Axillary Lymph Nodes Suspicious for Breast Cancer Metastasis: Sampling with US-guided 14-Gauge Core-Needle Biopsy—Clinical Experience in 100 Patients[1]

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Purpose: To study the clinical usefulness of ultrasonography (US)-guided core-needle biopsy (CNB) of axillary lymph nodes and the US-depicted abnormalities that may be used to predict nodal metastases.

Materials and Methods: This retrospective study was HIPAA compliant and institutional review board approved; the requirement for informed patient consent was waived. US-guided 14-gauge CNB of abnormal axillary lymph nodes was performed in 100 of 144 patients with primary breast cancer who underwent US assessment of axillary lymph nodes. A biopsy needle with controllable action rather than a traditional throw-type needle was used. US findings were considered suspicious for metastasis if cortical thickening and/or nonhilar blood flow (NHBF) to the lymph node cortex was present. The absence of any discernible fatty hilum was also noted.

Results: Nodal metastases were documented at CNB in 64 (64%) of the 100 patients. All 36 patients with negative biopsy results underwent subsequent sentinel lymph node biopsy (SLNB), which yielded negative findings in 32 (89%) patients and revealed metastasis in four (11%). All 44 patients who did not undergo CNB because of negative US results subsequently underwent SLNB, which revealed lymph node metastasis in 12 (27%) patients. Cortical thickening was found in 63 (79%) of the total of 80 metastatic nodes, but only a minority (n = 26 [32%]) of the nodes had an absent fatty hilum. NHBF to the cortex was detected in 52 (65%) metastatic nodes. Both absence of a fatty hilum (metastasis detected in 26 [93%] of 28 nodes) and cortical thickening combined with NHBF (metastasis detected in 52 [81%] of 64 nodes) had a high positive predictive value. No clinically important complications were encountered with the biopsy procedures.

Conclusion: Axillary lymph nodes with abnormal US findings can be sampled with high accuracy and without major complications by using a modified 14-gauge CNB technique.

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Axillary lymph node status is an important prognostic factor in the evaluation of patients with newly diagnosed breast cancer (1–3). Until recently, axillary lymph node dissection (ALND) was the reference standard for determining this status (4,5). With the detection of many small breast cancers at screening mammography, the yield of lymph nodes positive for breast cancer metastasis at ALND has decreased dramatically (6–8). The decrease in ALND-positive lymph nodes has fostered the alternative of sentinel lymph node biopsy (SLNB). Although SLNB is now widely accepted, surgeons must spend a considerable amount of time in the operating room harvesting sentinel lymph nodes (9–11). In addition, SLNB is not a perfect procedure; it results in no sentinel lymph nodes being elucidated in some patients or in more than three sentinel lymph nodes being detected (12).

If nodal positivity can be proved preoperatively, SLNB can be avoided. Preoperative lymph node staging in patients with breast cancer is increasingly being attempted as various new imaging modalities are developed (5,12–20). Ultrasonography (US) has been the most widely used modality for this purpose (15–20). Some investigators have reported high accuracy in preoperative lymph node staging with US and fine-needle aspiration combined (11,19–23). However, fine-needle aspiration—necessitating operator expertise and the cooperation of experienced cytologists—is known to be more operator dependent compared with core-needle biopsy (CNB). Therefore, our purpose was to study the clinical usefulness of US-guided CNB and the US findings that may be used to predict nodal metastasis.

Advances in Knowledge

- Of 97 patients in whom an abnormality was found in an axillary lymph node at US, 67 (69%) had histopathologically proved metastasis; this is significantly more patients compared with the number of patients with no US-depicted abnormality but histopathologically proved metastasis (13 [28%] of 47, $P < .001$).
- Both absence of a fatty hilum (93% [26/28]) and cortical thickening combined with nonhilar blood flow (81% [52/64]) had a high positive predictive value for metastasis.
- The method we used for core-needle biopsy (CNB) of axillary lymph nodes was efficient and safe; no clinically important complications were encountered with this procedure.

Materials and Methods

This retrospective study was Health Insurance Portability and Accountability Act compliant and was approved by the University of Chicago institutional review board. The requirement for written informed patient consent was waived.

Patients

We retrospectively reviewed the US images and histopathologic results (from US-guided CNB, SLNB, and/or ALND) of all patients who underwent US assessment of axillary lymph nodes between August 1, 2003, and December 31, 2006. Axillary lymph node US was performed in patients with lesions highly suspected to be invasive breast cancer and patients with newly diagnosed invasive breast cancer or extensive (at least 4 cm in extent) ductal carcinoma in situ (DCIS). US was performed by one or more of four radiologists (H.A., R.A.S., C.A.S., G.M.N.). One radiologist (H.A.) had fellowship training in breast imaging, with 3 years of dedicated breast imaging experience. The other three radiologists had 15–35 years experience in breast imaging, including 5–17 years experience in breast US. Axillary lymph node US was performed either at the same time as diagnostic breast US or after the diagnosis of breast cancer was established. Before December 1, 2004, axillary lymph node US was performed in only those patients in whom all diagnostic work-up, including biopsy, was performed at our institution. Since December 1, 2004, US of the ipsilateral axilla has been performed routinely not only in these patients but also in patients whose diagnostic work-up was performed partially at outside institutions. US of the axilla was also performed in patients with an abnormality in or near the axillary area, such as a palpable lesion or other anomaly deemed to be related to the axilla (Fig 1). The lymph node status of all patients was confirmed at histopathologic analysis.

Patients who underwent US-guided CNB.—One hundred patients were included in the study: 95 patients with concurrent breast cancer and five with a history of breast cancer treatment 2–12 years before lymph node biopsy. Five patients had been excluded: Two left our institution, and three did not undergo SLNB or ALND for histopathologic confirmation after CNB yielded

Implications for Patient Care

- Axillary nodes with abnormal US findings can be sampled with high accuracy and without major complications by using a modified 14-gauge CNB technique.
- This technique may enable one to avoid performing inoperative sentinel lymph node biopsy.

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Abbreviations:
ALND = axillary lymph node dissection
CNB = core-needle biopsy
DCIS = ductal carcinoma in situ
NHBF = nonhilar blood flow
SLNB = sentinel lymph node biopsy

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Guarantors of integrity of entire study, H.A., R.A.S.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; manuscript final version approval, all authors; literature research, H.A., R.A.S., clinical studies, H.A., R.A.S., C.A.S., J.S.M., G.M.N., experimental studies, H.A., R.A.S.; statistical analysis, H.A., R.A.S., K.K.; and manuscript editing, all authors

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negative findings. US assessment of the axilla was performed in the five patients who had undergone breast cancer treatment 2–12 years ago because of the following reasons: Two patients had a palpable lymph node at routine physical examination, one patient noticed the new onset of ipsilateral arm swelling on the side of prior breast surgery, one patient had abnormal axillary lymph nodes at recent chest computed tomography, and one patient reported having pain in the axilla. All patients with negative CNB results underwent SLNB. A median of three sentinel lymph nodes (range, 1–7) per patient were sampled at SLNB.

Patients ranged in age from 26 to 88 years (mean, 55 years). For all except two patients, lymph node biopsy was recommended by radiologists on the basis of suspicious findings at diagnostic US. The exceptions were two patients for whom biopsy of palpable lymph nodes was requested by surgeons. The histologic type of the primary lesion in the 100 patients was infiltrating ductal carcinoma in 78 (78%) patients, infiltrating ductal carcinoma with extensive DCIS in 13 (13%), DCIS greater than 4 cm in extent in four (4%), and infiltrating lobular carcinoma in five (5%). The sizes of the invasive components in the primary breast lesions are listed in Table 1.

Patients who did not undergo US-guided CNB.—Forty-four patients aged 39–90 years (mean, 59 years) with concurrent breast cancer underwent SLNB after receiving negative (no suspicious findings) directed axillary lymph node US results. Seven of these 44 patients underwent ALND after SLNB. The histologic type of the primary lesion was infiltrating ductal carcinoma in 35 (80%) of these 44 patients, infiltrating ductal carcinoma with DCIS in one (2%) patient, DCIS in three (7%) patients, and infiltrating lobular carcinoma in five (11%) patients.

Axillary US

Axillary lymph node US was performed with an ATL HDI 5000 US unit (Philips International, Potomac, Md) by using a 5–12-MHz linear transducer. The patient was placed in a supine or contralateral-side-down oblique position on the table, with the ipsilateral hand placed behind the head. US scanning typically started from the lower part of the axilla and continued upward toward the axillary fossa, with the goal of detecting at least one lymph node. US results were considered positive if cortical thickening (including loss of hilum) and/or nonhilar blood flow (NHBF) to the cortex was depicted. Cortical thickening, either diffuse or focal, was defined as a maximal cortical thickness equal to or greater than the width of the fatty hilum (Figs 2, 3). We made specific note of the absence of a fatty hilum. Color Doppler US was performed with low-velocity (4.4 cm/sec) parameter settings and high gain by using a slow scanning technique. US-guided CNB was recommended when positive US findings were obtained. When there were two or more abnormal lymph nodes, the lymph node with the most suspicious findings was selected for biopsy.

Biopsy Procedures

All biopsies, except those in a few difficult cases, were performed by one of three attending radiologists (H.A., R.A.S., C.A.S.) by using a previously described method (24). In the difficult cases, two radiologists each performed one biopsy to obtain better samples. In all except two patients, a 14-gauge Achieve needle (Cardinal Health, Dublin, Ohio) was used because it has an alternative firing mode of operation that is useful in the axilla (24). In two patients, biopsy was performed with a 14-gauge Magnum nee-

Figure 1

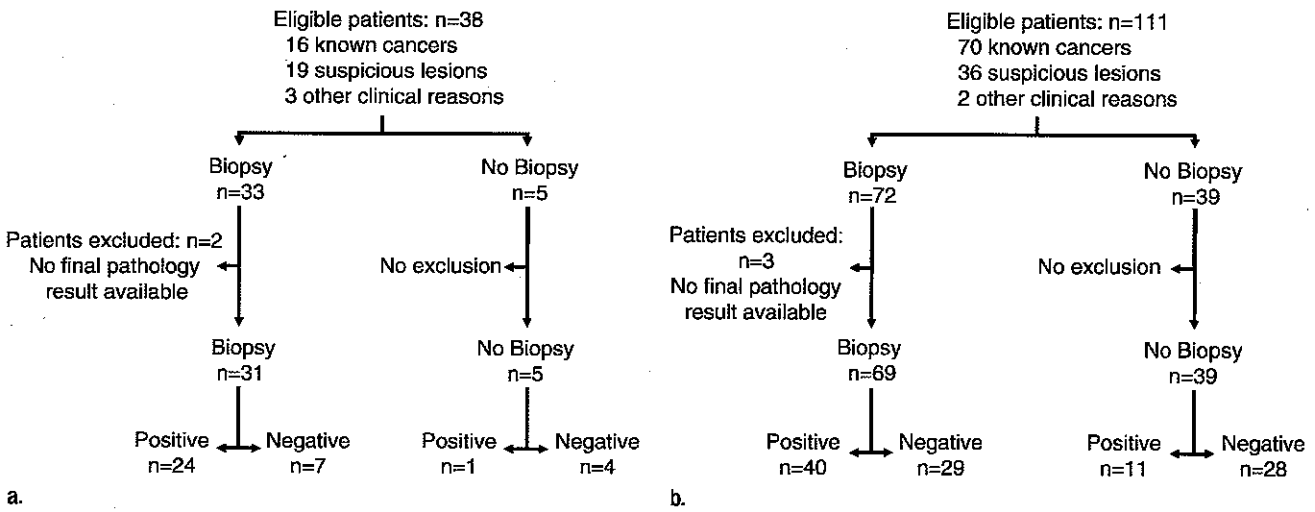

Figure 1: Flowcharts of the study group **(a)** before and **(b)** after the entry criteria were changed.

dle (Bard Biopsy Systems, Tempe, Ariz).

We considered the biopsy procedure to be successful when the obtained sample(s) contained a large portion of solid nonfatty tissue and/or sank in formalin. The mean number of samples obtained per lesion was 2.2 (range, 1–3). When histopathologic assessment findings confirmed the absence of lymph tissue in the specimen, this was regarded as mistargeting. Intolerable pain, considerable bleeding, and clinically important infection in patients were to be recorded. The histopathologic diagnosis was made by using specimens processed with standard hematoxylin-eosin stain. When changes secondary to prior CNB or chemotherapy were identified, they were described in the pathology report.

Twenty-four patients underwent axillary lymph node biopsy before or at the same time as biopsy of the primary lesion, while 71 patients underwent axillary lymph node biopsy after biopsy of the primary lesion; the mean interval between the two biopsies was 18.4 days (range, 1–250 days). In the five remaining patients, primary cancer surgery was performed 2–12 years before axillary biopsy.

Table 1

Final Histopathology Results: Axillary Node Metastatic Involvement and Size of Invasive Component

Size of Invasive Component (mm)	Metastatic Involvement	No Metastatic Involvement	Total
≤9	8 (38)	13 (62)	21
10–19	26 (53)	23 (47)	49
20–49	32 (68)	15 (32)	47
≥50	12 (71)	5 (29)	17
Nonmeasurable	0	3 (100)	3
No invasion (DCIS > 4 cm)*	2 (29)	5 (71)	7
Total	80 (56)	64 (44)	144

Note.—Data are numbers of patients, with percentages in parentheses.

* No invasive component was identified in the primary DCIS lesions. The histopathologic findings were positive for metastatic involvement in two and negative for metastatic involvement in five patients with these cancers.

Retrospective Review

Two radiologists (H.A., R.A.S.) retrospectively reviewed the US images in consensus to assess lymph nodes that had been sampled at biopsy. The long and short axes of the lymph nodes and the cortical thicknesses of the lymph nodes with a visible fatty hilum were measured. Three lymph nodes did not meet the criteria for biopsy: For two nodes, an attending surgeon requested biopsy on the basis of clinical suspicion, and one lymph node was prospectively interpreted to be abnormal.

Statistical Analyses

US and histopathology findings were compared, and the statistical analysis was performed by using the Yates χ^2 test. The US-based lymph node sizes (including cortical thickness and overall size) and histopathology results were compared, with the Welch t test used to determine statistical significance. The sensitivity and specificity of cortical thickness, with 3 and 4 mm as cutoff points, for the detection of metastatic lymph nodes were also calculated. Negative CNB results confirmed with SLNB were considered to be true negative. Positive CNB results were considered to be true positive.

Figure 2

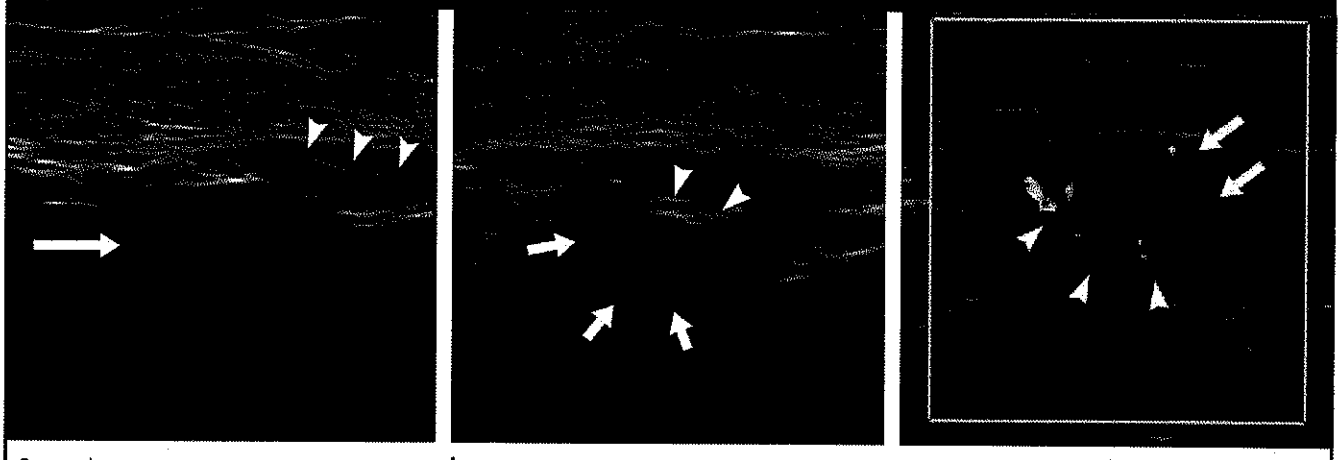

Figure 2: **(a, b)** Standard and **(c)** color Doppler axillary lymph node US images show three abnormal US findings (in three different patients). **(a)** Oval hypoechoic lesion (arrow) represents lymph node with absence of fatty hilum adjacent to normal lymph node with normal fatty hilum (arrowheads). **(b)** Lymph node with asymmetrically thickened cortex (arrows) and diminished fatty hilum (arrowheads). **(c)** Hilar blood flow (arrowheads) and NHBF (arrows) to the cortex at the periphery.

The significance level was set at .05. Statistical calculations were performed by using SPSS, version 11.01J, software (LEAD Technologies, Tokyo, Japan).

Results

Nodal metastases were found at CNB in 64 (64%) of the 100 patients (Table 2). ALND was performed in 49 of these 64 (77%) patients: 46 patients who proved to have nodal metastases at final histopathologic analysis and three without nodal metastasis, presumably as a result of complete response to neoadjuvant chemotherapy. ALND was not performed in 15 (23%) patients: eight patients who had other metastatic disease or another advanced cancer, two who refused to undergo ALND, two with no further information available, and three who did not undergo subsequent ALND after negative SLNB findings because of marked response to neoadjuvant chemotherapy. All 36 patients with negative CNB results underwent SLNB, at which 32 (89%) patients had findings that proved the negative CNB results; each of two (6%) patients had metastasis in one sentinel lymph node (2.3-mm focus and 2.5-mm focus of metastasis) and did not undergo subsequent full ALND; one (3%) patient had a region smaller than 0.2 mm that comprised isolated tumor cells and subsequently underwent ALND, which revealed no other nodal metastases; and one (3%) patient had one positive sentinel lymph node, with five of an additional 13 lymph nodes assessed at full ALND showing metastasis.

CNB had a negative predictive value of 89% (32 of 36 patients) and an overall sensitivity of 94% (64 of 68 patients). All three lymph nodes that did not fulfill the criteria for abnormality at retrospective review were negative for metastasis at US-guided CNB and subsequent SLNB.

In 11 (17%) of the 64 patients with positive US-guided CNB findings, only one metastatic node was found at subsequent ALND. In six (17%) of the 36 patients with negative CNB findings, there was some histopathologic evidence of changes secondary to prior CNB (fat necrosis, fibrosis, and/or hemosiderin deposition) in one of the sentinel lymph nodes.

Twelve (27%) of the 44 patients who had negative axillary lymph node US results and subsequently underwent SLNB had lymph node metastasis. Overall, lymph node metastasis was histopathologically proved in 80 (56%) of 144 patients (Tables 1, 3). The rate of positive biopsy results was 77% (24 of 31 patients) in the first 31 (of 100) patients, who underwent CNB before the entry criteria were changed, and 58% (40 of 69 patients) in the remaining 69 patients.

The data in Table 1 show the relationship between axillary node metastatic involvement and size of primary invasive component. As expected, the larger the primary invasive component was, the more frequently axillary nodal metastasis was found. Notably, two (29%) of seven patients with DCIS lesions greater than 4 cm in extent who did not have an identifiable invasive component at final histopathologic analysis had lymph node metastasis.

CNB revealed a metastatic lymph node in 14 (58%) of 24 patients who

Figure 3

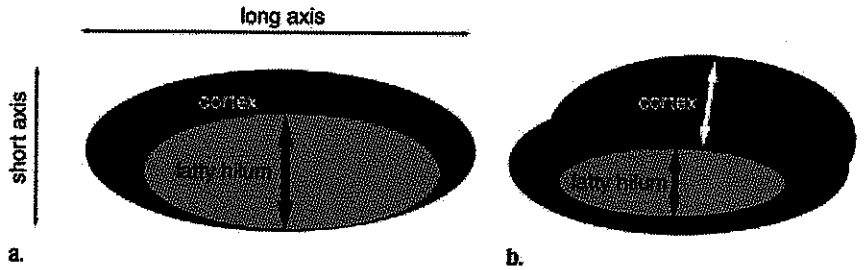

Figure 3: Drawings illustrate cortical thickness and width of fatty hilum. **(a)** The width of the fatty hilum is the length of this structure in the short axis (arrow), which is parallel to the short axis of the lymph node. **(b)** When the maximal thickness of the cortex (white arrow) is equal to or greater than the width of the fatty hilum (black arrow), it is defined as cortical thickening.

Table 2

Correlations between US-guided CNB and Surgical Pathology Results in 100 Patients

CNB Result	SLNB Result		ALND Result		Neither SLNB nor ALND Performed
	Positive	Negative	Positive	Negative	
Positive ($n = 64$)	0	3*	46	3*	12
Negative ($n = 36$)	4†	32	2†	0	0

Note.—Data are numbers of patients.

* SLNB or ALND was performed after neoadjuvant chemotherapy in these six patients.

† Two patients underwent both SLNB and ALND.

Table 3

Correlations between US and Histopathology Findings in 144 Patients

US Finding	Histopathology Finding		
	Malignant	Benign	Total
Positive	67	30	97
Negative	13	34	47
Total	80	64	144

Note.—Data are numbers of patients ($n = 144$). $P < .001$ for correlations between US and histopathologic results at χ^2 testing. Sensitivity, specificity, positive predictive value, and negative predictive value were 84% (67 of 80 patients), 53% (34 of 64 patients), 69% (67 of 97 patients), and 72% (34 of 47 patients), respectively.

underwent axillary lymph node biopsy before or at the same time as primary lesion biopsy and in 45 (63%) of 71 patients who underwent axillary biopsy after primary lesion biopsy ($P = .13$).

Cortical thickening, including that in 28 lymph nodes with absence of fatty hilum, was found in 86 (86%) of the 100 CNB-sampled lymph nodes, and NHBF was detected in 67 (67%) lymph nodes (Table 4). There were significant differences in cortical thickening, absence of fatty hilum, and NHBF to the cortex between the metastatic and nonmetastatic lymph nodes ($P < .01$).

Absence of a fatty hilum had the highest positive predictive value (93% [26/28]) (Table 4). Cortical thickening combined with NHBF in the same lymph node had the second highest positive predictive value (81% [52/64]), which was higher than those of cortical thickening alone (73% [63/86]) and NHBF alone (78% [52/67]) (Fig 4, Table 4). Cortical thickening had the highest sensitivity (79% [63/80])—but the lowest specificity (64% [41/64])—among the three findings.

There were significant differences in cortical thickness ($P < .001$) and overall size ($P < .01$) between the metastatic and nonmetastatic lymph nodes (Table 5). However, the median and mean cortical thicknesses of both the metastatic and nonmetastatic nodes were greater than 4 mm. With the cortical thickness cutoff point set at 3 mm, the sensitivity and specificity of this parameter for the detection of metastatic nodes were 95% (61 of 64 patients) and 6% (two of 36 patients), respectively. With 4 mm as the cutoff point, sensitivity decreased slightly to 88% (56 of 64 patients) and specificity increased to 42% (15 of 36 patients).

There were no major complications, such as clinically important bleeding, nerve injury, or infection, related to the CNB procedure. Three patients had minor complications: One patient experienced transient sharp pain, and two had a small amount of bleeding, which was stopped with simple compression. In all except one patient, the samples obtained at CNB contained a sufficient amount of tissue for histopathologic analysis. The samples from one patient showed no lymph tissue, and this was judged to be a result of mistargeting.

Discussion

All of the patients with positive CNB results—with the possible exception of those patients with a marked response to neoadjuvant chemotherapy—could have been spared SLNB. The patients with negative CNB results still needed to undergo SLNB for diagnosis confirmation. Among the 36 patients with negative CNB results, only four (11%)—including one patient with a small focus of tumor cells classified as isolated tumor cells, which are currently considered to be negative for nodal involvement (noncancerous) (25)—had SLNB results positive for nodal metastasis. The false-negative lesions in two other patients were isolated metastatic deposits smaller than 3 mm; current needle biopsy techniques are not expected to routinely detect such small metastases. Only one of the four patients with false-negative CNB results had clinically important nodal involvement, and retrospective analysis revealed this to be due to mistargeting.

US study of the axilla is beneficial for patients who are known or highly suspected to have invasive breast cancer or extensive DCIS (which might harbor invasive foci). The accuracy of preoperative US diagnosis of nodal metastasis has been reported by several investigators; sensitivity has ranged from 35% to 95% (11,16,17,20–22). Cortical thickening, large node size, and lobulated shape are often used as positive indicators. Our study results suggest that NHBF may be an important additional indicator of nodal metastasis. This increased blood flow probably reflects preexisting peripheral vessels that are engorged owing to a disruption of the hilar blood supply that results from infiltration by metastatic disease (26–28). NHBF may also be seen in other conditions such as inflammatory processes and reactive nodes. Nonetheless, our study revealed NHBF to have a high positive predictive value for nodal metastasis (78%) when it was detected in a patient known to have ipsilateral breast cancer.

An absent fatty hilum, previously reported as a good positive-result indicator (29,30), was the single best finding for detecting nodal metastasis in our study (positive predictive value, 93%), but it was infrequently present (sensitivity, 33%). Deurloo et al suggested that cortical thickening of at least 2.3 mm is a good predictor of lymph node metastasis, with 95% sensitivity and 44% specificity (20). However, the lowest cortical thickness of the lymph nodes sampled in our study was 2.7 mm. While the sensitivity of 3-mm cortical thickness in our study was high (95%) and identical to that of 2.3-mm cortical thickness in the Deurloo et al study, the specificity was unacceptably low (6%).

Table 4

Correlations between Specific US Findings and Histopathology Findings in 144 Patients

US Finding	Histopathology Finding*		Sensitivity†	Specificity†	PPV†	NPV†
	Malignant	Benign				
Cortical thickening	63	23	79 (63/80)	64 (41/64)	73 (63/86)	71 (41/58)
Absence of fatty hilum	26	2	33 (26/80)	97 (62/64)	93 (26/28)	53 (62/116)
NHBF	52	15	65 (52/80)	77 (49/64)	78 (52/67)	64 (49/77)
Cortical thickening and NHBF combined	52	12	65 (52/80)	81 (52/64)	81 (52/64)	65 (52/80)

* Data are numbers of lymph nodes (same as numbers of patients).

† Data are percentages, with the numbers of patients used to calculate the percentages in parentheses. NPV = negative predictive value, PPV = positive predictive value. $P < .001$ for all correlations between US and histopathologic findings at χ^2 testing.

Figure 4

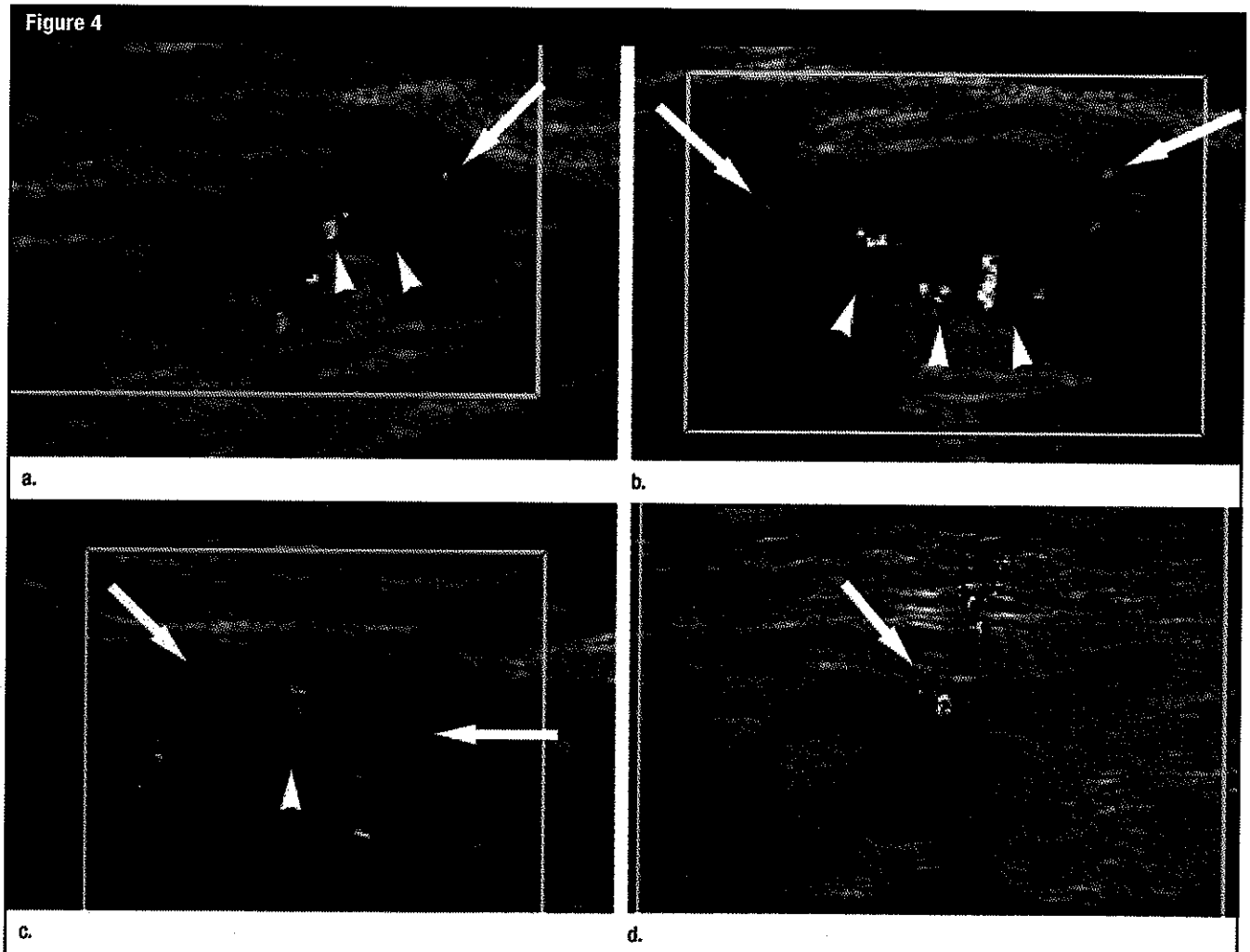

Figure 4: Color Doppler US images show examples of NHBF (arrows) to the cortex of the lymph node. **(a, b)** Bidirectional hilar blood flow (arrowheads) is a normal finding in lymph nodes, but when the cortical blood flow comes directly from outside the lymph node (NHBF), it is abnormal. A small degree of NHBF is seen in **a**, and marked NHBF is seen in **b**. **(c, d)** Hilar blood flow (arrowhead in **c**) may be diminished when NHBF is formed, and occasionally, only NHBF (**d**) is observed, without hilar blood flow.

Therefore, we devised a relative thickness measure of the cortex to the short axis of the lymph node instead of using absolute cortical thickness. Using our criteria, we achieved substantially higher specificity (64%) while maintaining relatively high sensitivity (79%) (Table 4).

Fine-needle aspiration is often performed to cytologically confirm the status of lymph nodes suspected of being malignant. Some investigators (20,21, 23) have reported high sensitivity (62%–86%) and specificity (99%–100%) with this technique. Some advantages of fine-needle aspiration are that it is less invasive, less expensive, more convenient, associated with lower risk, and faster compared with CNB. However, fine-needle aspiration requires operator expertise and the cooperation of experienced cytologists, which are not readily available at many institutions. On the other hand, CNB is a standard proce-

Table 5

Cortical Thickness and Overall Size of Lymph Nodes Sampled with US-guided CNB

Node Status	Cortical Thickness (mm)			Overall Size (mm)		
	Range	Mean	Median	Range	Mean	Median
Metastatic	2.7–27.3	10.3	8.1	6.9–39.4	16.5	12.9
Nonmetastatic	2.8–12.7	5.3	4.5	6.2–22.6	15.0	12.0

Note.—$P < .001$ for difference in cortical thickness between the metastatic and nonmetastatic lymph nodes. $P < .01$ for difference in overall size between the metastatic and nonmetastatic lymph nodes.

dure, is less operator dependent, and yields more material that can be readily examined with immunohistochemical staining. In addition, it was associated with negligible risk in our study. We believe that CNB of axillary lymph nodes can be performed quickly and safely by using our described techniques.

The main challenge in performing CNB within the axilla is to avoid damaging the major vessels and nerves. In one axillary lymph node CNB series, fine-needle aspiration was performed instead of CNB when the lymph nodes were in close proximity to vessels (31). To avoid complications, we used a modified CNB technique, which enables us to perform the biopsy and avoid nerve injury even when the target is immediately adjacent to a major vessel because the cutting cannula only traverses tissue that has already been passed through by the needle (24). Abdsaleh et al (32) reported using a similar technique for axillary lymph node biopsy without any complications in 21 cases by using a 14-gauge prototype semiautomated needle. Although only minor complications were reported in one previous study of axillary lymph node CNB performed by using regular automated CNB needles (33), we believe that use of a method involving a biopsy device with controllable needle action is safer.

A limitation of our study was that direct correlation between the CNB-sampled lymph nodes and the surgically removed lymph nodes was not always possible, so it is uncertain how often we were sampling a true sentinel lymph node or evaluating at preoperative US the lymph node ultimately found to have disease. Another limitation was selection bias: Although we are currently performing US in all patients with newly diagnosed breast cancer, this was not the routine protocol at the beginning of our study period. Thus, some patients with breast cancer did not undergo US for axillary screening.

In conclusion, axillary lymph node biopsy performed by using a 14-gauge controllable-action needle with US guidance in patients with breast cancer can yield a high positive result rate with no clinically important complications. Use of this procedure could obviate SLNB and thus facilitate surgical planning. A negative CNB result still necessitates SLNB, as the sensitivity of this procedure was only 94% in our study. The US finding of an absent fatty hilum had the highest positive predictive value for axillary lymph node metastasis, although it was not frequently detected; other signs such as cortical thickening combined with NHBF were useful and were detected more frequently.

References

1. Banerjee M, George J, Song EY, Roy A, Hryniuk W. Tree-based model for breast cancer prognostication. J Clin Oncol 2004; 22:2567–2575.
2. Cianfrocca M, Goldstein LJ. Prognostic and predictive factors on early-stage breast cancer. Oncologist 2004;9:606–616.
3. Krag D, Weaver D, Ashikaga T, et al. The sentinel node in breast cancer: a multicenter validation study. N Engl J Med 1998;339: 941–946.
4. Reynolds C, Mick R, Donohue JH, et al. Sentinel lymph node biopsy with metastasis: can axillary dissection be avoided in some patients with breast cancer? J Clin Oncol 1999; 17:1720–1726.
5. Lovrics PJ, Chen V, Coates G, et al. A prospective evaluation of positron emission tomography scanning, sentinel lymph node biopsy, and standard axillary dissection for axillary staging in patients with early stage breast cancer. Ann Surg Oncol 2004;11: 846–853.
6. Siegel BM, Mayzel KA, Love SM. Level I and II axillary dissection in the treatment of early-stage breast cancer: an analysis of 259 consecutive patients. Arch Surg 1990;125: 1144–1147.
7. Swenson KK, Nissen MJ, Ceronsky C, Swenson L, Lee MW, Tuttle TM. Comparison of side effects between sentinel lymph node and axillary lymph node dissection for breast cancer. Ann Surg Oncol 2002;9:745–753.
8. Mincey BA, Bammer T, Atkinson EJ, Perez EA. Role of axillary node dissection in patients with T1a and T1b breast cancer: Mayo Clinic experience. Arch Surg 2001;136:779–782.
9. Fraile M, Rull M, Julian FJ, et al. Sentinel node biopsy as a practical alternative to axillary lymph node dissection in breast cancer patients: an approach to its validity. Ann Oncol 2000;11:701–705.
10. McMasters KM, Giuliano AE, Ross MI, et al. Sentinel-lymph-node biopsy for breast cancer: not yet the standard of care. N Engl J Med 1998; 339:990–995.
11. de Kanter AY, van Eijck, van Geel AN, et al. Multicentre study of ultrasonographically guided axillary node biopsy in patients with breast cancer. Br J Surg 1999;86:1459–1462.
12. Kumar R, Jana S, Heiba S, et al. Retrospective analysis of sentinel node localization in multifocal, multicentric, palpable, or nonpalpable breast cancer. J Nucl Med 2003;44: 7–10.
13. Murray AD, Staff RT, Redpath TW, et al. Dynamic contrast enhanced MRI of the axilla in women with breast cancer: comparison with pathology of excised nodes. Br J Radiol 2002;75:220–228.
14. Ohta M, Tokuda Y, Saitoh Y, et al. Comparative efficacy of positron emission tomography and ultrasonography in preoperative evaluation of axillary lymph node metastases in breast cancer. Breast Cancer 2000;7:99–103.
15. Michel SC, Keller TM, Fröhlich JM, et al. Preoperative breast cancer staging: MR imaging of the axilla with ultrasmall superparamagnetic iron oxide enhancement. Radiology 2002;225:527–536.
16. Vaidya JS, Vyas JJ, Thakur MH, et al. Role of ultrasonography to detect axillary node involvement in operable breast cancer. Eur J Surg Oncol 1996;22:140–143.
17. Yang WT, Ahuja A, Tang A, Suen M, King W, Metreweli C. High resolution sonographic detection of axillary lymph node metastasis in breast cancer. J Ultrasound Med 1996;15:241–246.
18. de Freitas R Jr, Costa MV, Schneider SV, Nicolau MA, Marussi E. Accuracy of US and clinical examination in the diagnosis of axillary lymph node metastases in breast cancer. Eur J Surg Oncol 1991;17:240–244.
19. Tate JJ, Lewis V, Archer T, Guyer PG, Royle GT, Taylor I. Ultrasound detection of axillary lymph node metastases in breast cancer. Eur J Surg Oncol 1989;15:139–141.
20. Deurloo EE, Tanis PJ, Gilhuijs KG, et al. Reduction in the number of sentinel lymph node procedures by preoperative ultrasonography of the axilla in breast cancer. Eur J Cancer 2003;39:1068–1073.
21. van Rijk MC, Deurloo EE, Nieweg OE, et al. Ultrasonography and fine-needle aspiration cytology can spare breast cancer patients unnecessary sentinel lymph node biopsy. Ann Surg Oncol 2006;13:31–35.
22. Bedrosian I, Bedi D, Kuerer HM, et al. Impact of clinicopathological factors on sensi-

tivity of axillary ultrasonography in the detection of axillary nodal metastases in patients with breast cancer. Ann Surg Oncol 2003;10:1025–1030.

23. Krishnamurthy S, Sneige N, Bedi DG, et al. Role of US-guided fine-needle aspiration of indeterminate and suspicious axillary lymph nodes in the initial staging of breast carcinoma. Cancer 2002;95:982–988.

24. Abe H, Schmidt RA, Sennett CA, Shimauchi A, Newstead GM. Ultrasound guided core needle biopsy of axillary lymph nodes in patients with breast cancer: why and how to do it. RadioGraphics 2007;27(suppl 1):S91–S99.

25. Collaborative Staging Task Force of American Joint Committee on Cancer. Coding regional lymph nodes for breast. In: Collaborative staging manual and coding instructions. Version 01.03.00. NIH publication 04–5496. Bethesda, Md: National Institutes of Health, 2006; I-38.

26. Yang WT, Chang J, Metreweli C. Patients with breast cancer: differences in color Doppler flow and gray-scale US features of benign and malignant axillary lymph nodes. Radiology 2000;215:568–573.

27. Na DG, Lim HK, Byun HS, Kim HD, Ko YH, Baek JH. Differential diagnosis of cervical lymphadenopathy: usefulness of color Doppler sonography. AJR Am J Roentgenol 1997; 168:1311–1316.

28. Tschammler A, Ott G, Seelbach-Goebel B, Schwager K, Hahn D. Lymphadenopathy: differentiation of benign from malignant disease—color Doppler US assessment of intranodal angioarchitecture. Radiology 1998; 208:117–123.

29. Shin JH, Choi HY, Moon BI, Sung SH. In vitro sonographic evaluation of sentinel lymph nodes for detecting metastasis in breast cancer: comparison with histopathologic results. J Ultrasound Med 2004;23: 923–928.

30. Tateishi T, Machi J, Feleppa EJ, et al. In vitro B-mode ultrasonographic criteria for diagnosing axillary lymph node metastasis of breast cancer. J Ultrasound Med 1999;18: 349–356.

31. Damera A, Evans AJ, Cornford EJ, et al. Diagnosis of axillary nodal metastases by US-guided core biopsy in primary operable breast cancer. Br J Cancer 2003;89:1310–1313.

32. Abdsaleh S, Azavedo E, Lindgen PG. Ultrasound-guided large needle core biopsy of the axilla. Acta Radiol 2004;45:193–196.

33. Topal U, Punar S, Tasdelen I, Adim SB. Role of US-guided core needle biopsy of axillary lymph nodes in the initial staging of breast carcinoma. Eur J Radiol 2005;56:382–385.

RadioGraphics

US-guided Core Needle Biopsy of Axillary Lymph Nodes in Patients with Breast Cancer: Why and How to Do It[1]

TEACHING POINTS
See last page

Hiroyuki Abe, MD, PhD • Robert A. Schmidt, MD • Charlene A. Sennett, MD • Akiko Shimauchi, MD, PhD • Gillian M. Newstead, MD

Axillary lymph node status is an extremely important prognostic factor in the assessment of new breast cancer patients. Sentinel lymph node biopsy is now often performed instead of axillary dissection for lymph node staging but raises numerous issues of practicality. Sentinel lymph node biopsy can be avoided if lymph node metastasis is documented presurgically, making an alternative staging method desirable. Although not widely performed for axillary lymph node staging, ultrasonography (US)–guided core needle biopsy is a well-established procedure for the breast and other organs, with a higher success rate in terms of tissue diagnosis than fine-needle aspiration biopsy. Improvements in US have established it as a valuable method for evaluating lymph nodes. US findings in abnormal lymph nodes include cortical thickening and diminished or absent hilum. In addition, color Doppler US of abnormal axillary lymph nodes often shows hyperemic blood flow in the hilum and central cortex or abnormal (nonhilar cortical) blood flow. US-guided core needle biopsy of axillary lymph nodes in breast cancer patients can yield a high accuracy rate with no significant complications, given the use of a biopsy device with controllable needle action, a clear understanding of anatomy, and good skills for controlling the needle.

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Introduction

Until some future time when it is replaced with noninvasive imaging techniques, tissue diagnosis of axillary lymph nodes will remain one of the most important prognostic factors in the treatment evaluation of patients with newly diagnosed breast cancer (1–3). The standard of reference for axillary lymph node staging is dissection (4,5). However, this procedure can cause numerous postoperative problems, such as lymphedema (2%–18% of cases), pain (16%–56%), impaired shoulder mobility (4%–45%), and arm weakness (19%–35%). Furthermore, in this era of mammographic screening, axillary lymph node dissection yields negative results in 80%–85% of patients with T1 cancer (6–8). Therefore, in recent years, sentinel lymph node biopsy has replaced axillary dissection for lymph node staging at major medical centers in the United States. However, there are some practical issues to be resolved. For example, radiotracer distribution can be slow or faulty, valuable operating room time is expended, and pathologists must make quick decisions based on the analysis of frozen sections (9–12). If nodal positivity could be proved preoperatively, sentinel lymph node biopsy could be bypassed and a decision made to perform axillary dissection, which is the standard of care for staging in most node-positive patients. Minimally invasive determination of preoperative lymph node status in patients with breast cancer is of growing interest in the surgical community. Ultrasonography (US) is currently the main modality used for this purpose (13–17), with advantages over computed tomography and magnetic resonance imaging, including the capacity to help direct biopsy. Although fine-needle aspiration biopsy is helpful when used in combination with US for preoperative lymph node staging, it is known to be more operator dependent than core needle biopsy, necessitating operator expertise and the cooperation of experienced cytologists. Core needle breast biopsy is a standard procedure, is available at most institutions in the United States, is less operator dependent, and yields a higher reproducible success rate in terms of tissue diagnosis than does fine-needle aspiration biopsy. Nevertheless, core needle biopsy is not widely performed for axillary lymph node staging, partly because of the anatomic challenges it presents, and partly due to radiologists' unfamiliarity with the procedure.

In this article, we review the anatomy of the axillary lymph nodes and the imaging appearances of both normal and abnormal nodes. In addition, we discuss and illustrate US-guided core needle biopsy of axillary lymph nodes in breast cancer patients in terms of the biopsy device used, indications for the procedure, technical considerations, and associated complications.

Anatomy

Axillary lymph nodes are divided into three levels relative to the pectoralis minor muscle (18). Level 1 consists of nodes below the lateral border of the muscle, level 2 consists of nodes behind the muscle, and level 3 consists of nodes above the medial border of the muscle.

Most sentinel lymph nodes are level 1 nodes located in the inferior distribution of axillary nodes (1,19). In our experience over the past 3 years, abnormal lymph nodes are often seen in the tissues near the axillary tail, where core needle biopsy can be performed safely and easily. Although it has not yet been proved whether we are performing biopsy of a sentinel node when we use US evaluation and guidance, in over 15% of cases of positive US-guided core needle biopsy, the positive node was the only one found at subsequent axillary dissection—by inference, the sentinel node. We have received no reports from surgeons or pathologists that the sentinel node procedure, performed in all cases of negative US-guided core needle biopsy, was compromised or that diagnosis of the sampled nodes was made more difficult.

Teaching Point

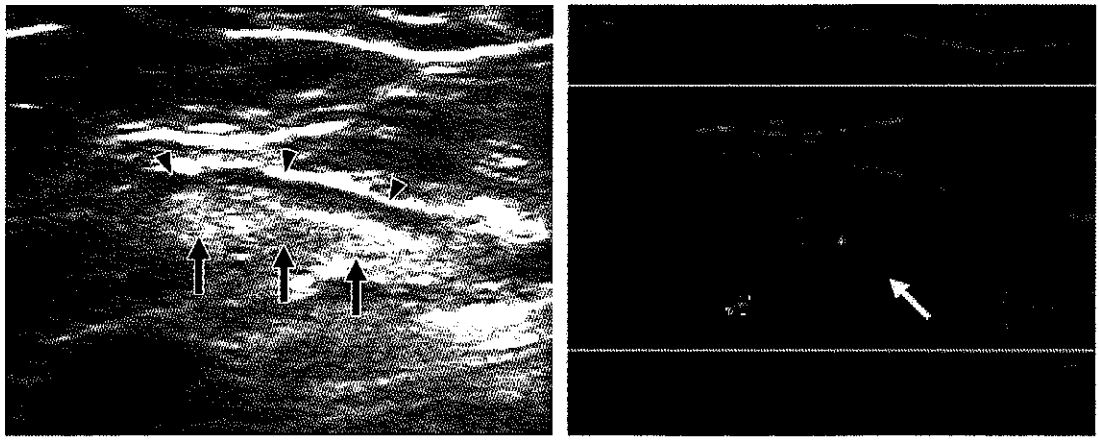
Normal Lymph Node

A normal lymph node has a thin cortex and a relatively large fatty hilum (Figs 1, 2). Blood flow usually passes through a single artery and drains into a single vein, with both vessels being located in the fatty hilum (20,21), much as in a small kidney. This normal blood flow is observed as bidirectional flow in the hilum. Microscopy demonstrates a vascular network within the lymph node cortex (20), but this network is not usually observed in a normal lymph node at color Doppler US. The size of the lymph node is not an indicator of benignity or malignancy, since normal lymph nodes larger than 5 cm can be present in the axilla and lymph nodes as small as 5 mm can contain metastases.

Abnormal Lymph Node

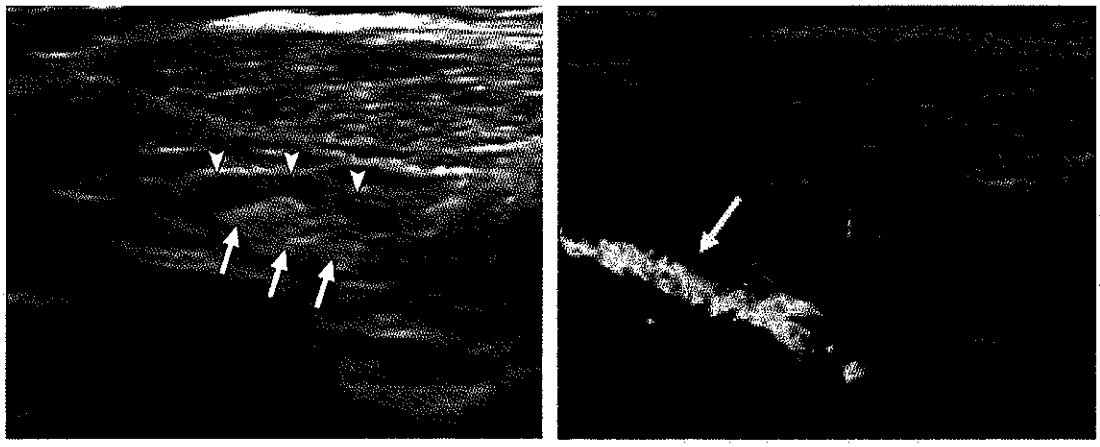
Teaching Point

An abnormal lymph node has a thickened or eccentrically bulging cortex and a diminished or absent hilum (Figs 3–5) (22,23). The thickened



a. b.

Figure 1. **(a)** US image shows a normal lymph node with a thin cortex (arrowheads) and a large fatty hilum (arrows). **(b)** Color Doppler US image shows normal bidirectional hilar blood flow (arrow).



a. b.

Figure 2. **(a)** US image shows a normal lymph node with a thin cortex (arrowheads) and a fatty hilum (arrows) (cf Fig 1a). **(b)** Color Doppler US image demonstrates an adjacent vein (arrow). Lymph nodes are often located near vessels and nerves.

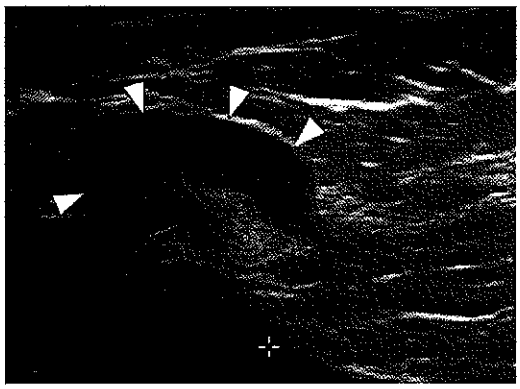


Figure 3. US image shows an abnormal lymph node with a uniformly thickened cortex (arrowheads). The thickness of the cortex exceeds that of the fatty hilum.

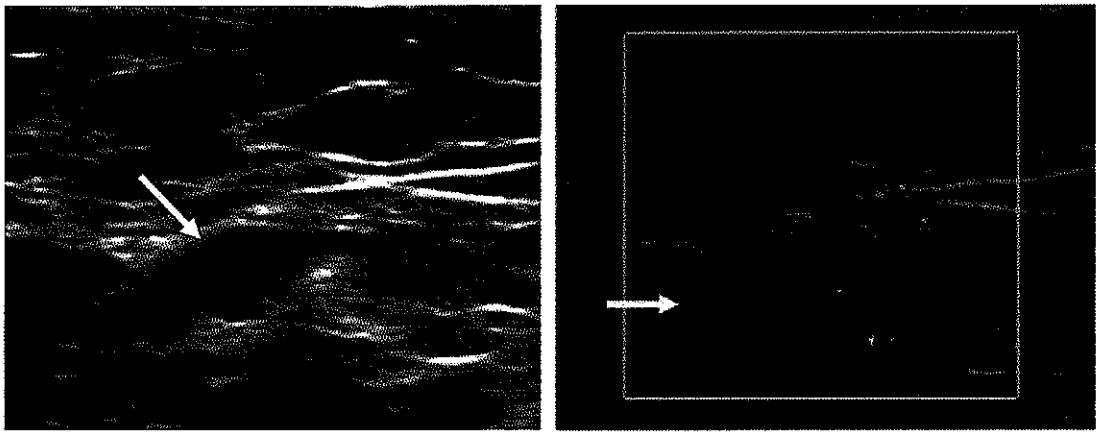


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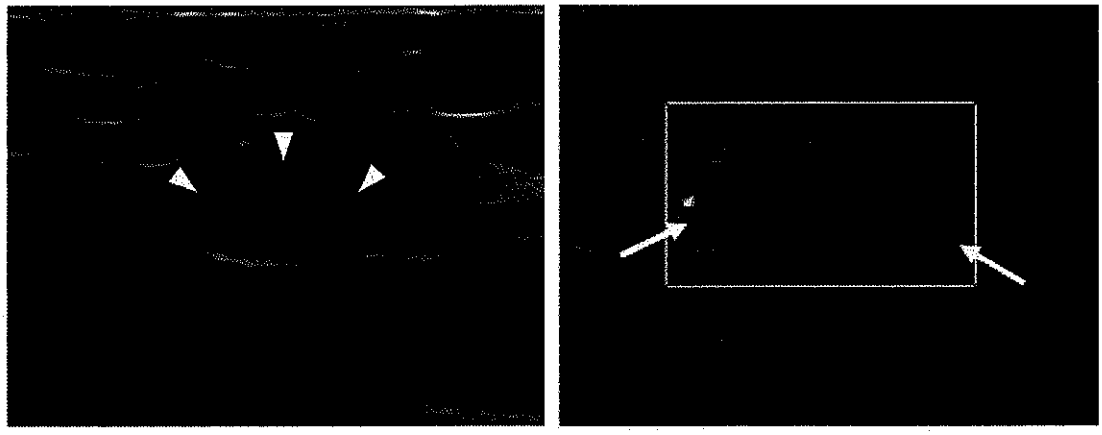
Figure 4. **(a)** US image shows an abnormal lymph node with asymmetric cortical thickening (arrow). **(b)** Color Doppler US image shows normal hilar blood flow as well as abnormal (nonhilar cortical) blood flow (arrow), with the latter finding probably representing enlarged capsular vessels.

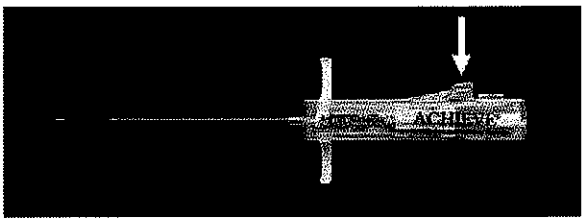


a. b.

Figure 5. **(a)** US image shows an abnormal lymph node with a hypoechoic thickened cortex (arrowheads) but no fatty hilum. **(b)** Color Doppler US image shows only abnormal (nonhilar cortical) blood flow (arrows); no normal hilar blood flow is seen.

Teaching Point

cortex should be the target at biopsy. Metastases embed subcortically in the end vasculature. Color Doppler US shows hyperemic blood flow in the hilum and central cortex or abnormal (nonhilar cortical) blood flow (24). In metastatic lymph nodes, this nonhilar cortical blood flow is probably due to angiogenesis of the tumor, and the vascular network of the cortex is enlarged; blood flow in this area becomes visible at US of an abnormal node. However, this abnormal blood flow is not pathognomonic for a metastatic lymph node; it can also be observed in other pathologic conditions such as reactive lymph nodes with inflammation. Maximizing the sampling of the cortex and specifically targeting the peripheral cortex are recommended for biopsy. We usually recommend biopsy when thickened cortex or nonhilar cortical blood flow is seen. We consider cortical thickening to be present if the cortex thickens to



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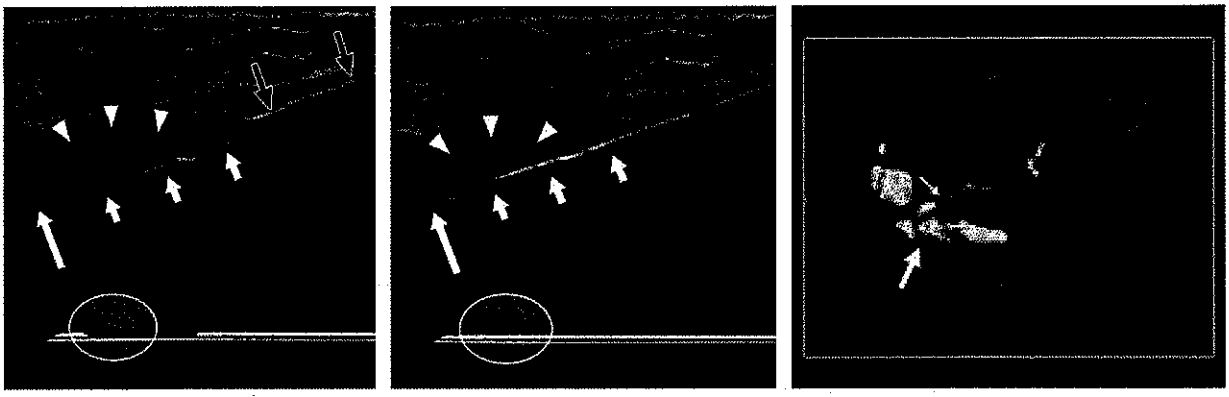


b. c. d.

Figure 6. Biopsy performed with the Achieve needle (Cardinal Health). **(a)** Photograph shows the biopsy device. Arrow indicates the "A" button, which the operator presses to release the outer cutting cannula. **(b)** Presampling US image with corresponding drawing shows how, after the needle has been inserted through the target lesion (arrowheads), the outer cutting cannula (black arrows) is cocked (pulled back) and the trough (short white arrows) is opened. At this point, the system is "charged" for releasing the outer cutting cannula. Long white arrow indicates the needle tip. **(c)** Postsampling US image with corresponding drawing shows how, when the "A" button is pressed, the spring-loaded cannula is released and the trough is covered, thereby retrieving the sample (short arrows). Note that the needle tip (long arrow) remains in the same position between pre- and postsampling (cf **b**). Arrowheads indicate the target lesion. **(d)** Color Doppler US image shows how biopsy can be performed even for a lymph node located right next to the axillary vein (large arrow), since the needle tip (small arrow) does not move during sampling. In this case, the distance between the axillary vein and the needle tip is less than 1 mm. Indeed, we have encountered no complications even when performing a biopsy with the needle tip almost touching the wall of a vessel.

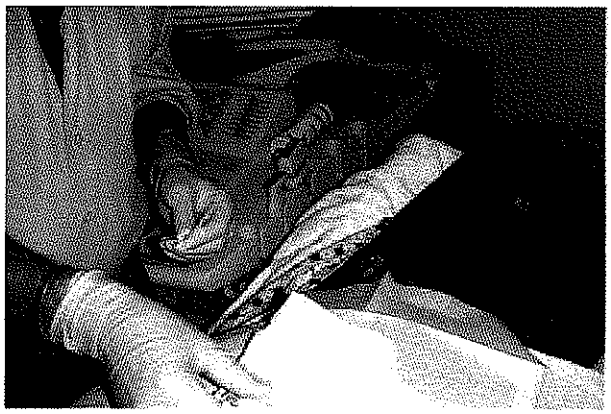
more than one-half the thickness of the lymph node in the short axis. We usually obtain two good-quality core samples, one centrally and one peripherally.

Biopsy Device

With standard spring-loaded 14-gauge biopsy needles, a tissue sample is retrieved by firing a stylet and then a cutting cannula at high speed in rapid sequence to capture the sample with the push of a button. However, this automated action is not desirable when there is a vessel immediately beyond the target, since the track of the needle is difficult to predict and the stroke can damage the vessel. To avoid this possible complication, we use a 14-gauge Achieve biopsy needle (Cardinal Health, Dublin, Ohio). This needle can retrieve a sample without advancing (firing) the tip of the needle beyond its initial placement, thus removing concerns about damaging vessels, nerves, or other tissue beyond the target. Biopsy performed with this needle is illustrated in Figure 6.

Indications

Our biopsy technique is useful for those new breast cancer patients in whom suspicious axillary lymph nodes are identified at ipsilateral axillary US, which is now part of our standard evaluation



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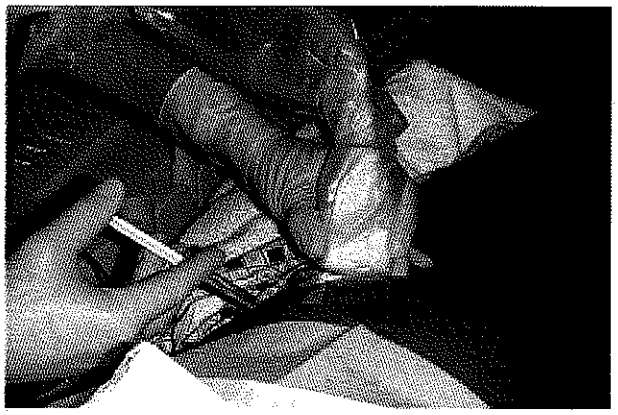

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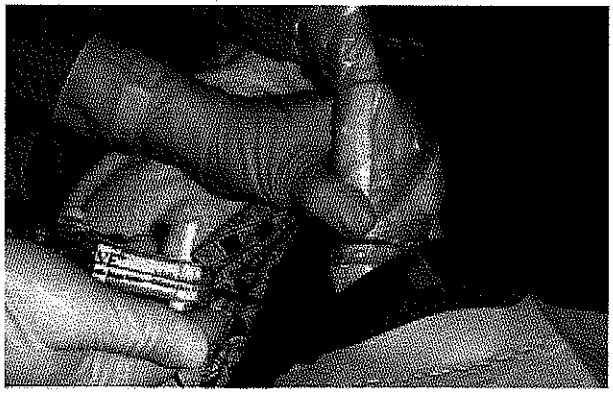


9.

Figures 7–9. (7) Clinical photograph shows how axillary core needle biopsy is performed with the patient's arm raised and with the axilla flattened with use of a wedge pillow. (8) Clinical photograph illustrates the injection of anesthetic. The operator can use the needle to probe any sensitive nerves, evaluate the distance and depth of the target, and simulate the appropriate angle of the biopsy needle. (9) Clinical photograph shows how, after a small skin incision has been made, the biopsy needle is advanced to the target (a thickened cortex) under real-time US guidance.

for invasive breast cancer or extensive ductal carcinoma in situ. Although we do not sample palpable lymph nodes at our clinic unless results of clinical fine-needle aspiration or unguided core needle biopsy are negative or equivocal, this technique can be used in patients with palpable lymph nodes if necessary.

Technique

Our approach is almost always from inferolateral to superomedial toward the target to avoid major vessels and muscles. To flatten the axilla, a wedge pillow is used to rotate the patient's body (Fig 7) and elevate the targeted area. The operator should visualize the target lymph node clearly at prebiopsy scanning and use color Doppler US to determine if there are large vessels around the target. The operator should determine the best approach at this time, with all information obtained at immediate prebiopsy scanning taken into account. After the puncture site and optimal needle approach have been determined, a local anesthetic is placed both superficially and deeply (Fig 8). During deep placement of anesthetic, the needle can be used as a probe to detect any sensitive nerves around the target and simulate the best approach. After the patient has been anesthetized, a small skin incision is made with a #11 scalpel blade. The biopsy needle is then advanced manually under real-time US guidance (Fig 9). Note that the outer cannula remains uncocked during manual needle advancement. In some cases, a tougher fascial layer under the superficial tissues necessitates a deeper incision or the use of a diamond-tipped guide cannula, and advancing the needle after cocking the outer cannula leaves a relatively thin and flexible portion of the stylet to withstand the insertion through the fascial tissues, potentially compromising placement accuracy or even bending the needle at the collection trough, the thinnest portion. Thus, we developed our protocol of advancing the entire uncocked needle—including the outer, more rigid cutting

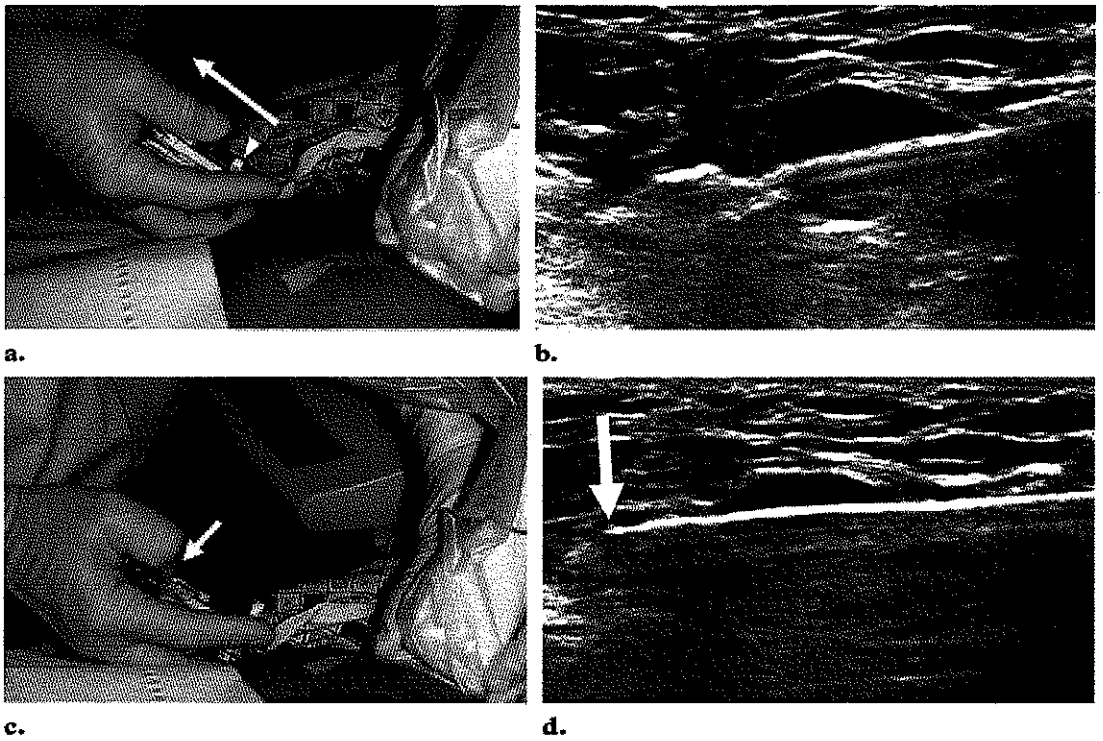
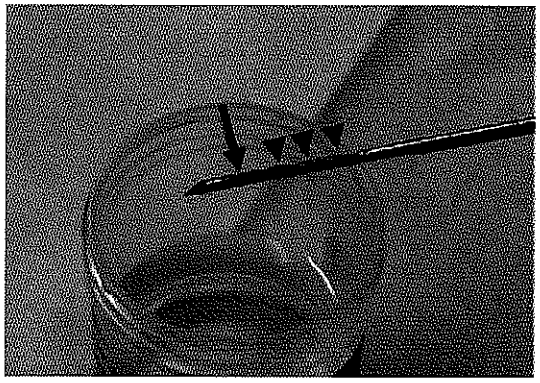


Figure 10. **(a)** Clinical photograph shows the direction (arrow) in which the loading lever (arrowhead) is cocked once the needle tip reaches the target. **(b)** US image shows the biopsy needle with the loading lever cocked. The trough can now be adjusted manually to center on the target. **(c)** Clinical photograph shows the operator pressing the "A" button (in direction of arrow) for sampling. **(d)** On a US image obtained immediately after the "A" button has been pressed, the outer cutting cannula is released and the trough is closed. The tip of the needle (arrow) should not move from its presampling location.

cannula—to or through the target (the cortex of the abnormal lymph node) and then cocking the needle to expose the inner collection trough. The operator should take care that the needle tip is visualized at all times, especially when there are large vessels around the target. Liberal use of color Doppler US is encouraged, both to avoid major vessels and to select a portion of the target node that is less likely to bleed. Somewhat surprisingly, targeting the central hilar area, even when considerable vascularity is present, has neither resulted in any significant hematoma nor compromised sampling or pathologic interpretation. At present, Doppler US at low flow rates (approximately 4 cm/sec) is highly sensitive for imaging blood flow and tends to lead to overestimation of the potential for vascular injury.

When the needle tip is just at or within the target, the gun is cocked once, which opens the trough without advancing the needle tip (Fig 10a). After manually adjusting the position of the trough to center on the target (Fig 10b), the operator presses the "A" button (Fig 10c), thereby releasing the outer cutting cannula and closing the trough (Fig 10d). This maneuver requires some practice and a modicum of physical strength but is easily accomplished with experience. We insert the needle with the bevel facing up to facilitate penetration of the superficial tissues and advance the needle with the plastic flanges used to cock the needle optimally positioned so as not to compromise the angle of advancement. The open trough can be positioned with exquisite accuracy just prior to sampling using this technique. It is recommended that a portion of the trough bridge the cortex and surrounding fat, which helps the pathologist see the interface between the target tissue and surrounding normal (usually fatty) tissue and thus more readily identify the target sample as being from a lymph node. Unlike with



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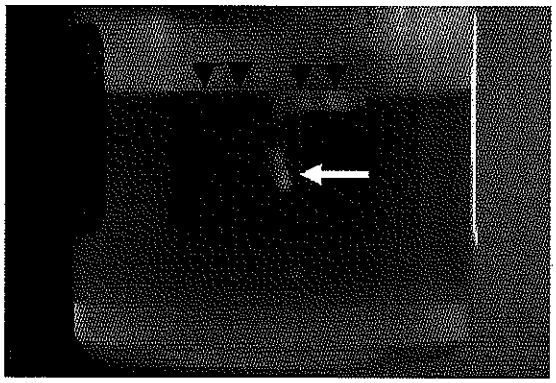

12.

Figures 11, 12. **(11)** Photograph shows a biopsy specimen on the trough of the needle. The white component (lymph node cortex [arrow]) is metastatic tumor, and the yellow component (arrowheads) is adjacent fatty tissue. **(12)** Photograph shows two core samples, taken from an axillary lymph node, in a jar filled with 10% formalin solution. As is typically the case, the lymph node cortical component (black arrow) or tumor component (white arrow) of the specimen sinks in the formalin solution, whereas the fatty tissue (arrowheads) floats. Because the trough of the biopsy needle is often longer than the lymph node, adjacent fatty tissue is usually sampled together with the target cortex.

most other US core needle biopsy procedures, the needle is placed through the lymph node manually rather than by firing the trocar and the cutting cannula automatically. The fatty tissue of the axilla and the relatively soft consistency of both normal and abnormal lymph nodes allows the firing of just the outer cutting cannula to produce a very good core specimen. Use of this procedure prevents inadvertent needle damage, since the needle does not move after placement and the cannula samples only tissue that has already been traversed by the specimen trocar—the same principle involved in stepping in the footprints made by a leader walking through a minefield.

After sampling and documentation of the needle throw position are achieved under US guidance, the needle is withdrawn, and the operator or an assistant should apply manual pressure on the biopsy site to minimize bleeding. The operator should evaluate the specimen visually both before and after placing the sample into a 10% formalin solution. The specimen should have a white (generally pathologic) or brown-tan (lymph node tissue) component, possibly with a yellow component representing adjacent fatty tissue (Fig 11). Because the trough of the needle (19 mm) is usually longer than the target lymph node, some adjacent fat (density, 0.9 g/mL) will often accompany the sampled lymph node tissue (density, 1.04–1.07 g/mL), causing the sample to float or partially sink. A lymph node replaced by tumor will usually produce a sample that sinks to the bottom of the container, sometimes after losing a few air bubbles that accompany the core initially (Fig 12). As mentioned earlier, we usually obtain two samples, one through the middle of cortex and one at the periphery. If the samples appear not to contain lymph node tissue (cortex) or tumor at visual assessment, additional sampling is advised. On average, we obtain about 2.2 samples per case. Occasionally, we will target more than one lymph node if another suspicious node is in the immediate vicinity, but this is not common.

Teaching Point

Complications

The main concern in performing axillary core needle biopsy is to avoid damaging blood vessels or nerves, since lymph nodes are often located near these structures. In our experience with more than 100 biopsies, there have been no major complications. To avoid significant complications, a biopsy device with controllable needle action (such as the Achieve needle) should be used, with a clear understanding of anatomy and good skills for controlling the needle. If, as rarely occurs, the patient complains of a sharp radiating pain on manual insertion of the needle, indicating possible contact with a nerve, choosing a slightly different direction for the approach invariably solves the problem. Use of the inferolateral-to-superomedial approach with the patient's ipsilateral arm raised but not fully extended allows most sampling to be performed parallel to major vessels.

Conclusions

US-guided core needle biopsy of axillary lymph nodes in patients with breast cancer can yield a high accuracy rate with no significant complications. Our positive biopsy yield is over 50%, with only three false-negative core needle biopsies to date: one due to mistargeting of the lesion and two in cases involving very small metastatic deposits (2 and 3 mm, respectively). Because many sentinel lymph nodes are located in the lower axillary region, core needle biopsy of these nodes can be performed safely. Core needle biopsy can be performed even for axillary lymph nodes located immediately adjacent to major vessels by choosing the approach with care and using a biopsy device with controllable needle action. If nodal positivity is confirmed with this procedure, time-consuming sentinel lymph node biopsy can be avoided. To obtain sufficient samples, accurate targeting of the thickened cortex and visual assessment of the sample are crucial. Use of an appropriate device, a clear understanding of anatomy, and good skills for controlling the needle are important for avoiding significant complications.

Teaching Point

References

1. Krag D, Weaver D, Ashikaga T, et al. The sentinel node in breast cancer: a multicenter validation study. N Engl J Med 1998;339:941–946.
2. Banerjee M, George J, Song EY, Roy A, Hryniuk W. Tree-based model for breast cancer prognostication. J Clin Oncol 2004;22:2567–2575.
3. Cianfrocca M, Goldstein LJ. Prognostic and predictive factors on early-stage breast cancer. Oncologist 2004;9:606–616.
4. Reynolds C, Mick R, Donohue JH, et al. Sentinel lymph node biopsy with metastasis: can axillary dissection be avoided in some patients with breast cancer? J Clin Oncol 1999;17:1720–1726.
5. Lovrics PJ, Chen V, Coates G, et al. A prospective evaluation of positron emission tomography scanning, sentinel lymph node biopsy, and standard axillary dissection for axillary staging in patients with early stage breast cancer. Ann Surg Oncol 2004;11:846–853.
6. Siegel BM, Mayzel KA, Love SM. Level I and II axillary dissection in the treatment of early-stage breast cancer: an analysis of 259 consecutive patients. Arch Surg 1990;125:1144–1147.
7. Swenson KK, Nissen MJ, Ceronsky C, Swenson L, Lee MW, Tuttle TM. Comparison of side effects between sentinel lymph node and axillary lymph node dissection for breast cancer. Ann Surg Oncol 2002;9:745–753.
8. Mincey BA, Bammer T, Atkinson EJ, Perez EA. Role of axillary node dissection in patients with T1a and T1b breast cancer: Mayo Clinic experience. Arch Surg 2001;136:779–782.
9. McMasters KM, Giuliano AE, Ross MI, et al. Sentinel-lymph-node biopsy for breast cancer: not yet the standard of care. N Engl J Med 1998;339:990–995.
10. de Kanter AY, van Eijck, van Geel AN, et al. Multicentre study of ultrasonographically guided axillary node biopsy in patients with breast cancer. Br J Surg 1999;86:1459–1462.
11. Fraile M, Rull M, Julian FJ, et al. Sentinel node biopsy as a practical alternative to axillary lymph node dissection in breast cancer patients: an approach to its validity. Ann Oncol 2000;11:701–705.
12. Kumar R, Jana S, Heiba S, et al. Retrospective analysis of sentinel node localization in multifocal, multicentric, palpable, or nonpalpable breast cancer. J Nucl Med 2003;44:7–10.
13. de Freitas R Jr, Costa MV, Schneider SV, Nicolau MA, Marussi E. Accuracy of ultrasound and clinical examination in the diagnosis of axillary lymph node metastases in breast cancer. Eur J Surg Oncol 1991;17:240–244.
14. Yang WT, Ahuja A, Tang A, Suen M, King W, Metreweli C. High resolution sonographic detection of axillary lymph node metastasis in breast cancer. J Ultrasound Med 1996;15:241–246.
15. Vaidya JS, Vyas JJ, Thakur MH, et al. Role of ultrasonography to detect axillary node involvement in operable breast cancer. Eur J Surg Oncol 1996; 22:140–143.
16. Tate JJ, Lewis V, Archer T, Guyer PG, Royle GT, Taylor I. Ultrasound detection of axillary lymph node metastases in breast cancer. Eur J Surg Oncol 1989;15:139–141.
17. Deurloo EE, Tanis PJ, Gilhuijs KG, et al. Reduction in the number of sentinel lymph node procedures by preoperative ultrasonography of the axilla in breast cancer. Eur J Cancer 2003;39:1068–1073.
18. Berg JW. The significance of axillary node levels in the study of breast carcinoma. Cancer 1955;8: 776–778.
19. Suga K, Yuan Y, Okada M, et al. Breast sentinel lymph node mapping at CT lymphography with iopamidol: preliminary experience. Radiology 2004;230:543–552.
20. Belz GT, Heath TJ. Pathways of blood flow to and through superficial lymph nodes in the dog. J Anat 1995;187:413–421.
21. Hay JB, Hobbs BB. The flow of blood to lymph nodes and its relation to lymphocyte traffic and the immune response. J Exp Med 1977;145:31–44.
22. Feu J, Tresserra F, Fabregas R, et al. Metastatic breast carcinoma in axillary lymph nodes: in vitro US detection. Radiology 1997;205:831–835.
23. Vassallo P, Wernecke K, Roos N, Peters PE. Differentiation of benign from malignant superficial lymphadenopathy: the role of high-resolution US. Radiology 1992;183:215–220.
24. Yang WT, Chang J, Metreweli C. Patients with breast cancer: differences in color Doppler flow and gray-scale US features of benign and malignant axillary lymph nodes. Radiology 2000;215: 568–573.

RadioGraphics

US-guided Core Needle Biopsy of Axillary Lymph Nodes in Patients with Breast Cancer: Why and How to Do It

Hiroyuki Abe, MD, PhD, et al

RadioGraphics 2007; 27:S91–S99 • Published online 10.1148/rg.27si075502 • Content Codes: BR OI US

Page S92
In our experience over the past 3 years, abnormal lymph nodes are often seen in the tissues near the axillary tail, where core needle biopsy can be performed safely and easily.

Page S92
An abnormal lymph node has a thickened or eccentrically bulging cortex and a diminished or absent hilum (Figs 3–5) (22,23).

Page S93
Color Doppler US shows hyperemic blood flow in the hilum and central cortex or abnormal (nonhilar cortical) blood flow (24).

Page S98
The specimen should have a white (generally pathologic) or brown-tan (lymph node tissue) component, possibly with a yellow component representing adjacent fatty tissue (Fig 11).

Page S99
Core needle biopsy can be performed even for axillary lymph nodes located immediately adjacent to major vessels by choosing the approach with care and using a biopsy device with controllable needle action.

BARD

BIOPSY SYSTEMS

Memorandum

TO: Biopsy Sales Team
FROM: Roger Anderson
DATE: September 2, 2009
SUBJECT: **Use of Ultrasound-Guided Axillary Node Core Biopsy in Staging of Early Breast Cancer**

The attached study authored by P.D. Britton, et al, was published by the *European Society of Radiology* in September 2008. This study strongly supports that performing axillary core needle biopsies is safe and significantly reduces the number of invasive procedures in women with breast cancer.

Study Background:
This study consisted of 139 patients diagnosed with invasive breast cancer. The objective was to see how effective ultrasound-guided core biopsy was at detecting lymph node involvement in patients with early breast cancer. 121 patients (87%) were selected for core biopsy. If this method identified malignancy, patients could bypass unnecessary sentinel lymph node (SLN) biopsy and proceed with axillary lymph node dissection – avoiding an additional invasive procedure.

Key Findings:

- Core biopsy of axillary lymph nodes diagnosed a substantial number of patients (53.4%) with lymph node metastases allowing them to avoid an additional surgical procedure.
- Fine needle aspiration cytology was also tested but was abandoned because of a high rate of inadequate samples.
- There was not a single report of axillary vascular damage from an axillary node biopsy.
- There were no reports of lymph node needle biopsy adversely affecting subsequent SLN biopsy.

Medical Device Equipment Involved:
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Use of ultrasound-guided axillary node core biopsy in staging of early breast cancer

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Abstract The aim of this study was to see how effective ultrasound-guided needle biopsy was at detecting lymph node involvement in patients with early breast cancer. Patients with newly diagnosed invasive breast cancer underwent axillary ultrasound (US) where lymph node size and morphology were noted. A core biopsy (CB) was undertaken of any node greater than 5 mm in longitudinal section. Patients with benign CBs proceeded to sentinel lymph node (SLN) biopsy, whereas those with malignancy underwent axillary lymph node dissection (ALND). US and CB findings were correlated with final surgical histology in all cases. One hundred and thirty-nine patients were examined, of whom 52.5% had lymph node metastases on final histology. One hundred and twenty-one patients (87%) underwent axillary node CB. The overall sensitivity of CB for detecting lymph node metastases was 53.4% (60.3% for macrometastases; 26.7% for micrometastases). The US morphological characteristics most strongly associated with malignancy were absence of a hilum and a cortical thickness greater than 4 mm. However, one third of patients with normal lymph node morphology had nodal metastases, and only 12% of these were diagnosed on CB. CB of axillary lymph nodes can diagnose a substantial number of patients with lymph node metastases, allowing these patients to proceed directly to ALND, avoiding unnecessary SLN biopsy.

Keywords Breast cancer · Axillary staging · Percutaneous biopsy · Histology · Ultrasound

Introduction

Metastatic involvement of axillary lymph nodes is the single most significant prognostic factor for patients with primary breast cancer, and staging of the axilla is an integral part of patient management [1]. Formerly, this was achieved by axillary lymph node dissection (ALND), which accurately staged and effectively treated metastatic lymph node involvement. However, for those patients whose nodes were free of disease, it conferred no benefit and, in some, was associated with significant morbidity. Sentinel lymph node (SLN) biopsy, developed and refined

over the last decade, offers a less intrusive way of staging the axilla [2]. Those patients whose SLN is free of disease require no further treatment and are spared unnecessary axillary surgery. However, SLN-positive patients require further intervention, which is most frequently a delayed ALND [3]. Since the advent of SLN biopsy, the preoperative diagnosis of metastatic lymph node involvement offers the potential to identify patients who require ALND as first-line surgery, removing the need for SLN biopsy [4]. The aim of this study was to determine the effectiveness of ultrasound (US)-guided needle biopsy at detecting lymph node involvement and hence reducing unnecessary SLN biopsies.

Materials and methods

From April 2005 until June 2007, female patients with either symptomatic or screen-detected invasive breast cancer, confirmed on CB, were invited to undergo an axillary US and possible needle biopsy. During the first 14 months consecutive patients whose invasive cancers measured 20 mm or more on US were recruited. The entry criteria for the remainder of the trial were extended to include grade 2 tumours of 15 mm or more and for grade 3 carcinomas of any size. By selecting patients with larger or higher grade tumours with a greater probability of lymph node metastases, we aimed to examine patients who were most likely to benefit from preoperative ultrasound and needle biopsy. The trial was approved by the local Research and Ethics Committee, and written consent was obtained from each patient. Patients, all of whom underwent initial axillary clinical examination, were usually recruited 1 week following their initial breast CB confirming the presence of invasive malignancy. The total duration of the procedure, i.e., from the patient entering to leaving the US room, was recorded. The axilla ipsilateral to the newly diagnosed breast cancer was carefully examined using a 12–16-MHz matrix linear-array transducer on a Toshiba Aplio Ultrasound platform (Toshiba Medical Systems, Tochigi, Japan). Examination of level I was routinely performed, and in those patients with abnormal lymph node morphology the examination was extended to include levels II and III. The number and position of the nodes were noted. The diameter in longitudinal section, transverse section and maximum cortical thickness of each node was recorded. The ratio of the longitudinal and transverse dimensions was calculated. The nodal morphology was recorded, including whether the outline of the node was smooth (Fig. 1), uni- or multi-lobulated (Figs. 2 and 3) and whether the hilum was normal (Fig. 1) or absent (Figs. 4 and 5). If a lymph node was greater than 5 mm in maximum longitudinal dimension and was not immediately adjacent to an axillary vessel, then a biopsy was undertaken. If more than one node was identified, the most morphologically abnormal node was selected for biopsy. Core biopsy was performed using a Bard Magnum device (Bard Medical Division, Covington, GA) and 16G needle. Depending upon the nodal size and proximity of vessels, either a long-throw (22 mm) or short-throw (15 mm) setting was selected. Between one and four cores were obtained and processed routinely in accordance with laboratory protocols, and three haematoxylin and eosin (H&E)-stained serial sections taken at 20-μm intervals were examined.

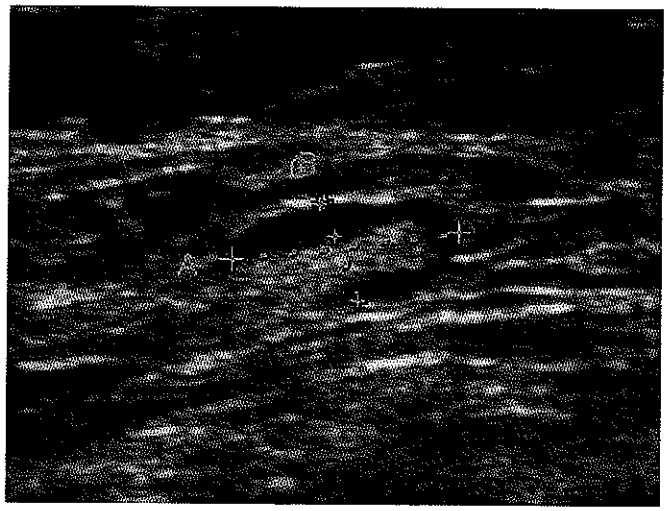

Fig. 1 Normal/benign lymph node with a smooth cortical outline and normal hilum; 36% of such nodes were found to have malignancy at final histology

Patients initially also underwent fine-needle aspiration cytology (FNAC) using multiple passes with a 21 or 22G needle. Following aspiration, needles were rinsed with ThinPrep® Cytolyt® (Cytyc Corporation, Marlborough, MA) solution and the suspension sent to the cytology

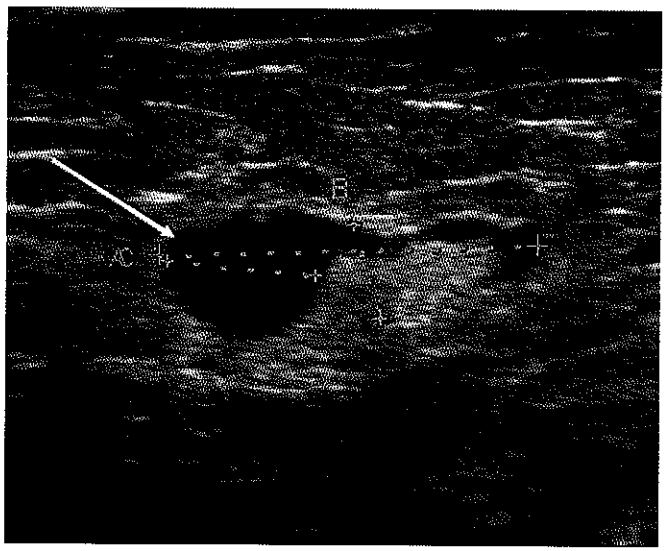

Fig. 2 Lymph node with a uni-lobulated (arrow) cortical outline and normal hilum; 65% of such nodes were found to have malignancy at final histology

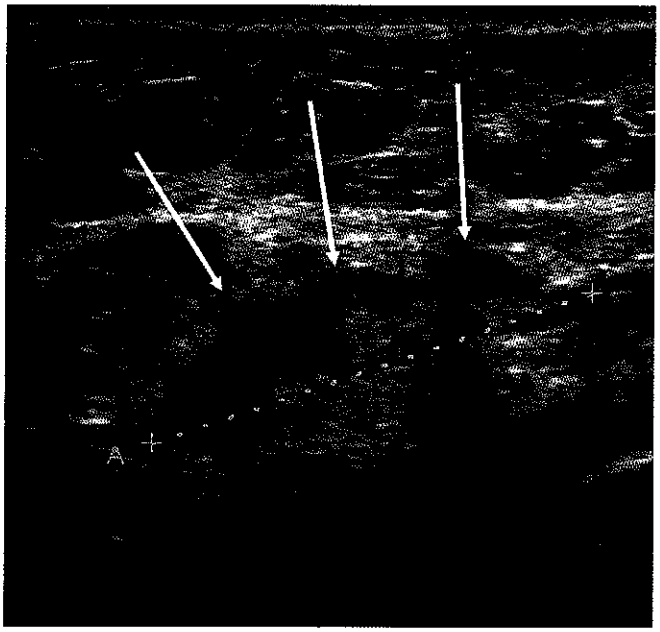

Fig. 3 Lymph node with a multi-lobulated (arrows) cortical outline and normal hilum; 71% of such nodes were found to have malignancy at final histology

laboratory, which obviated the need for slide preparation by the radiologist. A clot section was prepared then stained with H&E. As this unit has not routinely used FNAC in breast diagnosis for over 10 years, current experience with the technique is limited. Consequently, although results were collated for the trial, they were not used to direct patient management.

All CB results were discussed at a multi-disciplinary team meeting where decisions regarding further treatment

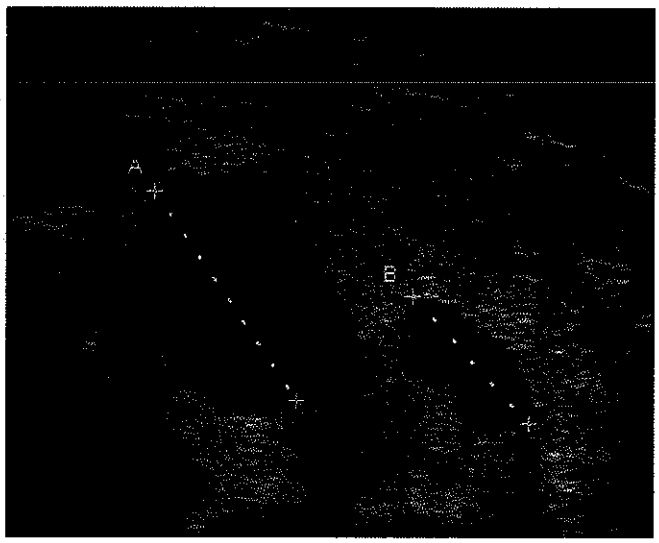

Fig. 4 Two lymph nodes with smooth cortical outlines and absent hila; 89% of such nodes were found to have malignancy at final histology

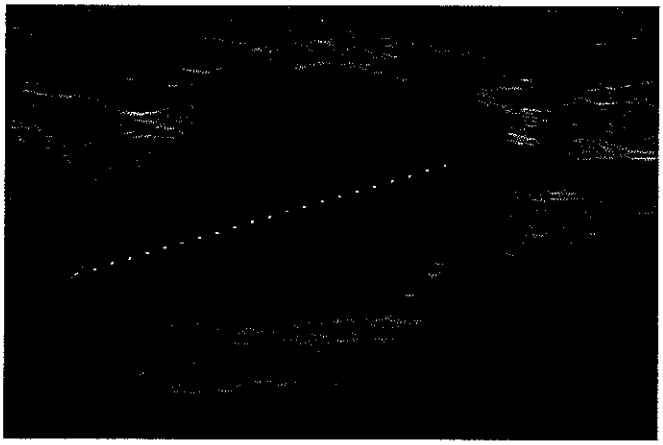

Fig. 5 Lymph node with an irregular cortical outline and absent hilum; 83% of such nodes were found to have malignancy at final histology

were taken. Patients who did not undergo a biopsy or whose biopsy results were inadequate or benign went on to have an SLN biopsy using dual localisation technique with blue dye and technetium-labelled nano-colloid. Those patients whose core biopsies confirmed malignancy subsequently proceeded directly to ALND as a single-stage procedure. Patients undergoing neo-adjuvant chemotherapy had axillary staging by CB and or SLN biopsy prior to commencement of treatment. If either CB or SLN biopsy revealed nodal metastases, ALND was performed after completion of chemotherapy.

All core biopsy and FNAC results were collated with the surgical histology of the excised nodes. Pathological analysis of excised lymph nodes was performed in accordance with National Health Service Breast Screening Programme (NHSBSP) guidelines for the handling of SLNBs [5]. All sentinel lymph nodes were fixed overnight in 10% neutral buffered formalin, then sliced at 2–3-mm intervals and submitted in their entirety for histological examination. Three H&E-stained slides taken at approximately 100-μm levels were examined from each block. Immunohistochemistry for epithelial markers was performed only if suspicious cells were identified, the nature of which was uncertain. Lymph nodes were designated positive for malignancy if they contained a macrometastasis (defined as a parenchymal tumour focus greater than or equal to 2 mm in diameter) or micro-metastasis (defined as a parenchymal tumour focus less than 2 mm in diameter, or deposits within subcapsular sinus between 0.2–2 mm in diameter) [6]. Lymph nodes were designated negative for malignancy if they were histologically normal or contained isolated tumour cells (tumour cell deposits less than or equal to 0.2 mm in the sub-capsular sinus) only.

The findings are presented as counts, percentages, means or ranges, as appropriate. Confidence intervals are given where appropriate. Potential predictors of lymph node positivity were examined using univariate, followed by

multivariate logistic regression. The effect sizes are presented as odds ratios with the corresponding 95% confidence intervals.

Results

One hundred and forty-two female patients with CB-proven unilateral invasive breast cancer were recruited and underwent axillary US. Three patients were excluded because of lack of histological confirmation of lymph node status. One hundred and thirty-nine patients were therefore included in the final analysis. The mean patient age was 56.7 years (range 23.7–82.1 years). One hundred and six symptomatic patients, almost all with breast lumps, and 33 screening patients, 29 with impalpable disease, were recruited to the study. Clinical axillary examination was normal in 116 patients (83%), benign-feeling nodes were palpated in 14 patients (10%), and clinically suspicious nodes were identified in 9 patients (7%). The mean US examination time was 23 min (range 9–60 min). The mean examination time for US was only 12 min compared with 24 min for those undergoing US and biopsy. The mean time between CB and SLN biopsy or ALND for all 139 patients was 25 days (range 3–199 days). There were 19 patients who underwent neoadjuvant chemotherapy, of whom 12 had benign CB and underwent SLN biopsy prior to chemotherapy (mean time 7.5 days, range 5–9 days). The remaining seven patients had proven axillary malignancy on CB and so underwent ALND after completion of chemotherapy (mean time 162 days, range 119–199 days).

Sixty-nine patients were confirmed lymph node positive at final surgical histological examination. Four patients with a malignant CB and post-chemotherapy nodal fibrosis at final histological assessment of the excised nodes were designated as macrometastasis positive. Seventy-three (52.5%) of the 139 study population were designated lymph node positive, of which 58 (79.5%) were regarded as macro- and 15 (20.5%) as micro-metastatic disease. Table 1 shows the final lymph node status by tumour type, grade and size. The comparison of CB results with final surgical histology and performance data is shown in Table 2. One patient, who did not undergo a CB, had no record of whether a lymph node had been identified or not. No nodes were identified on US in five (4%) patients, of whom two were subsequently found to contain nodal metastases. Lymph nodes were identified up to level 3 of the axilla in 1 patient, level 2 in 4 patients and isolated to level 1 in 128 patients. Lymph nodes were identified, but no biopsy performed in 13 patients; this was either because the lymph nodes were too small or their proximity to axillary vessels precluded safe biopsy. Four of these were subsequently shown to have lymph node metastases. The remaining 121 (87%) patients underwent CB. The mean number of needle passes was 2.9 (range 1–4). In five cases the CB samples failed to yield diagnostic material, resulting in an inadequate rate of 4.1%. No evidence of lymph node metastases was obtained in 77 core biopsies, 25 (32.5%) of which were subsequently shown to have lymph node metastases. Malignancy was identified preoperatively in 39 of 73 lymph node-positive patients. Thus, the overall sensitivity of US-guided core biopsy was

Table 1 Table comparing the surgical histological tumour type, grade and size with lymph node status

	Lymph node negative	Lymph node positive (micrometastases)	Lymph node positive (macrometastases)	Total lymph node positive	Total
Tumour type					
Invasive ductal cancer (NOS)	**55**	**11**	**48**	**59**	**114**
Invasive lobular cancer	**3**	**0**	**4**	**4**	**7**
Mixed invasive ductal and lobular cancer	**3**	**2**	**3**	**5**	**8**
Invasive ductal cancer special type (tubular, mucinous, medullary, apocrine, metaplastic)	**5**	**2**	**3**	**5**	**10**
Tumour Grade					
Gd 1	5	0	4	4	9
Gd 2	30	8	22	30	60
Gd 3	31	7	32	39	70
Tumour size (mm)					
0–9	2	0	0	0	2
10–14	12	3	3	6	18
15–19	14	1	2	3	17
20–24	14	4	10	14	28
25–29	11	0	8	8	19
30 or >	13	7	35	42	55
Total	66	15	58	73	139

Table 2 Comparison of core biopsy result with final nodal histology

Surgical histology	Core biopsy result				
	No biopsy	Inadequate	Normal lymph node	Malignant	Total
Lymph node –ve	12	2	52	0	66
Lymph node +ve	6	3	25	39	73
Total	18	5	77	39	139
Macrometastases	5	2	16	35	58
Micrometastases	1	1	9	4	15

Patients whose nodes are positive for malignancy have been subdivided into macro (>2.0 mm diameter tumour nodule) or micro (<2.0 mm diameter tumour nodule) metastases
Number of axillas examined 139
Number of axilla nodes identified on ultrasound 134 (96%)
Number of axilla core biopsies performed 121 (87%)
CB inadequate rate 4.1%
Lymph node +ve (surgery) 52.5%
CB sensitivity all positive nodes 53.4% (95% confidence interval: 41% to 65%)
CB sensitivity macrometastases 60.3% (95% confidence interval: 47% to 73%)
CB sensitivity micrometastases 26.7% (95% confidence interval: 8% to 55%)

53.4%. Core biopsy sensitivity for macrometastasis was 60.3%, but less than 30% for micrometastasis (see Table 2).

Eighty-nine patients also underwent FNAC, of whom 47 (53%) had an inadequate specimen. Malignancy was correctly identified in 15 (31%) of the 49 patients with nodal metastases. The sensitivity for diagnosing macrometastases was 38%, but 0% for micrometastases. In view of the high rate of inadequate samples, FNAC was abandoned during the latter stages of the trial.

Using univariate logistic regression (excluding the five cases for whom no nodes were observed on US and one case where the nodal appearance was not recorded), there was no association between the number of observed nodes and lymph node positivity. The sonographic features most strongly associated with malignancy were absence of a hilum [odds ratio 6.7 (95% CI: 1.5 to 31.1)] and cortical thickness [odds ratio of 5.8 (1.7 to 19.2) for nodes greater than 4 mm compared to under 2 mm]. Compared with a smooth cortex, a unilobulated cortex indicated a higher risk of malignancy [odds ratio of 2.1 (0.7 to 6.0)] and a multilobulated cortex, a significantly higher risk [3.8 (1.6 to 8.8)]. There was no clear evidence of a relationship with increasing longitudinal size or the LS:TS ratio. There was however a significant relationship with increasing size in the transverse plane. Compared with nodes smaller than 5 mm, the risk of malignancy nearly tripled for each increment of 5 mm in dimension [odds ratio 2.8 (1.6 to 4.9)]. In multiple regression, absence of identifiable hilum, non-smooth cortex morphology and size in transverse section remained significant independent predictors of lymph node positivity (Table 3).

Table 3 Independent predictors of lymph node positivity

	Odds ratio	Confidence interval
Hilum present	1	
Hilum absent	6.8	1.3 to 35.5
Smooth outline	1	
Uni-lobulated outline	2.4	0.8 to 7.7
Multi-lobulated outline	3.0	1.2 to 7.5
≤5 mm in transverse section	1	
5–9.9 mm	2.7	1.0 to 7.6
≥10 mm	7.4	2.0 to 27.2

Table 4 shows the relationship of US lymph node morphology with the results of CB and final histology. Of the 73 lymph node-positive patients, 5 (7%) exhibited suspicious US appearances with an irregular outline and absence of fatty hilum. All five (100%) of these yielded a malignant core biopsy result. Eight of the 73 lymph node-positive patients (11%) had morphology with smooth outline, but no fatty hilum, and 7 of these produced a malignant core biopsy result. A multi-lobulated node was identified in 22 (30%) of patients subsequently shown to have malignancy, and a malignant CB result was obtained in 17. A uni-lobulated node was identified in 11 (15%) patients subsequently shown to have malignancy, and a malignant CB result was obtained in 7. When the lymph node was smooth in outline with a fatty hilum, 25 (34%) patients were subsequently shown to be lymph node positive. However, only three of these patients with ultrasonically normal lymph nodes had a malignant CB result.

The procedure was well tolerated by all patients, and no immediate complications occurred. The only late complication occurred in one patient who developed a post-biopsy haematoma, and at surgery no isotope or blue dye containing SLN could be identified.

Table 4 Comparison of lymph node ultrasound morphology with surgical and core biopsy histological findings

	Lymph Node Morphology						
	LN not seen on US	Normal	Uni-lobulated cortex	Multi-lobulated cortex	Absent hilum smooth cortex	Absent hilum lobulated cortex	Total
							
Lymph Node -ve (surgery)	4(66%)	45 (64%)	6 (35%)	9 (29%)	1 (11%)	1 (17%)	66
Lymph Node +ve (surgery)	2 (33%)	25 (36%)	11 (65%)	22 (71%)	8 (89%)	5 (83%)	73
Total	6* (100%)	70 (100%)	17 (100%)	31 (100%)	9 (100%)	6 (100%)	139
CB result							
Malignant	0	3	7	17	7	5	39
Biopsy not done	6	11	0	1	0	0	18
Inadequate	0	4	0	1	0	0	5
Benign	0	52	10	12	2	1	77
Total	6	70	17	31	9	6	139

* Lymph node not seen on ultrasound = 5, lymph node morphology not recorded = 1.

Discussion

Accurate staging of axillary disease has always been an important aspect in the management of patients with breast cancer [1], and a variety of imaging modalities has been evaluated as predictors of histological findings [7–9]. Axillary ultrasound is readily available, non invasive and provides high-quality images [10]. It is recognised, however, that underlying malignancy can be found in lymph nodes that appear morphologically normal. In 6 studies of almost 1,000 patients, with lymph node positivity ranging from 31–39%, an average of 28% (range 26–52%) of patients with morphologically normal-appearing nodes had lymph node metastases [10–15]. A variety of morphological features that may be seen in pathological nodes has been described. The more axillary lymph nodes detected by US, the greater is the likelihood of malignant involvement [15]. The number of patients with identifiable nodes on US in the present study (96%) is higher than most other published reports, especially when taking into consideration the overall node positivity rate in the series. This may be due to a number of factors. Unlike most series, our patients were examined 1 week after initial breast core biopsy. It is recognised that reactive enlargement of axillary nodes can occur in response to breast biopsy. In addition the sensitivity of breast US has increased, enabling better tissue differentiation. In an in vitro study of excised nodes examined by CT, Uematsu et al. found that although in general the larger a node was in longitudinal or transverse section, the more likely it was to have malignant involvement, there was a large range in the dimensions of normal and abnormal nodes [9]. Although this current study found no significant correlation between the longitudinal to transverse ratio (LS:TS) in determining the likely presence of malignancy, Feu et al. found an LS:TS of <1.5 identified malignancy in 54% of cases and a ratio of >1.5 identified only 25% of nodes containing metastases [17]. Vassallo et al., in a series that included non-breast cancer patients, found an LS:TS of <2 was associated with malignant involvement in 94% of patients and an LS:TS >2.0 with 31% of nodes containing metastases [10]. These findings concur with a similar study by Uematsu et al. that reported 83% node positivity for a LS:TS of <2 and 9% when >2.0 [9]. These results have prompted numerous clinicians to adopt an LS:TS ratio of <2.0 as a criterion for biopsy.

The absence of a fatty hilum is also a feature well recognised as suspicious of malignancy and has been reported as occurring in approximately 45% of metastatic lymph nodes [10, 16]. Only 19% of malignant nodes in the present series, however, exhibited a lack of hilum. It should also be noted that such a finding is not pathognomonic of malignancy, and between 6 and 23% (13% in this current series) of these nodes contain no detectable malignancy [10–16]. Our study has also shown that cortical morphology of the node may suggest underlying metastases. Duerloo found that a diffusely thickened cortex of greater