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Preoperative Lymphoscintigraphy for Breast Cancer Does Not Improve the Ability to Identify Axillary Sentinel Lymph Nodes

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Objective

To evaluate the role of preoperative lymphoscintigraphy in sentinel lymph node (SLN) biopsy for breast cancer.

Summary Background Data

Numerous studies have demonstrated that SLN biopsy can be used to stage axillary lymph nodes for breast cancer. SLN biopsy is performed using injection of radioactive colloid, blue dye, or both. When radioactive colloid is used, a preoperative lymphoscintigram (nuclear medicine scan) is often obtained to ease SLN identification. Whether a preoperative lymphoscintigram adds diagnostic accuracy to offset the additional time and cost required is not clear.

Methods

After informed consent was obtained, 805 patients were enrolled in the University of Louisville Breast Cancer Sentinel Lymph Node Study, a multiinstitutional study involving 99 surgeons. Patients with clinical stage T1–2, N0 breast cancer were eligible for the study. All patients underwent SLN biopsy, followed by level I/II axillary dissection. Preoperative lymphoscintigraphy was performed at the discretion of the individual surgeon. Biopsy of nonaxillary SLNs was not required in the protocol. Chi-square analysis and analysis of variance were used for statistical comparison.

Results

Radioactive colloid injection was performed in 588 patients. In 560, peritumoral injection of isosulfan blue dye was also performed. A preoperative lymphoscintigram was obtained in 348 of the 588 patients (59%). The SLN was identified in 221 of 240 patients (92.1%) who did not undergo a preoperative lymphoscintigram, with a false-negative rate of 1.6%. In the 348 patients who underwent a preoperative lymphoscintigram, the SLN was identified in 310 (89.1%), with a false-negative rate of 8.7%. A mean of 2.2 and 2.0 SLNs per patient were removed in the groups without and with a preoperative lymphoscintigram, respectively. There was no statistically significant difference in the SLN identification rate, false-negative rate, or number of SLNs removed when a preoperative lymphoscintigram was obtained.

Conclusions

Preoperative lymphoscintigraphy does not improve the ability to identify axillary SLN during surgery, nor does it decrease the false-negative rate. Routine preoperative lymphoscintigraphy is not necessary for the identification of axillary SLNs in breast cancer.

Numerous studies have demonstrated that sentinel lymph node (SLN) biopsy for patients with breast cancer can provide accurate nodal staging information.[1–6] SLN biopsy is less invasive than level I/II axillary lymph node dissection and has been accepted at many institutions as a suitable alternative to axillary dissection for nodal staging of breast cancer. As this procedure becomes more widely accepted,

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attention has been focused on standardizing and optimizing the technical aspects of the procedure, as well as reducing cost and inconvenience for patients.

A variety of different techniques have been described for SLN biopsy in breast cancer. SLN biopsy is performed using injection of a vital blue dye (isosulfan blue), radioactive colloid (99-technetium sulfur colloid), or both. When radioactive colloid is used, a preoperative lymphoscintigram (nuclear medicine scan) is often obtained for ease of SLN identification. Lymphoscintigraphy is performed routinely in many institutions for localization of SLN in melanoma because anatomical predictions of lymphatic drainage are often unreliable, especially for lesions of the trunk or head and neck. A preoperative lymphoscintigram for melanoma is often useful because it may identify SLNs in unexpected locations or in multiple nodal basins.[7–10] Because of the predictable axillary nodal drainage in breast cancer, it is not clear whether preoperative lymphoscintigraphy adds diagnostic accuracy to offset the additional time and cost required.

Two critical factors are used to assess quality control for SLN biopsy: the SLN identification rate and the false-negative rate. The SLN identification rate is defined as the proportion of patients with attempted SLN localization in whom an SLN is found and removed. The false-negative rate is the proportion of patients with nodal metastases in whom the SLN is incorrectly found to be negative for tumor.[6] The present study was designed to determine whether preoperative lymphoscintigraphy improves the SLN identification rate and false-negative rate in a large multiinstitutional experience.

METHODS

Patients

The University of Louisville Breast Cancer Sentinel Lymph Node Study is a multiinstitutional study involving 99 surgeons. The study was approved by the institutional review board of each participating institution, and informed consent was obtained in writing from all patients after discussion of risks and benefits with the operating surgeon. Patients with biopsy-proven clinical stage T1–2, N0 breast cancer were eligible. A total of 16 patients were thought to have T2 tumors clinically that were found to be T3 tumors pathologically; these patients are included in the analysis.

Lymphoscintigraphy and SLN Biopsy

All patients underwent SLN biopsy followed by completion level I/II axillary dissection. Recommended guidelines for performance of SLN biopsy included peritumoral injection of 0.5 mCi of 0.2-μm filtered technetium-99 sulfur colloid in a volume of 6 mL at least 1 hour before surgery, followed by peritumoral injection of 5 mL isosulfan blue dye at the time of surgery. However, the decision to perform SLN biopsy using radioactive colloid alone, blue dye alone, or both radioactive colloid and blue dye in combination was left to the discretion of the operating surgeon. Biopsy of nonaxillary SLNs was not required in the protocol. The use of preoperative lymphoscintigraphy was determined by the individual surgeon and institution. Recommended guidelines for preoperative lymphoscintigraphy included gamma camera imaging in the oblique/lateral view and anterior view at least 45 to 60 minutes after injection. Delayed images were often obtained after 60 minutes. Intraoperative localization of SLNs was performed, even if the preoperative lymphoscintigram did not identify an SLN.

Pathology

Each SLN was examined by routine histology, with hematoxylin and eosin staining at a minimum of 2-mm intervals. Some institutions also performed immunohistochemistry using antibodies for cytokeratin.

Statistics

Statistical analysis was performed using chi-square analysis and analysis of variance, where appropriate. $P < .05$ was considered to be significant.

RESULTS

A total of 805 patients were enrolled in the study between August 1997 and June 1999. Radioactive colloid injection was performed in 588 patients; the 217 patients who underwent injection of blue dye alone were excluded from this analysis. In 560 of the 588 (95%), peritumoral injection of isosulfan blue dye was performed in addition to radioactive colloid injection. A preoperative lymphoscintigram was obtained in 348 of the 588 patients (59%). Injection of radioactive colloid was performed an average of 4.10 hours before surgery (range 24 minutes to 29 hours).

Patients in each group (preoperative lymphoscintigram vs. no preoperative lymphoscintigram) were well balanced in terms of age, tumor size, tumor location, T stage, pathology, type of surgical procedure for treatment of primary tumor (total mastectomy vs. partial mastectomy), and percentage with axillary nodal metastases (Table 1). Immunohistochemistry for cytokeratin was performed more frequently for patients in the preoperative lymphoscintigram group.

An SLN was identified in 89.1% and 92.1% of patients with and without preoperative lymphoscintigraphy, respectively (Table 2). The false-negative rates were 8.7% and 1.6% for the groups with and without preoperative lymphoscintigraphy, respectively. There were no significant differences in the SLN identification rates or false-negative rates, nor was there a significant difference in the mean number of SLNs removed per patient.

Results of preoperative lymphoscintigraphy are shown in

Table 1. CLINICOPATHOLOGIC CHARACTERISTICS OF PATIENTS UNDERGOING SENTINEL LYMPH NODE BIOPSY

Variable	Preoperative Lymphoscintigraphy	No Preoperative Lymphoscintigraphy
Radioactive colloid injection	348	240
Age (mean)	58.1	60.1
Tumor size (mean)	1.82 cm	1.99 cm
T1	72%	70%
T2	26%	26%
T3	2%	4%
Tumor location		
Upper outer quadrant	50%	56%
Upper inner quadrant	19%	9%
Lower outer quadrant	11%	15%
Lower inner quadrant	8%	6%
Central	13%	14%
Pathology		
Ductal	78%	78%
Lobular	11%	10%
Other	11%	12%
Type of surgery		
Total mastectomy	27%	29%
Partial mastectomy	73%	71%
Positive nodes	31%	28%
Immunohistochemistry performed on sentinel node	38%	20%

Table 3. Axillary SLNs were identified on the lymphoscintigram, either alone or concomitant with nonaxillary nodes in 196 of 348 patients (56%). Thirty-six percent (126/348) of lymphoscintigrams were negative studies—no SLN was identified on the scan. More than one draining nodal basin was identified in 18 of 348 patients (5.2%). Of the 44 patients with nonaxillary drainage identified on the scan, 26 had exclusively nonaxillary drainage, whereas 18 had concomitant axillary drainage as identified by the lymphoscintigram. Internal mammary nodes were identified on the lymphoscintigram in 27 of 348 patients (8%). Internal mammary nodal drainage on lymphoscintigraphy was associated with inner quadrant tumor location in 13 of 27 patients (48%). Biopsy samples were taken from internal mammary SLNs in two patients; both were negative for tumor. No supraclavicular node biopsies were performed in this study.

Of the patients with axillary SLNs identified on preoperative lymphoscintigraphy, intraoperative biopsy of an axillary SLN was successful in 98% (Table 4). When the lymphoscintigram was negative (no SLN visualized), an axillary SLN was identified during surgery in 78% of the patients. Further, when the preoperative lymphoscintigram identified exclusively nonaxillary SLNs, an SLN was found in the axilla 77% of the time. Overall, axillary SLNs could be identified during surgery in 78% (118/152) of patients in whom the preoperative lymphoscintigram showed either no drainage or exclusively nonaxillary drainage.

There were no significant differences in the SLN identification rate based on tumor location in the breast (Table 5).

Table 2. RESULTS OF SENTINEL LYMPH NODE BIOPSY

Preoperative Lymphoscintigram	SLN Identified	False-Negative Rate	Mean No. of SLNs Removed
Yes	310/348 (89.1%)	8.7%	2.00
No	221/240 (92.1%)	1.6%	2.16
Total	531/588 (90.3%)	6.1%	2.07

SLN, sentinel lymph node.

Table 3. RESULTS OF PREOPERATIVE LYMPHOSCINTIGRAPHY

SLN Identified on Preoperative Lymphoscintigram	No. of Patients (n = 348)	%
No drainage	126	36.2
Axillary only	178	51.1
IM only	14	4.0
SC only	1	0.3
Other only	11	3.2
Axillary + IM	13	3.7
Axillary + SC	2	0.6
Axillary + other	3	0.9

IM, internal mammary; SC, supraclavicular; SLN, sentinel lymph node.

Table 4. IDENTIFICATION OF SENTINEL LYMPH NODES BASED ON PREOPERATIVE LYMPHOSCINTIGRAM FINDINGS

Location of SLN on Preoperative Lymphoscintigram	Axillary SLN Identified During Surgery
Axilla	192 /196 (98%)
Nonaxillary site only	20 /26 (77%)
No SLN identified on preoperative lymphoscintigram	98 /126 (78%)

SLN, sentinel lymph node.

Axillary SLNs were reliably identified in most patients, even those with medial quadrant tumors.

DISCUSSION

Preoperative lymphoscintigraphy is performed routinely for SLN biopsy in melanoma.[9,10] This allows for identification of all lymphatic drainage basins at risk and for identification of SLNs in ectopic or unexpected locations. Melanoma, however, differs from breast cancer because lymphatic flow from the skin is reliable and easy to visualize on lymphoscintigraphy. The lymphatic drainage from the breast parenchyma is not as rich or reliably visualized as cutaneous lymphatic drainage. Often, the primary melanoma is located far enough from the nodal basin(s) that it is easy to distinguish the primary tumor injection site from the SLNs. This is often not true in breast cancer, in which the problem of "shine through" often obscures the SLNs on lymphoscintigraphy. Despite these factors, some investigators have suggested that preoperative lymphoscintigraphy is a useful procedure that improves SLN localization for breast cancer.[2,11–13]

Our results indicate that preoperative lymphoscintigraphy does not improve the ability to identify axillary SLNs for breast cancer. Specifically, preoperative lymphoscintigraphy was not associated with improvements in either the SLN identification rate or the false-negative rate. Indeed, the false-negative rate was greater in the group that underwent preoperative lymphoscintigraphy, although this did not reach statistical significance. This is not explained by a less intensive pathologic analysis of the SLNs in the preoperative lymphoscintigraphy group. In fact, immunohistochemistry was used almost twice as frequently in the preoperative lymphoscintigraphy group. Although this was not a randomized study, the data provide substantial evidence that preoperative lymphoscintigraphy is neither necessary nor helpful for the identification of axillary SLNs. This is also supported by the high rate of SLN identification by surgeons experienced in the use of blue dye alone, without radioactive colloid injection.[14,15]

The utility of preoperative lymphoscintigraphy for breast cancer, however, depends on the intended goal of the SLN procedure. For some, the goal is to biopsy regional SLNs—that is, axillary, internal mammary, supraclavicular, or other sites of nodal drainage that may be identified by lymphoscintigraphy. Certainly, preoperative lymphoscintigraphy may be helpful in some patients when this is the stated goal. However, most surgeons view SLN biopsy as a less morbid replacement for the standard level I/II axillary dissection and do not intend to perform internal mammary lymph node biopsies, even if drainage to this site is demonstrated on the study.

Some have suggested that preoperative lymphoscintigraphy may be valuable for detecting drainage to internal mammary nodes and other nonaxillary nodes.[16–18] Even when the lymphoscintigram suggested exclusively nonaxillary lymphatic drainage, we found concomitant axillary drainage in 77% of patients. The supraclavicular basin is easily assessed with the intraoperative gamma probe and does not require lymphoscintigraphy. The number of instances in which an internal mammary SLN contains metastatic cancer when the axillary SLN does not is small. The importance of nonaxillary SLN biopsy has not yet been determined in large studies and is under investigation in many centers. The poor sensitivity of preoperative lymphoscintigraphy for detection of axillary SLNs suggests that the ability to determine the presence of nonaxillary nodal drainage may suffer from similar limitations.

One reason for the poor sensitivity of lymphoscintigraphy for detection of axillary SLNs in this study may be related to the fact that this was a large multiinstitutional study, with

Table 5. SENTINEL LYMPH NODE IDENTIFICATION RATES BY TUMOR LOCATION WITHIN THE BREAST

Location of Tumor	Preoperative Lymphoscintigraphy	No Preoperative Lymphoscintigraphy	Total All Patients
Upper outer quadrant	151/171 (88.3%)	211/231 (91.3%)	362/402 (90.0%)
Upper inner quadrant	57/64 (89.1%)	33/37 (89.2%)	90/101 (89.1%)
Lower outer quadrant	36/39 (92.3%)	59/63 (93.7%)	95/102 (93.1%)
Lower inner quadrant	21/26 (80.8%)	22/25 (88.0%)	43/51 (84.3%)
Central	40/43 (93.0%)	45/55 (81.8%)	85/98 (86.7%)

variable quality of nuclear medicine imaging. Perhaps in centers with a large volume of experience and specialized nuclear medicine protocols, lymphoscintigraphy may provide a more reliable indication of lymphatic drainage for breast cancer. However, the present study provides a realistic and useful view of the quality of lymphoscintigraphy across a wide spectrum of surgical practices and hospital environments. Regardless, lymphoscintigraphy does not appear necessary for consistent and reliable identification of axillary SLNs.

Of the numerous studies on SLN biopsy for breast cancer, only about one third have included the use of preoperative lymphoscintigrams.[19] Arguments have been made in favor of lymphoscintigraphy as a "road map" for surgeons. Some studies report that a negative preoperative lymphoscintigram predicts inability to radiolocalize with the hand-held gamma probe.[2,11] However, the present study indicates that a negative preoperative lymphoscintigram is a poor predictor of intraoperative SLN biopsy failure. Even when no axillary SLN was identified on the lymphoscintigram, an axillary SLN was identified during surgery in 78% of patients. Similar results have been reported by other investigators, who found that most patients with negative lymphoscintigrams went on to have successful intraoperative SLN localization.[20,21] Some studies have excluded patients from SLN biopsy based on a negative preoperative lymphoscintigram.[22] Our results suggest that intraoperative gamma probe localization of the SLN is not dependent on visualization by gamma camera imaging, and that axillary SLN biopsy should be attempted regardless of the lymphoscintigram results.

It has been suggested that visualization of an SLN on preoperative lymphoscintigraphy virtually guarantees finding the SLN during surgery.[11,13] Our results confirm that finding, with a 98% SLN identification rate when an axillary SLN was visualized on the lymphoscintigram. However, there was a 92.1% SLN identification rate when no lymphoscintigram was performed. Although the finding of axillary drainage on preoperative lymphoscintigraphy may reassure the surgeon of impending success, this does not provide a sufficient rationale for performing the scan.

The time and cost required to perform preoperative lymphoscintigraphy must be considered as well. Preoperative lymphoscintigraphy requires the injection of radioactive colloid followed by gamma camera imaging before surgery. This time delay is neither convenient for patients nor conducive to efficient scheduling for the operating surgeon. The true cost of medical services is always a difficult issue to measure. Therefore, as an estimate of cost, total patient charges for lymphoscintigraphy at a representative institution were examined (Table 6). By injecting the radioactive colloid without obtaining a preoperative lymphoscintigram, patient charges were reduced by $545.

In conclusion, preoperative lymphoscintigraphy does not improve the ability to identify axillary SLNs during surgery, nor does it decrease the false-negative rate. Considering the extra time and cost required, the use of routine lymphoscintigraphy for identification of axillary SLNs is not justified. The value of lymphoscintigraphy for the identification of nonaxillary SLNs deserves further study.

Table 6. PATIENT CHARGES FOR LYMPHOSCINTIGRAPHY AT A REPRESENTATIVE HOSPITAL

Procedure	Lymphoscintigraphy	No Lymphoscintigraphy
Filtered technetium sulfur colloid	$ 56	$ 56
Injection	$105	$105
Imaging	$420	$ 0
Radiologist's interpretation fee	$125	$ 0
TOTAL	$706	$161

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Discussion

DR. EDWARD M. COPELAND III (Gainesville, Florida): I want to congratulate Dr. McMasters and his colleagues on getting 99 surgeons to participate in this study. Since all patients had a level I and II lymph node dissection, this paper represents a quality control of sentinel lymph node biopsy for the participating surgeons. The surgeons did great with a low false-negative rate. However, their nuclear medicine colleagues did not fare so well: 36% of patients who had radiocolloid injected failed to have a sentinel lymph node identified by lymphoscintigraphy.

The nuclear medicine physicians at our institution have had a particular interest in sentinel lymph node technology, and their concordance between visualization of the sentinel node and finding it at operation is virtually 100%. Since our lymphoscintigrams have proved so accurate, I have found them helpful, particularly if the scans are done sequentially over time. For example, if internal mammary nodes light up and an axillary sentinel node is positive, internal mammary node radiation therapy is indicated, particularly if the primary is medial in location. To state the reverse, if internal mammary lymph nodes do not light up under the same anatomic and pathologic circumstances, internal mammary lymph node irradiation is probably of no value. Of course, you need accurate lymphoscintigraphy to use the study for such therapeutic decisions. The 36% false-negative rate in your study would eliminate such a possibility.

Other investigators have reported that 3% of the positive lymph nodes discovered by lymphoscintigraphy lie outside the axilla. Also, many women who die of breast cancer have internal mammary lymph node metastasis at the time of postmortem.

Dr. McMasters, 12% of the patients in your study had extraaxillary drainage identified by scan. I note you biopsied internal mammary lymph nodes in only two of your patients. How do you propose that extraaxillary nodal basins identified by lymphoscintigraphy be managed therapeutically, especially in patients who have a positive axillary sentinel lymph node?

DR. DOUGLAS S. REINTGEN (Tampa, Florida): This paper from the multicenter group performing the breast lymphatic mapping trial organized by the University of Louisville states that preoperative lymphoscintigraphy was not helpful in identifying intraoperatively an axillary sentinel node, nor was it useful in preventing a false-negative sentinel node biopsy. This is good to know since the imaging of the radiocolloid in patients with breast cancer is not uniformly reimbursed by the insurance companies, and many times hospitals have to absorb these costs. However, one has to be aware that this nuclear medicine study may be technically demanding to perform, particularly for radiologists and, even worse, radiology technicians who may not be as facile as surgeons in the breast exam.

One question for the authors is what was the quality assurance for performing this preoperative study in the trial? They state that the ability to image an axillary sentinel node occurred 56% of the time, which seems low to us. The technique used to inject radiopharmaceutical is important for successful axillary sentinel node imaging and subsequent success by the surgeon finding the sentinel node intraoperatively.

The nuclear medicine technician or physician needs to inject diffusely around the palpable tumor, mammographic abnormality, or excisional biopsy scar, using increased volumes of injection, compared to what we use for the melanoma mapping.

Massage is used in the nuclear medicine suite to increase interstitial pressure and facilitate uptake of the mapping agent into the breast lymphatics. Proper positioning of the patient during imaging, the hand held above the head to maximize separation between the primary site and the regional basin, and the use of oblique and lateral views to unmask hidden sentinel nodes in the "star artifact" from the primary site injection are also important.

By increasing the volume of injection from 2 to 6 cc by increasing the diffuseness of the injection around the lesion or biopsy cavity, by assuring that the injection of radiopharmaceutical is outside the biopsy cavity by ultrasound, by proper positioning of the patients, and with 5 minutes of massage, the ability to image an axillary sentinel node at Moffitt Cancer Center increased from 70% to 85%, showing that there is a learning curve and it is a technically demanding procedure.

Preoperative lymphoscintigraphy has two potential uses in women with breast cancer, and we continue to perform the imaging to define these populations. The first use would be to identify the 10% of patients who have multidirectional lymphatic flow from the primary tumor, for instance to the axilla and to the internal mammary nodes. For this to make a difference, a treatment decision needs to be made based on this drainage pattern. What was the strategy in the trial if internal mammary nodal drainage was noted? Did the authors harvest these nodes, include them in the radiation ports in those women receiving breast conservation, or were they just ignored?

The second potential use of this nuclear medicine study is to identify a subgroup of women who may not drain at all to the axilla. Of course, in order to do that, high quality lymphoscintigraphy needs to be performed so that you can image an axillary sentinel node, not 58% of the time but perhaps as high as 85% of the time. There should also be good separation between the primary tumor and the axilla, so that shine-through from the primary site when probing at the skin level is not a concern. This will most often be the case, since most tumors that drain to the internal mammary nodes will be central or inner quadrant.

The final criterion would be using a well-collimated, shielded, very sensitive probe that can detect radioactivity in the axilla intraoperatively. At the University of South Florida, we have experience with 25 patients who meet all the above criteria. These women were taken to the operating room, and the vital blue dye injected, the axilla was opened, and even at the level of the lymph nodes, no blue dye or radiocolloid hot spots could be detected. The standard level I and II node dissection was performed, and these patients never had metastatic disease on their final pathology. In our series, axillary sentinel nodes are not found in 4% of the cases. We call them technical failures, but they may not represent technical failures at all. They may be a subgroup of women who have tumors that do not drain at all to the axilla and do not need any sort of axillary procedure to stage them.

The University of Louisville group continues to lead the way in designing, organizing, and performing national trials studying new surgical techniques. This effort is changing the standards of care for patients with melanoma and women with breast cancer, and I look forward to many more contributions from this particular group.

DR. DON M. MORRIS (Albuquerque, New Mexico): In my experience at my institution, this is a very reliable test, done by myself and one nuclear medicine person. We actually do it the day before, and then take the patient to the operating room first thing the next morning and perform our operation. That's worked very well for us.

Knowing exactly where it is—and I mark it in the nuclear medicine suite with the dye you use to mark radiation therapy patients—I can cut down directly on it, and it saves a tremendous amount of OR time, which is the most expensive commodity that I have in my practice.

I don't know where you inject these patients. Do you do it in the operating room? Do you do it a holding area? To take this kind of material outside the nuclear medicine suite, quite frankly, is not very dangerous, but most of the people I work with don't know that and they are afraid of it.

The other place I have found it's tremendously helpful is in certain obese people—having done the preoperative lymphoscintigraphy clearly makes the node easier to find.

Finally, where I work, the insurance companies love this. I have yet to have an insurance company refuse to allow me to do a sentinel node procedure, because if it's negative and a patient has a lumpectomy, they get their entire treatment as an outpatient, which is good for the insurance company.

DR. KELLY MCMASTERS (Closing Discussion): Dr. Morris asked whether we find that this is useful in heavier people. Again, we still find the sentinel lymph node in almost all cases, regardless of the size of the patient, without a lymphoscintigram. If we were having problems finding the sentinel lymph node without a lymphoscintigram, we would certainly go back to doing it, but we really have not had that problem.

What do we do in the case of a negative axillary sentinel lymph node exploration? We would recommend routinely an axillary lymph node dissection. But again, I believe that almost all breast cancers do drain to the axilla, even when they have concomitant internal mammary and supraclavicular lymph node drainage. As you get more experienced with this, you find the axillary sentinel node almost all the time.

I do think that it is more difficult to mark the location of the sentinel node in the nuclear medicine area because, the way that it's done under the camera, you need to come with a point source at different angles to identify the location of the sentinel node. Our radiologists would find sentinel node locations in the back, in the scapula and other places, which really were not the true location that you find with a gamma probe. It does not take long with the intraoperative gamma probe to percutaneously find the sentinel node in a couple of seconds intraoperatively.

Dr. Copeland has asked about the quality of nuclear medicine studies of the lymphoscintigrams that are being performed, and I believe that Dr. Copeland—correct me if I'm wrong—you are doing dermal injection of the radiocolloid. That would account for why you are very successful in finding the location of the sentinel node on the lymphoscintigram and also the reason that we find it very reliably with just the intraoperative gamma probe. But it's much easier to see and find the location of the sentinel node either way when you use dermal injection, as opposed to parenchymal injections. That may explain your high quality results, and it is also very clear—Dr. Reintgen also touched on this point—if you have a nuclear medicine department that's very dedicated to perfecting this technique and doing high-quality images, you will get more reliable detection of the sentinel nodes. Our data reflect a broad experience across community-practice surgery, looking at lymphoscintigraphy at a number of institutions, and perhaps reflect the real world of what goes on out there.

You also asked me what would I do if I find a positive axillary sentinel lymph node and also demonstrate internal mammary drainage. As I suspect you would do, I would consider the patient for internal mammary radiation therapy. However, we really have no data on which to base this decision, and I would suggest this is a good topic for a randomized clinical trial. Perhaps the American College of Surgeons oncology group might be interested in such a study.

Dr. Reintgen also asked about the quality assurance for lymphoscintigraphy. The guidelines for the injections and the technical details of lymphoscintigrams were blatantly and unceremoniously borrowed from the Moffitt Cancer Center protocol, and Dr. Reintgen should accept this as the highest form of praise, because we recognize that institution as a leader in providing high-quality studies. Although we had these specific guidelines, the quality of the imaging is no doubt variable from institution to institution and helps explain why it was not very helpful in finding these axillary sentinel lymph nodes overall.

Again, we did not have in the protocol an indication that we should go ahead and biopsy internal mammary and nonaxillary sentinel nodes, even if they were seen on the lymphoscintigram. This was left to the discretion of the individual surgeon. Two internal mammary lymph nodes were biopsied in the whole study, and they were both negative for tumor.

Dr. Reintgen also discussed the value of preoperative lympho-

scintigraphy for patients who have internal mammary drainage and possibly avoiding an unnecessary axillary exploration to find the sentinel lymph node. In 4% of his patients, there was no evidence of an axillary sentinel lymph node when the patients had internal mammary nodes seen on the lymphoscintigram. I think to do lymphoscintigrams on all the patients to benefit perhaps 4% may be a little excessive.

And I'm going to answer a question Dr. Copeland put to me yesterday that was not specifically addressed today, but I do want to answer it anyway, which is: why would all these surgeons want to participate in this large trial for which they were not compensated, for which they volunteered to take their time, busy surgeons in busy practices, to submit their data? In fact, we have been extremely surprised and pleased to see how interested surgeons across a wide variety of practices are in defining the quality of this procedure and making sure that it's being done right. Most people are very reluctant to abandon axillary dissection until they have proven that they can do this technique accurately, and I think a lot of people want to debunk the myth that this is a procedure that can only be done accurately in large academic centers.