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Correlation between Mammographic Features and Histological Findings in Female Breast Lesion at the University of Benin Teaching Hospital, Benin City. Edo State, Nigeria

Oriakhi S. N
Department of Surgery
University of Benin Teaching Hospital, Benin City
Email: nationoriakhi@gmail.com

ABSTRACT
Breast diseases constitute one of the most common contemporary diseases of females. Presently, breast cancer is the most prevalent cancer in the world over. It accounts for 18.4% of female cancers. In fact, 1:14 black women will develop breast cancer, during their life time. Mammography has become an invaluable tool for diagnosing breast lesion and detecting early breast cancer in women greater than 40 years in age. The aims and objectives of this study were to correlate the mammography BIRADS categories with the histological diagnosis in breast lesions and to determine the predictive values, sensitivity, specificity and accuracy of mammography in the diagnosis of breast lesions. It was a one year (March 2015-February 2016) prospective study of consecutive female patients above 40 years old who presented with breast lesions at the UBTH. All patients had mammography and core biopsy of the breast lesion using size 16 gauge biopsy gun. All biopsy specimens were subject to histological examination. The author and a consultant radiologist reported the mammograms using the BIRADS lexicon. Mammograms were categorized into BIRADS category 1 to 6. Patients with fungating breast lesion and patients who decline to be enrolled in the study. 101 patients were studied. 106 biopsies were performed. Data including Age distribution, clinical features of breast lesions, mammographic features and histology of tumors were analyzed and correlations between these findings were highlighted. The mean ages of patients with benign breast disease 47.0 ± 4.9 years while those with malignant breast disease 49.9 ± 8.5. P - Value was 0.080, this differences was not statistically significant. Fibrocystic disease 6 (5.6%) was the commonest benign disease whereas; invasive ductal carcinoma was the most common malignant breast disease 84(79.2%). BIRADS V correlates mostly with malignant breast disease (97.0%). P – Value was < 0.001 and was statistically significant. This study showed that mammography is very useful in the diagnosis of breast lesion in women above 40 years old. Patients with BIRADS category 3, 4 and 5 had step wise increasing correlation with malignant breast disease.

INTRODUCTION
Breast diseases constitute one of the most common diseases of females in any society[1]. These include both the benign and malignant types. Both

types are worrisome but breast cancers particularly shorten life expectancy. Cancer of the breast is the most common malignancy affecting women in many parts of the world[2]. Globally, it accounts for 18.4% of female cancers[2]. According to the American Cancer Society, it is the second most diagnosed cancer (after skin cancers) in United States of America[3]. In Nigeria and Ghana, it was the commonest malignancy by the year 2008[2]. The incidence of breast cancer in Nigeria in 2012 was 52.0 per 100,000 in Ibadan cancer registry and 64.6 per 100,000 in Abuja cancer registry[4]. The world records over 1.1 million new breast cancer cases (about 10% of all cancers), and over 410,000 female breast cancer deaths (over 1.6% of all female deaths) yearly. According to GLOBOCAN, breast cancer is the most prevalent cancer in the world (4.4 million survivors up to five years following diagnosis)[5,6]. Benign breast diseases include all non-malignant conditions of the breast and they include developmental abnormalities, inflammatory lesions, fibrocystic changes, stromal lesions and neoplasms. Typically, they do not convey an increased risk of malignancy[7], but benign lesions such as fibrocystic disease may increase the risk of breast cancer[8]. A 2 to 4 fold increase in risk of breast cancer has been shown in patients with fibrocystic disease[9].

Diagnostic imaging plays a central role in the diagnosis, treatment, planning and staging of patients with breast cancer. Mammography remains the mainstay in breast cancer detection[10]. A mammogram is a radiographic examination of the breast, either displayed on a film or on a computer monitor. A Screening mammography is carried out on women who are asymptomatic while indications for diagnostic mammography include women with symptoms or signs of breast cancer, a possible abnormality detected on screening mammography or other imaging or who have prior mammography findings requiring imaging follow-up[10]. It is essential that all mammography be performed and interpreted with the highest possible standard[11]. The American College of Radiology has developed the Breast Imaging Reporting and Data System (BI – RADS) to standardize the terminology employed for mammographic reports elaboration and for recommendations to be adopted. The fourth BI-RADS edition of November 2003 proposed seven categories for mammographic findings: negative for malignancy (1), benign (2), probably

benign (3), suspicious for malignancy (4), highly suspicious for malignancy (5), with proven malignancy (6) and requiring additional evaluation (0)[12], but category 4 is further subdivided into A, B and C. BIRADS 4A (low suspicion for malignancy), 4B (intermediate suspicion of malignancy), and 4C (moderate concern, but not classic for malignancy)[13].

Mammography may produce false negative results when mammograms appear normal even though breast cancer is present as well as false positive results when mammograms are abnormal but no cancer is actually present. Mammography is useful in breasts that contain little dense glandular tissue and composed predominantly of fat[10]. It is therefore performed after the age of 40 years[10]. It may be performed earlier if there is a strong indication but the density of the breasts makes the result unreliable. Ultrasonography is used in imaging dense breast tissue of young women below the age of 30 years, pregnant or lactating women and women with breast implants[10]. The mammographic findings relating to neoplasias include masses with spiculated margins, microlobulated(irregular) shape, lobular mass, fine branching microcalcifications and linear fine pleomorphic calcification[14]; thus placing these mammographic lesions into BIRADS categories is useful for predicting the presence of malignancy[15]. Pathological examination is used to confirm whether a breast mass is malignant or benign. It involves cytology and histology. Whereas the former entails the examination of the cells, the latter involves the examination of a histochemically prepared piece of tissue on a slide using a microscope. Several methods exist and they include:
Cytology:-Fine Needle Aspiration (FNA),
Histology: - Core Needle Biopsy
Open Biopsy (Incisional and Excisional)
This study was conducted to correlate the mammographic BI-RADS Categories with the histological diagnosis and to determine the predictive values, sensitivity and specificity of mammography in the diagnosis of breast lesions at the University of Benin Teaching Hospital (UBTH).

MATERIALS AND METHODS

This was a prospective descriptive cross sectional study that correlated biopsy reports of breast specimens obtained by core needle biopsy with the mammographic features of the same individual. It was conducted at the Departments of Radiology, Surgery and Pathology of the University of Benin Teaching Hospital (UBTH), Benin city, Nigeria, over a one year period from March 2015 to February 2016. Approval for the study protocol was obtained from the Hospital Research and Ethical Committee of UBTH. The study population was drawn from consecutive patients presenting to General Surgery Unit via Outpatient Department and other units of University of Benin Teaching Hospital with an initial diagnosis of breast lesion. All women from age of 40 years with clinically palpable lump or suspicious breast lesion or women from age 35 years with family history of malignancy or strong clinical suspicion of malignancy evidenced on mammogram were all included in the study. Patients excluded from the study were those with fungating breast lesion; clinically unstable patients too ill for a mammogram and/or biopsy; and those who decline even after adequate/ detained explanation.

The procedure was explained to the patient and informed consent was obtained. All consenting patients who satisfy the inclusion criteria were recruited during the period. Mammography was carried out in the mammography suite of Radiology department, University of Benin Teaching Hospital by a Radiographer, with either a Siemens Mammomat 3000 NOVA machine or a General Electric (GE) Performa machine using two standard views (craniocaudal and mediolateral oblique) and additional views where necessary. The mammograms were reported by the Radiologist using the BIRADS lexicon and categorization of the mammographic findings into BIRADS category 1 to 5. After the procedure, the patients then undergo a core needle biopsy procedure in the Surgical Outpatient department under aseptic condition with size 14/16-gauge needle of a spring loaded biopsy gun (HUNTER Automatic guillotine system by Tsunami medical) inserted into the lesion after infiltration with a local anaesthetics agent. Five samples were

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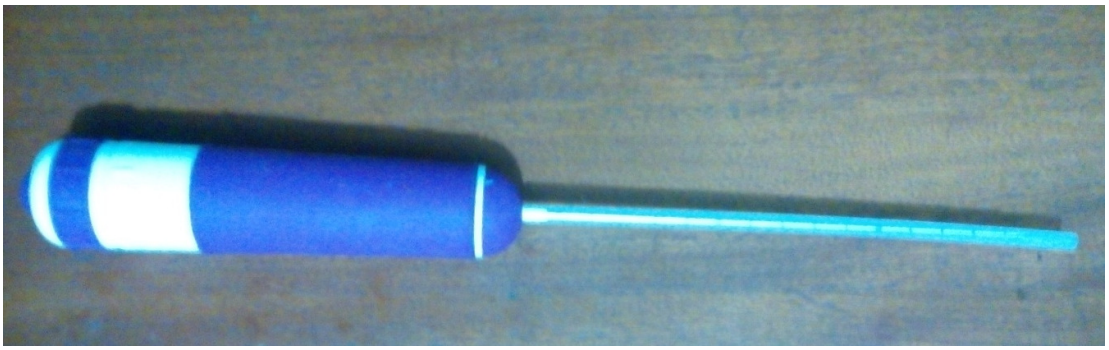
collected: one from the central portion, one each from positions 12- and 6- and 3- and 9 o'clock, all within the confines of the mass lesion. Each sample was submerged immediately in formalin solution in a specimen container. Sterile gauze was applied firmly to the biopsy site to ensure haemostasis. The samples were then sent for histopathological examination. The mammography and histology reports were retrieved, and the findings were then correlated.

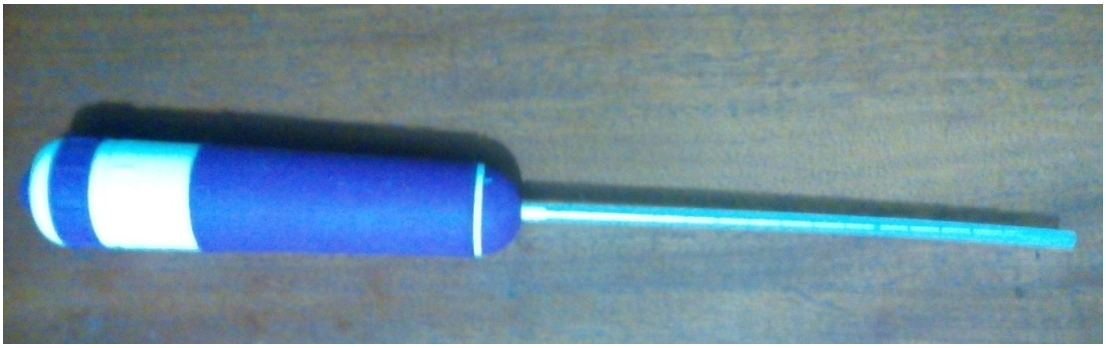


Biopsy Gun (Hunter Automatic Guillotine System by Tsunami Medical)

RESULTS

A total of 101 patients were evaluated and 106 biopsies were performed because five patients had bilateral breast disease. The ages of the patients ranged from 35 to 83 years, with a mean age of 49.6 ± 8.1 years. Eighty-eight out of the 101 patients (87.1%) were married, while 10 (9.9%) were single. Two of the 101 patients (2%) were widowed while one patient (1%) was divorced. Majority (98%) of the patients were Christian, while the rest 1% each practice Islam or traditional religion. Forty- five out of

the 101 patients (44.6%) had tertiary level of education, followed by primary level of education 28 (27.7%) while six patients (5.9%) had no formal education as shown in (Table 1). Using BIRADS III as Cutoff for malignancy, there would be 100% sensitivity, 36% specificity, 91% positive predictive value, 100% negative predictive value and 92.0% accuracy while BIRADS IV would have 91% sensitivity, 43% specificity, 91% positive predictive value, 43% negative predictive value and 85.0% accuracy for malignancy (Table 2). The area under the ROC curve was 0.823. Meaning, the overall accuracy for BIRADS was about 82% for the diagnosis of breast cancer (Figure 1).



The commonest benign histology was fibrocystic disease 5.6% while invasive ductal carcinoma was the commonest malignant histology 79.2%. (Table 3). The mean ages of patient with benign breast disease and malignant breast disease were 47.0 ± 4.9 years and 49.9 ± 8.5 respectively. Patients with malignant breast disease were older than patients with benign breast disease. P was 0.080, this differences was not statistically significant (Table 4). The peak age incidence of both benign and malignant breast disease occurred in the 5^{th} decade (41 – 45 years) Table 5. Mammographic feature of irregular shape 54 (98.2%) out of 55 was the commonest mass shape in breast with malignant histology while spiculated margin 32 (97.0%) out of 33 was the commonest mass margin and also occur in breast with malignant histology (Table 6). Lesion in BIRADS II (Benign) category had three (100%) benign histology, while BIRADS III (probably benign) category had nine lesions; one (11.1%) had benign histology whereas eight (88.9%) had malignant histology. BIRADS IV (Suspicious) category had 25 lesions; six (24.0%) had benign histology and 19 (76.0%) with malignant histology. BIRADS V (Highly

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suspicious) had 67 lesions; two (3.0%) had benign histology while 65 (97.0%) with malignant histology. P was <0.001 and was statistically significant (Table 7).

Table 1: Sociodemographics

Religion	Frequency	Percent
Christianity	**99**	**98.0%**
Islam	**1**	**1.0%**
Traditional	**1**	**1.0%**

Ethnic group	Frequency	Percent
Bini	**53**	**52.5%**
Igbo	**12**	**11.9%**
Ishan	**11**	**10.9%**
Urhobo	**7**	**6.9%**
Ika	**5**	**5.0%**
Akoko Edo	**4**	**4.0%**
Etsako	**3**	**3.0%**
Yoruba	**3**	**3.0%**
Isoko	**1**	**1.0%**
Kwale	**1**	**1.0%**
Itsekiri	**1**	**1.0%**

Marital status	Frequency	Percent
Married	**88**	**87.1%**
Single	**10**	**9.9%**
Widowed	**2**	**2.0%**
Divorced/Separated	**1**	**1.0%**

Level of Education	Frequency	Percent
None	**6**	**5.9%**
Primary	**28**	**27.7%**
Secondary	**22**	**21.8%**
Tertiary	**45**	**44.6%**

Table 2: BIRADS Category with respect to Sensitivity, Specificity, Accuracy and Predictive values

BIRADS Cutoff	Sensitivity	Specificity	Likelihood Ratio	PPV	NPV	Accuracy
2	1.00	0.14	1.17	0.88	1.00	0.89
3	1.00	0.36	1.56	0.91	1.00	0.92
4	0.91	0.43	1.60	0.91	0.43	0.85
5	0.71	0.86	4.95	0.97	0.31	0.73

Table 3: Histological types of breast lesions

Histology	Frequency	Percent
BENIGN		
Fibrolipoma	1	0.9
Fibrocystic Disease	6	5.6
Fibroadenoma	4	3.8
Mastitis	3	2.8
MALIGNANT		
Invasive Papillary Carcinoma	2	1.9
Medullary Carcinoma	2	1.9
Invasive Ductal Carcinoma	84	79.2
Intraductal Carcinoma	1	0.9
Intraductal Papillary Carcinoma	1	0.9
Invasive Lobular Carcinoma	1	0.9
Mucinous Carcinoma	1	0.9
Total	106	100.0

Table 4: Age with respect to Histology

	Histological Type of Breast Disease					
	Benign		Malignant		Total	
	Mean	SD	Mean	SD	Mean	SD
Age (years)	**47.00**	**4.88**	**49.98**	**8.46**	**49.59**	**8.13**

t =1.83, p=0.080

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Table 5: Relationship between Age range and Histology

Age (years)	Histological Type of Breast Disease		
	Benign N (%)	Malignant N (%)	Total N (%)
<= 40	1 (7.7%)	7 (8.0%)	8 (7.9%)
41 – 45	5 (38.5%)	27 (30.7%)	32 (31.7%)
46 – 50	4 (30.8%)	15 (17.0%)	19 (18.8%)
51- 55	2 (15.4%)	15 (17.0%)	17 (16.8%)
56 – 60	1 (7.7%)	18 (20.5%)	19 (18.8%)
> 60	0 (0.0%)	6 (6.8%)	6 (5.9%)

X_2 with trend= 0.840, p=0.359

Table 6: Association between Mammographic Features and Histological type of Breast Lesions

Mammographic feature	Histological Type of Breast Disease					
	Benign		Malignant		Total	
	N	%	N	%	N	%
Shape of Mass						
Round	2	50.0%	2	50.0%	4	100.0%
Oval	3	30.0%	7	70.0%	10	100.0%
Lobular	1	100.0%	0	0.0%	1	100.0%
Irregular	1	1.8%	54	98.2%	55	100.0%
Architectural distortions	1	25.0%	3	75.0%	4	100.0%
Margins of Mass						
Circumscribed	5	55.6%	4	44.4%	9	100.0%
Microlobulated	1	50.0%	1	50.0%	2	100.0%
Obscured	0	0.0%	0	0.0%	0	0.0%
Indistinct	0	0.0%	28	100.0%	28	100.0%
Spiculated	1	3.0%	32	97.0%	33	100.0%
Calcification – Morphology						
Typically Benign	0	0.0%	1	100.0%	1	100.0%
Intermediate Concern	0	0.0%	0	0.0%	0	0.0%
Higher Probability	0	0.0%	3	100.0%	3	100.0%
Calcification – Distribution						
Diffuse/Scattered	0	0.0%	2	100.0%	2	100.0%
Regional	0	0.0%	0	0.0%	0	0.0%

Grouped/Cluster	0	0.0%	0	0.0%	0	0.0%
Linear	1	25.0%	3	75.0%	4	100.0%
Segmental	0	0.0%	0	0.0%	0	0.0%
Asymmetry						
Focal	1	12.5%	7	87.5%	8	100.0%
Global	3	42.9%	4	57.1%	7	100.0%

Table 7: BIRADS Category with respect to Histology

BIRADS	Histological Type of Breast Disease					
	Benign		Malignant		Total	
	N	%	N	%	N	%
I	2	100.0%	0	0.0%	2	100%
II	3	100.0%	0	0.0%	3	100%
III	1	11.1%	8	88.9%	9	100%
IV	6	24.0%	19	76.0%	25	100%
V	2	3.0%	65	97.0%	67	100%

$X2=31.024$, $p<0.001$

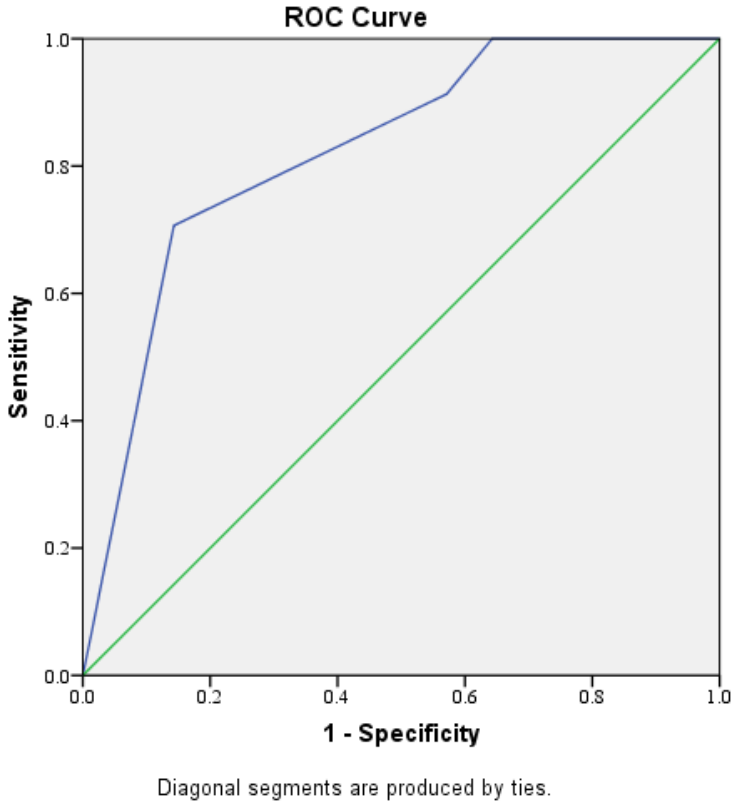

Figure 1: Sensitivity analysis for BIRADS using ROC Curve

The ROC curve shown in Figure 2 above has an area under the curve of 0.823 with 95% confidence intervals being 0.697 and 0.949.

DISCUSSION

This study showed that there was a correlation between mammographic features and histological findings of breast lesions in females. In this study, findings on age distribution were similar with the previous studies[16,17] that breast cancer affects younger population here in Nigeria. Peak age incidence in this study was 41 – 50 years as against 55 years and above in developed world[16,17] Although, the incidence of breast cancer increases with age with a palpable mass being the most common physical sign[18]. The most common histological type of breast cancer in this study was invasive ductal carcinoma which accounted for 79.2%, which was comparable to 75.5% reported in the study carried out in University of Benin Teaching Hospital by Ekanem et al[19] about a decade ago (2006), while fibrocystic disease was the most common benign histological type encountered, followed by fibroadenoma. These were similar to the findings reported in the literature[16,20,21], but Lacquement et al[22] reported infiltrating ductal carcinoma and ductal carcinoma in situ as the most common histological types of malignant breast lesions while fibroadenoma and fibrocystic changes as the most common histological types of benign breast lesions.

The American College of Radiology BIRADS was developed to provide a standardized reporting system for mammography. Prior to the implementation of the BIRADS lexicon, there was no uniformity in mammography reporting and this resulted in ambiguous reports, leading to confusion in the management and difficult medical audit. The main reason for the implementation of the BIRADS lexicon was to eliminate the confusion surrounding mammography reports such that the findings and recommendations would be made clear. Mammographic reports with a BIRADS category 1 (negative), category 2 (benign finding) and category 3 (probably benign findings) are classified as negative, while mammographic reports with a BIRADS category 4 (suspicious) and category 5 (highly suggestive of malignancy) are classified as positive. For those cases where additional evaluation is needed (BIRADS category 0), the assessment is classified as incomplete[23]. With the implementation of

the BIRADS lexicon, mammographic features were assigned into BIRADS category in the study. With lesion in BIRADS 4 or 5 classified as positive the mammography Sensitivity of the study ranged from 71% – 91%(identification of malignant lesions in patients with breast cancer), Specificity between 43% and 86%(patients without the disease, with negative tests), Positive predictive value ranged between 91% and 97% while the Negative predictive value ranged between 31% and 43%. The mammographic accuracy ranged between 73% and 85% in the differentiation between benign and malignant lesions with the use of BIRADS. These results were slightly different from the findings reported by Nascimento et al [14] where Sensitivity was 68% - 87%, Specificity was 44% - 76%, PPV was 51% - 53%, and NPV was 76% - 83% while accuracy was 62% - 75%.

Placing a lesion into BIRADS category 2 was 100% predictive of a benign lesion. BIRADS category 3, 4 and 5 showed a stepwise correlation with the diagnosis of breast cancer. However, few patients with BIRADS category 4 and 5 lesions had benign pathologies on biopsies, which imply that histopathological diagnosis was relevant in those category to preclude overtreatment. BIRADS category 3 findings of one benign, eight malignant histology and a PPV of 91% differs from the findings by Orel et al[15] who reported a PPV of 2% for BIRADS category 3 (probably benign) lesion, because placing a lesion into BIRADS category 3 was highly predictive of a benign lesion. Hence a short interval follow-up was recommended. But studies[15,24-26] reviewing mammographic follow-up of probably benign lesions have reported a very low incidence of malignancy in this group of lesions in which surveillance mammography was performed. However, Sickles et al[25] reported carcinoma in 17 (0.5%) of 3184 lesions classified as "probably benign" during mammography follow-up, while Varas et al[26] found carcinoma in nine (1.7%) of 535 "probably benign lesions". Their low incidence of malignancy was because they reported only lesions in BIRADS 3 category that had biopsy procedure, hence could not determine the frequency of carcinoma in BIRADS 3 lesions in which surveillance mammography was performed. The high rate of carcinoma in the probably benign lesions in the study may result from the fact that BIRADS 3 category is a heterogeneous group, comprising of lesion with microcalcifications in which there is high frequency of cancer

and another group without microcalcifications with a low frequency of cancer[27]. Moreso, experience of the Radiologist in reporting the mammography and assigning the features into BIRADS may also affect the analysis of these BIRADS 3 category[20,28]

The frequency of carcinoma was higher in BIRADS category 5 than in BIRADS category 4 lesions for all mammographic lesion types and these were similar to the findings reported by Liberman et al[29]. However, Berube et al [30], in their study to determine whether the BIRADS categories are useful predictors of malignancy and to assess their positive predictive value, correlated the mammographic features of the lesions, as defined by the BIRADS lexicon with the histological diagnosis after core needle biopsy and reported that all probably benign lesions (BIRADS 3 category) remained in the same category after core biopsy. Whereas, of the suspicious lesions (BIRADS 4), 91% were diagnosed as benign, only 4% was malignant while the remaining 5% has atypical hyperplasia. Among the lesions highly suggestive of malignancy (BIRADS 5), 54% were found to be malignant at core biopsy; hence they concluded that the BIRADS lexicon is helpful in discriminating between lesions that are probably benign and probably malignant from the mammographic features. Whereas, the rate of malignancy in the suspicious category was low[30] but this was different to what was obtained in these study where the rate of malignancy for the suspicious category was high. Thus, this study demonstrated a significant difference in the cancer detection among BIRADS categories 3, 4 and 5.

CONCLUSION

This study revealed a strong correlation between mammographic features and histological findings in breast lesion of women. It was revealed that mammography is very useful for screening and in making a diagnosis of breast lesion in females in University Of Benin Teaching Hospital. Patients with BIRADS category 3, 4, and 5 had a high chance of having malignant breast lesion while those with BIRADS category below 3 have a lower chance. It is suggested that mammography be used for screening and making early diagnosis of breast cancer so as to reduce the morbidity and mortality of breast cancer.

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