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.

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 between April 1998 and December 2000. All patients who had histologically proven melanoma, with a minimum Breslow depth of 1.00 mm (or ulceration) and staining with hematoxylin-eosin (H&E). Special immunohistochemical staining for S100, melan-A, and HMB-45 were performed in the setting of a positive lymph node. In addition, adjuvant radiation was recommended for patients when metastatic disease involved 3 or more lymph nodes or when extracapsular spread was identified. The remaining patients with a negative SLNB result were followed up clinically.

The University of Michigan Melanoma Database was used to define the population demographics. Main outcome measures included the percentage of positive SLNs, regional recurrence in the setting of a negative SLNB result (false-negative rate), and facial nerve injury.

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%), polymorphous 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 successful
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 SLN 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 2. Distribution of Sentinel Lymph Node Biopsy (SLNB) Results According to Breslow Depth*

<table>
<thead>
<tr>
<th>Patients</th>
<th>Breslow Depth, mm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>Total, No.</td>
<td>10</td>
</tr>
<tr>
<td>Positive SLN</td>
<td>2 (20)</td>
</tr>
</tbody>
</table>

*One patient did not have Breslow depth reported.

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

<table>
<thead>
<tr>
<th>Primary Tumor Site</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>

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

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, who 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 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 al, 1995</td>
<td>20</td>
<td>20</td>
<td>25</td>
<td>18.0</td>
<td>LSG + Dye</td>
</tr>
<tr>
<td>Wells et al, 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 al, 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 al, 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 al, 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>Raisgon, 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 al, 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 al, 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 al, 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.

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 involving 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 inappropriate 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 lymphoscintigram, but also to ensure that the appropriate lesion is mapped. Patients with melanoma often present with multiple lesions. It is imperative that only the invasive melanoma is injected with radioactive colloid. One regional failure in this study occurred in a patient who presented for simultaneous treatment of adjacent melanoma and Bowen’s disease of the scalp. Subsequent communication with the nuclear medicine team revealed that both lesions were injected, which may have adversely affected the accuracy of SLNB.

Lastly, the pathologist plays a critical role in the success of SLNB. Wagner et al reported the mean tumor volume in SLNs positive for metastatic melanoma to be only 4.7 mm³. Joseph et al 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 rigorous pathological analysis including serial sectioning, special immunohistochemical study when indicated, and interpretation by an experienced pathologist. Sentinel lymph node mapping with biopsy provides the pathologist with a limited number of nodes to thoroughly evaluate. Thereo-
fore, the histologic analysis of SLNs is more thorough and complete compared to the evaluation of the entire lymphadenectomy specimen.13

CONCLUSIONS

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,6 the accuracy of SLNB in the head and neck region demonstrated in the present study is quite promising.

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REFERENCES


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