In vivo micro-angiography by means of speckle-variance optical coherence tomography (SV-OCT) is able to detect microscopic vascular changes in naevus to melanoma transition

Editor

The transition from benign junctional melanocytic proliferation to *in situ* melanoma is based on clinical-histopathological evidence and partially understood *in vivo*.[1] Due to the high prevalence of naevi, the knowledge of early phenomena characteristic of the development of a melanoma would help to identify lesions that need excision. Dermoscopy[2] and reflectance confocal microscopy (RCM)[3] are among the most commonly used methods for the diagnosis of skin cancer.[4] Neither of these diagnostic technologies identifies *in vivo* features, which may characterize early phenomena related to tumour–matrix interaction.

Speckle-variance optical coherence tomography (SV-OCT) is a novel approach that allows the study of the vascular patterns of the skin in enface and transversal sections.[5] When blood cells pass through the infrared scanning beam, they interfere with the OCT signal changing the reflectivity of the tissue leading to increased brightness of the surrounding pixels. These changes can be detected through software analysis and affected areas are presented in red colour, generating images of the skin's micro-angiography.

We present the preliminary observation of this innovative technique showing changes in the micro-vascular organization during the junctional proliferation to melanoma *in situ* transition in a paradigmatic case, suggesting these micro-angiographic changes may help to identify the early events occurring in the malignant march.

Dermoscopy (Dermlitephoto®, 3Gen, S. Juan Capistrano, CA, USA) of the lesion (Fig. 1) showed regular pigment network at one pole and an island of homogenous pigmentation on the opposite pole, characteristic of melanoma arising on a naevus[2] *In vivo* RCM (Vivascope 1500®, MAVIG GmbH, Munich, Germany) showed, within the epidermis, regular ringed pattern in correspondence of the pigment network (Fig. 1c), and irregular architecture with atypical cells, in correspondence of the dermoscopic island (Fig. 1d).[3] Histology subsequently confirmed the diagnosis of junctional naevus and *in situ* melanoma respectively.

SV-OCT vascular pattern was evaluated on enface and transversal images by means of Vivosight® SV-OCT (Michelson Diagnostics Ltd., Orpington, Kent, UK). Corresponding to the benign lentiginous proliferation of melanocytes upon histopathology, SV-OCT showed micro-vasculature consisting of thin regular columns on transversal section, and regularly distributed dots or short curved lines, progressively assuming a regular reticulated architecture with depth in enface view (Fig. 1e). This pattern did not significantly differ from the vascular pattern of normal surrounding skin. On the other hand, in correspondence to the dermoscopic island (*in situ* melanoma upon histopathology), SV-OCT showed in the transversal section vessels organized in larger vertical columns, irregularly distributed. In the enface view, vascular pattern was characterized by numerous, densely packed dots progressively becoming irregular cloud-like structures with depth (Fig. 1f).

CD31 staining, an immunohistochemical marker of endothelium, showed two different vascular patterns, confirming the correspondence of SV-OCT images with skin vasculature. In the junctional naevus component, vessels were regularly distributed, presented thin lumina and a linear course (Fig. 1g). Although in the *in situ* melanoma component, vessels were increased in number, presented thicker lumina and a tortuous course. (Fig. 1h)

This observation represents a proof of concept for the interaction between melanoma development and matrix, highlighting the induction of vascular modifications at the very early stages, seemingly able to induce an increment of blood flow and also

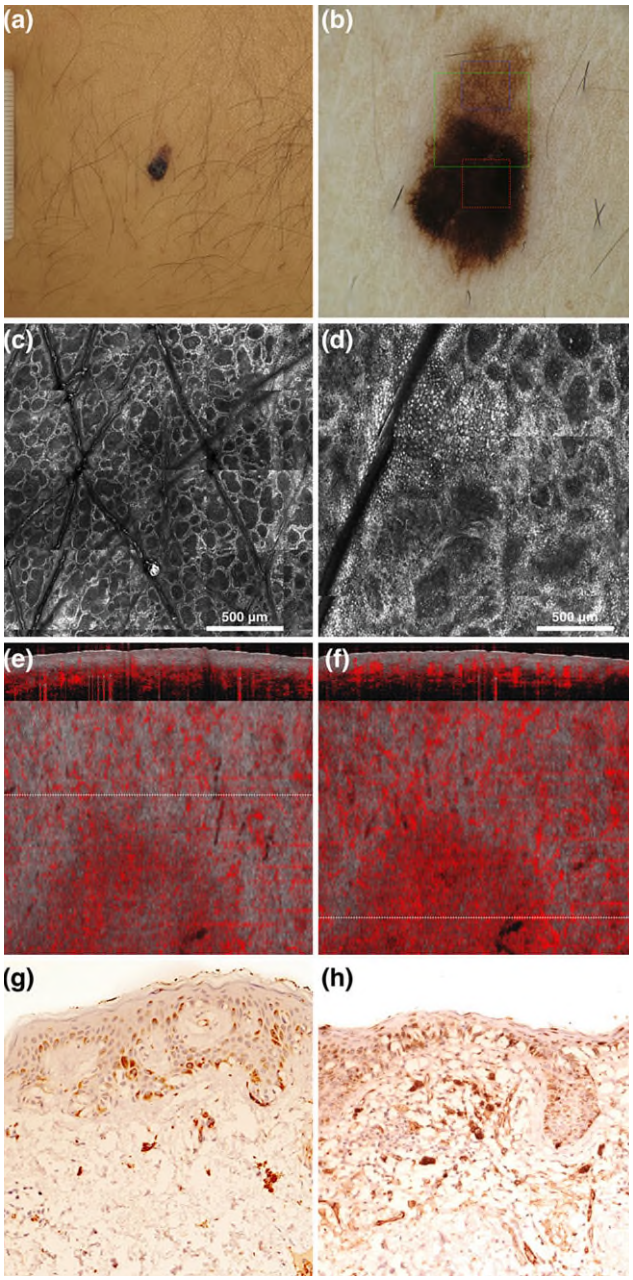

Figure 1 Melanoma *in situ* arising on junctional naevus. (a) clinical image. (b) Dermoscopy: reticular lesion with dermoscopic island of homogeneous pigmentation. Blue and red dashed squares depict the area of the corresponding RCM images below, (c and d, respectively), whereas the green-dashed square outline the area of the SV-OCT imaging. (c, d) RCM mosaic at the dermal–epidermal junction: ringed pattern without atypical cells (**c**) and architectural disarray and atypical cells (d). (e, f) SV-OCT transversal and enface sections: on the naevus portion presence of thin regular columns on the transversal SV-OCT in (e), and regularly distributed dots or short-curved lines at the papillary dermis [upper half of (e)] progressively assuming a regular reticulated architecture at the reticular dermis level [upper half of (f)]. On the melanoma portion, presence of vessels organized in large irregularly distributed vertical columns on the transversal SV-OCT in (f), and numerous vessels organized in densely packed dots [(e), lower part] progressively becoming irregular clod-like structures with depth [(f), lower part]. (g, h) CD31 immunohistochemistry. Junctional naevus (g) benign lentiginous proliferation of melanocytes and few regularly distributed vessels with thin linear lumina. *In situ* melanoma (h) junctional proliferation of atypical melanocytes and increased number of vessels presenting thicker lumina and a tortuous course.

the architectural transformation and disarray of the tumour-associated micro-vasculature, probably through induction of matrix component changes and neovascularization.[6] Although this study represents an observation of a single case, the uniqueness of the well-distinguished two portions, corresponding to a junctional naevus and an *in situ* melanoma, demonstrate the potential of SV-OCT to detect early alteration of the microscopic dermal vasculature, opening the possibility to identify biological processes related with tumour progression and aggressiveness *in vivo*.

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