Review paper

High-frequency ultrasound in the diagnosis and treatment of skin neoplasms

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Abstract

High-frequency ultrasonography (HFUS) is a non-invasive and highly repetitive medical imaging method with a great and still rising value in the diagnostic process of skin tumours. It accompanies the physician's examination, dermoscopy, and biopsy; facilitates real-time assessment of locoregional staging and planning of surgical excision; and provides postoperative inspection of treatment results. The aim of this review article is to discuss HFUS application in common cutaneous malignant tumours while depicting the use of both the grayscale and colour Doppler methods.

Key words: skin ultrasound, high-frequency ultrasonography, skin cancer, melanoma, non-melanoma skin cancer, basal cell carcinoma.

Introduction

Cutaneous malignancies are the most common cancers worldwide [1], therefore their early detection determines increase of morbidity and survival. Since the introduction of ultrasound in 1979 to measure cutaneous thickness [2], skin imaging has kept progressing, resulting in the invention of high-frequency ultrasonography (HFUS). This non-invasive method precisely depicts lesion characteristics, therefore increases diagnostic accuracy [3], reduces the need for biopsy [4] or supports excision planning.

Although the conventional ultrasound scanner may assist dermatological diagnosis, HFUS assessment is more accurate as wave resolution and penetration are frequency-dependent – with higher frequency wavelength diminishes, which results in lower ultrasound penetration and better resolution imaging of the skin and subcutaneous tissues [5].

According to the DERMUS Group guidelines [6], HFUS needs minimum 15 MHz frequency to differentiate between skin layers [7] (preferably 15–22 MHz [8], the lowest frequencies designated for deeper lesions). HFUS accompanied by colour Doppler imaging and spectral curve analysis evaluates tumour vascularities [6]. Colour Doppler ultrasound differentiates benign from malignant lesions by depicting vessel size, intra- and peritumoral circulation [9]. It also evaluates inflammation – high disease activity areas [10] show increased blood flow. Three-dimensional reconstruction based on large-scale serial tissue sections [11] may be performed.

Digital HFUS images should be stored for long-term follow-up combined with clinical observations and prospective histological outcomes [12].

Melanoma

Melanoma is a skin cancer with the lowest survival [12] and a rapidly rising incidence rate [13]. HFUS depicts melanoma as hypoechoic, inhomogeneous [14], oblong or oval, well-bordered by hyperechoic epidermis. In ulcerated malignancies the epidermis may be non-continuous or irregular [15].

In colour Doppler examination melanoma – as an angiogenic tumour – is hypervascular. The flow signal is easier to detect in lesions thicker than 2 mm. Vascularization corresponds with lymph node involvement and survival rate.

Preoperative HFUS may determine excision margin as HFUS-measured cancer's thickness resembles histopathologic results [16–22] especially in superficial melanomas, while evaluation of nodular and vertically spreading tumours is less reliable [23]. The correlation

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is adequate in neoplasms thicker than 2 mm, often enabling one-time excision without widening resections. Thinner lesions should be excised or reassessed with a 100 MHz probe [15, 21]. HFUS-measured cancer thickness might be slightly overestimated due to peritumoral inflammation [24] and post-excision tissue dehydration [15, 25, 26].

Hinz *et al.* indicated that 1325-nm optical coherence tomography (OCT) is more precise than 20 MHz HFUS in melanomas thinner than 1 mm [27]. However, Meyer *et al*. compared 25 MHz HFUS with 930 nm OCT, concluding that OCT is less accurate than HFUS in evaluating tumour thickness, especially when the cancer's depth exceeds 0.5 mm [21].

Postoperatively, HFUS surveils regional lymph node basins [28], detects satellite and in-transit melanoma metastases [29] as well-defined, hypoechogenic, rather homogenous, dermal or hypodermal structures [30, 31].

Basal cell carcinoma (BCC)

BCC constitutes the vast majority of non-melanoma skin cancers (NMSCs) and is the most common human malignancy [32].

HFUS presents BCC as an oval or subtly irregular well-bordered hypoechoic lesion with hyperechoic areas representing microcalcifications, corneous cysts or nests of apoptotic cells – "flower cotton" [33]. The presence of minimum seven hyperechoic spots (characteristic for morpheaform or micronodular BCC) indicates a high risk of recurrence [34]. BCC may be accompanied by low-flow vessels inside or at the bottom of the tumour [35]. The characteristics are isoechogenic sebaceous glands ("blurry tumour") [36] and peritumoral inflammation ("angles at the bottom"), which enlarges HFUS-measured tumour thickness [25].

HFUS may designate small, non-infiltrative BCCs for conservative treatment like photodynamic therapy or laser ablation [37]. Being crucial in follow-up, HFUS supports or re-evaluates the decision either of non-invasive or surgical management as it indicates cancer recurrence [19]. If surgery is necessary, HFUS helps to reduce excision margins or – contrarily – avoid an incomplete procedure [38]. This asset results from high HFUS accuracy in measuring tumour thickness, comparable with histopathology, which enhances radical treatment [16] and positive prognosis.

Cutaneous squamous cell carcinoma (cSCC)

Squamous cell carcinoma derives from squamous cells of epidermis and mucous membranes [39], in 80% of cases [40] presenting as a cutaneous form, more invasive than BCC [41].

HFUS-assisted lesion evaluation or follow-up of postoperative basin and surrounding lymphatic structures is advised in: recurrent cSCCs, poorly differentiated tumours, bigger than 2 cm in diameter or thicker than 2 mm, invading nerves, vessels, lymph routes and high-risk anatomical sites (lips, ears and perineum) [42, 43]. HFUS depicts cSCC as an irregular heterogeneous tumour, fully hypoechoic, tending to invade deeper tissues [44]. Discrete tumour vascularization can be found, with vessels amplified peripherally [35].

Merkel cell carcinoma (MCC)

MCC is a rare but boosting in morbidity highly aggressive neuroendocrine malignancy [45]. HFUS depicts MCC as a poorly-defined (except for well-bordered satellitosis), non-calcified dermal lesion tending to invade subcutaneous tissues [46]. The mainly hypoechoic MCC mass shows hyperechoic zones, mostly with posterior acoustic enhancement and thickening of epidermis [47]. Colour Doppler ultrasonography pictures the tumour interior as richly vascularized, the flow being less intense in recurrent lesions and more vivid in cutaneous satellitosis.

HFUS differentiates hypoechoic skin malignancies [48], precisely preoperatively marks tumour margins to avoid local recurrence [49] and detects MCC metastases – subcutaneous, in-transit or affecting lymph nodes – thus enabling to assess tumour staging that determines treatment methods and prognosis.

HFUS: role and limitations in dermatology

Ultrasonography in dermatology is increasingly more widespread as a highly retriable, non-invasive method. Especially valuable are high-frequency probes, which support locoregional staging and follow-up, detecting early local or nodal recurrences. HFUS also indicates prognostic factors implicating advised management, based on the estimated recurrence risk, metastases and survival rate.

HFUS may reduce excision biopsies in benign-looking cases – diminishing patient's stress, functional impairment, costs of materials and specialists' work. In lesions of greater oncological alert HFUS helps to select excision margins, enabling faster diagnosis, effective treatment [50] and potentially preventing premature death.

A crucial HFUS application is to detect skin malignancies infiltrating relevant anatomical structures, especially head tumours. Ultrasound is faster available than computed tomography or magnetic resonance imaging but equally accurate in descrying calvarium invasion [51]. Preoperative HFUS maps neurovascular peritumoral structures to lower the operation's risk and lift its aesthetic effect [52]. It can also support an aggressive management, reducing metastases and recurrence rate.

Despite diagnostic advancements, some skin cancers still present high morbidity and mortality. While the emphasis on discovering groundbreaking therapies for criti-

cally ill patients is fully appropriate, we should primarily struggle for the earliest possible neoplasm diagnosis. To achieve that we need to raise patients' awareness of cancer prevention and alarming symptoms, as well as clinicians' competencies and utmost oncological caution.

For worldwide HFUS application, training of medical doctors is necessary. Clinicians should attend practical courses and conduct HFUS regularly, preferably minimum 300 evaluations yearly [6]. Ultrasonographers should be trained in skin pathology to correlate HFUS images and physical examination with histopathology. Apart from education costs, HFUS machine may be a substantial expense.

HFUS should be evaluated in comparison to other advanced real-time three-dimensional (and high-priced) imaging methods, like line-field confocal OCT (LC-OCT), which combines standard OCT with reflectance confocal microscopy, thus achieving optimum penetration and excellent resolution for assessing cutaneous malignancies, especially NMSCs [53, 54]. LC-OCT shows a higher resolution than HFUS [55], unfortunately being significantly more time-intensive, which limits its broad-based clinical use.

Conflict of interest

The authors declare no conflict of interest.

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