Patterns of Drainage and Recurrence Following Sentinel Lymph Node Biopsy for Cutaneous Melanoma of the Head and Neck

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Objectives: To analyze lymphatic drainage patterns and recurrence patterns in patients undergoing sentinel lymph node biopsy (SLNB) for cutaneous head and neck melanoma.

Design: Retrospective review of a consecutive series with a mean follow-up of 35 months.

Setting: Tertiary cancer care center.

Patients: Fifty-one patients with clinically node-negative cutaneous melanoma of the head and neck region staged by means of SLNB.

Interventions: Sentinel lymph nodes (SLNs) were identified using preoperative lymphatic mapping along with intraoperative gamma probe evaluation and isosulfan blue dye injection. Patients with a positive SLNB finding by hematoxylin-eosin or immunohistochemical evaluation underwent completion lymphadenectomy of the affected lymphatic basin and were considered for further adjuvant treatment. Patients with a negative SLNB finding were observed clinically.

Main Outcome Measures: Location characteristics of SLNs, incidence of positive SLNs, same-basin recurrence, and disease-free survival.

Results: The mean number of SLNs per patients was 2.75. The extent of SLNB included removal of 1 node (n=11), multiple nodes from 1 basin (n=18), 1 node in multiple basins (n=7), and multiple nodes in multiple basins (n=15). Drainage to unexpected basins was found in 13 of 51 patients. Parotid region drainage was identified in 18 patients. There were no same-basin recurrences in patients with a negative SLNB finding. Thirty-six–month disease-free survival was 88.9% for patients with a negative SLN and 72.9% for patients with a positive SLN (P=.17).

Conclusions: The number and location of SLNs is variable and difficult to predict for head and neck cutaneous melanoma. Preoperative lymphoscintigraphy is an important planning instrument to guide complete removal of all SLNs. Based on 3-year follow-up, this procedure can be expected to provide low same-basin recurrence rates for patients with a negative SLN.

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The pathologic status of the sentinel lymph node (SLN) has been shown to be the most important prognostic factor for recurrence in cutaneous melanoma. The SLN biopsy (SLNB) provides accurate nodal staging with low morbidity and is useful in selecting patients who are most likely benefit from completion lymph node dissection (CLND) and possibly other adjuvant therapy. The SLN is defined as a node that receives direct independent drainage from the primary melanoma site. It is not necessarily the closest node, but it does exclude secondary nodes from flowing from that particular node as observed by lymphoscintigraphy.

Sentinel lymph node biopsy for the head and neck presents a number of unique challenges that may influence the accuracy of the procedure. Anatomic prediction of potential nodal metastatic sites is difficult because of complex lymphatic drainage in this region. The proximity of vital structures within the head and neck region as well as the proximity of the primary injection site to draining nodal basins increases the technical complexity. Our objective is to report the findings of a 3-year follow-up study of SLNB for the head and neck at a single institution and, specifically, to consider same-basin recurrence rates, disease-free survival, and parotid region drainage.

METHODS

PATIENTS AND PROCEDURES

The institutional review board of Baylor University Medical Center, Dallas, Tex, granted approval for this study. Over an 8-year period,
51 patients underwent lymphatic mapping and SLNB for cutaneous melanoma of the head and neck at Baylor University Medical Center. The inclusion criteria included a histologically confirmed cutaneous melanoma thicker than 1 mm or thicker than 0.7 mm with a Clark level of 4. The interval from biopsy to SLNB was less then 30 days in all cases. Preoperative evaluation of these patients, which included medical history, physical examination, chest radiograph, and liver function tests, did not show evidence of nodal or metastatic disease.

Prior to surgery, all patients underwent lymphoscintigraphy with intradermal injection of technetium Tc 99 sulfur colloid (0.2-1.2 mL; 7.4-44 μCi). Multiple injections were placed around the primary tumor site. Dynamic images of corresponding lymphatic basins were taken for 30 minutes after tracer administration. Areas identified by significant tracer uptake as draining lymph node were marked with indelible ink, and static scintigrams were produced.

The patient was taken to the operating room, and isosulfan blue dye was injected around the primary tumor site. A handheld gamma radiation detection probe (C-Trak; Carewise Medical, Morgan Hill, Calif) was used to identify the site of greatest radioactivity within the draining lymph node basin. Surgical exploration was undertaken through a limited incision oriented to facilitate CLND if necessary. The handheld gamma probe and visualization of blue-stained afferent lymphatic vessels leading to blue-stained SLNs guided surgical excision. An SLN was defined as one that localized blue dye and/or concentrated radiolabeled colloid (ratio of ex vivo radioactive count to residual nodal bed count, >10:1). After localization and excision of the SLN, a wide local excision of the primary melanoma was performed with margins appropriate for tumor thickness. In cases where the radioactivity associated with the injection site interfered with gamma probe investigation of the SLN, the excision of the primary tumor was performed first.

All SLNs were evaluated using serial sectioning with hematoxylin-eosin staining. Beginning in 1997, immunohistochemical stains (HMB-45 and/or S100) were routinely used for patients when hematoxylin-eosin did not reveal evidence of metastatic disease (n=38).

Patients whose SLN was found to harbor metastatic disease were offered CLND of the affected basin. This CLND included modified radical neck dissection of the affected side for patients with positive SLNs found in the neck and superficial parotidectomy along with modified radical neck dissection of the affected side for patients with positive SLNs in the parotid basin. Patients with a positive SLN after December 1997 were also offered participation in prospective clinical trials evaluating adjuvant therapy regimens.

**STATISTICAL ANALYSIS**

The χ² test was used to determine association between covariates in univariate models. Means testing of continuous variables (tumor thickness and age) was performed with the product-limit method and analyzed using the log-rank procedure.

**RESULTS**

**CLINICAL CHARACTERISTICS**

From March 1994 through April 2002, 51 patients underwent lymphatic mapping and SLNB for cutaneous melanoma of the head and neck at Baylor University Medical Center. The clinical characteristics of these patients are summarized in Table 1. The median age was 56.2 years and men made up 69% of the group. The sites of the primary melanomas categorized by anatomic regions included the face (n=12; 24%), ear (n=11; 22%), frontoparietal scalp (n=5; 10%), occipital scalp (n=7; 14%), and neck (n=16; 31%). The mean tumor thickness in the total population was 1.86 mm (range, 0.75-7.5 mm). Ninety-two percent of patients were found to have primary tumor thickness between 0.75 mm and 4.0 mm. One patient had a primary tumor depth less than 0.75 mm; the initial biopsy specimen in this case demonstrated a Clark level of 4, and there was question as to the involvement of the deep margin. Three patients with melanomas deeper than 4 mm underwent SLNB.

The number of SLNs per patient averaged 2.75 (range, 1-6). The extent of SLNB included removal of 1 node (n=11), multiple nodes in 1 basin (n=18), 1 node in multiple basins (n=7), and multiple nodes in multiple basins (n=15). The identification of multiple basins was based on primary pathways as observed by lymphoscintigraphy. The gamma probe was used in each “hot” spot, and the hottest node was identified. If residual counts in that area exceeded 10% of the counts of the hottest node then additional dissection was used to identify dominant secondary nodes. Analysis of the location of sampled SLNs allowed for categorization into regional basins, which included the parotid (n=18), anterocervical (n=33), posterocevical (n=10), and supravaculcavial regions (n=12). The parotid region was defined as the preauricular and infraauricular area near the angle of the mandible. Parotidectomy was performed as part of the sentinel lymphadenectomy in 6 patients and as part of the CLND for 2 patients. The pattern of drainage was thought to be discordant in 13 of 51 patients. The discordant drainage occurred mostly in frontoparietal primary tumors with Clark level 5 drainage (n=7) and facial primary tumors with Clark level 5 drainage (n=6). Discordant drainage was difficult to characterize in other primary tumor sites because almost all basins are theoretically possible.

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<th>Table 1. Clinical Characteristics of 51 Patients With Melanoma of the Head and Neck Region</th>
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<td><strong>Sex, No. (%)</strong></td>
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<td><strong>Site of primary tumor, No. (%)</strong></td>
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<td>Face</td>
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<td>Sentinel lymph node status, No. (%)</td>
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*Mean tumor thickness was 1.86 mm; median, 1.50 mm.
A positive SLN was identified by hematoxylin-eosin or immunohistochemical staining in 8 of the 51 patients. Sentinel lymph node status stratified by tumor depth is summarized in Table 2. For patients with a positive SLN, the average depth of the primary tumor was 3.38 mm (range, 1.13-7.5 mm). The incidence of positive SLN increased as the depth of the tumor increased; all the patients with a primary tumor depth greater than 4.0 mm (n=3) had a positive SLN. In the 8 patients with a positive SLN, an average of 2.9 nodes were harvested as SLNs. The number of positive SLNs in each case was either 1 (n=7) or 2 (n=1).

Seven of the 8 patients with a positive SLN underwent CLND of the involved lymphatic basin; 1 patient refused further treatment. Further lymphatic disease was identified in only 1 of these patients. This patient presented with a 1.8-mm lesion on the right cheek. A single SLN was identified along the inferior border of the right mandible. On completion of right modified radical neck dissection, 2 other positive lymph nodes were identified within the level I nodal region. This patient experienced recurrence at the primary site with subsequent systemic metastatic spread.

### HISTOLOGIC ANALYSIS

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### RECURRENCE

Of the 51 patients in this study, 7 had evidence of recurrence during a mean follow-up of 35 months. Of the 43 patients with a negative SLN, 5 patients (14%) experienced recurrence at a mean interval of 19.2 months. In the group of 8 patients with a positive SLNB finding, 2 patients (25%) evidenced signs of recurrence at a mean interval of only 6.7 months.

The pattern of recurrence is provided in Table 3 according to SLN status. Of the 7 total recurrences, the first clinical signs of recurrence were found to be local (n=2; 29%), nodal (n=1; 14%), and systemic (n=4; 57%). In the negative SLN group, there were no nodal-basin recurrences. In the positive SLN group, the first sign of recurrence occurred in the nodal or local sites, and all patients eventually died with systemic disease. Analysis of possible prognostic factors for recurrence is provided in Table 4. As expected, patients with recurrence had a greater mean melanoma thickness and a higher percentage of positive SLNs; however, none of the covariates tested were found to be statistically significant. This finding is not unexpected, given the small number of patients with recurrence in this population.

### PAROTID-REGION SLNs

Eighteen (35%) of the 51 patients had SLNs mapped to the parotid region. The sites of the primary lesions were the external ear (n=6), cheek and preauricular area (n=7), postauricular area (n=4), and forehead (n=1). The thickness of the primary lesions in this subgroup averaged 1.78 mm (range, 0.8-4.5 mm). The parotid was the sole draining basin in only 3 of these patients. Two of the 18 patients had positive parotid-region SLNs. Two other patients had metastatic disease identified in other SLNs that were sampled concurrently with the parotid-region SLNs.

In 9 patients, the SLNs were found to be located in the periphery of the parotid gland and were excised without parotid dissection. In the other 9 patients, the SLNs were embedded within the body of the parotid gland. Six of these patients underwent a superficial parotidectomy with ex vivo identification of the SLNs; the other 3 underwent intraparotid SLNB. During a mean follow-up of 35 months, only 1 patient who had undergone a superficial parotidectomy for intraparotid drainage and was found to have a negative SLN experienced systemic recurrence. There were no local or nodal recurrences in either the intraparotid or periparotid subgroup. There also were no instances of motor deficit in any of these 18 patients.

A 3-year Kaplan-Meier disease-free survival curve is presented in the Figure. The disease-free survival rates were 88.9% and 72.9% for patients with negative and posi-
Sentinel lymph node biopsy for cutaneous melanoma of the head and neck region is known to offer unique challenges. O’Brien et al6 categorized head and neck primary melanomas into 10 anatomic subgroups and then correlated lymphoscintigraphic findings with anatomic predictions. Discordant results were identified in 33 (34%) of 97 patients. In a similar assessment of the present series, 13 (26%) of 51 patients were found to have SLNs outside the anatomically expected sites of involvement. Predictions for lymphatic drainage may be further complicated by notable variability within expected drainage basins. This variability becomes technologically important for basins that may require distinctive surgical planning or incisions such as the parotid and supraclavicular regions. In the present series, all 11 primary lesions located on the external ear had an SLN located in the anterior cervical region; however, 4 of these patients also had SLNs located within the parotid region, while 7 did not. No distinguishing predictors of the parotid drainage were identified.

At our institution, the average number of SLNs per patient for the head and neck region was 2.75, which is significantly higher than the 2.1 average for trunk and extremity cutaneous melanoma in a similar series at our institution.8 Correspondingly, the percentages of patients with more than 1 SLN were 76.5% for head and neck and 63% for trunk and extremity melanoma.

This increased lymphatic complexity requires technical vigilance to ensure accurate assessment of the patient’s nodal status, as notably demonstrated in 1 case in our series. Prior to SLNB, a preoperative lymphoscintigram was performed for a lesion on the right cheek after 77.7 MBq of technetium Tc 99 sulfur colloid was injected intradermally. Three lymph nodes were identified within the right side of the neck; no parotid lymph nodes were visualized. After discussion with the nuclear medicine radiologist, it was decided to repeat the study at a later date with less sulfur colloid and fine matrix resolution in an attempt to visualize the parotid-region lymph nodes. Two weeks later, after an injection of 18.5 MBq of technetium Tc 99 sulfur colloid, which produced less injection site interference, an obvious parotid-region node was localized by lymphoscintigraphy and later by gamma probe evaluation. This node was excised along with the draining nodes in neck level II. We have also noticed an advantage to performing colloid injection the night before surgery: the radioactivity around the injection site is more dispersed by the time of evaluation, which allows for improved identification of draining nodes adjacent to the injection site.

PAROTID-REGION DRAINAGE

When considering surgical options for patients with SLN drainage to the parotid region, SLNs can be classified into 2 categories. The first includes those that are either adherent to the parotid gland or superficially embedded within the gland tissue. The second category includes SLNs that are distinctly embedded within the body of the gland. The present study and that of Ollila et al9 is that intraglandular dissection presents distinct technical challenges. The parotid-region nodes are consistently small (3-6 mm), are often densely adherent to surrounding fibrofatty tissue, and are often difficult to discretely localize by gamma probe. Removing all of the lymph nodes identified by lymphoscintigraphy can also prove challenging: Wells et al10 reported that 5 (21%) of 24 patients who underwent parotid selective lymphadenectomy without parotidectomy did not have all nodes that were identified on lymphoscintigraphy excised. The principal consideration for intraglandular dissection is the significant morbidity associated with damage to the facial nerve. The low morbidity rate of a standard superficial parotidectomy that has been repeatedly verified in large studies11-13 necessitates judicious use of intraglandular dissection if the facial nerve is not identified.

Distinguishing these 2 categories preoperatively has not proven straightforward. In our experience, preoperative lymphoscintigraphy is indispensable in identifying lesions with lymphatic drainage to the parotid region. Unfortunately, present nuclear medicine techniques do not accurately distinguish between periparotid and intraparotid SLNs. We have noticed a higher incidence of intraparotid SLNs among patients with preauricular primary lesions (5 of 6) than in those patients with primary lesions in other locations; however, this observation does not reach statistical significance in our population (P = .29).

In managing parotid-region SLNs, the practice at our institution is to first obtain a preoperative lymphoscintigram for all patients with cutaneous head and neck melano-
The risk of facial nerve injury is elevated in cases where there are (1) multiple areas of radioactive intensity within the gland; (2) large, diffuse glandular areas of radioactivity; and/or (3) poorly defined afferent lymphatics. In such scenarios it is sensible to first identify the facial nerve and then proceed with a superficial parotidectomy and ex vivo identification of SLNs. Based on these criteria, of the 18 patients in the present study with parotid-region SLNs, 9 underwent SLNB for periparotid SLNs; 3 underwent SLN excision without superficial parotidectomy for intraparotid SLNs; and 6 underwent superficial parotidectomy for intraparotid SLNs. There were no patients with postoperative motor deficits and no significant wound complications.

SAME-BASIN RECURRENCE RATES

The same-basin recurrence rate for negative SLNs is an important means of assessing the false-negative rate for SLNB. It is, however, dependent on a long period of follow-up for accuracy. Five recent studies with a mean follow-up range of 11 to 21 months have reported same-basin recurrence rates from 0% to 10.5%.14-18 Bostick et al10 in 1997 offered the study with the longest follow-up: in 82 patients with a mean follow-up of 46 months, there were no same-basin recurrences in the group of patients with a negative SLN. The present study offers similar validation of a low false-negative rate for SLNB of the head and neck region. Over a mean follow-up of 35 months, we have also found no same-basin recurrences among the 43 patients with a negative SLN.

Using the large database accrued through the Sunbelt Melanoma Trial, Chao et al20 recently reported a same-basin recurrence rate of 1.9% in the 278 patients found to have a negative SLN. The average follow-up for this group was only 15.5 months, so reports after longer follow-up will be of interest. This 1.9% false-negative rate of head and neck melanomas is significantly higher than the 0.5% false-negative rate reported for cutaneous trunk and extremity melanomas in the same study (P < .05). This significant difference is not unexpected, given the increased complexity of head and neck SLN.

In conclusion, SLNB for cutaneous head and neck melanoma can be expected to provide low false-negative rates based on 3-year follow-up. There is continued evidence for the variable pattern of lymphatic drainage in the head and neck region that must be given appropriate consideration when performing SLNB. Pre-operative lymphoscintigraphy is an important planning instrument to guide the removal of all SLNs. While many parotid-region SLNs can be safely excised without formal superficial parotidectomy, the potential for superficial parotidectomy to excise all SLNs with minimal risk to the facial nerve should be considered in preoperative planning.

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