ACCURACY OF ULTRASOUND-GUIDED VERSUS PALPATION-GUIDED BIOPSY OF PALPABLE BREAST MASSES IN WOMEN AT KENYATTA NATIONAL HOSPITAL: A RANDOMIZED CONTROLLED TRIAL

DR. MARYAM BADAWY

M.B.Ch. B (Cairo)

A DISSERTATION SUBMITTED IN PART-FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTER OF MEDICINE IN GENERAL SURGERY

UNIVERSITY OF NAIROBI

DECLARATION

I declare that this dissertation is my original work and has not been presented for a degree or any other award in any other institution

Dr. Maryam A. Badawy

Signed: …… Date: ……

DECLARATION BY UNIVERSITY OF NAIROBI SUPERVISORS

This dissertation has been submitted for examination with our approval as university supervisors

Dr. Elly Nyaim Opot

MBChB, M. Med General Surgery, FCS (ECSA)

Senior Lecturer Department of Surgery, University of Nairobi

Signed: …… Date: ……

Dr. Dan Kiptoon

MBChB, M. Med General Surgery

Lecturer Department of Surgery, University of Nairobi

Signed: …… Date: ……

Dr. Marilynn Omondi

MBChB, M. Med General Surgery

Tutorial fellow, Department of Surgery, University of Nairobi

Signed: …… Date: ……

DECLARATION BY KENYATTA NATIONAL HOSPITAL SUPERVISOR

This dissertation has been submitted for examination with my approval as a Kenyatta National Hospital supervisor

Dr. Wangari Maina

MBChB, M. Med Diagnostic Imagine and radiation medicine

Consultant radiologist, Radiology department, Kenyatta National Hospital

Signed: …… Date: ……

UNIVERSITY OF NAIROBI DECLARATION OF ORIGINALITY FORM

Name of Student:	Dr. Maryam A. Badawy
Registration number:	H58/80776/2015
College:	College of Health Sciences
Faculty/School/Institute:	School of Medicine
Department:	Surgery
Course Name:	Master of Medicine in General Surgery
Title of Work:	Accuracy of ultrasound-guided versus palpation-guided biopsy of palpable breast masses in women at Kenyatta National Hospital: a randomized controlled trial

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Dr. Julius Kiboi

Chairman

Department of Surgery, School of Medicine

University of Nairobi

Signed: …… Date: ……

DEDICATION

To my husband, **Dr. Swaleh H. Shahbal**, thank you for your unwavering support, encouragement and patience throughout this journey. To my children Aziza and Harith, thank you for your patience and understanding despite your young age.

To my parents **Alwy A. Badawy** and **Asma Khitamy**, throughout my life, you have supported and encouraged me to be the best I can be. For that, and many more, I say Thank you and God bless you.

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LIST OF ABBREVIATIONS

KNH:	Kenyatta National Hospital
SOPC:	Surgical Out-Patient Clinic
UON:	University of Nairobi
US:	Ultrasound
FNAC:	Fine Needle Aspiration Cytology
BIRADS:	Breast Imaging-reporting and data system
CBE:	Clinical Breast Examination

OPERATIONAL DEFINITIONS

Accuracy: Closeness of a measured value to a standard or known value

Sensitivity: The probability that a test will indicate 'disease' among those with the disease

Specificity: It is the fraction of those without disease who will have a negative test result

T-stage: Refers to the tumour size of cancer in the Tumour, Node and Metastasis (TNM) staging system

T-stage classification:

- T1= Tumour ≤ 2 cm in the greatest diameter
- T2= Tumour >2 but ≤ 5 cm in the greatest diameter
- T3= Tumour > 5 cm in the greatest diameter

ABSTRACT

Background: Breast cancer is one of the most common cancers in women. More than 90 percent of patients presenting to Kenyatta National Hospital with complaints of breast disease have a palpable breast mass. The American Society of Breast Surgeons has a consensus guideline stating that image guided biopsy of palpable and non-palpable breast lesions is the standard procedure for obtaining a histological diagnosis of a breast mass. At KNH, biopsies are currently performed using predominantly the palpation guidance method; however, the accuracy of the said method at KNH is not documented.

Objectives: To determine the accuracy of ultrasound-guided versus palpation-guided biopsy of palpable breast masses at KNH

Methodology: This was a single-blind randomized controlled trial carried out at Kenyatta National Hospital from January 2019 to January 2020, among women who were 18 year and above presenting with palpable breast masses, which were from T1-T3 and from BIRADS 3-5. Seventy-nine women who met the inclusion criteria were randomized into one of two arms, palpation guided or ultrasound guided biopsy. Demographic data, and appropriate physical examination carried out. Biopsy results determined further management as per standard guidelines. Biopsy results were compared with the final histology following surgical excision of the tumours. Data was entered into SPSS and analyzed for means, proportions. Inferential data on sensitivity, specificity, negative predictive value, and positive predictive value was determined from 4 by 4 table and means compared using student-t test. Statistically significant results were taken at $p<0.05$ with a confidence interval of 95%.

Results: There was no statistically significant difference in demographic data and other baseline characteristics. The sensitivity for ultrasound-guided biopsy was 95.7% compared to 87% for palpation-guided biopsy. The specificity and positive predictive values for the two methods was similar at 100%. The false negative rate was 18.8% for palpation-guided biopsy and 5.9% for image-guided biopsy.

Conclusion: This study has demonstrated that, in terms of accuracy, ultrasound guided biopsy is superior to palpation guided biopsy, with a higher sensitivity and a lower false negative rate.

CHAPTER ONE: INTRODUCTION

Breast cancer is the most common cancer in women worldwide including sub-Saharan Africa[1]. GLOBOCAN 2012 estimates an incidence of 20 to 40 per 100,000 in East Africa[2] with a large proportion of cases reporting a breast mass as their initial presenting symptom[3,4]. Clinical, radiological and histologic assessments (i.e. the modified triple assessment) are required to make the diagnosis of breast cancer[5].

Majority of cases presenting to the breast clinic in KNH undergo a core biopsy of their breast masses. As part of the modified triple assessment, approximately 70 palpation-guided core biopsies were performed at the minor theatre in KNH from January to July 2018, the majority of which were performed by the residents in the department of surgery. During the same period, a total of 35 ultrasound-guided core biopsies were performed in the KNH radiology department. However, the American Society of Breast Surgeons has a consensus guideline developed in November 2016, stating that image guided biopsy of palpable and nonpalpable breast lesions is the standard procedure for histological diagnosis of breast mass, this only changes after an initial histology is obtained [6].

In our setup, access to consultant radiologists could be a challenge especially in rural areas, considering that consultant radiologists are concentrated in urban areas. This leads to the necessity of doing core biopsies using the palpation guided method.

Although palpation guided biopsy is widely used in our setting, there have been no local studies justifying this practice. This study seeks to assess its' utility.

CHAPTER TWO: LITERATURE REVIEW

Breast cancer is the commonest type of cancer diagnosed in women worldwide, with 691,300 new cases diagnosed in developing countries in 2008[1]. Breast cancer is also the leading cause of cancer related mortalities in both developed and developing countries[1,7]. GLOBOCAN 2012 estimates an incidence of 20 to 40 per 100,000 in East Africa[2]. The Nairobi cancer registry states that breast cancer accounts for 23% of all cancers in Nairobi residents alone, with an age standardized incidence of 51.7 per 100,000[8].The disease is more aggressive in black women and they are more likely to die from breast cancer compared to white women[9].

Breast cancer presents with a variety of symptoms, including-but not limited to-a breast mass, nipple discharge and breast pain. The commonest presenting symptom in breast disease is a palpable breast mass. Studies done at KNH had more than 90% of patients presenting with a breast mass as their initial symptom [3,4].

The evaluation of a patient with a breast mass consists of implementing the modified triple assessment that includes: clinical examination, radiological and histological assessment of the breast mass to obtain a definitive diagnosis. Radiological assessment is carried out with a diagnostic mammogram or a breast ultrasound depending on the age of the patient. Patients aged 40 years and above normally undergo a diagnostic mammogram as recommended by the American college of radiology and the society for breast imaging[10].However, patients younger than 40 years of age undergo a breast ultrasound. This is due to the higher density of the breasts of a younger patient which would result in a higher rate of false positive results on mammography[11]. Upon radiological assessment, the result is reported and classified based on the Breast imaging-reporting and data system (BIRADS) which was developed by the American college of radiology[12]. The BIRADS assigns a specific category to each breast mass, ranging from 0 to 6, depending on the findings, with each category having a specific probability for malignancy. Ultrasound features suspicious for malignancy include a mass that is hypoechoic, nodular, taller more than it is wide, with spiculated margins and posterior acoustic shadowing [13]. In mammography, malignancy is suspected with the presence of a mass with irregular edges, architectural distortion and microcalcifications.

Following radiologic assessment, a cytological or histological diagnosis is obtained by means of a Fine needle aspiration cytology (FNAC) or a core needle biopsy, respectively.

Fine-needle aspiration cytology is cheap, easy to perform and readily available. But it requires great expertise in its interpretation, it is associated with an increased incidence of insufficient sampling and it cannot distinguish in-situ lesions from invasive cancer[14]. Core-needle biopsy has been shown to be more accurate in diagnosing cancer and can be used to biopsy non-palpable lesions with image guidance[15]. A systematic review was conducted in 2010 to evaluate the accuracy of core needle biopsy performed under image guidance, they found it was comparable with open surgical biopsy in the diagnosis of malignancy[16].

Core needle biopsies are obtained either by palpation or image guidance. However, image guidance has gained much popularity recently. Imaging modalities used include ultrasound, mammography and MRI. However, ultrasound is used more often as it has several advantages[17], namely; being cheaper, more available, has non-ionizing radiation and provides better comfort for the patient. On the other hand, ultrasound is disadvantaged by the inability to biopsy non-visible lesions like microcalcifications, which can only be viewed and biopsied with stereotactic guidance.

Palpation guided biopsy may be associated with sampling errors; due to the inability to confirm the location of the needle within a small mass, or the presence of peritumoural oedema and inflammation in large tumours, resulting in the sampling of inflammatory tissue [18].

The sensitivity of ultrasound guided biopsy, when compared with palpation guidance, has been reported to be above 90% from multiple retrospective studies. A study carried out in India prospectively investigated the superiority of image guidance over palpation guidance in a female population, with the aim to also determine the size of beneficial effect. They reported a sensitivity of 96.3% with ultrasound guidance versus 46.7% with palpation guidance. Ultrasound guided biopsy also resulted in a low false negative rate of 0.03% compared with 44.4% in palpation guided biopsy. They reported a diagnostic accuracy of 97.2% for ultrasound guided biopsy while palpation had an accuracy of 55.6%. However, they did not report the correlation with the breast mass size, where the masses ranged from 1-13 cm in diameter (average size was 4.4cm). They also cited their small sample size of 72 patients as a possible contributor to the higher positive rate[18]. In South Africa, a retrospective study reported the sensitivity to be 100% in detecting malignancy with a diagnostic yield of 98.5% [19]. A retrospective German study reported a sensitivity of 98% for ultrasound guidance and 79% with palpation guidance. However, there may have been selection bias in assigning patients to image or palpation guidance as larger masses were

more likely to be sent for palpation guided biopsy [20]. The use of ultrasound guidance has also been shown to have fewer false-negative rates and reduced the need for additional tissue sampling. In the United States, a retrospective study was conducted where they analyzed 27 cases of false negative core biopsies. These cases proved malignant upon excision of the mass. Of these 27 cases, 18 had been taken without ultrasound guidance. They concluded that the miss-rate was higher without image guidance(13.3% versus 3.6% miss-rate for image-guidance)[21]. However, in this study, the true positive results were not analyzed and correlated with the biopsy method used. Another retrospective study was conducted in New York, USA analyzing data of 115 palpable masses that had undergone image-guided biopsy (by use of ultrasound or stereotactic guidance) [22]. They concluded that ultrasound guidance reduced the need for repeat biopsy in 74% of patients. Despite these results, there was no arm of comparison with masses that were biopsied by palpation. There may also have been selection bias where image guided biopsy was performed to masses that were small, deep and vaguely palpable [22]. It also demonstrated that palpation guided biopsy was inferior to ultrasound guided biopsy in the United Kingdom [23] in this study, 24% of 410 biopsies were repeated under ultrasound guidance where in two-thirds, the histologic diagnosis was upgraded indicating a missed diagnosis at the initial palpation guided biopsy[23].

2.1 Statement of the Problem

Several studies have shown that ultrasound guided biopsy is superior to palpation guided, however in our setup, majority of breast masses are biopsied using the palpation-guided method, yet there is no data to support this practice.

2.2 Study Justification

This study aimed to determine the most accurate method for obtaining a core biopsy of breast masses, thus minimizing the rate of missing a malignancy while avoiding unnecessary cost on the patient with the blanket application of ultrasound guided biopsies for all breast masses.

2.3 Study Questions

- Is ultrasound-guided biopsy of palpable breast masses superior to palpation-guided biopsy?
- What is the sensitivity, specificity and accuracy of ultrasound-guided and palpation-guided biopsy of palpable breast masses?

2.4 Objectives

2.4.1 Broad Objective

To determine the accuracy of ultrasound-guided versus palpation-guided biopsy of breast masses

2.4.2 Specific Objectives

a) Determine sensitivity, specificity, and accuracy of ultrasound-guided versus palpation-guided biopsy

b) Determine negative and positive predictive values of ultrasound-guided versus palpation-guided biopsy

2.4.3 Secondary Objective

Determine the accuracy in relation to the size of the tumor (i.e T-stage)

2.5 Hypothesis

2.5.1 Null Hypothesis

With respect to breast masses that are palpable, ultrasound-guided biopsy is not superior to palpation-guided biopsy

2.5.2 Alternative Hypothesis

For palpable breast masses, ultrasound-guided biopsy is superior to palpation-guided biopsy in terms of accuracy

CHAPTER THREE: MATERIALS AND METHODS

3.1 Study Design

Randomized controlled single blinded trial

3.2 Study Site

The study was conducted in the following areas of Kenyatta National Hospital

- Breast clinic
- Accident and emergency department
- Surgical wards
- Minor theatre
- Radiology department
- Pathology department

3.3 Study Population

3.3.1 Inclusion Criteria

- Palpable breast masses presenting to any clinical service department in KNH
- Age 18 and above
- T1,2 & 3 tumors
- Breast ultrasound showing BIRADS 3, 4 and 5
- Informed consent given

3.3.2 Exclusion Criteria

- Patients referred for neoadjuvant therapy
- Benign lesions not planned for surgery
- Previous history of breast surgery
- Previous history of biopsy of a breast mass
- Previous history of breast cancer

3.4 Sample Size Determination

In a prospective study done by Hari S. et al. over a period of 18 months, looking at image guided versus palpation guided core needle biopsy of palpable breast masses, a total of 72 women with palpable breast masses were randomized into two arms of 36 each i.e. palpation guided and image guided biopsy arms. Malignancy was found in 30 of 36 women (83.3%) in palpation guided biopsy arm and 27 of 36 women (75.0%) in image guided biopsy arm.

Sample size calculation for clinical superiority design [24] the formula is:

$$n = 2 \times (\frac{Z_{1-\propto} + Z_{1-\beta}}{d - \delta_0})^2 \times p \times (1-p)$$

n = Desired sample size

$Z_{1-\propto}$ = value from standard normal distribution corresponding to desired confidence level - one tail (Z=1.645 for 95% CI)

$Z_{1-\beta}$ = value from standard normal distribution corresponding to 80% power (0.842)

d = real difference between treatment effects i.e. 0.083 (the difference from the two arms from the Hari S. et al study i.e. palpation guided (83.3%) and image guided (75.0%), therefore 0.833 – 0.750 = 0.083.)

δ_0 = clinically acceptable margin i.e. 0.25 (From the Hari S. et al. study); 19 of the 36 women (52.8%) required repeat biopsy because of inadequate samples (7 of 19), suspicious findings (2 of 19) or imaging-histologic discordance (10 of 19). On repeat biopsy, malignancy was found in all cases of imaging-histologic discordance i.e. 52.6%, therefore for this study a conservative and clinically acceptable margin of 25.0% will be used.

p = the response rate of the standard treatment i.e. 83.3% from the palpation guided

The sample size calculation for this study is:

$$n = 2 \times (\frac{1.645 + 0.842}{0.083 - 0.25})^2 \times 0.833 \times (1 - 0.833) = 62$$

A sample of 62 patients was required for each arm in this study.

3.5 Sampling Technique and Data Collection

Within a period of 12 months (January 2019 to 2020), consecutive patients presenting at clinical service departments in KNH had their relevant history taken and an appropriate physical examination was carried out by the principal investigator. During the study period, 80 patients met the inclusion criteria and were served with a consent form.

3.6 Randomization

At this stage, the research assistant took over randomization, this is because the principal investigator had to be blinded to avoid selective bias as they have examined the patient who has met the inclusion criteria. Patients included in the study were randomized by the research assistant into one of two arms; ultrasound-guided core biopsy or palpation-guided core biopsy, by block randomization based on the different T-stages (T1, T2 and T3). Each block contained an equal number of envelopes for palpation and ultrasound guided biopsy (i.e. randomization rate 1:1). Consecutive consenting patients belonging to each block were served with an envelope containing the method to be used for obtaining the core biopsy.

3.7 Procedure

3.7.1 Palpation Guided Biopsies

Palpation-guided biopsy was performed by surgical residents who have been trained by consultant breast surgeons and found to be competent to do this procedure, this was carried out under supervision of the consultant in the minor theatre at the surgical outpatient clinic (SOPC). Consent for the procedure was obtained. Procedure was done using strict aseptic technique. A 14-gauge automated Core biopsy needle (BARD Magnum needles with BARD Magnum reusable gun) was used to take biopsies under local anaesthesia (2% lignocaine). The patient was positioned in a supine position with the ipsilateral arm raised above the head to stretch the skin of the breast. Local anaesthesia was injected at the site of needle insertion and through the needle path. The shortest straight path to the lesion was used, with the path kept parallel to the chest wall to avoid thoracic injury. A minimum of 4 samples were collected in different areas of the mass. Cores were immediately placed in a 10% buffered formalin solution and labeled with patients' name and file number. Tissue samples were prepared with Hematoxylin & Eosin staining and examined at the pathology department by a pathologist.

3.7.2 Ultrasound Guided Biopsy

Ultrasound guided biopsies were carried out by the radiologist at the radiology department. A General Electric logic 5 machine was used, with a linear probe, the frequency of which is 5-12 MHz. A 14-gauge automated Core biopsy needle (BARD Magnum needles with BARD Magnum reusable gun) was used to take biopsies under local anesthesia (2% lignocaine)[(25)]. The patient was positioned in a supine position with the ipsilateral arm raised above the head to stretch the skin of the breast. Local anaesthesia was injected at the site of needle insertion and through the needle path. The shortest straight path to the lesion was used, with the path kept parallel to the chest wall to avoid thoracic injury. During ultrasound-guided biopsy, the cores are taken from suspicious lesions, keeping away from areas of necrosis. Visualization of the tip of the needle within the suspicious areas was required before taking the biopsy. A minimum of 4 samples were collected in different areas of the mass. Cores were immediately placed in a 10% buffered formalin solution and labeled with patients' name and file number. Tissue samples were prepared with Hematoxylin & Eosin staining and examined at the pathology department by a pathologist.

3.8 Materials/Equipment

a) 14-gauge automated Core biopsy needle (BARD Magnum needles with BARD Magnum reusable gun)

b) General Electric logic 5 machine will be used, with a linear probe, the frequency of which is 5-12 MHz

c) Sterile gloves

d) Sterile gowns

e) Personal protective equipment (PPE): gloves, masks, aprons

f) Betadine solution

g) 10% buffered formalin solution

h) Sterile biopsy containers

i) General sterile instrument set and drapes

j) Normal saline (0.9% NaCl) solution

k) Sterile dressing

3.9 Collection of Results and Interpretation

Histology results were reviewed, and further management was dependent on the diagnosis according to standard guidelines. 1 Lesion with histologic-imaging discordant was in the ultrasound-guided biopsy arm, this underwent further diagnostic sampling using excision biopsy at the surgical department. Patients indicated for surgery continued with the study and definitive management was done (mastectomy or lumpectomy). Post-operatively, histology of the resected specimens was compared to the initial biopsy results and correlated with biopsy method used.

Biopsy results were considered true positives or true negative when histology of surgically excised lesions was concordant with the initial biopsy result. Discordant and inconclusive results were considered false negative when surgical excision confirmed a malignancy. Discordant results were considered false positive when surgical excision confirmed the mass was benign.

In cases where the patient was operated on at another facility, we contacted the hospital at which they were operated on, to obtain the final histology results. This was done with the consent of the patient for obtaining those records from the other facility. If the histology from the other facility was discordant with initial biopsy, we were going to obtain the blocks to have them reviewed by a second pathologist at KNH. However, this scenario did not arise.

3.10 Data Collection and Management

Data was collected using a structured data collection sheet (APPENDIX II) at every stage; in the clinic, during biopsy and after obtaining histology report.

Only complete data collection sheets were entered into the software for analysis. To ensure accurate data entering, a random sample of 10% of the data was cross-checked. Daily data back-up was done. The raw data is stored in the department of surgery for future referencing and the soft copy is password protected.

3.11 Variables

3.11.1 Independent Variables

- Demographic characteristics: age, residence
- History and physical exam: number of breast masses, duration of symptoms, smoking, alcohol intake, other symptoms (pain, nipple discharge), size and location of mass, breast volume
- Imaging findings: BI-RADS score
- Biopsy method
- Biopsy results

3.11.2 Dependent/Main Outcome Variables

- Sensitivity
- Specificity
- Positive predictive value
- Negative predictive value

3.12 Recruitment and Randomization

3.12.1 Data Analysis

The collected data was entered into the Statistical Package for Social Sciences version 20.0 (SPSS 20.0). Means were used to describe normally distributed variables like age. While medians were used to describe skewed variables like tumour size. Associations within groups were determined using dependent sample t-test, while those between groups, will be determined using independent sample t-test. A four by four table was used to determine sensitivity, specificity, positive and negative predictive values for each investigative modality. Diagnostic accuracy was calculated in both the palpation and image guided groups as a proportion of correctly classified lesions (true positives+ true negatives) among all

subjects. A p value of <0.05 will be considered statistically significant for a 95% confidence interval.

3.13 Quality Assurance

- Palpation guided biopsies were performed by surgical residents who have been trained by consultant breast surgeons and found to be competent to do this procedure, this was carried out under supervision of the consultant
- Ultrasound guided biopsies were performed by consultant radiologists
- Histology specimens were examined by a consultant pathologist, in case when there was disagreement on the final diagnosis, a panel of pathologists examined the specimen and arrived at a final conclusive diagnosis by consensus.

3.14 Ethical Considerations

Institutional consent was sought from the Department of Surgery, University of Nairobi (UON) and Kenyatta National Hospital, Radiology department and Ethics and Research Committee of KNH (Appendix V). Informed consent was obtained from the patients (Appendix I and II). Confidentiality and privacy was observed. Confidentiality is ensured by non-disclosure of data collected to third parties and data collected was used for this research purposes only and anonymity was ensured by use of patient codes for identification instead of participants' names.

The raw data is stored in the department of surgery for future referencing and the soft copy is password protected. There is no conflict of interest for the patient, investigators or the institution. Patients had a right to withdraw from the study at any stage.

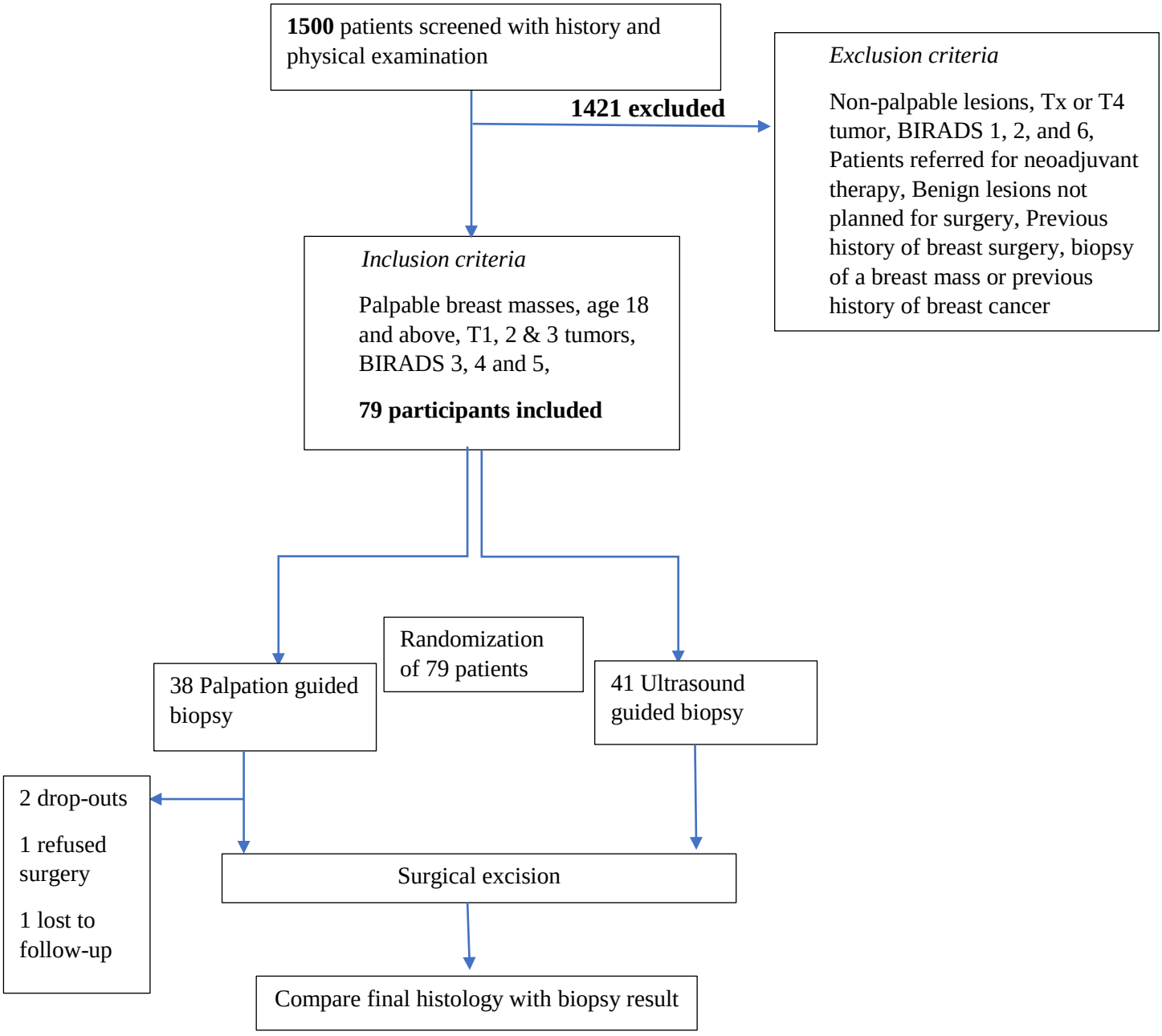
3.15 Study Results Dissemination Plan

Results have been made available to the department of surgery UON and KNH, college of health sciences library and the head of department for radiology, KNH. The study results will be published online for access to anyone who might require them. This will be done with consent from KNH research department.

CHAPTER FOUR: RESULTS

One thousand five hundred patients were screened at the different outpatient locations. 1421 patients were excluded from the study because they did not meet the inclusion criteria. A total of 79 patients met the inclusion criteria and were recruited into the study. Thirty-eight participants were enrolled into the palpation guided group and 41 into the ultrasound guided group. However, 2 dropped out of the study (from the palpation-guided group) before definitive surgical intervention and hence were not included in the analysis.

4.1 Patient Flow Chart



4.2 Baseline Characteristics

Baseline characteristics between the two groups (ultrasound-guided and palpation-guided) were compared. There were no statistically significant differences between the two groups, except for the parity, number of cores and duration of symptoms, which show a p value of 0.008, 0.05 and 0.02, respectively (Table1). However in a multivariate analysis, none was found to independently affect the results (Table 2).

Table 1: Comparison of baseline characteristics between the two groups

Variable		**Palpation Guided**	**Ultrasound Guided**	**P value**
Total number (%)		N37 (47.4%)	N41 (52.6%)	
Age	Means	42.2±16.6	43.0±13.0	0.80
Post-Menopausal	No	25(45.5)	30(54.5)	0.63
	Yes	12(52.2)	11(47.8)	
Parity	Nulliparous	12(80)	3(20)	0.008
	Multiparous	25(39.7)	38(60.3)	
Duration of symptoms(months)	Means	17.1± 13.1	8.2±10.6	0.02
Number of masses	Means	1.3±0.7	1.2±0.6	0.50
Mass Laterality	Left	18(42.9)	24(57.1)	0.73
	Right	14(51.9)	13(48.1)	
	Bilateral	5(55.6)	4(44.4)	
Number of masses	One	30(49.2)	31(50.8)	0.23
	Two	2(22.2)	7(77.3)	
	More than two	5(62.5)	3(37.5)	
Anatomical Location	UOQ	17(44.7)	21(65.3)	0.96
	LOQ	10(55.6)	8(44.4)	
	UIQ	4(50)	4(50)	
	LIQ	4(50)	4(50)	
	Retroareolar	2(40)	3(60)	
T-stage	T1	9(25.0)	12 (29.2)	0.40
	T2	18(50)	18(43.9)	
	T3	9(25.0)	11(26.8)	
BIRADS	BIRAD 3	15(41.7)	10(24.4)	0.28
	BIRAD 4	16 (43.2)	20(48.8)	
	BIRAD 5	6(6.6)	11(26.8)	
Number of Cores	Means	5.0±1.9	4.2±1.0	0.05

Table 2: Multivariate analysis

Variable	Wald	OR	95% C.I. for EXP(B)	
			Lower	Upper
Parity	4.330	0.166	0.031	0.901
Complaint duration	0.911	0.982	0.945	1.020
Adequate cores	1.712	0.741	0.472	1.161

4.3 Definitive Histopathologic Diagnosis

There was a total of 31 (40.25%) benign lesions, ranging from fibroadenoma to benign phylloides tumor (Figure 1).

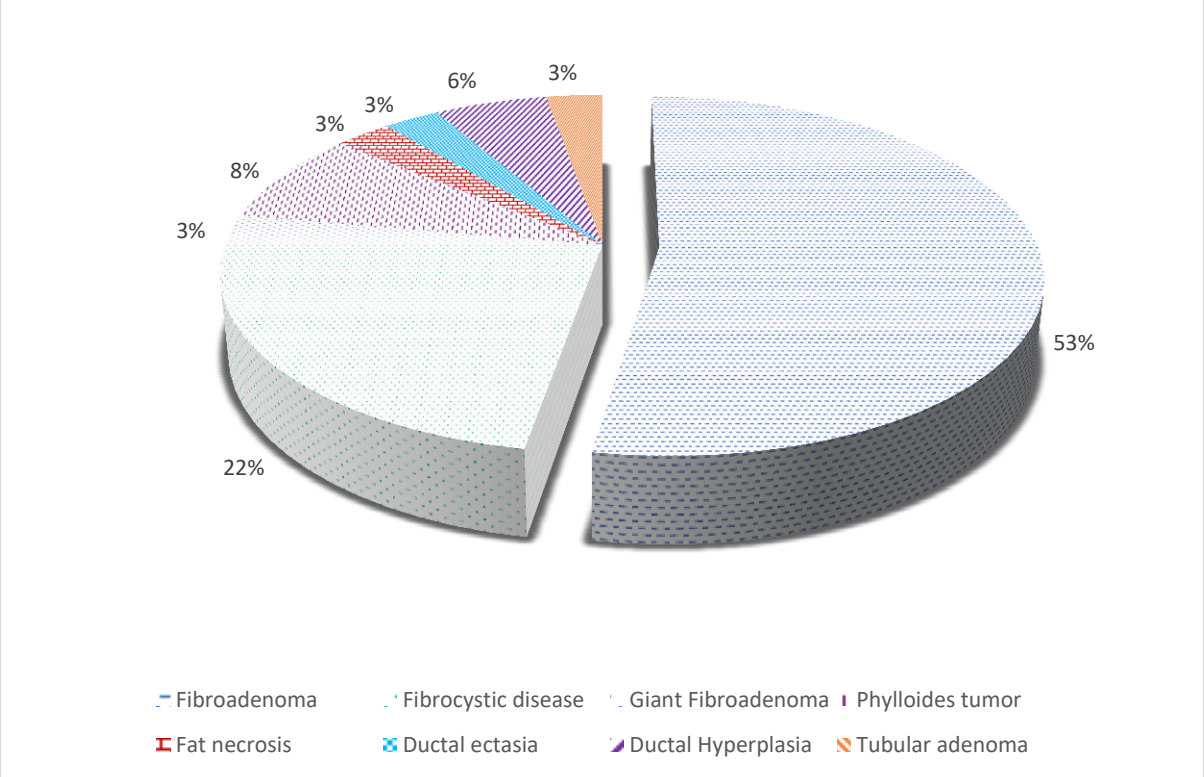


Figure 1: Distribution of benign breast masses

One patient had low grade DCIS and 46 patients (59.7%) had a malignant disease (Figure 2).

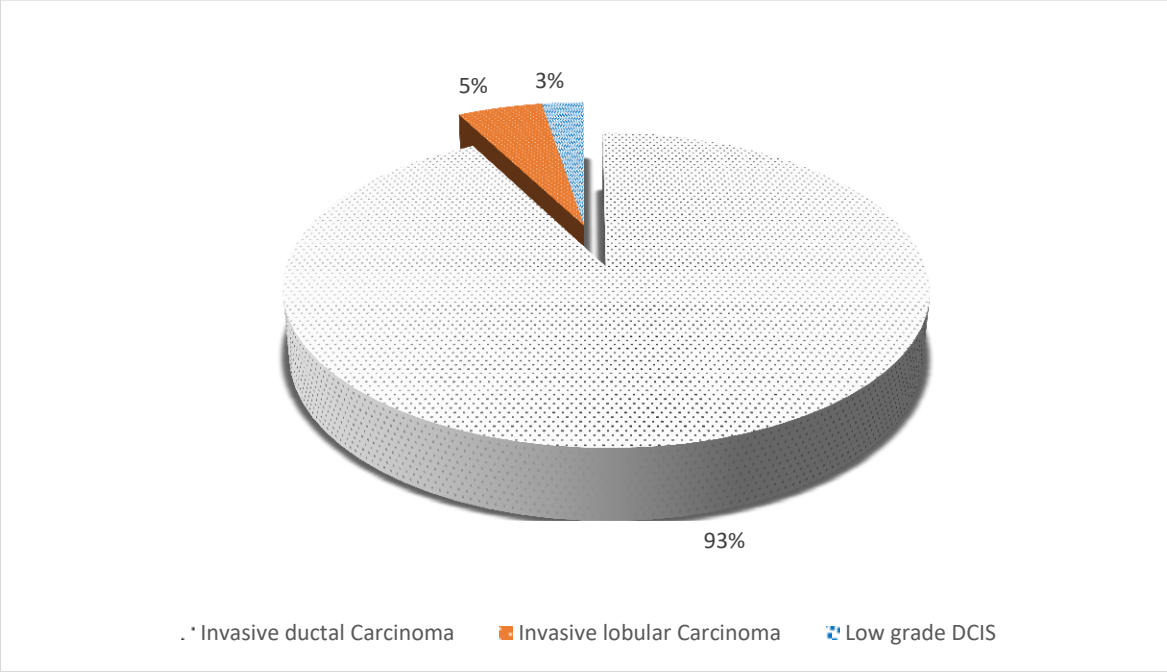


Figure 2: Distribution of malignant breast masses

One sample had imagine-histologic discordance requiring a repeat biopsy, this was from the ultrasound-guided biopsy arm. Subsequently, the participant underwent excision biopsy, which confirmed malignant disease.

4.4 Diagnostic Performance of Both Tests

The sensitivity and specificity were calculated using a 4x4 table for both diagnostic tests (Table 3 and 4).

Table 3: A 4x4 table showing the biopsy results and final histologic diagnosis in the palpation-guided biopsy group

		outcome		Total
		Malignant	Benign	
Test result	Malignant	20	0	20
	Benign	3	13	16
	Total	23	13	36

Table 4: A 4x4 table showing the biopsy results and final histologic diagnosis in the ultrasound-guided biopsy group

		Outcome		Total
		Malignant	Benign	
Test result	Malignant	22	0	22
	Benign	1	18	19
	Total	23	18	41

The sensitivity for palpation-guided biopsy was 87% while that for ultrasound-guided biopsy was higher at 95.7%. The specificity for diagnosing malignancy and the positive predictive value (PPV) were 100% for the two methods. Ultrasound-guided biopsy had a higher negative predictive value (NPV) at 94.7%, compared to 81.3% for palpation-guided biopsy. There was no case of false-positive results in our study. However, the false negative rate was higher for palpation-guided biopsy at 18.8% while that for ultrasound-guided biopsy was 5.3%. The true positive rate was 100% for both methods. The true negative rate was 81.3% for palpation-guided biopsy and 94.7% for ultrasound-guided biopsy.

4.5 ROC Curves

For ultrasound-guided biopsy, the area under the curve is equal to 0.54, cut off mass size for positivity is 2.5 cm (Figure 3). For palpation guided biopsy, the area under the curve is equal to 0.538, cutoff mass size for positivity is 2.5cm (Figure 4).

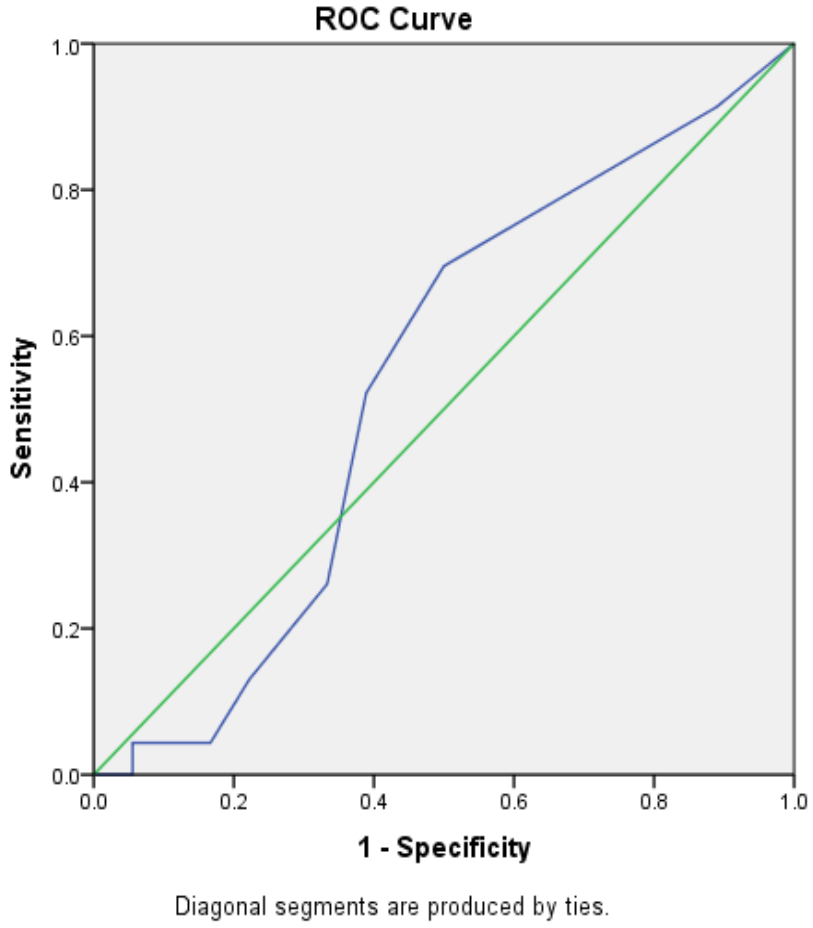


Figure 3: Ultrasound-guided biopsy ROC

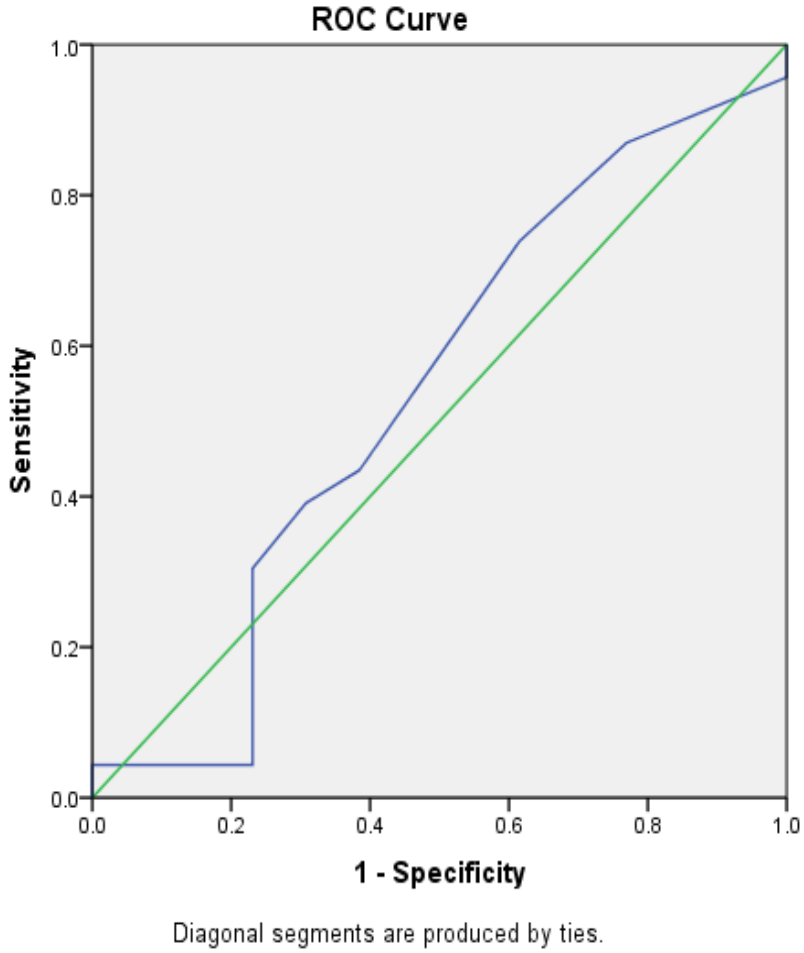


Figure 4: Palpation-guided biopsy ROC

CHAPTER FIVE: DISCUSSION, CONCLUSION & RECCOMMENDATIONS

5.1 Discussion

The accurate evaluation of a suspicious breast mass depends on adequate sampling of tissue for histologic diagnosis [26]. A minimum of 4 to 5 cores is usually required to improve the sensitivity for the diagnosis of cancer [27–29]. The number of cores in our population were 5.0±1.9 for the palpation-guided biopsy arm and 4.2±1.0 for the ultrasound-guided biopsy arm. In the study by Hari et al, the average number of cores obtained in each arm was 5 in both groups (18). However in our study, the sensitivity on either arm was not affected as the difference between the average number of cores was not statistically significant (OR = 0.74).

Our data reveals the propensity of breast masses to be on the left side more than the right. More than half 53.8% (n= 42) had left sided breast masses, while only 11.5% (n=9) had right sided breast masses, the remaining patients had bilateral masses, this has not been reported in other studies. It is noted from other studies that breast cancer tends to develop more on the left side than on the right [30,31]. However the reason for this remains unclear. Additionally, 49% of the breast masses in our patient population were located in the upper outer quadrant, while the remaining 51% are distributed between other locations within the breast. This is similar to other studies that report a higher propensity of breast mass location within the upper outer quadrant due to the higher density of breast tissue [32].

5.1.1 Diagnostic Performance of Both Tests

The results of our study show that ultrasound-guided biopsy is superior with a sensitivity of 95.7% compared to 87% for palpation-guided biopsy. Comparing with the study by Hair et al that had a similar methodology, it is noted that the sensitivity for image-guided biopsy in their study is almost similar at 96.3% , while that for palpation-guided biopsy is much lower (46.7%) than in our study [18]. The relatively higher sensitivity rate of palpation-guided biopsy that is demonstrated in this study, compared to the study by Hari et al. , may be explained by the higher number of cores obtained in the palpation-guided biopsy group which would result in a higher yield[33].

The results by Lorenzen and colleagues had revealed a sensitivity of 79% for palpation-guided biopsy, and 98% for ultrasound-guided biopsy, albeit retrospectively [20]. The negative predictive value (NPV) in our study is 94.1 % and 81.3 % for ultrasound-guided and palpation-guided biopsy, respectively. This was significantly different from the study by Hari

et al. whereby they had a negative predictive value of 27.3% for the palpation-guided biopsy group, while that for ultrasound-guided biopsy was 90%.

The specificity in obtaining a correct diagnosis (benign or malignant) and the positive predictive values were 100 % for the two biopsy methods. This is similar to the reported specificity in the Indian study by Hari et al [18].

There was no case of false positive results in our study. The same has not been reported in previous studies [18,20]. However, false negative results were reported in our study, at a rate of 18.8% for palpation-guided biopsy, and a significantly lower rate of 5.9% for ultrasound-guided biopsy. Indicating a significant risk of missing a malignancy for the palpation-guided method, despite the relatively low number of cases per arm. This is comparable to the results from the findings by Shah and colleagues whereby they detected a miss rate of 13.3 % for palpation-guided biopsy compared to 3.6% for biopsies done with ultrasound guidance[21]. Similarly, the study by Lorenzen and colleagues reported a false negative rate of 20.7% with palpation-guidance, while the false negative rate for ultrasound-guided biopsy was 2.2%.

In our population, we had only one case of image-histologic discordance. Surprisingly, this was a biopsy done with ultrasound guidance. Comparing with the study by Hari et al, they had 10 cases of image-histologic discordance, and all cases were in the palpation guided biopsy group, the repeat biopsy of which proved to be malignant. They did not report a similar incident in the ultrasound-guided biopsy group.

5.1.2 Accuracy within the Different T-Stages

Our secondary objective was to observe if breast mass size had an effect on the accuracy of the two diagnostic tests. In the study by Lorenzen and colleagues, they observed that the sensitivity was dependent on the breast mass size, where 82% of their false negative cases had a breast mass of 3 cm or smaller(20). However, they collected data retrospectively, where there might have been selection bias in assigning patients to either group. When comparing the different T-stages (breast mass size) in our study, it was observed that there was no statistically significant difference between the two groups ($p=0.4$). Similarly, the study by Hari et al demonstrated that the sizes of the lesions were similar between the two groups, hence it did not affect the superiority of ultrasound-guided biopsy. The ROC curve demonstrates that the cut-off size for sensitivity with both tests is 2.5 cm, however we cannot make a conclusion in view of the small sample size. We found no other studies comparing the two methods in relation to breast mass size.

5.2 Conclusions

This study has demonstrated that, at Kenyatta National Hospital, in terms of sensitivity and specificity of ultrasound guided biopsy is indeed superior to palpation guided biopsy, with a higher sensitivity and a lower false negative rate. A conclusion cannot be made with regards to the effect of breast mass size on the sensitivity and specificity due to the small sample size.

5.3 Study Limitations

- Patients lost to follow-up resulted in incomplete data collection
- Inability to quantify inter-observer variability in palpation guided biopsies.
- Inability to obtain the desired sample size of 124 because many patients were referred to KNH having had a biopsy done at an external facility.

5.4 Recommendations

- Ultrasound guided biopsy should be standard method for obtaining core biopsies of breast masses at KNH, this can be accomplished with the inclusion of the procedure charges under the National Health Insurance Fund (NHIF).
- Design a similar study while capping the number of maximum cores to be obtained, in order to control for that possible confounding factor.
- Examine the effect of the breast mass size (T-stage) on the accuracy of the two methods. This may require a multicenter study in order to obtain an adequate number of patients for each T-stage (i.e. T1,T2 and T3)

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APPENDICES

Appendix I: Consent Form (English Version)

"ACCURACY OF ULTRASOUND-GUIDED VERSUS PALPATION-GUIDED BIOPSY OF PALPABLE BREAST MASSES IN WOMEN AT KNH: A RANDOMIZED CONTROLLED TRIAL"

This informed consent is for patients presenting with palpable breast masses at the breast clinic at Kenyatta national hospital. We are requesting these patients to participate in this research project whose title is "Accuracy of ultrasound-guided versus palpation-guided biopsy of breast masses: a randomized controlled trial"

Principal investigator: Dr. Maryam A. Badawy

Institution: School of Medicine, Department of Surgery, University of Nairobi

Supervisors: Dr. Dan Kiptoon, Dr. Nyaim Opot, Dr. Marilyn Omondi and Dr. Wangari Maina

This informed consent has three parts:

1. Information sheet (to share information about the research with you)
2. Certificate of consent (for signatures if you agree to participate)
3. Statement by the principal investigator.

You will be given a copy of the full informed consent form

Part I: Information Sheet

My name is Dr. Maryam A. Badawy, a postgraduate student at the University of Nairobi's School of Medicine. I am carrying out a study to determine the '**Accuracy of ultrasound-guided versus palpation-guided biopsy of palpable breast masses in women at KNH'**. This will be determined by data collection through filling a data collection sheet. The findings may form a useful baseline of the most accurate method for breast mass biopsy at KNH.

Purpose of the Study

The study aims at determining the most accurate method for biopsy of breast masses at KNH (between palpation-guided and ultrasound-guided biopsy). This will assist in developing local protocols for use during the management of breast masses, will improve patient care and minimize the number of missed cases.

Voluntariness of Participation

I am inviting you to participate in my study and you are free to either agree immediately after receiving this information or later after thinking about it. You will be given the opportunity to ask questions before you decide. You may talk to anyone you are comfortable with about the research before deciding. After receiving this information concerning the study, please seek clarification from myself if there are words or details which you do not understand.

Procedure

As part of the evaluation of a breast mass, it is standard procedure that a tissue sample is taken to detect the nature of the mass, whether it is benign or malignant. The sample is taken by means of a needle inserted into the mass to obtain the tissue sample. Once the sample is taken, it is sent to the pathology lab for analysis. In this study, the method for sample acquisition is being tested. If you agree to participate, your sample will be taken with either the assistance of an ultrasound machine or without. Both methods are normally used.

The results of the biopsy will be compared with histology results obtained after surgery if your diagnosis requires you to undergo surgery. If surgery is not required, you will be followed up at our clinic for a minimum of 6 months. Should you decide to be operated on at another facility, by signing this consent form, you hereby consent for us to obtain the histology result from the other facility.

Benefits of Participation

There will be no monetary benefits in your participation into this study other than contributing to medical research.

Confidentiality

If you agree to participate, you will be asked to provide personal information and other details regarding your condition. All the information you provide will be kept confidential and only the researchers will see it. Your name will not appear in any research document. The information will be identified by a number and only the researchers can relate the number to you as a person. Your information will not be shared with anyone else unless authorized by the Kenyatta National Hospital/University of Nairobi-Ethics and Research Committee (KNH/UON-ERC).

Risks

Your involvement in this research will be through an interview, clinical evaluation and follow-up. Should your sample be collected using ultrasound, kindly be informed that ultrasound has an excellent safety record. It is based on non-ionizing radiation, unlike regular

X-rays. As with any sampling procedure, there is a slight risk of missing the mass during the biopsy, thus necessitating repeating the biopsy.

Biopsy procedure by either method carries the risk of pain, bleeding and infection. These will be addressed with analgesics, compression and aseptic technique,respectively.

Right to withdraw from the study

You may stop participating at any time with no consequences whatsoever. Participation in this study is out of your own free will, you will not be denied medical care in case you refuse to participate or withdraw from the study.

All the information that you give us will be used for this research only. The results of this research will be disseminated to you in your next routine follow-up visit. This proposal has been reviewed and approved by the KNH/UON-ERC, for a maximum duration of two years, which is a committee whose work is to make sure research participants like yourself are protected. It was submitted to them through the Chairman of the Department of Surgery at the School of Medicine of the University of Nairobi, with the approval of the four supervisors.

The contact information of these people is given below if you wish to contact any of them;

- **Principal investigator:**

  Dr. Maryam Badawy

  Department of Surgery, School of Medicine, University of Nairobi

  P. O. Box 19676 KNH, Nairobi 00202

  Mobile: 0718124704

- **University of Nairobi research supervisors**

  Dr. Dan Kiptoon

  Department of Surgery, School of Medicine, University of Nairobi

  P. O. Box 19676 Nairobi-00200, KNH

  Tel: 0202726300

  Dr. Elly Nyaim Opot

  Department of Surgery, School of Medicine, University of Nairobi

  P. O. Box 19676 Nairobi- 00200, KNH

  Tel: 0202726300

  Dr. Marilynn Omondi

  Department of Surgery, School of Medicine, University of Nairobi

  P. O. Box 19676 Nairobi- 00200, KNH

  Tel: 0202726300

- **Kenyatta National Hospital research supervisor**

  Dr. Wangari Maina

  Department of Radiology, Kenyatta National Hospital

  P.O Box 20723 Nairobi-00202

  Tel. 020-2726300

If you have any questions on your rights as a participant, contact the Kenyatta National Hospital/University of Nairobi-Ethics and Research Committee on;

P. O. Box 20723 KNH, Nairobi 0020

Phone: 2726300 Ext. 44355

Part II: Consent Certificate by Patient

I…… freely give consent to take part in the study conducted by Dr. Maryam Badawy, the nature of which has been explained to me by her. I have been informed and have understood that my participation is entirely voluntary and that I am free to withdraw my consent at any time if I so wish and this will not in any way alters the care given to me. The results of the study may directly be of benefit to myself and other patients and more significantly, to the medical profession. The results will be shared in my follow up visits.

Signature/ thumb print……

Date…….

Day/ Month/Year

Statement by the witness if participant is illiterate

I have witnessed the accurate reading of the consent form to the participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Name of witness……..

Signature of witness……Date…….

Day/Month/Year

Part III: Statement by the Researcher

I have accurately read out the information sheet to the participant, and to the best of my ability, I have made sure the participant understands the following:

- Refusal to participate or withdrawal from the study will not in any way compromise the quality of care and treatment given to the patient.
- All information given will be treated with confidentiality.
- The results of this study might be published to enhance the knowledge on the accuracy of ultrasound guided versus palpation guided biopsy of palpable breast masses. I confirm that the participant was given an opportunity to ask questions about the study, and all questions asked have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Informed Consent Form has been given to the participant

Name of researcher taking consent…….

Signature of researcher taking consent……..…… Date…….……

Appendix II: Consent Form (Swahili Version)

I Sehemu ya kwanza: Maelezo ya daktarin mtafiti

Kwa majina naitwa Dr. Maryam Badawy na ni mwanafunzi wa upasuaji katika Chuo Kikuu cha Nairobi. Nafanya utafiti wa kuangalia **"Accuracy of ultrasound-guided versus palpation-guided biopsy of palpable breast masses in women at KNH: a randomized controlled trial".** Ningependa kukuchagua katika utafiti huu.

Umuhimu wa utafiti huu

Utafiti huu utasaidia madaktari kuelewa tofauti katika usahihi wa kuchukua biopsy ya uvimbe wa matiti kutumia ultrasound na kutotumia kifaa hiki/kutumia hisia. Matokeo ya utafiti huu yatasaidia namna tutakavyo tibu wagonjwa wenye uvimbe wa matiti katika hospitali kuu ya Kenyatta kwa kutengeneza itifaki zitakazo fuatwa baadae.

Utaratibu

Katika uchunguzi wa uvimbe wowote wa matiti, ni lazima kuchukuliwe kinyama/biopsy kutokana na uvimbe huo. Kuna njia mbili za kuchukuwa kinyama hiki; moja ni kutumia ultrasound na pili kutumia hisia za daktari bila ultrasound. Katika utafiti huu tunajaribu kulinganisha usahihi wa njia hizi mbili, kwahivyo wewe unaweza kuangukia katika mkono wowote wa utafiti.

Uhuru wa kujihusisha na kujitoa katika utafiti

Kuhusika kwako katika utafiti huu hauna malipo yeyote ila ni kwa hiyari yako mwenyewe na pia unaweza kujiondoa kwenye utafiti wakati wowote bila kuhatarisha matibabu yako katika kospitali kuu ya Kenyatta.

Faida ya kujihusisha kwenye utafiti

Kuhusika kwako kwenye utafiti huu hauna malipo ya zaidi, lakini tutakuhakikishia tumefuatilia majibu ya biopsy yako kwa haraka.

Madhara

Kuhusika kwako kwenye utafiti huu hautakua na madhara makubwa dhidi ya afya yako. Ukiangukia kwenye mkono wa ultrasound, ni muhimu kujuwa kuwa kifaa hiki hakina mionzi, kwa hivyo ni kifaa ambacho hakina madhara. Ukiangukia kwenye mkono wa pili, kuna uwezekano wa daktari kukosa sehemu inayofaa kufanyiwa biopsy au uvimbe, kwa hivyo biopsy yako itabidi irudiwe.

Kufanyiwa biopsy kwa njiya yeyote huenda mtu ukapata maambukizi, uchungu ama kutokwa na damu. Utapatiwa madawa ikiwa umepatikana na matatizo hayo.

Siri

Majibu yako ya biopsy hatutoeleza mtu yeyote isipokuwa wewe. Jina lako halitaandikwa kwenye fomu yeyote. Matokeo ya utafiti huu yataelezwa kwako na kwa wahusika wowote katika siku maalum itakayo pangwa.

Unaweza kuuliza maswali yeyote kuhusu utafiti huu na ukiridhika tafadhali ijaze fomu ya idhini iliyopo hapa chini. Unaweza pia kuuliza swali lolote baadaye kwa kupiga simu ya mtafiti mkuu ama mkuu wa idara ya upasuaji katika chou kikuu cha Nairobi ama walimu wasimamizi wa utafiti ukitumia nambari za simu zifuatazo;

Katibu wa utafiti, hospitali kuu ya Kenyatta na chou kikuu cha Nairobi, sanduku la posta 20723 KNH, Nairobi 00202. Nambari ya simu : 2726300-9

- **Mtafiti**

  Daktari Maryam Badawy

  Idara ya upasuaji, shule ya tiba, chou kikuu cha Nairobi

  Sanduku la posta 19676 KNH Nairobi 00202

  Nambari ya simu 0718124704

- Walimu wasimamizi wa chou kikuu cha Nairobi:

a) Daktari Dan Kiptoon

Idara ya upasuaji, shule ya tiba, chou kikuu cha Nairobi

Sanduku la posta 19676 KNH Nairobi 00202

Tel: 0202726300

b) Dr. Elly Nyaim Opot

Idara ya upasuaji, shule ya tiba, chou kikuu cha Nairobi

Sanduku la posta 19676 KNH Nairobi 00202

Tel: 0202726300

c) Dr. Marylin Omondi

Idara ya upasuaji, shule ya tiba, chou kikuu cha Nairobi

Sanduku la posta 19676 KNH Nairobi 00202

Tel: 0202726300

- Mwalimu msimamizi wa hospitali kuu ya Kenyatta

d) Dr. Wangari Maina

Idara ya radiolojia, Hospitali kuu ya Kenyatta

Sanduku la posta 20723 KNH Nairobi 00202

Tel: 02 2724722

II Sehemu ya pili: Idhini ya mgonjwa

Mimi (jina)……. kwa hiari yangu nimekubali kushiriki katika utafiti huu unaofanywa na Daktari Maryam Badawy kutokana na hali ambazo nimeelezwa na sio kwa malipo ama shurutisho lolote.

Nimeelewa kwamba nina weza kujiondoa wakati wowote nitakapo na hatua hii haita hatirisha matibabu ninayoyapata. Matokeo ya utafiti yaweza kuwa na manufaa kwangu ama kwa wagonjwa wengine kwa jumla na hata madaktari wenyewe, kwa kuendeleza elimu. Matokeo nitaelezwa siku nyengine nitakapokuja kliniki.

Sahihi/alama ya kidole cha gumba……

Tarehe…….

Siku/Mwezi/Mwaka

Jina la shahidi…….

Sahihi……..

Tarehe…….

Siku/ Mwezi/Mwaka

III Sehemu ya tatu: Dhibitisho la mtafiti

Hii nikuidhinisha ya kwamba nimemueleza mgonjwa kuhusu utafiti huu na pia nimempa nafasi yakuuliza maswali.Nimemueleza yafuatayo;

- Kwamba kushiriki ni kwa hiari yake mwenyewe bila malipo.
- Kushiriki hakutasababisha madhara ama kuhatirisha Maisha kamwe.
- Anaweza kujiondowa kutoka kwa utafiti huu wakati wowote bila kuhatirisha matibabu anayoyapata katika hospitali kuu ya Kenyatta
- Habari ambazo atapeana hazita tangazwa hadharani kila ruhusa kutoka wake na pia kutoka kwa mdhamini mkuu wa utafiti wa hospitali kuu ya Kenyatta na chou kikuu cha Nairobi.

  Jina la mtafiti……

  Sahihi……Tarehe……

Appendix III: Data Collection Sheet

I. Demographics

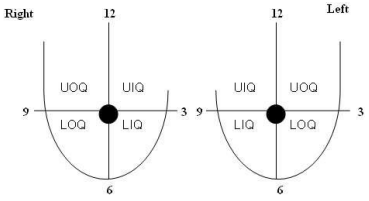
- Age…….. years
- IP number ……..
- Residence …….....
- Contact ……..

II. History

- Complaint ☐ palpable mass ☐ breast pain ☐ nipple discharge ☐ other ……..
- Duration of complaint …… days/weeks/months/years (circle whichever is applicable)
- Number of palpable masses ☐one mass ☐ 2 masses ☐ more than 2
- Side of breast mass ☐ right ☐ left ☐ bilateral
- Parity …….
- Menopause ☐ yes ☐ no
- Previous history of breast cancer ☐ yes ☐ no
- Family history of breast cancer (in a first degree relative) ☐ yes ☐ no
  - ➢ Number of first degree relatives affected ……

III. Examination

- Number of masses ☐one ☐ 2 ☐ more than 2
- Side of mass ☐ right ☐ left ☐ bilateral



- Location of mass (quadrant)……..
- Size of breast mass (largest diameter)…….cm

IV. Mammographic/ US finding at presentation:

- ➢ Mass size (largest diameter)…….
- ➢ BIRADS score…….

V. Biopsy procedure

- Method: ☐ Palpation guided ☐ Ultrasound guided
- Number of cores obtained ……

- Immediate complication…….

VI. Histology report

- Initial biopsy results…….....
- Number of adequate cores…….
- Post-operative histology results ……....

VII. Receptor status:……

VIII. Repeat biopsy needed ☐ Yes ☐No

Result of repeat biopsy ……....

IX. Reason for repeat biopsy

☐ imaging-histologic discordance ☐ insufficient sample ☐ NA

Appendix IV: Study Instruments/Equipment

a) 14-gauge automated Core biopsy needle (BARD Magnum needles with BARD Magnum reusable gun)

b) General Electric logic 5 machine will be used, with a linear probe, the frequency of which is 5-12 MHz

c) Sterile gloves

d) Sterile gowns

e) Personal protective equipment (PPE): gloves, maskes, aprons

f) Betadine solution

g) 10% buffered formalin solution

h) Sterile biopsy containers

i) General sterile instrument set and drapes

j) Normal saline (0.9% NaCl) solution

k) Sterile dressing

Appendix V: Ethical Approval

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/15

18th January, 2019

KENYATTA NATIONAL HOSPITAL APPROVED 18 JAN 2019 KNH/UoN-ERC P. O. BOX 20723 - 00202 NAIROBI

Dr. Maryam Badawy
Reg. No. H58/80776/2015
Dept. of Surgery
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Badawy,

RESEARCH PROPOSAL – ACCURACY OF ULTRASOUND- GUIDED VERSUS PALPATION-GUIDED BIOPSY OF PALPABLE BREAST MASSES IN WOMEN AT KENYATTA NATIONAL HOSPITAL; A RANDOMIZED CONTROLLED TRIAL (P663/09/2018)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 18th January 2019 – 17th January 2020.

This approval is subject to compliance with the following requirements:

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

Protect to discover

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

Yours sincerely,

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

c.c. The Principal, College of Health Sciences, UoN
The Director, CS, KNH
The Chairperson, KNH-UoN ERC
The Assistant Director, Health Information, KNH
The Dean, School of Medicine, UoN
The Chair, Dept. of Surgery, UoN
Supervisors: Dr. Dan Kiptoon, Dr. Elly Nyaim Opot, Dr. Marilynn Omondi

Appendix VI: Certificate of Plagiarism

turnitin Turnitin Originality Report

ACCURACY OF ULTRASOUND-GUIDED VERSUS PALPATION-GUIDED BIOPSY OF PALPABLE BREAST MASSES IN WOMEN AT KENYATTA NATIONAL HOSPITAL: A RANDOMIZED CONTROLLED TRIAL by Maryam Badawy

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