The utility of ultrasound for the diagnosis and treatment of primary and metastatic melanoma – a remaining oncological challenge

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Cutaneous melanomas (CMs) are malignant proliferations that arise from melanocytes located in the basal layer of the epidermis [1]. Although CM represent less than 5% of all types of cutaneous malignancies, they are responsible for almost 90% of all skin cancer-related deaths [2]. Due to its high aggressiveness and mortality rate, including in young people, a multidisciplinary effort was oriented towards an early, highly accurate diagnosis, as well as optimization of the therapeutic approach in order to increase the survival rate in affected patients. For this purpose, many different associations were involved, e.g. EADO (European Association of Dermatology) and EORTC (European Organisation for Research and Treatment of Cancer) in defining guidelines and identifying the best tools for the most appropriate characterization and management of this highly aggressive tumor [3,4].

The most important prognostic factors for CM patients are the tumor infiltration depth at time of diagnosis (Breslow index), as well as the presence of locoregional and/or distant metastases [5]. The dermatological diagnosis in CM patients is based on the clinical examination, patient history, and imagistic methods (dermoscopy, ultrasonography [US], magnetic resonance imaging (MRI), computer tomography (CT), optical coherence tomography, confocal microscopy) which allow us to characterize the primary tumor and identify potential locoregional or metastatic spread.

However, in comparison to other imagistic methods, US was shown to remain superior in the assessment of soft-tissue masses, offering clinicians a very good equity between resolution and penetration depth (up to 60 mm) of the lesions, a very good axial spatial resolution and a very accurate definition of the integumentary layers and adjacent structures [6,7]. According to Wortsman et al, US is the only imaging technique to define tumor depth without penetration issues, the best imaging modality to characterize the primary tumor in all axes and perform locoregional staging at the same time. Further, the axial spatial resolution of US was shown to be higher than MRI and CT [7]. Hence, the introduction of skin US in dermatology was a turning point, regarding the diagnosis, prognosis, tumoral staging, identification of the optimal therapeutic approach and follow-up in CM patients [8].

High-frequency US (HFUS) at frequencies ≥15 MHz offers essential, “in vivo” data regarding tumor morphology, blood supply, neovascularization and elasticity. Furthermore, the tumor infiltration depth, as assessed by HFUS in the pre-operative setting, was shown to have a very good correlation degree with the histological Breslow index [9-11].

The Breslow index at the time of diagnosis is essential in determining the therapeutic approach, the necessary safety margins as well as the need of a sentinel node biopsy, speeding up the diagnosis and therapy initiation [12]. Its pre-operative knowledge by HFUS hence allows in certain situations, e.g. CMs <0.8 mm thick a one-time excision with the required safety margins, sparing patients a second surgical intervention [13]. It also enables clinicians to determine the necessity of a sentinel node biopsy, usually recommended in patients with a Breslow index ≥0.8 mm or even <0.8 mm in the presence of other risk factors, such as ulceration, allowing the detection of subclinical lymphnode metastases [11,14].

The identification of locoregional spread in CM at the time of diagnosis is mandatory for guiding the therapeutic management. The US identification of satellite, “in-transit” or locoregional lymphnode metastases upstages patients directly into American Joint Committee on
Cancer (AJCC) stage III. In such cases, where stage III has been confirmed by biopsy or fine-needle aspiration biopsy under US guidance, excision of the primary tumor with clear margins suffices, avoiding more extensive safety margins of 1-2 cm and the need of a sentinel node biopsy becomes obsolete. These patients usually require a staging to rule out distant spread, and after individual discussion of the cases in interdisciplinary tumor boards, the appropriate therapy, e.g. adjuvant immunoncological or targeted systemic treatment and/or radiation can be initiated [3,11].

Locoregional metastases can not only be identified in the pre-operative setting when assessing the primary tumor area and the locoregional lymphatic basin, but also during follow-up, helping identify recurrences and tumor progress in an early stage. Studies on patients with CM, focused on locoregional evaluation of locoregional metastases by ultrasound and clinical examination, showed highly sensitivity (89.2%) and specificity (97%) of US in identifying occult metastases when compared to the clinical examination alone [15].

To conclude, US has become an essential non-invasive tool for dermatologists. The widespread of the US examination, miniaturization and portability of the machines, excellent resolution and delivery of multimodal “in vivo” information makes US an excellent imaging technique. The introduction of basic sonodermatology into the residents curriculum will surely “boost” the applications of this technique. Histology still remains the “gold standard” for confirming the diagnosis, however HFUS can provide a more broad perspective for the optimal management of CM. Being a fast imaging method, US can, in the hands of well trained operators spare patients not only more extensive and time-consuming diagnostic imaging methods (CT, MRI) but also avoid a delay in diagnosis, unnecessary surgical interventions, and facilitate an early therapy initiation.

References