

## Optimizing Outcomes for Cutaneous Head and Neck Melanoma

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**In this issue,** Moyer and colleagues<sup>1</sup> report long-term follow-up of a large cohort of patients with head and neck melanoma treated with a “square” staged excision technique using permanent sections for comprehensive margin assessment. The median follow-up of 9.3 years demonstrated excellent long-term disease control of 834 lesions with projected local recurrence rate of 2.2% at 10 years. The mean margin required for histologic clearance of tumor was 9.3 mm for melanoma in situ and 13.7 mm for invasive melanoma. The authors demonstrated that lesion size, presence of invasion, and prior incomplete excision were associated with larger surgical margins required for histologic clearance.

Melanoma of the lentigo maligna subtype accounted for nearly 75% of the head and neck melanomas in this series. This is a critical point because melanomas developing in an area of chronic photodamage in the head and neck region present many challenges. Lentigo maligna has had a long, confusing history. It was initially called Hutchinson’s melanotic freckle in the 1800s and felt to be an infectious process. Lentigo maligna is still misconstrued by some as a premalignant lesion. It is now well-recognized as a subtype of melanoma in situ. Once invasion is present, melanoma staging<sup>2</sup> and prognosis are directly related to tumor thickness, similar to other melanomas, with potential for metastasis and death, and should be treated according to current melanoma standards.<sup>3</sup> Following these guidelines, patients in this study underwent sentinel lymph node biopsy if indicated.

It is now well-established, in the dermatologic literature, that standard surgical margins for excision of melanomas on the trunk and extremities are frequently inadequate when applied to melanomas of the head and neck region. This study further supports this finding, because only 25% of melanoma in situ lesions were cleared with a 0.5-cm margin, and only 25% of invasive melanomas were cleared with a 1-cm margin. The National Comprehensive Cancer Network clinical practice guidelines clearly state that for melanomas of the “lentigo maligna type, greater than 0.5 cm may be necessary to achieve histologically negative margins,” and that “exhaustive histologic assessment of margins should be considered.”<sup>3</sup> The surgical treatment of melanoma of the lentigo maligna type has therefore evolved from standard wide excision to staged techniques that allow enhanced margin evaluation and reduce local recurrence. However, there remains debate in the field of dermatologic surgery over the ideal method of margin examination for these challenging melanomas, ranging from per-

manent sections using square, radial,<sup>4</sup> or en face sectioning to Mohs frozen sections. Irrespective of the technique used, dermatologic surgeons must understand the biological and histological nuances of melanomas arising in sun-damaged skin.

Multiple studies have evaluated the efficacy of various staged treatments for melanoma of the lentigo maligna type, but many are limited by small sample sizes with heterogeneous tumor types, variable follow-up duration, and inconsistent statistical analyses that fail to account for patient compliance with dermatologic follow-up. The study by Moyer et al<sup>1</sup> stands out for several reasons. The cohort consisted of 806 patients with 834 melanomas in the head and neck, the largest study to date. The study was allowed to mature, offering extended follow-up (median, 9.3 years, with 75% with 7.3 years) and the sound analytic methods nicely describe the disease process and surveillance methods used by the investigators. The low local recurrence rate confirms that comprehensive margin assessment is necessary. However, it is important to note that local recurrences occur late, with 36% of recurrences developing after 5 years (markedly different from melanoma of other subtypes). In our experience, 4 of 117 local recurrences occurred at a mean of 5.9 years following surgical treatment,<sup>5</sup> and a similar study<sup>6</sup> showed a mean time to local recurrence of 5.1 years.

When considering the reported efficacy of treatments for melanoma in sun-damaged skin, it is important to note how authors define local recurrence. For this melanoma subtype, defining local recurrence can be challenging when differentiating between field damage resulting in multiple primary melanomas vs a true local recurrence. Although there is no accepted standard definition, it is important to critically evaluate studies in this regard. Another issue to consider is whether the margin of clearance matters when treating melanomas in sun-damaged skin. In treatment of high-risk facial basal cell carcinoma with Mohs surgery, we readily accept microns of clearance without apparent associated increased rates of local recurrence. But in head and neck melanomas with trailing melanocytic atypia and potential for skip areas, a narrow margin of clearance could lead to recurrence over the long term. In this study,<sup>1</sup> additional 5-mm margins were excised when margins were involved and when anatomically feasible.

Melanomas arising in severely sun-damaged skin present multiple distinct challenges compared with other melanoma subtypes. Detecting the invasive component preoperatively is not easily achieved because complete excisional biopsies of these large lesions are not always feasible in anatomically sensitive locations. Up to 30% of cases have occult invasion,<sup>7</sup> and final pathologic staging can impact melanoma treatment. In this study, the

median lesion size was 96 mm<sup>2</sup>; the majority of patients presented with in situ melanoma, with invasive lesions having a mean depth of 0.455 mm. Despite microstaging biopsies, unsuspected invasion and melanoma upstaging was still noted in a small percentage of patients, highlighting the importance of permanent section pathology for final tumor staging. Furthermore, a clear definition of histologically clear margins is not straightforward in the setting of trailing melanocytic proliferation and melanocyte hyperplasia. Despite this challenge, in our experience similar to this study, immunostains are not typically needed with permanent sections. Nonetheless, excellent communication between surgeon and pathologist is of paramount importance when using a permanent sectioning technique.

Although 95% of patients in this cohort reported they were satisfied with their final result, a surgical margin close to 1 cm on cosmetically and functionally sensitive locations, such as those on the head and neck, is not insignificant. As newer patient-reported outcomes measures have emerged, such as the FACE-Q,<sup>8</sup> to assess the impact of facial skin cancer treatment on quality of life, studies are needed to better understand the effects of extensive facial surgery. This is particularly relevant for slowly progressive malignant abnormalities such as melanoma of the head and neck in the elderly population with medical comorbidities. On the other hand, with an average age of patients in this study of 65 years, a thoughtful long-term approach is required. In the setting of increased overall life expectancy and patients developing lentigo maligna at an earlier age with a female predominance, patient satisfaction may become an even more critical issue to understand.

As we look to the future, how will we optimize treatment of melanoma in sun-damaged skin in the head and neck region? Can we become more efficient and accurate in assessing these lesions preoperatively and offer targeted treatment paradigms in the new world of personalized medicine? Can topical therapies truly hold promise for long-term cures? To date the gold

standard for assessing the presence or absence of melanoma is histopathologic examination. However, advances in noninvasive imaging techniques may offer innovations to optimize diagnosis. In particular, reflectance confocal microscopy (RCM) provides high resolution real-time in vivo imaging of the skin and has been used to assess skin lesions.<sup>9</sup> This technology has been applied to diagnosis and treatment of melanoma of the lentigo maligna type including selection of scouting biopsy sites, delineating subclinical extent for surgical excision, and monitoring response to nonsurgical treatment in a longitudinal fashion.<sup>10,11</sup> However, the accuracy of RCM imaging in the setting of real-time clinically challenging lesions of lentigo maligna still needs to be validated. Progress along these fronts continues and CMS designated new *Current Procedural Terminology* codes in 2016 for RCM noninvasive imaging (96931-96936).<sup>12</sup>

When evaluating the efficacy of treatments for melanoma in the head and neck region, predominantly of the lentigo maligna type, investigators must consider the many inherent challenges: subtle histologic variations between atypical intraepidermal melanocytic proliferation and more fully developed melanoma, the often long time to local recurrence, and difficulty in distinguishing true local recurrence from a new primary lesion in a background of chronic actinic damage. This well-designed, large study with robust follow-up data reported by Moyer et al<sup>1</sup> addresses many of these issues and provides strong evidence for the efficacy of a staged surgical technique with permanent sections. In the treatment of these melanomas, dermatologists must be the ambassadors in educating our colleagues and other specialties about the specific care that is needed. Additionally, in today's medical environment, delivering effective care while reducing cost is prioritized. As we develop innovative technologies to diagnose melanoma and delineate melanoma margins, reduce the need for reexcision, and optimize techniques to minimize recurrence rates, patient morbidity and health care costs will continue to diminish.

#### ARTICLE INFORMATION

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**Published Online:** December 21, 2016.  
doi:10.1001/jamadermatol.2016.4604

**Conflict of Interest Disclosures:** None reported.

**Additional Contributions:** We thank Stephen Dusza, DrPH, Erica Lee, MD, and Anthony Rossi, MD, Memorial Sloan Kettering Cancer Center Dermatology Service, who shared their expertise and provided valuable feedback for this commentary. They were not compensated for their contributions.

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