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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

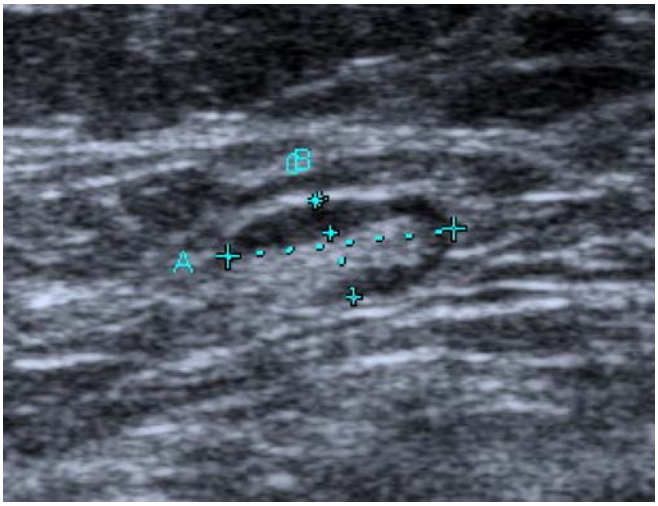

Fig. 1 Normal/benign lymph node with a smooth cortical outline and normal hilum; 36% of such nodes were found to have malignancy at final histology

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.

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

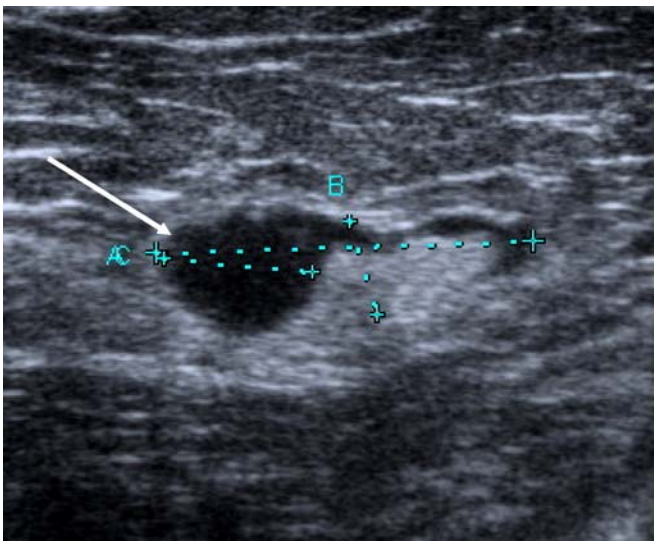

Fig. 2 Lymph node with a uni-lobulated (arrow) cortical outline and normal hilum; 65% of such nodes were found to have malignancy at final histology

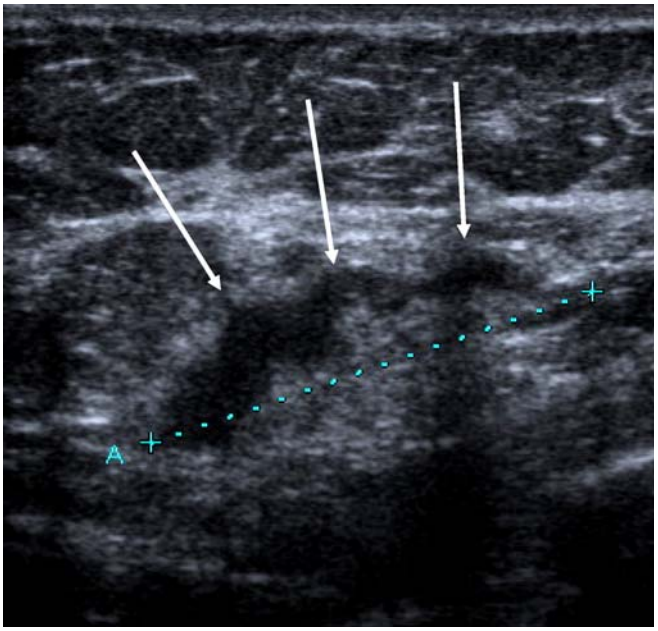

Fig. 3 Lymph node with a multi-lobulated (arrows) cortical outline and normal hilum; 71% of such nodes were found to have malignancy at final histology

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

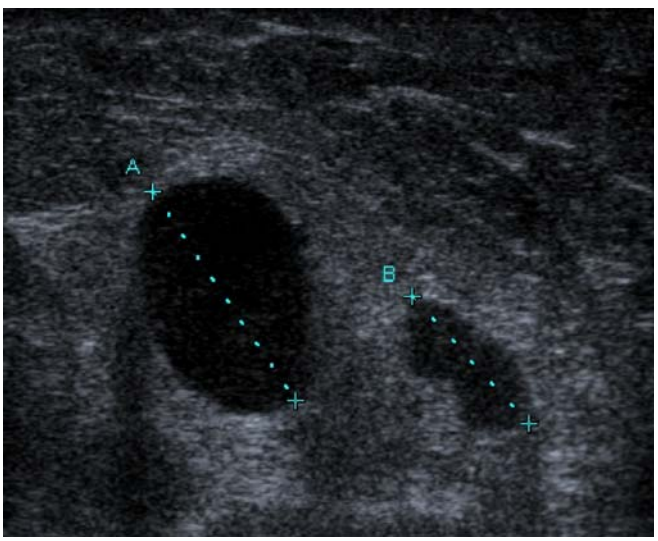

Fig. 4 Two lymph nodes with smooth cortical outlines and absent hila; 89% of such nodes were found to have malignancy at final histology

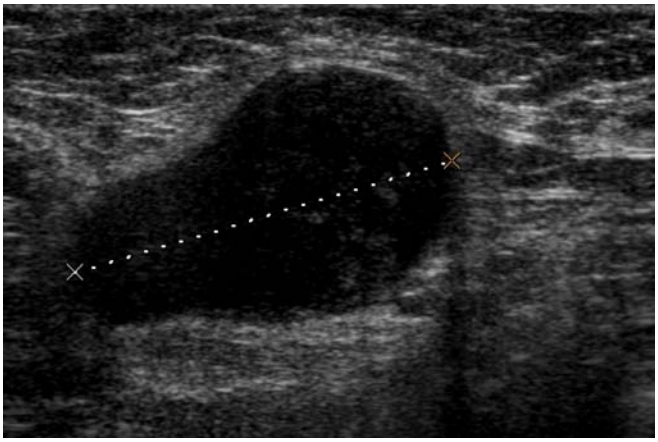

Fig. 5 Lymph node with an irregular cortical outline and absent hilum; 83% of such nodes were found to have malignancy at final histology

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

than 4.2 mm was 80% sensitive and 80% specific for malignancy [18]. If the cutoff was lowered to 2.3 mm, the sensitivity increased to 95%, but specificity dropped to 44% [18]. Vassallo described that diffuse cortical thickening was associated with malignancy in 47% of cases [10]. Duchesne found cortical thickening of >2 mm in 35% of all pathological nodes, and when present, a cortex of >2 mm was associated with malignancy in 30% and benignity in 70% [16]. A lobulated cortex is reported to be found in approximately 20% of malignantly involved nodes and is associated with malignancy in between 53 and 73% of patients [16, 17].

The variable accuracy of such findings, however, makes each morphological features, either alone or in combination, insufficiently reliable to assist in the decision as to whether an individual patient should be advised to proceed straight to ALND or undergo SLN biopsy. Any preoperative staging therefore requires needle biopsy to substantiate subsequent clinical decision making.

Comparison of published axillary lymph node biopsy performance data is presented in Table 5. The majority of publications on axillary node biopsy have used FNAC, and a wide range of sensitivities have been reported (21%–94%). Although FNAC was included in this study, the results were disappointing, especially the very high inadequate rate that does not match most other published series. The most likely reason for this is that FNAC on breast lesions has not been practised routinely in our institution since 1994 when CB replaced FNAC. None of the radiologists therefore has any recent experience in FNAC outside of this study, which was also why needle washings rather than smears were used for specimen preparation. Our experience in CB and the very encouraging results in breast diagnosis compared with FNAC [19, 20] made us wish to evaluate CB accuracy in staging the axilla. We modelled our series on the Nottingham trial of axillary CB [12], which biopsied 48 (29%) of 166 patients using one or two passes with a 14G needle. Their criteria for node biopsy were morphologically abnormal nodes with cortices greater than 2 mm in diameter and a LS:TS greater than 2. Overall sensitivity for detecting lymph node metastasis was 42%. The rationale for our study was to see whether submitting a greater proportion of patients to biopsy would result in improved sensitivity. In our series 87% of patients were biopsied, but the sensitivity for detecting lymph node metastasis only increased to 53% (95% confidence interval 41 to 65). This modest increment in sensitivity when compared with the Nottingham trial was only achieved by the addition of substantial numbers of negative biopsies. This may be partly explained by inadequate sampling of the affected node or possibly by biopsy of a node other than the SLN. A separate pathological review of the SLNs is this series is currently underway to see how many exhibit evidence of recent previous CB, which may reveal how often the actual SLN is being sampled during percutaneous biopsy. It is therefore disappointing to report that this aggressive biopsy approach does not appear to have resulted in a commensurate improvement in sensitivity.

Who then should be biopsied, and is node morphology important in guiding more intelligent biopsy? In this series, if the lymph node is morphologically normal on US, then malignancy is subsequently found in 36% of cases. However, CB of these nodes diagnosed malignancy in only 3 of 25 (12%). Until data correlating axillary node biopsy to targeting of the SLN are available, there seems little justification in trying to improve sensitivity of axillary lymph node biopsy by increasing the numbers of passes or the needle gauge. More intelligent targeting of the SLN is clearly required, and experimental work using radionuclide isotope [21] or US contrast agents [22] to aid identification of the SLN shows promise. Suga et al. have shown that injecting intra-parenchymal contrast can delineate sentinel nodes on computed tomography [23]. However, if biopsy of morphologically normal nodes is unrewarding at present, what criteria should the radiologist use to identify and biopsy the nodes? From the present series, and other published reports, it would seem reasonable to biopsy those nodes that are: greater than 10 mm in maximum transverse dimension, or have a cortex that is 4 mm or greater in thickness, have a uni- or multi-lobulated cortical margin, or have an absent hilum.

The entry criteria in this study were initially restricted to patients with larger tumours and then only to patients with smaller tumours of higher grade to focus resources on a population with a reasonable expectation of nodal involvement. The background level of nodal involvement in any study population will clearly affect the sensitivity achieved. Table 5 shows that the highest needle biopsy sensitivities are achieved in trials with high likelihood of metastatic disease. For CB, Topal's series had a high (85%) level of nodal metastasis and a 91% sensitivity [24]. For FNAC, Duchesne's series had a 78% level of lymph node metastasis and a 94% sensitivity [16]. It is likely, therefore, that the sensitivity for detecting lymph node metastases would drop if our entry criteria had included patients with invasive tumours of any size.

No major complications have been reported in any of the series reviewed in this paper. As far as we are aware, there has not been a single report of axillary vascular damage from an axillary node biopsy. There have also been no reports of lymph node needle biopsy adversely affecting subsequent SLN biopsy, although published numbers of CB, which might be expected to have a greater affect on lymphatic drainage of axillary nodes than FNAC, are currently extremely small. The SLN of one patient in this series could not be identified at the time of surgery, which was attributed to a post-needle biopsy haematoma. As stated above, this has not been previously reported in the literature, although it should also be taken into consideration that there is a technical failure rate for SLN biopsy, without prior needle biopsy, of between 1 and 4% [25, 26].

Table 5 Comparison of published performance statistics of ultrasound-guided axillary lymph node biopsy

Reference	This study	Topal et al.	Damera et al.	This study	Duchesne et al.	Bonnema et al.	van-Rijk et al.	de Kanter et al.	Duerloo et al.	Krishnamurthy et al.	Sapino et al.	K-Boumeester et al.
Reference no.	-	24	12	-	16	14	11	15	18	28	131	27
Date	2008	2005	2003	2008	2005	1997	2005	1999	2003	2002	2003	2003
Biopsy method	CB	CB	CB	FNAC	FNAC	FNAC	FNAC	FNAC	FNAC	FNAC	FNAC	FNAC
Number of patients	139	39.0	166	89	40	150	726	185	268	103	298	183
Lymph node positivity of study population	53%	85.0%	39%	55%	78%	41%	31%	47%	45%	77%	30%	46%
Nodes identified on ultrasound	134 (96%)	39 (100%)	103 (62%)	85 (96%)	100%	93 (62%)	NS	69 (37%)	93 (35%)	103	NS	183 (100%)
Number of biopsies	121 (87%)	39 (100%)	48 (29%)	89 (100%)	100%	54%	176 (24%)	69 (37%)	66 (25%)	103	95 (32%)	183 (100%)
Needle gauge	16	16.0	14	21/22	18	21	21/22	21	NS	20/21	22	21
Average number passes	2.9	2.0	2	1	NS	NS	NS	NS	NS	2.0	NS	NS
Inadequate rate	4.1%	0.0	NS	53%	NS	NS	NS	NS	11%	0%	11%	27%
% of all metastatic nodes diagnosed on biopsy	53%	91.0%	42%	31%	94%	63%	21%	36%	31%	50%	56%	44%
% of macro-metastatic nodes diagnosed on biopsy	62.3%	NS	NS	38%	NS	NS	NS	NS	41%	NS	NS	NS
% of micro-metastatic nodes diagnosed on biopsy	8.3%	NS	NS	0%	NS	NS	NS	NS	3%	NS	NS	NS

NS = not specified

Two published series have recorded false-positive results when using FNAC. Kuenen-Boumeester et al. had 3 cases in a series of 183 patients, and Van-Rijk et al. reported 1 false-positive FNAC in their study of 726 patients [11, 27]. To date, there has not been a single reported case of a false-positive CB from an axillary lymph node in a patient with invasive breast cancer.

Axillary lymph node US and biopsy have enabled the detection of 53% of patients with metastases in this series and obviates the need to perform initial SLN biopsy in such patients. However, a SLN biopsy is still required in patients with benign lymph node core biopsy. This study shows that lymph node US morphology is important when deciding whether and which node should be biopsied. We would suggest biopsy of those nodes that are: greater than 10 mm in maximum transverse dimension, or have a cortex that is 4 mm or greater in thickness, have a uni- or multi-lobulated cortical margin, or an absent hilum. More sophisticated

techniques are required to enable the SLN to be identified and biopsied under image guidance, which will provide a further improvement in preoperative diagnostic sensitivity for patients with axillary lymph node metastases.

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References

1. Fisher B, Bauer M, Wickerham DL, Redmond CK, Fisher ER (1983) Relation of number of positive axillary nodes to the prognosis of patients with primary breast cancer. An NSABP update. Cancer 52:1551–1557
2. Veronesi U, Paganelli G, Viale G, Luini A, Zurrida S, Galimberti V, Intra M, Veronesi P, Maisonneuve P, Gatti G, Mazzarol G, De Cicco C, Manfredi G, Fernández JR (2006) Sentinel-lymph-node biopsy as a staging procedure in breast cancer: update of a randomised controlled study. Lancet Oncol 7:983–990
3. Lyman GH, Giuliano AE, Somerfield MR et al (2005) American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer. J Clin Oncol 23(30):7703–7720
4. Cornford E, Evans A (2003) Editorial comment on "Reduction in the number of sentinel lymph node procedures by preoperative ultrasonography of the axilla in breast cancer" by Deurloo and colleagues. Eur J Cancer 39(8):1037–1038
5. NHSBSP Guidelines for Pathology Reporting in Breast Disease (2005) NHSBSP Pub. No. 58 http://www.cancerscreening.nhs.uk Accessed 3rd February 2008
6. Cserni G, Bianchi S, Boecker W et al (2005) European Working Group for Breast Screening Pathology. Improving the reproducibility of diagnosing micrometastases and isolated tumor cells. Cancer 103(2):358–367
7. Michel SC, Keller TM, Fröhlich JM et al (2002) Preoperative breast cancer staging: MR imaging of the axilla with ultrasmall superparamagnetic iron oxide enhancement. Radiology 225 (2):527–536
8. Stadnik TW, Everaert H, Makkat S et al (2006) Breast imaging. Preoperative breast cancer staging: comparison of USPIO-enhanced MR imaging and 18F-fluorodeoxyglucose (FDC) positron emission tomography (PET) imaging for axillary lymph node staging–initial findings. Eur Radiol 16 (10):2153–2160
9. Uematsu T, Sano M, Homma K (2001) In vitro high-resolution helical CT of small axillary lymph nodes in patients with breast cancer: correlation of CT and histology. AJR Am J Roentgenol 176(4):1069–1074
10. Vassallo P, Wernecke K, Roos N, Peters PE (1992) Differentiation of benign from malignant superficial lymphadenopathy: the role of high-resolution US. Radiology 183(1):215–220
11. van Rijk MC, Deurloo EE, Nieweg OE et al (2005) Ultrasonography and fine-needle aspiration cytology can spare breast cancer patients unnecessary sentinel lymph node biopsy. Ann Surg Oncol 13(1):31–35
12. Damera A, Evans AJ, Cornford EJ et al (2003) Diagnosis of axillary nodal metastases by ultrasound-guided core biopsy in primary operable breast cancer. Br J Cancer 89:1310–1313
13. Sapino A, Cassoni P, Zanon E et al (2003) Ultrasonographically-guided fine-needle aspiration of axillary lymph nodes: role in breast cancer management. Br J Cancer 88(5):702–706
14. Bonnema J, van Geel AN, van Ooijen B et al (1997) Ultrasound-guided aspiration biopsy for detection of nonpalpable axillary node metastases in breast cancer patients: new diagnostic method. World J Surg 21(3):270–274
15. de Kanter AY, van Eijck CH, van Geel AN et al (1999) Multicentre study of ultrasonographically guided axillary node biopsy in patients with breast cancer. Br J Surg 86(11):1459–1462
16. Duchesne N, Jaffey J, Florack P, Duchesne S (2005) Redefining ultrasound appearance criteria of positive axillary lymph nodes. Can Assoc Radiol J 56(5):289–296
17. Feu J, Tresserra F, Fábregas R et al (1997) Metastatic breast carcinoma in axillary lymph nodes: in vitro US detection. Radiology 205(3):831–835
18. Deurloo EE, Tanis PJ, Gilhuijs KG et al (2003) Reduction in the number of sentinel lymph node procedures by preoperative ultrasonography of the axilla in breast cancer. Eur J Cancer 39 (8):1068–1073
19. Britton PD (1999) Fine needle aspiration or core biopsy. The Breast 8:1–4
20. Britton PD, McCann J (1999) Needle biopsy in the NHS Breast Screening Programme: How much and how accurate? The Breast 8:5–11
21. Motomura K, Inaji H, Komoike Y et al (2001) Gamma probe and ultrasonographically-guided fine-needle aspiration biopsy of sentinel lymph nodes in breast cancer patients. Eur J Surg Oncol 27(2):141–145
22. Goldberg BB, Merton DA, Liu JB et al (2004) Sentinel lymph nodes in a swine model with melanoma: Contrast-enhanced lymphatic US. Radiology 230:727
23. Suga K, Yuan Y, Okada M et al (2004) Breast sentinel lymph node mapping at CT lymphography with iopamidol: preliminary experience. Radiology 230 (2):543–552
24. Topal U, Punar S, Taşdelen I et al (2005) Role of ultrasound-guided core needle biopsy of axillary lymph nodes in the initial staging of breast carcinoma. Eur J Radiol 56:382–385
25. Krag DN, Anderson SJ, Julian TB et al (2007) Technical outcomes of sentinel lymph node resection and conventional axillary lymph node dissection in patients with clinically negative breast cancer: results from the NSAPB B-32 randomised phase III trial. Lancet Oncol 8:881–888
26. Goyal A, Newcombe RG, Chhabra A et al (2006) Factors affecting failed localisation and false-negative rates of sentinel node biopsy in breast cancer–results of the ALMANAC validation phase. Breast Cancer Res Treat 99 (2):203–208
27. Kuenen-Boumeester V, Menke-Pluymers M, de Kanter AY et al (2003) Ultrasound-guided fine needle aspiration cytology of axillary lymph nodes in breast cancer patients. A preoperative staging procedure. Eur J Cancer 39:170–174
28. Krishnamurthy S, Sneige N, Bedi DG et al (2002) Role of ultrasound-guided fine-needle aspiration of indeterminate and suspicious axillary lymph nodes in the initial staging of breast carcinoma. Cancer 95:982–988