DIAGNOSTIC ACCURACY OF SONOGRAPHIC BI-RADS SCORE IN THE DIAGNOSIS OF BREAST LESIONS BASED ON HISTOPATHOLOGY AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET-KENYA

BY

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A research thesis submitted to the School of Medicine in partial fulfillment of the award of the degree of Master of Medicine in Radiology and Imaging in School of Medicine, Moi University

DECLARATION

Declaration by the Candidate

I declare that this thesis is my original work and has not been presented for a degree or any academic credit in any other University or examining body. No part of this thesis may be reproduced without the prior written permission of the author and/or Moi University.

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DEDICATION

I dedicate this work to my parents Mr. Boniventure Ombura and Mrs. Pamela Ombura who through their unending and amazing sacrifices and love have been very supportive throughout my education journey and on this research thesis. I would also like to acknowledge my daughter, Michelle Kendi who is my daily motivation to achieve the highest of dreams.

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LIST OF ABBREVIATIONS

ACR	American College of Radiology
BI-RADS	**Breast Imaging-Reporting and Data Systems**
CNB	**Core Needle Biopsy**
FNAC	Fine Needle Aspiration Cytology
NPV	**Negative Predictive Value**
PPV	**Positive Predictive Value**
U/S	Ultrasonography
INR	Internalized Normalized Ratio
MRI	Magnetic Resonance Imaging
VAB	**Vacuum Assisted Biopsy**
PLR	**Positive Likely Ratio**
NLR	**Negative Likely Ratio**
TDLUS	**Terminal Ductal Lobular Units**

DEFINITION OF TERMS

Diagnostic Accuracy: Diagnostic accuracy relates to the ability of a test to discriminate between the target condition and health. This discriminative potential can be quantified by the measures of diagnostic accuracy such as sensitivity and specificity, predictive values, likelihood ratios, Youden's index and diagnostic odds ratio

Ultrasound: Sound wave with frequencies higher than upper limit audible to human hearing (20Hz to 20KHz).

Diagnostic ultrasound: Is an imaging method that uses sound waves to produce images of structures within your body. Typical diagnostic scanner operates in the frequency range of 2-18MHz

BI-RADS (**Breast Imaging-Reporting and Data System**): Is a risk assessment and quality assurance tool developed by American College of Radiology that provides a widely accepted lexicon and reporting schema for imaging of the breast. It applies to mammography, ultrasound, and MRI

Breast lesion: An area of abnormal breast tissue. Can be benign or malignant and solid or cystic.

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ABSTRACT

Background: In Kenya, breast cancer leads in incidence with 5,985 new cases annually (12.5% of all new cancer cases) and it is third leading cause of all cancer deaths. Breast screening and diagnosis through imaging is important in the treatment and control of the disease. Breast Ultrasonography (US) should be the primary imaging tool for women who are pregnant, lactating, or younger than 30 years and for women > 40 years old it is complementary to both mammography and magnetic resonance imaging of the breast. Breast Imaging Reporting Data System (BI-RADS) is the reference for the presentation of clinical and medical results and communications. Its main objectives are to standardize the reports, facilitate the comparison of follow-up examinations and to allow a collection of data so as to follow treatment on an individual scale. However, the utilization of this standardized system has not been explored and no previous studies on diagnostic accuracy of sonographic BIRADS score exists in our setup. Therefore, the study aimed to establish the diagnostic accuracy of sonographic BI-RADS score based on histopathology in the diagnosis of breast lesions.

Objectives: To determine the sonographic and histopathological findings and to establish the diagnostic accuracy of sonographic BIRADS score in the diagnosis of breast lesions based on histopathology at Moi Teaching and Referral Hospital(MTRH).

Methods: This was a cross-sectional study done in MTRH from April 2021 to March 2022. A consecutive sampling technique was used to enroll 214 patients aged between 19-70years. Breast US was done using 7.5MHz linear transducer of the MINDRAY M7 ultrasound machine. Sonographic findings were described and classified into categories 0 to 6 according to the BI-RADS for breast US. A total of 295 breast US were done, however only 214 patients underwent core needle biopsy and their results were analyzed. Data collection form was used to record the demographics, clinical presentation, radiological findings (BIRADS category) and histopathological findings. BIRADS categorization and biopsy results were compared. Continuous variables were summarized using mean and categorical variables were summarized in frequencies and percentages. Cohens kappa statistics was used to determine the level of agreement between the sonographic findings and histopathology. A P-value of <0.05 was considered statistically significant.

Results: Majority of the study participants were female 204 (95.3%) with the mean age 44.14years. Clinically, 72% of patients presented with breast lump only, (8.4%) breast lump with pain, (8.9%) had ulceration. Sonographically, BIRADS-4(suspicious) was commonest at 33.6% followed by BIRADS-5(highly suspicious) at 24.8% and BIRADS-3 (probably benign) at 22.4%. Histopathologically, malignant breast lesions were the commonest at (59.3%) while the rest were benign at 40.7%. Commonest malignant and benign lesions was invasive ductal carcinoma (IDC) at (59.3%)n and fibrocystic change (41.4%) respectively. Sonographic BIRADS score had sensitivity (66.67%), specificity (51.14%), NPV (51. 72%), PPV (66.14%), NLR (0.65) and PLR (1.36). Correlating signs for malignancy were hypo-echogenicity (96.2%), uncircumscribed margins (95.7%) and posterior shadowing (77.4%) and for benignity were parallel orientation (96.5%), echogenic (95.1%), well circumscribed margins (91.8%) and oval/round shape (68%). There was slight agreement between the sonographic BIRAD-score and histopathology with two examinations having $\kappa = 0.178$ (95% CI 0.090 to 0.333).

Conclusion: Descriptors from the sonographic BI-RADS lexicon can be useful in differentiating benign from malignant masses. The low sensitivity and specificity for the BIRADS was due to high false positive and false negative numbers.

Recommendation: use of BIRADS as a standardized reporting tool should be mandatory. Use of high resolution transducers is recommended for high quality images and in detection of smaller abnormalities.

CHAPTER ONE: INTRODUCTION

1.1 Background

Breast diseases afflict women more than men worldwide. (Kaira, Aggarwal, & Kaira, 2017)

In India, 95.7% of breast lesions occur in females and 4.3% in men (Hatim, Laxmikant, & Mulla, 2017).

In Nigeria prevalence of benign breast, lesions are 22.7% (Registry & Registry, 2019).

In Kenya, the prevalence rate in male's ranges from 0 to 5.8%. The majority of male breast afflictions are benign with gynecomastia occupying the top slot. Among females, the distribution of pathology varies widely depending on age and geographical location. Benign lesions predominate at all ages accounting for 48.9% to 57% with a mean age of occurrence being 28.5 years. Five conditions namely fibro adenoma, invasive ductal carcinoma, breast abscesses, fibrocystic disease, and breast pain (mastalgia) account for over 85% of all breast ailments. (Otieno, Kimende, & Micheni, 2009).

Breast cancer is the most common type of malignancy in women, and one of the three most common cancers worldwide, along with lung and colon cancer. In 2012, there were approximately 1.7 million new cases of cancer worldwide, and about 31% of them led to death.(Iranmakani et al., 2020)

According to International Agency for Research on Cancer (IARC), it is predicted that by 2040 the breast cancer burden will increase to more than 3 million new cases per year (an increase of 40%) and more than 1 million deaths per year (an increase of 50%).

Breast cancer is a public health burden in sub-Saharan Africa (SSA). According to the 2020 GLOBOCAN data, 186,598 breast cancer cases were reported in Africa with 85,787 related deaths.(Anyigba, Awandare, & Paemka, 2021)

In south Africa, breast cancer is the most common female cancer and is a leading cause of death amongst South African women with increasing incidence of breast cancer is a major health concern with 19.4 million women aged 15 years and older at risk of contracting the disease and in 2013, it was responsible for 20.8% of female cancers and more than 10% of the entire cancer burden.(Smilg, 2018)

In Kenya, Breast Cancer leads in incidence with 5,985 new cases annually (12.5% of all new cancer case. It is the third leading cause of all cancer deaths. Five out of ten breast cancer cases in Kenya are diagnosed late (GLOBOCAN, 2018).

Pregnancy-associated breast cancer is the most common malignancy of pregnancy, occurring in 1 in 3000 to 1 in 10,000 pregnancies, and is the most common cause of cancer-related death in the pregnant and lactating patient. The mean age at diagnosis based on current studies is estimated to be between 32 and 34 years old.(Vashi, Hooley, & Philpotts, 2013)

A wide range of breast lesions can arise during pregnancy and lactation, from benign or inflammatory diseases to malignant tumors. Hormone-influenced physiological changes of the breast make the radiological evaluation of breast lesions challenging. Knowledge of the imaging features of normal physiological changes and common breast lesions during this period can help radiologists accurately diagnose and appropriately manage conditions. Most breast lesions detected during pregnancy and lactation are benign; however, the possibility of pregnancy-associated breast cancer (PABC) must be considered to avoid a delayed diagnosis.(S. E. Lee & Bae, 2020)

Breast US is usually the first line examination performed in women with implants to investigate breast implant complications that may present with pain, lumps, or asymmetries. It can be used to detect alterations of the implant structure, typically subdivided into intracapsular ruptures (when the implant envelope is broken but the silicon remains inside the capsule) and extracapsular ruptures (when the silicone leaks out of the broken capsule). Of note, the fibrotic capsule around the implant develops through a natural foreign body reaction of the breast tissues to the implant. Considering breast implant integrity, US is a very specific, although not very sensitive, method: if an implant rupture is suspected on US, the probability of a true rupture is high; conversely, if no rupture is visible on US, a rupture (mostly intra-capsular) is still possible. In addition, US is useful in diagnosing other implant complication such as infection, seroma, or granuloma.(Evans et al., 2018).

Common breast problems include breast mass, pain, and nipple discharge. Breast symptoms were reported in about 3% of all visits by female patients to family physician. Over a 10-year period, 16% of women 40 to 69 years of age had breast problems, and 10% reported breast symptoms at the time of mammography. The prevalence of cancer among women who report breast symptoms is estimated to be less than 10%, and those with breast lumps have a higher risk of malignancy than those with breast pain. Although most breast symptoms have benign causes, symptoms can cause significant anxiety. Breast masses are associated with an increased risk of breast cancer. Patients presenting with a palpable breast mass should be evaluated with a detailed history, clinical breast examination (CBE), and, for almost all women, imaging.(Salzman, Collins, & Hersh, 2019)

It has been consistently documented that women are somewhat more likely to be diagnosed with left breast cancer than right. Although the excess of left-sided tumors is not large and does not impact overall survival, it may influence subsequent management, especially in elderly patients with ischemic heart disease. For cases with left sided implantable devices, such as a pacemaker or defibrillator, that require radiation therapy to the left breast, the implantable devices need to be relocated to the right side prior to initiation of radiation therapy. Although the left predominance has since been repeatedly noted, no satisfactory explanation has been provided.(Amer, 2014)

Tumor location in the breast has been reported as an independent prognostic factor. Tumors in the upper outer quadrant (UOQ) are the most frequent site of tumor location. They are associated with better survival compared with other quadrants. survival for non-UOQ tumors such as lower inner quadrant (LIQ) or medial regions have demonstrated lower survival. Axillary LN metastasis has also been suggested to be significantly lower in the upper inner quadrant compared with all other quadrants.(Ji et al., 2019)

Benign breast diseases constitute a heterogeneous group of lesions arising in the mammary epithelium or in other mammary tissues and they may also be linked to vascular, inflammatory or traumatic pathologies. Some lesions are palpable masses, which may be nodular, some- times with specific or unspecific characteristics, but often (particularly in lesions of greater prognostic significance such as atypical hyperplasia) there are no specific clinical signs, and detection is difficult also at diagnostic imaging examinations.(Masciadri & Ferranti, 2011)

The malignant spectrum includes ductal carcinoma, lobular carcinoma, colloid carcinoma, and medullary carcinoma. The incidence of benign breast lesions begins during the 2nd decade of life and increases gradually in the 4th and 5th decades while the incidence of malignant lesions increases after menopause.(Yogalakshmi & Kavitha, 2019)

Reducing global breast cancer mortality by 2.5% per year would avert 25% of breast cancer deaths by 2030 and 40% by 2040 among women under 70 years of age. The three pillars toward achieving these objectives are: health promotion for early detection; timely diagnosis; and comprehensive breast cancer management (WHO, 2021)

Early detection of breast cancer through breast imaging plays an important role in the treatment and control of the disease.

The choice between using ultrasound or mammography for the evaluation of breast lesions depends on several factors like age and breast density.(Kutllovci, n.d.)

Mammography is the recommended method of screening for women in the average risk population. Clinical Breast Examination (CBE) should be considered as part of a physical examination and used as an opportunity to discuss and educate the woman on breast health. It should not be considered as a replacement for mammography screening. Ultrasound, when available and if conducted by a competent clinician, should be considered as an adjunct to CBE in women between 35 and 39 years. Ultrasound is not recommended for routine screening for the average risk population. It may be used to complement mammography in situations where patients have increased breast density. (2 | kenya national cancer screening guidelines, n.d.).

Breast Self-Examination (BSE) and Awareness BSE is not recommended as a screening method. However, women should be encouraged to be aware and to report changes in their breasts, such as nipple discharge, rash on nipples, inversion, dimpling or new mass in the breast or axilla. MRI is not recommended for routine screening in the average risk population. MRI may be used for screening in select high-risk populations or in specific circumstances as determined by a clinician such as previous lumpectomy, radiation or trauma to breast (2 | kenya national cancer screening guidelines, n.d.).

The imaging approach for the evaluation of breast lesions was standardized with the introduction of the Breast Imaging Reporting Data System (Bi-RADS), which was created by the American College of Radiology (ACR) in 1992. This systematization is a data control system that provides a lexicon for describing lesions, establishes levels of suspicion for breast cancer, and indicates the required subsequent steps for the evaluation and treatment of breast cancer (Zanello et al., 2011).

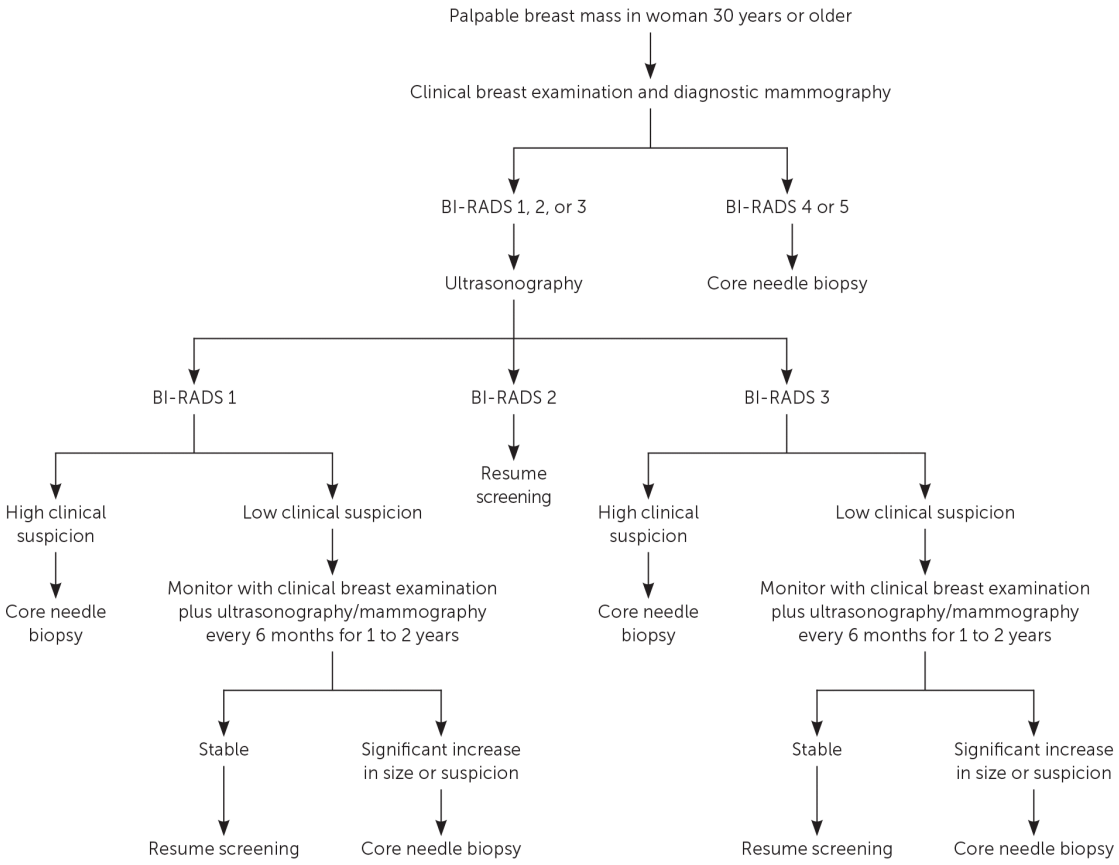


Figure 1: Evaluation of palpable breast masses in women 30 years and older. (BI-RADS = Breast Imaging Reporting and Data System.) (Salzman et al., 2019)

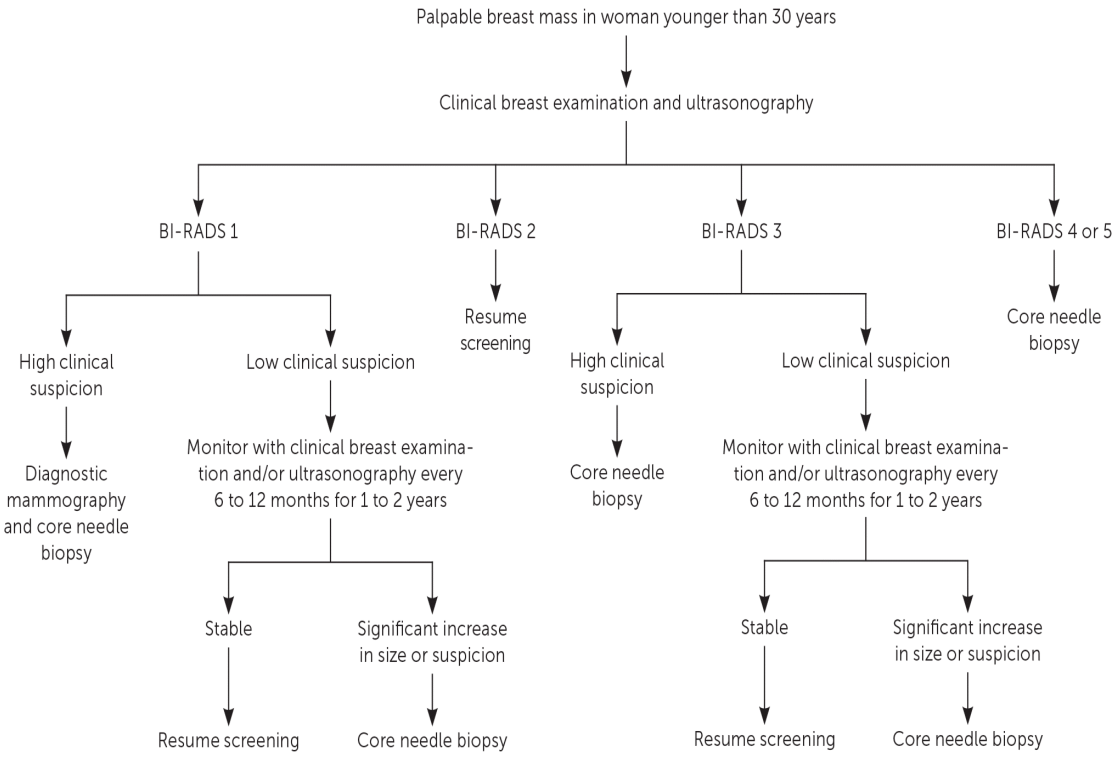


Figure 2: Evaluation of palpable breast masses in women younger than 30 years. (BI-RADS = Breast Imaging Reporting and Data System.) (Salzman et al., 2019)

Ultrasonography is in common use for diagnostic breast imaging,(Smilg, 2018).

It is an indispensable tool in breast imaging and should be the primary imaging tool for women with palpable lumps who are pregnant, lactating, or younger than 30 years. For women > 40 years old it is complementary to both mammography and magnetic resonance (MR) imaging of the breast. Advances in US technology allow confident characterization of not only benign cysts but also benign and malignant solid masses. (Hooley, Scoutt, & Philpotts, 2013).

Mammography, which has long been considered the gold standard for screening and early detection of breast cancer, is not always feasible, especially in limited-resource settings. This may be due to the high cost of purchasing and maintaining equipment as well as difficulty training and retaining skilled technologists and interpreting

radiologists. Breast ultrasound, which is used in high-resource settings to supplement mammography in certain clinical scenarios, offers a potentially viable alternative for early breast cancer detection in some resource- limited areas because it is portable, lower cost than mammography, and versatile across a wider range of clinical applications. Breast ultrasound has been proven to be an exceptionally effective tool for imaging palpable abnormalities and it is a particularly useful

diagnostic modality in dense breast tissue, often detecting breast cancers obscured on mammography (Brem, Lenihan, Lieberman, & Torrente, 2015).

With recent developments in ultrasound equipment, sonography is now a well-established tool in breast imaging, allowing identification of up to 27% of breast masses that are occult on mammography, especially in women younger than 50 years of age. In light of the widespread use of ultrasound, the ACR (American College of Radiology) in 2003 developed a BI-RADS lexicon for breast sonography to standardize the characterization of sonographic breast lesions. This lexicon includes descriptors of features such as mass shape, orientation, margin, and posterior acoustic transmission. Several studies have assessed the utility of such sonographic features in distinguishing between benign and malignant breast lesions. It has also suggested classifying each lesion into a single category after breast ultrasound, linked to the appropriate BI-RADS recommendation of management.(Heinig, Witteler, Schmitz, Kiesel, & Steinhard, 2008)

The ACR agreed with the idea that to improve report comprehension by the corresponding doctors and to facilitate the comparison of subsequent examinations, it was desirable to define the terms to be used according to the images encountered. The BIRADS lexicon for ultrasound was developed according to a basic principle: a maximum of terms would have to be shared with the BIRADS lexicon for

mammography. However, certain characteristics, such as the orientation of the lesion or the echogenicity are specific to ultrasound. The lexicon is supposed to be evolutionary. Its objective is to obtain an exact and concise report. As in mammography, a mass signifies a process occupying a space, thus, visible on two images, whereas the aspect of a normal anatomical structure (fatty lobule, ribs) will clearly change from one image to another. Seven categories should be documented using the best descriptor among those available. The shape can be oval, round, or irregular. An oval mass can be slightly lobulated or macro lobulated, meaning containing two or three lobulations (more than three constitutes an irregular mass). However, it should be noted that Radiologists can differ as to the classification between categories 4 and 5 for same lesions. Nevertheless, in most cases, this has no practical consequence, as their recommendations for supplementary examinations or biopsies turn out very often to coincide. With ultrasound, the types of lesions that can be classified in categories 4 or 5 are not yet clearly defined, as a lot of signs and their associations have to be evaluated.(Levy, Suissa, Chiche, Teman, & Martin, 2007)

Probably benign (BI-RADS 3) causes confusion for interpreting physicians and referring physicians and can induce significant patient anxiety. The 5th edition of the BIRADS atlas details the appropriate use of BI-RADS 3 for diagnostic mammography, ultrasound, and MRI, and discourages its use in screening mammography. Sonographic masses that meet criteria for BI- RADS 3, have a less than or equal to 2% likelihood of malignancy. This category reduces the number of false- positive biopsies and justifies a period of watchful waiting. The characteristics that determine a BI-RADS 3 mass on ultrasound include benign features such as an oval shape, well-circumscribed margins, parallel orientation, echogenicity less than fat with no posterior features or minimal posterior acoustic enhancement. Some

masses that are commonly assessed as BI-RADS 3 include classic appearing fibroadenomas, an isolated complicated cyst or cluster of microcysts that is perhaps diagnostically challenging or new in a postmenopausal woman not on hormonal therapy. BI-RADS 3 is used for both palpable and non-palpable masses and can accurately predict benignity when combining clinical information with imaging findings(K. A. Lee, Talati, Oudsema, Steinberger, & Margolies, 2018)

In countries that lack the resources to support the full implementation of BI-RADS, ensuring consistent reporting, tracking patient management, and improving performance and patient outcomes may be challenging. The Breast Health Global Initiative has proposed a phased implementation strategy to implement BI- RADS in low-resource areas. The use of a condensed version of BI- RADS, such as one containing limited descriptors from the breast US lexicon, is recommended before the transition to full BI-RADS for each phase of implementation. In Uganda, breast US education using a condensed BI-RADS resulted in improved interpretative performance and fewer unnecessary biopsies.(Eghtedari, Chong, Rakow-penner, & Ojeda-fournier, 2021)

Ultrasound elastography is a new screening modality in addition to sonography for detecting and identifying lesions in the breast. It can provide the investigator with another characteristic, stiffness, of the lesion. With light compression of the target lesion, it can noninvasively determine strain and elasticity distributions inside objects scanned and map the elasticity of the lesion by using a standardized color scale, with blue indicating regions with low elasticity (harder tissue areas) and red indicating regions with high elasticity (soft tissue).(Apesteguía & Pina, 2011)

Doppler study was initially considered very promising in the differential diagnosis between benign and malignant masses on the basis of morphological criteria (number

of penetrating vessels as well as central or peripheral distribution) and semi quantitative criteria (resistance and pulsatility indices, peak systolic velocity) which may identify the characteristic neo angiogenesis of malignant lesions. Power Doppler is better than color Doppler for detecting small vessels with slow blood flow and is therefore able to distinguish between solid and complicated cystic lesions, but it is more sensitive to artifacts. However, the literature has revealed a substantial overlap of aspects in the vascularity of benign and malignant lesions. The hypothesis that more vascularization means a higher probability that the lesion is malignant is absolutely not valid (for example, also benign papillary lesions are highly vascularized). However, vascularization within a solid lesion detected at color/power Doppler should increase the US operator's attention and suspicion.(S. E. Lee & Bae, 2020)

Lymph node involvement and tumor size are the most important factors in the prognosis of breast cancer and remain crucial for individual treatment decisions, hence in patients presenting with breast masses axillary node evaluation must be done(Fidan, Ozturk, Yucesoy, & Hekimoglu, 2016)

The primary nonsurgical imaging modality for evaluating axillary lymph node is US. High-frequency (7.57–17 MHz) linear-array transducer is generally used to examine the axillae and both breasts. The patient should lie in supine-oblique position with the arm abducted and externally rotated. It is important to examine the entire extent of the axillary contents. systematic review of the literature reports that the sensitivity of US has a wide range between 49% and 87% for depicting nonpalpable metastatic lymph nodes when based on size and between 26% and 76% when based on morphologic criteria.23 Specificity was between 55% and 97% when based on size and between 88% and 98% when based on morphologic characteristics(Choi et al., 2017)

Core needle biopsy (CNB) is the technique of choice for preoperative diagnosis of symptomatic or radiologically detected breast lesions in many centers. CNB has replaced fine-needle aspiration cytology in these centers, not only because it is more sensitive and specific, but also because it enables differentiation between invasive and in situ carcinomas in most cases. The introduction of CNB has led to a reduction in surgery on benign lesions. CNB yielded a ratio of benign to malignant surgical biopsies of 1:6.5.(Andreu et al., 2007)

Breast biopsy should be reserved for diagnostically challenging cases and when the evaluation of the invasiveness is mandatory in cases such as in papillary neoplasms. The histopathological report should be valid, reproducible, and accepted as the gold standard internationally. (Richie & P, 2019). ultrasound-guided core needle breast biopsy has become the first choice for performing a percutaneous biopsy for most lesions seen on ultrasound. Virtually any breast lesion that is clearly seen on ultrasound can be sampled under ultrasound guidance. Many surgical biopsies that had to be carried out in the past, because of suspicious radiological findings, are nowadays unnecessary due to the extensive use of ultrasound CNB. In addition, surgical specimens removed after a previously proven malignant result are usually more adequate for the tumor size. Consequently, the number of surgical procedures has drastically decreased both for benign and malignant lesions, thanks to the extensive use of ultrasound CNB and the other methods of percutaneous breast biopsies.(Apesteguía & Pina, 2011)

It should be noted that discordance between the assessment of imaging methods and pathological examination may be related to the type of tumor and breast density(Jahan, Rahman, Alam, & Islam, 2020)

Hence, there is a need to correlate the sonographic findings of breast lesions with histopathological diagnosis to evaluate the diagnostic accuracy of sonography before a therapeutic decision is made.(Richie & P, 2019)

Indeed, it should be noted that US cannot define the extension of carcinoma pre-operatively so correlating the sonographic findings with histopathologic features of carcinoma cells can determine the extension of carcinoma. And this demonstrates the importance of correlation between histopathological and the quality of US.(Kim et al., 2008)

1.2 Problem Statement

Globally, breast cancer is the leading cause of cancer-related deaths in women accounting for 12.5-30% of all cancer cases. Approximately 0.5-1% of breast cancer occurs in men (WHO, 2021).

It has been speculated that the lack of an early cancer detection program is responsible for the majority of women (77–89%) presenting at a late, symptomatic stage when cure is impossible.(Onono & Mubuuke, 2020)

The three pillars towards reducing global breast cancer mortality are: health promotion for early detection through imaging; timely diagnosis and comprehensive breast cancer management (WHO, 2021).

Breast ultrasonography (U/S) has gained widespread acceptance as a diagnostic tool for the evaluation of breast disorders and should be the primary imaging tool for women with palpable lumps who are pregnant, lactating, or younger than 30 years (Kumar & Kumar, 2018)

Ultrasound is not recommended for routine screening for the average risk population. It may be used to complement mammography in situations where patients have increased breast density (2 | kenya national cancer screening guidelines, n.d.).

The BI-RADS structured way of reporting ensures that all professionals communicate the same language and clearly alerts the clinician to the next management plan because each BI-RADS category dictates a management plan(Onono & Mubuuke, 2020)

However, the utilization of this standardized system of reporting breast ultrasound findings has not been explored in our setup

And no previous studies on diagnostic accuracy of sonographic BIRADS score has been performed in our setup

1.3 Justification/Significance

Breast changes either self-detected or found at clinical breast examination, is a common presenting symptom in women and (however rare in men) are a cause of anxiety and require a carefully targeted diagnostic process. Typical presenting symptoms such as pain, a palpable mass, and nipple discharge can be caused by a wide array of differential diagnoses and require targeted diagnostic imaging and others like cytological and histological examination. (Stachs, Stubert, Reimer, & Hartmann, 2019).

The credibility and reliability of BIRADS-lexicon for ultrasound need to be established for accurate reporting because it will be required for next course of management. (Belli et al., 2007)

Pre-operative pathology diagnosis constitutes an essential part of the work-up of breast lesions. The credibility and reliability of BIRADS-lexicon for ultrasound need to be established for accurate reporting.

Hence, this study aims to improve the patients' diagnosis by determining the diagnostic accuracy of sonographic BIRADS score in the diagnosis and screening of patients presenting with breast lesions in MTRH.

It will also be able to inform on the diagnostic criteria for patients with breast lesions conditions. This is an overall effort in improving patients' management and efficient service provision.

1.4 Research Question.

What is the diagnostic accuracy of sonographic BIRADS score in patients presenting with breast lesions based on histopathology at Moi Teaching and Referral hospital?

1.5 Objectives

1.5.1 Broad Objective

To determine the diagnostic accuracy of sonographic BIRADS score in patients presenting with breast lesions based on histopathology at Moi Teaching and Referral Hospital-Eldoret, Kenya

1.5.2 Specific Objectives

1. To determine the patterns of breast sonographic findings in patients presenting with breast lesions at Moi Teaching and Referral Hospital-Eldoret, Kenya
2. To determine the patterns of histopathological findings in patients presenting with breast lesions at Moi Teaching and Referral Hospital-Eldoret, Kenya
3. To establish the diagnostic accuracy of sonographic BIRADS score in patients presenting with breast lesions based on histopathology at Moi Teaching and Referral Hospital-Eldoret, Kenya

CHAPTER TWO: LITERATURE REVIEW

2.1 Breast anatomy and pathologies (it was recommended that I add the anatomy part in the literature review rather than in chapter one)

2.1.1 Breast embryology (Bistoni & Farhadi, 2015)

The breasts develop from the embryologic mammary ridges/milk lines, which extend from the axilla to the groin. During fetal development, the caudal portions of the milk lines regress with the persistence of the cranial portions, which overlie the pectoralis muscle groups. The nipple-areolar complex begins to form around 12 weeks of gestational age when mesenchymal cells differentiate into smooth muscles and form Montgomery glands and the mammary ducts. Breast development becomes quiescent until puberty when the breast mound and areola increase in size in response to sex hormones

2.1.2 Breast gross anatomy (Bistoni & Farhadi, 2015)

The adult female breast is a hemispheric structure with an axillary tail (of Spence). Normally, there are two breasts each situated in front of the thorax and each consisting of 15 to 20 lobes. A lobe consists of;

(i)Parenchymal elements i.e. ducts and lobules.

(ii) Supporting stromal tissues i.e. fibrous tissue and fat

A lobule consists of an intralobular segment of a terminal duct, ductules (acini) and intralobular stromal fibrous tissue. The Terminal Ductal Lobular Unit (TDLU) is the functional unit of the breast and consists of a lobule and an extra lobular terminal duct. The TDLU is the site of origin for most pathology and aberrations of normal development and involution of the breast.

The breast is entirely invested by an anterior and posterior mammary fascia. The anterior mammary fascia forms radial septa, the Cooper's ligaments, which divide the gland into lobules and attach it to the skin and the underlying posterior mammary fascia. The two fascial layers divide the breast into;

(i) Pre mammary zone.

(ii) Mammary zone

(iii)retro mammary zone

The pre mammary zone is subcutaneous and lies between the skin and the anterior mammary fascia. Lesions arising primarily from this zone are not true breast lesions but lesions of skin and subcutaneous tissue. The mammary zone lies between the anterior and posterior fascia. It contains the ducts, the TDLU and most of the fibrous stromal element of the breast. The retro mammary zone contains fat, blood vessels and lymphatics.

The base of the breast extends from the 2nd to the 6th rib and from the side of the sternum to near the mid axillary line. The breast lies mainly on the pectoralis major muscle but extends laterally over the serratus anterior muscle, the external oblique muscle and its aponeurosis. The nipple projects from the anterior surface of the breast. It is surrounded by the areola and its position is variable, but it usually lies over the 4th intercostal space in the non-pendulous breast.

In the male and pre pubertal female the breast is a rudimentary organ. During adolescence the growing breast becomes increasingly glandular.

The breast undergoes various changes during pregnancy and lactation in response to hormones such as estrogen, progesterone, and prolactin. During pregnancy, the

number and size of breast ducts and lobules increase. The fluid content of the breast also increases, accompanied by involution of the fibrofatty stroma. After delivery, prolactin induces milk accumulation and corresponding lobular growth and distension, and oxytocin induces the milk ejection reflex and facilitates the maintenance of milk production. These physiological changes result in increased breast volume with associated palpable nodularity and increased firmness, making the clinical detection of palpable lesions difficult. Spontaneous unilateral or bilateral bloody nipple discharge can occur during pregnancy and early lactation (in up to 20% of pregnant women and 15% of lactating women) due to proliferative changes in epithelial cells as well as increased breast vascularity. This condition is usually self-limiting. However, persistent unilateral bloody nipple discharge can be a pathological condition that occurs secondary to infection, papilloma, or breast cancer.

When lactation stops the glandular tissue involutes to less than pre-pregnancy state. Apart from the situation during pregnancy and lactation, parenchymal atrophy starts in early adulthood and is accelerated at menopause, with diminishing amounts of glandular tissue and an increasing amount of fat.

There are two breasts each situated in front of the thorax and each consisting of 15 to 20 lobes. A lobe consists of;

(i)Parenchymal elements i.e. ducts and lobules.

(ii) Supporting stromal tissues i.e. fibrous tissue and fat

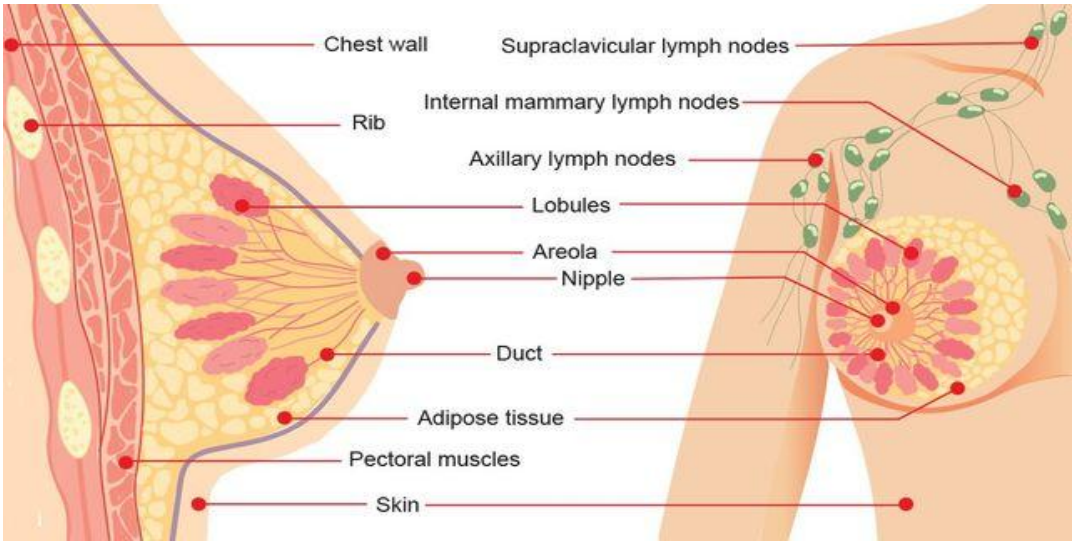


Figure 3: breast gross anatomy

2.1.3 Sonographic Anatomy of the breast

The anatomic components of the breast and surrounding structures have characteristic sonographic features which should be recognized.

The skin is seen as two thin echogenic lines demarcating a narrow hypoechoic band the dermis. Normal skin measures up to 0.2cm in thickness (may be thicker near the infra mammary fold). Fat, loose stromal fibrous tissue and individual TDLU are isoechoic structures.

Cooper's ligaments, the two mammary fascial layers, duct walls and compact stromal fibrous tissue are sonographically hyperechoic. The mammary ducts are arranged radially around the nipple in 7-20 segments and are recognized as tubular structures measuring 1 to 3mm in diameter and exhibiting progressive luminal enlargement as they converge on the nipple.

The nipple is of medium echogenicity and attenuates sound with resultant posterior acoustic shadowing. Axillary vessels present as tubular structures.

Lymph nodes are visible in the axilla and breast parenchyma as reniform structures with echogenic fatty hilum.

Most masses appear as hypoechoic or anechoic structures. Visualization of the pectoral muscle and the ribs seen as structures with posterior acoustic shadows behind the pectoralis muscle) is confirmation that the breast has been adequately penetrated

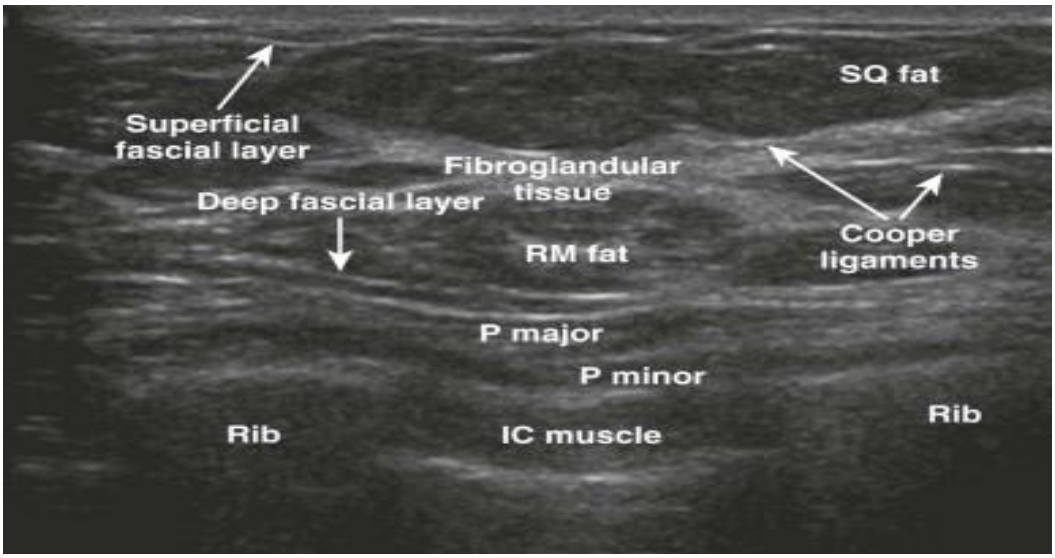


Figure 4: Sonographic anatomy of breast

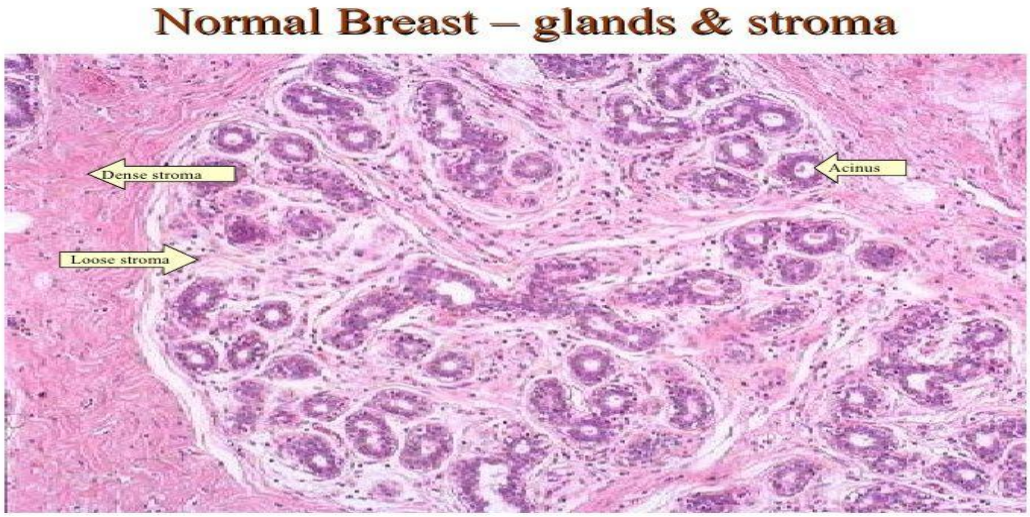


Figure 5: Normal histology of breast

2.1.4 Classification of breast Pathology

The pathologic categorization of breast disease is based on a combination of the architecture, cytological features and cell type of the lesion. The basic cell types are epithelial lining of the ducts and lobules, myoepithelium, surrounding the ducts and lobules, fibroblasts of the stroma, stromal blood vessels and nerves and adipocytes that make up the bulk of breast tissue. In addition, reactive and inflammatory processes may recruit tissue macrophages (histiocytic) and inflammatory cells to the breast. Each of these cell types can give rise to pathology and hence breast diseases can be broadly classified into inflammatory, epithelial, fibro epithelial, secondary lesions and other entities.

A) INFLAMMATORY LESIONS:

Breast abscess. This is due to duct obstruction during lactation leading to rupture, resulting in inflammation and abscess formation. Process is usually sub areolar.

Mammary duct ectasia. This condition of unknown etiology involves dilatation and filling of central ducts with proteinaceous material. Usually affects middle to older aged patients who present with nipple discharge or bleeding.

fat necrosis: This condition is fairly common. It may be spontaneous or may be due to trauma, surgery or radiation. Fat cells (adipocytes) are disrupted and this is accompanied by hemorrhage and histiocytic infiltration. Over time adipocytes degenerate and are surrounded by Iymphoplasmacyte infiltrate. Calcification and stromal fibrosis become prominent.

B) EPITHELIAL LESIONS.

These form the bulk of breast pathology. This category consists of fibrocystic changes, papillary proliferations, benign and atypical hyperplasia, carcinoma in situ and invasive carcinoma.

Fibrocystic changes. These are a constellation of benign alteration of ducts and stroma that occur alone or in combination with others. They are common and include cysts, unusual ductal hyperplasia, adenosis and sclerosing adenosis.

Papillary proliferations. These are lesions with a pattern of sequential branching of a fibro vascular stromal skeleton lined by a layer of epithelium. They include papilloma, papillary carcinoma and papillary proliferations partially involved by benign hyperplasia or carcinoma in situ.

Benign and atypical hyperplasia. This includes lactational adenoma and atypical ductal hyperplasia. The former occurs in pregnancy while latter are ductal lesions with a degree of cytological atypia that falls short of criteria for low grade ductal carcinoma in situ.

Carcinoma in situ. This refers to malignant epithelium without disruption of underlying basement membrane or invasion of stroma. Carcinoma in situ can either be of ductal or lobular differentiation.

Invasive carcinoma. This is sub classified as either ductal or lobular differentiation.

Invasive ductal carcinoma is defined by presence of glandular differentiation and cellular cohesion. A subset of invasive ductal carcinomas includes tubular, mucinous, cribriform, papillary, medullary, metaplastic and mucopapillary carcinoma

C) FIBROEPITHELIAL LESIONS. These entities comprise of a stromal and epithelial component. They include fibro adenoma which are benign, phylloides tumor which have a propensity for recurrence after excision, tubular adenoma, hamartoma, pseudo angiomatous stromal hyperplasia, fibromatosis and sarcomas. Breast sarcomas are uncommon and reported cases include malignant fibrous histiocytoma, osteosarcoma, chondrosarcoma, leiomyosarcoma, liposarcoma and rhabdomyosarcoma.

D) SECONDARY NEOPLASM: Secondary neoplasms of the breast are infrequent. They include lymphoma, melanoma, small cell carcinoma and adenocarcinoma from primaries in the stomach, kidney, ovary, cervix and thyroid.

E) OTHER ENTITIES. These include lipoma, hemangioma, collagenous spherulosis and calcification. Breast calcification is found in a wide range of entities including normal stroma, fibrocystic change, fibro adenoma, carcinoma in situ and invasive carcinoma.

It forms in duct lumens, stroma or blood vessel

2.2 Ultrasonography Findings of Breast Lesions

Breast cancer is still one of the leading causes of cancer-related death for women worldwide. Methods are being sought that allow early and accurate diagnosis of cancer. The use of diagnostic breast imaging in routine health examinations is important especially for the early detection of cancer. With recent developments in ultrasound equipment, sonography is now a well-established tool in breast imaging, allowing identification of up to 27% of breast masses that are occult on mammography, especially in women younger than 50 years of age.

Breast lesions and cancer are uncommon disease in men. As a result, the diagnosis may not initially be considered. Understanding the common benign and malignant entities affecting the male breast is critical for timely and accurate diagnosis in the primary care setting. Most patients present with a palpable breast mass or pain. The usual etiology is gynecomastia, the most common breast condition in males, but breast cancer must always be excluded through careful imaging evaluation when physical examination findings are suspicious or inconclusive.(Chau, Jafarian, & Rosa, 2016)

Women are more likely to develop tumor in the left breast than the right. in a study to evaluate breast cancer laterality, (Amer, 2014) assessed 687 patients with breast cancer between 2005 and 2012. They found out that 343 (50.9%) patients presented with left breast cancer, 311 (46.1%) with right breast cancer, and 20 (3.0%) with simultaneous bilateral malignancy. They also noted that there were no differences in survival in relation to breast cancer laterality, handedness, and presence or absence of a family history of cancer. However, there were significant similarities between patients and first-degree relatives in regards to breast cancer laterality, namely same breast (30/66, 45.5%), opposite breast (9/66, 13.6%), and bilateral cancer (27/66, 40.9, P=0.01163). they concluded that the high similarities between patients and their first-degree relatives in regards to cancer laterality and possibly age at initial diagnosis of cancer may suggest an underlying inherited genetic predisposition.

Tumor location within the breast has been proposed as an independent prognostic factor. For example, the frequency of axillary lymph node metastasis is found to be significantly lower in the upper inner quadrant compared to all other quadrants. In a study to evaluate the prognostic value of tumor site within the breast, (Rummel, Hueman, Costantino, Shriver, & Ellsworth, 2015) assessed 980 patients with defined

tumor location. They found out that tumor location was higher in the UOQ (51.5%) compared to the UIQ (15.6%), lower outer quadrant (LOQ, 14.2%), central (10.6%), or LIQ (8.1%). They also noted that central quadrants had a higher frequency of late-stage tumors (25%) compared to the other quadrants (range 7–13%), T3 tumors (16%) compared to other quadrants (range 0–5%) and metastatic lymph nodes (51%) compared to other quadrants (range 24–38%). Breast cancer mortality rates were highest in patients with tumors in the central quadrant (7%) compared to other quadrants (range 1–5%). They concluded that evaluation of tumor location as a prognostic factor revealed that although tumors in the central region are associated with less favorable outcome, the associations are not independent of location but rather driven by larger tumor size. Tumors in the central region are more difficult to detect resulting in larger tumor size at diagnosis and thus less favorable prognosis.

These results were echoed by (Ji et al., 2019) who investigated the clinicopathological characteristics of tumors of central and nipple area(TCNP) and to clarify their prognostic value. They found that TCNP patients were mainly in an older age group (age ≥66 years), with larger tumor sizes (>20 mm size) and higher TNM stages (II–III). This may because tumors within the central region are harder to detect during imaging may reach a substantially larger size before being detected by imaging. They concluded that TCNP relates to tumor burden and progression.

(Lehman, Lee, & Lee, 2014) describes breast ultrasound as a highly effective imaging tool for guiding effective evaluation of women with palpable breast abnormalities and that should be used for all women with suspicious findings at clinical breast examination and should be the primary imaging tool for women with palpable lumps who are pregnant, lactating, or younger than 30 years. For women 40 years old and older, mammography, followed in most cases by ultrasound, is recommended. For

women 30–39 years old, ultrasound or mammography may be performed first at the discretion of the radiologist, however (Draghi, Tarantino, Madonia, & Ferrozzi, 2011) argues that in imaging of the male breast, the use of mammography is the method of choice for evaluating lesions of the male breast, particularly those of a neoplastic nature, and ultrasonography are used only as complementary examination or as a guide for biopsy, this argument is echoed by (Chau et al., 2016) who also noted that Imaging of the male breast generally relies on mammography and ultrasound, with mammography employed as the initial imaging modality of choice and ultrasound when a mass is detected or suspected. They also noted that mammography has high sensitivity and high NPV and as part of ultrasound imaging of suspicious findings, the ipsilateral axillary basin should also be examined because 50% of male patients with breast cancer have axillary lymphadenopathy.

In a prospective study done at the University of Prishtina in Kosovo (2009) by (Kutllovci, n.d.) to determine a more accurate imaging test between mammography and ultrasound for the diagnosis of breast cancer based on the women's age and breast density with correlated histopathological findings. The study found that Sensitivity varied significantly with age and breast density. In the women who had both tests, ultrasound had a higher sensitivity than mammography in women younger than 45 years, whereas mammography had a higher sensitivity than ultrasound in women older than 60 years. The sensitivity according to age was 52,1% for mammography and 72,6% for the ultrasound. The specificity according to age was 88, 5% for ultrasound and 73, 9% for mammography. Comparing the sensitivity of mammography and ultrasound according to the breast density indicates that mammographic sensitivity was 82,2% among women with predominantly fatty breast, but 23.7% in women with heterogeneously dense breasts, with the increase of fibro

glandular density the level of sensitivity with mammography decreases, while ultra-sonographic sensitivity was 71,1% among women with predominantly fatty breast and 57,0% for heterogeneous dense breasts. The data indicated that sensitivity and specificity of ultrasound were statistically significantly greater than mammography in patients with breast symptoms for the detection of breast cancer and benign lesions particularly in dense breasts and in young women.

In a descriptive, comparative study, done in Khartoum Oncology Hospital in the period from February 2015 to April 2017, to compare between ultrasound and mammography in diagnosis of malignant breast masses, the study done in 201 women suffering from breast mass .(Key et al., 2018) established that ultrasounds was more sensitive and accurate than mammography for diagnosis of malignant breast mass it had sensitivity and accuracy of (97.98%) (83.08%) for ultrasound and mammography respectively.

Breast ultrasound can be used as complementary imaging to magnetic resonance (MR) imaging of the breast. In a study to evaluate the use of second-look ultrasonography (US) for investigating additional suspicious lesions detected on preoperative staging magnetic resonance imaging (MRI) for breast cancer. Between September 2008 and August 2010, 1,970 breast MRIs were performed by (M. J. Hong et al., 2015) to evaluate breast cancer before surgery. Second-look US was recommended for 135 patients with 149 suspicious lesions, following the MRI interpretation, and 108 patients with 121 lesions were included in this study. The detection rate on second-look US, according to the lesion type, diameter, and histopathological outcome, was analyzed. 105 lesions (86.8%) were correlated and 16 (13.2%) were not correlated with the findings of second-look US. Of the 105 correlated lesions, 29 (27.6%) were proven to be malignant and 76 (72.4%) were

benign. They found out that a second-look US identified 86.8% of the MRI-detected breast lesions and considered it a useful diagnostic tool for lesions incidentally detected on breast MRI.

Breast Sonography is the first-line modality in the workup of a palpable breast mass in a pregnant or lactating patient and the utility of breast ultrasound in detecting malignant lesions in these patients has been well established, with studies reporting 100% sensitivity and 100% negative predictive value for pregnancy-associated breast carcinoma. Moreover, ultrasound can detect most benign breast masses in these patients In a study to establish the role of breast imaging in detecting breast lesions in pregnant patients (Vashi et al., 2013) established the many advantages of ultrasound including safety secondary to its lack of ionizing radiation and a high sensitivity in the detection of pregnancy-associated breast cancer to be its merits of use in these patients.

Breast sonography is now a well-established adjunct to mammography and in light of its widespread use, the ACR (American college of radiology) developed a BI-RADS lexicon in 2003 for breast sonography to standardize the characterization of sonographic lesions. This lexicon includes descriptors of features such as mass shape, orientation, margin, and posterior acoustic transmission, and other sonographic features. Many studies indicate that the sonographic characteristics commonly seen in benign lesions include Smooth and well-circumscribed, Hyperechoic, isoechoic or mildly hypoechoic, thin echogenic capsule, Ellipsoid shape, with the maximum diameter being in the transverse plane. malignant lesions are commonly hypoechoic lesions with ill-defined borders. Typically, a malignant lesion presents as a hypoechoic nodular lesion, which is 'taller than broader' and has spiculated margins, posterior acoustic shadowing, and micro calcifications, while color Doppler may

show significant vascularity present within highly cellular types of malignancies. (A. S. Hong, Rosen, Soo, & Baker, 2005).

In an explorative qualitative study to explore staff perceptions regarding the use of the BI-RADS system in reporting breast masses on ultrasound as a way of ensuring patient safety in Mulago National Hospital-Uganda,(Onono & Mubuuke, 2020) interviewed 4 radiologist and 18 radiographers. they evaluated 3 themes including Standardization of breast ultrasound reporting: a precursor for patient safety; Need for more continuous professional development (CPD) and Challenges with the BI-RADS system. They found out that all the staff reported that the BI-RADS breast ultrasound system facilitated the classification of breast masses according to international standards and ensures that all staff use similar guidelines and characteristics to assess breast masses. They also established that The staff were pointing to the fact that despite using BI-RADS and its obvious benefits in maximizing patient safety, there was still a need to re-train staff periodically about this system and that there was a need to sensitize other clinicians about the importance of BI-RADS as a system for standardizing breast ultrasound reporting and ensuring patient safety. As per the last theme, the team noted that there was a negative attitude by some of the imaging staff towards this system because this standardized way limits their descriptive reporting that was previously used and that the BI-RADS standardized system was not being used all the time within the department. This results into situations where some reports are structured according to the BI-RADS system while others are not, which might also compromise quality of the breast ultrasound report.

Table 1:Lesion description characteristics(Glassman, 2010)

Ultrasound Lexicon		
Breast composition	a. homogeneous - fat b. homogeneous - fibroglandular c. heterogeneous	
Mass	**shape**	oval - round - irregular
	margin	Circumscribed ***or*** Not-circumscribed: indistinct, angular, microlobulated, spiculated
	orientation	parallel - not parallel
	echo pattern	anechoic - hyperechoic - complex cystic/solid hypoechoic - isoechoic - heterogeneous
	posterior features	no features - enhancement - shadowing - combined pattern
Calcifications	in mass - outside mass - intraductal	
Associated features	architectural distortion - duct changes - skin thickening - skin retraction - edema - vascularity (absent, internal, rim) - elasticity	
Special cases *(cases with a unique diagnosis)*	simple cyst - clustered microcysts - complicated cyst - mass in or on skin - foreign body (including implants) - intramammary lymph node - AVM - Mondor disease - postsurgical fluid collection - fat necrosis	

Table 2: BI-RADS evaluation categories (Levy et al., 2007)

category	Evaluation	Remarks
0	Incomplete	Further imaging examination is required. This may usually occur if ultrasound is the first exploration and there is a need for comparison with previous images or need for mammography
1	Negative	Normal ultrasound Theoretically, this is no problem, if the breasts are dense. However, what certainty is there when the breasts are fattily accompanied by a weak contrast (types 1 or 2) and no recent mammogram been performed? Possible solutions remain in the comparison to a clinical examination, mammography, and previous ultrasound, etc. A normal mammogram combined with a negative ultrasound implies a risk of cancer under 2%.
2	Benign findings	There is practically no risk that cancer will be present, and there is no reason to continue examinations. Abnormalities in this category are, in particular: simple cysts, typical intramammary lymph nodes, implants, stable post-surgical changes, stable possible or biopsy-proven fibro adenomas, well defined fatty lobules in dense echogenic breast tissue. Fine needle aspiration can be performed, when there are one or more big cysts with pain, or to improve the quality of the mammogram
3	Probably benign	Short term follow-up is recommended This is the most delicate category to deal with, because of its uncertainty. No change is expected during the monitoring period. Monitoring is justified because these probably benign lesions have a very weak risk of being malignant. The follow-up examinations will identify among the rare lesions that change in the interval, those which are malignant. These cancers will be diagnosed early in their evolution, still in a favorable stage. These lesions should still be non-palpable, and not be new or be in a state of progression compared to a previous ultrasound. Risk of malignancy >0%
4		A biopsy must be considered These lesions do not have all of the morphological characteristics of typical cancer, but they have a high "probability" of being malignant. The probability of malignancy of these lesions can vary from 3 to 94%. A histological examination is necessary.

	Categories	
	4A:	Low suspicion for malignancy > 2% to ≤ 10% likelihood of malignancy
	4B:	Moderate suspicion for malignancy > 10% to ≤ 50% likelihood of malignancy
	4C:	High suspicion for malignancy > 50% to < 95% likelihood of malignancy
5	Highly suggestive of malignancy	Appropriate action needs to be undertaken. These lesions have a high probability of being cancerous (≥95%). These are in particular irregular masses, with angular or spiculated margin, irregular masses with indistinct margin and posterior shadowing, etc. Imaging guided biopsies are useful to confirm the diagnosis, especially since the treatment considered includes sentinel lymph node technique, neo-adjuvant chemotherapy, or mastectomy
6	Proven malignancy	Appropriate action needs to be undertaken. Used in the pre-therapeutic assessment of biopsy-proven malignant lesions. There is no further need for this category after completion of treatment of the lesion

There are three objectives of BIRADS including to standardize the reports to improve medical treatment; on the other hand, facilitate the comparison of follow-up examinations coming from the same or different sources and finally, to allow a collection of data so as to follow treatment on an individual scale, and the results of the detection on a larger scale.(Levy et al., 2007)

To assess the accuracy of categorization of breast ultrasound findings based on scoring for malignancy using the sonographic breast imaging- reporting and data system (BI-RADS) (Suk et al., 2008), performed breast ultrasound in 2462 patients between 2001 and 2004 . Sonographic findings were then scored using analog criteria as in BI-RADS for breast ultrasound (mass shape, margin, orientation, posterior

acoustic features, lesion boundary, echo pattern). Each lesion was described using these features and then classified into categories 1 to 5 according to the BI-RADS for breast ultra- sound. Categorization and biopsy results were compared. Masses that were suspected of being malignant (Category 4) occurred in 225 (9.1%) patients and those highly suggestive of malignancy (Category 5) were found in 141 (5.7%) patient of the 203 sonographically suspicious lesions (Categories 4 and 5) for which a histological result was available, 116 (57.1%) were found to be malignant. They concluded that the use of the assessment categories, described in BI-RADS for ultrasound4, allows malignant solid masses to be distinguished from benign ones at least as accurately as does mammography

In a study to assess the reliability of the sonographic Breast Imaging Reporting and Data System (BI-RADS) classification in differentiating benign from malignant breast masses, with findings on cytology or histology taken as the reference standard, by (Belli et al., 2007) the following variables were used: Upper outer quadrant of the breast, including the border areas (intersection of outer quadrants and upper quadrants), Shape (irregular, oval, round), Diameters less or greater than 1.4 cm, Orientation (nonparallel, parallel), Presence or absence of circumscribed margins, Type of boundary (abrupt and echogenic halo), Hypoechoic pattern (presence/absence), Posterior acoustic features (enhancement, shadowing, none), Alterations of the surrounding tissue (presence/absence), Category (3, 4, 5), Ratio between horizontal and vertical diameter greater or less than 1 cm.

These study findings further confirmed the high sensitivity (that is, detection of malignant lesions in patients with breast cancer) (95.3%) and the high NPV (that is, detection of true negatives in the women without breast cancer) (92.3%) of the BI-RADS – US system. However, the system showed low specificity (48.4%) as a result

of a large number of false-positive results. They also found out that the greatest problem in differentiating benign from malignant lesions is linked to the overlap of category 4 lesions (benign: malignant ratio: 1.04).

This study finding also indicated that NPV for category 3 was 95.3%. with PPV of 4.7%. However, the results were affected by the small number of lesions assigned to this category. PPV for categories 4 and 5 were 48.9% and 88.1%, respectively. A careful analysis of the sonographic descriptors associated with category 4 demonstrated that malignant lesions were frequently associated with a hypoechoic pattern, indistinct margins, and nonparallel orientation. Although several benign lesions assigned to category 4 also had a hypoechoic pattern and indistinct margins, they were more often associated with an oval shape and parallel orientation. In this category, orientation and morphology are the most reliable features for differentiating benign from malignant lesions.

In a retrospective study at the University of Sao Paulo, to investigate the performance of the US as a secondary diagnostic tool and to assess the outcome of mammograms that were initially classified as Bi-RADS category 0, Of the 241 patients, ultrasonography was considered diagnostic in 146 (60.6%) patients and indeterminate in 95 (39.4%) patients. In the diagnostic group, 111 out of 146 patients (70.2%) had a sonogram result of Bi-RADS category 2 after a 2-year follow-up without evidence of malignancy. Furthermore, 35 out of 146 patients (29.8%) had a suspicious sonogram with a result of Bi-RADS category 4. After a tissue sampling procedure, 10 patients were confirmed to have breast cancer, and 25 had benign histopathological features without any evidence of malignancy after a 2-year follow-up (Zanello et al., 2011) concluded that the sensitivity of ultrasonography was 100%, specificity was 89.1%, and overall accuracy was 89.6%.

In a study to evaluate the applicability of the current BI-RADS for sonography to the assessment of synchronous breast nodules other than the primary malignant tumor in patients with breast cancer, (Suk et al., 2008) assessed One hundred eighty-nine synchronous nodules in 147 breast cancer patients which were surgically excised after localization, and 412 synchronous nodules in 191 patients were observed or biopsied or excised without localization. Among a total of 601 synchronous nodules, 372 nodules were ipsilateral and 229 were contralateral to a primary malignant tumor. They had 2 radiologists who retrospectively reviewed sonograms of these nodules and determined the sonographic BI-RADS category. For each nodule, the preoperative BI-RADS category and pathologic or follow-up results were then compared. Four hundred eighty-two nodules were classified category 3; 112 nodules, category 4; and seven nodules, category 5. Fifty-five (11.4%) of the category 3 nodules and 57 (47.9%) of the category 4 and 5 nodules were confirmed malignant. Thirty-six (21.2%) of 170 category 3 synchronous nodules in the same quadrant as the primary tumor were confirmed malignant, as were 12 (9.8%) of 122 nodules in a different quadrant and eight (4.2%) of 190 nodules in the contralateral breast. They concluded that uniform application of the current sonographic BI-RADS classification can lead to underestimation of the risk of malignancy, especially if the nodule is in same quadrant as the index lesion, hence biopsy is needed for synchronous nodules in the same quadrant as and maybe even in the same breast that contains a malignant tumor, even nodules considered probably benign according to conventional BI-RADS sonographic criteria.

In the evaluation of breast masses especially suspected malignancy the evaluation of axillary nodes is mandatory as it determines the prognosis and remain crucial for individual treatment decisions. Ultrasonography (US) is the most widely used

imaging method to detect axillary lymph node metastasis and for characterization of lymph nodes. New ultrasound techniques, including contrast- enhanced ultrasound (CEUS) and US elastography, have been deployed for lymph node evaluation. CEUS provides detailed visualization of the vascularity of lymph nodes and may thus be helpful in differentiating between benign and malignant nodes. In a study to determine the preoperative assessment with US of axillary lymph nodes in terms of metastasis, metastatic lymph node detection rates, and sensitivity and specificity of US compared with postoperative histopathological results (Fidan et al., 2016) evaluated Level I, II, and III lymph nodes in the axillary region, supraclavicular lymph nodes and internal mammary lymph nodes on the side of malignant breast lesions. They then classified each node sonographically according to the cortical morphological findings into three groups, including reactive (benign), suspicious, and metastatic lymph nodes (lymphadenopathy-LAP). In this study, In the benign group, hyperechoic lymph nodes had an invisible and thin diffuse hypoechoic cortex (< 3 mm) with significant echogenic "fatty" hilum. In the suspicious group, lymph nodes had asymmetrical focal or diffuse cortical thickening (> 3 mm), lobulated and more hypoechoic cortex compared to subcutaneous fat, with significant echogenic hilum and distorted hilum. In the metastatic group, the lymph nodes had obliterated and unselected hilum and were completely hypoechoic or anechoic in appearance. Cortical thickness of the lymph nodes was measured in the longitudinal section. They finally reported that the sensitivity and specificity of US in the pre-operative of axillary node was between 48 percent and 99 percent

Ultrasound elastography is a new screening modality in addition to sonography for detecting and identifying lesions in the breast. It can provide the investigator with another characteristic, stiffness, of the lesion. Through lightly compressing of the

target lesion, it can noninvasively determine strain and elasticity distributions inside objects scanned and map the elasticity of the lesion by using a standardized color scale, with blue indicating regions with low elasticity (harder tissue areas) and red indicating regions with high elasticity (soft tissue). Ultrasound elastography is superimposed on conventional sonography. In a study to evaluate the role of elastography in evaluation of solid breast masses, (Apesteguía & Pina, 2011) combined the use of conventional ultrasonography with elastography and they found out that when these 2 modalities were combined together, they improved the detection of breast cancer. The sensitivity, specificity, accuracy, and positive predictive value improved to 89.7%, 95.7%, 93.9%, and 89.7%, respectively, which were much higher than those of mammography and sonography alone. In addition, the negative predictive value improved to 95.7%, which was higher than that of sonography, and the false-negative rate dropped to 8 of 87 cancers, which was much lower than those of mammography (24/87) and sonography (25/87).

In another study, (S. E. Lee & Bae, 2020) evaluated the different elastic properties of the tissues which is best applied in the evaluation of breast lesions, as there is a substantial difference between fibroglandular tissue and nodules of different types. malignant lesions were generally less elastic than benign masses. A slight rhythmic compression was applied using the transducer positioned perpendicular to the breast, so that the relative deformation of the underlying tissues could be reconstructed and displayed on the monitor sometimes in black and white images. In color images, the lesions presented characteristics which were assigned a score from 1 to 5 (similar to the BI-RADS classification), where benign or probably benign lesions (more elastic) were green with possible blue points, whereas malignant lesions (less elastic) were

almost entirely blue with a possible halo which can be correlated with a desmoplastic reaction in the surrounding tissues.

2.3 Histopathological Findings of Breast Lesions

To reduce mortality from breast cancer it requires all professional groups involved to perform to the highest standards. The quality of pathological services is of the utmost importance; it is the pathologist who invariably makes the definitive diagnoses of breast cancer but additional features of in situ and invasive carcinomas that have prognostic significance are also required to determine the most appropriate management for individual patients.(Ellis et al., 2016)

Percutaneous image-guided needle biopsy is essential in the management of suspicious breast lesions detected by screening or during the assessment of clinical abnormalities.(Bick et al., 2020).

Triple assessment is useful for preoperative diagnosis of breast cancer. The triple assessment comprises of: Clinical breast examination (CBE), diagnostic imaging (mammography and/ or ultrasound) and pathological examination (FNAC and core needle biopsy) (Brem et al., 2015).

The use of the triple tests together gives a sensitivity of 100%. It is taken as positive if any of the three components, two are positive or positive FNAC/core needle biopsy and negative only if all of its component are negative for malignancy. (WHO., 2021).

Core biopsy has replaced fine needle aspiration for symptomatic and screen-detected breast lesions in most western countries. The frequency of non-diagnostic or inadequate sample reports is lower than that of FNAC and it is much less invasive and less expensive when compared with excision or incision biopsy for diagnosis. Also in

diagnostically challenging cases, clinically malignant masses and when evaluation of the invasiveness is mandatory in cases such as in papillary neoplasms, histopathological (biopsy) examination should be done, which is the gold standard for tissue diagnosis. It is valid, reproducible, and has been accepted as the gold standard internationally. For a good study, the reference test against which the diagnostic test in evaluation is compared should be the gold standard.(Sneige, Fornage, & Saleh, 1994).

Several arguments are used for choosing either fine-needle aspiration cytology (FNAC) or core needle biopsy (CNB) in the evaluation of breast lesions. Comparison of published data on both methods is complicated by differences in study design, calculations, and operator experience. In a study to make a direct comparison between these 2 methods where both ultrasound-guided FNAC and CNB were performed in the same session by the same operator on the same lesion, (Westenend, Sever, Beekman-de Volder, & Liem, 2001), found that Core needle biopsy and FNAC do equally well for sensitivity (88% vs. 92%), positive predictive value for malignancy (99% vs. 100%), and inadequate rate (7% vs. 7%). However, statistical differences are found for the specificity (CNB, 90%; FNAC, 82%). In addition, differences are found in the positive predictive value of both suspicious (CNB, 100%; FNAC, 78%) and atypia (CNB, 80%; FNAC, 18%) and for the suspicious rate (CNB, 5%; FNAC, 13%) reflecting difficulties in interpreting some FNACs. Combining the findings of both FNAC and CNB results in an increase in absolute sensitivity, a decrease in the positive predictive value of atypia compared with FNAC and CNB per se, and a decrease in the inadequate rate for cancers. They concluded that CNB has a higher specificity and lower suspicious rate. Combining results of FNAC and CNB leads to

an increase in absolute sensitivity without affecting specificity and a decrease in the inadequate rate for cancers.

Different modalities are available for image-guided breast biopsy and localization procedures, each of them with their own strengths and weaknesses.(Bick et al., 2020)

According to (Altinsoy, Güçlü, Coşkun, & Boğan, 2021),ultrasound-guided CNB (US-CNB) has been accepted as an alternative method with high sensitivity/specificity for the accurate diagnosis of breast cancers . It is faster, less invasive, and less expensive. Also, the increasing experience with this procedure makes the technique more preferable. Accurate targeting of the needle and adequate size of specimens are the most crucial factors affecting the underestimation rates and false-negative results. However according to (Bick et al., 2020) it is important to note that percutaneous needle biopsy may not provide a definitive diagnosis when the histopathological report describes the presence of a lesion with uncertain malignant potential (also called high-risk or B3 lesion). This occurs in 3 to 9% of cases, with a range of rates turning out to be malignant (10– 33% or also higher rates). These lesions include atypical ductal hyperplasia, benign phylloides tumors, flat epithelial atypia, classical lobular neoplasia, papillary lesions, radial scars.

The size of the needle used for CNB is one of the factors affecting the success of the biopsy. In a study, to evaluate and report on US-CNB experience with 14- and 18-gauge needles, (Altinsoy et al., 2021) found out that the size of the needle used for CNB is one of the factors affecting the success of the biopsy. They also noted that a variety of cutting needles (11-, 14-, 16-, and 18-gauge, respectively) being used by many centers, and the common reason to prefer larger needles is diagnostic quality. However, larger needle sizes have potential to increase complication rates, such as

hematoma formation, bleeding, and vasovagal reactions. While large size needles are recommended for ≤10 mm or non-mass lesions, most physicians in many different centers have been recommended to use smaller needles such as 16-gauge or 18-gauge.

Axillary lymph node assessment is an integral part of preoperative staging in patients with newly diagnosed invasive breast cancer. Information about possible metastatic involvement of axillary lymph nodes can help avoid unnecessary procedures, triaging patients directly to axillary lymph node dissection. Axillary lymph node US is the easiest way to identify abnormal lymph nodes. Tissue sampling with FNS or CNB is similar as in the breast. CNB seems to be more accurate than FNS in the diagnosis of axillary lymph node metastasis (Altinsoy et al., 2021)

There are two main objectives of percutaneous biopsy techniques: first, achieving the maximum degree of accuracy, and second, offering as much information as possible about the tumor (type, grade, invasion, hormonal receptors, HER-2 NEU, etc.)

In 2019, the World Health Organization's new classification of breast tumors (5^{th} edition) was published, which aims to examine the morphological categorization of breast carcinomas which is still principally based on histological features and follows the traditions of histological typing. It gives a subjective and critical view on the WHO classifications and their changes over time and describes the changes related to some of the most common or challenging breast carcinomas. According to(Cserni, 2020), the 5^{th} edition does not differ from earlier ones, it includes benign and malignant neoplasms and non-neoplastic disorders (e.g. usual ductal hyperplasia) which may be tumor-forming, but not all breast lesions that may be tumor-forming, even not all subsets of neoplastic lesions considered as given entities. The classification entails the following:

Non-invasive lobular neoplasia including the Lobular carcinoma in situ (classic, florid, pleomorphic)

Ductal carcinoma in situ (DCIS) includes

DCIS of low nuclear grade

DCIS of intermediate nuclear grade

DCIS of high nuclear grade -

Invasive breast carcinoma

Invasive breast carcinoma of no special type (including medullary pattern, invasive carcinoma with neuroendocrine differentiation, carcinoma with osteoclast-like stromal giant cells, pleomorphic pattern, choriocarcinomatous pattern, melanocytic pattern, oncocytic pattern, lipid-rich pattern, glycogen-rich clear cell pattern, sebaceous pattern) (Micro invasive carcinoma)

Invasive lobular carcinoma

Tubular carcinoma, Cribriform carcinoma, Mucinous carcinoma, Mucinous cystadenocarcinoma

Invasive micropapillary carcinoma

Carcinoma with apocrine differentiation - Metaplastic carcinoma (low-grade adenosquamous carcinoma, [high-grade adenosquamous carcinoma], fibromatosis-like metaplastic carcinoma, spindle cell carcinoma, squamous cell carcinoma, metaplastic carcinoma with heterologous mesenchymal [e.g. chondroid, osseous, rhabdomyoma, neuroglial) differentiation, mixed metaplastic carcinomas)

Acinic cell carcinoma, Adenoid cystic carcinoma, Secretory carcinoma Mucoepidermoid carcinoma, Polymorphous adenocarcinoma, Tall cell carcinoma with reversed polarity

Neuroendocrine neoplasms including the

Neuroendocrine tumor (Grade 1, Grade 2)

Neuroendocrine carcinoma

Papillary neoplasms including the

Papillary ductal carcinoma in situ

Encapsulated papillary carcinoma -

Solid papillary carcinoma (in situ and invasive)

Invasive papillary carcinoma

Epithelial-myoepithelial neoplasms that include

Malignant adenomyoepithelioma -

Epithelial-myoepithelial carcinoma

Tumors of the male breast that includes

In situ carcinoma -

Invasive carcinoma

According to (Ellis et al., 2016), benign breast lesions are histologically classified as solitary cysts, fibrocystic changes, columnar cell change without atypia, fibro adenoma, papilloma, sclerosing adenosis, sclerosing lesions, periductal mastitis/ductal ectasia, mastitis/ mammary duct fistula, reaction to breast implants, others(fat necrosis, lipoma, adenoma of the nipple, benign and borderline phylloides tumor).

In study to evaluate histopathological spectrum of breast lesions, (S. E. Lee & Bae, 2020), did retrospective study which they conducted in the Department of Pathology, Coimbatore Medical College and Hospital, from January 2017 to October 2018. They reviewed 120 specimens of which 116 specimens belonged to female patients (97%). The peak age of the occurrence of breast masses was in the 3rd decade (32% occurrence). The histopathological features were noted, and the tumors were

diagnosed based on the WHO classification and graded adopting modified Bloom–Richardson grading system. They found that Both malignant and non-malignant lesions were present in the specimens. Among the 98 benign lesions, 45 cases were of fibroadenoma (46%), 23 cases were of fibroadenosis (23%). Among the 22 malignant lesions, 17 cases were of infiltrative duct cell carcinoma (77%).they concluded that The pattern of breast lesions provides valuable information concerning clinicopathological profile of breast lesions. The clinical diagnosis of a breast lump must be correlated with histopathological diagnosis for correct and adequate treatment of patient.

2.4 Correlation of Sonographic with Histological Findings of Breast Lesions

Breast ultrasound is a non-invasive imaging-based technique that is widely used as a diagnostic modality for evaluating clinical or radiological suspected abnormalities and is an effective screening modality for detecting occult breast cancers in dense breasts.

Recent advances in ultrasound technology and transducer design permit greater spatial and contrast resolution. Discordance between the assessment of imaging methods and pathological examination may be related to the type of tumor and breast density.(Jahan et al., 2020).

In their study to determine the correlation of ultrasonographic features and histopathological findings, (Tamaki et al., 2010) retrospectively reviewed the US findings and the histopathologic features of 154 breast lesions. They evaluated the correlation of the US findings including shape, boundary zone, internal and posterior echo, anterior and posterior borders, estimated histological types and carcinoma infiltration with their corresponding histopathological findings of the same lesions. In particular, they found that for internal and posterior echoes, attenuation was

considered to be provided by a highly cellular fibroblastic proliferation. They also found out that some histological types demonstrated low concordance rates between estimated or the histological types estimated by ultrasonographic findings and actual histological types. Their final results demonstrated that the concordance rate between the US findings and the histopathologic features was 91.6%.

In another study aimed to evaluate the correlation of the US findings including shape, boundary zone, internal and posterior echo, anterior and posterior borders, estimated histological types and carcinoma infiltration with their corresponding histopathological findings of the breast lesions. A sample size of 50 breast lesions was analyzed by (Kumar & Kumar, 2018) .They found out that the overall detection rate of carcinoma extension by US was 86% (43 out of the 50 tumors).and that the ratio of the correlation of histological types by Ultrasound diagnosis and histopathological was 91.6%. the concordance rates between the ultrasound findings and IDC, DCIS, ILC and mucinous carcinoma were 95.2% (39 out of the 41), 25% (1 out of the 4 tumors), 66.7% (4 out of the 6) and 100% respectively. However, they noted that US cannot define the extension of carcinoma preoperatively and hence the need to correlate US findings with histopathologic features of carcinoma cells to determine the extension of carcinoma.

(Radhakrishna, 2013) in a retrospective analysis to study the concordance of radiological and histopathological findings in BI-RADS category 3, 4, and 5 lesions, where Women who had BI-RADS -3, 4 or 5 lesions on ultrasound (both palpable and non-palpable) were recommended to undergo a core biopsy for definitive histopathological correlation found out that positive predictive value for BI-RADS 5 lesions for malignancy was 93.25% and the negative predictive value of BI-RADS category 3 lesions for cancer was 98.4%. False-negative diagnosis on core biopsy was

0.85%. they hence concluded that the PPV and NPV for cancer are high with needle core biopsy in BI-RADS 3,4,5 lesions. And where there is no discordance between clinical, radiology, and pathology findings, surgery could be avoided in benign lesions, and that while in resource-poor countries FNAC continues to be a valuable method in the diagnosis of palpable and non-palpable breast lesions, the practice of needle core biopsy provides the most accurate and optimal diagnostic information.

According to (Apesteguía & Pina, 2011), despite performing an optimized biopsy procedure, a false negative result can occur. In the case of micro calcifications, the specimen radiograph is very useful for confirming them in the removed tissue. However, the specimen radiograph does not give additional information on non-calcified lesions. They however insist on the radiological–histological correlation which is crucial to avoid false-negative results. In their analysis, they found five situations of radiological–histological correlation that can occur. Which includes

-Concordant malignancy: a lesion that is radiologically suspicious for malignancy (BI-RADS category 4 or 5) is histologically diagnosed as malignant after core biopsy (B4 or B5). Adequate treatment should be performed. A typical example would be a spiculated mass seen on US that is diagnosed as invasive ductal carcinoma

- Discordant malignancy: a radiologically benign lesion (BI-RADS 2 or 3) is finally diagnosed as histologically malignant after core biopsy (B4 or B5). Adequate treatment should be performed. breast lesions that usually manifest as well-circumscribed masses include triple-negative or high nuclear-grade invasive ductal carcinomas not otherwise specified, metastatic lesions, lymphoma, and special-type tumors such as papillary carcinoma, mucinous carcinoma, medullary carcinoma, and metaplastic carcinoma

- Concordant benignity: the radiological findings are benign or low–intermediate suspicious (BI-RADS 2, 3, 4a, 4b), and histological features are benign (B1 or B2 categories). An adequate radiological–pathological correlation should be established, and imaging follow-up should be offered to avoid delayed false-negative results. Exceptionally, some of these lesions can be surgically or percutaneously excised because of patient anxiety, patient decision, or physician preference. It should be noted however that the reported percentage of missed cancers among concordant benign results using 14-gauge US-guided CNB ranges from 0% to 0.8%.

– Discordant benignity: a radiologically malignant lesion (BI-RADS category 4c or 5) is proved to be benign after core biopsy. In this case, both the imaging and the pathological findings should be reviewed again. It is imperative to find a diagnosis; therefore, a new percutaneous biopsy (including vacuum-assisted breast biopsy) or surgical removal can be offered. Benign lesions with spiculated findings can mimic malignancy on US, including granular cell tumor, sclerosing adenosis, postsurgical scar. However, approximately 4%-30.9% of discordant lesions after US- guided CNB are confirmed as cancer by subsequent surgical excision

– Borderline/high risk findings: This category refers to lesions that are not malignant but are considered to indicate an increased lifetime risk of developing breast cancer including atypical ductal hyperplasia, lobular recurrences after percutaneous biopsies vs surgical biopsies in patients with breast-conserving therapy, and found no significant differences in recurrence rates. Thus, whatever the method of biopsy, the recurrence rate was similar.

CHAPTER THREE: METHODOLOGY

3.1 Study site

The study was conducted at the Moi Teaching and Referral hospital, radiology and imaging department, in ultrasound unit, interventional radiology unit, and Chandaria breast clinic.

The Moi Teaching and Referral Hospital is located in Eldoret town, the headquarters of Uasin Gishu county. It is the second-largest referral hospital in Kenya after Kenyatta National Hospital It is 350km northwest of the Kenyan capital Nairobi. The hospital serves an estimated population of 16.24 million which is 42.5% of Kenya's population as per the 2010 Kenya population Census survey. It has a bed capacity of 800 with several departments including surgery, pediatrics, medicine, obstetrics and gynecology, radiology and imaging, accident and emergency department among others Directorates.

It is also the teaching hospital for Moi University College of Health Sciences that trains both Undergraduate Medical Students and several Masters in Medicine Specialist programs with over 240 postgraduate students (Registrars) distributed across several programs.(mtrh, n.d.)

3.2 Study design

This was a cross-sectional study design and was carried out for a period of one year from April 2021-March 2022

3.3 Study Population

The study was conducted for a period of 12 months and included adult patients who were referred for breast ultrasound and who further underwent core needle biopsy.

Target population-All patients who were referred for breast ultrasound.

3.4 Eligibility Criteria

3.4.1 Inclusion Criteria

All adult patients with breast complaints who were referred for breast ultrasound and who further underwent core needle biopsy (CNB). (The study only included patients who were done for breast ultrasound and who further underwent breast biopsy)

The indications for biopsy of benign and probably benign lesions were:

- Breast mass more than 2.5cm in size

- Strong family history of breast carcinoma

- Patients request

3.4.2 Exclusion criteria.

Previous ipsilateral breast surgery

Proven breast cancer and on treatment

BIRADS 0 and 1

Those who didn’t consent

Those who had contraindications

3.5 Sampling technique

Sample size calculation

The main aim of the study is to assess the accuracy of ultrasound in diagnosing breast lesions using histological findings as to the gold standard. A study done in Bangladesh by (Jahan et al., 2020) among patients presenting with breast lesions found the proportion of those with benign breast tumor by ultrasound to be 65.52%

and sensitivity and specificity of 100% and 91.6%% respectively. Assuming the same values in our settings the sample size will be estimated using Buderer's 1996 formula

$$n \geq \frac{Z^2{}_{1-\alpha/2}(S_N)(1-S_N)}{L^2 \times prevalence)}$$

S_N = the anticipated sensitivity taken as 100%

The proportion of benign tumors among those with breast lesions = 65.52%

1-α = size of the critical region (confidence level)

$Z^2{}_{\alpha/2}$ = standard normal deviation corresponding to the critical region α = 1.96

L^2 = absolute precision desired on either side (5%)

Substituting for the above figures the minimum sample size required is 211.

3.6 Study procedure

Patients who had breast complaints including pain, breast ulceration, breast discharge, and palpable mass from the history who were referred to breast ultrasound were screened and confirmation and classification as per BI-RADS lexicon for ultrasound criteria was done and this was based on lesion characterization including tissue composition, mass orientation, shape, margin, posterior enhancement. The diagnosis was made by the principal investigator and confirmed by a consultant radiologist. Consent was sought from all those with confirmed breast lesions and they were then recruited into the study. All these patients with confirmed breast lesions were booked and billed prior to recruitment into the study as per the hospital protocol for the charges of the procedure including waiving for inpatients. Information on the residence, age and sex at the time of the procedure were also obtained. All the patients' files were reviewed. For those who had any other investigation done as a

mode of investigation prior to diagnosis of the procedure, their reports were assessed by the principal investigator and the interventional radiologist and reviewed to confirm any other diagnosis. They were then assessed for any contraindications which included uncorrected coagulopathy, clinical instability and lack of safe access to the masses

All biopsies (for the image guided) were done by the interventional radiologist and clinicians (Chandaria breast clinic) and assisted by the principal investigator.

On the day of the procedure the arrival of the patient was confirmed. The vitals were taken; the laboratory results were evaluated. An I.V access was secured and the patients given pre-medication including pain medications and buscopan for smooth muscle relaxation.

The patients were then given hospital gowns, changed and was then directed onto the hospital bed, where the sleeping position depended on the location of the lesion. Then the patient was cleaned and draped.

The exact cutaneous entry site and proposed coaxial route were meticulously planned prior to needling and were based on the size, location, and anatomic relation of the breast lesion in ultrasound scan.

After that the local anesthesia was administered through subcutaneous injections of drugs (e.g., lidocaine). In the coaxial technique, a coaxial needle (usually gauge 13) was guided into the mass via ultrasound guidance and the stylet removed once the lesion has been accessed, the biopsy gun (usually gauge 14) was then advanced through the coaxial by the interventional radiologist, often through a small skin incision. The depth for needle insertion was the shortest distance from the entry site to the near wall of the masses to avoid reaching the chest wall cavity and causing

pneumothorax. once the needle was confirmed to be on target, a tissue sample (core) was obtained with a needle of variable length (from about 10 to over 20 mm), depending on the used device, and immediately fixed in small formalin containing jars. Since a lesion may be pushed ahead while shooting, the longer samples obtained from longer acquisition chambers are usually preferred.

A successful procedure was defined as one that resulted in a comfortable patient with no complications and adequate core biopsies.

Post Op-Observation

After the biopsy was done, the patient was taken to the recovery room for monitoring for 1 hour to evaluate for any early complications.

The patient was then officially discharged on antibiotics/painkillers and all patients were required to present to the department in cases of continued pain, difficulty in breathing and unstoppable bleeding from the site. However, most patients were informed that if they didn't have any complications they would follow-up the results from the histopathology laboratory and come back to the radiology department/ breast clinic with the results for referral to the relevant departments depending on the results.

3.7 Patient's Preparation

Patients for ultrasonography of the breast do not require specialized preparation, however, consent was sought before the procedure

Prior to CNB, all patients must be prepared by carrying out a coagulation profile and triple serology and a full haemogram. In the wake of covid 19 a covid 19 PCR test was included as screening tool for all patients prior to the procedure. These are part of the requirements for all patients prior to carrying out breast mass biopsy.

The coagulation screen includes prothrombin time and INR. PT should not be less than four seconds and the International Normalized Ratio should be less than 1.5. This is done to avoid or anticipate any complications that may occur during the procedure like bleeding. If the INR is higher patient is given I.V Vit k for 3 days prior to procedure and then re-evaluated again after the corrective measures.

No recommendation that broad- spectrum antibiotics be administered to the patients before breast CNB.

If the patient required sedation especially anxious patients, the patient was asked to fast for at least eight hours prior to the procedure. However, sedation was not carried out for majority of the patients in the study. The procedure was done under local anesthesia (0.5%-1% lignocaine) at dose of 5-300mg total dose for all patients including the patients who were sedated to assist with pain relief after the procedure.

After the procedure, 1hour of observation was recommended to assess for complications. Immediate complications were assessed at this stage including bleeding/hematoma formation.

3.8 Technique

3.8.1 Breast ultrasound

Equipment

Ultrasound machine MINDRAY M7

Probe with the frequency of 7-15MHz (linear or wide footprint probe. However, a lower frequency transducer was required for the larger attenuative breasts, inflammatory masses, and the axilla.

Ultrasound gel

Hospital gown, wipes, ultrasound couch

Patients position

Patient laid supine and in cases where there was a need to roll the patient slightly to 'spread' the breast evenly. the side being scanned was elevated with a wedge under the shoulder.

The patient was asked to raise the ipsilateral arm over the head.

Of note is that It was important to correlate the ultrasound with any palpable lumps indicated by the patient, these can include other imaging findings/data/modalities. Accordingly, if the patient could only identify the lump when erect then rescanning was done with the patient erect.

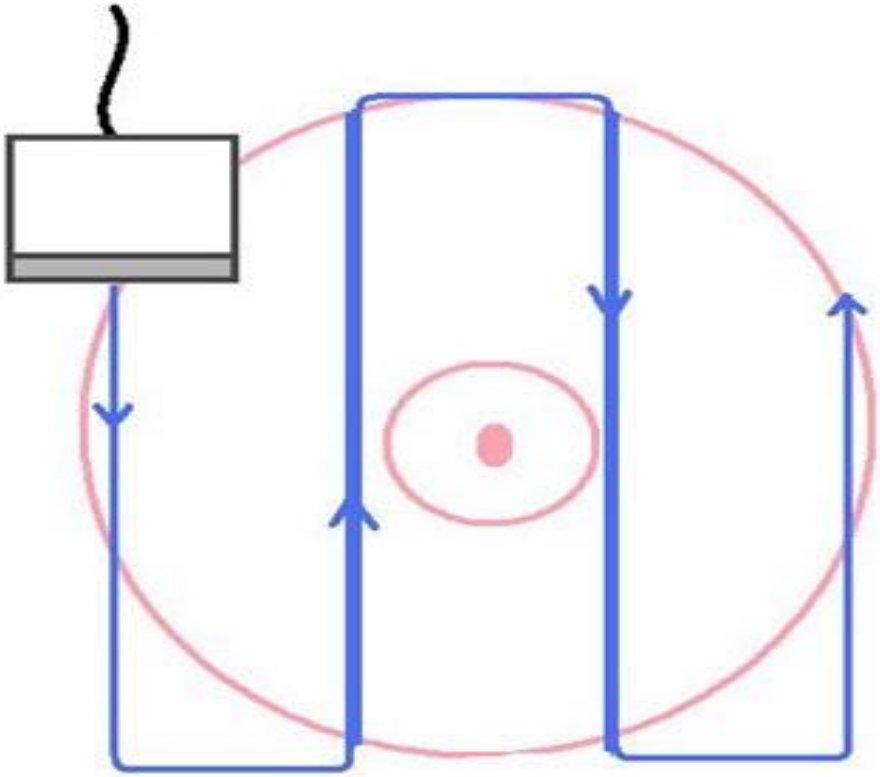
Techniques

The 2 commonest techniques used were:

1. Grid scanning technique followed by
2. Radial (clock face)

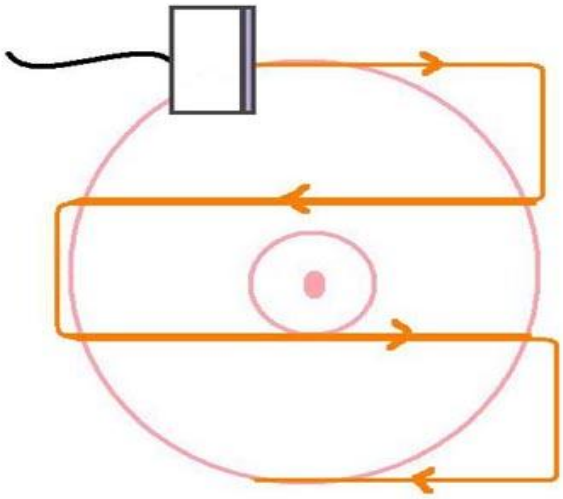
Grid scanning technique

This involved Scanning up and down the breast in rows, making sure that there was overlap each row slightly to ensure no breast tissue was overlooked.

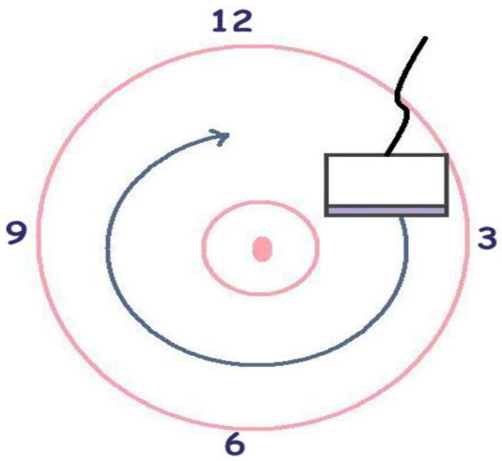


1. Begin in the upper outer quadrant, scanning in transverse. Slide inferiorly from top to bottom.
2. Move across and repeat the sweep inferior to superior.
3. Repeat this across the breast.
4. Rotate into a sagittal plane and repeat the pattern.

A variation, particularly in larger or mobile breasts, was to apply the grid pattern quadrant by quadrant in both axial and longitudinal two views.



Radial technique



The breast was scanned and described as a clock-face.

Begun at 12 o'clock in a sagittal plane with the toe of the probe at the nipple.

Scanned by rotating the probe around the nipple.

Depending on breast size, a second pass further from the nipple may be required.

If pathology was identified, then the probe was rotated 90degrees in the 'anti-radial' plane.

A breast series included the following minimum images:

12 O'clock,

2 O'clock

4 O'clock

6 O'clock

8 O'clock

10 O'clock

Nipple

Axillary tail

Axilla

any pathology found had to be documented in 2 planes, including measurements and any vascularity

3.8.2 Core needle biopsy

Equipment

The needles were selected and a 14-gauge conventional Tru-cut devices was the most commonly used.

High-frequency probes.

Alcohol swabs, povidone-iodine solution, sterile gloves, and drapes.

Technique

Local anesthesia was injected via ultrasound guidance or blindly then a small incision was required and the biopsy device was guided by ultrasound/ blindly and the procedure was performed using the free-hand technique: one hand holds the probe and the other hand holds the needle.

As a general rule, the shortest route from the skin to the lesion was used. A vertical approach would be the best, but sometimes not possible under ultrasound guidance. However, an oblique approach, as parallel to the chest wall as possible, should be used. In the case of very dense breasts, techniques used for access included: Coaxial technique: where once the coaxial needle was inserted in the lesion, the inner trocar was removed and replaced by the biopsy needle, a 16-gauge needle instead of a 14-gauge one, and stronger devices, such as vacuum-assisted devices & Devices with diamond-shaped needle tips because they transverse the fibrous tissue better than conventional needles.

The complications of ultrasound CNB are infrequent and not significant. Both hematomas and infections are very rare, accounting for less than 1/1,000 biopsies being similar to the complications of other percutaneous biopsy devices. The possibility of pneumothorax exists but it is very rare using the free-hand technique and a horizontal approach. One complication of all percutaneous biopsies is epithelial displacement

PROTOCOLS FOR BREAST CNB (it was recommended that I bring this here from the appendix section)

INTERVENTIONAL RADIOLOGY UNIT/BREAST CLINIC-CHANDARIA

Core biopsy has replaced fine needle aspiration for symptomatic and image-detected breast lesions in most western countries. The frequency of non-diagnostic or inadequate sample reports is lower than that of FNAC and it is much less invasive and less expensive when compared with excision or incision biopsy for diagnosis. Also in diagnostically challenging cases, clinically malignant masses and when evaluation of the invasiveness is mandatory in cases such as in papillary neoplasms, histopathological (biopsy) examination should be done, which is the gold standard for

tissue diagnosis. It is valid, reproducible, and has been accepted as the gold standard internationally. For a good study, the reference test against which the diagnostic test in evaluation is compared should be the gold standard.(Sneige et al., 1994)

Diagnostic criteria

Clinical diagnosis:

This is the most important criteria for referral for breast ultrasound and eventual CNB. Patients complains of breast lump, pain, have breast ulceration and breast discharge among other symptoms.

Laboratory diagnosis:

No specific laboratory findings can be tied to breast masses, however incases of infective process then CRP and leukocytosis can reflect the degree of sepsis and is useful for decision making

Imaging:

Clinical suspicion of breast lesions is often confirmed with imaging (ultrasound, CT, MRI or mammography)

Personnel

A breast biopsy should be performed by a physician (interventional radiologist) who understands the technology in the machine, physics used to produce an image, limitations of the technology as well as common artifacts associated with breast imaging.

Additionally, physicians and technicians must demonstrate knowledge of breast anatomy, and be able to recognize physiologic breast changes and common breast pathologies

Planning:

Assess pre-intervention images available to identify anatomical location of breast lesion and plan guiding modality and access route.

Assess breast lesion characters to guide on the biopsy equipment to be used

Choosing the modality for guidance: mostly US because it easier, cheaper, provides real-time guidance, however other modalities includes mammography and MRI.

Checking for Indications/Contraindications:

An absolute contraindication for an image-guided breast biopsy is the non-visualization of the lesion.

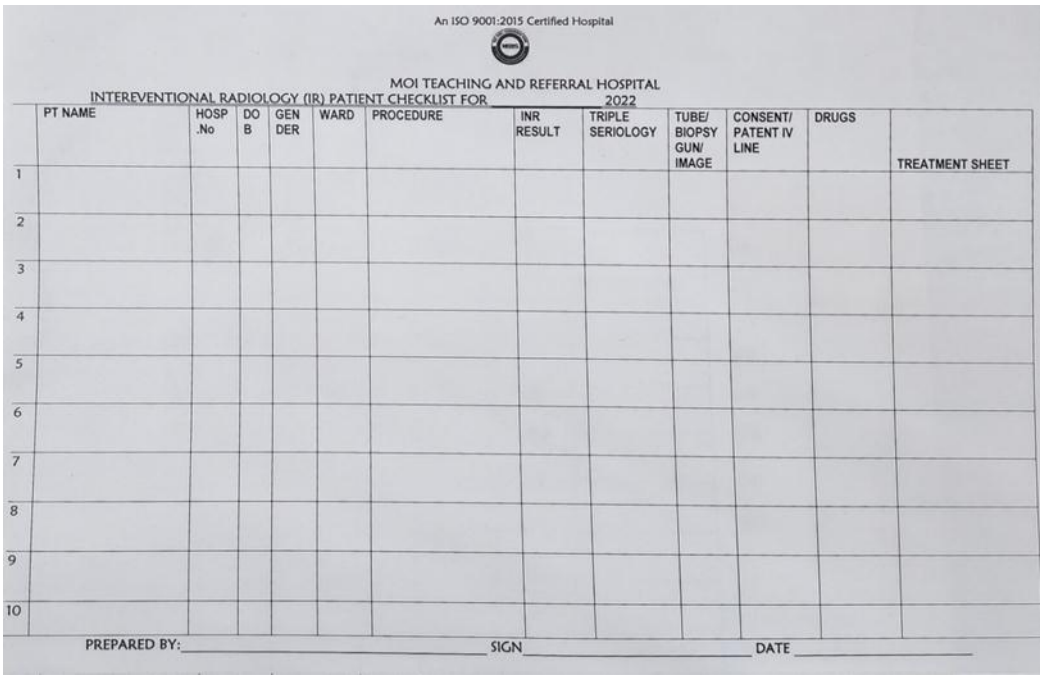
Relative contraindications are overlying skin infections and a high risk of bleeding demonstrated by a grossly abnormal international normalized ratio

Patient preparation:

Before any biopsy, the patient's previous imaging ……should be reviewed. At that time, a tentative plan is developed with an emphasis on patient positioning, the shortest distance from skin to the lesion, and the identification of important structures such as blood vessels and breast implants.

No indication for pre-surgical antibiotics. However, painkillers can be given to the patent before and after the procedure

Checklist should be filled



An ISO 9001:2015 Certified Hospital

MOI TEACHING AND REFERRAL HOSPITAL

INTEREVENTIONAL RADIOLOGY (IR) PATIENT CHECKLIST FOR _____ 2022

	PT NAME	HOSP .No	DOB	GENDER	WARD	PROCEDURE	INR RESULT	TRIPLE SERIOLOGY	TUBE/ BIOPSY GUN/ IMAGE	CONSENT/ PATENT IV LINE	DRUGS	TREATMENT SHEET
1												
2												
3												
4												
5												
6												
7												
8												
9												
10												

PREPARED BY:_____ SIGN_____ DATE _____

Interventional radiology (IR) is a fast-developing discipline with procedures and equipment getting more advanced and complicated by the day. Increasingly invasive procedures are being performed in a wide variety of patients, many of whom have not been evaluated by the interventional radiologist before the intervention. In IR, as in all medical disciplines, the need for improvements in quality and patient safety is increasingly being recognized. Standard operating procedures are useful and important but do not contribute to a more systematic workflow; nor do they cover the entire pathway of an intervention. Checklist have recently become an important aspect of patient management in IR. (Koetser et al., 2013)

The importance of safety checks has long been recognized in other areas, including aviation and other high-risk industries. In 2000, the Institute of Medicine recommended the implementation of verification processes, such as checklists, into medical practice to standardize processes and decrease reliance on human memory. Recently, the World Health Organization has introduced a safety checklist in the

operating room that reduces the rates of death and complications associated with surgery. An even greater effect on mortality and complications in hospitals with high standard of health care quality is seen after implementation of the surgical Patient Safety System (SURPASS) checklist that covers the entire surgical in-hospital pathway. (Koetser et al., 2013)

Because IR shares several features with surgery, a checklist may be equally effective to improve patient safety in IR. Recently the Cardiovascular and Interventional Society of Europe published a checklist for IR. This checklist was modified from the World Health Organization surgical safety checklist and the radiological Patient Safety System (RADPASS) checklist. The RADPASS checklist was the subject of a study done by Koetser et. al that was the first validated safety checklist for the complete pathway of radiological interventions. The aim of the study was to design a specific checklist for IR, and to assess the effect of this checklist on health care processes of radiological interventions. It showed that the use of the RADPASS checklist reduced deviations from the optimal process by three quarters and was associated with less procedure postponements. (Koetser et al., 2013)

Procedure

Planning an Access Route

Generally, the safest, straightest, shortest route to the breast lesion is chosen.

Think about patient comfort.

care must be taken to respect the patient's modesty and privacy and to ensure that the patient is lying comfortably

Traditionally US-guided breast biopsies are performed with the patient lying supine to slightly anterior oblique on an examination table.

To reduce shifting of tissue due to gravity, the side to be evaluated is elevated, and the ipsilateral arm flexed over or under the head (right breast right side is anterior oblique, and the right arm is positioned over the head)

When performing an ultrasound-guided biopsy, the transducer should be broad bandwidth, high frequency, and linear array. The transducer's focal zones and the machine's power, gain, and time-gain constant should be optimized.

Advanced US imaging, spatial compounding, harmonic imaging, extended field of view, elastography, 3D, and speckle reduction are commonly used,

After ensuring adequate quality control and identification of the target lesion, the overlying skin is anesthetized, followed by the deeper tissue along the expected biopsy trajectory

While maintaining appropriate transducer pressure and visualization of the target lesion, the needle is advanced into the breast. It is imperative the operator maintain constant visualization of the needle tip and entire length to ensure adjacent structures are not damaged, and the trajectory of the needle is parallel to the underlying chest wall, this is done to limit complications

Use color Doppler to avoid vessels.

This technique is real-time; the biopsy apertures should be visualized within the target lesion and image saved for post-biopsy review. Generally, 4 to 10 samples are taken to assist in tissue diagnosis. After completion of the biopsy, removal of the device,

and placement of a biopsy marker, manual pressure should be applied to mitigate the possibility of developing a hematoma.

A post-biopsy mammogram/ultrasonography can be subsequently obtained and compared to pre-biopsy imaging to confirm the on-target biopsy and appropriate biopsy marker placement. This is extremely important in cases where the imaging and tissue diagnosis are discordant

Endpoint: A comfortable patient leaving the interventional suite with adequate tissue biopsies and no complications. Immediate post-procedure care: Send a nursing post-care form with standard instructions to monitor pulse, blood pressure, temperature and prescribed analgesia. Position the patient to make the drain dependent. IV fluids may be required but rare.

Approaches/access

US guidance

If a lesion is visible on US, the best choice is to perform the biopsy under its guidance. US is readily available, does not expose the patient to ionizing radiation, and allows for real-time checking of needle placement.

US-guided biopsy can also be performed as a bedside procedure in bed-bound patients and there are virtually no contraindications or anatomical/technical restrictions for biopsy access to breast lesions.

Typically, US-guided biopsy is performed as CNB, allowing for a safe, fast, effective, and cheap procedure but US is also suited to guide FNS or VAB, taking into account that each system can have specific characteristics

The duration of a US-guided procedure is about 5 to 15 min, mainly depending on the type of needle used, number of samplings, lesion site, and radiologist's experience.

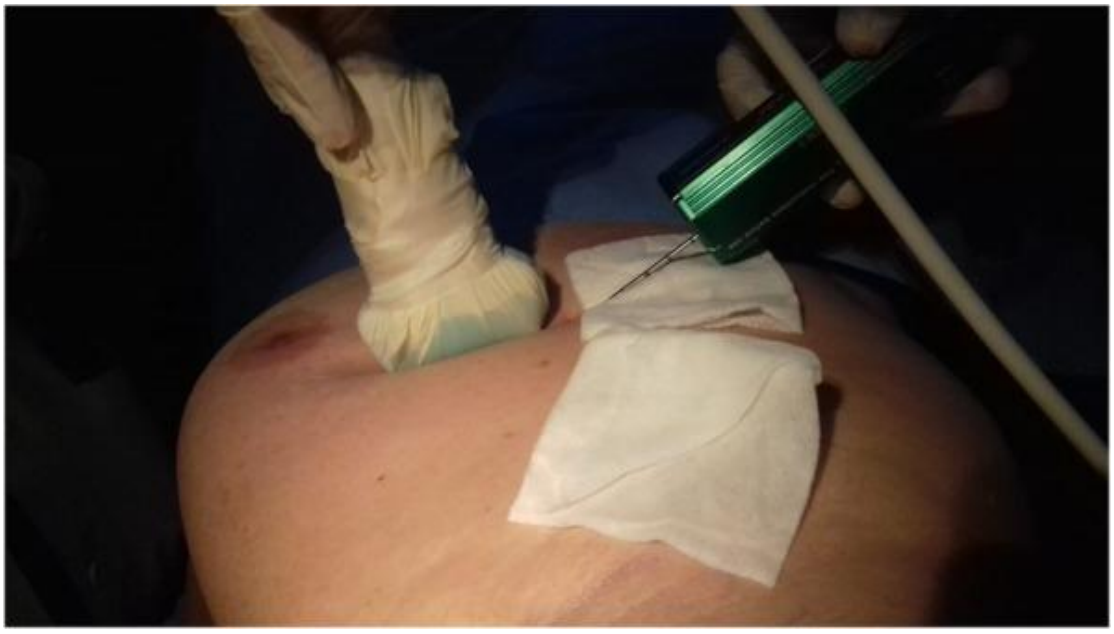


Figure 6: Ultrasound-guided core needle biopsy. The patient is in supine position. After local anesthesia, the ultrasound probe (on the left) guides the needle to the lesion

Depending on the size and type of biopsy performed (spring-loaded or VAD), a dermatome might be required**.** While maintaining appropriate transducer pressure and visualization of the target lesion, the needle is advanced into the breast

It is imperative the operator maintain constant visualization of the needle tip to ensure adjacent structures are not damaged, and the trajectory of the needle is parallel to the underlying chest wall.

This technique is real-time; the biopsy apertures **s**hould be visualized within the target lesion and image saved for post-biopsy review. Generally, 4 to 10 samples are taken to assist in tissue diagnosis.

After completion of the biopsy procedure, removal of the device, and placement of a biopsy site marker, manual pressure should be applied to mitigate the possibility of developing a hematoma.

A post-biopsy mammogram Imaging is subsequently obtained and compared to pre-biopsy imaging to confirm the on-target biopsy and appropriate biopsy marker placement

This is extremely important in cases where the imaging and tissue diagnosis are discordant or repeat biopsy required. The advantages of this technique are faster procedural time, real-time visualization of accuracy, lack of ionizing radiation, and increased patient comfort secondary to lack of breast compression

Mammographic guidance

Mammographic guidance is the method of choice for lesions detected by mammography which are not visualized on US.

Most of these lesions are suspicious calcifications, architectural distortions, or small masses. The well-established method for mammography-guided biopsy is called stereotaxis, a term that refers to the need of two oblique projections providing a two-view (*stereo*) information to the operator

Stereotactic interventions are performed using dedicated prone tables, where the biopsy equipment is located below the patient, thus not visible to the patient during the procedure, or upright mammographic add-on systems, with the patient usually sitting or lying in lateral decubitus during the procedure. A mild compression is required for breast immobilization

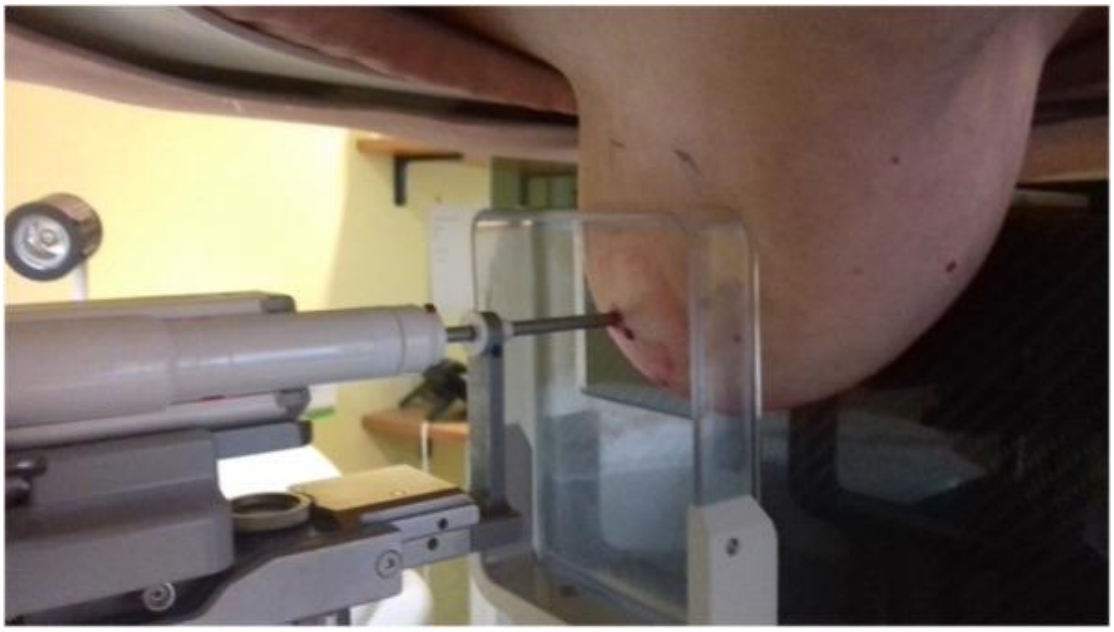


Figure 7: Mammography-guided (stereotactic) vacuum-assisted biopsy. The patient is in prone position lying on the table over the field of view of the image, with the breast pendent by gravity (she does not see the procedure). After local anaesthesia, the needle is guided to the lesion by the computer on the basis of specifically acquired mammographic images

Once adequate imaging is obtained, the breast is prepped and draped in a sterile fashion.

The skin overlying the predetermined entrance point is locally anesthetized, followed by the placement of anesthetic along the expected biopsy needle track.

At this time, some institutions repeat the scout images to ensure that the lesion has not moved. After confirmation of the lesion's location, a dermotomy is performed at the expected skin entrance point prior to the advancement of the biopsy needle.

The needle is then advanced through the dermotomy to the desired depth via the coordinate system. The second set of 15-degree and 15-degree images is then obtained to confirm accurate needle positioning.

Tissue sampling is performed with appropriate biopsy system along multiple axes. Usually, 6 to 12 samples are obtained. After sampling but prior to the removal of the

biopsy device, the tissue samples are evaluated under x-ray to ensure the target lesion was sampled.

Once adequate sampling and Site has been confirmed, the biopsy device is removed, and a subsequent biopsy marker is placed.

The patient is then brought out of compression, and manual pressure is provided to the biopsy site.

A post-biopsy mammogram is obtained and compared to pre-biopsy imaging to ensure appropriate sampling and biopsy marker placement

The advantage of this technique is the ability to target mammographic ally suspicious, but ultrasound occult lesions such as suspicious micro calcifications.

The disadvantages include cost adversity, time of the procedure (greater than ultrasound), and exposure to ionizing radiation

MRI guidance

MRI-guided VAB is a safe and accurate procedure that is mandatory when suspicious lesions are visible on MRI only

Of note, among MRI-detected lesions, 46 to 71% may be revealed by a subsequent targeted US (the so-called *targeted US* or *second-look US*), even if breast US performed before MRI did not detect any abnormalities

Importantly, identifying an MRI-detected lesion on US allows the biopsy to be performed under US guidance, in an easy, fast, comfortable, and cheap way Thus, the need for MRI-guided procedures is relatively limited.

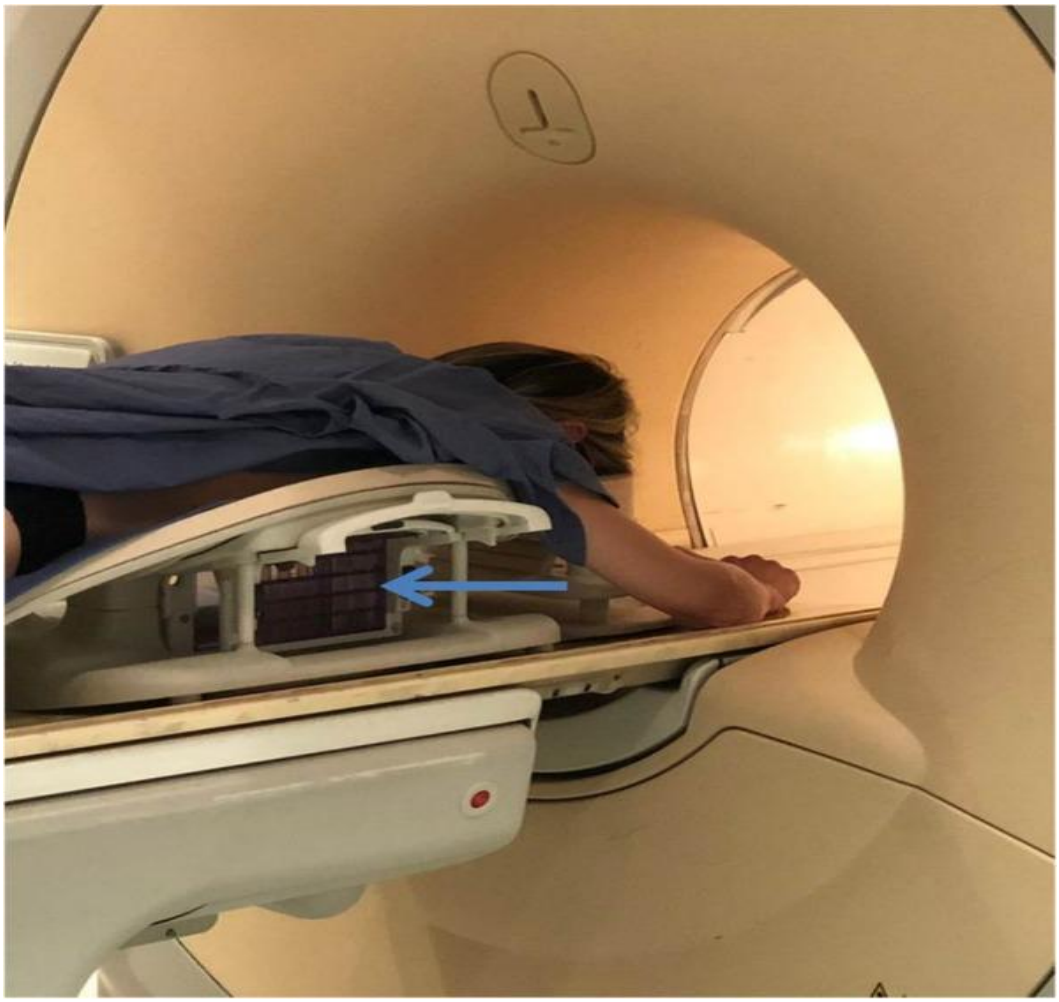


Figure 8: Magnetic resonance imaging-guided vacuum-assisted biopsy. The patient is prone, positioned on a dedicated coil that allows to insert the needle through a greed (light blue arrow), shown in the figure outside the magnet. After local anesthesia, the needle is guided to the lesion on the basis of specifically acquired magnetic resonance images. To conclude the procedure, the patient has to enter and exit the magnet at least three times

The biopsy is performed from the lateral to the medial aspect of the breast. Imaging guidance is provided using a basic grid type system, post, and pillar, as well as freehand. Commonly a sagittal T1 fat saturation pre and post-contrast sequences are obtained.

The needle is then advanced (sagittal plane) under intermittent imaging guidance. This process is repeated until adequate positioning is achieved. Then, as in

mammographic stereotactic biopsies, a VAD or spring-loaded device is used with 6 to 12 samples obtained. The needle is removed, and a biopsy marker is placed, followed by manual pressure. Most institutions obtain a post-biopsy mammogram to confirm biopsy marker placement

This technique is beneficial in that it allows a targeted biopsy of mammographically and ultrasound occult lesions and lacks the ionizing radiation exposure of mammographic guidance.

However, it is also the most cost adverse and time-consuming with variable specificity correlated to clinical presentation.

Additionally, there is a theoretical risk associated with gadolinium exposure.

Follow-Up and Post-Procedure Medications: These include analgesia and antibiotics. Post-procedure patient and wound care: The patient is advised to change the dressing after 24hrs initially unless the bleeding more

Equipment list

- 14G or 16G core biopsy needle, single or co-axial, with 10 mm or 20 mm cutting lengths
- trigger device/ GUN
- 1% or 2 % lidocaine without epinephrine
- chlorhexidine, surgical scalpel blade (usually n.11), needle and syringe for anesthetic, dressing, and sterile gloves
- imaging equipment

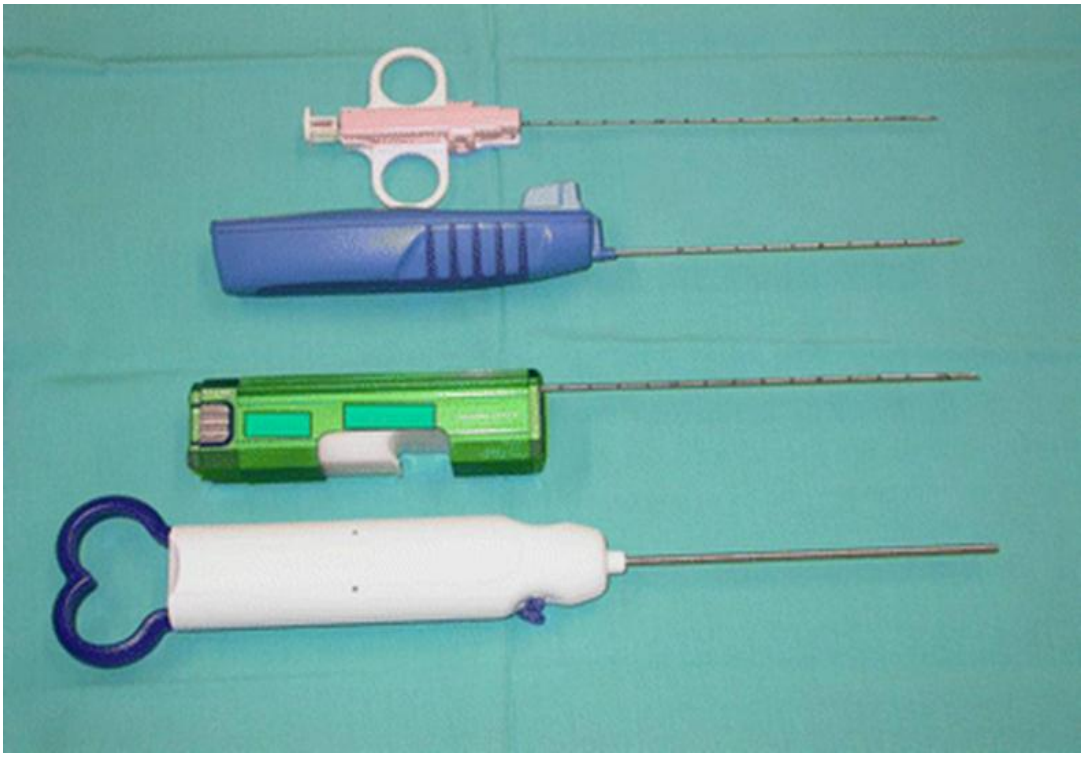


Figure 9: sample images of different biopsy guns that are used in breast biopsy

Things to Do

Specimen management:

Once the specimen is put into the formalin container, it is labelled including the patients name, age, in/outpatients name, date of specimen collection and the site of the specimen collected

Then a laboratory request form is written with full details included: this includes patient's demographics, small history of presenting illness or previous results, and description of the lesion

The specimen is recorded in the specimen book

The specimen is picked by the laboratory technologist, who counterchecks it with the nursing officer where they both countersign against the specimen

The specimen is then sent to the laboratory for histopathology

any other collection got during the procedure are also sent to the laboratory for Gram stain, culture, sensitivity, cytology

Who does what during the procedure?

Interventional Radiologist - Performs the CNB

Principal Investigator-Assists the Interventional radiologist carry out the procedure

Nurse – Assists in providing the necessary equipment needed for the procedure and gives pre and post medications to the patient.

General Preventive measures (SOPs)

A safety checklist must be filled for all patients presenting to the IR unit/breast clinic

All patients transferred to the IR unit must wear surgical masks same to for the porters.

All professionals working in the department must wear surgical scrubs and surgical masks throughout the work shift.

All professionals must wash their hands frequently

All work stations must be individualized

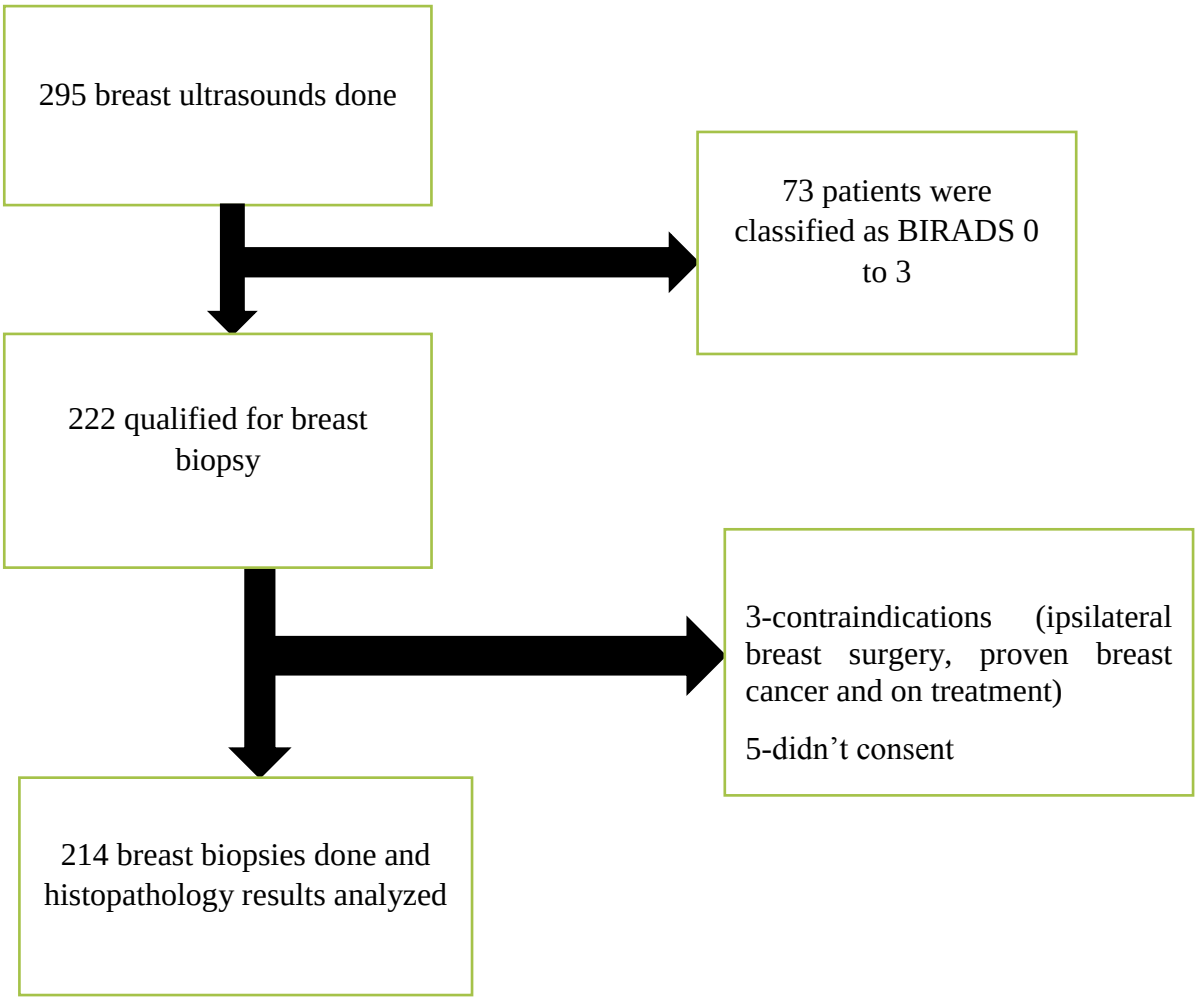
Consultations done from other departments must be done remotely

PROTOCOL SUMMARY

1. Patient either self/clinician referred to IR with a positive history of breast complaint and positive breast lesion during imaging evaluation
2. Patient assessed by the IR specialist
3. Patient prepared for the procedure
    a. Labs done including: Appropriate investigations +/- further clinical evaluation/management
    b. Procedure instruments acquired for the patient

4. Procedure done
5. Post-procedure instructions
6. Follow up done
7. Outcome evaluate

3.9 Study schema



3.10 Data management, analysis, and presentation

The data was collected using questionnaires that bore no patient's identification. For identification purposes, a study number was used instead. The questionnaires were filed in a study file which was kept under a lock and key to ensure confidentiality of information provided is maintained. To improve the quality of data, the researcher was to check on the completeness of the questionnaire on a daily basis before entering the data into a Microsoft access database.

Data was then imported into SPSS version 24 where coding, cleaning, and analysis will be done.

Descriptive statistics such as mean and corresponding standard deviation, the median, and the corresponding interquartile range were used to summarize the continuous data such as age. Frequencies and corresponding percentages were used to summarize categorical data such as the sex of patients.

Cohen kappa coefficient was used to estimate the level of agreement between sonographic findings and histopathology.

Parameters such as sensitivity, specificity and predictive values were used to describe the diagnostic accuracy of sonographic BI-RADS score

The data is presented in form of charts, tables, graphs, and prose form.

3.11 Ethical Considerations

Ethical approval was sought and obtained from Moi University/ MTRH Institutional Research and Ethics Committee (IREC)-Ref no: **0003854** and NACOSTI (National Commission for Science and Technology and Innovation)-Ref no: **848788**

Permission was sought from the management of MTRH for the study to be carried out at the facility. Informed consent was sought directly from the respondents undergoing the procedure.

Consent: Written consent was sought from patients above 18 years undergoing the procedure. Participation in the study was voluntary and the participants were free to withdraw at any time. Confidentiality of the respondents' information was maintained and codes were used instead of the respondents' names to protect their identity.

Confidentiality: The information provided by the respondents and that obtained from their medical records were kept confidential and were stored in a lockable cabinet. The data was entered into a password-protected computer and using codes in place of individual names.

Benefits: There was no direct monetary benefits in the participation of the study; however, the findings of the study will help in understanding the application and use of BI-RADS lexicon for ultrasound, and to ensure that there is concordance between imaging and histological findings of breast pathologies to ensure better service delivery to our patients.

Risks: No major risks existed as a result of participating in the study except the time that was spent in the participation of this study. Other risks are such the fear of personal data leaks which were handled well by maintaining the confidentiality of all the information provided.

3.12 Dissemination of results

The results will be presented to the department of radiology and imaging, Moi University School of medicine. A manuscript will be prepared and published in a reputable radiology journal. The results will also be presented in local and international radiology meetings, conferences, and seminars.

CHAPTER FOUR: RESULTS

4. 1: Socio-demographic characteristics

Table 4.1: Socio-Demographic characteristics

Variable		N 214	Frequency (n)	Percent (%)
Gender				
Male			10	4.7
Female			204	95.3
Age in Years				
Mean 44.14				
SD 14.84				
Below 40			95	44.4
40-49			53	24.8
50-59			28	13.1
Over 60			38	17.8
Total			214	100.0
County of residence	Uasin Gishu		73	34.1
	Kakamega		29	13.6
	Trans Nzoia		18	7.5
	Kisumu		10	4.7
	Kisii		7	3.3
	Baringo		25	11.7
	Others		12	5.6
	Total		214	100

Majority of the study participants were female 204 (95.3%). The mean age was 44.14 with a standard deviation of 14.84. Most of the participants 95 (44.4%) were aged below 40 years followed by those aged between 40 to 49 at 24.8%.

34.1% of the patients were residents of Uasin Gishu county while the bordering counties (Baringo, Kakamega and Trans Nzoia Counties contributed (32.8%) of the respondents

Table 4.2: Clinical presentation

Variable	Frequency (n)	Percent (%)
Breast lump	154	72.0
Ulceration	19	8.9
Pain, breast lump	18	8.4
pain	13	6.1
Breast discharge	9	4.2
Nipple retraction	1	.5
Total	214	100.0

Majority of the patients recruited in the study 154 (72%) presented with breast lump only. Eighteen 8.4% had breast lump accompanied with pain, 19 (8.9%) had ulceration, 13 (6.1%) presented with pain only, 9 (4.2%) with breast discharge and 1 (0.5%) with nipple retraction.

Objective 1: To determine the patterns of breast sonographic BIRADS-score in patients presenting with breast lesions at Moi Teaching and Referral Hospital.

Table 4.3: Breast Involved

Variable	Frequency (n)	Percent (%)
Left	89	41.6
Right	116	54.2
Bilateral	9	4.2
Total	214	100.0

One hundred and sixteen (54.2%) had complains in their right breast, 41.6 in their left breast and only 4.2 % with bilateral complaints.

Table 4.4: Distribution of patients based on location of lesion

Variable	Frequency (n)	Percent (%)
Upper outer quadrant	140	65.4
Upper inner quadrant	24	11.2
Nipple	23	10.7
Lower outer quadrant	14	0.7
Axillary tail	13	0.6
Sub-areolar	13	0.6
Lower Inner Quadrant-LIQ	7	0.3
Multiple Areas	3	0.14
Total	**214**	**100**

The Upper Outer Quadrant location of lesion on the right breast was the most common (65.4%) with multiple areas being the least at 0.3%.

Table 4.5: Lymph nodes involved

Variable	Frequency (n)	Percent (%)
Axillary (sonographic normal nodes)	130	60.7
Axillary group (suspicious)	82	38.3
Intramammary lymph nodes	2	.9
Total	214	100.0

Table 4.6: BI-RADS category of the study participants

Variable	Frequency (n)	Percent (%)
BI-RADS 2(benign)	41	19.2
BI-RADS 3(probably benign)	48	22.4
BI-RADS 4(suspicious)		
4A (Low suspicion)	17	7.9
4B (moderate suspicion)	0	0.0
4C (Moderate suspicion)	55	25.7
BI-RADS 5 (highly suspicious)	53	24.8
Total	214	100.0

According to the BI-RADS classification majority of the patients studied 55 (25.7%) had 4c (Moderate suspicion) followed by highly suspicious at 24.8%, patients with stage 4a were the least with 17 (7.9%). The rest of the results are displayed in table4.2 above.

Table 4.7: Lesions characteristics

		Frequency (n)	percentages
Mass shape	Lobulated	**103**	**48.1**
	Oval	82	38.3
	Round	29	13.6
Mass margin	Uncircumscribed	**116**	**54.2**
	circumscribed	98	45.8
Orientation	Non-parallel	**128**	**59.8**
	Parallel	86	40.2
Calcifications	Absent	**84**	**39.3**
	Microcalcification in mass	72	**33.6**
	Micro-calcification out mass	58	**27.1**
Posterior acoustic features	Posterior shadowing	**116**	**54.2**
	Posterior enhancement	72	34.1
	Absent features	25	11.7
echogenicity	Hypoechoic	**131**	**61.2**
	Hyperechoic	**83**	**38.8**

Objective 2: To determine the histopathological findings in patients presenting with breast lesions at Moi Teaching and Referral Hospital

Table 4.8: Histological Classification

Variable	Frequency (n)	Percent (%)
Benign	87	40.7
Malignant	127	59.3
Total	214	100.0

The histological examination revealed that malignant category was the most common category type which was found in (59.3%) as shown in table 4.8 above.

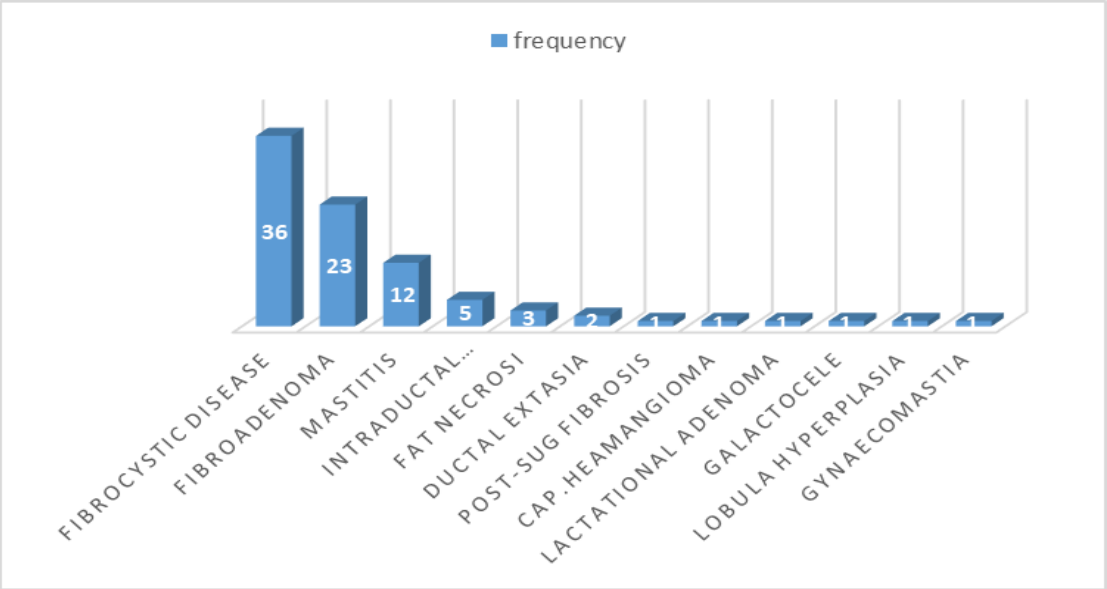


Figure 10:Bar graph showing Histopathological distribution of benign breast lesion.

As per the benign lesion distribution, fibrocystic diseases were the majority accounting for 41.4%, followed by fibro adenoma which accounted for 26.4%. the least percentage was shared by gynecomastia, galactocele, hemangioma each accounting for 1.15%.

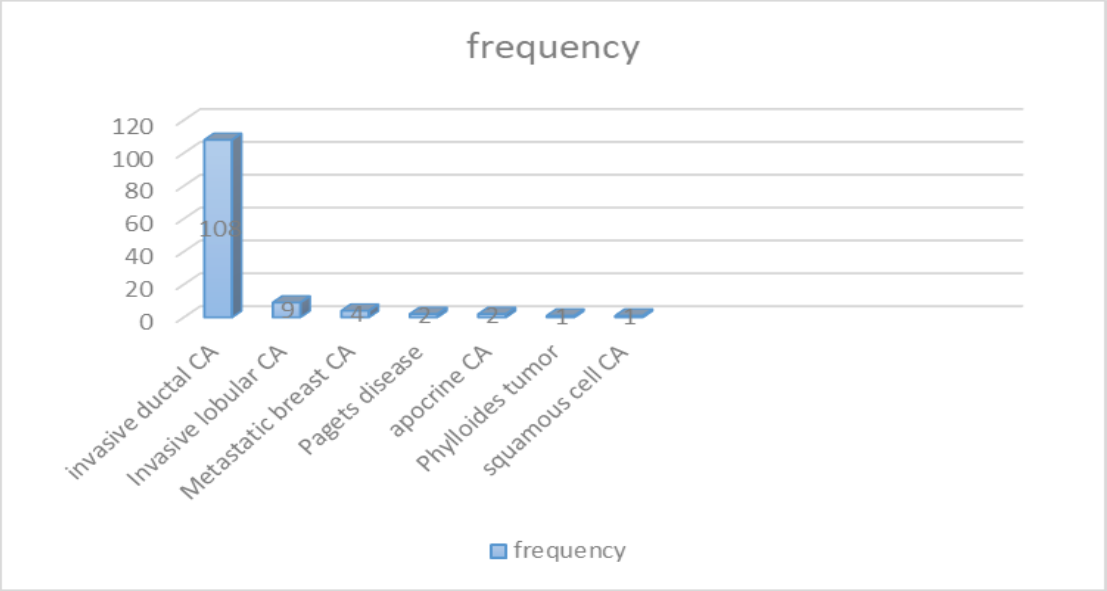


Figure 11:Bar graph showing Histopathological distribution of malignant breast lesions.

Invasive ductal CA accounted for 85% of all malignant lesions, followed by intraductal lobular CA (7.08%). Paget's disease (1.57%), apocrine CA (1.57%), phylloides tumor (0.78%) had the least distribution.

objective 3: To establish the diagnostic accuracy of sonographic BIRADS score in patients presenting with breast lesions in Moi Teaching and Referral Hospital

Table 4.9: Radiological-Histopathological correlation examination

		Pathological Classification (Gold standard)		Total
		malignant	benign	
Radiological findings (test)	Malignant	(TP)84	(FP)43	127
	Benign	(FN)42	(TN)45	87
Total		126	88	214

In ultrasound benign breast lesions were 88(41.1%) but in histopathology 87 (40.6%). In ultrasound malignant lesions were 126 (58.9%) but in histopathology 127(59.3%).

Cohen's Kappa was run to determine if there was agreement between radiological and histopathological examination. There was slight agreement between the two examinations with $\kappa = 0.178$ (95% CI, .090 to .333)

Table 4.10: Correlation of histopathological findings with sonographic BIRADS lesions characteristics

Lesion characteristic		frequency	Benign	malignant	P value
Mass shape	Oval	82	78	4	
	Round	29	26	3	
	Lobulated	103	35	68	**0.000**
Mass margin	Well circumscribed	98	90	8	
	uncircumscribed	116	5	111	**0.010**
Mass orientation	Parallel	86	83	3	
	Non-parallel	128	19	109	
Posterior acoustic features	Enhancement	15	14	1	
	No features	53	47	6	
	Shadowing	146	32	113	**0.000**
calcifications	Microcalcification in mass	58	3	55	
	Microcalcification out of mass	72	2	70	
	Absent	84	79	5	**0.001**
echogenicity	Hypoechoic	131	5	126	
	Hyperechoic	83	79	4	**0.000**

ultrasonographic features such as oval or round shape, parallel orientation, circumscribed margins, hyperechoic, enhancement or absence of posterior acoustic features, absence of surrounding tissue alterations represented a benign breast lesion, whereas, irregular shape, non-parallel orientation, posterior acoustic shadowing and abnormalities of the surrounding tissue regardless of echo pattern were shown to be associated with malignant lesions.

The most correlating signs for malignancy were hypo-echogenicity (96.2%), uncircumscribed margins (95.7%) and posterior shadowing (77.4%).

The most correlating signs for benignity were parallel orientation (96.5%), echogenic (95.1%), well circumscribed margins (91.8%) and ova/round shape (68%).

Table 4.11: Diagnostic accuracy parameters for sonographic BI-RADS score

Variable	Value	95% CI
Sensitivity	66.67%	57.72-74.81
Specificity	51.14	40.25-61.95
Negative Predictive Value	51. 72	43.75-59.62
Positive Predictive Value	66.14	60.41-71.43
Accuracy	60.28	53.39-66.89
Negative Likelihood Ratio	0.65	0.47-0.90
Positive Likelihood Ratio	1.36	1.07-1.75

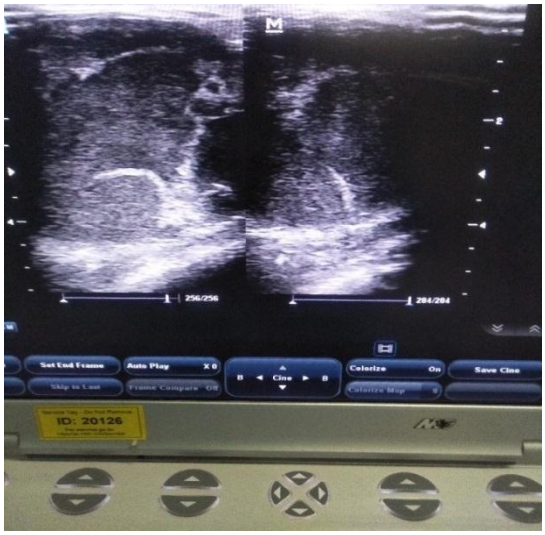
The sonographic BIRADS score had a sensitivity of 66.67% and specificity was 51.14%. The negative predictive value was 51.72% and the positive predictive value was 66.14%. The level of accuracy was 60.28%, the negative likelihood ratio was 0.65 while the positive likelihood ratio was 1.36.

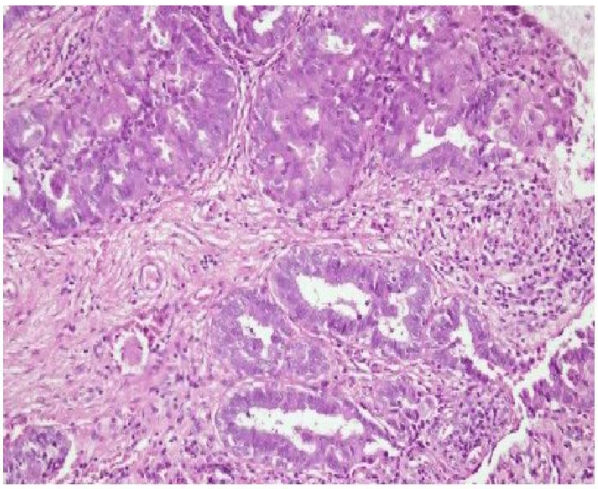
Table 4.12: Accuracy of BI-RADS characterization for benign and malignant lesions

BIRADS category	Sensitivity (%, 95% CI)	Specificity (%, 95% CI)	PPV (%, 95% CI)	NPV(%, 95% CI)	Accuracy(%, 95% CI)
2	23.4(17-35%)	100	14(12.5-20)	56.3(53.0-59)	65.2(55.3-69)
3	25.6 (18.2-34.8)	100 (96.5-100) 22.7	15.3(10.0-22.1%)	57.1 (54.3-59.9)	63.1 (56-69.2)
4A	22.3 (14.9-32)	22.7 (21.1-39.2)	24.1 (17.8-32.1)	27.9 (21.9-34.6)	25.8 (21.1-33.1)
4B	2.7 (0.5-7.9)	99.3 (95.1-100)	75.2 (24-96.5)	50.5 (50.1-52.1)	51.1 (44.1-57.9)
4C	13.9 (7.9-21.8)	98.1 (92-99.3)	82.8 (60.1-94.3)	53.2 (51-54.8)	56.1 (48.7-62.5)
5	59.9 (50.3-70.1)	100 (97-100)	100	72.1 (67.1-76.1)	79.9 (74.1-84.8)

Findings from this study show high rates of PPV for BI-RADS 4B, 4C and 5. This could provide some light at the end of the tunnel as using BI-RADS can potentially discriminate between benign and malignant masses and reduce not only unnecessary biopsies, but also unnecessary surgeries, an observation that has been alluded to in previous literature.

SAMPLE IMAGES

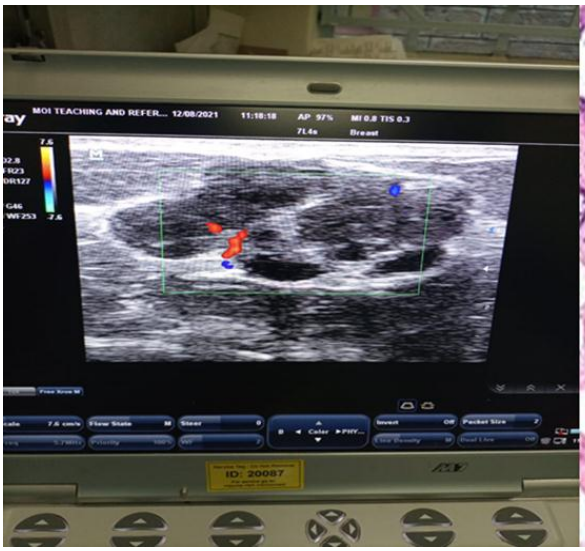


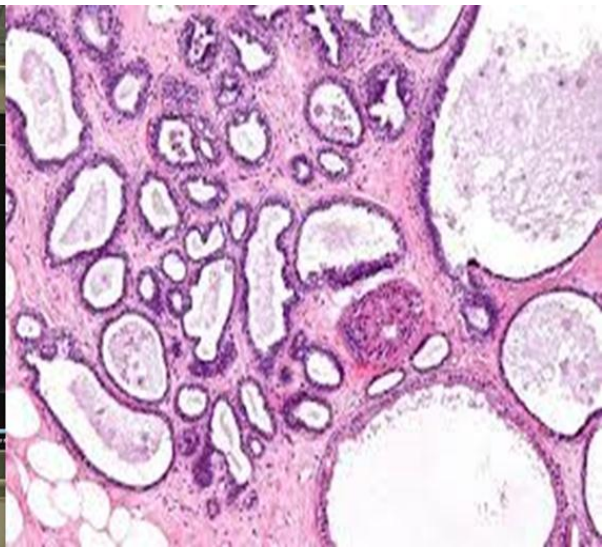


Sample image 1: 68year old male with right breast mass. This lesion demonstrated large necrotic area with thick peripheral solid component. This lesion was classified as (BIRADS-5). Histopathology showed invasive ductal CA

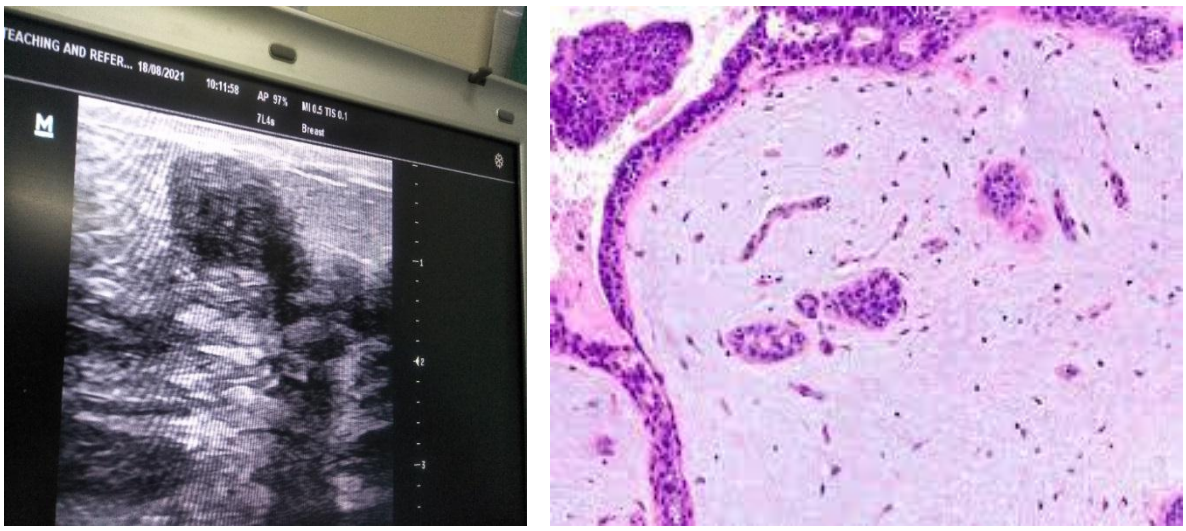
This lesion demonstrated heterogeneous echogenicity with cystic and solid areas. The solid areas showed internal vascularity.

The lesion was classified as birads-4. Histology showed fibrocystic disease of the breast





Sample image 2: 38-year-old female with left breast mass.



Sample image 3: 18years old with well circumscribed breast mass. This lesion was classified as BIRADS 3(probably benign). histology showed fibro adenoma

CHAPTER FIVE

5.0 DISCUSION

5.1 INTRODUCTION

Breast lesions are a major clinical presentation in hospitals with breast cancer being major cause of morbidity and mortality in the world and developing countries like Kenya bearing heavy causalities. The prompt diagnosis and hence management is needed to improve the outcome in case of malignancies. Hence radiological imaging especially breast ultrasound plays an important role in these scenarios. However, because of the frequent overlap of radiologic signs, suspected malignant breast lesions detected on sonography have to be examined with biopsy. The large number of biopsies performed for benign abnormalities because of patient's fear, physician uncertainty, or standard protocols is always recognized as an additional problem Excessive biopsies have adverse effects on society, increasing the costs of screening projects and health care. Reporting of breast ultrasound report is therefore required to be standardized for complete reporting and correlation with histopathology is a must for proper diagnosis and hence management

5.2 OBJECTIVE 1: To determine the patterns of breast sonographic findings in patients presenting with breast lesions in Moi teaching and referral hospital

Breast lesions were common in women at 95.3%(204) with the male population at 4.7%(10). These findings correlate well with a study done by (Yogalakshmi & Kavitha, 2019) who noted that the distribution of breast lesions were common in females at 97% and 3% in men.

These findings reinforce the notion that the breast lesions/complaints are common in women than men and could show better health seeking behavior in females.

Majority of patients in this study were below 40years accounting for 44.4% with mean age of 44.14 years. these results contrasted with research done by (Odedina et

al., 2018) in Nigeria, who noted that the mean age of women with breast disorders was 28.5 years, this could be explained by the fact that the research was done on expectant women and they had a large sample size of 1248. The study also contrasted with a study done by (Otieno et al., 2009) in Kenyatta National Hospital-Kenya, who found the mean age of the patients to be 34.17years, this contrast could be explained by the fact that the number of patients in their study was higher 1172 with a follow-up period of 2years.

This implies that more young people are involved and calls for greater awareness for self-breast examination, clinical breast examination and establishment/proper implementation of national breast screening programs.

Breast lump was the commonest presenting complaint in our study at 72% with the least presenting complaint being nipple retraction at 0.5%, this study findings were echoed by a study by (Kaira et al., 2017) in India, who studied 115 patients and their study showed 100% of their patients presenting with breast lump followed by pain at 7%, nipple discharge at 6%, ulcerations 4.4% and compounding non-breast complaints like weight loss and loss of appetite at 63%.

In our study the right breast was the commonest side affected by breast lesions at 54.2%, followed by left breast at 41.6% and with bilateral being 4.2%, this contrasted with a study done by(Kaira et al., 2017) in India, who found the left breasts to be the side affected most at 61.7% and right breast at 38.3% . our study also contrasted study done by (Key et al., 2018) in Sudan, whose study revealed that more than a half of breast masses occur in left side (50.75%) than in the right side (45.77%) and least occurs bilateral at 3.5%. These two studies however echoed our findings in the prevalence of bilateral breast lesions.

Upper outer quadrant was the most common site for breast lesions having a total of 28.5% and 11.2%% in the left and right breasts respectively. These results are similar to a study done by (Rummel et al., 2015) in USA, who found out that lesion location in the UOQ (51.5%) was significantly higher than in the UIQ (15.6%), LOQ (14.2%), central (10.6%), or LIQ (8.1%). Our study were also echoed by a study done by(Key et al., 2018) in Sudan, who found UOQ more involved at 54.23%.

Majority of the breast lesions had oval/round shape at 51.9% followed by lobulated masses at 48.1%. these study findings compares with a study by (Thibault et al., 2000) in France, who also established that most of their lesions had oval/round shape at 74% followed by lobulated lesions at 26%.

Most lesions had uncircumscribed margins (obscured, irregular or spiculated) at 52.4% followed by well circumscribed margins at 45.8%. these study finding compares with a study by (A. S. Hong et al., 2005) in USA,who found out that uncircumscribed lesions accounted for 52.1% followed by circumscribed lesions at 47.9%.

In our study breast lesions were predominantly hypoechoic at 65.9% followed by lesions that were hyper-echoic at 34.1%. these study findings compares with study by (Chiasawas, Boonjunwetwat, & Sampatanukul, 2011) in Thailand, who also noted that majority of breast lesions they evaluated were hypoechoic at 88.9% followed by hyperechoic lesions at 11.1%. The reason their values were high is because they evaluated only BIRADS-4/5 lesions.

According to posterior acoustic features of lesions we evaluated, majority of the lesions exhibited posterior shadowing at 54.2%, posterior enhancement at 34.1% and no features at 11.7%. these findings contrasts a study findings by (Tahira & Sarwar,

n.d.) in India, who found majority of the lesions to show posterior enhancement at 70%, followed by posterior shadowing at 19.3% and no features at 10.7%. This contrast could be explained by they had few patients at 150.

Majority of the breast lesions we evaluated showed didn't not show calcification at 39.9%, followed by lesion that had calcification within the mass at 33.6% and outside of the mass at 27.1%. these finding compare with a study by (A. S. Hong et al., 2005) in USA, who noted that majority of the lesions lacked calcification at 94.5% followed by those with calcification at 5.5%. These high values could be explained by the fact that they had high number of patients at 403.

The current study showed that most of our patients were classified as BIRADS-4(suspicious) at 33.6% followed by BIRADS-5(highly suspicious) at 24.8% and BIRADS-3 (probably benign) at 22.4%, however these findings contrast a study by (Tahira & Sarwar, n.d.) in India, who did a prospective study on 150 women only for period of 6 months. They found out that out of 150 patients using BIRADS system 82(54.6%) were category 2, 38(25.3%) patients were category 3. 18(12%) patients were category 4 and 12(08%) patients were category 5.

In our study, lymph node evaluation revealed that axillary lymph nodes were the commonest at 99%, followed by intra-mammary nodes at 0.9%. amongst the axillary nodes the benign nodes were at 60.7% and suspicious nodes at 38.3%. these findings correlated well with a study done by (Arslan, Altintoprak, Yirgin, Atasoy, & Celik, 2016) in Turkey, who prospectively evaluated 35 patients with breast cancer with preoperative ultrasonography (US) to determine the presence of axillary lymph node metastasis. they found that 83.5% and 16.7% of lymph nodes were benign and suspicious respectively.

These results stresses the importance of axillary evaluation and sonographic nodal characterization in patients presenting with breast lesions.

5.3 OBJECTIVE 2: To determine the patterns of histopathological findings in patents presenting with breast lesions in Moi teaching and referral hospital

In this study the malignant breast lesions were the commonest accounting for 59.3% followed by benign breast lesions at 40.7%, these findings were echoed by a study done by (Kaira et al., 2017) in India, who did a prospective study among 115 patients and found that , 47 cases (40.9%) were of Benign Breast Lesion and 68 cases (59.1%) were of Malignant Breast Lesion.

However these findings are contrasted with a study done by (Otieno et al., 2009) in KNH in which they found benign lesions to be the commonest at 78% followed by malignant lesions at 22%, this contrast could be explained by the fact that their study was retrospective with large number of patients 1172. Their result were also echoed by (Yogalakshmi & Kavitha, 2019) in India, who also found that benign lesions were the majority at 81.6% , while 18.3% constituted malignant lesions.

The commonest benign breast lesions were fibrocystic change at 41.4% followed by fibro adenomas at 26.4% with the least percentage being shared by gynecomastia, galactocele and hemangioma at 1.15%. these findings contrasted a study done by (Odedina et al., 2018) in Nigeria, who found that reactive lymph nodes were the commonest at (42.5%) and prominent ducts (27.1%). Other findings were fibro adenomas (9.6%), fibrocystic changes (2.5%) and breast cysts (3.8%. these contrast can be explained by the fact that their study was conducted among 1248 pregnant women in their first trimester of pregnancy and followed up till 26 weeks' gestational age and also that in our study the mean age of our study participants was 40yrs and

being the age in which fibrocystic disease are common.

The commonest malignant disease was invasive ductal carcinoma (85%) followed by intraductal lobular carcinoma at 7.08%. These findings correlated well with a study done by(Yogalakshmi & Kavitha, 2019) in India, who retrospectively found out that among the 22 malignant lesions, 17 cases were of infiltrative duct cell carcinoma (77%), two cases were of medullary carcinoma (9%), and one case each in invasive papillary carcinoma, metaplastic carcinoma, and apocrine carcinoma (5%).

5.4 OBJECTIVE 3: To determine the diagnostic accuracy of sonographic BI-RADS score in patients presenting with breast lesions in Moi teaching and referral hospital

In our study benign breast lesions detected by ultrasound and histopathology were 88(41.1%) and 87 (40.6%) respectively. Malignant lesions detected by ultrasound and histopathology were 126(58.9%) and 127(59.3%) respectively.

In our study findings ultrasonographic features such as oval or round shape, parallel orientation, circumscribed margins, hyperechoic, enhancement or absence of posterior acoustic features, absence of surrounding tissue alterations were seen in benign breast lesions, whereas irregular shape, non-parallel orientation, posterior acoustic shadowing and abnormalities of the surrounding tissue regardless of echo pattern were shown to be associated with malignant lesions

The most correlating signs for malignancy were hypo-echogenicity (96.2%), uncircumscribed margins (95.7%) and posterior shadowing (77.4%). These study findings compared well with findings by (Chiasawas et al., 2011) in Thailand, who found the most correlating signs for malignancy to be spiculated margins (100%), marked hypo-echogenicity (88.9%), , shadowing (81%) , irregular shape (72.2%).

The most correlating signs for benignity were parallel orientation (96.5%), echogenic (95.1%), well circumscribed margins (91.8%) and ova/round shape (68%). These study findings contrast findings by (Elverici et al., 2015) in Turkey, who retrospectively analyzed sonograms of 186 BI-RADS 4 non-palpable breast lesions with a known diagnosis. They noted that typical signs of benign lesions were oval shape (NPV, 77.1%), circumscribed margin (NPV, 67.5%), parallel orientation (NPV, 70%), and abrupt interface (NPV, 67.6%)

In our study findings sonographic BI-RADS score had a sensitivity of 66.67% and specificity was 51.14%. The negative predictive value was 51.72% and the positive predictive value was 66.14%. The level of accuracy was 60.28%, the negative likelihood ratio was 0.65 while the positive likelihood ratio was 1.36. These findings compares well with a study by (Naser et , 2021) in Iran, reported sensitivity, specificity, PPV, NPV and accuracy of 68.9%, 48.6%, 57%, 61.2% and 58.7% respectively.

This study findings also agrees with a study by (Mubuuke, Nassanga, & Galukande, 2023) in Uganda who studied comparative accuracy of sonography, mammography and the BI- RADS characterization of breast masses, reported that sonographic BI-RADS score had sensitivity, specificity, PPV, NPV and accuracy of 68.5%, 48.4%, 56.6%, 61% and 57.8% respectively.

Findings from this study show high rates of PPV for BI-RADS 4B, 4C and 5 at 75%, 82% and 100 % respectively. This study finding agrees with a study (Fu et al , 2011) in China who were studied influence of age on PPV on BIRDAS 3,4 and 5 categories found out that the PPV of BIRADS categories 4B,4C and 5 to be 65%, 79.6% and 99.6%.

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATION

6.1 Conclusion

1. Majority of the breast lesions demonstrated uncircumscribed margins, were hypoechoic, had parallel orientation, showed posterior acoustic shadowing and had no calcifications. BIRADS-4(suspicious) were the majority followed by BIRADS-5(highly suspicious).
2. Histopathologically, malignant lesions were the commonest**.** The commonest malignant and benign lesions were invasive ductal carcinoma and fibrocystic change respectively.
3. Sonographic BI-RADS score had a sensitivity and specificity of 66.67% and 51.14% respectively. There was a slight agreement between sonographic and histopathological findings with kappa score of 0.178.

6.2: Limitations of the study

This study was conducted in an urban level 6 hospital and had fewer number of patients hence the results may not be generalizable

6.3 Recommendations

1. All breast ultrasound reports should be standardized by ensuring that the final report is given as per the BIRADS-lexicon for breast sonography
2. Use of high resolution transducers is recommended for high quality images and in detection of smaller abnormalities with an overall aim in improving the sensitivity of breast sonography
3. Involvement of different stakeholders is recommended to increase awareness about breast cancer amongst the male gender and emphasis on triple test with an aim to increase early breast cancer detection

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APPENDICES

APPENDIX 1: PROTOCOL FOR ROUTINE HEMATOXYLIN AND EOSIN STAINING OF BREAST CNB SAMPLES IN MTRH –HISTOPATHOLOGY LABORATORY

Purpose: describes how to perform hematoxylin and eosin stain that is essential for recognizing various normal and abnormal tissue morphologies

Principle: hematoxylin is a basic stain that selectively stains cell nuclei while eosin is an acid that acts like counterstain that is selective for the cytoplasm

Recommended specimen: paraffin wax tissue sections

Equipment	supplies	reagents
Staining jars Slide racks Hot air oven microscope	Frosted edge glass slides coverslips	DPX Hematoxylin stain solution Eosin stain solution Xylene Ethanol Running tap water 1%acid alcohol Scotts tap water

SATETY PRECAUTION

1. Wear protective equipment to avoid harmful effects of reagents and infectious materials
2. Exercise the normal precautions required for handling infectious agents

PROCEDURE

1. Put tissue sample in the hot air oven for 30mins at 60-65degress to remove the excess wax and to allow the tissue sections to firmly attach to the microscope
2. Take tissue sections to water through xylene (4 changes) and descending grades of alcohol starting 90%, 70% and 50% and wash in water
3. Place sections in hematoxylin for 7-10mins
4. Differentiate in 1% acid alcohol for 30secs and wash in running tap water
5. Blue in Scotts water for 1min
6. Wash well in running ng tap water
7. Counter stain with eosin for 3-4mins
8. Wash well in water, dehydrate through 70%, 90% and three changes of absolute alcohol, clear in three changes of xylene
9. Mount with DPX and coverslip
10. Allow the slides to dry then dispatch to the pathologist for reporting

APPENDIX 2: CONSENT FORM

This informed consent form is for patients with breast complaints who are for breast ultrasound.

Introduction

My name is Dr. Jackline Anyango Ombura from the Department of Radiology and I am carrying out a study on establishing the diagnostic accuracy of sonographic BIRADS score in the diagnosis of breast lesions based on histopathology.

Breast lesions are a cause of concern and anxiety among women and men. Breast cancer is one of the leading causes of cancer-related deaths among women around the world and Kenya in particular. I am kindly requesting your participation in the study.

What is the study about?

The study is about the findings of breast lesions on ultrasound and how we ensure its accuracy by correlating these findings with histopathology which is considered as the gold standard. By you participating in the study you help us further enhance early diagnosis and appropriate management of breast lesions.

What will happen to me during the study?

On giving consent, you will be asked a few questions about yourself and your condition. I will then collect information about your clinical signs and symptoms, you will be told about the procedure and any risks involved, if present.

You will not incur any risks or acquire many benefits by participating in this study. You will be given the same medical care as the rest of the patients who do not participate in the study. You can choose whether or not you would like to participate

in the study. In case you refuse to be a part of the study you will not be forced to participate.

If you have any questions, please feel free to ask and I will be glad to assist you.

Certificate of assent

Do you understand this research study and are you willing to take part in it?

Yes: ☐ No: ☐

Has the researcher answered all your questions?

Yes: ☐ No: ☐

Do you understand that you can pull out of the study at any time?

Yes: ☐ No: ☐

I agree to take part in the study ☐

OR

I do not wish to take part in the study ☐

Signed: ……

Date: ……

APPENDIX III: DATA COLLECTION FORM

Instructions:

a) All sections should be filled accordingly.

b) Writings should be clear and legible.

c) The form is to be filled in by the principal investigator or assistant once the patient has given consent to be part of the study.

IP/OP No: …….

Serial No: …….

Date: …….

PART 1: DEMOGRAPHIC DATA

1. DOB/ Age ……....

2. Gender ……

3. County of Residence …….

4. Contact No: ……...

PART 2: FINDINGS

SECTION A: Clinical features and findings

Clinical features (tick as appropriate)

Breast complaints	
Pain	
Breast discharge	
Breast lump	
Ulceration	
Others(specify)	

Breast involved

Breast involved	**Tick as appropriate**
right	
left	
bilateral	

SECTION B: Radiological findings

What is the radiological diagnosis? (Include the breast quadrant, lymph node involvement, BI-RADS classification)

Breast quadrant/clock position/ICD codes

breast	**Quadrant/coding/clock**	**Tick as appropriate**
Right breast	**C50.2/(UIQ)/1'/2'oclock**	
	C50.2(LIQ)/4'/5'oclock	
	C50.5(LOQ)/7'/8'oclock	
	C50.4(UOQ)/10'/11'oclock	
	C50.0(NIPPLE)	
	C50.1(SUB-AREOLAR)	
	C50.6(AXILLARY TAIL)	
Left breast	**C50.4(UOQ)/1'/2'oclock**	
	C50.5(LOQ)/4'/5'oclock	
	C50.3(LIQ)/7'/8'oclock	
	C50.2(UIQ)/10'/11'oclock	
	C50.0(NIPPLE)	
	C50.1(SUBAREOLAR)	
	C50.6(AXILLARY TAIL)	

Lymph nodes involved

Lymph node group	**Tick as appropriate**
Axillary group	
Interpectoral nodes	
intrammamary	
parasternal	
others	
BI-RADS STAGINGS	TICK AS APPROPRIATE
0(incomplete)	
1(negative)	
2(benign)	
3(probably benign)	
4(suspicious)	
5(highly suspicious for malignancy)	
6(proven malignancy)	

Section c: histological findings

Histology classification	Tick as appropriate(specify)
Benign	
Malignant	

histopathological-sonographic correlation classification	Tick as appropriate
Concordant malignancy	
Discordant malignancy	
Concordant benignity	
Discordant benignity	
Borderline findings	

Sehemu ya c: matokeo ya histolojia

Uainishaji wa Histolojia	Jibu kama inafaa (taja
Benign	
Mbaya	

Uainishaji wa uwiano wa patholojia-sonografia	Jibu kama inafaa
Ukali wa concordant	
Ugonjwa mbaya	
Ukali wa concordant	
Ukosefu wa usawa	
Matokeo ya mipaka	

Appendix IV: IREC Approval

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3

MOI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
P.O. BOX 4606
ELDORET
Tel: 33471/2/3

Reference: IREC/2021/13
Approval Number: 0003854

15th April, 2021

Dr. Jackline Anyango Ombura,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

Dear Dr. Ombura,

ACCURACY OF SONOGRAPHIC BI-RADS SCORE IN DIAGNOSIS OF BREAST LESIONS AT MOI TEACHING AND REFERRAL HOSPITAL-ELDORET, KENYA

This is to inform you that ***MTRH/MU-IREC*** has reviewed and approved your above research proposal. Your application approval number is ***FAN: 0003854.*** The approval period is **15th April, *2021 – 14th April, 2022.***
This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by ***MTRH/MU-IREC***.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to ***MTRH/MU-IREC*** within 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to ***MTRH/MU-IREC*** within 72 hours.
v. Clearance for export of biological specimens must be obtained from ***MTRH/MU-IREC*** for each batch of shipment.
vi. 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.
vii. Submission of an executive summary report within 90 days upon completion of the study to ***MTRH/MU-IREC.***

Prior to commencing your study; you will be required to obtain a research license from the National Commission for Science, Technology and Innovation (NACOSTI) https://oris.nacosti.go.ke and other relevant clearances. Further, a written approval from the CEO-MTRH is mandatory for studies to be undertaken within the jurisdiction of Moi Teaching & Referral Hospital (MTRH), which includes 22 Counties in the Western half of Kenya.

Sincerely,

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
15 APR 2021
APPROVED
P. O. Box 4606-30100 ELDORET

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc CEO - MTRH Dean - SOP Dean - SOM
Principal - CHS Dean - SON Dean - SOD

Appendix VI: Hospital Approval (MTRH)

An ISO 9001:2015 Certified Hospital

MOI TEACHING AND REFERRAL HOSPITAL

Telephone :(+254)053-2033471/2/3/4
Mobile: 722-201277/0722-209795/0734-600461/0734-683361
Fax: 053-2061749
Email: ceo@mtrh.go.ke/directorsofficemtrh@gmail.com

Nandi Road
P.O. Box 3 – 30100
ELDORET, KENYA

Ref: ELD/MTRH/R&P/10/2/V.2/2010

16th April, 2021

Dr. Jackline Anyango Ombura
Moi University
School of Medicine
P.O .Box 4606-30100
ELDORET-KENYA

ACCURACY OF SONOGRAPHIC BI-RADS SCORE IN DIAGNOSIS OF BREAST LESIONS AT MOI TEACHING AND REFERRAL HOSPITAL-ELDORET-KENYA

In order to conduct research within the jurisdiction of Moi Teaching and Referral Hospital (MTRH) this includes 22 counties in the Western half of Kenya. You are required to strictly adhere to the regulations stated below in order to safeguard the safety and well-being of staff and patients seen at MTRH involved research studies.

1. The study shall be under Moi Teaching and Referral Hospital regulation.
2. A copy of MU/MTRH-IREC approval shall be provided.
3. Studies dealing with collection, storage and transportation of Human Biological Material (HBM) will not be allowed to export the HBM outside the jurisdiction of **MTRH.**
4. For those tests which are unavailable locally the PI is tasked to ensure sourcing of equipment and subsequent training of staff to build their capacity.
5. No data collection will be allowed without an approved consent form(s) to participants to sign.
6. Take note that **data** collected must be treated with due confidentiality and anonymity.

Permission to conduct research shall only be provided once all the requirements stated above have been met.

MOI TEACHING AND REFERRAL HOSPITAL
CEO
APPROVED
16 APR 2021
SIGN.....
P.O. Box 3-30100, ELDOR

16/04/2021
DR. WILSON K. ARUASA, *EBS*
CHIEF EXECUTIVE OFFICER
MOI TEACHING AND REFERRAL HOSPITAL

c.c. - Senior Director, Clinical Services
- Director of Nursing Services
- HOD, HRISM

Appendix VII: Nacosti Approval

REPUBLIC OF KENYA

NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Ref No: **848788**

Date of Issue: **06/May/2021**

RESEARCH LICENSE

This is to Certify that Dr.. Jackline anyango Ombura of Moi University, has been licensed to conduct research in Uasin-Gishu on the topic: ACCURACY OF SONOGRAPHIC BI-RADS SCORE IN PATIENTS PRESENTING WITH BREAST LESIONS IN MOI TEACHING AND REFERRAL HOSPITAL-ELDORET, KENYA for the period ending : 06/May/2022.

License No: **NACOSTI/P/21/10306**

848788

Applicant Identification Number

Director General
NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Verification QR Code

NOTE: This is a computer generated License. To verify the authenticity of this document, Scan the QR Code using QR scanner application.

THE SCIENCE, TECHNOLOGY AND INNOVATION ACT, 2013

The Grant of Research Licenses is Guided by the Science, Technology and Innovation (Research Licensing) Regulations, 2014

CONDITIONS

1. The License is valid for the proposed research, location and specified period
2. The License any rights thereunder are non-transferable
3. The Licensee shall inform the relevant County Director of Education, County Commissioner and County Governor before commencement of the research
4. Excavation, filming and collection of specimens are subject to further necessary clearence from relevant Government Agencies
5. The License does not give authority to tranfer research materials
6. NACOSTI may monitor and evaluate the licensed research project
7. The Licensee shall submit one hard copy and upload a soft copy of their final report (thesis) within one year of completion of the research
8. NACOSTI reserves the right to modify the conditions of the License including cancellation without prior notice

National Commission for Science, Technology and Innovation
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