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Reconstructive

Methods of Sentinel Lymph Node Identification in Auricular Melanoma

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Background: Sentinel lymph node biopsy is used to evaluate for micrometastasis in auricular melanoma. However, lymphatic drainage patterns of the ear are not well defined and predicting the location of sentinel nodes can be difficult. The goal of this study was to define the lymphatic drainage patterns of the ear and to compare multiple modalities of sentinel node identification.

Methods: A retrospective review of a prospectively maintained database evaluated 80 patients with auricular melanoma who underwent sentinel lymph node biopsy by comparing preoperative imaging with intraoperative identification of sentinel nodes. Patients were placed into two cohorts, based on the modality of preoperative imaging: (1) planar lymphoscintigraphy only (n = 63) and (2) single-photon emission computerized tomography combined with computerized tomography (SPECT-CT) only (n = 17). Sites of preoperative mapping and sites of intraoperative identification were recorded as parotid/preauricular, mastoid/postauricular, and/or cervical.

Results: In patients that underwent planar lymphoscintigraphy preoperatively (n = 63), significantly more sentinel nodes were identified intraoperatively than were mapped preoperatively in both the parotid/preauricular (P = 0.0017) and mastoid/postauricular (P = 0.0047) regions. Thirty-two nodes were identified intraoperatively that were not mapped preoperatively in the planar lymphoscintigraphy group (n = 63), two of which were positive for micrometastatic disease. In contrast, there were no discrepancies between preoperative mapping and intraoperative identification of sentinel nodes in the SPECT-CT group (n = 17).

Conclusions: SPECT-CT is more accurate than planar lymphoscintigraphy for the preoperative identification of draining sentinel lymph nodes in auricular melanoma. If SPECT-CT is not available, planar lymphoscintigraphy can also be used safely, but careful intraoperative evaluation, even in basins not mapped by lymphoscintigraphy, must be performed to avoid missed sentinel nodes. *(Plast Reconstr Surg Glob Open 2021;9:e4004; doi: 10.1097/GOX.0000000000004004; Published online 20 December 2021.)*

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INTRODUCTION

The incidence of melanoma in the United States has increased at a rate of approximately 1.5% per year over the past 10 years.[1] Mortality rates have improved by approximately 2.5% each year over the same time period, but melanoma remains responsible for approximately 65% of skin cancer deaths each year in the United States.[1,2] Melanomas of the head and neck account for approximately 20%–33% of all melanomas, with 7% of head and neck melanomas occurring on the external ear.[3–5] Most

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auricular melanomas occur on the sun-exposed areas of the helix.[6] Although auricular melanomas were once thought to be more aggressive,[7] more recent studies have suggested that Breslow-depth-adjusted mortality is comparable to other cutaneous melanomas.[8,9]

Sentinel node mapping has continued to be an important prognostic indicator to allow for staging in invasive melanoma. However, lymphatic drainage from the ear remains incompletely understood. Studies that have examined the lymphatic drainage patterns of the ear are few, with variable methods and differing conclusions.[6,10–12] In the most extensive study to date, Peach et al[6] reported the preoperative lymphoscintigraphic mapping in 111 patients with auricular melanoma. They characterized the lymphatic drainage patterns of various anatomical subunits of the ear based on the classical cervical lymphatic drainage basins (I–V) and concluded that the drainage of the ear is highly variable regardless of the sub-anatomical lesion site and "may occur in a retrograde, anterograde, or transaural fashion," most often to cervical levels II, V, and the postauricular region. However, this study did not compare preoperative mapping with intraoperative sentinel node identification. Other groups have reached different conclusions. Cole et al,[10] for example, found lymphatic drainage to the parotid and preauricular regions to be involved nearly 50% of the time, but Shpitzer et al[11] found cervical level II to be the most common site of drainage with no involvement of the postauricular nodes. One reason that lymphatic drainage of the ear may be so variable is that anastomotic pathways are common between draining lymphatic channels and may present the opportunity for multiple routes of spread from a single lesion.[12] However, drainage outside of the head and neck region or to the contralateral head and neck has not been reported in the literature.

Current surgical treatment of auricular melanoma involves wide local excision of the lesion, reconstruction of the ear, and sentinel lymph node biopsy (SLNB), rather than a strategy of whole-ear amputation which was common three decades ago.[2] Many surgical centers that treat auricular melanoma perform only day-of-surgery preoperative mapping using planar lymphoscintigraphy followed by intraoperative SLNB. Single-photon emission computerized tomography combined with computerized tomography (SPECT-CT) has been increasingly utilized in the United States since 2010 but is not available in all centers. At the Yale Melanoma Program, both preoperative mapping (at least 72 hours before surgery) followed by interval intraoperative sentinel node radioisotope injection by surgeons trained by the Department of Nuclear Medicine are performed in the treatment of auricular melanoma. The methods and safety of this approach were reported in a 2004 study by Ariyan et al,[13] which demonstrated that preoperative lymphoscintigraphy followed by intraoperative identification with radioisotope injection was able to identify draining sentinel nodes in all patients studied. Additionally, beginning in 2017, SPECT-CT became available at our center and was adopted in place of planar lymphoscintigraphy for preoperative sentinel node mapping, followed similarly by intraoperative sentinel node identification with radioisotope injection. The goals of our present study are (1) to report lymphatic draining patterns in auricular melanoma and (2) to assess a strategy of both preoperative imaging and intraoperative radioisotope injection in the treatment of auricular melanoma, comparing planar lymphoscintigraphy to SPECT-CT for preoperative mapping.

Takeaways

Question: How should sentinel lymph nodes be identified in auricular melanoma?

Findings: Eighty patients with auricular melanoma were evaluated by comparing preoperative imaging (either planar lymphoscintigraphy or SPECT-CT) and intraoperative identification of sentinel nodes. Thirty-two nodes were identified intraoperatively that were not mapped preoperatively in the planar lymphoscintigraphy group (n = 63). In contrast, there were no discrepancies between preoperative and intraoperative identification of sentinel nodes in the SPECT-CT group (n = 17).

Meaning: SPECT-CT is more accurate than planar lymphoscintigraphy for preoperative identification of sentinel nodes in auricular melanoma.

METHODS

Data Source and Patient Selection

A retrospective review of patient data from a prospectively maintained institutional database was used for analysis. From 1997 to 2021, patients with melanoma of the ear who underwent SLNB were evaluated with preoperative lymphoscintigraphy or SPECT-CT at least 72 hours before surgery, followed by intraoperative identification of draining nodes with radiotracer injection. To identify this cohort of patients, 138 patients with invasive auricular melanoma were reviewed. A total of 58 patients were excluded for the following reasons: (1) initial Breslow depth of less than 0.8 mm (n = 37), (2) initial Breslow depth between 0.8 mm and 1.0 mm with decision not to proceed with SLNB (n = 8), or (3) comorbidities that precluded general anesthesia or elected not to proceed with surgical management (n = 13). Criteria for inclusion are depicted in Figure 1. Strict inclusion criteria were defined before evaluating outcomes to prevent selection bias. This study was reviewed and approved by the Yale University Institutional Review Board.

For the 80 patients included in the study, demographic and clinicopathologic information were collected. Demographic variables included patient age, race, and gender. Clinicopathologic variables included anatomic location of the melanoma, Breslow depth of invasion, ulceration, type of melanoma, mitotic rate, history of other skin cancers, follow-up, and recurrence. Recurrence was defined as clinical or radiographic. Follow-up was reported based on the last documented follow-up. Patients underwent both preoperative mapping of draining lymph nodes (at least 72 hours before surgery) and intraoperative

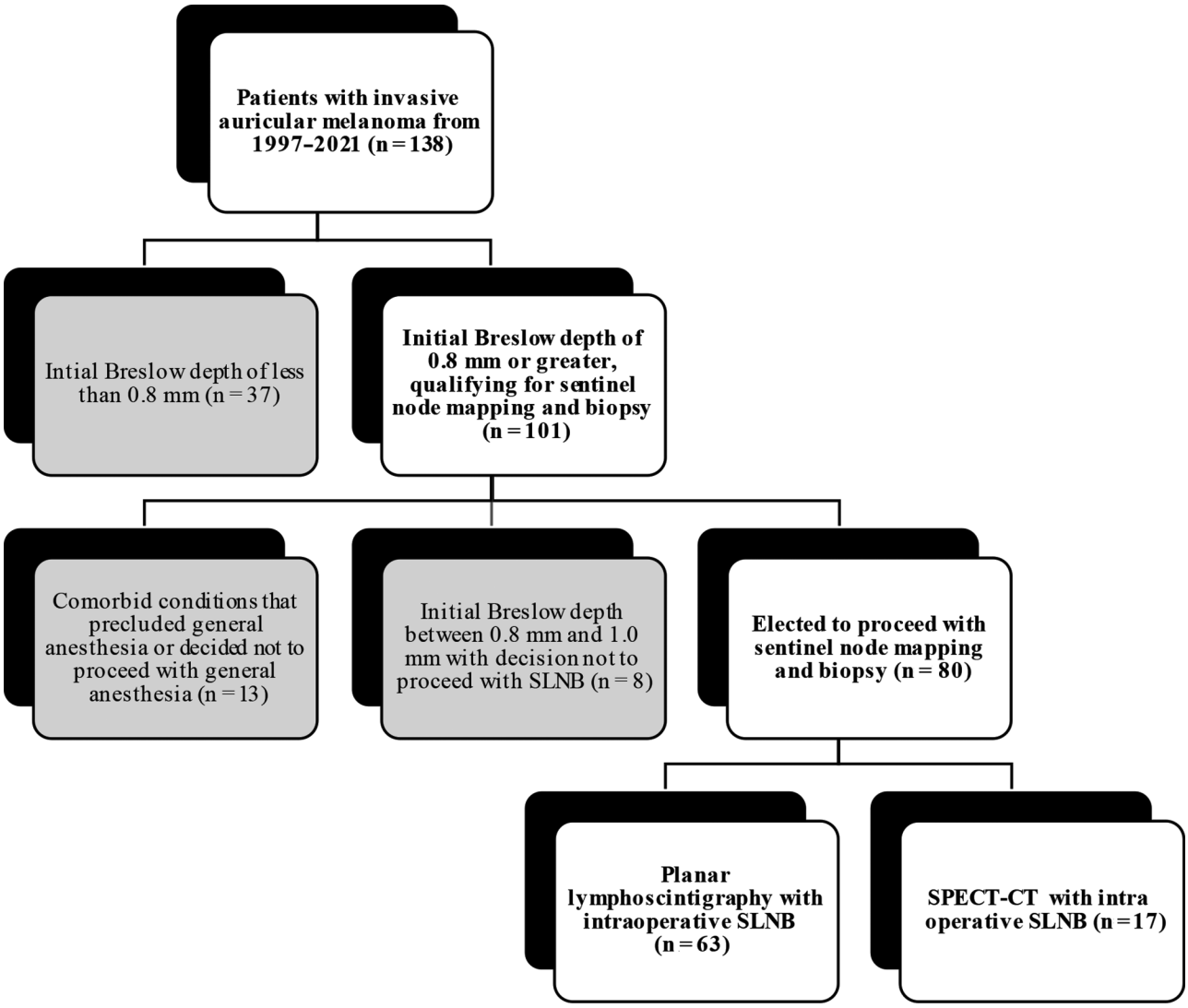

Fig. 1. Flow diagram of patients included and analyzed.

sentinel lymph node identification. In 63 patients, preoperative planar lymphoscintigraphy was performed; in 17 cases, patients underwent preoperative SPECT-CT.

Preoperative planar lymphoscintigraphy for sentinel lymph node mapping was performed after six circumferential intradermal injections totaling one mCi of 99m-Technitium filtered sulfur colloid at the primary lesion site, with initial dynamic flow imaging of the head and neck over 30 minutes and subsequent frontal and lateral static imaging of the head, neck, and chest. Beginning in 2017, SPECT-CT of the head and neck was performed in 17 patients in place of planar lymphoscintigraphy. Intraoperative sentinel node identification was performed by the surgeon injecting another circumferential dose of 99m-Technitium filtered sulfur colloid at the lesion site at the time of surgery and identifying draining nodes with a gamma probe and checking all nodal basins. Lymphatic drainage regions were classified as parotid/preauricular, mastoid/postauricular, or cervical (levels I–V of the neck), as shown in Figure 2.

Statistical Analysis

Summary statistics were reported as percentages for categorical variables and as medians with interquartile ranges (IQR) for continuous variables. McNemar's test was used to evaluate for differences in preoperative and intraoperative mapping. A backward selection logistic regression was used to evaluate covariates associated with recurrence. The following covariates were included in the model: age (defined as <65 or ≥65), gender (defined as men or women), nodal status (defined as negative or positive), Breslow depth (defined as <1 mm, 1–2 mm, 2–4 mm or ≥4 mm), mitoses (defined as <2, 2–3, 3–6, >6), and presence of ulceration (defined as present or absent). Overall follow-up and survival were reported in months.

RESULTS

The information regarding initial lesion site, patient demographics, and tumor-specific pathological features is stratified into those who underwent preoperative planar lymphoscintigraphy (n = 63) and those who underwent

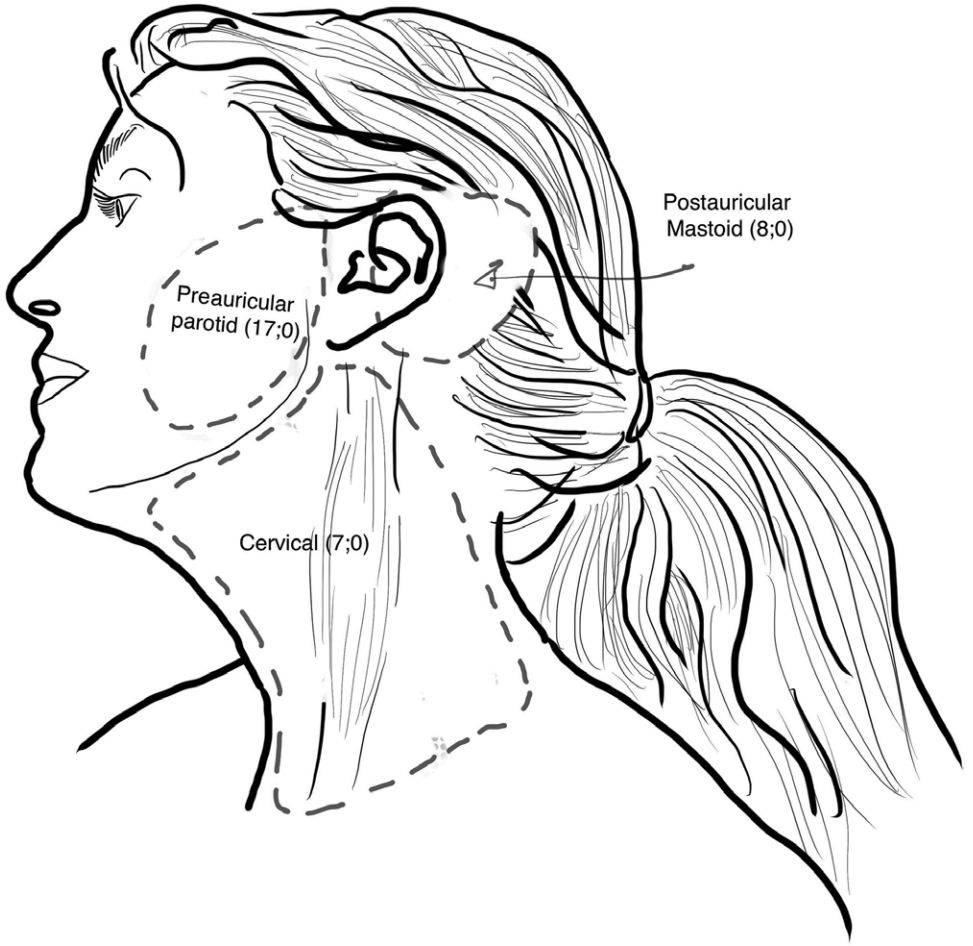

Fig. 2. Regions of lymphatic drainage of the ear utilized in this study: preauricular/parotid, postauricular/mastoid, and cervical, with numbers of un-mapped sentinel nodes for each region in the following format: planar lymphoscintigraphy (n = 63); SPECT-CT (n = 17).

preoperative SPECT-CT (n = 17) (see Table 1). The helix was the most common overall site of initial lesion, seen in 51 patients (63.8%).

Analysis of preoperative mapping and intraoperative sentinel node identification showed that the most common site of lymphatic drainage overall is the cervical region, seen in 90.0% of cases preoperatively and 95.0% of cases intraoperatively. Drainage to the parotid/preauricular region was also common, seen in 25.0% of patients on preoperative imaging and 42.5% of patients intraoperatively. Detailed lymphatic drainage patterns are described in Table 2. For three patients in the planar lymphoscintigraphy group, preoperative imaging did not reveal draining lymph nodes, but subsequent intraoperative injection did identify nodes. In all cases with SPECT-CT, draining lymph nodes were identified preoperatively.

In the 63 patients who had preoperative planar lymphoscintigraphy, there were significant differences in the rate at which lymph nodes were mapped on preoperative imaging and the rate at which nodes were identified intraoperatively after injection of radiotracer for both the parotid/preauricular and mastoid/postauricular regions. Preoperative planar lymphoscintigraphy mapped draining lymph nodes in the parotid/preauricular region in 23.8% of cases, whereas intraoperative radiotracer identified nodes in the parotid/preauricular region in 46.0% of cases ($P = 0.0017$). Similarly, preoperative planar lymphoscintigraphy identified draining lymph nodes in the mastoid/postauricular region in 4.8% of cases, whereas 17.5% of the same patients had nodes identified in the mastoid/postauricular region intraoperatively ($P = 0.0047$). For the cervical region, more patients had intraoperative identification of sentinel nodes with radiotracer relative to those that had preoperative planar lymphoscintigraphic mapping of sentinel nodes in the cervical region, but this difference was not significant ($P = 0.2059$). These findings are documented in Table 2. Importantly, there were no discrepancies between preoperative mapping of sentinel lymph nodes and intraoperative SLNB in the SPECT-CT group, as shown in Table 2.

Overall, 32 un-mapped lymph nodes (in 26 individual patients) were biopsied intraoperatively that were not identified on preoperative planar lymphoscintigraphy, whereas there were no un-mapped lymph nodes found following the use of preoperative SPECT-CT. Of these un-mapped sentinel nodes, 17 were located in the

Table 1. Initial Lesion Site, Patient Demographics, and Tumor-specific Pathological Features for the Total Population (n = 80), Patients Who Received Preoperative Planar Lymphoscintigraphy (n = 63), and Patients Who Received SPECT-CT Preoperatively (n = 17)

	Total Population (n = 80)	Planar Lymphoscintigraphy (n = 63)	SPECT-CT (n = 17)
Initial lesion site			
Helix	51 (63.8%)	39 (61.9%)	12 (70.6%)
Anti-helix/concha	4 (5.0%)	4 (6.3%)	0 (0.0%)
Tragus	2 (2.5%)	2 (3.2%)	0 (0.0%)
Antitragus	1 (1.3%)	1 (1.6%)	0 (0.0%)
Lobe	7 (8.8%)	3 (4.8%)	4 (23.5%)
Scapha	1 (1.3%)	1 (1.6%)	0 (0.0%)
Postauricular	10 (12.5%)	9 (14.3%)	1 (5.9%)
Preauricular	4 (5.0%)	4 (6.3%)	0 (0.0%)
Other/unknown	0 (0.0%)	0 (0.0%)	0 (0.0%)
Demographic information			
Median age (y) at surgery (IQR)	64.0 (*48.0–75.2*)	64.6 (*47.2–77.2*)	61.0 (*49.0–73.0*)
% White	96.3%	95.2%	100.0%
% Hispanic	3.7%	4.8%	0.0%
% Men	81.3%	79.4%	88.2%
% Women	18.7%	20.6%	11.8%
% History of other skin cancer	38.8%	42.8%	23.5%
Tumor-specific pathological features			
Median Breslow depth (mm) (IQR)	1.5 (*1.1–2.2*)	1.4 (*1.1–2.2*)	1.5 (*1.0–2.6*)
% Known ulcerated	28.1%	28.6%	29.4%
% Amelanotic*	14.1% (n = 71)	10.0% (n = 60)	30.7% (n = 13)
Median Mitoses per mm^2 (IQR)*	3.0 (*1.0–5.0*) (n = 71)	2.0 (*1.0–5.0*) (n = 55)	3.0 (*2.0–6.8*) (n = 16)

*Data for this variable were not available for all patients.

parotid/preauricular region, eight were located in the mastoid/postauricular region, and seven were located in the cervical region, as depicted in Figure 2. Two nodes (6.3%) had micrometastatic disease on SLNB after intraoperative identification, both sampled from the parotid region.

Additionally, there were six nodes visualized preoperatively on planar lymphoscintigraphy that were identified but not sampled intraoperatively, since radioisotope probe detected counts less than 10% of the "hottest" node. No patients had a recurrence during the follow-up period in the areas that were mapped preoperatively with planar lymphoscintigraphy but did not reach the 10% threshold for biopsy. There were no cases in which SPECT-CT identified a sentinel node preoperatively in a region that was not sampled intraoperatively.

In total, nine out of 80 patients (11.3%) included in this study had a positive sentinel node, seven in the planar lymphoscintigraphy group, and two in the SPECT-CT group. A total of 12 positive sentinel nodes were identified out of 491 sentinel nodes biopsied. There were three patients (3.8%) who were found to have micrometastatic nodal disease in more than one draining basin.

Median follow-up in this study was 38.3 months (IQR 9.3–84.1) overall, 57.6 months (IQR 24.4–124.6) in the planar lymphoscintigraphy group, and 20.4 months (IQR 6.7–25.6) in the SPECT-CT group. During this interval, 17 patients (21.3%) experienced a recurrence, 15 patients (23.8%) in the planar lymphoscintigraphy group (n = 63), and two patients (11.8%) in the SPECT-CT group (n = 17). However, only three of these patients experienced a nodal recurrence, all of whom underwent planar lymphoscintigraphy preoperatively and were alive at the time of publication. Three patients experienced a nodal recurrence in the planar lymphoscintigraphy group (n = 63), all outside of the original draining basin identified at the time of surgery. Two also had distant metastasis identified at the time of nodal recurrence. One of these patients had SLNB in the parotid/preauricular and cervical regions with nodal recurrence in the mastoid/postauricular region, and the other had SLNB in the cervical region with nodal recurrence in the parotid/preauricular region. The third patient experienced a nodal recurrence in the same nodal basin that was biopsied intraoperatively (cervical region) but was already being treated with immunotherapy due to the initial sentinel node being positive for micrometastasis.

Utilizing backward selection logistic regression, older age (OR5.179, 95% CI 1.127–23.796, $P = 0.0345$) and positive nodal status (OR 13.043, 95% CI 2.389–71.225, $P = 0.0030$) were significantly associated with recurrence in this study, whereas gender, Breslow depth, mitoses, and ulceration were not. During the submission of this article, 54 patients (67.5%) were alive with no evidence of disease, two patients (2.5%) were alive with evidence of disease, six patients (7.5%) were deceased from melanoma, 13 patients were deceased from other causes (13.8%), and seven patients (8.8%) were deceased from an unknown cause.

DISCUSSION

In this study, SPECT-CT was found to be a more sensitive and accurate imaging modality than planar lymphoscintigraphy for the identification of sentinel nodes

Table 2. Preoperative Mapping and Intraoperative Identification of Sentinel Nodes for the Total Population (n = 80), Patients Who Received Preoperative Planar Lymphoscintigraphy (n = 63), and Patients Who Received SPECT-CT Preoperatively (n = 17)

		Parotid/ Preauricular	Mastoid/ Postauricular	Cervical (I–V)
Planar lymphoscintigraphy (n = 63)	Preoperative	15 (23.8%)	3 (4.8%)	56 (88.9%)
	Intraoperative	29 (46.0%)	11 (17.5%)	60 (95.2%)
SPECT-CT (n = 17)	Preoperative	5 (29.4%)	1 (5.9%)	16 (94.1%)
	Intraoperative	5 (29.4%)	1 (5.9%)	16 (94.1%)
Total population (n = 80)	Preoperative	20 (25.0%)	4 (5.0%)	72 (90.0%)
	Intraoperative	34 (42.5%)	12 (15.0%)	76 (95.0%)

in auricular melanoma, with no discrepancies between preoperative mapping and intraoperative radiotracer identification (n = 17). In this way, SPECT-CT may be the preferred imaging modality for preoperative sentinel node identification in auricular melanoma. Other studies suggest that these findings may be generalizable to cutaneous malignancies in other parts of the body. For example, similar comparisons of SPECT-CT to planar lymphoscintigraphy have found SPECT-CT to be a more sensitive and accurate modality to identify sentinel nodes in the treatment of melanomas of the trunk, breast cancer, cervical cancer, and penile cancer.[14–17] In a study of cutaneous malignancies, including melanomas and squamous cell carcinomas, Doepker et al found that SPECT-CT identified additional sentinel nodes in 50% of patients that had previously been imaged with planar lymphoscintigraphy.[18]

However, SPECT-CT does have a major limitation: access. Although it has become widely available in the United States and Europe in the last decade,[19] SPECT-CT is not available at all centers and remains a rarity in many countries of the developing world. Additionally, even when SPECT-CT is available, insurance companies may limit access by denying coverage due to cost. This occurs even though there are data indicating that SPECT-CT improves cost-effectiveness in the treatment of cutaneous melanomas by allowing for a more precise surgical procedure, reducing operating time and minimizing morbidity from complications.[20] Of note, it is not clear how generalizable these cost-effectiveness data are to the United States or to auricular melanoma specifically, and thus further research is needed.

For cases in which SPECT-CT is not available or insurance companies deny coverage, preoperative planar lymphoscintigraphy is often used. However, preoperative planar lymphoscintigraphy must be combined with careful intraoperative assessment of nonmapped nodal basins with the gamma probe. In this study, the parotid/preauricular and mastoid/postauricular regions were identified as lymphatic draining basins more frequently with intraoperative gamma probe than with preoperative imaging in the planar lymphoscintigraphy group (n = 63). This was significant in the parotid/preauricular region (P = 0.0017) and in the mastoid/postauricular region (P = 0.0047), and indicates that false negatives, or preoperatively un-mapped nodes, are common in planar lymphoscintigraphy of the ear.

Critically, in two patients, a preoperatively "un-mapped" sentinel node with planar lymphoscintigraphy was identified, removed and found to be positive for micrometastatic disease after intraoperative radiotracer identification and SLNB. This suggests that sole reliance on the imaging produced with preoperative planar lymphoscintigraphy for sentinel node identification is insufficient in the operative planning and treatment of auricular melanoma. Preoperative nonvisualization of draining lymph nodes with planar lymphoscintigraphy is not uncommon in the head and neck. Nonvisualization is reported in about 10% of melanomas of the head and neck, compared with 0.56% of cutaneous melanomas in the rest of the body.[21] In the majority of cases, intraoperative identification and biopsy of nonvisualized sentinel nodes is still achieved via intraoperative radioisotope identification.[21]

In this study, no patients in the SPECT-CT group (n = 17) experienced a nodal recurrence, though follow-up is limited due to the relatively recent adoption of SPECT-CT at our center. Further, only one patient in the planar lymphoscintigraphy group (n = 63) experienced a recurrence in the nodal basin that was mapped and sampled intraoperatively (1.6%), and there had previously been a positive node in the same basin on initial SLNB. Therefore, our experience suggests that using preoperative planar lymphoscintigraphy is a reasonable alternative to preoperative SPECT-CT when SPECT-CT is not available, so long as careful intraoperative identification of sentinel nodes is performed with radioisotope injection and gamma probe localization. Although planar lymphoscintigraphy is less accurate than SPECT-CT, combination with intraoperative identification of sentinel nodes identified "missed" nodes preoperatively in our study. Further research is needed to assess if intra-operative identification of sentinel nodes is necessary in the setting of more accurate preoperative SPECT-CT.

A major limitation of this study is the size of the SPECT-CT group (n = 17). A larger study of SPECT-CT for melanoma of the ear is warranted, particularly to assess if intraoperative injection of radiotracer is necessary given the accuracy of SPECT-CT in our study.

CONCLUSIONS

The most common site of lymphatic drainage from auricular melanoma is the cervical region. SPECT-CT is more accurate than planar lymphoscintigraphy for the preoperative identification of draining sentinel lymph nodes in auricular melanoma and may be the preferred preoperative imaging modality. In the case that SPECT-CT is not available, preoperative planar lymphoscintigraphy can also be used safely, but fastidious use of the gamma probe intraoperatively is recommended, even in basins not mapped preoperatively.

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