Accuracy of Sentinel Lymph Node Biopsy for Patients with T_2 and T_3 Breast Cancers

SANDRA L. WONG, M.D.,* CELIA CHAO, M.D.,* MICHAEL J. EDWARDS, M.D.,* TODD M. TUTTLE, M.D.,† R. DIRK NOYES, M.D.,‡ DAVID J. CARLSON, M.D.,§ ALISON L. LAIDLEY, M.D.,¶ TERRE Q. McGLOTHIN, M.D.,¶ PHILIP B. LEY, M.D.,‖ C. MATTHEW BROWN, M.D.,** REBECCA L. GLASER, M.D.,†† ROBERT E. PENNINGTON, M.D.,§§ PETER S. TURK, M.D.,¶¶ DIANA SIMPSON, R.N.,* KELLY M. McMASTERS, M.D., PH.D.*

*From the *University of Louisville Breast Cancer Study Group, Division of Surgical Oncology, Department of Surgery, University of Louisville, Louisville, Kentucky; †Park Nicollet Clinic, Minneapolis, Minnesota; ‡LDS Hospital, Salt Lake City, Utah; §St. Mary's Medical Center and Deaconess Hospital, Evansville, Indiana; ¶Breast Surgeons of North Texas, Dallas, Texas; ‖Surgical Clinic Associates, Jackson, Mississippi; **Norton Hospital, Louisville, Kentucky; ††Kettering Hospital, Dayton, Ohio; §§General Surgeons, Inc., Richmond, Indiana; ¶¶Presbyterian Hospital, Charlotte, North Carolina*

Although numerous studies have demonstrated that sentinel lymph node (SLN) biopsy can accurately determine the axillary nodal status for early breast cancer some studies have suggested that SLN biopsy may be less reliable for tumors >2 cm in size. This analysis was performed to determine whether tumor size affects the accuracy of SLN biopsy. The University of Louisville Breast Cancer Sentinel Lymph Node Study is a prospective multi-institutional study involving 226 surgeons. The study was approved by the Institutional Review Board of each institution, and informed consent was obtained from all patients. Patients with clinical stage T_{1-2} N_0 breast cancer were eligible for the study. Some patients with T_3 tumors were included because they were clinically staged as T_2 but on final pathology were found to have tumors >5 cm. This analysis includes 2148 patients who were enrolled from August 1997 through October 2000. All patients underwent SLN biopsy using a combination of radioactive colloid and blue dye injection followed by completion Level I/II axillary dissection. Statistical comparison was performed by chi-square analysis. The SLN identification rate, false negative rate, and overall accuracy of SLN biopsy were not significantly different among tumor stages T_1, T_2, and T_3. We conclude that SLN biopsy is no less accurate for T_{2-3} breast cancers compared with T_1 tumors.

SENTINEL LYMPH NODE (SLN) biopsy is becoming increasingly accepted as a minimally invasive alternative to Level I/II axillary dissection for staging in breast cancer. For more than 100 years axillary lymph node status has been the most powerful predictor of recurrence and survival in breast cancer patients. Additionally the presence of nodal metastasis is an important component of the decision-making process for adjuvant therapy. Numerous studies have demonstrated that SLN biopsy can accurately determine the status of the axillary nodes in patients with invasive breast carcinoma.[1–9] However, there has been some evidence to suggest that SLN biopsy is less reliable for tumors greater than 2 cm in size.

Several previous studies have evaluated sentinel node biopsy in patients with T_2 tumors. O'Hea et al.[8] found a false negative rate of 25 per cent associated with T_{2-3} tumors. Winchester et al.[9] reported a 20 per cent false negative rate for tumors greater than 21 mm. However, it is important to note that, collectively, these two studies only represent results of 59 patients with T_2 or T_3 tumors. Indeed most studies of SLN biopsy for breast cancer include small numbers of patients with larger tumors.

This analysis was performed to determine whether tumor size affects the accuracy of SLN biopsy in a large multi-institutional study.

Presented at the Southeastern Surgical Congress 69th Annual Meeting and Postgraduate Course Program, New Orleans, Louisiana, February 2–6, 2001.

Supported by the Center for Advanced Surgical Technologies of Norton Hosital, Louisville, KY and the Links for Life Foundation, Louisville, KY.

Address correspondence and reprint requests to Kelly M. McMasters, M.D., Ph.D., University of Louisville, J. Graham Brown Cancer Center, 529 South Jackson Street, No. 318, Louisville, KY 40202.

Methods

The University of Louisville Breast Cancer Sentinel Lymph Node Study is a prospective multi-institutional study involving 226 surgeons. The study was approved by the Institutional Review Board of each institution, and informed consent was obtained from all patients.

Patients with clinical stage T_{1-2} N_0 breast cancer were eligible for the study. Some patients with T_3 tumors were included because they were clinically staged as T_2 but on final pathology were found to have tumors >5 cm. This analysis includes 2148 patients who were enrolled from August 1997 through October 2000. All patients underwent SLN biopsy followed by completion Level I/II axillary dissection. No patients received preoperative chemotherapy.

Blue dye, radioactive colloid, or a combination of the two agents was used at the discretion of the operating surgeon. A sentinel node was defined as any blue-stained node or any node with radioactive counts 10 per cent or more of the *ex vivo* count of the most radioactive sentinel node. SLNs were examined by hematoxylin and eosin staining at a minimum of 2-mm intervals. Immunohistochemistry with antibodies for cytokeratins was used for SLN evaluation in approximately 50 per cent of cases. Nonsentinel nodes were evaluated by routine histology.

Statistical comparison was performed by chi-square analysis. Significance was determined at $P < 0.05$.

Results

SLN biopsy was performed using blue dye, radioactive colloid, or a combination of both in 228, 120, and 1800 patients, respectively. Tumor size was available for 2085 (97.1%) patients; this analysis includes 1496 T_1 tumors, 545 T_2 tumors, and 44 T_3 tumors. Clinicopathologic data shown in Table 1. Patients with T_2 or T_3 tumors were more likely to undergo mastectomy than patients with T_1 tumors ($P < 0.0001$, chi square).

As expected there was an increasing incidence of axillary metastases with increasing tumor size (Fig. 1).

The SLN identification rates were 92.9, 93.5, and 100 per cent for stage T_1, T_2, and T_3 tumors, respectively ($P = 0.22$, chi square). The false negative rates were 9.0, 6.8, and 3.4 per cent for stage T_1, T_2, and T_3 tumors, respectively, and these results were not significantly different (Table 2). The negative predictive values, sensitivity, and overall accuracy rates of SLN biopsy were also similar in all groups.

When the results are broken down further into 1-cm increments there is a trend, although not statistically significant, that suggests that the SLN identification rate and false negative rate are actually slightly improved among patients with larger tumors (Fig. 2).

The sentinel node identification rate was significantly higher for palpable tumors than for nonpalpable tumors (Table 3). The SLN identification rate was greater for palpable tumors of all sizes compared with nonpalpable tumors, but the difference was only statistically significant for T_1 tumors. Tumor palpability did not affect the false negative rate in any tumor size category. Palpable tumors were more likely to have axillary metastases than nonpalpable tumors, especially in smaller tumors ($P < 0.0001$, chi square).

Discussion

SLN biopsy has become more widely accepted as a minimally invasive alternative to axillary dissection for nodal staging in breast cancer. Numerous studies

TABLE 1. *Clinicopathologic Characteristics of Patients Undergoing SLN Biopsy*

Variable	T_1	T_2	T_3
Age (median)	60	58	59
Pathologic subtype			
Ductal	1235 (82.6%)	436 (80.0%)	27 (61.4%)
Lobular	114 (7.6%)	53 (9.7%)	9 (20.5%)
Other	147 (9.8%)	56 (10.3%)	8 (18.2%)
Biopsy type			
Excisional	552 (36.9%)	152 (27.9%)	10 (22.7%)
Needle	943 (63.1%)	393 (72.1%)	34 (77.3%)
Surgery type			
Partial mastectomy	1105 (73.9%)	323 (59.3%)	17 (38.6%)
Mastectomy	391 (26.1%)	222 (40.7%)	27 (61.4%)
Tumor location			
Upper outer quadrant	727 (48.6%)	295 (54.1%)	19 (43.2%)
Other	769 (51.4%)	250 (45.9%)	25 (56.8%)
SLN injection technique			
Single agent	250 (16.7%)	81 (14.9%)	6 (13.6%)
Dual agent	1246 (83.3%)	464 (85.1%)	38 (86.4%)
Mean No. of SLNs Removed	2.28	2.41	2.40

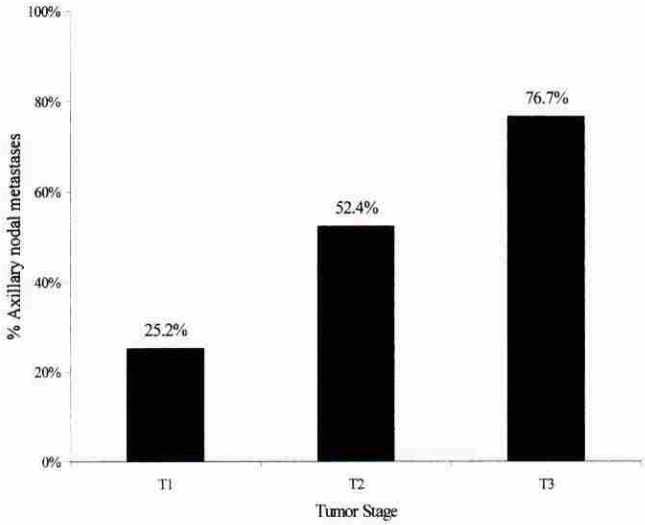

FIG. 1. Incidence of nodal metastases by tumor size.

have suggested that SLN biopsy can be used reliably to determine the axillary nodal status for early breast cancer. However, there has been some controversy as to its accuracy in larger tumors.

Our results indicate that the SLN identification and false negative rates are not significantly different among tumor sizes. Recent results from two other studies also speak to the accuracy of SLN biopsy in larger tumors. Bedrosian et al.[10] reported a SLN identification rate of 99 per cent and a 3.3 per cent false negative rate for T_2 tumors. In a follow-up to the previous report of the experience at their institution Olson et al.[11] concluded that there was no statistically significant difference in false negative rates between T_1 and T_2 tumors. In comparison with the initial analysis[8] the updated results reflect a larger sample size and increased surgeon experience.

Reasons previously cited for the inaccuracies include alternate lymphatic drainage pathways, inexperience with the procedure, and increased prevalence of axillary metastases in patients with larger tumors.[8] We do not believe there is any evidence to suggest that large tumors have different lymphatic drainage compared with small tumors. The increased incidence of axillary nodal metastases among T_2 and T_3 tumors does not correlate with an increase in the false negative rate in the present study. In fact, the false negative rates for T_2 and T_3 tumors are lower than that for T_1 tumors, although this was not statistically significant. As shown in Fig. 2 there is no difference in either SLN identification or false negative rates with increasing diameter of the primary lesion.

The current study reflects a large broad-based experience with SLN biopsy for breast cancer in a multiinstitutional setting. We report the results for sentinel node biopsy in 589 patients with T_2 or greater lesions, a sample size equivalent to or greater than that reported in all the collective literature on SLN biopsy for larger breast tumors. Our study includes surgeons who had very little if any prior experience with SLN biopsy before entering the study. Indeed, these results represent the initial validation studies at most participating institutions. Therefore there is no evidence that the degree of surgeon experience affects the accuracy of the procedure differently for T_1 tumors *versus* T_2 or T_3 tumors.

It is well established that larger tumors have a higher prevalence of axillary metastases.[12, 13] As expected, axillary node metastases were more frequent in T_2 and T_3 tumors than in T_1 tumors in the current study. Our data suggest that a higher likelihood of positive nodes does not affect the accuracy of the sentinel node in predicting axillary nodal status. Some might argue that the incidence of nodal metastases is so great in T_2 and T_3 tumors that routine axillary dissection should be performed instead of SLN biopsy. Although 52.4 per cent of patients with T_2 tumors have axillary nodal metastases the other 47.6 per cent of these patients can potentially avoid axillary dissection based on the SLN biopsy result. However, we believe that it is a reasonable decision to perform axillary dissection routinely for patients with T_3 tumors given the very high (76.7%) rate of nodal metastases.

In the present study palpable tumors were significantly associated with an increased SLN identification rate compared with nonpalpable tumors, with no difference in the false negative rates. Whether or not a tumor is palpable does not correlate with a difference in false negative rates. If a sentinel node is identified and removed it accurately reflects the status of the axilla in most cases. Improved SLN identification for palpable tumors may be attributable to more reliable injection of blue dye and/or radioactive colloid around the site of the palpable tumors. The majority of patients in this study received peritumoral injection of both radioactive colloid and blue dye. As we have shown previously, dermal injection of radioactive colloid (into the skin overlying the tumor) in conjunction with peritumoral blue dye injection may improve the SLN identification and false negative rates for nonpalpable tumors as well as palpable tumors.[14]

An increased incidence of positive axillary lymph nodes for palpable tumors compared with nonpalpable tumors within the same tumor size category has been reported.[15] We also found that the incidence of nodal metastases was greater for palpable tumors *versus* nonpalpable tumors overall ($P < 0.0001$, Table 3). Furthermore the incidence of nodal metastases was significantly greater for palpable tumors within the T_1 and T_3 categories but not for T_2 tumors. Although the explanation for the finding of increased incidence of

TABLE 2. *SLN Identification Rate and False Negative Rate by Tumor Stage*

T Stage	N	SLN ID Rate*	TP	FN	NPV*	Sensitivity*	FN Rate*	Overall Accuracy*
T1	1496	1378 (92.1%)	315	32	97.0%	90.8%	9.2%	97.7%
T2	545	508 (93.2%)	248	18	93.1%	93.2%	6.8%	96.5%
T3	44	43 (97.8%)	32	1	90.9%	97.0%	3.0%	97.7%

SLN ID, SLN identification rate; TP, true positive; FN, false negative; NPV, negative predictive value. Sensitivity equals the number of positive SLN biopsies divided by the number of patients with axillary lymph node metastases (in whom a sentinel node is identified; herein defined as true positive results + false negative results) × 100. Negative predictive value equals the number of patients without axillary lymph node metastases (in whom a sentinel node is identified) divided by the number of patients with a negative SLN biopsy × 100. Overall accuracy equals the total number of true positive and true negative SLN biopsies divided by the total number of patients in whom SLNs were identified. False negative rate equals number of false negative SLN biopsies divided by the number of patients (in whom a sentinel node is identified) with positive axillary lymph nodes × 100. Specificity equals the number of negative SLN biopsies divided by the number of patients (in whom a sentinel node is identified) without axillary lymph node metastases × 100. Positive predictive value equals the number of patients with axillary lymph node metastases (in whom a sentinel node is identified) divided by the number of patients with a positive SLN biopsy × 100. By definition specificity and positive predictive value for SLN biopsy is always one (100%).

* Not statistically significant.

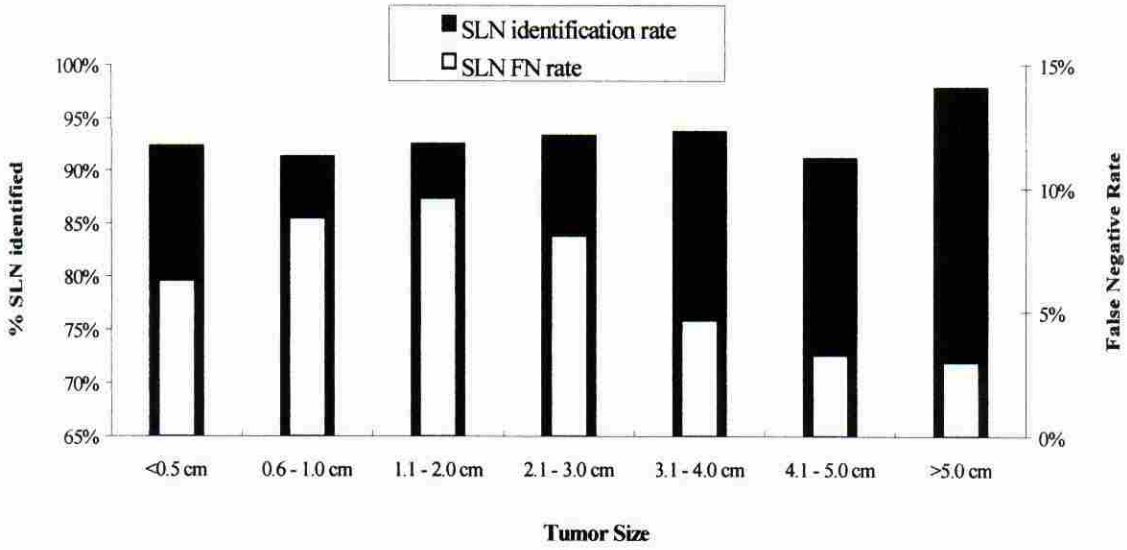

FIG. 2. Sentinel lymph node identification rate and false negative rates by tumor size.

TABLE 3. *SLN Biopsy Results by Tumor Palpability*

	SLN Identification Rate			SLN False Negative Rate			% Axillary Metastases		
	Palpable Tumor	Nonpalpable Tumor	*P* Value	Palpable Tumor	Nonpalpable Tumor	*P* Value	Palpable Tumor	Nonpalpable Tumor	*P* Value
T_1	93.8%	90.8%	0.035	8.8%	9.8%	0.76	33.3%	18.4%	<0.0001
T_2	93.8%	91.0%	0.29	7.0%	5.8%	0.75	52.1%	47.7%	0.42
T_3	96.7%	100%	0.49	0%	14.3%	0.05	90.0%	50.0%	0.0056
Overall	93.9%	90.8%	0.0058	7.7%	8.8%	0.64	41.1%	21.5%	<0.0001

Statistical comparison performed by chi-square analysis.

nodal metastases for palpable tumors compared with nonpalpable tumors within the same tumor size category is not readily apparent our data confirm this phenomenon (exclusive of T_2 tumors).

Because patients with clinical stage N_1, or N_2 disease (palpable or matted axillary nodes) were excluded from this study there is no way to evaluate whether palpable axillary nodes predicted the finding of positive SLN. We always recommend palpation of the axillary nodes intraoperatively. If there are any palpably suspicious nodes they should be removed along with any sentinel nodes found. However, the finding intraoperatively of palpable nodes in the axilla is not necessarily a reliable indicator of metastatic disease.

Some patients have enlarged nodes that are benign, which is presumably related to inflammation from the previous breast biopsy in some cases.

Patients with T_2 and T_3 tumors underwent mastectomy (as opposed to breast conservation) for treatment of the primary tumor more often than patients with T_1 tumors. Use of neoadjuvant therapy, although not shown to improve survival,[16] may allow more women to choose breast-conservation therapy by downstaging the tumor before surgery. Methods that accurately stage patients before any neoadjuvant regimen may be useful. Noninvasive methods such as clinical examination, CT scan, ultrasound, MRI, and positron emission scanning do not have sufficient sensitivity to replace pathologic staging of axillary nodes.[17–19] SLN biopsy may be valuable for pathologically staging the axillary nodes before the onset of neoadjuvant chemotherapy in patients with larger T_2 tumors and in patients with T_3 tumors who are highly motivated to attempt lymph node conservation. Because the long-term survival for women with locally advanced breast cancer who respond well to neoadjuvant chemotherapy is more favorable, quality-of-life issues such as the opportunity for breast conservation and/or immediate reconstruction become very important.[20]

Conclusions

Sentinel node biopsy is a feasible option for nodal staging in larger breast cancers. The SLN identification and false negative rates are similar for T_1 tumors compared with T_2 and T_3 tumors. SLN biopsy can accurately determine the nodal status in tumors greater than 2 cm and potentially spare further axillary dissection in those patients with negative sentinel nodes.

Acknowledgements

We thank the members of the University of Louisville Breast Cancer Study group for their dedicated and ongoing participation. We are grateful to Sherri Matthews for expert assistance with manuscript preparation and data management.

REFERENCES

1. McMasters KM, Tuttle TM, Carlson DJ, Brown CM, Noyes RD, Glaser RL, Vennekotter DJ, Turk PS, Tate PS, Sardi A, Cerrito PB, Edwards MJ. Sentinel lymph node biopsy for breast cancer: A suitable alternative to routine axillary dissection in multi-institutional practice when optimal technique is used. J Clin Oncol 2000;18:2560–6.

2. Turner RR, Ollila DW, Krasne DL, Giuliano AE. Histopathologic validation of the sentinel lymph node hypothesis for breast carcinoma. Ann Surg 1997;226:271–8.

3. Veronesi U, Paganelli G, Galimberti V, et al. Sentinel-node biopsy to avoid axillary dissection in breast cancer with clinically negative lymph-nodes. Lancet 1997;349:1864–7.

4. Krag D, Weaver D, Ashikaga T, et al. The sentinel node in breast cancer: A multicenter validation study. N Engl J Med 1998; 339:941–6.

5. Bass SS, Cox CE, Ku NN, et al. The role of sentinel lymph node biopsy in breast cancer. J Am Coll Surg 1999;189:183–94.

6. Giuliano AE, Jones RC, Brennan M, Statman R. Sentinel lymphadenectomy in breast cancer. J Clin Oncol 1997;15: 2345–50.

7. Hill AD, Mann GB, Borgen PI, Cody HS. Sentinel lymphatic mapping in breast cancer. J Am Coll Surg 1999;188:545–9.

8. O'Hea BJ, Hill ADK, El-Shirbiny AM, et al. Sentinel lymph node biopsy in breast cancer: Initial experience at Memorial Sloan-Kettering Cancer Center. J Am Coll Surg 1998;186:423–7.

9. Winchester DJ, Sener SF, Winchester DP, et al. Sentinel lymphadenectomy for breast cancer: Experience with 180 consecutive patients: Efficacy of filtered technetium 99m sulphur colloid with overnight migration time. J Am Coll Surg 1999;188: 597–603.

10. Bedrosian I, Reynolds C, Mick R, et al. Accuracy of sentinel lymph node biopsy in patients with large primary breast tumors. Cancer 2000; 88:2540–5.

11. Olson JA, Fey J, Winawer J, et al. Sentinel lymphadenectomy accurately predicts nodal status in T_2 breast cancer. J Am Coll Surg 2000;191:593–9.

12. Silverstein MJ, Gierson ED, Waisman JR, et al. Axillary lymph node dissection for T_{1a} breast carcinoma: Is it indicated? Cancer 1994;73:665–7.

13. Carter CL, Allen C, Henson D. Relation of tumor size, lymph node status, and survival in 24,740 breast cancer cases. Cancer 1989;63:181–7.

14. McMasters KM, Martin RCG, Wong SL, et al. Dermal injection of radioactive colloid is superior to peritumoral injection for breast cancer sentinel lymph node biopsy: Results of a multi-institutional study. Presented at the Southern Surgical Association Annual Meeting, December 2000.

15. Silverstein MJ, Gierson ED, Waisman JR, et al. Predicting axillary node positivity in patients with invasive carcinoma of the breast by using a combination of T category and palpability. J Am Coll Surg 1995;180:700–4.

16. Fisher B, Bryant J, Wolmark N, et al. Effect of preoperative chemotherapy on the outcome of women with operable breast cancer. J Clin Oncol 1998;16:2672–85.

17. Fisher B, Wolmark W, Bauer M, et al. The accuracy of clinical nodal staging and of limited axillary dissection as a determinant of histologic nodal status in carcinoma of the breast. Surg Gynecol Obstet 1981;152:765–72.

18. De Freitas R, Costa MV, Schneider SV. Accuracy of ultrasound and clinical examination in the diagnosis of axillary lymph node metastases in breast cancer. Eur J Surg Oncol 1991;17: 240–4.

19. Nieweg OE, Kim EE, Wong WH, et al. Positron emission tomography with fluorine-18-deoxyglucose in the detection and staging of breast cancer. Cancer 1993;71:3920–5.

20. McMasters KM, Hunt KK. Neoadjuvant chemotherapy, locally advanced breast cancer, and quality of life. J Clin Oncol 1999;17:441–4.

DISCUSSION

PAUL S. DALE, M.D. (Macon, GA): It has only been 6 years since Armando Giuliano first introduced the technique of sentinel lymphadenectomy for staging of breast cancers, and since that time multiple institutions including our own have published their experiences. Currently sentinel lymphadenectomy is accepted as a procedure for staging patients with smaller primary breast cancers. In 1999 the National Comprehensive Cancer Network issued guidelines regarding the utilization of sentinel lymphadenectomy for staging breast cancers and in those guidelines they recommended that patients with smaller T_1 tumors or small T_2 tumors could indeed undergo sentinel lymphadenectomy for staging. The authors have reported a lower incidence of false negative rates as well as a higher incidence of identification of the sentinel node with larger tumors, so indeed this is an area of controversy. This is the first large multicenter trial that actually evaluates tumor size as a variable for successful identification of the sentinel node. This study included many surgeons at different levels of expertise utilizing sentinel lymphadenectomy, and the authors found absolutely no difference in the sentinel node identification rate or false negative rates between smaller T_1 or T_2 and larger T_3 tumors. Larger tumors are often diagnosed *in vivo,* meaning you identify with fine-needle aspiration or true-cut biopsy.

My first question is: In those patients who underwent an excisional biopsy did this affect the sentinel node identification rate or the false negative rate? The technique of dye injection is often a very debated topic as well and we are experimenting with different dye injection techniques. You mentioned in your paper that you are using the dermal injection of the radioactive isotope. I was wondering if you could please comment on how you are doing this because I think this technique is very useful, and we should learn it. We have been utilizing it now for about a year in Macon and it certainly has improved our sentinel node identification technique, so could you please review your technique? Also you mentioned that of the large T_3 tumors 76 per cent of them had lymph node metastasis. While sentinel lymphadenectomy could certainly be used to stage these very large tumors we must consider completion axillary dissection in patients who have such a high rate of nodal metastasis. Any palpable node should also be removed at the time of surgery. Another thing that you did not mention was tumor grade; I would be interested to know if tumor grade had any erect on sentinel node identification rate or the false negative rate. I feel that probably as the grade becomes higher the sentinel node identification rate might indeed drop off. I was wondering if you noticed that in your experience. Certainly lymphadenectomy does accurately stage the axilla for breast cancer. This is a very well-written paper and it adds significantly to the growing literature which continues to expand this minimally invasive technique. Sentinel lymphadenectomy can be used to identify patients with large primary tumors; however, completion lymphadenectomy might be considered for those very large tumors. I think future studies will investigate whether or not we actually need to do the completion lymphadenectomy after a sentinel lymphadenectomy. Further dye technique studies and injection techniques should also be covered.

KIRBY I. BLAND, M.D. (Birmingham, AL): My question, which has been part of many prospective studies, involves evaluation of immunohistochemical activity, in particular for those who have H&E-negative nodes. I know that opinions differ on these issues, but I would like to know what Louisville's investigators consider to be the current standards regarding the IHC-positive, H&E-negative group of patients. This is important to know, now that the technology has been exported to the routine general surgeon in our communities. When IHC-positive nodes are evident surgeons feel obligated to go ahead and do an axillary dissection for further follow-up. What is your philosophy about this?

CHARLES E. COX (Tampa, FL): I would echo the same consensus as Dr. Bland. In your earlier description of this data, only 50 per cent of the patients had H&E and 50 per cent had cytokeratin analysis of their nodal tissues. My original comment about cytokeratin analysis is to remind the audience and the authors that the use of cytokeratin analysis was initiated to rule out falsely negative patients. I think that is a critical piece in this study. Even though it was stated that there was no difference in the pathology in these three groups of patients (T_1, T_2, and T_3) there were clearly only 61 per cent of the patients who had infiltrating ductal carcinomas in that T_3 grouping. Many of these patients must have had infiltrating lobular carcinomas and that may make a large difference in the rate of nodal positivity. That would be something I would want the authors to comment on in terms of the actual pathology. There was a 20 per cent difference in those three groups with the first two having 80 per cent infiltrating ductal and then in the T_3 group only 60 per cent had infiltrating ductal tumors.

EDWARD COPELAND, M.D. (Gainesville, FL): Do you believe in the sentinel node biopsy on patients who have T_2 and T_3 tumors? If you get a negative sentinel node, do you do an axillary dissection? Why do T_1 lesions that are palpable have more positive lymph nodes than T_1 lesions that are not palpable?

SANDRA L. WONG, M.D. (Closing Discussion): When we looked at our data for excisional biopsies *versus* core needle biopsies I can tell you that there is no difference in terms of identification rate or false negative rate with excisional biopsies. Secondly, about the injection technique: Recently Dr. McMasters presented this at the Southern Surgical Association showing that using dermal injection of radioactive colloid and peritumoral injection of blue dye resulted in an identification rate of 98 per cent and a false negative rate of about 6 per cent. These are very impressive results considering so many of the surgeons in this study had little previous experience with sentinel lymph node biopsy. I think this technique will bear out to be the technique of choice. Thirdly, and I think this will cover the question that Dr. Copeland had as well with T_3 tumors: You

saw that with T_3 tumors there is a pretest probability walking in the door of having a 75 per cent chance of axillary metastasis. I think this is something you need to keep in mind clinically but it does not deter from the accuracy of the sentinel lymph node biopsy itself. I agree with Dr. Dale that if you are intraoperative and you are palpating in the axilla and you palpate a sentinel lymph node, regardless of whether it's blue or hot or not, that it should be removed. Our database does not capture any information about tumor grade. I think this may be looked at retrospectively on our part and I think it would be something important to look at. In regard to Dr. Bland's and Dr. Cox's question about immunohistochemistry-positive nodes which happen to be H&E negative we at Louisville do not currently use immunohistochemistry staining on the sentinel nodes and this is based on a consensus statement issued by the American College of Surgeons based on Dr. Armando Giuliano's statements. In terms of the pathologic subtype or the histologic subtype in the T_3 tumors I think that the reason that you are seeing a difference in the numbers (which is not a statistically significant difference) is just because we did not have all that many patients in the T_3 group. χ^2 analysis on those numbers did not indicate any difference. Other studies have verified approximately 75 per cent positive sentinel nodes for T_3 tumors as well. We believe that for most patients with T_3 tumors this high risk of nodal metastasis warrants axillary dissection unless the patient understands the risk of a false negative result and is strongly motivated to attempt lymph node conservation.

Dr. Copeland asked why palpable tumors have a higher rate of positive nodes stage for stage. We do not have a definitive answer for that except that we are not the first to find this. There is an old study by Dr. Melvin Silverstein which showed that they had approximately 1500 patients that showed that palpable tumors had a higher incidence of axillary nodes than nonpalpable tumors and our results just seem to be consistent with that.