Pulmonologist-led ultrasound guided lung biopsy safety and efficacy: a 4-year experience from a tertiary centre in Northern Malaysia

Izzatul Nadzirah Ismail, MRCP(IRE), Arvindran Alaga, MRCP(UK)

Respiratory Department, Hospital Sultanah Bahiyah, Kedah, Malaysia

ABSTRACT

Introduction: Ultrasound guided lung biopsy (USLB) is a minimally invasive diagnostic tool with short examination time and real-time monitoring conducted bedside for accurate diagnosis in order to provide the best treatment. However, it is not widely performed by pulmonologists. We aim to explicate the efficacy and safety of USLB led by pulmonologists. The objective of this study is to assess safety and efficacy of USLB performed by pulmonologists in an outpatient setting.

Materials and Methods: We retrospectively enrolled patients who underwent the procedure from January 2018 to April 2022. Under real time ultrasound (Hitachi Medical ProSound F37), thoracic lesions adjacent to the chest wall were sampled with a full-core biopsy needle (CT Core Single Action Biopsy Device, 18G × 15 cm, Vigeo, Italy). Chest x-ray was performed 30 minutes post procedure ruling out pneumothorax. Patients were discharged home 1-2 hours post biopsy. Data was analysed using Microsoft Excel 2010 and Statistical Package for Social Science (SPSS) Version 26.

Results: A total of 18 patients (14 males, 4 females) underwent USLB for lung tumours. Biopsies were histologically deemed adequate with an overall diagnostic yield of 77.8% (14/18). A total of 57% were positive for thoracic malignancy (21% squamous cell carcinoma, 21% adenocarcinoma, 15% small cell carcinoma) and another 43% were positive for extra thoracic malignancy (1 hepatocellular carcinoma, 2 DLBCL, 1 Hodgkin's lymphoma, 1 seminoma, 1 thymoma). Four patients had inconclusive results but managed to get positive results from surgical or lymph node biopsy (thymoma and adenocarcinoma). Statistical analysis showed more than two passes are needed to achieve a positive HPE yield (*p* value<0.05). There were nil complications to all the cases done.

Conclusions: USLB can safely and effectively be performed by trained pulmonologists with excellent accuracy and low complication rate in outpatients.

KEYWORDS:
Ultrasound, lung biopsy, pulmonologist

INTRODUCTION

Lung cancer is the second most common cancer and the leading cause of cancer death worldwide in both males and females.[1] In Malaysia, lung cancer is the third most common cancer nationwide (1st most common in men and 4th most common in women) for the year 2020 accounting for 10% of all malignancies. Lung cancer is also the most common cancer-related death with 5-year observed survival rate of 9% and 5-year relative survival rate of 11% which is the lowest compared to other malignancies. However, 90% of patients were diagnosed at stage III, IV.[2,3] Hence it is crucial to evaluate each patient with any form of thoracic lesions in order to obtain an accurate diagnosis and manage accordingly. In recent years, there have been new advancements in lung cancer management, especially in molecular targeted therapy which has improved survival and quality of life.[4] However, to determine if a patient is suitable for the targeted therapy, better quality and quantity of samples are required for histological analysis.

There are various methods of lung biopsy such as surgical biopsy, bronchoscopy transbronchial lung biopsy (TBLB), endobronchial ultrasound (Linear or Radial EBUS)-guided biopsy, CT-guided biopsy, and ultrasound-guided biopsy.[5,6] Each of these methods has its own advantages and disadvantages. Ultrasound has been proven to be valuable as it is relatively inexpensive, mobile and widely available in most hospitals, including some district hospitals.

Ultrasound guided lung biopsy (USLB) is a minimally invasive diagnostic tool, requires short examination time and low complication rate with real-time monitoring at the bedside as compared to surgical biopsy.[6,7] USLB and CT-guided lung biopsy are preferable when diagnosing peripheral lung lesions as compared to bronchoscopy which is preferred for central lung lesions. USLB has an added advantage of no radiation exposure and is more economical with a similar success rate as CT-guided lung biopsy.

However, it is not widely performed by pulmonologists worldwide. Hence, we aim to explicate the efficacy and safety of USLB lead by pulmonologists in outpatient settings in Northern Malaysia. We hope to encourage pulmonologists to use this procedure in the future for accurate diagnosis in patients with lung mass.

This article was accepted: 19 September 2023
Corresponding Author: Izzatul Nadzirah Ismail
Email: izzatnadz@gmail.com

MATERIALS AND METHODS

Patients

We retrospectively enrolled and reviewed all the patients who underwent USLB as an outpatient in the Respiratory department, Hospital Sultanah Bahiyah, Alor Setar, Kedah, Malaysia from January 2018 to April 2022. Patients' demographic data, previous medical and surgical illness history was taken from electronic medical records (eHis), clinic files and procedure book. All patients provided a written consent prior to the procedure.

Procedure

Patients were positioned in lateral decubitus, dorsal decubitus or sitting position based on the puncture point. By using an ultrasound machine (Hitachi Medical ProSound F37), the location and size of the lesions are determined via a curvilinear or liner probe (example shown in Image 1A). Also based on these images and doppler scan, we were able to decide on the most suitable site for biopsy with the shortest and safest approach. Under real time ultrasound, thoracic lesions adjacent to the chest wall were sampled with a full-core biopsy needle (CT Core Single Action Biopsy Device, 18G × 15 cm, Vigeo, Italy) under local anaesthesia as shown in Image 1B. Chest x-ray was performed 30 minutes post procedure ruling out pneumothorax. Patients were discharged home 1-2 hours post biopsy. Each pulmonologist that performed this procedure has a minimum of t years of training in ultrasound thorax imaging and credentialed in performing USLB.

Statistical Analysis

Data was collected using Microsoft Excel 2010 and analysed using SPSS Version 26 via Wilcoxon signed rank test. P value of <0.05 was taken as significant.

RESULTS

A total of 18 patients (14 males, 4 females) with age ranging from 29 to 80 years old underwent USLB for lung tumours. Mean age group is 56.3±18.4 years old. Majority of the patients are male (78%) and mostly are Malay ethnicity (89%) while the rest are Chinese. Average duration of procedure is 20 minutes.

Location of lung lesions varies from right lung (45% in upper lobe, 5% in middle lobe, 5% in lower lobe), left lung (12% in upper lobe, 5% in lower lobe) to mediastinal area (28%). Only 12 out of 18 patients managed to get a CT Thorax done prior to procedure while another six patients did not undergo CT thorax prior to procedure in view of the availability and waiting time for CT thorax which included the period of COVID-19 pandemic from 2020 to 2022 where there is a lot of restriction in the access of CT scan. The biopsy was done prior to CT to reduce the waiting time to diagnosis as ultrasound is readily available in the procedure room and easily done prior to procedure after reviewing patients' latest chest x-ray.

The size of the lesion also varies but about 83% have lesions more than 7cm and 12% did not have proper documentation on lesion size. The mean size of lesion of those documented is about 11.3±4.1mm. Mean size of the sample taken for the biopsy is 1.92cm^2 which is adequate for histopathology and molecular testing. Summary of patients' characteristics as shown in Table I.

Biopsies were histologically deemed adequate with an overall diagnostic yield of 77.8% (14/18). Results as shown in Table II are as follows: 57% were positive for thoracic malignancy (21% squamous cell carcinoma, 21% adenocarcinoma, 15% small cell carcinoma) and another 43% were positive for extrathoracic malignancy (1 hepatocellular carcinoma, 2 DLBCL, 1 Hodgkin's lymphoma, 1 seminoma, 1 thymoma). Four patients had inconclusive results, however, were able to yield positive results from surgical or lymph node biopsy (thymoma and adenocarcinoma). Despite inconclusive results, there were no delays in obtaining the diagnosis as patients were promptly referred for surgical biopsy. These were not related to learning curve pattern as these results were across time from 2020 to 2022. These lung lesions were at a more difficult location and difficult to obtain via a trucut biopsy.

Mean number of passes done to obtain an adequate sample is 3.5±1.1. Statistical analysis showed >2 passes are needed to achieve a positive HPE yield (p value <0.05).

There were no complications for all the cases done either during or post procedure. All patients were discharged 2 hours post procedure once confirmed no complications via chest x-ray.

DISCUSSION

Imaging guided lung biopsy (Ultrasound or Computer Tomograph, CT) is traditionally performed by interventional radiologists. However, in recent years, USLB has gained traction among pulmonologists worldwide. USLB can be performed under local anaesthesia with real time monitoring which makes it a safe procedure to be performed in an outpatient setting in a general procedure room. Compared to traditional CT-guided lung biopsy, USLB demonstrates similar precision but added benefits of safety as there is no added radiation.[5] Hence, it can be performed at the bedside with less effort, time, and cost.

Literature search using PubMed and Google Scholar revealed no study from Malaysia has been previously published on pulmonologist led USLB.

Based on our study, it is eminent that the number of passes plays a significant role in acquiring a satisfactory diagnosis. More passes can safely be made, yielding more accurate results. There were four cases that did not obtain any yield by which one showed necrotic tissue, two showed normal cells and one resulted in a non-representative sample. Based on our analysis of these four cases, some only had two passes when retrieving the sample which may explain the negative results.

According to a study by Lee MH et al., USLB requires less passes as compared to CT guided biopsy in order to achieve adequate yield (mean, 3.1±1.8 vs. 4.4±1.9, respectively, p<0.001).[8]

Table I: Characteristics of patients who underwent ultrasound-guided lung biopsy

Subject characteristics	Number of patients (%)
Sex	
Male	14 (78%)
Female	4 (22%)
Age	
21-40	4 (22%)
41-60	5 (28%)
61-80	8 (44%)
>80	1 (6%)
Ethnicity	
Malay	16 (89%)
Chinese	2 (11%)
Indian	0
Others	0
Duration of procedure	
10-20min	3 (17%)
>20 min	15 (83%)
Location	
Right	
Upper lobe	8 (44%)
Middle lobe	1 (6%)
Lower lobe	1 (6%)
Left	
Upper lobe	2 (11%)
Lower lobe	1 (6%)
Mediastinal	5 (27%)
Size of lesion	
4-5cm	1 (6%)
>7cm	15 (83%)
Not documented	2 (11%)
No of passes	
2	4 (22%)
3	5 (28%)
4	7 (39%)
5	2 (11%)
Complications	
Yes	0
No	18 (100%)

Table II: Results of sample from ultrasound-guided lung biopsy

Pathological type	Number of cases
Thoracic malignancy	
Adenocarcinoma	3 (17%)
Squamous cell carcinoma	3 (17%)
Small cell carcinoma	2 (10%)
Extrathoracic malignancy	
Hepatocellular carcinoma	1 (6%)
Diffuse large B-cell lymphoma	2 (10%)
Hodgkin's lymphoma	1 (6%)
Germ cell tumour (seminoma)	1 (6%)
Thymoma	1 (6%)
Inconclusive	
Thymoma (surgical biopsy)	1 (6%)
Adenocarcinoma (surgical and lymph node biopsy)	2 (10%)
Non-representative	1 (6%)

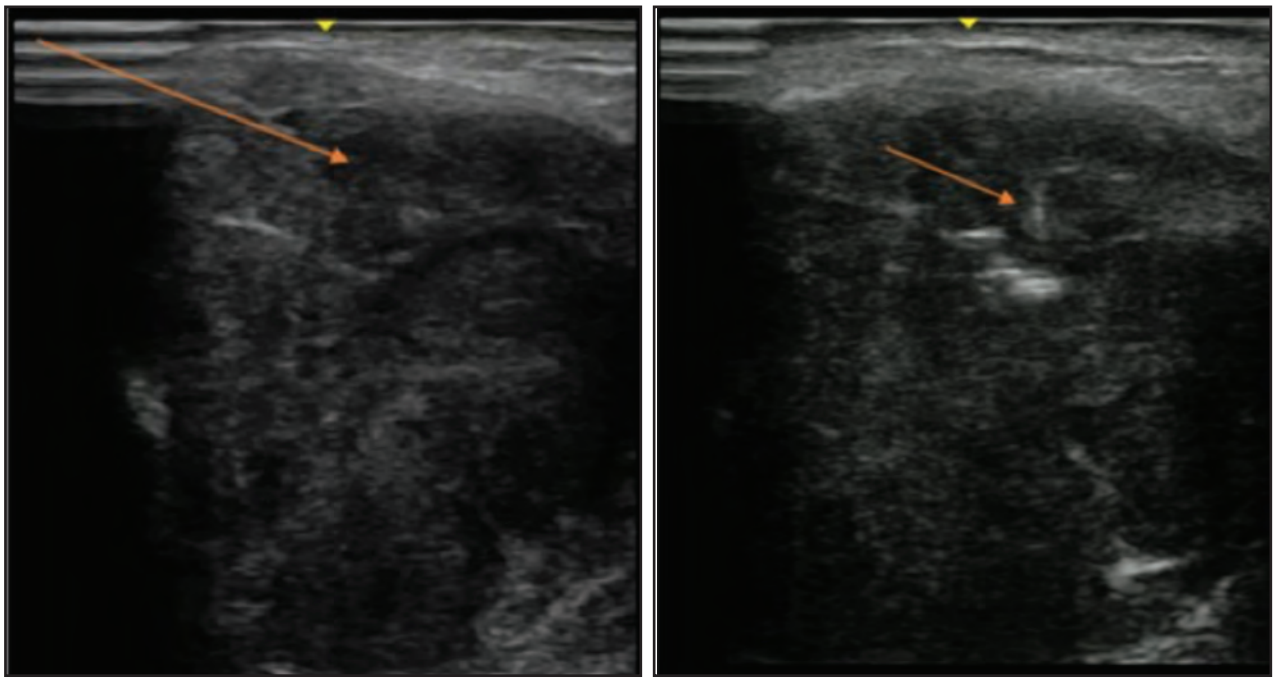

Image 1A Image 1B

Image 1A shows a lung mass (as shown by orange arrow) while image 1B showing full-core biopsy needle within the lesion (orange arrow).

USLB has shown a low rate of complications where none of the patients, involved in this study, developed any complications during or post procedure and were safely discharged within 2 hours after the procedure. Main complications that have been documented are pneumothorax and haemorrhage but at a negligible percentage in comparison to other methods.[9,10]

The risk of developing pneumothorax post USLB is higher in certain patients. The factors being older patients, patients with severe respiratory disease, smaller, deeper lung lesions and also technical factors such as the type and size of biopsy needle, longer procedure duration, biopsies in the middle or lower lobe, transgression of a fissure and multiple needle repositioning or pleural passes.[11]

The next most common complication of USLB is haemorrhage which is usually mild. But there is a higher risk of high-grade haemorrhage in the older age group, female sex, patients with emphysema, pulmonary hypertension, usage of coaxial technique, subsolid lesions, non-subpleural location and smaller lesions.[11] Lastly, the rarest complication of USLB is air embolism which is quoted to be 0.001-0.003% as quoted in a meta-analysis by Tomiyama et al.[12]

Nevertheless, these complications can be monitored in real time using the ultrasound post procedure and can be addressed in a timely manner.[5] The technical success rate of USLB based on our retrospective study is 100% as there were no documented complications during or post procedure. Multiple studies have also shown that USLB has fewer complications in comparison to CT-guided lung biopsy with a shorter duration of procedure.[8-11]

These findings are consistent with the findings in a study published by Diacon et al.,[13] that USLB can safely be done by pulmonologist for lesions 20 mm or more with high yield for malignant diseases including mesothelioma.[13]

On top of that, USLB has high efficacy of diagnosing malignancy which in our study only three cases of malignancy were missed. The histopathology results were divided into thoracic malignancy, extra thoracic malignancy and inconclusive results. Thoracic malignancy that was obtained were adenocarcinoma (17%), squamous cell carcinoma (17%) and small cell carcinoma (10%). On the other hand, extra thoracic malignancy includes diffuse large B-cell lymphoma (10%), hepatocellular carcinoma (6%), Hodgkin lymphoma (6%), germ cell tumour (6%) and thymoma (6%).

Another benefit of USLB by pulmonologist is a shorter waiting time (within 1 week) compared procedure done by interventional radiologist (within 2-4 weeks) which in turn leads to faster diagnosis and initiation of treatment. This procedure can be done under daycare setting by pulmonologist and thus avoiding unnecessary admission as compared to being done by interventional radiologist which requires admission about 2-3 days. There is no difference between procedure done by pulmonologist or interventional radiologist as both are trained in the procedure and use the same method.

Our study has certain limitations including small sample size of only 18 patients and it is a retrospective study for which it is prone to selection bias. A prospective study with larger sample size is needed to compare the efficiency of USLB with that of other methods.

Looking to the foreseeable future, there are now new technologies in ultrasound where contrast agents can be used to visualise microcirculation in lesions to differentiate the pathology of the lesion prior to the biopsy whether its benign or malignant.[14]

CONCLUSIONS

In conclusion, Ultrasound guided lung biopsy (USLB) can safely and effectively be performed by trained pulmonologists mainly for peripheral thoracic lesions with excellent accuracy and exceptionally low complication rate in outpatients. Mastering this technique also enables a pulmonologist to expedite the diagnosis of patients with lung mass.

REFERENCES

1. Dela Cruz CS, Tanoue LT, Matthay RA. Lung cancer: epidemiology, etiology, and prevention. Clin Chest Med 2011; 32(4): 605-44.
2. Rajadurai P, How SH, Liam CK. Lung cancer in Malaysia. J Thorac Oncol 2020; 15(3): 317–23.
3. World Health Organisation. Global cancer observatory (GCO). 'Malaysia Fact Sheet' [Internet]. March 2021 [cited 6 April 2021]. Available from: https://gco.iarc.fr/today/data/factsheets/populations/458-malaysia-fact-sheets.pdf
4. Goss G, Tsai CM, Shepherd FA, Bazhenova L, Lee JS, Chang GC, et al. Osimertinib for pretreated EGFR Thr790 Met-positive advanced non-small-cell lung cancer (AURA2): a multicentre, open-label, single-arm, phase 2 study. Lancet Oncol 2016; 17: 1643-52.
5. Christiansen IS, Clementsen PF, Bodtger U, Naur TMH, Pietersen PI, Laursen CB. Transthoracic ultrasound-guided biopsy in the hands of chest physicians - a stepwise approach. Eur Clin Respir J 2019; 6(1): 1579632.
6. Zhao ZL, Peng LL, Wei Y, Li Y, Wang GM, Yu MA. The accuracy of ultrasound-guided lung biopsy pathology and microbial cultures for peripheral lung lesions. J Thorac Dis 2020; 12(3): 858-65.
7. Prajapati P, Jindal S, Kapadia V, Tripathi S, Shah D, Bhatt P, et al. Study of safety and efficacy of ultrasound guided transthoracic tru-cut biopsy of lung mass. GCSMC J Med Sci 2019; 8(2): 17-20.
8. Lee MH, Lubner MG, Hinshaw JL, Pickhardt PJ. Ultrasound guidance versus CT guidance for peripheral lung biopsy: performance according to lesion size and pleural contact. AJR 2018; 210: W110-17.
9. Yamamoto N, Watanabe T, Yamada K, Nakai T, Suzumura T, Sakagami K, et al. Efficacy and safety of ultrasound (US) guided percutaneous needle biopsy for peripheral lung or pleural lesion: comparison with computed tomography (CT) guided needle biopsy. J Thorac Dis 2019; 11(3): 936-43.
10. Wafaa SE, Fawzy AE, Ayman HAB, Amr ME, Dalia EE. The diagnostic value of ultrasound-guided percutaneous transthoracic core-needle biopsy versus computed tomography-guided biopsy in peripheral intrathoracic lesions. Egypt J Bronchol 2016; 10: 12-9.
11. Anzidei M, Porfiri A, Andrani F, Martino MD, Saba L, Catalano C, et al. Imaging-guided chest biopsies: techniques and clinical results. Insights Imaging 2017; 8: 419–28.
12. Tomiyama N, Yasuhara Y, Nakajima Y, Adachi S, Arai Y, Kusumoto M, et al. CT guided needle biopsy of lung lesions: a survey of severe complications based on 9783 biopsies in Japan. Eur J Radiol 2006; 59(1): 60-4.
13. Diacon AH, Schuurmans MM, Theron J, Schubert PT, Wright CA, Bolliger CT. Safety and yield of ultrasound-assisted transthoracic biopsy performed by pulmonologists. Respiration 2004; 71: 519-22.
14. Fu Y, Zhang Y-Y, Cui L-G, Tan S, Sun Y. Ultrasound-guided biopsy of pleural-based pulmonary lesions by injection of contrast enhancing drugs. Front Pharmacol 2019; 10: 960.