MAMMOGRAPHIC BREAST PATTERN IN POSTMENOPAUSAL WOMEN IN IBADAN

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MAY, 2012
DECLARATION

I Dr. Bassey, Oku Sunday declare that this study was done by me and has not been published before or submitted for publication.

Sign..............................................

Date.............................................
ATTESTATION BY HEAD OF DEPARTMENT

I declare that the contents of this dissertation titled: ‘Mammographic Breast Pattern in Postmenopausal Women in Ibadan’, was carried out in the Department of Radiology, University College Hospital Ibadan, and was supervised by me. This study was developed based on the need to know the mammographic breast patterns in post menopausal women and any association with parity, age and demographic features as these are vital for breast cancer risk, diagnosis and prognostication.

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DEDICATION

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# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>TITLE PAGE</td>
<td>i</td>
</tr>
<tr>
<td>DECLARATION</td>
<td>ii</td>
</tr>
<tr>
<td>ATTESTATION</td>
<td>iii</td>
</tr>
<tr>
<td>ACKNOWLEDGEMENT</td>
<td>iv</td>
</tr>
<tr>
<td>DEDICATION</td>
<td>v</td>
</tr>
<tr>
<td>TABLE OF CONTENTS</td>
<td>vi</td>
</tr>
<tr>
<td>SUMMARY</td>
<td>1</td>
</tr>
<tr>
<td>INTRODUCTION</td>
<td>2</td>
</tr>
<tr>
<td>AIMS AND OBJECTIVE</td>
<td>4</td>
</tr>
<tr>
<td>LITERATURE REVIEW</td>
<td>5</td>
</tr>
<tr>
<td>MATERIALS AND METHODS</td>
<td>26</td>
</tr>
<tr>
<td>RESULTS</td>
<td>33</td>
</tr>
<tr>
<td>DISCUSSION</td>
<td>42</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>47</td>
</tr>
<tr>
<td>APPENDIX I</td>
<td>57</td>
</tr>
<tr>
<td>Study Data Sheet</td>
<td></td>
</tr>
<tr>
<td>APPENDIX II</td>
<td>59</td>
</tr>
<tr>
<td>IRB Approval</td>
<td></td>
</tr>
</tbody>
</table>
MAMMOGRAPHIC BREAST PATTERN IN POSTMENOPAUSAL WOMEN IN IBADAN

SUMMARY

INTRODUCTION: Mammographic density is a strong predictor of breast cancer. The mammographic breast pattern in all age groups is of great significance in the effort to understand the changes in breast pattern in pathological processes, and diseases prevalent in such age groups. It is also very important as the basis for national policy on breast diseases. Menopause has a significant effect on breast pattern and it is documented to have more important influence on the decline in mammographic densities than age. Breast changes in postmenopausal women are also affected by parity, positive family history of breast cancer and race. This study therefore aimed to describe the breast parenchymal pattern in post menopausal women. The study using ACR BIRADS Category has also correlated the socio-demographic and anthropometric characteristics with the described breast pattern.

METHODOLOGY: This is a retrospective descriptive study carried out in the Radiology Department of the University College Hospital Ibadan. The mammograms of 196 postmenopausal women which were reported by two experienced breast radiologists in the Department were retrieved and reviewed by the author. The BI-RADS breast parenchymal pattern was classified by the author into two groups, 1and2, and 3and4 for analysis to improve the sensitivity of the result from the small sample size. The final BI-RADS categories were also classified into 0, 1 – 2, 3 – 4 and 5 – 6 groups for the same reason. The report of the mammograms were matched with patients’ data and entered into R statistical package for analysis. Chi-square statistical test was used to assess the difference in proportion between these groups and the categorical variables. The p-value was set at 0.05.

RESULTS: The mean age of the women was 55.0±6.8 years and the mean age at menopause was 48.4±4.6 years. The combined BI-RADS 1 and 2 breast parenchymal patterns which are associated with low risk of breast cancer, were found in 82.1% of the study population. The mean age of the women at birth of their first child was 26.12 years. The mean difference in age at first birth between BI-RADS 1and2 and BI-RADS 3and4 was statistically significant p=0.035. Other variables show no significant statistical correlation likely due to the small sample size.

CONCLUSION: The higher percentage of BI-RADS 1 and 2 breast pattern in this study which is associated with lower incidence of breast cancer in African women supports previous publications, as the dense breast is an important singular risk factor for breast cancer. The clustering of low mean age at birth of first child, low mean age at menopause and multiparity, may be responsible for the higher percentage of BI-RADS 1 and 2 breast patterns in majority of the women in this study. Family and personal history of breast cancer and BMI also correlated with breast pattern; however these were not statistically significant, probably due to the small sample size. Further study with a larger sample size will clarify the statistical significance of these associations.
INTRODUCTION

Menopause by definition is the permanent cessation of menstruation in women\(^1\). It usually occurs in middle age and is heralded by changes in the vascular, urogenital, skeletal, skin and soft tissue (especially breast) as well as the psychological and sexual activity of women\(^2\). It has a significant effect on breast pattern and is documented to have more important influence on the decline in mammographic densities than age\(^3\). The mammographic breast pattern is also affected by other factors like age, race or ethnic group, parity and hormone use\(^4\). Menopause may be natural or induced (surgically or medically). Natural menopause varies in individuals and in races. It occurs between 45 and 55 years\(^5\) in the west, (mean 51 years)\(^5\), and 45 to 52 years in black women (mean 49 years)\(^5\). In India and Philippine the mean age for menopause is 44 years\(^5\). Surgical menopause occurs in middle aged women post bilateral ophoorectomy. Women with hysterectomy without ophoorectomy, whose ovaries are still functional - also categorized as ‘surgical menopause’ are not in the true sense menopausal since the disruption in menses in this case is due to the absence of the uterus. Medical menopause may be due to irradiation or medical disease like diabetes mellitus, as well as drug induced in the form of hormones or chemotherapy. Unexplained menopause occurring in women below the age of 40 years is considered premature menopause or premature ovarian failure (POF). As with normal menopause this varies with countries and race affecting about 1% of the population\(^6\). Irrespective of the cause, the overall effect of menopause in the various body systems remains the same, though the extent varies with individuals and race\(^7\). The menopausal symptoms occur long before any noticeable changes in menstrual cycle\(^7\).

Menopause appears to have a profound influence in the aetiology of breast cancer and is associated with a striking change in the slope of the age-specific incidence curve for breast cancer\(^8\). The age at menopause is known to influence risk of the disease\(^9\), and the large differences in rates of breast cancer that exist between countries are most marked after the age at which menopause usually occurs\(^10\).
Mammographic pattern reflects the tissue composition of the breast\textsuperscript{11,12}. Radiologically, dense tissue in the breast represents stroma and epithelium, whereas lucent tissue represents fat\textsuperscript{13}. Changes in the tissue composition of the breast occur with increasing age, with the amounts of stroma and epithelium decreasing, whilst the amount of fat increases\textsuperscript{14}. These changes results in an overall decrease in the mammographic densities with increasing age\textsuperscript{15}. Studies in other parts of the world have shown sharp reduction in the relative densities of the mammographic pattern in middle age women which also coincide with the age at menopause\textsuperscript{16}. In the Canadian National Breast Screening Survey [NBSS] the percentage breast densities and mammographic pattern according to age showed a 20\% difference in the glandularity of the breast in women between the age 40 – 44 years and 55 – 59 years\textsuperscript{14,15,16}. Menopause is however thought to be a more important influence than age, on the decline in mammographic breast densities\textsuperscript{3} during this period. This view is based entirely on cross-sectional data in which the mammographic pattern of different women were compared, rather than observation of longitudinal change in the radiological characteristics of the breast in individuals\textsuperscript{3,5}

In our environment where post menopausal hormone therapy is not commonly used, it is expected that mammographic pattern in postmenopausal women will be a true reflection of density changes in women in Nigeria, taking into consideration the effect of other fixed and non fixed variables such as body mass index, parity, age at menarche and age at first birth\textsuperscript{16}. The pattern of breast diseases in our study population has also been assessed\textsuperscript{17,18}. This study has therefore evaluated the mammographic breast patterns in postmenopausal women, and reported association between parity, age, weight and demographic features, as these are vital for breast cancer risk assessment, diagnosis and prognostication.
AIMS AND OBJECTIVES

BROAD:

This study is aimed at identifying and describing the breast parenchymal pattern in post menopausal women in Ibadan, South West Nigeria.

SPECIFIC:

1. To provide information on the predominant breast parenchymal pattern in postmenopausal women in Ibadan.
2. To show the correlation between the various breast parenchymal patterns with breast cancer risk factors in the study population.
3. To show any correlation of breast pattern with socio-demographic characteristics of the women in this study population.
LITERATURE REVIEW

ANATOMY OF THE BREAST

The breast overlies the second to sixth rib on the anterior chest wall. It is conical or hemispherical in shape and consists of fat and a variable amount of glandular tissue. It is entirely invested by the fascia of the chest wall, which splits into an anterior and posterior layer to envelop it. The fascia forms septae known as Coopers ligaments, which attaches the breast to the skin, anteriorly, pectoralis fascia posteriorly and through the breast substance to each other. These provide the supportive framework for the breast. The nipple projects from the breast anteriorly (fig. 1). The internal architecture of the adult female breast consists of 12 - 20 conical lobes. The base of each lobe lies on top of the pectoral muscles and ribs, and its apex is at the areola and nipple. Lobular (glandular) and ductal tissue lie within each lobe supported by intra-lobular connective tissue and adipose tissue. There is also extra-lobular connective tissue which binds the lobes together as well as extra-lobular adipose tissue. The breast receives its blood supply from internal mammary, axillary and perforating branches of anterior intercostal arteries.

The radiologic image of the breast is formed by the relative amount and arrangement of each of the structures in the breast. Adipose tissue is radiolucent on mammography and the visible densities on a mammogram are the images of lobular elements, ducts, fibrous connective tissue and blood vessels (figure 2). Ducts may be seen as thin linear radio-dense structures radiating from the nipple, if dilated they may be seen centrally while blood vessels are differentiated from ducts by their haphazard branching network usually of equal calibre. Lobules and their ducts are often superimposed with
connective tissue structures. Whether the mammographic appearance of a breast will appear more or less radiolucent will depend, for the most part on the quantity of extra-lobular connective tissue⁴,⁵.

Medical imaging of the breast came to public attention in the late sixties to the early seventies with direct exposure film mammography and xeromammography¹⁹,²⁰. These two imaging modalities eventually gave way to high quality mammography²¹. High quality analogue mammograms and digital mammography have remained the gold standard for breast cancer screening, work up and diagnosis of breast lesions. Despite the unprecedented growth of cross-sectional imaging modalities such as; ultrasound, computed tomography, tomosynthesis, magnetic resonance imaging, elastography and mammoscintigraphy, mammograms have remained the first line modality for population based screening²²,²³. Digital cross sectional imaging modalities may also be adapted to use computer aided diagnosis (CAD) system to improve lesion detection by the radiologist. The CAD system uses inbuilt specialized computer memory of normal variations in the breast to detect any variation that is not consistent with the overall pattern of the individual breast. The use of mammography in developed countries is largely due to its availability, acceptability, accessibility, cost effectiveness, consistency and sensitivity. Improvement in the technology of X-ray mammography machines and the use of the screen film technique have laid to rest the initial concern at inception of high radiation dose to the breast and low sensitivity of mammography²⁰. These attributes have made mammography the gold standard for breast cancer screening, work up and diagnosis of palpable and non palpable lesions²³.
Figure 1. Shows the sagittal image of the gross anatomy of the breast
Figure 2: A mediolateral oblique view of a conventional mammogram showing mammographic anatomy of the breast. Pectoralis muscle (a), vascular markings (b), retromammary fat (c), nipple (d), inframammary fold (e).
Xeroradiography was introduced in early 1970s as the second imaging modality for evaluation of the breast due to the poor performance of direct exposure film mammography\textsuperscript{20}. Direct exposure film mammography was fraught with motion blurring, due to the long duration of X-ray exposure required for image acquisition, and high radiation dose\textsuperscript{19,20}. Xeroradiography uses photocopying principle in which positively charged Selenium plate is used as the image receptor instead of a film. The charge pattern remaining on the imaging plate after exposure to x-ray corresponds to the various densities in the breast, according to the amount of radiation absorbed. A negatively charged blue toner powder was dusted onto the plate, and the amount of toner attracted to the plate was proportional to the residual charge pattern. This image is then transferred onto a sheet of plastic coated paper as a permanent image\textsuperscript{20}. The imaging plate can be cleaned and reused. Xeroradiography does not require chemical processing or a dark room. The advent of screen film mammography has however, rendered Xeroradiography obsolete because, the former uses far less radiation dose to image the breast\textsuperscript{21}. Excessive contrast and edge enhancement in Xeroradiography are also additional setback compared to a standard high quality mammograms\textsuperscript{20,21}.

Ultrasound (USS) evaluation of the breast uses high frequency sound waves in the region of 7-12MHz. Early studies with USS demonstrated low sensitivity with high inter-observer error and operator dependency\textsuperscript{24}. These limitations have been greatly reduced with the new dedicated breast ultrasound machines with high frequency and better designed transducers\textsuperscript{24}. However, increased false positive and biopsy rate remain known setbacks, when compared to mammography. Ultrasound is also inherently poor in the resolution of microcalcification, which is a common
presentation in ductal carcinoma in situ (DCIS)\textsuperscript{25}. This contributes to making USS less suitable, as a first line modality for breast cancer screening. However, majority of breast cancers are invasive ductal carcinoma\textsuperscript{26}, which present often as soft tissue mass and is easily masked in dense breasts, when less than one centimetre. These cancers and all forms of node negative subcentimetre cancers are detected well by USS\textsuperscript{26}.

Ultrasound is currently receiving attention in population based breast cancer screening programmes, as a second line screening modality in high risk women and women with mamographically dense breast\textsuperscript{25}. High risk women include women with a strong family history of breast cancer such as 2 or more first degree relatives with breast and/or ovarian cancer. Multicentric breast cancer in a first degree relative and BRCA1/BRCA2 gene mutation also confers increased risk. Women with Hodgkins disease and prior irradiation to the chest are also considered as high risk\textsuperscript{25}. The absence of the risk of ionizing radiation, cost and availability also makes ultrasound the modality of choice in the evaluation of breast in children and young adults\textsuperscript{27}.

The role of USS as an adjunct to complement mammography in the imaging of breasts in high risk patients is well established\textsuperscript{24}. Recent publications have shown an improvement in increase in the breast cancer detection rate from 1.3\% to 7.2\% additional cancers per 1000 high risk women when a single ultrasound screening is combined with mammography\textsuperscript{24,25}. This value is more than double the detection rate with mammography alone in the high risk population\textsuperscript{24}. Evidence abound, that the sensitivity of mammography is increased from 48\% to 94\% when combined with breast ultrasound, in patients with dense breast\textsuperscript{28}. Kolb et al\textsuperscript{26} in 2002 showed an
increase of 42% in yield of cancer detection, in non palpable invasive cancers in high risk patients when ultrasound was used with mammography for screening. The diagnostic accuracy of mammography is also markedly improved when combined with USS screening\textsuperscript{25}. Uchinda et al\textsuperscript{29} in 2008 demonstrated breast cancer detection rates of 83.5, 75.3, and 60.8\% respectively for mammography, breast ultrasound (BUS), and physical examination (PE)\textsuperscript{29}. The detection rates of the combinations of mammography and BUS, mammography and PE, then US and PE were 99.0, 88.7, and 81.4\%, respectively\textsuperscript{29}. In their study USS detected 15\% of the mammographically occult breast cancers\textsuperscript{29}. The sensitivity of USS for breast cancer screening is higher in women 50 years and below in the West, as more than 50\% of these women are documented to have the heterogenously dense or extremely dense breast pattern\textsuperscript{25,30, 31}.

Magnetic Resonance Mammography (MRM) utilizes magnetic fields to produce detail cross-sectional images of breast tissues, with inherent good soft tissue contrast. Contrast between tissues in the breast (fat, glandular tissue, lesions, etc.) depends on the mobility and magnetic environment of the hydrogen atoms in water and fat. These contribute to the measured signal that determines the brightness of tissues in the image. In the breast, this results in images showing parenchyma, fat, and lesions (if they are present). At inception, traditional spin-echo sequences of MRM showed poor outcome due to high percentage of fat in the breast, which is high intensity on T1 and T2 weighted images. However, Gradient Recall Echo (GRE) sequences and other manoeuvres which allow fat suppression have significantly improved the use of MRI in breast imaging. The use of intravenous gadolinium-based contrast agent also provides reliable detection of cancers and other lesions. Thus, contrast enhanced MRI has been shown to have a high sensitivity for detecting breast cancer in high
risk asymptomatic and symptomatic women, although specificity is variable\textsuperscript{32-34}.

Magnetic resonance mammography has no place currently, in general population breast cancer screening due to its high cost, time for study and other limitations as noted above\textsuperscript{35}. Magnetic resonance mammography as with BUS, is inherently poor in resolution of microcalcification with consequent low sensitivity in detection of DCIS. However, it is more sensitive in high risk women with a risk of 25\% and above. In some studies MRI shows sensitivity as high as 77\% when compared to 40\% for mammography in women with dense breast. However, specificity was lower for MRI compared to mammography with values of 81\% and 93\% respectively\textsuperscript{36}. MRI is invaluable in multi-centric or multifocal lesions as well as in differentiating scar tissue from tumours\textsuperscript{36}. It is therefore recommended in high resource setting as an adjunct to mammography or USS in diagnostic work-up of the breast\textsuperscript{35}.

Magnetic Resonance Elastography (MRE) of the breast is a phase-contrast-based MRI technique that depends on the quantitative differences in mechanical properties of normal and malignant tissues. The elastic modulus of cancerous tissue in the breast is about 5-20 fold higher than that of normal fibroglandular tissue. This results in marked reduction in compliance when subjected to electromechanical stress\textsuperscript{37,38}. Also the harder cancerous tissue will require higher electromechanical energy to attain the same degree of compliance or deformity with the surrounding normal breast tissues. MRE is done with MRI machines equipped with electromechanical driver and integrated radiofrequency coil unit. It measures the difference in deformation between breast cancer and normal fibroglandular tissue when a known stressor is applied to a volume of
breast tissue\textsuperscript{39}. Magnetic resonance elastography is currently the most sensitive anatomic modality for the diagnosis of breast cancer especially in women with dense breast, with sensitivity reaching 100% in most studies\textsuperscript{37}, however as with MRM, specificity in MRE is low\textsuperscript{40}. It is very expensive, not readily available and requires very skilled technologist and breast radiologist. These factors in concert make MRE a distant consideration in breast imaging.

Breast specific gamma imaging or Scintimammography (SMM) is a diagnostic modality that uses gamma emitting radioactive tracer in the diagnosis of breast cancer. The investigation is performed with a gamma camera after a bolus intravenous injection of radionuclide. The images show increased accumulation of the radionuclide in malignant tissues which appear as hot spots, when compared to background uptake in normal breast tissues.

There is a general consensus in the literature that SMM show high sensitivity in breast cancer detection\textsuperscript{41,42}, but with no statistical significance when compared with mammography, USS and MRM\textsuperscript{39}. It shows higher sensitivity than MRM in some cancers such as DCIS and invasive lobular carcinoma, with values of 91 and 88% of DCIS and 93 and 83% of invasive lobular carcinoma for SMM and MRM respectively\textsuperscript{39,41}. Scintimammography as with most other scintigraphy is affected by the size of the tumour with reported sensitivity as low as 29% in cancers less than 5mm\textsuperscript{43}. The specificity of SMM is generally low and the use of intravenous injection (which may be considered invasive) and ionizing radiation make SMM a diagnostic rather than a screening tool.
Computed Tomography (CT) and Positron Emission Tomography (PET) are also used either individually or in combination where the two modalities are co-registered in one unit as PET/CT machine. Computed tomography uses high energy, low dose X-ray to acquire sectional images of the patient’s breast in prone position. The main advantage of CT in evaluation of the breast include speed of examination, patient’s comfort and low incidence of motion artifacts especially when compared to MRI. The use of contrast medium also helps in the evaluation of extent of the disease including chest wall invasion by small retro-mammary or prepectoral tumours. However CT is less sensitive than mammography in detecting microcalcification which may be the sole manifestation of some breast cancers. This and the relative high cost make CT an adjuvant modality for evaluation of the breast.

Positron Emission Tomography uses 18 fluorodeoxyglucose (FDG) to diagnose as well as stage and monitor cancers. Malignant tissues usually show increased metabolic activity with greater demand for glucose which is usually evident with PET before obvious morphological changes are seen in anatomic imaging modalities. Radioactive glucose (FDG) unlike normal glucose when taken up by malignant cells is trapped within the cells. The increased accumulation of FDG in the malignant cells shows increased activity when imaged with PET machine. Positron emission tomography show high sensitivity, however it is inherently poor in precise anatomic localization of breast cancer\textsuperscript{44}. This limitation is reduced with PET/CT co-registration. In this combination, CT acquires good anatomic image in which lesions are well delineated, this anatomic image is superimposed or fused with the PET image to make accurate diagnosis. The sensitivity and specificity of PET/CT is reported as 80- 96% and 83-100% respectively in some studies\textsuperscript{44,45}. Despite the improvement in cancer detection with PET/CT, the diagnosis of subcentimeter cancers has remained a challenge with
PET/CT. PET also has limited value in identifying tumours that are histologically well differentiated, such as DCIS, and slow-growing cancers such as tubular carcinoma\textsuperscript{46,47}. These factors in addition to high cost have made PET/CT unrealistic in routine breast imaging.

Breast imaging with X-Ray modalities currently includes conventional screen-film mammography, Full Field Digital Mammography (FFDM) and Digital Breast Tomosynthesis (DBT). Digital breast tomosynthesis is the latest of these three modalities. In DBT the X-ray tube moves in a specified arc, but the digital image receptor may be stationary or moves with x-ray tube. It acquires multiple thin cross sectional 2D images (up to 50) in one view which could be viewed in batches or cine mode. Images could also be reformatted analogous to helical CT images and viewed in a 3D mode with better localization of lesion for surgical planning\textsuperscript{48}. The main advantages of DBT are elimination of overlapping tissues, improved visualisation of lesions and better characterisation of lesion margins\textsuperscript{49}. These features have greatly improved the sensitivity of X-Ray imaging of heterogeneously dense and extremely dense breast. Positioning during image acquisition is as in conventional mammography or FFDM. Tight compression for even distribution of the breast tissue is not necessary with DBT, making it a more comfortable and better tolerated investigation\textsuperscript{48}. Various studies have reported reduction of patient's recall rate after BDT by 40-50\%\textsuperscript{50} with lower or same amount of radiation dose used in FFDM\textsuperscript{51,52}. However, loose compression is required to minimise motion artefact. Digital breast tomosynthesis is poor in resolving microcalcification when compared to mammography, it is also prone to motion artefact due to slightly longer acquisition time\textsuperscript{48,50}. Digital breast tomosynthesis is also more expensive and requires additional training for technologist and breast radiologist. It is used
as adjunct to mammography in evaluation of heterogeneously dense and extremely dense breast.

Full field digital mammography uses digital image receptor (Caesium iodide or Selenium) and digital image display system, but positioning and use of compression paddle for even distribution of breast tissues remain the same as in screen-film mammography. At inception this technology was inferior to conventional mammography; however recent improvement in the acquisition and display system as well as the use of computer assisted diagnosis (CAD) has made FFDM a much better screening tool\textsuperscript{53,54}. Various studies have consistently shown statistically significant difference in the sensitivity and accuracy of FFDM compared to screen-film mammography in the evaluation of heterogeneous and dense breast\textsuperscript{54}. However these parameters were similar in population based screening which included women with fatty replaced breast pattern\textsuperscript{55}. Other advantages of FFDM include lower dose of radiation without compromise on image quality and reduction in recall rate especially in women with dense breast\textsuperscript{54,55}. Images on FFDM work station can be manipulated to improve contrast resolution and can also be stored, transferred and handled with ease. Cost is the main disadvantage of FFDM over screen-film mammography with some units up to 4 times more expensive. Spatial resolution of FFDM is also lower compared to conventional screen-film systems\textsuperscript{53}. In low resource economies and where limited access to available technology to support the use of FFDM, screen-film system with USS as an adjunct in evaluation of heterogeneous and dense breast, provides an excellent alternative to FFDM in population based breast cancer screening.
Conventional screen-film mammography has been in use for more than five decades. It is the best studied and most conversant screening tool for breast cancer among breast radiologist. Over the years it has provided the baseline for the assessment of newer modalities for breast cancer screening. Screen-film mammography uses fluorescent material as a single screen in good contact with a single emulsion. This screen-film combination improves the performance of conventional mammography in detecting breast lesions by allowing low radiation dose with maximum contrast. The acquired image is then processed in a processor with the right chemical and temperature to obtain the final image which is available only in a hard copy. Before the advent of FFDM conventional screen-film mammography was the most effective screening modality for the early detection of breast cancer. The reduction in breast cancer mortality with mammography is greater for women above 50 years whose breast pattern is mammographically transparent.

Mammograms with screen-film systems are acquired with automatic exposure control (AEC) using molybdenum anode and double filter [molybdenum and rhodium]. This is to achieve the optimal monoenergetic radiation for the less dense and dense breast respectively. Images are acquired using compression pad to distribute breast tissues evenly on the imaging plate [screen-film] thereby reducing scatter and motional blurring. A single screen-film combination is used to improve differentiation of the various soft tissues of the breast which have virtually the same atomic number and X-ray attenuation characteristics. The screen size depends on the breast size with the aim of achieving breast thickness of about 3-8mm and also reducing radiation dose to the patient. Two standard views Cranio-caudal (CC) and Medio-lateral oblique (MLO) views are conventionally done on both breasts for screening mammography.
Depending on the country or Institutional protocol, one standard view (MLO) may also be done for screening mammography due to concern about radiation risk\textsuperscript{58}. Additional views such as spot magnification and spot compression views may be required to better define lesions seen on the standard views or to magnify detected calcifications.

The extended MLO may be required in women with large breast or breasts with huge axillary tail. In some instances mammograms on very large breasts are done in overlapping segments known as the ‘Mosaic technique’\textsuperscript{59}. In this case the breast is divided into 2-4 imaginary segments depending on the film/cassette size available. The various segments are imaged independently with some overlap with the adjacent segments. The various overlapping segments are viewed together for complete assessment of the breast\textsuperscript{59}. Mammography is associated with minimal risk of ionizing radiation because a limited body surface area (breast) is exposed. This risk is generally accepted as safe with regards to the benefits of mammography\textsuperscript{23}.

However some authorities believe that, with regular screening the dose to the breast tissue is sufficient to trigger an otherwise quiescent lesion, into full cancer especially in young high risk women\textsuperscript{58}. This risk is increased with screen-film mammography with relative high radiation dose and attendant repeat due to poor quality images in these dense breasts. This concern is addressed in part, with current generation of digital mammographic machine which use low radiation dose, and the repeat rate is reduced due to manipulation of the image on the display system to improve contrast\textsuperscript{23,54,55}. The use of other imaging modalities, such as USS and MRI as alternative to x-ray modalities in high risk women, also help to address this concern. Conventional screen-film mammography is well
established world wide as the most cost-effective, sensitive and reliable tool in radiological evaluation of the breast\textsuperscript{60}. In most developing economies it is the only modality available for population based breast cancer screening at the moment.

Mammography is known to contribute to the understanding of the biology of breast cancer\textsuperscript{60}. The transition from low to high malignancy grade, associated with some early diagnosed small cancers over time, is sufficient evidence that some cancers evolve as they grow. The biology of cancers is also demonstrated by rapid growth of some interval tumours in women with dense breast, between two screenings in a screening programme. This attribute of interval tumours is also seen more often in women under the age of fifty years compared to those above fifty years\textsuperscript{60}. In Sweden, a screening programme with a mean follow-up period of 6 years showed that patients with casting-type calcification on mammography had six fold increase in mortality compared to other type of cancers\textsuperscript{61}. This biologic behaviour of casting-type calcification attracted appropriate attention to women with this type of cancer.

The time interval between an existing but mammographically occult cancer and when the tumour becomes visible (Sorjourn time) is well demonstrated by mammography. Various screening trials have provided good evidence on the sojourn time and show some age dependency in the differentiation of cancers\textsuperscript{60}. This has inadvertently explained much of the age difference in the effectiveness of mammographic screening\textsuperscript{9}. Mammographic density is an important predictor of future breast cancer risk and also an important determinant of mammographic screening sensitivity\textsuperscript{60}. A dense breast pattern has been shown to be consistently linked with a greater risk of breast cancer due to the increased proportion of epithelial and stromal
tissues. These tissues are usually the primary site of origin of breast cancer, and show a direct relationship with incidence of breast cancer\textsuperscript{62}. The increased density also masks small cancers with consequent reduction in the sensitivity of mammography in patients with heterogeneous and extremely dense breast\textsuperscript{62-64}.

Though the main interest in mammography has been in breast cancer screening, mammograms over the years in various parts of the world have inadvertently generated extensive amount of longitudinal data, on the relationship of mammographic features and future risk of breast cancer. The percentage of the various amounts of breast tissues contributes, both to tumour behaviour and the future risk of breast cancer in the normal population\textsuperscript{60}. The Swedish two county study reported higher interval cancer rates in women below 50 years of age, when compared to older women\textsuperscript{65}. These younger women had higher mammographic density, and a smaller proportion of stage 1 cancers were detected in this cohort compared to the older women\textsuperscript{65}. More recently, the analysis of the UK national screening data from East Anglia\textsuperscript{66}, demonstrated a significant increase in interval cancers in women with mammographically dense breast\textsuperscript{66}. They also show higher grade cancers at diagnosis, compared to women with fatty replaced breast pattern.

Race or ethnic variation and its relationship with breast cancer risk have also been established with mammography\textsuperscript{67}. Studies in the west have shown higher grade tumours and increased incidence of breast cancer in young women of African descent compared to Caucasians. Though the incidence of cancer in women of African descent is less compared to the Caucasians, Yip et al\textsuperscript{67,68} have shown mortality to incidence ratio of 0.43 compared to 0.3 in low-income and high-income countries respectively\textsuperscript{69}.  

20
This difference in mortality to incidence ratio is mainly attributed to early diagnosis of breast cancer from population based mammographic screening\textsuperscript{70}, which is the practice in the West unlike in Arica.

Unfortunately, there is no "normal" appearance on a mammogram that can be memorized. What constitutes "normal" varies within a wide spectrum\textsuperscript{5}. In addition, the appearance of the breast differs during pregnancy and in the postpartum period. This varying spectrum is due to the differences in breast composition, at the different stages of a woman’s life. A breast with a high composition of adipose tissue will appear darker on a mammogram than a breast with a high composition of connective tissue (stroma) which gives lighter density\textsuperscript{22}. From a population perspective, the mammogram will appear radiographically dense in a higher percentage of younger women than in older women due to the relatively higher stromal and epithelial tissues in the breast of the former\textsuperscript{71}. Even for an individual female, mammographic appearance may vary over the years. Such changes are often gradual and the trend is generally towards a less dense breast, the so called fatty resolution. However the reverse may happen during weight loss, which is associated with general loss of body fat including fat in the breast. Postmenopausal women on hormone replacement therapy will also show mammographic density higher than their counterpart who are not on hormonal therapy\textsuperscript{72}. This is basically due to the effect of oestrogen in hormone replacement therapy on oestrogen receptors in the breast, which invariably sustains proliferation of epithelial and stromal tissues, hence delaying fatty involution of the breast\textsuperscript{71,72}.

Mammographic density is also affected by the age at delivery of a woman’s first child, the number of children and also child spacing\textsuperscript{73}. Some authors in the West have documented that women who have their first live birth
before the age of 30 years are more likely to have a less dense breast pattern as they grow older\textsuperscript{73,74}. These authors believe that, early pregnancy causes permanent alteration in the cyclical changes during breast development with a net reduction in epithelial and stromal tissues with age\textsuperscript{74}.

In the early 1970’s Wolfe\textsuperscript{19} pioneered the use of X-ray mammography to classify breast patterns according to breast density. He empirically classified the breast parenchyma into N1; primarily fatty, P1; < 25% prominent ducts, P2; >25% prominent ducts and DY; dense fibroglandular tissue\textsuperscript{19}. The last category is known to markedly degrade the sensitivity of mammogram, thus making it difficult to detect small cancers. It is also documented to be associated with up to 4-6 times the risk of breast cancer when compared to the primarily fatty breast pattern\textsuperscript{63}. Wolfe\textsuperscript{20} also pioneered the use of xero-radiography to improve breast lesion detection due to its better definition of lesion margins\textsuperscript{20}. This effort has led to the present day use of high quality mammograms in breast imaging\textsuperscript{21}. The American College of Radiology (ACR) against this background established the Breast Imaging Reporting and Data System (BIRADS) which classifies the mammographic breast density into four categories from the fatty breast through the scattered fibroglandular, heterogeneous fibroglandular to the extremely dense breast\textsuperscript{16}. This category is represented numerically as follows:
<table>
<thead>
<tr>
<th>Bi-rads Category</th>
<th>Breast Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>fatty</td>
</tr>
<tr>
<td>2</td>
<td>scattered fibroglandular</td>
</tr>
<tr>
<td>3</td>
<td>heterogenous fibroglandular</td>
</tr>
<tr>
<td>4</td>
<td>extremely dense.</td>
</tr>
</tbody>
</table>

The American College of Radiology also classifies the final breast assessment of each mammogram into categories called the final BIRADS category which is also represented numerically as shown below

<table>
<thead>
<tr>
<th>Final Bi-rads Category</th>
<th>Final assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>1</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>–</td>
</tr>
<tr>
<td>4</td>
<td>–</td>
</tr>
<tr>
<td>5</td>
<td>–</td>
</tr>
<tr>
<td>6</td>
<td>–</td>
</tr>
</tbody>
</table>

Presently, the Wolfe classification has been replaced with the ACR BI-RADS breast classification and all mammographic reports must include the BI-RADS parenchymal breast pattern and the final BI-RADS assessment Category\textsuperscript{16,60.}

A greater percentage of fat relative to epithelial and stromal tissues has been reported in developed countries in the middle age and elderly women\textsuperscript{71}. When other fixed and non fixed variables such as parity,
menopause and post menopausal hormone use are taken into consideration there appears to be a significant reduction in breast density and parenchymal features in favour of fatty replaced breast for the same age group in menopausal women compared to their non menopausal counterparts\textsuperscript{4,8}. Other normal variations of breast tissue include asymmetric patterns and asymmetric size. Although the breasts usually develop symmetrically, differences in the symmetry of breast tissue patterns or breast size are documented\textsuperscript{1}.

Since the pioneering work of Wolfe\textsuperscript{19} on mammographic breast pattern and the increased risk of breast cancer in women with breast pattern BIRADS 3 and 4, various authors in the Western Countries have consistently agreed that breast density is an independent risk factor for breast cancer\textsuperscript{75,76}. Racial differences in breast cancer risk are also demonstrated by some of these authors\textsuperscript{63,77,78}. In Northern America, Caucasian women show higher absolute breast density compared to African American women, while the Asian Americans have higher absolute breast density compared to Caucasians. Del Carmen\textsuperscript{63} demonstrated that African American women have the least mammographic density in a large series of 15,292 women in America. Ursing et al\textsuperscript{78} in a study across America and Asia demonstrated breast density difference in Japanese women in Japan and Japanese women in USA. Breast density differences were also seen in Japanese women in Japan, and America compared to Caucasians in the USA\textsuperscript{78}. This study by Ursing\textsuperscript{78} suggests the role of environmental factor in breast density pattern in the same race. The variation in the risk of breast cancer in different racial groups is adduced to the differential densities in mammographic pattern in these groups\textsuperscript{71}. Recent publications by Obajimi and Akinola et al\textsuperscript{79,80,81} in Ibadan and Lagos both in Nigeria also supported this age long concept on the breast density and cancer risk association in Nigerian Women.
However, del Carmen et al\textsuperscript{63} more recently in their retrospective study reported that the relationship between mammographic density and breast cancer risk is not absolute. In their study, they showed that when corrected for age and body mass index (BMI) there is no racial differences in mammographic density except in Asian women who show higher breast density (absolute and corrected for age and BMI) when compared to Caucasians and African Americans\textsuperscript{63}. The American National Institute of Health classifies BMI into 4 categories; 18.5kg/m\textsuperscript{2} or less is underweight, 18.6 – 24.9kg/m\textsuperscript{2} is normal, 25 – 29.9kg/m\textsuperscript{2} is overweight and 30kg/m\textsuperscript{2} or greater is obesity\textsuperscript{63}. This classification is used in most institutions including UCH. Mammographic density is documented to have an inverse relationship with BMI\textsuperscript{63}.

Furthermore, Asian women have less breast cancer incidence rate (97 per 100,000) compared to the Caucasians (141/100,000) and African American (122/100,000)\textsuperscript{82}. This appears to contradict the status quo as the Asian women are supposed to have higher incidence rate of breast cancer or lesser breast density\textsuperscript{63,83}. The study by del Carmen\textsuperscript{60} has demonstrated that racial differences in breast cancer risk does not correlate with racial differences in breast density pattern. The mammographic density difference across racial groups is also said to be more pronounced in women over 50 years probably reflecting variation in the pattern of breast involution in these group\textsuperscript{63,83}. However, there is consensus that within a racial group and groups with similar BMI, mammographic density is a strong risk factor for breast cancer\textsuperscript{63}. 
MATERIALS AND METHOD

MATERIALS

This is a retrospective study of mammographic records of post menopausal women obtained over a period of 2 years (January 2009 to December 2010). The study venue is the Department of Radiology, University College Hospital (UCH), Ibadan.

SAMPLE SIZE

A total of 196 post menopausal women excluding women with surgical and medical menopause were selected from the pool of women who had screening or diagnostic mammogram done in the Department of Radiology during the study period.

INCLUSION CRITERIUM

Postmenopausal women whose last menstrual period (LMP) was more than six months before they had mammograms done in UCH during the study period.

EXCLUSION CRITERIA

1. Premenopausal status.
2. Women whose LMP were less than six months before their mammograms.
3. Women with history of previous hysterectomy and/or bilateral ophorectomy.
4. Women on postmenopausal hormone therapy
CONSENT
Consent for the study was obtained from the institutional review board (IRB) to retrieve patient’s data from the departmental archive for the study (appendix ii).

METHOD
Mammograms and reports of 196 women, reported earlier by two experienced breast radiologists in Radiology Department of University College Hospital Ibadan, met the inclusion criteria as stated above and were retrieved for this study. They were viewed with a dedicated trans-illuminated viewing box in a conducive environment by the author. The assessed breast pattern, impression and final BIRADS Category were documented. Any disparity with the previous report was clarified by one or both of the experienced radiologists in the department, and a final decision was taken in consensus. The breast pattern of the reviewed mammograms were categorised numerically using the ACR classification 1–4. Each mammogram was also given a final BI-RADS assessment that was also classified numerically into 0 - 6 final BI-RADS assessment Categories as stipulated by the ACR. The BI-RADS breast parenchymal pattern in this study was further classified into two groups, 1and2, 3and4 for analysis to improve the sensitivity of the result from the small sample size. The final BI-RADS category was also classified into 0, 1 – 2, 3 – 4 and 5 – 6 groups for the same reason. Reports with final BI-RADS 0 in this grouping were considered independently in the analysis. This is due to the fact that, in practice, additional imaging is usually required for definitive diagnosis, which will place BI-RADS 0 in one of the other six categories. Additional imaging was done for patients with BI-RADS 0 in this study and the final diagnosis and categorisation was made for each of them. Relevant information on patients’ data sheet, including patients’ weight and height, positive family
history of breast cancer and age were extracted from the routine data sheet (Appendix I), completed by patients before the mammograms were done. Data on menarche were not included in the data sheet and could not be used in the analysis of the results.

The mammographic reports were matched with patients’ data and entered into R statistical package (Auckland, New Zealand) for analysis. The distribution of age, age at delivery of first child, age at menopause and BMI were compared between the BI-RADS breast pattern groups as well as the final BI-RADS groups. Chi-square statistical test was then used to assess the difference in proportion between these groups and the categorical variables. The p-value was set at 0.05. The final BI-RADS category groups were also stratified against the BI-RADS breast parenchymal pattern groups. The results are reported in tables and charts.
Figure 3, A Craniocaudal view of the left breast showing the homogenous fatty replaced breast pattern, BI-RADS category 1.
Figure 4. A Mediolateral oblique view of the left breast showing the scattered fibroglandular breast pattern, Bi-RADS category 2.
Figure 5.A Craniocaudal view of the right breast showing the heterogeneously dense breast pattern, Bi-RADS category 3.
Figure 6, A Mediolateral oblique view of the left breast showing the homogenously dense pattern, Bi-RADS category 4.
RESULT

The data of 196 women who met the Study criteria were selected. The studied population showed a mean age of 55.0 ±6.8 years, while their median age was 54.0 years with age ranging between 38 years and 76 years (Table 1). Most of the women (81.6%) were 50 years and above, with only 18.4% below 50 years of age. Fatty replaced breast pattern (BI-RADS 1) was predominant (46.4%) among the postmenopausal women studied; this was followed by the scattered fibroglandular pattern BI-RADS 2 (35.7%). The heterogeneously dense breast pattern BI-RADS 3 was found in 16.3% and the extremely dense pattern BI-RADS 4 was the least, 1.5%. There was no correlation between age and breast density pattern, p=0.66. Figure 7 on next page, shows the distribution of breast pattern among the menopausal women. Data on some of the sociodemographic features were missing, further reducing the frequency of these features used to correlate with breast pattern.

The predominant breast parenchymal pattern in patients below 50 years was BI-RADS 1 and 2 (15.3%). BI-RADS 1 and 2 was also seen in majority of those 50 years and above, 66.8%. BI-RADS 3 and 4 was seen in 3.1% and 14.8% of women below 50 years and those 50 years and above respectively. The difference in the percentage of women with both BI-RADS group (1 and 2 or 3 and 4) was not statistically significant, (p=0.97), Table 1. The higher percentage of both BI-RADS group in women above 50 years when compared to women below 50 years may be due to the skewed population of the study in favour of women above fifty years of age.
Figure 7: Distribution of Breast Pattern by BI-RADS Category in the study population

Key:

BIRADS 1- Fatty replaced
BIRADS 2- Scattered fibroglandular

BIRADS 3- Heterogeneous
BIRADS 4 - Extremely dense
Extremely dense breast pattern was however found in 2% of those 50 years and above. Figure 8, shows the variation of breast pattern with age among the postmenopausal women. The mean age at menopause for the study group was 48.4±4.6. The mean age at menopause for women with BI-RADS 1&2 was 48.3±4.7 while the mean age at menopause for patients with BI-RADS 3and4 breast parenchymal pattern was 48.9±4.3. There was no statistically significant difference in the mean age at menopause in these two groups, (p=0.44). Ninety five (48.5%) of the women were menopausal at or below 48.4 years while 98 (50.5%) became menopausal above 48.4 years. Two of the subjects had menopause below 40 years (38 and 39 years), this was not sufficient for any useful statistical analysis with breast pattern or other socio-demographic features and are considered as outliers.

Most of the women (95.4%) were multiparous while only 4.6% were either nulliparous or primipara. Majority of the parous women (81.1%) had their first child before the age of 30 years. The mean age of the women at birth of their first child was 26.1±5.5 years with a range of 16 to 50 years. Women with BI-RADS 1and2 tend to have their first child below the mean age of 26 years. There was statistically significant difference in the breast pattern of women who had their first child below and above the mean age of 26 years, p=0.035 (Table 1).
Table 1. Association between mammographic breast density pattern (in BI-RADS categories) and selected socio-demographic and clinical variables.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Breast Pattern</th>
<th></th>
<th></th>
<th></th>
<th>Chi-square value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 and 2</td>
<td>3 and 4</td>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 50 years</td>
<td>30 (15.3)</td>
<td>6 (3.1)</td>
<td>36 (18.4)</td>
<td></td>
<td>0.001</td>
<td>0.97</td>
</tr>
<tr>
<td>≥ 50 years</td>
<td>131 (66.8)</td>
<td>29 (14.8)</td>
<td>160 (81.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at Menopause N(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 48.44</td>
<td>80 (40.8%)</td>
<td>15 (7.7%)</td>
<td>95 (48.5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 48.44</td>
<td>79 (40.3%)</td>
<td>20 (10.2%)</td>
<td>99 (50.5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>2 (1.0%)</td>
<td>0 (0%)</td>
<td>2 (1.0%)</td>
<td></td>
<td>0.375</td>
<td>0.54</td>
</tr>
<tr>
<td>Age at 1st child birth</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD [min, max]</td>
<td>25.74 ± 5.5</td>
<td>27.84 ± 4.9</td>
<td>26.12 ± 5.5</td>
<td></td>
<td>-2.16</td>
<td>0.035</td>
</tr>
<tr>
<td>Age at first child birth N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 30 years</td>
<td>133 (67.9)</td>
<td>26 (13.3)</td>
<td>159 (81.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 30 years</td>
<td>19 (9.7)</td>
<td>6 (3.1)</td>
<td>25 (12.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>9 (4.6%)</td>
<td>3 (1.5%)</td>
<td>12 (6.1%)</td>
<td></td>
<td>0.428</td>
<td>0.513</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Para 0or1</td>
<td>7 (3.6%)</td>
<td>2 (1.0%)</td>
<td>9 (4.6%)</td>
<td></td>
<td>0.009</td>
<td>0.924</td>
</tr>
<tr>
<td>Para 2 or&gt;</td>
<td>154 (78.6%)</td>
<td>33 (16.8)</td>
<td>187 (95.4%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 24.9</td>
<td>18 (11.1%)</td>
<td>7 (4.3%)</td>
<td>25 (15.4%)</td>
<td></td>
<td>1.097</td>
<td>0.295</td>
</tr>
<tr>
<td>≥ 25</td>
<td>114 (70.4%)</td>
<td>23 (14.2%)</td>
<td>137 (84.6%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family Hx. of Breast Ca</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>150 (76.5%)</td>
<td>30 (15.3%)</td>
<td>180 (91.8%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>9 (4.6%)</td>
<td>5 (2.6%)</td>
<td>14 (7.2%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>2 (1.0%)</td>
<td>0</td>
<td>2 (1.0%)</td>
<td></td>
<td>2.029</td>
<td>0.1543</td>
</tr>
<tr>
<td>Previous Hx of Breast Ca</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>151 (77.0%)</td>
<td>33 (16.8%)</td>
<td>184 (93.9%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>7 (3.6%)</td>
<td>2 (1.0%)</td>
<td>9 (4.6%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>3 (1.5%)</td>
<td>0</td>
<td>3 (1.5%)</td>
<td></td>
<td>0.014</td>
<td>0.9068</td>
</tr>
</tbody>
</table>

N – frequency, *34 values were missing in the calculation of BMI, Hx – history, Ca – cancer.
Figure 8: Distribution of Breast Parenchymal Pattern by Age in postmenopausal Women in Ibadan.

**Key:**

BIRADS 1 - Fatty replaced

BIRADS 2 - Scattered fibroglandular

BIRADS 3 - Heterogeneous

BIRADS 4 - Extremely dense
Body mass index was estimated in 162 of the women, out of which 84.6% were either overweight or obese while 15.4% were underweight or with normal weight. The box plot (Figure 9), shows the graphic presentation of BMI in the two groups. Patients in group 1 (BIRADS 1 and 2) had a higher mean BMI when compared to patients with group 2 (BIRADS 3 and 4). The plot also shows 3 unrealistic BMI values that were recorded as outliers in both groups. This may be due to error in data acquisition from the retrospective study. There was no statistically significant association between the BMI of the subjects and their mammographic breast pattern, p= 0.29 (Table 1).

In the final BI-RADS categories, BI-RADS 1-2 were the predominant categories found, representing 65.8% of cases (Table 2). Among these women with final BI-RADS categories 1-2, 84.4%(109/129) had either homogenous fatty or scattered firoglandular breast pattern. This shows that normal or benign findings are more likely in women with BI-RADS breast pattern 1 and 2.

<table>
<thead>
<tr>
<th>Final BI-RADS</th>
<th>BI-RADS BREAST PATTERN</th>
<th>Total</th>
<th>Chi-square value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1&amp;2</td>
<td>17(8.7%)</td>
<td>2(1.0%)</td>
<td>19(9.7%)</td>
</tr>
<tr>
<td>1-2</td>
<td>109(55.6%)</td>
<td>20(10.2%)</td>
<td>129(65.8%)</td>
<td></td>
</tr>
<tr>
<td>3-4</td>
<td>28(14.3%)</td>
<td>11(5.6%)</td>
<td>39(19.9%)</td>
<td>4.069</td>
</tr>
<tr>
<td>5-6</td>
<td>4(2.0%)</td>
<td>1(0.5%)</td>
<td>5(2.5%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>3(1.5%)</td>
<td>1(0.5%)</td>
<td>4(2.0%)</td>
<td></td>
</tr>
</tbody>
</table>
BI-RADS 1 and 2 breast pattern was also predominant in final BI-RADS 3-4 (66.7%), and 5-6 (80%) respectively. Figure 10, shows the distribution of final BI-RADS category among the women. Only 2.5% of the study population was in final BI-RADS category group 5-6, out of which 80% had BI-RADS 1&2 and 20% had BI-RADS 3&4 breast density pattern. There was no statistically significant correlation between final BI-RADS category and breast density pattern p=0.25, likely due to the small sample size of the study population.

Five (35.7%) out of 14 women with family history of breast cancer had either the heterogeneously dense or extremely dense breast pattern compared to their counterpart with no family history of breast cancer 16.7%. This difference was not statistically significant, p=0.15 (Table 1). Women with personal history of breast cancer also show higher percentage of BI-RADS 3&4 breast pattern (22.2%) compared to their counterpart with no personal history of breast cancer (17.9%), p=0.09 (Table 1).
Figure 9: Distribution of Body Mass Index (BMI) with Breast Pattern in the women.

**Key**

1 – BI-RADS 1 & 2

2 – BI-RADS 3 & 4
Figure 10: Distribution of final BI-RADS assessment in the study population.
DISCUSSION

Mammographic breast pattern is well documented by different authors as an independent risk factor for breast cancer\(^5\,8,\,8^4\). Breast parenchymal pattern on a mammogram is modulated by several factors including non-hereditary and hereditary factors. Among the non-hereditary factors, age, menopause, reproductive, demographic and anthropometric factors individually and in concert affects the mammographic breast density thereby affecting breast cancer risk\(^1\).

In this study, the mean age of 55.0 ±6.8 years of the study population was similar to the mean age in most studies in developed countries\(^5\,5,\,5^7\). High incidence of BI-RADS 1and2 (82%) breast density pattern, which is associated with lower risk of breast cancer, is demonstrated in this study. This result is in consonance with the study by Obajimi et al\(^7\,9\) in the same setting where 80% of the women in the same age group had BI-RADS 1and2 breast density pattern. However, there was no significant correlation between breast pattern and age in this study, p=0.66 unlike the other studies\(^1,\,5,\,7\,9\). Only 18% of the women in the study population had the dense breast pattern (BI-RADS 3and4), when compared to Caucasian women of the same age group where 34% of BI-RADS 3and4 was reported\(^1\,9,\,3\,0\). This finding has no doubt contributed to the low incidence of breast cancer in our environment.

Age is an important determinant of breast parenchymal density as well as breast cancer risk\(^1,\,5\,7\). The decline in the prevalence of mammographically dense breast in the population that occurs with age is based among other things on the concept of breast tissue aging\(^1,\,8\). This concept is closely associated with exposure (and duration), of breast tissues to hormones
(endogenous and exogenous hormones), and the effect of hormones on the kinetics of breast cells, rather than just the chronological age alone\(^1,8\).

In this study, the mean age at menopause of 48.4±4.6 years is similar to the mean age at menopause of 48.0±5.9 years in 1189 women, in a study by Olaolorun et al\(^8\) in the same setting, and to that found among African-American women in the diasporas (49years)\(^5\). Menopause however showed no significant correlation with breast pattern of the women in this study, \(p=0.44\). Conversely, the mean age at menopause of Caucasian women is reported to be 51 years\(^5,57\), which is significantly higher than the values for African and African-American women. In this study 1% of the women had premature menopause and this was not sufficient for statistical analysis to correlate their breast pattern with those of women with normal menopause. However, similar trends have been reported in Caucasians with premature menopause seen in about 1% of the population and 1.4% of African - American women is also reported to have premature menopause\(^6\).

It is highly probable that the higher percentage of BI-RADS 1and2 in this study population is due to the lower mean age at menopause\(^1,8\) of the study population, as menopause is documented to have more effect on mammographic pattern than age\(^1\).

Breast development is a continuous process which is cyclical during child bearing age and punctuates at menopause. This process is altered by pregnancy, parturition and breast feeding with corresponding effect on the breast density pattern\(^70,71\). In this study, there was a statistically significant difference between women with mean age at delivery of first child less than or greater than mean value of 26 years, and their type of breast pattern (\(p = 0.035\)). The mean age at delivery of first child in the study population is comparably lower than studies in Caucasian women where most women
deliver their first child after the age of 30 years\textsuperscript{71}. Several studies\textsuperscript{70,71} have documented positive correlation between age at delivery of first child and mammographic breast pattern. Caucasian women who had their first child before the age of 30 years in these studies, were reported to have lower mammographic breast density pattern with corresponding low incidence of breast cancer\textsuperscript{70,71}.

Multiparity is known also to correlate positively with low breast density pattern\textsuperscript{70}. Majority of the women in this study (95.4\%) are multiparous and have predominantly the BI-RADS 1 and 2 breast pattern. However no significant association of parity with breast density pattern was found, (P=0.92). This finding was at variance with the study of 498 women by Obajimi et al\textsuperscript{79} where nulliparity showed significant positive correlation with breast density pattern. However, the study by Obajimi et al\textsuperscript{79} was not limited to post menopausal women, further confirming the important role of menopause in breast density pattern. This feature together with other sociodemographic features individually or in concert has contributed to the greater percentage of BI-RADS 1 and 2 seen in this study population.

Most of the women (84.6\%) were overweight or obese with a mean BMI of 30.0 kg/m\textsuperscript{2}. The mean BMI in women with BIRADS 1 and 2 (30.2 kg/m\textsuperscript{2}) was higher than that of women with BIRADS 3 and 4 (29.3 kg/m\textsuperscript{2}). This finding though not statistically significant (P=0.48) appears to be at variance with obesity as a risk factor for breast cancer. Obesity as a risk factor for breast cancer is however, documented to be independent of breast density pattern in the literature\textsuperscript{23,86}. The greater percentage of women with BI-RADS 1 and 2 (58.2\%) showing BMI $\geq$25 kg/m\textsuperscript{2} compared to BI-RADS 3 and 4 (11.7\%) is in agreement with most published studies in developed countries, where BMI is documented to have inverse relationship with breast density pattern\textsuperscript{60}. 
This finding is also consistent with findings in women of African descent in the Diaspora\textsuperscript{23,60}.

Women with family (14.2\%) and personal (7.6\%) history of breast cancer in this study showed positive correlation with breast pattern though not statistically significant, \(P=0.15\) and 0.9 respectively. These findings as with studies in Caucasians show that family history of breast cancer is a stronger risk factor than personal history of the disease\textsuperscript{23,86}, confirming the role of family history of breast cancer in mammographic screening data. Ding et al\textsuperscript{86} reported studies of a large population of mono and dizigotic twins showing a detailed relationship with genetic factors accounting for up to 60\% of breast cancer risk. Various studies as with our study have shown BI-RADS 3 and 4 breast pattern to predominate in women with family history of breast cancer\textsuperscript{87,88}. 
CONCLUSION

The low incidence of dense mammographic breast pattern in this study reiterates previous findings of low risk of breast cancer in African women, as the dense breast is an important singular indicator of breast cancer. This study has shown the prevalence of most of the known factors (age at menopause, age at delivery of first child and multiparity) associated with low breast density pattern in the study population. These factors individually or in concert may be responsible for the low breast cancer incidence in women of African descent. Further study with a larger sample size is suggested to clarify the statistical significance of these associations.
REFERENCES


55. Pisano ED, Gadsnisis C, Hendrick E, Yaffe M, Baum JK et al. Diagnostic Performance of Digital versus Film Mammography for Breast Cancer


DATA SHEET

MAMMOGRAPHIC BREAST PATTERN IN POSTMENOPAUSAL WOMEN IN IBADAN

A. Serial no.................. Telephone no:...........................

B. BIOMEDICAL DATA
1. Name (Initials)..............
2. Age..................
4. Educational level Primary Secondary Tertiary
5. Height.................................
6. Weight.................................
7. Age at menarche............
8. Any history family planning Yes/No. If yes specify.............................................
9. Number of children. 1 2 3 4 5 >5
10. Duration of breast feeding for each child; 3mo..... 6mo..... 12mo..... >12mo.....

Others specify..........................................................
11. Age at birth of first child..........................................
12. Last menstrual period................................................
13. Age at menopause...................................................
14. Any history gynaecological surgery? Yes/No. If yes specify.....................................
15. Any (Hormonal) treatment for menopause? Yes/No. If yes specify..............................

C. MAMMOGRAM HISTORY/BREAST DISEASE.
1. Have you had mammogram before Yes/No. If yes for what indication and what were the findings....................................................
2. What is the indication for present mammogram please specify
3. Do you have any breast disease?
Rt.                                   Lt.
Lump/mass                 ..........................................................
Skin thickening           ..........................................................
Nipple discharge           ..........................................................
Nipple retraction          ..........................................................
Pain                      ..................................................................
Others specify            ..................................................................

4. Any treatment for breast disease? Needle/surgical biopsy, cyst aspiration, lumpectomy, mastectomy, breast implant/reduction, others specify ..........................................................

5. Do you have breast implant? Yes/No

6. Any family member or first degree relative with history of breast cancer? If yes specify relationship and age at diagnosis ...........................................................................