Original Article

First Asia-Pacific experience of trans-bronchial core biopsy with a Franseen needle

Michael V. Brown[1,2#^], Katherine Lavrencic[1,2#^], Arash Badiei[1,2^], Hubertus Jersmann[1,2^], Andrew Fon[2,3^], Sean Chang[4], Phan Nguyen[1,2^]

[1]Department of Thoracic Medicine, Royal Adelaide Hospital, Adelaide, Australia; [2]Faculty of Health and Medical Sciences, Adelaide Medical School, University of Adelaide, Adelaide, Australia; [3]Department of Respiratory and Sleep Medicine, Queen Elizabeth Hospital, Adelaide, Australia; [4]SA Pathology, Adelaide, Australia

Contributions: (I) Conception and design: MV Brown, K Lavrencic, P Nguyen; (II) Administrative support: P Nguyen; (III) Provision of study materials or patients: P Nguyen, A Badiei, H Jersmann, A Fon, S Chang; (IV) Collection and assembly of data: MV Brown, K Lavrencic, S Chang, P Nguyen; (V) Data analysis and interpretation: P Nguyen, MV Brown; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work and should be considered as co-first authors.

Correspondence to: Michael V. Brown, MBBS (Bachelor of Medicine, Bachelor of Surgery). Department of Thoracic Medicine, Royal Adelaide Hospital, 1 Port Road, Adelaide, SA 5000, Australia. Email: MichaelV.Brown@sa.gov.au.

Background: Endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) is the standard for evaluating mediastinal and hilar lesions. EBUS-TBNA is limited by small volume of material obtained for immunohistochemistry (IHC) and ancillary studies important for oncological therapies. The Franseen Acquire™ needle is designed for EBUS-transbronchial needle core biopsy (TBNB) allowing larger core sizes with evidence in gastroenterology literature but little in pulmonology. This study reports the first Asia-Pacific experience of EBUS-TBNB and adequacy of samples for diagnosis and ancillary studies.

Methods: A retrospective cohort study of EBUS-TBNB at the Royal Adelaide Hospital was conducted between December 2019 and May 2021. Diagnostic rate, adequacy for ancillary studies and complications were evaluated. Samples were flushed into formalin for histological processing with no rapid on-site cytological evaluation (ROSE). For suspected lymphoma, samples were flushed into HANKS for flow cytometry. Cases performed with the Olympus Vizishot™ during the same 18-month were similarly analysed.

Results: One hundred and eighty-nine patients were sampled with the Acquire™ needle. Diagnostic rate was 174/189 (92.1%). Where reported [146/189 (77.2%)], average core aggregate sample size was 13.4 mm × 10.7 mm × 1.7 mm. For non-small cell lung cancer (NSCLC) cases, 45/49 (91.8%) had adequate tissue for programmed cell death-ligand 1 (PD-L1). 32/35 (91.4%) adenocarcinoma cases had sufficient tissue for ancillary studies. There was one false negative malignant lymph node at the first Acquire™ procedure. There were no major complications. One hundred and one patients were sampled with the Vizishot™ needle. Diagnostic rate was 86/101 (85.1%) with only 25/101 (24.8%) having reported tissue cores (P<0.0001 of Vizishot™) with the remaining samples processed via cell block.

Conclusions: Acquire™ EBUS-TBNB diagnostic rate is comparable to historical data with >90% of cases having sufficient core material for ancillary studies. There appears to be a role for the Acquire™ alongside the standard of care for the work up of lymphadenopathy and particularly for lung cancer.

^ ORCID: Michael V. Brown, 0000-0002-6678-1407; Katherine Lavrencic, 0000-0002-4139-0733; Arash Badiei, 0000-0002-9237-8355; Hubertus Jersmann, 0000-0003-1763-2736; Andrew Fon, 0000-0001-9940-5996; Phan Nguyen, 0000-0002-8573-3574.

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Introduction

This study represents the first Asia-Pacific experience of the Boston 22G Acquire™ Franseen needle in pulmonary medicine. Endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) has become the standard of care as the initial diagnostic procedure for assessment of lesions, particularly lymph nodes, in the mediastinum and central hilar area. The most common indication for the procedure is the diagnosis and staging of lung cancer, but it is also used to diagnose a variety of other pathologies including extra-thoracic malignancy, lymphoproliferative disorders, sarcoidosis and tuberculosis (1-3).

Until recently, the preferred instrument for EBUS-TBNA has been the Olympus Vizishot™ 21G, however it is limited by the small volume of diagnostic material yielded for cytological analysis and the associated destruction of the microscopic architecture of the lesion during the sampling process. This approach often fails to yield adequate material for immunohistochemical and molecular studies in cases of non-small cell lung cancer (NSCLC). In cases of advanced stage lung cancer at time of diagnosis, the diagnostic biopsy is often the only specimen available for molecular studies. As no surgical specimen is available in these cases, it is crucial that there is adequate tissue to avoid the need for repeat procedures (4). In addition, the diagnosis of conditions such as sarcoidosis relies on the preservation of the histological architecture and structure, limiting the diagnostic utility of fine needle aspiration (FNA). Lymphoproliferative disorders require larger volume tissue samples for additional processing. Studies to date do not demonstrate effective diagnostic yield using EBUS sampling (5,6). Alternatives to the conventional 21G Olympus Vizishot™ needle have been trialled and include the 19G Vizishot™ Flex needle and the Cook ProCore needle (7). Sensitivity and specimen adequacy appear similar between the ProCore Cook needle and the Olympus Vizishot™ needle though randomized trial data is limited.

The Boston Scientific Acquire™ 22G needle has now become commercially available for endobronchial ultrasound guided transbronchial needle core biopsy (EBUS-TBNB). The Acquire™ needle has several features which may allow for larger sample size, including a three-point needle tip (Franseen) designed to provide stability at the puncture and fully formed heels designed to maximise tissue capture and minimize fragmentation. This needle type was originally used in gastroenterology procedures to sample intra-abdominal lymph nodes and masses and has only recently been found to have an application in respiratory medicine (8).

Traditional EBUS-TBNA has an overall diagnostic yield of up to 89% (9), with sufficient material for immunohistochemical studies. With advances in therapies for lung cancer and the shift towards personalised therapy an increasing number of diagnostic tests are required. Firstly, differentiation of NSCLC into subtypes is required with immunohistochemistry (IHC). In Australia, the

Highlight box

Key findings
- First Asia-Pacific experience of the Boston Acquire Franseen needle for EBUS-TBNA.
- Diagnostic yield was 174/189 (92.1%).
- Large cores with adequate tissue for PD-L1 testing in 45/49 (91.8%) and for ancillary studies in 32/35 (91.4%) cases.
- One false negative malignant lymph node.
- Explored the role for the Acquire™ needle alongside the Vizishot™ standard of care.

What is known and what is new?
- The Acquire™ needle has an established role in gastrointestinal literature.
- Increasing demand for histological tissue for oncological testing has led to a requirement for new sampling techniques designed to increase tissue yield.

What is the implication, and what should change now?
- There is a role for the Acquire™ Franseen needle alongside the standard of care particularly when the pre-test probability of malignancy is high.
- There are multiple technical considerations when choosing the Acquire™ needle.

standard biomarker panel consists of thyroid transcription factor 1 (TTF1), Napsin A, p40, Cytokeratin (CK)5/6 and CK7. Predicted rate of response to immunotherapy is assessed by measuring programmed cell death-ligand 1 (PD-L1) expression on tumour cells. In cases of lung adenocarcinoma further ancillary studies can be performed to determine potential molecular targets. This entails an assessment for driver mutations in anaplastic lymphoma kinase (*ALK*) gene and *ROS1* oncogene, as well as somatic mutations in epidermal growth factor receptor (*EGFR*) (10-12). These driver mutations have historically been identified with IHC, polymerase chain reaction (PCR) and IHC then fluorescence in situ hybridization (FISH) respectively. With continuing, rapid advancement in oncology therapeutics it is predicted that there will be an ever-growing number of significant molecular targets identified and as a result, demand for larger biopsy samples for additional testing. This is particularly relevant given the increasing role for next-generation sequencing (NGS). NGS assays provide more comprehensive information on genetic abnormalities in malignancy including the detection of both additional mutations [for example, V-Raf murine sarcoma viral oncogene homolog B (*BRAF*) kinase, re-arranged during transfection (*RET*) and mesenchymal epithelial transition factor receptor (*MET*)] as well as detecting conventional mutations like *EGFR* which were not identified in the original targeted PCR regions (13). The literature supports EBUS-TBNA in reliably providing adequate tissue for NGS in 86.1–92.8% of cases (13-15) but in institutions where cytology and cell block experience is not readily available, then histological cores could prove advantageous.

Our centre was provided with pre-commercial access to the Boston 22G and 25G Acquire™ needle and was the first hospital in the Asia-Pacific region. The aim of this study was to assess the diagnostic adequacy of mediastinal lymph node sampling with the new Boston Scientific Acquire™ Franseen tip needle for EBUS-TBNB. Additional aims included determining the average size of biopsy samples, the adequacy of samples in providing enough tissue for ancillary testing for malignancy and the safety profile. We also reviewed results in parallel with the Olympus Vizishot™ (Model NA-U401SX-4021) within the same period in order to identify and demonstrate the real-world role of the Acquire™ needle alongside the standard of care. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-1747/rc).

Methods

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Ethical approval was obtained from the Central Adelaide Local Health Network Human Research and Ethics Committee. Individual Consent for this retrospective analysis was waived. This was a retrospective cohort study of patients who underwent mediastinal lymph node sampling with the Boston Scientific Acquire™ 22G needle and Olympus Vizishot™ 21G over an 18-month period between December 2019 and May 2021 inclusive. The start date was the first time our department had access to the Acquire™ 22G needle. The 8th edition of the tumor-node-metastasis (TNM) classification for lung cancer were used to define each lymph node station (16).

Procedures were performed under either general anaesthetic or conscious sedation with intravenous midazolam and fentanyl. A trainee senior medical registrar and supervising specialist attended every procedure. The BF-UC180F linear ultrasound bronchoscope and EU-ME2 ultrasound processor (Olympus Medical Corporation, Tokyo, Japan) were used without routine elastography prior to puncture. A stylet was used for all cases and suction applied. The decision to use the Boston Acquire™ needle or Olympus Vizishot™ was left to the discretion of the supervising specialist as was the needle depth and number of passes per puncture. Although not controlled, generally 3–6 punctures of the target lesion and 15–20 passes per puncture are performed at our institution based on historical teaching from the primary EBUS-TBNA specialist. Tissue samples were primarily flushed directly into formalin with saline rinses for culture or cell block if required. No rapid on-site cytological evaluation (ROSE) was performed. Physicians looked for histological 'worms' (macroscopic needle cores) in formalin as a surrogate marker of tissue adequacy. In cases where macroscopic needle cores could not be seen, samples were flushed into HANKS preservative as an alternative. *Figure 1* shows example macroscopic cores. Samples were then assessed by clinical pathologists as per standard procedure. Any samples in formalin considered insufficient for histological analysis were prepared into a cell block.

Patient demographics, lymph node station or site sampled, lymph node size [short axis diameter (SAD)] and average size of tissue core aggregate were analysed. Based on patient presenting complaint and imaging, a retrospective assessment of the pre-linear EBUS probability

of malignancy was also made. High pre-test probability was reserved for patients with lung masses and associated lymphadenopathy, a prior history of malignancy with enlarging lymph nodes or the presence of a confirmed solid organ tumour with new pathological lymph nodes.

In the event of a malignancy diagnosis, the adequacy of material for IHC ancillary studies was examined. In our centre, the standard ancillary testing includes IHC for PD-L1, IHC for fusions of *ALK* gene and *ROS1* (followed by FISH), and PCR for *EGFR* genes. The rate of adverse events was also reported.

Statistical analysis

Descriptive statistics were used to analyse the data reported as mean and interquartile range (IQR) and independent samples *t*-test to compare results between the two needle types.

Figure 1 Example macroscopic samples.

Results

Demographics

Of the 290 patients who underwent linear EBUS over the 18-month period, 182 (62.8%) patients were male. The average age of patients was 64.5 years. The Acquire™ group were more likely to have a high pre-test probability of malignancy compared to the Vizishot group (P<0.001) (*Table 1*).

Boston Acquire™ results

Over the 18 months between December 2019 and May 2021, 189 patients underwent TBNB with the Boston Acquire™ needle. A total of 254 different lymph node stations or masses were targeted. The most frequent site of biopsy was the station 7, subcarinal lymph nodes (n=129, 50.8%). The other sites are outlined in *Table 2*. One hundred and eleven patients (38.3% of all patients) had a high pre-test probability that the target lymph node would be malignant. The average target lymph node size was 18.7 mm (SAD) (*Table 1*). Patient tissue core aggregates were reported in 146/189 (77.2%) of cases with an average size of 13.4 mm (IQR, 10.0–15.8 mm) × 10.7 mm (IQR, 7.0–14.0 mm) × 1.7 mm (IQR, 1.0–2.0 mm) (*Table 3*). *Figure 2A*,*2B* demonstrates comparative histological cores between the Acquire™ and Vizishot™ needles at varying magnifications stained with haematoxylin and eosin (H&E) stain. The diagnostic rate for all cases was 174/189 (92.1%) and conversely 15/189 (7.9%) of cases had inadequate tissue for a diagnosis to be made (*Table 3*).

A total of 98/189 (51.9%) of patients were identified as having malignancy. Of these, 69/98 (70.4%) had primary lung carcinomas. Primary lung adenocarcinoma was the

Table 1 Demographics

Demographic	All patients	Acquire™ patients	Vizishot™ patients	P value
Male	182 (62.8%)	116 (61.4%)	66 (65.3%)	
Female	108 (37.2%)	73 (38.6%)	35 (34.7%)	
Age (years)	64.5	63	67.8	
High pre-test probability of solid organ malignancy*	158/290 (54.5%)	111/290 (38.3%)	47/290 (16.2%)	<0.0001
Average lymph node size (mm) (mean short axis diameter)	17.4	18.7 (IQR, 13–23)	15.1 (IQR, 11–18)	0.0002

*, patients with lung masses and associated lymphadenopathy, a prior history of malignancy with new lymphadenopathy or the presence of a confirmed solid organ tumour with new pathological lymph nodes. IQR, interquartile range.

Table 2 Olympus Vizishot™ and Boston Acquire™ results—sites targeted

Location	Number of times sampled (Acquire™)	Number of times sampled (Vizishot™)	P value
Station 7	129/254 (50.8%)	45/137 (32.8%)	0.00064
Station 4R	46/254 (18.1%)	26/137 (19.0%)	0.83
Station 4L	18/254 (7.1%)	13/137 (9.5%)	0.40
4L technical success rate	13/18 (72.2%), 5 converted to Vizishot™	13/13 (100.0%)	0.04
Station 11R	17/254 (6.7%)	28/137 (20.4%)	<0.0001
Station 11L	12/254 (4.7%)	10/137 (7.3%)	0.29
Station 10R	9/254 (3.5%)	7/137 (5.1%)	0.45
Paratracheal mass	6/254 (2.4%)	1/137 (0.7%)	
Right hilar mass	6/254 (2.4%)	1/137 (0.7%)	
Left hilar mass	5/254 (2.0%)	3/137 (2.2%)	
Station 2R	–	2/137 (1.5%)	
Station 2L	–	1/137 (0.7%)	
Station 3	2/254 (0.8%)	–	
Right lower lobe mass	2/254 (0.8%)	–	
Right upper lobe mass	1/254 (0.4%)	–	
LB6 mass	1/254 (0.4%)	–	

Table 3 Olympus Vizishot™ and Boston Acquire™ yields

Outcome	Acquire™	Vizishot™	P value
Overall diagnostic yield	174/189 (92.1%)	86/101 (85.1%)	0.07
Malignant diagnoses	98/189 (51.9%)	31/101 (30.7%)	0.006
Benign diagnoses	76/189 (40.2%)	55/101 (54.5%)	0.02
Reported core samples	146/189 (77.2%)	25/101 (24.8%)	<0.0001
PD-L1 testing sufficient	45/49 (91.8%)	11/16 (68.8%), (12 adenocarcinoma, 2 NSCLC-NOS, 2 SCC)	0.02
EGFR/ALK/ROS ancillary testing sufficient	32/36 (88.9%)	10/14 (71.4%) (12 adenocarcinoma, 2 NSCLC-NOS)	0.13

PD-L1, programmed cell death-ligand 1; NSCLC-NOS, non-small cell lung carcinoma-not otherwise specified; SCC, squamous cell carcinoma; EGFR, epidermal growth factor receptor; ALK, anaplastic lymphoma kinase; ROS, ROS proto-oncogene 1.

most common (35/69, 50.7%) followed by small cell carcinomas (19/69, 27.5%), primary lung squamous cell carcinoma (13/69, 18.8%), NSCLC not otherwise specified (1/69, 1.4%) and atypical carcinoid (1/69, 1.4%) (*Table 4*). Ancillary testing results were obtained in 49 patients (35 primary lung adenocarcinoma, 13 squamous cell carcinomas and 1 unspecified non-small cell lung carcinoma). There was sufficient tissue for PD-L1 in 45/49 (91.8%) of cases and sufficient tissue for adenocarcinoma ancillary testing of *EGFR*, *ALK* and *ROS1* in 32/36 (88.9%) of cases (*Table 3*).

TBNB established extra-thoracic malignancy with metastasis to the mediastinal and hilar lymph nodes in the 29/98 (29.6%) remaining malignancy cases (*Table 4*). 23/98 (23.5%) of these were metastasis from solid organ tumours and 6/98 (6.1%) were haematological malignancies. Breast carcinomas (n=5), melanoma (n=4) and colorectal adenocarcinoma (n=4) represented the most common solid organ tumours.

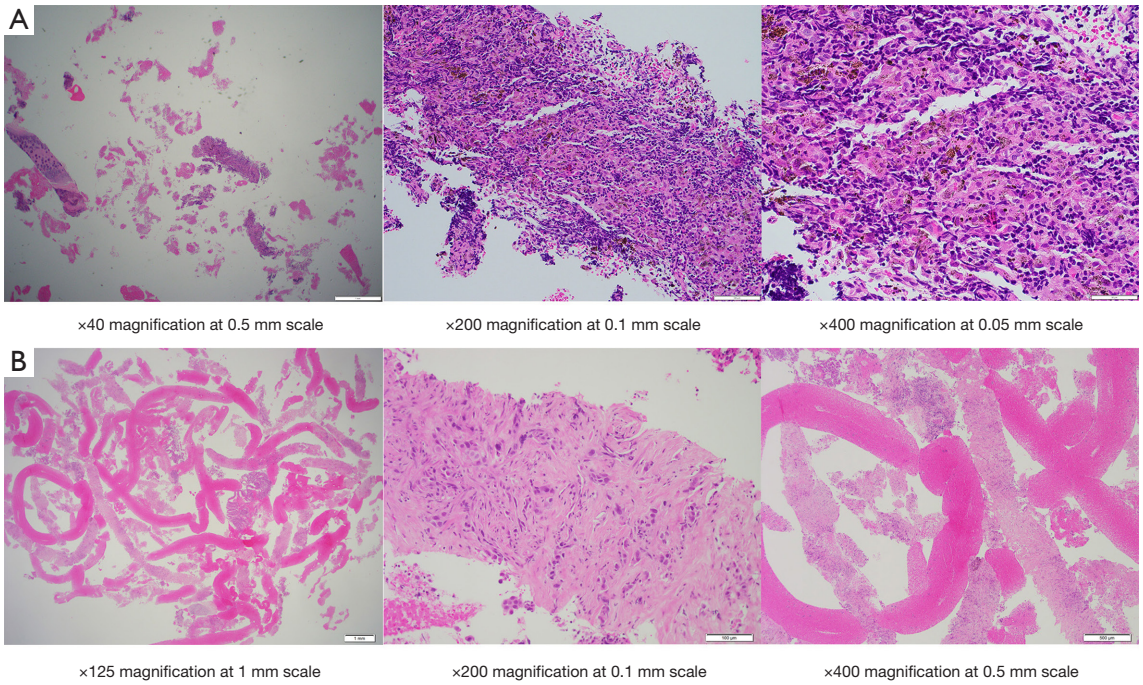

Figure 2 Comparative histological cores between the Acquire™ and Vizishot™ needles at varying magnifications. (A) Histological cores from Vizishot™ needle. (B) Histological core from Acquire™ needle—demonstrating more abundant tissue obtained. Staining method: haematoxylin and eosin.

A benign diagnosis was made in 76/189 (40.2%) cases (*Table 4*). 36/76 (47.4%) of these had normal lymph node tissue with normal flow cytometry. 23/76 (30.3%) had non necrotising granulomas (subsequently diagnosed as sarcoidosis), 12/76 (15.8%) had anthrasilicosis and 5/76 (6.6%) had tuberculosis.

The following 15/189 (7.9%) patients had inadequate tissue for a diagnosis to be made:

- 6 of these had stable lymph nodes on imaging follow-up at greater than 6 months;
- 4 had biopsy of a concurrent lung mass with benign nodes at surgery;
- 2 were treated as sarcoidosis on the basis of their imaging;
- 1 case was staged surgically with no evidence of malignancy on lymph node resection;
- 2 required repeat procedures which subsequently yielded diagnostic results.
  - 1 of these was non necrotising granulomas suggestive of sarcoidosis and the other was primary lung adenocarcinoma.

Out of a total of 99 malignancies, there was only 1 false negative node using the Acquire™ needle.

Notably, the steeper angle of the Olympus Vizishot™ needle was more favourable for certain lymph nodes prompting a change from the Acquire™ to the Vizishot™ needle. This most commonly occurred at the station 4L node (n=5/18, 27.8%) but also occurred in the station 7 node (n=2/129, 1.6%), station 4R node (n=1/46, 2.2%) and station 10R node (n=1/9, 11.1%). These cases were considered to be technical failures and were included in the calculations as non-diagnostic samples. We did not utilise the 25G Acquire™ needle, which allegedly has a similar approach angle to the Olympus Vizishot.

Olympus Vizishot™ results

Over the same 18-month period, 101 patients underwent TBNA with the Olympus Vizishot™. A total of 137 lymph nodes were aspirated and the most common site of sampling was the station 7, subcarinal lymph node (*Table 2*). Forty-seven patients (16.2% of all patients) had a high pre-test probability the target lymph node would be malignant. The average target lymph node size was 15.1 mm (SAD) (*Table 1*). 25/101 (24.8%) of patients had reported tissue cores with an average size of 10 mm (IQR, 6–11.75 mm) × 7.9 mm (IQR,

Table 4 Pathology results of samples taken with the Boston Acquire™ needle

Histopathology results	Number of patients
Primary lung carcinomas	69 (70.4%)
Primary lung adenocarcinoma	35 (50.7%)
Small cell carcinoma	19 (27.5%)
Primary lung squamous cell carcinoma	13 (18.8%)
Non-small cell lung carcinoma-not otherwise specified	1 (1.4%)
Atypical carcinoid	1 (1.4%)
Other malignancies	23 (23.5%)
Breast carcinoma	5
Melanoma	4
Colorectal adenocarcinoma	4
Undifferentiated carcinoma	2
Adenocarcinomas of unknown primary	2
Oesophageal carcinoma	1
Pancreatic carcinoma	1
Prostate carcinoma	1
Renal cell carcinoma	1
Chordoma	1
Leiomyoma	1
Haematological malignancy	6 (6.1%)
Hodgkin's lymphoma	2
Chronic lymphocytic leukaemia	2
B cell non-Hodgkin's lymphoma	1
Diffuse large B cell lymphoma	1
Benign	76 (40.2%)
Normal lymph node tissue (normal flow cytometry)	36
Non necrotising granulomas/sarcoidosis	23
Anthrasilicosis	12
Tuberculosis	5
No tissue obtained	15

5–10 mm) × 1.4 (IQR, 1–2 mm) (*Table 3*). *Figure 2* shows Vizishot™ histological samples and demonstrates that more abundant tissue is obtained with the Acquire™ needle at the lower power view, though we acknowledge the scaling is not equivalent. At the ×200 magnification at 0.1 mm scaling, there is more detail from the Acquire™ sample. Acellular samples were reported in 15/101 (14.9%) of cases.

A malignant diagnosis was established in 31/101 (30.7%) cases (*Table 5*). The most common was primary lung adenocarcinoma (n=12) followed by small cell lung carcinoma (n=6) and carcinomas of unknown primary. Solid organ tumours (gastrointestinal carcinoma and renal cell carcinoma) as well as haematological malignancy (diffuse large B cell lymphoma and Hodgkin's lymphoma) were also represented. A benign diagnosis was made in 55/101 (54.5%) of cases. Normal lymph node tissue was identified in the vast majority of these (n=41).

Of the primary lung malignancy population, sufficient pathological material for PD-L1 testing was obtained in 11/16 (68.8%) of cases. For adenocarcinoma there was sufficient tissue for ancillary testing of *EGFR*, *ALK* and *ROS1* in 10/14 (71.4%) of cases (*Table 3*).

Boston Scientific Acquire™ vs. Olympus Vizishot™ comparative results

Given the retrospective nature of this analysis, the two needles cannot be compared head-to-head.

There was no significant difference in the overall diagnostic yields between the two needles: 86/101 (85.1%) for Olympus Vizishot™ and 174/189 (92.1%) for Boston Scientific Acquire™ (P=0.07) (*Table 3*). The Acquire™ needle was favoured for bulky mediastinal nodes in late-stage disease [in particular the subcarinal region (P=0.00064)] where it was felt that ancillary testing would be important and larger tissue volume was preferable. Further supportive data showed that average target lymph node size was larger [18.7 mm (IQR, 13–23 mm) *vs.* 15.1 mm (IQR, 11–18 mm), P=0.0002] and there were more cases of high pre-test probability of a malignant target lymph node for the Acquire™ needle (*Table 1*).

Our technical experience of the needles favoured the

Table 5 Pathology results of samples taken with the Olympus Vizishot™

Histopathology results	Number of patients
Malignant diagnosis	31/101 (30.7%)
Primary lung adenocarcinoma	12
Small cell lung carcinoma	6
Carcinomas presumed primary lung on imaging—insufficient for immunohistochemical diagnosis (not included in calculations)	5
Non-small cell lung carcinoma-not otherwise specified	2
Squamous cell carcinoma	2
Gastrointestinal carcinoma	1
Renal cell carcinoma	1
Diffuse large B cell lymphoma	1
Hodgkin's lymphoma	1
Benign	55 (54.5%)
Normal lymph node tissue	41
Anthrasilicosis	6
Non necrotising granulomas/sarcoidosis	4
Tuberculosis	2
Cryptococcus	1
Mycobacterium bovis (granulomas on aspirate)	1

Vizishot™ for the right upper hilar nodes (10R, R11s) (P<0.0001) and 4L lymph nodes (P=0.04) (*Table 2*).

Recognising the needle preference bias, core samples were reported significantly more frequently in the Acquire™ group with significantly greater tissue volumes. In addition, there was better adequacy of tissue for PD-L1 [45/49 (91.8%) *vs.* 11/16 (68.8%) Vizishot™ (P=0.02)] and a trend to higher success of other ancillary studies (*Table 3*).

From a safety perspective, there were no pneumothorax, infection or significant bleeding complications within either group. Significant bleeding was defined as grade 2 bleeding or above as stratified in the Delphi Consensus statement (17).

Discussion

EBUS-TBNA has been demonstrated to be a safe and minimally invasive method for the initial diagnostic evaluation of mediastinal adenopathy. The overall yield of EBUS-TBNA for a specific diagnosis has consistently been in the range of 80–90% for both malignant and benign pulmonary pathologies with a consistently good safety profile (2,3,9).

For the diagnosis and staging of lung cancer, meta-analysis has calculated a pooled sensitivity of 0.93 and pooled specificity of 1.00. The sensitivity could be improved further when lymph nodes were targeted in conjunction with positive computed tomography (CT) and positron emission tomography (PET) scan results for lymph node metastasis (2,18). A second meta-analysis (19) indicated that there was high yield for molecular analysis with EBUS-TBNA such that the probability of obtaining a sufficient sample for *EGFR* mutations was 94.5% and 94.9% for *ALK* mutations.

The Boston Acquire™ needle has been documented in the gastrointestinal literature. Studies have identified its role in the sampling of pancreatic masses, abdominal adenopathy and submucosal lesions. In the presence of ROSE one study obtained core tissue in 145/200 cases and only 13/200 required a repeated procedure (20). In pancreatic masses alone, the Acquire™ needle compared to FNA resulted in larger tissue aggregates, 6.1 *vs.* 0.28 mm^2, better retained tissue architecture and a higher cell block diagnostic yield (97.8% *vs.* 82.6%, P=0.03) (21). A similar study of solid pancreatic lesions (22) had an increased yield of histological specimens in 92.9% of patients undergoing fine needle biopsy *vs.* 68.9% in fine-needle aspiration patients. In liver biopsy a multicentre trial had a diagnostic yield of 98% of samples with no increase in adverse events compared to traditional methods (23).

Limited published data in the pulmonology field has demonstrated a similar safety profile and diagnostic rate to EBUS-TBNB (8) with a diagnostic yield of 97%. The yield for granulomatous lymphadenopathy was 95.6% which characteristically requires larger tissue samples to preserve histological architecture and structure.

The results from our study suggest that EBUS-TBNB performs well in cases of suspected primary lung malignancy with mediastinal adenopathy where large cores of tissue are required for diagnosis, staging and ancillary testing. The use of this needle has the potential to reduce the number of procedures the patient is required to undergo in the initial malignancy work up.

A recent study has suggested a novel technique; EBUS guided transbronchial mediastinal cryobiopsy, may have higher diagnostic yield than conventional TBNA (91.8% compared to 79.97%, P=0.001) (24). Of the total population

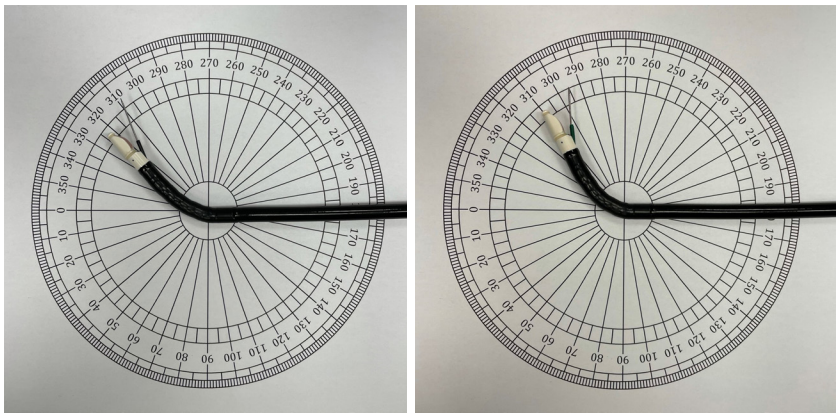

Figure 3 Acquire™ *vs.* Vizishot™ needle angles.

(n=194), cryobiopsy appeared to be particularly beneficial for diagnosing uncommon tumours (lymphoma, n=7) and benign lesions (sarcoidosis, n=15; tuberculosis, n=16). In our similar sized population, the Acquire™ needle also performed favourably for diagnosing sarcoidosis (n=23/26), tuberculosis (n=5/5) and lymphoma (n=6/6) in our analysis on first diagnostic attempt. EBUS-TBNB is also significantly more cost effective than EBUS-cryobiopsy and the technique is almost identical to EBUS-TBNA, which therefore makes it easier for respiratory physicians to perform this procedure. No trial comparing TBNB *vs.* cryobiopsy currently exists. An additional novel technique for the sampling of intrathoracic lymphadenopathy is EBUS-guided intranodal forceps biopsy which, whilst being technically complex, has demonstrated high diagnostic accuracy in feasibility studies. The role alongside other sampling techniques is currently unclear (25).

Our clinical experience

ROSE

There has been conflicting evidence in the literature for the role of ROSE in determining the adequacy of nodal sampling. Some studies, including randomised trial data, have argued that ROSE does not increase the diagnostic efficacy of EBUS-TBNA (26,27). Other studies have reported high agreement between the on-site and final pathological evaluation during EBUS-TBNA (28) and have reported an increased diagnostic yield up to 30% (4,29). The advantages of ROSE have been identified as reducing the need for additional sampling with fewer passes needed for an adequate sample in addition to a lower risk of procedural complication. A role has also been suggested for diagnostic triage in determining the requirement for extra material and the method of material preservation for ancillary studies. Disadvantages include the need for an experienced on-site cytopathologist, the need for extended procedure time and an equivocal on-site diagnosis potentially leading to a premature end to a procedure (30).

With adequate tissue cores or cell blocks, the findings from this study would support the current literature that ROSE may not be needed for successful EBUS-TBNB. The Acquire™ needle in this study provided ample tissue for diagnosis in almost all cases with only 1 patient needing a repeat procedure to identify lung cancer. Similarly, patients had adequate tissue for PD-L1 and ancillary studies (*EGFR*, *ALK*, *ROS1*) in 91.8% and 88.9% of cases respectively. Additionally, perhaps in the Olympus Vizishot™ group, prioritising the specimens into formalin may be a better method of preserving tissue for histological assessment.

Technical considerations

From our experience of 290 cases in an 18-month period, when choosing the Vizishot™ *vs.* the Acquire™ a number of technical aspects should come into consideration. Firstly, currently the Acquire™ needle is only compatible with the Olympus BF-UC180F convex bronchoscope not the newer Olympus BF-UC190F convex bronchoscope. Secondly, the fabrication of the needle with cobalt chromium does not allow for full flexion of the bronchoscope when compared to the Vizishot™ needle (*Figure 3*). This results in a shallower angle of needle penetration (*Figure 4*). Other characteristics of the Acquire™ compared to the Vizishot™ needle includes an electropolished needle tip to create a smooth cutting surface and three fully formed

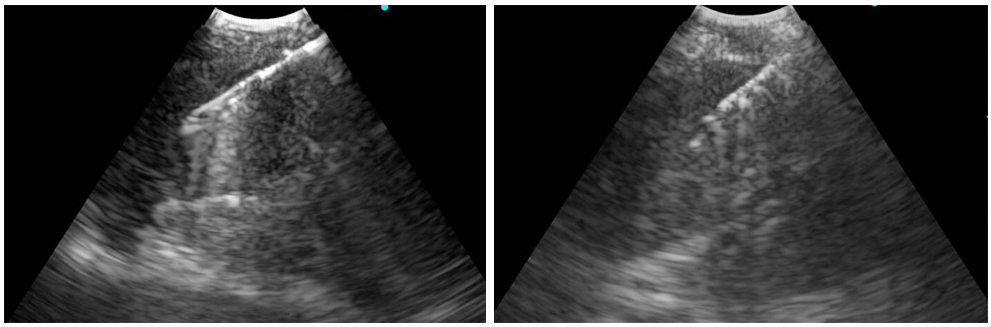

Figure 4 Acquire™ *vs.* Vizishot™ needle penetration angles.

heels that promote a circular cut during sampling which maximises tissue capture and minimises tissue tearing and fragmentation. The Acquire™ is also designed to have 3 angled points to promote tissue stability however, in our experience the reinforced, bevelled tip of the Vizishot™ needle with greater flexion actually has greater stability. These technical factors need to be taken into consideration for small nodes and certain anatomical locations. It may be more appropriate to sample the right upper hilar nodes (11R or R11s) with the Vizishot™ needle due to this more predictable angle of entry and the ability to have greater flexion of the EBUS scope (*Table 2*). For the station 4L node, a steeper angle of entry is also required and hence the Vizishot™ may be preferentially selected. In our experience a conversion from the Acquire™ to the Vizishot™ needle was required in 5/18 (27.8%) of cases and diagnostic tissue was routinely, reliably obtained with the Vizishot™ (13/13, 100.0%) in this instance (P=0.04).

To overcome the technical difficulties within the paratracheal region an attempt using more balloon inflation with full EBUS scope flexion could be effective due to the resultant increased pressure against the paratracheal wall and the increased angle at which the Acquire™ needle enters the node. For lymph nodes in the 4L region an EUS-B approach can be considered in centres experienced with this. There also appears to be a role for 25G Franseen needles which are more flexible and may help to access difficult targets (8).

Our experience would favour the use of the Acquire™ needle for bulky disease where it is felt that ancillary testing would be important. An early observation by the specialist respiratory proceduralists was that tissue volume and macroscopic 'worms' appeared greater with the Acquire™ needle. This was confirmed from pathologist feedback at the time of histological processing. Hence this led to selection bias of using this needle in cases of late-stage malignant disease or bulky mediastinal adenopathy. We would favour the Vizishot™ for smaller nodes and in technically challenging sites requiring a steeper needle angle including 4L and right upper hilar lymph nodes.

Limitations

This study has several limitations. It is a single centre, retrospective review but has a large enough sample of patients to demonstrate sufficient experience with this technique. The procedure was not standardized, particularly the number of passes through each lesion. The choice of needle was also not randomized giving rise to a needle selection bias with the reasons addressed earlier. In particular, the target lesion for the Acquire™ needle was often larger. Smaller lesions were perceived to be more accessible with the Vizishot needle due to stability at the puncture site and steeper needle angulation. The greater capacity for flexion with the Vizishot™ meant it was also favoured for the lymph nodes requiring up-angulation such as 4L and 10R. Due to these factors, a comment on whether Vizishot™ or Acquire™ is diagnostically superior has not been made and instead yields have been compared to historical data. Future studies comparing diagnostic yield when both needles are applied to the same patient and same target lesion could be trialled. Similarly, a future randomised trial comparing cryobiopsy, TBNB and TBNA could be considered.

Conclusions

In conclusion, this study suggests that the Boston Scientific Acquire™ needle is a safe method of obtaining core samples of mediastinal lesions. The overall diagnostic yield is

comparable between both the Olympus Vizishot™ and the Acquire™ needle and historical meta-analysis data. The diagnostic yield for EBUS-TBNB was also favourable for benign granulomatous conditions and unusual malignancies. For lung cancer, there was consistently ample tissue for PD-L1 and ancillary testing on first procedure. Our first documented Asia-Pacific experience of the Acquire™ Franseen needle supports its role in lung cancer work-up but also other common benign conditions and demonstrates a role for this needle as an additional diagnostic tool alongside the current standards of care.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-1747/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-1747/coif). PN has had presentation fees from Boston Scientific Australia relating to the content of this manuscript. PN has had consultancy fees from Olympus Medical Corporation Australia not relating to contents of this manuscript. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Ethical approval was obtained from the Central Adelaide Local Health Network Human Research and Ethics Committee. Individual Consent for this retrospective analysis was waived.

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