Utility of confocal microscopy in the management of lentigo maligna and lentigo maligna melanoma

To the Editor: Lentigo maligna and lentigo maligna melanoma (LM/LMM) often present in cosmetically sensitive regions with poorly defined borders, subtle pigmentation, and areas of discontinuity, creating a diagnostic and therapeutic challenge. Wood's lamp and dermoscopy are often insufficient for accurate peripheral margin determination. Confocal microscopy (CM) enables real-time imaging of the epidermis, dermoepidermal junction, and papillary dermis, and has potential to optimize the current surgical approach to LM/LMM. We systematically reviewed the literature for CM application to LM/LMM management and identified 13 relevant publications (Supplemental Fig 1; Supplemental Table I, available via Mendeley at https://data.mendeley.com/datasets/9tv8cbg5kc/2).

Studies reproducibly demonstrated correlation between histopathologically detected and CM-detected margins (Supplemental Table II). Five of these studies were prospective in design. One prospective study (n = 23 patients) reported histopathologic clearance in 91% of all CM-negative margins.[1] In another prospective study (n = 23 cases), 63% of the CM-mapped quadrants had no difference with the final surgical margins that were blinded to CM mapping, 27% of the quadrants underestimated required margins, and 10% overestimated them.[2] One retrospective study (n = 37 patients) demonstrated a 3.2% false-positive rate and a 8.3% false-negative rate of CM melanoma margins compared with histopathology.[3]

CM margin assessment of LM/LMM can also help visualize lesion extension beyond what is visible on dermoscopy and Wood's lamp examination (Supplemental Table II).[1-5] In 1 prospective study (n = 23 patients), CM achieved margin accuracy in 91% compared with 26% by dermoscopy.[1] In another prospective study (n = 23 cases), CM extended the dermoscopically visible margin in 44% of LM/LMM quadrants.[2]

CM may improve surgical planning for LM and LMM by reducing repeat excisions and conserving tissue; however, current evidence is insufficient to draw firm conclusions. Two prospective studies (n = 33; n = 70 patients) demonstrated CM-directed margin clearance with 1.2 and 1.1 stages of excisions, respectively. Single excision was insufficient to clear LM/LMM margins after CM mapping in a few rare cases (n = 2 of 23 patients; n = 1 of 1 patient) in 2 other prospectively designed studies (Supplemental Table I).[1] Two retrospective studies (n = 16; n = 47 patients) with a comparison group demonstrated 1.3 to 1.4 stages were required for margin clearance with CM guidance, and 1.7 to 2.2 stages were required without CM.

A CM-guided surgical approach may achieve minimal tumor recurrence rates at long-term follow-up (Supplemental Table II). Prospective studies demonstrated no tumor recurrence after CM-guided treatment at an average of 10 to 44 months after treatment.[1] Local recurrence was found in 1 patient with a follow-up of 6 months. Metastatic disease was found in 1 patient; however, invasive disease was found at initial diagnosis (1.7 mm depth).

CM clinical application has limitations with regard to acquiring images and melanoma margin assessment. The initial cost and the learning curve for CM limit widespread adoption.[1,3] In addition, reported durations of 20 to 75 minutes for margin mapping with hand-held CM create practical challenges. Deep margin evaluation beyond 200 μm also remains a technologic limitation. CM margin evaluation can also be limited in the presence of widespread epithelioid or dendritic melanocytes at the dermoepidermal junction[1]; however, this remains a challenge in histopathologic examination as well.[1,2] Although larger prospective controlled studies are warranted, the current data demonstrates promising roles for CM in margin evaluation and surgical management of LM/LMM.

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Funding sources: None.

Conflicts of interest: None disclosed.

IRB approval status: Not applicable.

Reprints not available from the authors.

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https://doi.org/10.1016/j.jaad.2020.08.101

Application of 3-dimensional reflectance confocal microscopy: Melanocytic proliferations as three-dimensional models

To the Editor: Melanoma on chronically sun-damaged skin (MSDS) is challenging to detect.[1] Reflectance confocal microscopy (RCM) increases diagnostic accuracy but relies upon interpretation of 2-dimensional (2D) horizontal sections. Our objective was to determine whether existing technology could be used to create 3-dimensional (3D) models, which would expand on data available for discriminating skin biology.

Melanocytic cells have different morphologic appearances dependent on developmental stage, activation status, and pathogenic genetic and epigenetic alterations. Cell shape, therefore, can provide clues to a cell's behavior. We reconstructed individual melanoma cells from stacks of RCM images (Fig 1; Supplemental Fig 1, available via Mendeley at https://data.mendeley.com/datasets/7kx38d9h2v/3). Distinct morphologies could be identified, including spindle, spheroid, and heavily dendritic cell forms. These 3D reconstructions also allowed for modeling of the nuclear shapes (Fig 1, *insets*). Because image sizes are known, it is possible to calculate nuclear and cellular volumes, which may also increase diagnostic accuracy.[2]

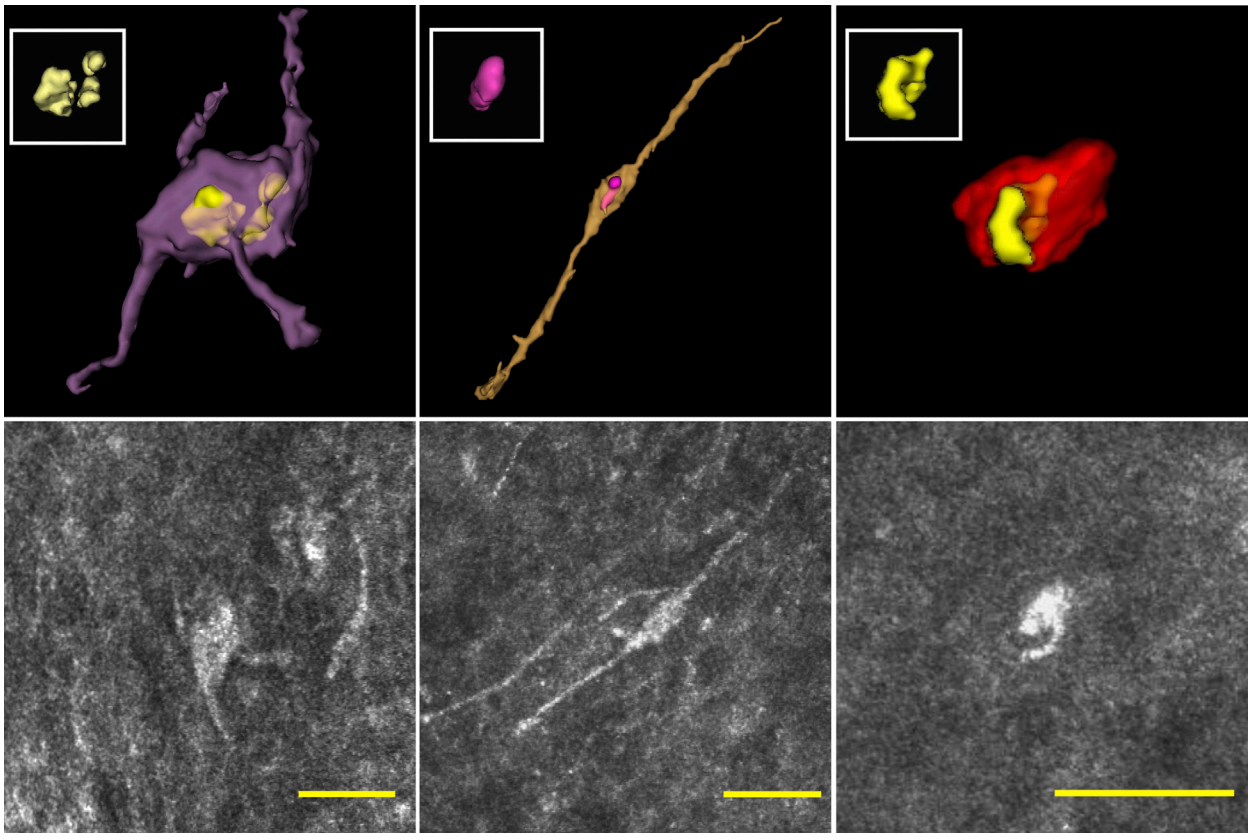

Fig 1. Three-dimensional reconstructions of atypical melanocytic cells revealing different morphologies. The *insets* illustrate nuclear morphology. A single slice from the confocal stack is shown below each cell. The reconstructions are enlarged to show features. Scale bar is 50 μm. A 3-dimensional model can be downloaded and rotated freely to examine from any angle, see Supplemental Fig 1 (.OBJ and associated .MTL)