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GUEST EDITORIAL

Sentinel Lymph Node Biopsy for Thin Melanoma-Con

MICHAEL S. SABEL, MD*
University of Michigan, Ann Arbor, Michigan

When sentinel lymph node biopsy (SLNB) for the regional staging of melanoma was first introduced, it was recommended for any patient with a melanoma between 1.0 and 4.0 mm in Breslow thickness. Patients with thin melanomas were not felt to have a sufficiently high risk to warrant the additional cost and morbidity of the procedure. As experience grew, several retrospective series identified risk factors beyond Breslow thickness that were associated with an increased risk of regional metastases, and should therefore prompt consideration of SLN biopsy for patients with melanomas shy of 1.0 mm (generally considered to be 0.76–0.99 mm). These were quite varied and included Clark level IV or V, ulceration, mitotic rate (MR), angiolymphatic invasion, and the age of the patient (younger patients having a higher rate of SLN metastases than their older counterparts), with the last three being the most consistent. SLN biopsy is also often recommended for patients with thin melanoma who have significant regression or a positive deep margin, as the true Breslow thickness is often unknown.

When the most recent version of the AJCC staging system for melanoma was released [1], one of the most significant changes was the classification of stage T1b as any melanoma $\leq$1.00 mm with ulceration or a MR of $\geq$1/mm^2. Despite the caveat that ''the AJCC Melanoma Staging Database did not contain sufficient data to assess risk of occult nodal micrometastases in this population,'' many surgeons have advocated extending the indications for SLNB to include any T1b melanoma. This would include any melanoma $<$0.76 mm with a MR of at least 1/mm^2. However, this is not an accurate interpretation of the data. One might assume that the majority of these patients recur regionally first, then distally, and survival may be impacted because of regional recurrence. However, recent data suggests that this is not true; T1b status does not impact regional recurrence but does increase the likelihood of distant recurrence [2]. These data support the new AJCC staging system for prognostication, but not for selection for SLNB.

So should SLN biopsy be performed for patients with T1b melanoma? As with most debates in medicine, most of the controversy centers on the semantics. Are there some patients with T1b melanomas who require SLN biopsy? Absolutely, this has never been in debate, as discussed above. So the real controversy centers on two questions:

1 What is the risk of identifying regional disease in patients with melanoma $<$0.76 mm?
2 Among these patients, does a MR of $\geq$1/mm^2 sufficiently increase risk to justify the procedure?

Regarding the risk of regional disease for patients with melanomas $<$1.00 mm, most of the data comes from retrospective series where patients routinely had SLNB for melanoma $\geq$1.00 mm (or $>$0.75 mm in some series) and selectively had SLNB for thinner melanomas. Estimated risks for melanomas $\leq$0.75 mm are based on extrapolations from statistical models. However, a careful analysis of papers advocating SLNB for thin melanomas show most if not all potential benefit is limited to patients with melanomas between 0.76 and 0.99 mm, the group for whom we currently recommend consideration. Retrospective series consistently show a SLN positivity rate of less than 2–3% for melanoma $<$0.75 mm [3]. As these patients were already specifically selected for SLNB based on adverse features, this may over-estimate the risk among the entire T1b population.

Performing SLNB even for intermediate thickness melanoma remains slightly controversial, as the Multicenter Selective Lymphadenectomy Trial-1 (MSLT-1) has yet to demonstrate an overall survival benefit to the addition of SLNB to wide excision of intermediate-thickness (1.2–3.5 mm) melanoma.[4] This is primarily because any potential benefit is limited to the node positive population (16% in the MSLT-I trial) and subset analysis suggests the benefit is only around 10–15%. With a decreasing likelihood of finding regional metastases, the absolute benefit of the procedure also decreases, and the risk-benefit ratio tilts significantly more towards risk. As the addition of SLNB to wide excision significantly increases both the costs and the morbidity, it is difficult to justify the use of SLN biopsy in patients with melanoma $\leq$0.75 mm [5–7].

The second question centers on whether a MR of 1/mm^2 or greater justifies performing SLN biopsy. A cut-off of $<$1 and $\geq$1 mm^2 clearly discriminates between patients with a worse outcome, but does not necessarily identify a group of patients with thin melanoma who harbor a sufficient risk of regional disease [1,2]. While MR is associated with the risk of finding a positive SLN, it is best considered as a continuous variable, and the impact of MR on risk varies with both age and Breslow thickness [8–10]. The contribution of MR as an adverse risk factor when selecting patients with thin melanoma for SLN biopsy must not only be based on the value (as opposed to simply $<$1 or $\geq$1) but also in the context of increasing age and decreasing Breslow thickness. While they are both staged as T1b, the recommendations for SLN biopsy should be not be the same for a 65-year old patient with a 0.6 mm melanoma and a MR of 2 compared with a 33-year old patient with a 0.6 mm melanoma and a MR of 12.

*Correspondence to: Dr. Michael S. Sabel, MD, 3304 Cancer Center, 1500 East Medical Center Drive, Ann Arbor, MI 48109. Fax: 734-647-9647. E-mail: msabel@umich.edu

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Data from large national databases suggest that SLNB is only being utilized in a fraction of patients with intermediate-thickness melanoma, those patients most likely to benefit from the procedure [11,12]. At this time, our efforts and resources are better spent addressing the utilization of SLNB among this population. In addition, we should continue our attempts to identify clinical, molecular, or proteomic markers associated with a sufficient risk of regional metastases among patients with melanomas <0.75 mm so as to identify a subset who should be offered the procedure. Until that time, the standard recommendations for SLNB (melanoma ≥ 1 or 0.76–0.99 mm with adverse features) should not be extended to include all T1b patients.

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