PREVALENCE AND ACR BI-RADS CATEGORIZATION OF MAMMOGRAPHIC CALCIFICATIONS WITH HISTOPATHOLOGICAL CORRELATION OF THE SUSPICIOUS CATEGORIES AT THE KENYATTA NATIONAL HOSPITAL

A CROSS SECTIONAL DESCRIPTIVE STUDY AT THE KENYATTA NATIONAL HOSPITAL

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DECLARATION

This dissertation is my original work and has not been presented for the award of a degree in any other university.

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DEDICATION

I dedicate this dissertation to my families, the Sehdeva, Gadhia and Mour family.

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LIST OF ABBREVIATIONS

ACR - American college of Radiology.

AJR - American journal of roentgenology

ALARA- As low as reasonably achievable

BIRADS - Breast imaging reporting and data system

DCIS - Ductal carcinoma in situ

ERC- Ethics and research committee

KNH - Kenyatta national hospital

LIUQ - Left inner upper quadrant of breast

LILQ - Left inner lower quadrant of breast

LOUQ - Left outer upper quadrant of breast

LOIQ - Left outer inner quadrant of breast

MRI - Magnetic resonance imaging

RIUQ - Right inner upper quadrant of breast

RILQ - Right inner lower quadrant of breast

ROUQ - Right outer upper quadrant of breast

ROIQ - Right outer inner quadrant of breast

UON - University of Nairobi

MLO - Medio lateral view

TLDU - Terminal duct lobular unit

WHO - World Health Organization

DEFINITIONS

Pathophysiology: Disordered mechanical, physiological and biochemical changes associated with a disease process.

Prevalence: Proportion of a given population with a particular condition at a specific point in time.

Incidence: Occurrence of new cases of disease or injury in a population over a specified period of time.

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ABSTRACT

Background: The incidence of breast cancer has been on the rise. Breast cancer causes the third highest number of deaths in relation to all cancers in Kenya.

Mammography is currently the optimal screening and diagnostic imaging modality for identifying breast cancer and breast calcifications. Other imaging modalities such as breast ultrasound and MRI are suboptimal in detecting calcifications.

Mammographic Calcifications, when present, are known indicators of benign and malignant breast diseases. Their distribution and morphology can determine the next course of action for diagnosis and management.

Mammographic calcifications patterns have been utilized in western countries based on extensive studies done there. The breast calcification patterns in terms of morphologies and distribution guide further imaging and management. There is need for local studies to form a baseline for our breast imaging.

Broad Objective: The objective of this study was to determine the prevalence and pattern of mammographic calcifications and to correlate the suspicious categories to histopathology in clients undergoing mammography at the radiology department at the Kenyatta National Hospital.

Study design and site: Prospective descriptive study at the radiology department, mammography unit of Kenyatta National Hospital, serving the women in Nairobi county and as a national referral institution for other counties and East African region.

Methodology: Ethical approval was sought from KNH-UoN ERC. The study enrolled 190 participants from the clients who required mammographic evaluation as per inclusion and exclusion criteria following informed consent obtained, between February and June 2021. Their demographic and relevant risk factors as well as mammographic characteristics were collected in a predesigned data collection tool. Mammographic images obtained were analyzed and reports prepared by the principal investigator and breast imaging specialists with a composite experience of 10 years. Participants whose mammograms had suspicious calcifications (BIRADS 3-5) underwent ultrasound guided core needle biopsy. Differential and inferential data analysis was done using SPSS Chicago Illinois version 21.

Main outcomes: The mean age of the clients was 53.9(SD=10.8) years respectively. The median age was 53.0 (IQR=46.0-60.) years. They were all females. The ages of the clients ranged between 35-101years. Mammographic calcifications were detected in 40% of the participants. Macro calcifications were 45 (23.7%) while micro calcifications were 32 (16.8%) of the total population. The most frequent type of macro calcification was the vascular type,12 (15.6%) whereas for micro calcifications it was the punctate type, 12 (15.6%). Majority of calcifications were found at the upper outer quadrant of the breast, seen in 20 (26%). The most frequent categories were 1 and 2, accounting for 52 (67.5%) of all the calcifications. In the correlation of 25 suspicious calcifications (categorized as BIRADS 3 to 5) with their histopathological analysis, the sensitivity was 94.7%, specificity was 16.7%, positive predictive value was 78.3%, negative predictive value was 50%, diagnostic accuracy was 76.0%.

Conclusion and recommendations: The study has shown that mammographic calcifications are a common finding, with the benign category being commoner. Suspicious categories have a relatively significant diagnostic accuracy with histopathological analysis. Spot compression with magnification view and/or follow up in 6months is recommended for all suspicious categories (BIRADS 3) especially if there is low index of suspicion for malignancy. Biopsy is recommended for BIRADS 4 & 5 in cases of high suspicion for malignancy. Overall mammographic micro calcifications can help to identify breast malignancy.

CHAPTER ONE

INTRODUCTION

Breast cancer is the second most commonly occurring cancer worldwide and most common in Kenya. There were 2.09 million cases reported worldwide in 2018. In Kenya the cases were at 5985, having risen from 4465 in 2012. The attributed deaths were recorded at 627,000 worldwide making it the 4th highest cancer related mortality in comparison to Kenya where it was the 3rd highest (1,2).

The incidence of breast cancer is very high in the developed countries at 87 per 100, 000 women. In Eastern Africa it stands at 19.3 per 100,000 women and specifically in Kenya it is 40 per 100,000 women(1,2).

Despite this lower incidence rate, the 5-year survival rate for breast cancer clients in developing countries is below 40%, as compared to 80% in developed countries. Less developed countries carry the burden of all the breast cancer cases worldwide at 50% with 58% of the attributed deaths This is partly attributed to delayed diagnosis resulting from lack of early detection programs (1,2).

There are multiple pathologies that affect the breast. Most are benign (75%) and include a large spectrum of lesions with fibro adenoma being the commonest. Minority are malignant but largely responsible for the total attributed mortality (3) . Clients tend to seek medical help at advanced stages. About 80 % of patients in Kenya seek medical care at advanced stages of breast disease. (4). Majority of women with breast cancer at KNH had invasive disease, of which 90% were invasive ductal carcinoma (5)

In evolution of breast cancers, the in-situ forms are non-systemic diseases, which if untreated progress to invasive forms. An opportunity to halt progression to advanced stages is possible, improving the treatment options available to client as well as the outcomes (6). It is useful to have imaging characteristics that can help predict presence of breast cancer early. Mammographic calcifications are an example of such an imaging characteristic. add reference

This study aims to determine the prevalence and pattern of calcifications and the histopathological correlation of the suspicious categories seen on mammograms of clients attending evaluation at the mammography unit of the department of radiology at KNH.

CHAPTER TWO

LITERATURE REVIEW

2.1.0 BACKGROUND

There are many known risk factors for developing breast cancer. These include hereditary and family history of breast cancer, hormonal influences as evidenced by early menarche, late menopause, hormonal replacement therapy, hormonal family planning pills and nulliparity which increase the risk of occurrence of breast cancer (7–9). Lifestyle factors including obesity and diet, diabetes mellitus are also known risk factors to the development of breast cancer. These increase the index of suspicion while imaging the breast tissue (10).

A palpable lump in the breast is the commonest symptom (79%). This is followed by breast pain in 27% (11,12). Other clinical symptoms that can be suggestive of breast disease include breast swelling, nipple discharge, nipple retraction/inversion, changes of skin overlying the breast tissue including redness and dimpling of skin. These clinical signs are usually indicative of advanced disease and lead to higher morbidity and mortality overall (11,13).

Breast cancers can be broadly classified in to two, invasive or noninvasive forms. Invasive forms are seen in up to 90% of the breast cancers in Kenya. The non-invasive cancers do not grow beyond the basement membrane. They are usually not palpable. They may progress to malignancy (11).

Majority of breast cancers are ductal carcinoma in situ (DCIS), accounting for 80% of all breast cancers worldwide. They originate from epithelium within the ducts and spread through them. Atypical cells within mammary ducts and lobules grow at a higher than normal rate, accumulating within and expanding the ducts and lobules. There is no invasion of the basement membrane. Up to 53% advance into invasive ductal carcinoma (14). There are various microscopic subtypes including papillary, micro-papillary, comedo, cribriform, solid and mixed subtypes (15).

In younger clients, DCIS is detected mostly using mammographic calcifications, whereas in older women, it is by presence of masses in the breast (16). On mammography it has 3 major presentations: micro-calcifications (72%), soft tissue masses (10%), combination of both (12%) (17).

Identifying and characterizing breast calcifications is vital to detect DCIS before progression into invasive ductal carcinoma. An organized screening done in UK increased detection of DCIS from 3 per 100,000 in the late 1980s to 23 per 100,000 mammograms in 2013. This six-fold increase was due to identification of mammographic micro calcifications, mostly linear branching type (18). 85-93% of DCIS are diagnosed by presence of micro calcifications. (16,18,19) DCIS are usually associated with 10 or more calcifications per cubic centimeter.

J J Mordang showed in his study that if calcifications were picked up earlier, the rate of development of new cancers might have been reduced by 16%, and invasive cancers by 31% (20).

The remaining pre-invasive breast cancers are lobular carcinoma in situ(LCIS). They do not distort the anatomy of the breast. They often demonstrate no mammographic findings and are discovered incidentally on biopsy specimens (21,22).

Invasive Breast Cancers extend beyond the basement membrane, eventually leading to formation of palpable breast masses and metastasis in later stages. About 80% of these are invasive ductal carcinomas, which were initially DCIS/LCIS. The remaining are invasive lobular carcinoma (21). Primary osteosarcomas of the breast are a very rarely occurring type of breast malignancy.

In 1949, Raul Leborgne reported findings of radiographically visible micro calcifications in 30% of breast cancers (20). Later in 1986, Sickles classified these calcifications based on their risk stratification into benign, probably benign, and suggestive of malignancy, which has since been revised by the BIRADS 5th edition of the American College of Radiology in 2013 (23–25)

There are two proposed mechanisms by which breast calcifications are laid down. First is an active cellular process where benign cells and lower grade tumor cells excrete fluid in to the extracellular matrix which then precipitate in to calcifications. Second is cellular degeneration, where abnormal breast cells grow unopposed which compete for nutrients. Some of these cells die and attract other chemicals in the body, and together they harden and cause areas of calcification. (18,26)

Breast micro calcifications are made up of mostly calcium oxalate and calcium phosphate. They are mostly benign. Some can be malignant dependent on their composition and distribution. Calcium oxalate is produced by apocrine cells of the breast. It is not metabolized by human cells and on histology it is easily recognized. It is mainly

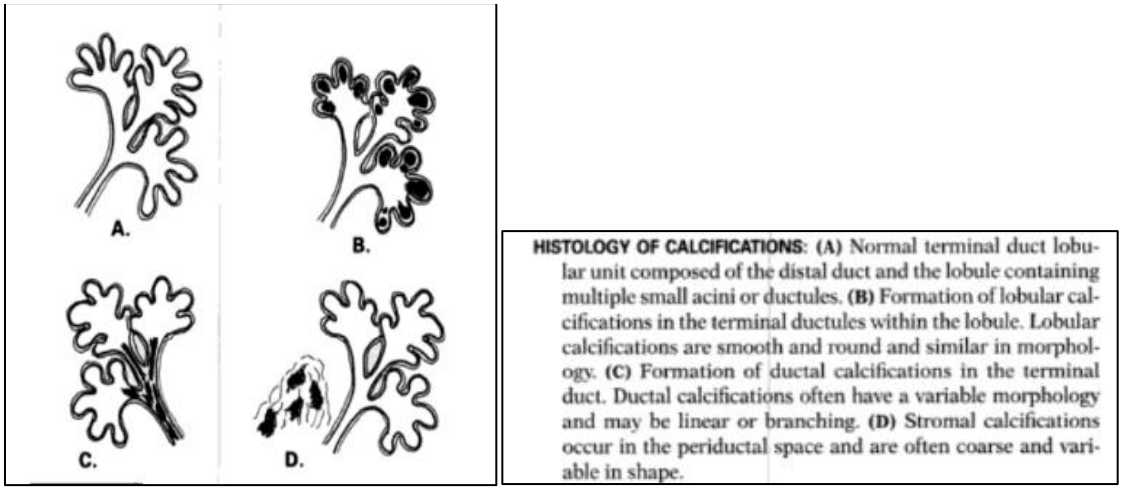
related to benign cystic changes. Calcium phosphate is deposited in form of calcium hydroxyapatite, similar to the one in bone mineralization or skeletal growth. It is mostly associated with malignant changes and stains purple on hematoxylin and eosinophil on histology so is also easily recognizable (18,26).

The functional unit of the breast is called the terminal ductal lobular unit (TDLU). It consists of 10-100 acini that drain in to the terminal duct. The terminal duct drains into larger ducts and finally in to the main duct of lobe that drains in to nipple (21)

The TDLU is the site of origin for various breast diseases including invasive cancers, ductal and lobular carcinoma in situ, fibro adenomas, fibrocystic disease, and adenomas among many others. Most calcifications originate in the TDLU and are therefore ductal calcifications (18,26). Calcified cellular debris and calcific secretions are deposited in to ducts may fragment and give a non-uniform appearance, different shapes and sizes and varying densities. These give rise to pleomorphic calcifications. The secretions may sometimes form a cast in the ductal lumen taking up shape of the ducts, so that there will be fine linear or fine branching types of calcifications. These are usually suggestive of malignancy and are considered as BIRADS 4/5 (27–31)

Other calcifications are deposited external to the breast parenchyma, in the skin and vessels (27–31).

Figure 1: Location of calcifications



courtesy: Atlas of Mammography (31,32)

Calcifications can be found in 30% of all breast malignancies and 55% of non-palpable (16,19,26,33). Mammographic calcifications can help detect rare entities like primary osteosarcoma of the breast, as well as in papillary invasive ductal carcinoma (15)

Invasive cancers with calcifications have higher rates of metastasis, lymphatic invasion and higher local recurrence They also tend to be positive for her2/neu, progesterone receptors and estrogen receptors. (34–37). Biopsied malignant calcifications have a 36% chance of being positive for malignancy (38,39)

Her2/neu receptors are responsible for accelerated uncontrolled cell growth. They are seen in 15-30% of breast cancers. They have a worse prognosis (40)

Estrogen/progesterone receptor positive breast cancers cause cell proliferation by inducing cyclin G1 expression. They have a worse prognosis than estrogen/progesterone receptor negative. Hormone receptor status has been widely studied in breast cancers due to the importance in selecting the chemotherapy agents required. Breast calcifications presence will have an influence on the selection of chemotherapy agent in treatment of breast cancer. (41).

Calcifications can be seen to be intra lesional or extra lesional. In extra-lesional cases, they delineate the true extent of the cancer that can be underestimated based on the size of the margins of a mass alone. surgical margins of excision can be therefore be informed (24).

The presence of micro calcifications, mostly the ductal branching type are recognized to increase risk of recurrence of breast cancer with increased local and distant metastasis. Breast conservative surgery should not be recommended for clients with micro calcifications. Post breast conservative treatment, 43% of mammographically detected cancers manifest as calcifications. Pleomorphic or granular micro calcifications are suggestive of residual malignancy and should be biopsied (37).

A study done in 2017 on prevalence of silent breast cancer in autopsy specimens of asymptomatic clients who had no breast related complaint/illness identified mammographic calcifications, especially the malignant types (BI-RADS 4/5). Their histology correlated with malignancy. This information can help determine the true pattern of breast cancers in a population (42). Put the figures for prevalence.

2.1.1 MORPHOLOGY OF MAMMOGRAPHIC CALCIFICATIONS

Morphology describes the shape and structure of the calcifications. It is considered the most important aspect of determining benign or malignant potential.

2.1.1.0 BENIGN CALCIFICATIONS

They are usually larger, measuring larger than 1mm in diameter, while the malignant ones are usually 0.05mm to 0.5mm (micro calcifications) (25).

Table 1: Mammographic features of benign calcifications. Table adapted from references (23,25)

Type of calcification	location	Mammographic appearance	size	Seen in
Skin calcifications	Sebaceous glands	Polygonal, with lucent centers. Tattoo sign	1-2mm	Chronic folliculitis
Vascular	Mammary arteries	Smooth parallel tracks with a serpentine course	Varying lengths	Age related and due to arterial atherosclerosis
Coarse/popcorn	TDLU	Large, thick popcorn	2-3mm	fibro adenomas
Large Secretory rod-like	Periductal or intra-ductal	Rod-like with or without lucent centers and smooth regular edges. Have ductal distribution	More than 0.5mm	ductal ectasia, plasma cell mastitis
Ring	TDLU	Lucent lesions with peripheral rim of calcification	Several mm to cm	post trauma
Dystrophic	TDLU	Coarse irregular lava shaped. may coalesce	More than 1mm	irradiated breast and post trauma
Milk of calcium	TDLU	Clustered micro and macro cysts with mobile calcifications. Tea cup appearance on 90 degrees Medio	Variable	peri-menopausal and premenopausal

		lateral		
suture	TDLU	Linear/tubular with knots	Depends on size of suture	Post-surgical
Round	TDLU	Round/oval homogeneous	>0.5mm	fibrocystic disease
punctate	TDLU	Pearl homogeneous	< 0.5mm	fibrocystic disease

Uncommon calcifications that may occur include paraffin/silicone induced, parasitic and venous calcifications in Mondor's disease. (23)

Pseudo-calcifications can be seen and may be a result of droplets from creams or deodorants, dust from cassettes and finger prints (23).

2.1.1.1 SUSPICIOUS MORPHOLOGY

These can be associated with malignancy.

Table 2: Mammographic features of suspicious calcifications. Table adapted from

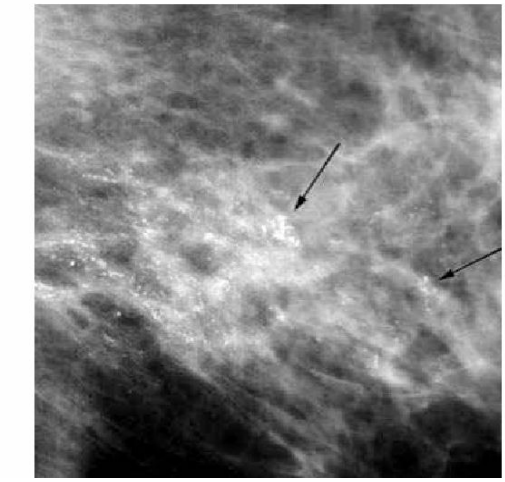
Type of calcification	location	shape	Size in mm	Seen in
Coarse heterogeneous	TDLU	Rough irregular heterogeneous	>0.5 -<1	fibro adenoma, fibrosis, post traumatic-fat necrosis, DCIS.
Amorphous powdery	TDLU	Difficult to determine	<1	sclerosing adenosis, adenomas, or pappilomas
Fine pleomorphic	TDLU	Varying shapes, sizes and density	0.5- 1	Breast tumors
Fine linear/ fine branching	TDLU	Irregular thin linear / curvilinear. May be discontinuous	< 0.5	Breast tumors

references: (23,25)

The stability of lesions over 2 years is considered to be a sign of a benignity. However, for suspicious morphology calcifications, it is not a sure sign of benignity and biopsy is indicated (43).

Calcifications that are larger at first diagnosis and grow faster when followed up have a relatively higher risk of being malignant than those that are initially smaller and with a slower growth rate (43).

Figure 2:Suspicious calcifications



Magnification view shows a segmental distribution of fine, linear, branching calcifications and two groups of pleomorphic calcifications (arrows). Diagnosis was invasive ductal carcinoma with extensive intraductal component (85)

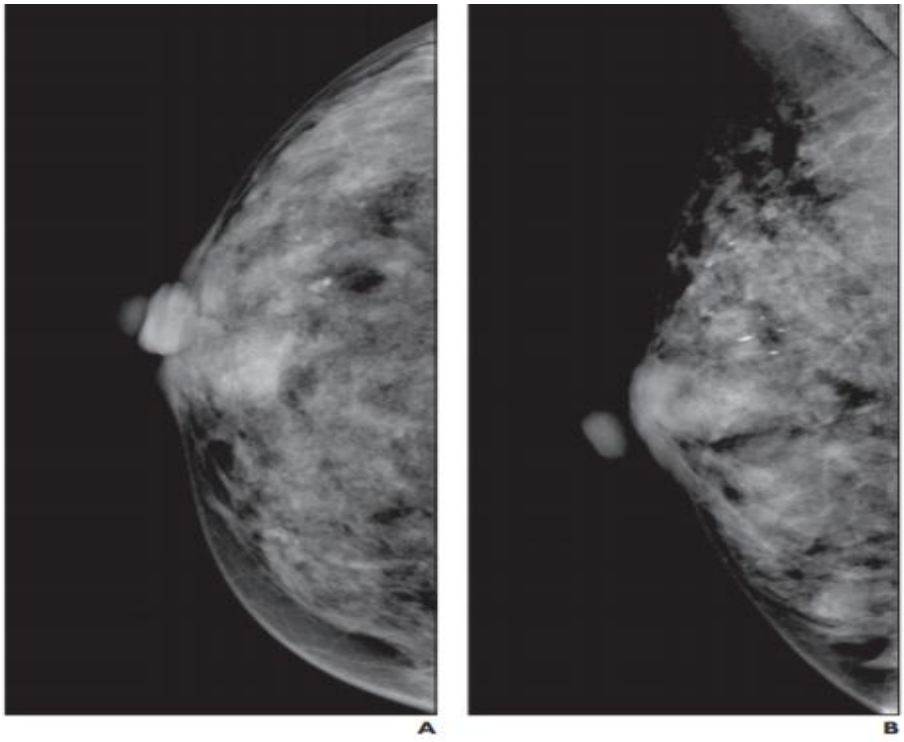
2.1.2 DISTRIBUTION OF MAMMOGRAPHIC CALCIFICATIONS

Distribution is the pattern of spread of calcifications in the breast and is usually valuable when the morphology is indeterminate. When combining morphology and distribution, the predictive value becomes more accurate than for either of the two characteristics alone.

Table 3: Types of distributions of mammographic calcifications. Table adapted from references: (25,44)

type	Description	classification
Diffuse/scattered	Multiple similar clusters of calcifications in whole breast	benign
Regional	Scattered in >2cc of breast tissue. Non ductal distribution.	Benign
Clustered	At least 5 calcifications in <2cc	Benign or malignant
Segmental	Within ducts and branches of a segment or lobe	Malignant

Figure 3: Diagrammatic representation of distribution of calcifications



Segmental Breast Calcifications. Milk of calcium. A and B, Craniocaudal (A) and Medio lateral oblique (B) images of right breast in 46-year-old woman show classic appearance. Due to effects of gravity on calcium sedimentation, calcium-fluid levels are poorly seen in Craniocaudal view but easily visualized in Medio lateral oblique view (45)

For linear calcifications with segmental or linear distribution the malignant proportion or segmental distribution of pleomorphic calcifications were 100%, clustered distribution of linear morphology was 80%. (53).

The distribution and morphology may sometimes be indeterminate, in which cases other characteristics are considered. These include the size, number and stability of calcifications (23)

2.1.3 BREAST IMAGING-REPORTING AND DATA SYSTEM (BIRADS) CLASSIFICATION

This is an international standardized reporting tool by the American College of Radiology, for breast findings on mammography. It has been extended to report findings on sonography and MRI of the breast (23).
BIRADS description can be used to categorize calcifications into the various categories, however the grade can be altered based on the morphology and/or distribution. (25,44)

Table 4: BI-RADS categorization . Table adapted from references (46)

BIRADS	CATEGORY	COMMENTS	PROBABILITY OF MALIGNANCY %
0	inconclusive	Requires further imaging/comparison images	n/a
1	Negative	negative	0%
2	Benign	Symmetrical. No masses, architectural distortions.	0%
3	Probable benign	Probable benign	<2%
4	Suspicious for malignancy	4A	2-9%
		4B	10-49%
		4C	50-94%

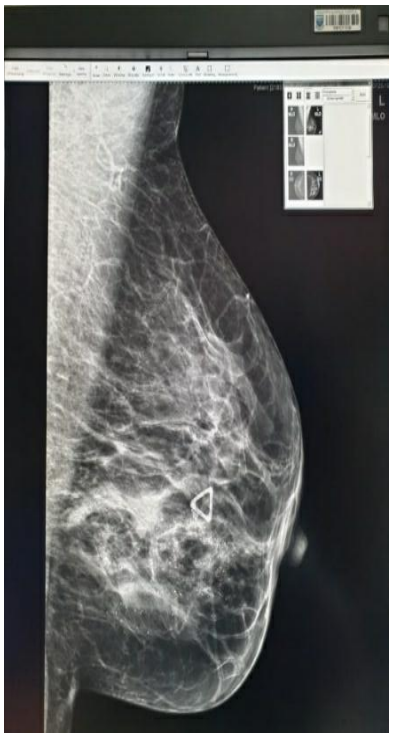
5	Highly suspicious for malignancy	Highly suspicious for malignancy	>95%
6	Known biopsy proven malignancy	Known biopsy proven malignancy	100%

Table 5: BIRADS categorization of calcification. Table adapted from references (46)

Calcification type	BIRADS category
Vascular	3
Skin	2
Milk of calcium	2
Thick linear	2
Popcorn	2
Dystrophic	2
Round/punctate scattered or isolated	2
Ring	2
Suture	2
Round grouped	3
Coarse rough heterogeneous	4B
Amorphous	4B
Fine pleomorphic	4B
Linear/branched linear	4C
Linear and new branching linear and segmental distribution	6

Figure 4: mammogram

Courtesy: KNH. Pleomorphic clusters of calcifications noted adjacent to the marker for a palpated breast lump. Note the different shapes, sizes and densities of the clustered micro calcifications with segmental distribution.



2.1.4 ASSOCIATED FEATURES OF MAMMOGRAPHIC CALCIFICATIONS

Some features associated with calcifications cause a higher risk of malignancy.
Architectural distortional appearances including spiculations, focal retraction, straightening or thickening of cooper ligaments, compression of tissue around a mass can represent either benign or malignant disease and when occurring concurrently with micro calcifications can represent benign sclerosing adenitis, or malignant ductal carcinoma in situ (47).
Duct changes such as asymmetric dilatation, especially in a non-retro areolar or lateral region of the breast, with branching micro calcifications warrant a biopsy due to high risk of malignancy (31).
Skin thickening with calcifications can be seen in malignancy which later can become focally retracted. Dermal calcifications are usually benign, but rarely inflammatory breast cancer can lead to pleomorphic dermal calcifications (48).

Associated enlargement of lymph nodes (intra mammary or axillary) with a high density, rounded irregular shape or ill defined, with or without intranodal calcifications are highly suggestive of malignancy (44,49).

2.1.5 IMAGING OF CALCIFICATIONS.

There are mainly three imaging modalities used in detecting breast cancers, and mammographic calcifications.

Mammography is the optimal modality for detecting breast calcifications (23)

Ultrasound is mostly able to visualize large sized calcifications or those associated with nodules and cysts, usually in clients who are symptomatic. The characterization of the breast calcification in terms of shape and size is also not very accurate. Hence ultrasonography is not used for this study.(50)

MRI has the highest sensitivity in detecting soft tissue changes in the breast. Its ability to detect calcifications is limited. It is not cost-friendly, or time –effective and does not allow for targeted tissue sampling while imaging real time. (23).

Mammograms are a non-invasive, relatively accessible type of high-resolution x-ray specific for compressed breast imaging, with the exposure factors adjusted to improve detection of abnormalities and maintain radiation safety (21). Mammography dates back to 1913 (51).

Figure 5: Senoessential GE machine

Courtesy: Kenyatta National hospital.

There are two types of mammograms, screening and diagnostic mammograms. Appropriate type is selected based on each client's individual requirements.

Screening mammograms are performed for clients with no breast-related complaints. The approved Screening imaging modality by WHO for breast cancer is mammography. Women above 50 years do routine screening mammograms for breast cancer mandatorily in some countries. In Kenya, despite of policy recommendations, there is still low screening, physician-prescribed or self-prescribed mammography done. Younger women who are at high risk are screened routinely. High risk factors includes previous history of breast cancer in family.(21)

Diagnostic mammography is for older women, above 40 years, with breast related complaints. Younger women, who have denser breasts usually undergo sonography, with

supplementary mammography in case of presence of calcifications. Men also undergo this type of mammography when they have breast related complaints.(21)(25,44,46).

Correct positioning, adequate compression and exposure factors in mammography are very important in order to reduce artefacts, client discomfort and thereby increase the final image quality (61). The conventional images are taken in Medio-lateral(MLO) and Cranio-caudal views(CC). To optimize the characterization of micro calcifications, magnification views are done in the true lateral MLO and CC views, and tangential views are useful for intradermal calcifications (15,52).

Magnification mammography utilizes a smaller focal spot size which focuses at a smaller targeted volume of the breast being imaged, to cause geometric enlargement of calcifications especially those that are clustered together to characterize them better. This increased resolution in comparison to the conventional mammography occurs without an increase in unsharpness of the mammographic image which occurs when a normal conventional image is zoomed to increase the size of the calcifications (53). The principal impact of magnification mammography can be observed in the evaluation of clustered breast micro calcifications. Sickles showed in his study that majority of clients' interpretations were changed from "equivocal" to either "benign" or "malignant". They were reclassified because of the increased detail with which small calcifications portrayed in the additional magnification mammogram. Calcifications could be identified in both conventional and magnification images, but the magnification technique more clearly defined the extent of the lesion (number, distribution, and especially shape of the calcifications). Overall there was increased number of correct interpretations in 40 % of the cases (from 62/216 = 29% to 150/216 = 69% (53). Perisinakis showed that electronic magnification and processing of the digital film gives similar information while identifying calcifications as magnification while at the same time the additional radiation dose due to magnification view is avoided.(54)

Tomosynthesis is a three-dimensional mammographic imaging modality that can be used to detect calcifications. There has been no significant difference noted in the detection rates when compared to the conventional digital mammography. A paired study done by M Lee comparing 100 mammograms with calcifications, demonstrated that tomosynthesis detected only 75% of the mammograms to have calcifications whereas the full field digital mammography detected in 84% (55).

BIRADS recommends biopsies for calcifications and lesions that are classified as BIRADS 4 or 5. They are best carried out by radiologists rather than a surgeon as the micro calcifications are too small to be visible to the naked eye. The radiologist can

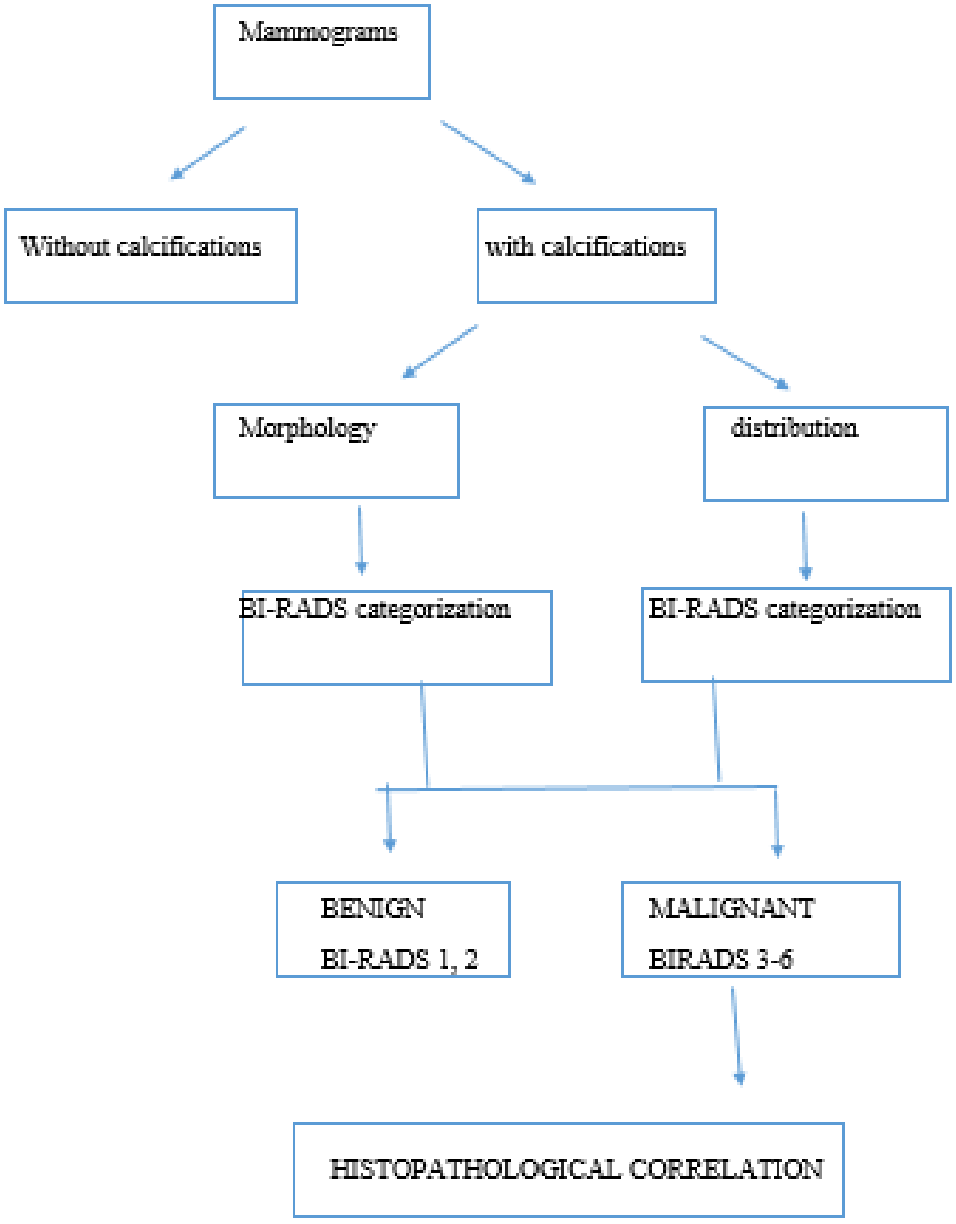
perform biopsies under guidance of ultrasound or mammography (56). In this study calcifications considered BI-RADS 3 (malignancy potential is 2%) will also be biopsied as their follow up may require more time than the study time frame.

Mammographic stereotactic biopsy (S- biopsy) is the method of choice to biopsy. It is not technically achievable in cases where clients who are obese, in whom the lesion is too superficial or too close to the chest wall. S-biopsies are useful for non sonographically visible calcifications and those that are too small to be seen by the naked eye. It however has specific machinery requirements of the mammographic machine.

In a study done by Mary Scott, of the 111 suspicious calcifications identified mammographically, only 23% were sonographically visible. However biopsies identify other findings that can suggest the malignancy of the calcifications such as architectural distortion, metaplasia of cells (57)

During ultrasound guided- biopsy the breast is not compressed. The client is more comfortable in a supine position and the procedure is less time consuming. The radiologist also has more flexibility with inserting needle in to the skin, and real time observations can be made (58). Conventional gray-scale examination may however limit the identification of calcifications, especially those located outside of a mass or duct, due to the lack of contrast with the normal breast parenchyma. Recent technical advances have improved the detection of calcifications by ultrasound (50).

2.1.6 CONCEPTUAL FRAMEWORK



2.2 STUDY JUSTIFICATION

Breast cancer is a very debilitating disease worldwide.

There are multiple causes of the delays that occur in diagnosing breast cancer. Knowledge gaps in performance and interpretation of the mammograms is one of the causes.
Breast calcification pattern is one of the few known mammographic imaging characteristic that can help make diagnosis of the commonest type of breast cancer, ductal carcinoma in situ especially at an early stage.

Knowledge of the mammographic calcifications' prevalence and patterns, histopathology of suspicious categories in our setting will raise the index of suspicion for radiologists. They can be guided on how to recommend further imaging or follow up. They may in future guide the surgeons regarding surgical modes of treatment including biopsies and excisions, and pathologists to carry out qualitative analysis of the calcifications as appropriate.

This study may also become the basis for other studies in future that could correlate breast calcifications with presence of hormonal receptors and immunological factors that are highly predictive of the overall outcome of breast cancers and important when selecting the treatment options such as chemotherapy medications.

2.3 STUDY QUESTION

What is the prevalence and ACR BI-RADS categorization of mammographic calcifications and histopathological correlation of suspicious categories on mammography at the radiology department at Kenyatta National Hospital?

2.4 OBJECTIVES

2.4.1 MAIN OBJECTIVE

To determine the prevalence and ACR BI-RADS categorization of mammographic calcifications and histopathological correlation of suspicious categories on mammography at the radiology department at Kenyatta National Hospital.

2.4.2 SPECIFIC OBJECTIVES

1. To determine the prevalence of mammographic calcifications of clients undergoing mammography at the radiology department of Kenyatta national hospital.

2. To determine the ACR BI-RADS categorization of mammographic calcifications in terms of morphologies, distributions, and location of clients undergoing mammography at the radiology department of Kenyatta national hospital.
3. To correlate suspicious mammographic categories (BI-RADS 3-5) with histopathology of clients undergoing mammography at the radiology department of Kenyatta national hospital.

CHAPTER 3: METHODOLOGY

3.1 STUDY DESIGN

The study was a prospective descriptive study.

3.2 STUDY SITE

This study was carried out at the mammography unit of the department of radiology at Kenyatta National Hospital (KNH). KNH is a national referral hospital in Nairobi, the capital city of Kenya. The main catchment area was Nairobi, Central and surrounding Eastern parts of Kenya. KNH is also a teaching institution for both undergraduate and postgraduate medical students and various other disciplines in health. The main area of the study was the mammographic imaging department.

3.3 STUDY POPULATION

The study population was all clients presenting for mammographic evaluation at the mammography unit of the department of radiology at Kenyatta National Hospital (KNH).

3.3.1 CASE DEFINITION

The case in consideration for this study were the mammographic images of clients imaged at the mammography unit of the department of radiology at KNH.

3.3.2 INCLUSION CRITERIA

1. All clients undergoing mammography who provided informed consent to participate in the study.

3.3.3 EXCLUSION CRITERIA

1. Clients who had declined consent.
2. Clients who had any major surgical intervention or chemo-radiation. They will require comparison studies with previous images to check for changes in the morphology and number of calcifications. Comparison with previous images was not part of this study.

3.4 SAMPLE SIZE

Sample size was calculated using the (Daniel, 1999) formula;

$$n = \frac{Z^2 x\ P(1-P)}{d^2}$$

Where,

n = Desired sample size

Z = value from standard normal distribution corresponding to desired confidence level (Z=1.96 for 95% CI)

P = expected true proportion (estimated from a prospective study of 894 mammograms done in the Radiology Department of the University College Hospital, Ibadan over a 7-year period (2006–2013), of clients with calcifications was 23.8%. This study was chosen as it was carried out in a developing country similar to Kenya, with clients sharing similar demographics.

d = desired precision (0.05)

$$n_0 = \frac{1.96^2 x\ 0.238(1-0.238)}{0.05^2} = 280$$

This amounted to approximately 600 mammograms done per annum. Adjusting the sample size for finite populations less than 10,000

$$nf = \frac{n_0}{1 + \frac{n_0 - 1}{N}} = \frac{280}{1 + \frac{280 - 1}{600}} = 187$$

3.5 SAMPLING METHOD

The sampling method was consecutive sampling till the appropriate sample size was attained.

3.6 PROCEDURE/DATA COLLECTION

A prospective descriptive study was carried out at the mammography unit of the department of radiology at Kenyatta National Hospital (KNH). Ethical approval was obtained from the ethics committee of KNH.

Clients seeking mammographic examinations underwent mammography at the unit using the automated Senoessential GE mammography machine.

The clients were asked for permission to analyze their mammograms and utilize them for the study if they consented. The principal investigator (PI) obtained the request forms with history of symptoms and signs recorded by the requesting physician/surgeon. Additionally, the pre-procedural mammographic client form and questionnaire form filled by the assisting radiographer was collected into the data collection tool.

The PI applied the eligibility criteria and filtered those to be included in the study.
The PI prepared mammogram reports for all the clients, which were verified by the supervisors (who have experience in reporting mammograms for over ten years), and thereafter the reports were finalized.

The mammograms of consenting patients were used to fill the data collection tool. Calcifications were categorized as per the ACR-BIRADS categorization system.

The suspicious category calcifications were recommended to undergo ultrasound guided biopsy. The pathologists were blind to the study and no information regarding the inclusion of the participants in the study was recorded on the histopathology request forms. The biospies were done within a timeline of maximum 5months from date of reporting to avoid introduction of changes to the calcifications.

Data from the mammograms and the histopathology reports was collected on the following variables:

I. Morphology of calcifications.
II. Distribution of calcifications.
III. Presence of associated findings.
IV. Location of calcifications
V. Histopathological results of biopsied calcifications.

Data collection tools was pretested and designed to capture the pattern of mammographic calcifications as well as other associated and incidental findings that were reported. Analysis was done using the SPSS at 95% CI.

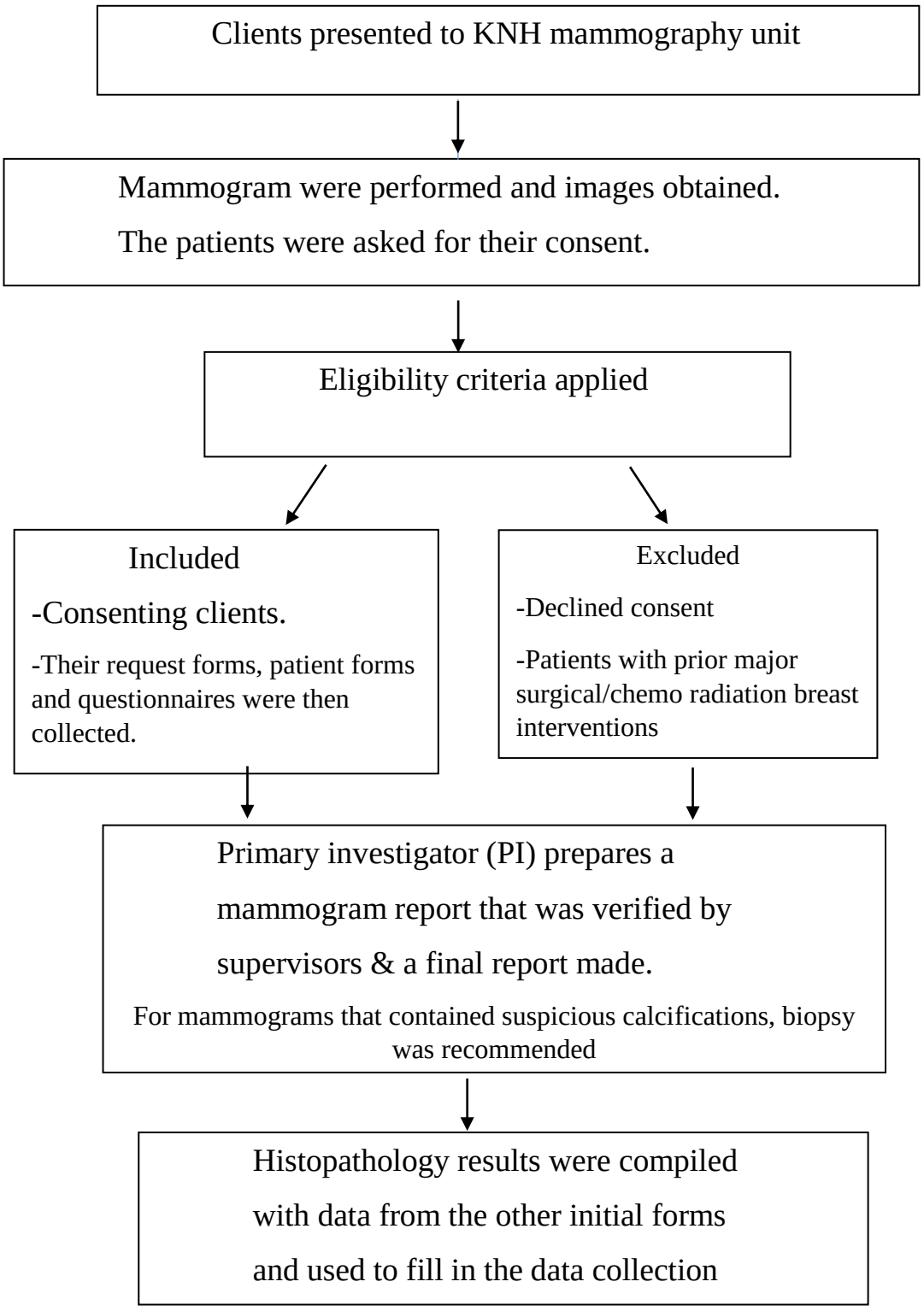
3.6.1 STUDY ENTRY POINT

All clients who presented at KNH mammography unit, radiology department, KNH.

3.6.2 STUDY INSTRUMENTS

A study proforma was used, part of which is the KNH client form, to collect socio-demographic and clinical data e.g. sex, age, duration of illness. APPENDIX I was used as the auditing tool.

3.6.3 STUDY FLOW



3.6.4 QUALITY ASSURANCE

Corona pandemic associated precautions

The recommendations related to the corona pandemic as issued by the Ministry of Health of Kenya were adhered to throughout the study (70).

A hand basin was available, along with liquid soap, sanitizers, and surgical masks for every client and study assistant, radiographers, and primary/secondary investigators.

Additionally, face shields and surgical gloves were availed for persons involved in this study. Non powdered gloves were used so that there is no glove powder of fingerprints of the technician. These could cause pseudo-calcifications.

The mammography machine, table and seats were wiped with 70% alcohol sanitizer after every client exits.

At any point only 1 woman could be attended to during the procedures. The seat for the client was at least 1.5metres away from each individual involved in the study. Every attempt was made to keep a distance between the client and radiographer during the process of positioning.

Quality assurance before mammography image acquisition

Quality checks were done as per the instructions of the manufacturer and include full field artefact evaluation and system check, detector calibration, image quality evaluation, automatic exposure control calibration.

The principal investigator together with the mammography technicians will go through the techniques for positioning during mammography for both standard and supplementary views.

The questionnaire and auditing tools were tested for its user-friendliness, also the study assistants were adequately trained by the PI on the data collection process prior to the onset of the data collection thus the assistant was well vast with the research tools and all clarifications were made beforehand. This will minimize errors during the data collection process. There was a data verification process done by the PI at the end of each data collection day.

Prior to every procedure, decontamination of the mammography equipment was done using methylene spirit, (including the compressor pedal and the breast support). Adequate client preparation was done, and this included talking to the client and explaining the procedure earlier to ensure compliance and good understanding of the procedure.

The breasts were cleaned gently with alcohol wipes, which will allow for removal of particles such as talc powder or deodorant that may cause confusion to be an abnormality or artefacts while reporting. The mammograms were performed in the same sequence every single time to avoid confusing the left and right sides of the breasts.

Quality assurance during report processing

Optimal lighting was low, but not pitch dark, and at the same time ensuring that any light entering from the doors or windows was eliminated. The sitting arrangement was done so that the reader saw the images from a central point and also be comfortable while reporting.

Each received image was counter checked to see if it belongs to the client whose request form is being used. The demographics of the client and associated history was checked if they match as the one of the soft copy images. The image quality was assessed before reporting could be initiated. Images that are suboptimal in quality was rejected and appropriate decision made for possible repeat or supplementary views being conducted. The reports will also be viewed with magnified views to ensure all calcifications were captured. The reports which were made by the principal investigator were saved and the on the PACS system of the hospital for referencing during verification with the supervisors. Any previous studies done will also be considered while preparing the report. Every report prepared by the principal investigator was rechecked by the supervising investigators and thereafter a final report was made, which was given to the client. Quality assurance after the images have been acquired and the corresponding reports processed. All images were saved in the hospitals electronic storage system for future referencing. The histopathology reports were kept confidential with records maintained in a similar manner as the mammographic reports with involvement of the personnel involved from the pathology department.

3.7 ETHICAL CONSIDERATION

Ethical Approval was obtained from the University of Nairobi and KNH research and ethics committee before commencement of data collection.

Radiation protection for the clients were strictly maintained as per the ALARA technique. Optimal technique was maintained so that mammographic examinations were not unnecessarily repeated. Two standard views were performed (CC, MLO). Supplementary views will only be added only if the required information is not available on standard views. Exposure times were kept at minimum limits. Radiation protection was maintained for all personnel working in the mammography unit. The staff is already issued with radiation dose monitoring devices that were routinely evaluated on a monthly basis for the maximum dosage allowance.

Clients' confidentiality was maintained by assigning codes to the data collection forms and computerized data. Data collection forms were stored in a lockable case that were accessible only to the principal investigator and personnel involved in the study directly. The sole purpose of the collected data was to meet the objectives of this study. The client shall be protected off any emotional, socio-economic harm. The staff is well aware on the sensitivity required when involving with clients in the health facility. There were no additional costs incurred by the client due to participating in this study, the imaging and/or tissue sampling for pathological evaluation that was undertaken is what the client would have undergone even if not involved in the study.

The overall benefit would be that the client care will be improved in the future based on recommendations that the study will make and include higher suspicion of malignancy by the radiologists who will later be able to guide other involved specialists.

3.8 STUDY PERIOD

The study was conducted over a period of 6 months.

3.9 DATA MANAGEMENT AND ANALYSIS

All data from the study pro forma was coded, entered and managed in Microsoft access database. Data cleaning was conducted at the conclusion of data entry. Data analysis was done using the SPSS Chicago Illinois version 21. Study population was defined using clinical and socio-demographic characteristics. Continuous variables were summarized as mean and standard deviation while categorical variables e.g. age, sex, were presented as proportions. Pattern of the mammographic calcifications were analyzed relevant results were represented in tables.

CHAPTER 4

RESULTS

The main objective of the study was to determine the prevalence of mammographic calcifications in clients, categorize them according to the BIRADS classification and correlate the suspicious categories with histopathology.

A total of 190 consecutive clients presented at the radiology department with requests for mammography during the study period, February to June 2021. They were all females whose ages ranged between 35-101 years. Out of 190 clients, 77 clients had mammographic calcifications. Suspicious calcifications (as per BIRADS categorization, BIRADS 3-5) accounted for 25 mammograms, of which 76% were found to be malignant on histopathology.

Sociodemographic and characteristics of the clients (Table 6)

A total of 190 consecutive clients presented at the radiology department of Kenyatta National Hospital with requests for mammography during the study period. They were all females.

The mean age of the clients was 53.9(SD=10.8) years respectively. The median age was 53.0 (IQR=46.0-60.) years. The ages of the clients ranged between 35-101years.

Majority of the clients had up to primary education (48%).

Majority of the clients had normal age at menarche, 73%, and 61% were postmenopausal. Most clients had between 1-4 children ,73.7 % and a small percentage, 20.5% had more than 4 children (multiparous) and very few had no children. Hormonal family planning was used by 65.8% of the clients at some point in their lives. Previous known breast cancer was seen only in minority (6.8 %). Chronic conditions like diabetes mellitus and hypertension were relatively common and seen in 19.5 %.

Table 6: Socio demographics and Characteristics of the clients

Age	Frequency *(n=190)*	Percent (%)
30-40	17	8.9
41-50	57	30.0
51-60	71	37.4
61-70	31	16.3
More than 70	14	7.4
Level of education		
No formal education	13	7
Up to primary education	91	48
Secondary education	66	35
Above secondary education	19	10
Age at menarche		
Early-less than 12	9	4.7
Normal-12-15	140	73.7
Late-More than 15	41	21.6
Parity		
Nulliparous	11	5.8
1-4 children	140	73.7
Multiparous, more than 5 children	39	20.5
Hormonal FP		
Yes	125	65.8
No	65	34.2
Medical disease in patient		

Breast cancer	13	6.8
Other cancers	8	4.2
Other conditions including DM/HTN	37	19.5
LMP		
Less than 1 week ago	13	6.8
More than 1 week ago	60	31.6
Post-menopausal	117	61.6

Clinical Presentation of the clients (Table 7)

Most clients requesting for mammograms usually had a breast related complaint as listed in table 7.0 below. The most common presentation was breast mass, 33.2 %, followed by breast pain which was reported in 30.5% of the population. Rarely, between 1 to 2.1% of patients presented with either nipple discharge, skin thickening, or axillary mass/node each as their major complaint.

Clients who had reported clinical symptoms mostly came with delayed presentation (Presentation after 3months), 45.8%, followed by those who presented between 1 to 3 months, 18.9%. Very few patients presented earlier in less than a month. This represents overall delayed presentation of the clients.

Table 7: Clinical Presentation of the clients

Clinical Presentation	Frequency *(n=190)*	Percentage
Axillary mass/node	4	2.1
Breast mass	63	33.2
Breast pain	58	30.5
Nipple discharge	2	1.1
Skin thickening	4	2.1
No complaints	59	31.1
Duration of presentation		
Up to 1 month	8	4.2

1 month to 3 months	36	19.0
More than 3 months	87	45.8
None	59	31.0

Predictors of breast calcifications (Table 8)

Women above 60 years of age at examination had two times higher risk of having micro calcification clusters (OR=2.0; 95% confidence interval [CI] = (0.9 – 4.1) compared to younger women (<50 years). Women with normal menarche had a 5times higher probability of having calcifications than women with early menarche, OR = 5.0 (95% CI =0.6-41.3). A probable association was seen in clients who had a delayed presentation (more than 3months) as these clients were twice more likely to have calcifications than those who presented earlier (OR = 2.1; 95% CI = 0.4-11.1).

Table 8: Predictors of breast calcifications

		Calcifications			
	n	Yes, *n (%)*	No, *n (%)*	OR (95% CI)	p-value
Age in years					
≤50	71	21 (31.3)	50 (40.7)	1.0	
50 – 60	74	26 (38.8)	48 (39.0)	1.3 (0.6 – 2.6)	0.475
>60	45	20 (29.9)	25 (20.3)	2.0 (0.9 – 4.1)	0.105
Age at menarche					
Early-less than 12	9	1 (1.5)	8 (6.5)	1.0	
Normal-12-15	140	54 (80.6)	86 (69.9)	5.0 (0.6 – 41.3)	0.133
Late-More than 15	41	12 (17.9)	29 (23.6)	3.3 (0.4 – 29.4)	0.283
LMP					
Less than 1 week ago	13	3 (4.5)	10 (8.1)	1.0	
More than 1 week ago	60	22 (32.8)	38 (30.9)	1.9 (0.5 – 7.8)	0.355
Post-menopausal	117	42 (62.7)	75 (61.0)	1.9 (0.5 – 7.2)	0.363
Duration of presentation					
Up to 1 month	8	2 (3.0)	6 (4.9)	1.0	
1 month to 3 months	36	11 (16.4)	25 (20.3)	1.3 (0.2 – 7.6)	0.756
More than 3 months	87	36 (53.7)	51 (41.5)	2.1 (0.4 – 11.1)	0.375

None	59	18 (26.9)	41 (33.3)	1.3 (0.2 – 7.2)	0.750
Hormonal FP					
Ever	125	39 (58.2)	86 (69.9)	1.0	
Never	65	28 (41.8)	37 (30.1)	1.7 (0.9 – 3.1)	0.105
Parity					
Nulliparous	11	1 (1.5)	10 (8.1)	1.0	
1-4 children	140	50 (74.6)	90 (73.2)	5.6 (0.7 – 44.7)	0.107
Multiparous, ≥ 5 children	39	16 (23.9)	23 (18.7)	7.0 (0.8 – 59.9)	0.077

Mammographic Characteristics Table (9.0)

Majority of the patients underwent diagnostic mammography, 135(68.1%). Most patients as seen had scattered fibro glandular breast tissue, at 43.2%. Calcifications were seen in 40.5% of the mammograms. Some patients had more than 1 type of calcification, so that the total number of calcifications were 77. The prevalence of calcifications was 40.5% overall. The macro calcifications were commoner than the micro calcifications by about 7%.

Table 9: Mammographic characteristics

Type of mammogram	Frequency(n=190)	percentage
Diagnostic	135	68.1
Screening	59	31.1
ACR category		
A (predominantly fatty)	49	25.8
B (scattered fibro glandular tissue)	82	43.2
C (heterogeneous fibro glandular tissue)	51	26.8
D (dense fibro glandular tissue)	8	4.2
Mammographic calcifications found in number of patients		
Present	77	40.5

Absent	113	59.5
Mammographic calcifications type		
Macro calcifications	45	23.7
Micro calcifications	32	16.8
Total	77	40.5

Mammographic macro calcifications (Table 10)

The most common type of macro calcifications was vascular, at 15.6 % of the total calcifications and 6.3% of the total population. It was followed by round calcifications which were11.7 %. popcorn calcifications were third most common. Milk of calcium was the least common in occurrence.

Majority of all macro calcifications had linear distribution, of which most were due to vascular calcifications. Segmental distribution was the least common for all macro calcifications.

In most cases the macro calcifications were located bilaterally in all the quadrants of the breasts. The next most common locations were RUOQ, RLOQ and LUOQ.

Mammographic macro calcifications (Table 11)

	Frequency	Percent of cases *(n=77)Total calcifications*	Percent of cases *(n=190)Total population*
Morphology			
Vascular calcifications	12	15.6	6.3
Round calcifications	9	11.7	4.7
Popcorn	7	9.1	3.7
Egg shell calcifications	6	7.8	3.2
Secretory rod like calcifications	6	7.8	3.2
Skin calcifications	2	2.6	1.1
Dystrophic calcifications	2	2.6	1.1
Milk of calcium	1	0.5	0.5

Distributions		
Linear	15	19.5
scattered	12	15.6
Regional	11	14.3
Grouped	6	7.8
Segmental	1	0.5

Location		
LLIQ	2	2.6
LLOQ	2	2.6
LUIQ	1	0.5
LUOQ	5	6.5
RLIQ	3	1.6
RLOQ	4	5.2
ROUQ	1	
RUOQ	7	9.1
Whole breasts	20	26.0

Mammographic micro calcifications (Table 12)

The most common type of micro calcifications were Punctate calcifications, at 15.6% of the total calcifications, and 6.3% of the total population. Fine pleomorphic calcifications were second most commonly occurring at 13% of the total calcifications and 5.3% of the total population. Fine linear calcifications were the least in number.

The most common distributions were grouped and scattered at 14.3% and 13.0% respectively of the total calcifications distributions, corresponding to the most common morphological types; the punctate and fine pleomorphic calcifications. Similar to macro calcifications, the micro calcifications were located bilaterally in all the quadrants of the breasts in most cases followed by RUOQ, and LUOQ.

Table 13: Mammographic micro calcifications

	Frequency	Percent of cases	Percent of cases *(n=190)Total*

		(n=77)Total calcifications	*population*
Morphology			
Amorphous calcifications	5	6.5	2.6
Coarse heterogeneous calcifications	3	3.9	1.6
Fine linear calcifications	2	2.6	1.1
Fine pleomorphic calcifications	10	13.0	5.3
Punctate calcifications	12	15.6	6.3
Distribution			
Grouped	11	14.3	
Linear	2	2.6	
Regional	2	2.6	
Scattered	10	13.0	
Segmental	7	9.1	
Location			
LLIQ	2	2.6	
LLOQ	3	3.9	
LUIQ	2	2.6	
LUOQ	6	7.8	
RLIQ	1	0.5	
RLOQ	6	7.8	
RUOQ	2	2.6	
Whole breast	10	13.0	

Mammographic BIRADS Categorization Of Calcifications (Table 14)

Most calcifications based on their morphology and distribution were actually considered benign, and categorized as BIRADS 1 or 2, a sum of 62.4% (39.0% and 23.4%

respectively) of the total calcifications, and a total of 25.5% (15.8 % and 9.5% respectively) of the total population.

The suspicious calcifications accounted for 35.6% of the total calcifications. The mammographic calcifications that were considered suspicious on BIRADS categorization (BIRADS 4-5) were ultrasound guided biopsies biopsied. BIRADS 3 calcifications were also biopsied instead of the follow-up scan, since the timeline of the study did not extend up to the timeline of 6months to 1 year which is recommended for follow up as per the ACR guidelines. The clients made an informed consent for these biopsies.

Almost three quarters (76%) of the suspicious calcifications were found in breast with ACR B/C categories.

Table 15: Mammographic BIRADS categorization of calcifications

Mammographic BIRADS categorization	Frequency	Percent of cases *(n=77)Total calcifications*	Percent of cases *(n=190)Total population*
Benign			
1-benign calcifications	34	44.1	16.3
2-benign calcifications	18	23.4	9.5
Suspicious			
3-suspicious calcifications	2	2.6	1.1
4a-suspicious calcifications	7	11.7	4.7
4b-suspicious calcifications	1	0.5	0.5
4c-suspicious calcifications	6	9.1	3.7
5-suspicious calcifications	9	11.7	4.7

Suspicious calcifications occurrence in different ACR breast densities	Frequency *(n=25)Total calcifications*	Percent of cases

A	5	20
B	10	40
C	9	36
D	1	4

Other Mammographic findings (Table 16)

Majority of the patients presented with masses (ill-defined and well defined), 29%.

Table 17: Other Mammographic findings (excluding calcifications)

Mammographic findings	Frequency	Percent of cases *(n=190)*
Well defined mass	48	17.8
Ill-defined mass	32	11.9
Benign axillary nodes	30	11.2
Benign intramammary nodes	25	9.3
Skin thickening	25	9.3
Architectural distortion	14	5.2
Asymmetry	13	4.8
Dilated ducts	5	1.9
Suspicious axillary nodes	3	1.1
Skin para-papules	1	0.4%

Histopathological correlation of suspicious categories (Table 14)

Overall the most common findings in the mammograms were masses, a sum of 29.7% for both the well-defined and ill-defined masses. Skin thickening and enlarged axillary and intramammary nodes were also common. Asymmetry was also seen in some cases, 4.8%. 27.1% of the patients had no other findings.

Majority of the mammographic calcifications, about 2/3 of the population, were considered benign, hence not biopsied further. In the entire population the benign calcifications were seen in almost 1/3 of the population.

Table 18: Histopathological correlation of suspicious categories.

Histopathological type	Frequency	Percent of cases *(n=77)*	Percent of cases *(n=190)*
Others			
Benign calcifications so no biopsy required	52	67.5	27.4
Benign tissue	2	2.6	1.1
Fibro adenoma	2	2.6	1.1
Fibrocystic change	2	2.6	1.1
Ductal carcinoma			
DCIS	1	1.3	0.5
Invasive ductal carcinoma	12	15.6	6.3
Invasive ductal carcinoma not otherwise specified	5	6.5	2.6
Lobular carcinoma			
Invasive lobular carcinoma	1	1.3	0.5

Histopathological analysis of mammograms categorized as suspicious (Table 15)

Micro calcifications were rarely reported on pathological specimens of biopsies of suspicious calcifications. Most of the data was missing.

Table 19: Histopathological analysis of mammograms categorized as suspicious.

	Frequency *(n=190)*	Percent
Presence of calcifications		
Dystrophic calcifications	1	0.5
Micro calcifications seen	1	0.5
No calcifications found	23	12.1
Not applicable	165	86.8
Histological grade		

G1	0	0
G2	12	6.3
G3	5	2.6
Missing	8	4.2
Not applicable	165	86.8
Histological lymphovascular invasion		
Present	11	5.8
Absent	6	3.2
missing	8	4.2
Not applicable	165	86.8
Histological node invasion		
Positive	3	1.6
Negative	3	1.6
Missing data	19	10
Not applicable	165	86.8
Histological LCIS		
Positive	0	0
Absent	10	5.3
Missing data	15	7.9
Not applicable	165	86.8
Histological DCIS		
Present	2	1.1
Absent	12	6.3
Missing data	11	5.8
Not applicable	165	86.8

Correlation of BIRADS category with histopathology (Table 16)

The calcifications categorized as BIRADS 3 demonstrated malignancy in 50% (1 out of 2), whereas for BIRADS 5 it was seen in 89%(8 out 0f 9).

Table 20: Histopathology outcome of BIRADS categories

BIRADS category	Correlation with histopathology					
	Benign		Malignant		Total	
	Frequency	Percentage (%)	Frequency	percentage (%)	Frequency	percentage (%)
3	1	50	1	50	2	100
4A	5	71	2	29	7	100
4B	1	100	0	0	1	100
4C	5	83	1	17	6	100
5	8	89	1	11	9	100

Diagnostic indices (Table 17)

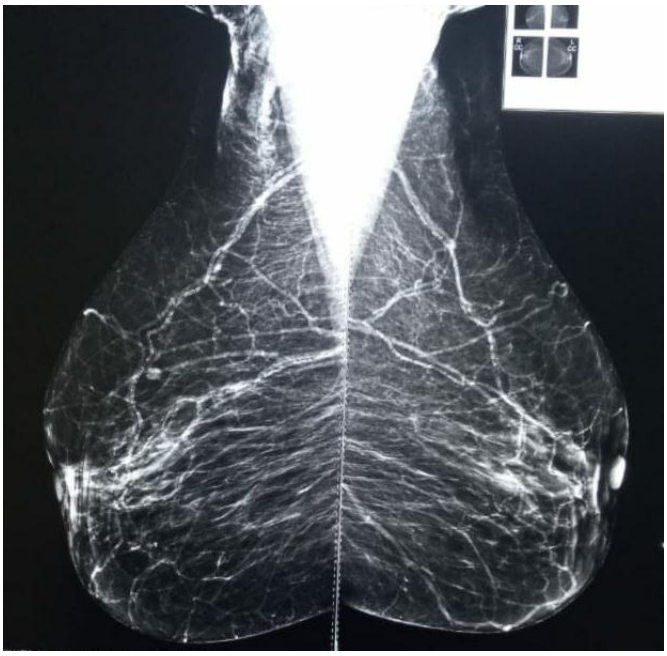
The diagnostic indices (sensitivity, specificity, positive predictive value, negative predictive value) were calculated using standard statistical method. The diagnostic accuracy was 76.0%.

Table 21:Diagnostic indices

Sensitivity	specificity	Positive Predictive value	Negative Predictive value	Diagnostic accuracy
94.7%	16.7%	78.3%	50.0%	76.0%

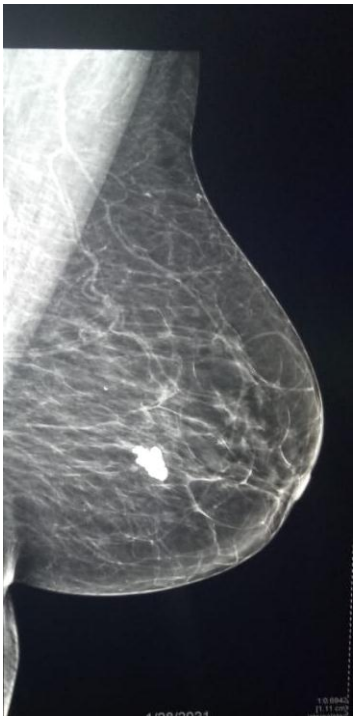
SAMPLE RESULTS

Figure 6: mammogram image 1



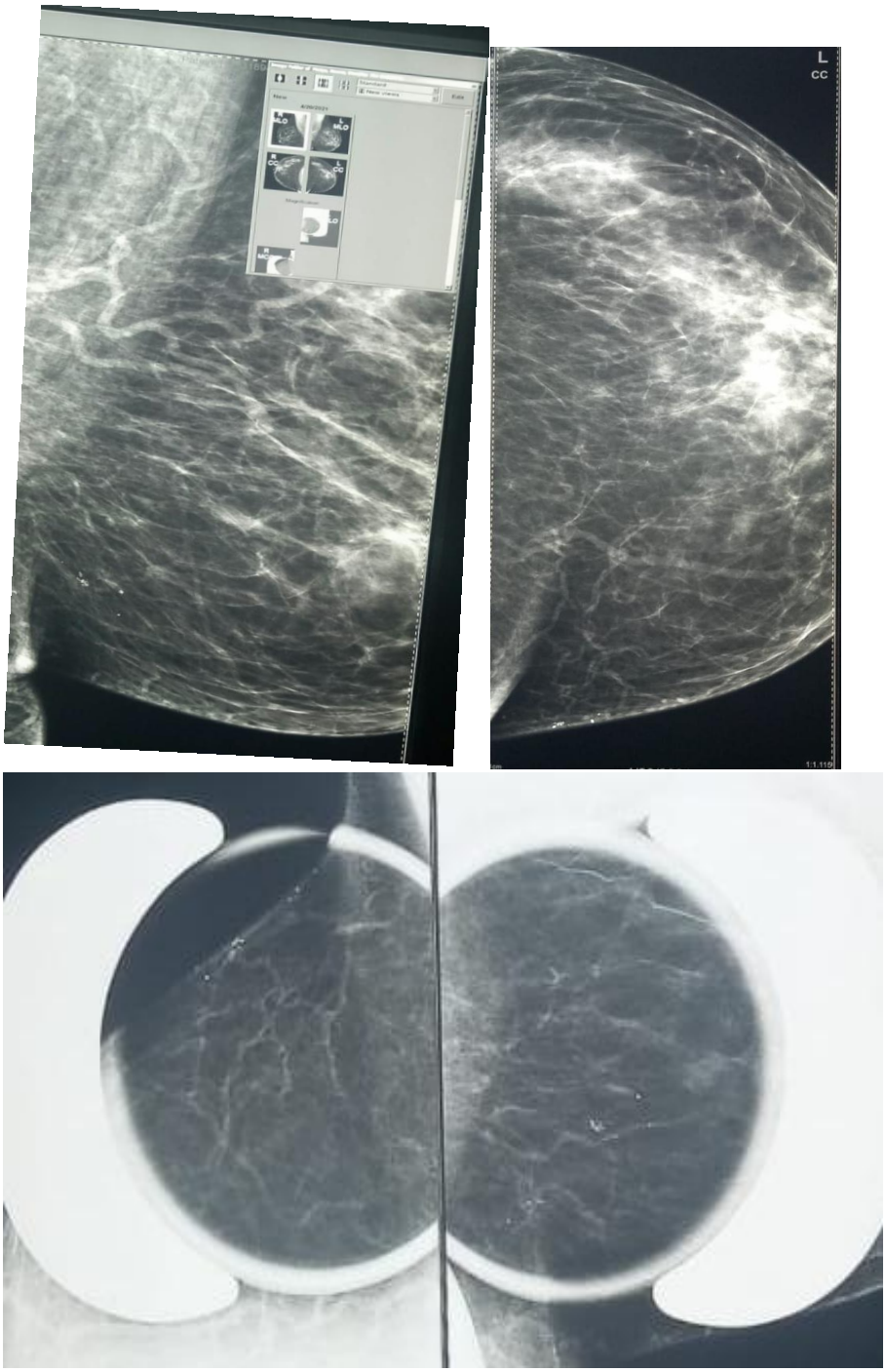
101 year old patient who underwent screening mammography. She was a known hypertensive patient with known pelvic rhabdomyosarcoma. MLO view showed bilateral vascular macrocalcifications. It was categorised as BIRADS 2. No biopsy was recommended.

Figure 7: Mammogram image 2



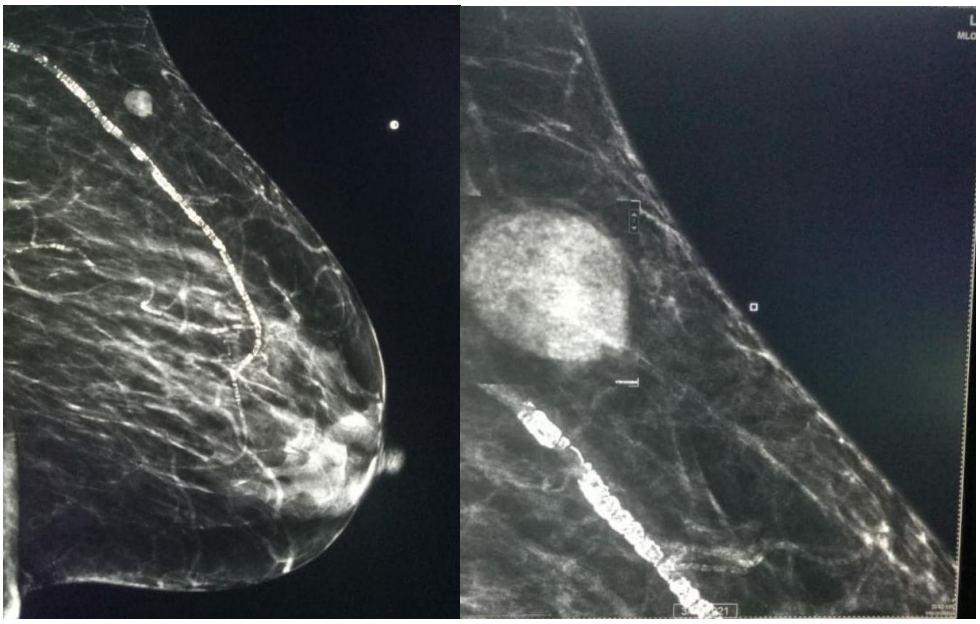
52-year-old female with slowly enlarging painless breast lump on right breast. MLO view showed a well-defined lobulated mass at the right lower quadrant, with popcorn calcifications. BIRADS 2 categorization was described for it.

Figure 8:Mammmogram image 3



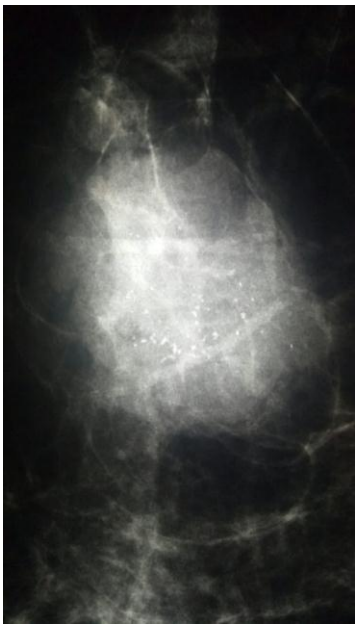
52 years woman who underwent screening mammography. Left breast MLO, CC and spot compression views showed skin calcifications. These are considered benign and bilateral breast were categorised as BIRADS 2.

Figure 9: Mammogram image 4



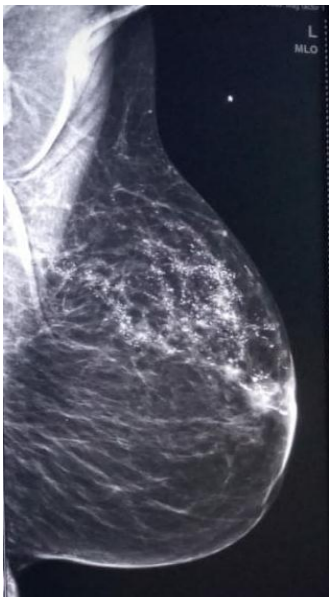
56 years old hypertensive woman who presented with a small painless non mobile breast lump at the left upper breast. Above are her right MLO view and a zoomed in view. There are vascular calcifications and a round dense mass with micro-lobulated margins. It was associated with internal grouped amorphous calcifications and categorized as BIRADS 4C. Biopsy on the mass showed invasive ductal carcinoma.

Figure 10: Mammogram image 5



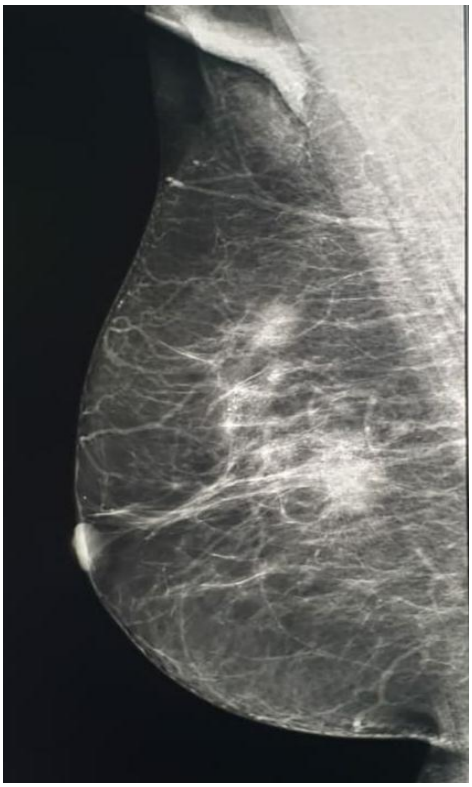
36 years old woman who presented with a painless progressively enlarging mass on her left upper breast. There was positive history of breast cancer in her mother. Zoomed in image of the poorly circumscribed dense breast mass showed intralesional grouped pleomorphic microcalcifications, this was categorised as BIRADS 5. Biospy proved this to be a invasive ductal carcinoma.

Figure 11: Mammogram image 6



55-year-old woman who presented with left sided nipple discharge. MLO view demonstrate isolated segmental heterogeneous calcifications at the left upper quadrant that are distributed towards the nipple. It was categorized as BIRADS 4C. Biopsy proved it to be invasive ductal carcinoma.

Figure 12: mammogram image 7



65 years old patient who presented with right painless breast lumps. Right MLO view showed multiple ill-defined masses with spiculations and associated local architectural distortion. There was punctate intra and extra lesional micro calcifications associated with grouped and regional distribution. Classified as BIRADS 4C. Biopsy proved it to be invasive ductal carcinoma.

CHAPTER 5
DISCUSSION

Participant characteristics

There were a total of 190 clients' mammograms as part of this study done at Kenyatta National Hospital. All the clients were women.

The clients of the study were mostly of the ages between 51-60 years. This was in contrast to study done by Opili et al in Trans Nzoia in Kenya where the most common age group was 41-50 years (59). KNH is a referral hospital, therefore most patients present at an advanced stage of the breast disease (11), which may be attributed to negative interpretation of symptoms by patients, fear of being diagnosed with cancer, lack of trust in the medical care system and access to healthcare, as reported by Andrew Donkor et al in 2015, where they reviewed 9 studies done in Africa (including Kenya) to identify the factors contributing to the late presentation or delayed diagnosis of breast cancer in Africa (60).

Older age group is generally linked with advanced stage breast disease. Studies done by Azam et al (2021), Nuzhat and Abouzaid et al (2017) showed that older age is associated with higher number of breast cancers and calcifications (61,62).

Most of the clients in this study were postmenopausal accounting for 61.6% of the total number of clients. Azam showed statistical significance between postmenopausal status and the presence of calcifications with statistically significant p value of less than 0.01 (61).

Majority of our clients attained primary and secondary level education. There was no consistency seen in studies regarding association between higher education level and increased occurrence of breast cancer. No association was shown in the study done by Lund et al 1991, where he showed that the relative risk for death from breast cancer was unchanged by level of education, with reference odds ratio of 1.0 for those who studied for less than 7 years and 1.1 for those who studied for more than 7 Years (62). The findings in these studies are in contrast to a meta-analysis by Akinyemiju (2017) in which 9 distinct studies were evaluated to look for association in early socioeconomic position (including education). This meta-analysis included studies done in America in 2012 by Pudrovska et al and Lope et al inn Spain in 2016 among others. Some of the observations made in the studies included higher occurrence of breast cancer in women with higher level of education as they would be of an older age at first birth and had lower parity, but with higher chances of survival due to their educational background and indirectly higher socioeconomic status. Women with a lower early life socioeconomic position had a higher likelihood of being overweight and with a higher body mass index which was associated with lower risk of breast cancer was reported by Ruder et al(2008) and according to her one mechanism by which childhood body mass index could potentially

influence breast cancer risk is via effects on reducing mammographic density (63). There is no consensus on the influence of education on occurrence of breast cancer.

In the current study we observed that majority of our clients (62%) had used hormonal family planning. This was similar to a Kenyan study done by Rispah where the use of hormonal family planning was found to be more than 50% (64). Bassuk and Mansion (2014) carried out a meta-analysis on observational studies published between 2000 and 2012 on ever versus never on use of combined oral contraceptives. The use of oral contraceptives increases the risk of breast cancer. That study showed a summary odds ratio at 95% confidence interval of 1.08 (1.00-1.17), with an increased lifetime risk of 0.89% (66).

In this study, most of the patients did not have a family history of breast cancer (6.87%). This was similar to a study done in Uganda and Cameroon in 2020 by Babatunde et al on breast cancer genetics. In the Babatunde study, out of a total of 382 participants, 13 cases (3.4%) had a positive family history of breast cancer. In western countries however, there is a hereditary component seen in 25% of breast cancers (66).

Mammographic Calcifications

Out of the 190 mammograms in this study,129 (68%) were of the diagnostic type with patients being symptomatic already. This is in contrast to study done by Adenike in South West Nigeria in 2015 where most mammograms were of the screening type (53.5%) (67). The higher proportion of diagnostic mammograms found in this study may be attributable to the lack of a national mammography screening program in our country and lower awareness of breast cancer in the population as stated in the study conducted in Kenya by Shahin et al in 2016 at three different sites including Aga Khan University Hospital, Tenwek Missionary hospital and Kisii Teaching and Referral Hospital. Shahin's study showed that less than 50% of the participants had knowledge about how breast cancer is diagnosed (68).

The policy recommendations are available from the Western world as well local guidelines, however, carrying out breast cancer screening is costly in most resource limited countries (68)(69).

Mammographic calcifications were seen in 40.5% of our clients' mammograms, while in the study by Adenike in Nigeria, 23.8% of the clients had mammographic calcifications. The increase in mammographic calcifications in our study may be due to the increasing use of hormonal family planning which increases the likelihood of occurrence of breast calcification. Studies have shown that hormonal contraceptive use in Kenya is significantly higher (53%) than in Nigeria (15%) as shown by the data in the demographic health surveys in an analytic study done by Aliyu et al in 2018 (70).

Morphological pattern of calcifications

Mammographic macro calcifications were more common than micro calcifications which is similar to findings in other studies. Macro calcifications are considered to be benign, and correlates to benign BIRADS categories, BIRADS 1 and 2 (46).

We found that the most common type of morphologic macro calcifications was the vascular type, at 15%. Other studies done in Nigeria by Akinola showed them to range between 9-17%, with a prevalence of up to 50% in clients aged 50 years and above which correlates well with our study population (71).

The most common micro calcification morphology was the punctate type usually considered benign BIRADS 1 and 2 categories. The second most common micro calcification was the pleomorphic type which are usually associated with invasive ductal carcinoma and most were categorized as BIRADS 4 – 5 (25).

Linear calcifications are usually seen in the early stages of ductal breast cancers. Their frequency was very low as most of our clients presented late (12 weeks after first detection of symptoms). The late presentation of clients at an advanced stage of breast disease was comparable to study done at KNH in 2018(11) by Abinya et al and another by Kantelhardt in 2016 in his meta-analysis of studies done in sub Saharan countries including south Africa and Nigeria (11,72).

Distribution of breast calcifications

The most common distribution pattern was the scattered type. This type of distribution is associated with benign BIRADS categorization and correlates with the majority of breast diseases. Micro calcifications were mostly associated with grouped distribution and linear distribution. All the 13 grouped and linear distributions of micro calcifications were associated with malignancy on BIRADS categorization and histopathology as is recommended in ACR BIRADS (25). No studies were found specifically correlating distribution of micro calcifications independently with histopathology.

Location of breast calcifications

The most common locations of calcifications were the upper outer quadrants of the breasts found in 10% (19) of the sample size. Multiple studies show that breast cancer is detected in the upper outer quadrant mostly. This location is known to have the highest breast density and breast tissue, but there has been no study that scientifically proves that the upper outer quadrant is directly related to cancer occurrence. It is possible that this observation is to do with the fact that in the division of the breast, the upper outer quadrant has been assigned the highest breast area (73–75).

Categorization of the mammographic calcifications

The categorization helps to predict the outcome of the identified calcifications based on both their morphology and distribution. The suspicious categories corresponded to the summative effect of suspicious morphologies and distribution as is based in the ACR.(46)

In our study, the benign calcifications (BIRADS 1 and 2) were almost double the malignant ones (BIRADS 3-5). A similar pattern was seen in study of Adenike et al. This is related to majority of breast diseases also being benign (3).

Histopathological correlation of suspicious categories (BIRADS 3-5) of mammographic calcifications

The sensitivity (94.7%) and specificity (16.7%) of the current study was comparable that of Muller et al, Lo et al trial B and Muhammad et al studies (95.7%, 96.0 %, 97.0%) and (21.2%, 28.0%, 64.5%) respectively. The specificity in the study done by Muhammad showed higher specificity than all other studies and this could be because they had excluded all dense breasts (ACR D) as high density breasts may obscure calcifications.

The positive predictive value of this study was higher (78.3%) than 37.8%, 46.6% and 55.7% for Muller et al, Lo et al and Muhammad et al respectively. This could be attributed to a symptomatic and diagnostic sample population in our study. The negative predictive value was lower in our study (50%) while of Muhammad was 90.9% for a similar reason. The diagnostic accuracy was 76% and was comparable to Muhammad's 71.5% (76–78).

False negative

This study had one false negative in the BIRADS 3 cases which represented benign calcifications (classified as BIRADS 4A pre-biopsy) coincidentally near an ill-defined mass that was classified on histology as malignant.

<u>False positives</u>

Six false positives were identified in this study.

Two of the false positives in this study were assigned categories BIRADS 4A and 4B, which on histology were due to fibrocystic disease of the breast. Fibrocystic disease of the breast is a benign proliferative condition. It commonly presents as micro calcifications (amorphous, punctate or pleomorphic) which are identified in up to 40-55% of cases. Invasive ductal carcinoma is also associated with similar micro calcifications and can be a differential diagnosis and so these micro calcifications are often assigned a malignant BIRADS category resulting in false positives on histology (79) (80).

In one case, the micro calcifications which were suspicious and pleomorphic was assigned BIRADS 4C and it was associated with a well-defined mass. The mammogram was recalled after biopsy showed it to be benign. It was reclassified as BIRADS 2 because the pleomorphic calcifications were located peripherally in the well-defined mass. Fibroadenomas have been found to produce pleomorphic calcifications and which

may be difficult to differentiate from suspicious calcifications in the early stages, however the eccentric location of calcifications is a clue to the benignity (81,82)

For the other cases no specific reason for the discordance was discerned. A possible explanation could be under-sampling of the micro calcifications due to usage of ultrasound guided core needle biopsy rather than stereotactic guided vacuum biopsies which sample a larger volume. A specific diagnostic accuracy for ultrasound guided biopsy was 1.7% as shown by Mary et al while for the stereotactic biopsy was 8.9% in a study with 2427 participants who underwent imaging guided breast biopsies in 2015 (83).

There were twenty-five calcifications biopsied, only three biopsy reports mentioned the presence of calcifications. Missing data in the biopsy reports and lack of capacity for polarization of calcifications was however a limitation. This is in contrast to a study done by Madiha et al in which the mammographic micro calcifications appearing on mammography had almost equal detection on pathology samples. Our low yield of micro calcifications on histology could be attributable to our biopsy techniques and tissue preparation techniques resulting in measurement bias. Madiha et al carried out stereotactic core biopsies for micro calcifications and where they did not find micro calcifications initially, the slides were polarized to find polarized calcium crystals. If there were no micro calcifications on polarization, the pathology blocks were further x-rayed and cut on deeper levels until the micro calcifications were identified (84).

CONCLUSION

Mammographic calcifications are a relatively common finding in our set up as they were found in slightly above 1/3 of the population. The majority were benign.

Categorization by the BIRADS system is useful as the suspicious categories (BIRADS 3, 4, 5) have a significant diagnostic accuracy (76%) using histopathological analysis as the gold standard.

Spot compression with magnification views should be done routinely to avoid false positives and negatives for all suspicious mammographic calcifications.

LIMITATIONS

Lack of stereotactic biopsy capacity and lack of capacity of polarization of calcifications for their identification on histopathology in the hospital led to possible inadequate sampling and reporting of calcifications as we only used ultrasound guided biopsy results for this study.

RECOMMENDATIONS

- Spot compression with magnification views should be done routinely to avoid false positives and negatives for all suspicious mammographic calcifications.

- Stereotactic biopsies should be performed for all breasts with suspicious calcifications and on histopathology immunofluorescence polarization for calcifications should be performed if calcifications are not identified initially .
- Correlation of suspicious calcifications should be done with immunohistochemistry to look for association with Hers 2, BRCA genes, hormonal receptors.
- Having a small hospital based sample size may not truly represent a population of over 47 million. A more robust study involving multiple centers would be useful to provide more robust and generalizable data.

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APPENDICES

APPENDIX I (a): CONSENT FORM

INFORMATION AND CONSENT FORM

Title of study: Prevalence and Pattern of breast Calcification in Women undergoing mammography at Kenyatta National Hospital

Principle investigator: Dr. Sehdeva M. K (MMed Radiology student, University of Nairobi),

Supervisors: Dr. Mwango (University of Nairobi), Dr. Mugi (Kenyatta National Hospital),

Participant Number: - _____

Introduction

I would like to tell you about this study being conducted by the above named investigators. The purpose of this form is to give you the information that will help you decide whether you want to take part in this study or not. Feel free to ask any questions regarding the purpose of this study, what happens if you participate, the possible risks and benefits, your right as a volunteer and anything else about this research or form that is not clear. When we have answered all your questions to your satisfaction, you may decide to be in this study or not. Once you understand and agree to be in this research I will request you to sign your name in this form. You should understand the general principles that apply to all participants in a medical research: I) your decision to participate is entirely voluntary, ii) you may withdraw from the study at any time without necessarily giving a reason for your withdrawal, iii) refusal to participate in this research will not affect the services you are entitled to in this health facility or other facilities. We will give you a form of this copy for your records.

May I continue? Yes, or no?

What is this study about?

The breast is an important organ in the body. The breast can however be involved in multiple disease processes, some that are easily treated and others that can be harmful and need urgent attention. Calcium deposits in the breast can help to predict the nature of the breast disease. The researchers listed above are conducting a research to determine the prevalence and pattern of calcium deposits seen in the breast on mammographic

images of women undergoing this imaging in Kenyatta National Hospital. Approximately 243 participants were selected to participate in this study. we are asking for your consent to participate in this study.

What will happen if you decide to be in this research question?

If you agree to participate in this study, the following things will happen:

You will undergo mammographic imaging and the findings of the mammogram reports, were collected as part of the raw data for this study.

Are there any risks, harms, discomforts associated with this study?

Medical research has the potential to introduce psychological, social, emotional, and physical risks. Effort should always be put in place to minimize the risks. One potential risk of being in this study is the loss of privacy. We will keep everything you tell us as confidential as possible. We will use a code number to identify you in a password-protected computer database and will keep all your paper records in a locked file cabinet. However, no system of protecting your confidentiality can be absolutely secure, so it is still possible that someone could find out you were in this study and could find out information about you.

There could be an additional magnification view that can be carried out if necessary to better view clustered breast calcifications, which could slightly increase the radiation dose by approximately double the dose of the standard two views used in 2-digital mammography for the breast undergoing an additional magnification view. This increase in dose is still lower than maximum acceptable dose in a mammography (3MGy per breast).

Are there any benefits in this study?

you may not directly benefit as a client, but the study will aim in development of standardized imaging protocols which are pivotal in imaging of the breast cancer. There was no direct compensation for participating in this study.

will being in this study cost you anything?

Participation is free and voluntary.

Will you get refund for money spent as part of this study?

There is no expense involved in participating in this study. you will not be compensated.

Contacts: what if you have a question in the future?

If you have any questions or concerns about participating in this study, please call or send a text message to the principal investigator, Dr. Manpreet Kaur Sehdeva, 0738798666. For more information about your rights as a participant in this research, you may contact the secretary/chairperson, Kenyatta National hospital- University of Nairobi Ethics and Research committee telephone number 2726300 ext 44102, Email uonknh_erc@uonbi.ac.ke. The study staff will pay you back for your charges to these numbers if the call is for study-related communication.

What are your other choices?

Your decision to participate in this research is voluntary. You are free to decline participation in the study, and can withdraw from the study at any time without suffering negative consequences. You will continue to receive the care and treatment needed even if you do not wish to participate in this study.

CONSENT FORM (STATEMENT OF CONSENT)

Participant's statement

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counsellor. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw at any time. I freely agree to participate in this research study.

I understand that all efforts will be made to keep information regarding my identity confidential.

By signing this consent form, I have not given up any of the legal rights that I have as a participant in a research study.

I agree to participate in this research study: yes no

Participant printed name: _____

Participant signature/thumb stamp: _____ Date: _____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this study to the participant named above and believe that the participant has understood and has willingly and freely given her consent.

Researcher's name: _____ Date: _____

Researcher's signature: _____

Role in the study: _____

Witness (if a witness is necessary, a witness is a person mutually acceptable to both the researcher and participant).

Name: _____

Contact information_____

APPENDIX I (b): CONSENT FORM-SWAHILI

FOMU YA HABARI NA RIDHI

Title of study: Prevalence and Pattern of breast Calcification in Women undergoing mammography at Kenyatta National Hospital

mtafiti mkuu: Dk. Sehdeva M. K (MMed Radiology student, University of Nairobi)
Watafiti weza: Dk Mwango (University of Nairobi), Dk. Mugi (Kenyatta National Hospital)

Utangulizi

Ningependa kukuambia juu ya utafiti huu uliofanywa na watafiti waliotajwa hapo juu. Madhumuni ya fomu hii ni kukupa habari ambayo itakusaidia kuamua ikiwa unataka kushiriki katika utafiti huu. Jisikie huru kuuliza maswali yoyote kuhusu kusudi la utafiti huu, ni nini kitatokea ikiwa utashiriki, hatari na faida zinazowezekana, haki yako kama kujitolea na kitu kingine chochote juu ya utafiti huu au fomu ambayo haijulikani wazi. Wakati tumejibu maswali yako yote kukuridhisha, unaweza kuamua kuwa katika utafiti huu au la. Mara tu utakapoelewa na kukubali kuwa katika fomu hii, nitakuomba utie saini jina lako katika fomu hii. Unapaswa kuelewa kanuni za jumla ambazo zinatumika kwa washiriki wote katika utafiti wa matibabu: I) uamuzi wako wa kushiriki ni wa hiari kabisa, ii) unaweza kujiondoa kwenye utafiti wakati wowote bila kutoa sababu ya kujiondoa kwako, iii) kukataa kushiriki katika utafiti huu hautaathiri huduma unazostahiki katika kituo hiki cha afya au vituo vingine. Tutakupa fomu ya nakala hii kwa kumbukumbu zako.

Naweza kuendelea? Ndio au hapana?

Utafiti huu unahusu nini?
Matiti ni kiungo muhimu mwilini. Matiti hata hivyo inaweza kuhusika katika michakato mingi ya magonjwa, zingine ambazo hutibiwa kwa urahisi na zingine ambazo zinaweza kudhuru na zinahitaji uangalifu wa haraka. Amana za kalsiamu kwenye matiti zinaweza kusaidia kutabiri hali ya ugonjwa wa matiti. Watafiti walioorodheshwa hapo juu wanafanya utafiti ili kujua kuenea na muundo wa amana za kalsiamu zinazoonekana kwenye kifua kwenye picha za mammografia za wanawake wanaofikiria hii katika

Hospitali ya Kitaifa ya Kenyatta. Takriban washiriki 243 watachaguliwa kushiriki katika utafiti huu. tunaomba idhini yako kushiriki katika utafiti huu.

Ni nini kitatokea ikiwa utaamua kuwa katika swali hili la utafiti?
Ikiwa unakubali kushiriki katika utafiti huu, mambo yafuatayo yatatokea:
Utapitia taswira ya mammografia na matokeo ya ripoti za mammogramu, zitakusanywa kama sehemu ya data ghafi ya utafiti huu.

Kuna hatari, madhara, usumbufu unaohusishwa na utafiti huu?
Utafiti wa kimatibabu una uwezo wa kuanzisha hatari za kisaikolojia, kijamii, kihemko, na kimwili. Jitihada inapaswa kuwekwa kila wakati ili kupunguza hatari. Hatari moja ya kuwa katika utafiti huu ni kupoteza faragha. Tutaweka kila kitu unatuambia kama siri iwezekanavyo. Tutatumia nambari ya kukutambulisha kwenye hifadhidata ya kompyuta inayolindwa na nywila na tutaweka rekodi zako zote za karatasi kwenye kabati la faili lililofungwa. Walakini, hakuna mfumo wowote wa kulinda usiri wako ambao unaweza kuwa salama kabisa, kwa hivyo bado inawezekana kwamba mtu anaweza kugundua kuwa ulikuwa kwenye utafiti huu na angeweza kupata habari kukuhusu.
Kunaweza kuwa na maoni ya kukuza ambayo yanaweza kufanywa ikiwa ni lazima ili kuona vizuri hesabu za matiti zilizoshonwa, ambazo zinaweza kuongeza kipimo cha mionzi kwa takriban mara mbili kipimo cha maoni mawili ya kawaida yaliyotumiwa katika mammografia ya dijiti 2 kwa kifua kinachopitia nyongeza. mtazamo wa kukuza. Ongezeko hili la kipimo bado ni la chini kuliko kipimo kinachokubalika katika mammografia (3MGy kwa kila titi).

Kuna faida yoyote katika utafiti huu?

unaweza kufaidika moja kwa moja kama mgonjwa, lakini utafiti huo utakusudia kukuza protokali za upigaji picha ambazo ni muhimu katika taswira ya saratani ya matiti. Hakutakuwa na fidia ya moja kwa moja ya kushiriki katika utafiti huu.

kuwa katika utafiti huu kutagharimu chochote?

Kushiriki ni bure na kwa hiari.

Utarudishiwa pesa uliyotumia kama sehemu ya utafiti huu?

Hakuna gharama inayohusika katika kushiriki katika utafiti huu. hautalipwa.

Mawasiliano: vipi ikiwa una swali baadaye?

Ikiwa una maswali yoyote au wasiwasi juu ya kushiriki kwenye utafiti huu, tafadhali piga simu au tuma ujumbe mfupi kwa mchunguzi mkuu, Dk Manpreet Kaur Sehdeva, 0738798666. Kwa habari zaidi juu ya haki zako kama mshiriki wa utafiti huu, unaweza kuwasiliana na katibu / mwenyekiti, hospitali ya kitaifa ya Kenyatta- Kamati ya Maadili na Utafiti ya Chuo Kikuu cha Nairobi nambari ya simu 2726300 ext 44102, Barua pepe uonknh_erc@uonbi.ac.ke. Wafanyakazi wa utafiti watakulipa malipo yako kwa nambari hizi ikiwa simu ni ya mawasiliano yanayohusiana na utafiti.

Chaguzi zako zingine ni zipi?

Uamuzi wako wa kushiriki katika utafiti huu ni wa hiari. Uko huru kukataa kushiriki katika utafiti, na unaweza kujiondoa kutoka kwa utafiti wakati wowote bila kupata athari mbaya. Utaendelea kupata matunzo na matibabu inahitajika hata ikiwa hutaki kushiriki katika utafiti huu.

APPENDIX II: AUDITING TABLES

AGE DISTRIBUTION AMONG STUDY POPULATION

Age	Total
BELOW 30 YEARS	
31-40	
41-50	
51-60	
61-70	
70+	
TOTAL	

CLINICAL PRESENTATION VS AGE GROUP

Clinical Presentation	AGE in years					
	31-40	41-50	51-60	61-70	70+	TOTAL
Palpable mass						
Breast pain						
Breast discharge						
Skin thickening						
Nipple retraction or inversion						
Nipple discharge						
Palpable nodes						
Distortion of the breast						

FREQUENCY OF MACRO CALCIFICATIONS

Age Group	Macro calcifications						
	Skin	Vasc-ular	Popcorn	Egg Shell	Dystrophic	Milk of Calcium	Fat Necrosis
BELOW 30 YEARS							
31-40							
41-50							
51-60							
61-70							
71+							
TOTAL							

FREQUENCY OF MICRO CALCIFICATIONS

Age Group	Micro calcification			
	Amorphous	Coarse Heterogeneous	Fine Pleomorphic	Fine Linear
31-40				
41-50				
51-60				
61-70				
71+				
TOTAL				

FREQUENCY BY DISTRIBUTION OF CALCIFICATIONS

Location	Frequency
Diffuse	
Regional	
Grouped	
Linear	
Segmental	
TOTAL	

FREQUENCY DISTRIBUTION BY LOCATION OF CALCIFICATIONS

Location	Frequency	
	Macro calcifications	Micro calcifications
Left Inner Lower Lobe		
Left Outer Lower Lobe		
Left Inner Upper Lobe		
Left Outer Upper Lobe		
Right Inner Lower Lobe		
Right Outer Lower Lobe		
Right Inner Upper Lobe		
Right Outer Upper Lobe		
Retro areolar region		
Skin		
TOTAL		

Histopathological correlation

category	Histopathology correlation
3	
4	
5	

APPENDIX III: SCHEDULE AND BUDGET

Table 5 Schedule of activities

2020	Dec	Jan	Feb	March -July	July	June
Proposal Development						
Protocol presentation						
Ethical approval						
Data collection						
Data analysis						
Results presentation						

APPENDIX IV: BUDGET

Table 6 Budget

ITEM	Quantity	Unit Price (Ksh)	Total (Ksh)
Writing pens and notebooks	1	500.00	500.00
Printing Paper	5rims	400.00	2,000.00
Cartridge	1pc	6,000.00	6,000.00
Internet Surfing	200 hrs.	60.00 per hr.	12,000.00
Flash discs	2pcs	2,000.00	4,000.00
Printing drafts and final proposal	5 copies	1,000.00	5,000.00
Photocopies of questionnaires	100 copies	10.00	1000 .00
Photocopies of final proposal	3 copies	1,000.00	3000 .00
Binding copies of proposal	3 copies	200.00	600 .00
Ethical review fee	1	2,000.00	2,000 .00
Transport			10,000.00
Subtotal			40,6000.00

Personnel

Research Assistant	1		30 000 .00
Biostatistician	1	30 000 .00	30 000 .00
Subtotal			**60 000 .00**

Data Collection, Data Analysis and Thesis Development

Printing of thesis drafts	10 copies	1 000 .00	10 000 .00
Printing final thesis	3 copies	1 000 .00	3 000 .00
Binding of thesis	3 copies	300 .00	900 .00
Dissemination cost			10 000 .00
Subtotal			**23900 .00**
Contingency			**10,000 .00**
Grand Total			**139,00.00**

APPENDIX IV: QUESTIONNAIRE

Biodata

Participant number: _____

Age: _____ Residence/county: _____

Ethnicity: _____

General history

Last normal menstrual period: _____

Age at menarche: _____

Parity: _____

Method of family planning:

Pills ____ IUD ____ Injection ____ coil ____

History of prior breast disease including cancer in self: _____

Benign ____ malignant _____

History of prior breast disease including cancer in family: (mention who and what)

History of any other systemic illness:

Who: _____ what disease: _____

Benign ____ malignant _____

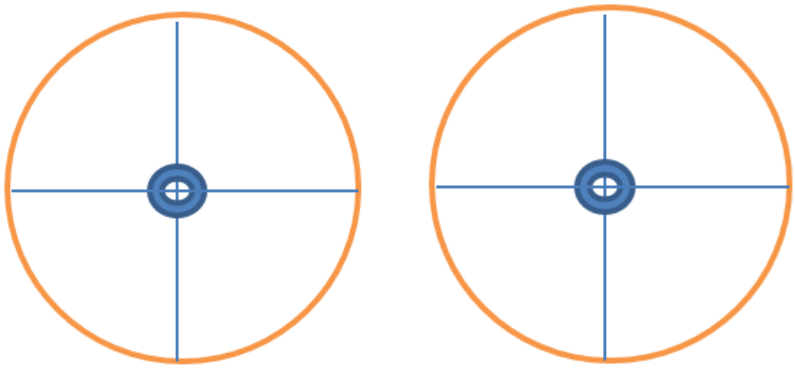
Presenting complaints

Nipple discharge: _____ if Yes, what is the color of the discharge_____

Breast related complaints: _____

Duration: _____

Breast involved and location: right ___ left: ____



Examination

Size symmetry: yes____ no _____ which one is larger: _____

Breast tenderness: yes _____ no _____

Breast mass: yes _____ no_____

Draw the mass in the location:

Nipples position: normal_____ inverted_____

Nipple discharge: yes _____ no _____, if yes, what color: _____

Skin: normal _____ thickened _____

UNIVERSITY OF NAIROBI (UoN)

COLLEGE OF HEALTH SCIENCES

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Facebook: ttps://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC

KENYATTA NATIONAL (KNH)
P O BOX 20723 Code 0020
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nair

KNH-UoN ERC APPLICATION FORM

ETHICS RESEARCH COMMITTEE

Application Number P572/10/2020

Submit one copy of this form with original inked signatures. **Handwritten and /or incomplete forms** will not be accepted. All relevant appendices e.g. consent forms, questionnaires, instruments, drug information summary, data collection forms, debriefing statements, advertisements, etc.) must be included at the back of the proposal.

I. **PRINCIPAL INVESTIGATOR**: Provide the information requested below:

Last Name **SEHDEVA** First name **MANPREET** Academic degrees **MBChB**

Professional titles and/or work position within your home institution __Medical Doctor__

Home institution(s) and/or department (s) approving this research project.
__University of Nairobi__
Mailing address, telephone and fax numbers, and email address

P. O. Box 1967-00200 0738798666 sehdevamanpreet@gmail.com

All correspondence shall be addressed to the Principal Investigator. Research Administrators may have delegated signatory authority only when listed as Co-investigators.

II **PROJECT TITLE**

Prevalence and ACR BIRADS categorization of mammographic calcifications with histopathological correlation of the suspicious categories at the Kenyatta National Hospital

As the Principal Investigator in this research I declare that:

1) Any change to this protocol and/or procedure shall be notified to and effected only after approval by the KNH-UoN ERC.
2) I shall notify the KNH-UoN ERC of intended publication, or any other form of dissemination of results of this study and provide the draft contents.
3) Other members of the research team are bound by 1) and 2) above.

Resub P572/10/2020

DR Manpreet K. Sehdeva
H58/7014/2017
Department of diagnostic imaging
School of medicine
College of health sciences'
University of Nairobi
P. O. Box 1967-00200

REF KNH-ERC/RR/834

The secretary

KNH-UON ERC

Kenyatta National Hospital

P. O. Box20723-00200

Nairobi

Dear Sir,

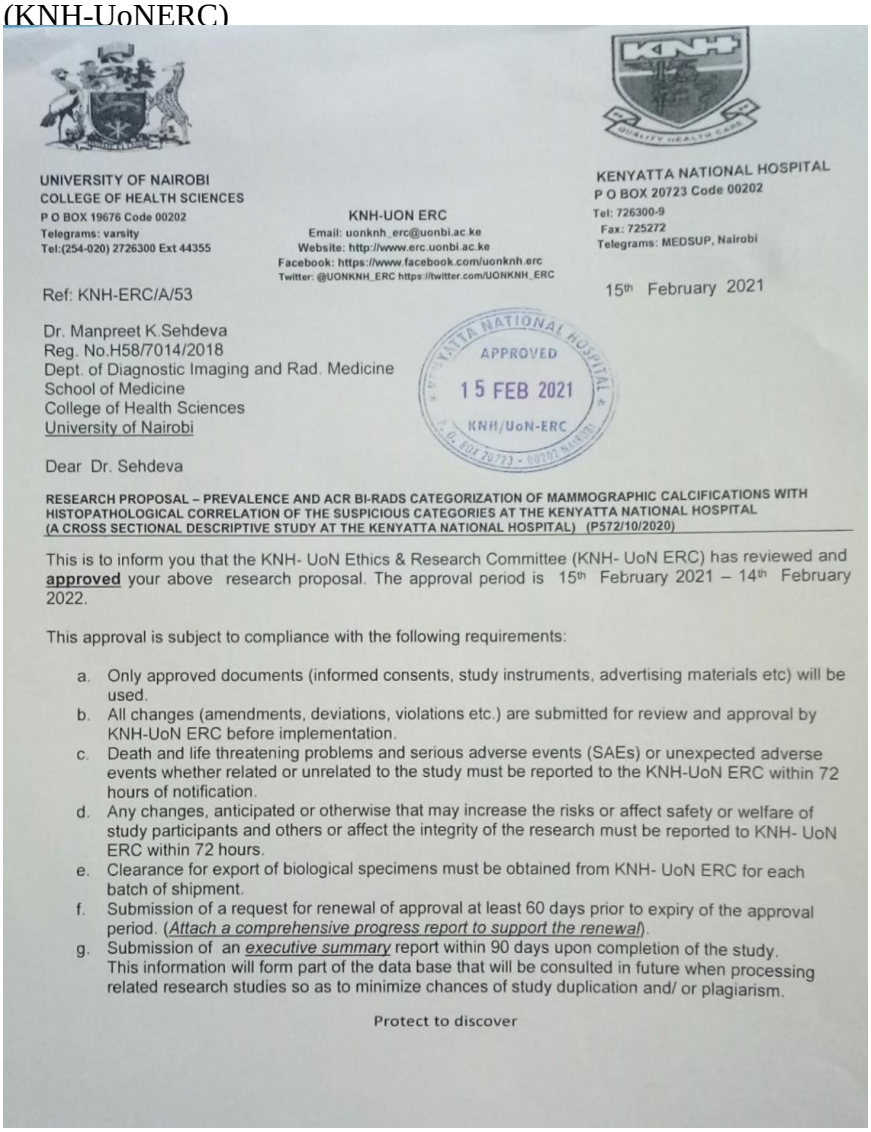
RE: CORRECTED PROPOSAL P572/10/2020

This is to acknowledge the receipt of your letter dated 9th December, 2020 with corrections to my proposal as earlier forwarded to the KNH-UON committee for review.

Here in attached kindly find 2, two, copies of my revised proposal as guided in the table below:

Correction Number	Observation from ethics	Changes made	Page number
1	Study title needs revision	Revised to "prevalence and ACR BIRADS categorization of mammographic calcifications with histopathological correlation of the suspicious categories at the Kenyatta national hospital	Title page
2	Structuring of the abstract:	Has been revised as per the	iv

APPENDIX V: APPROVAL FROM ETHICS REVIEW COMMITTEE (KNH-UoNERC)



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15th February 2021

Dr. Manpreet K.Sehdeva
Reg. No.H58/7014/2018
Dept. of Diagnostic Imaging and Rad. Medicine
School of Medicine
College of Health Sciences
University of Nairobi

KENYATTA NATIONAL HOSPITAL
APPROVED
15 FEB 2021
KNH/UoN-ERC
P.O. BOX 20723 - 00202 NAIROBI

Dear Dr. Sehdeva

RESEARCH PROPOSAL – PREVALENCE AND ACR BI-RADS CATEGORIZATION OF MAMMOGRAPHIC CALCIFICATIONS WITH HISTOPATHOLOGICAL CORRELATION OF THE SUSPICIOUS CATEGORIES AT THE KENYATTA NATIONAL HOSPITAL (A CROSS SECTIONAL DESCRIPTIVE STUDY AT THE KENYATTA NATIONAL HOSPITAL) (P572/10/2020)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 15th February 2021 – 14th February 2022.

This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
g. Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

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For more details consult the KNH- UoN ERC website http://www.erc.uonbi.ac.ke

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Senior Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information Dept, KNH
The Dean, School of Medicine, UoN
The Chair, Dept. of Diagnostic Imaging and Rad. Medicine, UoN
Supervisors: Dr. Gladys Mwango, Dept. of Diagnostic Imaging and Rad. Medicine, UoN
Dr. Beatrice Mugi, Dept. of Radiology, KNH

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