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Extent of ulceration in cutaneous melanoma: is this biomarker ready for primetime?

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COMMENTARY

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Extent of ulceration in cutaneous melanoma: is this biomarker ready for primetime?

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After Breslow thickness (BT), the presence or absence of ulceration is the most significant prognostic indicator for primary cutaneous melanoma. For this reason, it forms an integral part of the American Joint Committee on Cancer (AJCC) classification. The presence of ulceration for any AJCC BT category corresponds to a reduced melanoma-specific survival similar to the next-highest tumour thickness category without ulceration.¹ While this is well established, the impact of the extent of ulceration on prognosis is not routinely considered in clinical decision-making. In this issue of the *BJD*, Portelli and colleagues examine the prognostic impact of the extent of ulceration and suggest the inclusion of this as a routine biomarker in histopathology reporting.²

Having robust and reproducible biomarkers in melanoma has become crucial in this new era of effective systemic therapies. Reliable biomarkers enable better decision-making for patients. They aid clinicians in stratifying risk and evaluating the benefits of adjuvant therapy. A reliable biomarker assists in identifying patients at high risk of disease relapse who could derive the most benefit from adjuvant therapy.

Several prognostic markers are routinely used internationally as they have consistent evidence for correlation with disease recurrence and poor survival. These include BT, presence of ulceration and sentinel lymph node status.³ While other factors have shown association with increased risk of recurrence and melanoma-specific survival, they lack consistent evidence as independent prognostic indicators or have limitations in their

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reproducibility. Therefore, factors such as mitotic rate, lymphovascular invasion, tumour-infiltrating lymphocytes and size of sentinel lymph node deposit are not included in the staging system.^{1,4,5}

Numerous studies have shown that the extent of ulceration provides more accurate prognostic information than the mere presence of ulceration.^{6,7} The latest study by Portelli *et al.*² concludes that extent of ulceration is an independent prognostic factor in primary cutaneous melanoma with BT ≤ 2 mm. They identify an extent of ulceration > 2 mm to be significant in patients with melanomas with BT < 2 mm but not for melanomas with BT > 2 mm. Interestingly, this raises the question of whether they have identified that a small extent of ulceration may not carry the prognostic significance that the AJCC 8th edition suggests in T1–2 tumours.

With all of the supporting evidence available on ulceration extent why is it not routinely incorporated into risk stratification? Biomarkers need to be easily reproducible outside of specialist centres. Cases at extremes are straightforward to categorize but borderline cases are not. Pathologists' correct assessment and reporting of parameters relevant for staging is paramount.⁸ To facilitate collaboration, allow accurate analysis of patient data and advance our understanding of the impact of ulceration extent on prognosis, standardization of reporting is needed. This requires both a clear definition of the extent of ulceration and a consensus of reporting that is unambiguous and easily reproducible.

The results of the study by Portelli *et al.* provide further data to support the need for a consensus among pathologists for the reporting of extent of ulceration.² The study also raises intriguing questions around the complex biological mechanisms of how ulceration extent correlates with tumour-related inflammation and host-immune surveillance, which may provide further advances in treatment strategies.

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