PERCUTANEOUS 17/18-GAUGE COAXIAL CT GUIDED CORE NEEDLE BIOPSIES OF LUNG NODULES AND MASSES AT KENYATTA NATIONAL HOSPITAL: DIAGNOSTIC YIELD, COMPLICATION RATES AND RADIOLOGICAL PATTERN OF HISTOLOGICALLY PROVEN PRIMARY LUNG CANCER HISTOLOGICAL SUBTYPES

A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT FOR THE DEGREE OF MASTER OF MEDICINE IN DIAGNOSTIC IMAGING AND RADIATION MEDICINE, UNIVERSITY OF NAIROBI

DR. WANJIKU JOHN MWANGI (MBCHB, UoN)

H58/68988/2013

UNIVERSITY OF NAIROBI

DECLARATION

I, **Dr. Wanjiku John Mwangi,** declare that the work contained herein is my original work and has not been presented in any other university or published anywhere to the best of my knowledge.

Signature ……..Date……

APPROVAL BY SUPERVISORS

This dissertation has been submitted with my approval as a University supervisor.

Dr. Peter Magabe Chacha, M. B. Ch. B (UoN), Mmed. Diagnostic Imaging (AKUH, Nbi), Fellow, VIR (Israel)

Vascular and Interventional radiologist, Lecturer

Department of diagnostic imaging and radiation medicine

University of Nairobi.

Signature …… Date……...

This dissertation has been approved with our approval as University co-supervisors

Dr. Daniel Kibaya, M. B. Ch. B (UoN), Mmed. Diagnostic Imaging (UoN), Fellow, VIR (Singapore)

Vascular and interventional radiologist,

Kenyatta National Hospital.

Signature……..…… Date……

Dr. Lawrence Mugambi M'Arithi, M. B. Ch. B (UoN), Mmed. Diagnostic imaging (UoN),

Radiologist,

Kenyatta National Hospital.

Signature ……. Date……

DECLARATION OF ORIGINALITY FORM

Declaration Form for Students

UNIVERSITY OF NAIROBI

This form must be completed and signed for all works submitted to the University for examination.

Name of Student _____

Registration Number _____

College _____

Faculty/School/Institute_____

Department _____

Course Name _____

Title of the work_____

DECLARATION

1. I understand what Plagiarism is and I am aware of the University's policy in this regard
2. I declare that this _____ (Thesis, project, essay, assignment, paper, report, etc) is my original work and has not been submitted elsewhere for examination, award of a degree or publication. Where other people's work, or my own work has been used, this has properly been acknowledged and referenced in accordance with the University of Nairobi's requirements.
3. I have not sought or used the services of any professional agencies to produce this work
4. I have not allowed, and shall not allow anyone to copy my work with the intention of passing it off as his/her own work
5. I understand that any false claim in respect of this work shall result in disciplinary action, in accordance with University Plagiarism Policy.

Signature _____

Date _____

DEDICATION

This work is dedicated to my family.

To Carolyne, the love of my life and to our handsome boy, Master Alvin, for their immense support and patience during the many long hours that I invested in the compilation of this book. May God's grace and favour be upon you always.

To my mum and my siblings for standing with me in prayers. May the Almighty father bless you abundantly.

ACKNOWLEDGEMENTS

My sincere gratitude goes to my supervisors, Dr Chacha, Dr Kibaya and Dr Mugambi for their guidance and support throughout the process of preparing this book. May God bless you.

Special thanks go to my stastician, Mr. Philip Ayieko for a wonderful analysis of the raw data. Your support was invaluable.

I am truly grateful to the staff who worked with me at the KNH CT suite especially Mr. Kidali and Mr. Gitonga. Your commitment to the study was awesome.

I will remain forever indebted to all the patients who trusted us to perform the procedures. Without you this study would not have been possible.

Special appreciation goes to my family for their love, prayers and moral support. You were my strong pillars during the entire process.

I cannot forget my fellow residents especially Dr Norah Ger and all those who contributed in one way or the other towards the successful compilation of this work. May God bless you.

Above all, I give thanks to the Almighty God for His grace is always sufficient.

ACRONYMS AND ABBREVIATIONS

CT scan	-	Computed Tomography Scan
KNH	-	Kenyatta National Hospital
CNB	-	Core Needle Biopsy
TTFNAB	-	Transthoracic Fine Needle Aspiration Biopsy
UoN	-	University of Nairobi
VIR	-	Vascular Interventional Radiology
ACCP	-	American College of Chest Physicians
FNA	-	Fine Needle Aspiration Biopsy
TCNB	-	Transthoracic Core Needle Biopsy
PI	-	Principal Investigator
ALARA	-	As Low As Reasonably Achievable
WHO	-	World Health Organization
NSCLC	-	Non Small Cell Lung Cancer
SCLC	-	Small Cell Lung Cancer
SPN	-	Solitary Pulmonary Nodule
HRCT	-	High Resolution CT Scan
NCR	-	Nairobi cancer registry

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

Percutaneous 17/18-gauge coaxial CT guided core needle biopsies of lung nodules and masses at Kenyatta National Hospital: diagnostic yield, complication rates and radiological pattern of histologically proven primary lung cancer histological subtypes.

Background: Percutaneous CT guided transthoracic core needle biopsy has become the procedure of choice for the diagnosis of pulmonary lesions [1-4]. This method is effective, safe and minimally invasive thereby providing a real alternative to more invasive surgical procedures like diagnostic thoracotomy [1, 4-6]. Co-axial biopsy needle system is becoming increasingly used as a diagnostic technique in the diagnosis of focal pulmonary pathology.

The objective of this study was to determine the diagnostic yield and complication rates of percutaneous 17/18-gauge coaxial CT guided core needle biopsies of lung nodules and masses as seen at a tertiary national referral center. Radiological pattern of the histologically proven bronchogenic carcinoma was also described.

Materials and Methods

A total of 51 patients with demonstrable lung nodules and masses at imaging were prospectively referred for CT guided biopsy. Pre biopsy CT chest was carried out to confirm the location of the lesion and map out entry site. A 17 gauge coaxial needle was then inserted into the lesion, adjusted and optimal position of the tip confirmed with CT. An 18 gauge trucore biopsy needle was subsequently inserted through the guiding coaxial needle and at least three trucore biopsies obtained for histology. Radiological description of the histologically proven lung cancer was done after histopathological confirmation.

Results

Forty nine (96.1%) biopsies yielded adequate specimens for histopathological diagnosis. Two specimens were non diagnostic. There were 36(73.5%) malignant lesions and 13(26.5%) benign lesions. Primary lung cancer can accounted for 69.4% while metastatic deposits constituted 4.1% of the cases. Among the primary lung cancers, 32(94.1%) cases were of the NSCLC type and 2(5.9%) cases were of small cell carcinoma type. Squamous cell carcinoma was the most prevalent histological subtype involving 24(70.6) cases followed by adenocarcinoma 8(23.5%). Small cell carcinoma was seen in 2(5.9%). There were no cases of

large cell carcinoma. Of the total number of patients with primary lung cancer, 27 (70.4%) were males and 7(20.6%) were females.

More than half (58.8%) of primary lung cancers in the study presented as solid tumours while the rest had a mixture of both solid and ground glass CT attenuation. There were no tumours that presented with pure ground glass attenuation.

Squamous cell carcinoma presented most commonly as a central speculated mass while adenocarcinoma presented mainly as a large well outlined homogenous mass with peripheral extension. Cavitation within the primary lung cancers was rare and only seen in squamous cell carcinoma and adenocarcinoma. Calcification was commonest in squamous cell histological subtype. Spiculated mass lesion of either peripheral or central location was the commonest radiological pattern seen in the primary lung cancers.

A total of 15 complications occurred in 51 lung biopsies done, 9 (17.6%) being cases of post biopsy pneumothorax and 6(11.8%) being cases of minor lung parenchymal haemorrhage. Only two patients (3.9%) had a pneumothorax of more than 3cm requiring chest tube drainage.

Conclusion

Percutaneous 17/18 gauge coaxial CT guided core needle biopsies of lung lesions has a high diagnostic yield with low complication rates and is recommended for routine biopsies of lung lesions. Squamous cell carcinoma was the commonest histological subtype presenting most commonly as a central speculated mass.

1.0 CHAPTER ONE: INTRODUCTION

Percutaneous transthoracic needle biopsy of lung lesions under image guidance has been shown to be a safe and effective minimally invasive method of obtaining adequate specimen for either histological or cytological analysis [1, 3-4, 7-12]. Computed tomography offers the most accurate method of localizing lung biopsies[13]. Development and improvement of specific needle types have led to the acceptance of this technique making it an indispensable method in diagnosis of focal pulmonary pathology[14]. Indeed, it provides a viable alternative to other available diagnostic methods such as bronchoscopy, sputum analysis and thoracotomy[6]. Percutaneous CT guided biopsies of lung lesions are performed either by using fine needle aspiration biopsy (FNAB) or core needle biopsy technique with or without the coaxial system.

FNAB technique is used to obtain aspiration material for cytological evaluation while core needle biopsy technique is used to obtain tissue specimen for histological analysis. Several studies have been done to assess the diagnostic yield of these two techniques. Both techniques show high diagnostic accuracy, sensitivity and specificity for malignancy [15]. However, with development of individualized and targeted therapy of specific lung cancer histological subtypes, CT guided core needle biopsy technique has gained more ground as it avails more tissue both for histological and biomarker profile analysis[16-17]. It provides multiple larger specimens for more accurate classification and specific diagnosis. In malignant lesions core needle biopsy has shown higher diagnostic accuracy compared to FNAB without significant increase in complication rates.

The use of the coaxial system improves the biopsy procedure by helping to avoid multiple pleural punctures and thus reducing the incidence of pneumothorax which is the most common complication. It also allows multiple sampling and therefore improves the diagnostic yield[16].

Different coaxial automated CNB systems are now available in the market. A guiding outer needle is first inserted through the skin and towards the lesion. Multiple samples are harvested by use of the inner CBN while maintaining the guiding outer needle in position, thus greatly minimizing the incidence of potential complications[18]

The coaxial biopsy needle system continues to be refined with the use of smaller diameter guiding and core biopsy needles. In this study we used a 17 gauge guiding needle and

18gauge core biopsy needle, a system which in a few studies has been shown to further increase the diagnostic yield while reducing the incidence of complication rates such as pneumothorax and haemorrhage [17-20].

The aim of this study was to evaluate the effectiveness and complications of 17/18 gauge coaxial system technique in CT guided core biopsies of lung nodules and masses. Where complications occurred possible risk factors were identified.

1.1 Literature Review

Percutaneous transthoracic lung biopsy was introduced by Leyden for diagnosis of pneumonia. This technique was then extended to the diagnosis of malignancies from 1930s onwards [14]. The use of large bore needles at that time was associated with many complications post procedure.

However, around 1960s and 1970s it gained widespread use due to development of high resolution image intensification and improved cytological techniques that allowed the use of smaller needles resulting to lower complication rates [14]

The first CT guided thoracic biopsy was reported by Haaga and Alfidi in 1976. Since then great strides have been made in technological improvement of CT as well as refinement of equipment available to interventional radiologists. With its high sensitivity, specificity and diagnostic accuracy percutaneous transthoracic CT guided biopsy technique has established itself as major diagnostic tool in thoracic oncology. Careful preprocedural evaluation as well as precise technique is key to achieving high diagnostic yields[21].

1.2 Diagnostic Yield

According to literature, both fine needle aspiration and core needle biopsy of pulmonary lesions have shown high diagnostic yield with acceptable rates of complications. However, with improvement of technique and specific needle types in the recent decades several studies have demonstrated excellent diagnostic accuracy with low incidence of complications for automated core needle biopsy technique compared to FNAB technique [2, 5, 22-24].This has made automated core needle biopsy technique to be adopted in many centers especially in cases where specific diagnoses of both malignant and benign lesions are being sought. This technique initially proved particularly effective in stable patients and for larger, superficial pulmonary lesions with unknown malignant status[21-22]On the other hand, FNAB was

recommended for small, deep and potentially malignant pulmonary lesions and is said to play a role in critical patients [20].

Recently a systematic review carried out by Yao et al [25], comparing FNAB and core needle biopsy in diagnosing lung cancer showed that the overall diagnostic characteristics for both benign and malignant lesions were better for core needle biopsies. In their study, the sensitivity ranges were 81.3-90.8% and 85.7-97.4% while diagnostic accuracy ranges were 79.7-91.8% and 89-96.9% for FNAB and core needle biopsy respectively.

Similar analysis of 305 percutaneous CT guided procedures of pulmonary lesions by Choi et al [26] revealed better performance of core needle biopsies compared to FNAB. The sensitivity, specificity and diagnostic accuracy was 93.6%, 100%, and 95.2% respectively for core needle biopsies compared to 89.2%, 97.4% and 93.4% for FNAB.

Further studies to define the best needle option for specific diagnosis by Gumaraels et al [22] and Beslic et al[23] reported a higher percentage of adequate biopsy samples obtained via core needle biopsy of up to (96.9%) compared to 84% for FNAB. Significantly, more specific diagnoses for bening and malignant lung lesions were recorded based on specimen collected by core needle biopsy method[22].

The presence of an onsite pathologist at the time of performing FNAB is essential to ascertain the diagnostic quality of the specimen obtained[27] .However, due to logistics of having a pathologist in the imaging department as well as cost considerations many centers are not able to meet this conditions and this makes core needle biopsy the best method for obtaining appropriate specimen for making specific diagnosis of both malignant and benign conditions[17]. In addition, core biopsy needle technique provides sufficient sample for biomarker profile analysis contributing immensely in targeted therapy for lung cancer histological subtypes[2, 28].

1.3 Complications

Many studies have shown transthoracic core needle biopsy to be an effective and safe procedure with very low morbidity and extremely rare mortality [1-4]. However, post procedure pneumothorax remains the most common complication with reported incidences of between 8% and 64% [29-31]. Fortunately most pneumotharaces resolve spontaneously and only a few are treated with chest tube thoracostomy. Other rare complications may occur and include hemorrhage, haemoptysis, systemic air embolism and pericardial tamponade[32-33].

In an effort to improve diagnostic yield and reduce the incidence of complication rates, major leaps in technological advancement and refinement in equipment used in CT guided transthoracic needle biopsy techniques are continually being made. Introduction of coaxial biopsy systems diminishes the number of passes through the visceral pleura to only a single puncture[18]. This ideally should reduce the likelihood of pneumothorax. However, few studies to have not statistically proven this concept [29-30, 34-37]

Haramati et al[38] evaluated 33 consecutive biopsies using non coaxial automated needle biopsy system technique and found that 9% of the patients developed post biopsy pneumothorax. None of these cases required chest tube insertion for drainage. A study conducted by McSweeny et al[39] using 19/20gauge coaxial biopsy needle system found that pneumothorax was the most common post biopsy complication. They reported a pneumothorax rate of 20% with 4 patients (5.3%) requiring chest tube for treatment. Luciderme et al[20] employed 18g coaxial system and recorded a pneumothorax rate of 34% . 3% of the cases met the criteria for chest tube placement. Pulmonary parenchymal haemorrhage occurred in 9% of the patients. Guimaraes et al[6] combined both 18g and 20g coaxial needle system depending on the lesion size and recorded a relatively low pneumothorax rate of 7.2% and a modest bleeding rate of 3.1%.

1.4 Risk Factors Associated With Complications

Refinement of specific needle types and development of small bore needles have had remarkable improvements in TCNB outcomes. Some studies have associated large cutting needles with clinically significant bleeding but not with unacceptable pneumothorax rates[3, 32, 40]. In their study of 846 consecutive CT guided TNAB procedures, Geraghty et al[41] reported significant reduction in pneumothorax rate with comparable diagnostic yield when smaller coaxial stabilizing needle was used. Similarly small gauge needle are preferred since they have been shown to facilitate access of very small lesions with significant reduction in bleeding complications and without reduction in diagnostic yield [2-3, 34, 36, 42-43]. However, a few studies have contradicted this concept and failed to associate large gauge needles with increased rates of pneumothorax or chest tube placement [44-46]. Infact Moore et al[47], in their study to determine the effect of needle gauge on cytological yield and complications in CT guided lung biopsy, supported the use of large gauge(18g) needles since it required few passes, had similar complication rates and equivalent diagnostic yield with that of smaller gauge needle(19.5 and 21g).

Apart from the needle size, several other factors have been found to influence the development as well as the severity of post biopsy complications. A study conducted by Wang et al[48] concluded that smoking, supine position and longer needle path within normal lung parenchyma were significant risk factors for post biopsy pneumothorax. Eva Branden et al[8] observed that there was an increased risk for pneumothorax when the biopsied lesion was small or when the emphysema was in the path of the biopsy needle.

Stanley et al[49] conducted a study to evaluate the diagnostic yield and complications of CT guided thoracic biopsy. The study associated pneumothorax rate with traversed lung length, lesion size and lesion depth. Risk factors influencing haemoptysis rate were found to be the traversed lung length and lesion size.

Analysis of risk factors affecting complications of CT guided lung biopsies by Nakatani et al[50] revealed that the incidence of pneumothorax and bleeding increased with smaller lesion size and greater lesion depth. Patients who had pulmonary emphysema were noted to experience less significant parenchymal bleeding.

Khan et al[51] noted a higher incidence of pneumothorax rate when the lesion was located in the lung parenchyma compared to lesion located at the pleura. A similar observation was noted by Guimaraes et al[6] in their study that evaluated 362 biopsies.

A study conducted by Yeow et al[52] evaluating the risk factors for pneumothorax and bleeding concluded that lesion depth was the most important predictor of post biopsy pneumothorax with the highest incidence reported for subpleural lesions.

1.5 Radiological Evaluation of Bronchogenic Carcinoma

Bronchogenic carcinoma forms the highest percentage of all primary lung tumours[53]. It tops the list of cancer related deaths accounting for 27% of all cases [54]. This carcinoma is broadly divided into small cell lung carcinoma (SCLC) and non small cell lung carcinoma (NSCLC). Histologically, NSCLC is sub classified further into three main categories: Squamous cell carcinoma, adenocarcinoma and large cell carcinoma[55]. NSCLC accounts for up to 85% of all cases of lung cancer with over 50% of this group being adenocarcinoma[54]. A change in biology of lung cancer has been reported with relative increase of adenocarcinoma and declining numbers of Squamous cell carcinoma. Moreover, there is increasing incidence of lung cancer in women[53, 56]. A better understanding of NSCLC biology has led to development of novel treatment strategies with remarkable

improvement in the prognosis. Histologically guided and genotype based targeted therapies predominantly for lung adenocarcinoma has opened new frontiers towards personalized therapy for lung cancer[54]. Lung cancer most frequently presents as pulmonary parenchymal nodule or a mass on imaging. A mass is a nodule that is larger than 3cm in diameter and is easily diagnosed on plain chest radiograph or on a CT scan of the chest. A lung nodule is defined as a radiographic opacity less than 3cm in diameter. Small nodules less than 1cm are known as indeterminate nodules and are diagnosed on HRCT of the chest[57]. Determination of malignant or benign nature of a nodule or mass will influence the treatment plan and the disease prognosis. Even though radiology alone cannot determine the disease status of a nodule or mass, it plays a vital role in suggesting the likelihood of malignancy or benignity noninvasively[57]. Different variables assessed on CT to determine the disease status of nodule or mass include the following:-

1.5.1 Size

The chances of malignancy increases with increasing size of a lung nodule[58]. As a general rule, a solitary pulmonary nodule (SPN) of more than 3cm in diameter is highly likely to be malignant. A clear correlation between the prevalence of malignancy and nodule size has been reported with 0-1% for nodule less than 5mm, 6-28% for nodules 5-10mm, 33-60% for nodules 11-20mm and 64-82% for nodules greater than 20mm[59-60].

1.5.2 Margins

Though not an absolute indicator, the interface between a lung nodule and the surrounding normal lung parenchyma provides very vital information regarding the disease status of the nodule. Smooth peripheral margins on CT are frequently associated with benign lesions while speculated, lobulated and irregular margins indicating neoplastic infiltration and distortion on neighbouring tissues are suggestive of malignancy[61]. Zwirewich et al[62] evaluated 96 solitary pulmonary nodules and found speculation in 95% of primary lung carcinoma. In the same study speculation was seen in 45% of benign lesions while lobulation was predominantly associated with malignancy. Pleural tags were noted in 58% of malignant lesions and in 27% of benign lesions.

1.5.3 Calcification

Though calcification is seen in both benign and malignant pulmonary lesions, the pattern of calcification is different for the two types of lesions. Laminated, dense central and popcorn

patterns of calcification characterize benign nodules whereas stippled, punctate and eccentric patterns of calcification suggest malignancy[63].

1.5.4 CT attenuation

Ground glass attenuation of a nodule on CT represents lepidic growth pattern or mucin production. This characteristic has been associated with more aggressive behavior of a lung nodule with a high potential for developing early stage adenocarcinoma and bronchoalveolar carcinoma than that of solid nodule[64-65]. Nakata et al[66] found malignancy rate of nodular ground glass opacity with solid component of 93%. Henschke et al[67] reported a malignancy rate of 63% and 18% respectively for nodular ground glass opacity with solid component and nodular ground glass opacity without nodular components.

1.5.5 Cavitation

Cavitation is seen in both benign and malignant nodules. However, thicker and irregular walls are associated with malignancy. Pseudocavitation which is a result of lepidic growth pattern is seen in bronchoalveolar adenocarcinoma. Cavitation occurs in 2-16% of lung cancer[68]. A 5mm thickness of the wall of a cavity and the presence of nodular internal margins due to tumour excresences may be seen in a malignant lung nodule.

1.6 Radiological Appearance of Bronchogenic Carcinoma Subtypes

Multiple synchronous primary lung cancers of the same or different cell types account for less than 3% of all lung cancers[69]. In addition, different cellular elements may be found within the same tumour as reported by Roggli et al[70] who found 45% of lung cancers in their study had more than one major histological subtype. Despite this overlap different radiographic patterns have been described for specific cell types.

1.6.1 Adenocarcinoma

The incidence of adenocarcinoma has been rising overtime accounting for more than 50% of NSCLC in recent studies compared to an incidence of 4-8% reported in the 1960s[53-54]. It presents most commonly as a solitary peripheral or subpleural mass. Approximately 50 % of these lesions will have hilar or mediastinal involvement at the time of diagnosis. Adenocarcinoma is the most common histological subtype of lung carcinoma associated with superior sulcus tumour[53]. Other imaging features of adenocarcinoma include

pseudocavitation, speculation, irregular margins forming a star like pattern, pleural tags and heterogeneous attenuation[71].

1.6.2 Squamous Cell Carcinoma

Squamous cell cancer most commonly presents as a central lung tumour[72-73]. However Quinn et al[56] contradicted this finding and reported no significant difference between central and peripheral tumours. Intraluminal tumours may produce complete lobar collapse resulting in volume loss. Radiological features of volume loss include ipsilateral mediastinal shift and hemidiaphragmatic elevation[53]. Cavitation is also commonly associated with squamous cell carcinoma. In their study to evaluate radiographic patterns in lung cancer, Sharma et al[72] reported that 75% of cavitating lung malignancies in their study were of squamous cell type.

1.6.3 Small Cell Lung Carcinoma

This subtype of lung cancer is highly malignant and usually shows metastasis at the time of diagnosis. The most common presentation of this tumour is a central mass with only 10% presenting as peripheral lesions[56, 72-73].

1.6.4 Large cell carcinoma

This histological entity of lung carcinoma accounts for 9% of all lung cancers. It presents as a large bulky peripheral mass on imaging[53, 74].

2.0 CHAPTER TWO: STUDY JUSTIFICATION

A multitude of literature have shown core needle biopsy to be superior than FNAB[1, 4-6] and use of coaxial systems reduces the frequency of pneumothorax. This has led to adoption of coaxial core needle biopsy technique by many centers. However, review of literature reveals conflicting results as regards the size of both outer stabilizing cannula and inner biopsy needle. As a result some centers select needles sizes based on lesion characteristics with small gauges being preferred for small and deep seated lesions and large gauges are used in relatively large lesions.

Very few studies have specifically evaluated the diagnostic yield of 17/18 gauge coaxial system in CT guided transthoracic needle biopsy of lung lesions [17-20] and to the best of our knowledge in English literature. Studies done assessing coaxial core needle systems have reported diagnostic yields and complication for much finer systems.

Our institution, a national referral center, has recently started performing CT guided coaxial transthoracic core needle biopsies. There was no previous data documenting the local experience. This study seeks to establish the diagnostic yield of 17/18 gauge coaxial core needle system in the national referral center. This system is readily available and affordable. Findings of this study will fill the local experience gap as well as contribute to the body of knowledge of outcomes of this specific system which has not been extensively evaluated. In addition, the study may lay the foundation for other future studies evaluating the diagnostic yield of other core needle biopsy systems used in the diagnosis of lung lesions.

2.1 Study Question and Objectives

2.1.1 Research question

What are the diagnostic yields and complications rates of percutaneous 17/18 gauge coaxial CT guided core needle biopsies of lung nodules and masses at Kenyatta national hospital?

2.2 Study objectives

2.2.1 Broad objective of the study

- To determine diagnostic yield and complication rates of percutaneous 17/18gauge coaxial CT guided core needle biopsies of lung masses and nodules at KNH.

2.2.2 Specific objectives

- To determine diagnostic yield of 17/18 gauge coaxial CT guided core needle biopsies of lung masses and nodules at KNH.
- To determine the complications associated with this coaxial technique.
- To identify risk factors associated with complications of this coaxial technique.
- To describe the radiological appearance of histologically proven bronchogenic carcinoma subtypes.

3.0 CHAPTER THREE: METHODOLOGY

3.1 Study Design

This was a descriptive prospective cross sectional study which was conducted over a period of one year from 1st of December 2015 to 30th of December 2016.

3.2 Sample Size Estimation

The sample size was calculated using Cochran formula (1963)

$$n_0 = \frac{Z^2 * p(1-p)}{e^2}$$

[Cochran (1963)]

Where

n_0 is the sample size for target population> 10, 000

Z^2 is the abscissa of the normal curve that cuts off an area at the tails (1 - α equals the desired confidence level, e. g, 95%).

e is the desired level of precision,

p is the estimated proportion of an attribute that is present in the target population,

The study desired a 95% confidence level and +5% precision.

Since no there was no study found conducted in similar settings, our study assumed p=50%.

The sample size became

$$n_0 = \frac{1.96^2 * 0.5(1-0.5)}{0.05^2} = 384$$

Since the target population was less than 10,000 (i.e. target population= 48 patients per year) then the sample size was adjusted downwards.

The sample size (n_0) was adjusted using:

$$n_1 = \frac{n_o}{1 + \frac{(n_o - 1)}{N}}$$

Where

n_1 is the adjusted sample size

N is the target population size

Therefore the adjusted sample size became:

$$n_1 = \frac{384}{1 + \frac{(384-1)}{48}} = 43$$

Since the study allowed for 10% loss of information, the sample size was adjusted upwards by 4 participants (i.e. 10% of 43). The final sample size became

n=43+4=47

3.3 Study Population and Recruitment

This research was carried out at the radiology department of Kenyatta national hospital which is a national referral and teaching centre. The principal investigator (P.I) and a research assistant were stationed at the radiology department during operating hours (each weekday between 8am and 4pm). All consecutive patient referrals for percutaneous CT guided transthoracic lung biopsies were approached and assessed for study eligibility. Eligible patients meeting the study criteria were asked to consent to participate in the study. Those patients who provided informed consent were recruited prior to administration of any study procedures and completion of study tools. A total of 51biopsies were carried out.

3.4 Ethical Considerations

The study only commenced upon approval by the university of Nairobi and Kenyatta National Hospital Scientific and Ethics Review Committee. The study objectives, the process of biopsy procedure, likely complications, treatment and other available alternative methods for diagnosis were fully explained to the eligible participants. Only the patients who gave informed consent were enrolled for participation in the study and they were made to understand that they had the right to withdraw from the study at any stage. Those who

declined participating in the study were not in anyway denied the treatment they deserved because of their decision to decline. There was no extra cost incurred for participating in the study. Data collected was entered into an excel spread sheet in a password protected computer and only accessible to personnel involved in the project. Confidentiality and privacy was observed at all times and the datasheets were destroyed upon completion of the study. There was no monetary gain by the principal investigator

3.5 Inclusion Criteria

The study included all patients who were consecutively referred for percutaneous CT guided transthoracic biopsy with focal pulmonary pathology presenting as lung nodule, mass or consolidation. It was mandatory for the participants to have normal platelet counts, prothrombin time and activated prothrombin time four prior to undergoing the biopsy. Only patients who gave informed consent were included in the study after a thorough explanation of the benefits and risks of needle lung biopsy as well as the alternative diagnostic procedures available.

3.6 Exclusion Criteria

The study excluded those patients referred for percutaneous CT guided biopsy of lung masses but failed to consent for the procedure. Patients with abnormal coagulation parameters and those who already had a histological diagnosis were excluded from the study.

3.7 Quality Assurance and Control

All study exclusions and reasons for exclusion were documented. The biopsy procedure was standardized and only performed by three radiologists experienced in interventional radiology work and the principal investigator under the supervision of one of the three radiologists. All specimens were analyzed in one laboratory, Kenyatta national hospital, and by one senior experienced pathologist to avoid inter-observer bias.

3.8 Materials and Methods

3.8.1 Materials

A coaxial 17gauge automated core needle biopsy system (BARD systems) was used. The system consists of a 17-gauge 15.1cm coaxial needle with an introducer stylet that is used for positioning and guidance and an 18-gauge 25cm core cutting biopsy needle that is passed through the coaxial needle for biopsy sample.

A 16 slice multidetector CT scan (Phillips Medical Systems) was used to guide all biopsies. Selected images were acquired in the area of interest using optimum parameters in line with the ALARA principle.

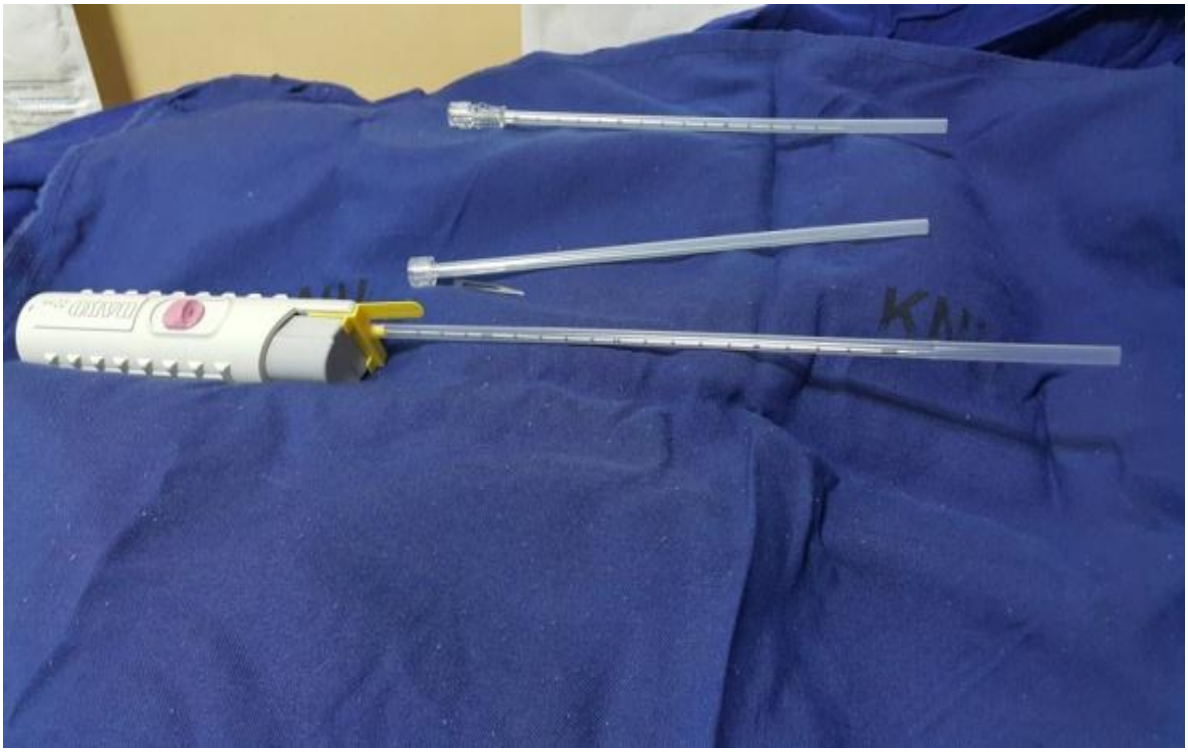

Figure 1: Photograph of the coaxial needle system used at KNH

3.8.2 Pre-Biopsy Preparations

Coagulation screening was done to all study participants to ensure all parameters are within normal limits (prothrombin time: 9.50 -14.00s, activated prothrombin time: 25-35s, international normalizing ratio: 0.8-1.5). Patient receiving anticoagulant and antiplatelet drugs were advised to stop their medication five days prior to the procedure. All patients were informed about the purpose, methodology and possible complication and treatment of those complications. Written and informed consent was obtained from all participants. All available thoracic images were reviewed to localize the lesion and to plan the optimal patient position that allowed for the safest access route avoiding the ribs, fissures, bullae and vessels. For standardization, the biopsy procedure was performed by two experienced interventional radiologists, one general radiologist experienced in transthoracic needle biopsy technique and

one radiology resident who is the principal investigator under the supervision of the experienced interventional radiologists.

3.8.3 Biopsy Procedure

IV premedication was given. All biopsies were performed using multidetector CT scan guidance. The patient was positioned either prone, supine or lateral decubitus depending on the site of the lesion. Selected images (4-5 slices) were acquired in the region of interest. Patient was instructed to breath in a slow, shallow and regular manner both during the time of performing the biopsy and during the time of image acquisition. They were encouraged to stay calm and to abstain from talking or coughing during the procedure and also during the observation period.

An initial CT scan with or without contrast was done to localize the mass and reveal its current status. The safest and the shortest distance to reach the lesion was determined. The entry point was identified. The distance between the skin, pleura and the lesion was measured and recorded. The marked skin entry site and the surrounding area were thoroughly cleaned with povidone iodine solution. The area was then covered with sterile drapes. The area was infiltrated with 10cc of 2% lidocaine hydrochloride (Xylocaine, AstraZeneca).

A small cruciate incision was made on the skin at the entry site. The 17 gauge introducer coaxial needle was inserted gradually in small increments in the chest wall until just before crossing the pleura. Limited [biopsy protocol] repeat-CT scans were performed at the area of interest to ensure the coaxial needle is aligned to the planned needle path towards the lesion. Once satisfactory alignment was achieved, the needle was advanced swiftly beyond the pleura into the lesion. After ensuring the needle trajectory is correct the needle was advanced rapidly through the pleura in one swift move and limited CT scans obtained to confirm the appropriate position of the needle within the lesion. In case of misalignment, the introducer needle was positioned in small increments without exiting the lungs.

The inner stylet of the coaxial needle was removed and an 18g cutting core automated biopsy needle was placed inside the needle guide to obtain core biopsy tissues [figure 2] of the mass obtained. After obtaining the specimen the core biopsy needle was carefully removed from the guiding needle hub and put in 10% formalin solution. More specimens up to a maximum of five were obtained in a similar fashion while directing the biopsy needle in different parts of the lesion. A core needle biopsy specimen was only considered adequate if histopathology

showed a definite malignant diagnosis such as adenocarcinoma or a benign diagnosis such as aspergilloma. If histopathological analysis did not reveal a specific diagnosis and contained phrases in the report such as atypical cells, highly suspicious among other terms, the sample was considered inadequate or non-diagnostic.

Figure 2: Photograph of a patient undergoing biopsy in prone position. The tru core biopsy [arrow] has been inserted through the guiding coaxial needle in readiness for first core biopsy

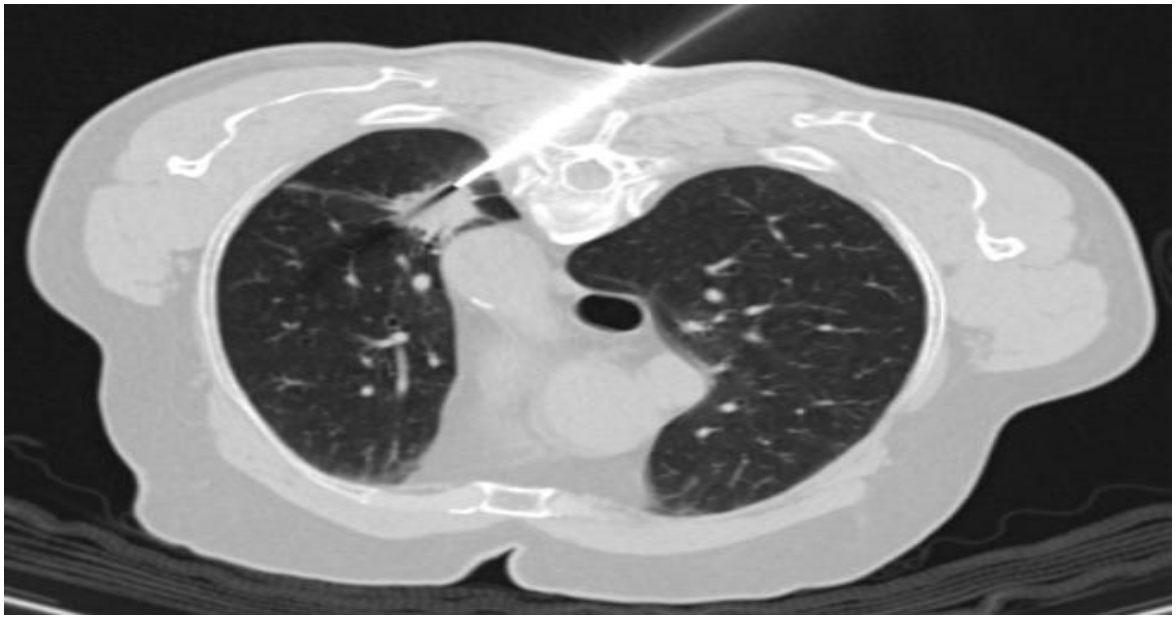

Figure 3: Prone limited CT scan of the same patient as in figure 2 showing successful optimal positioning of the coaxial needle within the margins of the lesion. Several tru core biopsies were obtained via the coaxial needle.

Figure 3: Prone limited CT scan of the same patient as in figure 2 showing successful optimal positioning of the coaxial needle within the margins of the lesion. Several tru core biopsies were obtained via the coaxial needle.

3.8.4 Imaging of Post Biopsy Complications

After withdrawal of the introducer co axial needle the biopsy site was dressed with sterile gauzes and a post biopsy CT chest done to evaluate for the presence of parenchymal haemorrhage or pneumothorax. Parenchymal haemorrhage was identified as areas of hyperattenuation around the lesion or along the needle path. Pneumothorax was identified as low attenuation free air outside of the lungs in the pleural cavity. The grade of pneumothorax and haemohrrage was determined according to known CT criteria [37, 38]. Small asymptomatic immediate pneumothorax was treated conservatively while placement of tube thoracostomy was reserved for patients with signs of respiratory compromise.

The patient was transferred to the observation room and monitored for four hours in order to detect possible complications. Imaging either CT chest or plain radiograph was repeated if necessary. Asymptomatic patients with mild pneumothorax were followed with no intervention. Drainage of the pneumothorax post procedure was done for symptomatic patients who meet criteria for drainage based on clinical and radiological findings.

3.9 Data Collection

Each patient was assigned a unique number that was filled at the top of the data collection form. Information on key demographic data and clinical history focusing on identification of possible risk factors for bronchogenic carcinoma was entered on the data abstraction form. Neither the name nor the patient number was used for confidentiality purposes. Enquiry on medical history was made to identify any co-morbidities of interest as per the data collection form. The participants were requested to submit any prior thoracic images to assist in lesion localization and biopsy procedure planning. The patients were then followed into the CT scan room and the preferred position for biopsy procedure noted and documented. Confirmation of the correct biopsy needle system, amount and type of local anaesthetic drug prepared for use was noted. The biopsy procedure was then carried out using CT guidance. The number of specimen collected documented. Details of variables under study were obtained from the CT consul and recorded on the data collection form.

All data was recorded in Ms excel data sheet that was saved in a password protection only accessed by personnel involved in the project. At the end of each day the P. I. inspected and verified all completed questionnaires to minimize errors and ensure no relevant study data was missing.

Confidentiality and privacy was observed and the data sheets were destroyed upon completion of the study.

3.10 Study Variables

Four different categories of variables were analyzed. These included variables related to the patient, lung lesion, procedure and complications.

3.10.1 Independent variables

Patient variables

Age
Sex
Occupation
Residence
Smoking
Comorbidity status

Lesion variables

Location in the lung parenchyma
Size
Depth
Radiological texture

Procedure

Duration
Participant position
Number of specimens obtained.

3.10.2 Dependent variables

Complications

Parenchymal haemorrhage

Pneumothorax

Haemoptysis

3.11 Data Management and Analysis

3.11.1 Data Management

Databases designed in Microsoft (Ms) excel was used for data entry. Data collected was entered in to an excel spreadsheet in a password protected computer. The data bases contained range and validity checks for each variable to ensure that data entry errors were minimized. Any inconsistencies noted during data entry were investigated by cross checking database entries to the source questionnaire. During this process integrity checks were used to detect invalid entries and outliers. Data cleaning was carried out using frequency distributions and cross tabulations until no more errors could be detected.

3.11.2 Data Analysis

In order to achieve the objectives of the study, data analysis was done by cross tabulation with chi square.

This analysis was carried out using the following steps;

3.11.3 Univariate analysis

The univariate analysis involved frequency distributions for categorical variables and descriptive statistics (means, medians, standard deviations) for continuous variables. Categorical variables (e.g. gender) were presented using pie charts and frequency distribution tables. Bar graphs were used to present age. Univariate analysis was used to give an understanding of the characteristics of the finding.

3.11.4 Bivariate analysis

Bivariate analysis was used to investigate any association or difference between variables. Selected variables related to the patient e. g. age, occupation, smoking history and co-morbidity, those related to the lung lesion such as diameter of the lesion and depth of the lesion from the pleura and those related to the core needle biopsy technique including

participant position during the procedure and duration of the procedure were correlated with complications such as pneumothorax and parenchymal haemorrhage by cross tabulation with chi square. P value less than 0.05 was reported as significant.

The spectrum of histopathological findings of the core needle biopsy specimens analyzed using frequency statistics.

Final computed results were presented in form of bar graphs, frequency tables and pie charts.

4.0 CHAPTER FOUR: RESULTS

4.1 Participants' Characteristics

A total of 51 patients underwent CT guided core needle lung biopsies using 17/18g coaxial needle system. There were 34(66.7%) males and 17(33.3%) females, giving a male to female ratio of 2:1

The mean age was 58.4 years with an age range of 22 to 94 years. The mean age of males was 61.7 while that of females was 51.6 years.

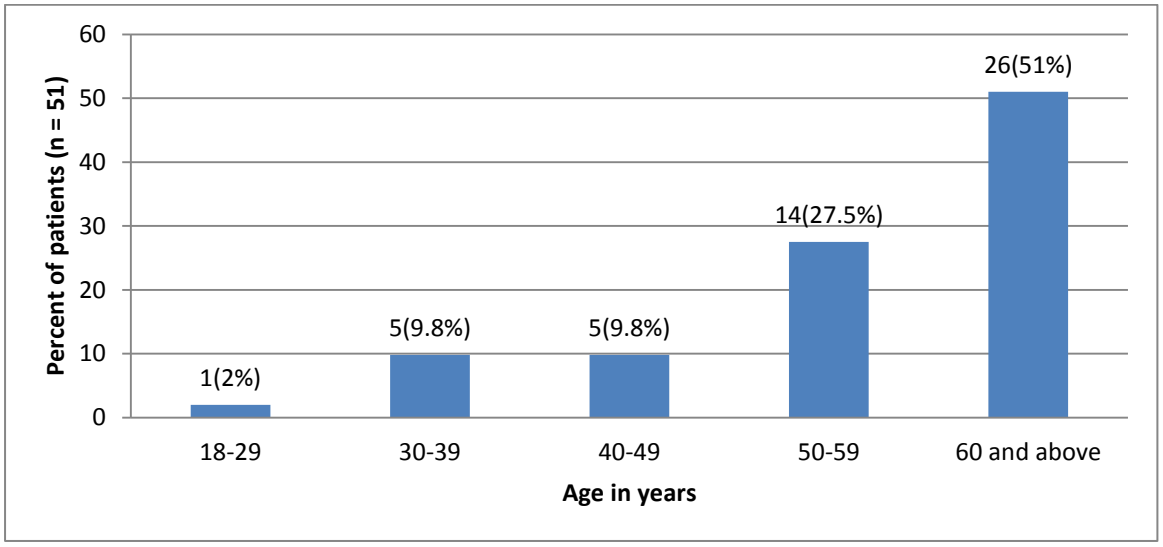

Figure 4: Bar graph of patients' age distribution. Most of the patients were aged 50 years and above.

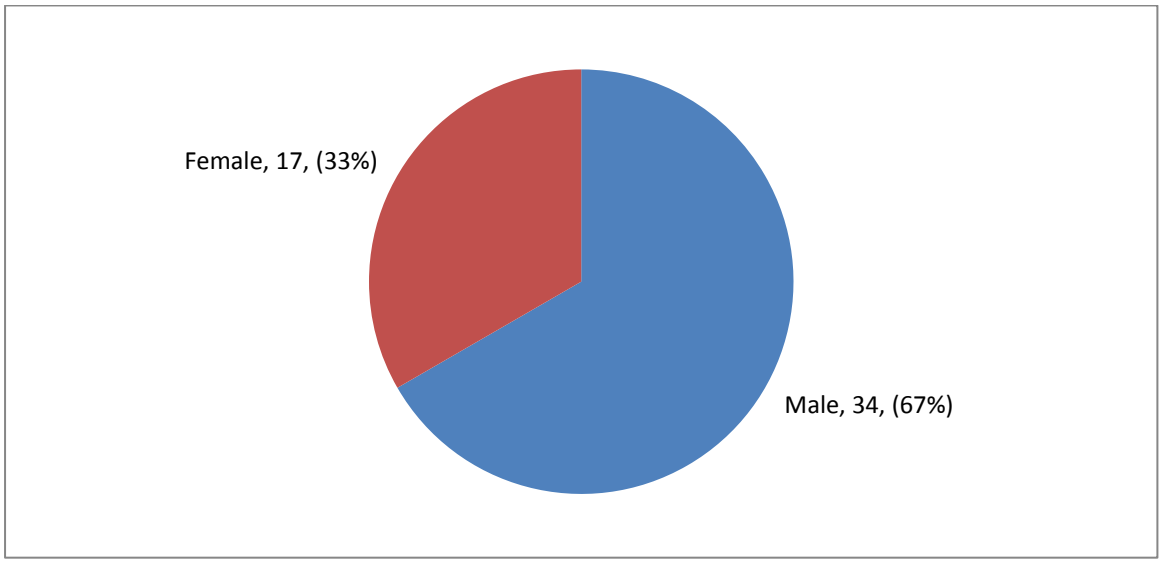

Figure 5: Pie chart of the study group showing a predominant male population

4.2 Local Geographic Distribution of the Study Population

The highest number of participants (45.1%) came from the Eastern region. This was followed by central region with 15(29.4%) participants. There was only one participant (2%) who came from north Eastern province. Western, Nairobi and central Rift valley had 3(5.9%), 4(7.8%) and 5(9.8%) participants respectively.

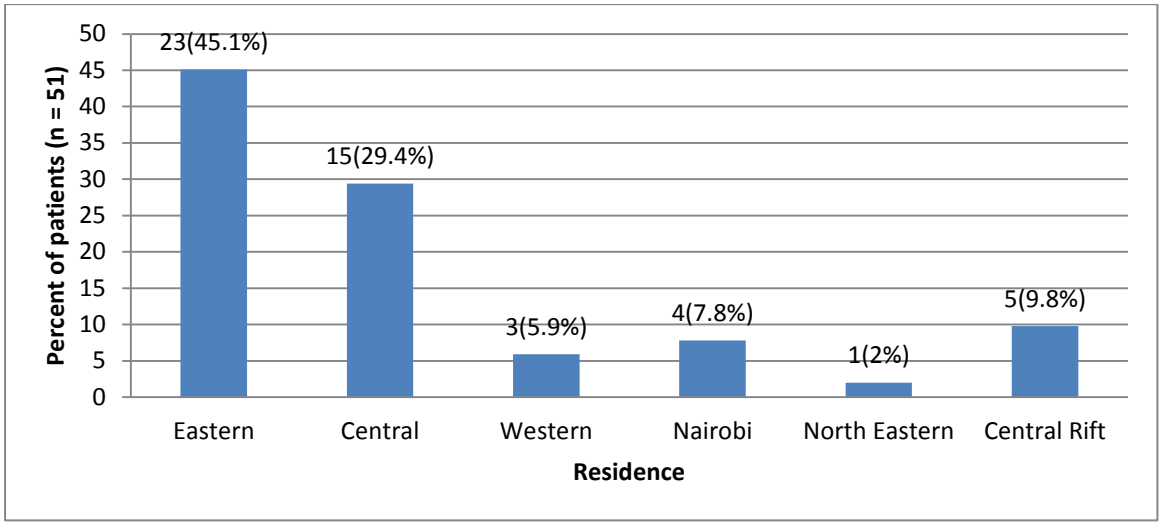

Figure 6 : Bar graph of geographic distribution of study population. Eastern Kenya accounted for the highest number of patients in the study

4.3 Smoking History

Of the 51 patients, 20(39.2%) of them were active smokers and the remaining 31(60.8%) had no history of smoking. All the smokers were males. The highest number of patients with smoking history came from the Eastern region 9(45%) followed by central region with 8(40%) active smokers. The average number of pack years among smokers was 28.7 with a range of 0.2 to 102.

4.4 Histopathological Results

Forty nine (96.1%) core needle biopsy specimens were considered adequate for histopathological analysis and the remaining two (3.9%) samples were considered non diagnostic. There were 36(70.6%) malignant lesions and 13(25.5%) benign lesions. Of the 36 malignant lesions 34(94.4%) were primary lung cancers while 2(5.6%) lesions were metastatic lung deposits. Among the primary lung cancers, 30(94.1%) cases were of the NSCLC type and 2(5.9%) cases were of small cell carcinoma type. Squamous cell carcinoma

was the most prevalent histological subtype involving 24(70.6) cases followed by adenocarcinoma 8(23.5%). Small cell carcinoma was seen in 2(5.9%). There were no cases of large cell carcinoma. Males had a higher incidence of primary lung cancer (79.4%)

Table 1: Spectrum of Histopathological Results

	n	%
Histological diagnosis		
Primary lung malignancies	34	66.7
Metastatic deposits	2	3.9
Benign nodules	1	2
Benign non-neoplastic conditions	12	23.5
Inadequate sample	2	3.9
TOTAL	**51**	**100**

Table 2 : Table Showing Histological Subtypes of Primary Lung Cancer.

Cell types	**Males**	**Females**	**Total**
Squamous cell carcinoma	20(58.8%)	4(11.8%)	24(70.6%)
Adenocarcinoma	5(14.7%)	3(8.8%)	8(23.5%)
Small cell carcinoma	2(5.9%)	0(0.0%)	2(5.9%)
Total	**27(79.4%)**	**7(20.6%)**	**34(100%)**

4.5 Primary Lung Cancer Histological Correlation with Smoking.

Among the 20 participants who were smokers 17(85.5%) were found to have primary lung carcinoma with squamous cell carcinoma subtype being the commonest. In the non smoking group, 17(54.8%) participants had primary lung cancer. Squamous cell carcinoma was the most prevalent subtype in both the smoking and non smoking group. The highest number of adenocarcinoma was seen in the non smoking group [table 4]. There were two (10%) cases of small cell carcinoma and these were found in the smoking group. Three (5.9%) non-smoking females with an active smoking spouse were found to have primary lung cancer; two adenocarcinoma and one squamous cell carcinoma [table 4]. Primary lung carcinoma was more prevalent in patients above the age of 50 years.

Table 3 ; Table Showing Histological Subtypes of Primary Lung Cancer Correlated With Smoking

	Small cell carcinoma	**Squamous cell carcinoma**	**Adenocarcinoma**	**Total**
No. of patients	**2(5.9%)**	**24(70.6%)**	**8(23.5%)**	**34(100%)**
Smokers	2(100.0%)	14(58.3%)	1(12.5%)	17(50%)
Non-smokers	0(0.0%)	10(41.7%)	7(87.5%)	17(50%)
Male smokers	2(100.0%)	14(58.3%)	1(12.5%)	17(50%)
Female smokers	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)
Smoking spouse	0(0.0%)	1(4.2%)	2(25.0%)	3(8.8%)

4.6 Complications

A total of 15 complications occurred: - 9 (17.6%) cases of pneumothorax and 6 (11.8%) cases of pulmonary parenchymal bleeding. Two (3.9%) patients had pneumothoraces of more than 3cm and required chest tube drainage. The rest of pneumothoraces were small and resolved spontaneously. Non of the pulmonary parenchymal haemorrhages required intervention and completely resolved in subsequent follow up .

Table 4 : Table Showing Post Biopsy Complications. Only Two Patients Required Intervention By Chest Tube Drainage For Resultant Pneumothorax.

Complication	Number	Intervention
Pneumothorax		
Less than 3cm	7	None
More than 3cm	2	Chest tube drainage
Parenchymal haemorrhage	6	None

4.7 Illustrative Cases

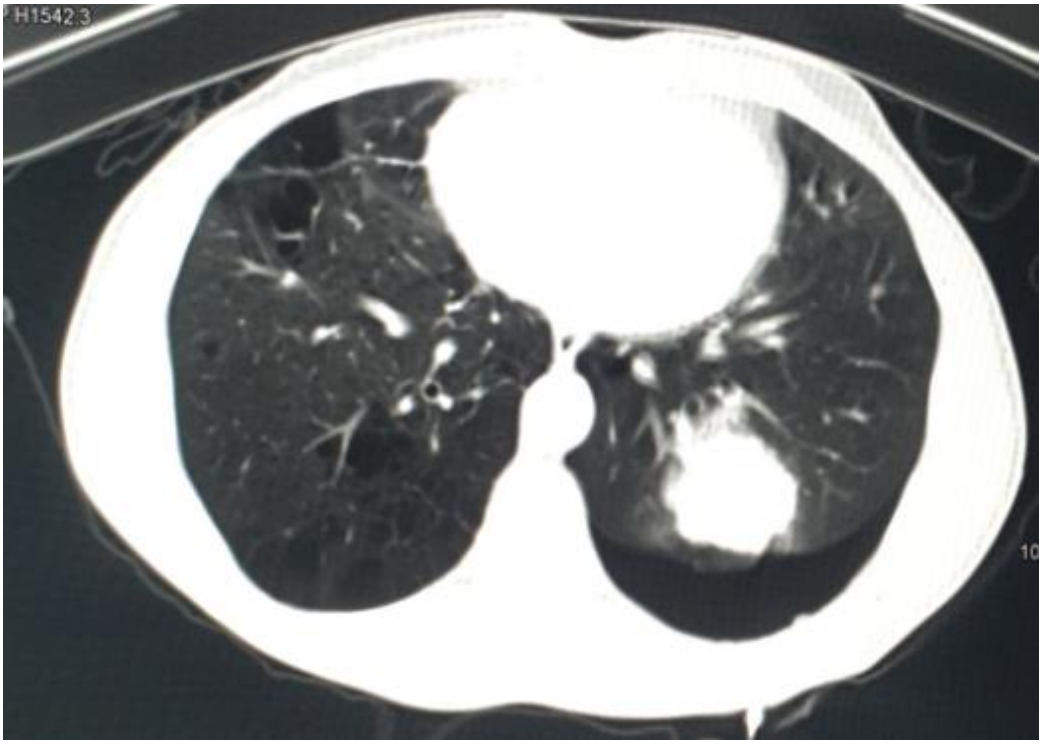

Figure 7 : Axial post biopsy CT chest of a 50 year old male chronic smoker demonstrating a left sided pneumothorax of less than three centimeters which resolved spontaneously on subsequent follow up.

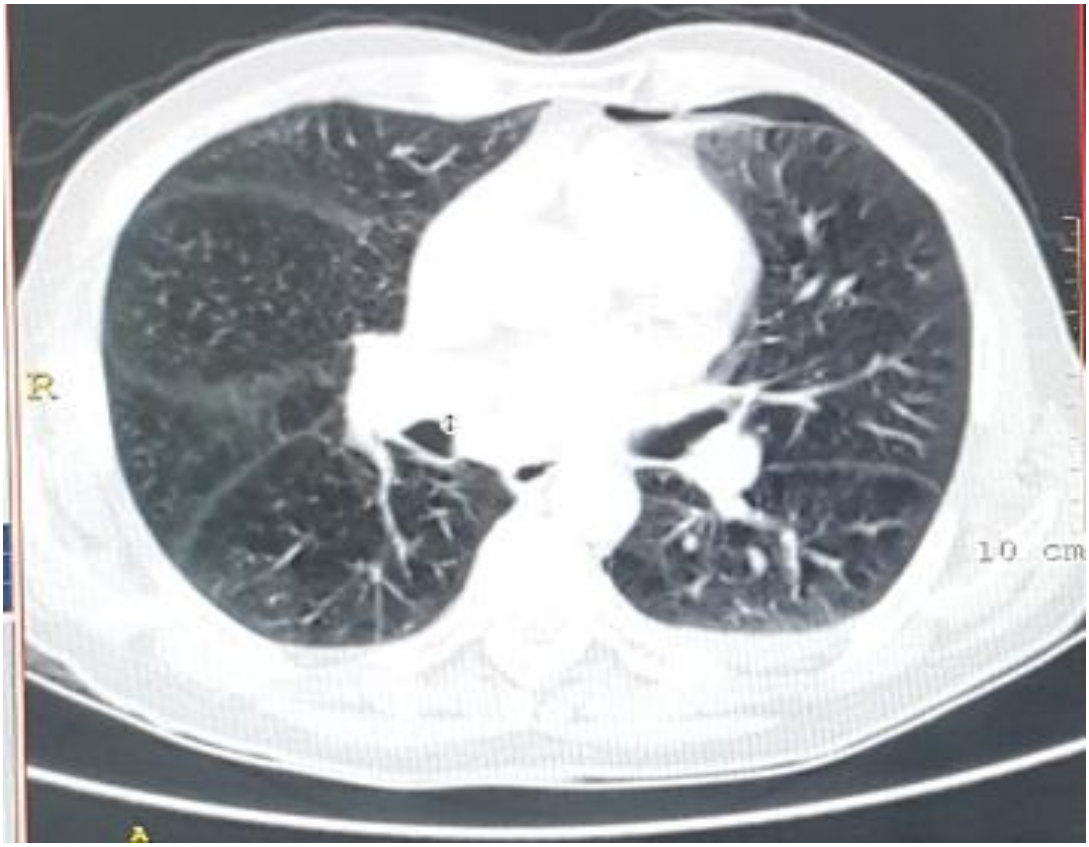

Figure 8: Post biopsy CT chest of a 74 year old male chronic smoker showing a small left sided post biopsy pneumothorax which resolved spontaneously on subsequent follow up

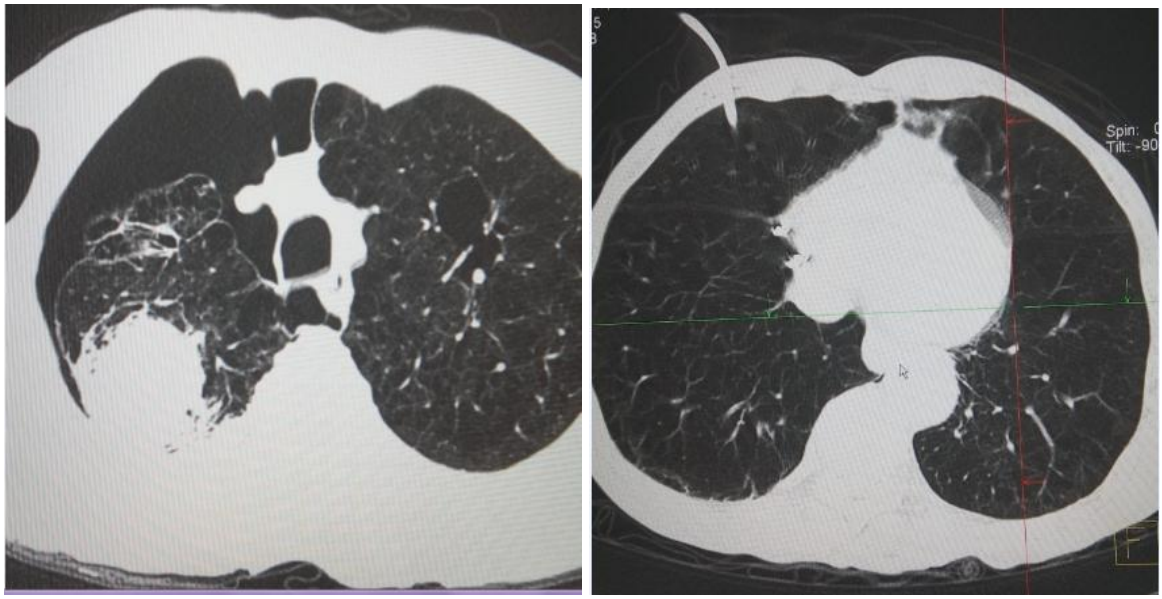

Figure: 9a **Figure 9b**

Figure 9: Post biopsy CT chest images of a 68 year old male chronic smoker showing a large right sided post biopsy pneumothorax (figure 9a). Figure 9b shows immediate re-expansion of the right lung after drainage of the pneumothorax using a pigtail catheter.

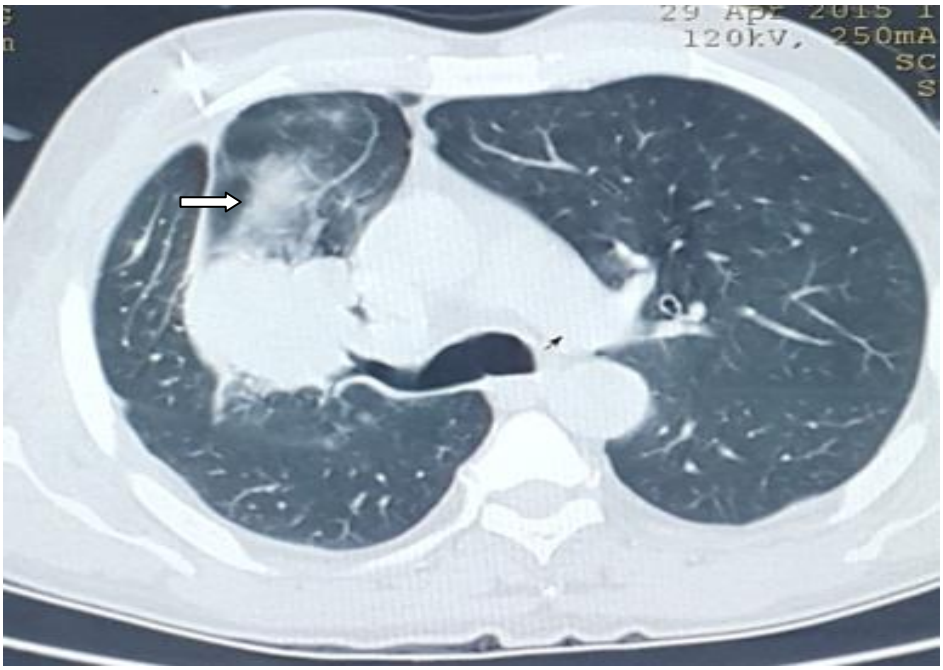

Figure 10:Post biopsy CT chest image of a 53 year old chronic smoker demonstrating a right sided linear ground glass attenuation (arrow) consistent with lung parenchymal hemorrhage along the needle path and a central hilar mass posterior to the haemorrhagic focus.

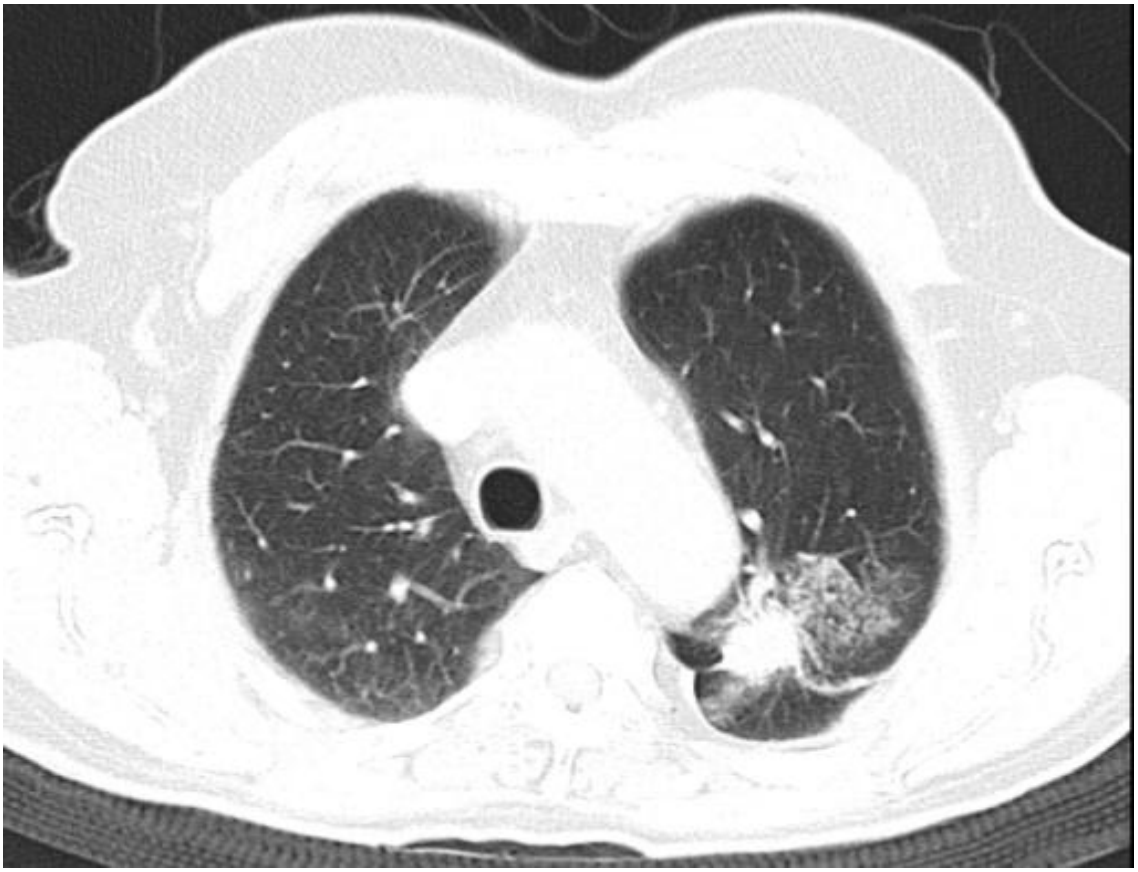

Figure 11: Post biopsy CT chest image of 77 year old showing ground glass attenuation adjacent to a spiculated left upper lobe lung mass consistent with parenchymal haemorrhage

4.8 Lesion Size, Depth and Pneumothorax

This study demonstrated positive correlation between lesion size and post biopsy pneumothorax with larger lesions having a low risk of developing pneumothorax ($p<0.05$). Lesion depth did not significantly influence development of pneumothorax. However, the highest incidence of post biopsy pneumothorax in this study was observed for sub pleural lesions which accounted for 49.5% of the cases.

Table 5: Association between Lesion Size, Depth and Post Biopsy Pneumothorax

	Pneumothorax		
	Yes	**No**	**P**
Lesion depth from the pleura			
0	6(16.2)	31(83.8)	0.63
0.1 to 2.0	2(33.3)	4(66.7)	
2.1 to 4.0	1(20.0)	4(80.0)	
> 4.0	0(0.0)	3(100.0)	
Lesion size			
< 2.0	1(25.0)	3(75.0)	0.025*
2.0-4.0	4(50.0)	4(50.0)	
> 4.0	4(10.3)	35(89.7)	

4.9 Emphysematous Lungs and Pneumothorax

The study showed a strong positive association between post biopsy pneumothorax rate and emphysematous lung parenchyma ($p<0.05$)

Table 6: Association Between Post Biopsy Pneumothorax And Emphysematous Lung Parenchyma

	Pneumothorax		
	Yes	**No**	**P**
Emphysema			
Yes	4(50.0)	4(50.0)	0.009*
No	5(11.6)	38(88.4)	

4.10 Needle Approach Site and Pneumothorax

The study did not show any significant association between needle approach and post biopsy pneumothorax rate ($p>0.05$). However, pneumothorax occurred in the only patient where lateral approach was used to perform biopsy procedure.

Table 7 ; Association between needle approach and post biopsy pneumothorax

	Pneumothorax		
	Yes	**No**	**P**
Needle approach			
Prone	5(18.5)	22(81.5)	0.081
Supine	3(13.0)	20(87.0)	
Lateral decubitus	1(100.0)	0(0.0)	

4.11 Post Biopsy Parenchymal Bleeding

When the effect of lesion depth on parenchymal bleeding after core needle biopsy of the lung was evaluated, a strong positive association was found ($p<0.05$) with the risk of haemorrhage increasing with increasing lesion depth. Lesion size did not statistically influence the tendency to parenchymal haemorrhage although bigger lesions tended to bleed less.

Table 8 : Association between Lesion Depth, Size and Post Biopsy Parenchymal Bleeding.

	Parenchymal hemorrhage		
	Yes	**No**	**P**
Lesion depth			
0	1(2.7)	36(97.3)	<0.001
0.1 to 2.0	1(16.7)	5(83.3)	
2.1 to 4.0	3(60.0)	2(40.0)	
> 4.0	1(33.3)	2(66.7)	
Lesion size			
< 2.0	1(25.0)	3(75.0)	0.059
2.0-4.0	1(12.5)	7(87.5)	
> 4.0	4(10.3)	35(89.7)	

Out of the 51patients who participated in the study 34(66.7%) were found to have primary lung carcinoma. The right lung was the most commonly involved (50%) followed by the left lung (44.1%). Both lungs were involved by two cases of adenocarcinoma.

More than half (58.8%) of primary lung cancers in the study presented as solid tumours while the rest had a mixture of both solid and ground glass CT attenuation. There were no tumours that presented with pure ground glass attenuation.

Squamous cell carcinoma presented most commonly as a central spiculated mass while adenocarcinoma presented mainly as a large well outlined homogenous mass with peripheral extension.

Cavitation within the primary lung cancers was rare and only seen in squamous cell carcinoma and adenocarcinoma. Calcification was commonest in squamous cell histological subtype.

Table 9 : Table of Radiological Features of Primary Lung Cancer.

	Small cell carcinoma	**Squamous cell carcinoma**	**Adenocarcinoma**	**Total**
No. of patients	**2(5.9%)**	**24(70.6%)**	**8(23.5%)**	**34(100%)**
Site of tumor				
Right sided	0(0.0%)	14(58.3%)	3(37.5%)	17(50%)
Left sided	2(100.0%)	10(41.7%)	3(37.5%)	15(44.1%)
Both right and left side involved	0(0.0%)	0(0.0%)	2(25.0%)	2(5.9%)
Location				
Central	0(0.0%)	11(45.8%)	1(12.5%)	12(35.3%)
Peripheral	0(0.0%)	1(4.2%)	0(0.0%)	1(2.9%)
Both Central & Peripheral	2(100.0%)	12(50.0%)	7(87.5%)	21(61.8%)
Margin				
Spiculated	0(0.0%)	13(54.2%)	2(25.0%)	15(44.1%)
Smooth	0(0.0%)	1(4.2%)	2(25.0%)	3(8.8%)
Lobulated	0(0.0%)	6(25.0%)	1(12.5%)	7(20.6%)
Irregular	2(100.0%)	4(16.7%)	3(37.5%)	9(26.5%)
Consistency				
Pure consolidated	2(100.0%)	14(58.3%)	4(50.0%)	20(58.8%)
Mixture	0(0.0%)	10(41.7%)	4(50.0%)	14(41.2%)
Pure ground	0(0.0%)	0(0.0%)	0(0.0%)	0(0%)
Special features				
Cavitation	0(0.0%)	2(8.3%)	2(25.0%)	4(11.8%)
Calcification	0(0.0%)	4(16.7%)	2(25.0%)	6(17.6%)

4.12 Illustrative Cases

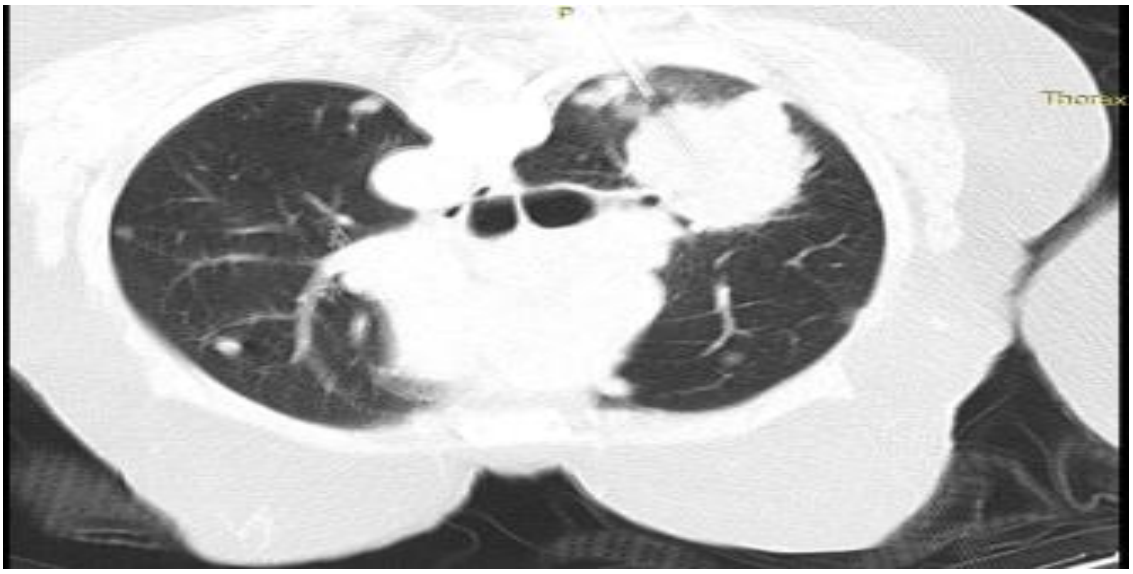

Figure 12: Prone CT scan of 75 year old male chronic smoker showing a spiculated hilar mass extending to the periphery with local pulmonary metastases bilaterally. Histology showed infiltrating poorly differentiated squamous cell carcinoma.

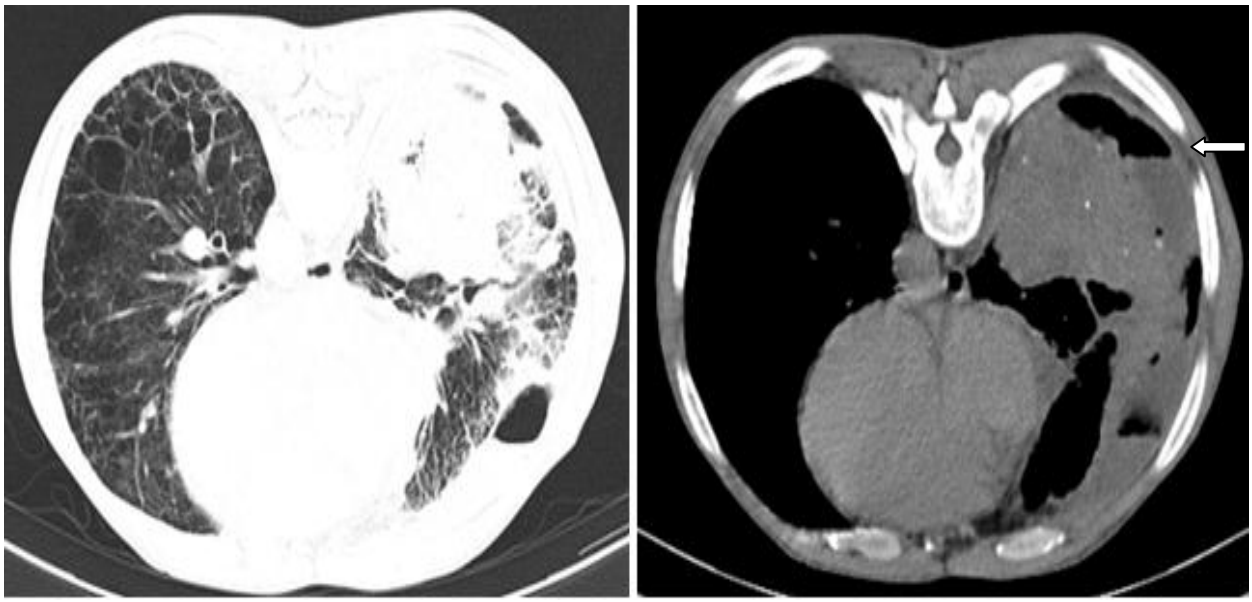

Figure 13a **Figure 13b**

Figure 13: Prone pre biopsy axial CT scan images of a 61 year old male lung window [figure 13a] and mediastinal window [figure 13 b]. Left lower lobe lung mass with punctate calcification is demonstrated. There was left sided loculated pleural effusion (arrow) with bilateral emphysematous changes. Histology showed moderately differentiated squamous cell carcinoma

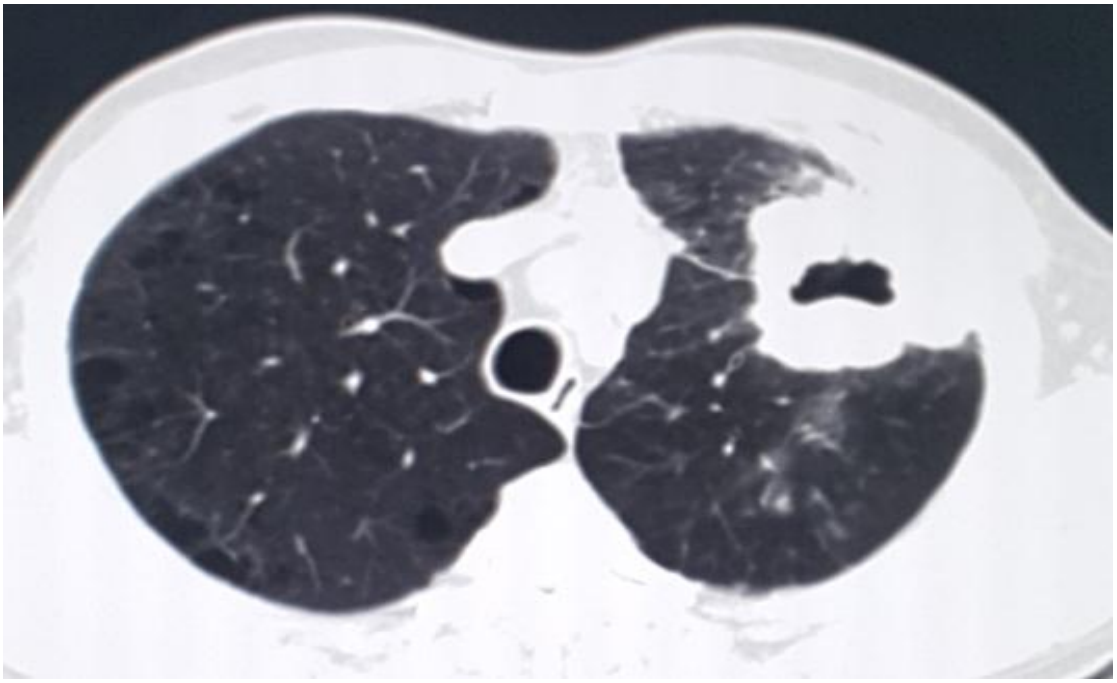

Figure 14: Supine pre biopsy axial CT scan of 52 year old chronic smoker. The cavitating lesion seen in the left upper lobe was confirmed to be squamous cell carcinoma

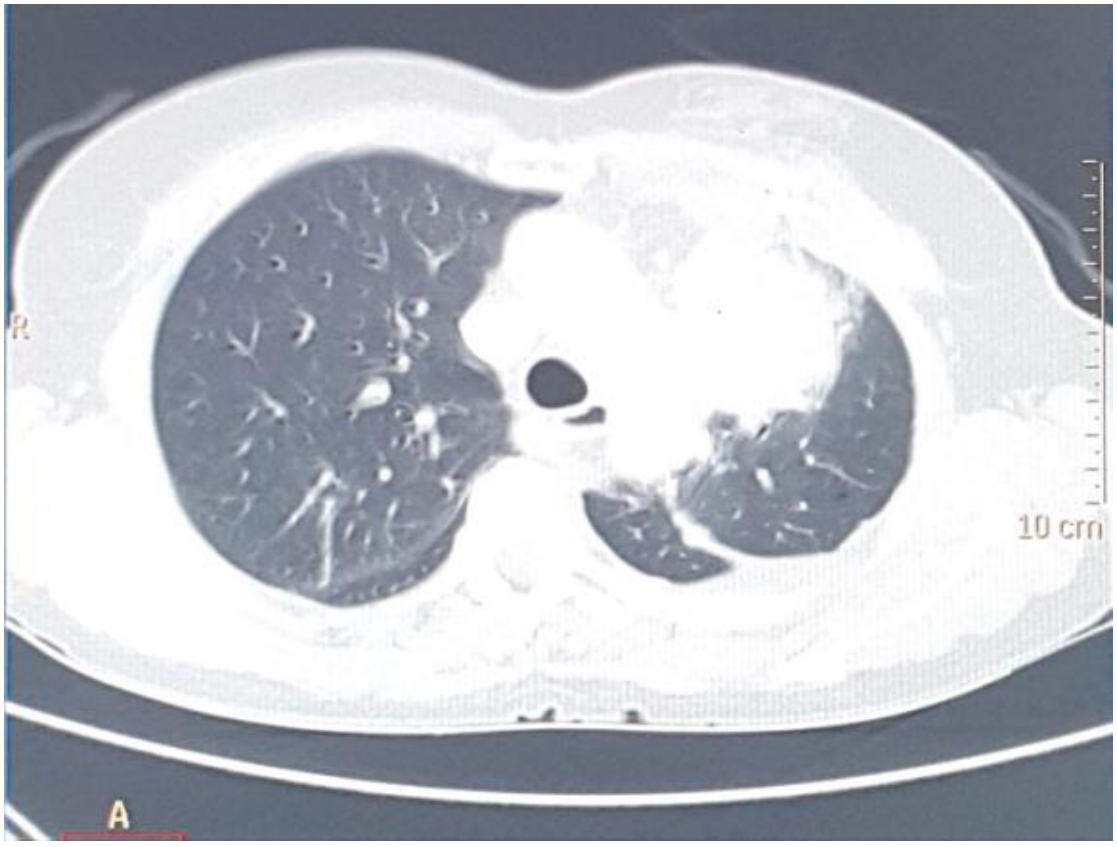

Figure 15 : Supine pre biopsy CT chest of a 66 year old female passive smoker. Left upper lobe mass with ipsilateral lung volume loss is demonstrated. This turned out to be an invasive moderately differentiated adenocarcinoma on histology.

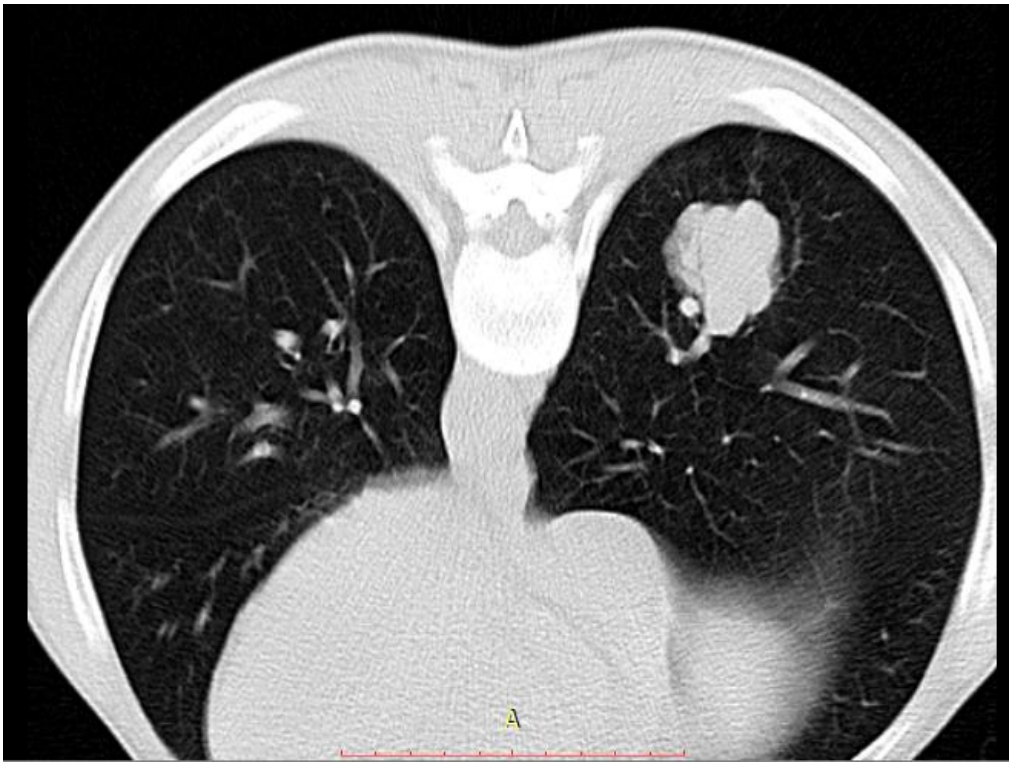

Figure 16 : Prone pre biopsy CT chest of a 51 year old nonsmoker showing a lobulated peripheral left lower lobe mass. Histology showed adenocarcinoma.

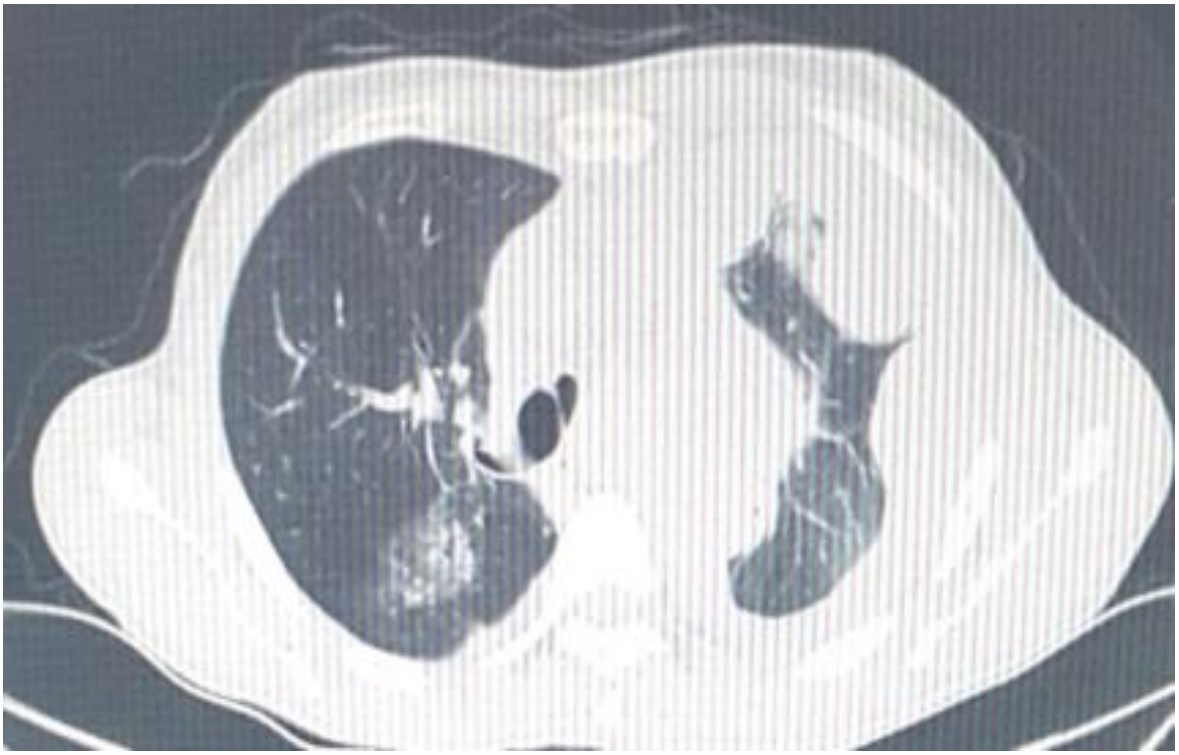

Figure 17 : Supine pre biopsy CT chest of 44 year old male chronic smoker showing a mass involving the left lung and pleura with hilar adenopathy and a subsolid nodule in the contra lateral lung. This turned out to be a case of small cell carcinoma on histology.

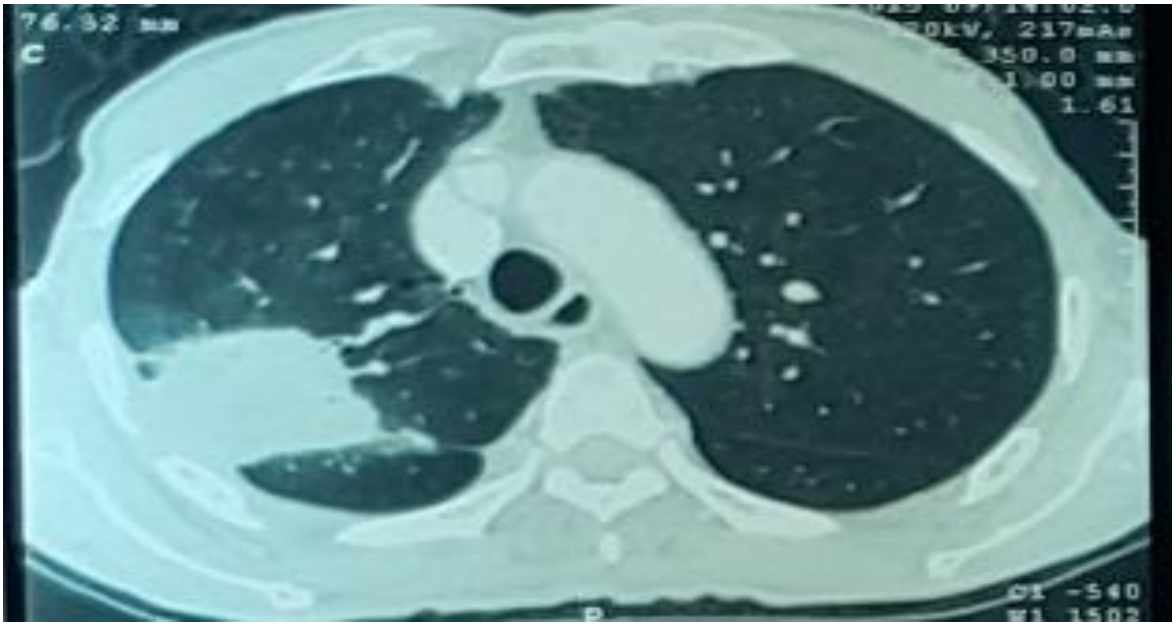

Figure 18 : Supine axial pre biopsy lung window CT scan of an eighty year old male chronic smoker showing a right upper lobe lung mass. Histology showed metastatic carcinoma.

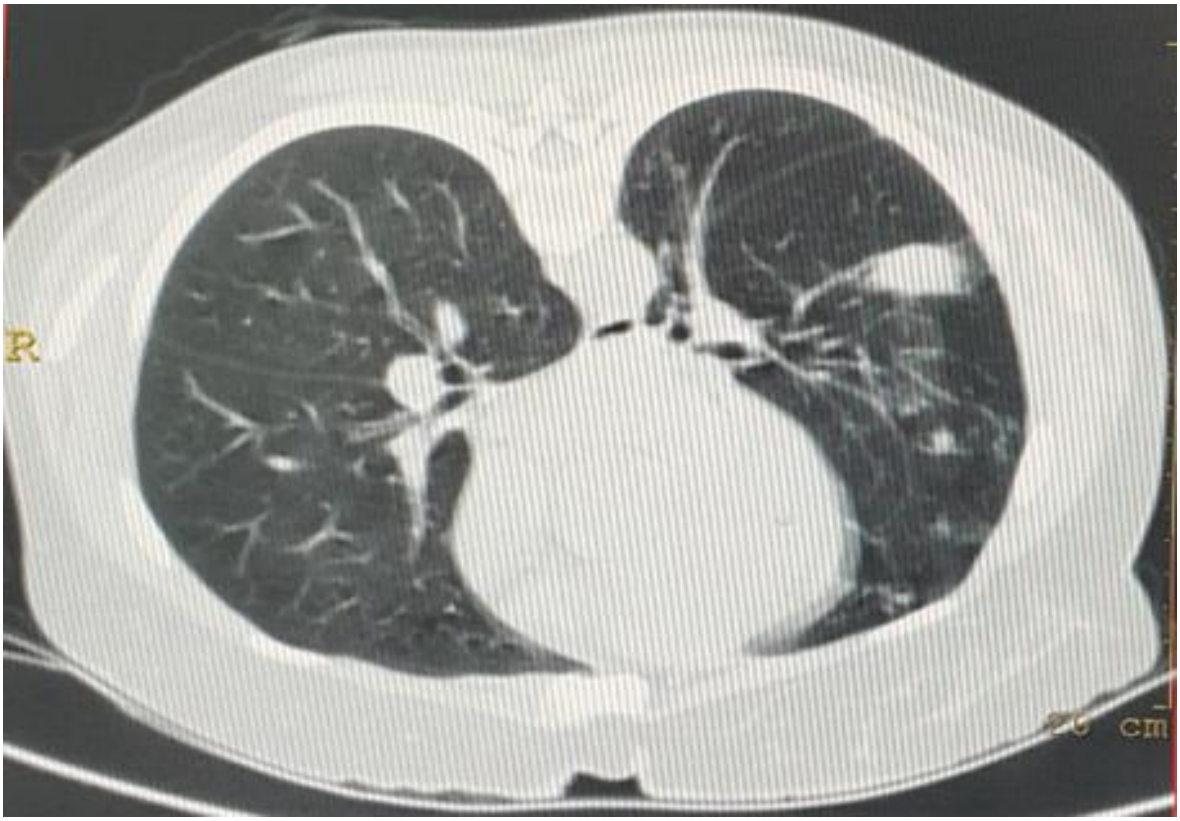

Figure 19 : Prone pre biopsy axial CT scan of a 40 year old female non smoker showing a solitary pulmonary nodule in the lingular segment. Histology showed a fibrotic lung nodule.

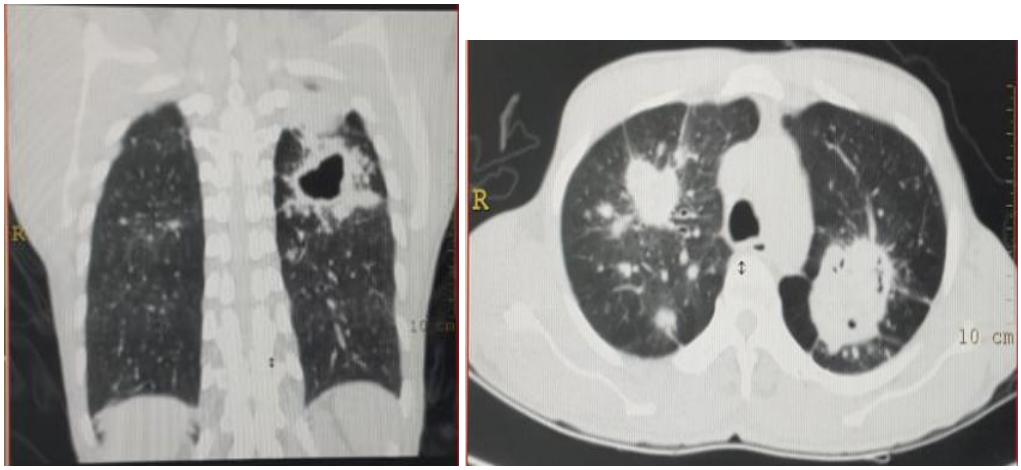

Figure 20a **Figure 20b**

Figure 20: Coronal and axial CT chest of a 48 year old male non smoker showing a left upper lobe cavitating lesion [figure 20a] with multiple satellite lesions in both lung fields [figure 20b]. Histology showed fibrosing alveolitis due to pneumoconiosis.

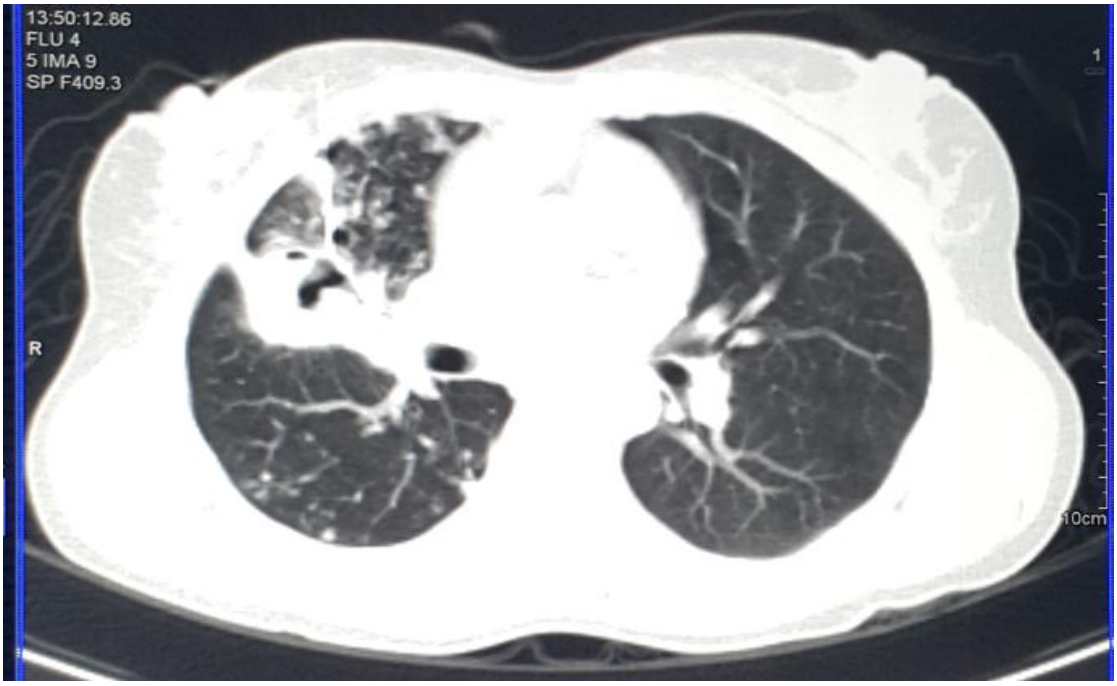

Figure 21: Supine axial CT scan chest of a 32 year old female non smoker showing a right middle lobe cavitating lesion. Histology showed pulmonary tuberculosis.

5.0 CHAPTER FIVE: DISCUSSION

Lung cancer causes the highest number of cancer related deaths in the whole world[75]. With the development of targeted therapies, histological subtyping is paramount in the management process of lung cancer[54]. The quality and quantity of the tissue obtained at lung biopsy determines the success of the biomarker profile analysis which is essential in the process of histological subtyping of this highly fatal malignancy[8]. The ability of CT guided core needle biopsy to obtain adequate and appropriate material for histopathological analysis has placed it at the heart of the management process of primary lung cancer. Its high diagnostic yield coupled with low complication rates has given it an edge over FNAB which merely obtains aspiration material for cytological analysis [22-23, 25-26]. In addition a cytopathologist is not required during the performance of CNB procedure[18]. With reported rising incidence of lung cancer locally (NCR), this procedure is gaining momentum and our study is the first local study to evaluate its diagnostic yield and complication rates as well as radiological pattern of histologically proven primary lung carcinoma.

The study found 94.4% of primary lung carcinoma out of the total biopsies done. This compares well with the reported findings in literature[53]. Non-small cell carcinoma accounted for 94.1 % with Squamous cell carcinoma accounting for the majority of cases (70.6%). Adenocarcinoma accounted for 23.5% in our series. This pattern is in contrast to the current reported lung cancer pattern in the west where adenocarcinoma is the most prevalent histological subtype[76]. This difference may be explained by various factors including the rising incidence of female smokers in the west who tend to develop adenocarcinoma. Smoking is not common among Kenyan women as reflected in our study. Social and racial differences may be the other contributing factors though unproven. The pattern compares favourably with a study done by Sharma et al[77] which reported Squamous cell carcinoma as the most common histological subtype in their study which evaluated 373 Indian patients with primary lung cancer. Smoking is known to be a major risk factor for bronchogenic carcinoma. A meta analysis conducted by Sadik A Khuder[78] found that smoking is associated with all the histological subtypes with a stronger association for squamous cell carcinoma. This study recorded similar findings with 82.4% of primary lung cancer among smokers falling in the squamous cell subtype. Small cell carcinoma, although rare, was seen in two patients who were smokers. This histologic subtype almost invariably occurs in smokers[79]. Adenocarcinoma has been reported as the most prevalent histologic subtype

among women and lifelong nonsmokers[76] . This was the case in this study where 87.5%% of this histological subtype occurred among the nonsmoking males and females.

Passive smoking has been reported as a risk factor for primary lung cancer [80-81]. This series confirmed this finding as all the three females who reported positive history of a smoking spouse were found to have lung cancer.

Eastern and central regions form the major catchment area for the national referral center and recorded the highest percentage of primary lung cancer in this study.

5.1 Diagnostic Yield

In this series, using large bore 17/18g coaxial CT guided CNB system, we obtained adequate specimens for histopathological analysis in 49(97%) out 51 enrolled participants. The yield was high and compared favourably to similar studies using similar systems conducted by Loubeyre et al [18]and Guimaraes et al[6] whose diagnostic yields were 97% and 96.9% respectively.

5.2 Complications

Pneumothorax

The complications rate of 17/ 18 coaxial CNB system in this series was well within the reported range in other thoracic biopsy systems including TFNAB technique [29-31]. Pneumothorax rate (17.6%) generally fell within the range reported in several studies of between 9% and 64%. Specifically, this compared fovourably with rates observed in similar studies by Loubeyre et al [18]and Guimaraes et al[6] who reported pneumothorax rates of 19% and 7.2%. The modest pneumothorax rate without any case requiring chest tube drainage reported in the Guimaraes study is explained by the use of a smaller gauge needle for smaller lesions thus reducing the risk of post biopsy pneumothorax. Eva Branden et al[8] used a larger gauge system of 16/18g and recorded a higher pneumothorax rate (29%) than our study(17.6%) with 16% requiring treatment with a chest tube. In this study, only two patients (3.9%) required treatment with a chest tube. This finding was concordant with findings of a similar study by Luciderme et al[20] who recorded a pneumothorax rate of 34% with 3% of the cases requiring chest tube thoracostomy. Most of the patients in our study presented late with large lesions most of which contacted the pleural surface. Lesions with a diameter of more than 3cm accounted for 82.4% while lesions with a diameter of below 3cm accounted

for 17.6% of the cases. This may have contributed to our high diagnostic yield and low complication rates. In addition, apart from the principal investigator, all the biopsies were performed by experienced interventional radiologists.

Parenchymal Haemorrhage

Parenchymal haemorrhage accounted for 11.8% of the cases in our study. This corroborated well with findings of similar studies done by Loubeyre et al [18]and Luciderme et al[20] who recorded parenchymal bleeding rates of 22% and 10% respectively.

5.3 Risk Factors Influencing the Rate of Complications

Pneumothorax

This study found very low rates (17.6%) of pneumothorax as a complication. In the biopsies where pneumothorax occurred there was significance correlation with lesion size. Smaller lesions were shown to have higher incidences of post biopsy pneumothorax. This compares favourably with studies done by Stanley et al[49] and Nakatani et al[50].

Lesion depth and needle approach had no significant correlation to occurrence of pneumothorax, although a few superficial lesions tended to develop pneumothorax. This is in contrast to other studies in literature [6, 49-52]. This finding may have been due to the fact that majority of the lesions biopsied in this series were large masses extending to the lung periphery.

On analyzing the effect of emphysema to the incidence of pneumothorax, this study demonstrated that there was a high risk of post biopsy pneumothorax when the biopsy needle cut through the emphysematous lung parenchyma. Similar findings were reported by Eva Branden et al[8] in their study that evaluated the complication rates and diagnostic yield of CT guided core biopsies.

Parenchymal Haemorrhage

There was a strong positive association between lesion depth and parenchymal haemorrhage. Lesions located less than 2cm below the pleural surface had proportionately lower bleeding rate. This study therefore confirms the positive correlation between parenchymal bleeding rate and lesion depth as reported by several other studies [49-50, 52]. Lesion size did not statistically influence the tendency to parenchymal haemorrhage although bigger lesions

tended to bleed less. This finding contrasts reports by both Stanley et al[49] and Nakatani et al[50]. This may be explained by the fact that this series had very few small lesions (<2cm).

5.4 Radiological Appearance of Histologically Proven Bronchogenic Carcinoma

Lung cancer reported in this series had a slight preponderance to the right lung. This is consistent with what is reported in literature[77]. Similar to the Mayo clinic study[82], squamous cell carcinoma in this study presented most commonly as central spiculated lung mass. This however contrasts the findings of the Marshfield study[56] which showed no significant difference between central and peripheral lung masses with this histology.

Majority of adenocarcinoma in this study presented predominantly as both central and peripheral masses. This is in line with Marshfield study[56] but contrasted the findings of Sharma et al[77] where most adenocarcinoma in their study presented as peripheral masses. We think this is because most of the patients in our study presented late with larger masses spanning both central and peripheral lung fields.

Cavitation is most commonly associated with Squamous cell carcinoma. Our study showed equal incidence of cavitating lesions in both Squamous cell carcinoma and adenocarcinoma. Sharma et al[77] evaluated 373 chest radiographs of patients with lung cancer and found that 66% of cavitating lung tumours in their study were of Squamous cell carcinoma histological subtype. The same study found that calcification was more commonly associated with Squamous cell carcinoma, a finding that is in concordance with our study where 66.7% of calcific lung tumours were of squamous cell histology.

Majority of lung cancers in these series presented as consolidations. This is consistent with what is reported in literature[77]. Whereas most tumours tended to be spiculated and irregular, a small percentage (8.8%) in this series had smooth margins mimicking benign lesions.

5.5 Conclusions

Percutaneous 17/18 gauge coaxial CT guided core needle biopsies of lung lesions has a high diagnostic yield. Squamous cell carcinoma was the commonest histological subtype presenting most commonly as a central speculated mass.

Complication rates are low, with pneumothorax being the commonest and in which a very small percentage require thoracostomy drainage. The small number of lung parenchymal bleeds that occur post biopsy do not require intervention and nearly always resolve

spontaneously. We therefore recommend this needle biopsy system for routine biopsies of lung lesions.

5.6 Study Limitations

Late presentation of patients with large masses may have introduced selection bias and this may have overestimated our diagnostic yield and underestimated our complication rates.

5.7 Recommendations

- Raise awareness to the clinicians of the high diagnostic yield and low complication rates of this procedure.
- Adoption as a standard routine protocol.
- Future studies on yields and practical applicability of much finer needle gauge systems.

REFERENCES

1. Chojniak R, I.R., Viana LM, et al. , *Computed tomography guided needle biopsy: experience from 1, 300 procedures.* Sao Paulo Med J, . 2006. **124**(1): p. 5.
2. Klein JS, S.G., Stewart EA *Transthoracic needle biopsy with a coaxially placed 20 gauge automated needle:Results in 122 patients.* Radiology. , 1996. **198**(3): p. 6.
3. Westcott JL, R.N., Colley DP, *Transthoracic needle biopsy of small pulmonary nodules.* Radiology, 1997. **202**: p. 96.
4. Yu LS, D.D., Younes RN *Computed tomography-guided cutting needle biopsy of pulmonary lesions.* Rev Hosp Clin Fac Med Sao Paulo., 2002. **57**: p. 4.
5. Arakawa H, N.Y., Kurihara Y, , *CT guided transthoracic needle biopsy: a comparison between automated biopsy gun and fine needle aspiration.* Clin Radiol, 1996. **51**: p. 4.
6. Guimaraes MD, C.R., Gross JL, *Predictive success factors for CT guided fine needle aspiration biopsy of pulmonary lesions. Clinics.* Sao Paulo Med J, 2010. **65**(9): p. 4.
7. Haaga JR, A.R., *Precise localization by computer tomography.* Radiology, 1976. **118**(3): p. 5.
8. Branden E, W.S., Hogberg *Computed tomography guided core biopsies in a county hospital in Sweden: Complication rate and diagnostic yield.* Ann Thorac Med, 2014. **9**(3): p. 5.
9. Atkas AR, G.E., Yilmaz O et al. . ; , *CT-guided transthoracic biopsy: Pathology results and complication rates.* Diagn Interv Radiol DOI 2014.
10. Piplani S, M.R., Lalit M *Cytologic-radiologic correlation using transthoracic CT guided FNA for lung and mediastinal masses: our experience.* 2014.
11. Mondal SK, N.D., Das . *Computed tomography guided fine needle aspiration of lung mass with histological correlation A study in Eastern India.* South Asian J cancer, 2013. **2**(1): p. 5.
12. Prashant, R.C., Pattbhariman R, Attili SSV. , *Feasibility, safety and efficacy of CT guided fine needle aspiration cytology of lung lesions.* . Indian journal of medical and paediatric oncology., 2007. **28(**(2): p. 10.
13. Haaga JR, A.R., Zelch MG *Computed tomography of the pancreas.* Radiology, 1976;. **120**: p. 7.
14. Manhire AR, R.C., Gleeson FV *Lung biopsy guidelines-for the obedience of fools and guidance of the wise men.* Thorax, 2003. **58**: p. 2.
15. Kulkarni S, K.A., Roy D *Percutaneous computed tomography- guided core biopsy for the diagnosis of mediastinal masses.* 2003. **3**(1): p. 5.
16. Tsai IC, T.W., Chen MC, Chang GC, Tseng WS, Chan SW, *CT guided core biopsy of lung lesions: a primer.* AJR Am J Roentgenol, 2009. **;193**(5): p. 8.
17. Guimraes MD, d.A.M., da fonte AC, et al, *computed tomography guided core needle biopsy of lung lesions: an oncology center experience.* Radiol Bras, 2011. **44**(2).

18. P Loubeyre, M.C., P.Y. Dietrich, *Percutaneous ct guided multisampling core needle biopsy of thoracic lesions.* AJR Am J Roentgenol, 2005. **185**(5): p. 5.
19. Atkas AR, G.E., Yilmaz O et al, *CT-guided transthoracic biopsy:Histopathology results and complication rates.* Diagn Interv Radiol DOI 2015. **21**(1): p. 4.
20. Lucidarme O, H.N., Finet JF, *Intrapulmonary lesions: percutaneous automated biopsy with a detachable, 18-gauge, coaxial cutting needle.* Radiology, 1998. **207**: p. 7.
21. Wu CC, M.M., *CT guided percutaneous needle biopsy of the chest: preprocedural evaluation and technique.* 2011. **195**: p. 1.
22. Guimaraes MD, M.E., *CT-guided biopsy of lung lesions. Defining the best needle option for a specific diagnosis.* Clinics (Sao Paulo), 2014. **69**(5): p. 6.
23. Beslic S, Z.F., Milisic S *percutaneous transthoracic CT guided biospsies of lung lesions; fine needle aspiration biopsy versus core biopsy.* Radiol Oncol, 2012. **46**(1): p. 4.
24. Moulton JS, M.P., *Coaxial percutaneous biopsy technique with automated biopsy devices: Value in improving accuracy and negative predictive value.* Radiology, 1993. **186**.
25. Yao X, G.M., Tsao MS, Allen CJ, Geddie W, Sekhon H, *Fine needle aspiration biopsy versus core needle biopsy in diagnosing lung cancer: a systematic review.* Curr Oncol, 2012. **19**(1): p. 12.
26. Choi SH, C.E.K.J., *Percutaneous CT-guided aspiration and core biopsy of pulmonary nodules smaller than 1cm: Analysis of outcomes of 305 procedures from a tertiary referral center* 2013. **201**: p. 1.
27. Priola AM, P.S., *Diagnostic accuracy and complication rate of CT-guided fine needle aspiration biopsy of lung lesions: A study based on the experience of the cytopathologist.* Acta Radiologica, 2010. **51**: p. 7.
28. LB, H., *CT guided automated needle biopsy of the chest.* AJR J Roentgenol, 1995. **165**: p. 3.
29. Laurent F, L.V., Vergier B *Percutaneous CTguided biopsy of the lung: Comparison between aspiration and automated cutting needles using a coaxial technique. .)* Cardiovasc Intervent Radiol, 2000. **23**(4): p. 7.
30. Laurent F, M.P., Latrabe V et al *Pneumothoraces and chest tube placement after CT guided transthoracic lung biopsy using a coaxial technique.* AJR Am J Roentgenol, 1999. **172**: p. 4.
31. Yamagami T, N.T.L.S.e.a., *Management of pneumothorax after Percutaneous CT guided lung biopsy.* Chest, 2002. **121**: p. 6.
32. Perlmutt LM, J.W., Dunnick NR, *Percutaneous transthoracic needle aspiration: a review.* AJR Am J Roentgenol, 1989. **152**.
33. Tolly TL, F.J., Czerneck D, *Air embolism complicating Percutaneous lung biopsy.* AJR Am J. Roentgenol, 1988. **150**: p. 2.
34. Cox JE. Chiles, C., McManus, CM *Transthoracic needle aspiration biopsy: variables that affect risk of pneumothorax.* Radiology, 1999. **212**: p. 4.

35. EH, M., *Technical aspects of needle aspiration lung biopsy: a personal perspective.* Radiology, 1998. **208**: p. 15.
36. Li H, B.P., Shepard JO et al. . *Diagnostic accuracy and safety of CT guided Percutaneous needle aspiration biopsy of the lung. Comparison of small and large pulmonary nodules.* AJR Am J. Roentgenol 1996. **167**: p. 5.
37. Tsukada H, S.T., Iwashima A et al. , *Diagnostic accuracy of CT guided automated needle biopsy of lung nodules.* AJR Am J Roentgenol, 2000. **175**: p. 5.
38. LB, H., *CT guided automated biopsy of the chest.* AJR Am J Roentgenol, 1995. **165**(1): p. 3.
39. McSweeney SE, O.R.K., Mc Laughlin PD, Crush L, Maher MM, *Evaluation of the efficacy and safety of percutaneous biopsy of lung.* Open Respir Med J, 2012. **6**: p. 9.
40. Herman PG, H.S., *The diagnostic accuracy and complications of closed lung biopsies.* Radiology 1977. **125**: p. 4.
41. Geraghty PR, K.S., McFarlane G, , *CT-guided transthoracic needle aspiration biopsy of pulmonary nodules: needle size and pneumothorax rate.* Radiology, 2003. **229**: p. 13.
42. Brown KT, B.L., Getrajdman GI et al.. *Outpatient treatment of iatrogenic pneumothorax after needle biopsy*. Radiology, 1997. **205**: p. 4.
43. Ko JP, S.J., Drucker EA et al., *Factors influencing pneumothorax rate at lung biopsy: are dwell time and angle of pleural puncture contributing factors?* Radiology, 2001. **218**: p. 6.
44. A Fukushima, K.A., N aso et al, *CT guided needle biopsy of the lung: Factors affecting risk of complications.* Nippon Igaku Hoshasen Gakkai Zasshi, 2001. **61**(3).
45. A. M. Priola, S.N.a.S.M.P., *Factors affecting risk of pneumothorax in CT guided transthoracic needle lung biopsy of lung lesions: results of 708 consecutive procedures. .* Journal of Thoracic Oncology, 2007. **2**(8): p. 1.
46. Swischwak JL, C.F., Patel JC *Percutaneous transthoracic needle biopsy of the lung: Review of 612 lesions.* J Vasc Interv Radiol, 1998. **9**(2): p. 6.
47. William M, A.S., Cindy L et al, *Needle gauge and cytological yield in CT guided lung Biopsy.* Pulmonology, 2011: p. 4
48. Wang Y, L.W., *Computed tomography guided core needle biopsy of lung lesions: Diagnostic yield and correlation between factors and complications.* Oncol Lett, 2014. **7**(1): p. 7.
49. Stanley EL, D.D., Sudhakar KV et al., *CT-guided thoracic biopsy: Evaluating diagnostic yield and complications.* Annals of the Academy of Medicine Singapore, 2013. **42**(6).
50. Nakatani M, T.N., Kariya S et al., *Analysis of factors influencing accuracy and complications in CT-guided lung biopsy.* 2012. **21**(6): p. 8.
51. Khan MF, S.R., Moghaddam SR, Maataoui A, Gurung J, Wagner TO, *Variables affecting the risk of pneumothorax and intrapulmonal haemohrrage in CT-guided transthoracic biopsy.* Eur Radiol, 2008. **18**(7): p. 8.

52. Yeow KM, S.I., Pan KT, Tsay PK, Lui KW, Cheung YC, *Risk of pneumothorax and bleeding: multivariate analysis of 660 CT-guided coaxial cutting needle lung biopsies.* Chest, 2004. **126**(3): p. 7.
53. O, P.B., *The radiographic appearance of lung cancer.* ONCOLOGY, 1997. **11**(9): p. 16.
54. Jon Z, A.B., Juan AN et al., *The new IASLC/ATS/ERS lung adenocarcinoma classification from a clinical perspective: current concepts and future prospects.* J Thorac Dis, 2014. **6**(5): p. 11.
55. Travis WD, B.E., Müller-Hermelink HK, et al, *Pathology and Genetics of Tumours of the Lung, Pleura, Thymus and Heart.* Lyon: IARC Press, 2004.
56. Quinn D, G.A., Broste S., *The changing radiographic presentation of bronchogenic carcinoma with reference to cell type.* Chest 1996. **110**.
57. Azra A, N.A., Sajid M et al, *Radiological and pathological correlation of lung nodules in a background of metastatic disease.* Journal of Cancer & Allied Specialties, 2015. **1**(1).
58. Suresh T. T., X.Z., *Differentiation of benign and malignant solitary pulmonary nodule: literature review.* Advances in lung cancer, 2015. **4**: p. 8.
59. Gould MK, F.J., Lannetoni MD et al, *Evaluation of patients with pulmonary nodules: when is it lung cancer? ACCP Evidence based clinical practice Guidelines (2nd edition).* chest, 2007. **132**: p. 221.
60. Jeong YJ, Y.C., Lee KS, *Solitary pulmonary nodules: Detection, characterization and guidance for further diagnostic work up and treatment.* AJR 2007. **188**.
61. Siegleman S. S, Z.E.A., Leo F. P et al., *CT of the solitary pulmonary nodule.* AJR, 1980. **135**(13).
62. Zwirewich CV, V.S., Miller RR et al. *Solitary Pulmonary Podule: High Resolution CT and Radiologic-Pathologic correlation.* Radiology, 1991. **179**: p. 7.
63. AP, F., *Pulmonary Disease and Disorders.* McGraw Hill. New York 2nd edition , , 1988.
64. Takashima S, S.S., Li F et al. *Small Solitary Pulmonary Nodules (<1cm). Detected at Population-Based CT screening for lung cancer. Reliable High Resolution CT features of benign lesions.* AJR, 2003. **180**: p. 9.
65. Noguchi M, M.A., Kawasaki M et al. , *Small adenocarcinoma of the lung.* Cancer, 1995. **75**: p. 9.
66. Nakata M, S.H., Takata I et al, *Focal ground glass opacity detected by low dose helical CT.* Chest, 2002. **121**: p. 4.
67. Henschke CI, Y.D., Mirtcheva R et al. , *CT screening for lung cancer: Frequency and significance of part- solid and Non solid nodules.* AJR, 2002. **178**: p. 5.
68. Felson B, W.J., *Some less familiar roentgen manifestations of carcinoma of the lung.* Semin Roentgenol, 1977. **12**: p. 20.

69. Bower SL, C.R., Muss HB. , *Multiple primary bronchogenic carcinomas of the lung.* AJR 1983. **140**: p. 6.
70. Roggli VL, V.R., Greenberg SD et al, *Lung cancer Heterogeneity: A blinded and randomized study of 100 consecutive cases.* Hum PATHOL 1985. **16**: p. 11.
71. Kulman JE, F.E., Kahajda FP et al *Solitary bronchoalveolar carcinoma. CT criteria.* Radiology, 1988.
72. C.P Sharma, D.B., A.N aggurwal et al. , *Radiographic patterns in lung cancer.* Indian J. Chest Dis Allied Sci 2002. **44**.
73. Brud RB, C.D., Miller WE et al. , *Radiographic abnormalities in carcinoma of the lungs as related to histologic cell types.* Thorax, 1969. **24**.
74. ANONYMOUS, *Pretreatment evaluation of non- small cell lung cancer. The American Thoracic Society and the European Respiratory Society.* Amer J. Respir Crit Care Med, 1997. **156**: p. 13.
75. Jemal A, B.F., Center MM et al, *Global cancer statistics.* CA Cancer J clin 2011. **61**(2): p. 61-90.
76. Nakamura H, s.H., *World wide trend of increasing primary adenocarcinoma of the lung.* Surg Today, 2014. **44**(6): p. 1004-12.
77. C P Sharma, D.B., A. N Aggurwal et al, *Radiographic patterns in lung cancer.* Indian J Chest Allied Sci 2002. **44**: p. 25-30.
78. Khuder, S.A., *Effects of cigarette smoking on major histological types of lung cancer: a metaanalysis.* Lung cancer 2001. **31**(2-3): p. 139-148.
79. Semin Cheng, K.s.L., Myung Jin Chung et al, *Neuroendocrine Tumours of the lung. Clinical, Pathologic and imaging findings.* Radiographics 2006; 26(1), 2006. **26**(1).
80. A Charloux, E.Q., G pauli, *Passive smoking and bronchogenic cancer. A difficult relationship to establish.* Revue de Pneumologie Clinique. , 1996. **52**(4): p. 227-34.
81. T . H. Lam, I.T.K., C. M Wong et al *Smoking, passive smoking and histological types in lung cancer in Hongkong chinese women.* British Journal of Cancer., 1987. **56**(5): p. 673-678.
82. Brud RB, C.D., Miller WE et al, *Radiographic abnormalities in carcinoma of the lungs as related to histologic cell type.* Thorax 1969; 24: 573-75, 1969. **24**: p. 573-75.

APPENDICES

Appendix A: Participant Consent Form

This consent has three parts

Participant Information sheet –to share information about the research

Consent form- for signing

Statement by the researcher

PARTICIPANT INFORMATION SHEET

Introduction

My name is Dr. John Mwangi Wanjiku, a post graduate student at the University of Nairobi School of medicine, department of diagnostic imaging and radiation medicine. I am conducting a study to evaluate the diagnostic yield and complications of 17/18 gauge coaxial CT guided core needle biopsy of lung nodules and masses.

Voluntariness of participation

I am inviting you to participate in my study. You will be given an opportunity to ask questions before you make a decision. You are free to consult any person of your choice before making a free decision. Your treatment will not be affected in any way if you choose to decline participation and no explanation will be required.

Compensation

There will be no compensation for participating in the study

Summary of the procedure

Following your consent to participate in this study we shall record your personal data and a brief clinical history. We will ask you to submit any prior thoracic images and laboratory tests. With the help of the CT scan machine we shall obtain small tissue specimens from the abnormal part of your lungs using a very thin needle. This procedure will take approximately 30 minutes

Risks of the procedure

During the procedure a few complications may occur. These include bleeding within the lungs which in some cases can make you cough blood. Air may also escape from your lungs making your breathing difficult. Please note that these complications only occur in a small proportion of the patients who undergo this procedure. I want to assure you that we shall do our level best to avoid the occurrence of these complications but in case we fail, prompt management will be instituted. Internationally approved protocols will be used during the acquisition of CT scan images of your chest to ensure you receive as little radiation as is reasonably achievable.

Confidentiality

Information obtained from this study will be highly confidential. It will not be shared with anyone unless authorized by the Kenyatta National Hospital/ University of Nairobi Ethics and Research Committee.

Thank you very much.

CONSENT FORM TO PARTICIPATE IN RESEARCH STUDY

TITLE OF STUDY: Percutaneous 17/18 gauge coaxial CT guided core biopsies of lung nodules and masses at Kenyatta National Hospital: diagnostic yield and complication rates.

NAME OF RESEARCHER: Dr. Wanjiku John Mwangi, M.B.Ch.B (UoN)

Postgraduate radiology resident

University of Nairobi, Department of Diagnostic Imaging and Radiation medicine

I hereby confirm that the doctor has explained to me about the above study and I understand fully. I have been given the opportunity to ask questions which have been adequately answered.

I understand that my participation is voluntary and that I have not been forced to participate. I understand that I can decline without giving any reason, without my medical care or legal rights being affected.

I understand that I will not receive any compensation either financial or otherwise, and will not receive any preferential treatment, gift or reward, for participating in the above study.

I understand that my personal information will be kept confidential, but that any relevant medical information regarding the results of my scans and the data collected will be accessible to the researcher, and may be looked at by his supervisors where relevant to the study. I give them permission to have access to this information.

If need be, you can contact me or my supervisor or the Kenyatta National Hospital /University of Nairobi Ethics and Research secretariat using the contacts given below.

I hereby consent to take part in the above study

Name of participant ……date……signature……

Mobile……

Name of parent/guardian providing consent for the minor …….....

Date……signature……..

Name of person taking consent ……

Date……..signature…….

Name of witness……

Date…….. Signature……

Dr John Mwangi

Depart of radiology, UoN

P.O. Box 37441-00100

Nairobi.

Phone number: 0723700911

Supervisor

Dr. Peter Magabe Chacha

Depart of radiology, UoN

P.O. Box 19676-00202

Nambari ya simu- 0722293104

KNH-UoN ERC Secretariat

Secretary,

KNH-UoN-ERC

P.O. Box 20723-00202 KNH

Nairobi

Tel: 7263009

Fax: 725272

Email: UoNknherc@UoNbi.ac.ke

STATEMENT BY THE RESEACHER

I hereby confirm that I have accurately read out the contents of the information sheet to the participant. To the best of my ability, I have made sure the participant understands the following;

Participation in this study is on voluntary basis and no compensation will be given.

Refusal to participate or withdraw from the study at any point will not in any way compromise the quality of care accorded to the patient.

All the information that shall be given will be treated with confidentiality.

Name …….

Signature……

Date ……..

Appendix B: Maelezo Kwa Mshirika

Kuhusu mtafiti

Mimi nafahamika kama daktari John Mwangi, mwanafunzi wa shahada ya uzamili katika fani ya radiology, chuo kikuu cha Nairobi. Ninafanya utafiti kuhusu matumizi ya kifaa kwa jina la 17/18-gauge coaxial core needle chini ya uelekezi wa CT scan katika kuchuna kijisehemu kidogo cha uvimbe ulio nao katika mapafu yako.

Kujitolea kwa hiari

Ni muhimu kuelewa kwamba kushiriki katika utafiti huu ni kwa hiari yako mwenyewe. Unaweza ukabadili nia yako kuhusu kwendelea kushiriki wakati wowote bila ya kuathiri huduma zako za kiafya.

Fidia yakushiriki katika utafiti

Hakuna malipo yoyote utakoyopokea kwa kushiriki katika utafiti huu.

Maelezo kwa ufupi kuhusu utafiti

Baada ya kutoa idhini yako, tutakagua vipimo na picha zako za kiafya kisha kijisehemu kidogo kitachunwa kutoka kwa uvimbe ulio nao katika mapafu yako chini ya uelekezi wa CT scan Machine.

Madhara

Katika harakati ya kuchuna kijisehemu cha uvimbe, madhara machache yanaweza kutokea ingawa kwa watu wachache tu. Madhara haya ni kama kuvunja kwa damu na hewa katika mapafu. Ninatoa hakikisho kwamba tutafanya juu chini kuzuia madhara haya. Hata hivyo, madhara yakitokea yatakabiliwa kwa matibabu yanayostahili. Isitoshe, utumizi wa CT scan Machine utafuata mujibu uliowekwa kimataifa ili kuzuia madhara.

Siri ya utafiti

Habari zote na matokeo ya utafiti huu yatalindwa vilivyo na kuwekwa katika hali ya siri.

Ahsante sana kwa ushirikiano wako.

FOMU YA IDHINI ILI KUSHIRIKI KATIKA UTAFITI

Kichwa cha utafiti

Matumizi ya 17/18 gauge coaxial core biopsy needle chini ya uelekezi wa CT scan katika kuchuna sehemu ndogo ya uvimbe wa mapafu ya wagonjwa katika hospitali kuu ya Kenyatta.

Jina la mtafiti

Dakt. WANJIKU JOHN MWANGI, M. B. Ch. B (UON)

Mwanafunzi wa shahada ya uzamili katika fani ya radiology.

Chuo kikuu cha Nairobi, idara ya Radiology.

Mini ninatoa thibitisho ya kwamba daktari amenieleza vilivyo kuhusu utafiti ambao kichwa chake kimetajwa hapo juu.

Ninakiri pia nimepewa fursa ya kuuliza maswali kuhusu utafiti huu na nimeridhika.

Ninaelewa kwamba kushiriki katika utafiti huu ni kwa hiari yangu na wala sijalazimishwa kamwe kuhusika.

Ninaelewa fika kwamba sitapokea fidia yoyote iwe fedha au vinginevyo wala sitapokea matibabu yoyote ya upendeleo, zawadi au tuzo kwa ajili ya kushiriki katika utafiti huu.

Naelewa kwamba taarifa yangu binafsi itakuwa siri. Hata hivyo, habari kuhusu matokeo ya uchunguzi zitakazokusanywa wakati wa utafiti zitaangaliwa na kuchambuliwa na mtafiti mkuu na hata wasimamizi wake pindi itakavyohitajika.

Ukiwa na swali lolote, unaweza kuwasiliana nami, msimamizi wangu, au kamati ya utafiti ya chuo kikuu cha Nairobi na Hospitali Kuu ya Kenyatta kupitia anwani kama ilivyodokezwa hapa chini

Ninatoa idhini yangu kushiriki katika utafiti huu.

Jina la mshirika……..Tarehe……

Sahihi…… Nambari ya simu……

Jina la mzazi /mlezi anayetoa idhini kwa niaba ya mshirika wa umri mdogo ……

Tarehe……. Sahihi ……

Jina la mtu anayechukua idhini ……

Tarehe……sahihi……

Jina la shahidi…….**.....**tarehe……..

Sahihi……..

Dr John Mwangi W.

Idara ya radiology-Chuo Kikuu cha Nairobi

Sanduku la posta 37441-00100

Nairobi.

Nambari ya simu-0723700911

Msimamizi

Dr. Peter Magabe Chacha

Idara ya Radiology- Chuo Kikuu cha Nairobi

P.O. Box 19676-00202

Nambari ya simu- 0722293104

KNH-UoN ERC Secretariat

Katibu wa utafiti

Chuo kikuu cha Nairobi-Hopitali Kuu ya Kenyatta

Sanduku la posta, 20723-00202 KNH

Nairobi

Nambari ya simu: 72600-9

Fax: 725272

Email: UoNknherc@UoNbi.ac.ke

DHIBITISHO LA MTAFITI

Ninadhibitisha ya kwamba nimemwelezea mshirika mambo yafuatayo kuhusu utafiti huu

Kwamba kushiriki ni kwa hiari yake
Hatapokea fidia yoyote kwa ajili ya kushiriki katika utafiti.
Anaweza kubadili nia ya kushiriki wakati wowote bila kuathiri haki yake ya huduma zake za kiafya.
Haki zake zitalindwa na habari atakayotoa au ile itakayopatikana kumhusu itawekwa katika hali ya siri wakati wote na itatumika kwa ajili ya utafiti peke yake.

Jina……

Sahihi ……

Tarehe ……..

Appendix C: Data Collection Form

BIODATA

Serial number ……Date……..

Age……. Sex……

County…….

Location……

Phone no……

Occupation……..

SMOKING HISTORY

	Patient	Spouse
Smoker		
Type of cigar		
Number of sticks per day		
Pack years		

CLINICAL SUMMARY

Presenting complains and duration

1……

2……

3……

4……

Date of first presentation……

Place and date of first review by a clinician……

Initial radiological investigation……

Latest radiological investigation……

Comorbidity status……

LESION CHARACTERISTICS

Location

	central	peripheral
Right upper lobe		
Right middle lobe		
Right lower lobe		
Left upper lobe		
Left lower lobe		

Size…… Number of masses……

Depth (from pleura to edge of lesion)……..

Other lesions……

Lesion margins

Speculated ☐

Smooth ☐

Lobulated ☐

☐

Irregular

Lesion consistency

Pure ground glass ☐

Pure consolidation ☐

Mixture of consolidation and ground glass ☐

PROCEDURE CHARACTERISTICS

Time at the start of procedure……

Time at the end of procedure……

Needle approach: Supine ☐ Prone ☐ Lateral decubitus ☐

Biopsy frequency 1st ☐ other ☐

Number of specimens obtained…….

COMPLICATIONS

Post biopsy pneumothorax (ACCP guidelines)

Small (<3cm) ☐

Large (>3cm) ☐

None ☐

Pulmonary haemorrhage (Fleischner society)

	Type I(along needle path)	Type II (perilesional)
Low grade (<6mm)		
High grade (>6mm)		

Other complications

1……..

2……

HISTOPATHOLOGY REPORT

……..

……..

Appendix D: KNH/UON –ERC Letter of Approval

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
(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/488

3rd December 2015

Dr. Wanjiku John Mwangi
H58/68988/2013
Dept.of Diagnostic Imaging and Rad. Medicine
School of Medicine
University of Nairobi

KENYATTA NATIONAL HOSPITAL APPROVED 03 DEC 2015 KNH-UON ERC P.O. BOX 20723-00202 NAIROBI

Dear Dr. Mwangi

Revised research proposal: Percutaneous 17/18-Gauge Coaxial CT guided Core Needle biopsies of Lung nodules and Masses at Kenyatta National Hospital: Diagnostic Yield and Complication rates (P689/10/2015)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH-UoN ERC) has reviewed and **approved** your above proposal. The approval periods are 3rd December 2015 – 2nd December 2016.

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) 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*).
f) Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
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.

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 Deputy Director CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Dean, School of Medicine,UoN
The Chair, Dept.of Diagnostic Imaging & Rad. Medicine,UoN
Supervisors: Dr. Daniel Kibaya, Dr. Lawrence Mugambi M'Arithi

Turnitin Originality Report

PERCUTANEOUS 17/18-GAUGE COAXIAL CT GUIDED CORE NEEDLE BIOPSIES OF LUNG NODULES AND MASSES AT KENYATTA NATIONAL HOSPITAL: DIAGNOSTIC YIELD, COMPLICATION RATES AND RADIOLOGICAL PATTERN OF HISTOLOGICALL by John Wanjiku

From Department of Radiology (Medicine)

- Processed on 07-Jun-2017 20:04 EAT
- ID: 822980764
- Word Count: 10798

Similarity Index
12%
Similarity by Source
Internet Sources:
6%
Publications:
8%
Student Papers:
3%
sources:
1

1% match (Internet from 22-Oct-2010)

http://www.ajronline.org/cgi/content/full/185/5/1294
2

1% match (publications)

&NA;, . "15th World Conference on Lung Cancer :", Journal of Thoracic Oncology, 2013.
3

1% match (publications)

&NA;. "Abstracts", Journal of Thoracic Oncology, 09/2009
4

1% match (Internet from 03-Mar-2003)

http://intouchlive.com/journals/oncology/o9709d.htm
5