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### High Resolution Ultrasound Imaging of Melanocytic and Other Pigmented Lesions of the Skin

Laurent Machet, Mahtab Samimi, Gabriella Georgesco, Youssef Mourtada, Michaël Naouri, Jean Marc Grégoire, Frédéric Ossant, Frédéric Patat and Loïc Vaillant Department of Dermatology, CHRU Tours, UMRS Inserm U930, CNRS ERL 3106, Tours, CIC-IT, CHRU Tours, Université François Rabelais, Tours, France

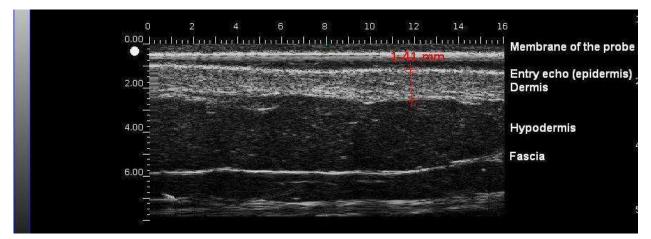
#### 1. Introduction

For two main reasons, dermatology is one of the later medical disciplines to use imaging techniques: 1) skin lesions are readily visible to the naked eye or through a magnifying glass, allowing clinical diagnosis with no invasive examination, 2) skin lesions can easily be biopsied or removed for histological study. This approach has therefore remained the basis of clinicopathological diagnosis of skin diseases for a long time. There has also been a third factor, i.e. the technical factors limiting image resolution (1-12). It is often necessary to visualise sub-centimeter lesions or even smaller, as in the case when measuring the thickness of a melanoma, and this cannot be achieved using traditional 7-10 MHz ultrasound. However, such techniques are useful in dermatology, especially in detecting lymph node spread of melanoma (6,13,14).

Other techniques such as optical coherence tomography and confocal microscopy are now available, with better resolution than 20-100 MHz ultrasound. However, both are more expensive and more time-consuming than ultrasound. Moreover, in certain European countries (e.g. France and Germany) ultrasound examination of the skin is reimbursed by health insurance services.

High resolution ultrasound imaging systems enable ultrasound to differentiate structures of less than 100 microns on the beam axis (axial resolution) and 200 microns on the scan axis (resolution axis). This can be achieved by the use of ultrasound frequencies above 15 MHz. Several groups have been working to extend the limits of existing machines by increasing the frequency (11,12,15,16). Working in our group, Berson et al. proposed a new ultrasound device operating at 17 MHz (1). This device was compact and had a very handy probe with an acoustic window enclosed by a thin membrane, allowing easier exploration of skin tumours on the face where they are more frequent than on other sites of the skin. We currently use a device derived from this prototype (Dermcup 2020®, Atys Medica, St

Soucieu en Jarrest, France) (2). The frequency ranges from 20 to 50 MHz, allowing visualisation of the superficial layer of the skin (epidermis and dermis, and the upper part of hypodermis) (Fig. 1), where the majority of lesions and skin tumors are located.



#### Fig. 1. Normal skin

Ultrasound imaging has been routinely used by dermatologists in our department for over ten years. The main indication is in the initial management of malignant tumors (including helping in the differential diagnosis and measurement of thickness). Moreover, ultrasound of the skin may be useful in the diagnosis of local recurrence and of locoregional melanoma, especially on certain very fibrous scars that are not easily accessible to palpation.

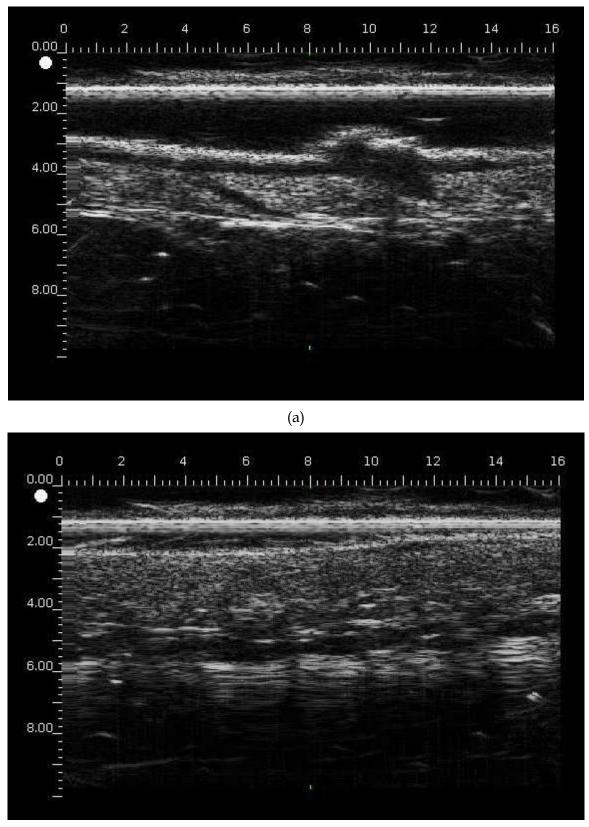
#### 2. Ultrasound imaging of melanocytic lesions

Melanocytic lesions are often benign (melanocytic naevus) and affect many individuals. Melanoma is a highly malignant tumor, whose incidence has doubled every 20 to 30 years (1 to 2 new cases/10 000 inhabitants/year, representing a 1% probability of developing melanoma during a lifetime). The overall mortality rate is 20% and it is greater in the case of lesions thicker than 4 mm (50%). On the other hand, the overall survival of thin lesions (less than 0.5 mm thick) is excellent. The diagnosis of melanocytic lesions is initially clinical, frequently assisted by dermoscopy, and in the case of suspected malignancy, the second step is surgical removal and histology examination which remains the gold standard. Dermoscopy and ultrasound are both non-invasive techniques that can be combined to increase preoperative diagnostic accuracy in pigmented skin lesions (17). Dermoscopy has been proved to improve the sensitivity and the specificity of clinical examination. The goal is to remove all *in situ* or less than 0.5 mm thick melanomas and to reduce the unnecessary removal of benign melanocytic lesions. How can ultrasound imaging help in the management of such lesions?

#### 2.1 Ultrasound imaging of naevi

The lesions are mainly hypoechoic, with many small echoes, symmetrical, and usually well delimited from the adjacent dermis (Fig. 2a). They are usually very thin in the case of junctional naevi (Fig. 2b) and thicker in the case of dermal naevi. However, the ultrasound image of clinically atypical naevi (which are often those that pose a problem of differential diagnosis) may be only slightly different from that observed in thin melanoma. Acoustic

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(b)

Fig. 2. a) echographic appearance of benign congenital melanocytic naevus; b) small acquired melanocytic naevus.

shadowing and retrolesional echogenicity may assist the diagnosis between benign naevus and melanoma (18) Quantitative discrimination of pigmented lesions seems possible using three-dimensional high-resolution ultrasound reflex transmission imaging (19). Blue naevi are also hypoechoic, and often have a dish shape or an ovoid shape (Fig.3a and 3b) (20).

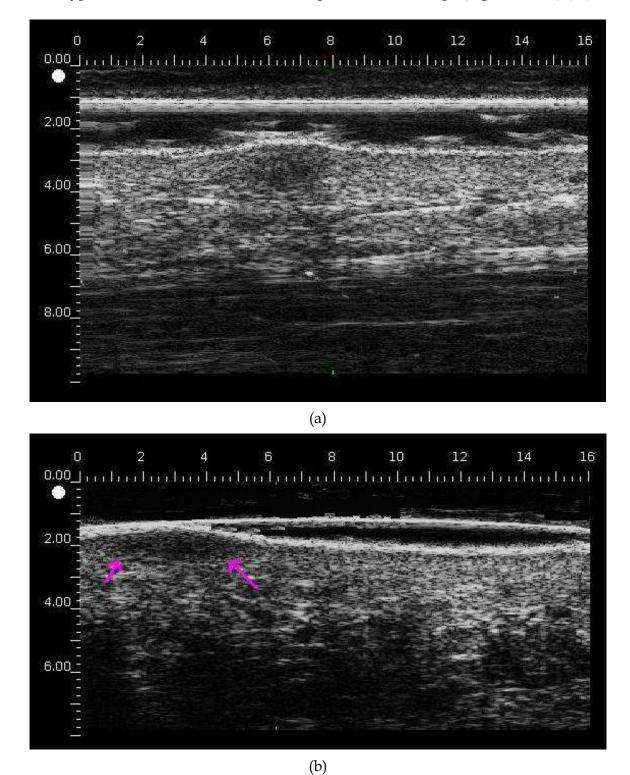


Fig. 3. a) Ovoid shaped benign blue naevus, b) dish shaped naevus

#### 2.2 Ultrasound imaging of primary melanomas

The lesions are homogeneous and hypoechoic, often more so than benign naevi in our experience. Echo entry is usually clearly visible, but it is less visible in the case of ulcerated lesions. The lateral dermal component of superficial spreading melanoma is usually well delimited from the dermis, but the intra-epidermal part cannot be seen (Fig. 4) A thin melanoma with Breslow thickness below 0.5 mm may be hard to visualise on the face of an elderly person due to the Sub Epidermal NonEchogenic Band (SENEB). The vertical part of the lesion is easily shown within the dermis and to a lesser extent within the hypodermis (Fig. 5).

## 2.3 Ultrasound imaging of local or in transit recurrence and distant cutaneous metastasis:

Recurrences appear as hypoechoic nodules located within the dermis or the hypodermis. They are not well delimited and often infiltrate adjacent structures (Fig. 6). They are often visible or palpable, and may simulate a benign blue naevus. However, the shape of the lesion is different for a blue naevus and a recurrence of melanoma (20). Moreover, ultrasound examination is able to detect subclinical in transit recurrence in some cases.

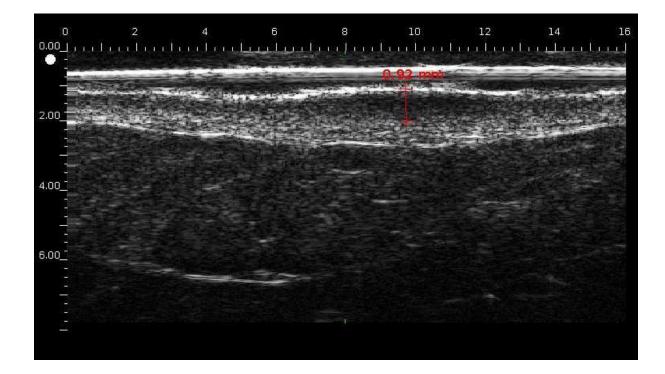


Fig. 4. Thin maligant melanoma.

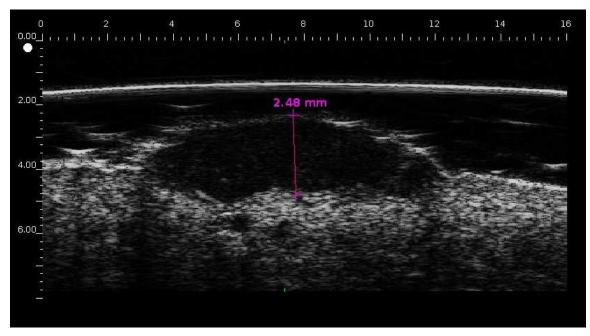


Fig. 5. Thick and ulcerated nodular malignant melanoma.

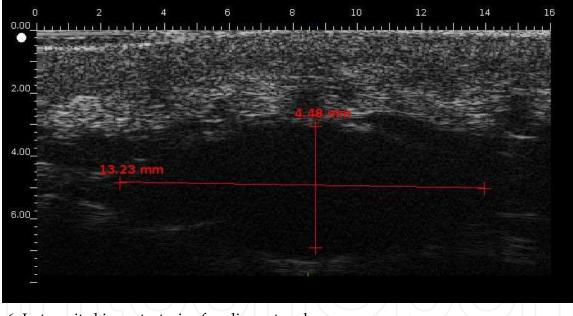


Fig. 6. In transit skin metastasis of malignant melanoma

#### 2.4 Ultrasound measurement of thickness of melanocytic lesions:

The shape of a melanoma is often different from that of a benign naevus. However, the value of ultrasound imaging is mainly to measure the thickness of the lesion (3, 15,16,17, 21,23,24). Ultrasound thickness is well correlated with histological thickness (Fig. 7). This was recently demonstrated in a systematic review of the literature which identified 14 studies. Pearson's coefficient is generally good, ranging from 0.88 to 0.97 (21). However, there are some marked differences, as demonstrated in some cases using the graph of Bland and Altman (Fig. 8). This is particularly clear for thick melanomas, and in some particular locations (nail or plantar melanoma). Nevertheless, the width of surgical margins can be

Measurement of thickness of 61 melanomas r = 0,91**Breslow thickness** 12 10  $\left( \begin{array}{c} \mathbf{m}_{6}^{8} \\ \mathbf{m}_{6}^{6} \\ \mathbf{m}_{4}^{6} \end{array} \right)$ . 4 2 0 0 2 4 6 8 10 Ultrasound thickness (mm)

correctly determined from ultrasound thickness, allowing the patient to be operated on in a single operation in nearly 75% of cases (Table 1) (21).

Fig. 7. Measurement of melanoma thickness with ultrasound (horizontal axis) as compared with histology, i.e. Breslow thickness (vertical axis), in a series of 61 melanomas treated in department.

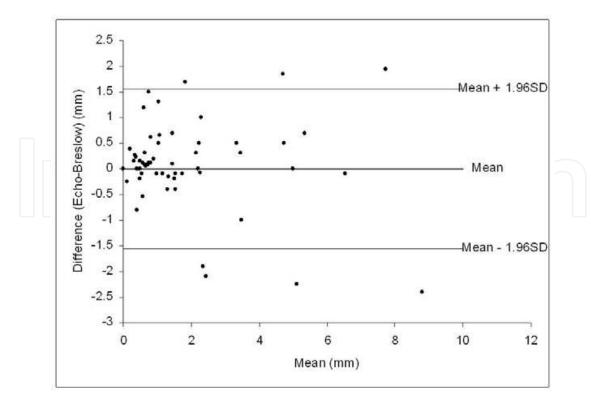


Fig. 8. Graph of Bland and Altman.

#### 3. Differential diagnosis: ultrasound imaging of other frequent lesions

Ultrasound may assist the diagnosis of other pigmented or non pigmented tumors, as melanomas are sometimes achromic.

#### 3.1 Basal Cell Carcinoma (BCC)

This is the most common skin cancer, most often located on areas of skin subjected to chronic sun exposure. The incidence is steadily increasing due to population aging and sun exposure habits. The pigmented variant of BCC may be confused with melanoma. In elderly subjects the tumor is mainly located on the face of. The first line of treatment is surgery, which allows complete excision and histological diagnosis. Radiotherapy or cryosurgery are therapeutic alternatives to surgery, with somewhat lower success rates (7% and 10% recurrence, respectively, versus 5% after surgery).

Ultrasound imaging may help in the diagnosis of BCC (25,26). The sonographic appearance is often stereotyped: overall anechoic tumor, including large focally dense echoes (Fig. 9). It is usually well delimited from the surrounding dermis.Ultrasound may also assist the detection of early recurrence, especially when surgical removal is incomplete or in cases treated with radiotherapy or cryosurgery. Ultrasound may also be used to help to determine the surgical margins or to delimitate the area treated with radiotherapy or cryosurgery (25, 27-32). This may decrease the rate of relapse.

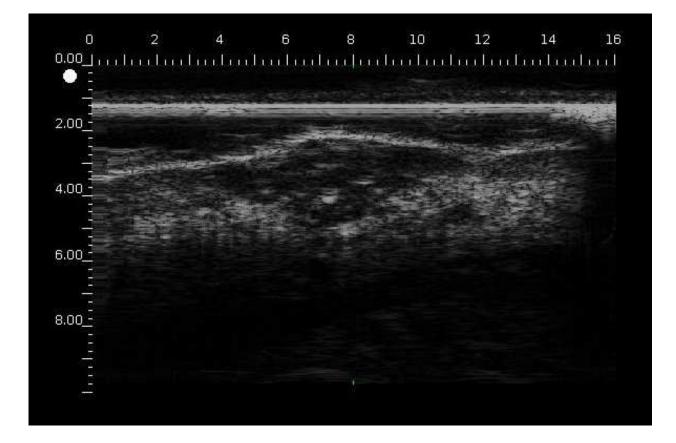


Fig. 9. Pigmented basal cell carcinoma showing some thick echoes within the tumor.

*Epidermal cysts* are limited, pushing the adjacent structures, and they have a heterogeneous structure, with both very echogenic and low echogenic areas (Fig. 10).

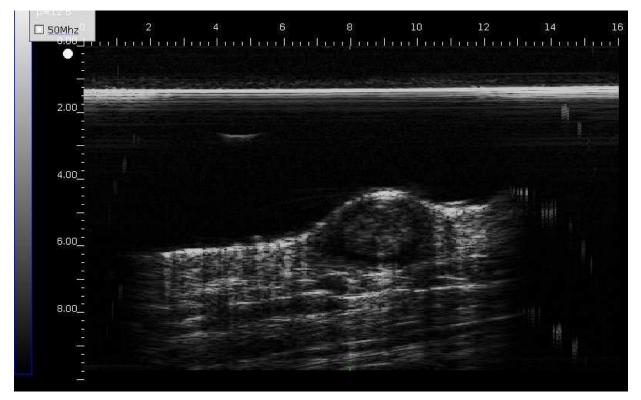


Fig. 10. Epidermal cysts showing a heterogeneous structure, with both very echogenic and low echogenic areas

*Fibrous histiocytomas* are fairly homogeneous, less echogenic than the normal dermis , with multiple small echoes, and their boundaries are poorly demarcated from the surrounding dermis (Fig. 11).

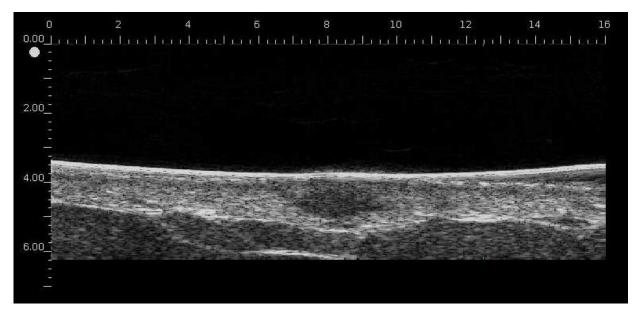


Fig. 11. Pigmented fibrous histiocytoma

*Seborrheic keratoses* are very well delimited, very superficial, as though laid on the skin, and may be misdiagnosed as melanoma. Ultrasound examination shows a dense echo input, under which there are very hypoechogenic lesions, in which one can sometimes see dense echoes (horny pseudocysts) (18) (Fig.12).

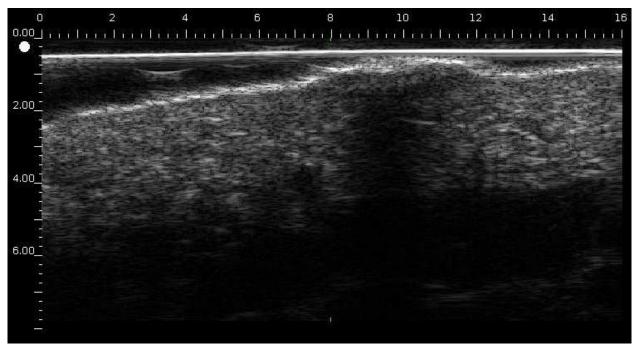


Fig. 12. Seborrheic keratosis with retrolesional acoustic shadowing

*Acquired angiomas* are sometimes a cause for concern especially in cases of inflammation or thrombosis, or sometimes in the differential diagnosis with amelanotic melanoma. They are fairly homogeneous lesions, less echogenic than the dermis, whose echogenicity is quite similar to that of the lip structure that is richly vascularized (Fig. 13).

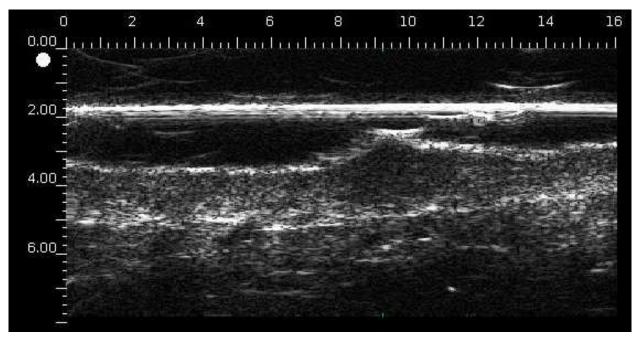


Fig. 13. Acquired hemangioma of the jaw.

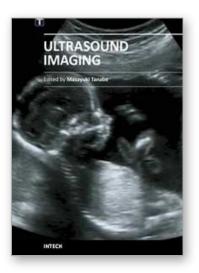
#### 4. Conclusion

Pathology examination remains the ultimate gold standard for diagnosis of skin tumors. However, it is not concievable to remove every skin lesion. Clinical examination (possibly assisted by dermoscopy) is often sufficient to determine whether a lesion has to be removed. However, ultrasound imaging provides additional information such as depth and lateral delimitation of the lesion, homegenous or heterogeneous structure, and hypo or hyperechoic appearance. These elements may of themselves be effective in terms of diagnostic accuracy and they are also valuable in the initial management or surveillance of patients.

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In this book, we present a dozen state of the art developments for ultrasound imaging, for example, hardware implementation, transducer, beamforming, signal processing, measurement of elasticity and diagnosis. The editors would like to thank all the chapter authors, who focused on the publication of this book.

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