ADDIS ABABA UNIVERSITY

COLLEGE OF MEDICINE AND HEALTH SCIENCES

SCHOOL OF GRADUATE STUDIES

DEPARTMENT OF RADIOLOGY

A Prospective Study on Diagnostic Yield, Complication Rate and Associated Factors of Computed Tomography (CT) Guided Transthoracic Needle Biopsy in Tikur Anbessa Specialized Hospital, Addis Ababa University, Addis Ababa, Ethiopia.

Principal investigator: AbdulKerim Girma, MD (Radiology resident)

A research paper to be submitted to the radiology department, college of health science, Addis Ababa University in preparation for partial fulfillment of the requirements for the specialty certificate in radiology.

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ACRONYMS

- CNB - Cutting needle biopsy
- COPD - Chronic obstructive pulmonary disease
- CT - Computed tomography
- DLP - Dose-length product
- FNA - Fine needle aspiration
- FNAB - Fine needle aspiration biopsy
- FNAC - Fine needle aspiration cytology
- TASH - TikurAnbessa Specialized Hospital
- TNB - Transthoracic needle biopsy

ABSTRACT

Introduction: Percutaneous image-guided transthoracic needle biopsy is a safe, minimally invasive, accepted, easy and accurate procedure that provides useful diagnostic information and avoids more invasive and expensive exploratory surgeries especially in medically treatable or unresectable cases. Computed tomography (CT) guided transthoracic needle biopsy involves the insertion of a needle under the guidance of a CT scan to a mediastinal, pleural or pulmonary lesion from which a tissue specimen is taken for cytological evaluation. Any solid or cystic lesion between chest wall and mediastinum can be biopsied percutaneously by a needle provided that it is not accessible by a bronchoscopy. Although it is a safe and minimally invasive procedure, CT guided a transthoracic needle biopsy (TNB) can have some complications. Although it is a well-accepted procedure worldwide with determined accuracy and complication rate our study was intended to specify this hospital experience, to settle a base for an institutional guidelines for selecting fit patients for CT guided transthoracic needle biopsy, for directing ways for rapid detection of complications and management if any occurs.

Objective: To determine the diagnostic yield, complication rate and associated factors of CT guided transthoracic needle biopsy in TikurAnbessa specialized hospital, Addis Ababa University, Addis Ababa, Ethiopia.

Methodology: An institutional-based prospective study was conducted on all patients for whom CT guided TNB was done for mediastinal, pleural, pulmonary or multi-compartmental mass lesions and have pathology result from July 2018 to July 2019 G.C. The collected data wereprocessed and analyzed using IBM SPSS statistics software version 25 and it is presented by statements, figures, graphs, and tables.

Result:CT guided transthoracic biopsy was done on 57 males (56.4%) and 44 females (43.6%) whose mean age was 49.12 years. The location of the lesions was lung (72.28%), mediastinal (12.87%), pleural (10.89%), and multi-compartmental (3.96%). Average of 3 pleural punctures were required for adequate lesion access. A minimum of 3 and a maximum of 8 scans (mean 4.8) were taken during the procedures with a mean DLP of 159.3 mG cm. The mean time required to perform biopsy was 24.8 minutes. The study found that the cooperative patients had statistically significant lower number of scans and short procedure duration than uncooperative patients. The conclusive rate of the procedure was 76.2%. Adenocarcinoma was the most common pathologic result of biopsied lung lesions whereas Thymoma and adenocarcinoma infiltrate were the most common findings in mediastinal and pleural lesions. This study didn’t find statistically significant differences between the conclusive and non-conclusive patient groups in terms of age, sex, lesion characteristics or technical factors. Among the 101 biopsies, 20.8% had complications of which the most common was pneumothorax 12.9% followed by alveolar hemorrhage (5%). Complications had a strong positive correlation with the traversed aerated lung and negative correlation with the mean size of the lesion along the planned trajectory.

Conclusion and Recommendation:CT-guided percutaneous transthoracic needle biopsy can be performed easily and safely with patient comfort, high conclusive rate, and few associated complications. Lesion size and distance of traversed aerated lung tissue are correlated with complications but no associated factor was found with diagnostic yield. However, it is possible that larger sample size and correlation with the surgical outcome and follow-up imaging could show more subtle trends. The procedure can be done with low dose protocols and shorter duration provided that the patient position selection and line of trajectory are settled at the pre-procedural time.

CHAPTER 1. INTRODUCTION

1.1 Background

Thorax consists of different types of tissues and organs starting from the outer most chest wall having a bony skeleton of the spine and ribs to the inner mediastinum and lung parenchyma. Cardiac chambers, great vessels, and large airways form the mediastinum with lymphatic drainages and neural structures [1]. There is a wide variety of mass lesions that affect these structures including non-neoplastic lesions like acute and chronic inflammatory or granulomatous lesions and neoplastic conditions ranging from benign to malignant lesions. The malignant lesions can be of primary or metastatic [2, 3].

Transthoracic needle biopsy has made advances since it is popularized by a nordenstorm in the 1960s [4]. The needles have been changed from large cutting, non-automated needles to thin-walled, small-gauge coaxial needle systems that offer the ability to obtain aspiration and automated core biopsy specimens with a single positioning [5, 6]. Different imaging modalities can be used for guidance including fluoroscopy, computed tomography (CT), and ultrasound [6]. CT plays an important role in the accurate delineation of nodules because of its high resolution and for pre-procedure planning although it exposes the patient for radiation risk and fails to provide real-time imaging [7]. CT guided transthoracic needle biopsy involves the insertion of a needle under the guidance of a CT scan to a mediastinal, pleural or pulmonary lesion from which a tissue specimen is taken for cytological evaluation[8]. It has a variable diagnostic accuracy rate ranging from 74% to 100% based on lesion characteristics and technical factors[3, 9-13].

Lung biopsies may be cytological or histological, fine-needle aspiration biopsy (FNA, FNAB) gives cytological specimens andcutting needles (CNB) produce histological specimens [6].Different approaches can be used for mediastinal lesions based on clinical circumstances, the location and size of the target lesion, the presence of any comorbid conditions, the availability of a procedure at the institution, and the experience of the performing physicians. Approaches with less risk of pneumothorax like parasternal, paravertebral, trans-sternal, and suprasternal approaches are a direct mediastinal approaches that avoid the pleural space and lung parenchyma. However trans-pulmonary approach or trans-pleural approaches are alternatives with a substantial risk of pneumothorax[14].

Although it is a safe and minimally invasive procedure, CT guided transthoracic needle biopsy can be complicated by subcutaneous emphysema, pneumothorax, hemothorax, air embolism, vasovagal reaction, pericardial hemorrhage and tumor seeding [15-21].

Hemorrhage can occur after damage to the pulmonary vessel or systemic arteries including the subclavian, axillary, internal mammary, and intercostal arteries although it is minimal and asymptomatic during damage to a pulmonary vessel under normal physiologic conditions. It can manifest as a focal opacity on CT and in advanced cases, there may be cough and hemoptysis.Air embolism is a rarely reported but life-threatening serious complication. The proposed mechanisms of its occurrence are of two types. First, aspiration of atmospheric air to the pulmonary veins when a needle lodged in the pulmonary vein is opened to the atmospheric air especially during rapid inspiration. Second, when a needle punctures an air-containing space and pulmonary vein simultaneously, air can be sucked to the venous system during coughing which can also be caused by the hemorrhage itself[5, 15].

Patients should stay in hospital at least their first post-procedural hour at which time an erect chest radiograph should be taken which is sufficient to detect the majority of complications. Based on its result further management and follow-up can be modified. The management for the complications is variablyaffected bythe patient presentation and the type and amount of complications. Observation, aspiration and drain insertion are management options for pneumothorax while oxygen administration and general resuscitation should be done for large symptomatic hemorrhages and the clinical team should be contacted. It has been recommended that resuscitation facilities and chest drainequipment should be immediately availablein the procedure room[6, 15]. Prevention of the complications by proper pre-procedural planning with appropriate technique and post-procedural care is the most important way of minimizing potential complications [15].

1.2 Statement of the problemand significance of the study

Cancer is a leading cause of death worldwide. Malignant lesions that affect the components of the thorax have a great health burden. Especially lung cancer is the leading cause of cancer-related mortality, 1.18 million cancer-related deaths [22]. Defining a lesion as benign or malignant plays a significant role in further management, prognosis and psychological condition of a patient.Aside from the continuing search for a cure, hugeglobal efforts are being made to improve the prevention, detection, and treatment of cancer anda very large proportion of this progress is beingmade in the field of medical imaging. Imaging plays a major role in the detectionof cancer as it provides a detailed insight into the exact location and extent of thedisease as well as to guide for sampling[23].

Percutaneous image-guided transthoracic needle biopsy is a safe, minimally invasive, accepted, easy and accurate procedure that provides useful diagnostic information and avoids more invasive and expensive exploratory surgeries, especially in medically treatable or unresectable cases [7, 20, 24-26]. CT guided transthoracic needle biopsy can be performed on an outpatient base with similar accuracy and complication rates if patients with high risk like those with borderline lung function and those with significant co-morbid pathology or inadequate home support are excluded [6, 27].

Any solid or cystic lesion between chest wall and mediastinum can be biopsied percutaneously by a needle provided that it is not accessible by a bronchoscopy.It should be the first invasive procedure in the diagnostic workup of patients with pulmonary nodules and non-endobronchial masses, and for staging of disease that has spread to the hilus, mediastinum, chest wall, and beyond and for mediastinal and pleural masses[6, 20, 24]. Especially it is useful for carcinoma staging, determining unresectability and diagnosis of non-carcinomatous lesions [25]. It can be done whenever it imposes a significant change in the treatment strategy and when the procedure is technically feasible.The benefits should also outweigh the risks (complications)[6, 28].Several factors influence the occurrence of complications and their severity. Lesion characteristics like its size, depth, and location, patient cooperation, underlying lung disease, technical factors like the number of puncture and needle insertion angle are ascribed for the variable frequency of complications occurrence [5, 15, 21, 27, 29, 30].

CT guided transthoracic needle biopsy is being given in TikurAnbessa Specialized Hospital (TASH) sincethree years back. For a diagnostic procedure to be chosen as an investigation modality it should have a determined complication rate and diagnostic performance [17]. Although it is a well-accepted procedure worldwide with determined accuracy and complication rate our study was intended to specify its yield in our hospital.

If possible the goal will be expanded to settle the base fordeveloping an institutional guidelines for selecting fit patients for CT guided transthoracic needle biopsy, for directing ways for rapid detection of complications and management if any occurs. It was also intended to have a role in creating teamwork for adequate pre-procedural assessment of patients and post-procedure handling of complications. As per the knowledge of the principal investigator of this research, there are no regional or local studies made public on this topic so it can also be used as a base for the future.

CHAPTER 2. LITERATURE REVIEW

2.1 Diagnostic yield of CT guided transthoracic needle biopsyand factors affecting it

CT guided transthoracic needle biopsy provides a tissue specimen to classify lesions into benign, malignant or inflammatory/infectious category. Different factors manipulate its diagnostic accuracy. Among 150 difficult thoracic lesions diagnosis was made in 82.7% of them according to Eric vanSonnenberg and associates report, 86.3% of malignant lesions and 65.4% of benign lesions, including 86of 107 lung nodules (80.4%), 28 of 31mediastinal lesions (90.3%), and tenof 12 pleural masses (83.3%). The top three benign lesions were granuloma, histoplasmosis, and lymphocele and the commonest malignant lesions include bronchogenic carcinoma, mediastinal metastasis and pulmonary metastasis[31].

A six-year retrospective analysis of 631 CT-guided percutaneous coaxial cutting needle biopsy of lung lesions in Chang Gung Memorial Hospital, Taiwan revealed that its accuracy is 95% with lesion size and the final diagnosis of the lesion (benign or malignant) affecting its accuracy. Malignant lesion compromise 65% of the cases with the remaining being benign. Malignant lesions and lesions of greater than 1.5cm and less than 5cm of diameter had higher accuracy (99% and 96% respectively) [11]. Malignancy remained the most common diagnosis (75.6%) in a series of 127 CT-guided lung FNACcases with benign lesions accounting for 21.2%. A specific diagnosis was achieved in 85.8% of cases[32]. CT guided cutting needle biopsy lung lesions in 185 consecutive cases histology reveals malignancy in 81.1% and benign in 12.4%. The most common malignant lesion was squamous cell carcinoma followed by adenocarcinoma. Organizing pneumonia predominates in the benign group [27].

A study on 73 CT-guided percutaneous transthoracic biopsies for the diagnosis ofmediastinal masses revealed that 8.2% (6/73) of samples had a benign diagnosis, whereas 91.8% (67/73) were malignant. Thymoma, Hodgkin’s lymphoma, and mesenchymal tumors were the commonest tumors in decreasing order[24].On a 15 year experience of 139 cases by Zafar, N. and S. Moinuddin diagnosis is reached in 128cases (92%) of which 33cases (26%)had benign diagnosis and the remaining 95 (74%)had malignant diagnosis with metastasis the most common (80 of 95cases). An overall cytologicaldiagnostic accuracy was 99%. Nodular sclerosis variantof Hodgkin’s disease was the main component of inadequate samples[33]. It was also the predominant diagnosis of unrepresentative samples in a review of 136 fine needle aspiration (FNA) biopsies of mediastinal masses. Thymoma (malignant), Hodgkin’s lymphoma and metastasis were the predominant lesions in increasing order [34].A study of 52 patients with anterior mediastinal mass had indicated that the diagnostic yield of CT-guided percutaneous biopsy is 77%. There was no factor that had a significant association with accuracy rate [12].Thymic lesions and metastasis have a higher rate of specific histologic typing where as lymphoma is less reliably diagnosed [12, 24].

CT-guided core needle biopsy of pleura done on 88 patients showed that 63% were malignant, 31% were benign and 5% were undetermined. Mesothelioma was the commonest malignant lesion followed by adenocarcinoma while tuberculous and inflammatory pleuritis were the leading benign lesions [35].Of 21 patients with confirmed malignant mesothelioma who underwent percutaneous image-guided cutting needle biopsy (CNB), 18 patients had a correct diagnosis (86% sensitivity and 100% specificity)[36].

Image-guided pleural biopsy was performed in 82 patients, five under ultrasoundguidance and 80 under CT guidance, seventy-five of the 85 biopsies were diagnostic,with a sensitivity of 76% and specificity of 100%[13].

2.2 Complications of CT guided transthoracic needle biopsy and associated factors

Pneumothorax is the most common complication of CT guided transthoracic needle biopsy. In a large survey in the UK involving 5444 percutaneous lung biopsies, 20.5% of pneumothorax and 3.1% of pneumothorax requiring chest drain was reported[37].A meta-analysis of 12,753 procedures revealed that 25.3 % of core biopsy and 18.8 % fine needle aspiration(FNA) were complicated by pneumothorax[17]. Nour-Eldin, N.-E.A., et al. found 23.2- 27 % of pneumothorax complicating 650 coaxial and non-coaxial CT-guided lung biopsy[30].

There are patient-related and technical factors and lesion characteristics that affect the occurrence of pneumothorax.Underlying lung disease like chronic obstructive pulmonary disease (COPD) and emphysema are major patient-related factors for the development of biopsy related pneumothorax[15, 30, 38].Larger lesion diameter andavoiding aerated lung along the biopsy tract have been mentioned as a protective factor for pneumothorax [17, 18, 27, 30, 38]. Needle type and operator experience have no significant association with the pneumothorax [17, 24, 39, 40]. There is no agreed data on the effect of the number of punctures on the incidence of pneumothorax[5].

Hemorrhage, the second most common complication, was reported from 6.4-42% [17, 21, 29]. However,hemothorax complicates CT guided TNB rarely with a reported value of less than 5% [29, 30, 41]. The mentioned factors associated with increased risk of hemorrhage are decreased lesion size and traversing aerated lung parenchyma [29].

Air embolism is a rare disastrous complication with only case reports and if it occurs usually fatal. Two cases of air embolism to the heart, one fatal cerebral air embolism and 6 cases of air embolism to an unspecified location are reported[41-45].Tumor seeding along the biopsy tract,tension pneumothorax, heart arrest, shock, respiratory arrest, and death are reported as very rare complications accounting $\leq$0.1% in a survey of severe complications of 9783 CT-guided needle biopsy of lung lesions[41]. Vasovagal reaction, infection and cardiac tamponed are also rarely reported complications [5].

2.3 Number of scans and radiation dosage

In CT guided TNB static CT images are used after each adjustment of the needle to guide it to the desired target. The reported median DLP (dose-length product)ranges from 403 mGy cm to 845 mGy cm [8, 46].Kallianos, K.G., et al. found that median DLP can be decreased by 64% by setting low-dose protocol[47]. Lesions that are smaller or deeper in the lung result in a higher number of CT scans, resulting in increased radiation dose and procedure time, with most of these performed during the needle insertion step[8].

CHAPTER 3. OBJECTIVES

3.1 General Objective

- To determine the diagnostic yield, complication rate and associated factors of CT guided TNB in TikurAnbessa specialized hospital.

3.2 Specific Objectives

- To determine the diagnostic yield of CT guided TNB
- To assess the incidence of complicationsin CT guided TNB
- To assess factors affecting diagnostic accuracy and complication rate of CT guided TNB
- To determine the time required to do CT guided TNB.
- To determine the mean number of scans and DLP of the procedure

CHAPTER 4. METHODS AND MATERIAL

4.1 Study area

The study was conducted at TASH, College of health science, Addis Ababa University, Addis Ababa Ethiopia. TASH, located in the nation's capital Addis Ababa, is the largest referral as well as the main teaching hospital. The hospital provides a tertiary level referral treatment with over 900 beds and is open 24hrs for emergency services.

4.2 Study design and period

An institutional-based prospective study was conducted from July 2018 to August 2019 G.C.

4.3 Population

4.3.1 Source population

All patients with a mediastinal, pleural, pulmonary or multi-compartmental mass lesions.

4.3.2 Study population

All patients for whom CT guided TNB is done for mediastinal, pleural, pulmonary or multi-compartmental mass lesion and have pathology result.

4.4 Inclusion and Exclusion criteria

4.4.1 Inclusion criteria

- All patients who underwent CT-guided TNB at the radiology department of TASH between July 2018 and July 2019 G.C having a post-procedural histo-pathologic results.
- Patients with adequatehepatic and hematological function for those having coagulation abnormalities and who take drugs affecting the coagulation profile.

4.4.2 Exclusion criteria

- Patients with uncorrectable coagulopathy, positive-pressure ventilation or severe respiratory compromise.
- Patients with a significant decrease in size and extent of the lesion in the pre-biopsy scan.
- Patients who refused the procedure.
- Aborted biopsies in which no samplewas obtained (eg, patient intolerance of the procedure).

4.5 Sampling technique and sample size determination

Non-probability sampling technique was used and all patients who undergo CT guided TNB and hadhistopathologic results during the study period were included.

4.6 Data collection technique

A total of 107 CT guided core needle biopsy in 100 patients were performed between July 2018 and Jun 2019 in TASH. Seven biopsies were repeat procedures because of the inconclusive finding of the first biopsy. Seventy-seven (71.96%) were located in the lung, fifteen (14.02%) in the mediastinum, eleven (10.28%) in the pleura, and two (3.74%) multi-compartmental.

During patient arrival to the radiology department with a CT guided TNB request its feasibility was assessed by a senior radiologist and radiology resident. A review of patients' more recent chest CT was used to determine patient and lesion selection, patient positioning and biopsy approach. It was also reviewed before the procedure for the lesion size, location, lesion vascularity, and important structures located in the biopsy path. Patients who full filled the inclusion criteria and had no contraindication were enrolled after informed about the pros and cons of the procedure. The procedure was done by either experienced cardiothoracic radiologist, cardiothoracic radiology fellow or radiology residents under the supervision of a cardiothoracic radiologist.

Patients were positioned in either supine, prone, lateral decubitus or oblique positions based on the lesion characteristics. Patients were instructed to abstain from moving, coughing, talking, or deep breathing during the procedure. Pre-procedural CT was done on a GE 64-row detector volumetric CT scanner with the following parameters: 5mm slice thickness, 50 or 40 mAs and 100 kV. On the scout image, the anatomic area containing the lesion was collimated. Lesions which showed a significant interval size reduction or complete disappearance were indications for termination of the procedure during which benign or infectious conditions were considered based on the patient's clinical data. For cases in which the procedure was decided to proceed the suitable slice number which avoids crossing interlobar fissures, visible bronchi, thoracic wall, and central vessels and has a minimum distance of traversed aerated was selected. Based on this CT localization was done by laser lights and markers on the skin. Patients were instructed to abstain from moving, coughing, talking, or deep breathing during the procedure. Biopsies were performed using an 18-gauge automated core needle biopsy.

Under possible aseptic conditions, local anesthesia was administered by 10 cc syringe up to the pleura which was kept insitu in order to be sure that the path was correct for further core needle biopsy advancement. After the advancement of the biopsy needle, the position of its tip is confirmed by CT images. In cases of needle misplacement, it was removed and replaced along the predicted trajectory. Then after the automated biopsy system was fired after which the needle was removed and the sampled tissue was detached and inserted to the prepared formalin solution. The same procedure was repeated two to three times until the operator decides that the sampled tissue was adequate. At the end of the last needle biopsy, the patient was kept in place and the pre-collimated anatomic area was scanned for any complication. During complication detection, the patient was told to stay around the radiology department for the first post-procedural hour. All the patients had no complications that needs admission and further management like drainage tube placement. Additional chest radiographs were taken in patients with chest pain and new respiratory symptoms. All patients were sent home after instructed to abstain from coughing, shouting, and Valsalva maneuvers related to lifting heavy items or straining in the bathroom for 24 hours following the procedure. They were given instructions to telephone or return to the hospital if they develop breathlessness, chest pain, or hemoptysis. Any new air collection in the pleural cavity or an increase in depth of preexisting air collection was considered as procedure-related pneumothorax complication. A new post-procedural ground-glass opacity along the trajectory path or surrounding the lesion was recorded as alveolar hemorrhage. Patients were considered cooperative if they were following the operator's instruction appropriately, like breath-holding.

The sample tissue was sent to the department of pathology in a formalin solution. The pathology results were collected monthly. Among the 107 core needle biopsy samples the pathology results were collected for 101 cases (94.35%) (Seventy-three lung (72.28%), thirteen mediastinal (12.87%), eleven pleural (10.89%), and two multi-compartmental (3.96%)). The result of the remaining patients were lost from the pathology unit for which they were excluded from the analysis.

Pathology results with the definitive diagnosis were considered as conclusive and those results which are reported as inconclusive or non-representative and did not allow for a therapeutic decision to be made are considered as inconclusive. In case of strong radiologic suspicion for malignant lesions, pathology results having a description of no malignant cells without a definitive diagnosis were also considered inconclusive.

The length of biopsy procedures was calculated by the difference between the clock reading on the first scout view and the time on the CT image obtained through the chest after removal of the guide needle. The automatically calculated DLP was recorded from the CT dose report.

4.7 Data quality and management

A clear understanding of the questioner among the radiology residents was assured by providing a pretest. Data were evaluated for completeness and patients with incomplete records and pathology data were excluded from the study to avoid bias in the correlation.

4.8 Data entry and analysis

The collected data were processed and analyzed using IBM SPSS statistics software version 25. Data cleaning was performed to check for frequencies, accuracy, and consistencies and missed values and variables.

Complication rate and its associated factors, as well as pathologic conclusive rate and its associated factors, were determined by descriptive statistics and the association was demonstrated. Chi-square was used to see the relationship between nominal variables while the association between scale and nominal variables were analyzed by independent t-test for those having only two variables and ANOVA with eta squared for those having more than two variables. The data is presented by statements, figures, graphs, and tables.

4.9 Study variables(Independent & dependent)

4.9.1 Independent variables

- Age
- Sex
- Lesion location and characteristics
- Technique used

- Underlying lung disease and patient cooperation

4.9.2 Dependent variables

- Diagnostic yield
- Complications
- Number of scan and dosage

4.10 Ethical considerations

Ethical clearance has been obtained from Addis Ababa University College of health sciences research and ethical clearance committee. Written consent was acquired before any procedure. Any piece of information will be kept confidential. A written formal letter will be obtained from the respective authorities and a formal letter was written from the radiology department to pathology unit before commencing the data collection process.

4.11 Dissemination of the result

The final result from the study will be submitted and presented to the radiology department of Addis Ababa University College of Health Science. Efforts will be made for presentations in regional and international conferences and journals.

4.12 Limitation

Only one out of the two CT-scanners was functional during the study period. There wasa huge patient burden on the CT scanner for which CT guided TNB has been done only for one or one and half hours per day. The only available CT scanner was not functional for a one and half month. Therefore an adequate number of procedures and sample size was not acquired.The needle required for CT guided TNB was also not available in the TASH compound. Except in some rare cases, the only available biopsy needle was CNB and found only in some private centers which were costly. It had also an impact on the sample size especially when patients can't afford it. Rooms were not provided for post-procedure follow-up for complications.

CHAPTER 5. RESULTS

CT guided transthoracic biopsy was done on 57 males (56.4%) and 44 females (43.6%) after the exclusion of the six patients in which pathology result was not available. The mean age of the patients was 49.12 years (SD: ±16.59) with a range of 14 to 85 years.

The target lesions were mainly located in the upper lobe (31.7%) from the lungs and in the anterior compartment (7.9%) from the mediastinum. The lower lobes (26.7%) and posterior mediastinum (3%) were the second most common localization of lung and mediastinal lesions respectively. Nine patients had pleural effusion and four patients had emphysema.

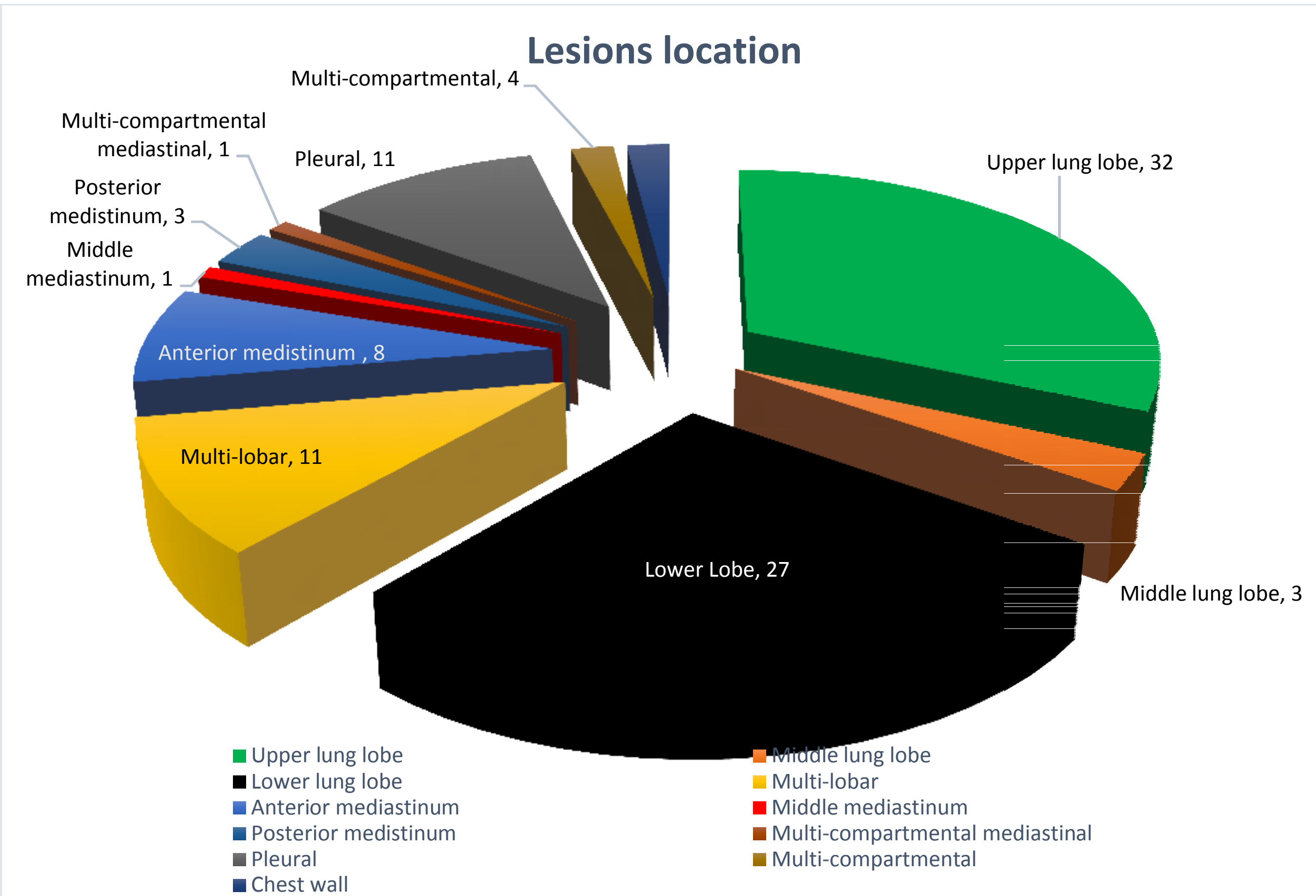

Figure 1 Compartments of lesions for which CT guided biopsy was done

The mean target size along the trajectory path was 5.69 cm (SD: ±2.49 cm, range: 1.5 to 14.6 cm). The mean depth of the lesions from the skin along the planned trajectory was 3.95 cm (SD: ±1.94 cm, range: 1.35 to 10 cm) and their mean distance from the nearest diaphragm was 3.89 cm (SD: ±3.65 cm, range: 0 to 14 cm).

The most preferred patient positioning was prone (40.5%) followed by supine position (31.1%). Lateral and oblique positions were also used for 12 and 9 patients respectively. Average of 3 pleural punctures were required for adequate lesion access and sampling with a range of 1 to 6 punctures. The mediastinal, pleural and multi-compartmental lesions were sampled 3 times on average. Among the biopsied lung lesions some of them were adjacent to the pleura with no traversed aerated lung but a maximum of 5.15 cm was traversed resulting in a mean distance of traversed aerated of 0.27 cm (SD: ±0.77 cm).

More than half of the procedures were done by radiology residents (58.1%). The chest radiologist did 35.1% of the biopsies although all the biopsies done by the radiology residents were supervised by him. A minimum of 3 and a maximum of 8 scans (mean 4.8) were taken during the procedures with a mean DLP of 159.3 mG cm (SD: ±70.52 mG cm, range: 42 to 410.51 mG cm). The mean time required to perform biopsy was 24.8 minutes (SD ±5.17) with a range of 17 to 48 minutes.

Table 1Descriptive values for patients age, lesion characterstics and technical factors

	Minimum	Maximum	Mean	Std. Deviation
Age	14	85	49.12	16.59
Size along the long axis (in cm)	1.50	14.60	5.69	2.49
Depth from the chest wall along the planned trajectory (in cm)	1.35	10.00	3.95	1.94
Distance from the nearest diaphragm (in cm)	0.00	14.00	3.89	3.65
Number of pleural puncture	0	6	2.72	1.37
Pleural-needle angle	20	107	80.13	17.64
Distance of aerated lung traversed (in cm)	.00	5.15	.27	.77
No of scans	3	8	4.78	1.21
DLP (in mG cm)	42.00	410.51	159.30	70.52
Duration of the procedure (in minutes)	17	48	24.80	5.17

Patient cooperation had a significant effect on the number of scans, DLP level and duration of the procedure. The study found that the cooperative patients had statistically significantly lower number of scans (M = 4.68, SD = 1.12), DLP level (M = 155.98 mG cm, SD = 66.7 mG cm) and short procedure duration (M = 24.49 min, SD = 4.88 min) than uncooperative patients (for number of scans M = 6.8, SD = 1.1, t(99)= 4.14, *p* = .000. for DLP level M = 223.00, SD =

115.40, t(99)= 2.11, *p* = .038. for procedure duration M = 30.60, SD = 7.77, t(99)= 2.66, *p* = .009).

Of the 101 biopsies, there were inadequate tissue for diagnosis in 24 (23.8%) biopsies. Of this 18 were lung lesions, 3 mediastinal and 3 pleural lesions. Adenocarcinoma was the most common pathologic result of biopsied lung lesions followed by squamous cell carcinoma and undifferentiated carcinoma. Two cases of tuberculosis were also identified. Thymoma and lymphoma were the 1st and 2nd most common pathology revealed diagnosis of the mediastinal lesions. There were 5 cases of pleural adenocarcinoma infiltrates and one case of tuberculosis.

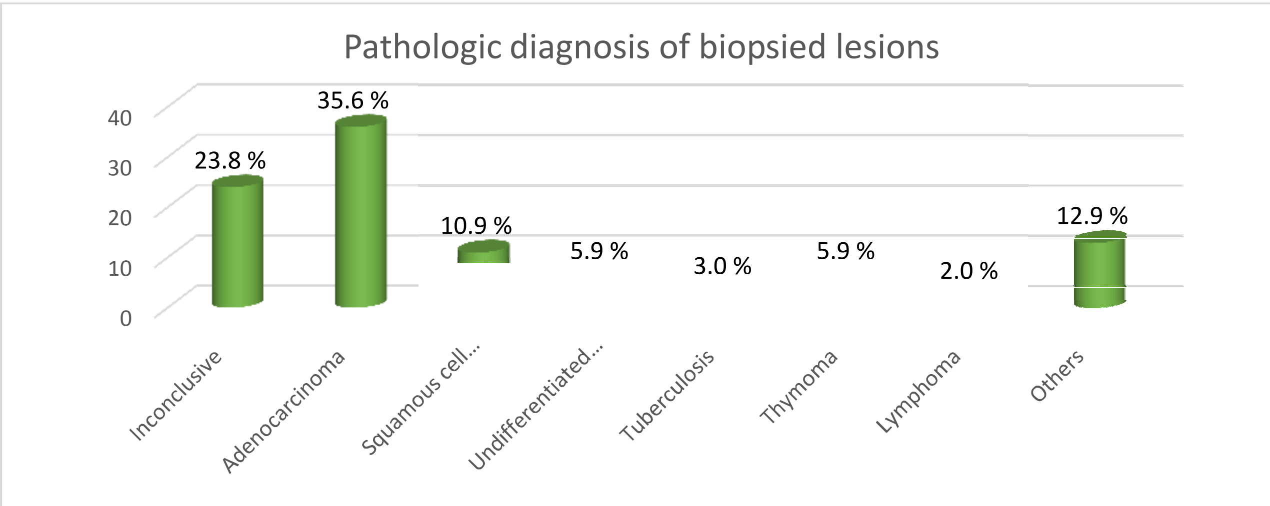

Figure 2 Pathologic diagnosis of the biopsied lesions under CT guidance.

Table 2Pathologic diagnosis of biopsied lesions by compartement

Mediastinal pathology	Frequency	%	**Lung pathology**	Frequency	%	**Pleural pathology**	Frequency	%
Inconclusive	3	23.1	Inconclusive	18	24.3	Inconclusive	3	27.3
Thymoma	6	46.2	Adenocarcinoma	31	41.9	Adenocarcinoma	5	45.5
Lymphoma	2	15.4	Squamous cell carcinoma	11	14.9	Tuberculosis	1	9.1
Others	2	15.4	Undifferentiated Carcinoma	6	8.1	Others	2	18.2
Total	13	100.0	Tuberculosis	2	2.7	Total	11	100.0
			Others	6	8.1			
			Total	74	100.0			

There was no statistically significant difference in the means of age, a number of pleural punctures, size and depth of the lesion between inconclusive and conclusive pathologic yield groups as determined by independent samples t-test ($p > 0.5$). A cross-tabulation with chi-square determination did not reveal a statistically significant correlation between the pathologic yield and the sex of the patient and the location of the lesion ($p > 0.5$).

Among the 101 biopsies, complications were observed in 21 patients (20.8%). Most of them (20 patients, 95.2% of complications) occurred during biopsy of lung lesions and the remaining one occurred during pleural lesion biopsy. There was no complication correlated to the biopsy of the multi-compartmental or mediastinal lesion. The most common complication was pneumothorax which occurred in 13 patients (12.9%), they were treated conservatively and none of them underwent insertion of chest tubes or admission. Five patients (5%) had alveolar hemorrhage for which no specific therapy was required except for observation. Subcutaneous emphysema appeared in two patients, and one patient had syncope and vomiting for which he was seen in the emergency department for an hour and discharged improved. A dedicated room for post-procedural complications follow-up was not provided during the study period.

A one-way between-subjects ANOVA was conducted to compare the effect of distance of traversed aerated lung and size of the lesion along the planned trajectory on complications for pneumothorax, alveolar hemorrhage, and others. There was a significant effect of distance of traversed aerated lung and size of the lesion along the planned trajectory on complications at the $p<.05$ level for the three complications [$F(3, 70) = 21.4$, $p = 0.001$] and [$F(3, 70) = 6.04$, $p = 0.001$] respectively. Post hoc comparisons using the Tamhane's T2 post hoc test indicated that the mean distance of traversed aerated score for the pneumothorax ($M = 1.65$, $SD = 1.43$) was significantly different than the no complication ($M = 0.06$, $SD = 0.23$) with partial eta square of 0.688. The mean size of the lesion score for the pneumothorax ($M = 4.02$, $SD = 1.33$) as well as that for alveolar hemorrhage ($M = 3.84$, $SD = 0.49$) were also significantly different than those having no complication ($M = 6.38$, $SD = 2.30$) with partial eta square of 0.206. However, complication had no correlation with a number of pleural punctures, the age of the patient as well as the depth of the lesion ($p>0.05$). An independent sample t-test was performed for possible correlation of complications with underlying lung disease but didn't reveal a significant correlation ($p>0.05$).

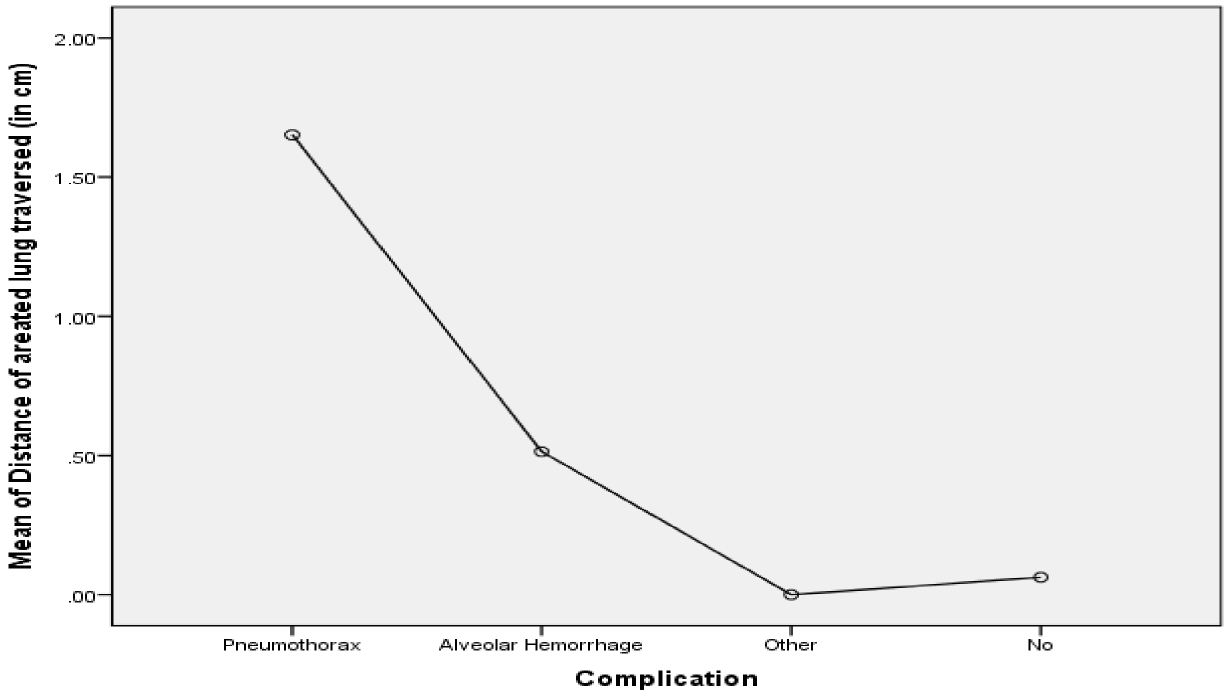

Figure 3 Correlation of complications to the mean distance of traversed aerated lung tissue

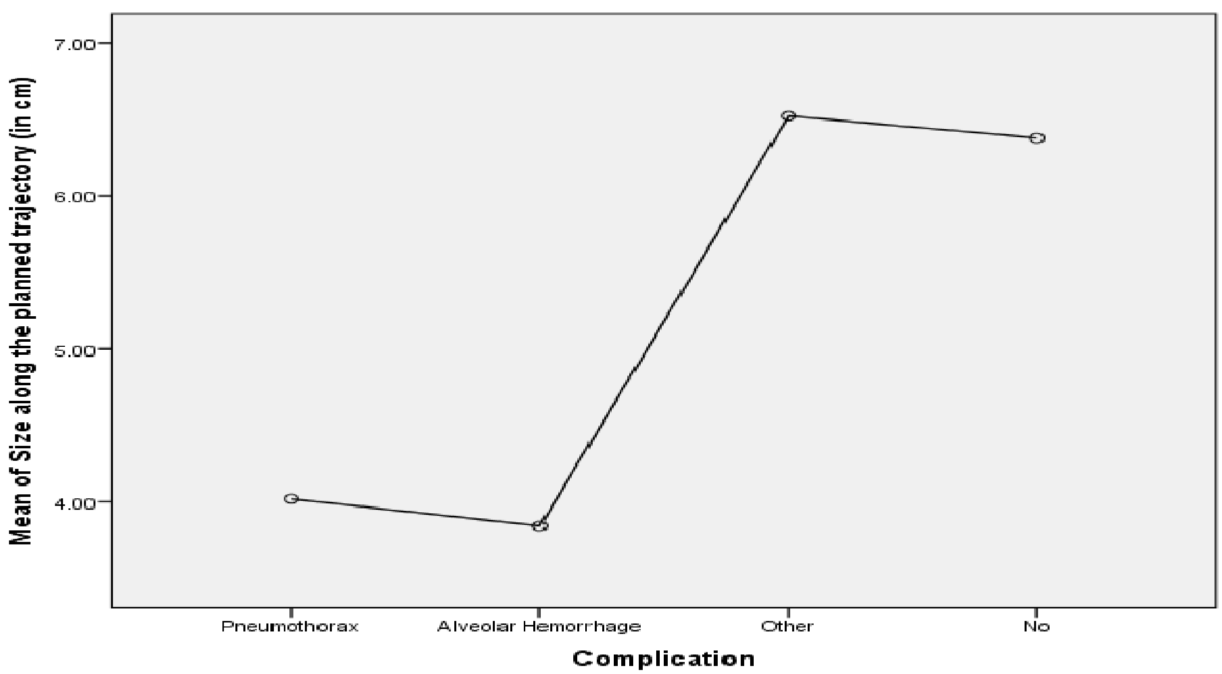

Figure 4 Correlation of complications to the mean size of the lesion

CHAPTER 6. DISCUSSION

As modern medical therapy requires precise and accurate diagnosis of lesions avoiding or minimizing complications, minimally invasive techniques are getting worldwide acceptance. Percutaneous image-guided transthoracic needle biopsy has made advances since it is popularized by a nordenstorm in the 1960s [4]. CT guided transthoracic needle biopsy provides a tissue specimen to classify lesions into benign, malignant or inflammatory/infectious category. It is a safe, minimally invasive, accepted, easy and accurate procedure that provides useful diagnostic information and avoids more invasive and expensive exploratory surgeries, especially in medically treatable or unresectable cases [7, 20, 24-26].

CT guided transthoracic needle biopsy has been used for sampling of mediastinal, pleural, pulmonary or multi-compartmental masses since 3 years ago in TikurAnbessa Specialized Hospital (TASH). For the past year, it was done for a total of 107 lesions on 100 patients of which 7 were a repeat biopsy. Excluding the lesions for which biopsy result was not found the locations of the lesions were lung (72.28%), mediastinal (12.87%), pleural (10.89%), and multi-compartmental (3.96%). The mean age of patients was 49.12 years with male predominance (56.4%). A similar mean age of presentation has been seen in other studies [21, 48, 49].

This study demonstrates that CT guided a transthoracic needle biopsy of intrathoracic lesions yields adequate material to establish a conclusive diagnosis based solely on cytologic and histologic interpretation in up to 76.2% of cases. The diagnostic yield for lung, mediastinal and pleural lesions were 76.6%, 80%, and 72.7 % respectively. The accuracy of CT guided lung biopsies was low in this study compared to the previous studies having a range of 80.4% - 95% accuracy rate [9, 11, 31, 50]. In most of the studies, CT guided biopsy procedures were accompanied by pathologists who assess the adequacy of the sampled tissues immediately. This can be an explanation for the different accuracy rates. Although the number of cases was small, transthoracic needle biopsy of the mediastinal lesion showed similar accuracy with most of the previous studies [12, 34, 46, 51]. Pleural biopsies were less accurate in this study than vanSonnenberg, E., et al, Benamore et al and Niu et al studies which showed the accuracy of 83.3%, 82 % and 89.2% respectively [13, 35]. It can be because of the small size of the current study population.

Out of the 101 biopsied lesions, only 9 cases showed benign and infectious cause. Adenocarcinoma was the most common pathologic result of biopsied lung lesions followed by squamous cell carcinoma and undifferentiated carcinoma. Two cases of tuberculosis were also identified. Thymoma and lymphoma were the 1st and 2nd most common pathology revealed diagnosis of the mediastinal lesions. There were 5 cases of pleural adenocarcinoma infiltrates and one case of tuberculosis. The predominance of malignant lesions in the biopsied lesions is in concordance with another large sample as well as small sample studies [11, 24, 27, 32, 33, 35].

Although Yeow, K.-M., et al showed that lesion size and the final diagnosis (benign or malignant) determines the diagnostic yield, Niu, X.-K. et al, Petranovic, M., et al and this study didn't find statistically significant factors associated with the diagnostic accuracy [11, 12, 35]. The present study did not find statistically significant differences between the conclusive and non-conclusive patient groups in terms of age, sex, or lesion characteristics such as size or depth of the lesion. The other studies compared the diagnostic accuracy to the surgical outcome or to the follow-up imaging but this study only had a single pathology report of the biopsy which was not compared to the surgical outcome which may increase or decrease the diagnostic accuracy.

Among the 101 biopsiesthe 20.8% had complications of which the most common was pneumothorax 12.9% followed by alveolar hemorrhage (5%). This complication rate is much less than the reported rate ranging from 23.2 to 27 % of pneumothorax and 6.4 to 42 % of alveolar hemorrhage [17, 21, 29, 30, 37]. This can be because of the small number of the current study sample size and the patient selection method. Most of the complications (95.2%) occurred during biopsy of lung lesions and the remaining one occurred during pleural lesion biopsy. There was no complication correlated to the biopsy of the multi-compartmental or mediastinal lesion. All the complications were managed by observation.

Like that of the other studies complications, especially pneumothorax and alveolar hemorrhage hada strong positive correlation with the distance of traversed aerated and negative correlation with the mean size of the lesion along the planned trajectory [17, 18, 27, 30, 38]. But in contrary to the studies done by Wu, C.C., et al, Nour-Eldin, N.-E.A., et al and Cox, J.E., et al underlying lung disease like COPD had no significant effect on the occurrence of complications [15]. The likely explanation is the small number of included patients with COPD. The number of pleural punctures also had no significant effect on complications like that of the study done by Elizabeth, H.M. [5].

A mean scan number of 4.8 was taken during the procedures with a mean DLP of 159.3 mG cm. This is much lower than the mean dose reported in other studies (403 mGy cm to 845 mGy cm)[8, 46].The smaller scan length and mA applied for low dose protocol in this study may be the reason for the lower mean DLP value. It is approximate to the low dose protocol (113.8 mGy cm) instituted by Kallianos, K.G., et al [47]. The mean time required to perform biopsy was 24.8 minutes with range of 17 to 48 minutes. The study found that the cooperative patients had statistically significantly lower number of scans and short procedure duration than uncooperative patients.

CHAPTER 7. CONCLUSION AND RECOMMENDATIONS

A CT-guided percutaneous transthoracic needle biopsy was used as an initial procedure for evaluating mediastinal, pleural, pulmonary as well as multi-compartmental lesions with the overall diagnostic conclusive rate of 76.2%. No significant differences between the conclusive and non-conclusive patient groups in terms of patient factors, lesion characteristics as well as technical factors. However, it is possible that larger sample size and correlation with the surgical outcome and follow-up imaging could show more subtle trends, and discovering such trends would help in further guiding referring physicians as to the likelihood of obtaining a diagnostic specimen. We recommend an on-site cytopathologist for the assessment of tissue adequacy to increase the diagnostic accuracy of this minimally invasive procedure.

A CT-guided percutaneous transthoracic needle biopsy can be performed easily and safely with patient comfort and few associated complications. It is a rapid technique and can avoid invasive procedures requiring patient admission and anesthesia. Although there was no dedicated room for the management of procedural complications, in this study we did not come across a severe complication requiring admission, chest drain or resuscitation. Lesion size and the distance of traversed aerated lung tissue were the determinant factors for the occurrence of complications. We recommend a dedicated room having materials for the post-procedural follow-up of patients with any complications occurring during a CT guided transthoracic needle biopsy.

The procedure can be done with low dose protocols and shorter duration provided that the patient position selection and line of trajectory are settled at the pre-procedural time. The cost and availability of the core biopsy needle as well as the only available single partially functional CT scanner made this simple and safe procedure to be done for a few patients. As this hospital is a tertiary hospital there are a lot of patients eligible for this procedure for which the radiology department and the hospital managing team should take responsibility to advance the quality and quantity of this diagnostic workup. We also recommend further studies and implementations to be taken by the government to apply and use this diagnostic workup in other centers who have a functional CT scanner.

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ANNEX I: CONSENT FORM

Patient agreement to CT guided a needle biopsy

Statement of the health professional
I have explained the procedure to the patient. *In particular, I have explained:*

The intended benefits
- A clear diagnosis that will inform future treatment options

Mild complication
- Bruising

More serious complications
- Slight bleeding
- Pneumothorax

Very serious complications
- Bleeding requiring surgery
- Air embolus
- Death The overall risk of a serious complication ordeath is one in 5,000.

Statement of patient
I agree with the procedure or course of treatment described in this form and had the opportunity to ask questions.
I agree with the use of photography for the purpose of diagnosis and treatment and I agree with photographs being used for medical teaching and education.
I understand that any tissue removed as part of the procedure or treatment may be used for diagnosis, stored or disposed of as appropriate and in a manner regulated by appropriate, ethical, legal and professional standards.
I understand that any procedure in addition to those described on this form will be carried out only if necessary to save my life or to prevent serious harm to my health.

Patient
Name:.…….………..........…...................
Signature:.……...………........…………..
Date:…………….....................................

ANNEX II: DATA COLLECTION FORMAT (QUESTIONNAIRE)

Date: ____________________
Name: ____________________
MRN: ____________________
Phone number: ____________________
Pathology serial number: ____________________

A. Demography:

1. Age: ____
2. Sex: ____
3. Region: ____________

B. Patient medication history and laboratory data

1. Clotting function (PT, PTT and INR) **A)** Normal **B)** Abnormal **C)** Not done
2. Platelet **A)** Normal **B)** Abnormal **C)** Not done
3. Medication that affect platelet/clotting function **A)** Yes **B)** No

C. Pre-procedural chest CT evaluation

1. Lesion characteristics

1.1. Location: (Mark √)

Lung			Mediastinum				Pleural	Multi-compartmental
Upper	Middle	Lower	Anterior	Middle	Posterior	Multi-compartmental		

1.2. Size along the long axis (in cm): ______

1.3. Depth (From the chest wall along the planned trajectory) (in cm): ______

1.4. Adjacent structures: **A)** Large vessels(specify): ____________________

B) Large air ways (specify): ____________________

1.5. Distance from the nearest diaphragm (in cm): _______

2. Underlying disease

A) No **B)** Yes, if yes what type: (Mark √)

Emphysema	
Pulmonary HTN	
Other(specify):	

D. Procedure

1. Patient positioning: (Mark √)

Supine		Prone		Lateral		Oblique	

2. Pleural puncture:

2.1. Number of pleural puncture: _____

2.2. Pleural-needle angle: ______

3. Distance of aerated lung traversed (in cm): ______

4. Needle manipulation in the lung: **A)** Yes **B)** No

5. No of scans: _____

6. DLP (mGy cm): ______

7. Duration of the procedure (from the first scan to the last): __________

8. Patient cooperation (breath hold): **A)** Cooperative **B)** Uncooperative

E. Post-procedure

1. Complications (Mark √): More than one can be marked. If no skip Q no 2 and 3.

No	
Pneumothorax	
Tension pneumothorax	
Hemorrhage	
Hemothorax	
Subcutaneous emphysema	
Air embolism	
Cardiac tamponed	
Death	
Other(specify):	

3. Type of complication management taken(Mark √): More than one can be marked

Observation	
Intra-nasal O_2	
Admission	
Aspiration	
Chest drain	
Resuscitation	
Other(specify):	

2. Complication detected by

A) Immediate CT **B)** 1hour CXR