REVIEW ARTICLE

Skin cancer: findings and role of high-resolution ultrasound

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Abstract
Currently available high-resolution transducers allow a detailed ultrasound (US) assessment of skin tumors. US complements clinical examination, dermoscopy, and biopsy in the initial differential diagnosis, surgical planning, locoregional staging, and follow-up of patients with skin malignancies. It is important for dermatologists, skin surgeons, and US operators to be aware of the US imaging findings and to recognize the clinical scenarios where imaging is indicated in the management of skin cancer. The purpose of this review article is to address the most common indications for US in skin oncology and to provide a comprehensive guide to the gray-scale and color-Doppler findings in cutaneous malignant tumors.

Keywords Skin ultrasound · Dermatology ultrasound · Skin tumors · Soft tissues · Melanoma

Abbreviations

CM	Cutaneous melanoma
BCC	Basal cell carcinoma
DFSP	Dermatofibrosarcoma protuberans
KS	Kaposi sarcoma
MCC	Merkel cell carcinoma
PCL	Primary cutaneous lymphoma
SCC	Squamous cell carcinoma
US	Ultrasound

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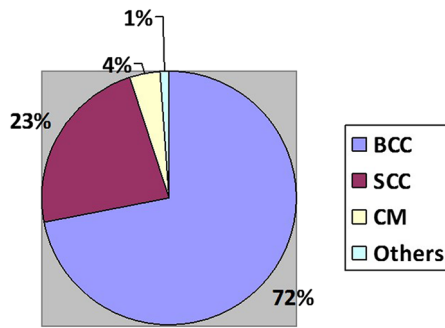   Santiago, Chile

Introduction

Skin tumors are by far the most frequent malignancies of the body. These tumors are classified according to their cells of origin (known or putative). These cells can be located in the epidermis, dermis or skin appendages. Malignant tumors arising from the epidermis include cutaneous melanoma (CM) and non-melanoma cancers, such as basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and Merkel cell carcinoma (MCC). Main malignancies developing from dermal components are atypical fibroxanthoma, dermatofibrosarcoma protuberans (DFSP), angiosarcoma, and Kaposi's sarcoma (KS). Malignant tumors of skin appendages include sebaceous carcinoma, eccrine porocarcinoma, and microcystic adnexal carcinoma. To all these histotypes, primary and secondary cutaneous lymphomas, as well as skin metastasis, must also be added. CM only represents the 4% of all skin cancers, but it is by far the most important one because of its lethality. BCC and SCC are grouped as epitheliomas and represent up to 95% of skin malignancies (BCC, 3/5 and SCC, 2/5) [1, 2] (Fig. 1). The remaining skin tumors are uncommon but some of them can have a very aggressive behavior.

Although clinicians primarily rely on their eyes, a number of instruments have been developed to improve skin tumors assessment. These include digital photography, dermoscopy, reflectance confocal microscopy, optical coherence tomography, and high-frequency ultrasound (US). US is being employed with increasing frequency in

Fig. 1 Approximate prevalence of skin cancers. *BCC* basal cell carcinoma, *SCC* squamous cell carcinoma, *CM* cutaneous melanoma

the assessment of skin disorders [3–11]. In this article, we review the scanning methodology, the B-mode and Doppler findings, and the practical role of US in patients with skin malignancies.

Scanning methodology

High frequency (≥ 15 MHz), broadband, linear transducers are necessary [3]. Transmission frequency, depth, and time-gain compensation curve are regulated according to the position of the lesion (dermis, superficial hypodermis, deep hypodermis) [4–7]. Beam focus is placed at level of or immediately below the lesion. Gain is regulated to maximize image contrast. Volume acquisition of multiplanar and 3D images can be helpful [3, 8].

Color/power-Doppler mode is set to detect slow flows, which means high Doppler frequency, low pulse repetition frequency, low wall filter, and color gain immediately below the noise threshold [3, 7, 8]. Focus is placed right below the lesion. Spectral analysis of intratumor vessels may be obtained, recording the peak velocity and the resistive index.

An abundant amount of gel is placed on the lesion. Gel pad spacers may also be employed, although they may compress the thin vessels. The hand pressure applied on the probe is minimized (both for B-mode and Doppler mode) and the little finger can be put below the probe footprint to improve the stability. Lesions are imaged according to longitudinal and transverse planes. Both the maximal width and the vertical thickness at the deepest point of the lesion is measured (electronic zoom may be useful).

Basal cell carcinoma

BCC occurs in the elderly on sun-exposed areas, particularly the face [12]. While BCC is rarely metastatic, large or aggressive, tumors can infiltrate critical anatomic structures [13]. It classically presents as a pearlescent nodule or ulcer.

Some lesions may appear as poorly defined plaques or areas of skin induration. Nodular variant, the most common, consists of well-circumscribed nodules of basaloid cells with characteristic peripheral palisading, retraction artifact, and stromal mucin. More infiltrative variants include the micronodular pattern and the morpheic pattern. These infiltrative histologic variants generally require wider surgical margins or Mohs surgery, in contrast with non-infiltrative variants, which may be treated with standard surgical excision [13]. Up to 7% of BCCs are pigmented, mimicking melanoma [12]. For BCC, as well as for SCC and adnexal carcinomas, but not MCC, the current staging system consider T1 for lesions with a larger diameter up to 20 mm, T2 for a 20–39 mm diameter, and T3 for a diameter 40 mm or above [14]. Tumors thicker than 6 mm or tumors invading below the subcutaneous layer are automatically classified as T3, whatever their diameter is [14].

BCC lesions appear as well-defined, oval or slightly irregular, hypoechoic lesions that usually present hyperechoic spots [12, 15, 16]. A high density of hyperechoic spots, representing nests and not calcifications, has been reported to be more frequent in high-risk of recurrence subtypes such as micronodular or morpheaform variants [17]. Low flow arterial and venous vessels are detected within or at the bottom of the lesion. The appearance of tortuous vessels should suggest other tumors [7]. At elastography BCC is usually rather stiff. However, infiltrative BCCs have increased marginal stiffness in comparison with non-infiltrative BCCs (88% vs. 19%) and this finding may help predicting before treating the presence of an infiltrating variant [13] (Fig. 2 and 3).

Squamous cell carcinoma

SCC arises on sun-exposed sites of fair-skinned individuals. The head, neck, and dorsal hands are commonly affected. SCC may be associated with local invasiveness, recurrence, and lymph nodes metastasis. US imaging of SCC (primary tumor/surgical scar and regional lymph nodes) is indicated for patients with recurrent tumors, tumors > 2 cm in diameter or > 2 mm in depth, poorly differentiated histology, perineural invasion, lymphovascular invasion, and specific anatomic site (ears, lips, anogenital regions) [2, 18, 19]. Some SCCs present as red patches or plaques, others as hyperkeratotic or ulcerated lesions. The classical form of SCC comprises sheets and nests of relatively large atypical epithelial cells with pleomorphic nuclei and variable numbers of mitotic figures. Poorly differentiated lesions show a greater degree of cytological atypia and are scarcely keratinized. Deep keratinization is present instead in better differentiated tumors. Spindle cell (sarcomatoid) variant also occurs.

At US imaging SCC presents as a heterogeneously hypoechoic lesion with irregular borders, lack of hyperechoic

Fig. 2 Basal cell carcinoma of the nasion. Patient photograph (**a**). Ultrasound scan with tumor thickness measurement (**b**). The lesion is hypoechoic and relatively homogeneous, with some hyperechoic spots. It is adherent to the bony cortex
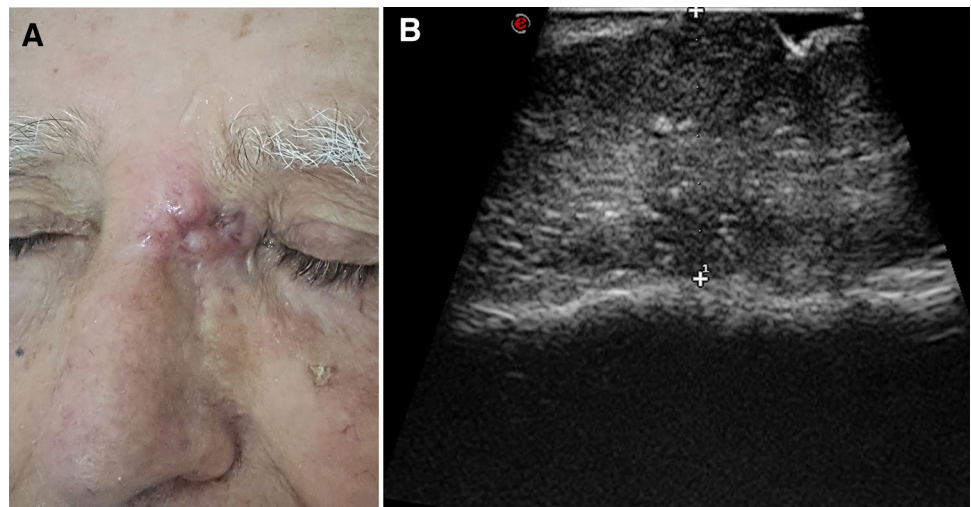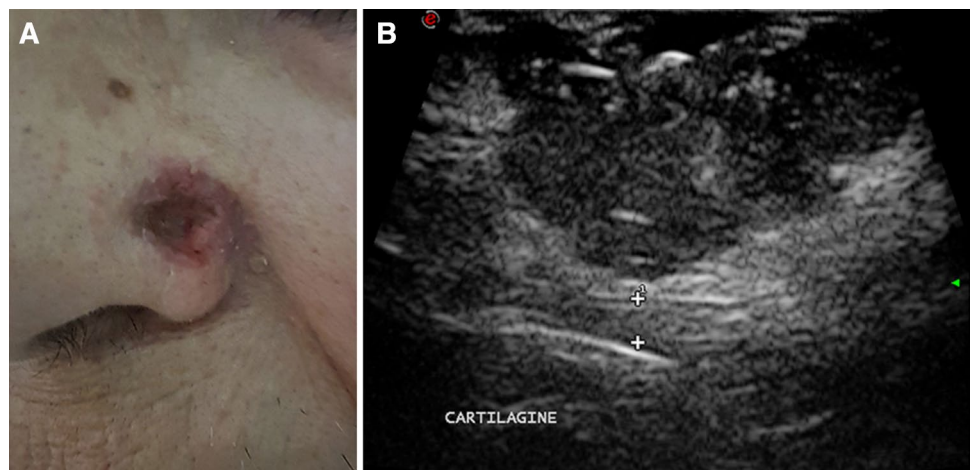

Fig. 3 Ulcerated basal cell carcinoma of the nose ala. Patient photograph (**a**). Ultrasound scan (**b**). The lesion is hypoechoic and relatively homogeneous, with some hyperechoic spots. The tumor does not infiltrate the cartilage (calipers)

spots, and tend to involve the deeper layers [16]. The low-flow vascular pattern is increased diffusely throughout the entire lesion but particularly at the periphery [7] (Fig. 2 and 4).

Cutaneous melanoma

CM typically occurs in pale-skinned Caucasians. Rare in childhood, this tumor is predominantly seen in the middle aged and elderly. However, the worldwide incidence of CM is rising, particularly among younger individuals. About 87,000 new cases/year are diagnosed in the USA, with more than 9000 people dying of invasive CM. Overall 5-year survival is 60%, although behavior is variable. Head, back, and lower extremities (particularly in women) are the most common sites [10]. CM is a malignancy of skin melanocytes and fall into four basic categories: superficial spreading CM, lentigo maligna, acral lentiginous

CM, and nodular CM. CM presents as pigmented macules or nodules, that can show irregular borders and ulceration. Amelanotic CM account for about 5% of cases. CMs are asymmetrical and poorly circumscribed lesions with architectural disturbance and usually marked cytological atypia. Melanoma cells can be categorized in epithelioid and spindle cells. The current standard for regional lymph nodes staging is represented by the sentinel lymph-node excision biopsy procedure. However, it is important to indicate if histologically involved lymph nodes were clinically occult or detectable [14].

At US melanoma appears as an oval/fusiform, well-defined, homogeneous, and echo-poor lesion [20, 21]. The hyperechoic epidermis line is seen above the tumor, except that for ulcerated CMs. Acoustic transmission is frequently increased. Correlation of the sonographic and histologic thickness has been reported as excellent. However, peritumoral inflammatory infiltrates may be present, falsely increasing the tumor depth measurement. Satellite

Fig. 4 Ear scapha squamous cell carcinoma. Patient photograph (**a**). Ultrasound scan (**b**). The 7-mm thick lesion (calipers) is hypoechoic and relatively homogeneous. There is no infiltration of the cartilage. Color-Doppler scan (**c**). Discrete vascularization, with vessels mostly arranged vertically, starting from two deep vascular poles
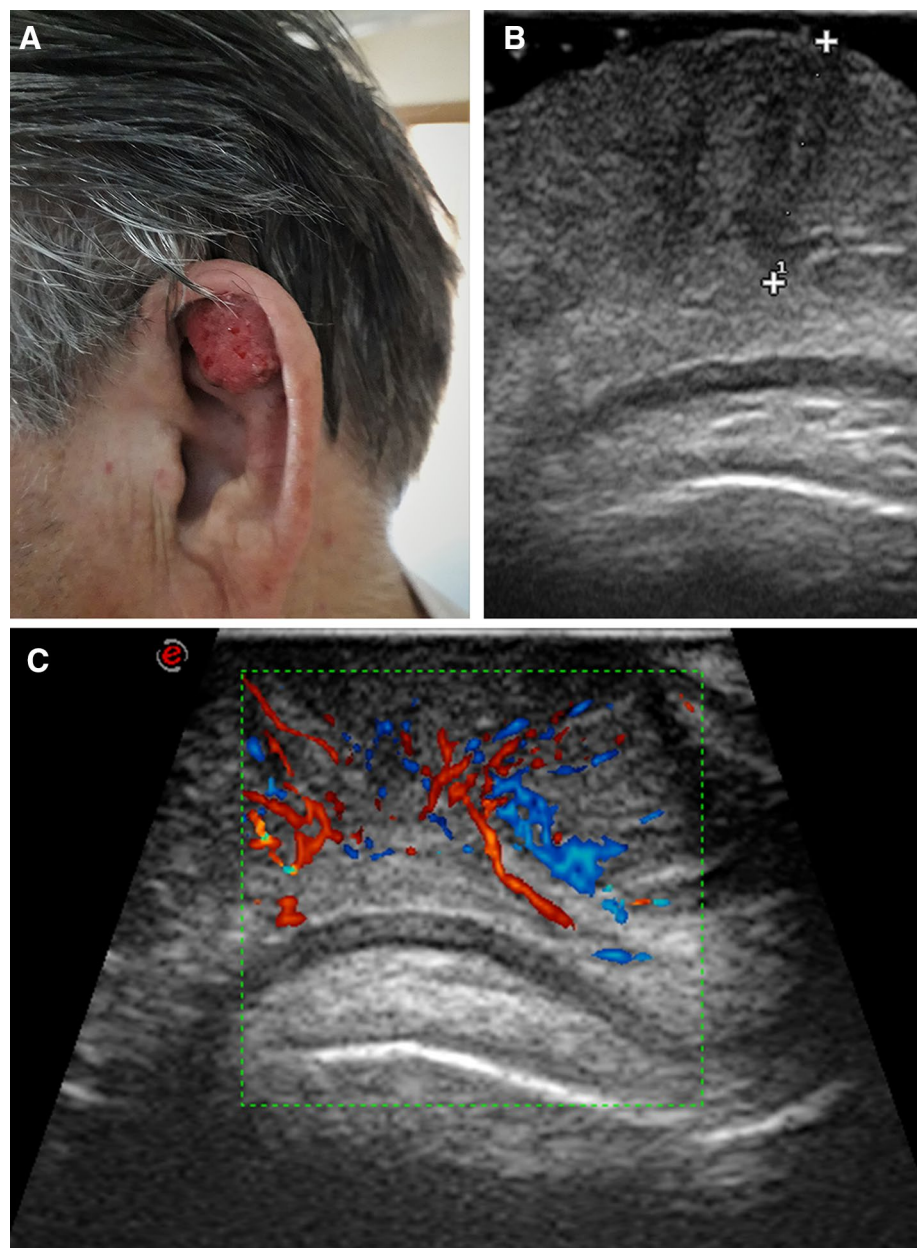
and in-transit nodules appear as markedly hypoechoic, relatively homogeneous and well demarcate, within the dermis or hypodermis [20–22].

Differently from nevi, CMs are hypervascular, although flow signal can be hard or impossible to detect in very thin lesions. CM tend to show hypervascularity due to their angiogenic capability [20, 21]. The degree of tumoral vascularization correlates with the risk of locoregional of the lymph nodes and with patient prognosis (Fig. 5).

Merkel cell carcinoma

MCC is a relatively rare but increasing neuroendocrine tumor. Mean age at diagnosis is around 70 years, with a moderate prevalence of males. Risk factors include ultraviolet exposure and immunosuppression. The 5-year survival rate is 64% for local disease, 39% for regional nodal involvement, and 18% for distant metastatic disease. Most cases arise in the face, neck, upper extremities, and buttocks [23]. Sentinel lymph-node biopsy is included specifically in the MCC current pN staging system [14].

MCC typically presents as an asymptomatic, rapidly expanding, firm-elastic, pink–purple, dome-shaped nodule.

Fig. 5 Sole melanoma. Patient photograph (**a**). Ultrasound scan (**b**). The 3-mm thick tumor is hypoechoic and homogeneous. Directional power-Doppler scan (**c**). Very intense tumor vascularization
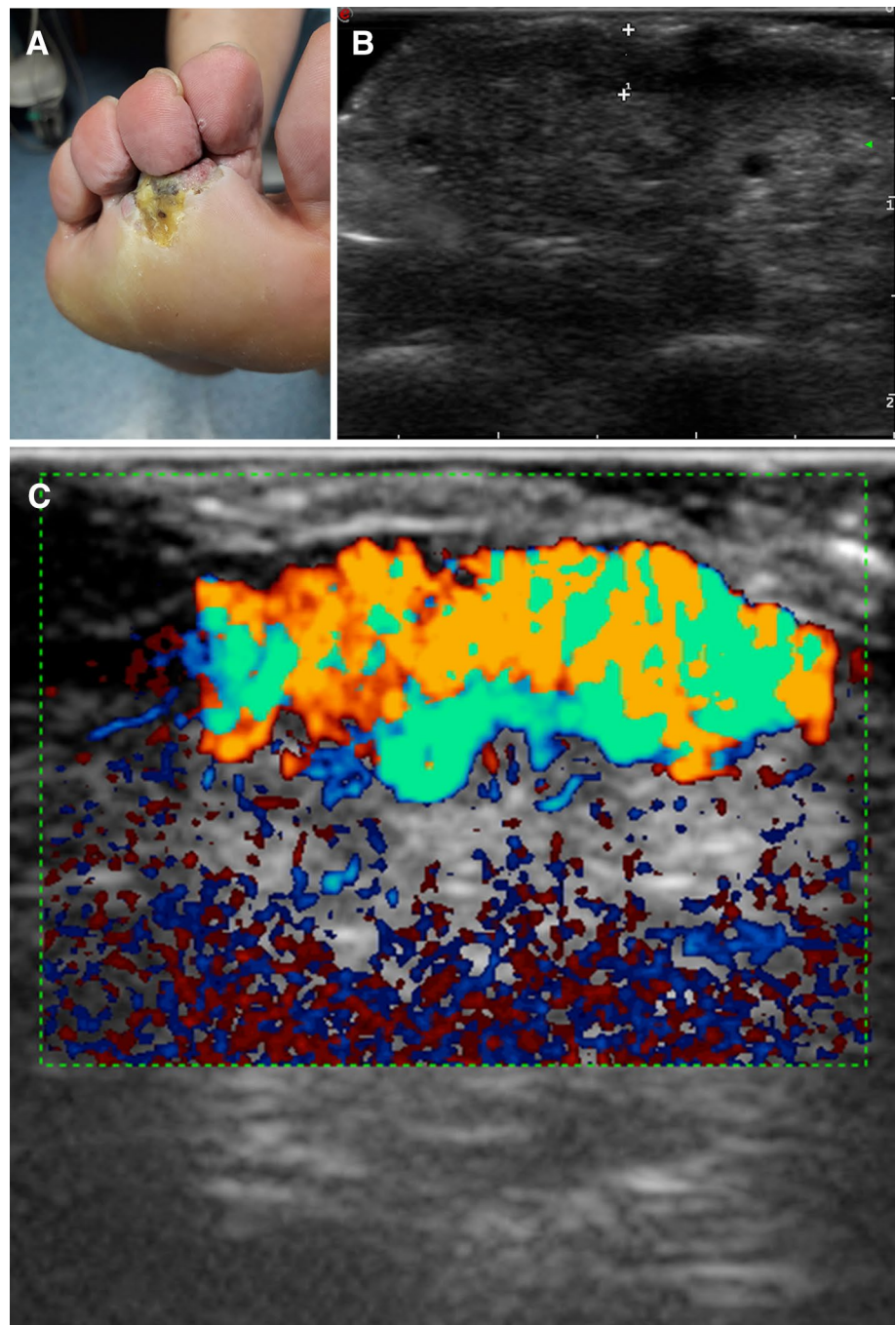
It is a localized, ill-defined dermal proliferation of uniform, small blue cells, arranged in strands and nests.

MCC lesions are located in the dermis and may be oval or dome-shaped. They are hypoechoic, with variable degrees of heterogeneity. Borders are usually ill-defined. Calcifications are absent. A slight dorsal enhancement may be seen, as well as a thickening of the overlying epidermis [23, 24]. Vascularization is typically rich and shows vessels with a chaotic distribution, although a kind of vertical arrangement can be seen. Arterial flows show a mean systolic velocity of 11 cm/s and a mean resistive index of 0.57 [23, 24].

Dermatofibrosarcoma protuberans

DFSP is a rare monoclonal cutaneous fibroblastic sarcoma. It typically arises on the trunk or extremities in the fourth decade and is more common in males. It may be locally aggressive and recurring. The deeply infiltrating growth

of DFSP can make tumoral extent challenging to predict based on a clinical examination alone [18]. DSFP starts as a firm dusky plaque and slowly grows into a nodular or multinodular pattern. It is composed of bland monomorphic spindle cells with elongated nuclei, arranged in a storiform pattern, with poorly defined infiltrative tumor margins. About 10% of cases develop a small fibrosarcomatous component, with an associated risk of metastasis. DFSP lesions are located in the subcutaneous fat layer, abutting against the skin, and have a broad base.

US demonstrates an ill-defined hypoechoic pattern in the surface and hyperechogenicity in the deep part. This tumor commonly invades fascial or muscular layers [7, 25]. Hypercellular DSFP are rather homogeneous while tumors with large fibrous tissue components show a mixed appearance with echoic areas. The margin can be focally lobulated or may show irregular pseudopodia-like projections to the fascial or muscle layers. Flow signals can be detected throughout the entire tumor or only at its peripheral portions [25] (Fig. 6).

Kaposi sarcoma

KS is a low-grade mesenchymal tumor involving the blood and lymphatic vessels. It is associated with HIV infection but may also occur endemically (Jewish and Mediterranean African populations) and in transplant recipients. KS lesions are usually identified in the lower leg, except in the case of AIDS-related KS where the lesions mainly affect the face and trunk [26]. KS presents as asymptomatic purple patches, later developing into nodules or plaques. Histology demonstrates a proliferation of endothelial-lined slit-like vascular channels and spindle cells.

KS lesions appear as solid and hypoechoic lesions, located in the dermis but sometimes extending to the subcutaneous [27]. Nodules are usually rather homogeneous, with well-defined, frequently lobulated, borders. Plaques are less homogeneous, showing irregular edges and acicular morphology. Infiltration of deeper structures is possible [26]. The intralesional vascularization is more marked at the lower pole in nodules and poor or absent vascularization in plaques. AIDS-KS lesions may show a greater vascularization than classic KS ones [26] (Fig. 7).

Primary cutaneous lymphoma

Primary cutaneous lymphoma (PCL) is rare and must be distinguished from secondary skin involvement by systemic lymphoma. Mycosis fungoides is a neoplastic proliferation of T-cells, which accounts for approximately half of PCLs.
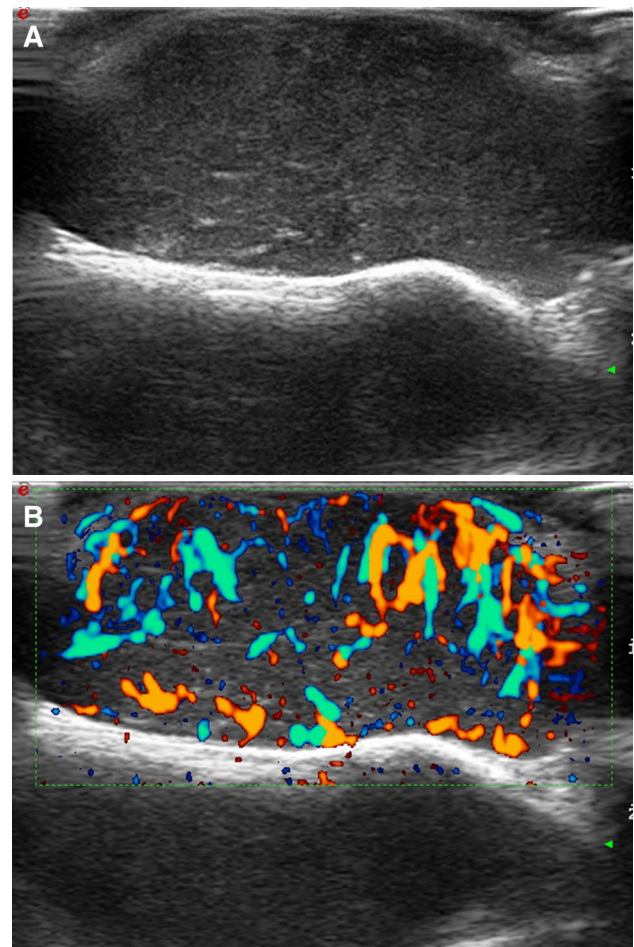

Fig. 6 Dermatofibrosarcoma protuberans of the head (frontal region), local recurrence. Ultrasound scan (**a**). Thick, homogeneous, and ill-defined lesion, adherent to the bone surface. Directional power-Doppler scan (**b**). Strong, irregular vascularization at power-Doppler imaging

Patch, plaque and tumor stages of disease are recognized. Mycosis fungoides shows atypical, cerebriform lymphocytes with a surrounding halo infiltrating the epidermis, arranged individually or in small aggregates. Cutaneous B cell lymphoma comprises a heterogeneous group of tumors, often presenting as infiltrated plaques and irregular infiltration of lymphoma cells between dermal collagen bundles.

Lymphoma cell varieties have mixed echo patterns. The echo poor areas may be mistaken for fluid collections or cysts [7, 28, 29]. Although rarely, a subcutaneous panniculitis-like pattern can also be seen, particularly in T-lymphoma. This pattern may sometime mimic cellulitis (panniculitis) [28]. Vascularity of cutaneous lymphomas is variable, ranging from the less common hypovascular pattern to the more common hypervascular one [28, 29]. A vertical disposition of the vessels may be seen. The resistive index is relatively low.

Fig. 7 Thigh metastases from Kaposi sarcoma. Patient photograph (**a**). Ultrasound scans, taken at 13.5 MHz (**b**) and at 22 MHz (**c**). The latter image shows the two hypodermis, hypoechoic nodules with a superior detail compared to the former
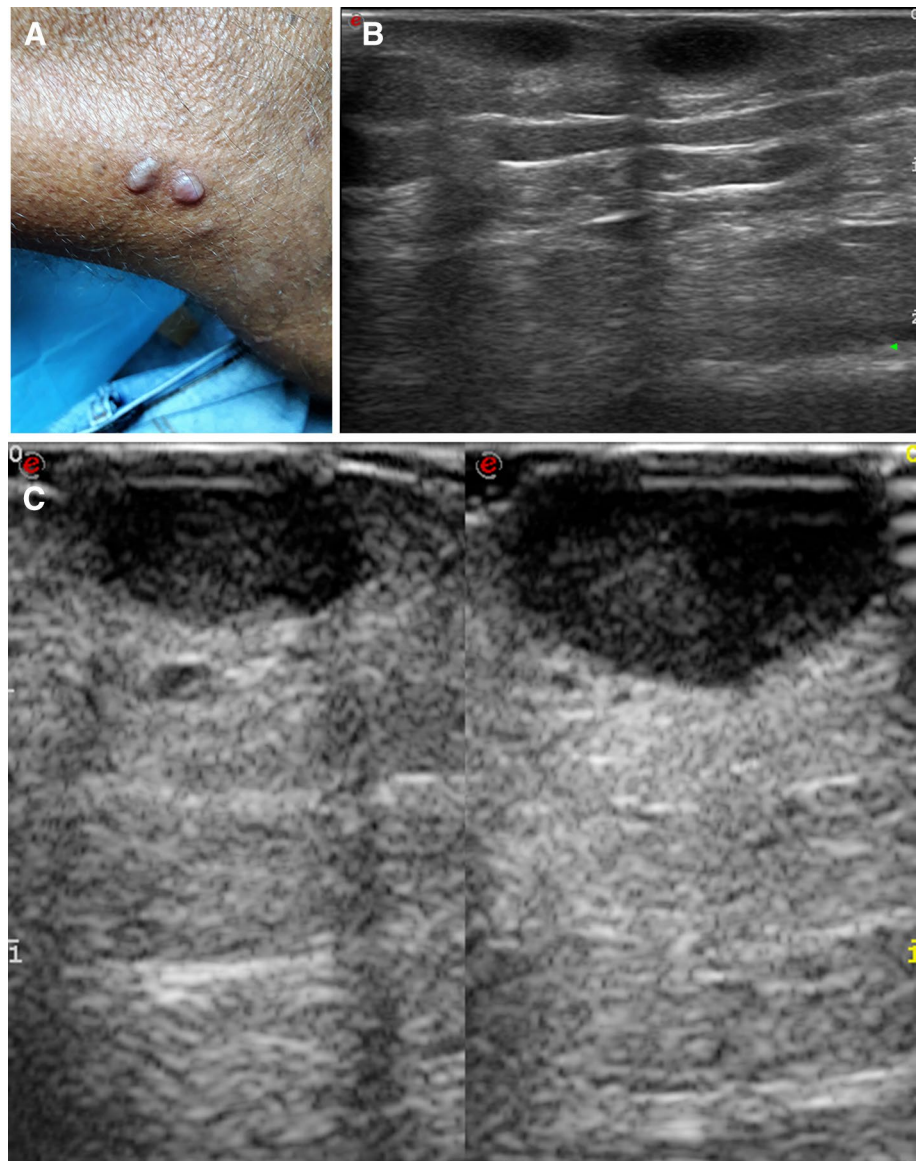
Role in US patients with skin cancer

Although the majority of skin tumors can be treated without additional information provided by imaging studies, large or aggressive high-risk cancers or those that compromise relevant anatomic structures necessitate additional information to optimize management [17, 18]. US examination allows a fast and accurate assessment of the tumoral diameters, including thickness, as well as provides the extent of involvement of deeper layers and improves the performance of loco-regional staging [4–6, 14, 17, 30]. US-based categorization of epitheliomas into superficial (thickness < 5 mm) and deep (thickness ≥ 5 mm) may help to decide for non-surgical treatments, such as brachytherapy [31]. Appropriate pre-surgical assessment of tumor extent can help reducing the extent of surgical defects. On the other side, infiltration of relevant anatomic structures, including fascia, muscles, cartilages, and bone cortex, can be effectively recognized using US and help the surgeon for choosing a more aggressive approach. The presence of a firm, fixed tumor mass or focal tenderness over a bony or cartilaginous margin is suspicious for invasion, and an US imaging is indicated in these cases [11]. Particularly in the head, where the subcutaneous layer is very thin, there is risk of bony involvement and US is an effective alternative to CT and MRI in establishing the presence of calvarium infiltration. Moreover, an US-guided pre-operative mapping of the lesion and the detection of relevant neurovascular structures close to the lesion can decrease the surgical risk and improve the cosmetic prognosis of the patient [1, 8, 30]. Non-palpable, satellite lesions may also be detected. Pre-surgical information provided by US

allows improving the surgical planning, which can help to decrease the time spent on surgery and to establish the site and size of the excision and identify the optimal technique for surgical closure. Moreover, post-surgical surveillance of high-risk cases allows an early detection of local or nodal recurrence [30]. It is, however, our experience that, with some notable exceptions, US is underemployed by dermatologists and surgeons in the assessment of skin tumors and that more efforts are needed to make spread this US application worldwide.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This is a review article. The images included are from current clinical practice. Anyway, all procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent This is a review article. The images included are from current clinical practice. For retrospective chart reviews, the authors obtained the consent requirement to be waived.

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