# EFFECTIVENESS OF ULTRASOUND GUIDED FINE NEEDLE ASPIRATION IN DETECTING AXILLARY LYMPH NODE METASTASES IN EARLY BREAST CANCER AT KENYATTA NATIONAL HOSPITAL.

This dissertation is submitted as part fulfilment of the award of the Degree of Masters of Medicine (General Surgery), University of Nairobi (UON).

By

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DECLARATION

I declare that this study is my original work and has not been presented for the award of any degree at any other institution or university.

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APPROVAL BY THE DEPARTMENT

The research proposal has been presented at the surgical departmental meeting and is hereby approved for presentation to the Kenyatta National Hospital Ethics and Research committee.

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## ABBREVIATIONS

| | |
|---|---|
| ALND | Axillary lymph node dissection |
| CNB | Core Needle Biopsy |
| ERC | Ethical and Research Committee |
| FNA | Fine needle aspiration |
| KNH | Kenyatta National Hospital |
| LN | Lymph Node |
| MRM | Modified Radical Mastectomy |
| NHLNF | None Hilar Lymph Node Flow |
| NPV | Negative predictive value |
| PPV | Positive predictive value |
| ROC | Receiver operator curve |
| SLNB | Sentinel Lymph Node Biopsy |
| U/S | Ultrasound |

ABSTRACT

**Background:** Breast cancer is the second commonest malignancy among women in Kenya. Axillary nodal status is key to its management. Ultrasound guided FNA and sentinel lymph node biopsy (SLNB) can be used. In our set up axillary staging is mainly performed by clinical examination and histopathological results of axillary dissection. The latter has a high morbidity. There is paucity of studies locally involving US guided FNA in staging the axilla. This study aimed to compare the effectiveness of Ultrasound guided FNA cytology in axillary nodal status staging with axillary lymph node dissection.

**Objective:** To determine effectiveness of ultrasound guided FNA in detecting axillary lymph node metastasis in early breast cancer at KNH

**Study Design:** A Prospective Study.

**Setting:** Kenyatta National Hospital, Nairobi Kenya

**Methodology:** This was a 12 month prospective study done between March 2016 and March 2017. Seventy nine female surgical patients seen in surgical outpatient clinics and wards diagnosed with early breast cancer were participated. The bio data including age and sex of the patient, size of the primary tumour were taken. Axillary ultrasound for determination of the presence of lymph node, its characteristics was done. Axillary lymph node ultrasound guided FNA was done and specimen taken for cytology. Patients then underwent modified radical mastectomy with ALND. The histopathology results of the lymph node FNA was done. Modified radical mastectomy outcome was taken as the definitive diagnosis.

**Results;** A total of seventy nine patients were enrolled between a period of March 2016 and to May 2017. A total of 51patients had results of axillary u/s guided FNA

and ALND .Patients who didn't have axillary FNA results were 19 while 6 patients were missing ALND results. Patients with negative FNA of axilla were 19 while a total of 13 patients had axilla FNA which was non diagnostic. Twenty five patients had positive lymph nodes on FNA . Data was entered in an Excel, cleaned then exported to SPSS version 23 for analysis. The FNA results of the axilla in 51 patients were compared with ALND. The sensitivity of u/s guided FNA was 90%.Only two patient who had non diagnostic results on FNA cytology returned positive results on ALND. The nondiagnostic (indeterminate) was treated as negative. The positive predictive value was high at 94.74%.The specificity was high at 96.88. % . The negative predictive value was high at 93.9%.The ultrasound results of axillary lymph node morphology was recorded. The average size of axillary lymph nodes was 2.5cm.The primary tumour average T2.

**Conclusion:** Ultrasound guided FNA cytology of the axilla may be useful in predicting axillary lymph node metastasis and determining patients who may require ALND for the positive metastatic nodes or a less morbid procedure of sentinel lymph node biopsy for a negative axillary nodes.

# CHAPTER ONE

# INTRODUCTION

## 1.1 **Background**:

Breast cancer staging is performed primarily through the Tumour size (T), Nodal involvement (N) and screening for metastasis (M). The evaluation for the T and N has remained clinical with a difference pathological staging prefix after histopathology.

The axillary lymph nodes receive 75% of lymphatic from the breast [1]. Cancer cells are transported through this drainage into the axilla, where they infiltrate the nodes causing it to enlarge and subsequently fuse forming a conglomerate mass clinically becoming palpable. Later the cells may grow outside the nodes and get fixed to the extra nodal tissue.

Although more than 95% of the women who die of breast cancer have distant metastases, the most important prognostic correlation of disease-free and overall survival is axillary lymph node status [1, 2]. Women with node-negative disease have less than a 30% risk of recurrence, compared with as much as a 75% risk for women with node-positive diseases [1].

It is this interest in prognostic advantage of axillary involvement which has invoked several methods of staging the axilla in breast cancer.

Clinical determination of axillary lymph node metastases has an accuracy of only 33 %.[1]

Guiliano first described sentinel lymph node biopsy (SLNB) in 1994 with breast cancer using the methyl blue dye [3]. The accuracy and clinical utility of SLNB is its ability to identify the presence or absence of metastasis in the lymph nodes.

The morbidity associated with the SLNB such as bleeding, seroma, has given rise to possibility of newer methods of assessing the axilla [4,5]

The fine needle aspiration used in conjunction with ultrasound has been proposed as an alternative to SLNB in diagnosing nodal metastasis with lesser morbidity. While many studies report specificity of 100% , the sensitivity varies between 50% and 98.4% [4,5,6,7]. There has been no study in our environment on this subject. This study seeks to determine effectiveness of ultrasound guided FNA in detecting axillary lymph node metastasis in early breast cancer at KNH.

## 1.2 Statement of the Problem

In managing breast cancer with clinically suspected axillary metastasis, axillary dissection is done for treatment as well as for staging in the surgical unit at Kenyatta National Hospital. This is because Sentinel Lymph Node Biopsy (SLNB) which is used for staging purposes to determine axillary metastasis is rarely done in the surgical unit. However, in early breast cancer, chances of Axillary involvement are limited. Therefore, in relation to the above challenges, Can Ultra sound guided FNA, help in staging Axillary metastasis in early breast cancer, to determine which patient will benefit from Axillary dissection?. This study is therefore intended to assess the effectiveness of Ultrasound Guided Fine Needle Aspiration (FNA) In Detecting Axillary Lymph Node Metastasis in Early Breast Cancer at KNH

## 1.3 Objectives

### 1.3.1Main Objective

The aim of study was to assess effectiveness of ultrasound guided FNA in detecting axillary lymph node metastasis in early breast cancer at KNH

### 1.3.2 Specific Objectives

1. To determine the specificity of u/s guided-FNA of axillary lymph node in breast cancer
2. To determine sensitivity of u/s guided-FNA of axillary lymph node in breast cancer
3. To correlate the US guided-FNA with ALND

## 1.4 study question Null hypothesis

Ultrasound guided FNA cytology of the axilla is not effective in diagnosis of axillary metastasis in patients with early breast cancer compared with ALND.

## 1.4 Study Justification

- In our set up frozen section for SLNB is limited and therefore ultrasound guided FNA could bridge the gap in staging and managing the axilla in early breast cancer.
- ALND and sentinel node biopsy is associated with complications. Use of ultrasound guided FNA cytology may reduce these complications.
- Validate the uptake of ultrasound guided fine needle aspiration in our set up.

# 2.0 CHAPTER TWO: LITERATURE REVIEW

## 2.1 Axillary Lymph Node Dissection

Axillary lymph node staging remains the most important prognostic indicator of outcome in patients with breast cancer. Axillary lymph node dissection (ALND) is the reference standard because it is the most conclusive method of evaluating the axilla, but it is associated with substantially increased morbidity[1, 3]. Early wound complication was documented in as many as 50%, this include seroma in the majority of patients[9].

Level I-II ALND has low rate of recurrence (<3%) but this is at the cost of significant morbidity, with an acute complication rate of 20%-30% and a chronic lymphedema rate as high as 20%-30%. There is no consensus in the use of routine ALND in breast cancer patients who have a low risk of axillary metastasis or who would risk of axillary metastasis or who would receive adjuvant therapy regardless of axillary involment[10.]

## 2.2 Sentinel Lymph Node Biopsy (SLNB)

The advances in research away from ALND occurred in 1977, when Cabanas was able to localize a sentinel lymph node in a patient with penile cancer. Morton in 1992 was able to localize the SLN in a patient with melanoma .After several animal model trials, Guilliano was the first to describe the SLNB in breast in 1994[1,]

A trial was conducted in developmental phase of adapting SLNB from a cutaneous tumour system (melanoma) to a parenchyma tumour system ( breast cancer ).Sentinel nodes were detected in 114 of 174 patients(65%) who underwent

dye directed SLNB followed by ALND. The sentinel node accurately reflected axillary tumour status in 109 of 114 SLND procedures (95.6%).During this phase of development, the optimal amount of dye needed and the interval from dye injection to dissection were determined [(10)].

Sentinel lymph nodes were successfully identified in 65 of the 88 cases (74%) in a study done in 1999. Sentinel lymph nodes were negative in 40 cases including four cases with non-sentinel-node-positive breast cancer (specificity, 100%; sensitivity, 86%). In nine (31%) of the 29 cases with histological node-positive breast cancer, the sentinel lymph nodes were the only lymph nodes affected. Axillary lymph node status was accurately predicted in 61 (94%) of the 65 cases. [(11]

While sensitivity and specificity of SLNB has improved quite significantly as above ,there was still associated morbidity .Although postoperative morbidity after SLNB alone was significantly lower than after SLNB and completion ALND in the investigation, there were still 39% of patients in the former group who suffered from at least one complication .[(12).]One would think that the removal of a median number of two axillary lymph nodes through a small incision should not lead to problems or complications but investigations provide compelling evidence that morbidity is not negligible and occur even after SLNB alone.[10] This finding is important in the assessment of a new surgical technique in comparison with a standard procedure, not only for quality assurance, but it enables also to provide accurate informed consent to patients undergoing breast cancer surgery.[(12,13,)]

### 2.3 Axillary Ultra Sound (U/S) /Core Biopsy/Fine Needle Aspiration (FNA)

Although SLNB is now widely accepted [(14,15)] surgeons must spend a considerable amount of time in the operating room harvesting sentinel lymph nodes .([13])

Furthermore in some studies for quality control, the breast surgeon requires to perform the ALND until the SLN is mastered [10]

In addition, SLNB is not a perfect procedure; it results in no sentinel lymph nodes being harvested in some patients or in more than three sentinel lymph nodes being detected.[13] If nodal positivity can be proved preoperatively, SLNB can be avoided.[13] Preoperative lymph node staging in patients with breast cancer is being investigated .Ultrasonography (US) has become a widely used modality for this purpose. Some investigators have reported high accuracy in preoperative lymph node staging with US and fine-needle aspiration combined. [4, 13, 16].

## 2.4 Ultrasound Imaging of Axillary Lymph Nodes

Ultrasound result is considered positive if cortical thickening (including loss of hilum) and/or non-hilar blood flow (NHBF) to the cortex is depicted.[4, 5] This increased blood flow probably reflects pre-existing peripheral vessels that are engorged owing to a disruption of the hilar blood supply that results from infiltration by metastatic disease .NHBF may also be seen in other conditions such as inflammatory processes and reactive nodes. [13]

Cortical thickening, either diffuse or focal, is defined as a maximal cortical thickness equal to or greater than the width of the fatty hilum. Deurloo et al suggested that cortical thickening of at least 2.3 mm is a good predictor of lymph node metastasis, with 95% sensitivity and 44% specificity.

However, in other studies the lowest cortical thickness of the lymph nodes sampled was 2.7 mm. [4, 5, 13, 15]

While the sensitivity of 3-mm cortical thickness in the Koelliker et al study [4] was high (95%) and identical to that of 2.3-mm cortical thickness in the Deurloo et al study, [5,23] the specificity was unacceptably low (6%) [4].Therefore, another way was

devised using a relative thickness measure of the cortex to the short axis of the lymph node instead of using absolute cortical thickness. Using these criteria, the workers achieved substantially higher specificity (64%) while maintaining relatively high sensitivity (79%). [4,5

The ultrasound can also detect absence of a fatty hilum. An absent fatty hilum, previously reported as a good positive-result indicator , was the single best finding for detecting nodal metastasis (positive predictive value, 93%), but it was infrequently present (sensitivity, 33%) [4,5,13].

**2.5 Ultrasound Guided Core Needle Biopsy**

U/S-guided core needle biopsy (CNB) is recommended when positive U/S findings were obtained. When there were two or more abnormal lymph nodes, the lymph node with the most suspicious findings was selected for biopsy [10]. The main challenge in performing CNB within the axilla is to avoid damaging the major vessels and nerves. In one axillary lymph node CNB series, fine-needle aspiration was performed instead of CNB when the lymph nodes were in close proximity to vessels, because of risk of bleeding [(13).]

**2.6 Ultrasound Guided Fine Needle Aspiration.**

Ultrasonography (U/S) evaluation of the axilla with U/S-guided fine-needle aspiration (FNA) has been shown to offer a means of nonsurgical staging of the axilla. Axillary lymph nodes are depicted at U/S, and the most suspicious lymph node is identified. FNA is guided by using U/S to sample the most suspicious area. The specimen is evaluated with cytological examination. The procedure has almost no morbidity, is quick, and is minimally painful. [4, 5,6,17]

The addition of US-guided FNA to the evaluation of the axilla offers the benefit of nonsurgical detection of axillary metastases, and US-guided FNA is typically faster to perform, is more easily tolerated, and allows more rapid cytological interpretation than a surgical procedure. When the US-guided FNA finding is negative, the patient undergoes SNB for further evaluation.

However, when the US-guided FNA finding is positive, SNB can be omitted and the patient can undergo ALND, which minimizes the number of surgeries. In addition to its use in preoperative staging, US-guided FNA can be used to stage the axilla before neoadjuvant chemotherapy. [4, 10,11,12,13]

U/S-guided FNA is more sensitive for detecting lymph node metastasis in patients with larger primary tumors because lymph node metastases tend to be larger in these cases. False-negative findings at US-guided FNA involved lymph nodes with small (<5 mm) metastatic foci. Sensitivity declined with smaller tumor size, although the specificity (100%) was excellent. US-guided FNA is such a quick and easily tolerated procedure, a sensitivity of 56% in T1 lesions (<2 cm) is acceptable because half the patients with a positive axilla would not have to undergo SNB.[4, 5, 11, 13]

While lymph nodes that appeared abnormal at U/S were more likely to be positive at US-guided FNA, the results suggest a benefit of performing U/S-guided FNA in lymph nodes that appear normal at U/S, particularly in patients with a high likelihood of having nodal disease. Criteria used to distinguish benign from malignant lymph nodes include cortical thickness, contour, and echogenicity and the appearance of the hilum ([4, 5, 11, 13). The most predictive features of lymph node tumor involvement in one of the studies were hypo echoic cortex, eccentric hilum, and completely replaced hilum. The nodal size was of limited value as a

distinguishing feature. This was also confirmed in other studies which indicate that changes in cortical morphology may precede any changes in the overall size or echogenicity of the hilum[4,5].

For axillary lymph nodes that appeared normal at U/S, it remains unclear which lymph node should be sampled. In some studies it was found out that the largest node and the node closest to the breast most likely is the sentinel node and more appropriate for biopsy[4,5] By performing U/S-guided FNA in lymph nodes that were normal at U/S, the workers increased the rate of preoperative detection of axillary lymph node metastases by (13.0% and 11% of benign-appearing axilla at U/S respectively). [4, 16]

The subjective nature of assessment of the U/S appearance of lymph nodes may further support the use of U/S-guided FNA in both normal- and abnormal-appearing axilla. This may prove more important with patients with larger tumors, who are more likely to have positive axilla. It may be less beneficial to perform U/S-guided FNA in an axilla that was normal at U/S when the chance of axillary nodal involvement is small, such as in patients with primary tumors of T1 size [4, 16.] False-positive results ranging from 1.4% to 1.6% have been reported only rarely. These results have been reported to occur occasionally because of interpretive errors and mistaking reactive lymphoid cells or mesothelial cells for metastatic carcinoma. The majority of cases believed to be false-positive may indeed be true-positive cases because of complete response to neoadjuvant chemotherapy or, occasionally, failure to detect minimal volume disease on final pathologic examination. .[4, 5, 13]

U/S-guided FNA is a well-tolerated, minimally invasive procedure. In staging the axilla of a patient with known carcinoma, a cytologic result positive for metastatic

adenocarcinoma is sufficient to replace SNB and to proceed to ALND or neoadjuvant chemotherapy.[4]

Although CNB is an alternative to U/S-guided FNA ,in one of the studies the researchers were able to demonstrate success with FNA in 75 patients with only one with insufficient sample .The quality of the sample also didn't depend on skill because the sample was collected directly into fixative solution. [4]

While core biopsy is preferred for the evaluation of the primary tumor because of the histological information (invasive vs. in situ carcinoma) obtained, a positive cytology result from a lymph node is indicative of metastatic tumor, and histological evaluation is not necessary for diagnosis. [4,5.]

In conclusion, U/S-guided FNA is useful in the initial axillary staging of breast cancer.Staging of axillary lymph nodes in patients with early stage (T1 or T2) breast cancer helps the surgeon select the appropriate surgical management of axilla[(5]. Patients who have no evidence of metastatic disease in the preliminary staging process are selected for SLN biopsy, whereas those with evidence of metastatic disease undergo complete dissection of the axillary lymph nodes nodes [4, 5,11,13,16,18,19,20]

## 3.0 CHAPTER THREE. MATERIALS AND METHODS.

### 3.1 Study Design:

This was a prospective descriptive study involving female surgical patients seen in surgical outpatient clinics and wards diagnosed with breast cancer and underwent modified radical mastectomy within the time limit of the study.

### 3.2 Study Setting:

The study was conducted in all surgical out patients, wards, breast clinics, pathology and radiology department at Kenyatta national hospital, over a period of twelve months.

### 3.3 Inclusion Criteria

**The following cases were considered eligible for inclusion in the study:**

1. All women > 18 yrs with diagnose OF EARLY breast cancer
2. All women who had MRM
3. women with clinically non palpable nodes ( patient who should otherwise undergone sentinel lymph node biopsy

### 3.4 Exclusion Criteria

**The following cases were excluded from the study:**

1. Patients with metastatic breast cancer
2. Patients who had undergone neoadjuvant radiotherapy
3. Patients who had ALND and or SLNB

4. Patients with breast cancer T4 and above.
5. patients declining to give consent

### 3.5 Sample size calculation

There was an estimated number of 6 patients with early breast cancer seen in KNH per month. It was estimated that a total of 54 patients would be accessible within the 12 months of the study. A representative sample was drawn from the population and the sample size calculation was obtained using a formula for finite population (less than 10,000). The calculation was as follows:

$$n' = \frac{NZ^2P(1-P)}{d^2(N-1)+Z^2P(1-P)}$$

Where

$n'$ = sample size with finite population correction,

$N$ = size of the target population = 54

$Z$ = Z statistic for 95% level of confidence = 1.96

$P$ = Estimated proportion of patients with positive ALDA

$d$ = margin of error = 5%

Substituting into the formula,

A minimum sample size of 51 patients was needed to estimate a proportion within 5% level of significance.

### 3.6 Technique

The patient was placed in a supine or contra lateral-side-down oblique position on the table, with the ipsilateral hand placed behind the head. US scan was done from the lower part of the axilla and continued upward toward the axillary fossa, with the goal of detecting at least one lymph node.

A 22-gauge needle was attached to a 10ml syringe and 2 to 3 excursions were performed to obtain sample containing a large portion of solid non-fat tissue.

### 3.7 Procedure

#### 3.7.1 Ultrasound Findings

All patients who met the inclusion criteria were subjected to ultrasound of the lymph node: the size was recorded and the largest node was followed by Fine Needle Aspiration (FNA), using gauge 22 needles attached to a 10-mL syringe, with suction applied by using numerous short excursions in and out of the area being sampled. Three samples was obtained from each node and direct smears were fixed in alcohol for papanicolaou staining at the same setting. The harvest was done by observing all the aseptic techniques (using sterile cut down tray, sterile gloves, sterile needles, Iodine solution for swabbing the site, and the ultra sound probe shall be covered with the sterile dressing ) to prevent any infection of the site and contamination of the specimen collected. All patients were seen by principle investigator within 1 week and there was no complications.

The specimen was marked and sent to KNH/UON LAB for cytology examination. The resulting slide was covered with a cover slip, and evaluated by a pathologist with expertise in cytology.

All patients underwent MRM with ALND the pathological results was collected and compared with US guided FNA.

The data was analysed using Statistical Package for Social Sciences (SPSS) for Windows Version 22.

### 3.7.2 Quality Assurance

To ensure quality and reproducibility of results, the standard procedure protocol was put in place and was strictly followed by the research team. This was in addition to training of the research team in their respective area of speciality (Consenting process, Ultra sound and harvesting stage, Cytology preparation, examination and reporting). Data collection worksheet was verified for completeness and double entry was made in SPSS version 22.0

### 3.7.3 Ethical Consideration

The study commenced upon approval by the department of surgery (UON) and KNH Ethics and Research committee.

A pre-consent counselling of the participants was carried out, and then an informed consent obtained from each of the participant prior to enrolment in the study. Those who decline participation were not denied treatment they deserve because of their decision not to participate.

There was no extra cost incurred for participating in the study. All data was recorded in MS Excel data sheets and saved under password protection only accessed by personnel involved in the project. Hard copy back-up copies was securely locked in a cabinet under lock and key only accessed by personnel involved in the project. Confidentiality and privacy was observed. Data collected was destroyed upon completion of dissertation

## 4.0 CHAPTER FOUR: RESULTS

A total of 79 patients participated between a period of March 2016 and to March 2017. A total 51 patients had results of axillary FNA and ALND and therefore met criteria of the study. Nineteen patients didn't have axillary FNA while six patients were missing ALND results. Nineteen patients had negative FNA of axilla. Thirteen patients had axilla FNA which was non diagnostic. Only 25 patients had FNA which was positive .One patient had liver metastasis on staging u/s and was send for chemotherapy. One patient had lymphoma and another patient had not been operated by the time study ended. The results was analyse using SPSS on the 51 patients which meet the corrected samples size.

**Table 1: Demographic characteristics**

| **Variable** | **Frequency (%)** |
|---|---|
| **Age**<br>Mean (SD)<br>Min-Max | <br>42.2 (12.2)<br>18-76 |
| **Gender**<br>Female | <br>51 (100.0) |

The total number of patients was 51 who did u/s guide FNA of axilla and underwent Surgery of modified radical mastectomy


*Figure 1: Age distribution*

**Table 2**

| Variable | Mean (SD)/Median (IQR) | Min-Max |
|---|---|---|
| Breast mass size | 4.1 (1.9) | 0.5-8.0 |
| U/S AXILLA | 2.5 (1.5-5.3) | 0.5-16.0 |

The breast size with the highest measures 8cm.No skin or chest wall involvement. The axilla size was average 2.5cm by u/s.The highest being 16cm.

**Table 3:**

| Variable | Frequency (%) |
|---|---|
| **FNA of axilla** | |
| Positive (malignant) | 19 (37.3) |
| Negative (benign) | 19 (37.3) |
| Non-diagnostic(indeterminate) | 13 (25.5) |
| **ALND** | |
| Positive (malignant) | 20 (39.2) |
| Negative(benign) | 31 (60.8) |

The patients who did u/s guided FNA with results and proceeded to do surgery (MRM).with axillary dissection.

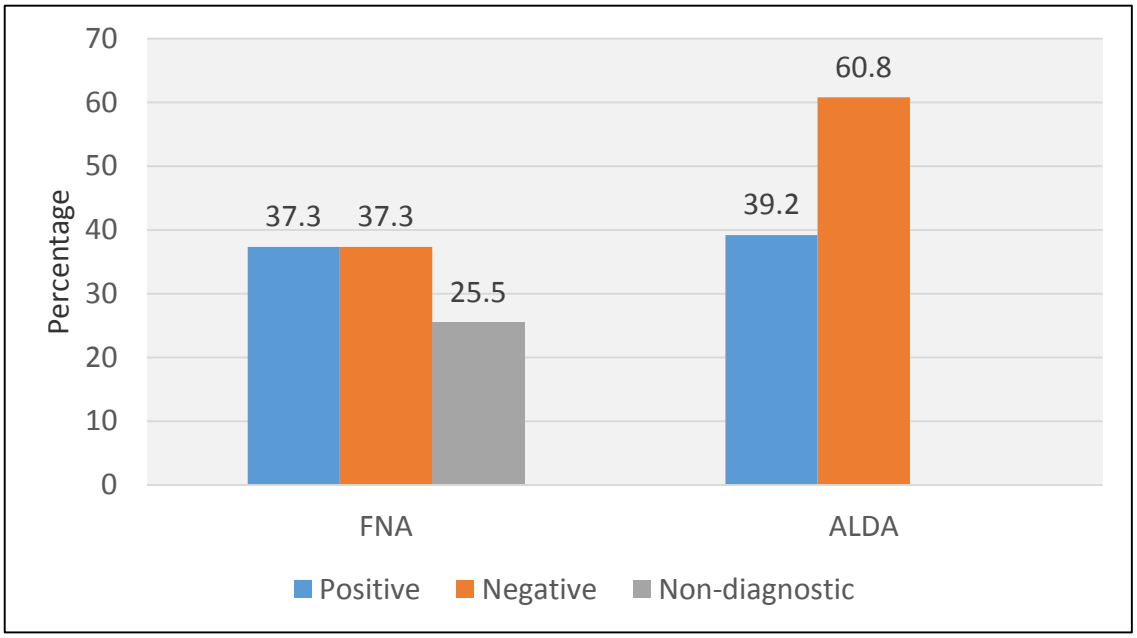


*Figure 2:*

**Table 4: Sensitivity and specificity of FNA**

| | ALND | | Total |
|---|---|---|---|
| | Positive | Negative | |
| **FNA** | | | |
| Positive | 18 | 1 | 19 |
| Negative | 0 | 19 | 19 |
| Non-diagnostic | 2 | 11 | 13 |
| **Total** | 20 | 31 | 51 |

The outcome on the table was either (malignant) positive or benign (negative). The 13 non diagnostic outcomes were treated as negative for analytical purpose. Refer koelliker et al[4].

| **Parameter** | **Value** | **95% CL** |
|---|---|---|
| Sensitivity | 90% | 68.3%-98.77% |
| Specificity | 96.88% | 83.78%-99.92% |
| Positive predictive value (PPV) | 94.74% | 72.23%-99.2% |
| Negative predictive value(NPV) | 93.94% | 80.61-98.3% |
| Positive likelihood ratio(PLR) | 28.8 | 4.16-199.34 |
| Negative likelihood ratio(NLR) | 0.10 | 0.03-0.38 |

**Correlation between breast mass size and ALND positivity**

| **Variable** | **ALND** | | **P value** |
|---|---|---|---|
| | Positive | Negative | |
| Breast mass size, mean (SD) | 4.4 (1.7) | 3.6 (2.2) | 0.242 |

# 5.0 CHAPTER FIVE: DISCUSSION

The average age of the patients were 43 years with the highest age of 79.The average breast mass size was 4cm although there was two patients with over 4cm. Two patients with T3 were included. The FNA results of the axilla was compared with the gold standard ALND. The sensitivity of u/s guided FNA was 90 %.The positive predictive value was high at 94.74%.The only criteria of picking the most likely sentinel node by ultrasound was largest size of the node. Other features like the nodal flow or cortical thickness were not included .This is an area where radiological improvement may be needed to identify gaps. Positive predictive value for U/S guided FNA cytology of axilla was 94.74%.Our sensitivity was 90% compared to 67% in the koelliker study .This was because in our study the average primary tumour size was T2 in contrast to the koelliker study which had most tumours within T1.The positive predictive value in the same study approached 100% for larger primary tumors which was equivalent to our study which had an average tumour size or 4.4cm, or T2. The invasive axillary cancer in our population was 38.4%.

The specificity was high at 98.88% all the indeterminate was treated as negative. The negative predictive value was high at 93.4%. The specificity was higher than 50 % which shows that about 50% of the population may not really have to undergo ALND but may hope for a least morbid SLNB especially in early breast cancer tumors below T1.the role of indeterminate is significant and may be cytologist experienced may play a role. The cost of redo FNA for indeterminate results is not justifiable considering 84 % of indeterminate was negative after ALND but further resource may need to be invested to enable objective determination of repeat cytology for indeterminate results .The negative predictive value was 93.9% is lower than koelliker at al[4] 100% and could be attribute to

better cytological interpretation .The significance of the study to stage the axilla was high within the 95% CI, compared with clinical assessment because most of the axilla enlargement after the core biopsy could as well be inflammatory and not necessarily metastatic. The FNA can supplement the clinical work as adjunct for staging the axilla especially in early breast cancer who might wish to undergo breast conserving surgery, while informing the surgeon on the need for ALND on positive nodal status or a sentinel lymph node biopsy on the benign FNA results. This study had no morbidity on review of patients after FNA. The morbidity of ALND compared SLNB was significant in Igor langer et al [12] study with the former at 19% and the lather at 3.5%. Based on the above results half of the population with negative axilla may opted for SLNB instead of ALND. The FNA also can be useful in neoadjuvant setting in staging the axilla before and after but studies need to be done .The Kenyatta study was funded by KNH to a tune of 400,000,with the FNA initially at cost of 5000 it was revised upwards to 12000 but most of the patients had underwent FNA ,this in future is prohibitive . The installation of patients imaging results in machine archive will facilitated future research on the same.

## 5.1 CONCLUSION

The study which was fully funded showed, sensitivity was 90% and the specificity was 96.88% was within the 95% CI and therefore significant to compare well with ALND especially with primary tumours of T2.This may be lower especially in T1 tumours which might need better radiological input on features of malignant node in addition to the size alone and therefore identify gaps in performing u/s of axilla to identify the most suspicious node. In addition the cytological interpretation yielding indeterminate may need to improve. FNA gives the surgeon added tool which may assist in selecting patients who need axillary dissection for the positive FNA of axilla in early breast cancer or less morbid SLNB on the negative FNA of the axilla.

## 5.2 RECOMMENDATION

The study found the cost of u/s guided FNA which was revised upwards from 5000 to 12000 was prohibitive and a discussion needs to be done so that, patients who are suspicious and have paid for the core biopsy of breast should undergo staging FNA of axilla at no added cost to the patient upon clinician request .The installation of patients imaging results in machine archive will also facilitated future research .

STUDY BUDGET.

| Budget Item | Amount (K.shs.) |
|---|---|
| Research fee for technical<br>Lead supervisor | 1700000<br>100000 |
| UoN/KNH ERC Fee | 2000 |
| Statistician consultation fee | 20,000 |
| Stationery;(a) Printing<br>(b)photocopying<br>(c)binding<br>(d)pens | 10000<br>3000<br>7000<br>500<br>Total=20500 |
| Research assistants fee<br>@15000 each (two assistants) | 30,000 |
| Contingency fund | 40000 |
| **Total** | **382,500** |

TIME FRAME

| ACTIVITY | 2015 MAY-DEC | 2016 FEB | 2016 MAR | 2016 APR | 2016 MAY | 2016 OCT | 2016 NOV | 2016 SEP | 2017 JAN | 2017 APR | 2017 MAY |
|---|---|---|---|---|---|---|---|---|---|---|---|
| PROPOSAL DE VELOPMENT | | | | | | | | | | | |
| ETHICAL APPROVAL | | | | | | | | | | | |
| DATA COLLECTION | | | | | | | | | | | |
| DATA ANALYSIS | | | | | | | | | | | |
| PRESENTATION | | | | | | | | | | | |

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DATA COLLECTING WORK SHEET

Age----------

Sex----------

PRIMARY BREAST CANCER;

- Size; using tape measure……..cm, by US.....
- Histological grade…….
- Breast cancer stage.....

**Primary breast cancer imaging**

- Breast ultrasound findings……
- Mammogram findings……..

UTRASOUND FINDINGS OF AXILLARY NODES

Axillary Nodal size----------

Cortical Nodal thickness----------mm

Nodal Height width ratio----------

Nodal Cortex hilum ratio----------

Hillar flow----------yes/no

Ultrasound guided FNA cytology ---------- yes /no

Cytology ---------- positive/negative

Sentinel node biopsy---------- yes/ no

If yes ----------histology positive/negative

Axillary lymph node dissection done----------yes/no

Histology of axillary lymph node Dissection----------cancerous/no cancer

INFORMED CONSENT FORM

**STUDY TOPIC:** Effectiveness of ultrasound guided fine needle aspiration in staging axillary lymph nodes in early breast cancer.

This informed consent form is for patients who are Diagnose with breast cancer and are undergoing staging of axilla as part of other investigation and treatment at KNH. I am inviting you to participate in this research on a voluntary basis.

**Principal Investigator:** Dr. Henry Kipronoh Ngenoh

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

This Informed Consent Form has three parts:

1) Information Sheet (to share information about the research with you).
2) Certificate of Consent (for signatures if you agree to take part).
3) Statement by the researcher/person taking consent.

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

## PART I: Information Sheet

### Introduction

My name is Dr Henry Kipronoh Ngenoh, a post graduate student in General Surgery at the University of Nairobi. I am carrying out a research to determine the effectiveness of ultrasound-guided lymph node aspiration to stage the axilla in early breast cancer at KNH.

**Purpose of the research**

Breast cancer is the second leading malignancy among women in Kenya. The survival and life expectancy of diseases depends very much on the spread of tumor in the axillary lymph nodes. Accurate staging of the axilla with newer methods which has less complication will be advantageous in decision of the treatment plan on whether to perform axillary Dissection or initiate neoajuvant therapy or perform less extensive operation without axillary dissection. The current Diagnosis which involves assessing the lymph nodes by physically palpating the axilla is less sensitive, and the other method of doing Sentinel Lymph Node Biopsy is limited in our institution because of need to do frozen section. The purpose of this research is to determine the lymph node if there is cancer cells by using a small needle injected into the lymph node and the cells aspirates are taken for histology. There will be no operation involve. The findings will be correlate with those found after the surgery for breast.

I am going to give you information and invite you to be a participant in this research. There may be some words that you do not understand or that you may need clarification. Please ask me to stop as we go through the information and I will explain or clarify.

**Type of Research Intervention**

This research will involve physical examination of your breast and the axilla and the rest of the body. The results of your breast cancer imaging and histology will be recorded. You will be sent to ultrasound room where the specialist will check your armpit using the Ultrasound to see the lymph node and will do an injection on the lymph node which is suspicious of cancer cells and send for histology. Those lymph nodes which will show signs suggesting there are no cancer cells will be

subjected to needle aspiration to determine by histology that indeed there are no cancer cells.

**Voluntary participation/right to refuse or withdraw**

It is your choice whether to participate or not. Whether you choose to participate or not, all the services you receive at this hospital will continue and nothing will change. If you choose not to participate in this research project, you will be offered the treatment that is routinely offered in this hospital for your condition. You have a right to refuse or withdraw your participation in this study at any point.

**Confidentiality**

The information obtained will be treated with confidentiality and only be available to the principal investigator and the study team. Your name will not be used. Any information about you will have a number on it instead of your name. We will not be sharing the identity of those participating in this research.

**Sharing the results**

The knowledge that we get from this study will be shared with the policy makers in the Ministry of Health, KNH and doctors through publications and conferences. Confidential information will not be shared.

**Risks**

There is no direct risk resulting from your participation in the study.

**Cost and compensation**

There will be no extra cost incurred for participating in this study nor is there compensation offered. However your time will be required to participate in the interview.

This proposal has been reviewed and approved by UoN/KNH Ethics Committee, which is a Committee whose task is to make sure that research participants are protected from harm.

PART II: CERTIFICATE OF CONSENT

**Who to contact:** If you wish to ask any questions later, you may contact:

**1. The Principal Researcher:**

Dr Henry kipronoh Ngenoh

Department of Surgery, School of Medicine, University of Nairobi

P.O. Box 19676 KNH, Nairobi 00202.

Mobile no. 0721959547

**2. The University of Nairobi Supervisors**:

i. Dr Kimani Wanjeri,
MBCh.B, M.MED (Gen Surg.), Plastic and reconstructive surgery,

Consultant Surgeon/Lecturer,

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

P.O. Box 19676 KNH, Nairobi 00202.

Mobile no. 0722708051

ii. Dr Joseph Githaiga
MBCh.B, M, MED (Gen Surg), Senior Lecturer,

Consultant Surgeon,

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

P.O. Box 19676 KNH, Nairobi 00202.

Mobile no. 0722526274

If you have any ethical concerns, you may contact:

iii. Secretary,
KNH/UoN-ERC,

P.O. Box 20723 KNH, Nairobi 00202

Tel +254-020-2726300-9 Ext 44355

Email: KNHplan@Ken.Healthnet.org

I have read the above information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.

Print Name of Participant

_____

Signature of Participant

_____

Date

_____

If Illiterate :

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

Print Name of witness_____

Signature of witness _____

Date _____

Thumb print of participant

PART III:  STATEMENT BY THE RESEARCHER

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

- Refusal to participate or withdrawal from the study will not in any way compromise the care of treatment.
- All information given will be treated with confidentiality.
- The results of this study might be published to facilitate treatment and diagnosis of prostate cancer.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant 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 provided to the participant.

Name of researcher/person taking consent

_____

Signature of researcher/person taking consent

_____

Date_____

FOMU YA MAKUBALIANO YA KUJIUNGA NA UTAFITI SEHEMU YA KWANZA

**SWALA LA UTAFITI:** Matumizi ya picha ya U/S kusaidia kutoa celli kwenye matesi ya kwapa ili ifanyiwe uchunguzi kama ina saratani.

Hii fomu ni kwa ajili ya wagonjwa ambao wana saratani ya matiti na wanafanyiwa uchunguzi kuona kama saratani imeenea hadi kwenye matesi ya kwapa na pia wanaendelea na matibabu katika KNH. Mimi nakukaribisha wewe kushiriki katika utafiti huu kwa hiari yako.

**Mtafiti mkuu:** Dkt. Henry Kipronoh Ng'eno

**Kituo:** Kitengo cha Upasuaji, Shule ya Afya, Chuo Kikuu cha Nairobi.

Fomu hii ya makubaliano ina sehemu tatu:

1) Habari itakayokusaidia kukata kauli
2) Fomu ya makubaliano (utakapowekasahihi)
3) Ujumbe kutoka kwa mtafiti

Utapewa nakala ya fomu hii.

SEHEMU YA KWANZA: UKURASA WA HABARI

## Kitambulizi

Jina langu ni . Dkt. Henry Kipronoh Ng'eno. Mimi ni daktari ninaesomea upasuaji katika Chuo Kikuu cha Nairobi. Ninafanya utafiti kwa anwani ya, "Matumizi ya ya picha ya U/S kusaida kutoa celli kwenye matesi ya kwapa kwa wagonjwa walio na saratani ya matiti na wanapata matibabu hospitali kuu ya Kenyatta."

## Nia ya utafiti huu

Saratani ya titi ni ya pili katika kusababisha vifo vya akina mama humu nchini. Kuenea kwa ugonjwa huu hadi kwenye matesi ya kwapa ni mojawapo ya ishara inayotumiwa na madakitari kufanya uamuzi wa aina ya kimatibabu au upasuaji. Mojawapo ya kauli inayofaa kufanywa ni iwapo kama titi lote pamoja na matesi ya kwapa yanafaa kung'olewa au la. Matumizi ya mikono kuchuguza matezi ya kwapa iwapo ina saratani huwa haipeani hakikisho kamili. Njia nyingine ni ya matumizi ya SNL biopsy ambayo inahitaji watalamu na vifaa vya frozen section.kwa sababu ya changamoto kuhusu vifaa na watalamu, hii njia ya pili haiwezi kutumika katika hospitali kuu ya Kenyatta. Matumizi ya picha ya u/s katika kutoa celli kwenye matesi ya kwapa inaendelea kupata umarufu kwa sababu ni rahisi na haitaji kuwepo kwa vifaa na wataalamu wa kufanya frozen section. Nia ya utafiki huu ni kuthibitisha kwamba matumizi ya picha ya U/S kusaidia kutoa celli kwenye matezi ya kwapa inaweza kutupea hakikisho ilio na uzito zaidi kuliko njia zinazotumika sasa.Nitakupa habari na kukualika kuwa mshiriki katika utafiti huu. Kunaweza kuwa baadhi ya maneno ambayo huelewi.Ikiwa kuna chochote huelewi, tafadhali nisimamishe ndio nikueleze kwa kina.

## Aina ya Utafiti

Utafiti huu utahusu kufanyia mwili , kwapa na matiti yako uchunguzi. Utapigwa picha ya U/S na mtalaamu kisha utadungwa sindano kwenye kwapa ili celli zitolewe kwa ajili ya kufanyiwa uchunguzi kuona kama zina saratani.

**Haki ya kukataa utafiti**

Kushiriki kwako kwa utafiti huu ni kwa hiari yako. Una uhuru wa kukataa kushiriki, na kukataa kwako hakutatumiwa kukunyima matibabu. Uko na haki ya kujitoa katika utafiti wakati wowote unapoamua.

**Tandhima ya siri**

Ujumbe kuhusu majibu yako yatahifadhiwa .Ujumbe kuhusu ushiriki wako katika utafiti huu utawezekana kupatikana na wewe na wanaoandaa utafiti na wala si yeyote mwingine. Jina lako halitatumika bali ujumbe wowote kukuhusu itapewa nambari badala ya jina yako.

**Hatari unayoweza kupata**

Hakuna hatari yeyote ambayo yaweza kutokea kwa sababu ya kuhusishwa kwa utafiti huu. Muda wako ndio utakaotumiwa wakati wa mahojiano.

## SEHEMU YA PILI: FOMU YA MAKUBALIANO

**Anwani zaWahusika:** Ikiwa uko na maswali ungependa kuuliza baadaye, unaweza kuwasiliana na:

1. Mtafiti Mkuu:

   Dkt. Henry Kipronoh Ng'eno

   Kitengo cha Upasuaji, Shule ya Afya, Chuo Kikuu cha Nairobi,

   SLP 19676 KNH, Nairobi 00202.

   Simu: 0721959547

2. Wahadhiri wahusika:
   i Dkt. Githaiga
   MBCh.B, M.MED (Gen Surg.),

   Consultant Surgeon/Mhadhiri,

   Idara yaUpasuaji, Shule ya Afya, Chuo Kikuu cha Nairobi,

   SLP 19676 KNH, Nairobi 00202.

   Simu: 0722322246

   ii Dkt. Kimani Wanjeri,
   MBCh.B, M.MED (Gen Surg.), Plastic and Reconstruction Surgery,

   Consultant Surgeon/Mhadhiri,

   Idara yaUpasuaji, Shule ya Afya, Chuo Kikuu cha Nairobi

   SLP 19676 KNH, Nairobi 00202.Simu: 0722708051

3. Wahusika wa maslahi yako katikaUtafiti:

   Karani,

   KNH/UoN-ERC

   SLP 20723 KNH, Nairobi 00202

   Simu: +254-020-2726300-9 Ext 44355

   Barua pepe: KNHplan@Ken.Healthnet.org

Nimeelezewa utafiti huu kwa kina. NakubaIi kushiriki kwenye utafiti huu kwa hiari yangu. Nimepata wakati wa kuuliza maswali na nimeelewa kuwa iwapo nina maswali zaidi, ninaweza kumwuliza mtafiti mkuu au watafiti waliotajwa hapo chini.

Jina la Mshiriki_____

Sahihi ya mshiriki _____

Tarehe_____

**Kwa wasioweza kusoma na kuandika:**
Nimeshuhudia usomaji na maelezo ya utafiti huu kwa mshiriki. Mshiriki amepewa nafasi yakuuliza maswali.Nathibitisha kuwa mshiriki alipeana ruhusa ya kushiriki bila ya kulazimishwa.

Alama ya kidole cha mshiriki

Jina la shahidi _____

Sahihi la shahidi _____

Tarehe _____

## SEHEMU YA TATU: UJUMBE KUTOKA KWA MTAFITI

Nimemsomea mshiriki ujumbe kiwango ninavyoweza na kuhakikisha kuwa mshiriki amefahamu yafuatayo:

- Kutoshiriki au kujitoa kwenye utafiti huu hautadhuru kupata kwake kwa matibabu.
- Ujumbe kuhusu majibu yake yatahifadhiwa kwa siri.
- Matokeo ya utafiti huu inaweza chapishwa kusaidia katika ucunguzi na matibabu ya wagonjwa walio na saratani.

Ninathibitisha kuwa mshiriki alipewa nafasi ya kuuliza maswali na yote yakajibiwa vilivyo. Ninahakikisha kuwa mshiriki alitoa ruhusa bila ya kulazimishwa.

Mshiriki amepewa nakala ya hii fomu ya makubaliano.

Jina la mtafiti _____

SahihiyaMtafiti _____

Tarehe_____