ECRONICON OPEN ACCESS

EC PULMONOLOGY AND RESPIRATORY MEDICINE

Research Article

Comparing the Use of 19-Gauge and 21 or 22-Gauge Needle in Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration (EBUS-TBNA)

Kristin Yee-Hsien Hsu[1]*, Tuck-Yean Yong[2], Esther Yong-Mei Tan[3] and Shanka Karunarathne[3]

[1]*Department of Medical Oncology, Flinders Centre for Innovation in Cancer, Flinders Medical Centre, Bedford Park, Australia*

[2]*Flinders Private Hospital, Bedford Park, Australia*

[3]*Department of Respiratory Medicine, Lyell McEwin Hospital, Elizabeth Vale, Australia*

***Corresponding Author:** Kristin Yee-Hsien Hsu, Department of Medical Oncology, Flinders Centre for Innovation in Cancer, Flinders Medical Centre, Bedford Park, Australia.

Received: May 03, 2019; **Published:** August 30, 2019

Abstract

Background and Objectives: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a minimally invasive procedure used to obtain tissue samples to evaluate mediastinal or hilar lymphadenopathy or masses. This is conventionally done using 21 or 22-Gauge (G) needles. The introduction of the EBUS 19-G needle may allow larger samples to be obtained. This study aimed to compare the diagnostic yield, sample adequacy for further immunohistochemistry (IHC) and molecular characterisation, and complication rates.

Methods: A retrospective study involving 50 patients who underwent EBUS-TBNA between June 2016 and August 2017 was conducted. Biopsies were obtained using either a 19-G, 21-G or 22-G needles. Information on patient's demographic data, diagnosis, sample adequacy for IHC and molecular analyses, sample quality and procedure complication data were collected.

Results: The diagnostic yield was not significantly different between the 19-G and 21 or 22-G EBUS-TBNA needles (96% vs 88%; p = 0.61). Samples were adequate for immunohistochemistry (IHC) and testing could be performed in 91% of patients who had the 19-G needle compared to 56% of patients with the 21 or 22-G needle (p = 0.049). In both groups, molecular mutation analyses were achieved in 100% of patients with primary lung adenocarcinoma. Complication rates were comparable between the groups (20% with 19-G vs 4% with 21/22-G; p = 0.19).

Conclusion: The diagnostic yield and complication rates were comparable between the 19-G and 21 or 22-G needles in EBUS-TBNA. In this study, sample adequacy for IHC was significantly better with the 19-G needle compared to other needles. Further research is needed to establish the role and advantages of 19-G aspiration needle in EBUS-TBNA.

Keywords: *Bronchoscopy; Carcinoma; Endobronchial Ultrasound; Lymphadenopathy; Needle Aspiration*

Abbreviations

ALK: Anaplastic Lymphoma Kinase; CT: Computed Tomography; EBUS-TBNA: Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration; EGFR: Epidermal Growth Factor Receptor; FISH: Fluorescent *In Situ* Hybridization; G: Gauge; IHC: Immunohistochemistry; NSCLC: Non-Small Cell Lung Cancer; PCR: Polymerase Chain Reaction; PD-L1: Programmed Death-Ligand 1; SCLC: Small Cell Lung Cancer

Introduction

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a well-established minimally invasive procedure that has an important role in evaluating patients with mediastinal and hilar lymphadenopathy or masses and staging of lung cancer [1],

with high specificity of 100% and sensitivity 92% [2]. Even so, the diagnostic performance of EBUS-TBNA can be improved by potentially improving sampling. Until recently, EBUS-TBNA has usually used 21 or 22-G needles.

According to results of the American College of Chest Physicians Quality Improvement Registry, Education, and Evaluation Registry, adequate samples were obtained in 95% of cases and diagnosis achieved in 51% with the 21 or 22-G needles [3]. The result of this study, and also in several other studies [4,5], described no significant difference in the diagnostic yield using the 21 or 22-G needles. However, studies by Lockman., *et al.* [6] and Saji., *et al.* [7] have suggested that increasing the sample volume may improve sampling and diagnostic yield.

The role of EBUS-TBNA is well established in diagnosing and staging of primary lung malignancy [8,9]. With the advent of novel treatments such as immune checkpoint inhibitors and tyrosine kinase inhibitors targeting specific molecular mutations in non-small lung cancer (NSCLC), pathologists are increasingly requiring greater volumes of diagnostic material in order to optimally characterise lung malignancies [10,11].

However, with cases of suspected lymphoproliferative disorders, the use of EBUS-TBNA remains controversial. A meta-analysis by Erer., *et al.* [12] reported that the diagnostic sensitivity of lymphoma with EBUS-TBNA is generally low (between 28% and 90%), particularly in diagnosing Hodgkin's lymphoma. At present, the latest National Comprehensive Cancer Network guidelines also do not recommend fine needle aspiration (FNA) biopsy for diagnosis of non-Hodgkin's and Hodgkin's lymphoma [13].

The 19-G needle in EBUS-TBNA has been proposed to obtain samples similar to a core biopsy with greater tissue yield and improved sample size to better characterise primary lung cancer or lymphoproliferative disorders. As the requirement evolve for molecular profiling of malignant lesions, the ability to collect larger tumour samples can be beneficial.

Ben., *et al.* [14] was the first group to report the use of the 19-G needles to perform aspiration from mediastinal lymph nodes, and so far, published studies using 19-G EBUS-TBNA have included a small number of patients [15,16]. However few studies have compared the diagnostic yield of using 19-G compared with 21-G or 22-G needles.

Aim of the Study

The primary aim of this study was to assess the adequacy of sample for diagnosis among patients who had the 19-G needle aspiration compared with those performed using 21 or 22-G needles. The secondary aims were to determine the adequacy of specimens for immunohistochemistry (IHC) and molecular testing among those with malignant lesions and the rate of complications in these groups of patients.

Methods

Study design

This was a retrospective study conducted at the Lyell McEwin Hospital in South Australia between June 2016 and August 2017. All patients who underwent EBUS-TBNA with the 19-G needle were included. For comparison, we randomly selected the same number of EBUS-TBNA cases performed using the 21 or 22-G needle during the same study period. This study was approved by the The Queen Elizabeth Hospital/Lyell McEwin Hospital/Modbury Hospital Human Research Ethics Committee (HREC/17/TQEH/186). All patients provided written consent for the EBUS-TBNA procedure.

EBUS-TBNA procedure

EBUS-TBNA was done under conscious sedation or general anaesthesia. This was performed with a flexible ultrasonic puncture bronchoscope. After the target lesion was identified with ultrasound, the 19-G needle (Olympus ViziShot Flex Model No: NA-U402SX-4019) or the 21 or 22-G needle (Olympus ViziShot Flex Model No: NA-201SX-4021 and NA-201SX-4022-A respectively) was inserted through the

2.2 mm channel in the bronchoscope and advanced into the target mass. One bronchoscopist was involved in this procedure. The decision on which needle gauge to use was determined by the size of the lesion on CT imaging and the degree of clinical suspicion of malignancy or lymphoproliferative disorder.

Processes in analysing aspirated specimens

All specimens were reviewed with rapid on-site cytological evaluation (ROSE). A portion of the initial sample obtained from the EBUS-TBNA was smeared onto glass slides, dried, stained, fixated and analysed under the light microscope. The remaining specimen was put into the Hank's Buffered Salt Solution and sent to the pathology laboratory for further analysis.

Specimens were considered sufficient for histopathological analysis and diagnosis if lymphocytes or abnormal cells were present. When cells were abnormal, further IHC testing would be carried out for further characterisation if sufficient specimen was present. IHC testing comprised of various staining procedures to determine the specific type of malignancy and its origin based on the pattern of cell markers. To diagnose non-small cell lung cancer (NSCLC) for example, specific markers such as thyroid transcription factor 1 (TTF-1), Napsin A, cytokeratin 7 (CK7), cytokeratin 5 or 6 (CK5/6) and tumour protein 63 (P63) have excellent sensitivity [17].

After the type of malignancy was determined and if the sample was diagnosed as primary lung adenocarcinoma, further molecular testing for epidermal growth factor receptor (EGFR) mutations and anaplastic lymphoma kinase (ALK) inhibitor gene rearrangements was performed according to the local hospital pathology testing guideline. This would involve testing for EGFR mutations using polymerase chain reaction (PCR) based methods. ALK gene rearrangements were detected using IHC, fluorescent in situ hybridization (FISH), and PCR based techniques.

Specimen quality was evaluated by assessing the degree of blood staining under the microscope, which was described in the cytology report.

Collection of data

Information was collected from patients' electronic and handwritten medical records, which included the patient's demographic data, needle gauge used, findings on CT imaging, number of nodes biopsied, number of passes in each node, diagnosis, sample adequacy for molecular mutation testing, sample quality and procedure complication rate.

Statistical analysis

Normally distributed continuous data were expressed as means and standard deviations, while non-parametric continuous data were described as medians and interquartile ranges. Categorical data were described as absolute numbers and proportions. Differences between the groups were compared statistically using student's t-test for continuous variables, and Fisher's exact tests for categorical variables.

Results

Baseline characteristics

During the study period, 25 patients had EBUS-TBNA performed with the 19-G needle. A second group comprising of 25 patients who underwent the same procedure with the 21 or 22-G needle (control group) were randomly selected for inclusion. Patient demographics and baseline characteristics of the nodes biopsied are shown in table 1. Mean age, sex, number of nodes biopsied and number of needle passes per procedure were not significantly different between the two groups. The average size of the nodes biopsied were significantly larger in the 19-G group compared with the 21 or 22-G needle group ($p = 0.0005$).

Characteristics	19-G (*n* = 25)	21/22-G (*n* = 25)	P value
Age ± SD, years	64.96 ± 13.68	67.32 ± 9.71	0.4852
Female sex, n (%)	10 (40)	13 (52)	0.5709
Characteristics of lymph nodes			
Mean ± SD number of nodes biopsied	1.92 ± 0.64	1.84 ± 0.80	0.6979
Average size of nodes biopsied	30.00 ± 10.52	19.80 ± 8.87	0.0005
Average number of needle passes to lymph nodes	5.36 ± 1.15	5.16 ± 1.90	0.6545

Table 1: *Patient's baseline data and characteristics of lymph nodes.*

Diagnoses, sample adequacy and quality

The diagnoses obtained based on histopathology reports from EBUS-TBNA is presented in table 2. Among those who had biopsies with the 19-G needle, eight had NSCLC including four cases of primary lung adenocarcinoma, and four cases of squamous cell carcinoma. Five had small cell lung carcinoma (SCLC), two had non-Hodgkin's lymphoma. Other diagnoses included two cases of adenocarcinoma favouring gastrointestinal origin, one had adenocarcinoma of uncertain origin, one had large cell malignancy (subsequently determined to be primary lung adenocarcinoma) and one had malignant melanoma. In the 21 or 22-G group, five had NSCLC and one had SCLC, two had malignant cells that were unable to be characterised further. There were more malignancies diagnosed in the 19-G group compared with the 21 or 22-G group (80.0% vs 32.0%).

Diagnosis	19-G (*n* = 25)	21/22-G (*n* = 25)
Malignant (n, %)	20 (80)	8 (32)
Non-small cell lung cancer	8	5
Small cell lung cancer	5	1
Non-Hodgkin's lymphoma	2	0
Others	5	2
Non-malignant (n, %)	4 (16)	14 (56)
Sarcoidosis	4	1
Reactive lymphadenopathy	0	13
Insufficient tissue/incorrect diagnosis (n, %)	1 (4)	3 (12)

Table 2: *Summary of diagnoses obtained with the 19-G and 21/22-G EBUS-TBNA needles.*

With the non-malignant diagnoses, there were more reactive or inflammatory and granulomatous lymph nodes found in the 21 or 22-G group (56.0% vs 16.0%). To confirm the diagnosis, these patients had repeat computed tomography (CT) scans three to six months after the EBUS-TBNA procedure. CT imaging which showed unchanged or reduced mediastinal lymphadenopathy or lesions were considered benign.

In the 19-G group, one patient was incorrectly diagnosed due to insufficient tissue, and a repeat EBUS-TBNA revealed non-Hodgkin's lymphoma. Three cases were not able to be diagnosed in the 21 or 22-G group; one underwent a repeat EBUS-TBNA which showed adenocarcinoma, one had two further EBUS-TBNA procedures which eventually revealed small cell carcinoma, and another patient had repeat CT images which showed stable lymphadenopathy.

In terms of quality of specimens, heavy blood staining on slides was present in two cases (8.0%) with the 19-G needle, and in eight cases (32.0%) with the 21 or 22-G needle, which was not significantly different (p = 0.074) (See table 3).

Overall, the diagnostic yield was 96% in the 19-G needle group compared with 88% in the 21 or 22-G needle group (p = 0.61). Samples were adequate for immunohistochemistry testing in 91% of patients with the 19-G compared with 56% with the 21 or 22-G needle (p = 0.049). With samples found to be primary lung adenocarcinoma based on IHC testing, EGFR and ALK testing was achieved with all samples (see table 3).

	19-G	21/22-G	P-value
Diagnostic yield	24/25 (96%)	22/25 (88%)	0.6092
Sample adequacy			
Immunohistochemistry	19/21 (91%)	5/9 (56%)	0.0492
Molecular mutation testing	4/4 (100%)	3/3 (100%)	-
Quality of specimens			
Slides stained with blood	2/25 (8%)	8/25 (32%)	0.0738
Complications			
Bleeding	5/25 (20%)	1/25 (4%)	0.1895

Table 3: *Diagnostic yield, sample adequacy, specimen quality and complications.*

Complications

Five patients (20.0%) in 19-G needle group developed bleeding complications compared to one (4.0%) in the 21 or 22-G group (See table 3), which was not statistically significant. All the bleeding incidents were moderate according to the British Thoracic Society Guidelines[18] and required cold saline and compression to control, with no additional intervention required. None required blood transfusion and no patient developed pneumothorax or pneumomediastinum.

Discussion

This study showed that there was no statistically significant difference in diagnostic yield and complication rates between the use of the 19-G and 21 or 22-G EBUS-TBNA needle. In comparison with 21 or 22-G needles, the 19-G needle provided significantly higher specimen adequacy for IHC analyses. The complication rates with the use of 19-G needle were comparable with the other needles.

The high diagnostic yield with 19-G needles of the present study is consistent with studies done using the 19-G EBUS needles obtained by Tyan., *et al.* (47 participants; 89% diagnostic yield) and Gnass., *et al.* (22 participants; 100% diagnostic yield) [15,16]. However, when compared with 21-G and 22-G needles, results regarding diagnostic yield and tissue characterisation are conflicting.

A randomized clinical trial involving 78 participants with suspected lung cancer in a single centre compared the Flex 19-G needles and 22-G needles and found that that tissue core procurement and sample adequacy for diagnostic yield was not different between these two needles [19]. In addition, this study observed that specimens obtained using the 19-G needle were bloodier than those with the 22G needle but this did not compromise the diagnostic assessment. The complication rates were also comparable between these two needles in this study. However, this study did not evaluate patients suspected to have lymphoproliferative disorders. Therefore, authors of this study concluded that the choice between Flex 19-G and 22-G needles could be based on the need for a larger tissue and tumour surface area fon the cell block preparation for further analysis.

In the study by Garrison and colleagues, additional aspiration performed with the 19G needle appear to increase diagnostic yield compared to 22-G alone. No difference in yield was observed when direct comparison was made between needle gauges [20]. On the other hand, Chaddha., *et al.* found no difference in diagnostic yield between 19-G needle and 22-G needle in an alternating sampling method [21].

Four studies which investigated tissue acquisition and/or characterization have found different results [22,23]. Two studies found the 19-G needle provided better tissue acquisition and subclassification of disease [22,23]. One randomized study demonstrated no difference in tissue procurement but Porfyridis and colleagues reported that the 19-G needle yielded better samples [19,24]. In the present study, tissue adequacy was high (96%) in the 19-G needle group.

The yield for molecular analysis with the use of 19-G needle has also been consistently high with the use of the 19-G needle. Tyan., *et al.* reported 75% success rate for molecular analysis for advanced lung cancer using the 19-G needle [16], while analysis for EGFR was completed in 100% of patients included in a Polish study [15]. In a prospective single-centre observational cohort study, the cell area of aspirated tissue using the 19-G needle was significantly larger than that obtained with the 21-G needle [25].

For evaluation of suspected granulomatous disease such as sarcoidosis, the diagnostic yield of EBUS-TBNA in a systematic review was 79% [26]. This result was reproduced in the GRANULOMA trial published in 2013 [27]. The study by Tyan., *et al.* also reported a better diagnostic yield for sarcoidosis with the 19-G needle [16]. Similar findings were also reported by Balwan [28]. In another study, only one patient who had the 19-G needle aspiration returned a non-diagnostic result, out of ten who had sarcoidosis diagnosed [25]. In the current study, four patients were accurately diagnosed with sarcoidosis using the 19G needle. This has stimulated further interest in using the 19-G needle to obtain lymph node samples from patients with suspected sarcoidosis.

Emerging research suggest that EBUS-TBNA is also effective for the diagnosis of lymphoma and can be considered as a diagnostic approach in patients with suspected lymphoma but only has isolated mediastinal lymphadenopathy. Tyan and colleagues suggested that the 19-G needle may improve the diagnosis and subtyping of lymphoproliferative diseases but this involved only a small sample [16]. The current study showed that lymphoma can be diagnosed and subtyped with the 19-G needle but this finding is also based on a small number of patients.

EBUS-TBNA is associated with a number of complications including bleeding, which were slightly higher in patients undergoing EBUS-TBNA with the 19-G needle compared to the 21 or 22-G EBUS-TBNA. Kinoshita., *et al.* indicated that 19-G needle is safe and provides larger volumetric tissue samples that can be appropriate for histopathological analyses in selected cases where greater tissue acquisition is required [23]. Although 19-G is a larger needle, higher rates of major complications have not been observed with its use. Other studies involving the 19-G EBUS-TBNA needle have also described a very low bleeding rate with its use [14-16].

The main benefits for the 19-G needle may be in cases where there is high clinical suspicion of lymphoma, and in advanced NSCLC requiring molecular testing or for more specific testing required in a clinical trial setting. Larger trials (Clinical-trials.gov identifiers: NCT02592837 and NCT029164599) are currently being undertaken to clarify the results with the use of 19-G needle in EBUS-TBNA. Whether or not the use of a 19G needle is indeed more effective than a 21- and 22G needle is unclear from the present results. A larger study is required to confirm these findings. Until additional data is available, it is it is recommended that different gauge needles are used judiciously depending on the characteristics of the target lymph node and the feedback were given by an on-site pathologist.

The present study has several limitations. Firstly, this is a retrospective study and as a result, some data may be missing or incompletely recorded. Secondly, patients were not randomised, and potential selection bias may have affected the results. The sample size is relatively small and may not be representative of the range of diagnoses that might arise in mediastinal or hilar lesions or lymphadenopathy. Thirdly, programmed death-ligand 1 (PD-L1) was not routinely performed at the time of this study period, which is currently a useful

marker to characterize and tailor treatment in NSCLC. Fourthly, the selected population of patients, particularly in the 19-G needle group, have significantly larger mediastinal lymph nodes or masses biopsied. Furthermore, all EBUS-TBNA in this study was performed by one bronchoscopist

Conclusion

In conclusion, using the 19-G needle in EBUS-TBNA is effective and safe with a promising diagnostic yield including the ability to provide adequate specimen for molecular testing required in advanced lung carcinoma. Sample adequacy for IHC was higher among patients who had the 19-G needle, compared with 21 or 22-G needles. Further multicentred randomized studies are needed to characterize the utility of 19-G needle in the diagnosis of lymphoproliferative disorders and sarcoidosis.

Acknowledgements

Dr Tom Dodd and Dr Neeru Arora, Pathologists, Department of Pathology, Lyell McEwin Hospital

Conflict of Interest

None to declare.

Bibliography

1. Medford AR., *et al*. "Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA): applications in chest disease". *Respirology (Carlton, Vic)* 15.1 (2010): 71-79.
2. Chandra S., *et al*. "Diagnostic accuracy of endobronchial ultrasound-guided transbronchial needle biopsy in mediastinal lymphadenopathy: a systematic review and meta-analysis". *Respiratory Care* 57.3 (2012): 384-391.
3. Yarmus LB., *et al*. "Comparison of 21-gauge and 22-gauge aspiration needle in endobronchial ultrasound-guided transbronchial needle aspiration: results of the American College of Chest Physicians Quality Improvement Registry, Education, and Evaluation Registry". *Chest* 143.4 (2013): 1036-1043.
4. Nakajima T., *et al*. "Comparison of 21-gauge and 22-gauge aspiration needle during endobronchial ultrasound-guided transbronchial needle aspiration". *Respirology (Carlton, Vic)* 16.1 (2011): 90-94.
5. Giri S., *et al*. "Meta-analysis of 21- versus 22-G aspiration needle during endobronchial ultrasound-guided transbronchial needle aspiration". *Journal of Bronchology and Interventional Pulmonology* 22.2 (2015): 107-113.
6. Lockman H., *et al*. "M10 21G VS 22G EBUS-TBNA needle sampling and cell morphology of the core biopsies and needle washings: Is bigger better?" *Thorax* 68.3 (2013): A199.
7. Saji J., *et al*. "Comparison of 21-gauge and 22-gauge Needles for Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration of Mediastinal and Hilar Lymph Nodes". *Journal of Bronchology and Interventional Pulmonology* 18.3 (2011): 239-246.
8. Almeida FA. "Bronchoscopy and endobronchial ultrasound for diagnosis and staging of lung cancer". *Cleveland Clinic Journal of Medicine* 79.1 (2012): eS11-S16.
9. Detterbeck FC., *et al*. "Invasive mediastinal staging of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition)". *Chest* 132.3 (2007): 202S-20S.

10. Lindeman NI., *et al*. "Molecular testing guideline for selection of lung cancer patients for EGFR and ALK tyrosine kinase inhibitors: guideline from the College of American Pathologists, International Association for the Study of Lung Cancer, and Association for Molecular Pathology". *Journal of Thoracic Oncology* 8.7 (2013): 823-859.

11. Moran C. "Importance of molecular features of non-small cell lung cancer for choice of treatment". *The American Journal of Pathology* 178.5 (2011): 1940-1908.

12. Erer OF., *et al*. "Diagnostic yield of EBUS-TBNA for lymphoma and review of the literature". *Endoscopic Ultrasound* 6.5 (2017): 317-322.

13. Network NCC. NCCN Clinical Practice Guidelines in Oncology (2018).

14. Ben S., *et al*. "Endobronchial ultrasound transbronchial needle aspiration: a hybrid method". *Journal of Thoracic Disease* 7.4 (2015): S287-S291.

15. Gnass M., *et al*. "Initial Polish experience of Flexible 19 gauge Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration". *Advances in Respiratory Medicine* 85.2 (2017): 64-68.

16. Tyan C., *et al*. "Flexible 19-Gauge Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration Needle: First Experience". *Respiration International Review of Thoracic Diseases* 94.1 (2017): 52-57.

17. Gurda GT., *et al*. "Utility of five commonly used immunohistochemical markers TTF-1, Napsin A, CK7, CK5/6 and P63 in primary and metastatic adenocarcinoma and squamous cell carcinoma of the lung: a retrospective study of 246 fine needle aspiration cases". *Clinical and Translational Medicine* 4 (2015): 16.

18. Du Rand IA., *et al*. "Summary of the British Thoracic Society guideline for diagnostic flexible bronchoscopy in adults". *Thorax* 68.8 (2013): 786-787.

19. Dooms C., *et al*. "A Randomized Clinical Trial of Flex 19G Needles versus 22G Needles for Endobronchial Ultrasonography in Suspected Lung Cancer". *Respiration International Review of Thoracic Diseases* 96.3 (2018): 275-82.

20. Garrison G., *et al*. "Use of an Additional 19-G EBUS-TBNA Needle Increases the Diagnostic Yield of EBUS-TBNA". *Journal of Bronchology and Interventional Pulmonology* 25.4 (2018): 269-273.

21. Chaddha U., *et al*. "Comparison of Sample Adequacy and Diagnostic Yield of 19- and 22-G EBUS-TBNA Needles". *Journal of Bronchology and Interventional Pulmonology* 25.4 (2018): 264-268.

22. Jones RC., *et al*. "The effect of 19-gauge endobronchial ultrasound-guided transbronchial needle aspiration biopsies on characterisation of malignant and benign disease. The Bristol experience". *Monaldi Archives for Chest Disease* 88.2 (2018): 915.

23. Kinoshita T., *et al*. "Clinical evaluation of the utility of a flexible 19-gauge EBUS-TBNA needle". *Journal of Thoracic Disease* 10.4 (2018): 2388-2396.

24. Porfyridis I., *et al*. "Comparison of diagnostic performance of 19-gauge and 21-gauge needles during endobronchial ultrasound-guided transbronchial needle aspiration". *European Respiratory Journal* 50.61 (2017): PA823.

25. Pickering EM., *et al*. "Tissue Acquisition During EBUS-TBNA: Comparison of Cell Blocks Obtained From a 19G Versus 21G Needle". *Journal of Bronchology and Interventional Pulmonology* (2018).

26. Agarwal R., *et al*. "Efficacy and safety of convex probe EBUS-TBNA in sarcoidosis: a systematic review and meta-analysis". *Respiratory Medicine* 106.6 (2012): 883-892.

27. von Bartheld MB., *et al*. "Endosonography vs conventional bronchoscopy for the diagnosis of sarcoidosis: the GRANULOMA randomized clinical trial". *Journal of the American Medical Association* 309.23 (2013): 2457-2464.

28. Balwan A. "Endobronchial Ultrasound-guided Transbronchial Needle Aspiration Using 19-G Needle for Sarcoidosis". *Journal of Bronchology and Interventional Pulmonology* 25.4 (2018): 260-263.

Volume 8 Issue 9 September 2019