ORIGINAL ARTICLE

Concordance of handheld reflectance confocal microscopy (RCM) with histopathology in the diagnosis of lentigo maligna (LM): A prospective study

Tyler D. Menge, BA,[a] Brian P. Hibler, BS,[b] Miguel A. Cordova, MD,[b]
Kishwer S. Nehal, MD,[b] and Anthony M. Rossi, MD[b]
Ann Arbor, Michigan, and New York, New York

Background: Reflectance confocal microscopy (RCM) provides real-time noninvasive imaging of cell structure and may be useful in diagnosing lentigo maligna (LM). Few studies have compared performance of RCM with histopathology in diagnosing LM, and specific features influencing RCM interpretation are not well described.

Objective: We sought to determine concordance rate between RCM and histopathology in the evaluation of suspected LM and to identify factors that may obscure diagnosis.

Methods: We designed a prospective study involving 17 participants seen for evaluation at a large tertiary referral center. Cases included primary lesions and possible recurrent and/or previously treated lesions. A total of 63 clinically equivocal sites were assessed by RCM and histopathology.

Results: RCM and histopathology interpretations were concordant in 56 of 63 sites (89%). There were no false-negative and 7 false-positive results using RCM (sensitivity 100%, specificity 71%, positive predictive value 85%, negative predictive value 100%). Features suggestive of LM in the false-positive group included the presence of numerous hyperreflectile large cells at the dermoepidermal junction and follicular localization of these cells.

Limitations: A larger test set is needed to more reliably distinguish LM from benign lesions using RCM and to improve specificity.

Conclusion: RCM shows excellent sensitivity for detecting LM although features of benign macules on a background of actinically damaged skin can obscure diagnosis and limit its specificity. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2015.12.045.)

Key words: confocal laser scanning microscopy; diagnosis; histopathology; lentigo maligna; melanoma; nevi; pigmented lesions; reflectance confocal microscopy.

Lentigo maligna (LM) is a form of melanoma in situ that occurs on chronically sun-damaged skin and its incidence has risen sharply in recent decades.[1-3] LM has long been considered a disease of the elderly, although it is increasingly being seen in patients younger than 49 years of age.[1] Although disease-specific mortality in patients with LM remains low, accurate recognition of disease is needed for early diagnosis and to limit its recurrence or progression to invasive melanoma. The rate of progression of LM to invasive melanoma if left untreated has been reported to be 5% to 15%.[4,5]

LM may appear as a pigmented, asymmetric macule that spreads slowly, often on cosmetically and functionally sensitive areas of the head and neck.[1,6,7] Dermoscopy and Wood's light examination

From the University of Michigan Medical School,[a] and Dermatology Service, Memorial Sloan Kettering Cancer Center, New York.[b]

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Reprint requests: Anthony M. Rossi, MD, Dermatology Service, Memorial Sloan Kettering Cancer Center, 16 E 60 St, New York, NY 10022. E-mail: rossia@mskcc.org.

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are commonly used to clinically diagnose LM, although these tumors frequently share many overlapping features with benign pigmented lesions. LM can thus be difficult to distinguish from benign lesions, particularly on a background of heavily sun-exposed skin, and biopsy is required for definitive diagnosis. However, biopsy specimens are prone to sampling error because of the heterogeneous nature of LM and its characteristic subclinical extension. Histologically LM can be challenging to diagnose as it often occurs in areas with high background melanocytic hyperplasia. The costs and morbidity associated with multiple biopsy specimens in patients with a high burden of actinic disease can be substantial.

CAPSULE SUMMARY

- Lentigo maligna is a form of melanoma in situ that can be challenging to differentiate from benign pigmented lesions.
- Handheld reflectance confocal microscopy shows excellent sensitivity in the diagnosis of lentigo maligna, including on anatomically difficult areas of the head and neck.
- Reflectance confocal microscopy may be useful in the identification of lentigo maligna without the need for biopsy.

Reflectance confocal microscopy (RCM) provides real-time noninvasive imaging of intact skin at a resolution comparable with conventional histology. Several studies have demonstrated that RCM may improve diagnostic accuracy of melanoma compared with dermoscopy or Wood's light examination.[8-14] A recent meta-analysis performed by Stevenson et al[15] reports a sensitivity and specificity of 93% and 76%, respectively, for RCM when used as a second-level test for diagnosing pigmented lesions that are clinically equivocal. Few studies have compared the performance of RCM with histopathology specifically in the diagnosis of LM and data are lacking regarding use of a newer handheld version of the microscope that can move more freely and assess anatomically difficult areas in real time.[16-18] Here, we report on the degree of concordance between RCM and histopathologic analysis in a series of patients undergoing evaluation for suspected LM and we describe factors that may obscure diagnosis of LM using RCM.

METHODS

Study design

We designed a prospective study involving participants being seen in consultation by the dermatology service at Memorial Sloan Kettering Cancer Center in New York, NY. Eligible participants included men and women seen for evaluation of known or suspected LM between August 1, 2014, and August 31, 2015. Cases included primary lesions and possible recurrent and/or previously treated lesions. Both pigmented and amelanotic lesions were included. The study was approved by the Memorial Sloan Kettering Cancer Center Institutional Review Board, and all participants provided their written informed consent.

Clinical evaluation

All study participants were seen in consultation by at least 1 dermatologist (A. M. R. or K. S. N.) for head and neck lesions that were clinically concerning for LM or had been partially biopsied by an outside provider. Sites clinically equivocal for LM were identified for biopsy and a baseline clinical photograph was taken of each lesion.

Intervention with RCM

New solitary lesions or areas surrounding a partial biopsy site were imaged using a commercially available handheld RCM (Vivascope 3000, Caliber Imaging and Diagnostics, Rochester, NY). The microscope uses an 830-nm near-infrared laser beam to provide a 0.75- × 0.75-mm field of view at depths up to about 200 μm, which corresponds to the superficial reticular dermis. Lateral and axial resolutions of about 1.25 μm and 5 μm, respectively, are achievable with the device. Confocal sections were visualized in real time across the entire lesion, including previous biopsy sites (if present), and representative videos or images extending from the stratum corneum to the papillary dermis were captured for each lesion. The new, handheld device provides real-time video imaging, which differs from prior models that only allowed still-captured images taken at a fixed point on the lesion.

Two confocal experts (A. M. R. or M. A. C.) assessed real-time video imaging for LM using an algorithm adopted from Guitera et al[16] (Table I). In their algorithm, an LM score is calculated based on the presence or absence of 6 features associated with LM. There are 2 major features (nonedged dermal papillae, presence of round large pagetoid cells) that are scored +2 points each and 3 minor features (nucleated cells in dermal papillae, ≥3 atypical cells at the dermoepidermal junction in five 0.5- × 0.5-mm^2 images, and follicular localization of atypical cells) that are scored +1 point each. There is also 1