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Guidelines for Sentinel Node Biopsy and Lymphatic Mapping of Patients With Breast Cancer

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Objective

To define preliminary guidelines for the use of lymphatic mapping techniques in patients with breast cancer.

Summary Background Data

Lymphatic mapping techniques have the potential of changing the standard of surgical care of patients with breast cancer.

Methods

Four hundred sixty-six consecutive patients with newly diagnosed breast cancer underwent a prospective trial of intraoperative lymphatic mapping using a combination of vital blue dye and filtered technetium-labeled sulfur colloid. A sentinel lymph node (SLN) was defined as a blue node and/or a hot node with a 10:1 *ex vivo* gamma probe ratio of SLN to non-SLN. All SLNs were bivalved, step-sectioned, and examined with routine hematoxylin and eosin (H&E) stains and immunohistochemical stains for cytokeratin. A cytokeratin-positive SLN was defined as any SLN with a defined cluster of positive-staining cells that could be confirmed histologically on H&E sections.

Results

Fine-needle aspiration (FNA) or stereotactic core biopsy was used to diagnose 195 of the 422 patients (46.2%) with breast cancer; 227 of 422 patients (53.8%) were diagnosed by excisional biopsy. The SLN was successfully identified in 440 of 466 patients (94.4%). Failure to identify an SLN to the axilla intraoperatively occurred in 26 of 466 patients (5.6%). In all patients who failed lymphatic mappings, a complete axillary dissection was performed, and metastatic disease was documented in 4 of 26 (15.4%) of these patients. Of the 26 patients who failed lymphatic mapping, 11 of 227 (4.8%) were diagnosed by excisional biopsy and 15 of 195 (7.7%) were diagnosed by FNA or stereotactic core biopsy. Of interest, there was only one skip metastasis (defined as a negative SLN with higher nodes in the chain being positive) in a patient with prior excisional biopsy. A mean of 1.92 SLNs were harvested per patient. Twenty percent of the SLNs removed were positive for metastatic disease in 105 of 440 (23.8%) of the patients. Descriptive information on 844 SLNs was evaluated: 339 of 844 (40.2%) were hot, 272 of 844 (32.2%) were blue, and 233 of 844 (27.6%) were both hot and blue.

At least one positive SLN was found in 4 of 87 patients (4.6%) with noninvasive (ductal carcinoma *in situ*) tumors. A greater incidence of positive SLNs was found in patients who had invasive tumors of increasing size: 18 of 112 patients (16%) with tumor size between 0.1 mm and 1 cm had positive SLNs. However, a significantly greater percentage of patients (43 of 131 [32.8%] with tumor size between 1 and 2 cm and 31 of 76 [40.8%] with tumor size between 2 and 5 cm) had positive SLNs. The highest incidence of positive SLNs was seen with patients of tumor size greater than 5 cm; in this group, 9 of 12 (75%) had a positive SLN ($p < 0.001$).

Conclusions

This study demonstrates that accurate SLN identification was obtained when all blue and hot lymph nodes were harvested as SLNs. Therefore, lymphatic mapping and SLN biopsy is most effective when a combination of vital blue dye and radiolabeled sulfur colloid is used. Furthermore, these data demonstrate that patients with ductal carcinoma *in situ* or small tumors exhibit a low but significant incidence of metastatic disease to the axillary lymph nodes and may benefit most from selective lymphadenectomy, avoiding the unnecessary complications of a complete axillary lymph node dissection.

Every paper for the past 5 years has described 185,000 women who in the past year have been afflicted with breast cancer. However, population statistics reveal that until 1970, approximately 11 million women were at risk for breast cancer. This year, approximately 10 million women will be turning 50, at a rate of 5000 per day.[1] Based on the age incidence data for breast cancer, within the next 10 years 269,000 women per year will be afflicted with breast cancer.[2] More startling is the fact that in another 10 years, 420,000 women per year will be afflicted with this disease. These projections represent a significant increase in prevalence without a change in incidence and will require new strategies in the care and treatment of breast cancer (Fig. 1).

Some basic tools that have been incorporated into the authors' practice have made a dramatic difference in the ability to provide rapid and efficient breast cancer care: first, the application of touch preparation cytology for the evaluation of diagnostic biopsies,[3] intraoperative margin analysis,[4] and intraoperative lymph node assessment for metastatic disease[5]; second, lymphatic mapping of the axillary lymph nodes using a combination of technetium-labeled sulfur colloid and Lymphazurin blue dye[6]; and third, the use of immunohistochemical staining of lymph nodes for the identification of metastatic disease.[7,8] Lymphatic mapping for breast cancer has independently been reported by Giuliano et al.[9] and Krag et al.[10] with the use of Lymphazurin blue dye and technetium-labeled sulfur colloid, respectively. The current authors previously published their modification of this procedure, which combined the two agents and demonstrated improved capability for detecting sentinel lymph nodes (SLNs).[6]

The role of axillary dissection may be the most controversial topic in the treatment of breast cancer.[11–17] Nearly 100 years ago, Halstead demonstrated the curative potential of radical mastectomy. Fifty years later, Patey proved that modified radical mastectomy could yield similar survival with limited morbidity. The controversy now rages over the current role of axillary dissection in the management of operable breast cancer.[11] Since the time of Halstead to the current day, the status of the regional nodal basin remains the single most important independent variable in predicting prognosis. Advocates of axillary dissection contend that there is a benefit for breast cancer patients because axillary dissection renders regional

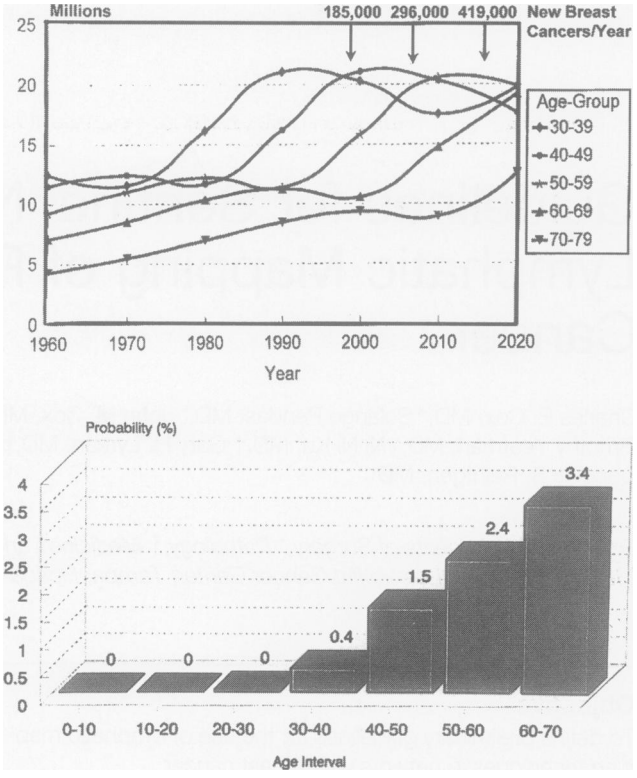

Figure 1. The epidemiology of breast cancer. The upper panel demonstrates the number of women at risk for breast cancer for the whole population divided by decades of age. The rapid increase of 10 million women beginning with 1970 is a result of the "baby boomer" population moving through successive decades of life. The lower panel shows a probability distribution by decade of age of the percentage of women who have been demonstrated to have developed breast cancer. Along the top of the upper figure are extrapolations of the predicted number of breast cancer cases per year based on the current number of cases and the probabilities by age of the lower panel. Dramatic increases will be seen in prevalence, although the incidence will not change.

control of axillary disease. Critics of axillary dissection maintain that overall survival depends on the development of distant metastases and is not influenced by axillary dissection in most patients.[11,13] They contend that patients with microscopic axillary metastases might be cured with adjuvant chemotherapy with or without nodal irradiation in the absence of axillary dissection. Many have even advocated abandoning axillary dissection in early breast cancer.[11,13]

The purpose of this article is to demonstrate that through lymphatic mapping, individual tumor behavior can be predicted with greater accuracy and sensitivity with limited morbidity. This study prospectively reviews the outcomes of the data collected on 466 consecutive patients in which SLNs were mapped. On the basis of these outcomes, the authors have developed a set of guidelines for the use of lymphatic mapping in patients with breast cancer.

METHODS

From April 1994 to November 1997, all patients presenting to the Comprehensive Breast Cancer Program at the H.

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Lee Moffitt Cancer Center at the University of South Florida, Tampa, with suspected breast cancer were evaluated for enrollment in a breast lymphatic mapping study. All patients diagnosed by fine-needle aspiration (FNA) biopsy, core needle biopsy, advanced breast biopsy instrument, or excisional breast biopsy were included. In all patients, physical examination indicated that the axilla was not involved. Pregnant women were excluded. Four hundred sixty-six women were enrolled in the study after they gave written informed consent.

The study was made up of three specific studies. The initial phase I protocol included the training phase of lymphatic mapping in which the SLN along with a complete axillary lymph node dissection was performed. Also included were patients enrolled in a phase II protocol that involved removal of only the SLN or SLNs, without a complete lymph node dissection, provided that the SLN or SLNs were negative intraoperatively by gross examination and by touch preparation cytology.[5] Cytokeratin immunohistochemical staining was subsequently performed on each SLN. Complete axillary dissection was performed on all patients with histologic-positive nodes by hematoxylin and eosin (H&E) or cytokeratin-positive staining. The final group of patients included in this review were a group of patients enrolled in a Department of Defense-funded study for polymerase chain reaction evaluation of SLNs, bone marrow aspirates, and peripheral blood. Each of the studies was reviewed and approved by the Institutional Review Board at the University of South Florida for the protection of human subjects.

The 466 consecutive patients with newly diagnosed breast cancer underwent a prospective trial of intraoperative lymphatic mapping using a combination of Lymphazurin blue dye and filtered technetium-labeled sulfur colloid. An SLN was defined as any blue and/or hot node with a 10:1 *ex vivo* gamma probe ratio of SLN to non-SLN.

All patients were scheduled for either a lumpectomy or mastectomy with selective lymphadenectomy and possible complete axillary lymph node dissection, depending on the patient's clinical presentation and personal preference. Sixty-three percent of the women elected and underwent breast preservation.

Patients underwent intraoperative lymphatic mapping using filtered technetium-labeled sulfur colloid 450 μCi (425 to 495 μCi) (Syncor International, Tampa, FL), which was injected 1 to 6 hours before the operative procedure. This was followed by the injection of a vital blue dye 5 cc (2.5 to 7.5 cc) (isosulfan blue [Lymphazurin], Zenith Parenterals, Rosemont, IL) just before the skin preparation and operative intervention. Four hundred fifty microcuries of technetium-labeled sulfur colloid in 6 cc of saline were injected in six 1-cc aliquots in separate sites at the periphery of the tumor or at the site of the previous excisional biopsy, as directed by palpation or ultrasound. A hand-held gamma-detection probe (Neoprobe 1000 or 1500, Neoprobe Corp., Dublin, OH) was used to assist in SLN detection. The probe was used before making the incision. The axillary incision was made to include the area of greatest activity. Careful dissection was used to identify the blue-stained afferent lymphatic channels. The gamma probe was used to confirm the location of the SLN and to guide the dissection when the afferent lymphatics were difficult to identify.[6]

Radiation Safety

All physicians (surgeons, pathologists, radiologists) and intraoperative personnel (perioperative nursing personnel, nuclear medicine staff, pathology staff) were routinely badged and monitored for radiation exposure. Radiation monitoring of the operating room and pathology cutting areas was accomplished on a case-by-case basis. All pathologic materials were quarantined for 48 hours before being processed for permanent section analysis. Samples for estrogen and progesterone receptor analysis were harvested fresh and frozen but held in quarantine for 48 hours before being submitted for analysis.

Pathology

Excised lumpectomy margins were evaluated by touch preparation cytology; on rare occasions, frozen sections were performed to evaluate intraoperative margins or tumor masses.[4] All nodal tissue excised was submitted to the pathology department. Every SLN was identified by number (*e.g.*, SLN 1, SLN 2). NonSLNs were also identified, and remaining tissues were identified simply as axillary contents. All lymph nodes were identified and dissected from the surrounding fat and connective tissue. Intraoperative evaluation of bisected lymph nodes was accomplished using imprint cytology.[5] After this, the bivalved nodes were entirely submitted for paraffin blocks, and sections were stained with H&E. Additional sections of each SLN were likewise stained with immunohistochemical stain using the peroxidase–antiperoxidase technique with monoclonal antibody against low-molecular-weight cytokeratin (CAM 5.2; Becton Dickinson Immunocytometry Systems, San Jose, CA). A cytokeratin-positive SLN was defined as any SLN with a defined cluster of positive-staining cells that could be confirmed histologically on H&E sections.

Statistics

Statistical inference of the probability of nodal involvement was based on the binomial distribution (binomial test) applied to on-time pairs of observations (*i.e.*, when only SLNs were involved). False-negative SLN localization was defined as negative SLNs with other nodes in the basin positive for metastatic breast cancer. Sensitivity was calculated by the number of patients in whom the histologic characteristics of the SLN reflected the histologic characteristics of the rest of the nodes in the basin. The unit of analysis was patients, not the number of lymph nodes re-

Table 1. LYMPHATIC MAPPING: SUCCESS RATE (466 PATIENTS)*

Successful Mapping	Failed Mapping	False Negative Mapping
440 (94.4%)	26 (5.6%)	1 (0.21%)

* This table demonstrates the overall success rate of detecting the sentinel lymph node(s) in the 466 patient study population. This table also demonstrates the failure rate and the false negative rate for this mapping series.

moved. Confidence intervals for the sensitivity and other proportions were based on an exact formula that uses percentiles of the F distribution.

RESULTS

Lymphatic Mapping *Versus* Biopsy Technique

Lymphatic mapping results were first evaluated in patients with intact breast lesions that were diagnosed by either FNA or stereotactic core biopsy, under the hypothesis that nonexcisional biopsy may lead to less lymphatic disruption. Therefore, patients undergoing stereotactic core biopsy and FNA as the initial diagnostic procedure were compared with patients undergoing excisional biopsy. Of the 466 patients enrolled in the study, 422 provided data that could be evaluated for biopsy comparison. FNA or stereotactic core biopsy was used to diagnose 195 of the 422 patients (46.2%). Excisional biopsy was performed for diagnosis in 227 of the 422 patients (53.8%). Failure to identify an SLN intraoperatively occurred in 26 patients; 15 of 195 (7.7%) of these patients were diagnosed by FNA or stereotactic biopsy and 11 of 227 (4.8%) were diagnosed by excisional biopsy. There was only one (0.21%) skip metastasis (defined as a negative SLN with higher nodes in the chain being positive) in a patient initially diagnosed with prior excisional biopsy.

Lymphatic Mapping Success Rate *Versus* Detection Method

The SLN was successfully identified in 440 of the 466 patients (94.4%). Failure to identify an SLN to the axilla intraoperatively occurred in 26 of the 466 patients (5.6%) (Table 1). Patients who failed mapping underwent a complete axillary dissection, and metastatic disease was documented in 4 of 26 (15.4%) of these patients. A total of 844 SLNs were successfully removed, and 169 (20%) were positive for metastatic disease in 105 of the 440 patients (23.8%).

Subsequently, lymphatic mapping results were evaluated as a function of the detection method used to identify the SLN. Under the hypothesis that both the radiocolloid and the vital blue dye would independently detect the SLN, it was our initial postulate that the SLN should be both blue and hot. We therefore collected information to determine the variance in detection methodology of radiocolloid *versus* vital blue dye. Of the 466 patients enrolled in the study, 450 had data available for comparison; 844 SLNs were evaluated in this subgroup. Based on our initial hypothesis, 233 of the 844 SLNs (27.6%) were demonstrated to be both blue and hot. However, an additional 106 SLNs, or 339 of 844 (40.2%), were detected as being hot using technetium-labeled sulfur colloid. Radiocolloid thus detected 67.8% of the nodes. Finally, 39 additional SLNs, or 277 of 844 (32.2%), were identified as blue by Lymphazurin injection. Lymphazurin thus detected 59.8% of the nodes. These results confirmed the added benefit in detecting SLNs using both Lymphazurin blue dye and technetium-labeled sulfur colloid, for an overall success in mapping of 94.4% of patients.

Lymphatic Mapping *Versus* Tumor Size

As demonstrated in previous publications, lymphatic mapping has clearly demonstrated a more sensitive capacity to detect lymph node metastases.[9,10] Under this operative premise, using the immunohistochemical techniques for metastatic detection in SLNs, all patients, including those with ductal carcinoma *in situ* (DCIS), were mapped and evaluated.[10] Of the 466 patients enrolled in the study, 418 were evaluated for histology and tumor size. Positive SLNs were found in 4 of 87 patients (4.6%) with TIS (DCIS) tumors. Patients with invasive tumors defined as T_{1A} were combined with T_{1B}, which grouped tumor sizes between 0.1 mm and 1 cm. In this subgroup, 18 of 112 patients (16%) demonstrated positive SLNs on lymphatic mapping. T_{1C} tumors (1 to 2 cm) demonstrated positive SLNs in 43 of 131 (32.8%). T_2 tumors (2 to 5 cm) demonstrated positive SLNs in 31 of 76 (40.8%). Finally, a small subgroup of T_3 tumors (>5 cm) demonstrated positive SLNs in 9 of 12 (75%) ($p < 0.001$) (Table 2).

Table 2. LYMPHATIC MAPPING: POSITIVE SENTINEL LYMPH NODE(S) (SLNs) *VERSUS* TUMOR SIZE (418 PATIENTS)*

	Number of Patients (% of total)	Number of Patients with Positive SLNs	% Positive
T0 (DCIS)	87 (20.8)	4	4.6
T1A–T1B	112 (26.8)	18	16.0
T1C	131 (31.3)	43	32.8
T2	76 (18.2)	31	40.8
T3	12 (2.9)	9	75.0

DCIS = ductal carcinoma *in situ*.

* This table demonstrates the number of patients (of 418 evaluated) that were detected to have positive SLNs compared with the tumor size following lymphatic mapping with blue dye and radiocolloid.

DISCUSSION

The current standard of care for the management of invasive breast cancer is the complete removal of the cancer with documented negative margins by either mastectomy or lumpectomy followed by complete axillary lymph node dissection.[12,15]

As pointed out in the presentation of the data, 23.8% of patients will be detected as having metastatic disease to the lymph glands. The remaining 76.2% patients with negative lymph nodes may easily be treated entirely in an outpatient environment, shifting the care from the previously defined inpatient role to the outpatient setting. This should generate significant cost savings to the health care system. The added cost of the lymphatic mapping and blue dye techniques should be easily offset by the reduction in intensity of care currently being delivered in the inpatient operating room. The additional cost of reoperation for the 10% added detection of metastatic disease by immunohistochemical staining of lymph nodes will likewise need to be offset by the move to the outpatient setting for the majority of the patients. Further investigations using more rapid techniques for immunohistochemical staining of lymph nodes in the intraoperative setting are ongoing and should improve the current rate of reoperation for complete axillary dissection as a result of this upstaging.

The use of immunohistochemical staining of lymph nodes has increased the detection of occult lymph node metastases and has upstaged approximately 10% of the overall population who underwent lymphatic mapping. Upstaging node-negative patients to stage II using immunohistochemical staining of SLNs may have a significant impact on subsequent adjuvant treatment and overall survival. Therefore, this group of patients may require a new subset in the staging system. The importance of micrometastatic disease in SLNs has yet to be determined; however, based on the data accrued from previous studies, it would appear that micrometastatic disease may have therapeutic significance.[10] Stage 1 breast cancer patients have approximately a 10% percent 5-year failure rate. Ultimately, if these failures can be attributed to patients with submicroscopic metastatic nodal disease, then perhaps the remaining patients who are true stage I patients with no metastatic disease may not require additional chemotherapy. This should be the focus for new trials in breast cancer management with randomized treatment or control arms based on the presence or absence of microscopic (positive immunohistochemical stains) or submicroscopic (positive on polymerase chain reaction) disease.[10,18,19]

GUIDELINES

1. **Complete axillary dissection:** The current standard of care for any invasive breast cancer is complete axillary dissection.[12,15] Cady,[11] Fisher,[21] and others have challenged this standard.[13,14] However, it remains our position to perform complete axillary node dissections on patients when lymphatic mapping fails or positive nodes are encountered by H&E or cytokeratin-positive staining. The surgeon and patient alike should tacitly understand that the current standard of care for invasive breast cancer is the complete removal of the axillary lymph nodes.
2. **Institutional review board protocols:** The therapeutic use of lymphatic mapping in patients with breast cancer should adhere to the institutional requirements for an investigational procedure. This may require the filing of appropriate institutional review board documents, including appropriate consent forms. Institutions without such a review board may contact the United States Department of Health and Human Services, Public Health Service, National Institutes of Health Office of Extramural Research, Office For Protection From Research Risks, Bethesda, MD 20892, for information on establishing a review board.
3. **Radiation safety:** Safeguards must be established by each institution for the use of radioactive materials. Appropriate radiation safeguards must be employed for the operative staff, surgeons, and pathologists. Likewise, each state's radiation safety requirements must be satisfied.
4. **Training:** Programs involved in teaching lymphatic mapping procedures should include the training of surgeons and nuclear medicine and radiology personnel as well as the pathologists of the institution that will be participating in the investigational procedure. Such a course should provide adequate exposure and experience to those who will be involved in the management of lymphatic mapping patients. In addition, appropriate hands-on procedures for each team member should be provided.[20]
5. **Data collection:** There should be ample documentation and data collection to validate the technical competency of each institution. The surgeons should also document their clinical competency over time and their ability to detect SLNs. It has generally been the authors' experience that approximately 20 procedures are required for a surgeon to attain competency in the procedure. A review of each surgeon's experience after performing approximately 20 procedures should indicate a success rate of approximately 90% or better when dual agents (technetium-labeled sulfur colloid and Lymphazurin blue dye) are used simultaneously. During this training phase, the protocol should include removal of the SLN followed by complete axillary lymph node dissection to validate the actual rate of skip metastasis and the surgeon's capacity to identify the SLNs.
6. **Self-credentialing:** This can be achieved with the collection of the data via the national data registry through the Internet (http://mapping.rad.usf.edu).

This allows institutions and physicians to review their data and the collective data before moving to a secondary protocol for removal of the SLN only. Institutions should adhere to the initial protocol that requires the removal of the SLN followed by complete axillary lymph node dissection until each surgeon has achieved an appropriate level of training and can validate his or her success rate. This method would be appropriate and safe before moving forward to SLN removal alone.

7. **Sensitivity and specificity:** The current technique of SLN mapping for breast cancer uses both radiocolloid (technetium-labeled sulfur colloid) and Lymphazurin blue dye injected intraparenchymally into the breast. Methods currently in use worldwide include the use of radiolabeled microcolloidal human serum albumin injected subdermally over the lesion, technetium-labeled sulfur colloid injected intraparenchymally, and Lymphazurin blue dye, also injected intraparenchymally. Each of these methods appears to be accurate in detecting SLNs, with an efficacy in the range of 92% to 97%.[6–10] Whichever method is used, it should be appropriately validated by trials in which all nodes are removed in addition to the SLNs. Appropriate immunohistochemical techniques should be used for each SLN, with comparative sectioning and H&E staining to evaluate the true morphology of the cells.
8. **Follow-up:** Ongoing and continuous follow-up is required of patients who undergo SLN biopsy, not only to evaluate the incidence of potential axillary nodal recurrence but also to evaluate treatment failures and skip metastases. Finally, long-term follow-up and evaluation of the effect of micrometastatic disease on recurrence and survival are critical to discovering whether these findings make a difference in therapeutic outcome. Only then will we know of the long-term benefit of this new procedure.
9. **Early disease:** Lymphatic mapping used in extensive DCIS and T_{IA} or T_{IB} breast cancers may redefine the true incidence of micrometastatic disease in patients with such lesions. Therefore, mapping of these lesions should be included in the data base for future reference so that the impact of this procedure in evaluating minimally invasive disease can be assessed. This procedure may detect previously unrecognized metastatic disease or micrometastatic disease using the more sensitive technique of immunohistochemical analysis.
10. **Late disease:** Advanced local disease may result in the use of neoadjuvant radiation or neoadjuvant chemotherapy or may be the cause of extensive tumor involvement of the lymphatic pathways, as seen in advanced disease or inflammatory breast cancer. Advanced disease would appear to be a specific contraindication to lymphatic mapping; to date, mapping has been used only as a means of lymph node identification in these patients to verify involvement before neoadjuvant chemotherapy.
11. **Anatomic consideration:** Some anatomic concerns related to lymphatic mapping may preclude or influence the successful location of the SLN. Inner-quadrant lesions pose the problem of draining into the internal mammary nodes, which may be obscured by the radioactive shine-through of the injection site. This may also be a problem when an intramammary node is present that is also the SLN. When an internal mammary node is the only site of lymphatic drainage, a decision must be made whether to pursue it surgically, with the attendant morbidity of potential pneumothorax. There is additional morbidity and deformity associated with costal cartilage injury or removal. Antecedent tissue injury and surgical disruption of normal lymphatic drainage are important considerations in assessing the accuracy of lymphatic mapping. Such problems include previous breast-reduction surgery, surgical implants, extensive injuries, burns, previous reconstructive surgery to the breast or axilla, surgery for hidradenitis, or congenital lymphatic problems. The authors have encountered several of these conditions and have attempted lymphatic mapping in some of these patients.

Acknowledgments

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Discussion

DR. EDWARD M. COPELAND (Gainesville, Florida): Thank you, Dr. Wells. Dr. Cox and his colleagues have adapted sentinel node biopsy to patients with breast cancer. We owe a debt of gratitude to Don Morton and his colleagues in Los Angeles for resurrecting the concept of sentinel lymphadenectomy and for providing convincing data that the technique works for melanoma.

Lymphatic distribution of the skin, however, is more predictable than the drainage from the breast. Nevertheless, reports from both Guilliano and colleagues at John Wayne Cancer Institute and Dr. Cox and his group at the Moffitt Cancer Center indicate that there is a sentinel node in the axilla of breast cancer patients that is representative of the remainder of the lymph nodes in the axilla.

Dr. Cox, I note that you inject your radiolabel several hours prior to the operative procedure. In our experience, a filtered colloid passes rapidly to the lymph nodes and lights up multiple nodes. This rapidity of passage has led us to do a lymphoscintigraphy with 5 second frames to insure that the sentinel node is identified. Also, the time from injection of the blue dye in and around the lesion and the expiration of the axilla is made more exact.

I'm one of those people who believes that axillary dissection improves survival and reduces uncontrolled recurrence in the axilla. I feel women are going to demand to have this procedure, and it will become a widely practiced technique before long-term follow-up of the patients who have intact axillary lymph nodes becomes available.

The technique is somewhat cumbersome and requires attention to detail. As more surgeons are forced to do the procedure because of patient demand, there will be women out there who have undetected axillary metastases.

Often, I hear this technique of sentinel lymphadenectomy compared to laparoscopic cholecystectomy for gallbladder disease, in that all of us are going to become sentinel lymph node biopsiers. And, in fact, Dr. Cox mentions that in his paper.

Sentinel lymphadenectomy is not a comparable technique to laparoscopic cholecystectomy because one is applied to malignant disease, and a technical failure has a more grave import than laparoscopic cholecystectomy that is applied to benign disease, and failure is known rather immediately.

Dr. Cox, I have several questions. Do you use preoperative lymphoscintigraphy, and if so, how? Your success rate with identification with blue dye is less than other published series. Do you have an explanation? When in your own practice did you feel comfortable enough with the technique to abandon axillary dissection when the sentinel node was negative?

You report the average number of sentinel nodes removed, and as I recall it was 1.9 or so. What was the average of the total lymph nodes removed from your sentinel lymphadenectomy?

And, last, do you think this new procedure will put the long thoracic nerve at greater risk as we, for lack of a better term, root around the axilla trying to find the sentinel node?

I appreciate the opportunity to comment on the paper. Congratulations. [Applause]

DR. ROGER S. FOSTER (Atlanta, Georgia): Dr. Wells, Dr. Copeland, Fellows, and Guests.

This is a large series of patients and a carefully analyzed study. I believe that sentinel node mapping and biopsy are going to be adopted increasingly in the management of breast cancer patients, particularly after publication of the sort of data we have heard today.

But many of us who have used these techniques have found the procedures must be performed with precision and that there is a learning curve.

I have several questions for the authors. I was somewhat surprised by the relatively high rates of failure in mapping for both the blue dye and radionuclide techniques independently. However, you were successful at a high rate by using both techniques. Have you examined your data? You mentioned there is a learning curve, but you didn't show us the data for the learning curve for sentinel node identification for each of the techniques. Did your identifications go up with experience? Was there variability from surgeon to surgeon in success rates?

The next question has to do a little bit also with Dr. Copeland's comments about variability and lymphatic drainage from the breast. Umberto Veronesi of Milan has suggested that one can inject the label into the skin that lies over the tumor in the breast rather than a peritumoral injection, which I believe was today's technique. This implies there is either a perfect or a near perfect correlation between the dermal lymphatics and the lymphatics in