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Dermatologic Ultrasound

Fernando Alfageme[1], Ximena Wortsman[2], Gastón Roustan[1], Maria Crisan[3], Radu Badea[3]

[1]Dermatology Service. Hospital Universitario Puerta de Hierro Majadahonda. Madrid. Spain

[2]IDIBAPS. Dermatology and Radiology Department Clinica Seervet. Universidad Católica y Santiago de Chile. Chile

[3]Radiology and Dermatology UMPh Iuliu Hatieganu, Cluj-Napoca. Romanaia

Corresponding author:

Prof. Dr. Fernando Alfageme

Dermatology Service

Hospital Universitario Puerta de Hierro Majadahonda (Madrid)

Associate Professor Dermatology

Universidad Autónoma de Madrid, Spain

Ultrasonography of normal skin and appendages (hair and nails)

The skin covers all our human body, but its function goes further than being just a physical barrier. It is necessary to know exactly the dermatologic structures and its ultrasound features. The skin is composed by three anatomically distinct layers: epidermis, dermis and hypodermis or subcutaneous tissue. There are anatomical regional variations of these strata depending on the location (face, trunk, palm or sole). Besides the skin there are the skin appendages, especially the nail and the hair for ultrasound purposes. And finally there are other structures (glands, vessels, nerves) that we will have to take into account in our ultrasound examinations. Maybe the best way to classify skin disease is according to the skin structure affected: epidermis, dermis, subcutaneous fat, hair or nails. We will need a high frequency linear transducer (> 12 MHz) and Doppler for a suitable skin ultrasound study.

Epidermis

It is the external layer of the skin and it is composed mainly of keratinocytes. In turn, we may differentiate five strata: the basal layer, the spinosum stratum, the granulous layer, the stratum lucidum (only in palm and soles) and the most superficial stratum, the stratum corneum, a cornified external membrane that is mainly formed of keratin. It is the thinnest layer, 0,04 mm (eyelid)-1,6 mm (sole).

On ultrasound examination we will find a single hyperechogenic band, except in areas where is specially thick like palms and soles, where we will identify a bilaminar hyperechoic structure [(1)]. As the epidermis has no vessels or vascular structures, there is no blood flow in color Doppler. Melanocytes and melanin are not well identified by ultrasound, neither Langerhans nor Merkel cells.

Dermis

Dermis is the middle layer of the skin. It is composed mainly of connective tissue, collagen and elastic fibers, within them are embedded the hair follicles and the sebaceous, appocrine and eccrine glands; as well as blood vessels, lymphatics, nerves and the arrector pili muscle. It is 15-40 times thicker than epidermis, being the back the most width.

Dermis we may be divided in two compartments: the papillary dermis and the reticular dermis.

1. Papillary dermis is the most near to the epidermis (between them we found the dermoepidermal junction). It is characterized by many digitiform dermal projections that ascend towards the epidermis (dermal papillae). Lax collagen bundles and elastic fibers are disposed perpendicularly.
2. Reticular dermis goes from the papillary dermis to the subcutaneous fat. We find dense collagen bundles parallel to the skin surface with a network of elastic fibers.

On ultrasound examination there will be a thin moderate hypoechoic homogeneous band just below the epidermis (the papillary dermis), and a thicker more hyperechoic slightly heterogeneous band beneath the latter (the reticular dermis). Intermingled in the reticular dermis we may identify hair follicles.

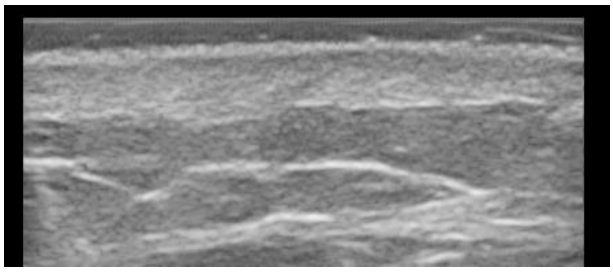
Normal dermis will show no blood flow or minimal in color Doppler studies. What we are going to see varying amounts of small-size blood vessels depending on the anatomical region.

Subcutaneous tissue

It is the deepest layer of the skin. There are two main structures in the hypodermis: lobules and septa. Lobules are composed of adipocytes distributed like irregular rectangular boxes separated by thin bands, the septa, formed mainly by collagen fibers, small and medium-sized blood vessels and lymphatics.

On ultrasound examination we will observe a usually thick homogeneous hypoechoic band with inserted hyperechoic lines. With color Doppler we will appreciate the blood vessels, with a low-flow pattern.

Figure 1 Normal skin of the arm sonography. From top to bottom: hyperechoic linear band (Epidermis), slighltly thin hipoechoic band (papillary dermis), thick hyperechoic structure (reticular dermis) wide hypoechoic layer with linear hyperechoic lines/septa (subcutaneous fat).



Hair unit

Humans have hair in all the body surface, except palms, soles and mucous membranes. There are three types of hair: vellus, sebaceous and terminal. Its life cycle has three stages: anagen (growing phase, the longest), catagen (involution) telogen (resting phase). They are composed of a cuticle (outer layer), cortex (middle layer, hard keratin) and medulla (inner layer, soft keratin).

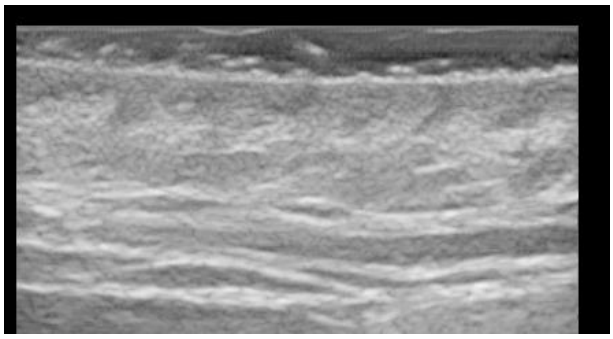
We have to differentiate between:

1. hair shaft (with a extracutaneous portion and a intracutaneous portion inside the follicle) and
2. hair follicle (all of it is intracutaneous). Terminal hair follicle is thick, entering to reticular dermis and subcutaneous fat, especially if they are in anagenic phase; while vellus hair follicle is very thin.

On ultrasound studies we will see hair shafts as an extracutaneous hyperechoic linear structures parallel to each other with a oblique orientation over the surface of the epidermis. With a high resolution probe we will be able to differentiate an inner hypoechoic band in terminal hairs, the medulla, what it gives a trillaminar appearance to the hair shaft. In the other hand the follicles are hypoechoic bands dermal structures with a tendency of be wider at the bottom, also parallel to each other with a oblique orientation, so it is very

important not to put the transducer in a longitudinal way. Follicles in superficial dermis usually correspond to telegenic phase and deeper follicles to anagenic phase.

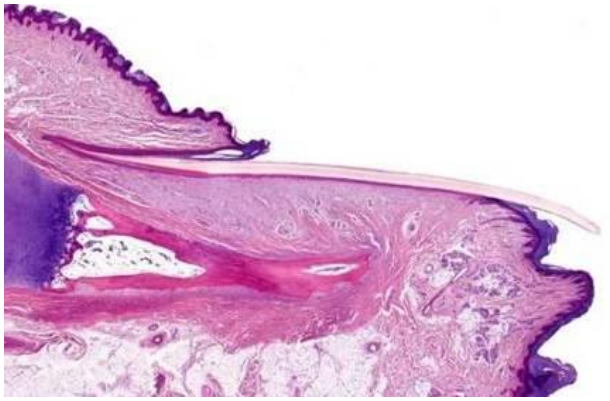
Figure 2 Terminal follicles in the face sonography. Oblique hypoechoic shadows slightly globular in the dermis.



Nail unit

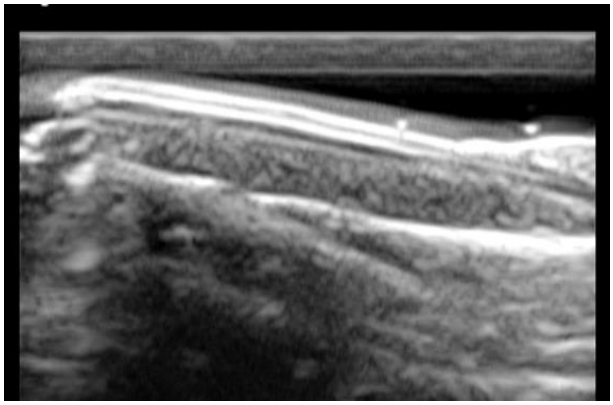
The nail is composed of many structures: 1) the nail plate or lamina, in the surface, keratinized, with three layers: ventral plate, interplate space, dorsal plate; 2) the nail bed, just beneath the nail plate, contains connective tissue with collagen fibers, a capillary network and glomus bodies 3) the ungueal matrix or germinal layer located in the proximal area of the nail bed; and 4) the periungueal folds: distal, proximal and lateral. We should underline the importance of the nail unit and its relation with adjacent structures; the distal phalanx and the extensor/flexor tendon insertion.

Figure 3 Nail unit, longitudinal histological features. From top to bottom: nail fold, nail plate, nail bed, distal phalanx. Courtesy of Dr. Luis Requena.



Ultrasound enables us to differentiate each structure. Nail plate linear is characterized by a slightly convex multilaminar band: two well defined homogeneous parallel hyperechoic lines (dorsal and ventral) and a hypoechoic space between them. Nail bed is seen as a thick homogeneous hypoechoic area below and attached to the nail plate. There are many capillaries, so a low-flow pattern with Doppler is frequently observed. Nail matrix is an ill-defined slightly hyperechoic area in the proximal area of the nail bed.

Figure 4 Nail unit sonography. See a billaminar hyperechoic nail plate with a hypoechoic interplate space, a hypoechoic band underneath that corresponds to nail bed, and the distal phalanx at the bottom



Other Skin Appendages

Skin appendages as sebaceous and apocrine glands (part of the hair unit); and eccrine glands are not identified by ultrasound.

Ultrasound of common skin cancers

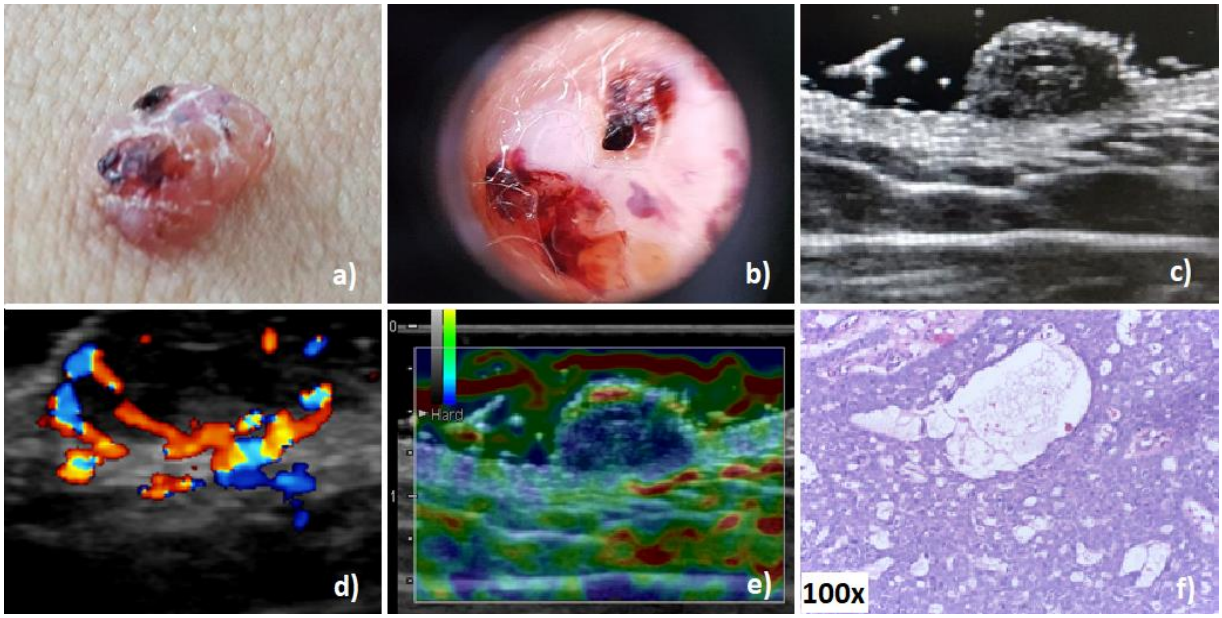
Skin cancer is the most common type of cancer in humans and can be divided into two groups: non-melanoma skin cancer (NMSC) and melanoma. Malignant melanoma makes up 4-11% of all skin cancers and it is estimated that 75-80% of all NMSC are basal cell carcinomas (BCC) and up to 25% squamous cell carcinomas (SCC) [(1-3)]. Some of the well-known causes of skin cancer include exposure to UV-radiation, infections, exposure to carcinogens, iatrogenic immunosuppression and chronic inflammatory skin diseases. The risk factors include clinical aspects (skin phenotype, incomplete excision of primary tumor, anatomical site localization, size, borders, history of a prior skin tumor) and histological aspects of which the most important for both prognosis and therapeutic approach is the tumor thickness (Breslow index) [(3-5)].

Basal cell carcinoma

BCCs arise from basal keratinocytes and grow by direct extension. Although they rarely metastasize, BCCs have local invasion and destruction potential [(1, 2)]. Chronic intermittent UV rays' exposure is correlated with the development of BCCs, however, this type of malignancy can also occur on sun protected areas. Regular sonographic examination of the skin is recommended to be included in the follow-up of patients with BCCs, due to the increased risk of local recurrences. High frequency ultrasonography (HFUS) can help distinguish between different histological types of BCC: nodulocystic, superficial, keratotic etc. [(6, 7)]. It is important to keep in mind that in the same lesion different histological types may also be encountered.

Figure 5 Nodular Basal Cell Carcinoma. a) Clinical aspect: nodular tumor with superficial ulceration, covered with hemorrhagic crusts; b) Dermoscopy: typical superficial

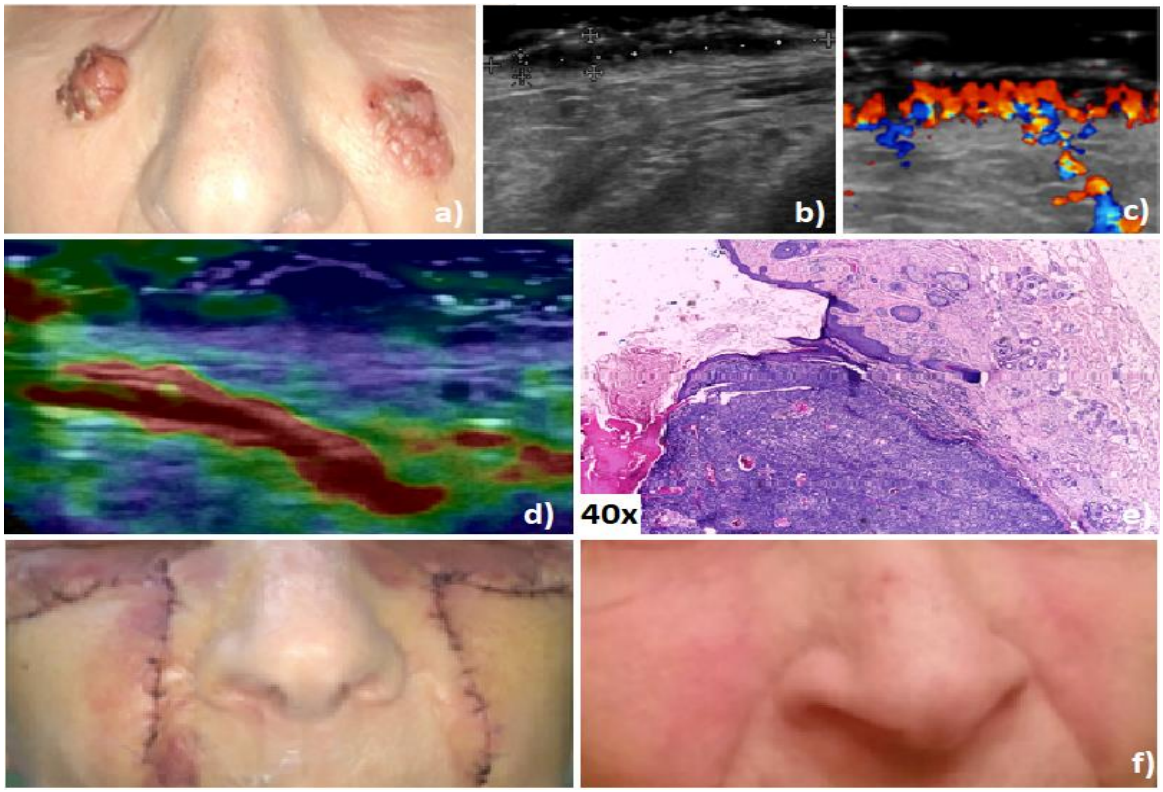
dilated and arborizing vessels; c) Grey scale HFUS: well-defined hypoechoic, exophytic, solid heterogeneous lesion with several echoic and hyperechoic reflecting spots and few hypoechoic irregular structures corresponding to the histological type; the lesion displays regular borders, a superficial ulceration, a lateral extension of 11 mm and 5.5 mm thickness; the clinical lateral extension correlates with the sonographic extension; d) Color Doppler: increased vascularity with arborizing pattern and two vascular pedicles; e) Elastography: increased rigidity; f) Histology: large nests of basaloid cells displayed in a nodular type with adeno-cystic differentiation; Breslow index 5.5 mm; note the high correspondence with the sonographic thickness (5.5mm).



Squamous cell carcinoma

Cutaneous SCCs arise from the epidermal keratinocytes and can metastasize and be locally destructive. Continuous and cumulative UV rays' exposure represents the greatest risk factor for SCC development. The most common anatomical sites where SCC arises are the scalp, the back of the hand as well as the superior surface of the pinna [(1, 8)] [Figure 6].

Figure 6 **Squamous cell carcinoma (facial symmetric lesions). a) Clinical aspect: two symmetric, exophytic and ulcerated lesions, located on the face; b) Grey scale HFUS: hypoechoic lesion involving epidermis and dermis with superficial ulcerations, inhomogeneous structure, hyperechoic spots corresponding to cysts, 3 cm lateral extension, 3 and 4 mm thickness; c) Color Doppler: intense vascularity within the lesion; two vascular pedicles; d) Elastography: increased rigidity of the tumor; e) Histology: well-differentiated squamous cell carcinoma, fibrous stroma, peritumoral inflammatory infiltrate (Breslow 2 and 3 mm); f) Post-operative aspect at 10 days and 6 weeks (9).**

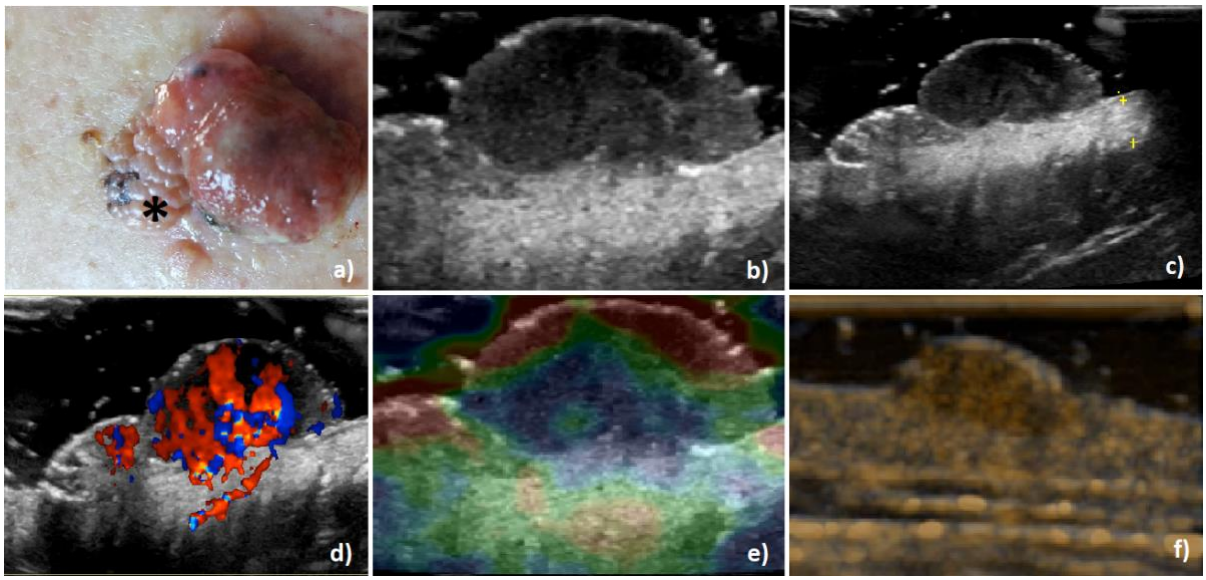


Cutaneous melanoma

Although primary cutaneous melanoma (CM) is not the most common type of skin malignancy, it is the most aggressive one. Moreover, up to 40% of lesions have a high recurrence rate. Sunburns during childhood, a positive family history of melanoma and pre-existing melanocytic nevi make up the most essential risk factors for developing CM [(1, 3,

4)]. Breslow index is the most important factor for prognosis and therapeutic management in melanoma patients [(1, 10)]. CMs have a potential to metastasize, thus regular follow-up is required (clinical examination and sonography) [Figure 7].

Figure 7 **Amelanotic malignant melanoma. a) Clinic aspect: exophytic nodular amelanotic ulcerated tumor, developed on top of a compound nevus (*); b,c) Grey scale HFUS: well-defined hyperechoic inhomogeneous structure involving dermis and hypodermis, with regular contour, associated with a smaller well-defined echogenic structure corresponding to a compound nevus; hyperechoic underlying adipose tissue; HFUS thickness 5,7 mm, Breslow histological index 5,5 mm; d) Color Doppler: hypervascularization within the tumor, central pattern, some blood vessels displayed in a parallel pattern; more than 2 vascular pedicles; e) Elastography: increased rigidity of the tumor; f) Contrast enhanced ultrasonography: fast inhomogeneous uptake and quick wash up time.**



Dermatological diagnosis

The dermatological diagnosis is based on physical, dermoscopical and histological examination. HFUS supports the dermatological diagnosis and offers real-time information which is strongly correlated with the histological findings [(1, 7, 11)]. The most important and relevant sonographic parameters that can be identified in skin cancer are related to morphology, vascularization and elasticity [Table 1].

Table 1 Sonography parameters suggestive for BCC, SCC and melanoma.

Basal Cell Carcinoma (BCC)	
Grey scale (Morphology)	• Well-defined hypoechoic and inhomogeneous structure; • Hyperechoic spots inside the tumor; • Sharply/poorly defined borders (difficulty in assessing the tumor margins of morpheaform and infiltrative types); • High correlation between tumor thickness and Breslow index; • Anechoic/hyperechoic areas (suggestive for cysts) [(1, 7, 12)]
Doppler (Macrocirculation)	• 1-2 vascular pedicles; • Blood flow prominent at the bottom of the tumor (usually) [(7, 13, 14)]
Elastography	• Increased rigidity [(15, 16)]
Squamous Cell Carcinoma (SCC)	
Grey scale (Morphology)	• Hypoechoic well-defined lesion with/without hyperechoic spots; • Frequently invading the deeper structures; • Shadows running perpendicularly on the skin structure induced by superficial scales or crusts; • Tumor size may be overestimated due to hyperkeratosis/abundant inflammatory infiltrate [(1, 8, 9, 17)]; • Loco-regional lymph-nodes should be examined (risk of metastasis);
Doppler (Macrocirculation)	• Compared to BCC, SCC have a more prominent vascularization; • Internal and peripheral disposed blood vessels that create a mixed pattern; • 2 or more vascular pedicles [(1, 7, 13)]
Elastography	• Increased rigidity [(1, 16)]
Cutaneous Melanoma (CM)	
Grey scale (Morphology)	• Well-defined oval/fusiform homogeneous hypoechoic structure; • Irregular contour; • Increased echogenicity of the underlying subcutaneous tissue; • The area around the tumor should be examined for local/in-transit metastasis [(10, 11, 18, 19)]

Doppler (Macrocirculation)	• Intense chaotic vascularization composed mostly of arterial vessels with low flow [(1, 7, 13)]
Elastography	• Increased rigidity [(1, 18)]
Tips	• Check for satellites/in transit metastasis; • Provide extension in all axes [(1)];
Metastasis (satellite lesions or in-transit metastasis)	• Hypoechoic/anechoic heterogeneous structures; • Oval/round/irregular shape; • Enhanced acoustic in the underlying subcutis; • Variable degree of vascularization; • Round shaped structure with nodular thickness of the cortex, loss of central medullae hyper echogenicity, peripheral vascularization [(1, 20)]

Sonographic imaging is used as a preoperative assessment of skin tumors. HFUS acquires images at frequencies between 18 and 20MHz [(7, 13)]. Although HFUS is highly sensitive (detection of the tumor is very accurate), it has a low specificity, therefore it cannot precisely differentiate between NMSC and CM, or between benign or malignant lesions. However, certain morphology aspects and vascular characteristics can be of use in suggesting the type of malignant lesion or in telling apart malignant from benign lesions. HFUS assessment of cutaneous tumors provides information which is essential for therapy management of cutaneous tumors [(1, 7, 11, 21)]. Of notice, sonographic artifacts may in some cases appear. For example, the “blurry tumor” appearance may be caused by local sebaceous gland hyperplasia while the “angels of the bottom” appearance is caused by inflammatory infiltrate and dilated vessels. Difficulty in image interpretation may be due to elastosis and by association with other lesions, as seen in CM developed in close proximity to nevi [(18, 20)]. Other oncological applications of HFUS are assessment of skin lymphomas, angiosarcomas, Kaposi sarcomas, adnexal carcinomas etc. [(1, 13)].

Ultrasound of inflammatory skin diseases

Inflammatory skin diseases can be, in general terms, the result of an infectious or non-infectious disease. Within this last group, psoriasis, hidradenitis suppurativa and rheumatologic diseases stand out as most common pathologies.

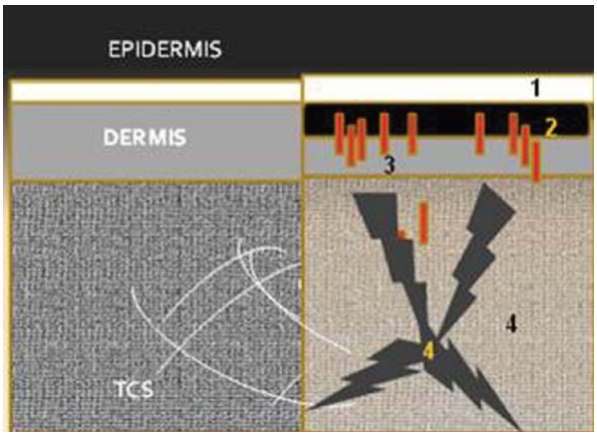
Cutaneous ultrasound can provide information on the extension of the inflammation and also on eventual complications that may come from that inflammation, thus becoming a very useful tool to monitor the treatments prescribed to the patients.

Basic principles of ultrasound of cutaneous inflammatory diseases

Pathophysiologically any skin inflammation is accompanied by an increase in the blood flow of the affected area [(22)]. The superficial vascular plexus, found in the dermoepidermal junction, is the structure with the highest capacity of intravascular and extravascular exchange. Given this, the first sign of inflammation that is visible in ultrasound is the increase in the vascular flow of the affected area, compared to the flow registered in surrounding areas [(2)]. This increased flow will lead to the accumulation of intravascular serum and mediator inflammation cells and mediators. This phenomenon is characterized in ultrasound as hypoechogenicity of the superficial dermal band which corresponds anatomically to papillary dermis [(23)].

If the inflammatory infiltrate reaches the subcutaneous tissue increased vascular flow in this tissue will be observed together with this being identifiable hypoechogenicity of the interlobular septa and the changes in echogenicity of fatty lobules [(23)] which increase echogenicity in *a cobblestone pattern.* If the vascular inflammation becomes very intense it can lead to necrosis, which is characterized in ultrasound images of hypoechoic and unstructured areas in dermis or subcutaneous tissue. Reparation processes after inflammatory events of the skin, are characterized by the replacement of inflamed tissue by a scar [(22)] (mainly composed of collagen) that is hypoechogenic in the first stages and then becomes hyperechogenic when the contraction and remodeling process is completed.

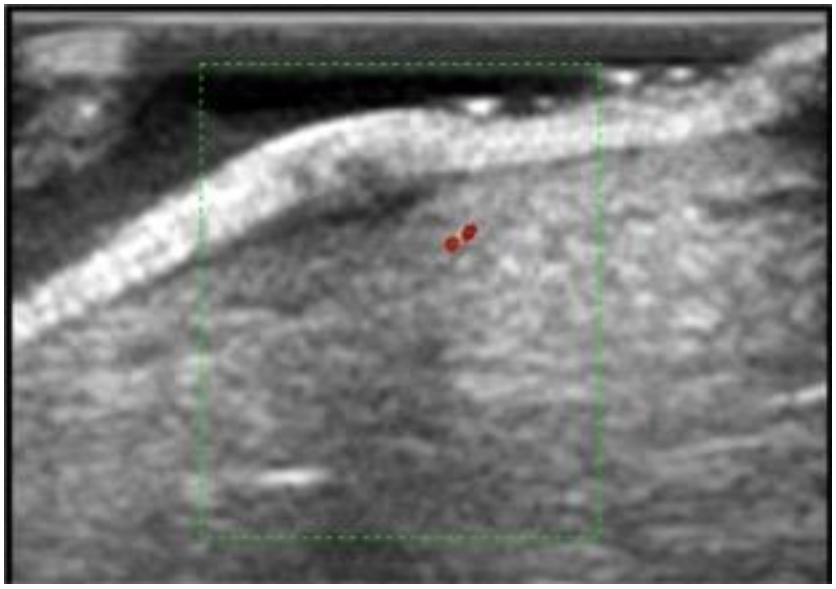
Figure 8 **Ultrasound of skin inflammation (schema). Ultrasonograhic changes of skin inflammation are 1. Epidermal thickening 2. Dermal hypoechogenicity, 3. Increased dermal vascularization 4. Changes in subcutaneous tissue echogenicity**



Ultrasound of skin infectious diseases

Microbial infection (caused by viruses, bacteria or fungi) of the skin is normally accompanied by an inflammation of the infected layer. Viruses often infect more superficial layers of the skin. The viral infection better characterized from the sonographic point of view are those caused by human papilloma virus (HPV). HPV type 1 affects mainly plantar surfaces and the infection is characterized by an inflammation of both superficial and deep tissues [Figure 9].

Figure 9 Viral wart. Thickened epidermis with underlying dermal hypoechogenicity and local increased vascularization.



The second histologic feature of HPV infection is hyperkeratosis of superficial layers. The inflammatory process is accompanied by inflammation of deeper structures such as joint bursae [(24)]. In this sense, ultrasonography becomes very useful for the diagnosis of plantar warts and to guide treatment in recalcitrant cases. Cryotherapy, ablative and vascular laser are efficient treatment modalities in which ultrasound indicates if inflammation is progressively reducing in from deep to superficial layers. The reaction of the body to an inflammation caused by *bacterial infection* is frequently the isolation of the focus of the infection through the formation of pyogenic abscesses. These may not be clinically evident, which is problematic because they need drainage to be treated [(25, 26)]. Ultrasound clearly defines the abscess limits, which is essential to guide the drainage process. Regarding mycoses, ultrasound is useful in the differential diagnosis of onychomycoses with psoriatic onycopathy [(27)]. In the case of psoriasis ventral thickening of nail plate is evident in contrast with onychomycoses in which dorsal plate involvement is also present. Together with increased vascularization of nailbed in psoriasis, this sonographic difference is relevant to prescribe antifungal drugs, which are not exempt of secondary effects, or high potency corticosteroids, which are keystone treatment for, nail psoriasis.

Non-infectious inflammatory skin diseases: Psoriasis

Psoriasis is nowadays considered a systemic inflammatory disease that affects the skin, the nails and the joints. Methods used to quantify the extent or severity of skin psoriasis (PASI-NAPSI) are subjective and highly susceptible to inter-observer variation. These variations make early psoriasis detection and treatment follow up difficult to evaluate [(28)]. Ultrasound of the psoriatic plaque follows the same general ultrasonography principles of skin inflammation:

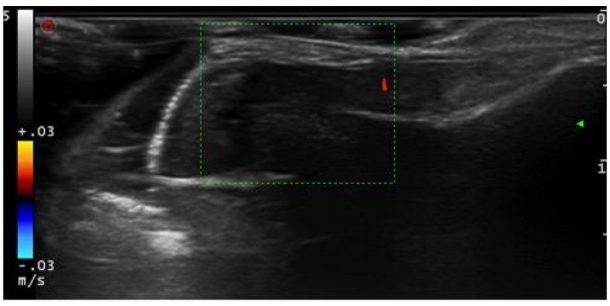
1. Dermo-epidermal thickening.
2. Appearance of hypoechoic band in the superficial dermis that correlates with inflammation.
3. Increased flow in the dermis visible with Doppler.

Regarding nails, general features of psoriatic onicopathy are [Figure 10]:

1. Thickening of the nail bed (measured from the table to the phalanx)
2. Loss of definition of the ventral nail plate
3. Increased flow in the nail bed.

Ultrasonographic follow up of topical and systemic treatments in psoriasis have proven to be sensitive for changes induced by the use of these treatments [(29)]

Figure 10 Psoriatic nail. Increased vascularization in matricial area with distal thickening and irregularities in ventral plate.



Ultrasonography of inflammatory skin diseases: Lupus, dermatomyositis, morphea

This group of diseases have two phases: an active inflammatory phase and an atrophy-sclerosis phase Most rheumatologic skin diseases are best treated in the *active* inflammatory phase therefore, the use of ultrasound to discriminate between these two phases is relevant above all in the case of deep sclerosing diseases in which clinical findings are usually inconclusive.

Active phase ultrasound findings in this group of diseases are:

• Changes in epidermis

• Hypoechoic dermis

• Increased echogenicity of subcutaneous cellular tissue.

• Increased flow at the dermis and at the subcutaneous cellular tissue.

Dermatomyositis and systemic sclerosis can cause calcinosis, which is characterized by signs of calcification (hyperechoic, posterior acoustic shadowing) and vascular thrombosis. The appearance of both these signs indicate poor prognosis in these diseases.

Inactive or atrophic phase ultrasonograhic findings in rheumatological diseases are :

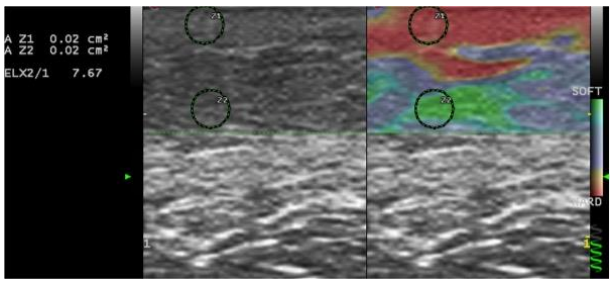
• Thinning of the dermis and of subcutaneous tissue

• Increase of the fibrous component in the dermis and hypodermis

• Decreased vascularization.

New ultrasonographic techniques such as elastography are being used to assess skin sclerosing diseases in the atrophic phase [Figure 11].

Figure 11 Morphea plaque B mode and elastography. Increased strain can be observed in the underlying dermis and subcutaneous tissue



Ultrasonograhy in hidradenitis suppurativa

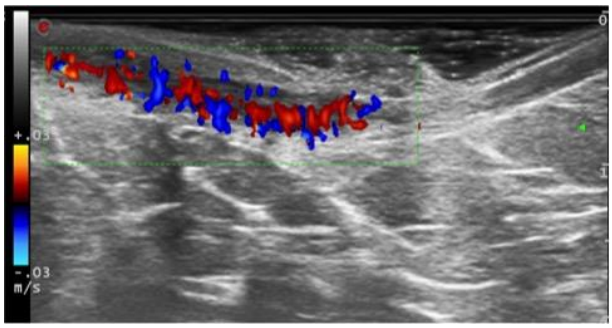
Hidradenitis suppurativa (HS) is an immune mediate disease targeting follicles in the apocrine areas of the body (axila, groin gluteal, submmamary). This chronic debilitating disease is usually underestimated due to the deep location of the lesions that are felt by the patient but that in many occasions are occult to the naked eye. The role of ultrasound in the management of this disease is key to fully avoid irreversible atrophic scars that may lead to functional impairment and social exclusion due to foul discharge of the structurally established lesions.

In the spectrum of HS lesions three elementary forms can be observed

1. **Pseudocyst**: Limited hypoechoic area in dermis.
2. **Fistulous tracts**: Lineal dermal-subdermal areas that connect several follicles.
3. **Fluid collections**: Subdermal hypoechoic areas or purulent content.

Adequate treatment of HS depends mainly in sonographic staging according these lesions. While as pseudocysts may be treated with topical antibiotics, fistulae or collections indicate the need of a systemic or combined surgical treatment.

Figure 12 Hidradenitis suppurativa Color Doppler (longitudinal view axilla). Fistulous tract between dermis and subcutaneous tissue.



Ultrasound in aesthetic dermatology

Nowadays, aesthetic procedures have presented an explosive growth in the last two decades due to the constant development of agents and techniques that are produced for enhancing the beauty and preserve youth. Each year millions of people worldwide undergo these procedures [(30, 31)], which are not free from complications. In this review, we provide the ultrasound appearance of the most commonly used cosmetic fillers and other aesthetic procedures.

As reported, the sonographic features of complications should be kept in mind because the presence of adverse reactions in this field is not infrequent [(32, 33)]. For adding complexity to the situation, there are patients with a history of multiple procedures performed by different operators, not all of them well-trained physicians, and sometimes these cosmetic techniques have been applied from non-medical personnel. Thus, the history of these cases may be not sufficiently reliable, occasionally confusing or merely non-existent, because whatever the reason, some of these cases deny the performance of cosmetic procedures. Furthermore, some of these patients are policonsultant and go to different operators for a wide range of aesthetic procedures. Most of these operators work in private institutions or offices, and some of them in different cities or countries. Therefore, the real clinical information can be complicated to obtain.

Ultrasound is the first imaging technique for studying aesthetic procedures because it is the only technique that can reliably identify the most common types of cosmetic fillers and can observe with high-definition the anatomical changes in other common cosmetic procedures [(34, 35)].

The dermatologic ultrasound technique for examining these cases relies on the already published guidelines for performing dermatologic ultrasound examinations, among other publications [(36)].

Knowledge of the sonographic anatomy of the skin and its changes with the age and exposure to the sun is a must for interpreting well the images. For example, the cutaneous damage produced by prolonged exposure to the sun is called photoaging and produces a hypoechoic band in the upper dermis called SLEB (subepidermal low echogenic band). This band is related to the increased deposition of glycosaminoglycans in the dermis and should not be confused with active or chronic inflammation [(37, 38)].

For academic reasons, we will divide the aesthetic procedures into fillers and non-fillers.

Fillers

They are nanoparticles that are used for treating sagging skin, wrinkles or increasing the volume of specific regions [(39-43)]. Ultrasound allows to detect, identify, locate and measure the extent of the deposits of cosmetic fillers as well as support the diagnosis and follow up the complications derived from these injections [(39-42)].

There are multiple types of cosmetic fillers, and each year the industry supplies new products to the worldwide market that can be new formulations of the old products or new agents [(30-32)].

There are several types of classifications of fillers according to their physical properties such as biodegradable (i.e., absorbable) and synthetic (i.e., not-biodegradable) or hydrophilic (i.e., retain water) and hydrophobic (i.e., repel water). Nowadays, several fillers contain mixed chemical properties because they are manufactured to present longer durations [(44)].

Some of the fillers are not FDA-approved and are injected illegally in many countries. An example of this issue is the silicone oil injection, which can cause well-known complications. Therefore, the recognition of these synthetic deposits is a must, and its ultrasonographic pattern is included among the fillers [(40-42)].

Fillers are sometimes misnamed “dermal fillers.” On imaging, it is possible to see that most of the deposits are located in the hypodermis and not in the dermis.

Inflammatory signs can be detected in the periphery of the deposits such as increased echogenicity of the fatty hypodermal tissue or regional hypervascularity.

To date, MRI can detect silicone due to the silicone-only sequence that was designed to identify the breast silicone implants. CT can show some formulations of calcium hydroxyapatite due to the calcium component. In spite of some articles report the use of MRI for identifying fillers [(45, 46)], our experience has shown that in the real world, MRI and CT are rarely used for identifying cosmetic fillers. Probably, this is related to the lack of characteristic patterns necessary to discriminate the most common types of fillers; however, these imaging modalities can significantly support anatomical information on the extent and degree of inflammation and the presence of granulomatous reaction.

In PET-CT, these deposits produce hypermetabolic areas due to inflammation and should not be misinterpreted as metastasis [(47)].

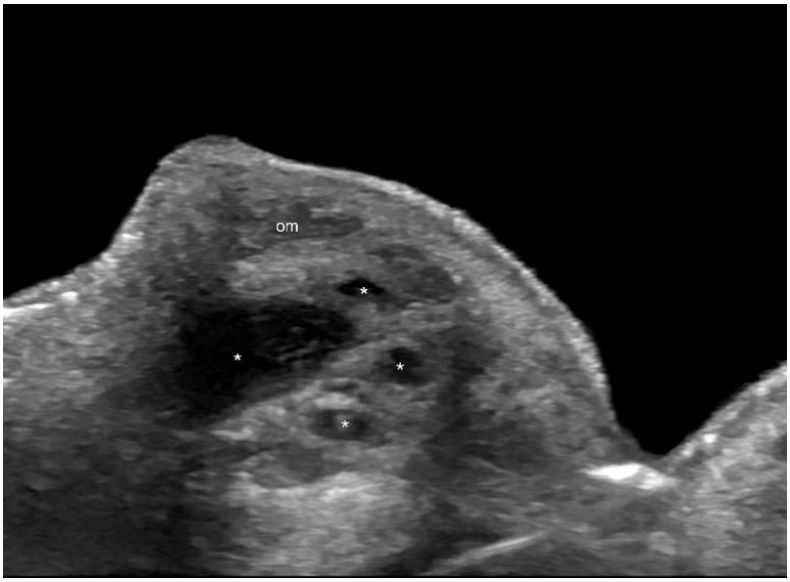
Ultrasound Appearance of Common Types of Cosmetic Fillers

The most commonly used cosmetic fillers worldwide are:

Hyaluronic Acid (HA)

It is a hydrophilic and the most frequently injected filler worldwide. Its pure form is biodegradable in 3 to 6 months; however, the new families of cross-linked products are mixed with excipients and can last several years. It shows as oval-shaped, anechoic or hypoechoic, pseudocystic structures that usually modify their size over time (months) [Figure 13] [(48, 49)].

Figure 13 Hyaluronic acid (longitudinal view). Oval shaped, anechoic, pseudocystic deposits (*) in the orbicularis muscle and hypodermis of the upper lip.

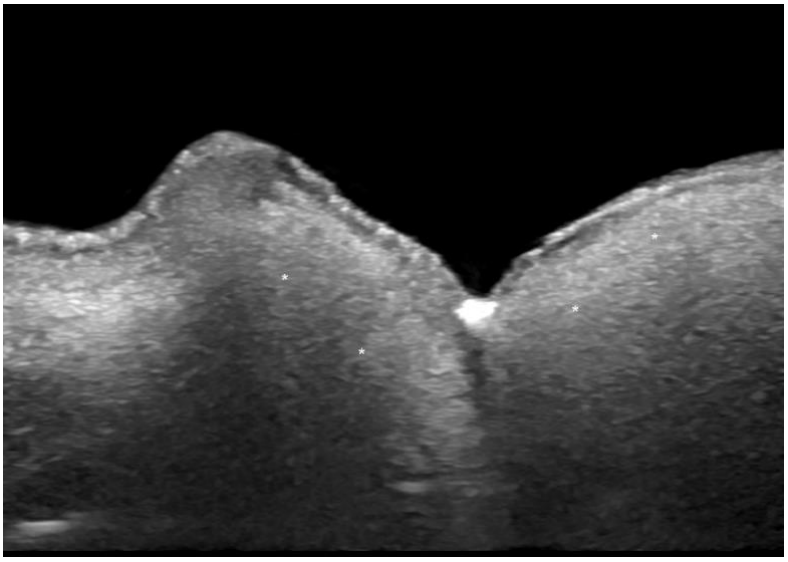


Silicone

It is a synthetic and hydrophobic filler, and it has a pure form and an oily formulation that present different ultrasound appearances. The pure form is composed of oval-shape,

commonly taller than wide, anechoic deposits. Its oily formulation appears as hyperechoic deposits that produce a diffuse reverberation artifact that had been named “snow storm.” In some parts of the oily formulation, pure silicone deposits can be seen. This filler easily passes through the superficial layers, including the muscles and can migrate to other corporal locations due to gravity effect or through the lymphatic system [Figure 14] [(49)].

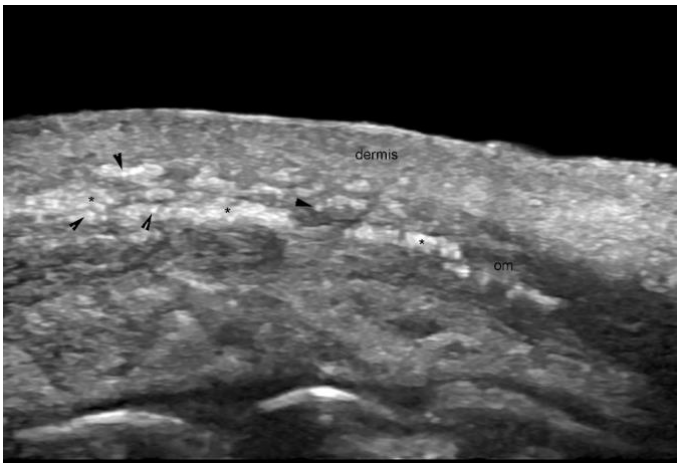
Figure 14 Silicone oil (longitudinal view). Hyperechoic deposits (*) in the upper and lower lip that produce a diffuse posterior acoustic reverberance artifact, also called “snow storm.” Notice the blurriness of the dermis, hypodermis and orbicularis muscles due to the presence of the filler in all the layers.



Polymethylmethacrylate (PMMA)

It is a synthetic and hydrophobic filler. These deposits appear as hyperechoic and generate small spots with tiny posterior reverberation artifact that had been called the mini-comet tail artifact [Figure 15] [(44)].

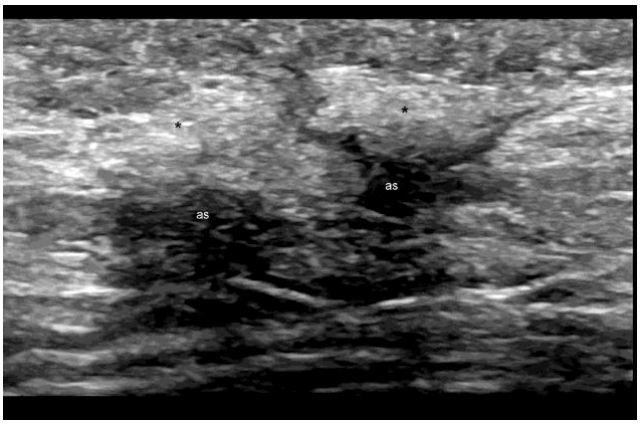
Figure 15 Polymethylmethacrylate (transverse view). Hyperechoic deposits (*) that produce a mini-comet tail artifact (arrowheads) in the orbicularis muscle of the upper lip.



Calcium Hydroxyapatite (Ca-OH)

It is a synthetic and hydrophobic filler that shows as hyperechoic deposits that commonly produce a posterior acoustic shadowing artifact due to the presence of calcium [Figure 16] [(39)].

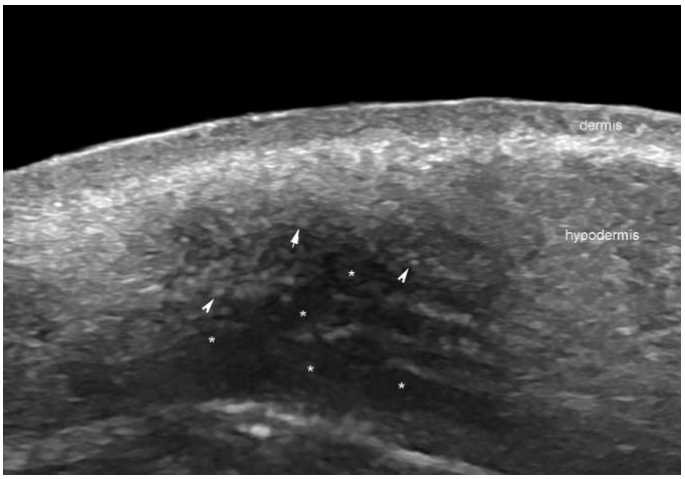
Figure 16 Calcium hydroxyapatite (transverse view). Hyperechoic deposits (*) that produce posterior acoustic shadowing artifact (as) in the hypodermis of the anterior abdominal wall.



Polycaprolactone (PCL)

It is a mix of synthetic and hydrophilic components. Recent injections appear as hypoechoic deposits that contain multiple hyperechoic dots that produce a mini-comet tail artifact. The hydrophilic component tends to decrease in size over time, usually after a year, and the synthetic hyperechoic dots remain in the tissues [Figure 17] [(50)].

Figure 17 Polycaprolactone (transverse view). Hypodermal deposits in the left perioral region with a hypoechoic matrix (*) that corresponds to the hydrophilic part and multiple hyperechoic spots that present a mini-comet tail artifact (arrowheads) and represent the synthetic part with microspheres.



Complications of Fillers

For academic purposes, these can be divided into immediate (first 24 hours after the injection), mediate (< 2 months after injection) or delayed (≥ 2 months after injection) [(44)]. Immediate complications are severe but fortunately very rare. Most of these complications are derived from technical issues and imply the vascular injection or embolization of fillers. They are more commonly seen in the injections around the glabellar or nasal regions and can produce blindness or brain infarcts. Additionally, sites with epidermal necrosis can be observed [(42)]. Knowledge of the vascular anatomy, color Doppler ultrasound and spectral curve analysis of the facial vessels is a must in these complications. Additionally, if needed, ultrasound can guide the percutaneous injections of hyaluronidase (i.e., an enzyme that break down the hyaluronic acid) [(51, 52)].

Mediate complications are commonly related to the type or amount of filler; however, it may also be an autoimmune reaction to the filler. These can cause erythema, swellings, bumps or palpable nodules that on ultrasound commonly present as signs of dermal and hypodermal edema or inflammation [(39)].

Delayed complications are mostly related to an autoimmune response of the host to the filler. On ultrasound, they show variable degrees of edema, lymphedema, acute inflammation, panniculitis, collections, fistulous tracts, encapsulating chronic inflammation and granulomas [(48)].

The mix of different types of fillers usually has a higher rate of adverse reactions. An example of this is the mix of pre-existent silicone oil with hyaluronic acid. A limitation of ultrasound is that it can not unveil the exact date of injections of the fillers. To date, this capability is not available in other imaging techniques, but this question is often asked in medico-legal consultations or trials. Importantly, ultrasound can significantly support the diagnosis and management of these complications [(44)].

Non-Fillers Procedures

The objectives of these procedures are to decrease the amount of fatty hypodermal tissue, also called lipolysis, and increase the production of collagen, also named neo-collagenesis. There is an increasing number of aesthetic procedures such as platelet-rich plasma, mesotherapy (i.e., injection of lipolytic agents), cryolipolysis (i.e., cold for generating lipolysis), radiofrequency (i.e., heat for producing lipolysis) [(39)].

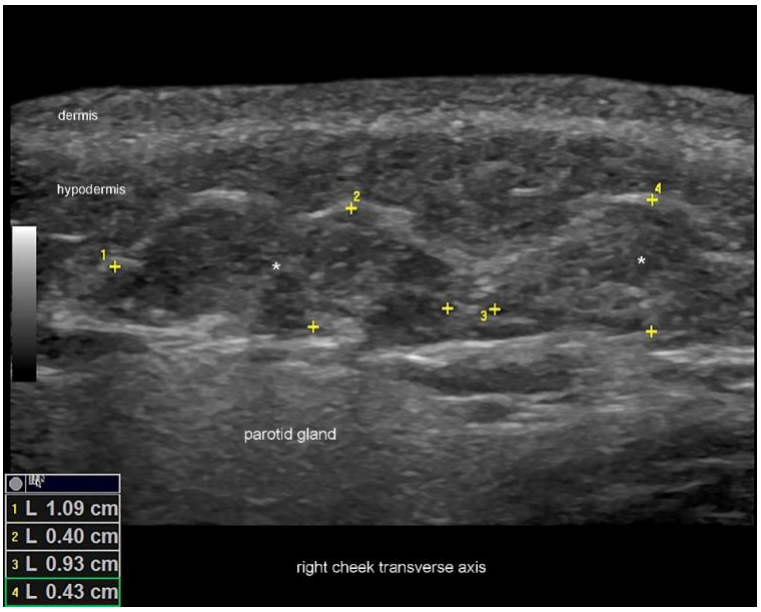
In most of these cases, the ultrasound examination will show variable degrees of edema and inflammation in the dermis and hypodermis according to the intensity and date of the procedure. Therefore, decreased echogenicity of the dermis and increased echogenicity of the hypodermis are common findings. On color Doppler, there are variable degrees of hypervascularity according to the level of inflammation, usually with low flow arterial and venous vessels. In some cases, areas with reduced or absent hypodermal fat can be detected, generally with some patchy-type of distribution and secondary to scarring. After platelet-rich plasma, anechoic sero-hematic fluid collections can also be identified [(49)].

Fat Grafting

Also called lipotransfer or lipofilling, this procedure usually implies the autologous extraction and injection of fat. Commonly, it is used for filling wrinkles or scars, but it has also been reported among the treatments for radiodermatitis, which is an adverse cutaneous reaction to radiotherapy [(29)]. On ultrasound, these fatty implants present as round or oval shaped

hypoechoic deposits that resemble the appearance of lipomas; however, in contrast to lipomas, these fat grafts do not follow the axis of the skin layers and sometimes show a disorganized distribution. They are commonly injected in the hypodermis; nevertheless, they can also be located intramuscularly such as in the orbicularis muscles of lips or eyelids or the gluteal muscles [Figure 18] [(53, 54)].

Figure 18 Fat grafts (transverse view). Two well-defined hypoechoic hypodermal nodules (*) that measure 1.09 x 0.4 cm and 0.9 x 0.43 cm respectively, and located on top of the right parotid gland.



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