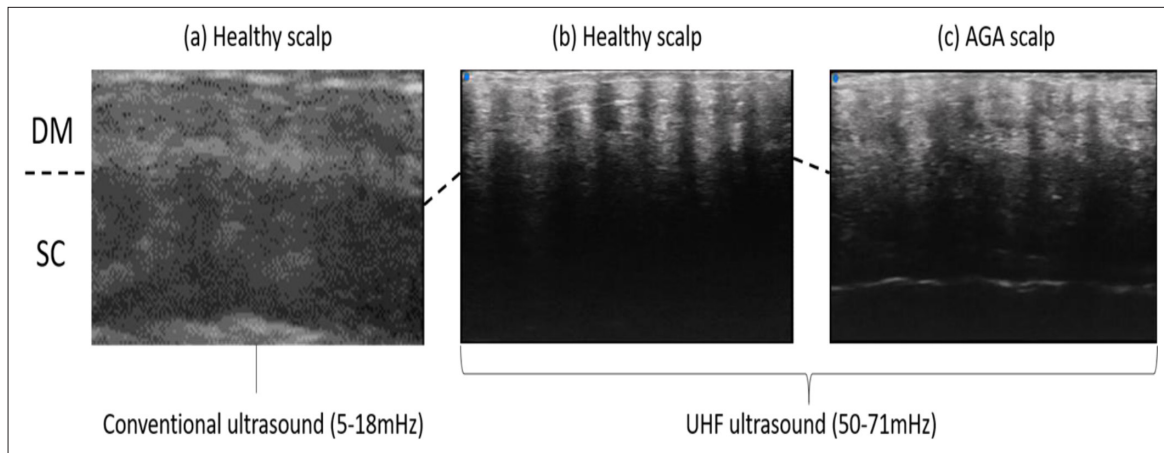


Figure 3. The ultrasonographic images of conventional and newly developing ultrasound. (a) Healthy scalp depicted by conventional ultrasound. (b) Healthy scalp depicted by ultra-high-frequency (UHF) ultrasound. (c) Scalp of androgenetic alopecia depicted by UHF ultrasound. AGA, androgenetic alopecia; DM, dermis; SC, subcutis.

Figure S11).⁶⁷ On color Doppler, they frequently present hypervascularity.⁶⁷

Subungual Exostosis

This bony outgrowth protrudes into the nail bed and may simulate other nail conditions. The US examination demonstrates a band-like hyperechoic structure with a posterior acoustic shadowing artifact and connected to the underlying bony margin (Supplemental Figure S11).⁶⁸

Onychocriptosis

This is the embedding of the nail plate into the periungual nail fold. The US examination shows the hyperechoic bilaminar fragment in the periungual region and the hypoechoic inflammatory in the surrounding tissue. On color Doppler, there is a variable degree of hypervascularity.⁶⁹

Exogenous Material

US can be useful in diagnosing foreign bodies, (Supplemental Figure S12) and cosmetic fillers. A study by Bray et al. showed that US had a Sensitivity of 9% (CI 89% to 97%) and specificity of 99% (CI 96% to 100%) in detecting foreign bodies.⁷⁰ They appear as hyperechoic linear structures surrounded by a hypoechoic halo due to inflammation or granuloma formation. This is useful in determining the location of foreign bodies to guide surgical removal.⁷⁰

US also can detect the most common types of cosmetic fillers. Thus, US is sometimes used in the management of the complications of cosmetic fillers such as granuloma or inflammation.⁷¹

Conclusion

US is a useful non-invasive modality in the field of dermatology that can provide critical information to complement the clinical examination. It can accurately assess disease severity and activity in several inflammatory dermatoses. It is also useful in the diagnosis and preoperative planning of skin tumors. Moreover, it could mitigate the need for skin biopsy in some situations which is especially helpful in the pediatric population, nail/hair disorders.

Declaration of Conflicting Interests


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Supplemental Material

Supplemental material for this article is available online.

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