

## Sentinel Lymphadenectomy: A New Alternative for Managing Early Breast Cancer

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**Key words:** lymphatic mapping, sentinel lymphadenectomy, breast cancer

*IMAJ 2002;4:803–809*

With one million new cases each year worldwide, breast cancer is the most common malignancy in women. Constituting 18% of all cancers in women, breast cancer also accounts for approximately 30% of all malignancies diagnosed in the United States [1].

Breast-conserving therapy is widely accepted as an effective treatment option for patients with early-stage carcinomas of the breast. The use of BCT became widespread after randomized studies demonstrated survival rates similar to those following radical mastectomy [2,3]. In a stepwise manner, less radical surgery was proven as effective as more extensive operations. Modified radical mastectomy was found to have equivalent results to radical mastectomy without being as morbid and disfiguring. Subsequent studies later provided evidence that survival rates following breast conservation with axillary dissection and postoperative radiotherapy were equivalent to rates following modified radical mastectomy. Axillary dissection, however, has remained unchanged for the past century. Since this procedure is essential for staging, regional control, and perhaps improving survival, the fact that it causes morbidity is considered an acceptable price for its efficacy.

Over the last few years, however, the role of axillary dissection for women with invasive breast cancer has been questioned. This is in part due to the earlier stage detection of smaller tumors, malignancies with fewer nodal metastases, and more widespread use of tumor characteristics to determine the need for chemotherapy regardless of nodal status.

Axillary lymphadenectomy for patients with early-stage invasive breast cancer removes lymph nodes from levels I and II. This dissection may result in significant morbidity, with lymphedema reported in 15–30% of patients. The incidence and severity of lymphedema increases, however, with both the extent of axillary surgery and the addition of radiation therapy. While lymphedema is the most widely reputed morbidity with ALND, other complications have been noted, including seroma or wound infection (3–20%), numbness (70%), pain (33%), stiffness (10–15%), arm weakness (25%), decreased shoulder range of motion, and neurologic changes (15–20%) [4]. Vascular injury and brachial plexus injury are also serious but rare complications, greatly increasing the cost,

morbidity, hospital stay, and recovery time following ALND. Since most patients with early breast cancer who undergo axillary dissection have no evidence of nodal metastases they are unlikely to benefit from the procedure.

Recently, surgical treatment of breast cancer has entered a new era with the introduction of the lymphatic mapping/sentinel lymphadenectomy concept. This procedure, also known as sentinel node biopsy, is an important recent development in surgical oncology [5,6]. This operation preserves the accurate staging ability of ALND, identifies patients most likely to benefit from ALND, yet minimizes morbidity and expense by identifying patients who are unlikely to benefit from ALND, thereby obviating more radical surgery.

The propensity of solid tumors to spread to regional lymph nodes was originally described in the eighteenth century by François LeDran (1685–1770) in patients with breast cancer [7]. Historically, examples of preferential sites of tumor metastasis have been recognized, such as Virchow's node for gastric cancer, the Delphian node for thyroid cancer and Sister Mary Joseph's node. The urologist Ramon Cabanas first coined the term "sentinel lymph node." In 1977 he determined that, by using lymphangiography, squamous cell carcinomas of the penis initially drain to a group of lymph nodes in the groin [8]. The concept of identifying a lymph node that is most likely to have metastatic melanoma in order to minimize surgery was first utilized by Morton and colleagues in patients with stage I cutaneous melanoma. They defined the sentinel node as the first lymph node or nodes to drain a primary melanoma and the node most likely to contain metastases if the melanoma has spread to the regional lymph nodes [9]. Thus, they showed that if the sentinel nodes were melanoma-free, the remaining regional nodes would also be tumor-free. This subsequently became significant in its application for operative staging of regional lymph node basins. In 1991, Giuliano modified this procedure in order to apply the technique to patients with breast cancer.

### **Intraoperative lymphatic mapping using vital-blue dye in patients with breast cancer**

After administration of general or local anesthesia with intravenous sedation, isosulfan blue (3–5 ml, Lymphazurin 1%) is injected into the breast parenchyma along the axillary peritumoral region or into

BCT = breast-conserving therapy  
ALND = axillary lymphadenectomy



**Figure 1.** Axillary sentinel node with its associated blue-stained lymphatic track easily visible using the blue dye injection technique.

the axillary side of the wall of the cavity after biopsy. Dye is injected below the subcutaneous fat into the parenchyma to avoid skin tattooing and to assure parenchymal uptake by breast lymphatics, the same lymphatics that drain the tumor. If the lesion is not palpable, a mammographic or ultrasound-guided localization is necessary. After injection, the area is massaged for approximately 5–7 minutes to augment the action of the lymphatic pump to improve passage of the dye to the sentinel node [6,10]. A transverse incision is then made at the inferior aspect of the hair-bearing area of the axilla. The incision is carefully carried through the subcutaneous fat and pectoral fascia to the surface of the axillary fat. Blunt dissection is performed to identify a blue-stained lymphatic channel within the axillary fat pad. Abduction of the arm above the patient's head facilitates identification of the lymphatic tract or blue-stained node [Figure 1]. The axilla should be palpated for suspicious nodes, which may be removed. If the sentinel node is found to have metastatic cells or cannot be identified, a full ALND is usually performed.

Several factors contribute to the success of the lymphatic mapping/sentinel lymphadenectomy technique. Tumor location, size, injection technique including dye volume and injection depth, addition of massage, method of dissection, and histopathologic evaluation of the sentinel node all influence success. Timing of the axillary incision after injection is also crucial to successful identification, as “washout” of the dye from the sentinel node occurs after a prolonged period. Patient selection also influences outcome, as older age, large breasts and high body fat have been shown to cause a decreased rate of sentinel node identification. Finally, LM/SL after excisional biopsy has been demonstrated to produce sub-optimal results in some studies [6,11] but not in ours [12].

In 1994, Giuliano et al. [6] published a large feasibility trial using intraoperative LM/SL with vital-blue dye. In this study 172 patients had 174 breast cancers, with 2 patients having synchronous bilateral tumors. All patients underwent LM/SL followed by a level

I and II ALND in addition to surgical treatment of the primary lesion. Using 1% isosulfan blue dye, the sentinel node was identified in only 66% of patients overall, but the identification rate improved as the investigators developed the technique. The staging accuracy of the procedure, however, was 96% even in this initial feasibility trial. In this study there were five false negative cases in which the pathology of the sentinel node did not accurately predict the status of the axilla. All false negatives occurred in the first 87 cases. Analysis of these five cases revealed that three of them did not contain lymphatic tissue, with axillary fat misidentified as the sentinel node. One patient was found to have occult metastases when evaluated by immunohistochemical staining using anti-cytokeratin antibodies. While this patient would have been identifiable today with this technique, this method was not utilized in the initial protocol. Only one of the five patients examined had a true false negative sentinel node, improving the staging accuracy rate from 96 to 99%. Although the initial identification rate using the blue dye technique was only 66%, this was at first interpreted as a “learning curve,” however in reality it was not only a learning curve but a demonstration of the evolution of the technique. Giuliano and co-workers reported all patients who were injected with blue dye, including those in whom blue-stained fat was misidentified as a sentinel node. Since this was a feasibility trial to determine the safety and efficacy of the procedure, all patients who consented underwent sentinel lymphadenectomy followed by ALND. This included patients in whom the procedure is now clearly inappropriate, namely, those with large, locally advanced tumors, and those with palpable or matted nodes. It also included patients for whom the appropriate volume of dye and time to incision were unknown and that we now recognize were clearly inadequate. In this study, the technique, safety and indications were defined. At the time of operation, the anatomic level of the sentinel node was recorded in the 54 most recent cases. In 43 cases the sentinel node was identified and 27 of them (62.7%) were level I, whereas 10 (23.7%) exhibited drainage of isosulfan blue directly to a sentinel node in level II. Six cases had blue-stained sentinel nodes in levels I and II.

A subsequent study of LM/SL at the John Wayne Cancer Institute was performed after the technique had matured. In this series of 107 patients at least one sentinel node was identified in 94% of patients using blue dye alone. There were no false negative results and sensitivity and specificity were 100%. This increased success was attributed to definition and refinement of the technical details and indications for the procedure [13].

These two studies comparing sentinel lymphadenectomy with ALND in the same patients provided clear evidence for the feasibility and staging accuracy of the procedure. More recently, series rates of 99% have been achieved with blue dye alone.

### **Radioisotope and gamma probe-guided method**

In contrast to the dye-only method, Krag et al. [5] published the first pilot study of LM/SL using isotope alone in patients with invasive breast cancer. In this study of 22 patients, unfiltered technetium sulfur colloid injected 1–9 hours prior to the surgery was used to map the lymphatic tract and identify the sentinel node.

LM/SL = lymphatic mapping/sentinel lymphadenectomy

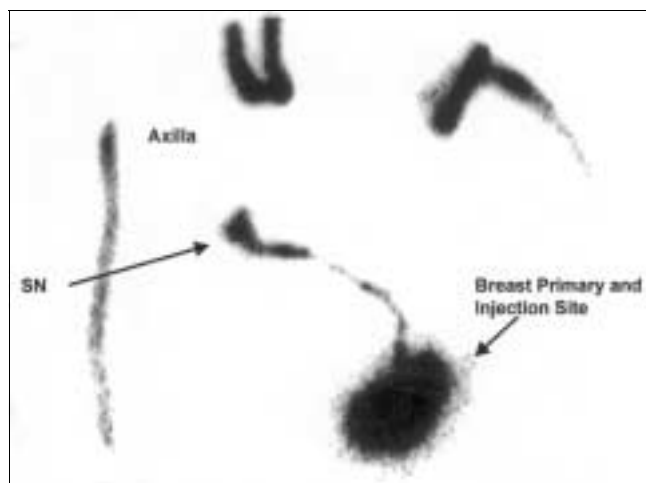
The sentinel node was identified in 18 of 22 cases (82%) and was 100% predictive of the axillary status. Krag et al. [14] subsequently updated their results in 248 cases. In this cohort, the sentinel node was then identified in 95.5% of patients with a false negative rate of 6.5%.

Since then, the technique using isotope without dye has progressively matured. The lymphoscintigram, while valuable for mapping and visualization, was not felt to be mandatory and probe-only detection is practiced at some centers. One significant advantage of the lymphoscintigram is that it provides information on the routes of draining regional lymph node basins and thus possible metastases, on the number of sentinel nodes that require harvesting, and on the location within the basin. This method may aid the surgeon in cases of unexpected drainage from the breast to supraclavicular nodes, infraclavicular nodes or internal mammary nodes, which occurs predominantly in medial lesions. The presence or absence of internal mammary node metastases is important for estimating the prognosis of breast cancer patients, particularly in those without axillary metastases [15–17].

Identification of internal mammary sentinel lymph nodes also allows proper planning of radiotherapy in patients who might not otherwise be recognized as high risk for metastases in this location. The gamma probe facilitates the LM/SL considerably by locating the sentinel node non-invasively and aiding the surgeon in placement of the skin incision. The use of lymphoscintigraphy is generally a more desirable approach to localization than the probe alone since distant or unusual nodal basins can easily be documented peri-operatively. In general, probes have inferior spatial resolution compared with modern gamma cameras.

As the accuracy of the technique became refined, so did attempts to define a sentinel node. Krag et al. [5] defined a sentinel node as “hot” by radioactivity levels being three times that of background and at least 15 counts per 10 seconds. Veronesi and colleagues [18] defined the sentinel node as the node with the highest radioactivity, and Albertini et al. [19] defined it as the node with a tenfold increase in radioactivity of neighboring lymph nodes.

In the USA, the most commonly used agent is technetium-labeled sulfur colloid [13,18,20]. Some investigators use filtered agents, which have a faster transit time, while others prefer unfiltered sulfur colloid. Nonetheless, lymphoscintigraphy can rarely be obtained with the unfiltered agent, necessitating reliance solely on the intra-operative probe. The timing of the injection is dependent on the type of radioactive colloid used. The size of the colloidal solution is important since the rate of migration of radiocolloids through lymphatics and nodal basins is inversely proportional to particle size. A very small particle such as Tc-99m antimony sulfide, which has a particle size of 3–12 nm, provides extensive spill or overflow of tracer to non-sentinel nodes. This agent is widely used in Australia. Conversely, excessively large particles such as those in non-filtered Tc-99m sulfur colloid (50–100 nm) [21,22] show poor migration within the lymphatics and less intense labeling of the sentinel node [5]. The ideal dimensions for



**Figure 2.** Lymphoscintigram shortly after injection, demonstrating the primary injection site and sentinel node (SN = sentinel node).

such a molecule are between 10 and 200 nm. Albertini et al. [19] used filtered (200 nm filter) Tc-99m sulfur colloid. In contrast, Pijpers et al. [15] reported that selective targeting and intranodal retention in the sentinel node was best achieved with Tc-99m colloid albumin (3–80 nm). Tc-99m colloid is available in Israel.

Veronesi et al. [18] reported results for 163 patients who underwent LM/SL using technetium-labeled human serum albumin with a particle size of 50–200 nm. The radioisotope was injected subdermally and superficial to the tumor, and the sentinel node was identified using a gamma counter. The sentinel node was identified in 160 patients, and its tumor status was predictive of axillary status in 156 patients of the cohort (97%).

Prior to surgery, patients receive an injection of Tc-99m-labeled colloid usually into the peritumoral parenchyma of the breast. After injection by intratumoral, subdermal or parenchymal peritumoral methods, imaging with a scintillation camera should begin immediately in order to identify lymph channels and the first sentinel node [Figure 2]. The patient should be positioned in a manner similar or identical to that used in surgery, with the arm elevated for visualization of axillary nodes. The location of the sentinel node should be determined precisely and skin marks applied directly over the node for the operating surgeon. A hand-held gamma detection probe is used to identify the area of greatest activity in the axilla prior to skin incision. The signal emitted by the probe is used to guide isolation and removal of the nodes intra-operatively.

### **Combination of radioisotope and vital-blue dye**

In addition to techniques utilizing only dye or radioactivity, the most commonly used method of sentinel node detection uses both pre-operative isotope injection and intra-operative injection of dye. The radioactive colloid is injected pre-operatively to facilitate intra-operative identification of the sentinel nodal drainage basin, which may also be identified with dye [15,22]. If lymphoscintigraphy is performed, the most radioactive region, the “hot spot,” in the axilla is marked on the skin. This mark helps the surgeon find the sentinel node by localizing the region where it is located. The blue dye

Tc-99m = technetium

method is then used intra-operatively to increase the likelihood of identifying a sentinel node.

Albertini's team [19] used a combination of isosulfan blue dye and filtered technetium sulfur colloid for lymphatic mapping. He identified a sentinel node in 57 of 62 cases (92%). In 45 cases, the node was identified by both blue dye and radiolabeled colloid. In 12 cases it was identified by colloid alone. Metastases were found in 18 sentinel nodes, all of which were identified by both dye and colloid. No patient had a positive non-sentinel node in the absence of a positive one (100% sensitivity). These investigators concluded that the combination of blue dye and colloid increased the sentinel node identification rate, and that this method is therefore superior to colloid or dye alone. Such results are significant because lymphatic mapping and selective lymphadenectomy could lead to more conservative surgical treatment of women with breast cancer [Table 1]. This combination may be the best technique for the team just starting a sentinel node biopsy program as it provides the surgeon with two modalities to identify the sentinel node [23].

Cox et al. [24] undertook a prospective trial of intra-operative lymphatic mapping using a combination of vital-blue dye and filtered technetium-labeled sulfur colloid. A sentinel node was defined as a blue node and/or radioactive node with a 10:1 gamma probe ratio of *ex vivo* sentinel node to non-sentinel node counts. The node was successfully identified in 440 of 466 patients (94.4%). In all patients who failed lymphatic mapping (5.6%) a completion axillary dissection was performed. This study led Cox to conclude that accurate LM/SL is most effective when a combination of vital-blue dye and radiolabeled sulfur colloid is used, but a randomized trial by Morrow and associates [25] showed no difference. In this trial, among 92 patients randomized to either blue dye or radioactivity and blue dye, sentinel nodes were identified in 88% and 86% of patients, respectively. Identification method made no difference in the predictive value of the node for axillary metastases, and those patients at highest risk for non-identification of the sentinel node were patients who were older or had a larger body mass index, those with non-palpable tumors, and those with tumors requiring localization.

Dupont and team [26] used filtered Tc-99 sulfur colloid to map drainage to axillary sentinel nodes found in 335 of 516 patients

(65%), and to internal mammary or extra-axillary nodes found in 52 patients (10%). By using sensitive hand-held probes and vital-blue dye intra-operatively, the overall success rate of finding an axillary sentinel node was 85%. Of the 335 patients in whom an axillary sentinel node was identified with imaging, all had successful sentinel lymphadenectomies. Although no sentinel nodes could be imaged in 181 patients, 153 of these patients (85%) had an axillary sentinel node identified with intra-operative mapping. For 28 patients in whom lymphoscintigraphy was negative and intra-operative mapping was unsuccessful, complete axillary lymphadenectomy was performed and 13 of these patients (46%) were found to have metastatic disease in the basin.

Pijpers and co-workers [15] reported the use of peritumoral injection of Tc-99m labeled colloidal albumin in 37 patients. These authors reported a 92% success rate with the sentinel node 100% predictive of the axillary status. Borgstein's group [20] used Tc-99m-labeled colloidal albumin in patients with T1 or T2 tumors. The identification rate was 94% and the false negative rate 1.7%.

There is considerable variation in techniques for injection of both colloid and dye. Both peritumoral and intraparenchymal injections as well as para-areolar and intradermal injections have found success and have their respective advocates. The technique used in the initial study at the John Wayne Cancer Institute [6] comprised a peritumoral intraparenchymal injection of isosulfan blue alone and, subsequent to the initial learning curve, was noted to have a 0% false negative rate and to be 100% predictive in 107 consecutive cases with axillary dissection [13]. The Multicenter Validation Study by Krag et al. [27] also used the peritumoral intraparenchymal injection location but with Tc-99m. Their results demonstrated 97% accuracy and 100% specificity with a positive predictive value of 100% and negative predictive value of 96%. While several series combine intradermal isotope injection and intraparenchymal blue dye yielding sentinel node identification rates of approximately 97% [28], subareolar injection of blue dye alone has also demonstrated potential with one series of 40 women demonstrating a sentinel node identification rate of 98% with a 100% positive predictive value for the axilla [29]. Thus, while many argue that peritumoral injections seem most logical from a drainage standpoint, considerable well-supported variation and controversy exists regarding the most appropriate method for injection of dye and radionuclide. There is, unquestionably, an advantage in not tattooing the skin when using dye with the intraparenchymal method.

**Table 1.** Identification and success rate of sentinel lymph nodes in breast cancer patients

Author	Mapping technique	SN identification (%)
Albertini, 1996 [19]	Gamma probe & isosulfan blue	57/62 (92%)
Veronesi, 1997 [18]	Lymphoscintigraphy & gamma probe	160/163 (98%)
Krag, 1993 [5]	Gamma probe	18/22 (82%)
Giuliano, 1994 [6]	Isosulfan blue feasibility trial	114/174 (66%)
Pijpers, 1997 [15]	Lymphoscintigraphy & gamma probe	34/37 (92%)
Giuliano, 1997 [13]	Isosulfan blue	100/107 (94%)
Cox, 1998 [24]	Gamma probe & isosulfan blue	440/466 (94%)

## Histopathology

Sentinel lymphadenectomy has resulted in an increased awareness of the accurate pathologic staging of breast cancer. Since the sentinel node is the most likely site of axillary metastasis, the pathologist can concentrate efforts on detecting metastases in this node.

Giuliano et al. [30] compared 162 patients who underwent a sentinel lymphadenectomy followed by a complete axillary lymphadenectomy (sentinel node group) with 134 patients who underwent axillary lymphadenectomy alone (ALND group). All sentinel nodes were evaluated with standard hematoxylin and eosin

techniques, and sentinel nodes without evidence of metastasis underwent immunohistochemical stains using low and intermediate molecular weight cytokeratin antibodies. All non-sentinel nodes were evaluated by hematoxylin and eosin alone. The sentinel node and ALND groups had 42% and 29% incidences of nodal metastases respectively ( $P < 0.03$ ) with the difference primarily due to more focused examination of the sentinel node in contrast to random sections of non-sentinel nodes. Among the patients with nodal metastases, micrometastases (defined as metastatic foci = 2 mm) comprised only 10.3% of the ALND group versus 38.2% of the sentinel node group, with 42% of these only identified by immunohistochemical stains. Examination of the sentinel nodes therefore improved the sensitivity by enabling the pathologist to not only increase the number of nodal sections examined per node, but to utilize the stain to improve detection, which in a full dissection may be prohibitively expensive and labor-intensive.

At the present time, the clinical significance of micrometastases is unclear. A micrometastasis is defined as a focus of cells 2 mm or less in greatest dimension. Numerous studies have shown that multiple sectioning of lymph nodes can detect micrometastases missed by routine sectioning [31,32]. It has also been demonstrated that histopathologic detection of axillary metastases overall was significantly higher with LM/SL than with axillary lymphadenectomy, probably due to the examination of multiple sections of a sentinel node as compared to random sections of many non-sentinel nodes. Thus, LM/SL may be beneficial in detection of micrometastases.

In 40–60% of cases the sentinel node is the only involved lymph node and non-sentinel nodes are free of tumor, however the natural history of micrometastases is unknown and the current published literature evaluating the impact of micrometastases on survival is contradictory. Early studies using serial sectioning and H&E staining showed no significant difference in survival between patients with negative nodes and those with occult metastases, while other studies have shown decreased survival with the detection of micrometastases. The size of the micrometastasis appears to be prognostically important and IHC stain-detected micrometastases are usually very small. The tumor cell clusters detected by IHC stains are on average one-tenth the size of micrometastases (0.1 mm versus 1.0 mm) detected by H&E [33].

Trojani et al. [34] demonstrated a 14% increase in micrometastases with the addition of IHC stain to routine H&E in patients whose nodes were felt to be tumor-free, which correlated with lower survival. The largest trial examining the prognostic effect of occult metastases was reported by the International (Ludwig) Breast Cancer Group [35]. Multiple sections and IHC staining were used to reevaluate axillary lymph node specimens previously considered to be tumor-free by routine H&E staining. The group reevaluated 921 breast cancer specimens by sectioning the axillary nodes at six different levels and examining with hematoxylin and eosin. The incidence of nodal metastasis increased by 83 patients (9%). The 5

year disease-free and overall survival rates for these 83 patients were significantly lower than for patients whose axillary specimens were confirmed to be tumor-free by multiple sectioning and IHC staining (58% vs. 74%,  $P = 0.003$ ; and 79% vs. 88%,  $P = 0.002$  respectively).

The use of immunohistochemical staining on the entire axillary specimen is impractical due to both time and financial constraints, however adding it to hematoxylin and eosin for the examination of the sentinel node alone may improve detection of micrometastases and later clarify their natural history.

The clinical significance of IHC stain-positive sentinel node micrometastases and of bone marrow micrometastases is currently being evaluated in a large multicenter study (American College of Surgeons Oncology Group Z0010). In this trial, patients with T1 and T2, N0 breast cancers undergo lumpectomy, LM/SL, and bilateral iliac crest bone marrow aspiration biopsy. The sentinel nodes and bone marrow are examined in a double-blinded fashion at a central laboratory using IHC staining and reverse transcriptase polymerase chain reaction. A concurrent study (ACOSOG Z0011) randomizes women with involved sentinel nodes to either no further regional therapy or completion lymphadenectomy. This trial is designed to evaluate whether completion axillary lymphadenectomy presents a therapeutic advantage over LM/SL with systemic adjuvant therapy and whole breast irradiation.

The use of frozen sections in the setting of LM/SL has also been a subject of considerable debate. Criticism mainly focuses on the high false negative rate compared with standard H&E examination. Weiser et al. [36] reported a benefit from the use of frozen section in selected breast cancer patients who underwent sentinel node biopsy, and found this to be 58% sensitive. The sensitivity of a frozen section critically depended upon the primary tumor size, and increased from 4% in patients with T1a lesions to 38% in those with T2 primaries. Dixon et al. [37] reported an overall 73% sensitivity, which was believed too low to justify routine use of a frozen section. Polymerase chain reaction assays and other new technologies will probably improve the detection rate. Once established, these techniques may prove too costly and labor-intensive for routine use in axillary lymphadenectomy specimens or even standard sentinel node evaluation.

Turner and colleagues [38] reviewed 278 consecutive patients undergoing sentinel lymphadenectomy concurrent with breast cancer excision in order to examine intra-operative frozen section and imprint cytology H&E accuracy for staging. In this study a false negative rate was defined as the number of false negative results (imprint cytology and frozen section) divided by the sum of the false negative results and true positive results. The accuracy of sentinel node imprint cytology and frozen section when compared with permanent paraffin H&E examinations was 93%, but dropped to 79% of final IHC stain results because of the identification of 39 metastases by IHC stains not evident by H&E (sensitivities of 74% and 48%, respectively). The imprint cytology and frozen section false negative rate was 26% compared with paraffin H&E, versus 52% when compared with paraffin IHC stain. The study also noted that imprint cytology and frozen section accuracy decreased as the diameter of the sentinel node increased, and the accuracy of intra-

H&E = hematoxylin and eosin

IHC = immunohistochemical

operative imprint cytology and frozen section correlated with the pathologist's experience reading the slides, when gauging by the permanent IHC stain standard.

## Conclusion

The sentinel node is the first lymph node to receive lymphatic drainage from a primary breast cancer and, therefore, the node most likely to contain metastatic tumor cells [9]. Intra-operative LM/SL is a new technique that may accurately stage patients with minimal morbidity. The most important question resulting from the emergence of sentinel node technology is whether LM/SL can replace routine axillary lymphadenectomy. Our group feels that experienced centers may replace axillary dissection with LM/SL in clinically node-negative patients with T1-T2 breast cancers without adverse consequences. Results at the John Wayne Cancer Institute recently demonstrated the safety and efficacy of LM/SL without routine completion lymphadenectomy. In 133 patients who underwent LM/SL, sentinel nodes were identified in 132 (99%) with blue dye alone. Eight sentinel node-negative patients were excluded, and none of them had axillary metastases. Of the remaining 125 patients, 57 had tumor-positive sentinel nodes. One underwent an unsuccessful mapping procedure, and 67 received no further axillary-specific therapy after LM/SL alone. The rate of minor wound complications (seroma, cellulitis, drain site infection) was 35% after axillary lymphadenectomy versus 2% after sentinel lymphadenectomy. At median follow-up of 39 months and more than 4 years at the time of this writing, there have been no local or axillary recurrences. The absence of axillary recurrence supports LM/SL as an accurate staging procedure and suggests that routine axillary lymphadenectomy may be eliminated for patients with negative sentinel nodes at centers with experience in this procedure [39]. At the John Wayne Institute, Turner and team [40] reported that the probability of non-sentinel node involvement detectable by hematoxylin and eosin was 0% of 157 sentinel nodes and <0.1% using immunohistochemical staining when there was no evidence of micrometastasis within the sentinel node by H&E or IHC staining.

Quality control is paramount for successful application of this technique and involves not only surgeons, but also radiologists, pathologists, and nuclear medicine physicians. Axillary dissection should not be abandoned until the entire team is able to achieve highly accurate results.

Finally, not all patients are candidates for this procedure. Those pregnant and lactating and with clinically positive nodes, and those with multicentric tumors are not good candidates. Those with large tumors or large biopsy cavities may have a higher rate of false negative sentinel nodes, and patients with prior axillary surgery may not be suitable due to the likelihood of previous axillary lymphatic disruption. The effects of pre-operative chemotherapy or radiation on this procedure are also unknown and further investigation is needed to determine whether these patients are candidates for this procedure.

**Acknowledgment.** Supported by funding from the Fashion Footwear Charitable Foundation, New York, USA.

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