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#### REFERENCES

1. Ormerod AD, Thomas KS, Craig FE, et al; UK Dermatology Clinical Trials Network's STOP GAP Team. Comparison of the two most commonly used treatments for pyoderma gangrenosum: results of the STOP GAP randomised controlled trial. *BMJ*. 2015;350:h2958.

- 2. Weenig RH, Davis MDP, Dahl PR, Su WPD. Skin ulcers misdiagnosed as pyoderma gangrenosum. *N Engl J Med.* 2002;347(18):1412-1418.
- 3. Maverakis E, Ma C, Shinkai K, et al. Diagnostic criteria of ulcerative pyoderma gangrenosum: a Delphi consensus of international experts [published online February 14, 2018]. *JAMA Dermatol.* doi:10.1001/jamadermatol.2017.5980
- 4. Ashchyan HJ, Butler DC, Nelson CA, et al. The association of age with clinical presentation and comorbidities of pyoderma gangrenosum [published online February 14, 2018]. *JAMA Dermatol*. doi:10.1001/jamadermatol.2017.5978
- 5. Langan SM, Groves RW, Card TR, Gulliford MC. Incidence, mortality, and disease associations of pyoderma gangrenosum in the United Kingdom:

- a retrospective cohort study. *J Invest Dermatol*. 2012:132(9):2166-2170.
- **6.** Ahronowitz I, Harp J, Shinkai K. Etiology and management of pyoderma gangrenosum: a comprehensive review. *Am J Clin Dermatol*. 2012; 13(3):191-211.
- 7. Su WP, Davis MD, Weenig RH, Powell FC, Perry HO. Pyoderma gangrenosum: clinicopathologic correlation and proposed diagnostic criteria. *Int J Dermatol.* 2004;43(11):790-800.
- **8**. Binus AM, Qureshi AA, Li VW, Winterfield LS. Pyoderma gangrenosum: a retrospective review of patient characteristics, comorbidities and therapy in 103 patients. *Br J Dermatol*. 2011;165(6):1244-1250.

## Dermoscopy and Overdiagnosis of Melanoma In Situ

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**In this issue** of *JAMA Dermatology*, Lallas et al<sup>1</sup> state that "our goal today is to detect melanoma, if possible, before it becomes invasive." Given the challenges related to the early de-



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tection of melanoma faced by clinicians and patients alike, this goal can only be achieved through further improving

clinical training of clinicians, allied health care workers, and consumers alike, combined with heightened individual awareness and advanced imaging technologies.<sup>2</sup>

Recently at the 2017 World Congress of Melanoma in Brisbane, Australia, Wolfgang Weyers, MD, also commented that in regard to the detection of melanoma, "the earlier the better; however, this is only true if the melanoma can be recognized." Weyer's statement raises 2 questions that have seen much debate in the scientific and medical communities. The first question is, how early is too early? From a clinical perspective, the smaller the malignant neoplasm, the better the outcomes. However, in an era of "cancer overdiagnosis" and tighter government spending, screening programs and improved diagnostic approaches are scrutinized for early detection of indolent lesions. This leads to the second question, is it a melanoma? In this context, the recent article by Elmore et al<sup>3</sup> highlights the difficulties in addressing this question at the histopathologic level. In particular, early-stage disease (melanoma in situ) resulted in diagnosis that was neither reproducible nor accurate. For example, of 187 pathologists, only 40% made a diagnosis of melanoma in situ in agreement with the reference diagnosis (obtained from 3 dermatopathologists).<sup>3</sup>

The significance of the findings by Elmore et al<sup>3</sup> in relation to melanoma management is that the majority of cases diagnosed within the "melanoma epidemic" are disproportionally attributed to melanoma in situ. Although noninvasive itself, melanoma in situ results in an increased risk of invasive melanoma<sup>4,5</sup> and increased risk of several other cancers. These risks are not trivial and can lead to serious medicolegal consequences if invasive melanoma were to develop, or on the other end of the spectrum,

lead to increased anxiety, excisions, and cost to patients for potentially benign lesions.

Since its clinical implementation in the late 1980s, dermoscopy has significantly enhanced diagnostic accuracy over naked-eye examination<sup>6-8</sup> and complemented histopathologic analysis through whole-lesion morphological characterization.<sup>9</sup> Melanomas are detected and diagnosed dermoscopically using various guidelines including, but not limited to, the ABCD rule (asymmetry, irregular borders, >1 or uneven distribution of color, or a large [>6 mm] diameter), 7-point checklist, Menzies method, or the AC rule (asymmetry, color variation).<sup>10</sup> Although effective, many of the studies establishing these criteria consisted of laterstage invasive melanomas and as such fall short for early-stage "dermoscopically featureless" melanoma, particularly melanoma in situ. These difficult-to-diagnose melanomas highlight a problematic shortfall in dermoscopic criteria, making identification and diagnosis challenging.

The study by Lallas and colleagues¹ addresses the limitations of current dermoscopy criteria by investigating the accuracy of melanoma criteria specifically for the diagnosis of melanoma in situ. The authors identified 5 dermoscopic criteria as positive markers for melanoma in situ compared with commonly occurring benign pigmented lesions.¹ Lallas et al¹ believe that implementation of their criteria will have the potential to reduce the burden on patients, clinicians, and the health care system (eg, anxiety around metastasis and resulting treatment, medicolegal ramifications from wrong diagnosis and cost). However, given today's controversy around early detection and overdiagnosis of clinically indolent lesions, implementation of these refined dermoscopic criteria into new guidelines and screening programs should address those who benefit most.

One potential benchmark that is also often raised in the overdiagnosis debate is the number needed to biopsy. The recent article by Lott et al<sup>12</sup> determined that more than 90% of biopsies were attributed to benign or low-risk lesions (Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis class I and II), with melanoma in situ (class III) contrib-

uting 4.5%. However, with the influence of "diagnostic drift," pressure of medical liability, and variability in histopathological diagnosis, the accurate diagnosis of melanoma in situ is critical for appropriate management. Given that dermoscopy has been shown to reduce the number of biopsies by improving the benign to malignant ratio, <sup>13</sup> it further emphasizes the importance of the study by Lallas et al<sup>1</sup> in establishing optimal criteria for early equivocal lesions.

The individuals who will benefit most from improved diagnostic accuracy are those with multiple nevi and a personal or family history of melanoma. It is not feasible from a patient or practical perspective to excise every nevus, so accurate noninvasive diagnostic tools are needed. The recent Special Report by Thomas and Puig<sup>14</sup> discusses the benefits and challenges of dermoscopy for early detection of melanoma in high-risk individuals. Of note is the role that digital dermoscopy plays in continued surveillance: "comparisons of good quality [accurate and reproducible] images provide additional opportunities to make an accurate diagnosis of an initially featureless melanoma." Yet, even with the established benefits, dermoscopy uptake and util-

ity still faces challenges. This is in part due to a perceived complexity of dermoscopic criteria inhibiting a willingness of clinicians to become qualified and experienced with routine dermoscopy. <sup>14</sup> Therefore, studies similar to that by Lallas et al<sup>1</sup> are needed to refine and simplify dermoscopic criteria and promote its clinical utility for early melanoma detection.

While the debate of overdiagnosis will continue, the anxiety around underdiagnosis remains from both a medicolegal and a human point of view. The integration of dermoscopy (and total-body photography<sup>15</sup>) within screening programs, particularly for high-risk individuals, is the optimal method to detect and monitor for melanoma in situ. However, dermoscopy is just one, albeit essential, weapon in the battle against melanoma, and we foresee that a holistic approach incorporating current risk assessment tools, genetic profiling, total-body photography, and sequential dermoscopy imaging will play a crucial role in early melanoma detection and management.<sup>2</sup> The tools for achieving the goal of Lallas et al<sup>1</sup> of detecting noninvasive melanoma are available; it is just a matter of putting them into our daily practice.

#### ARTICLE INFORMATION

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### **REFERENCES**

- 1. Lallas A, Longo C, Manfredini M, et al. Accuracy of dermoscopic criteria for the diagnosis of melanoma in situ [published online February 21, 2018]. *JAMA Dermatol*. doi:10.1001/jamadermatol.2017.6447
- **2**. Smithers BM, Dunn J, Soyer HP. Whither melanoma in Australia? *Med J Aust*. 2017;207(8): 330-331.
- **3**. Elmore JG, Barnhill RL, Elder DE, et al. Pathologists' diagnosis of invasive melanoma and

melanocytic proliferations: observer accuracy and reproducibility study. *BMJ*. 2017;357:j2813.

- 4. Wassberg C, Thörn M, Yuen J, Hakulinen T, Ringborg U. Cancer risk in patients with earlier diagnosis of cutaneous melanoma in situ. *Int J Cancer*. 1999:83(3):314-317.
- 5. Mocellin S, Nitti D. Cutaneous melanoma in situ: translational evidence from a large population-based study. *Oncologist*. 2011;16(6): 896-903
- **6**. Pehamberger H, Steiner A, Wolff K. In vivo epiluminescence microscopy of pigmented skin lesions. I. pattern analysis of pigmented skin lesions. *J Am Acad Dermatol*. 1987;17(4):571-583.
- 7. Steiner A, Pehamberger H, Wolff K. In vivo epiluminescence microscopy of pigmented skin lesions. II. diagnosis of small pigmented skin lesions and early detection of malignant melanoma. *J Am Acad Dermatol.* 1987;17(4):584-591.
- 8. Soyer HP, Smolle J, Kerl H, Stettner H. Early diagnosis of malignant melanoma by surface microscopy. *Lancet*. 1987;2(8562):803.
- **9**. Soyer HP, Smolle J, Hödl S, Pachernegg H, Kerl H. Surface microscopy: a new approach to the diagnosis of cutaneous pigmented tumors. *Am J Dermatopathol*. 1989;11(1):1-10.
- **10**. Luttrell MJ, Hofmann-Wellenhof R, Fink-Puches R, Soyer HP. The AC Rule for melanoma: a simpler

tool for the wider community. *J Am Acad Dermatol*. 2011;65(6):1233-1234.

- 11. Neila J, Soyer HP. Key points in dermoscopy for diagnosis of melanomas, including difficult to diagnose melanomas, on the trunk and extremities. *J Dermatol.* 2011;38(1):3-9.
- 12. Lott JP, Boudreau DM, Barnhill RL, et al. Population-based analysis of histologically confirmed melanocytic proliferations using natural language processing [published online November 1, 2017]. *JAMA Dermatol.* 2017. doi:10.1001/jamadermatol.2017.4060
- **13.** van der Rhee JI, Bergman W, Kukutsch NA. The impact of dermoscopy on the management of pigmented lesions in everyday clinical practice of general dermatologists: a prospective study. *Br J Dermatol.* 2010:162(3):563-567.
- 14. Thomas L, Puig S. Dermoscopy, digital dermoscopy and other diagnostic tools in the early detection of melanoma and follow-up of high-risk skin cancer patients [published online July 5, 2017]. Acta Derm Venereol. doi:10.2340/00015555-2719
- 15. Banky JP, Kelly JW, English DR, Yeatman JM, Dowling JP. Incidence of new and changed nevi and melanomas detected using baseline images and dermoscopy in patients at high risk for melanoma. *Arch Dermatol.* 2005;141(8):998-1006.

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