

Melanomas

Reliability of Lymphatic Mapping After Wide Local Excision of Cutaneous Melanoma

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Background: Since the advent of sentinel lymph node (SLN) biopsy, patients with cutaneous melanoma have been referred to surgeons for consideration for SLN biopsy, sometimes even after the wide local excision (WLE) of the primary melanoma has been performed. This has raised the question of the reliability and validity of a lymphoscintigram performed for lymphatic mapping of the SLN after there has been anatomic rearrangement of the skin following the WLE of this primary melanoma.

Methods: We conducted a prospective study of 20 consecutive patients with cutaneous melanomas with thickness less than 1.00 mm, who volunteered to undergo preoperative and postoperative lymphatic mapping to determine if there were any changes in the lymph nodes that were identified following the WLE of the primary melanoma. Each of the patients had a resection with a minimum of 1.0 cm margin, and closure of their wounds with either transposition flap or double advancement flaps.

Results: Lymphatic mapping was clearly identified in all 20 patients. One patient declined to undergo postoperative lymphatic mapping. Postoperative lymphatic mapping performed in the remaining 19 patients 2–4 weeks following WLE was identical to the preoperative mapping in 13 patients (68%), showed additional lymph nodes in 4–5 patients (21–26%), and showed fewer lymph nodes in 1–2 patients (5–10%).

Conclusions: Lymphatic mapping performed after a WLE of a primary cutaneous melanoma should be as reliable in identifying the SLN as a preoperative lymphatic mapping in 90% of the patients.

Key Words: Melanoma—Sentinel lymph nodes—Lymphoscintigraphy.

One of the most powerful predictors of survival and cure of cutaneous melanoma is the presence or absence of tumor cells metastatic to the regional draining lymph nodes. The introduction and popularization of the concept of sentinel lymph node

(SLN) biopsy by Morton et al.¹ has played a major role in defining the surgical management of the regional nodes, the staging of the disease, and the adjuvant treatment of the patients.

The technique of SLN biopsy was based on the concept that all lymphatic fluid from a certain portion of skin is filtered by specific regional lymph nodes; as such, the first (or sentinel) lymph node(s) filtering a specific site could be removed and evaluated for presence or absence of metastatic malignant cells. Initially, these SLNs were identified with the help of vital blue dye injected into the dermis, coloring the draining lymphatic vessels, and allowing the identifi-

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cation of each specific SLN that took up the blue dye, identifying the SLN in more than 80% of the patients. Lymphoscintigraphy, which was introduced by Sherman and TerPogossian² in 1953 to study lymphatic flow in the hopes of treating lymph node metastases, subsequently became more helpful for identifying ambiguous sites of regional draining lymph nodes.³ Since then, subsequent investigators reported that the combination of preoperative lymphatic mapping and the intraoperative use of radioactive colloid increased the identification and successful removal of these SLNs to reach 98–99% of the cases.^{4–7}

This approach has been straightforward in the evaluation and treatment of the vast majority of patients with primary cutaneous melanoma. Occasionally, however, some patients were referred for sentinel lymph node biopsy and evaluation of their lymph nodes after their primary cutaneous melanoma had already been treated with a wide local excision. Since the architecture at the site of the primary melanoma had been altered because of the surgical rearrangement of the tissues, there was concern as to the validity or reliability of the lymph nodes identified by lymphatic mapping to represent the true “sentinel” lymph nodes for that site.

Nevertheless, after advising the patients regarding the limitation of the procedure, many surgeons proceeded to perform the SLN biopsy with the understanding that if they identified metastases in the regional lymph nodes, the patient could then proceed with the completion lymphadenectomy. In fact, two published data, with small numbers of patients, have shown that 23–34% of these patients harbored metastatic melanoma within their identified SLN.^{8,9} However, it did not answer the question of whether any true SLN were missed in the group of patients who had negative lymph nodes.

Therefore, we decided to evaluate the SLNs in a prospective manner by lymphatic mapping performed before and after surgical resection of cutaneous melanoma among a group of patients who volunteered to have the studies performed to see how often there were any changes in the lymph nodes identified.

METHODS

Twenty consecutive patients with cutaneous melanomas (1.0 mm or less invasion) who were treated at the Yale Melanoma Unit with SLN biopsies by a single surgeon during October 1, 1997 through September 30, 2001 were evaluated. Each patient was

informed that the study had been approved by our institutional review board (Yale Human Investigation Committee), that they did not need any lymphatic mapping or SLN biopsy because their risk of nodal involvement was less than 5%, and that their participation would only help us get data for future patients to determine if there are any changes in the SLN identification by the lymphatic mappings. They were informed that for this study each site of the primary melanoma would be resected with a standard 1.0 cm margin, and the wound site would be closed with either a transposition flap (rhomboid flap) or by double advancement flaps, by dissecting along the deep subcutaneous fascia or muscle fascia; the choice of the flap would be based on the simpler of the two depending on the site of the excision. They were further informed that the postoperative lymphatic mapping is not performed in standard cases and was only being requested for the investigation of this study. The charges for the lymphatic mappings for this study were absorbed by the Yale–New Haven Hospital as part of its support for clinical research at the Medical Center.

The preoperative and postoperative lymphatic mapping were performed at the same facility. The preoperative study was usually performed within 2 weeks (range 1–29 days) prior to the scheduled resection, and the postoperative study was usually performed within 2 months (range 14–176 days) after the resection and coverage.

Each study involved the intradermal injection of filtered technetium-99, sulfur colloid filtered to less than 0.2 μm particles. The dose was 1 mCi in 0.6 mL volume. The colloid dose was injected in 6 intradermal injections circling the primary site to a total volume of 0.5–0.8 mL. The whole body images were then scanned 1–3 hours later. This technique was used in all cases.

All 20 consecutive patients agreed to enter the study. One patient declined to have a postoperative study because the patient felt the preoperative study injections were “too painful to endure again,” and was excluded from the study. The other 19 patients completed the second lymphatic mapping. Their demographic data is illustrated in Table 1.

The preoperative and postoperative studies were reviewed independently by the senior surgeon, another surgeon, and an attending in nuclear medicine, each independently and at their leisure on separate days. None of the sets of images that were evaluated for each patient had any data other than the number assigned (1–19) and whether the study was preoperative or postoperative. Furthermore, none of the

TABLE 1. Demographic data of the 19 patients in the study

Patient No.	Primary location	Thickness (mm)	Preop (days)	Postop (days)
1	L scapula	0.35	1	119
2	L back	0.3	21	94
3	Mid-abdomen	0.4	10	113
4	R anterior thigh	0.3	13	52
5	R scapula	0.27	15	57
6	L back	0.8	12	43
7	L flank	0.25	5	176
8	R shin	0.35	13	36
9	R shoulder	0.68	6	137
10	L mid-back	0.8	29	29
11	R upper arm	0.35	9	48
12	L anterior thigh	0.25	14	14
13	L back	0.75	4	38
14	Mid-vertex scalp	0.70	11	36
15	L anterior thigh	0.4	11	34
16	Mid-vertex scalp	0.5	5	109
17	L posterior shoulder	0.25	5	69
18	R neck	0.3	13	34
19	L flank	0.85	21	100
Median		0.35	11	52
Range		0.25-0.85	1-29	14-176

TABLE 2. Diagnostic evaluation of lymphatic mapping in 19 patients following wide local excision of and repair of primary site of cutaneous melanoma

Evaluator	No. patients same	No. patients added sites	No. patients dropped sites
Senior surgeon	13 patients	No. 2, 10, 13, 19	No. 3, 16
Attending surgeon	13 patients	No. 2, 10, 13, 19	No. 3, 16
Attending nuclear medicine	13 patients	No. 1, 3, 10, 13, 19	No. 16

evaluators were given access to the reports of the original studies, so that they would not be influenced by those reports.

RESULTS

All three of the physicians evaluating the lymphatic mappings found the two studies identified the same lymph nodes in 13 of 19 patients (Table 2). Figure 1 shows a representation of two such patients that all three evaluators agreed were the same in the preoperative and postoperative studies.

All three of the evaluators found that four or five of the patients had radioisotope uptake in one or more LNs in addition to the same preoperative LN. All three evaluators selected the same three patients (No. 10, 13, 19). Figure 2A shows the two studies in patient No. 19 with a melanoma of the left flank, and Fig. 2B shows an example of left groin nodes in the preoperative study of patient No. 13 and bilateral groin nodes postoperatively. On the other hand, the two evaluators felt patient No. 2 had one more LN in the postoperative study that the third evaluator felt was not different from the preoperative study (see

Fig. 2C). Furthermore, one evaluator thought that patient No. 1 had additional nodes, while the other two evaluators felt that patient had the same nodes in both studies (see Fig. 2D).

Finally, two evaluators felt that the preoperative study of patient No. 3 showed more LNs than the postoperative study (Fig. 2D), but the third evaluator felt the postoperative study showed one additional LN.

With the exception of patient No. 3 noted previously, all three evaluators felt that patient No. 16 had one LN in bilateral neck drainages preoperatively and one LN in only the right neck postoperatively (see Fig. 3A).

DISCUSSION

Since the popularization of the SLN examinations, patients have been selected who would benefit from completion lymphadenectomy. Although there are still discussions whether the lymphadenectomy at the time of the original diagnosis alters the outcome when compared with therapeutic lymphadenectomy among those patients who subsequently show clinical

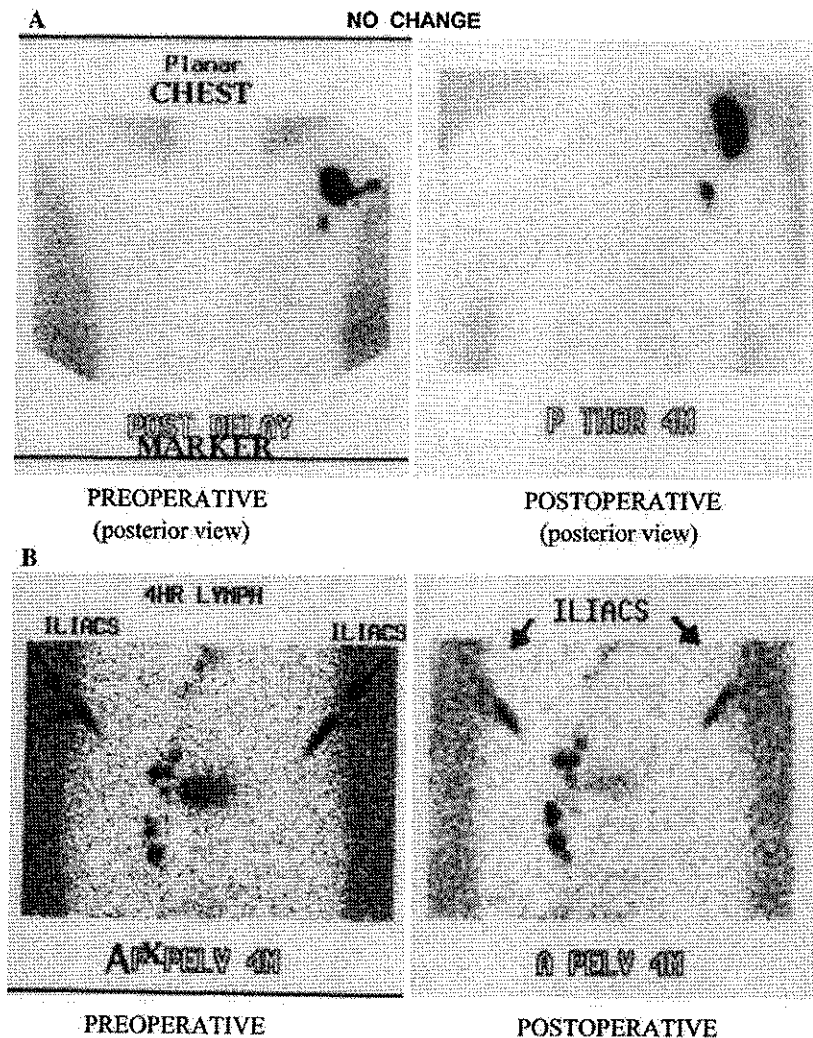


FIG. 1. Two examples of patients who had no change in the LN identified in both the preoperative and postoperative studies. (A) Patient No. 9 with a melanoma of the right posterior shoulder had one LN identified in the ipsilateral axilla in both studies. (B) Patient No. 12 with a melanoma of the right anterior thigh had the same right inguinal and right iliac LNs identified in both studies.

evidence of metastases, there is no question that the demand for these studies has increased over the past decade.

Most surgeons who see patients referred for SLN biopsy after the original melanoma has been resected have advised the patients and the referring physicians that the results of the lymphoscintigraphy, and the SLN removal may not be conclusively reliable. Nevertheless, the procedures have been performed with that admonition. Some comfort has been felt due to the reports by Kelemen et al.,⁸ and Karakousis et al.,⁹ showing that the SLN biopsy results in these patients were positive in the same proportion as would have been expected if they had not had a previous surgery and anatomic alteration of the tissues.

However, with the help of our patients who volunteered to have lymphoscintigraphy prior to and

subsequent to their surgical resections, we have confirmed the reliability of identifying the correct draining of the SLN in such cases. This study proposes that the SLNs do not necessarily provide drainage to several square centimeters of skin, but rather to regional areas of skin. This is illustrated by the work of Suami and Taylor,¹⁰ who demonstrated the lymphatic pattern of the skin of the upper extremity.

To further illustrate this, let us look at the area of the chest. The drainage from the breast goes to the ipsilateral axillary nodes. Others have shown that the proper SLN can be identified whether the parenchyma is injected around the tumor with the radiocolloid material, or whether the areola of that same breast is injected with the marker. Nathanson¹¹ compared peritumoral injection (66 patients) and

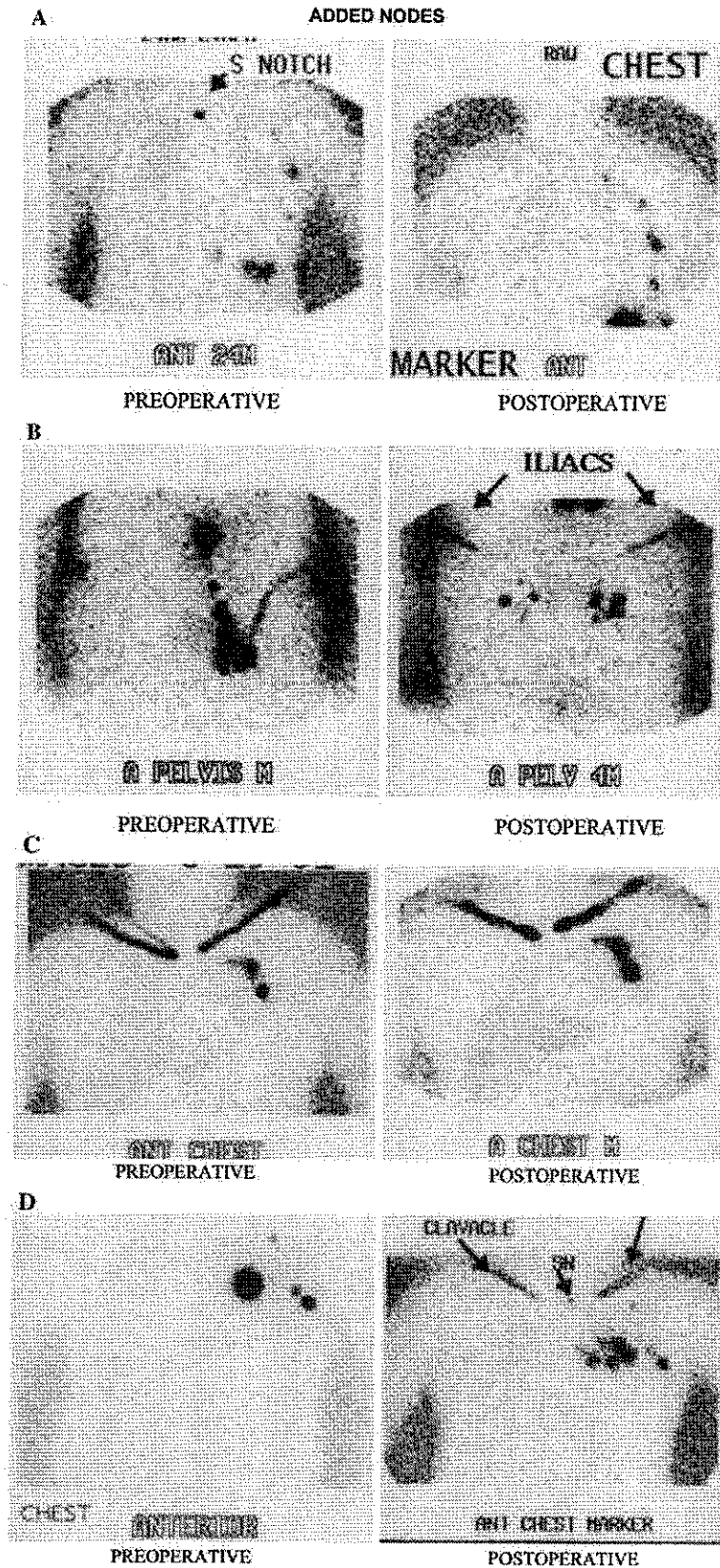


FIG. 2. Two examples of patients who had additional LN identified in the postoperative studies. **(A)** Patient No. 19 with a melanoma of the left flank. The surgeons felt there was an additional LN, but the radiologist thought the study represented the same LN. (The arrowhead at the top of the left image points to a radioactive marker placed on the suprasternal notch)—it is not a mediastinal lymph node. **(B)** Patient No. 13 with a primary melanoma of the left paramedian back had left groin nodes identified in the preoperative study (left) and bilateral groin nodes identified in the postoperative study (right). **(C)** Patient No. 2 with a melanoma of the left back with preoperative scan showing drainage to the left axillary SLN (left). Two evaluators felt the postoperative scan showed an additional SLN, while the third evaluator felt the two studies were the same. **(D)** Patient No. 1 with a melanoma of the left scapula and drainage to the left axillary SLN (left). One evaluator felt the postoperative scan showed additional SLN, while the other two evaluators felt the additional radioactivity represented the injection sites of the radioactive colloid at the site of the repair (former site of the primary).

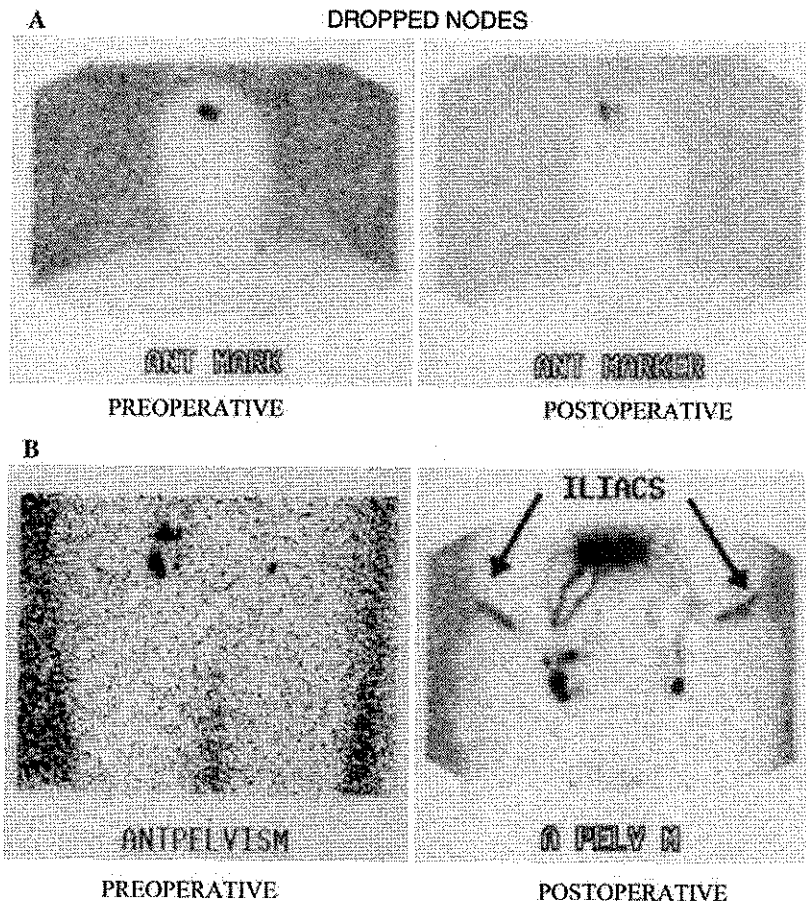


FIG. 3. Two examples of patients who had less LN identified in the postoperative studies. (A) Patient No. 6 with a melanoma of the midline scalp had bilateral lower cervical LN identified preoperatively (left) and only a right lower cervical LN identified postoperatively (right). (B) Patient No. 3 with a midline abdominal wall melanoma. The surgeons felt the preoperative study (left) shows more LN than the postoperative study (right), but the radiologist feels the postoperative study actually shows one more LN.

parenchymal injection of a different breast quadrant (53 patients) and found that the SLNs were both blue and radioactive in 94% and 93% of the patients in these respective groups. D'Eredita et al.¹² compared peritumoral injection (group 1 = 115 patients) and subareolar injections (group 2 = 40 patients), and they identified the SLN in 95% and 97.5% of the patients in these respective groups; the false negative rates after completion lymphadenectomy was 9% in group 1 and none in group 2. A recent multi-institutional study of 3961 patients comparing subareolar and periareolar injections identified the SLN in 99% and 96% of the patients respectively, with false negative rates of 8% and 9% of the respective groups after completion lymphadenectomy.¹³ Zavagno et al.¹⁴ studied 137 patients with breast cancer who had intrasubdermal injections of radioactive colloid over the tumor site; they compared 117 patients who had the addition of blue dye injected in the subareola (group 1) to 20 patients who had the blue dye injected in the subdermal area of the quadrant of the breast opposite to the tumor (group 2). They identified the

SLN in 98% of all the patients, and they included blue dye in 83% of group 1 and 85% of group 2. Therefore, these studies support the belief that the lymphatic drainage of the breast is the same for the parenchyma as well as for the areola, and most likely the skin of the breast, to the same SLN in the axilla.

In a similar fashion, the drainage from the scapula, shoulder tip, arm, lateral chest, and lower pectoral region is also channeled to the axillary nodes. We believe that it is quite likely that individual nodes within a LN group may filter larger anatomic areas rather than smaller portions. As such, if an entire arm, or a large portion of an arm drains to two or three SLNs, then any surgery to a portion of that area will not be sufficient to alter the lymphatic drainage. Therefore, lymphoscintigraphy should be reasonably accurate in most patients in spite of previous surgery.

We understand that the limitation of the number of patients in this study precludes us from making any conclusions about any specific site. Primary melanomas in the head and neck region are often under the site of the primary injection sites and require special

attention even if previous surgery has not been performed.

We believe this method can be employed in patients who have had a skin graft applied because the injection will be along the normal skin outside of the graft. This should have the same drainage as patients in whom this surrounding skin has been used with flaps. Those wounds that are covered by a skin graft have had no dissection of the surrounding skin and soft tissue and as such have had no alteration of the lymphatics in the periphery.

Finally, even though we studied patients with 1 cm margins, we believe it would be similar in patients who have had a 2 cm margin of excision.

CONCLUSIONS

This moderate series of patients from a single institution attests to the reliability of lymphatic mapping performed after a WLE of a primary cutaneous melanoma and tissue rearrangement to repair the site. This report demonstrates that lymphoscintigraphy in the postoperative period identified the same or additional SLNs when compared with the preoperative studies in 89–95% (17 of 19 to 18 of 19) of the patients studied.

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