Sentinel Lymph Node Biopsy for Cutaneous Head and Neck Melanomas

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Objective: To report the results of sentinel lymph node biopsy (SLNB) for cutaneous head and neck melanomas (CMHNs).

Design: Consecutive series followed for a median of 20 months.

Setting: Tertiary cancer care center.

Patients: Fifty-six individuals with clinically node-negative CMHN, median Breslow thickness, 2.6 mm (range, 0.2-20.0 mm).

Interventions: Preoperative technetium 99m sulfur colloid lymphoscintigraphy (PLSG) followed within 4 hours by intraoperative handheld gamma probe localization (IHGP). Intraoperative injection of 1% isosulfan blue dye (IBD) was used in 48 patients. Immediate completion nodal dissection was performed for metastatic SLNs on intraoperative frozen section analysis and monitoring for negative SLNs.

Main Outcome Measures: Rate of SLN identification, SLN and non-SLN positivity, same-basin recurrence, and disease-specific and recurrence-free survival.

Results: Combination of IHGP and IBD improved SLN identification to 96% from 93% for IHGP and 73% for IBD alone. Four patients had a positive SLN on frozen section analysis. A negative SLNB correctly predicted regional nodal control in 47 of 48 patients but missed 1 of 5 patients who had regional lymphatic disease. All 4 patients who failed SLNB remain alive and free of recurrent disease. Two-year Kaplan-Meier disease-specific and relapse-free survival was 91% and 88%, respectively. Two-year disease-specific survival was 93% for SLN-negative patients and 50% for SLN-positive patients ($P=0.20$).

Conclusions: Combining PLSG with IHGP and IBD improves the success rate of SLNB. Although SLNB is a reliable indicator of the status of the draining lymphatic basins in CMHN, patients with negative SLNs must be observed for longer periods to understand the true implications of the procedure.


Regional nodal metastases occur infrequently in thin cutaneous melanomas (<1 mm thick), and elective neck dissection (ELND) is therefore not recommended. Thicker lesions (>4 mm) are associated with a high incidence of distant metastases, and, therefore, ELND may not affect survival in this population. Active debate continues as to the clinical effect of ELND in patients with intermediate-thickness melanomas (1-4 mm thick). Even in this group, only approximately 15% of patients will have histologically demonstrable metastatic nodes, so that the remaining 85% undergoing routine ELND may be considered to have undergone an unnecessary procedure. Four randomized trials$^{1-4}$ and 1 large, retrospective study$^5$ of patients with intermediate-thickness melanomas have not demonstrated any improvement in survival after ELND. Against this background, the advantage of sentinel lymph node biopsy (SLNB) for cutaneous head and neck melanoma is the potential to avoid the morbidity of routine ELNDs while accurately and pathologically staging the regional nodes at risk for micrometastases. This has clear implications for patient prognosis and for their eligibility to participate in clinical trials of adjuvant therapy. The usefulness and reliability of SLNB has been well described in the literature since it was first reported in 1990.$^6$ In contrast to other sites within the body, the head and neck region presents unique challenges in terms of the anatomy, the technique, and the interpretation of SLNB results. This study was undertaken to assess our experience with SLNB, with a special focus on these issues.

RESULTS

We identified at least 1 SLN in 52 (93%) of 56 patients. Previous surgery; the site, morphologic characteristics, thickness, and
PATIENTS AND METHODS

PATIENTS

Between February 1, 1996, and February 15, 2000, 56 patients underwent SLNB for a cutaneous malignant melanoma of the head and neck. Clinical data, surgical details, and histopathologic and outcome data on these patients were entered prospectively into a computerized database and form the basis of this study. There were 15 females (27%) and 41 males (73%) aged 12 to 86 years (median, 62 years).

PRIMARY TUMORS

The site of the primary lesion was the scalp in 18 patients (32%), the cheek in 15 (27%), the ear in 11 (20%), the neck in 8 (14%), and other sites on the face in 4 (7%). The median thickness of the primary tumor was 2.6 mm (range, 0.2-20.0 mm; mean, 3.5 mm). Most tumors (n=35 [62.5%]) were of intermediate thickness (1-4 mm), 17 (30.4%) were greater than 4-mm thick, and 4 (7.1%) were less than 1-mm thick. Thirty-six patients (64%) had Clark level IV tumors, 10 (18%) had level III tumors, 8 (14%) had level V tumors, and 1 (2%) had level II tumors; 1 patient (2%) could not be staged because of previous shave biopsy. Fifty-four patients (96%) had previously undergone excision (n=29 [52%]) or biopsy (n=25 [45%]) of the lesion, and 2 patients (4%) had previously unviolated tumors.

TECHNIQUES

All 56 patients underwent preoperative lymphoscintigraphy (PLSG) to facilitate identification of nodal basins at risk and to identify extra-anatomic and in-transit SLNs. Briefly, 0.05 mCi (1.9 MBq) of radioactive technetium Tc 99m sulfur colloid (CIS-US, Inc, Bedford, Mass) filtered through a 0.22-µm filter in a volume of 0.5 mL was injected into 4 quadrants of the primary lesion or around the biopsy scar. Injection was performed beginning immediately after injection at a rate of 1 frame per minute for approximately 10 minutes. Anterior and lateral static images were obtained at 5-minute intervals for 20 minutes. A radioactive lead marker was placed in the external auditory canal in selected patients to provide orientation in interpretation of the images.

The SLNB was performed within 4 hours of injection of the radiocolloid, and the images were used to guide the procedure in the operating room. The operating room setup for SLNB includes equipment for injection of 1% isosulfan blue dye (Lymphazurin; Hirsch Industries, Inc, Richmond, Va) and localization of the radioactive colloid. A tuberculin syringe was used to inject the blue dye in an intradermal plane on the side of the lesion nearest to the relevant draining nodes identified by PLSG. Most commonly, a volume of 0.5 mL or less was used, as larger volumes tend to dissipate into the subcutaneous tissue and cause artifacts, complicating the procedure. Blue dye injection was used in 48 of the 56 patients, and it successfully identified an SLN in 35 (73%).

Clark level of the primary lesion; and features such as histologic type, ulceration, growth phase, and lymphovascular or perineural invasion were not statistically associated with success or failure of SLNB (data not shown). One of the 4 patients in whom an SLN was not identified underwent immediate superficial parotidectomy. Elective nodal dissection was not performed in any of these patients, and all 4 are alive and free of disease (Table 1).

Table 1

HISTOPATHOLOGIC EXAMINATION OF SLNs

Frozen section analysis of the SLNs was performed in 51 patients. Each SLN was bisected from the hilum to its periphery. Half of the node was immediately processed for frozen section evaluation using conventional hematoxylin-eosin staining, and the other half was processed for immunohistochemical staining with antibodies to S100 protein and HMB-45. All lymphatic and parotid tissue was then embedded in paraffin and processed per routine departmental protocols. Sentinel lymph nodes were positive for melanoma on frozen section analysis in 4 patients (8%), and these patients underwent immediate completion lymph node dissection. Serial sectioning and immunohistochemical analysis for S100 and HMB-45 were performed in 31 patients, and no additional nodal metastases were identified. Of the remaining 25 patients, 4 had a positive SLN on frozen section analysis, an SLN could not be identified in 4, and these investigations were not performed in 17. Two of these 17 patients recurred at distant sites (1 died of disease and 1 is alive with disease), and the remaining 15 are alive and free of disease.

STATISTICAL METHODS

Data were analyzed using a statistical software package (JMP 4.0; SAS Institute Inc, Cary, NC). Follow-up was calculated in months from the date of SLNB to the date of last follow-up or death, and the disease-free interval was calculated from the date of SLNB to the date of first recurrence. For disease-specific survival, patients who were alive with disease at last follow-up (2 [4%] of 56) were censored. Disease-specific and recurrence-free survival rates were calculated using the Kaplan-Meier method. Nonparametric qualitative and quantitative comparisons were performed using the Fisher exact test and the Mann-Whitney test, respectively, setting the level of statistical significance at a P<.05.
Sentinel lymph nodes were identified in the neck in 37 patients (66%), parotid gland in 8 (14%), and parotid and neck in 7 (13%). Most SLNs (47 [90%] of 52) were located in the same side as the primary lesion. Of 6 patients whose primary lesions were close to or in the midline, 1 had bilateral occipital SLNs, 2 had unilateral upper posterior triangle SLNs, 1 had unilateral parotid and level II SLNs, and 1 had no SLNs. One patient with a primary lesion in the neck at right level II had a contralateral SLN at level II. Most patients (37 [71%] of 52) had SLNs in a single basin, 13 (25%) had SLNs in 2 draining basins, and 2 (4%) had SLNs in 3 basins. Sentinel lymph nodes were sampled (alone or in combination with other basins) from level I in 12 patients (23%), level II in 13 (25%), level III in 4 (8%), level IV in 2 (4%), level V in 10 (19%), the parotid in 15 (29%), and the occipital triangle in 8 (15%).

A total of 137 SLNs were harvested (range, 1-11 [median, 2] per patient). One SLN was harvested in 38 patients (73%). Six SLNs (4%) of the 137 harvested in 4 patients contained metastatic malignant melanoma on intraoperative frozen section analysis. These 4 patients (8%) with positive SLNs underwent completion lymph node dissection at the time of the procedure. A total of 283 non-SLNs were harvested, 116 in the 48 patients who had negative SLNs and 167 in the 4 patients who underwent completion nodal dissection for positive SLNs. None of the 48 patients with negative SLNs had metastases in non-SLNs, whereas 1 of 4 patients with positive SLNs had 2 positive non-SLNs in the nodal dissection specimens. No positive non-SLNs were therefore detected in any patients with negative SLNs. However, only 31 of these 48 patients were studied with immunohistochemical analysis and serial sectioning, and, therefore, some micrometastases may have been missed in the remaining 17.

### PAROTID REGION SLNs

Fifteen patients had SLNs that mapped to the parotid region. The site of the primary lesion in these patients was the external ear in 6 (40%), the cheek in 5 (33%), the scalp in 3 (20%), and the eyelid in 1 (7%). All lesions except 1 in a patient who had a midline scalp melanoma were well lateralized and drained to the ipsilateral parotid region. The thickness of the primary lesions ranged from 0.2 to 9.5 mm (median, 2.8 mm); thickness was classified as intermediate in 10 patients (67%), thick in 4 (27%), and thin in 1 (7%). The parotid gland was the sole draining basin in 8 patients (53%), whereas 7 (47%) drained to additional nodal basins in the neck: 5 to level II, 2 to level I, and 1 to level V and the occipital region. All but 1 of the SLNs was visualized on PLSG, whereas blue dye injection was successful in 11 (79%) of 14 patients with parotid SLNs. Six patients (40%) underwent subtotal parotidectomy, whereas only the SLNs was biopsied in the remaining 9 (60%). Temporary postoperative facial nerve weakness was noted in 4 (27%) of the 15 patients, and all 4 regained complete function. The facial nerve and its branches were identified and preserved in the 6 patients who underwent superficial parotidectomy; temporary postoperative facial nerve weakness was recorded in 3 of these patients. Of 9 patients who underwent intraparotid SLNB, the facial nerve or its branches were not identified during surgery in 5 patients, none of whom developed facial nerve weakness; 1 of the remaining 4 patients in whom the nerve was identified had evidence of postoperative facial nerve weakness. These differences were not statistically significant. The number of parotid region SLNs ranged from 1 to 11 (median, 2) per patient. Two SLNs (4%) (in the same patient) of 48 parotid SLNs were positive for metastatic disease, whereas none of the 80 non-SLNs were positive for melanoma. The 1 patient (7%) who had metastatic disease in parotid region SLNs underwent immediate superficial parotidectomy with neck dissection, which did not identify any other positive non-SLNs. With median follow-up of 19.6 months (range, 1-48 months), 1 of these 15 patients had recurred in the neck (described in detail in the following paragraph) and 2 had recurred at distant sites.

### OVERALL OUTCOME

With limited follow-up (median, 20 months; range, 1-48 months), 7 patients (13%) had recurrent disease: 3 at distant sites, 1 locally, 2 at local and distant sites, and 1 in the sampled nodal basin (Figure 1). Of 5 patients that

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**Table 1. Description of 4 Patients in Whom an SLN Was Not Found**

<table>
<thead>
<tr>
<th>No.</th>
<th>Primary Tumor</th>
<th>Preoperative Lymphoscintigraphy</th>
<th>Intraoperative Gamma Probe</th>
<th>Intraoperative Blue Dye Injection</th>
<th>Extent of Surgery</th>
<th>Outcome (Follow-up, mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cheek, 2.0-mm thick; previous biopsy</td>
<td>SLN in adjacent parotid gland</td>
<td>Difficult to interpret</td>
<td>Failed</td>
<td>Superficial parotidectomy; no neck dissection</td>
<td>NED (18)</td>
</tr>
<tr>
<td>2</td>
<td>Midline parietal scalp, 4.4-mm thick; previous biopsy</td>
<td>SLN in left parotid gland</td>
<td>Weak activity in parotid gland; no SLN identified</td>
<td>Failed</td>
<td>No superficial parotidectomy or neck dissection</td>
<td>NED (28)</td>
</tr>
<tr>
<td>3</td>
<td>Cheek, 1.1-mm thick; previous excision</td>
<td>No SLN imaged</td>
<td>Failed</td>
<td>Not performed</td>
<td>No superficial parotidectomy or neck dissection</td>
<td>NED (18)</td>
</tr>
<tr>
<td>4</td>
<td>Neck, 1.2-mm thick; previous biopsy</td>
<td>SLN in close proximity to primary lesion</td>
<td>Failed</td>
<td>Not performed</td>
<td>No superficial parotidectomy or neck dissection</td>
<td>NED (20)</td>
</tr>
</tbody>
</table>

*SLN indicates sentinel lymph node; NED, no evidence of disease.*
A little more than half of the patients in our experience had undergone either local excision or biopsy of the lesion so that the potential for alteration of the regional lymphatic patterns existed in these patients. However, none of these patients had undergone reconstruction with either skin grafts or local flaps. Kelemen et al9 reported their experience of SLNB in patients who had undergone previous local excision of primary melanoma. Most of these patients had lesions of the extremity and had been excised with margins of 2 cm. Of 47 patients who underwent the procedure, 11 were reported to have positive SLNs, of which 8 were solitary nodal metastases. With median follow-up of 36 months, 3 SLN-negative patients had developed nodal recurrence. Two of these patients had positive SLNs on retrospective reexamination of the pathologic specimen and were believed to be pathologic misses, not failures of the lymphatic mapping technique. The third patient developed in-transit metastasis and delayed nodal recurrence. A fourth patient developed nodal recurrence in the basin opposite that identified by PLSG. The overall false-negative rate was therefore reported as 26%, since 4 of 15 patients with positive nodes were missed by SLNB. Based on these findings, the authors advised caution in the use of this technique in patients who have undergone antecedent wide excision, especially with split-thickness skin grafts or closure with flap rotations, and in patients in whom the melanoma occurs in the head and neck or trunk region. However, as we have shown, the success of SLNB can be maintained in patients who have had previous surgery as long as extensive mobilization or transposition of the skin around the lesion has not been undertaken. A history of surgical manipulation should, therefore, not automatically deny the potential benefits of SLNB to these patients.

Shah et al8 previously reported on the unpredictability of lymphatic metastases from cutaneous melanomas of the head and neck. In contrast to studies that have attempted to delineate patterns of metastasis from retrospective examination of neck dissection specimens, O’Brien et al9 reported the patterns of SLNs based on the primary subsite in the head and neck region in a group of 97 patients who underwent PLSG for cutaneous melanoma of the head and neck. At least 1 SLN was identified by PLSG in 95 of 97 patients, with a mean of 2.7 per patient. Twenty-two percent of their patients had SLNs failed at distant sites, 4 had primary tumors thicker than 4 mm. The patient who recurred in the sampled nodal basin had a primary melanoma of the parietal scalp, 6.5-mm thick, which had been previously biopsied. At SLNB, 2 SLNs in the ipsilateral parotid were hot and blue, whereas 2 nodes at level II were blue but not hot. Frozen section analysis, routine hematoxylin-eosin staining, and immunohistochemical analysis did not identify the presence of metastatic disease in any of these SLNs, and no further surgery was undertaken at this time. A year later, the patient developed recurrent disease at level II, within the sampled nodal basin, and underwent modified radical neck dissection. A single 1.8-cm-diameter metastatic node was identified at level II, and the remainder of his neck specimen was negative. The patient did well for another year before developing a soft tissue recurrence, again at level II, which was excised, and postoperative adjuvant radiation therapy was given. Within 2 months of completion of therapy, the patient developed contralateral neck metastases, along with massive mediastinal disease, and died of aspiration pneumonia secondary to a tracheoesophageal fistula.

A negative SLNB finding, therefore, correctly predicted regional nodal control in 47 (98%) of 48 patients and missed 1 (20%) of the 5 patients who had regional lymphatic disease. Two-year disease-specific and recurrence-free survival determined using the Kaplan-Meier method were 90.6% and 87.4%, respectively. The presence of metastatic disease in SLNs was not a statistically significant predictor of 2-year disease-specific survival (93.2% in SLN-negative patients vs 50.0% in SLN-positive patients; \( P = 0.20 \)) (Figure 2).

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**Figure 1.** Results and outcomes in 56 patients undergoing sentinel lymph node biopsy (SLNB). NED indicates no evidence of disease; DOD, died of disease; DFI, disease-free interval; and AWD, alive with disease.

**Figure 2.** Disease-specific survival rates in sentinel lymph node (SLN) –negative vs SLN-positive patients.
in sites other than the parotid gland and the 5 standard cervical levels on PLSG. Using a schema of anterior vs posterior primary sites, draining to corresponding anterior or posterior nodal basins, 33 (34%) of 97 lesions demonstrated drainage outside their clinically predicted nodal basin. In the current cohort, 10 (19%) of the 53 patients had an SLN that was outside the clinically predicted area of drainage based on PLSG (data not shown).

The site of the primary cutaneous melanoma can affect the outcome of SLNB. For instance, the technique needs to be modified for lesions that are in close proximity to a nodal basin, for example, a cheek lesion that lies close to the parotid gland or a neck primary lesion in close proximity to underlying nodes. Interpretation of PLSG scans in these instances is almost always inaccurate, and it may be better to rely on intraoperative gamma probe evaluation, frequently after the primary lesion has been excised, to evaluate the draining basin. As seen in our patients (Table 1), identification of an SLN may be impossible even after excision of the primary lesion with the adjacent nodal basin.

The type and particle size of the agent used for PLSG may have an impact on the results of the procedure if the dynamics of migration of the radioactive agent are not considered. The variables generally considered important are uptake of the tracer by initial lymphatics after injection into the skin, easy migration along the collecting vessels, and retention of most of the tracer material for a long period in the SLN, mimicking the behavior of tumor cells. None of the currently available radiopharmaceuticals is ideal, and there are conflicting reports on the superiority of one agent over the other and of filtered vs unfiltered colloids. Whether the “improved results” reported with a particular agent translate into improved sensitivity of the technique can only be answered through large clinical trials and long-term follow-up. With the growing acceptance and applicability of SLNB, the mechanisms of radiocolloid localization in lymph nodes are beginning to be investigated, and there is considerable interest in developing techniques to ensure greater migration of tracer material from the injection site while increasing retention in the SLN.

The combination of blue dye injection and radiocolloid injection has been documented to improve accuracy. Bostick et al reviewed their experience with 117 patients with primary cutaneous melanoma of the upper chest and head and neck undergoing PLSG with SLNB. Data on the 82 patients who had head and neck primary lesions were not reported separately. The authors compared the efficacy of blue dye injection alone vs a combination of blue dye and radiocolloid injection. An identical number of SLNs were identified per basin by using either technique (mean, 1.4). The basin identification rate was 92% for the blue dye and 96% for the blue dye plus radiocolloid method. The lymphatic metastasis rate was identical at 11% for each group. The authors concluded that the combination of blue dye and injection with technetium Tc 99m and use of the gamma probe may be a more sensitive method to detect SLNs. The results of our study are in agreement with these previous findings, and our current preference is to use PLSG with technetium Tc 99m sulfur colloid combined with intraoperative hand-held gamma probe localization and injection of 1% isosulfan blue dye.

Although the median number of SLNs identified per patient was 2, as many as 11 nodes were sampled, mainly based on achieving the previously described level of radioactivity in the resection bed. This is a crucial consideration in ensuring adequate sampling, as was demonstrated in a recent analysis of patients in the Sunbelt Melanoma Trial, which showed that if only the hottest SLN in each basin had been sampled, 13.1% of positive nodal basins would have been missed. Twenty-five percent of these nodal basins were in the neck, and, based on these data, the authors recommended that all nodes that measure 10% or more of the ex vivo radioactive count of the hottest SLN should be harvested to minimize sampling error.

None of our patients who had a negative SLN had a positive non-SLN. With median follow-up of 20 months, we had 1 same-basin nodal recurrence after negative SLNB. If accurate pathologic regional nodal staging is considered the end point, the procedure correctly predicted regional lymph nodal status in 47 (98%) of the 48 patients who had a negative SLNB but failed to identify 4 (20%) of the 5 patients with subclinical lymph node metastases in our experience. Wells et al reported a 95% success rate in identifying an SLN in 58 patients with melanomas of the head and neck region. With limited median follow-up of approximately 1 year, they found no evidence of metastatic disease in the SLN basin or in other nodal basins in the 49 patients with negative SLNs. In the 6 patients (11%) who had positive SLNs, they found no additional metastatic lymph nodes within the completion neck dissection specimens. This last observation is in contrast to our finding of 2 positive non-SLNs in 1 of the 4 patients who underwent completion nodal dissection for a positive SLN.

The issue of parotidectomy and, indeed, parotid region SLNB in patients with cutaneous melanomas continues to generate considerable debate. When an SLN is detected in the substance of the parotid gland, options include formal parotidectomy with facial nerve dissection and inspection of the parotid specimen on the back table for the SLN vs intraparotid gland dissection in vivo with identification and excision of the SLN with preservation of the parotid gland. Although the latter approach has the potential for inadvertent facial nerve injury, with increasing experience, our technique has evolved over time from the former to the latter.

Ollila et al reported on the technique of intraparotid gland dissection without formally identifying the facial nerve in 39 patients with cutaneous melanoma. They were able to identify an SLN in 37 (95%) of 39 patients, and the 2 patients (5%) in whom the SLN could not be identified underwent superficial parotidectomy. The mean number of SLNs was 2.3 per patient. A positive SLN was identified in 4 (10%) of 39 patients. The tumor-positive SLN was anterior to the parotid gland in 2 patients, in an intraparotid gland in 1, and at the inferior edge of the gland in 1. On completion parotidectomy and modified neck dissection, there was no residual metastatic melanoma of the parotid gland, although 2 of the 4 patients exhibited metastatic melanoma in the modified neck dissection.
Table 2. Published Results of SLNB in Recent Series

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<tbody>
<tr>
<td><strong>Patients with head and neck tumors, No.</strong></td>
<td>56</td>
<td>82</td>
<td>58</td>
<td>58</td>
<td>52</td>
<td>58</td>
</tr>
<tr>
<td><strong>Preoperative lymphoscintigraphy, %</strong></td>
<td>95</td>
<td>96</td>
<td>NA</td>
<td>90</td>
<td>99</td>
<td>98</td>
</tr>
<tr>
<td><strong>Blue dye injection, % (No.)</strong></td>
<td>14 (8/56)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Overall results of SLNB, %</strong></td>
<td>73 (35/48)</td>
<td>92</td>
<td>67</td>
<td>57</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>SLNs per patient, range, No.</strong></td>
<td>1-11 (median, 2)</td>
<td>NA (68% had 1 SLN)</td>
<td>1-5</td>
<td>1-5 (mean, 2.6)</td>
<td>1-8 (mean, 2.5)</td>
<td>NA (mean, 2.7)</td>
</tr>
<tr>
<td><strong>Positive SLNs, %</strong></td>
<td>8</td>
<td>12</td>
<td>10</td>
<td>90</td>
<td>99</td>
<td>96</td>
</tr>
<tr>
<td><strong>Desmoplastic or spindle cell histology of the primary tumor, No. (%)</strong></td>
<td>12 (21)</td>
<td>NA</td>
<td>NA</td>
<td>0</td>
<td>1 (1)</td>
<td>4 (7)</td>
</tr>
<tr>
<td><strong>Same-basin recurrence in SLN-negative patients, No. (%) [follow-up, mo]</strong></td>
<td>All NED [median, 20] (N = 58)</td>
<td>All NED [median, 11.6] (N = 30)</td>
<td>2/19 (10.5) (N = 70)</td>
<td>1/58 (2) [median, 11] (N = 70)</td>
<td>1/47 (2) [median, 15.9] (N = 70)</td>
<td></td>
</tr>
<tr>
<td><strong>“False-negative” rate, No. (%)§</strong></td>
<td>1/5 (20)</td>
<td>0/14</td>
<td>0/6</td>
<td>2/10 (20)</td>
<td>1/13 (8)</td>
<td>1/11 (9)</td>
</tr>
</tbody>
</table>

*SlnB indicates sentinel lymph node biopsy; NA, not available; and NED, no evidence of disease.
†Results reported in 70 SLNs identified overall.
‡Data for head and neck patients are not reported separately.
§Number of same-basin recurrences ÷ (number of same-basin recurrences + number of SLNB-positive patients).

In addition, 6 patients had a second SLN identified in the cervical region. One of these contained metastatic melanoma in the setting of a negative parotid SLN. With median follow-up of 33 months, they reported 1 recurrence in the 33 patients whose parotid SLN was negative, so that 1 (20%) of the 5 patients whose parotid SLNs harbored tumor was missed on SLNB. There were no major complications, and 1 patient (3%) developed temporary facial paresis that resolved completely. Based on these results, the authors concluded that intraparotid and periparotid lymph node dissection without formal parotidectomy is safe and effective SLNB procedure. To date, we have seen no parotid region recurrences after negative SLNB; although 4 of 15 patients developed postoperative facial weakness, all of them regained complete function. It cannot be overemphasized that this technique should be used only by the experienced parotid surgeon who has a sense of the depth and course of the main trunk and of the branches of the facial nerve. As was the case in 6 of 15 patients, if an SLN is not readily apparent, it is always safer to perform a standard superficial parotidectomy, identifying the main trunk and relevant branches of the facial nerve. There is no indication for removal of parotid tissue deep to the plane of the facial nerve because the deep lobe of the parotid or parapharyngeal nodes are generally not thought to be at risk in cases of cutaneous melanoma. Although most centers do not routinely use frozen section analysis in assessing SLNs, this investigation is especially valuable in assessing parotid region SLNs. Delayed completion parotidectomy may place the facial nerve at greater risk of injury, and this situation can be avoided if parotidectomy is performed at the time of SLNB, when metastases are detected on frozen section.

Reporting the false-negative rate for this procedure is problematic because of the difficulty in reliably assessing the status of the remainder of the basin by using nonsurgical means. The most accurate approach would be to have each patient undergoing SLNB have an immediate completion lymph node dissection so that the status of the entire nodal basin at risk can be compared with that of the SLNs. In an ideal situation, after such a policy of immediate completion ELND, SLNs and non-SLNs would be examined in equal detail using immunohistochemical methods and serial step sectioning to allow a truly valid evaluation of the technique, but this is obviously impractical. The current, more acceptable method to determine false-negative rates is to document the rate of nodal failure within SLN-negative basins over time. The incidence of same-basin recurrences after negative SLNB has been reported to be as high as 10.5% (Table 2). With limited median follow-up of 20 months, we have had 1 failure within a sampled basin after a negative SLN, and the true predictive accuracy of SLNB in our hands will be apparent only with time.

As Table 2 demonstrates, our results are comparable to those of other recent series. Although the incidence of positive SLNs has been reported to be as high as 27%, only 8% of our patients had a positive SLN. It is possible that this relatively low incidence of positive SLNs may correlate with the higher percentage of desmoplastic and spindle cell melanomas in our series vs others.
(Table 2). In addition, high-risk factors that are known to predispose to nodal metastases, such as ulceration of the primary tumor, were present relatively infrequently in our patients (13%) compared with other reported series (data not shown). Although SLNs harvested from patients with spindle cell and desmoplastic melanomas have been shown to consist of only rarely harbor micrometastases, we could not demonstrate a significant difference in positivity rates in spindle cell and desmoplastic tumors (n = 12, no positive SLNs) vs other tumors (n = 44, 4 positive SLNs in 40 patients).

With an increasing understanding of the molecular and immunologic mechanisms of the disease, assays such as reverse transcriptase–polymerase chain reaction for tyrosinase, or one of the other markers, such as GP-100, MAGE-3, and MART-1, are being evaluated to detect disease at the molecular level. The clinical relevance of these tests, however, is not clear and is currently being assessed in the multi-institutional Sunbelt Melanoma Trial on a prospective basis. The validity and usefulness of SLNB, nevertheless, is well established, and even using conventional histopathologic evaluation, it is a reliable predictor of the status of the draining nodal basins.

In summary, patients with cutaneous melanomas of the head and neck provide a unique anatomic consideration because they often have multiple SLNs and an unpredictable pattern of involvement. Particular concern exists in terms of intraparotid lymph node biopsy and ultimate facial nerve function. The combination of PLSG and blue dye injection improves the success rate of SLNB. Although SLN mapping is a reliable indicator of the status of the draining lymphatic basins in cutaneous melanomas of the head and neck, given the incidence of false-negative results reported in this and other series, patients with negative SLNs need to be observed for longer periods to understand the true implications of the procedure.

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