Lymphatic Mapping for Staging of Head and Neck Cancer

Jai Balkissoon, Barry M. Rasgon, and Laurie Schweitzer

Lymphatic mapping with sentinel lymph node (SLN) biopsy can accurately stage the nodal basins in patients with melanoma of the trunk and extremities and has become a routine, well-accepted diagnostic method for melanoma at these anatomic locations. Melanoma of the head and neck (16% of all cases of melanoma) is complex and difficult to manage because of the rich abundant interlacing lymphatic drainage patterns, as well as watershed areas, which can lead to unusual and unexpected drainage patterns. Radioguided surgery in combination with blue dye facilitates localization of the SLN in the head and neck; however, this type of radioguided surgery is an evolving technique of some difficulty and thus requires careful coordination among the surgeon, nuclear medicine physician, and pathologist. Applications of this technique to other sites in the head and neck are currently being investigated for conditions including squamous cell carcinoma (SCC) of the oral cavity, thyroid cancer, and Merkel cell cancer. More studies of patients with head and neck cancer are needed—and technical issues must be resolved—before radioguided surgery can be recommended as the standard of care for these patients.

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P RIMARY CUTANEOUS melanoma of the head and neck is uncommon and occurs on all areas of the scalp, face, and neck. The condition is seen more commonly in males and is more aggressive and has a worse prognosis and higher recurrence rate than melanoma of similar thickness in the trunk or extremities.1

The head and neck lymphatics are located within six nodal basins in addition to the parotid region (Fig 1).2 Because these areas are highly vascularized and contain an abundant network of overlapping lymphatic channels, collateral drainage, and watershed areas, drainage patterns are unpredictable and variable. Primary melanoma of the head and neck frequently develops superficially or adjacent to the sentinel lymph node (SLN) basins, which can make preoperative lymphoscintigraphy and intraoperative localization problematic. Because the head and neck are the most visible parts of the body, any surgery in this location must consider cosmesis.

Blue dye has been used by itself to localize the SLN. The drawback of using this method is that the afferent blue lymphatic channel leading to the SLN cannot be visualized unless a skin incision has been made. When this procedure is done in the head and neck, subplatysmal flaps must be raised and the blue channel observed along its course to the lymph nodes. In patients who have unusual ipsilateral, bilateral, or contralateral drainage, SLNs can be missed if this blue dye method is used. The method also complicates identification of SLNs in unusual locations, such as the supraclavicular or axillary areas. Melanomas in the lower parts of the neck and upper parts of the chest can drain to these areas.

Identifying SLNs in the parotid area can be especially difficult. SLNs drain to the parotid area in 30% to 56% of affected patients and most commonly accompany lesions on the ear, anterior aspect of the scalp, and temporal area.3,4 When blue dye alone is used, drainage to the parotid basin is difficult to detect: nodes may be concealed in the substance of the parotid gland, and the SLNs—which are often very small—can resemble surrounding tissue.

Varying success rates have been reported for finding blue-stained SLNs in the head and neck. Chao et al5 reported that 59% of SLNs in the head and neck stained blue compared with 68.6% in the trunk and 74% in extremities. Other studies reported blue staining in 29% (J.B., unpublished data, 2002) and 28%6 of SLNs in the head and neck. These rates are much lower than the rate reported by Bostick et al,7 who found blue-stained SLNs in 92% of patients with head and neck melanoma. This discrepancy in reported success rates may reflect variation in elapsed time from injection to exploration or may reflect use of a different staining procedure (ie, not reinjecting blue dye).

The blue dye migrates rapidly to the SLN and washes out easily because of extensive lymphatics.
and vascularity in the head and neck; Therefore, timing of injection of the blue dye is critical. If injection is done too early, by the time the flaps are being developed and subcutaneous dissection is being done to find the blue channels, the blue dye will have passed through the first echelon nodes. To prevent this rapid transit from being a problem, many surgeons recommend injecting the blue dye 3 to 5 minutes before incision. The blue dye should be re-injected intradermally around the primary site every 15 to 20 minutes. Nontechnical drawbacks of using blue dye in the head and neck region include a cosmetic concern: possible blue staining of skin surfaces that is easily visible. Most blue-stained tissue eventually fades or is removed when the melanomatous tissue is completely excised. Also of concern is the small but real risk of the patient having an anaphylactic reaction to the blue dye.

Imaging techniques using blue dye, radioactive colloid, and gamma probe detection have together increased the SLN detection rate to between 98% and 100%. Most of these imaging studies (Table 1) have described melanoma of the trunk and extremities and not of the head and neck. Most series describing large numbers of melanoma patients do not include many with primary tumors of the head and neck.

**Preoperative Lymphoscintigraphy**

Use of preoperative lymphoscintigraphy has greatly improved our ability not only to identify all the nodal basins at risk but also to identify multiple SLNs and their location within each nodal basin (Table 2). Preoperative lymphoscintigraphy of the head and neck shows between one and three lymph node basins and one to five SLNs per patient. Balkissoon (unpublished data, 2002) has reported visualizing 1.31 nodal basins and 1.75 SLNs.

![Diagram shows lymph node basins of neck. Reprinted with permission. Copyright © 2002, American Medical Association. All rights reserved.](image)

### Table 1. Reported Sensitivity Rates for Lymphatic Mapping

<table>
<thead>
<tr>
<th>Study</th>
<th>Blue Dye Sensitivity</th>
<th>Gamma Probe + Lymphoscintigraphy Sensitivity</th>
<th>Combined Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leong et al, 1999</td>
<td>—</td>
<td>90% (patients)</td>
<td>—</td>
</tr>
<tr>
<td>Wagner et al, 2000</td>
<td>—</td>
<td>—</td>
<td>99% (patients)</td>
</tr>
<tr>
<td>Carlson et al, 2000</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Bostick et al, 1997</td>
<td>92% (basins)</td>
<td>98% (patients)</td>
<td>96% (basins)</td>
</tr>
<tr>
<td>Wells et al, 1998</td>
<td>50% (patients)</td>
<td>—</td>
<td>95% (patients)</td>
</tr>
<tr>
<td>Alex et al, 1998</td>
<td>67% (patients)</td>
<td>91% (patients)</td>
<td>—</td>
</tr>
<tr>
<td>O’Brien et al, 1994</td>
<td>—</td>
<td>98% (patients)</td>
<td>—</td>
</tr>
<tr>
<td>Peralta et al, 1998</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Davison et al, 2001</td>
<td>82% (patients)</td>
<td>94% (patients)</td>
<td>100% (patients)</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td>73%</td>
<td>94%</td>
<td>98%</td>
</tr>
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per patient with melanoma of the head and neck area. Rasgon\(^4\) has reported visualizing 1.4 nodal basins and three SLNs per patient. The multiplicity and widespread distribution of SLNs may result from the complexity of the lymphatic system in the head and neck area.\(^1\)\(^6\) In addition, the elapsed time between injection of radioactive colloid and SLN biopsy is prolonged enough to allow the tracer to diffuse into secondary-echelon nodes previously identified falsely as SLNs.\(^6\) In a study of 97 patients, 85% of whom had multiple SLNs, O’Brien et al\(^8\) reported identifying one or more SLNs in 95 of 97 preoperative lymphoscintigrams. Rasgon\(^4\) found SLNs in 26 (96%) of the 27 patients, whereas Balkissoon et al (unpublished data, 2002) identified SLNs on preoperative lymphoscintigrams of 14 (78%) of 18 patients. Preoperative lymphoscintigraphy can help identify these SLNs and can allow the surgeon to plan surgery accordingly.

Background radiation from the primary injection site can constitute a shine artifact that incorporates the SLN and can thus make localization of SLNs difficult—or impossible—during preoperative lymphoscintigraphy. For example, this shine artifact occurs in the treatment of melanoma of the pinna and cheek because these locations are adjacent to or directly superficial to the parotid gland nodes. Every attempt should be made to decrease the shine artifact from the primary injection site and to increase the distance between the primary melanoma site and its potential nodal basin. Radiation doses commonly used for melanoma of the extremities and trunk (500 to 2,000 \(\mu\)Ci) may be too high for melanoma of the head and neck if the primary site is near or overlaps the

| Table 2. Nodal Basins in the Head and Neck Region Where SLNs May Be Located |
|---------------------------------|-----------------|
| **Cervical**                    |                 |
| Anterior cervical               |                 |
| Posterior cervical              |                 |
| Submental                       |                 |
| SuprACLavicular                 |                 |
| Parotid                         |                 |
| Cervical, other (occipital, mastoid, ectopic) | |

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Fig 2. Lymphoscintigrams compare use of high-dose (500 \(\mu\)Ci) \(\textsubscript{99m}\)Tc sulfur colloid for melanoma of right pinna and left cheek. Shine artifact incorporates parotid, postauricular, and suboccipital nodal basins; thus, treatment with lower activity levels of \(\textsubscript{99m}\)Tc sulfur colloid allows better visualization of adjacent nodal basins. Reprinted with permission from Rasgon BM. Use of low-dose technetium \(\textsubscript{99m}\) sulfur colloid to locate sentinel lymph nodes in melanoma of the head and neck: preliminary study. Laryngoscope 2001;111:11366-11372.\(^4\)
nodal basin in the head or neck (Fig 2). Rasgon has suggested that for patients with primary melanoma near or overlapping the nodal basin in the head and neck, SLN biopsy can be done accurately using technetium 99m sulfur colloid at low activity levels (10 to 60 μCi). The closer the melanoma to the nodal basin, the smaller the volume and dose needed (Fig 2).

Preoperative lymphoscintigraphy allows identification of unusual drainage patterns in the head and neck (Fig 3), which can occur in 34% to 84% of cases (Table 3). All nodal basins showing an SLN must be identified so that no potentially positive SLNs remain undetected. For this reason, the entire head and neck, upper part of the chest, and both axillary areas must be included in preoperative lymphoscintigraphy. Lymphoscintigraphy shows bilateral drainage in 10% of cases and fails to detect existing SLNs in 10% of cases. Elective lymph node dissection should be considered for patients with melanoma of the head and neck who do not have an SLN visualized.

The injection site must be covered with a lead shield to decrease the shine artifact and thus make the SLNs more visible. The patient’s neck should be flexed or extended so that it is positioned to maximize the distance between the injection site and the nodal basin. Use of a cobalt radiation source also helps outline landmarks in the head and neck.

**INTRAOPERATIVE LYMPHATIC MAPPING AND SLN BIOPSY**

The surgeon and the nuclear medicine physician must both review lymphoscintigrams before beginning the planned surgery. This procedure enables the surgeon to discuss with the patient any

<table>
<thead>
<tr>
<th>Location of Primary Site</th>
<th>Unusual SLN Location</th>
<th>Expected SLN Location</th>
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<tbody>
<tr>
<td>Cheek</td>
<td>Level 2A only</td>
<td>Parotid, level 2</td>
</tr>
<tr>
<td>Lateral neck</td>
<td>Supraclavicular</td>
<td>Level 2-4</td>
</tr>
<tr>
<td>Anterior neck</td>
<td>Supraclavicular</td>
<td>Level 2-4</td>
</tr>
<tr>
<td>Anterior neck</td>
<td>Axillary</td>
<td>Level 2-4</td>
</tr>
<tr>
<td>Posterior neck</td>
<td>Supraclavicular (ipsilateral)</td>
<td>Occipital</td>
</tr>
<tr>
<td>Posterior neck</td>
<td>Supraclavicular (contralateral)</td>
<td>Occipital</td>
</tr>
<tr>
<td>Postauricular</td>
<td>Level 2-4</td>
<td>Occipital</td>
</tr>
</tbody>
</table>
additional findings that could affect informed consent (eg, if an SLN is located over the parotid or submandibular area and thus increases the risk of facial nerve injury). Another example is drainage to parotid lymph nodes, an event that can occur in 30% to 50% of cases: Being aware of this finding would lead the surgeon to discuss with the patient the comparative operative risks of performing superficial parotidectomy versus sentinel lymphadenectomy and the risk of injury to branches of the facial nerve. Preoperatively, the surgeon may also plan to use a facial nerve monitor during the procedure.\(^4\) In addition, an SLN shown by preoperative lymphoscintigraphy in the tail of the parotid may actually be located in level 2b. The surgeon must be aware of this finding before beginning dissection in and around the parotid gland and must take extra steps intraoperatively to identify a level 2b SLN. Because structures in the head and neck are close together, the surgeon must use all techniques that can help decrease the shine artifact emanating from the injection site. This will maximize identification of the SLN on preoperative lymphoscintigraphy and intraoperatively. Removing the primary melanoma site initially with appropriate margins or shielding the injection site with malleable lead can accomplish this goal.

After location of the SLN has been identified and designated by a mark on the overlying skin, the surgeon must decide what initial skin incision is needed to remove the SLN; this decision will be determined by the surgical approach most likely to minimize morbidity. In addition, thought must be given to the possibility of the SLN being positive and thus mandating future lymph node dissection. The initial incision should be properly planned so that it will not interfere with either a standard parotid incision or neck dissection. Biopsy of SLNs in the head and neck should not violate standard oncologic principles.

SLNs in the parotid area can be problematic and should be approached through a standard preauricular parotid incision. This method gives excellent visualization of small SLNs and minimizes the risk of injury to branches of the facial nerve. Some surgeons recommend superficial parotidectomy in patients who have a parotid SLN identified by lymphatic mapping.\(^{11,16}\) Advocates of this approach believe that superficial parotidectomy reduces the risk of facial nerve injury. Moreover, if these nodes are found positive, superficial parotidectomy will already have been performed, thus avoiding the need for reoperation in the parotid area, with the attendant risk of facial nerve injury. Others\(^{18}\) believe that sentinel lymphadenectomy in the parotid basin is a feasible and safe approach. Ollila et al\(^{18}\) described sentinel lymphadenectomy without parotidectomy in 37 patients with SLNs found in the parotid gland; one (2.6%) of these 37 patients had surgical morbidity of the facial nerve (the patient had transient facial paresis that resolved completely).\(^{18}\) Sentinel lymphadenectomy without parotidectomy was done also in a series of 25 patients with drainage to the parotid gland.\(^{4}\) A facial nerve monitor was used for all patients, none of whom had any facial nerve morbidity.

Most identified parotid SLNs are superficial to the facial nerve. If sentinel lymphadenectomy is done in the parotid area, removing an SLN through a transverse incision directly over the parotid gland is not recommended; this approach is not cosmetically acceptable and could lead to partial necrosis of the flap if parotidectomy becomes necessary. Instead, the incision should be placed in the preauricular crease so that it can be incorporated into a standard parotid incision if parotidectomy becomes necessary. The incision in the neck should also be placed in a location that will allow incorporation into a standard neck dissection incision.

When multiple SLNs are found in a nodal basin, a preferable approach may be to perform selective neck dissection or superficial parotidectomy to encompass all nodes in the basin (Fig 4).\(^{11}\) A recommended approach for removing all SLNs in a nodal basin is to resect the entire sentinel nodal basin (sentinel basin lymphadenectomy) and isolate the SLN ex vivo; this approach reduces operative morbidity and facilitates identification and isolation of SLNs.\(^{16}\) Because the SLNs are small and encased by fibrolymphatic tissue (making identification difficult), this approach is important, particularly in the suboccipital and posterior auricular areas. After all SLNs have been identified, the decision to perform elective lymph node dissection should be based on frozen sections but on permanent histology sections and immunohistochemical stains.

The incidence of positive SLNs in the head and neck ranges from 11% to 15%. Although mela-
noma in the head and neck is inherently more aggressive than in other anatomic areas, Chao et al.\textsuperscript{5} reported a lower incidence of nodal metastasis in patients with head and neck melanoma than in patients with melanoma located at other anatomic sites. According to these investigators, this finding may indicate that SLN biopsy for melanoma of the head and neck may be less reliable and technically more challenging than SLN biopsy done at other anatomic sites.

Reliability of this technique depends on the false-negative rate. Several studies of SLN biopsy in the head and neck\textsuperscript{6,7,9,17} reported false-negative rates ranging from 0% to 10%. At least two studies\textsuperscript{6,7} as well as our own study reported false-negative rates of 0% to 1%. The true false-negative rate may remain unknown until longer follow-up studies are done and more cases of same-basin recurrence are seen. Carlson et al.\textsuperscript{12} reported the highest false-negative rate, 21%. The incidence of false-negative results is higher in patients with melanoma of the head and neck than in patients with melanoma of the trunk and extremities.\textsuperscript{8} The lowest false-negative results are seen in studies of a combined technique: lymphoscintigraphy plus blue dye and intraoperative use of the gamma probe.\textsuperscript{4,6,7}

**DISCORDANT RATES FOR LYMPHATIC MAPPING**

Lymphatic mapping in the head and neck is technically challenging and can show many unusual and unexpected drainage patterns. The highest rates of discordance are seen in the head and neck area\textsuperscript{9} and can range from 34% to 84%.\textsuperscript{8,18} Balkissoon (unpublished data, 2002) found discordance in 44% of patients. O’Brien et al.\textsuperscript{8} reported that 22% of patients had SLNs in other anatomic sites than the parotid area or in the five standard neck levels. That most of these SLNs were located in the posterior auricular and occipital regions—areas where SLNs are not usually reached during standard neck dissection—explains most of the discordance in reported results. This discordance rate was calculated as 34%.\textsuperscript{8}

In 21 (84%) of 25 patients, lymphoscintigraphy showed lymphatic drainage to sites not predicted clinically.\textsuperscript{19} Chao et al.\textsuperscript{5} reported that only 25% of SLNs harvested from the head and neck were found near the parotid area. Rasgon\textsuperscript{4} reported a higher incidence of parotid SLNs, ie, as many as 50%. In contrast to these high discordance rates, data from the Sydney [Australia] Melanoma Unit showed a high rate of disease control using clinically predicted drainage patterns, and false-negative results were rare.\textsuperscript{20} In that study,\textsuperscript{20} in which 106 patients had modified elective or selective neck dissections done by the same surgeon within a 6-year period, only three patients had recurrence outside the dissected fields. Despite these excellent results, the variably discordant results of treating melanoma in the head and neck are yet to be reconciled.

**SENTINEL LYMPH NODE BIOPSY FOR SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY**

Squamous cell carcinoma (SCC) is the most common cancer of the oral cavity, where the condition most often affects the tongue. The most important prognostic factor in SCC of the oral cavity is the status of regional lymph nodes. In
cases where these nodes test positive, the cure rate is decreased by half.

Management of the neck that is clinically negative for SCC of the oral cavity continues to evolve. In the past, the main treatment was radical neck dissection, as first described by Crile in 1906.\(^21\) This operation included removal of all lymphatic basins in the neck (levels I through V) (Fig 1), as well as removal of the sternocleidomastoid muscle, internal jugular vein, and spinal accessory nerve (Fig 1). This operation resulted in clinically significant morbidity (including shoulder dysfunction) and cosmetic deformity.

Twenty percent to 34% of patients with stage I or II SCC of the oral cavity are found to have occult metastasis in the neck when undergoing elective neck dissection.\(^22-25\) For cases in which only the primary node level is resected, the recurrence rate in the neck may be as high as 42%.\(^26\) Because of this high recurrence rate, current therapy attempts to reduce morbidity by using various forms of selective neck dissection. This approach is based on the concept of orderly lymphatic drainage by known routes, a strategy that depends on the anatomic site in the oral cavity or pharynx.\(^27\)

Currently accepted practice for treating stages I and II SCC of the oral cavity is supraomohyoid neck dissection (ie, selected neck dissection at levels I through III) with sparing of the sternocleidomastoid muscle, internal jugular vein, and spinal accessory nerve. This practice is controversial; many critics view selective neck dissection as a staging procedure only.\(^23,25,28\) If pathologic nodes are found, more comprehensive neck dissection or radiation therapy is required.\(^21,25,28\) Other investigators believe that more extensive neck dissection is necessary because of the possibility of metastasis skipping to level IV. The estimated rate of such metastasis in patients with an N0 neck varies from about 2% to 10%,\(^24,29,30\)

Clinical examination and imaging techniques—computed tomography (CT) scan, magnetic resonance imaging (MRI), and positron emission tomography (PET) scan—have not accurately identified micrometastases in a clinically negative neck.\(^31,32\)

Currently, for patients with stage I and II SCC of the oral cavity and pharynx, the most accurate way to stage the clinically negative neck is with elective neck dissection and microscopic examination of the neck nodes. In approximately 20% to 34% of patients with clinically negative necks, micrometastases are found\(^22-25\) thus, 66% to 80% of patients may be receiving unnecessary surgery.

Because of the success rate of SLN biopsy in melanoma of the head and neck, interest in using SLN mapping in patients with stages I and II squamous cell carcinoma of the oral cavity and oropharynx is growing. For these patients, the potential advantage of SLN biopsy would be to identify patients with possible micrometastases; such identification would distinguish patients who would benefit from elective neck dissection from those who would not. This method of minimizing use of surgery would not only reduce overall morbidity but would reduce costs of treatment.

Several reports on SLN biopsy for SCC of the oral cavity and pharynx have been published.\(^33-41\) Unfortunately, these studies included only a limited number of patients, few of whom received long-term follow-up. Nonetheless, most of these investigators stated their belief that SLN mapping is a feasible technique for patients with stages I and II SCC of the oral cavity and that this technique seems to adequately predict presence of occult metastases in the neck.

Currently, for patients with SCC of the oral cavity, no uniformity exists for determining the dose or volume of radiolabeled colloid injected around the primary site or how the primary site should be injected. Some surgeons inject the radiolabeled colloid mucosally around the primary; others inject the radiolabeled colloid submucosally around the primary; still others inject both submucosally and intramuscularly around the primary site. Timing of injection also is inconsistent: some surgeons inject the radiolabeled colloid within about 2 hours before surgery, whereas others inject the colloid approximately 24 hours before surgery.

Unlike melanoma—for which most investigators agree that the combined technique is more accurate than either technique used alone—use of blue dye in patients with SCC of the oral cavity and pharynx gives mixed results. Pitman et al\(^38\) and Rasgon et al (unpublished data, 1998) did not find blue dye in any of their patients injected. Stoeckli et al\(^39\) found blue dye in only two of the first seven patients injected and abandoned use of blue dye in the remaining patients. However, both Shoai\(^35,36\) and Mozillo et al\(^41\) found blue-stained lymph nodes in many patients and stated that the combined technique is beneficial. Pitman
et al\textsuperscript{38} and Rasgon both used isosulfan blue; Stocek et al\textsuperscript{39} used methylene blue. Shoaib et al\textsuperscript{35,36} and Mozzillo et al\textsuperscript{41} both used patent blue V dye. The discrepancy in success rates for localizing these blue lymph nodes may be due to any or all of several factors: the technique of injection around the primary tumor; the timing of injection (because blue dye washes out very rapidly in the head and neck); or the type of blue dye injected.

One of the most important technical difficulties of lymphatic mapping in patients with SCC of the oral cavity and pharynx results from close proximity of the primary tumor site to the first-echelon lymphatic basins. The shine artifact emanating from radiocolloid injection at the primary site may incorporate levels Ia, Ib, 2a, or 2b, depending on location of the primary cancer site in the oral cavity or pharynx. This shine artifact can make the SLN difficult to identify on preoperative lymphoscintigrams and can make intraoperative localization problematic (ie, because of the large amount of radiation emanating from the primary injection site) and thus can conceal the SLN.

Technical maneuvers to improve identification of SLNs on preoperative lymphoscintigrams are to use a low dose (30 to 60 $\mu$Ci) and small volume (0.2 mL) of radiocolloid when injecting the primary tumor site\textsuperscript{4} (Rasgon, unpublished data, 1998) (Fig 5). Other techniques include injecting a large dose of radiocolloid (0.4 to 3 mCi the day before surgery. Because the half-life of $^{99m}$Tc is 6 hours, only a low dose of the radiocolloid remains the next day at the injection site\textsuperscript{33,35,36,40}; the decrease in background radiation facilitates intraoperative identification of SLNs. Rinsing the patient’s mouth after injection of the primary tumor site can decrease spillage of radiocolloid from the injection site; such spillage can interfere with identification of SLNs on preoperative lymphoscintigrams. Another helpful practice for facilitating preoperative identification of SLNs on lymphoscintigrams is to shield the primary tumor site with malleable lead (whenever possible) to decrease the shine artifact from the primary injection site.

Intraoperative identification of SLNs can be improved by initially excising the primary cancer site or by using a malleable lead shield (if feasible) to decrease both the shine artifact from the primary injection site as well as background radiation. However, this initial excision of the primary cancer site does not completely eliminate the shine artifact near the first-echelon nodes. The shine artifact emanating from the primary injection site may be decreased also by angling the neoprobe away from the primary site and using a collimator on the tip of the neoprobe. Despite all these modifications, however, identifying the SLN can be difficult.

General consensus holds that SLN mapping in the oral cavity can be technically challenging and that further investigation should be pursued before this technique is recommended. All patients studied so far have received SLN biopsy in conjunction with selective neck dissection; in most of these cases, the SLN could be found and reflected.
the remainder of the nodal basin. However, these studies included small numbers of subjects, most of whom had limited long-term follow-up. Currently, for patients with SCC of the oral cavity, SLN biopsy should not be used to determine the need for elective neck dissection. Large, prospective, multi-institutional studies are needed to determine the accuracy of this technique and to resolve the technical difficulties seen with this procedure when used in patients with SCC of the oral cavity.

Because SLN biopsy for patients with SCC of the oral cavity and pharynx is still evolving and because further studies are needed before this can be recommended as the standard of care, how can we use this technology now to help improve our current approach to diagnosing and treating the clinically negative neck of a patient with SCC?

Selective neck dissection at levels I through III—currently the standard of care for treating stages I and II SCC of the oral cavity—can fail for three reasons. First, some important nodal basins might not be included in the selective neck dissection (ie, skip metastasis to level IV or V or contralateral drainage; Fig 6). Skip lesions have been reported at rates ranging from 2% to 10%. Second, because of insufficient thoroughness in operating within the field of dissection, the surgeon might fail to incorporate all the high-risk nodes. This omission has been reported based on recurrence rates of approximately 3% to 4% in the dissected basins of patients who received selective neck dissection at levels I through III and have necks that tested negative for pathology. Finally, in standard selective neck dissection at levels I through III, the pathologist scrutinizes the high-risk nodes less closely than SLNs and therefore might fail to detect micrometastases.

An abundance of evidence indicates that micrometastatic disease carries prognostic connotations. Presence of micrometastatic disease also has therapeutic implications. In a study by Byers et al, patients with a clinically negative neck and nodes positive for tumor who received postoperative radiation therapy had a 0% recurrence rate, whereas similar patients who did not receive postoperative radiation therapy had a 36% recurrence rate and all recurrences were in the dissected nodal basins. Thus, identification and microscopic examination are essential for the lymph nodes most likely to contain micrometastatic disease.

Information on high-risk nodal basins can be ascertained by incorporating preoperative lymphoscintigraphy with standard therapy. In addition, if “hot” nodes are identified outside levels I through III, selective neck dissection can be extended to include the nodal basins not normally incorporated in selective neck dissection. Moreover, after neck dissection is completed, the neck may be rescanned using the gamma probe to ensure that all “hot,” high-risk nodes have been removed. The surgeon may also dissect out the SLNs from the selective neck dissection once the selective neck dissection is complete. The SLNs are then labeled separately and sent to pathology where they are examined (by using serial sectioning and immunohistochemical staining) so that the SLNs can be examined for micrometastases. This excision of the SLNs would enable more accurate staging and treatment of the neck and would help surgeons to identify patients with positive histology results who would benefit from postoperative radiation therapy or from additional surgery.

LYMPHATIC MAPPING AND SLN BIOPSY FOR THYROID CANCER

The utility of SLN biopsy for treating well differentiated thyroid cancer has yet to be determined. At present, thyroidectomy without lymph node dissection is the standard treatment for papillary thyroid cancer in a patient whose neck is
clinically negative for pathology. However, 82% of patients may have occult metastasis. Using blue dye only, Dixon et al found SLNs in 65% of patients with thyroid neoplasms. The series included two SLNs that yielded false-negative results. Other investigators reported a higher (88%) success rate for identifying SLNs in patients with thyroid disease.

Lymphatic mapping is also being investigated for use in treating medullary thyroid cancer. When the technique is used for that condition, 7% of thyroid metastases appear in the lateral compartment only and bypass the central lymph node compartment. SLN mapping can thus identify high-risk nodes in the lateral compartments when these nodes otherwise would be missed by dissection in the central compartment only. The usefulness of this procedure for detecting occult metastases may help reduce the high recurrence rate for medullary thyroid cancer.

The technique of lymphatic mapping and SLN biopsy described by Dixon et al involves injecting blue dye directly into the tumor or nodule. Care is taken not to stain any surrounding structures with blue dye. All SLNs are then removed. One key technical point noted by Dixon et al to facilitate visualization of SLNs is to minimize dissection before injecting the blue dye. Dixon et al also noted that the parathyroid glands can also stain blue and thus cause a parathyroid gland to be mislabeled as an SLN. Because few data on lymphatic mapping and SLN biopsy for thyroid neoplasms are available and because these methods present technical issues that must be resolved, we cannot draw any conclusions at this time. Future considerations should include preoperative use of lymphoscintigraphy in conjunction with the handheld gamma probe to facilitate identification of SLNs in the lateral compartments.

LYMPHATIC MAPPING AND SLN BIOPSY FOR MERKEL CELL CANCER

Merkel cell cancer is an uncommon, highly malignant neuroendocrine tumor of the skin. Treatment for this neoplasm is controversial and has included surgery with wide excision alone or combined with elective lymph node dissection. Radiation therapy and chemotherapy have also been used. Despite our best efforts at treatment, overall survival has not improved, and recurrence rates remain clinically significant. Most surgeons would agree that Merkel cell cancer in the head and neck must be treated aggressively because this approach may help improve the prognosis. As in patients with melanoma, regional nodal status remains the most important predictor of survival in patients with Merkel cell cancer. A more selective approach is possible for identifying patients who might benefit from elective lymph node dissection; this possibility for patients with Merkel cell cancer is intriguing because many of these patients are older and have an increased risk for morbidity. As in patients with melanoma, preoperative lymphoscintigraphy can be performed in patients with Merkel cell cancer to identify the nodal basins at risk. The combined technique can then be done to identify all SLNs. Several investigators have shown that this procedure for treating Merkel cell cancer is technically feasible and results in minimal morbidity. However, until a large, randomized prospective trial is completed, we cannot recommend this procedure as the standard of care for patients with Merkel cell cancer of the head and neck.

CONCLUSIONS

SLN biopsy remains an evolving treatment for melanoma of the head and neck. Clinicians should present all treatment options to patients diagnosed with intermediate-thickness melanoma in the head and neck. To reduce operative morbidity, lymphatic mapping and SLN biopsy using a combined technique can be offered as an alternative to elective lymph node dissection in patients with clinically negative nodes. However, close follow-up is necessary. Patients must be informed that this technique is not yet the standard of care in the community. The success of this technique depends on particularly complex technical considerations as well as on the experience of the treating surgeon. Patients who choose not to have SLN biopsy and who prefer elective lymph node dissection should be encouraged to have preoperative lymphoscintigraphy. This procedure shows nodal basins at high risk and can identify ambiguous drainage patterns. These patterns may either be used in lymph node dissection or be closely monitored postoperatively.

Lymphatic mapping in SCC of the oral cavity is also evolving and presently appears feasible, but large multi-institutional studies are needed before the technology can be recommended for this con-
dition. Until then, the technology can be used as an adjunct to standard treatment for the clinically negative neck. Preoperative lymphoscintigraphy can allow for better preoperative planning so that selective neck dissection can be modified accordingly. The gamma probe can thus assure that all high-risk nodes have been removed from the nodal basin after selective neck dissection is complete. Last, the gamma probe can then be used to identify the SLN in the just-dissected tissue. These SLNs can be dissected out from the selected neck dissection, labeled separately, and sent for detailed histopathologic examination. This approach is therefore consistent with oncologic principles.

Finally, lymphatic mapping for thyroid cancer is still experimental and warrants further investigation before any recommendations can be made.

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**REFERENCES**