High-resolution ultrasound imaging of cutaneous lesions

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Abstract

High-resolution variable frequency ultrasound imaging is increasingly being used in the noninvasive evaluation of various cutaneous diseases. It plays a complimentary role to physical examination in the assessment of cutaneous lesions. It is the only imaging modality useful in the evaluation of superficial cutaneous lesions that are too small to be evaluated on computed tomography (CT) or magnetic resonance imaging (MRI) and is helpful in reducing invasive procedures like biopsies and fine needle aspirations.

In this article, we seek to describe the relevance and basic principles of cutaneous ultrasound, imaging findings of normal skin, current applications of high-resolution ultrasound in the diagnosis and management of various dermatological conditions, along with the features of some commonly encountered lesions.

Key words: Color Doppler; dermatology; high-resolution ultrasound; skin

Introduction

Ultrasonic imaging has been used in the field of dermatology for nearly 30 years.[1] In 1979, Alexander and Miller first introduced ultrasonography (USG) as a noninvasive technique to measure normal skin thickness, and in the 1980s and 1990s, high-resolution ultrasonography (HRUS) was used for noninvasive assessment of skin nodules and cutaneous diseases.[2-4] The diagnosis of most skin diseases, both focal and diffuse, has been mainly relied upon physical examination findings.[5] Studies show that high frequency ultrasonography (HFUS) is superior to clinical examination alone by providing valuable information in the detection and accurate measurement of many clinical and subclinical cutaneous lesions.[6] The requirements for the noninvasive ultrasonic investigations of human skin from the dermatologist point of view were defined as it is expected to determine the size, contour, structure, and penetration depth of skin lesions.[7] The procedure involving USG is a noninvasive method allowing “in vivo” and “in real time” histologic assessment of the cutaneous structure as well as its specific conditions.[8] In the evaluation of cutaneous lesions, HRUS with color Doppler is useful as a safe, noninvasive, economical, and repeatable diagnostic procedure that can reduce and replace invasive procedures like fine needle aspirations and biopsies.[9]

Methods

References for this review were obtained from Medline, PubMed, Scopus, and EMcare databases.

Instrumentation

The HRUS for cutaneous imaging in radiology department generally uses variable frequency transducers (5-20 MHz) that are able to focus on different tissue layers by modifying the applied frequency according to the depth of the tissue imaged. This enables “real time” visualization of the skin layers, underlying musculo-tendinous, cartilaginous, and bony structures, along with vasculature and perfusion patterns at the same resolution.[10] The selection of the probe frequency depends mainly on the size, site, and surface of the lesions. Lower frequencies (7.5-13 MHz) depict flat and regular surfaces effectively and provide a wider field
of surface vision, while higher frequencies (10-20 MHz) provide excellent study of superficial structures and irregular surfaces.[9] The examination should be started with lower frequencies and continued through higher frequencies till the lesion’s structure and characteristics have been adequately imaged. The frequencies of USG and corresponding tissue visualization are given in Table 1.[1]

Examination protocol

The evaluation of cutaneous lesions in radiology department is generally carried out with linear array high-frequency transducers (operating bandwidth of 6-18 MHz) with standardized scanner’s settings (overall gain, time gain compensation, Doppler gain, power output). Color Doppler and Power Doppler are used to assess the vascularity of the lesions. A copious amount of gel is used over the surface of the lesions and any hair present is displaced with gel towards the lesion margins to minimize artifacts. Compression is avoided in superficial lesions because this may result in a false thinning or superficial nodules might move outside the field of view.[9] The mirror image or contralateral unaffected skin should be used as a control for skin thickness in inflammatory skin diseases. The HRUS examination of each lesion should consist of: (a) a morphologic study analyzing the structural sonographic pattern and margins; (b) the measurement of the largest transverse diameter and thickness; (c) Color Doppler USG for intralesional and perilesional vessels and, if possible, spectral analysis is obtained; and (d) in cases suspicious for malignancy, the surrounding areas are scanned for locoregional metastasis.

Indications

USG has been used in the evaluation of benign and malignant neoplasms, inflammatory diseases, infectious diseases, and in the forum of cosmetic dermatology. The current indications for HRUS in dermatology are as follows:[1,5,8-11,12]

1. Measurement of thickness, invasion depth, and assessment of the borders of skin tumors, and follow-up after surgery, cryotherapy, and laser treatment (e.g. malignant melanoma, basal cell carcinoma, hemangioma, fibroma, seborrheic wart)
2. Monitoring the course and therapeutic efficacy of the treatment of diseases with skin sclerosis (e.g. morphea, systemic scleroderma, scleroderma-like diseases), edematous (e.g. lipodermatosclerosis) and chronic inflammatory dermatoses (e.g. psoriasis)
3. Monitoring the effects of topical and systemic drugs on the skin (e.g. corticosteroids, estradiol)
4. Evaluation of allergic dermatitis, nodular erythema, dermatomyositis, sarcoidosis, lymphedema of the limbs, wound healing, scars and follow-up of localized burn lesions
5. Evaluation of exogenous components like foreign bodies and cosmetic fillers in the skin
6. Evaluation of nail involvement in systemic diseases and nail bed lesions like glomus tumors, nail bed cysts, subungual exostosis.

Anatomy

In vivo, normal skin is made of three layers: The epidermis (thickness 0.06-0.6 mm) on the most external surface; the underlying dermis (thickness 1-4 mm) consisting of connective tissue, nerves, blood, and lymphatic vessels, glands, mast cells, fibroblasts, histiocytes, etc.; and the subcutaneous tissues (thickness 5-20 mm), mainly made of adipose cells providing a cushion between the underlying bone and the dermo-epidermal layers.[5]

B-scans provide images that resemble anatomic cross sections of scanned tissues.[13] HRUS of the normal skin shows a well-defined hyperechoic band known as epidermal “entry echo” at the interface between the transducer and the skin. Underneath, the dermis is seen as a hyperechoic layer with small hypoechoic areas, corresponding to hair follicles, vessels, and sebaceous glands. The next layer, subcutaneous tissue, is hypoechoic with hyperechoic connective tissue septa separating the adipose lobules. More deeply, the superficial fascia covering the muscular tissues can be seen as a hyperechoic regular line [Figure 1A and B].[14-15] The nail unit structure on HRUS shows superficial bilaminar hyperechoic parallel lines representing dorsal and ventral plates and underlying hypoechoic nail bed [Figure 2A and B].[16]

Skin tumors

On HRUS, majority of the skin lesions appear as hypoechoic cutaneous or subcutaneous thickening.[6] The biological nature of tumors based on vascularity and density, reflecting differences in keratin, collagen, and water content of tissues, may affect the extent to which high-frequency sound waves are transmitted through them.[1,16,17] Skin tumors present as focal hypoechoic areas within the hyperechoic epidermis and the dermis. Color and Power Doppler studies help to identify vascularity in the lesions. Presence of abnormal intra- or peritumoral low-resistance pulsatile flow signals suggests the malignant nature of the cutaneous lesion.[11] Previous studies have shown that the vascular density in tumor identified by color Doppler directly correlates with its

Table 1: Frequency of ultrasound and corresponding tissue visualization

<table>
<thead>
<tr>
<th>Frequency of ultrasound (MHz)</th>
<th>Approximate depth of penetration (cm)</th>
<th>Visualization</th>
</tr>
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<tbody>
<tr>
<td>7.5</td>
<td>&gt;4.0</td>
<td>Subcutis and lymph nodes</td>
</tr>
<tr>
<td>13.5-50</td>
<td>3.0-0.3</td>
<td>Epidermis and dermis</td>
</tr>
<tr>
<td>20</td>
<td>0.6-0.7</td>
<td>Epidermis and dermis</td>
</tr>
<tr>
<td>50-100</td>
<td>0.3-0.015</td>
<td>Epidermis only</td>
</tr>
</tbody>
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metastatic potential, and hence, assessment of tumor perfusion by Color Doppler is very important.\textsuperscript{[18,19]} USG differentiation of the various histological types of skin tumors, either benign or malignant, is not at present feasible, and only the depth, area, and demarcation from the adjacent structures can be defined, possibly affecting prognosis.\textsuperscript{[11,15,17]} Review of literature shows that HRUS has significant role in the detection and evaluation of benign and malignant dermatological conditions, and the sensitivity and specificity of various parameters evaluated in some previous studies are given in Table 2.\textsuperscript{[6,10,17-20-22]} Determination of tumor margins is very important in the surgical planning of cutaneous tumors to avoid incomplete excision and re-intervention, while prevention of functional and esthetic defects is of significant interest in tumors that commonly involve head and neck, face, and sun-exposed regions.\textsuperscript{[23]} USG may help in determining the best treatment approach by preoperative assessment of cutaneous neoplasms, usefully integrating clinical findings, and is also helpful in the follow-up of the patients after surgery, cryotherapy, or laser treatment.\textsuperscript{[11,20,24,25]}

**Benign dermatological conditions**

Seborrheic keratoses are epidermal in origin, well delimited, very superficial, as though laid on the skin, and may be misdiagnosed as melanoma. HRUS shows them just beneath the entry echo as hypoechoic lesions with dense echoes (horny pseudocysts), mostly avascular on Color Doppler [Figure 3A and B]. Harland et al., reported that high attenuation, prominent entry echo, and irregular surface were seen in seborrheic keratosis, which differentiated it from melanomas and other benign nevi, due to surface keratinization of these tumors which makes them reflective and irregular with shadowing.\textsuperscript{[17]}

Von Recklinghausen disease (neurofibromatosis) usually presents as multiple nodules localized in the epidermis. They are well-defined, hypoechoic, and avascular on USG [Figure 4A and B]. In case of neoplastic degeneration of a nodule, variations in the sonographic pattern with inhomogeneous structure and ill-defined margins are seen.\textsuperscript{[26]}

Nevi are polychromic maculopapular or slightly elevated plaque-like pigmented lesions with irregular contour. On USG, they often appear as very thin lesions not identifiable with probes of 10-13 MHz frequency.\textsuperscript{[26]} HRUS shows them as round-to-oval hypoechoic lesions with relatively well-defined borders, usually very thin in the case of junctional nevi and thicker in the case of dermal nevi [Figure 5A and B]. The nevic cells are located at the dermo-epidermal junction, and during malignant transformation, the transition from the radial growth phase to the vertical growth phase begins with progression in depth.\textsuperscript{[27,28]} USG is the optimal method for monitoring of congenital and dysplastic nevi which usually undergo malignant transformation.\textsuperscript{[20]} HRUS reveals the epidermal lesions, their regression areas, and their degree of dermal penetration during malignant transformation into melanomas, and also helps in the assessment of location and size for the excision with safety margin of suspicious lesions.\textsuperscript{[28]}

Pilonidal cysts commonly develop in intergluteal region from entrapped hair follicles, and chronic repetitive local trauma may play a role in etiology.\textsuperscript{[12]} They present as acute or chronic abscesses with intermittent purulent discharge or bleeding. USG shows them as irregular hypoechoic tracts in dermis and subcutaneous tissue with linear internal foci corresponding to hair fragments [Figure 6A and B]. HRUS helps in preventing postoperative recurrences by providing

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**Table 2: Significance of HRUS evaluation in cutaneous lesions**\textsuperscript{[6,10,17-20]}

<table>
<thead>
<tr>
<th>Previous studies</th>
<th>Feature evaluated</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harland et al. (2000)</td>
<td>Distinguishing melanoma from common benign pigmented skin lesions</td>
<td>100</td>
<td>79</td>
</tr>
<tr>
<td>Bessoud et al. (2003)</td>
<td>Distinction of melanoma from non-melanomatous lesions by HRUSG</td>
<td>100</td>
<td>32</td>
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<tr>
<td>Wortsman et al. (2010)</td>
<td>Comparison of USG diagnoses with clinical diagnoses</td>
<td>99</td>
<td>100</td>
</tr>
<tr>
<td>Music et al. (2010)</td>
<td>HRUS detection of primary melanoma &gt;1 mm</td>
<td>92</td>
<td>92</td>
</tr>
<tr>
<td>Chami et al. (2011)</td>
<td>Vascular ultrasound Doppler for malignancy</td>
<td>90-100</td>
<td>34-100</td>
</tr>
<tr>
<td></td>
<td>US contrast agents for diagnosis of malignant skin lesions</td>
<td>51-99</td>
<td>86-99</td>
</tr>
<tr>
<td>Mandava et al. (2012)</td>
<td>Predictive value of HRUS and color Doppler for malignancy in pigmented skin lesions</td>
<td>81</td>
<td>94</td>
</tr>
</tbody>
</table>

HRUS: High-resolution ultrasonography, USG: Ultrasonography
accurate details regarding the location, depth, extent, and branching of pilonidal sinus.[21,29] Preoperative USG helps the surgeon in planning the optimum approach to surgery, facilitating complete excision of sinus tract.[21,29]

Pilomatrixoma, also known as calcifying epithelioma of Malherbe or trichomatricoma, is a benign skin tumor arising from hair follicle matrix.[21,30] On HRUS, it is commonly seen in dermis and subcutaneous tissue as a hypoechoic lesion with hyperechoic center corresponding to calcification, giving a target appearance [Figure 7A].[12,21,30]

HRUS and Color Doppler can evaluate vascular lesions like hemangiomas and vascular malformations that are seen superficially in cutaneous layers as multiple arterial and venous vessels with arteriovenous shunts.[12] HRUS can also monitor the progression of these lesions with age (involvement in hemangiomas and growth in case of vascular malformations) and response to therapies like laser, surgery, or embolization [Figure 7B].[12]

Malignant tumors
Basal cell carcinoma (BCC) is the most common skin cancer, often located in head and neck regions and areas of skin subjected to chronic sun exposure. HRUS shows them as heterogeneous hypoechoic tumors with irregular contour and large, focally dense internal echoes, and Color Doppler shows internal vascularity [Figure 8A and B]. Uhara et al., have reported that majority of the BCCs showed hyperechoic spots on USG (corresponding to keratin nests on histology), which was not seen in any melanoma; therefore, this feature may be used to differentiate BCC from melanoma.[31] BCC has a high recurrence rate, and preoperative HRUS is helpful in reducing the rate of relapse by accurate determination of the area and margins of tumor for either surgical excision or nonsurgical treatment with radiotherapy or cryosurgery.[32] HRUS may also assist the detection of early recurrence, especially when surgical removal is incomplete or in cases treated with radiotherapy or cryosurgery.

Squamous cell carcinoma is the second most common...
cancer of the skin with a major tendency to local relapse and with frequent lymph nodal metastases. The tumor growth causes infiltration of the adjacent tissue and erosion of the underlying cartilages and bones. It is seen on USG as a lesion with marginal irregularities and inhomogeneous hypoechoic structure, and Doppler may show the presence of low-resistance pulsatile flow signals within or at the periphery of the tumor [Figure 9A and B]. In some cases of squamous cell carcinoma, the hyperkeratotic epidermis may lead to total reflection of the ultrasound waves, making the measurement of tumor thickness impossible. 

Malignant melanoma is a lethal but curable skin cancer and early detection is the basis for reducing the mortality rate. HRUS shows melanoma as a solid, homogeneously hypoechoic lesion with a thin “entry echo” and quite well-delimited contours [Figure 10A and B]. The histopathologically measured thickness (Breslow index) is the single most important prognostic factor in the management of malignant melanoma which can be measured accurately and noninvasively by using HRUS. Serrone et al. have reported that for melanomas of thickness greater than 0.75 mm, the correlation between sonographic thickness and histological thickness was significantly high. Intraläsional Color Doppler signal correlates with the Breslow index and patient survival. Lassau et al., reported that the tumor thickness indicated by Breslow index as well as the vascular density in tumor identified by Color Doppler were significantly and independently correlating with metastatic potential and dissemination in melanomas. Skin or subcutaneous metastases of melanoma appear as hypoechoic nodules on USG. They are described as “satellite” metastases when they are found within 2 cm of the primary tumor or its scar and “in-transit” metastases if they are more than 2 cm from the primary lesion but are not beyond the regional nodal basin. These satellite and in-transit metastases develop within dermal and subdermal lymphatics before reaching the regional lymph nodes, and studies have shown that HRUS is more sensitive and specific than palpation in the detection of these metastases. Catalano et al., in their study of lymph node metastasis in patients with cutaneous melanoma have concluded that HRUS can replace the complex and expensive sentinel lymph node biopsy procedure in the staging of patients with melanoma as cases with positive nodes on HRUS can directly undergo radical surgery with lymphadenectomy. USG is also used during patient follow-up, having been proven more accurate than physical examination in detecting locoregional relapses.

Cutaneous metastases involving the skin and subcutaneous tissue are seen in 0.5–9% of all malignancies and they commonly present as nodules on the trunk, abdomen, or scalp. Skin involvement typically occurs near the site of the primary tumor, and the most common primary lesions that metastasize to the skin are breast carcinoma, malignant melanoma, and lung cancer. Metastases on HRUS appear as well-defined, homogeneous, hypoechoic, subcutaneous nodules and on Color Doppler may show high vascularity with multiple peripheral and internal vessels 

Cutaneous lymphoma can present itself in a diffuse or a nodular form. In the diffuse form, the sonographic aspect is generally that of a hyperechoic area with poorly defined margins, with an increase of thickness of the dermis and the subcutaneous layers, and the nodular lymphoma is seen as a hypoechoic coalescing solid nodule with well-defined margins. Color Doppler USG may be useful by showing, in the florid phase of the disease, vessels branching regularly, perpendicular to the cutaneous layer.

**Diffuse cutaneous diseases**

HFUS is also useful in the evaluation of diffuse cutaneous diseases. HFUS systems are suited to follow inflammatory skin diseases over time, for example, dermatitis, hypersensitivity reactions, and psoriasis.

Psoriasis is seen in 1-2% of the population of any age-group and presents as thickening of the epidermis with the formation of large scales on the surface of the skin (hyperkeratosis). The thickness of the skin in psoriatic plaques is increased on an average by 55% in comparison to normal skin, and HFUS can provide a valid morphologic representation of the psoriatic cutaneous lesions. The epidermis is thickened, hyperechoic as the superficial scales produce a hyper-reflective epidermal band, and a hypoechoic band of variable thickness may be

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**Figure 9:** (A) Invasive squamous cell carcinoma arising from a neglected, chronic nonhealing ulcer. (B) HRUS shows irregular, hypoechoic, highly vascular, heterogeneous lesion invading the dermis and subcutaneous layers, with loss of normal cutaneous architecture

**Figure 10:** (A) Malignant melanoma seen as an elevated pigmented lesion with irregular shape and borders. (B) HRUS shows well-defined, solid, homogeneously hypoechoic lesion in the dermis with multiple vessels arising from the base, suggestive of high vascular density
seen in dermis in the acute phase [Figure 13A and B]. USG and Power Doppler may be a useful and feasible method for short-term monitoring of disease activity in psoriatic plaques. Scleroderma is a sclerosis of the skin of unknown etiology that can manifest itself in localized (morphea) or generalized forms. It is characterized by thickening of the dermis, and subcutaneous layers with the formation of gross connecting bands, in advanced stages. HRUS of sclerotic skin, when compared to normal skin, shows wide entry echo, and hyperechoic and thicker dermis and subcutaneous layers due to the accumulation of collagen fibers in the affected areas [Figure 14A and B]. USG findings in scleroderma vary depending on the disease activity. In scleroderma patients, HRUS is useful to identify the edematous phase, detect skin involvement early if the diagnosis is uncertain, and assess the severity of overall skin involvement and response to treatment.

Contact dermatitis is an inflammatory skin reaction (dermatitis) resulting from exposure of skin to allergens (allergic contact dermatitis) or irritants (irritant contact dermatitis). HRUS of the affected areas in these cases shows significantly increased thickness of dermis with inhomogeneous echotexture and gross foci of hypoechoic edema [Figure 15A and B].

In dermal edema, echogenicity of dermis is decreased, but there are marked differences in the distribution of the low echogenic region in various diseases. In lipodermatosclerosis, a decrease of echogenicity is noted mainly in the subepidermal region, whereas in lymphedema and allergy reactions, edema spans the entire dermis [Figure 16A and B] and in cardiac insufficiency, echogenicity decreases in the lower portion of the dermis adjacent to the subcutaneous tissue.

Exogenous components
Foreign bodies can be found in skin and subcutaneous tissue in the setting of post-trauma or post-therapeutic procedures. They can be fragments of wood, metal, glass, suture materials, subcutaneous implantable devices, orthopedic implants, tissue expanders used in plastic and reconstructive surgery, etc. The USG appearance of foreign body is typical and consists of a small, strong reflector surrounded by hypoechoic tissue [Figure 17A and B]. The combination of this appearance and a positive clinical history is virtually pathognomonic of the diagnosis. HRUS is also useful in the detection of complications of intradermal and subcutaneous foreign bodies like abscesses, draining sinus tracts, apart from guiding the removal of foreign bodies. Cosmetic fillers or dermal fillers are biologically inert nanoparticles (1-100 nm in size) that are injected to fill wrinkles or cutaneous defects and are being increasingly used world over in cosmetic procedures. Fillers can be biodegradable and temporary like hyaluronic acid (most commonly used) or permanent nonreabsorbable molecules like silicone, polymethylmethacrylate, and calcium hydroxyapatite. On HRUS, hyaluronic acid and pure silicone are anechoic while polymethylmethacrylate, silicone oil, and calcium hydroxyapatite appear hyperechoic.
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HRUS is also useful in the evaluation of complications of filler therapy like swellings, palpable nodules, hyperpigmentation, and fistulous tracts.[51]

Interventions
HRUS is of significant value in the management of nonpalpable or slightly palpable cutaneous tumors or lymph nodes suspicious for malignant involvement. It can be used to guide percutaneous procedures like fine needle aspirations and biopsies for cytology and histology sampling and also for surgical excision of lesions using a dermographic marker or a guidewire.[36]

Limitations
The limitation of USG is that in its current version, it cannot detect lesions that are epidermal only or that measure less than 0.1 mm in depth.[21] USG may overestimate the tumor thickness compared to the actual histological thickness in lesions with inflammatory peritumoral infiltration like melanomas and BCC, and also underestimate the thickness in ulcerated lesions.[10] Finally, hyperkeratotic squamous cell carcinomas may not be well visualized on HFUS.[8]

Future developments
Contrast-enhanced USG is a recent technique under evaluation using ultrasound contrast agents to increase the sensitivity of Doppler examination. It is useful in morphologic and functional assessment of lesions, providing quantitative perfusion parameters, which can be biomarkers for new antiangiogenic therapy monitoring.[6] In future, higher-frequency probes and newer USG techniques like tissue harmonic imaging, spatial compound imaging, panoramic views, and 3D reconstruction views may provide images with increased resolution and quality to the clinician and surgeon for better management of cutaneous lesions.[36] Ultrasound elastography is a noninvasive method in which stiffness or strain images of soft tissue are used to characterize tissue, and it is found that malignant tumors have significantly lower elasticity than benign lesions. Ultrasound elastography can help in noninvasive detection and characterization of malignant cutaneous tumors, while reducing unnecessary biopsies. Recent studies have also reported that ultrasound elastography has considerable clinical potential in the assessment of cutaneous pressure ulcers, lymphedema, and age-related changes in the skin.[52]

Conclusion
HFUS has multiple applications both in the clinical and research settings. An important goal of future studies is to distinguish between benign and malignant lesions. HRUS is a simple, reliable, relatively cost-effective, generally available, noninvasive method that can be used along with the physical examination for the assessment, diagnosis, and management of many cutaneous diseases.

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