Discordancy Between Clinical Predictions vs Lymphoscintigraphic and Intraoperative Mapping of Sentinel Lymph Node Drainage of Primary Melanoma

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Objective: To evaluate discordancy between clinical predictions and lymphatic drainage patterns of primary cutaneous melanoma as determined by preoperative lymphoscintigraphy and intraoperative lymphatic mapping of sentinel lymph nodes (SLNs).

Design: Before selective SLN dissection, 226 consecutive patients with melanoma underwent preoperative lymphoscintigraphy.

Setting: Teaching hospital tertiary care center.

Main Outcome Measure: Correlation of lymphatic drainage patterns from the following 3 data sources: clinical predictions preoperatively based on anatomical location of primary melanoma, lymphatic drainage patterns as determined by preoperative lymphoscintigraphy, and identification of SLNs during surgery.

Results: Preoperative lymphoscintigraphy was successful in identifying at least 1 SLN in all 226 patients. In head and neck melanomas, at least 1 SLN was identified in an area outside what would have been clinically predicted in 11 (36.7%) of 30 cases. Discordancy for trunk melanomas was seen in 24 (25.3%) of 95 cases. Extremity melanomas showed drainage to unexpected SLNs in 6 (13.6%) of 44 and 3 (5.3%) of 57 patients for the upper and lower extremities, respectively. The overall rate of discordancy was 44 (19.5%) of 226. The SLNs were identified in surgery in all but 4 cases.

Conclusions: Discordancy is most frequent in melanomas of the head and neck region, followed by that of the trunk. Preoperative lymphoscintigraphy identifies the occasional cases in the upper and lower extremities where drainage occurs to a basin that is not clinically predictable. Preoperative lymphoscintigraphy is a prerequisite for characterizing the lymphatic drainage pattern in patients with primary melanoma, especially for sites such as head and neck as well as trunk, before selective SLN dissection.

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PATIENTS AND METHODS

Two hundred forty-two consecutive patients with invasive cutaneous melanoma seen at the University of California–San Francisco (UCSF) Mount Zion Cancer Center from November 1, 1993, through June 30, 1997, underwent evaluation for admission into our study. Sixteen patients were excluded because they had a previous wide excision of their primary melanoma site with adequate margins. Thus, all 226 eligible patients underwent a punch, shave, or narrow biopsy before SSLND. There were 131 male and 95 female patients with a mean age of 51.6 years (range, 17-88 years). The median Breslow thickness for the primary melanoma was 1.8 mm (range, 0.4-14.5 mm). At the UCSF–Mt Zion Cancer Center, all patients with a primary melanoma with Breslow thickness of at least 1.0 mm are recommended to undergo an SSLND. If a shave biopsy was performed that resulted in a diagnosis of less than 1.0 mm, an SSLND was also recommended because the true thickness of the lesion may be underestimated. Other patients with Breslow thickness of less than 1.0 mm underwent an SSLND if their primary melanoma showed high-risk features such as ulceration, regression, or lymphatic invasion. Overall, patients with Breslow thickness of at least 1.0 mm constituted 94.7% of the entire group of 226 patients.

All patients underwent preoperative lymphoscintigraphy on the morning of their surgery. The technique has been described in detail previously. Briefly, technetium Tc 99m (99mTc) sulfur colloid filtered through a 22-µm filter was injected intradermally around the primary melanoma or the biopsy site. Immediate dynamic imaging was performed to assess the uptake of radiotracer by the lymphatic channels. Delayed imaging was then performed to evaluate the focal accumulation of the radiotracer in the lymph nodes. Median delayed imaging duration was 60 minutes (range, 10-165 minutes). The locations of these nodes were marked on the skin using indelible ink. An average of 19.6 MBq (range, 3.0-63.6 MBq) of 99mTc sulfur colloid was used. In 222 patients, iodosulfan blue (Lymphazurin; Hirsch Industries, Richmond, Va) was injected intradermally around the primary site immediately before surgery. An average of 3.7 mL (range, 0.8-10.0 mL) of blue dye was injected. The SSLND procedure was then performed, in addition to a wide local excision of the primary site. Using a handheld gamma probe (Neoprobe Corporation, Dublin, Ohio), lymph nodes with high gamma emissions were localized. High lymph node-to-background count ratios or blue color were used to identify the SLNs.

Clinical predictions of the location of the nodal basin draining the primary site were made according to standard drainage patterns. For the lower extremities, cutaneous lymphatic drainage was expected to the inguinal (femoral) area only. Drainage to the popliteal area was considered to be discordant. For the upper extremities, drainage was expected to the axillary area only. Drainage to the epitrochlear or supraclavicular area was considered to be discordant.

For patients with truncal melanomas, drainage was expected to occur to the nearest axillary or inguinal basin. If a primary melanoma was located within 2.5 cm of the midline, then drainage could occur to either side or both sides and was not considered to be discordant. Similarly, for primary melanomas located within 2.5 cm of the Sappey line, drainage could occur to the ipsilateral groin, axilla, or both. For example, a primary melanoma located at the umbilicus or at L2 could drain to any combination of axillary or inguinal basins and not be considered discordant.

For patients with head and neck primary melanoma sites, the algorithm for determining discordant drainage was based directly on the patterns illustrated by O’Brien et al. The primary melanoma lesions were classified by location into 10 regions on the head and neck. Drainage areas were identified as parotid (area 1), submandibular and submental triangles (area 2), upper jugular (area 3), midjugular (area 4), lower jugular (area 5), posterior triangle (area 6), and occipital area (area 7). If a primary melanoma site exhibited drainage to an area outside the predicted areas, then the drainage was considered to be discordant. The following tabulation shows the predicted drainage areas:

<table>
<thead>
<tr>
<th>Primary Site</th>
<th>Predicted Area of Drainage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior scalp</td>
<td>1-4</td>
</tr>
<tr>
<td>Coronal scalp (5-cm band)</td>
<td>1-6</td>
</tr>
<tr>
<td>Posterior scalp</td>
<td>2-5, 7</td>
</tr>
<tr>
<td>Face</td>
<td>1-4</td>
</tr>
<tr>
<td>Ear</td>
<td>1-6</td>
</tr>
<tr>
<td>Anterior upper neck</td>
<td>1-5</td>
</tr>
<tr>
<td>Coronal neck (5-cm band)</td>
<td>1-6</td>
</tr>
<tr>
<td>Posterior upper neck</td>
<td>2-5, 7</td>
</tr>
<tr>
<td>Anterior lower neck</td>
<td>3-5</td>
</tr>
<tr>
<td>Posterior lower neck</td>
<td>3-5</td>
</tr>
</tbody>
</table>

than 95% of the time. However, the accuracy of the SSLND technique depends on the reliability of preoperative lymphoscintigraphic localization of the SLN. Lymphoscintigraphy has been shown to be an excellent predictor of lymphatic drainage from primary melanoma based on nodal recurrence as demonstrated by long-term follow-up.

Early lymphoscintigraphic studies have demonstrated variability in the lymphatic drainage patterns from different sites of the primary melanoma. Although the head and neck region appears to show greatest variability, the trunk region also demonstrates significant variation, especially for melanomas arising on the midline and near the Sappey line. Drainage from extremity melanomas has been considered to be less variable.

Preoperative lymphoscintigraphy and intraoperative mapping of the SLN may constitute a preferable alternative to the traditional method of elective lymph node dissection based on anatomical predictions. Preoperative lymphoscintigraphy will identify the draining nodal basin accurately, after which intraoperative mapping of SLN will facilitate the SSLND for accurate staging of the nodal basin, thus sparing about 80% of patients with melanoma a formal elective lymph node dissection. Therefore, our goals are to evaluate the lymphatic drainage patterns of cutaneous malignant melanoma based on preoperative and lymphoscintigraphy.
and intraoperative mapping of SLNs, and to compare these patterns with those based on traditional anatomic and clinical predictions.

**RESULTS**

All 226 patients included in this study underwent a successful lymphoscintigraphy that identified at least 1 SLN in 1 basin. A single basin draining a primary melanoma site was identified in 178 patients (78.8%). Thirty-one patients (13.7%) had 99mTc sulfur colloid localization of patients with at least 1 SLN in 1 basin. A single basin draining a primary melanoma site was identified in 178 patients (78.8%). Thirty-one patients (13.7%) had 99mTc sulfur colloid localization

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- **Head and neck (n = 30)**
  - Standard: None (19)
  - Drainage to area not consistent with predicted pattern: Standard drainage (11)

- **Trunk (n = 95)**
  - Standard: None (71)
  - Contralateral axilla: Drainage across midline (8)
  - Contralateral groin: Drainage across midline (1)
  - Posterior and/or anterior cervical: Nonstandard drainage (4)

- **Supraclavicular:**
  - Nonstandard drainage (4)
  - Chest wall: Nonstandard drainage (4)
  - Lower back: Nonstandard drainage (2)
  - Posterior triangle: Nonstandard drainage (1)

- **Upper extremity (n = 44)**
  - Axillary: None (38)
  - Axillary and epitrochlear: Additional basin (2)
  - Axillary and supraclavicular: Additional basin (2)
  - Axillary and subclavicular: Additional basin (1)
  - Supraclavicular only: Nonstandard drainage (1)

- **Lower extremity (n = 57)**
  - Inguinal: None (54)
  - Inguinal and popliteal: Additional basin (3)

The SLNs were identified in surgery in all but 3 cases. One patient had primary melanoma in the preauricular area, with lymphoscintigraphy indicating drainage to the parotid. Another patient had a right occipital scalp melanoma with drainage to right upper jugular lymph nodes. The third exhibited discordant drainage from a primary melanoma in the right postauricular area to the right submandibular and upper jugular areas.

Of the 27 patients in this group with successful harvesting of SLNs, 2 had SLNs with micrometastasis. The first case involved a primary melanoma located in the midline upper occipital area with concordant drainage to the occipital lymph nodes. The second case involved a patient with a postauricular melanoma with drainage to the upper jugular lymph nodes as well as discordant drainage to the supraclavicular area. An SLN from each basin was determined to contain micrometastasis.

### HEAD AND NECK

Thirty patients with primary melanoma in the head and neck area underwent successful preoperative lymphoscintigraphy. Of these patients, 19 (63.3%) had drainage concordant with clinical prediction as illustrated in Table 1, and 11 (36.7%) had discordant drainage.

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### TRUNK

A total of 95 patients had a primary melanoma in the truncal region. Of these, 71 (74.7%) had concordant drainage, and 24 (25.3%) had discordant drainage. Types of discordant drainage are listed in Table 1. The SLNs were identified in all but 1 patient. This patient had a primary site located in the left upper back with discordant drainage to the left supraclavicular area only and no drainage to the left axillary area.

Of the 94 patients in this group with a successful SSLND, 24 had an SLN with positive findings. Of these 24 patients, 19 (79.2%) had concordant and 5 (20.8%) had discordant lymphoscintigraphy. Thus, the percentage of discordant drainage was similar between the positive-SLN subgroup and the entire group of patients with truncal melanomas.

### UPPER EXTREMITIES

A total of 44 patients had a primary melanoma located on the upper extremity. Of these, 38 (86.4%) had concordant drainage and 6 (13.6%) had discordant drainage as summarized in Table 1. The SLNs were identified in all 44 patients. Seven patients had at least 1 SLN that exhibited micrometastasis. Of these 7 patients, 3 had concordant and 2 had discordant drainage. Of these 2, one patient had drainage to the supraclavicular area only, and the other had drainage to the supraclavicular and axillary basins. In this latter case, the axillary SLN was positive for micrometastasis.

### LOWER EXTREMITIES

A total of 57 patients had a primary melanoma located in the lower extremities. Of these, 54 (94.7%) had concordant lymphoscintigraphy and 3 (5.3%) had discordant lymphoscintigraphy. One patient had an external iliac SLN and 2 patients had a popliteal SLN in addition
to the inguinal or femoral drainage. All 57 patients had an SLN identified in surgery. Of these, 16 patients had at least 1 SLN with positive findings. All 16 patients with positive SLN findings had concordant drainage. The discordancy rates for all anatomical sites are summarized in the Figure.

**NODAL BASINS AND SLN STATUS**

Table 2 summarizes the mean number of basins identified by lymphoscintigraphy per patient by anatomical site of the primary melanoma. Primary sites of the upper and lower extremities averaged slightly over 1 basin per patient, whereas primary sites on the head, neck, and trunk drained to almost 1.5 basins on average. About 20% of patients with extremity melanoma had SLNs with positive findings. One quarter of the patients with primary melanoma on the trunk had an SLN with positive findings, whereas less than 7% of the patients with a primary melanoma on the head or neck had an SLN with positive findings.

**COMMENT**

Multiple studies have established the combined technique of preoperative lymphoscintigraphy and intraoperative mapping for the harvesting of SLNs. The overall success rate for using blue dye alone ranges from 75% to 85%, vs more than 98% using a combination of blue dye and $^{99m}$Tc. The intraoperative handheld gamma probe guides the surgeons to the area of greatest radioisotope uptake with pinpoint accuracy.

With the perfection of the intraoperative SLN mapping method, the combination of preoperative lymphoscintigraphy and intraoperative mapping of SLN should become the standard approach for the harvesting and assessment of SLN for patients with primary malignant melanoma but without clinically palpable nodal disease. To achieve a high rate of accurate and successful identification of the SLNs, it is imperative that surgeons, physicians of nuclear medicine, and pathologists work together closely as a multidisciplinary team. The significant discordancy rate shown by this study is consistent with that of other studies. Given the discordancy rates, especially in head and neck (36.7%) and trunk (25.3%), preoperative cutaneous lymphoscintigraphy is recommended for detection of relevant draining lymph node basins over the traditional anatomical method.

Based on follow-up studies from Gershenwald et al and one from our group (S.P.L.L., T.A.A., F.A.H., I.S., R.E.A., M.K.-S., R.S., J. R. Miller, MD, P. Ituarte, PhD, MPH, K. R. Abbey, JD, P. Treseler, MD, and S. Mraz, MD, unpublished data, 1999), patients with SLNs with positive findings have reduced disease-free survival compared with those with SLNs with negative findings. The SLN status analyzed using univariate and multivariate analysis in comparison with the other prognostic factors influencing the outcome of melanoma SLN status was found to be the most important prognostic factor influencing disease-free survival in patients with stages I and II melanoma. These findings support the contention that lymphatic mapping of SLNs and SSLND accurately select the lymph node most likely to harbor micrometastasis. Therefore, the role of SSLND is to provide accurate staging at the initial diagnosis of primary melanoma.

To have an accurate staging result from SSLND, it is mandatory to have preoperative lymphoscintigraphy. For that reason, physicians such as dermatologists and surgeons should be familiar with this technique and the potential use of it as a staging purpose, and wide local excision should be reserved until the SLN harvesting is completed. Because the discordancy rate is substantial in the head and neck as well as in the trunk, wide local excision before SLN detection may accentuate this discordancy rate. Even in the upper extremities, with relatively reliable clinical predictions, there is still a 13.6% discordancy rate with involvement of an epitrochlear, supraclavicular, or subclavian lymph node. As to the lower extremities, the involvement of the external iliac...
lymph node as well as the popliteal lymph node may be encountered.

CONCLUSIONS

Preoperative lymphoscintigraphy is an essential prerequisite to an SSLND. For patients with a primary melanoma on the upper or lower extremity, lymphoscintigraphy allows for identification of rare drainage to basins other than the axilla or groin. For truncal primary sites, standard drainage patterns may include bilateral and ipsilateral drainage, and discordant drainage may involve in-transit and unusual drainage basins. For the head and neck, drainage is variable, and lymphoscintigraphy provides a reliable tool to guide the surgeon to the areas that drain a particular melanoma site. Preoperative lymphoscintigraphy allows drainage patterns to be defined on an individual basis and, thus, greatly contributes to the success of the selective SLN dissection.

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