

Comparative Study of Core Needle Biopsy and Fine Needle Aspiration Cytology in Palpable Breast Lumps: Scenario in Developing Nations

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ABSTRACT

Objective: The purpose of this study was to evaluate the utility of core needle biopsy as a diagnostic tool for palpable breast lumps in developing countries as compared to fine needle aspiration cytology.

Material and Method: All patients attending the surgery outpatient department with palpable breast lumps were subjected to fine needle aspiration cytology and core needle biopsy by the same operator in a single session. Fine needle aspiration cytology was performed by the standard technique. Core needle biopsy was done freehand using a 14G manual core biopsy needle. Reporting categories of the two techniques were taken from the standard National Health Service Breast Screening Programme criteria and were compared with the final histopathology results.

Results: A total of 107 patients underwent fine needle aspiration cytology and core needle biopsy simultaneously. Histopathology was available for 85 cases. Statistical analysis of fine needle aspiration cytology and core needle biopsy showed no significant difference between the diagnoses offered by core needle biopsy and histopathology while there was a significant difference between fine needle aspiration cytology and histopathology diagnoses.

Conclusion: Core needle biopsy detected more breast carcinomas as compared to fine needle aspiration cytology with a sensitivity 95.83% as opposed to 64.58%. Though both the techniques were equally specific (100%), Core needle biopsy was able to correctly categorize borderline / inadequate lesions into definitely benign and malignant categories. We suggest that core needle biopsy should be preferred over fine needle aspiration cytology for the diagnosis of palpable breast lumps with fine needle aspiration cytology being reserved for definitely benign lesions.

Key Words: Fine needle aspiration, Core needle biopsy, Breast carcinoma

INTRODUCTION

Breast carcinoma is one of the leading causes of cancer in women worldwide both in developed and developing countries. Due to lack of breast screening practices in developing nations, patients present with palpable breast lumps. Studies regarding the comparison of core needle biopsy (CNB) and fine needle aspiration cytology (FNAC) in palpable breast lumps within the same patient population are relatively scarce whereas those of screen-detected breast lesions are plenty. We therefore decided to evaluate the utility of CNB as a routine diagnostic procedure for palpable breast lumps as compared to FNAC.

MATERIAL and METHODS

This prospective study was conducted in a tertiary care hospital over a period of two years. Study subjects were all patients attending the surgery outpatient department

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(OPD) for breast pathology. A detailed clinical history and examination was done using a standardized proforma. Patients with a positive clinical examination (palpable breast lump/nodularity) were subjected to simultaneous FNAC and CNB by the same surgeon (GT). Patients with palpable axillary lymph nodes were excluded from the study.

After patient selection, FNAC from the lumps was done using the method described by Frable WJ et al. (1). Both wet fixed in 95% ethanol and air-dried smears were prepared. All cytology smears were stained by May Grunwald Giemsa, Papanicolaou and Hematoxylin & Eosin stains. The average number of FNA passes recommended for adequate sampling of most palpable breast masses was two-four (2). Adequate smears were defined as aspirates containing more than four to six well visualized cell groups. A cell group can be an acinous (cluster of at least 6 cells) or a flat sheet (no fewer than 10 cells) (3).

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CNB was performed freehand/unguided on the breast lumps in a single session as FNA with a manual 14 gauge needle (Shoney Cut Biopsy Needle with 20 mm specimen notch) after informed consent and coagulation profile. Core biopsy was performed as per the procedure described (4). The specimens were fixed in 10% neutral buffered formalin for a minimum of 6 hours as recommended (5). Typically three to five samples were taken through different parts of the lesion to ensure adequacy of sampling. No more than five needle core biopsies (for a maximum aggregate length of 100 mm) were processed in one block (6). Whenever possible the cores were arranged in parallel arrays. All of the core needle biopsies were submitted for microscopic examination. At least three histological levels were prepared from each block. Additional levels were prepared as required.

The outcomes of FNAC and CNB were reported using the standard National Health Service Breast Screening Programme (NHSBSP) criteria. The diagnoses offered by FNAC and CNB were not accepted blindly and were interpreted in the light of corresponding clinical and radiological findings. Whenever there was a discrepancy in this triple assessment, appropriate action was initiated.

RESULTS

A total of 107 breast lumps were subjected to simultaneous FNAC and CNB in this study and histopathology was available for 85 cases. The patients ranged in age from 13 to 73 years (average age, 31-50 years). Lesions ranged in size from 1 cm to 15 cm. The palpable lumps had two peaks. Twenty-four cases (22.42%) had lumps of size up to 2 cm while 26 cases (24.29%) had breast lumps more than 5 cm in size. Ninety-eight patients (91.58%) had a single lump in either breast. Nine patients (8.41%) had multiple lumps, out of which 4 patients had multiple lumps in a single breast while 5 patients had lumps in both breasts.

The FNAC and CNB diagnoses for the 107 cases are shown in Table I. Specific diagnoses for the B2 and B5 categories of CNB are presented in Table II.

The comparison between FNAC and CNB diagnoses was as follows (Table III): Percent positivity of malignant diagnosis on CNB (B5) was 44.85% while that on FNAC (C5) was 30.84%. Thus CNB detected 14.01% more malignant cases than FNA. The suspicious rates for FNAC (C3&C4) expressed as a percentage of the total number of cases was 38.31% compared to the suspicious rate of CNB (B3&B4) of just 2.80%. Percentage of benign cases diagnosed on FNAC (C2) was 28.03 while that on CNB (B2) was 44.85. Thus there was a 16.82% increase in definitive benign diagnosis by CNB over FNA.

CNB and histopathology of C1 (unsatisfactory) category of FNAC: Three cases were unsatisfactory (C1) on FNAC. Their CNB and histopathology diagnoses were concordant in two cases (infiltrating duct carcinoma (IDC) and lipoma), whereas one case was upgraded from suspicious (B4) on CNB to IDC on final histopathology. Both the IDC were Grade II on histopathology.

CNB and histopathology of C2 (benign) category of FNAC: Thirty cases were benign (C2) on FNAC. CNB was done in all cases while histopathology was available for 14 cases. Cytology-CNB-Histopathology concordance was seen in eleven cases consisting of fibroadenoma (n=7) and benign phyllodes tumor (n=4). One case diagnosed as inflammatory on FNAC was given a diagnosis of fat

FNAC	Cases	%	Spe	ecific cytology d	CNB	Cases	%		
C1	3	2.80	-	-	-	-	B1	8	7.47
C2	30	28.03	Infl(6)	BBL (7)	FA (12)	BPT (5)	B2	48	44.85
C3	35	32.71	PBD(19)	PBD-A (13)	PL (1)	LC-A (2)	B3	1	0.93
C4	6	5.60	ADH/DCIS(3)	SM (3)	-	-	B4	2	1.86
C5	33	30.84	DC(25)	MC (1)	SCC (1)	MMT (1)	B5	48	44.85
			LC(3)	UC (1)	PC (1)				
Total	107	100	-	-	-	-	Total	107	100

Table I: Distribution of cases according to FNAC & CNB diagnoses

Infl: Inflammatory, BBL: Benign breast lesion, FA: Fibroadenoma, BPT: Benign phyllodes tumor, PBD: Proliferative breast disease, PBD (A): Proliferative breast disease with atypia, PL: Papillary lesion, LC-A: Low cellularity with atypia, SM: Suspicious for malignancy, DC: Duct carcinoma, LC: Lobular carcinoma, MLC: Medullary-like carcinoma, UC: Undifferentiated carcinoma, SCC: Squamous cell carcinoma, PC: Papillary carcinoma, MMT: Malignant mesenchymal tumor. C1/B1: Unsatisfactory, C2/B2: Benign, C3: Atypia probably benign, B3: Benign, but of uncertain malignant potential, C4/B4: Suspicious for malignancy, C5/B5: Malignant.

Diagnosis B2	No. of cases	%	Diagnosis B5	No. of cases	%
BBL	8	16.66	IDC	37	77.08
FCC	6	12.5	ILC	3	6.25
SA	5	10.41	IPC	1	2.08
Fat necrosis	1	2.08	МС	2	4.16
Inflammatory		10.41	MLC	1	2.08
Nonspecific	3				
Granulomatous	2				
Duct ectasia	1	2.08	SCC	1	2.08
Lipoma	1	2.08	MPT	1	2.08
FA	12	25	MMT	2	4.16
BPT	5	10.41	-	-	-
EH-UT	4	8.33	-	-	-
Total	48	100	Total	48	100

Table II: Distribution of cases according to CNB diagnosis- category B2 & B5

BBL: Benign breast lesion, **FCC:** Fibrocystic change, **SA:** Sclerosing adenosis, **FA:** Fibroadenoma, **BPT:** Benign phyllodes tumor, **EH-UT:** Epithelial hyperplasia-usual type, **IDC:** Infiltrating duct carcinoma, **ILC:** Infiltrating lobular carcinoma, **IPC:** Intracystic papillary carcinoma, **MC:** Metaplastic carcinoma, **MLC:** Medullary like carcinoma, **SCC:** Squamous cell carcinoma, **MPT:** Malignant phyllodes tumor, **MMT:** Malignant mesenchymal tumor, **B2:** Benign, **B5:** Malignant.

Table III: Comparative study of FNAC and CNB

FNAC	CNB							
	B1	B2	B3	B4	B5	Total		
C1		1		1	1	3 (2.80%)		
C2	4	24			2	30 (28.03%)		
C3	4	22	1	1	7	35(32.71%)		
C4		1			5	6 (5.60%)		
C5					33	33 (30.84%)		
Total	8 (7.47%)	48 (44.85%)	1 (0.93%)	2 (1.86%)	48 (44.85%)	107 (100%)		

FNAC: Fine needle aspiration cytology, CNB: Core needle biopsy, C1: Unsatisfactory, C2: Benign, C3: Atypia probably benign, C4: Suspicious of malignancy, C5: Malignant.

necrosis on CNB and histopathology. Two cases were discordant and were diagnosed as benign breast lesion (BBL) and benign phyllodes tumor (BPT) on FNAC but were given a diagnosis of IDC and malignant phyllodes tumor (MPT) on CNB and histopathology. Twelve cases showed cytology-CNB-radiology concordance and thus the lesions were not excised. The remaining four C2 cases showed unsatisfactory material (B1) on CNB. Since the radiology/clinical examination was benign, no further intervention was done.

CNB and histopathology of C3 (Atypia probably benign) category of FNAC: Thirty-five cases were atypical (C3) on FNAC. CNB was performed for all the 35 cases while

histopathology was available for 31 cases. Nineteen cases were classified as benign on CNB (B2) and histopathology. These were diagnosed as fibrocystic change (FCC) (n=9), sclerosing adenosis (n=3), fibroadenoma (n=1), BPT (n=1) and epithelial hyperplasia of usual type (n=4). One case diagnosed as BBL on CNB turned out to be hamartoma on histopathology. Seven cases were given a malignant diagnoses on CNB (B5) and histopathology. Six cases were IDC on CNB, with 2 cases of Grade I, 2 cases of Grade II and 2 cases of Grade III on subsequent histopathology. One case that was given a diagnosis of papillary neoplasm on FNAC was given a diagnosis of papillary carcinoma on CNB and turned out to be intracystic papillary carcinoma on histopathology. One case diagnosed as suspicious for malignancy (B4) on CNB turned out to be malignant, IDC – Grade II on histopathology.

Out of 35 cases, 4 cases were placed in the B1 (unsatisfactory) category on CNB. The subsequent histopathological diagnoses of all 4 cases turned out to be FCC.

Another case diagnosed as C3 on FNAC remained the same (B3) on CNB and could not be further classified. This patient was lost to follow up. Three cases with a B2 CNB diagnosis of chronic mastitis, duct ectasia and BBL with benign radiology were not excised for obvious reasons.

CNB and histopathology of C4 (suspicious of malignancy) category of FNAC: Six cases were suspicious (C4) on FNAC. Their CNB and histopathology diagnoses were concordant in all the cases. Four cases were diagnosed as IDC, one case as infiltrating lobular carcinoma (ILC) and one case as sclerosing adenosis. Three cases were of Grade I IDC and one case of Grade II IDC on histopathology.

CNB and histopathology of C5 (malignant) category of FNAC: Thirty-three cases were malignant (C5) on FNAC. CNB was done in all cases while histopathology was available for 31 cases. Cytology-CNB-Histopathology concordance was seen in 27 cases consisting of IDC (n=23), ILC (n=2), metaplastic carcinoma (n=1) and squamous cell carcinoma (n=1). Two cases diagnosed as ductal carcinoma on FNAC were given a diagnosis of medullary like/ IDC-NST with lymphocyte rich stroma and metaplastic carcinoma on CNB and histopathology. One case diagnosed as lobular carcinoma on FNAC turned out to be IDC on CNB and histopathology. Another case diagnosed as papillary carcinoma on FNAC was given a diagnosis of IDC with papillary features on CNB and histopathology. Out of the 25 cases of IDC, 14 cases were of Grade I, 8 cases were of Grade II and 3 cases were of Grade III on final histopathology. Two cases diagnosed as malignant mesenchymal tumor and undifferentiated carcinoma on CNB were lost to follow up and hence no histopathology was available for these cases.

Statistical analysis of FNAC and CNB was done using McNemar's Chi square test (Table IV). Cases for which final histopathology was available were analysed. They were divided into malignant (C5&B5) and non-malignant (C1-C4&B1-B4) categories for both FNAC and CNB. McNemar's Chi square for FNAC was 17; df.=1, p<0.001, i.e. highly significant. This indicates that there was a statistical difference between the diagnoses offered by histopathology and FNAC, which was also reflected by the false negative rate of FNAC of 35.41%. McNemar's Chi square for CNB was 2.00, p=0.1573, i.e. not significant. This indicates that there was no statistical difference between the diagnoses offered by histopathology and CNB, which was also reflected by the false negative rate of CNB of 4.16% and no false positive results. The sensitivity and specificity for FNAC was 64.58% and 100% respectively while that for CNB was 95.83% and 100% respectively. Positive predictive value (PPV) and negative predictive value (NPV) for FNAC was 100% and 68.51% respectively while the respective values for CNB were 100% and 94.87% in this study.

DISCUSSION

Breast carcinoma is the most common cancer in women all over India and accounts for 25% to 31% of all cancers in women in Indian cities (7). Due to lack of awareness and almost non-existent breast screening practices, patients present with palpable breast cancers, a profile very different from their counterparts in developed countries where most of the breast cancers are screen detected. Triple assessment (clinical palpation, radiology and FNA) has been the standard of care for palpable breast lumps in most centers in developing countries. Studies regarding the comparison of CNB and FNAC in palpable breast lumps within the same patient population are relatively scarce whereas those of screen-detected breast lesions are plenty. We therefore decided to test the utility of CNB as compared to FNA in palpable breast lumps.

Many surgeons are reluctant to accept the cytological report as the only criterion for performing definitive

FNAC	Histopathology		Total	CNB	Histopathology		Total
	Malignant	Non-Malignant			Malignant	Non-Malignant	
Malignant	31	0	31	Malignant	46	0	46
Non-Malignant	17	37	54	Non-Malignant	2	37	39
Total	48	37	85	Total	48	37	85

FNAC: Fine needle aspiration cytology, CNB: Core needle biopsy, Malignant : (C5/B5 category), Non-Malignant : (C1-C4/B1-B4 category).

surgery since no distinction is possible between infiltrating and non infiltrating lesions and also because certain cases of clinically apparent malignancy require preoperative chemotherapy based on estrogen and progesterone receptor (ER and PR) and c-erb-B2 status (8, 9). Percutaneous core needle biopsy (CNB) is an accurate test for sampling breast lesions and is therefore increasingly replacing fine needle aspiration cytology (FNAC) in breast diagnosis.

The sensitivity of FNAC in detecting malignancy was 64.58% in this study, which is similar to other studies of palpable breast lumps in which both FNA and CNB were done (10-15). The specificity and positive predictive value of FNAC was found to be 100% i.e., the cases that were assigned to C5 (malignant) category in fact proved to be malignant on subsequent histopathology which is comparable with other studies of palpable breast lumps (13,15). However, a significant number of cases (17) were missed/ underdiagnosed on FNAC in this study, which is reflected by the false negative rate of FNAC of 35.41% and a negative predictive value of 68.51%. They were placed in C1 (2 cases), C2 (2 cases), C3 (8 cases) and C4 (5 cases) categories. The cases that were placed in C1 and C2 categories and were later found out to be malignant on CNB were missed on FNAC due to sampling error. One case, that of malignant phyllodes tumor, deserves special mention as it was diagnosed as benign phyllodes tumor on FNAC whereas the malignant change was picked up by CNB. As stated by Jacklin et al., the accuracy of FNAC in the diagnosis of phyllodes tumor of the breast depends on an adequate and representative sample (16). Sampling problems can arise in phyllodes tumors because of the heterogeneous nature of these tumors which means that the sampling should be thorough to minimize the risk of sampling error, both with FNA and CNB.

CNB was able to correctly categorize C3 and C4 cases into either benign or malignant categories. B3 (Benign, but of uncertain malignant potential) category had only a single case as compared to the C3 category of FNAC that had 35 cases. This implies that the lesions diagnosed as borderline or suspicious (C3, C4) on FNAC should be confirmed by a biopsy, either open biopsy or minimally invasive core biopsy, a view also supported by other authors (11, 17-24). Besides, none of the cases placed in the B2 category were found out to be malignant on FNAC/histopathology. Also none of the B4 cases had a malignant FNAC diagnosis. Thus FNAC was unable to improve upon any of the diagnoses offered by CNB in any of the categories. On the contrary, CNB improved the preoperative diagnosis more often than did FNAC, a finding also observed in other studies (14, 15, 25). This was also reflected in the statistical analysis using McNemars Chi-square test where there was a concordance between the diagnoses offered by CNB and histopathology, whereas any discordance between FNAC and histopathology diagnoses was quite apparent.

CNB detected more breast carcinomas as compared to FNAC in this study with a sensitivity of 95.83%, which is comparable to other studies of palpable breast lumps (8,10-13, 15, 26). The specificity and positive predictive value of CNB was found to be 100%, i.e., the cases that were assigned to B5 (malignant) category in fact proved to be malignant on subsequent histopathology, a finding also observed in other studies of palpable breast lumps (8, 13, 14, 26, 27).

Typing of breast carcinomas on CNB co-related well with the final histopathological diagnoses in all the cases while grading was not attempted. Other studies have also found typing of breast carcinoma to be more accurate than grading on core biopsy (11, 28). Thus grading of breast carcinomas is not mandatory on CNB or on FNAC, a view also proposed by a recent review article (29).

The inadequate rate (category B1) of CNB in this study was 7.47%. This inadequate rate was slightly higher than that seen in the studies of Shannon et al. and Poon and Kocjan who report an inadequate rate of 5% and 2.3% respectively (11, 14). FCC was the final histopathological diagnosis in half of the cases that were missed on CNB and placed in C3 (Atypia probably benign) category of FNAC. Thus the rubbery consistency of the lesions made the CB needle to slip, making procurement of tissue difficult and yielding an inadequate core of tissue. Comparing the inadequate rates of CNB and FNAC by Pearson's Chi square test (p=0.122) showed no statistical difference between CNB and FNAC as far as the number of reported inadequate cases were concerned.

In this era of neoadjuvant therapy and personalised medicine, ancillary immunohistochemical (ER, PR, cerb2) and molecular tests can be more reliably and easily performed on CNB than on FNAC (23, 30). CNB is also more robust in distinguishing between invasive lobular and invasive ductal carcinoma, based on histological and immunohistochemical features. This distinction has important clinical implications. Also, CNB contains RNA/ DNA in sufficient quantity and quality for molecular testing, which can be difficult to obtain in the case of FNAC which has limited yield.

Regarding cost effectiveness, FNAC is fast and therefore must be preferred for some palpable, probably benign lesions, staging of breast carcinoma, in particular preoperative axillary lymph node FNAC, and the diagnosis of metastatic disease. In the case of (potential) malignancy, the speed advantage of FNAC over CNB seems irrelevant in view of the required multidisciplinary meeting to arrive at a therapy plan. An interesting study showed that an indefinite diagnosis using FNAC required additional CNB and surgical excision biopsies in 32% and 21% of cases respectively (31). Another large meta-analysis assessing the diagnostic value of FNAC for breast mass concluded that underestimation rate for FNA is 27.5% with C1 cytological analysis requiring further core biopsies/open surgical biopsy to minimize the chance of missing breast cancer (32). Also since CNB is an OPD procedure which is less costly and minimally invasive as compared to an open biopsy, it can be used in place of an open biopsy whenever tissue diagnosis is needed in cases of indeterminate FNAC. Therefore, FNAC, though much cheaper as a single procedure, is likely to be more expensive overall to obtain a definitive diagnosis.

To conclude, taking into account the benefits and limitations of both techniques, we argue that CNB should be preferred over FNAC for the diagnosis of palpable breast lumps with FNAC being reserved for definitely benign lesions. Freehand CNB detects more breast carcinomas as compared to FNAC in palpable breast lumps. and correctly categorizes borderline / inadequate breast lumps on FNAC into benign & malignant categories, thus reducing indeterminate results and treatment delays. It can therefore be used as an alternative to open biopsy.

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