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Intraoperative Lymphatic Mapping and Sentinel Lymph Node Dissection in Breast Cancer

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Abstract

Because the tumor status of the regional lymph nodes is the most important prognostic factor in patients with early-stage breast cancer, accurate histopathologic assessment of these nodes is essential for optimal management, including the selection of candidates for adjuvant systemic therapies. Intraoperative lymphatic mapping using a vital blue dye, with or without a radiocolloid, can identify the first axillary node to receive lymphatic drainage from a primary breast carcinoma. Focused histopathologic assessment of this sentinel node can be used to determine the tumor status of the entire axillary basin.

The minimal morbidity and high accuracy of sentinel lymph node dissection (SLND) in breast cancer have been validated by multiple independent investigators, and the data suggest that this surgical technique may eventually replace complete lymph node dissection as the preferred axillary procedure for the management of early-stage disease. In experienced hands, SLND can be successfully performed in more than 90% of eligible breast cancer patients; the tumor status of the sentinel node accurately predicts the status of all axillary nodes in more than 95% of cases.

This article reviews the current status, controversies, and future directions of SLND as a staging technique for patients with primary breast carcinoma. (CA Cancer J Clin 2000;50:279-291.)

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Introduction

Axillary lymph node dissection (ALND) has been an integral part of breast cancer management since Halsted introduced radical mastectomy in the mid-1800s. Although the impact of resecting axillary lymph nodes on survival is currently a subject of controversy, accurate assessment of axillary nodal status provides the most important prognostic information for patients with primary breast cancer.[1,2]

Information about regional nodal involvement often directs selection of adjuvant systemic therapy,[3,4] and it may be the key factor in the decision to initiate such therapy when the primary breast tumor is small. As improved imaging techniques continue to increase the proportion of breast cancer patients diagnosed with small primary tumors,[5] axillary nodal assessment is likely to become even more important in planning adjuvant systemic therapy.

At present, ALND with histopathologic study of the axillary specimen is the gold standard for detecting axillary nodal involvement and determining the number of nodes containing tumor.[6] Although level I-II ALND provides accurate information regarding axillary involvement and is associated with a low (less than 3%) rate of axillary recurrence,[7-9] its morbidity is significant; the acute complication rate can be as high as 20% to 30% and the rate of chronic lymphedema (see Petrek et al, page 292) can reach 20% to 30%.[10-14]

As yet, there are no accurate noninvasive techniques for assessment of axillary status in patients with primary breast cancer. Clinical assessment is associated with a 29%-to-38% false-negative rate, and radiographic methods (mammography, computed tomography, and positron emission tomography) have not achieved the level of accuracy required for management decisions.[15-19]

Limiting the extent of axillary dissection by random sampling of axillary nodes or removal of only level I nodes may decrease the complication rate but is associated with an unacceptably high false-negative rate: 40% false-negative rate for random axillary nodal sampling and 10% to 15% for excision of level I nodes alone.[20]

The recent introduction of intraoperative lymphatic mapping and sentinel lymph node dissection (SLND) for patients with primary invasive breast cancer allows directed and accurate assessment of axillary involvement with minimal morbidity.[21]

Development of Breast SLND

Morton et al[22] developed and first published a description of the SLND technique for clinical stage I cutaneous melanoma in 1992. This technique has since been validated by other melanoma investigators.[23,24] SLND is based on the concept that the tumor-bearing status of the sentinel node, i.e., the first node in the regional nodal basin that drains a primary tumor, reflects the tumor status of the entire nodal basin. Our group adapted the dye-directed SLND technique in melanoma (a cutaneous tumor system) for use in primary breast cancer (a parenchymal tumor system).[21]

Our initial trial was conducted during the developmental phase of SLND for breast cancer and involved 174 patients (T1, T2, or T3 primary tumors) with or without palpable axillary nodes who underwent dye-directed SLND followed by ALND.[21] All sentinel nodes were examined with hematoxylin and eosin staining (H&E).

Sentinel nodes were detected in 114 patients (65.5%), and the sentinel node accurately reflected axillary tumor status in 109 of 114 SLND procedures (95.6%). The 59% rate of sentinel node detection in the first 87 patients increased to 72% in the remaining 87 patients; the detection rate reached 78% by the last 50 cases in this series.

False-Negative Results

Of the five false-negative results, all occurred in the first 87 cases. Three of the five were related to misidentification of blue-stained fat as a sentinel lymph node; frozen section analysis of the sentinel node has since been incorporated into the procedure to prevent this error and to prepare our pathologists for the replacement of ALND by SLND.

The two other false-negative sentinel nodes were re-examined with immunohistochemical staining (IHC) employing anti-cytokeratin antibodies. IHC revealed micrometastases in one of the sentinel nodes. We now use IHC routinely for histopathologic examination of sentinel nodes. Thus, of the five false-negative cases, only one remained falsely negative after refining the technique.

After we had improved technical aspects and better defined patient selection criteria, we examined the accuracy of

SLND in 107 patients with T1-2 breast cancer. All patients also underwent completion ALND.[25] SLND was successful in 100 patients (93.5%). There were no false-negative results, and sentinel node status was 100% predictive of axillary tumor involvement. Based on the results of this study, in 1995 we stopped performing completion ALND in patients whose sentinel nodes were tumor-free by both H&E and IHC.

In our recent study encompassing the period from October 1995 to July 1999, 133 women with invasive breast carcinomas < 4 cm and clinically normal axillary nodes were prospectively enrolled in a trial of SLND using vital blue dye.[26] All patients underwent SLND; if no sentinel node was identified or if any sentinel node contained metastases, the patient also underwent completion ALND. Eight patients were excluded from the study, either because they refused to undergo ALND after identification of sentinel node metastases (three cases) or because they underwent subsequent mastectomy for unsuspected multifocal carcinoma (five cases).

Of the 125 evaluable patients, 57 had tumor-positive sentinel nodes and underwent completion ALND; ALND was also performed for one patient in whom a sentinel node was not identified.

Sixty-seven patients (54%) underwent SLND as the only axillary procedure. There were no local or axillary recurrences at a median follow-up of 39 months. The complication rate was 3% (two patients) following SLND without ALND, compared with 35% (20 patients) following SLND with ALND ($p = 0.001$).

Confirming the Sentinel Node Hypothesis

During a routine histopathologic workup of an axillary nodal specimen, the pathologist bisects the lymph node and stains sections of each half with H&E to search for tumor cells. However, only a small area of the lymph node is examined. To determine whether a more thorough examination of the nodal specimen would better identify metastases, we compared the incidence of metastases in 134 patients who underwent ALND alone with 162 patients who underwent SLND followed by completion ALND.[27]

All lymph nodes (sentinel and nonsentinel) were examined by standard H&E. However, if a sentinel node was negative, additional sections of this node were examined using IHC. The incidence of metastases was 42% in the SLND group and 29.1% in the ALND group. The higher incidence of metastases in SLND specimens reflected the increased detection of micrometastases using serial sectioning and IHC.

The small size of the SLND specimen (one to two lymph nodes) allows a focused examination that is too costly and time-consuming to be undertaken for the much larger ALND specimen (15 to 25 lymph nodes). However, to prove that the tumor status of the sentinel node reflects the tumor status of remaining nodes in the axillary lymphatic drainage basin, we undertook an exhaustive IHC assessment of 1,087 nonsentinel nodes removed from 60 breast cancer patients who had no H&E or IHC evidence of tumor cells in multiple sections of their sentinel nodes.[28] These patients were identified from a cohort of 103 consecutive breast cancer patients undergoing SLND.

We identified only one tumor-positive nonsentinel node, an error rate of 0.1% (1 of 1,087 lymph nodes) and an axillary status staging error rate of 0.9% (1 of 103). This confirmed the validity of the sentinel node hypothesis in breast cancer: The sentinel node is the lymph node most likely to harbor metastases if the tumor spreads to the axilla.

Other Experience

Dye-directed SLND

Results of dye-directed SLND have been reported by other investigators. In a group of 145 patients who underwent

SLND followed by ALND, Guenther et al[29] successfully identified a sentinel node in 103 patients (71%). However, this study should be interpreted as a feasibility trial as it included tumors ranging from T0 to T4. Moreover, the SLND technique was not standardized in the initial phase of the study. Nonetheless, histopathologic examination of the sentinel node accurately reflected the axillary status of 100 patients (97%); as in our study, the three false negatives occurred in the early phase of the trial.

Dale et al[30] reported their initial SLND experience in 20 patients who underwent dye-directed SLND followed by ALND. One patient in this series had bilateral SLND followed by ALND. A sentinel node was identified in 14 of 21 drainage basins (66%), and its status was 100% predictive of axillary nodal status.

Recently, Koller et al[31] reported their breast SLND experience using either methylene blue 1% or patent blue dye. A sentinel node was found in 96 of 98 patients (98%) undergoing dye-directed SLND followed by ALND, and the accuracy of sentinel node status in predicting axillary status was 97% (93 of 96).

Probe-directed Intraoperative Mapping

Other investigators have mapped lymphatic drainage using a hand-held gamma probe and a radioactive tracer. Krag et al[32] first described probe-directed intraoperative mapping in breast cancer using Tc-99m sulfur colloid as the tracer material. Sentinel nodes were detected in 18 of 22 patients (82%).

Pijpers et al[33] used peritumoral injection of TC-99m labeled colloidal albumin to identify a sentinel node in 34 of 37 breast cancer patients (92%). Two patients refused ALND, but in the remaining 32 patients, the histopathologic status of the sentinel node was 100% predictive of the histopathologic status of the ALND specimen.

Veronesi et al[34] reported subdermal injection of Tc-99m-labeled human serum albumin colloid for probe-directed mapping in 163 consecutive breast cancer patients. The sentinel node was identified in 160 patients (98.2%), and its tumor status matched that of the ALND specimen in 156 patients (97.5%).

Borgstein et al[35] reported their experience with probe-directed SLND using Tc-99m labeled colloidal albumin in patients with T1-T2 breast cancer. The sentinel node was detected in 122 of 130 patients (94%), and the technique had a sensitivity of 98% with a false-negative rate of 1.7%.

Miner et al[36] used ultrasonography to guide the peritumoral injection of unfiltered Tc-99m sulfur colloid in 42 breast cancer patients undergoing SLND followed by ALND. A sentinel node was localized in 41 patients (98%) and was falsely negative in one case. Thus, the accuracy rate of SLND was 98% for predicting axillary status.

Offodile et al[37] used Tc-99m labeled dextran as the radioactive tracer to identify a sentinel node in 40 of 41 patients (98%) who underwent SLND followed by ALND; the sensitivity of the sentinel node in predicting axillary tumor status was 100%, with no false-negative sentinel nodes.

Crossin et al[38] reported peritumoral injection of Tc-99m sulfur colloid for lymphatic mapping and SLND in 50 clinically node-negative breast cancer patients. The SLND success rate was 84% and the accuracy rate of sentinel node status in predicting axillary nodal status was 98%.

Most recently, Krag et al[39] reported the results of a multicenter trial studying probe-directed SLND. The overall rate of sentinel node identification among the 11 participating surgeons practicing in a variety of settings was 91% (405 of 443 patients). The histopathologic status of the sentinel node was 97% accurate (392 of 405 patients) in predicting the histopathologic status of the axilla. In this study, the sentinel node was outside the axilla in 8% of the cases.

Combination Techniques

Albertini et al[40] combined dye-directed and probe-directed mapping in 62 patients with primary breast cancer. The sentinel node was blue-stained in 73% of the patients and radioactive in an additional 19%, increasing the total sentinel node detection rate to 92%. Sensitivity was 100% and there were no falsely negative sentinel nodes, i.e., no sentinel node was tumor-negative if any nonsentinel node removed during completion ALND contained tumor cells.

Barnwell et al[41] recently reported their experience with this combination approach in 42 patients undergoing SLND followed by level I/II ALND. Sentinel nodes were detected in 38 patients (90%) and were 100% accurate in predicting the tumor-bearing status of the axilla.

With the combination technique, O'Hea et al[42] reported a SLND success rate of 93%, identifying a sentinel node in 55 of 59 breast cancer patients. The sentinel node status was 95% (52 of 55) accurate in predicting axillary tumor involvement.

Finally, Cox et al[43] compiled results from three breast SLND protocols with 466 patients. In one protocol, only patients with a positive sentinel node underwent completion ALND. The overall SLND success rate was 94% (440 of 466).

Table 1 summarizes the various studies of SLND as a staging tool in breast cancer patients. In general, the rate of sentinel node identification is greater than 90%, and the accuracy of sentinel node status as a predictor of axillary nodal status exceeds 95%—much higher than the reported accuracy of any noninvasive method. The average number of sentinel nodes removed was similar with all three of the techniques: 1.2 to 2.7 for dye-directed SLND; 1.2 to 2.9 for probe-directed SLND; and 1.0 to 2.2 for the combination mapping technique.

The similar results achieved using different techniques indicate that SLND can be successfully performed in a great majority of patients using dye and/or radioactive tracer with a variety of subtle technical modifications.

Surgical Technique

The sentinel node to be excised during SLND is identified intraoperatively by lymphatic mapping using a vital blue dye and/or a radioactive tracer. Regardless of mapping technique, identification of the sentinel lymph node can be performed with local anesthesia and heavy sedation, or with general anesthesia.

For dye-directed lymphatic mapping and SLND, preoperative lymphoscintigraphy is recommended to demonstrate axillary drainage if the primary tumor is in the medial half of the breast. Rarely, a tumor located in the medial half may drain only to lymph nodes in the internal mammary chain; this decreases the likelihood of finding an axillary sentinel node.

To date, no study has demonstrated the effectiveness of SLND for an internal mammary lymph node. In our practice, we attempt to identify an axillary sentinel node. If an axillary sentinel node is not found, we will perform a standard ALND and recommend that, for patients with internal mammary drainage, the internal mammary nodal chain be included in the radiation port.

At the time of surgery, 3 to 5 ml of isosulfan blue dye (Lymphazurin®)[25,27,29,30] are injected into the breast parenchyma. The dye is injected laterally, adjacent to the breast mass and below the subcutaneous fat, to avoid tattooing the overlying skin. If the primary tumor has already been excised, dye is injected into the wall of the biopsy cavity. If the primary tumor is not palpable, dye is injected through a needle inserted under mammographic guidance for tumor localization.

For five to seven minutes after dye

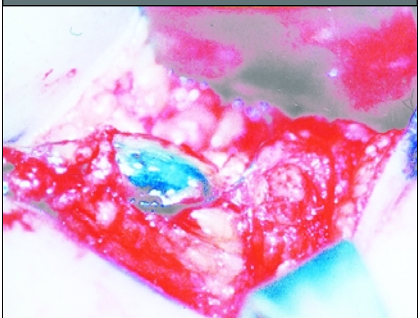
Table 1
Success Rate and Accuracy of SLND in Breast Cancer

Study	N	Mapping Technique	Pathology Technique	SLND Success Rate	Accuracy	Average Number of Sentinel Nodes	Rate of Sentinel-only Metastases
Krag 1993 [32]	22	Probe	H&E	18 / 22 (82%)	18 / 18 (100%)	—	43%
Giuliano 1994 [21]	174	Dye	H&E	114 / 174 (66%)	109 / 114 (96%)	1.8	38%
Albertini 1996 [40]	62	Dye + Probe	H&E	57 / 62 (92%)	57 / 57 (100%)	2.2	67%
Pijpers 1997 [33]	37	Probe	H&E	34 / 37 (92%)	32 / 32 (100%)*	2.2	64%
Veronesi 1997 [34]	163	Probe	H&E	160 / 163 (98%)	156 /160 (98%)	1.4	38%
Giuliano 1997 [25]	107	Dye	H&E + IHC	100 / 107 (94%)	100 / 100 (100%)	1.8	67%
Guenther 1997 [29]	145	Dye	H&E	103 / 145 (71%)	100 / 103 (97%)	—	43%
Dale 1998 [30]	21	Dye	H&E	14 /21 (66%)	14 / 14 (100%)	1.2	60%
Borgstein 1998 [35]	130	Probe	H&E + IHC	122 / 130 (94%)	103 / 104 (99%)†	1.2	59%
Barnwell 1998 [41]	42	Dye + Probe	H&E	38 / 42 (90%)	38 / 38 (100%)	1.0	33%
O'Hea 1998 [42]	59	Dye + Probe	H&E	55 / 59 (93%)	52 / 55 (95%)	2.2	41%
Miner 1998 [36]	42	Probe	H&E	41 / 42 (98%)	40 / 41 (98%)	2.9	57%
Offodile 1998 [37]	41	Probe	H&E + IHC	40 / 41 (98%)	40 / 40 (100%)	3.0	—
Cox 1998 [43]	466	Dye + Probe	H&E + IHC	440 / 466 (94%)‡	—	1.9	—
Koller 1998 [31]	98	Dye	—	96 / 98 (98%)	93 / 96 (97%)	2.7	27%
Crossin 1998 [38]	50	Probe	—	42 / 50 (84%)	41 / 42 (98%)	2.0	—
Krag 1998 [39]	443	Probe	H&E	405 / 443 (91%)	392 / 405 (97%)	2.6	60%

* Two patients refused complete lymph node dissection and were censored from this analysis.
† 18 patients refused complete lymph node dissection and were censored from this analysis.
‡ Majority of patients with negative SLND did not undergo completion ALND.

H&E = hematoxylin and eosin staining
IHC = immunohistochemical staining

Figure 1



The blue-stained sentinel node is identified by following the dye-filled lymphatic tract. Reprinted with permission from Hsueh.[68]

Figure 2

Preoperative lymphoscintigram demonstrates the lymphatic drainage tract from primary tumor to the sentinel node. Reprinted with permission from Hsueh.[68]

injection, the breast is gently compressed to enhance lymph flow. A transverse incision is then made just below the hair-bearing area in the axilla. The amount of dye injected and the interval between dye injection and skin incision increase with the distance of the tumor from the axillary drainage basin. Blunt dissection is performed to identify the dye-filled lymphatic tract. This tract is then followed proximally and distally to a blue-stained sentinel node (Fig. 1). If more than one dye-filled lymphatic tract is identified, each is followed. These tracts usually drain to the same sentinel node or to additional neighboring sentinel nodes.

Probe-directed mapping using a radioactive tracer is performed by injecting technetium-99m (Tc-99m) labeled sulfur colloid,[32,36,38,39] albumin colloid,[33-35] or dextran[37] one to 24 hours prior to operation. A lymphoscintigram is usually obtained preoperatively to determine the axillary drainage pattern from the primary tumor (Fig. 2).

At the time of surgery, a hand-held gamma-ray counter is positioned over the axilla to identify the area of greatest radioactivity in counts per second. A background count is established by measuring radioactivity over a neutral site. The skin is incised over the area of greatest radioactivity, and the probe is held over the incision to measure the in vivo radioactivity of axillary lymph nodes. The sentinel node is usually the node with the highest absolute count. After this node is excised, in vivo radioactivity of the axillary basin is reassessed. Some SLND investigators will continue to search for additional sentinel nodes if the absolute count of the basin still exceeds background.

Because of differences in the type, dose, and timing of radioactive tracers used, there are no uniform criteria for identifying the sentinel node by its radioactive count. Krag et al[39] injected 37 MBq (1 mCi) of Tc-99m labeled unfiltered sulfur colloid around the tumor and defined a sentinel node as any node with radioactivity three times greater than background and at least 25 counts per 10 seconds. Veronesi et al[34] injected 7 MBq of Tc-99m labeled albumin colloid subdermally over the tumor and defined a sentinel node as the node with the highest radioactive count. Albertini et al[40] injected 16 MBq of Tc-99m labeled filtered sulfur colloid around the tumor and defined the sentinel node as the node with greater than 10 times the radioactivity of neighboring nonsentinel nodes; these investigators also searched for additional sentinel nodes if the basin count remained 150% higher than background. Thus, the definition of a "hot" sentinel node varies greatly.

Histopathologic Analysis of Sentinel Nodes

Because the SLND specimen contains only one or two lymph nodes, it can be routinely examined in multiple sections with IHC staining for low and intermediate molecular weight cytokeratin. This meticulous histopathologic assessment increases the sensitivity of detecting micrometastases.

In our study, the 42% rate of axillary metastasis in 162 patients undergoing SLND followed by ALND was significantly ($p < 0.03$) higher than the 29.1% rate in 134 patients undergoing ALND alone.[27] The corresponding rates of axillary micrometastases (≤2 mm) were 38.2% (26 of 68) and 10.3% (4 of 39). Eleven of the 26 micrometastases in the SLND group were identified by IHC after H&E was negative. Therefore, a detailed examination of the sentinel node "upstaged" an additional 16% (11 of 68) of patients.

Because the application of IHC increased the rate of detecting axillary nodal metastases, we further evaluated the use of multiple-step sections and IHC in 60 sentinel nodes (42 patients) that were tumor-free on frozen section and on H&E staining of permanent sections from levels 1 and 2.[44] Previous IHC staining of levels 1 and 2 had identified micrometastases in nine of the 60 nodes (eight patients). The paraffin blocks of the sentinel nodes were further sectioned at eight additional levels (levels 3 to 10), separated by 40 µm and then re-examined with IHC.

Of the 51 previously negative sentinel nodes, only two nodes—both from the same patient—contained metastatic cancer cells in levels 3 to 10. Thus, the additional step of sectioning and IHC staining did not significantly increase the number of patients with tumor-positive sentinel nodes.

Significance of Axillary Micrometastases

Although the significance of axillary micrometastases has not been validated in a prospective fashion, several retrospective studies suggest that micrometastases are associated with poor outcome (Table 2).[45-51] The International (Ludwig) Breast Cancer Study Group used serial sectioning of axillary lymph nodes to identify micrometastases in 9% (83 of 921) of breast cancer patients whose nodes were tumor free by routine histopathological examination.[47] Patients with micrometastases had lower rates of five-year disease-free survival ($p = 0.0003$) and overall survival ($p = 0.002$) than did those whose nodes remained negative: 58% and 79%, respectively, versus 74% and 88%, respectively.

Two subsequent large ($n > 100$) retrospective analyses also demonstrated the prognostic importance of identifying occult micrometastases when H&E results were negative. De Mascarel et al[49] used IHC to identify micrometastases in 50 of 218 patients (23%) whose ALND specimens stained negative for tumor cells with H&E. In patients with invasive ductal carcinoma, IHC-detected micrometastasis was the most significant factor associated with recurrence (multivariate p-value = 0.011). IHC-detected micrometastasis was also significantly associated with overall survival on multivariate analysis ($p = 0.027$).

Hainsworth et al[50] used IHC to identify occult metastases in 41 of 343 "node-negative" patients (12%), and reported that the presence of occult metastases increased the five-year recurrence rate

Table 2
Prognostic Significance of "Occult" Axillary Micrometastases

Study	Number of Patients	Histologic Examination	Incidence of Occult Micrometastases (%)	Decrease in Disease-Free Survival Associated with Detection of Occult Micrometastases* (%)
Trojani[1987] [45]	162	IHC	14	22
Sedmak[1989] [46]	45	IHC	11	11
Ludwig group[1990] [47]	921	Multiple sections + IHC	9	16
Chen[1991] [48]	80	IHC	29	16
De Mascarel[1992] [49]	218	IHC	23	10
Hainsworth[1993] [50]	343	IHC	12	15
Clare[1997] [51]	86	Multiple sections + IHC	13	28

IHC = immunohistochemical staining.
*Duration of follow-up varies.

from 16% to 32%. Numerous other studies, however, failed to show an association of micrometastases with diminished survival.[52-55] A prospective study of the significance of IHC-detected occult metastases is being sponsored by the American College of Surgeons.

Conclusion

Intraoperative lymphatic mapping and sentinel node biopsy may alter the surgical management of patients with invasive breast cancer. Because only about one third of patients with clinically negative axillae have histopathologic evidence of metastases in the ALND specimen,[15,56-58] routine ALND places a significant number of patients at risk for operative morbidity without certain benefit.

The risk of axillary metastasis from a small primary breast cancer is low but not negligible,[59-62] and the tumor status of the axillary nodes in this subset of patients often determines the need for and type of adjuvant systemic therapy.[63] An accurate and minimally morbid axillary staging tool such as SLND not only would be extremely valuable in managing these patients but also would provide important prognostic information for patients with larger primary tumors[64,65] With minimal risk of complications, SLND can accurately distinguish patients who may not benefit from ALND from those who may benefit from complete axillary staging and regional nodal control with ALND. Nevertheless, surgeons should not consider SLND as a first-line axillary surgical option until they have completed a learning phase to validate its high accuracy and low rate of complications.

The SLND Learning Curve

Compelling phase II data notwithstanding, SLND should be considered an experimental technique because its staging efficacy has been demonstrated only in relatively small trials. Surgeons interested in using SLND should progress along their own "learning curves," performing a completion ALND after each SLND. This will document the rate of sentinel node identification—and the accuracy of SLND at their institutions. The staging accuracy of the sentinel node procedure depends not only on the surgeon's proficiency but also on the expertise of the nuclear medicine physician and the pathologist. Mapping, excision, and histopathologic examination of the sentinel node is a multidisciplinary technique; a concerted effort by the surgeon, the nuclear medicine physician, and the pathologist is necessary to assure quality control and accuracy.

The sentinel node is often the only lymph node that contains tumor cells. In our previous study of 107 consecutive patients,[25] 67% (28 of 42) of those with sentinel node involvement had no other tumor-positive nodes in the axillary basin. Likewise, the rate of axillary involvement confined to the sentinel node ranges from 27% to 67% in other studies (Table 1). Although there is no accurate means of predicting which patients will have axillary metastases limited to the sentinel node, the size of the primary tumor and the size of the sentinel node metastasis may predict the likelihood of nonsentinel node metastases.[66] If so, then completion ALND may not be necessary in all patients who have sentinel node metastasis.[26] This possibility requires further study.

The emergence of intraoperative lymphatic mapping and sentinel node biopsy for patients with invasive breast cancer is exciting because it may spare node-negative patients the morbidity of complete ALND. Avoiding the morbidity of complete ALND is especially important in elderly breast cancer patients,[67] in whom any operative complication is more likely to impair quality of life. However, the long-term success of SLND as an adjunct for management of breast cancer depends on uniform selection criteria, standardization of the technique, and reproducibility of results.

Centers should avoid offering SLND without completion ALND until their multidisciplinary SLND team has demonstrated consistent success; all of the peer-reviewed breast SLND studies in the literature report routine use of completion ALND during the initial phase of each group's SLND experience, regardless of the technique or mapping material used.

Quality control is paramount, yet the optimal type of quality control for SLND—a multidisciplinary technique—is still not adequately defined. In addition, we have yet to establish the true definition of a "hot" sentinel node, the ideal location for injection, and the indications for SLND. All of these issues must be resolved before SLND can be widely incorporated into the daily practice of surgeons.

In the US, a multicenter prospective trial sponsored by the American College of Surgeons and another large-scale prospective study sponsored by the National Surgical Adjuvant Breast and Bowel Project are currently examining SLND versus ALND. The results of these trials will validate the clinical utility of SLND in the management of patients with breast cancer. CA

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