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Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration (EBUS-TBNA)

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Introduction

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is an outpatient minimally invasive procedure which is increasingly used, over the last decade, as a technique to visualise and sample structures within and adjacent to the airways and the mediastinum. It is an evolving technique with many applications and is most widely used in staging and diagnosis of lung cancer and unexplained mediastinal lymphadenopathy. This article provides a simple overview of the procedure itself and its main clinical applications, focussing on linear probe EBUS-TBNA specifically. The related endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is not discussed in detail here.

Outline of Procedure

The reader is directed to other sources for a more comprehensive review[1]. Briefly, a flexible bronchoscope with an ultrasound probe at its end is guided through the airways under conscious sedation (or general anaesthesia in some centres). Significant differences are that the patient is typically supine and intubated by the oral route due to the greater external diameter of the scope.

Ultrasound probes are of two types, with contrasting specifications and applications (see Table 1).

Table 1:
EBUS Probes - Features and Applications

Features	Radial probe	Linear probe
Frequency	20-30 MHz	7.5 MHz
Resolution	Higher (<1mm) – 360 degree view	Lower – 50 degree scanning range
Depth penetration	Less (5 cm)	More (9 cm)
Use	Peripheral lesion sampling	Real-time sampling of accessible mediastinal lesions
	Evaluation of central airway wall	

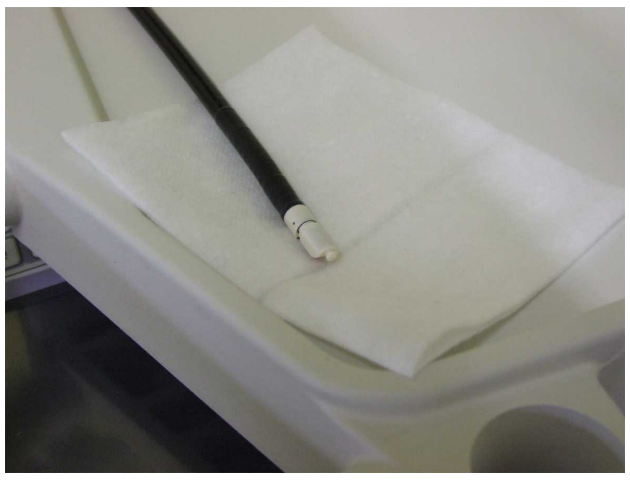

Figure 1
Convex probe bronchoscope

The linear ultrasound probe (see Figure 1) produces a B-mode (or Colour Doppler mode) sonographic image of the targeted areas, lymph nodes or masses, which are then sampled via an extended needle passed through the bronchoscope under real-time imaging (see Figure 2).

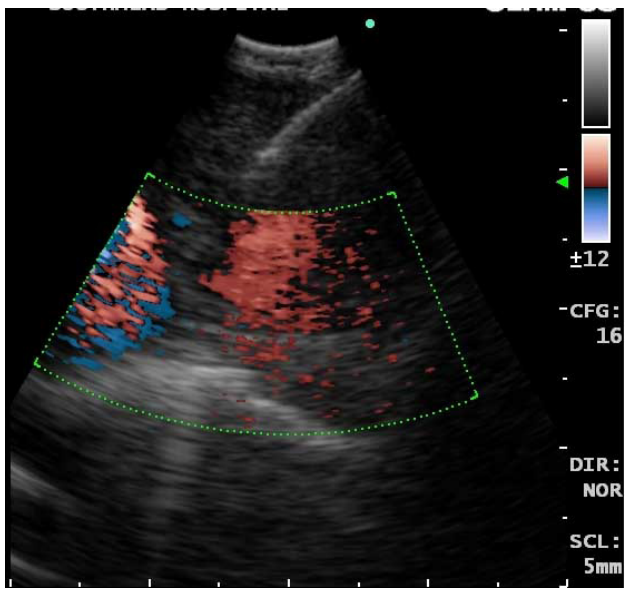

Figure 2
Real-time sampling of aorto-pulmonary lymph node (needle coming in top right) with colour Doppler on to illustrate proximity of vessels

The radial probe is also used but for peripheral lesions. It does not allow real-time sampling and is not discussed further in this paper but the reader is directed to a comprehensive review [2]. Sonographic and conventional bronchoscope images are often displayable on the same monitor in dual display format on more recent models. Colour and Doppler features aid identification of vascular structures both within and around the nodes (see Figure 2). If the image is poor an inflatable balloon can be placed on the probe at the start, in practice this is seldom needed. Enough material is usually available for immunostaining (see Figures 3a-c).

Lung cancer and EBUS

Early diagnosis and accurate staging are crucial to lung cancer management. Mediastinal assessment is a key component of the staging process as mediastinal spread (N2 and N3 disease) predicts survival and determines treatment options (in the absence of distant metastases)[3].

Radiological staging modalities, computed tomography (CT) and positron emission tomography (PET) are very good at directing where tissue can be obtained from but are themselves limited by their sensitivity[4]. The mediastinal spread identified on CT as enlarged nodes (short axis diameter >1cm) or on PET scan as metabolically active nodes requires biopsy.

Sampling techniques to assess N2-3 disease include the traditional gold standard surgical techniques: mediastinoscopy (accessing stations 1–4, 7, see Figure 4), and anterior mediastinotomy (accessing stations 5–6); and minimally invasive needle techniques: EBUS-TBNA and conventional TBNA (both capable of accessing stations 1–4, 7, 10–11) and EUS-FNA (accessing stations 5,6,7-9).

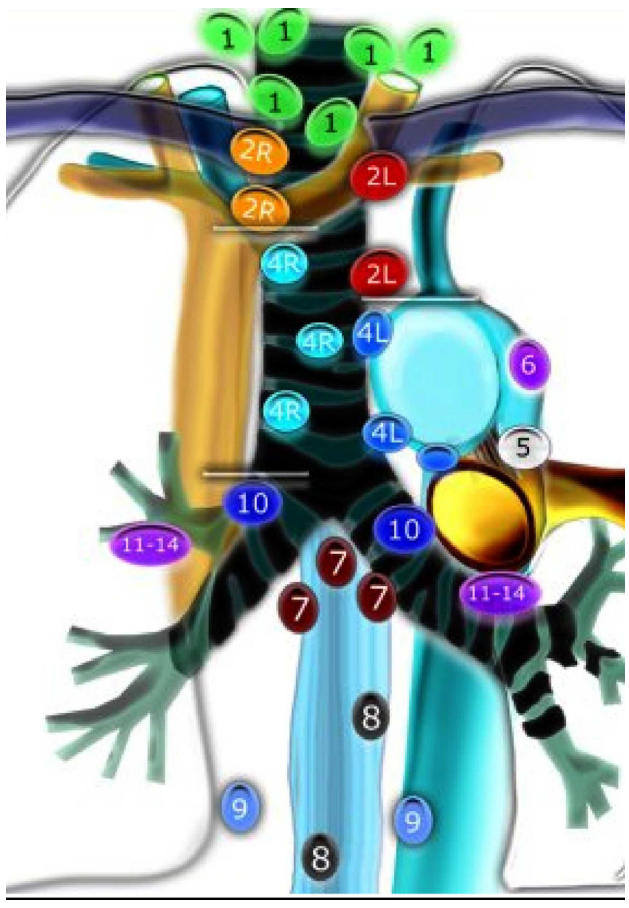

Figure 4 Mediastinal nodal station classification based on American Thoracic Society lung cancer staging. Adapted from: http://www.radiologyassistant.nl/en/4646f1278c26f , Dr Robin Smithuis (with permission).

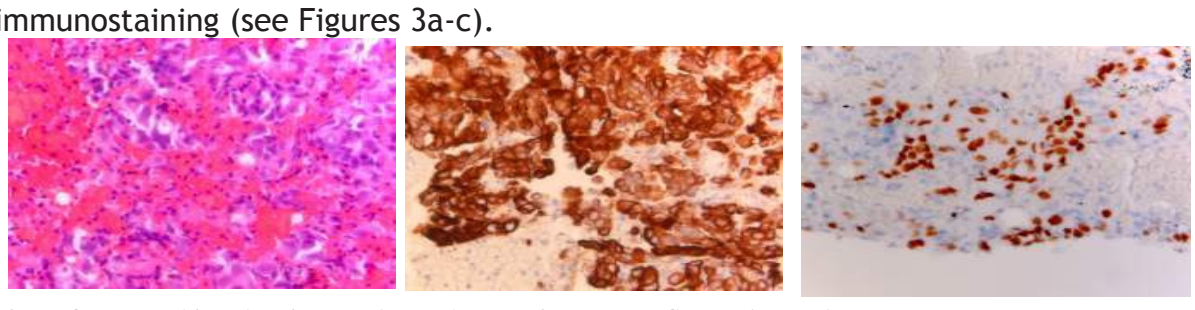

Figure 3 Immunohistochemistry on lung adenocarcinoma EBUS-TBNA sample.
3a (left): haematoxylin and eosin, 3b (middle): cytokeratin-7, 3c (right): TTF-1.

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Comparison of mediastinal sampling techniques

Pros Versus conventional TBNA	Pros Versus Mediastinoscopy	Cons
See node under direct vision, real-time sampling, less risk of puncture	Minimally invasive , no general anaesthesia	Inferior negative predictive value to mediastinoscopy (less core tissue), if negative result need to proceed to mediastinoscopy if high clinical suspicion
Better access to remote nodal stations and smaller nodes	Cheaper: day case , no general anaesthesia, theatre, shorter procedure time	Initially longer procedure than conventional TBNA
Higher sensitivity	Not limited to thoracic surgeons	Training and learning curve
Longer tissue size with more cellular integrity	Access to hilar nodes (TB, sarcoidosis)	Higher costs than conventional TBNA; staff costs, vulnerability to tariff changes, higher repair costs

Table 2:
Pros and cons of EBUS-TBNA compared to conventional TBNA and mediastinoscopy

Mediastinoscopy is currently regarded as the gold standard. EBUS-TBNA however is being increasingly used and is regarded as superior to conventional TBNA. EUS-FNA is also complementary to EBUS-TBNA.

Table 2 summarises the key pros and cons of each technique.

A recent randomised multicentre controlled trial (ASTER trial) of endosonography (combined EBUS-TBNA and EUS-FNA versus surgical staging have been reported[5]. Sensitivity is improved by adding endosonography (94% versus 79%) and this can also reduce unnecessary thoracotomies, but extrapolation to assessing the value of EBUS-TBNA alone is difficult given this study included combined endosonography and was performed only in tertiary endosonography centres.

Another randomized controlled trial, Lung BOOST trial (in progress) will ascertain whether EBUS-TBNA and EUS-FNA early on in the investigative pathway will speed-up time to diagnosis, minimise other diagnostic tests and save costs[6]. Further outcome studies on survival, morbidity and health-related quality of life are needed to determine whether EBUS-TBNA improves hard outcome measures.

Other clinical applications

EBUS is a relatively new and evolving technique which has role in many other diagnostic and therapeutic applications (see Table 3).

Table 3
Indications for linear probe EBUS

Most widely used	Other specialist applications
Staging and diagnosis of lung cancer	Aspiration of mediastinal cysts
Unexplained mediastinal node sampling (benign/malignant)	?Assess pulmonary vascular disease (possible)
Tissue banking	

Outside lung cancer, its major role is in diagnosis of unexplained mediastinal lymphadenopathy and may prove a valuable tool in diagnosis of granulomatous disease, adding to existing bronchoscopic techniques in sarcoidosis [7], and being of value in mediastinal tuberculosis even via the oesophageal route using the same scope[8]. It can also be used in lymphoma using flow cytometry, although results (57% sensitivity) do not currently compare to its performance in cancer and granulomatous disease[9].

Safety profile and complications

It is a safe procedure and no major complications have been reported in literature so far with frequency. Complications are similar to those from conventional bronchoscopy. There are a small number of reports of asymptomatic bacteraemia, and mediastinal infection (more rarely[10]) and more recent studies[11] suggesting occasional metal particle installation into the lymph nodes specific to EBUS-TBNA, of uncertain significance. Chest radiography is not routinely required post EBUS-TBNA although some centres perform this after hilar node sampling.

Training issues and setting up a service

Training in EBUS-TBNA requires adequate knowledge of thoracic anatomy and competence in basic flexible bronchoscopy with sufficient experience in all standard bronchoscopic techniques, including conventional TBNA., however even experienced bronchoscopists have a slow and varied learning curve[12]. Experience in ultrasound in other domains, e.g. Royal College of Radiology level 2 competency in thoracic ultrasound[13] can be an advantage as neck node sampling and imaging is a useful transferable skill to EBUS-TBNA. Early on, help from interventional gastroenterologists (performing EUS-FNA) or interventional radiologists can be invaluable as well as getting cytology support; post-CCT interventional pulmonology training fellowships[14] also provide a valuable framework for learning but are scarce. The European Respiratory Society and American Thoracic Society[15] suggest forty supervised procedures to gain competence and 25 procedures per year to maintain the skill but this applies to radial probe EBUS and is not likely to be translatable to linear probe EBUS-TBNA. British Thoracic Society guidelines are in progress in what is an evolving area. Extrapolating from experience[12] and EUS-FNA training guidelines[16], higher numbers are likely to be required in units with high numbers of cases. Training is also needed for the nursing staff in parallel.

Financial costs include the capital costs of the ultrasound processor and scope, running costs of the disposable EBUS-TBNA needles and staff (an assistant to the operator is advisable), and increased time of the procedure in the learning phase. Coding accuracy remains paramount given the specific EBUS-TBNA tariff [17]. However, linear EBUS-TBNA has been reported to take a mean of 12.5 (range 8–21) minutes in expert hands [18], although this will be significantly longer initially in units where the operator, nursing staff and cytology department are all in learning phase.

New developments

In non-small cell lung cancer, the presence of mutations in epidermal growth factor receptor (EGFR) may determine the efficacy of treatment with EGFR tyrosine kinase inhibitors. Multi-gene mutation analysis in EBUS-TBNA samples of metastatic lymph nodes may guide clinicians to choose such appropriate treatments[19]. Other potential longer-term uses are providing a non-ionising radiation modality to assess pulmonary vascular disease and central emboli[20], and asthma[21] (using a radial probe to look at airway remodelling providing a surrogate to HRCT).

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