Mammographic Calcifications in Women in Ibadan, South-West Nigeria: A Seven Years Review

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ABSTRACT

Background/Aims: The purpose of this paper is to present the various types of calcifications seen on mammograms in Nigerian women in Ibadan. The study was to describe calcifications using the American College of Radiology Breast Imaging Reporting and Data System (ACR-BIRADS) classification, document the incidence of the various types of calcifications in a Nigerian population and also report on any association between these calcifications and the demographic variables. **Materials and Methods:** A prospective study of 894 mammograms done in the Radiology Department of the University College Hospital, Ibadan over a seven year period (2006–2013). The mammographic evaluation was carried out by two radiologists. Calcifications were described and classified using the ACR-BIRADS system. Patients' demographic data were obtained using the departmental breast imaging questionnaire. **Results:** Of the 894 women (with an age range of 30–82 years), 213 (23.8%) had calcifications on their mammograms. Macro-calcifications (81.2%) were more common than micro-calcifications (18.8%). The most common distribution of these calcifications was the clustered type. Vascular calcifications (31.2%) were the common morphologic type of macro-calcifications while the punctate calcifications (15.5%) were the common morphologic type of micro-calcifications. About 12.3% of the women had associated masses, 3.3% had associated asymmetric density and 1.9% had associated architectural distortion. A quarter of micro-calcifications fell under 'higher probability of malignancy' (BIRADS 3) and 39% fell under 'intermediate concern of malignancy' (BIRADS 2). 18.4% of the women were asked to undergo further imaging studies. **Conclusion:** We have reported the various types, distributions and morphology of calcifications seen in an African population, similar to those seen in developed countries.

Key words: Calcifications; distribution; mammography; morphology; type

Introduction

Calcifications are important and common findings on mammograms.[1] They may be intramammary, ductal, periductal, intralobular, dermal, vascular, and of stromal origin. They can appear with or without an associated lesion and their morphologies and distribution provide clues to their etiology which may be benign or malignant.[2]

Certain calcification patterns are almost always associated with a benign process and in such cases, no further analysis is required. On the other hand, a mass with pleomorphic irregularly shaped calcifications, heterogeneous in shape and morphology raises concern about malignancy. However, some calcifications are indeterminate and may require further workup to arrive at a diagnosis.[3]

Micro-calcifications are calcifications <0.5 mm in size while macro-calcifications are those >0.5 mm in size.[4] Most micro-calcifications are better seen at mammography using

Access this article online	
Quick Response Code:	Website: www.wajradiology.org
	DOI: 10.4103/1115-3474.162147

How to cite this article: Adeniji-Sofoluwe AT, Obajimi MO, Olusunmade D. Mammographic calcifications in women in Ibadan, South-West Nigeria: A seven years review. West Afr J Radiol 2015;22:76-81.

the spot magnification technique. This makes an assessment of the individual calcifications possible; more so in a cluster where calcifications may be monomorphic (similar shape and size) or pleomorphic (different shapes and sizes).[4,5] Four parameters of calcifications usually assessed are size, shape, distribution, and association with a mass.[5] However, sedimented calcifications like the milk of calcium type of micro-calcifications are better seen on the mediolateral oblique (MLO) view because the calcifications tend to layer out with a straight upper margin giving the so-called "teacup sign" different from the round "smudge" seen on the craniocaudal (CC) view.[4,5] Furthermore, computer-aided detection (CAD) systems may be utilized in the detection of micro-calcifications.[6] Detection sensitivities between 86% and 99% have been reported for malignant calcifications on mammography.[6] Micro-calcifications demonstrated in the early stage of breast cancer and may be the only presenting sign of the disease in some patients, making the diagnosis of breast cancer in the non-mass, non-palpable, and clinically non-evident stage possible.[7] Micro-calcifications seen in the earliest form of breast cancer (ductal carcinoma *in situ* [DCIS] and lobular carcinoma *in situ* [LCIS]) may be the comedo or cribriform pattern depending on the tumor biology; low or high nuclear grade, respectively.[4,7] Macro-calcifications, on the other hand, pose less threat and are demonstrated in benign breast lesions, which can be followed-up over a period of time. They usually do not require the spot magnification technique to aid their detection.[1,3,4]

When calcifications with a higher chance of being malignant are found without an associated mass, they are usually biopsied with the stereotactic guidance. However, if a mass is associated with the suspicious calcification, ultrasound guidance may be employed so long as the mass can be visualized sonographically.[7,9]

Breast calcifications might be an indication of systemic diseases in conditions like secondary hyperparathyroidism from chronic kidney diseases, but they do not simulate those found in breast cancer.[10] Post radiation calcifications can develop in patients being treated for breast cancer.[11]

Materials and Methods

A descriptive, prospective study carried out over a seven years period (2006–2013) in the Radiology Department, University College Hospital, Ibadan. Ethical approval was obtained from our Institutional Review Board and Ethics Committee. All women with calcifications in their mammograms were recruited into the study. The general electric (GE) senographe DMR+ mammographic unit with the filmscreen system was used for the mammographic examination. Informed consent was obtained from the women. The patients' demographic data were obtained using the departmental breast imaging questionnaire. Two standard views, the CC and MLO views were obtained for both breasts. Spot compression and spot magnification views were acquired when needed. The American College of Radiology Breast Imaging Reporting and Data System (ACR-BIRADS) have classified calcifications into three categories. These are the typically benign, those of intermediate concern and those with a higher probability of malignancy denoted as BIRADS 1, 2, and 3, respectively based on morphology and distribution of the calcifications.[3,7,8]

Mammographic calcifications were categorized by interpreting radiologists MO and ATS using the ACR-BIRADS classification into 1 (benign), 2 (intermediate), and 3 (higher probability for malignancy).

The purpose of this paper is to present the various types of calcifications seen on mammograms of Nigerian women in Ibadan. The study describes the calcifications using the ACR-BIRADS, documents the incidence of the various types of calcifications, and describes the pattern of distribution of the calcifications. Correlations between the calcifications and demographic variables are also discussed.

Results

A total of 894 women were imaged in the Department of Radiology, University College Hospital, Ibadan between 2006 and 2013. Of the 894 women, 213 (23.8%) had calcifications on their mammograms. The age range of those that had calcifications was 30–82 years with a mean of 51 ± 10 years. One hundred and eighteen (55.4%) of the women were premenopausal while 203 (95.3%) were parous.

A slightly higher proportion of the women presented for screening mammograms (114/53.5%) than those (99/46.5%) who presented for diagnostic mammograms.

Macro-calcifications were the majority found on the mammograms of 173 (81.2%) women while 40 (18.8%) women had micro-calcifications on their mammograms. Twenty-four women (0.1%) had a combination of micro and macro-calcifications.

Table 1 shows the frequency of calcifications by breast side and quadrant location. More of the calcifications were bilateral (42%). The majority (29%) of the calcifications were detected in the upper outer quadrant of the breasts whereas 22% were found in the lower inner quadrant. Calcifications were few (3%) in the axillary tail.

Figure 1 depicts the distribution pattern of calcifications for both micro and macro-calcifications.

The calcifications seen were distributed in the clustered (59%), diffuse/scattered (11%), and linear/segmental (30%) patterns.

Twenty-six (12.2%) mammograms of women with calcifications had associated masses, 7 (3.3%) had associated

Table 1: Frequency of calcifications by breast side and quadrant location. Bilateral lesions were most common but right sided calcifications were more common than left sided calcifications and AT location were least frequent

Location	
Breast side (%)	**Quadrant (%)**
Right (32)	UOQ (29)
	UIQ (20)
Left (26)	LOQ (12)
	LIQ (22)
Bilateral (42)	RA (14)
	AT (3)

UOQ – Upper outer quadrant; UIQ – Upper inner quadrant; LOQ – Lower outer quadrant; LIQ – Lower inner quadrant; RA – Retro-areolar; AT – Axillary tail

asymmetric density, and 4 (1.9%) had associated architectural distortion.

Vascular calcifications (54) and dermal calcifications (32) were the most common radiologic diagnoses made as shown in [Figure 2].

Punctate calcifications (33%) were the most common morphologic type of micro-calcifications while vascular calcifications (31.2%) were also the most common morphologic type of macro-calcifications as depicted in Figures 3 and 4 respectively; also showing the various morphologic appearances of calcifications as seen on the mammograms in our study.

Only 18.4% of the women were asked to do further imaging studies. Final BIRADS assessment of categories 2 (benign findings) and 3 (probably benign findings) accounted for a greater proportion of the diffuse/scattered distribution of calcifications similar to the clustered distribution of calcifications. On the other hand, most calcifications were placed in the BIRADS 1 and 2 categories for calcifications. Most (86%) calcifications with diffuse or scattered distribution pattern were of low (BIRADS 1) and intermediate (BIRADS 2) concern.

Discussion

Mammographic calcifications can be benign or malignant which affects the management of the patient. Calcifications seen on mammography are better evaluated with magnification techniques.[9] The morphology and size are two critical factors that must be assessed. Most macro-calcifications are >2 mm and tend to be benign, while micro-calcifications are typically <0.5 mm and require more rigorous evaluation and possibly biopsy to rule out malignancy. Furthermore, bilateral lesions are more likely benign.[9,10]

Three hundred and four women without breast masses but with mammographic calcifications and breast cancer were evaluated over a ten years period in New York by Stomper *et al*.[12] Majority of the calcifications found in

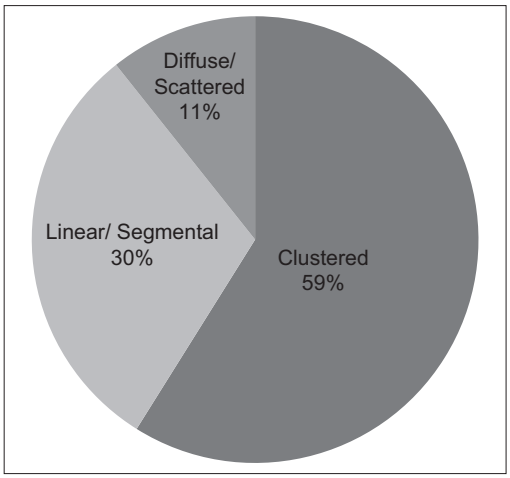

Figure 1: Distribution of calcifications (macro- and micro-calcifications). The majority (59%) of calcifications had a clustered distribution with diffuse/scattered distribution accounting for only 11% of calcifications encountered

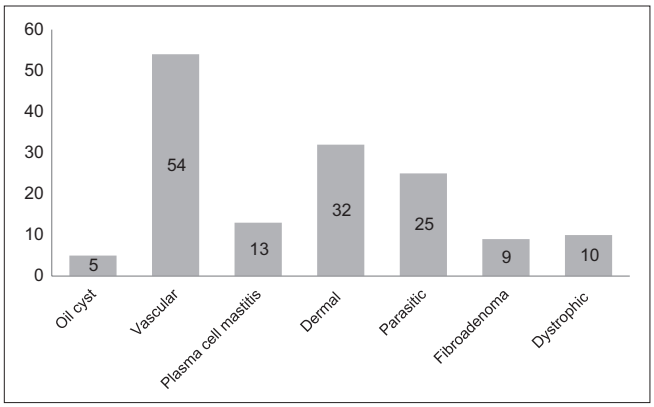

Figure 2: Spectrum of diseases with macro-calcifications. Oil cyst and fibroadenomas were the least frequent lesions associated with macro-calcifications. Dermal calcifications accounted for about a third of macro-calcifications

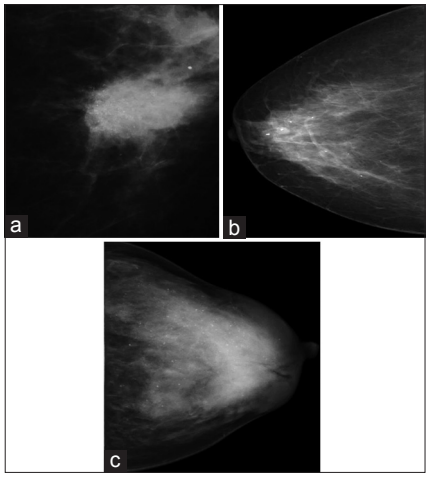

Figure 3: Morphologic appearances of micro-calcifications. (a) Cluster of pleomorphic, (b) scattered indeterminate, (c) diffuse pleomorphic micro-calcifications

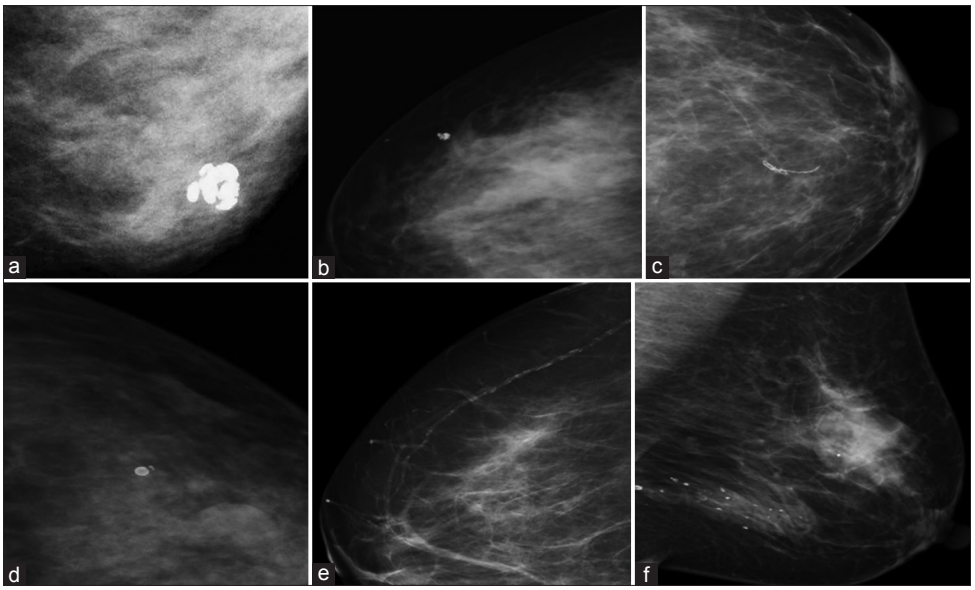

Figure 4: Morphologic appearances of macro-calcifications. (a) Coarse (popcorn) macro-calcification, (b) coarse heterogeneous, (c) coiled, tubular and discontinuous calcification consistent with a parasitic calcification, (d) lucent-centered / rim calcification (Oil Cyst), (e) vascular calcifications, (f) fat necrosis

the study were 1–10 mm in size but the granular type was predominant. In comparison to our study, the study period was over seven years and 213 women with and without breast masses were evaluated. Furthermore, the size of calcifications detected were similar but the granular type was not common in our cohort, this might be due to women presenting earlier for evaluation with imaging due to increased awareness in contrast to the late presentation that has been observed in several studies in our country.[13,14] Early presentation connotes a more fine granular type of micro-calcifications easily identified with digital mammography and with CAD, which was also not employed in our study. The heterogeneous fibroglandular pattern was the most common background breast pattern found, in consonance with our study.[10] DCIS and invasive ductal carcinomas were the most frequent histologic diagnosis made overall and principal in the >50 age group.[10] This is in agreement with our study except for the diagnosis of DCIS, which was rarely made because women still present too late for the diagnosis to be made. One of the factors responsible for late presentation is a low level of awareness about the use of mammography as a screening tool; others include socioeconomic, religious, and psychological factors. Therefore, the diagnosis of invasive breast cancer (ductal/lobular cancer) was made in the majority of cancer cases in our study, due to a late presentation from aforementioned factors.[13.14]

Sedimented calcifications are benign and seen in about 4–6% of symptomatic mammograms but we found no sedimented calcifications.[13] This might be due to the use of the non-digital technique for acquiring the images. Sedimented calcifications may be scattered and clustered in bilateral breast exams. The majority remain unchanged even on follow-up studies.[15]

A review of the surgical pathology database of mucocele-like breast lesion over a 3-years period found 30 lesions. The features on mammography included a related calcifications reported as indeterminate with the majority 56% being benign and 25% DCIS.[16]

Although indeterminate calcifications accounted for approximately 5% of the micro-calcifications detected in our study, they were unrelated to mucoceles.

Linear and branching calcifications were not the predominant morphologic type of micro-calcifications seen in our study. Likely because most cancers we detected are palpable resulting from late presentation and poor attendance at mammography screening. Linear and branching calcification was the most common reason for undertaking biopsy in 300 consecutive non-palpable breast cancers.[17] The calcifications biopsied were those within masses visible on breast ultrasound examination. Other calcifications not associated with masses were not biopsied because our analog mammography screening system stereotactic component was not functional. A few cases of those with a higher probability for malignancy with a BIRADS 3 were excised based on the managing surgeons' decision via a quadrantectomy; thereafter the sample was subjected to histological analysis.

Homer *et al*. in their study of radio pathologic correlation of masses, found most masses with calcifications confined within related masses.[18] Only 12.3% (923/213) of our cohort had associated masses with calcifications. A cluster of micro-calcifications is one of the key conventional signs of early breast cancer, which was the most common distribution pattern in our study.[19] Five such calcifications

in a 1 cm^3 volume of breast tissue is considered a cluster. Although the clustered distribution pattern was the most frequent distribution pattern, we were unable to make an accurate diagnosis in the majority of cases as the calcifications were not biopsied as discussed earlier. We are also likely to have missed quite a number of cancers at the DCIS and LCIS stages, which usually present with this kind of distribution. Linear, curvilinear, and branching calculations < 0.5 mm are best assessed by spot magnification mammography and hand-held magnification device used for evaluating the mammograms of all our patients with micro-calcifications.[19]

In a study carried out over a ten year period in the United Kingdom, 41 cases out of 356 screening-detected cases were of the basal cell type. Basal phenotype was defined according to the expression of basal cytokeratins, 10% or more of tumor cells expressing cytokeratin 5/6 or cytokeratin.[16] Tumors with <10% reactivity were classified as non-basal and these were the majority, which were also more likely to have the non-comedo type of calcifications and ill-defined masses.[20] In contrast, the basal type of breast cancer has been reported as common in our environment; however the mammographic appearance of this type of cancer has not been extensively studied in our environment. Furthermore, no particular pattern of masses associated with BIRADS 3 calcifications was noted. The result of such a study with a large sample size would be of interest in our locality.[16,20]

Calcifications in the breast can also be an indication of systemic diseases in conditions like secondary hyperparathyroidism from chronic kidney diseases, but they do not simulate those found in breast cancer.[10] The presence of systemic diseases was not completely excluded by laboratory tests. Post radiation calcifications can develop in patients being treated for breast cancer but calcifications detected prior to radiation therapy can disappear or remain stable.[11] A few cases in the study group were women on follow-up imaging for breast cancer post radiotherapy. They predominantly had dystrophic calcifications and fat necrosis which is not unusual.

Secretory calcification also called plasma cell mastitis is related to duct ectasia.[21] We found rod-like calcifications present in about 7.5% of our study population. In another study, it constituted just over 3% of calcifications on mammograms.[21] Large rod-like calcifications were bilateral in 80% of cases.

Vascular calcifications are benign and are one of the most commonly seen calcifications in mammography.[4,22] Certain diagnosis can be made by imaging alone. Vascular calcifications in the breast represent calcification in the media of vessel unlike intimal calcification seen in the atherosclerotic disease.[4,5,22] Initial studies suggested an association between breast vascular calcifications and diabetes, but later found the association to be weak.[5,22,23] Other studies have suggested a relationship between visualized breast calcifications and an increased risk for coronary artery disease.[22,23] Granting that vascular calcifications were very frequent in these women, we were unable to correlate these findings with the presence or risk of coronary artery disease as data was not gathered to evaluate this. Diabetes was also not completely ruled out by laboratory means.

Segmental or grouped, scattered, and regional are terminologies that describe the distribution of calcifications. Diffuse and regional calcification is usually benign, but the morphology has to be characterized to draw this conclusion.[24] Those that are suspicious require biopsy. In our study, only BIRADS 3 calcifications that had a related mass visible on ultrasound could be biopsied. Others unrelated to masses were not biopsied as the stereotactic component of our mammography machine could not be used due to unresolvable mechanical faults with the component. Only 14% of our study population were diffuse and in the high-risk group; BIRADS 3 whereas 20% were also in the same BIRADS category but of the clustered variety. Malignant causes of diffuse calcifications are DCIS, IDC with the extensive intraductal component.[24] Common benign causes are plasma cell mastitis and dermal lesions. Dermal calcifications were also frequently seen in our study. Parasitic calcifications were common and not unexpected since *Wuchereria bancrofti* and *Brugia malayi* are endemic in the tropics and especially in the South-Western part of Nigeria with as much as 25% of the population infected.[25] In a study of mammographic parasitic calcifications carried out in the same region, 39/547 (7.5%) mammograms of women demonstrated parasitic calcifications whereas, they only made up 14.5% of all the calcifications seen.[26]

We were faced with a lot of challenges in terms of the imaging device utilized for the screening mammographic examination. The quality of the images acquired was not consistently high as the manual processing method with its antecedent problems was still employed to develop the images acquired. This could have a profound effect on the detection rate of these calcifications in our study. Furthermore, the stereotactic device on our analog system used for the study was faulty. Therefore, a major limitation of the study was our inability to correlate mammographic assessments with histology. In conclusion, we have described the various types, distributions, the morphology of calcifications seen in an African population, which is not different from the spectrum seen in other (Western) populations.

The future direction of our study is to review mammographic calcifications using a digital system with functional stereotactic capability. We hope to compare future findings with those in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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