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Localization of the sentinel lymph node in melanoma without blue dye

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INTRODUCTION

Since its original description in 1992, sentinel lymph node biopsy (SLNB) has become a vital component of the staging protocol for melanoma.¹ More than any patient demographic or tumor characteristic, the most powerful prognostic indicator in early-stage melanoma is the status of the sentinel node.² Sentinel node localization in melanoma was originally described using vital dyes to permit intraoperative mapping. Using this technique alone, node localization rates ranged from 52% to 95%.³ By the late 1990's, the addition of radiolabeled colloids led to localization rates of 98–99%.^{4–8} Within this body of work, radiocolloid guidance alone had a sentinel node localization failure rate of 2–5%, indicating a continuing role for blue dye.^{7, 9}

Over the past decade, there has been mounting evidence that visual localization using blue dye may not confer a clinically-meaningful benefit over radioguidance alone.^{10–13} In the setting of breast cancer, compared with radioguidance alone, the combined modality of blue dye plus radioguidance confers only a 2% localization rate advantage.^{14, 15} Juxtaposed against this marginal benefit are rare but potentially serious adverse events associated with blue dye, including prolonged cutaneous staining,³ skin reactions, and anaphylaxis rates ranging from 0.1–2.7%.^{16–19} Finally, because Medicare does not allow for separate reporting of vital dye injection for reimbursement, its routine use may also incur unnecessary costs to the provider.

Whether the increased sentinel node localization rate conferred by blue dye results in clinically-meaningful benefit is unclear. The purpose of this study is to report recurrence outcomes among patients with melanoma who undergo SLNB without blue dye. We hypothesized that SLNB with radioguidance alone would result in node positivity and regional recurrence rates that are comparable to existing reports of combination localization modalities.

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METHODS

We conducted a retrospective review of a prospectively-collected database of consecutive patients with primarily trunk and extremity melanoma who underwent SLNB from January 2005 to December 2008 for primary cutaneous melanoma at our institution. During this period, patients received SLNB if their primary cancer had a Breslow thickness of ≥ 1.0 mm, Clarks level ≥ 4 , had high-risk characteristics such as ulceration, or had a positive deep margin on shave biopsy. Between 2005–2007, selected patients with thin melanomas (< 1.0 mm) with regression also were offered SLNB.²⁰ Following surgery, patients underwent follow-up visits every 4–12 months (depending on overall risk) during the first 2 years, every 6–12 months to year 5, then annually thereafter. Patients were identified from a prospectively collected clinical database approved for research use (IRB #10803). For all patients, data were accrued on demographics, cancer characteristics, length of follow-up, pathology results, and recurrence outcomes. Operative characteristics, including node and background radioactivity counts, were determined by retrospective chart review.

Patients received preoperative lymphoscintigraphy using Technetium 99m-labeled sulfur radiocolloid injected intradermally at the site of prior biopsy on the morning of surgery or the afternoon of the prior day. Lymphoscintigraphy images were made available to the surgeon in order to determine the surgical approach to regional lymphatic drainage basins. Intraoperatively, a hand-held gamma probe was used to guide the placement of biopsy incisions and to localize radioactive nodes. For each excised node, an ex vivo radioactivity count was recorded. Biopsy criteria followed the 10% guideline, meaning nodes were excised until the resection bed contained a residual radioactivity level less than 10% that of the “hottest” node removed. The removed nodes were considered to be the sentinel nodes within the dissected basin. Two patients did not receive preoperative lymphoscintigraphy imaging due to scheduling difficulties. Two additional patients received preoperative lymphoscintigraphy, but no lymphatic drainage was visualized on preoperative images. These patients’ operations were guided solely by intraoperative localization using the gamma probe. For two more patients, the gamma probe was not available upon incision, thus, intradermal injection of 1.5 mL lymphazurin blue dye was used for visual localization of sentinel nodes. These two were the only patients who received blue dye guidance over the study period. However, for both patients, the gamma probe became available at the time of node extraction, and nodes were removed based on radioactive criteria. For 33 out of 215 patients (15.3%), the 10% criterion for residual bed radioactivity was not satisfied, despite diligent dissection.

Following removal, all excised sentinel nodes were submitted for pathologic analysis: each node was serially partitioned into sections 1 mm thick. Sections were examined using hematoxylin and eosin (H&E) staining. Immunohistochemistry (IHC) using antibodies to MART-1/Melan A, S-100, Tyrosinase, or gp100 (HMB45) was performed at the discretion of the supervising dermatopathologist. Patients who had a tumor-positive sentinel lymph node were offered completion lymphadenectomy. We defined a false-negative outcome as recurrence in a nodal basin which was previously negative for metastases during the original SLNB (regional recurrence). Recurrences within 5 cm of the primary cancer site were

considered local, while those located between the excision site and the mapped nodal basin were considered in-transit.

For statistical analyses, Breslow depth was discretized to ≤ 2 mm and > 2 mm based on the American Joint Committee on Cancer (AJCC) staging system, and mitotic rate was discretized based on sample median. To determine clinical and pathologic factors associated with overall survival and recurrence of any type, univariate analyses were performed using the Fisher's exact test for categorical variables. Multivariate analysis using logistic regression was performed for factors associated with recurrence on univariate analysis. Kaplan-Meier curves and the log-rank test for significance are used to show recurrence-free survival. Multivariate analyses for overall survival were not performed due to a low rate of death ($N=27$). For all statistical analyses, p -values < 0.05 were considered significant, and calculations were performed using SAS statistical software (version 9.3; SAS Institute, Inc). This study was approved by the University of Virginia Institutional Review Board (IRB-HSR protocol #17273).

RESULTS

A total of 215 patients were included in the analysis. Clinicopathologic characteristics of the patient population are shown in Table 1. Median length of follow-up was 4.2 years (interquartile range, IQR 1.2 – 6.1). Median Breslow thickness was 1.56 mm (IQR 1.01 – 2.57). The majority of primary cancers were located on the trunk (51.6%, 111/215).

One or more sentinel nodes was excised from every targeted lymphatic basin (100% success at node localization), totaling 545 nodes removed from 279 basins (Table 2). An average of 2 nodes were removed per basin (IQR 1 – 3). Forty patients had at least one sentinel node positive for metastasis (18.6%). Of these, 32 (80%) subsequently underwent completion lymphadenectomy, 7 (22%) of which yielded additional positive nodes.

Overall, 44 patients (20.5%) experienced recurrence after a median of 1.9 years (IQR 0.87 – 2.9). Under univariate analysis, cancer recurrence was significantly associated with Breslow depth > 2 mm, Clark level ≥ 4 , mitotic rate > 2 per mm^2 , and positive SLNB (Table 3). Residual counts exceeding 10% of the count of the hottest node was not associated with recurrence at the univariate level. After incorporating significant risk factors from the univariate model into a logistic multivariate model, only mitotic rate and Breslow depth were significantly associated with cancer recurrence (Figure 1). Analyses were also repeated treating Breslow depth and mitotic rate as continuous variables, in which case both factors were significant predictors of recurrence at the univariate level, but only mitotic rate proved significant on multivariate analysis (data not shown). Over the study period, the mortality rate was 12.6% (27/215), with a 3-year survival rate of 83%. The only risk factor significantly associated with overall mortality at the univariate level was positive SLNB status (38.2% vs 8.3%, $p < 0.001$).

Recurrences occurred in 20% (35/175) of patients who had a negative SLNB result. These included 2 local, 8 in-transit, and 19 distant recurrences. There were 6 (3.4%) regional node recurrences, which were considered false negatives. Three of these occurred in axillary

basins, while the other 3 were in groin basins. Thus, the negative predictive value of SLNB was 96.6% (169/175), and the false negative rate was 13.0% (6/(40+6)). Six patients presented with recurrence in more than one location.

During surgery, the residual radioactivity count in the node basin was less than 10% of the count of the hottest sentinel node for 246/279 basins (88%). Thirty-three basins did not satisfy the 10% guideline (12%); the most commonly-cited reason within operative records was risk of injury to adjacent structures (nerves, vasculature) with further dissection, in the setting of having removed the dominant hot node(s) identified by lymphoscintigraphy. The distribution of these basins was similar to the overall distribution of the study: 17 axillary basins (51.5%), 9 groin basins (27.3%), 3 head and neck basins (9.1%), and 4 other basins. None of the patients in this subgroup experienced regional recurrence.

DISCUSSION

To maximize success rate and to minimize false negatives, SLNB is traditionally performed using a combination of radiocolloid and visual localization with a vital blue dye. This study demonstrates that SLNB performed using radiocolloid guidance alone may result in a high biopsy success rate and negative predictive value. By excluding blue dye from the operation, providers can avoid skin complications and rare but serious allergic reactions. Although anaphylactic reactions can be easily managed under general anesthesia, omitting blue dye may support SLNB under local anesthesia, which offers advantages in cost and safety.^{21, 22}

The recurrence patterns within our results are concordant with several collections of multi-institutional data. Early work by Gershenwald, et al noted a regional recurrence rate of 5.8% in a population that closely resembles our dataset, with a 16% positive sentinel node rate and median Breslow thickness of 1.6 mm.²³ More recently, the Sunbelt Melanoma Trial, the Multicenter Selective Lymphadenectomy Trial and others have reported regional recurrence rates in previously negative node basins ranging from 2.7% to 4.8%.^{24–27} These studies involve strict protocols that dictate combination localization techniques. Our data showing a regional recurrence rate of 3.4% demonstrate that comparable sampling accuracy is attainable without the additional cost and risk of blue dye.

Several works have scrutinized the expected utility of blue dye localization in the setting of melanoma. As early as 2004, Gipponi reported that, among 126 patients receiving a combination localization protocol, blue dye did not confer additional localization benefit to radio-guidance.¹⁰ With a similar combination protocol involving a newer radiocolloid, Sondak and colleagues reported a 100% detection rate of tumor-positive sentinel nodes by radioguidance, compared to 80% by blue dye.¹³ In a larger retrospective study, Liu, et al compared radiocolloid alone (n=581) to radiocolloid plus blue dye (n=571). The miss-rate of positive sentinel nodes were 2% and 1% in these two groups, respectively (p = 0.56). The authors concluded that there is no significant impact of adding blue dye in terms of the identification of sentinel nodes or in the miss-rate of positive nodes.¹¹ Surgeons in that study adopted the radiocolloid-only technique as they became more comfortable with it; however, that study did not address clinical outcomes. An early large multicenter trial of sentinel node biopsy, in which we participated, reported recurrence outcomes with radiocolloid with or

without blue dye, but did not focus on the long term outcomes without blue dye.¹² To our knowledge, no study has reported clinical results of adopting a radioguidance-only biopsy protocol. The results from our study corroborate existing data, and support our hypothesis that, among experienced surgeons, biopsy using radiocolloid alone yields regional recurrence rates comparable to established reports using both radiocolloid and blue dye.

There may be indications, however, for using blue dye in select patients. When a gamma probe is unavailable, blue dye localization is superior to no guidance. Combined localization could also potentially reduce operative duration by facilitating visualization. Finally, when complex anatomy is anticipated, particularly for previously-dissected or irradiated basins within the head and neck, blue dye or SpectCT imaging may help focus the dissection and reduce risk of nearby injury. More recently, near-infrared fluorescence imaging has emerged as an attractive alternative to blue dye for real-time visual localization of sentinel nodes within surrounding anatomy. Much like blue dye, fluorescence imaging is best used in conjunction radiocolloid localization due to tissue attenuation of signal. Fluorescence imaging is relatively inexpensive compared to isosulfan blue, and has not been reported to cause anaphylaxis.²⁸ Recent reports suggest that its accuracy in sentinel node detection is 88%–97% within a variety of nodal basins, superior to that of isosulfan blue.^{29–31} As this innovative technology continues to be explored, we anticipate that its implementation will especially benefit providers who frequently perform SLNB for head and neck melanomas and those who perform SLNB at lower volumes.

A randomized prospective trial would be needed to test the added value of blue dye definitively, but this is not likely to be performed. As a single-institution non-randomized case series, this study has inherent limitations. First, routine performance of IHC may increase detection of micrometastases. However, serial sectioning through the node is expected also to add value over bivalving the node. In this setting, the added utility of IHC over H&E staining and optional IHC is not known, and is an area of interest for future study.^{32, 33} Furthermore, criteria for offering SLNB were fluid over our study period as pervading evidence regarding the prognostic value of regression and Clark level continued to mature.^{20, 34} Our multivariate analysis assessing for predictors of recurrence was limited by study size to four risk factors. We found that tumor thickness and mitotic rate are associated with recurrence, in concordance with prior studies.^{35–37} It is therefore relevant that our study population's median Breslow thickness (1.56 mm) is slightly lower than those in recent trials incorporating blue dye and radiocolloid localization, which have ranged from 1.6–1.8 mm.^{26, 27, 36} Although positive SLNB status was strongly associated with recurrence on univariate analysis, the association was not significant after accounting for mitotic rate and Breslow depth. Despite this, SLNB status was predictive of overall survival, and we anticipate that in larger datasets, the capacity of SLNB to predict recurrence would likely prove significant. Finally, 11.8% (33/279) of the biopsied basins in our study had residual radioactivity greater than 10% that of the hottest node. Our protocol is to follow the 10% guideline, but with exceptions when the residual bed count appeared to represent non-sentinel secondary nodes and all hot spots seen on lymphoscintigraphy had been accounted for,³⁸ especially when the residual bed counts are very close to 10%. Within our study, no patient whose operation violated the 10% guideline developed regional recurrence.

However, abiding by this guideline can reduce the false negative rate associated with SLNB,^{11, 39} and we do not recommend routine indifference toward this important guideline.

Although most reports of sentinel lymph node biopsy employ combined radioguidance and visual localization, radioguidance alone yields a high sentinel node sampling rate. Our regional recurrence rate in node-negative basins is in the range that has been reported in other large studies with blue dye plus radiocolloid. Blue dye is visible through thin layers of tissue, but not through the skin or deep in node-bearing basins. Also, radiocolloid, but not blue dye, is retained in the sentinel nodes for many hours, and can be reliably detected over time. Isosulfan blue can cause anaphylaxis, and carries added costs; thus, successful localization without it can be advantageous for the patient and for the health system. Prior reports show that blue dye does not increase detection of tumor positive nodes.^{10,11} The present report corroborates those findings and presents supportive clinical outcomes data. By forgoing blue dye guidance, experienced surgeons may anticipate reliable nodal sampling while avoiding unnecessary costs and risks.

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ABBREVIATION LIST

AJCC	American Joint Committee on Cancer
IHC	immunohistochemistry
IQR	interquartile range
SLNB	sentinel lymph node biopsy

References

1. Morton DL, Wen DR, Wong JH, et al. Technical details of intraoperative lymphatic mapping for early stage melanoma. *Arch Surg.* 1992; 127:392–399. [PubMed: 1558490]
2. Balch CM, Soong SJ, Gershenwald JE, et al. Prognostic factors analysis of 17,600 melanoma patients: validation of the American Joint Committee on Cancer melanoma staging system. *J Clin Oncol.* 2001; 19:3622–3634. [PubMed: 11504744]
3. Ariyan S, Ariyan C, Farber LR, et al. Reliability of identification of 655 sentinel lymph nodes in 263 consecutive patients with malignant melanoma. *J Am Coll Surg.* 2004; 198:924–932. [PubMed: 15194074]
4. Bartolomei M, Testori A, Chinol M, et al. Sentinel node localization in cutaneous melanoma: lymphoscintigraphy with colloids and antibody fragments versus blue dye mapping. *Eur J Nucl Med.* 1998; 25:1489–1494. [PubMed: 9799344]
5. Kapteijn BA, Nieweg OE, Liem I, et al. Localizing the sentinel node in cutaneous melanoma: gamma probe detection versus blue dye. *Ann Surg Oncol.* 1997; 4:156–160. [PubMed: 9084853]
6. Landi G, Polverelli M, Moscatelli G, et al. Sentinel lymph node biopsy in patients with primary cutaneous melanoma: study of 455 cases. *J Eur Acad Dermatol Venereol.* 2000; 14:35–45. [PubMed: 10877250]
7. Gesuelli GC, Sartelli M, Berbellini A, et al. Sentinel lymph node identification in the staging of cutaneous melanoma. Blue dye vs. radioguided localization. *Minerva Chir.* 2000; 55:513–516. [PubMed: 11140105]

8. Kretschmer L, Peeters S, Beckmann I, et al. Intraoperative detection of sentinel lymph nodes in cutaneous malignant melanoma -- blue dye alone versus blue dye plus gamma detection. *J Dtsch Dermatol Ges.* 2005; 3:615–622. [PubMed: 16033480]
9. Villa G, Agnese G, Bianchi P, et al. Mapping the sentinel lymph node in malignant melanoma by blue dye, lymphoscintigraphy and intraoperative gamma probe. *Tumori.* 2000; 86:343–345. [PubMed: 11016724]
10. Gipponi M, Di Somma C, Peressini A, et al. Sentinel lymph node biopsy in patients with Stage I/II melanoma: Clinical experience and literature review. *J Surg Oncol.* 2004; 85:133–140. [PubMed: 14991885]
11. Liu LC, Parrett BM, Jenkins T, et al. Selective sentinel lymph node dissection for melanoma: importance of harvesting nodes with lower radioactive counts without the need for blue dye. *Ann Surg Oncol.* 2011; 18:2919–2924. [PubMed: 21468784]
12. Harlow SP, Krag DN, Ashikaga T, et al. Gamma probe guided biopsy of the sentinel node in malignant melanoma: a multicentre study. *Melanoma Res.* 2001; 11:45–55. [PubMed: 11254115]
13. Sondak VK, King DW, Zager JS, et al. Combined analysis of phase III trials evaluating [(9)(9)mTc]tilmanocept and vital blue dye for identification of sentinel lymph nodes in clinically node-negative cutaneous melanoma. *Ann Surg Oncol.* 2013; 20:680–688. [PubMed: 23054107]
14. Kim T, Giuliano AE, Lyman GH. Lymphatic mapping and sentinel lymph node biopsy in early-stage breast carcinoma: a metaanalysis. *Cancer.* 2006; 106:4–16. [PubMed: 16329134]
15. Bines S, Kopkash K, Ali A, et al. The use of radioisotope combined with isosulfan Blue dye is not superior to radioisotope alone for the identification of sentinel lymph nodes in patients with breast cancer. *Surgery.* 2008; 144:606–9. discussion 609–10. [PubMed: 18847645]
16. Bezu C, Coutant C, Salengro A, et al. Anaphylactic response to blue dye during sentinel lymph node biopsy. *Surg Oncol.* 2011; 20:e55–9. [PubMed: 21074413]
17. Clarke SA, Molajo A, Powell BW. Incidence of adverse reactions to patent blue dye in melanoma sentinel node biopsy: a major UK centre experience. *J Plast Reconstr Aesthet Surg.* 2013; 66:1299–1300. [PubMed: 23582508]
18. Leong SP, Donegan E, Heffernon W, et al. Adverse reactions to isosulfan blue during selective sentinel lymph node dissection in melanoma. *Ann Surg Oncol.* 2000; 7:361–366. [PubMed: 10864344]
19. Mansel RE, Fallowfield L, Kissin M, et al. Randomized multicenter trial of sentinel node biopsy versus standard axillary treatment in operable breast cancer: the ALMANAC Trial. *J Natl Cancer Inst.* 2006; 98:599–609. [PubMed: 16670385]
20. McClain SE, Shada AL, Barry M, et al. Outcome of sentinel lymph node biopsy and prognostic implications of regression in thin malignant melanoma. *Melanoma Res.* 2012; 22:302–309. [PubMed: 22610274]
21. Luini A, Gatti G, Frasson A, et al. Sentinel lymph node biopsy performed with local anesthesia in patients with early-stage breast carcinoma. *Arch Surg.* 2002; 137:1157–1160. [PubMed: 12361425]
22. Covarelli P, Badolato M, Tomassini GM, et al. Sentinel lymph node biopsy under local anaesthesia versus general anaesthesia: reliability and cost-effectiveness analysis in 153 patients with malignant melanoma. *In Vivo.* 2012; 26:315–318. [PubMed: 22351676]
23. Gershenwald JE, Tseng CH, Thompson W, et al. Improved sentinel lymph node localization in patients with primary melanoma with the use of radiolabeled colloid. *Surgery.* 1998; 124:203–210. [PubMed: 9706139]
24. Carlson GW, Page AJ, Cohen C, et al. Regional recurrence after negative sentinel lymph node biopsy for melanoma. *Ann Surg.* 2008; 248:378–386. [PubMed: 18791358]
25. Leong SP, Kashani-Sabet M, Desmond RA, et al. Clinical significance of occult metastatic melanoma in sentinel lymph nodes and other high-risk factors based on long-term follow-up. *World J Surg.* 2005; 29:683–691. [PubMed: 15895193]
26. Morton DL, Thompson JF, Cochran AJ, et al. Final trial report of sentinel-node biopsy versus nodal observation in melanoma. *N Engl J Med.* 2014; 370:599–609. [PubMed: 24521106]
27. Scoggins CR, Martin RC, Ross MI, et al. Factors associated with false-negative sentinel lymph node biopsy in melanoma patients. *Ann Surg Oncol.* 2010; 17:709–717. [PubMed: 19967459]

28. Gilmore DM, Khullar OV, Gioux S, et al. Effective low-dose escalation of indocyanine green for near-infrared fluorescent sentinel lymph node mapping in melanoma. *Ann Surg Oncol*. 2013; 20:2357–2363. [PubMed: 23440551]
29. Brouwer OR, Buckle T, Vermeeren L, et al. Comparing the hybrid fluorescent-radioactive tracer indocyanine green-99mTc-nanocolloid with 99mTc-nanocolloid for sentinel node identification: a validation study using lymphoscintigraphy and SPECT/CT. *J Nucl Med*. 2012; 53:1034–1040. [PubMed: 22645297]
30. Cloyd JM, Wapnir IL, Read BM, et al. Indocyanine green and fluorescence lymphangiography for sentinel lymph node identification in cutaneous melanoma. *J Surg Oncol*. 2014; 110:888–892. [PubMed: 25124992]
31. van den Berg NS, Brouwer OR, Schaafsma BE, et al. Multimodal Surgical Guidance during Sentinel Node Biopsy for Melanoma: Combined Gamma Tracing and Fluorescence Imaging of the Sentinel Node through Use of the Hybrid Tracer Indocyanine Green-Tc-Nanocolloid. *Radiology*. 2014:140322.
32. Gibbs JF, Huang PP, Zhang PJ, et al. Accuracy of pathologic techniques for the diagnosis of metastatic melanoma in sentinel lymph nodes. *Ann Surg Oncol*. 1999; 6:699–704. [PubMed: 10560857]
33. Messina JL, Glass LF, Cruse CW, et al. Pathologic examination of the sentinel lymph node in malignant melanoma. *Am J Surg Pathol*. 1999; 23:686–690. [PubMed: 10366151]
34. Balch CM, Gershenwald JE, Soong SJ, et al. Final version of 2009 AJCC melanoma staging and classification. *J Clin Oncol*. 2009; 27:6199–6206. [PubMed: 19917835]
35. Azzola MF, Shaw HM, Thompson JF, et al. Tumor mitotic rate is a more powerful prognostic indicator than ulceration in patients with primary cutaneous melanoma: an analysis of 3661 patients from a single center. *Cancer*. 2003; 97:1488–1498. [PubMed: 12627514]
36. Gershenwald JE, Thompson W, Mansfield PF, et al. Multi-institutional melanoma lymphatic mapping experience: the prognostic value of sentinel lymph node status in 612 stage I or II melanoma patients. *J Clin Oncol*. 1999; 17:976–983. [PubMed: 10071292]
37. Clary BM, Brady MS, Lewis JJ, et al. Sentinel lymph node biopsy in the management of patients with primary cutaneous melanoma: review of a large single-institutional experience with an emphasis on recurrence. *Ann Surg*. 2001; 233:250–258. [PubMed: 11176132]
38. Dengel LT, More MJ, Judy PG, et al. Intraoperative imaging guidance for sentinel node biopsy in melanoma using a mobile gamma camera. *Ann Surg*. 2011; 253:774–778. [PubMed: 21475019]
39. Kroon HM, Lowe L, Wong S, et al. What is a sentinel node? Re-evaluating the 10% rule for sentinel lymph node biopsy in melanoma. *J Surg Oncol*. 2007; 95:623–628. [PubMed: 17345610]

Figure 1.

Kaplan-Meier curves for recurrence-free survival, categorized by Breslow depth (a), mitotic rate (b), and sentinel lymph node status (c).

Table 1

Clinicopathologic characteristics

Characteristic	Median N	IQR %
Age (years)	59	47 – 69
Follow-up (years)	4.2	1.2 – 6.1
Breslow (mm)	1.56	1.01 – 2.57
Mitotic rate	2	1 – 6
Female	100	46.5%
Clark level		
1	3	1.4%
2	3	1.4%
3	39	18.1%
4	150	69.8%
5	11	5.1%
Unknown	9	4.2%
Ulceration		
Yes	52	24.2%
No	149	69.3%
Unknown	14	6.5%
Regression		
Yes	31	14.4%
No	141	65.6%
Unknown	43	20.0%
Primary tumor		
Head and neck	6	2.8%
Trunk	111	51.6%
Upper extremity	40	18.6%
Lower extremity	58	27.0%

Table 2

Operative characteristics

Characteristic	N	%
Basins biopsied	279	
Axillary	156	55.9
Groin	75	26.9
Head and Neck	18	6.5
In-transit	23	8.2
Other	7	2.5
Total nodes removed	545	
Basins per patient	1.30	
Nodes per basin	2.01	
Residual basin radioactivity		
< 10%	246	87.8
10–19%	29	10.4
20%	4	1.4
Unknown	1	0.4
Patients with positive SLNB	40	18.6
Positive completion node dissection	7	17.5
Negative completion node dissection	25	62.5
No completion node dissection	8	20
Patients with negative SLNB	175	81.4
Recurrences	35	20
Local	2	1.1
In-transit	8	4.6
Regional	6	3.4
Distant	19	8.8

Table 3

Risk factors for cancer recurrence. Multivariate C-statistic: 0.747

Risk Factor	Univariate analysis			Multivariate analysis		
	No Recur	Recur	p-value	OR	95% CI	p-value
Female	47.4%	44.2%	0.709			
Age	56.2	61.9	0.060			
Positive sentinel node	11.1%	34.1%	<0.001	1.97	0.75 – 5.17	0.170
Residual 10%	11.8%	11.6%	1.000			
Primary Pathology						
Breslow > 2 mm	32.7%	64.3%	<0.001	2.86	1.18 – 6.93	0.020
Clark 4	75.2%	90.2%	0.036	1.67	0.44 – 6.42	0.455
Mitotic rate > 2 ^a	39.1%	71.4%	<0.001	2.84	1.21 – 6.63	0.016
Ulceration	22.4%	39.0%	0.085			
Regression	18.3%	17.1%	0.879			
Primary Location						
Trunk	49.1%	60.5%	0.246			
Upper Extremity	20.5%	11.6%	0.273			
Lower Extremity	27.5%	25.6%	0.851			
Head & Neck	2.9%	2.3%	1.000			

^aMitotic rate reported as number per mm²