Reliability of Sentinel Lymph Node Mapping With Biopsy for Head and Neck Cutaneous Melanoma

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Objectives: To determine (1) the reliability of sentinel lymph node mapping with biopsy (SLNB) in head and neck cutaneous melanoma to accurately stage nodal basins and (2) the safety of SLNB in both the neck and parotid regions.

Design: Retrospective cohort study with a median follow-up of 25 months. All patients had a minimum follow-up of 1 year.

Setting: Academic medical center.

Patients: Eighty evaluable patients diagnosed as having head and neck cutaneous melanoma and staged using SLNB.

Interventions: Sentinel lymph nodes were identified using preoperative lymphoscintigraphy and a combination of intraoperative gamma probe and isosulfan blue dye. Patients with a SLN positive for melanoma underwent therapeutic lymphadenectomy followed by an evaluation for adjuvant therapies. Patients with a negative SLNB result were followed up clinically.

Main Outcome Measures: Percentage of positive SLNs, regional recurrence in the setting of a negative SLNB result (false-negative rate), and procedure complications.

Results: The mean Breslow depth was 2.35 mm. A SLN was identified in 77 (96.3%) of cases, with an average of 2.18 nodes per patient. Of the sentinel nodes identified, 74% were from the neck region. The remaining 26% were from the parotid basin. No facial nerve complications occurred. Of the patients, 14 (18%) were SLN positive for metastatic melanoma. The regional failure rate in the setting of a negative SLNB result was 4.5%.

Conclusions: Sentinel lymph node mapping with biopsy is a reliable technique to diagnose regional spread from head and neck cutaneous melanoma. This procedure can be performed in both neck and parotid nodal basins with safety and accuracy similar to non–head and neck sites.


NUMEROUS QUESTIONS surround the management of head and neck cutaneous melanoma, especially with respect to the role for elective treatment of regional nodal basins. Prospective randomized trials have failed to demonstrate a survival benefit for patients with melanoma undergoing elective lymphadenectomy.1,2 While nodal status is clearly recognized as the most significant prognostic factor for patients diagnosed with cutaneous melanoma, only 10% to 20% of patients present with occult lymph node metastasis. This risk for nodal metastasis increases as primary tumor thickness increases. Lesions less than 1 mm thick are associated with a less than 5% rate of regional metastasis, while lesions thicker than 4 mm are associated with a 30% to 50% rate of nodal involvement.3,4

In an attempt to identify this small group of patients harboring occult nodal disease using a minimally invasive procedure, Morton et al5 introduced sentinel lymph node mapping with biopsy (SLNB) for the evaluation of patients with trunk and extremity cutaneous melanoma. They demonstrated that the status of the SLN accurately represented the status of the entire nodal basin from which it was obtained. In doing so, SLNB provided a means of identifying patients with occult nodal metastasis who warranted therapeutic lymphadenectomy and adjuvant therapy, while sparing the remaining 80% of patients without regional disease the morbidity associated with formal lymphadenectomy. Recent multivariate analysis involving patients with stage I and II melanoma by Gershenwald et al6 found the pathological status (positive or negative for
metastasis) of the SLN to be the most important prognostic factor for recurrence and survival.

While SLNB has a defined role in the evaluation of cutaneous melanoma of the trunk and extremities, several questions remain unanswered with respect to its application in the head and neck region. The complexity of the head and neck lymphatic system has caused concern surrounding the reliability of SLNB to accurately reflect the status of the entire nodal basin. The popularity of SLNB in this region has also been limited by technical difficulties, concern surrounding damage to vital structures such as the facial nerve, and the necessity for nuclear medicine staff as well as pathologists who specialize in SLNB technique. The objective of this retrospective cohort study was to determine the reliability of SLNB for regional staging of head and neck cutaneous melanoma.

### METHODS

Approval for this study was granted by the University of Michigan Medical School Institutional Review Board for Human Subject Research, Ann Arbor. This retrospective cohort study included 87 patients (7 of whom were lost to follow-up) treated for head and neck cutaneous melanoma who were staged using SLNB by the senior authors (C.R.B. and R.S.R.). Patients were identified through a query of the prospective University of Michigan Melanoma Database from April 1998 through December 2000. Eighty-seven patients treated between April 1998 and December 2000 met the inclusion criteria for this study. Seven patients were lost to follow-up. Of the remaining 80 evaluable patients, 54 (68%) were men and 26 (32%) were women. The median patient age was 55 years (range, 7-86 years). The mean Breslow depth was 2.35 mm (range, 0.7-7.0 mm). Melanoma subtypes included superficial spreading (32%), unclassified (21%), nodular (20%), lentigo maligna (19%), desmoplastic (5%), spindle cell (1%), polypoid melanoma (1%), and neurotropic (1%). Seventeen percent of the lesions were ulcerated. The distribution of the primary melanoma lesions are listed in Table 1.

### RESULTS

Eighty-seven patients treated between April 1998 and December 2000 met the inclusion criteria for this study. Seven patients were lost to follow-up. Of the remaining 80 evaluable patients, 54 (68%) were men and 26 (32%) were women. The median patient age was 55 years (range, 7-86 years). The mean Breslow depth was 2.35 mm (range, 0.7-7.0 mm). Melanoma subtypes included superficial spreading (32%), unclassified (21%), nodular (20%), lentigo maligna (19%), desmoplastic (5%), spindle cell (1%), polypoid melanoma (1%), and neurotropic (1%). Fourteen percent of the lesions were ulcerated. The distribution of the primary melanoma lesions are listed in Table 1.

Using the combined techniques of lymphoscintigraphy, intraoperative gamma probe, and isosulfan blue dye, a SLN was found in 77 (96%) of the 80 cases performed. The average number of SLNs identified per patient was 2.18 (range, 1-7 nodes). Of the 168 SLNs, 74% were identified in neck nodal basins. The remaining 26% were found within the parotid bed. Of the 30 patients with SLNs that drained to the parotid basin, 28 (93%) underwent successful SLNB. One patient underwent success-

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**Table 1. Distribution of Head and Neck Cutaneous Melanoma**

<table>
<thead>
<tr>
<th>Location</th>
<th>No. (%) of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cheek</td>
<td>16 (20)</td>
</tr>
<tr>
<td>Scalp</td>
<td>16 (20)</td>
</tr>
<tr>
<td>Neck</td>
<td>13 (16)</td>
</tr>
<tr>
<td>Auricle</td>
<td>13 (16)</td>
</tr>
<tr>
<td>Forehead</td>
<td>5 (6)</td>
</tr>
<tr>
<td>Temple</td>
<td>4 (5)</td>
</tr>
<tr>
<td>Mentum</td>
<td>4 (5)</td>
</tr>
<tr>
<td>Preauricular</td>
<td>4 (5)</td>
</tr>
<tr>
<td>Cutaneous lip</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Nose</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Postauricular</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Eyelid</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

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ful SLNB in a neck nodal basin but required a superficial parotidectomy because of the deep location of a second SLN within the superficial lobe. This parotid SLN was identified in the surgically removed lobe using the gamma probe. The “hot” node was sent separately for histologic review and was found to be negative for metastatic disease. A second patient experienced significant intraoperative bleeding from the parotid tissue. The procedure was aborted due to the associated risk to the facial nerve, and the patient was followed up clinically. This patient remains free of disease at a follow-up interval of 36 months.

There was minimal morbidity related to this procedure. No anaphylactic reactions occurred following injection of isosulfan blue dye. There were no cases of cranial nerve damage, and all patients had normal postoperative cranial nerve function, including the facial nerve. No damage to vital neck structures was reported.

Of the patients, 14 (17.5%) had metastatic melanoma identified using SLNB. A breakdown of SLNB results according to Breslow depth is provided in Table 2. All of these patients subsequently underwent therapeutic lymphadenectomy. Specifically, the neck nodal basins were treated with a modified radical neck dissection sparing the sternocleidomastoid muscle, internal jugular vein, and spinal accessory nerve. A posterolateral neck dissection was completed when clinically indicated. Lymphadenectomy of the parotid nodal basin entailed a superficial parotidectomy. The median follow-up for the positive SLN group was 25 months (range, 12-43 months).

The remaining 66 (82.5%) of patients with a negative SLNB result were followed up clinically. Median follow-up for the negative SLN group was 25 months (range, 12-47 months). During this follow-up interval, 8 (12%) of 66 patients developed recurrent disease. The distribution of recurrences is summarized in Table 3. Three patients had a recurrence of isolated regional disease in a previously mapped nodal basin. Thus, the regional failure rate in the setting of a negative SLNB result, also referred to as the false-negative rate, was 4.5% at a median follow-up interval of 25 months.

<table>
<thead>
<tr>
<th>Breslow Depth, mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.0</td>
</tr>
<tr>
<td>Total, No.</td>
</tr>
<tr>
<td>Positive SLNB result, No. (%)</td>
</tr>
</tbody>
</table>

*One patient did not have Breslow depth reported.

Comment

There are 4 reasons that necessitate the use of SLNB for accurate regional staging of cutaneous melanoma. First, the technique provides important prognostic information to the physician and patient in guiding subsequent treatment options. Second, it helps to identify patients harboring nodal metastases, which then may benefit from early therapeutic lymphadenectomy. Third, it identifies patients who are candidates for adjuvant treatment including interferon alfa-2B and radiation. Fourth, accurate regional staging enables the identification of a homogeneous population of patients for enrollment into clinical trials. Regional metastasis is recognized as an important prognostic factor. Without accurate pathologic staging, stratification is impossible and results of clinical trials will remain inconsistent and difficult to interpret. Fortunately, SLNB provides a minimally invasive means of regional staging.

While SLNB is routinely performed for cutaneous trunk and extremity melanoma, the role of this procedure remains uncertain for head and neck cutaneous melanoma. The main concern surrounds the reliability of the SLN to accurately predict the disease status of the entire nodal basin within this region. The interlacing network of cervical lymphatic vessels is often deemed watershed in nature. The complexity of this lymphatic system was demonstrated by O’Brien et al who reported a 34% discordance between the clinical prediction of lymphatic drainage and lymphoscintigraphy findings in 97 cases of head and neck cutaneous melanoma.

Our study demonstrated that the complexity of the head and neck lymphatic system does not preclude the use of SLNB for staging of cutaneous melanoma. Sentinel lymph node mapping with biopsy in the head and neck region accurately predicts the status of the nodal basin, with 14 (17.5%) of 80 patients identified with a positive SLNB result and 3 (4.5%) of 66 patients developing regional recurrence following a negative SLNB result. A review of other institutional experiences in the use of SLNB for head and neck cutaneous melanoma is presented in Table 3. Studies were included only if information specific to the head and neck sentinel nodes could be ascertained. The 17.5% rate of SLN positivity and the 4.5% false-negative rate reported in our study compares favorably with the success of SLNB achieved in other anatomic sites.

Reported regional recurrence rates following a negative SLNB result in the head and neck region were quite variable, ranging from 0% to 25% (Table 4). Follow-up time is likely one reason for this variability. Two thirds of recurrences from cutaneous melanoma are expected to occur within 3 years following diagnosis.

Table 2. Distribution of Sentinel Lymph Node Biopsy (SLNB) Results According to Breslow Depth

<table>
<thead>
<tr>
<th>Breslow Depth, mm</th>
<th>&lt;1.0</th>
<th>1.01-2.0</th>
<th>2.01-4.0</th>
<th>&gt;4.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total, No.</td>
<td>10</td>
<td>34</td>
<td>23</td>
<td>12</td>
</tr>
<tr>
<td>Positive SLNB result, No. (%)</td>
<td>2 (20)</td>
<td>4 (12)</td>
<td>5 (22)</td>
<td>3 (25)</td>
</tr>
</tbody>
</table>

*Case contributing to false-negative rate of sentinel lymph node mapping with biopsy.

Table 3. Location of First Recurrence for 8 Patients in Negative Sentinel Lymph Node Group

<table>
<thead>
<tr>
<th>Primary Tumor Site (Breslow Depth, mm)</th>
<th>Area of Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lateral neck (5.0)</td>
<td>Regional*</td>
</tr>
<tr>
<td>Auricle (1.12)</td>
<td>Regional*</td>
</tr>
<tr>
<td>Scalp (3.12)</td>
<td>Regional*</td>
</tr>
<tr>
<td>Auricle (1.3)</td>
<td>Satellite/in-transit</td>
</tr>
<tr>
<td>Scalp (2.09)</td>
<td>Satellite/subcutaneous</td>
</tr>
<tr>
<td>Scalp (2.46)</td>
<td>Skin and pulmonary metastasis</td>
</tr>
<tr>
<td>Scalp (3.7)</td>
<td>Lung and liver metastasis</td>
</tr>
<tr>
<td>Cheek (2.1)</td>
<td>Lung metastasis</td>
</tr>
</tbody>
</table>

*Regional metastasis compared with 17.5% success of SLNB achieved in other anatomic sites.
rotidectomy over the mapping procedure,8 we success-
SLNB has led some authors to advocate superficial pa-
and neck cutaneous melanoma who underwent preop-
clinical nerve monitoring. Concern has also been expressed
senior surgeons, regardless of the use of continuous fa-
fully removed 39 nodes from 28 parotid basins without
variability, and a 30-case learning curve has previously
was moderate in duration. Repeat analysis at the 5- to
median follow-up of 25 months (range, 12-47 months)
low-up interval beginning 1 month following SLNB. Our
1.9% failure rate reported by Patel et al20 included a fol-
the learning curve contributed to regional fail-
Following completion of the recommended num-
cases that represents the learning curve, 1 re-
gional failure involved the 19th case for one surgeon, while
remaining 2 failures involved the 43rd and 45th case for the second surgeon. This observation reflects the techni-
O'Brien et al11 reported that 33% of patients with head
and neck cutaneous melanoma who underwent preop-
erative lymphoscintigraphy had drainage to lymph nodes
within the parotid bed. Our distribution was similar, with
30 (26%) of 80 patients mapping to this region. We suc-
erve at increased risk when reopera-
tion is required to definitively treat the parotid basin in
the setting of a positive SLN.8 In our study, patients with
a positive parotid SLN underwent a superficial paroti-
dectomy as a subsequent procedure, and normal facial
nerve function was achieved postoperatively in all cases.
Our findings are consistent with other reports demonstr-
ing that SLNB can reliably and safely be performed
within the parotid nodal basin.24,25
While the surgeon’s experience and technical skill
are both vital to the success of SLNB, we attribute our
overall low regional failure rate to a team effort involv-
ing surgeons, dermatologists, nuclear medicine staff, and
pathologists. Appropriate patient selection is imperative
because patients with regional or distant metastatic
disease or previous surgical disruption of the lymphatic
system are not candidates for SLNB. An experienced
nuclear medicine staff is necessary because inappropri-
ate administration of the radioactive tracer can lead to
“shine through,” which will render the intraoperative
gamma probe useless. Communication with the nuclear
medicine team is helpful not only in interpreting the lym-
phoscintigram, but also to ensure that the appropriate
lesion is mapped. Patients with melanoma often present
with multiple lesions. It is imperative that only the in-
vasive melanoma is injected with radioactive colloid. One
regional failure in this study occurred in a patient who
presented for simultaneous treatment of adjacent mel-
oma and Bowen’s disease of the scalp. Subsequent com-
munication with the nuclear medicine team revealed that
both lesions were injected, which may have adversely af-
ected the accuracy of SLNB.
Lastly, the pathologist plays a critical role in the suc-
cess of SLNB. Wagner et al26 reported the mean tumor
volume in SLNs positive for metastatic melanoma to be
only 4.7 mm3. Joseph et al27 reported identification of only
73% of metastatic SLNs using standard H&E staining.
Therefore, occult lymphatic metastasis from cutaneous
melanoma can be difficult to detect and warrants rigor-
ous pathological analysis including serial sectioning, spe-
cial immunohistochemical study when indicated, and in-
terpretation by an experienced pathologist. Sentinel lymph
node mapping with biopsy provides the pathologist with
a limited number of nodes to thoroughly evaluate. There-

Table 4. Previous Reports of SLNB for Head and Neck Cutaneous Melanoma

<table>
<thead>
<tr>
<th>Source</th>
<th>No. of Patients</th>
<th>Positive SLNB Result, %</th>
<th>Regional Failure Rate Following a Negative SLNB Result, %</th>
<th>Median Follow-up, mo</th>
<th>Treatment Modality</th>
</tr>
</thead>
<tbody>
<tr>
<td>O'Brien et al11 1995</td>
<td>20</td>
<td>20</td>
<td>25</td>
<td>18.0</td>
<td>LSG + Dye</td>
</tr>
<tr>
<td>Wells et al14 1997</td>
<td>58</td>
<td>11</td>
<td>0</td>
<td>11.6</td>
<td>Dye ± LSG + GP†</td>
</tr>
<tr>
<td>Alex et al13 1998</td>
<td>23</td>
<td>14</td>
<td>5</td>
<td>30.0</td>
<td>LSG + GP + Dye</td>
</tr>
<tr>
<td>Jansen et al18 2000</td>
<td>30</td>
<td>26.7</td>
<td>9.1</td>
<td>21.0</td>
<td>LSG + GP ± Dye‡</td>
</tr>
<tr>
<td>Carlson et al21 2000</td>
<td>58</td>
<td>17.5</td>
<td>21.3</td>
<td>15.9t</td>
<td>LSG + GP + Dye§</td>
</tr>
<tr>
<td>Raison15 2001</td>
<td>24</td>
<td>20.8</td>
<td>10</td>
<td>18.0</td>
<td>LSG + GP + Dye</td>
</tr>
<tr>
<td>Jacobs et al19 2001</td>
<td>12</td>
<td>0</td>
<td>8.3</td>
<td>24.0</td>
<td>LSG + GP</td>
</tr>
<tr>
<td>Patel et al20 2002</td>
<td>56</td>
<td>7.1</td>
<td>1.9</td>
<td>20.0</td>
<td>LSG + GP ± Dye</td>
</tr>
<tr>
<td>Chi et al21 2001</td>
<td>19</td>
<td>15.8</td>
<td>10.5</td>
<td>23.3</td>
<td>LSG + GP</td>
</tr>
</tbody>
</table>

Abbreviations: Dye, vital blue dye; GP, intraoperative gamma probe; LSG, lymphoscintigraphy; plus sign, with; plus/minus sign, with or without; SLNB, sentinel lymph node mapping with biopsy.
*Of the patients, 38% underwent mapping with vital blue dye alone.
†Of the patients, 52% underwent mapping with all 3 treatment modalities.
‡Mean follow-up reported.
§Vital blue dye used in a few sporadic cases.
||Of the patients, 85.7% underwent mapping with all 3 treatment modalities.

Regional recurrence rate of 0% reported by Wells et al14 included a follow-up interval of only 11.6 months. The 1.9% failure rate reported by Patel et al20 included a follow-up interval beginning 1 month following SLNB. Our median follow-up of 25 months (range, 12-47 months) was moderate in duration. Repeat analysis at the 5- to 10-year follow-up interval is warranted to confirm our initial findings.

The experience of the surgeon may also account for variability, and a 30-case learning curve has previously been suggested.7 Studies with higher regional failures compared with our reported 4.5% often involved smaller cohorts of only 20 to 30 patients (Table 4). At our institution, most SLNBs for head and neck melanoma are performed by the 2 senior surgeons. Although retrospective studies often reveal higher failure rates at the beginning of a surgeon’s experience, our study did not show that the learning curve contributed to regional failures.14,23 Following completion of the recommended number of cases that represents the learning curve, 1 regional failure involved the 19th case for one surgeon, while the remaining 2 failures involved the 43rd and 45th case for the second surgeon. This observation reflects the technical challenges involved in performing SLNB.
Many questions surround the treatment of head and neck cutaneous melanoma. This retrospective study addresses the reliability and safety of SLNB to accurately determine the presence of occult regional spread for head and neck cutaneous melanoma. With a median follow-up of 25 months, 17.5% of patients had a positive SLNB result and only 4.5% of patients developed regional recurrence following a negative SLNB result. The procedure was performed with equivalent safety in both the neck and parotid nodal basins. There were no reported complications of facial nerve weakness or injury to other vital structures. This documented accuracy reported in the setting of minimal morbidity indicates that SLNB is a reliable procedure for regional staging of head and neck cutaneous melanoma. Given that the SLN status is the most important prognostic factor for patients with melanoma, the accuracy of SLNB in the head and neck region demonstrated in the present study is quite promising.

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