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FREEHAND VERSUS ULTRASOUND GUIDED CORE NEEDLE BIOPSY OF PALPABLE BREAST MASSES: A PROSPECTIVE RANDOMIZED STUDY

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Abstract:

Background: The most common malignancy diagnosed in women worldwide is carcinoma breast, accounting for more than 1 in 10 new cancer diagnoses each year. Nowadays, percutaneous core needle biopsy is a reliable alternative to surgical biopsy as it provides adequate sample for histological analysis. **Aim:** To verify the improved diagnostic accuracy of ultrasound guided over freehand core needle biopsy in palpable breast masses and to determine the factors associated with false negative freehand biopsies in palpable breast masses. **Methods:** Prospective randomized study was conducted in Post graduate department of General Surgery, Pathology and Radiodiagnosis, Government Medical College Jammu from November 2019 to October 2020. A total of 40 women presenting to the department of general surgery meeting the inclusion criteria were included in the study. Patients were equally randomized into freehand and ultrasound guided core needle biopsy arms, 20 patients each, with the help of computer generated randomization application. The study protocol was approved by the institutional ethical committee of the Government Medical College Jammu. A detailed history was recorded and complete physical examination was done. All biopsies were performed under local anaesthesia using 14 gauge automated core biopsy needles. Ultrasound by a single operator was used for image guidance. **Results:** Mean value of age (years) of study subjects was 45.38 ± 10.9 with median (25th-75th percentile) of 45(38-51). In 52.50% and 45% of patients, left and right side was involved respectively. Both sides were involved in only 1 out of 40 patients (2.50%). Concordance was seen in majority of patients in Freehand and USG guided biopsy; 75% in freehand and 95% in USG guided and discordance was seen in 25% of patients in freehand and 5% of patients in USG guided with no significant difference in them (p value=0.182). Core needle biopsy (CNB) HPE reported malignancy in majority of patients in Freehand and USG; 50% in freehand and 55% in USG. Benign pathology was found in 40% of patients in freehand and 45% of patients in USG. CNB HPE report was inconclusive in very few patients; 10% of patients in freehand and 0% of patients in USG. Sensitivity (95% CI) was comparable in free hand and USG (83.33% vs 91.67% respectively, p value = 0.774). Diagnostic accuracy was comparable in free hand and USG (88.89% vs 95% respectively, p value = 0.924). **Conclusion:** We conclude that whenever available, USG guided core needle

biopsy should always be preferred over freehand biopsies to maximize the diagnostic accuracy and obviate the need for repeat biopsies. However, in the absence of imaging modalities, only those breast mass biopsies should be done by freehand which are unlikely to be missed.

Keywords: Breast biopsy, breast cancer, ultrasound guided, freehand core needle biopsy.

Introduction:

The most common malignancy diagnosed in women worldwide is carcinoma breast, accounting for more than 1 in 10 new cancer diagnoses each year. An estimated 1.67 million women across the world were diagnosed with breast cancer in 2012, accounting for 25% of all cancers in women**. [1]**In 2019, an estimated 268,600 new cases of invasive breast cancer have been diagnosed among women and approximately 2,670 cases been diagnosed in men. It is the second most common cause of death from cancer among women in the world.

Due to lack of screening modalities, most of the patients in developing countries present with a palpable breast lump. Although the majority of palpable lumps are benign, a new palpable breast mass is a common presenting sign of breast cancer**. [2]**

Clinical breast examination (CBE) is recommended as the initial tool for assessing breast diseases. Despite its accuracy, clinical breast examination alone is not adequate for definitive diagnosis of breast cancer**.[3]**

Triple assessment is the combination of results from clinical breast examination, imaging and tissue sampling. When the three assessments are performed adequately and produce concordant results, the triple test diagnostic accuracy approaches 100 percent**.[4]** Triple test score was developed to help physicians interpret discordant results**. [5]**

Nowadays, percutaneous core needle biopsy is a reliable alternative to surgical biopsy. Core needle biopsy provides adequate sample for histological analysis. Compared with FNA, it takes more time and requires specific training and patient anesthesia, but has a higher positive predictive value for suspicious and atypical results and may provide an overall cost benefit**.[6]** As compared to open surgical biopsy, it has several advantages like better patient tolerance, better cosmetic outcome and low cost**. [7]** It is less invasive than surgery can be performed quickly and complications are rare. The histological material from a core biopsy can also be used to determine estrogen, progesterone and HER 2 neu receptor status. Multiple tumour tissue samples can be taken in core needle biopsy due to increased cross section diameter, with an amount of up to 20 mg for which the diagnostic process is easier. It is reported that an accuracy rate of up to 90.1% can be achieved with the first core needle biopsy sample. The thickness of the needles can be selected, varying from 18 to 8 gauge. Introduction of 14G core biopsy needle and automated large core biopsy gun improves diagnostic efficacy and the procedure becomes easier**.[8]**In 2010, the European Society of Breast Cancer Specialists, EUSOMA, suggested that 90% of all the women with breast cancer (invasive or ductal carcinoma in situ) should have a preoperative diagnosis by means of percutaneous biopsy**.[9]**The ability to obtain a diagnosis of cancer prior to surgery can allow for proper pre-

operative planning with concomitant staging of the axilla, decrease the subsequent positive margin rate, and thus decrease the re-excision rate.

Methods:

The present study was conducted in the Department of General Surgery, in collaboration with department of Pathology and Radiodiagnosis at Government Medical College Jammu over a period of 1 year from 1st November 2019 to 31st October 2020.

All patients presenting with palpable breast masses meeting the inclusion criteria and not falling into any of the exclusion criteria were included in the study. The study protocol was approved by the institutional ethical committee of the Government Medical College Jammu. A detailed history was recorded and complete physical examination was done. Patients were subjected to ultrasound examination and/or mammography and BIRADS categories were assigned. Masses which were reported as definitely benign on imaging were excluded. Thus patients with BIRADS 3, 4 and 5 were included. Patients were equally randomized into two arms of freehand and ultrasound guided core needle biopsy arms with the help of computer generated randomization application. Procedure was explained to them in detail and informed written consent was taken.

All biopsies were performed under local anaesthesia using 14 gauge automated core biopsy needles. Ultrasound by a single operator was used for image guidance. On ultrasound guided biopsy, visualization of needle tip in the lesion was assured. An average of 7-10 cores were taken. Adequacy of cores was assessed visually based on size, consistency and grade of immersion of the samples. Histopathological results were related with clinical and imaging findings to establish imaging-histologic concordance. Inconclusive, suspicious or imaging-histologic discordant biopsies were repeated. All repeat biopsies were USG guided. Those with concordant findings were offered definitive treatment. The patients with benign findings who were managed conservatively were advised for regular follow ups.

OTHER PARAMETERS ASSESSED IN THE STUDY:

- Age of the patient
- Laterality of the mass
- Location of the mass
- Size of the mass
- Duration of symptoms
- Depth of the lesion.

Statistical analysis:

The presentation of the categorical variables was done in the form of number and percentage (%). The presentation of the continuous variables was done as mean ± SD and median values. The comparison of the variables which were qualitative in nature was analyzed using Fisher's Exact test. Chi square test was used for comparing sensitivity and diagnostic accuracy. Inter-rater kappa agreement was used to find out the strength of agreement between freehand and

USG with final biopsy report. Univariate logistic regression was used to find out factors affecting concordance rate in free hand and USG.

The data entry was done in the Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) for software version 21.0, Inc, Chicago, USA. For statistical significance, p value of less than 0.05 was considered as significant.

Results:

37.50% of patients belonged to age group <=40 years age group and 41-50 years age group each followed by 51-60 years (15.00%). Age group was >60 years in only 4 out of 40 patients (10.00%) [Table 1].

Table 1:-Distribution of age (years) of patients with breast masses

Age (years)	Frequency	Percentage
<=40	15	37.50%
41-50	15	37.50%
51-60	6	15.00%
>60	4	10.00%

In majority (50.00%) of patients, location was upper outer quadrant followed by lower outer (17.50%), lower inner (12.50%), upper inner (10.00%) and retroareolar area (5.00%). Location was upper and retroareolar and upper inner and retroareolar in only 1 out of 40 patients (2.50%) each [Table 2].

Table 2:-Distribution of location of breast masses

Location	Frequency	Percentage
Lower inner	5	12.50%
Lower outer	7	17.50%
Retroareolar	2	5.00%
Upper and retroareolar	1	2.50%
Upper inner	4	10.00%
Upper inner and retroareolar	1	2.50%
Upper outer	20	50.00%

55% of the patients presented with a lesion at a depth of >4-6mm followed by 20% who presented with a lesion at a depth of >2-4mm. Mean value of depth (mm) of study subjects was 6.28 ± 3.83 with median (25th-75th percentile) of 5(4.875-6) [Table 3].

Table 3:-Descriptive statistics of depth (mm) of breast masses

Depth (mm)	Frequency	Percent
<=2	Nil	0%

>2-4	8	20%
>4-6	22	55%
>6-8	4	10%
>8	6	15%

Concordance was seen in majority of patients in Freehand and USG guided biopsy; 75% in freehand and 95% in USG guided and discordance was seen in 25% of patients in freehand and 5% of patients in USG guided with no significant difference in them. (p value=0.182) [Table 4].

Table 4:-Comparison of concordance between Freehand and USG guided biopsy with BIRADS

Concordance with BIRADS	Freehand n(%)	USG n(%)	Total	P value
No	5 (25%)	1 (5%)	6 (15%)	0.182*
Yes	15 (75%)	19 (95%)	34 (85%)	
Total	**20 (100%)**	**20 (100%)**	**40 (100%)**	

***-Fisher Exact test**

CNB HPE reported malignant pathology in majority of patients in Freehand and USG; 50% in freehand and 55% in USG. Benign pathology was found in 40% of patients in freehand and 45% of patients in USG. CNB HPE report was inconclusive in very few patients; 10% of patients in freehand and 0% of patients in USG [Table 5].

Table 5:-Distribution of CNB HPE in Freehand and USG guided biopsy

CNB HPE	**Freehand n(%)**	**USG n(%)**	**Total**
Benign	**8 (40%)**	**9 (45%)**	**17 (42.50%)**
Inconclusive	**2 (10%)**	**0 (0%)**	**2 (5%)**
Malignant	**10 (50%)**	**11 (55%)**	**21 (52.50%)**
Total	**20 (100%)**	**20 (100%)**	**40 (100%)**

USG had sensitivity of 91.67% followed by free hand (83.33%). On the other hand, USG and free hand had specificity of 100% each. Highest positive predictive value was found in USG(100%) and free hand (100%) each and highest negative predictive value was found in

USG (88.89%). So overall USG was best predictor of malignancy.Sensitivity (95% CI) was comparable in free hand and USG (83.33% vs 91.67% respectively, p value = 0.774). Diagnostic accuracy was comparable in free hand and USG (88.89% vs 95% respectively, p value = 0.924) [Fig 1].

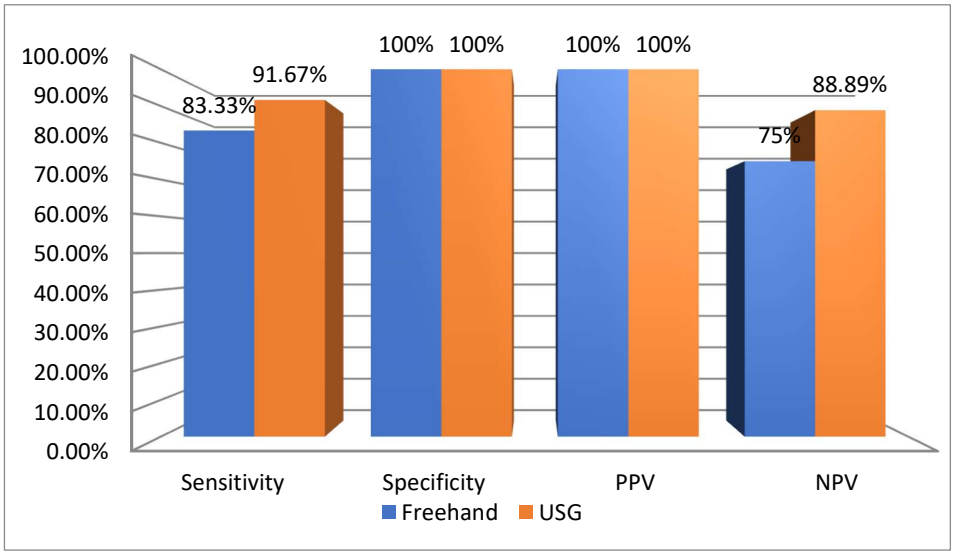

Fig 1.

There was no complication of biopsy in majority (97.50%) of patients. Haematoma was seen in only 1 out of 40 patients (2.50%) [Fig 2].

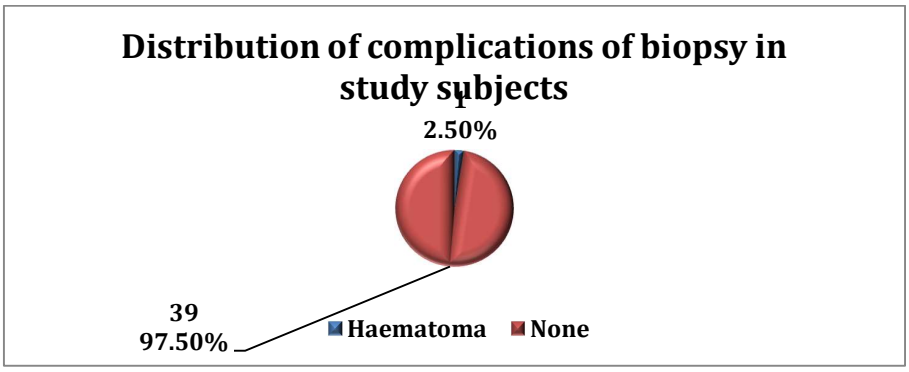

Fig 2.

Discussion:

The present study included 40 women with a mean age of 45.38±10.9 years and median age of 45 years. **Youk JH *et al.*, (2008)[10]** in their study "Sonographically guided 14- gauge core needle biopsy of breast masses", conducted in Seoul, South Korea, included 2420 patients in the age group of 12-88 years, with the mean age of 45.3 years and median age of 45 years.

In our study the mean diameter of the lump biopsied in the study group was 4.09± 2.04 cm with the range of the lumps being 1-8 cm. The mean diameter is comparable to the study by **Hari S *et al.*, (2016) [11]** in which the mean diameter of the lump undergoing image guided

biopsy was 4cm with the range of 1-13 cm and in those undergoing palpation guided biopsy, the mean diameter was 4.4cm and the range being 2-13 cm.

In our study, among the 20 freehand biopsies, 10 (50%) were malignant, 8 (40%) were benign and 2 (10%) came out to be inconclusive. Out of the 8 benign biopsies 5 were concordant with BIRADS whereas 3 were discordant which were subsequently subjected to re-biopsy. The re-biopsy result came out to be malignant for 2 patients and benign for 1 patient. In the 2 inconclusive freehand biopsy results, the re-biopsy turned out to be malignant for 1 patient and benign for another. Amongst the 20 USG guided biopsies, 11 were malignant and 9 were benign. There was no case of inconclusive biopsy. Only 1 biopsy out of the 9 benign biopsies came out to be discordant with BIRADS whereas 8 were concordant. The re-biopsy in the patient with discordant result turned out to be malignant.

Hari S *et al.*, (2016) [11] divided their study population in two groups which included 36 patients each. In the palpation guided biopsy group, the biopsy results turned out to be malignant for 14 patients, benign for 13 patients, inconclusive for 7 patients and suspicious for 2 patients. The biopsy results for10 patients in the benign group were discordant with BIRADS and on re-biopsy turned out to be malignant. The 7 inconclusive biopsy results on re-biopsy turned out to be malignant for 4 patients and benign for 3 patients. The 2 suspicious biopsy results on palpation guided biopsy turned out to be malignant for both the patients. In the image guided biopsy group of 36 patients, the results were malignant for 26 patients, benign for 9 patients and suspicious for 1 patient. The re-biopsy of suspicious patient came out to be malignant.

Dillon MF *et al.*, (2005) [12] in their study "The accuracy of ultrasound, stereotactic and clinical core biopsies in the diagnosis of breast cancer, with an analysis of false negative cases" conducted in Dublin, Ireland, performed core biopsies in a total of 2427 patients. Out of 2427 core biopsies, 1228 were diagnosed with malignant disease, 1008 had benign disease & 191 patients demonstrated atypical disease. On re-biopsy, 1384 patients had a final diagnosis of malignant disease, 954 were diagnosed with benign disease and 89 with atypical disease.

In the present study, ultrasound guided core needle biopsy had a sensitivity of 91.67% for predicting malignancy whereas freehand biopsies had a sensitivity of 83.33%, proving USG guided biopsies to be superior than freehand biopsies. Both the USG guided and freehand biopsies had specificity of 100 % each. Highest positive predictive value was 100% for both USG guided and freehand biopsies. The highest negative predictive value was found in USG guided biopsies (88.89%). So overall, USG guided biopsy was the best predictor of malignancy. Sensitivity (95% CI) was comparable in freehand and USG guided biopsies (83.33% vs 91.67% respectively, p value= 0.774). Diagnostic accuracy was comparable in free hand and USG guided biopsies (88.89% vs 95% respectively, p value = 0.924).

Good agreement exists between final biopsy report and freehand biopsy with kappa= 0.769 and p value=0.001.Overall concordance rate was 88.89% and overall discordance rate was 11.11% between final biopsy report and freehand biopsy report.

Very good agreement exists between final biopsy report and USG guided biopsy report with kappa= 0.898 and p value=0.0001. Overall concordance rate was 95% and overall discordance rate was 5% between the final biopsy report and USG guided biopsy report.

In the study by **Hari *et al.*, (2016) [11]** the sensitivity of image guided biopsy for diagnosing a malignant lesion was 96.3% (26 of 27; 95% CI, 81- 99.4%). On the other hand, palpation guided biopsy group yielded sensitivity of 46.7% (14 of 30; 95% CI, 28.4- 65.7%). Specificity as well as positive predictive value in both the groups was 100% for diagnosis of malignancy. There was a significant ($p<0.001$) difference in negative predictive value between both the groups for diagnosis of malignancy; 90% (9 of 10; CI, 55.4- 98.3%) in the image guided biopsy group as against 27.3% (6 of 22; CI, 10.8- 50.2%) in the palpation guided biopsy group. In the study by **Dillon MF *et al.*, (2005)[12]** the false negative rate for each biopsy modality was 1.7% (13 of 769) for ultrasound guided biopsy, 8.9% (16 of 179) for stereotactic guided cores and 13% (56 of 436) for clinically guided cores.

The complications of the core needle biopsy are infrequent and not significant. In the present study, there was no complication of biopsy in majority (97.50%) of patients. Hematoma was seen in only one out of 40 patients (2.50%). The results of our study are broadly consistent with the results published by other studies in this parameter.

Parker SH *et al.*, (1994) [13] in their study "Percutaneous large core breast biopsy: a multi-institutional study", described that both hematoma and infections are very rare, accounting for less than 1/1000 biopsies.

O'Connor A *et al.*, (2002) [14] in their study "Complications of breast core biopsy", conducted in Perth, Australia, also demonstrated that serious complications related to the breast core biopsy are rare. The commonest problem is bleeding, which is usually easy to control at the time of procedure. Rarer complications include infection and abscess formation, pneumothorax, milk fistula formation, cosmetic deformity and seeding of tumour along the biopsy track.

Conclusion:

On completion of our study, we found that USG guided core needle biopsy is superior to free hand biopsy in terms of sensitivity, false negative rates, negative predictive value, accuracy and repeat biopsy rates. The higher false negative rates or inconclusive results with freehand biopsy results in repeated procedures with increased costs and diagnostic delays.

These false negative rates are due to multiple factors, including sampling from inappropriate sites. There was found a significant statistical association between false negative biopsy and depth of the lump, deeper lumps being more likely to be missed by palpation alone. Also biopsy in younger women with denser breasts and those with smaller lumps are more likely to be missed on palpation alone. However, no statistical association with these factors was seen in our study. The patients who present late with large malignant masses, having gross edema, induration and peritumoral infiltration making it difficult to differentiate these changes from true tumour mass on palpation are also likely to get false negative results.

We conclude that whenever available, USG guided core needle biopsy should always be preferred over freehand biopsies to maximize the diagnostic accuracy and obviate the need for repeat biopsies. However, in the absence of imaging modalities, only those breast mass biopsies should be done by freehand which are unlikely to be missed.

To reduce the burden on radiologists and delays in performing the procedure and obtaining the diagnosis, ultrasound guided biopsy can be carried out by the surgeons themselves in their own setting/ department.

Conflict of interest: Nil

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