Ann Surg Oncol (2021) 28:3449–3451
https://doi.org/10.1245/s10434-021-10038-6

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

EDITORIAL – MELANOMA

Sentinel Lymph Node Biopsy for Thin Melanoma—Some Need It, Some Don't. So Now What?

Michael E. Egger, MD, MPH, FACS, FSSO

Hiram C Polk, Jr, MD, Department of Surgery, Division of Surgical Oncology, University of Louisville, Louisville, KY

Having lost limb perfusions, metastasectomies, and lymph node dissections to immunotherapy, intralesional therapies, and targeted therapies, melanoma surgeons are now forced to ponder the relevance of the last great melanoma operation—sentinel lymph node biopsy (SLNB). If we are not careful, we may lose this operation to gene expression profiling, but until that happens, we should continue to evaluate its appropriate use. Selectively applied, the SLNB procedure has the power to risk-stratify patients, provide reassurance and comfort to the anxious and afraid, and to provide a path forward for surveillance and treatment for those with stage III disease. However, we run the risk of overusing SLNB if we apply it indiscriminately to patients with a very low likelihood of benefiting from the operation. We may collectively be doing just that in patients with thin ($\leq$1.0 mm thick) melanoma. Having demonstrated the safety and efficacy of the operation, we must now pay the piper and justify its use from an economic standpoint for patients with thin melanoma. We have ample evidence in the literature to predict the risk of a positive SLNB in these patients based on clinical and pathologic information. Now we must take a stand and choose a risk cut-off at which point we should recommend an SLNB. In doing so, we will promote responsible stewardship of the last great melanoma operation and benefit patients by doing so.

First Received: 24 March 2021
Accepted: 3 April 2021;
Published Online: 22 April 2021

M. E. Egger, MD, MPH, FACS, FSSO
e-mail: michael.egger@louisville.edu

The article by Herb et al. in this edition of *Annals of Surgical Oncology* provides some valuable data to help us critically assess how we are using SLNB in low-risk, thin melanoma patients[1]. Using the surveillance, epidemiology, and end results (SEER) data, Herb et al. take a 30,000 foot, population-level view of American Joint Committee on Cancer (AJCC) 8th edition T1b melanoma patients without ulceration (thickness 0.8–1.0 mm), and report that half of these patients undergo an SLNB. Overall, the SLNB positivity rate is 4.1% in this group. The usual suspects predict higher rates of positive SLNB: younger age, presence of mitoses, sex, and truncal tumor location. The authors then apply a rudimentary cost analysis, using the Medicare reimbursement fee schedule, to compare the cost difference between a wide local excision under local anesthesia and a wide local excision under general anesthesia with an SLNB. Unsurprisingly, the addition of an SLNB adds significant cost to a simple wide local excision. Herb et al. provide a range of numbers needed to biopsy to find a positive node and the Medicare costs needed to identify a positive node. Depending on the risk factors, one may need to perform anywhere from over 40 SLNBs to a dozen or so to identify a positive SLN.

The authors correctly point out the potential benefit of using population-based SEER data over hospital-based registries such as the National Cancer Database (NCDB). They correctly suggest that papers (including one from your humble editorial writer) that have used the NCDB to estimate the risk of a positive SLNB in thin melanoma are likely providing an overestimate of the overall risk of SLNB in all thin melanoma patients[2–4]. However, studies such as this one and others, regardless of whether they use institutional data, NCDB data, or SEER data, provide us with risk factors by which we can select high- or low-risk patients for *selective* use of SLNB in thin melanoma patients. The point of these papers is that we need a more

nuanced approach to selecting SLNB in patients with thin melanoma. Herb et al. argue this in their conclusion, stating that selective use of SLNB in thin melanoma patients is warranted. I hope readers were able to see the Great Debate at the most recent SSO 2020—International Conference on Surgical Cancer Care, in which Drs. Mark Faries and Jonathan Zager argued this very point to a draw. Yes, some should get it, some should not. But who? We need to decide. This question is important because as the long-term follow-up data from the Melanoma Institute Australia have shown us, a disturbing number of T1 melanoma patients die of melanoma when followed for several decades[5].

What this paper and others have clearly demonstrated is that we cannot rely on the AJCC staging system, which is designed to predict long-term survival, to tell us when to do an SLNB. We must make our decision based on the risk of a positive SLN. We are dancing around the 5% risk of a positive SLN as a cut-off, as promoted in the National Comprehensive Cancer Network (NCCN) guidelines[6]. But is 5% the right number? Only a more formal economic evaluation, complete with the costs of diagnosis and treatments based on false positives, false negatives, extensive surveillance imaging, and potential adjuvant immunotherapy can help answer this question. Herb et al. take a stab at this question but leave me wanting more. What is the appropriate number needed to biopsy to find a positive SLN? What is the acceptable cost to a health system to identify a stage IIIA melanoma in a population that usually consists of young, healthy patients with thin melanoma? In this study, a female patient with > 1 mitosis per mm^2 who is younger than 50 years of age and has a truncal melanoma has a risk of a positive SLNB of 17%. This results in a number needed to biopsy of approximately 6, and a cost to the system of somewhere between $12,000 and $18,000 per positive lymph node. Is that low enough? I think most of us would perform an SLNB on that patient every day of the week and twice on Sunday, even if (heaven forbid) one must do a peer-to-peer call with the insurance company. Some studies have attempted to answer these questions but more work is needed[7–9]. We have plenty of data now to predict the rate of a positive SLNB in these patients, based on age, mitoses, and whatever other factors you choose. If we can then determine the cut-off for SLN positivity, we will be well on our way to responsible use of SLNB in thin melanoma patients.

How do we value the peace of mind that comes with a negative SLNB in these patients? This point was raised by Dr. Faries in the SSO Great Debates: there is tremendous value to the patient's well-being when a negative SLNB is obtained. Is that worth $2800, or the out-of-pocket expense of $500–$600? I would argue (without consulting the Medicare fee schedule) that more cost-effective peace of mind may be achieved with a negative SLNB than with extensive positron emission tomography (PET) scan imaging, genetic profiling, and surveillance imaging—yet another paper that needs to be written. On the contrary, consider the peace of mind of the surgeon (and the anesthesiologist) when the elderly patient comes into your office in her wheelchair, right after her coumadin clinic appointment, but before she goes to her dialysis appointment. I can rest easy that night after telling her that her 0.8 mm melanoma with no mitoses with a 3% chance of a positive SLN will be managed just fine with a simple wide local excision under local anesthesia, thank you very much. I imagine she rests easy as well.

How do I approach SLNB for non-ulcerated T1b melanoma patients? I have a copy of our algorithm printed off in the clinic[4]. If the patient has a mitotic rate of 0, I do not offer an SLNB. For young patients (≤ 50 years of age) with a mitotic rate of at least $1/mm^2$, I offer an SLNB. If they have a thickness of 1.0 mm with mitoses, then I offer an SLNB. If they are aged ≥ 60 years with mitoses but have only a 0.8–0.9 mm-thick primary, then I favor omitting an SLNB, unless we reach the conclusion together that they prefer an SLNB.

We must answer these questions of utility and cost effectiveness with regard to SLNB in thin melanoma patients. These are the majority of patients I see in practice now. Step one has been developing predictive models to estimate a patient's risk of a positive SLNB. This has been accomplished and Herb et al. have added to the literature in a meaningful way regarding this question. The next step is to partner with our medical decision-making scientists and economist colleagues to determine where we should draw the line for these patients to recommend an SLNB.

FUNDING Research support was received from SkylineDX and the authors entered into a consultancy agreement with Iovance Biotherapeutics

REFERENCES

1. Herb JN, Olila DW, Sititzenberg KB, Meyers MO. Use and costs of sentinel lymph node biopsy in non-ulcerated T1b melanoma: analysis of a population based registry. *Ann Surg Oncol*. 2021;239:S279-80.
2. Sinnamon AJ, Neuwirth MG, Yalamanchi P, et al. Association between patient age and lymph node positivity in thin melanoma. *JAMA Dermatol*. 2017;153:866–73.
3. Sinnamon AJ, Gimotty PA, Karakousis GC, Yang YX. Survival outcomes following lymph node biopsy in thin melanoma—a propensity-matched analysis. *Ann Surg Oncol*. 2021;28:1634–41.
4. Egger ME, Stevenson M, Bhutiani N, Jordan AC, Scoggins CR, Philips P, et al. Should sentinel lymph node biopsy be performed for all T1b melanomas in the new 8(th) Edition American Joint Committee on Cancer Staging System? *J Am Coll Surg*. 2019;228:466–72.
5. Lo SN, Scolyer RA, Thompson JF. Long-term survival of patients with thin (T1) cutaneous melanomas: a breslow thickness cut point

of 0.8 mm separates higher-risk and lower-risk tumors. *Ann Surg Oncol*. 2018;25:894–02.
6. Cutaneous Melanoma (Version 1.2019). Available at: https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf. Accessed 20 Nov 2018
7. Agnese DM, Abdessalam SF, Burak WE Jr, Magro CM, Pozderac RV, Walker MJ. Cost-effectiveness of sentinel lymph node biopsy in thin melanomas. *Surgery*. 2003;134:542–7.
8. Hu Y, Briggs A, Gennarelli RL, Bartlett EK, Ariyan CE, Coit DG, et al. Sentinel lymph node biopsy for t1b melanoma: balancing prognostic value and cost. *Ann Surg Oncol*. 2020;27:5248–56.
9. Serra-Arbeloa P, Rabines-Juárez ÁO, Álvarez-Ruiz MS, Guillén-Grima F. Sentinel node biopsy in patients with primary cutaneous melanoma of any thickness: a cost-effectiveness analysis. *Surg Oncol*. 2016;25:205–11.