



EVALUATION OF BENIGN BREAST DISEASE, ITS CLINICAL PRESENTATION, INDICATIONS FOR MAMMOGRAPHY AND BIOPSY, RESULTS OF TREATMENT

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ABSTRACT

BACKGROUND- Benign breast disease is a neglected entity despite the fact that it constitutes the majority of breast complaints. Breast cancer has taken precedence over benign breast disease since it is more fearsome although the number of females with benign breast diseases is substantial. Benign breast diseases can occur any time during the life span of a female, though its manifestation in a male is limited. The incidence of suspicious benign breast diseases and those benign breast diseases which are not reacting to medical line of management is still unknown and requires evaluation. Another important question remains is the risk of malignancy associated with these lesions. Correlation of histologic and imaging findings is essential for providing appropriate recommendations regarding risk management. Occasionally, pathologic findings may not be concordant with the imaging findings noted by the radiologist and the malignancy can be missed resulting in delayed diagnosis of breast cancer. To investigate these questions this study was conducted to evaluate benign breast diseases with their clinical features and finding out the risk of malignancy associated with suspicious breast lesions and benign breast diseases which are not reacting to medical treatment. This study also aims at finding out the role of mammography and biopsy in benign breast diseases, finding out the chance of malignancy which can be missed by mammography and biopsy and finding out those high risk lesions which need regular follow up for subsequent development of breast cancer.

MATERIAL AND METHODS- This was a prospective study carried out at AVBRH, Sawangi, (Meghe) over a period of about 2 years starting from Oct. 2015 to Sept. 2017. All female patients visiting the surgical clinic with breast problems were included in the study. Patients who on clinical examination are diagnosed as carcinoma are excluded from the study. Only those benign breast diseases which were not reacting to medical treatment and when there was suspicion for malignancy clinically were included in the current study. During the course of study, a total of 120 female patients presented with breast diseases were examined clinically. When there was suspicion for malignancy (without a definitive signs of malignancy) and when benign breast diseases were not reacting to medical treatment underwent diagnostic mammography followed by USG guided true cut biopsy. The mammography and true cut biopsy reports were collected. Subsequently excisional biopsy in all these cases were done (except two cases of tuberculous mastitis and 20 cases of invasive ductal carcinoma on true cut biopsy). All the excised specimen obtained were subjected to histopathology. The collected reports of mammography and true cut biopsy were correlated with the final histopathological report. Patients were assessed periodically, and were followed for 3 months during

study period clinically. The response to treatment was assessed clinically. Data is entered on pre-designed proforma and informed written consent were taken from all the patients before including in the study.

RESULTS- The overall age of the patients ranged from 19 yrs to 75 yrs. The maximum no. of patients n=50(41.67%) were found in the age group of 29-38 yrs. In the present study of 120 patients with benign breast diseases clinically, 72 (60%) patient had right sided breast involvement while 47 (39.17%) patient had left breast involvement whereas bilateral involvement was seen in 1 (0.83%) patient. In the present study, among total 120 patients of benign breast diseases clinically, it was found that upper outer quadrant was involved most commonly constituting 51 (42.50%) cases followed by upper inner quadrant constituting 39 (32.50%) cases. It was found that there were 66 (55%) patients of benign breast disease not reacting to medical treatment and 54(45%) patients had suspicion for malignancy on first clinical examination. There were 7 cases which were high risk lesions and require intensive surveillance. There were total 28 cases of malignancy in the present study out of which 8 cases were missed by mammography and true cut biopsy but had clinical

suspicion for malignancy. The sensitivity of true cut biopsy was 71.43%. The specificity was 100%, positive predictive value was 100%, negative predictive value was 91.84% and diagnostic accuracy was 93.22%. The false negative rate in this study was 8.16%. The sensitivity of mammography was 60.71%, specificity was 100%, positive predictive value was 100%, negative predictive value was 89.11%, diagnostic accuracy was 90.6%. The false negative rate in our study was 10.89%. The probability of malignancy in BIRADS II in the present study was 3.70%, 3.22% in BIRADS III, 57.14% in BIRADS IV and 100% in BIRADS V. Complete response was seen in 63 (68.48%) patients after the medical treatment in the present study. There were 21 (22.83%) patients who showed partial response and no response was seen in 8 (8.70%) patients.

INTRODUCTION

Benign breast disease is a neglected entity despite the fact that it constitutes the majority of breast complaints.^[1] Breast cancer has taken precedence over benign breast disease since it is more fearsome although the number of females with benign breast diseases is substantial. Benign breast diseases can occur any time during the life span of a female, though its manifestation in a male is limited.

Breast is a dynamic structure, which undergoes changes throughout women's reproductive life, and superimposed on this cyclical changes throughout menstrual cycle. The pathogenesis involves disturbance in breast physiology extending from an extreme normality to well defined disease process.

India with its multilingual, and multiethnic society has reported breast cancer as the commonest cancer in urban Indian females, and the second commonest in the rural Indian women (ICMR, 2016). As per the ICMR-HBCR data, breast cancer is the commonest cancer among women in urban registries of Delhi, Chandigarh, Mumbai, Chennai, Guwahati, and Trivandrum where it constitutes 20 - 30% of all cancers in female.^[2] Benign breast disease is the most common cause of breast problems in females and it is more frequent than the malignant ones^[3-8].

The main problem from patient of view is fear that such lump may be a cancer. The clinician must therefore provide a degree of diagnostic accuracy. Most women with a clinically suspicious palpable lump need an imaging and histologic evaluation. Ultrasound and mammography, when used appropriately, are effective and safe for triage of most women to clinical follow-up, a small portion to imaging follow-up, and the minority to image-guided core needle biopsy^[9-11]. These primary imaging modalities and minimally invasive needle biopsy techniques play a central role in reducing costs and morbidity associated with unnecessary advanced imaging (e.g., MRI) and surgery in this specific patient population.

Breast lesions have many subtypes. But there are certain lesions which raises suspicion of malignancy. These lesions must be diagnosed early and malignancy must be ruled out. To make an early diagnosis of breast cancer, the physician must have a high degree of suspicion regarding all breast lesions, as well as a basic knowledge of the following factors:

- (1) the common types of breast lesions and their relative frequency;
- (2) the age periods at which these lesions usually occur;
- (3) the characteristic symptom complexes and features favouring malignancy;
- (4) the various high risk lesions that increase a patient's chance for developing breast cancer in future.

During the past decade there has been increasing interest in benign breast diseases for number of reasons:-

1. Patients started demanding investigation and treatment for the benign breast diseases. These have participated in scientific studies, classification and treatment of their conditions.

2. There is a question of pre-malignant disorders and histological features, which imply an increased risk of breast cancer. Increasing understanding of these conditions may prove important in understanding the pathogenesis of breast cancer and defining the high risk groups in whom regular surveillance may be beneficial.

It is well known that certain types of nonmalignant lesions predispose patients to increased risk of developing breast cancer. **Dupont and Page^[159]** were the first to retrospectively review benign breast biopsies and determine the inherent risk they presented. Over 10,000 specimens were divided into three groups: nonproliferative lesions, proliferative lesions without atypia, and proliferative lesions with atypia. Their findings suggested a 1.9 times greater risk for proliferative lesions without atypia and 5.3 times greater risk for proliferative lesions with atypia.^[159]

Correlation of histologic and imaging findings is essential for providing appropriate recommendations regarding risk management. Occasionally, pathologic findings may not be concordant with the imaging findings noted by the radiologist and the malignancy can be missed resulting in delayed diagnosis of breast cancer.

Also the incidence of suspicious benign breast diseases and those benign breast diseases which are not reacting to medical line of management is still unknown and requires evaluation. Another important question remains is the risk of malignancy associated with these lesions.

To investigate these questions this study was conducted to evaluate benign breast diseases with their clinical features and finding out the risk of malignancy associated with suspicious breast lesions and benign breast diseases which are not reacting to medical treatment. This study also aims at finding out the role of

mammography and biopsy in benign breast diseases, finding out the chance of malignancy which can be missed by mammography and biopsy and finding out those high risk lesions which need regular follow up for subsequent development of breast cancer.

AIMS AND OBJECTIVES

AIMS

1. To evaluate benign breast disease clinically and its treatment and to find out indications for mammography and/or biopsy and to evaluate its impact on further treatment.

OBJECTIVES

1. To find out clinical presentation in benign breast disease.
2. To find out utility of mammography and biopsy in the treatment of benign breast disease.
3. To find out associated risk of malignancy and/or presence of malignancy.
4. To find out effectivity of medical treatment and/or surgical treatment.

MATERIAL AND METHODS

The current study was conducted at rural tertiary health care centre—Acharya Vinobha Bhave Rural Hospital, Sawangi, Wardha.

1. **Duration of study:** From October 2015 to September 2017.
2. **Study design:** Prospective study.
3. **Study population:** Attending OPD and admitted to JNMC
4. **Inclusion criteria:** All symptomatic patients of benign breast disease.
5. **Exclusion criteria**
 - A. Asymptomatic patients of benign breast disease.
 - B. Patients who on clinical examination are diagnosed as carcinoma of breast.
6. **Sample size:** 120 patients.

This was a prospective study carried out at AVBRH, Sawangi, (Meghe) over a period of about 2 years starting from Oct. 2015 to Sept. 2017. All female patients visiting the surgical clinic with breast problems were included in the study. Patients who on clinical examination are diagnosed as carcinoma are excluded from the study. Only those benign breast diseases which were not reacting to medical treatment and when there was suspicion for malignancy clinically were included in the current study. Detailed histories of patients were recorded that included age, menstrual history, past history and family history. Family history of breast diseases especially breast cancer, is recorded.

Breast was examined with respect to nipple, areola, details of the lump including size, site, surface, margins, mobility, consistency, tenderness, local temperature, nipple discharge, skin over the lump. Axilla of same side is examined for lymph nodes. The local examination was

completed only after the examination of opposite breast and axilla. Detailed examination of lump and axilla is made with especial attention to any clinical signs of malignancy.

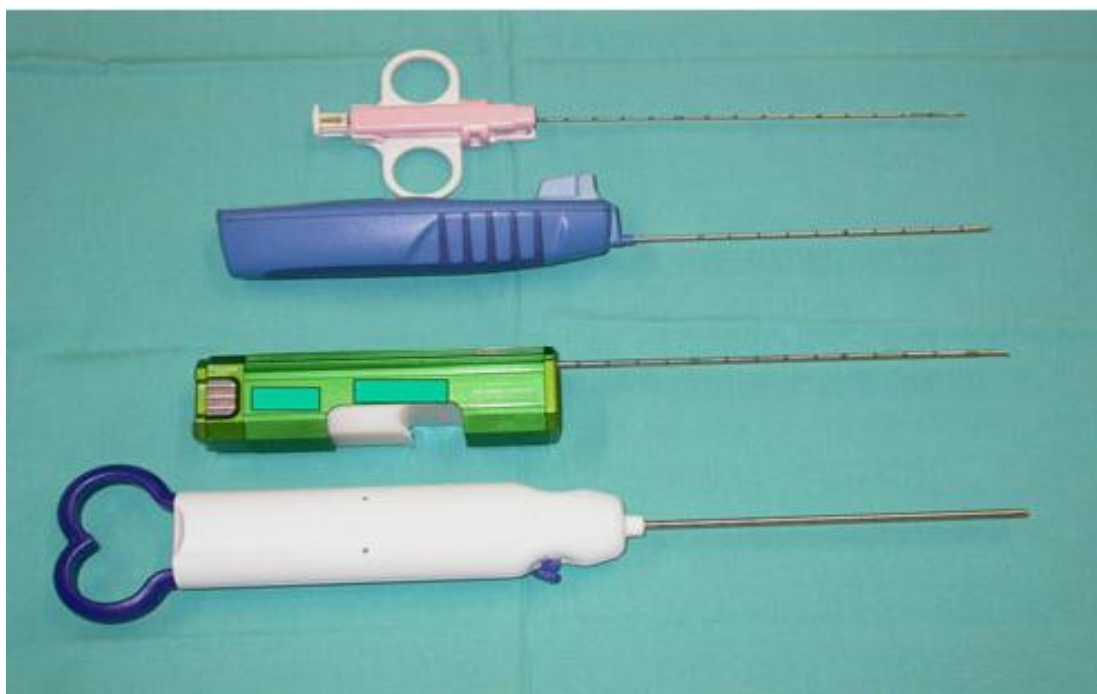
During the course of study, a total of 120 female patients presented with breast diseases were examined clinically. When there was suspicion for malignancy (without a definitive signs of malignancy) and when benign breast diseases were not reacting to medical treatment underwent diagnostic mammography followed by USG guided true cut biopsy. The mammography and true cut biopsy reports were collected. Subsequently excisional biopsy in all these cases were done (except two cases of tuberculous mastitis and 20 cases of invasive ductal carcinoma on true cut biopsy). All the excised specimen obtained were subjected to histopathology. The collected reports of mammography and true cut biopsy were correlated with the final histopathological report.

USG guided true cut biopsy was done with 18-gauge true cut biopsy needle and spring loaded automated gun under the sonographic guidance with 10-12MHz linear probe as it is cost effective and easy to use and 18 gauge needle prevents mass displacement while performing the procedure.

Patients were assessed periodically, and were followed for 3 months during study period clinically. The response to treatment was assessed clinically. Data is entered on pre-designed proforma and informed written consent were taken from all the patients before including in the study.



USG Guided true cut biopsy.



A small sample of the great variety of biopsy devices that can be used under ultrasound guidance.

OBSERVATIONS AND RESULTS

During the course of study, a total of 120 female patients presented with breast diseases were examined clinically. When there was suspicion for malignancy (without a definitive signs of malignancy) and when benign breast diseases were not reacting to medical treatment underwent diagnostic mammography followed by USG guided true cut biopsy.. The mammography and true cut biopsy reports were collected. Subsequently excisional biopsy in all these cases were done (except two cases of tuberculous mastitis and 20 cases of invasive ductal

carcinoma on true cut biopsy). All the excised specimen obtained were subjected to histopathology. The collected reports of mammography and true cut biopsy were correlated with the final histopathological report. All the patients were followed for 3 months and results were interpreted as follows:

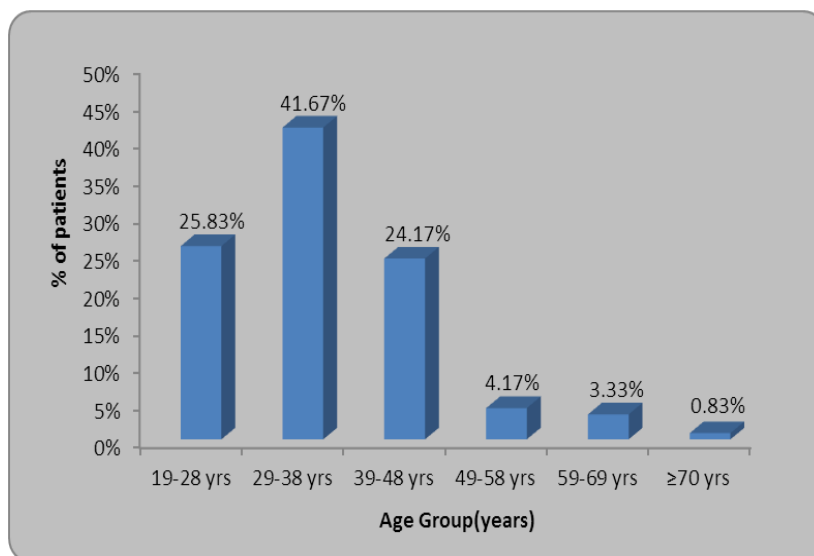
Age

The overall age of the patients ranged from 19 yrs to 75 yrs. The maximum no. of patients n=50(41.67%) were found in the age group of 29-38 yrs.

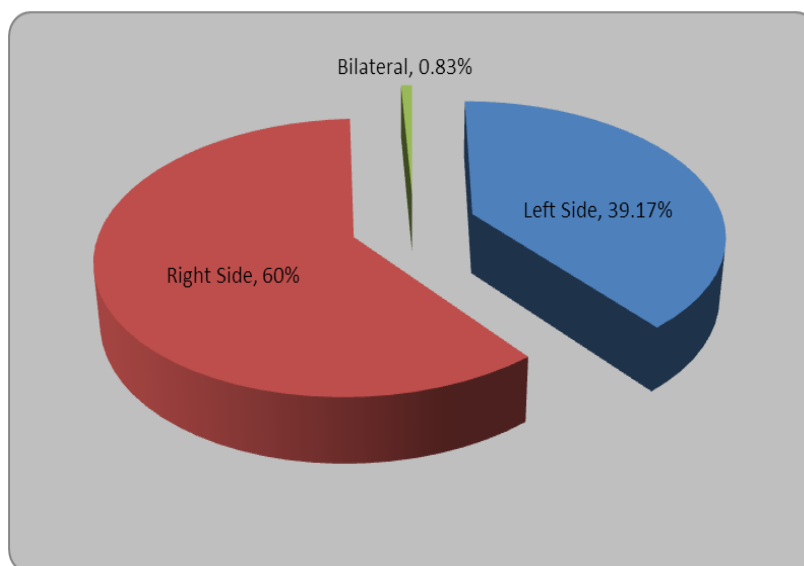
Table 1: Distribution of patients according to their age(yrs).

Age Group(yrs)	No of patients(n)	Percentage(%)
19-28 yrs	31	25.83
29-38 yrs	50	41.67
39-48 yrs	29	24.17
49-58 yrs	5	4.17
59-69 yrs	4	3.33
≥70 yrs	1	0.83
Total	120	100
Mean±SD	34.97±9.99(19-75 yrs)	

The mean age of all the patients presenting with breast diseases was found to be 34.97±9.99 yrs.

**Graph 1: Distribution of patients according to their age(yrs).****Table 2: Distribution of patients according to side of involvement.**

Side of involvement	No of patients	Percentage(%)
Left Side	47	39.17
Right Side	72	60
Bilateral	1	0.83
Total	120	100

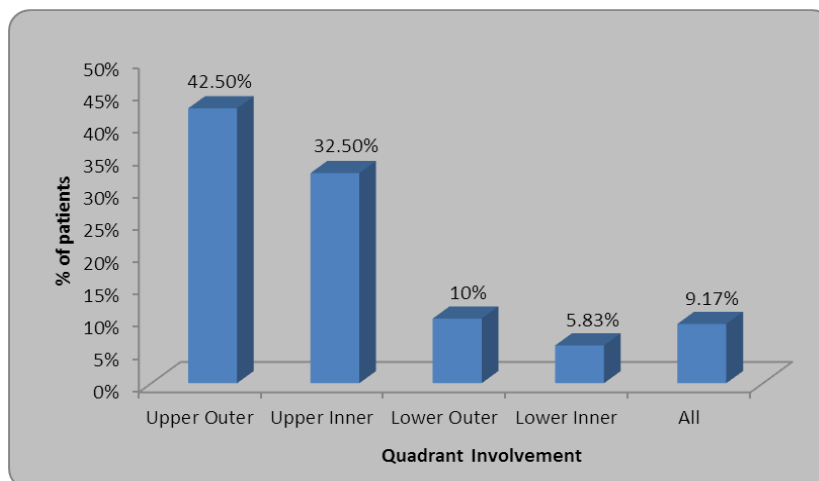
**Graph 2: Distribution of patients according to side of involvement.**

In the present study of 120 patients with benign breast diseases clinically, 72 (60%) patient had right sided breast involvement while 47 (39.17%) patient had left

breast involvement whereas bilateral involvement was seen in 1 (0.83%) patient.

Table 3: Distribution of patients according to quadrant involvement.

Quadrant involvement	No of patients	Percentage(%)
Upper Outer	51	42.50
Upper Inner	39	32.50
Lower Outer	12	10.00
Lower Inner	7	5.83
All	11	9.17
Total	120	100



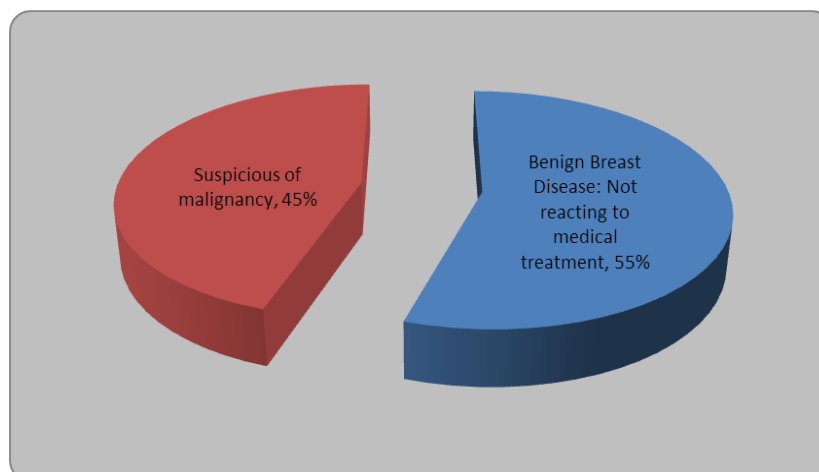
Graph 3: Distribution of patients according to quadrant involvement.

In the present study, among total 120 patients of benign breast diseases clinically, it was found that upper outer quadrant was involved most commonly constituting 51 (42.50%) cases followed by upper inner quadrant constituting 39 (32.50%) cases. The lower outer quadrant

was next commonly involved constituting 12 (10.00%) cases. Lower inner quadrant was involved in 7 (5.83%) cases. All quadrant involvement was seen in 11(9.17%) cases.

Table 4: Distribution of patients according to clinical diagnosis.

Clinical Diagnosis	No of patients	Percentage(%)
Benign Breast Disease: Not reacting to medical treatment (BBD-NRMT)	66	55.00
Suspicious of malignancy (SOM)	54	45.00
Total	120	100



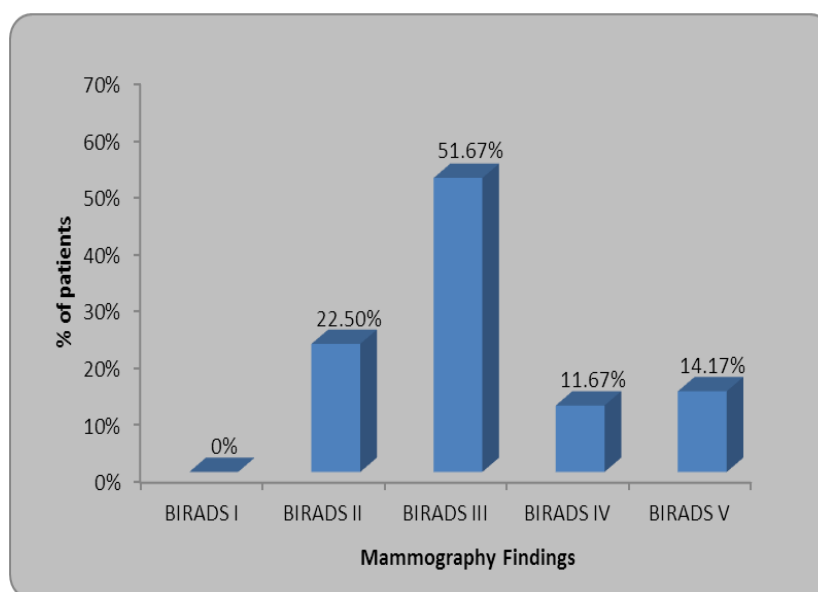
Graph 4: Distribution of patients according to clinical diagnosis.

In the present study of 120 patients, all the cases were clinically diagnosed as benign breast disease not reacting to medical treatment (BBD:NRMT) or suspicious of malignancy (SOM). It was found that there were 66

(55%) patients of benign breast disease not reacting to medical treatment and 54(45%) patients had suspicion for malignancy.

Table 5: Distribution of patients according to mammography findings.

Mammography Findings	No of patients	Percentage(%)
BIRADS 0	0	0.00
BIRADS I	0	0.00
BIRADS II	27	22.50
BIRADS III	62	51.67
BIRADS IV	14	11.67
BIRADS V	17	14.17
Total	120	100



Graph 5: Distribution of patients according to mammography findings.

In the present study, all 120 patients were subjected to mammography after the clinical diagnosis of BBD:NRMT and SOM was made. The most common mammography finding was BIRADS III seen in 62 (51.67%) patients. 27 (22.50%) patients had BIRADS II

as mammography finding. There were 17 (14.17%) patients who had BIRADS V as mammography finding, 14 (11.67%) patients had BIRADS IV as mammography finding in the present study. There were no cases of BIRADS 0 and I in the present study.

Table 6: Distribution of patients according to True Cut Biopsy Findings.

True Cut Biopsy Findings	No of patients	Percentage(%)
Acute on Chronic Mastitis	4	3.33
Atypical Ductal Hyperplasia	1	0.83
Atypical Ductal Hyperplasia with Sclerosing Adenosis	1	0.83
Benign Phylloides Tumour	9	7.50
Chronic Granulomatous mastitis	4	3.33
Chronic mastitis	2	1.67
Adipose Tissue	1	0.83
Chronic non specific granulomatous mastitis	1	0.83
Chronic non specific mastitis	2	1.67
Duct Ectasia	1	0.83
Fibroadenoma	20	16.67
Fibroadenoma with fibroadenosis	32	26.67
Fibroadenoma with fibrocystic change	1	0.83
Fibroadenosis	2	1.67

Fibrocystic change of breast	2	1.67
Fibrocystic change of breast with atypical ductal hyperplasia	1	0.83
Fibrocystic disease of breast	3	2.50
Granulomatous mastitis	3	2.50
Highly Suspicious of epithelial malignancy	1	0.83
Idiopathic Granulomatous mastitis	1	0.83
Invasive Ductal Carcinoma	20	16.67
Non Caseating Granulomatous Mastitis	1	0.83
SclerosingAdenosis	3	2.50
SclerosingAdenosis with fibrocystic change	1	0.83
Suspicious of epithelial malignancy	1	0.83
Tuberculous mastitis	2	1.67

In the present study all the patients were subjected to USG guided true cut biopsy after the clinical diagnosis of BBD:NRMT and SOM was made. It was found that fibroadenoma with fibroadenosis was the most common finding on true cut biopsy in 32 (26.67%) patients. There were 20 (16.67%) cases of fibroadenoma found on true cut biopsy which was the next most common finding of true cut biopsy in this study. There were 20 (16.67%) cases of invasive ductal carcinoma found out on true cut biopsy. It was found that 9 (7.50%) patients had benign phylloids tumor as true cut biopsy finding. 4 (3.33%) patients showed chronic granulomatous mastitis as true cut biopsy finding.

There was 1 (0.83%) patient of atypical ductal hyperplasia, 1(0.83%) patient of atypical ductal hyperplasia with sclerosingadenosis, 1 (0.83%) patient of chronic non specific granulomatous mastitis, 1 (0.83%) patient of duct ectasia, 1 (0.83%) patient of

fibroadenoma with fibrocystic change,1(0.83%) patient of sclerosingadenosis, 1 (0.83%) patient of fibrocystic change of breast with atypical ductal hyperplasia, 1 (0.83%) patient of idiopathic granulomatous mastitis, 1 (0.83%) patient of sclerosingadenosis with fibrocystic change as true cut biopsy finding. There were 4 (3.33%) patients whose true cut biopsy showed acute on chronic mastitis. There were 2 (1.67%) patients of chronic mastitis, 2 (1.67%) patient of fibroadenosis, 2 (1.67%) patients of chronic non specific mastitis as true cut biopsy finding. There were 3 (2.50%) cases of granulomatous mastitis as true cut biopsy finding. There were 5 cases of fibrocystic disease/change of breast. There were 2 (1.67%) cases of tuberculous mastitis found out on true cut biopsy. There were 2 cases whose true cut biopsy showed highly suspicious of epithelial malignancy and suspicious of epithelial malignancy. There was 1 case whose true cut biopsy showed adipose tissue as its finding.

Table 7: Distribution of True Cut Biopsy Findings according to clinical diagnosis.

True Cut Biopsy Findings	No of patients	Percentage(%)
Benign Breast Disease: Not reacting to medical treatment(n=66)		
Acute on Chronic Mastitis	4	6.06
Chronic Granulomatous mastitis	4	6.06
Chronic mastitis	2	3.03
Chronic non specific granulomatous mastitis	1	1.52
Chronic non specific mastitis	2	3.03
Duct Ectasia	1	1.52
Fibroadenoma with fibroaadenosis	32	48.48
Fibroadenosis	2	3.03
Granulomatous mastitis	3	4.55
Idiopathic Granulomatous mastitis	1	1.52
Invasive Ductal Carcinoma	11	16.67
Non Caseating Granulomatous Mastitis	1	1.52
Tuberculous mastitis	2	3.03
Suspicious of malignancy(n=54)		
Atypical Ductal Hperplasia	1	1.85
Atypical Ductal Hyperplasia with SclerosingAdenosis	1	1.85
Benign Phylloides Tumour	9	16.67
Fibroadenoma	20	37.04
Fibroadenoma with fibrocystic change	1	1.85
Adipose Tissue	1	1.85
Fibrocystic change of breast	2	3.70
Fibrocystic change of breast with atypical ductal hyperplasia	1	1.85

Fibrocystic disease of breast	3	5.56
Highly Suspicious of epithelial malignancy	1	1.85
Invasive Ductal Carcinoma	9	16.67
SclerosingAdenosis	3	5.56
SclerosingAdenosis with fibrocystic change	1	1.85
Suspicious of epithelial malignancy	1	1.85

Out of total 120 patients in the present study, 66 patients were diagnosed as benign breast disease not reacting to medical treatment (BBD:NRMT) clinically. Of this 66 patients, 32 (48.48%) patients had fibroadenoma with fibroadenosis as the most common finding on true cut biopsy. There were 11 (16.67%) cases of invasive ductal carcinoma on true cut biopsy report. There were 2 (3.03%) patients of tuberculous mastitis on true cut biopsy report. There were 4 cases each of acute on chronic mastitis and chronic granulomatous mastitis on true cut biopsy. There were 3 (4.55%) cases of granulomatous mastitis on true cut biopsy. There were 2 (3.03%) cases each of chronic mastitis, fibroadenosis, chronic non specific mastitis on true cut biopsy. There were 1 (1.52%) cases each of chronic non specific granulomatous mastitis, idiopathic granulomatous mastitis and non caseating granulomatous mastitis on true cut biopsy.

Out of total 120 patients in the present study, 54 patients were diagnosed as suspicious of malignancy clinically. Out of this 54 patients, 20 (37.04%) patients had fibroadenoma as the most common finding on true cut biopsy. There were 9 (16.67%) cases of invasive ductal carcinoma on true cut biopsy report. There were 9 (16.67%) cases of benign phyllodstumour on true cut biopsy report. There were 5 cases of fibrocystic change/disease of breast on true cut biopsy. There were 1 cases each of atypical ductal hyperplasia, atypical ductal hyperplasia with sclerosingadenosis, fibroadenoma with fibrocystic change, fibrocystic change of breast with atypical ductal hyperplasia, adipose tissue, sclerosingadenosis with fibrocystic change, on true cut biopsy report. There were 3 (2.50%) cases of sclerosingadenosis on true biopsy report. There were 1 cases each of highly suspicious of epithelial malignancy and suspicious of epithelial malignancy on true cut biopsy.

Table 8: Distribution of patients according to final histopathological diagnosis.

Histopathological Diagnosis	No of patients (n=118)	Percentage(%)
Acute on Chronic Mastitis with E/O Fat Necrosis	1	0.85
Atypical Ductal Hperplasia	1	0.85
Benign PhylliodsTumour	8	6.78
Benign PhylloidsTumour with Focal Atypical Ductal Hyperplasia	1	0.85
Chronic Granulomatous mastitis	5	4.24
Chronic mastitis	2	1.69
Chronic non specific mastitis	1	0.85
Duct Ectaisa with fibrocystic change	1	0.85
Duct ectasia with chronic non specific granulomatous mastitis	1	0.85
Ductal Ectasia with acute on chronic mastitis	2	1.69
Fibroadenoma	19	16.10
Fibroadenoma with fibroadenosis	32	27.12
Fibroadenoma with fibrocystic change	2	1.69
Fibroadenosis	2	1.69
Fibroadenosis with extensive chronic non specific mastitis	1	0.85
Fibrocystic change with fibroadenosis and duct ectasia	1	0.85
Fibrocystic disease of breast with benign epithelial hyperplasia	1	0.85
Fibrocystic disease of breast with sclerosingadenosis	1	0.85
Granulomatous mastitis	2	1.69
Granulomatous mastitis with superadded infection	1	0.85
Idiopathic Granulomatous mastitis	1	0.85
Invasive Ductal carcinoma	27	22.88
Mucin Secreting Adenocarcinoma (Colloid Carcinoma)	1	0.85
Non Caseating Granulomatous Mastitis	1	0.85
SclerosingAdenosis	2	1.69
Sclerosingadenosis with simple fibrocystic change of breast	1	0.85

In the present study of 120 patients, final histopathology report was collected in 118 patients. Fibroadenoma with fibroadenosis was the most common finding accounting for 32 (27.12%) cases. There were 27 (22.88%) cases of invasive ductal carcinoma and 1(0.85%) case of mucin secreting adenocarcinoma. So out of 118 patients, there were total 28 patients whose final histopathology report came out to be malignant. 8 (6.78%) patient's final histopathology report showed benign phyllodes tumor as its finding and 1 (0.85%) case had benign phyllodes tumor with focal atypical ductal hyperplasia as final histopathology report. There were 19 (16.10%) cases of fibroadenoma on final histopathology report. There were 5 (4.24%) cases whose final histopathology report showed chronic granulomatous mastitis as its finding.

There were 2 (1.69%) cases each of chronic mastitis, ductal ectasia with acute on chronic mastitis,

fibroadenoma with fibrocystic change, fibroadenosis, granulomatous mastitis and sclerosingadenosis on final histopathology report.

There were 1 (0.85%) case each of acute on chronic mastitis with evidence of fat necrosis, atypical ductal hyperplasia, chronic non specific mastitis, duct ectasia with fibrocystic change, duct ectasia with chronic non specific granulomatous mastitis, fibroadenosis with extensive chronic non specific mastitis, fibrocystic change with fibroadenosis and duct ectasia, fibrocystic change with benign epithelial hyperplasia, fibrocystic disease of breast with sclerosingadenosis, granulomatous mastitis with superadded infection, idiopathic granulomatous mastitis, non caseating granulomatous mastitis, sclerosingadenosis with simple fibrocystic change of breast.

Table 9: Distribution of patients of BBD:NRMT with clinical features.

	No of patients(n=66)	Percentage
Lump		
Vague Lump	63	95.45
Well Defined Lump	3	4.55
Side Involved		
Right Side	37	56.06
Left Side	29	43.94
Quadrant Involved		
Upper Outer	30	45.45
Upper Inner	21	31.82
Lower Outer	9	13.64
Lower Inner	5	7.58
All	1	1.52
Tenderness		
Present	62	93.94
Absent	4	6.06
Mobility		
Mobility	57	86.36
Restricted Mobility	9	13.64
Margins		
Ill Defined	63	95.45
Well Defined	3	4.55
Consistency		
Firm	66	100
Hard	0	0
Surface		
Smooth	21	31.82
Granular	43	65.15
Irregular	2	3.03
Nipple Discharge		
Yes	26	39.39
No	40	60.61
Axillary Lymph Node		
Yes	8	12.12
No	58	87.88

Out of 120 patients, there were 66 (55%) cases of benign breast diseases which were not reacting to medical treatment. Out of these 66 patients, vague lump was

present in 63 (95.45%) patients and 3 (4.55%) patients had well defined lump. Right sided involvement was seen in 37 (56.06%) patients and left side involvement

was seen in 29 patients (43.94%). Upper outer quadrant involvement was involved most commonly in 30 (45.45%) patients. Upper inner quadrant was involved in 21 (31.82%) patients, lower outer quadrant in 9 (13.64%) patients. 5 (7.58%) patients had lower inner quadrant involvement where as there was 1(1.52%) patient whose all quadrant were involved. Tenderness was present in 62 (93.94%) patients and breast were non tender in 4 (6.06%) patients.

The lump was mobile in 57 (86.36%) patients where as there was restricted mobility in 9 (13.64%) patients. 63 (95.45%) patients had ill defined margins and 3 (4.55%) patients had well defined margins. The lump was firm in all the 66 (100%) cases. The surface was smooth in 21 (31.82%) cases, 43 (65.15%) cases had granular surface whereas irregular surface was seen in 2 (3.03%) cases. Nipple discharge was seen in 26 (39.39%) patients. Axillary lymph node involvement was seen in 8 (12.12%) patients.

Table 10: Distribution of patients of SOM with clinical features.

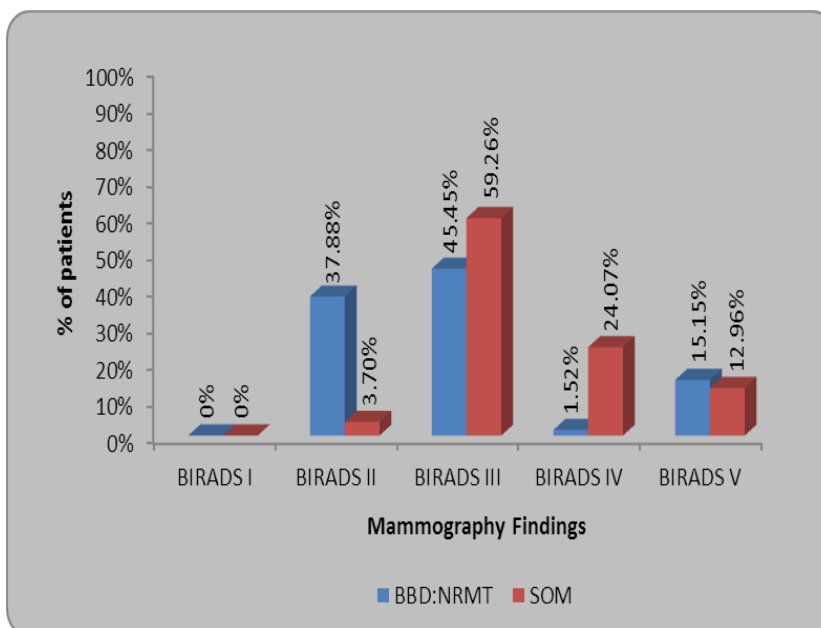
	No of patients(n=54)	Percentage
Lump		
Vague Lump	27	50.00
Well Defined Lump	27	50.00
Side Involved		
Right Side	35	64.81
Left Side	18	33.33
Bilateral	1	1.85
Quadrant Involved		
Upper Outer	21	38.89
Upper Inner	18	33.33
Lower Outer	3	5.56
Lower Inner	2	3.70
All	10	18.52
Tenderness		
Present	0	1.85
Absent	54	98.15
Mobility		
Mobility	30	55.56
Restricted Mobility	24	44.44
Margins		
Ill Defined	30	55.56
Well Defined	24	44.44
Consistency		
Firm	48	88.89
Hard	0	0.00
Varigated	6	11.11
Surface		
Smooth	13	24.07
Granular	0	0.00
Irregular	31	57.41
Bosselated	10	18.52
Axillary Lymph Node		
Yes	41	75.93
No	13	24.07

In the current study, there were 54 (45%) patients of suspicious of malignancy out of total 120 patients. Out of this 54 patients, 27 (50%) patients had vague lump and 27 (50%) had well defined lump. Right sided involvement was seen in 35 (64.81%) patients, left sided involvement was seen in 18 (33.33%) patients, and 1 (1.85%) patient had bilateral involvement. Upper outer quadrant was involved most commonly in 21 (38.89%) patients. Upper inner quadrant was involved in 18 (33.33%) patients, lower outer in 3 (5.56%) and lower inner 2 (3.70%) patients whereas all quadrants were

involved in 10 (18.52%) patients. Tenderness was absent in all of these patients. The lump was mobile in 30(55.56%) patients and mobility was restricted in 24 (44.44%) patients. The lump was firm in 48 (88.89%) patients whereas variegated consistency was seen in 6 (11.11%) patients. The surface of lump was smooth in 13 (24.07%) patients, it was irregular in 31 (52.41%) patients and bosselated surface was seen in 10 (18.52%) cases. Axillary lymph node involvement was seen in 41 (75.93%) patients.

Table 11: Correlation between clinical diagnosis and mammography.

Mammography Findings	BBD:NRMT	SOM
BIRADS 0	0(0%)	0(0%)
BIRADS I	0(0%)	0(0%)
BIRADS II	25(37.88%)	2(3.70%)
BIRADS III	30(45.45%)	32(59.26%)
BIRADS IV	1(1.52%)	13(24.07%)
BIRADS V	10(15.15%)	7(12.96%)
Total	66(100%)	54(100%)

**Graph 11: Correlation between clinical diagnosis and mammography.**

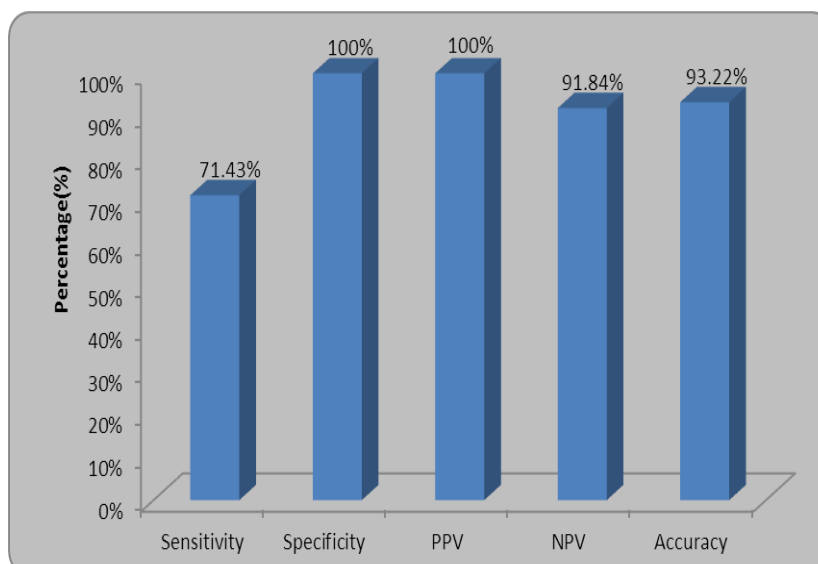
In the present study of 120 patients, there were 66 patients of benign breast diseases which were not reacting to medical treatment. Out of these 66 patients, BIRADS III was most common finding seen in 30(45.45%) patient. BIRADS II was seen in 25 (37.88%) patients, BIRADS IV seen in only one (1.52%)patient. BIRADS V was seen in 10 (15.15%) patients.

Out of 54 patients of suspicious of malignancy, BIRADS III was most common mammography finding seen in 32(59.56%). BIRADS II was seen in only 2 (3.70%) patients. BIRADS IV was seen in 13(24.07%) patients and BIRADS V in 7 (12.96%) patients.

Table 12: Correlation between true cut biopsy and final histopathological diagnosis

True Cut Biopsy	Final Histopathological Diagnosis		Total
	Malignant	Benign	
Malignant	20	0	20
Benign	8	90	98
Total	28	90	118

- X2-value=77.40,p-value=0.0001,Significant
- Sensitivity=71.43%(95% CI=51.33-86.78%)
- Specificity=100%(95% CI=95.98-100%)
- Positive Predictive Value=100%(95% CI=83.16-100%)
- Negative Predictive Value=91.84%(95% CI=84.55-96.41%)
- Diagnostic Accuracy=93.22%
- False Negative Rate=8.16%



Graph 12: Correlation between true cut biopsy and final histopathological diagnosis.

In the current study, final histopathological report was collected in 118 patients and diagnostic value of true cut biopsy was assessed by correlating with final histopathology report. Out of this total 118 patients, there were 20 patients which were malignant both on true cut biopsy and final histopathology report. There were 8 cases which were benign on true cut biopsy but came out to be malignant on final histopathology report after excisional biopsy was done. There were total 90 patients which were benign both on true cut biopsy and final histopathology report.

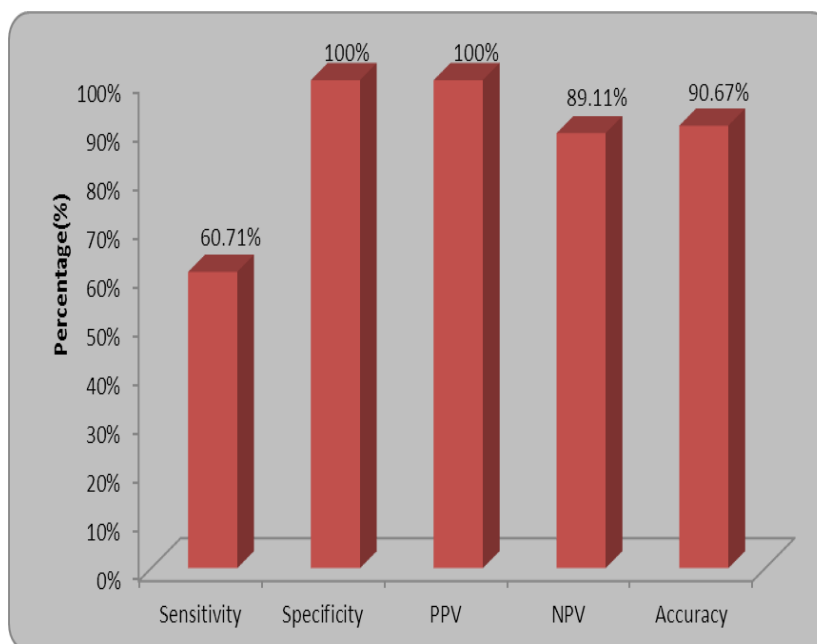
Thus from the above data, sensitivity, specificity, negative predictive value, positive predictive value, diagnostic accuracy and false negative rate of true cut biopsy was calculated and the results are as follows:

- X²-value=77.40, p-value=0.0001, Significant
- Sensitivity=71.43% (95% CI=51.33-86.78%)
- Specificity=100% (95% CI=95.98-100%)
- Positive Predictive Value=100% (95% CI=83.16-100%)
- Negative Predictive Value=91.84% (95% CI=84.55-96.41%)
- Diagnostic Accuracy=93.22%
- False Negative Rate=8.16%

Table 13: Correlation between final histopathological diagnosis and mammography.

Mammography	Final Histopathological Diagnosis		Total
	Malignant	Benign	
Malignant	17	0	17
Benign	11	90	101
Total	28	90	118

- X²-value=63.84, p-value=0.0001, Significant
- Sensitivity=60.71% (95% CI=40.58-78.50%)
- Specificity=100% (95% CI=95.98-100%)
- Positive Predictive Value=100% (95% CI=80.49-100%)
- Negative Predictive Value=89.11% (95% CI=81.35-94.44%)
- Diagnostic Accuracy=90.67%
- False Negative Rate=10.89%



Graph 13: Correlation between final histopathological diagnosis and mammography.

In the present study of 120 patients, final histopathological report was collected in 118 patients, there were 17 patients which were malignant on both mammography and final histopathological report. There were 11 patients which were benign on mammography but came out to be malignant on final histopathological report. There were 90 cases which were benign both on mammography and final histopathological report.

Thus from the above data, sensitivity, specificity, positive predictive value, negative predictive value,

diagnostic accuracy and false negative rate of mammography were calculated and result are as follows:

- X2-value=63.84, p-value=0.0001, Significant
- Sensitivity=60.71% (95% CI=40.58-78.50%)
- Specificity=100% (95% CI=95.98-100%)
- Positive Predictive Value=100% (95% CI=80.49-100%)
- Negative Predictive Value=89.11% (95% CI=81.35-94.44%)
- Diagnostic Accuracy=90.67%
- False Negative Rate=10.89%

Table 14: Correlation between true cut biopsy and final histopathological diagnosis of patients of BBD:NRMT

True Cut Biopsy	Final Histopathological Diagnosis		Total
	Malignant	Benign	
Malignant	11	0	11
Benign	0	53	53
Total	11	53	64

- X2-value=64, p-value=0.0001, Significant
- Sensitivity=100% (95% CI=71.51-100%)
- Specificity=100% (95% CI=93.28-100%)
- Positive Predictive Value=100% (95% CI=71.51-100%)
- Negative Predictive Value=91.84% (95% CI=93.28-100%)
- Diagnostic Accuracy=100%

In the present study, there were 66 patients of benign breast diseases which were not reacting to medical treatment. Out of these 66 patients, there were 2 patients of tuberculous mastitis for which excisional biopsy was not done. So out of these remaining 64 patients, there were 11 patients which were malignant both on true cut biopsy and final histopathological report. There were 53 patients which were benign both on true cut biopsy and final histopathological report. There was no discordance

between true cut biopsy and final histopathological report in these group of patients.

From the above data, sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of true cut biopsy was calculated in these group of patients and results are as follows:

- X2-value=64, p-value=0.0001, Significant
- Sensitivity=100% (95% CI=71.51-100%)
- Specificity=100% (95% CI=93.28-100%)

- Positive Predictive Value=100%(95% CI=71.51-100%)
- Negative Predictive Value=91.84%(95% CI=93.28-100%)
- Diagnostic Accuracy=100%

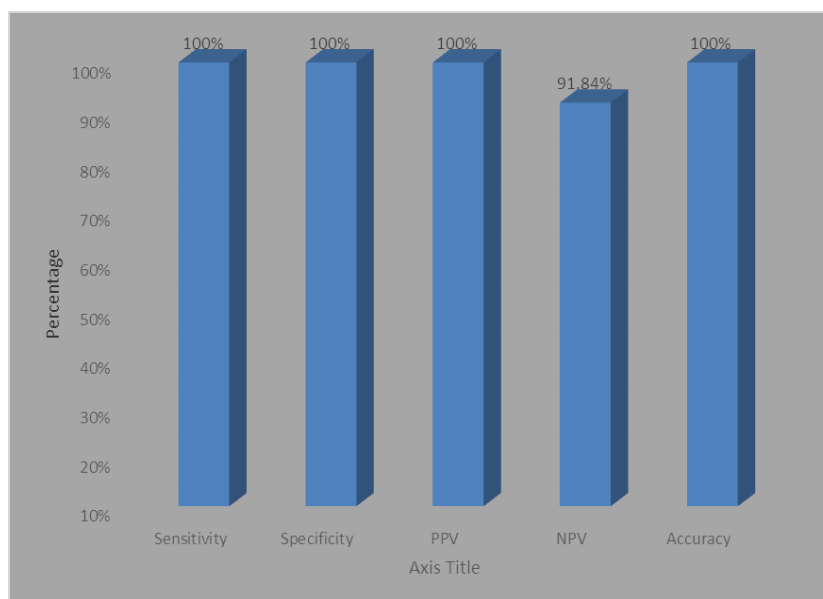
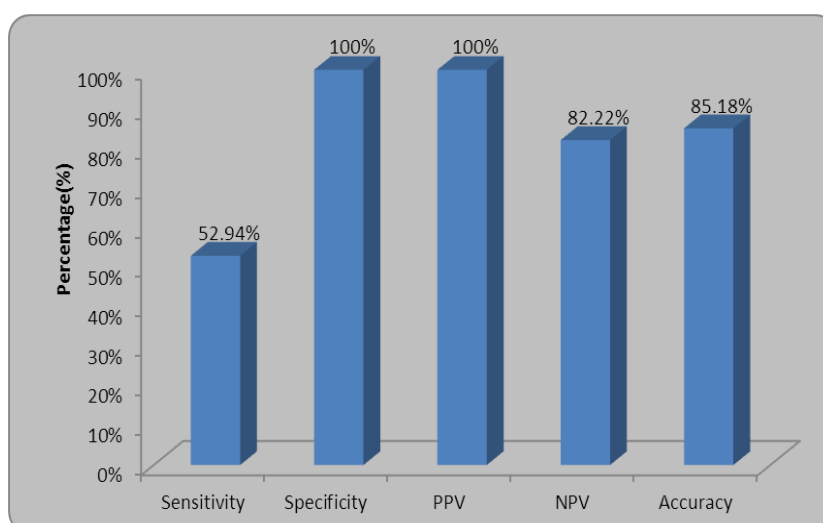


Table 15: Correlation between true cut biopsy and final histopathological diagnosis of patients of SOM.

True Cut Biopsy	Final Histopathological Diagnosis		Total
	Malignant	Benign	
Malignant	9	0	9
Benign	8	37	45
Total	17	37	54

- X2-value=23.50,p-value=0.0001,Significant
- Sensitivity=52.94%(95% CI=27.81-77.02%)
- Specificity=100%(95% CI=90.51-100%)
- Positive Predictive Value=100%(95% CI=66.37-100%)
- Negative Predictive Value=82.22%(95% CI=67.95-92%)
- Diagnostic Accuracy=85.18%



Graph 15: Correlation between true cut biopsy and final histopathological diagnosis of patients of SOM.

There were 54 patients of suspicious of malignancy in the present study. Out of this 54 patients, there were 9 patients which were malignant both on true cut biopsy and final histopathology report. There were 37 patients which were benign both on true cut biopsy and final histopathological report. However, there were 8 patients which were benign on true cut biopsy but came out to be malignant on final histopathological report.

From the above data, sensitivity, specificity, positive predictive value and negative predictive value and

diagnostic accuracy of true cut biopsy was calculated in these group and results are as follows:

- χ^2 -value=23.50, p-value=0.0001, Significant
- Sensitivity=52.94%(95% CI=27.81-77.02%)
- Specificity=100%(95% CI=90.51-100%)
- Positive Predictive Value=100%(95% CI=66.37-100%)
- Negative Predictive Value=82.22%(95% CI=67.95-92%)
- Diagnostic Accuracy=85.18%

Table 16: Correlation of patients of malignancy which were missed by true cut biopsy and mammography with clinical features.

	No of patients	Percentage(%)
Age(years)	47.37±15.79(25-75 yrs)	
Side		
Left	3	37.5
Right	5	62.5
Total	8	100%
Quadrant		
All	1	12.5
LI	1	12.5
UI	5	62.5
UO	1	12.5
LO	0	0.00
Total	8	100%
Mobility		
Mobile	2	25.0
Restricted Mobility	6	75.0
Total	8	100%
Margin		
Ill Defined	7	87.5
Well Defined	1	12.5
Total	8	100%
Consistency		
Firm	7	87.5
Variegated	1	12.5
Total	8	100%
Surface		
Bosselated	1	12.5
Irregular	4	50
Smooth	3	37.5
Total	8	100%
Axillary Lymph Node		
Present	8	100
Absent	0	0
Total	8	100%

In the present study of 120 patients, there were total 28 patients of malignancy. Out of these 20 patients, there were 8 patients of malignancy which were missed by true cut biopsy and mammography but clinically had suspicion for malignancy. There were 5 (62.5%) patients having right sided involvement and left sided involvement was seen in 3(37.5%) patients. Out of 8 patients, upper inner quadrant involvement was seen in 5 (62.5%) patients. There was 1 patient each of where

upper outer, lower inner and all quadrant was involved. The lump was mobile in 2 (25%) patients and the mobility was restricted in 6 (75%) patients. The margins were ill defined in 7 (87.5%) patients and well defined in 1(12.5%) patient. The lump was firm in consistency in 7 (87.5%) patients and it was variegated in 1 (12.5%) patient. The surface over the lump was irregular in 4 (50%) patients, smooth in 3 (37.5%) patients and

bosselated in 1 (12.5%) patient. The axillary lymph nodes were involved in all the 8 patients.

Table 17: Correlation of patients of malignancy which were missed by true cut biopsy and mammography with clinical diagnosis, true cut biopsy and mammography.

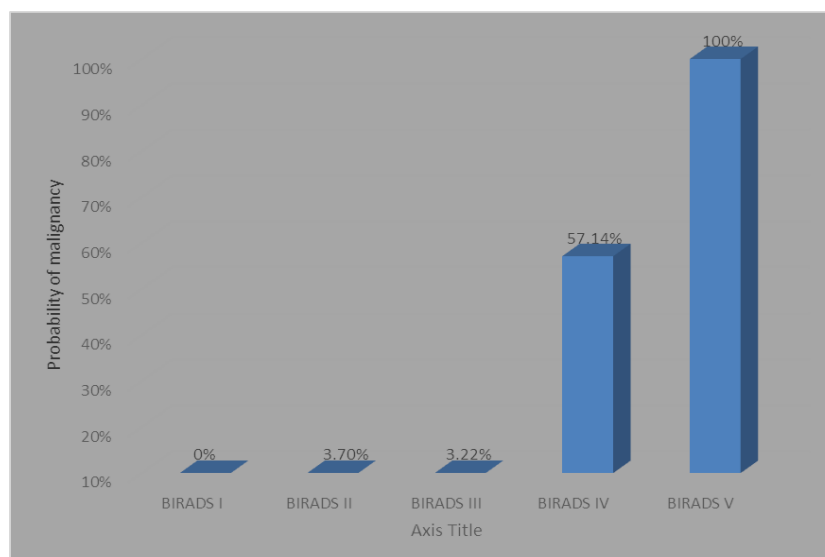
Clinical diagnosis		No of patients	Percentage(%)
	Mammography		
	BIRADS 0	0	0.00
	BIRADS I	0	0.00
SOM	BIRADS II	1	12.5
SOM	BIRADS III	2	25
SOM	BIRADS IV	5	62.5
SOM	BIRADS V	0	0
	Total	8	100%
	True cut biopsy		
SOM	Atypical Ductal Hperplasia	1	12.5
SOM	Atypical Ductal Hyperplasia with SclerosingAdenosis	1	12.5
SOM	Fibrocystic change of breast	1	12.5
SOM	Fibrocystic change of breast with atypical ductal hyperplasia	1	12.5
SOM	Highly Suspicious of epithelial malignancy	1	12.5
SOM	SclerosingAdenosis	1	12.5
SOM	SclerosingAdenosis with fibrocystic change	1	12.5
SOM	Suspicious of epithelial malignancy	1	12.5
	Total	8	100%

All the 8 patients of malignancy which were missed by true cut biopsy and mammography had suspicion for malignancy clinically. Out of these 8 patients, there were 5 (62.5%) patients having BIRADS IV as mammography finding. There were 2 (25%) patients of BIRADS III grading and 1 patient of BIRADS II as mammography finding.

There was 1 patient each of atypical ductal hyperplasia, atypical ductal hyperplasia with sclerosingadenosis, fibrocystic change of breast, fibrocystic change of breast with atypical ductal hyperplasia, highly suspicious of epithelial malignancy, sclerosingadenosis, sclerosingadenosis with fibrocystic change and suspicious of epithelial malignancy having true cut biopsy finding.

Table 18: Probability of malignancy according to BIRADS Grading.

Mammography	No. of patients.	No of patients with malignancy on final histopathology	Probability of malignancy(%)
BIRADS 0	0	0	0.00
BIRADS I	0	0	0.00
BIRADS II	27	1	3.70
BIRADS III	62	2	3.22
BIRADS IV	14	8	57.14
BIRADS V	17	17	100
Total	120	28	23.33



Graph 18: Probability of malignancy according to BIRADS Grading.

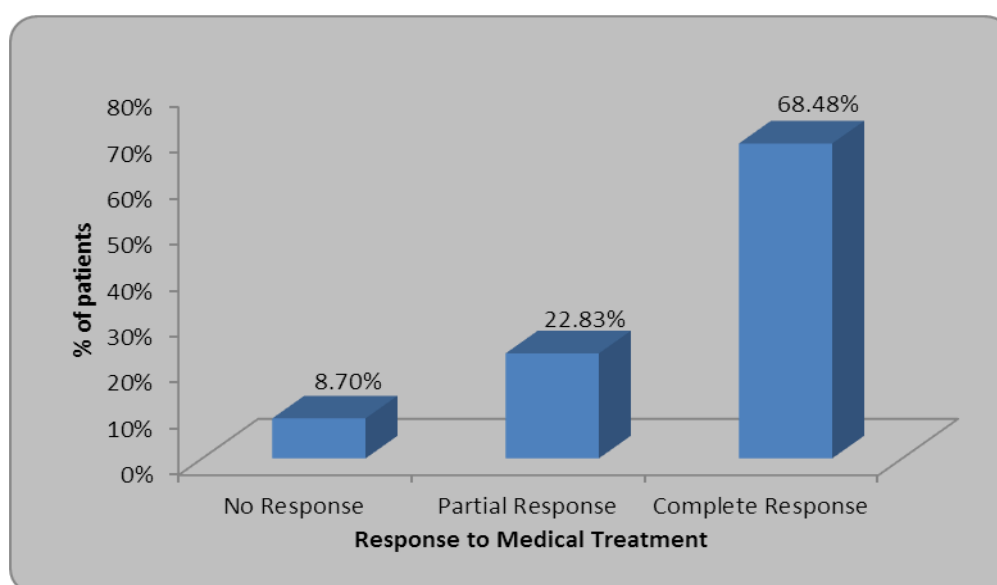
There were total 28 patients of malignancy in the current study. Mammography showed BIRADS II in 27 patients. Out of these 27 patients there was only one patient which came out to be malignant on final histopathological report. So the probability of malignancy in BIRADS II in this study was 3.70%. There were 62 patients whose mammography finding was BIRADS III and out of these 62 patients, 2 patients turned out to be malignant on final histopathological report. So the probability of malignancy in BIRADS III was 3.22%.

Mammography report of 14 patients was BIRADS IV and 8 patients turned out to be malignant on final histopathological report. So the probability of malignancy in BIRADS IV was 57.14% in this study.

There were 17 patients of BIRADS V in the present study. And all of these patients were found to be malignant on final histopathology. So the probability of malignancy in BIRADS V was 100%.

Table 19: Distribution of patients according to response to medical management.

Response to medical management	No of patients	Percentage(%)
No Response	8	8.70
Partial Response	21	22.83
Complete Response	63	68.48
Total	92	100



Graph 19: Distribution of patients according to response to medical management.

In the present study, all the patients of benign breast diseases were followed up for 3 months after the excisional biopsy was done and response to medical treatment was assessed clinically. Complete response was seen in 63 (68.48%) patients after the medical treatment. There were 21 (22.83%) patients who showed partial response and no response was seen in 8 (8.70%) patients.

Statistical analysis was done by using descriptive and inferential statistics using Chi square test, sensitivity and specificity and software used in the analysis were SPSS 20.0 version and GraphPad Prism 6.0 version and $p < 0.05$ is considered as level of significance.

DISCUSSION

Benign lesions of the breast can confuse both the clinician and patient. Much of the decisionmaking falls onto clinical judgement as many lesions are confusing and because every patient is different (eg, family history, level of fear in patient, comorbidities).

The treatment of breast disease in the developing countries is late because of unawareness, illiteracy, fear of malignancy, not ready to get examined by male doctor resulting in delay in diagnosis, especially in malignancy as well as in benign lumps in breast.

For correct diagnosis of breast disease, background knowledge of general clinical features of breast disease like incidence, age distribution, symptoms and palpatory findings are very important. In the course of diagnosis of a disease, the clinical evaluation is always followed by the reports derived from reliable investigation tools to strengthen the accuracy of the clinical diagnostic skill.

1. Age wise distribution of patients

In the present study of 120 patients, the overall age of the patients ranged from 19 yrs to 75 yrs. The maximum no. of patients $n=50$ (41.67%) were found in the age group of 29-38 yrs. The mean age of all the patients presenting with breast diseases was found to be 34.97 ± 9.99 yrs.

In a study by **Out AA**^[34], majority of the patients of benign breast diseases were below the age of 30 years.

Ihekwa in his study from Western Africa showed that about 80.5% of the BBD occur in females between 16-35 years of age^[35].

Chaudhary et al found almost equal incidence of BBD in patients between age group of 21 - 30 & 31 - 40 years^[36]. However **Dunn et al.**, contradicts the results of all above mentioned studies in which the mean age of the patient with BBD was 50 years^[37].

Thus, our findings are in agreement with the data given above.

2. Distribution of patients according to side of involvement

In the present study of 120 patients with benign breast diseases clinically, 72 (60%) patient had right sided breast involvement which is the most common side of involvement, while 47 (39.17%) patient had left breast involvement whereas bilateral involvement was seen in 1 (0.83%) patient.

In a study done by **Sangma et al**^[38], right sided involvement in benign breast diseases was seen in 48%, left side involvement was seen in 40% and bilateral involvement was seen in 12%.

In a study done by **Abhijit MG et al**^[39], out of 110 patients, right sided involvement was seen in 52 patients, 48 patients had left sided involvement and 10 patients had bilateral involvement.

This shows that our findings are concordance with the literature given above.

3. Distribution of patients according to quadrant involvement

In the present study, among total 120 patients of benign breast diseases clinically, it was found that upper outer quadrant was involved most commonly constituting 51 (42.50%) cases followed by upper inner quadrant constituting 39 (32.50%) cases. The lower outer quadrant was next commonly involved constituting 12 (10.00%) cases. Lower inner quadrant was involved in 7 (5.83%) cases. All quadrant involvement was seen in 11 (9.17%) cases.

The studies done by **Haque et al (1980)**^[288], **Gupta JC et al (1983)**^[289], **Alam et al (1991)**^[290], **Hussain et al (1994)**^[291], **Iyer SP et al (2000)**^[292], show that upper outer quadrant is most commonly involved in benign breast diseases.

This shows that our data is concordant with above studies.

4. Distribution of patients according to clinical diagnosis

There are two types of patients of breast diseases clinically: malignant and non malignant. Those patients which are not malignant clinically are included in this study. Among these non malignant patients, there are patients of benign breast diseases which are not showing response to medical treatment and there are patients where there is a suspicion for malignancy on first clinical examination. In these subgroup of patients, definitive diagnosis is necessary so that definitive treatment can be planned. With the current study, an attempt is made to make a definitive diagnosis in this subgroup of patients and definitive treatment can be provided accordingly and also to confirm that malignancy is not missed in these patients.

In the present study of 120 patients, it was found that there were 66 (55%) patients of benign breast disease not reacting to medical treatment and 54(45%) patients had suspicion for malignancy on first clinical examination.

5. Distribution of patients according to mammography findings

In the present study of 120 patients, the most common mammography finding was BIRADS III seen in 62 (51.67%) patients. 27 (22.50%) patients had BIRADS II as mammography finding. There were 17 (14.17%) patients who had BIRADS V as mammography finding and came out to be malignant on true cut biopsy and final histopathology after the excisional biopsy. These 17 cases were thought to be benign or had suspicion for malignancy on clinical diagnosis. 14 (11.67%) patients had BIRADS IV as mammography finding in the present study. There were no cases of BIRADS 0 and I in the present study.

In a study done by **Timmers JM et al 2012^{xyz1}**, there were 811 (53%) patients of BIRADS 0, 578 (37%) patients of BIRADS IV and 156 (10%) patients of BIRADS V. In this study of dutch breast cancer screening programme, the sample size was quite large as compared to our study thus affecting the results. Also in this screening programme, BIRADS category 0 and III were merged in one group. This study programme was a mass based screening programme and the current study is a hospital based study. In the dutch screening programme, the targeted population consisted of women age 50-69 years and later on age limit was raised upto 75years. In our study there is no defined age group for women who were included in the study. These can be the possible explanations for this discordance.

In a study done by **Fatima N et al 2011^{xyz2}**, mammography was performed in 564 patients. There were 227 (40%) patients of BIRADS I, 110 (20%) of BIRADS II, 53 (9%) of BIRADS III, 130 (23%) of BIRADS IV and 44 (8%) in BIRADS V category. In this study by Fatima N et al, the sample size was 1104 women out of which mammography was performed on 564 patients constituting much larger study population as compared to our study. Also not all the women were subjected to mammography in this study, only those women who were more than 40 years of age and selected cases of less than 40 years (suspicious for malignancy and family history of breast cancer) women were subjected to mammography. Therefore, the large sample size and selected women who were subjected to mammography can be the cause for this disparity.

6. Distribution of patients according to true cut biopsy finding

In the current study, it was found that fibroadenoma with fibroadenosis was the most common finding on true cut biopsy in 32 (26.67%) patients. There were 20 (16.67%) cases of fibroadenoma found on true cut biopsy which was the next most common finding of true cut biopsy in

this study. There were 20 (16.67%) cases of invasive ductal carcinoma found out on true cut biopsy which were thought to be benign on clinical examination or had suspicion for malignancy clinically. Final confirmation was done after the final histopathology report. It was found that 9 (7.50%) patients had benign phylloids tumor as true cut biopsy finding. 4 (3.33%) patients showed chronic granulomatous mastitis as true cut biopsy finding.

There was 1 (0.83%) patient of chronic non specific granulomatous mastitis, 1 (0.83%) patient of duct ectasia, 1 (0.83%) patient of fibroadenoma with fibrocystic change, 1 (0.83%) patient of idiopathic granulomatous mastitis as true cut biopsy finding. There were 4 (3.33%) patients whose true cut biopsy showed acute on chronic mastitis. There were 2 (1.67%) patients of chronic mastitis, 2 (1.67%) patients of fibroadenosis, 2 (1.67%) patients of chronic non specific mastitis as true cut biopsy finding. There were 3 (2.50%) cases of granulomatous mastitis as true cut biopsy finding. There were 5 cases of fibrocystic disease/change of breast. There were 2 (1.67%) cases of tuberculous mastitis found out on true cut biopsy which were missed clinically. There were 2 cases whose true cut biopsy showed highly suspicious of epithelial malignancy and suspicious of epithelial malignancy and were confirmed to be malignant on final histopathology report. There was 1 case whose true cut biopsy showed adipose tissue as its finding concluding that the core of the lesion might not get hit while performing the procedure. This patient had past history of toilet mastectomy done on opposite breast for invasive ductal carcinoma. Final histopathology report came out to be atypical ductal hyperplasia.

There was 1 (0.83%) patient of atypical ductal hyperplasia, 1(0.83%) patient of atypical ductal hyperplasia with sclerosing adenosis, 3(2.50%) patient of sclerosing adenosis, 1 (0.83%) patient of fibrocystic change of breast with atypical ductal hyperplasia, 1 (0.83%) patient of sclerosing adenosis with fibrocystic change as true cut biopsy finding.

These high risk lesions are of utmost importance because in one study, 8% of core biopsies demonstrating sclerosing adenosis had associated cancer^[154]. With regards to breast cancer risk, sclerosing adenosis carries a 1.5 to 3.7 times relative risk of developing invasive cancer^[153,155].

Atypical ductal hyperplasia occupies a transitional zone between benign and malignant disease, because it contains some of, but not all, the requisite features of a cancer and is thus considered to be premalignant^[164-166]. In studies with long term follow up, atypical ductal hyperplasia has been shown to confer a relative risk for future breast cancer of 4^[159-162,167,168].

With the current use of percutaneous core needle biopsy for diagnosis, when atypical ductal hyperplasia is found,

there is a possibility that a cancer was missed as a result of sampling error. Therefore, surgical excision of the site of the atypical hyperplasia biopsy is recommended in the National Comprehensive Cancer Network (NCCN) guidelines^[175]. In the case of atypical ductal hyperplasia, the frequency of finding breast cancer (“upgrading”) with surgical excision is 15% to 30% or even higher, despite the use of large-gauge (9-or 11-gauge) core-needle biopsy with vacuum assisted devices^[176,177]. Thus, excision remains the current standard when atypical ductal hyperplasia is identified by core biopsy.

Therefore, these high risk lesions requires definitive treatment, intensive surveillance and follow up whether found on true cut biopsy or after the excisional biopsy.

In a study done by Moschetta M et al 2014^{xyz3}, there were total 400 patients. Out of these 400 patients, there were 190 cases of fibroadenoma on true cut biopsy, 144 cases of invasive ductal carcinoma, 30 cases of invasive lobular carcinoma, 23 cases of flogosed cyst, 2 cases whose true cut biopsy showed fibrosis, 2 cases of phyllodes tumour, 2 cases of diabetic mastopathy, 4 cases of sclerosing adenosis, 2 cases of zonal mastitis and 1 case of papilloma. In our study, fibroadenoma was included only when there was clinical suspicion for malignancy. So in our study many cases of fibroadenoma which were not raising clinical suspicion for malignancy were not included. We didn't find any case of invasive lobular carcinoma, flogosed cyst, fibrosis, diabetic mastopathy and papilloma in our study.

7. Distribution of true cut biopsy finding according to clinical diagnosis

Out of total 120 patients in the present study, 66 patients were diagnosed as benign breast disease not reacting to medical treatment (BBD:NRMT) clinically. Of this 66 patients, 32 (48.48%) patients had fibroadenoma with fibroadenosis as the most common finding on true cut biopsy. There were 11 (16.67%) cases of invasive ductal carcinoma on true cut biopsy report which were thought to be benign breast disease not reacting to medical treatment clinically. Final confirmation was done after the final histopathology report. There were 2 (3.03%) patients of tuberculous mastitis on true cut biopsy report which were also thought to be benign breast disease not reacting to medical treatment clinically. There were 4 cases each of acute on chronic mastitis and chronic granulomatous mastitis on true cut biopsy. There were 3 (4.55%) cases of granulomatous mastitis on true cut biopsy. There were 2 (3.03%) cases each of chronic mastitis, fibroadenosis, chronic non specific mastitis on true cut biopsy. There were 1(1.52%) cases each of chronic non specific granulomatous mastitis, idiopathic granulomatous mastitis and non caseating granulomatous mastitis on true cut biopsy.

Out of total 120 patients in the present study, 54 patients were diagnosed as suspicious of malignancy clinically. Out of this 54 patients, 20 (37.04%) patients had

fibroadenoma as the most common finding on true cut biopsy. There were 9 (16.67%) cases of invasive ductal carcinoma on true cut biopsy report which also raised suspicion for malignancy clinically. Final confirmation was done after the final histopathology report. There were 9 (16.67%) cases of benign phylloids tumour on true cut biopsy report. There were 5 cases of fibrocystic change/disease of breast on true cut biopsy. There were 1 cases each of atypical ductal hyperplasia, atypical ductal hyperplasia with sclerosing adenosis, fibroadenoma with fibrocystic change, fibrocystic change of breast with atypical ductal hyperplasia, adipose tissue, sclerosing adenosis with fibrocystic change, on true cut biopsy report. There were 3 (2.50%) cases of sclerosing adenosis on true biopsy report. There were 1 cases each of highly suspicious of epithelial malignancy and suspicious of epithelial malignancy on true cut biopsy report which were found to be malignant on final histopathology report.

There were 11(16.67%) and 9 (16.67%) cases of malignancy on true cut biopsy in subgroup of BBD:NRMT and SOM respectively. This suggests that the probability of malignancy on true cut biopsy in both the subgroups was 16.67% in the present study.

8. Distribution of patients according to final histopathological diagnosis

In the present study of 120 patients, final histopathology report was collected in 118 patients. Fibroadenoma with fibroadenosis was the most common finding accounting for 32 (27.12%) cases in this study.

There were 27 (22.88%) cases of invasive ductal carcinoma and 1(0.85%) case of mucin secreting adenocarcinoma. So out of 118 patients, there were total 28 patients whose final histopathology report came out to be malignant. Out of this 28 cases of malignancy, there were 8 cases of malignancy which were missed by true cut biopsy and mammography but had suspicion for malignancy on first clinical examination.

Breast cancer may include not only neoplastic cells but also regions of fibrosis, necrosis, typical and atypical intraductal or intralobular proliferations or inflammatory components. Furthermore, there are certain high risk lesions which are difficult to distinguish them with malignancy on true cut biopsy. The true cut biopsy extracts a very small size of sample and the extracted sample may not be from the core of the lesion. This histopathological heterogeneity of the lesion (coexistence of cancer and inflammation; “underestimation”) can be the probable cause of missing those 8 cases of malignancy on true cut biopsy.

8 (6.78%) patient's final histopathology report showed benign phyllodes tumor as its finding and 1 (0.85%) case had benign phyllodes tumor with focal atypical ductal hyperplasia as final histopathology report. There were 19 (16.10%) cases of fibroadenoma on final histopathology

report. These 19 cases had suspicion for malignancy clinically but came out to be fibroadenoma i.e. benign on final histopathology. There were 5 (4.24%) cases whose final histopathology report showed chronic granulomatous mastitis as its finding.

There were 2 (1.69%) cases each of chronic mastitis, ductal ectasia with acute on chronic mastitis, fibroadenoma with fibrocystic change, fibroadenosis, granulomatous mastitis and sclerosing adenosis on final histopathology report.

There were 1 (0.85%) case each of acute on chronic mastitis with evidence of fat necrosis, chronic non specific mastitis, duct ectasia with fibrocystic change, duct ectasia with chronic non specific granulomatous mastitis, fibroadenosis with extensive chronic non specific mastitis, fibrocystic change with fibroadenosis and duct ectasia, fibrocystic change with benign epithelial hyperplasia, fibrocystic disease of breast with sclerosing adenosis, granulomatous mastitis with superadded infection, idiopathic granulomatous mastitis, non caseating granulomatous mastitis, sclerosing adenosis with simple fibrocystic change of breast. There was 1 (0.85%) case of atypical ductal hyperplasia on final histopathology report. The true cut biopsy report of this patient showed adipose tissue as its finding. This patient had past history of toilet mastectomy of opposite breast done for invasive ductal carcinoma. So there was high clinical suspicion for malignancy in opposite breast but final histopathology report came out to be atypical ductal hyperplasia and therefore required regular follow up. There was no case of atypical lobular hyperplasia in the present study.

In a study done by **Ohri P et al 2017^[201]**, there were 20 (40%) cases of fibroadenomas on final histopathology, 16 (32%) cases of malignancy on final histopathology, 4 (8%) cases each of simple cyst and fibrocystic disease of breast, 1(2%) cases each of phyllodes and lipoma and 2 (4%) cases of lactational mastitis and chronic inflammatory disease of breast.

In a study done by **Uwaezuoke SC et al 2014^{xyz4}**, there were 104 (45.6%) cases of fibroadenoma, 60 (26.3%) patients of fibrocystic change, 19 (8.3%) patients of inflammatory lesions, 2 (0.9%) patients of atypical ductal hyperplasia, 9 (4%) cases of gynaecomastia, 6 (2.6%) of lipoma, 6 (2.6%) patients of epidermal cyst, 5 (2.2%) cases each of tubular adenoma and lactating adenoma, 3 (1.4%) patients of sclerosing adenosis, 2 (0.9%) cases each of lactational changes, benign phylloides tumour and fibroepithelial polyp, 1 (0.4%) case each of intraductal polyp, granular cell tumour and keloid on final histopathology.

In our study, only those cases of fibroadenoma were included when there was suspicion for malignancy on clinical examination. The cases of fibroadenoma which were not raising suspicion for malignancy were not

included in this study. So many cases of fibroadenoma are missing in this study. This can be the possible reason for this discordance between above mentioned studies and our study.

9. Clinical features of BBD:NRMT and SOM patients

Clinical examination is a simple method to detect breast lumps and their nature as it is inexpensive and noninvasive and if found to be accurate, might be of great value as a diagnostic tool. This would prove to be highly useful particularly in rural areas where funds and/or facilities may not be available for more sophisticated diagnostic methods. There is an overall consensus that clinical breast examination is useful in screening as well as in evaluation of a lump. About 3 % to 45 % of cancer diagnoses missed by mammography were reported as having been detected by clinical breast examination^{xyz5}.

The main problem in clinical breast examination utility as a diagnostic tool is its lack of standardization because there is variation in its performance and reporting by different examiners. Recommendations that have been made regarding standardization of CBE to enhance its sensitivity include following a particular sequence of examination, focusing on clinical signs which can raise suspicion and spending sufficient time on examination emphasizing that a structured evaluation can maximize cancer detection and minimize unnecessary investigations and procedures.

Our data suggests that a standardized sequence of examination should be chosen and if certain clinical signs are focused and found to be present, then the diagnosis of benign swellings can raise suspicion for malignancy. This can lead to the early detection of malignancy resulting in the better and favorable outcome for the patient. These sinister signs are firm to hard or hard consistency of lump, irregularity, early skin dimpling overlying lump, early fixity or restricted mobility, axillary Lymphadenopathy.

In the current study of 120 patients, there were 66 (55%) cases of benign breast diseases which were not reacting to medical treatment. Out of these 66 patients, vague lump was present in 63 (95.45%) patients and 3 (4.55%) patients had well defined lump. Right sided involvement was seen in 37 (56.06%) patients and left side involvement was seen in 29 patients (43.94%). Upper outer quadrant involvement was involved most commonly in 30 (45.45%) patients. Upper inner quadrant was involved in 21 (31.82%) patients, lower outer quadrant in 9 (13.64%) patients. 5 (7.58%) patients had lower inner quadrant involvement where as there was 1(1.52%) patient whose all quadrant were involved. Tenderness was present in 62 (93.94%) patients and breast were non tender in 4 (6.06%) patients.

The lump was mobile in 57 (86.36%) patients where as there was restricted mobility in 9 (13.64%) patients. 63 (95.45%) patients had ill defined margins and 3 (4.55%) patients had well defined margins. The lump was firm in all of these 66 (100%) cases. The surface was smooth in 21 (31.82%) cases, 43 (65.15%) cases had granular surface whereas irregular surface was seen in 2 (3.03%) cases. Nipple discharge was seen in 26 (39.39%) patients. Axillary lymph node involvement was seen in 8 (12.12%) patients.

In the current study, there were 54 (45%) patients of suspicious of malignancy out of total 120 patients. Out of this 54 patients, 27 (50%) patients had vague lump and 27 (50%) had well defined lump. Right sided involvement was seen in 35 (64.81%) patients, left sided involvement was seen in 18 (33.33%) patients, and 1 (1.85%) patient had bilateral involvement. Upper outer quadrant was involved most commonly in 21 (38.89%) patients. Upper inner quadrant was involved in 18 (33.33%) patients, lower outer in 3 (5.56%) and lower inner 2 (3.70%) patients whereas all quadrants were involved in 10 (18.52%) patients.

Tenderness was absent in all of these patients. The lump was mobile in 30(55.56%) patients and mobility was restricted in 24 (44.44%) patients. The lump was firm in 48 (88.89%) patients whereas variegated consistency was seen in 6 (11.11%) patients. The surface of lump was smooth in 13 (24.07%) patients, it was irregular in 31 (52.41%) patients and bosselated surface was seen in 10 (18.52%) cases. Axillary lymph node involvement was seen in 41 (75.93%) patients.

10. Corelation between true cut biopsy and final histopathological diagnosis

In this study, the sensitivity of true cut biopsy was 71.43% which is in the range of 65%-95% given in the literature^[293-297]. The specificity was 100%, positive predictive value was 100%, negative predictive value was 91.84% and diagnostic accuracy was 93.22%. The false negative rate in this study was 8.16% which is within the range of 1%-15% given in the literature^[298-304].

In a study done by **Homesh et al. 2005**^[227], sensitivity of true cut biopsy was 92.3%, specificity was 94.8%, positive predictive value and negative predictive value was 100% and diagnostic accuracy was 93.4%.

In a study done by **Brunner et al. 2009**^[228], sensitivity was 95%, specificity and positive predictive value was 100% and negative predictive value was 90%.

In a study done by **Kulkarni et al. 2009**^[229], sensitivity was 97.7%, specificity was 94.2%, positive predictive value was 93.1%, negative predictive value was 98.1% and diagnostic accuracy was 95.5%.

In a study done by **Bdour et al. 2009**^[230], sensitivity was 97% and specificity was 100%.

In a study done by **Ahmed et al. 2010**^[231], sensitivity was 94.64%, specificity was 91.3% and diagnostic accuracy was 94.87%.

In a study done by **Lacambra et al. 2012**^[232], sensitivity was 96%, specificity and positive predictive value was 99% and negative predictive value was 94%.

In a study done by **Rikabi and Husain et al. 2013**^[233], sensitivity was 95.1%, specificity and positive predictive value was 100%, negative predictive value was 97.2% and diagnostic accuracy was 98.2%.

In a study done by **Dimitrov D et al. 2016**^[234], sensitivity was 98.67%, specificity was 100%, positive predictive value was 100% negative predictive value was 80% and diagnostic accuracy was 98.73%.

Thus from the above discussion, it is clear that our data is concordant with the literature given above.

11. Corelation between mammography and final histopathological diagnosis

In the present study, sensitivity of mammography was 60.71%, specificity was 100%, positive predictive value was 100%, negative predictive value was 89.11%, diagnostic accuracy was 90.6%. The false negative rate in our study was 10.89% which is in the range of 4%-34% given in the literature^[200-209].

In a study done by **Shaikh R et al 2017**^[200], sensitivity of mammography was 91.3%, specificity was 87.2% and diagnostic accuracy was 90%.

In a study done by **Ohri P et al 2017**^[201], sensitivity of mammography was 100%, specificity was 79.41%, positive predictive value was 69.57%, negative predictive value was 100% and diagnostic accuracy was 86%.

In a study done by **Omranipour R et al 2016**^[202], sensitivity of mammography was 80.5%, specificity was 73.3%, positive predictive value was 85.45%, negative predictive value was 66% and diagnostic accuracy was 76.9%.

In a study done by **Duijm LE et al 1997**^[203], sensitivity of mammography was 92%, specificity was 97.7%, positive predictive value was 68%, negative predictive value was 99.6%.

In a study done by **Tiwari et al 2017**^[305], sensitivity of mammography was 77.8%, specificity was 97.7%, positive predictive value was 87.5% and negative predictive value was 95.6%.

In our study, the sample size is very small. Our setup is a rural general setup and the above mentioned studies were done at dedicated cancer setups or hospitals. In our setup, the mammography reporting is done by radiologist who

does not do executive reporting of mammography only. This explains the reason for the discordance between our study and above mentioned studies.

12. Correlation between true cut biopsy and final histopathological diagnosis of patients of BBD:NRMT

In the present study, there were 66 patients of benign breast diseases which were not reacting to medical treatment. Out of these 66 patients, there were 2 patients of tuberculous mastitis for which excisional biopsy was not done. So out of these remaining 64 patients, there were 11 patients which were malignant both on true cut biopsy and final histopathological report. There were 53 patients which were benign both on true cut biopsy and final histopathological report. There was no discordance between true cut biopsy and final histopathological report in these group of patients.

From the above data, sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of true cut biopsy was calculated in these group of patients and results are as follows:

- X2-value=64, p-value=0.0001, Significant
- Sensitivity=100%(95% CI=71.51-100%)
- Specificity=100%(95% CI=93.28-100%)
- Positive Predictive Value=100%(95% CI=71.51-100%)
- Negative Predictive Value=91.84%(95% CI=93.28-100%)
- Diagnostic Accuracy=100%

13. Correlation between true cut biopsy and final histopathological diagnosis of patients of SOM

There were 54 patients of suspicious of malignancy in the present study. Out of this 54 patients, there were 9 patients which were malignant both on true cut biopsy and final histopathology report. There were 37 patients which were benign both on true cut biopsy and final histopathological report. However, there were 8 patients which were benign on true cut biopsy but came out to be malignant on final histopathological report.

From the above data, sensitivity, specificity, positive predictive value and negative predictive value and diagnostic accuracy of true cut biopsy was calculated in these group and results are as follows:

- X2-value=23.50, p-value=0.0001, Significant
- Sensitivity=52.94%(95% CI=27.81-77.02%)
- Specificity=100%(95% CI=90.51-100%)
- Positive Predictive Value=100%(95% CI=66.37-100%)
- Negative Predictive Value=82.22%(95% CI=67.95-92%)
- Diagnostic Accuracy=85.18%

14. Correlation of patients of malignancy which were missed by true cut biopsy and mammography with clinical features

In the present study of 120 patients, there were total 28 patients of malignancy. Out of these 20 patients, there were 8 patients of malignancy which were missed by true cut biopsy and mammography but clinically had suspicion for malignancy. There were 5 (62.5%) patients having right sided involvement and left sided involvement was seen in 3(37.5%) patients. Out of 8 patients, upper inner quadrant involvement was seen in 5 (62.5%) patients. There was 1 patient each of where upper outer, lower inner and all quadrant was involved. The lump was mobile in 2 (25%) patients and the mobility was restricted in 6 (75%) patients. The margins were ill defined in 7 (87.5%) patients and well defined in 1(12.5%) patient. The lump was firm in consistency in 7 (87.5%) patients and it was variegated in 1 (12.5%) patient. The surface over the lump was irregular in 4 (50%) patients, smooth in 3 (37.5%) patients and bosselated in 1 (12.5%) patient. The axillary lymph nodes were involved in all the 8 patients.

15. Correlation of patients of malignancy which were missed by true cut biopsy and mammography with clinical diagnosis, true cut biopsy and mammography.

All the 8 patients of malignancy which were missed by true cut biopsy and mammography had suspicion for malignancy clinically. Out of these 8 patients, there were 5 (62.5%) patients having BIRADS IV as mammography finding. There were 2 (25%) patients of BIRADS III grading and 1 patient of BIRADS II as mammography finding.

There was 1 patient each of atypical ductal hyperplasia, atypical ductal hyperplasia with sclerosing adenosis, fibrocystic change of breast, fibrocystic change of breast with atypical ductal hyperplasia, highly suspicious of epithelial malignancy, sclerosing adenosis, sclerosing adenosis with fibrocystic change and suspicious of epithelial malignancy having true cut biopsy finding.

These all 8 cases which were confirmed to be malignant on final histopathology had clinical suspicion for malignancy. There were 5 cases of BIRADS IV, 2 cases of BIRADS III and 1 case of BIRADS II on mammography and no case of BIRADS V. In these 8 cases, true cut biopsy showed benign/high risk finding or suspicion for malignancy. This suggests that clinical suspicion remains to be the most important factor for deciding excisional biopsy.

16. Probability of malignancy according to BIRADS Grading

There were total 28 patients of malignancy in the current study. Mammography showed BIRADS II in 27 patients. Out of these 27 patients there was only one patient which came out to be malignant on final histopathological report. So the probability of malignancy in BIRADS II in

this study was 3.70%. There were 62 patients whose mammography finding was BIRADS III and out of these 62 patients, 2 patients turned out to be malignant on final histopathological report. So the probability of malignancy in BIRADS III was 3.22%.

Mammography report of 14 patients was BIRADS IV and 8 patients turned out to be malignant on final histopathological report. So the probability of malignancy in BIRADS IV was 57.14% in this study.

There were 17 patients of BIRADS V in the present study. And all of these patients were found to be malignant on final histopathology. So the probability of malignancy in BIRADS V was 100%.

According to **American College of Radiology**^[194], the probability of malignancy in BIRADS III is less than 2%, in BIRADS IV the range is from 2% to 95% and in BIRADS V it is more than 95%.

In our study, the probability of malignancy in BIRADS II is higher than BIRADS III. The reason for this can be the technical error or the radiologist are not dedicated to do mammography reports only in our setup.

Thus from above discussion, remaining findings of BIRADS IV and V are in agreement with the literature.

17. Distribution of patients according to response to medical management

In the present study, all the patients of benign breast diseases were followed up for 3 months after the excisional biopsy was done and response to medical treatment was assessed clinically. Complete response was seen in 63 (68.48%) patients after the medical treatment. There were 21 (22.83%) patients who showed partial response and no response was seen in 8 (8.70%) patients.

This data is in agreement with the literature discussed earlier^[236,243,253,262,275,278].

In the present study, there was no recurrence and no benign breast disease or high risk lesions turned out to be malignant after 3 months of follow up.

LIMITATIONS

- The sample size in the current study was 120 which is quite small to evaluate these group of patients of BBD:NRMT and SOM and to find out the risk of malignancy associated with these cases.
- Since our study group is rural population with low education level, it does not reflect the picture of general population. A study on urban population especially educated working women may reveal different statistics based upon which stakeholders can plan their health education strategies.
- The needle used for USG guided Core needle Biopsy in our study was 18-gauge needle thus

increasing the chances of sampling error which can be the cause of false negative cases on true cut biopsy in our study.

- Follow up period was 3 months in our study which is very short. High risk lesions like atypical ductal hyperplasia and sclerosing adenosis require long term follow up as these lesions can turn out to be malignant in future.