Service	Endobronchial Ultrasound (EBUS)-Transbronchial Needle Aspiration

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REVISION HISTORY

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Executive Summary

Endobronchial ultrasound (EBUS) is a bronchoscopic procedure performed largely in a day case setting. It is a pivotal diagnostic and staging test in the lung cancer pathway. Efficient access to high quality EBUS services is paramount to facilitate the implementation of the National Lung Cancer Optimal Pathway and achieving new national cancer targets such as the 28 day faster diagnosis standard.

This document classifies EBUS into two different types of procedure that require differing levels of skill and expertise. This is an important distinction for commissioners to understand and consider building their EBUS pathways around. A *diagnostic EBUS* is indicated when the focus of the procedure is to obtain adequate tumour samples to guide systemic therapy in advanced stage disease. A *staging EBUS* is indicated in patients that may be suitable for curative intent treatment and nodal staging is required to define the optimal treatment.

A **diagnostic EBUS** is usually indicated in patients that are not suitable for treatment with curative intent, either because they have advanced stage, are not fit enough for or do not wish to undergo the suggested treatment. It is important that enough tumour tissue of sufficient quality is obtained for accurate tumour sub-typing, and molecular & immuno-oncology profiling. This is essential to guide treatment with increasingly specific targeted systemic anti-cancer therapy. Obtaining tumour tissue for diagnostic purposes only is generally a faster and more straightforward procedure.

A **staging EBUS** is indicated where there is a potential for treatment with curative intent. The type of treatment is defined by the presence or absence of nodal metastases which is provided by a systematic examination of the mediastinal and hilar lymph nodes with ultrasound and sampling where appropriate. The most recent (2019) NICE guideline update cements the critical need for high quality staging EBUS procedures in defining the most appropriate treatment and ensuring the very best patient outcomes. Staging EBUS generally requires a higher degree of skill because a greater number of sites are often sampled and the nodes can be small. The procedure is often longer so better bronchoscopic skills are required to ensure the procedure is tolerated by the patient and all required areas are sampled adequately.

Commissioning implications

Consideration should be given to staging EBUS being provided within high volume EBUS centres serving the population of several hospitals within a geographical area. This must be considered carefully against any potential barriers to accessing these centres by increasing the travel required for patients. This service specification provides *recommendations* on the minimum number of procedures per year to maintain the appropriate skills to deliver staging EBUS. Commissioners may consider whether individual hospitals, outside of their staging EBUS centres, provide rapid access diagnostic EBUS (as well as potentially utilising EBUS in the management of benign respiratory conditions such as tuberculosis and sarcoidosis) in additional hospitals.

Most importantly, this service specification sets out standardised performance metrics for both types of EBUS procedures as well as metrics that cover pathway time, safety and patient experience. EBUS services must record, audit and publish their performance. The 2019 NICE guidelines have mandated this audit process for all EBUS services. Where performance is below that set out in this document a clear mechanism to provide support to and enhance these services is required.

Chapter 1: Service Specification

1.1 Aims

The key objectives of this specification are:

1. To provide a framework for the delivery of high quality, safe, efficient and sustainable EBUS-TBNA services across the NHS
2. To describe a standardised dataset for audit and service evaluation
3. To provide quality assurance standards, and describe key performance metrics.

In addition, this specification will describe measures to ensure access to services is geographically equitable and timely throughout the year.

It will acknowledge the National Optimal Lung Cancer Pathway aspirations to ensure patients referred with suspected lung cancer attain referral to diagnosis and MDT discussion in 21 calendar days, and recognises that EBUS-TBNA should not be viewed as a stand-alone test (by provider or commissioner) but viewed in the context of the full patient experience and journey.

1.2 Evidence Base

There is an extensive and robust evidence base on the performance of EBUS-TBNA and this evidence has been reviewed as part of the NICE guidelines for the Diagnosis and Management of Lung Cancer both in 2011 and 2019. A list of further reading of important publications is provided at the end of this document and note is made of a recent UK consensus statement on recommended performance characteristics for EBUS-TBNA, according to the indication for the procedure (Evison et al, Br J Cancer 2016).

1.3 General Overview

Endobronchial ultrasound transbronchial needle aspiration (EBUS-TBNA) is a bronchoscopic technology for the management of suspected lung cancer (and other thoracic conditions) that requires skill in patient selection, technical proficiency and the appropriate management of results, delivered as part of a lung cancer multidisciplinary team and a wider team including bronchoscopy nurses. It enables sampling of a lymph node or lesion under ultrasound guidance, typically performed under conscious sedation (although it can be performed under general anaesthetic) using a flexible fibreoptic bronchoscope passed down the trachea and main airways.

The primary role of EBUS-TBNA in lung cancer is in lymph node staging, although tissue acquisition for diagnosis only is also common where nodal staging will not influence treatment. Staging in lung cancer is required to accurately assess the extent of the disease and is crucial to offering curative treatment. In addition to diagnosis and staging in lung cancer, EBUS-TBNA can be utilised to assess mediastinal or hilar lymph node enlargement in other settings

1. Re-staging of lung cancer following previous treatment or induction treatment
2. Confirmation of lung cancer recurrence following previous treatment
3. Repeat sampling in advanced stage lung cancer for molecular testing and targeted therapies
4. Lymphadenopathy in the setting of extra-thoracic malignancy, such as metastases from the breast or other organs
5. Isolated mediastinal or hilar adenopathy, such as seen in TB, lymphoma or sarcoidosis

1.4 Definition of a Diagnostic EBUS

A diagnostic EBUS is performed to confirm the pathology within an abnormal lymph node, identified on pre-procedure imaging (abnormal size, morphology or metabolic activity). The procedure 'targets' the abnormal lymph nodes only with the sole aim of identifying the pathology within them. In lung cancer this procedure is reserved for patients with advanced stages of the disease where sufficient samples need to be obtained from malignant lymph nodes in order to sub-type the tumour and complete all required molecular or immune profiling to define a personalised strategy for palliative systemic anti-cancer therapy.

1.5 Definition of a Staging EBUS

A staging EBUS is reserved for those patients with suspected or confirmed lung cancer and potentially suitable for curative-intent treatment. The aim of the procedure is to accurately define the exact location and extent of any nodal metastases. This is achieved through a systematic examination and sampling of appropriate lymph nodes. A staging EBUS should routinely complete a systematic examination of the mediastinal and hilar lymph nodes beginning with the nodal stations contralateral to the primary tumour (N3) followed by N2 stations and finally N1 (a suggested systematic approach is outlined in Appendix 1). During this examination, the following recommendation is made with regard to lymph node sampling:

- Sample any lymph node identified as abnormal (defined as >10mm short axis on staging CT, any FDG avidity above that of the mediastinal blood pool on PET regardless of node size or any node regardless of size showing abnormal sonographic characteristics *(an example of sonographic assessment of lymph nodes during EBUS is provided by Fujiwara et al 2010 and is based on size, shape, margin, echogenicity, central hilar structure and coagulation necrosis sign).*
- Staging EBUS may be indicated where CT shows nodes with abnormal morphology even where nodes are <10mm short axis.

Note: The 2019 NICE guidelines state that PET-CT is performed <u>prior</u> to staging EBUS. This is of critical to ensure any PET avid nodes are sampled during the procedure.

A substantial evidence base for staging the mediastinum has evolved but this evidence base is derived from a small number of high volume expert centres and it is not established whether this translates readily into everyday NHS practice. Indeed, work across one large cancer network has shown disparate outcomes across important performance indices amongst the four established EBUS providers. Nodal staging is a critical part of ensuring the most appropriate treatment and therefore the performance of a staging EBUS service must be monitored to ensure the very best patient outcomes are achieved.

1.6 Indications for Staging EBUS

A staging EBUS is required when pathological confirmation of the presence or absence of loco-regional nodal metastases will define treatment options and when there is a risk of nodal metastases of greater than 5-10%. Specifically it is used to differentiate between early stage lung cancer where surgical resection is the standard care versus locally advanced lung cancer where multi-modality treatment of differing forms are recommended. Staging EBUS is a pivotal test in the lung cancer pathway with clear evidence and guidelines when it is indicated. Figure 1 and Appendix 1 provide additional detail on this topic. In summary, Staging EBUS is not indicated in cases of peripheral tumours with a normal hila & mediastinum on both CT and PET, because the risk of occult N2/3 disease is less than 5%. Here, curative treatment may be offered without pathological nodal staging. However, in patients with

discrete enlargement of hilar or mediastinal lymph nodes on CT, nodal staging is mandated regardless of PET findings because the latter, although mostly accurate, yields too many false positives and negatives to guide treatment (ACCP Staging of Lung Cancer Guidelines 2013, Schmidt-Hansen et al JAMA 2015).

Taking all these considerations into account, commissioned EBUS services and cancer alliances need to ensure that:

- *All patients with suspected lung cancer who are deemed fit for treatment with curative intent and have no evidence of distant metastases on CT/PET but with ANY enlarged (>10mm) hilar or mediastinal lymph nodes on CT or ANY FDG avid hilar or mediastinal lymph nodes on PET-CT are referred for a staging EBUS.*

1.7 Role and place of Mediastinoscopy

Although EBUS is the preferred first test in mediastinal diagnosis and staging, mediastinoscopy may be performed where there is a reasonable suspicion that EBUS results are unreliable, for example where the procedure is not well tolerated, the samples are scanty or where there were technical difficulties. Individuals who cannot tolerate EBUS can either have EBUS under anaesthetist led deep sedation or where this is not possible, mediastinoscopy, accepting the latter may be suboptimal for sampling some of the nodal stations. Mediastinoscopy is also recommended in cases of a negative staging EBUS but the suspicion of mediastinal metastases remains high and the presence of nodal metastases would influence the management decision.

Figure 1: Which patients with suspected lung cancer need a staging EBUS?
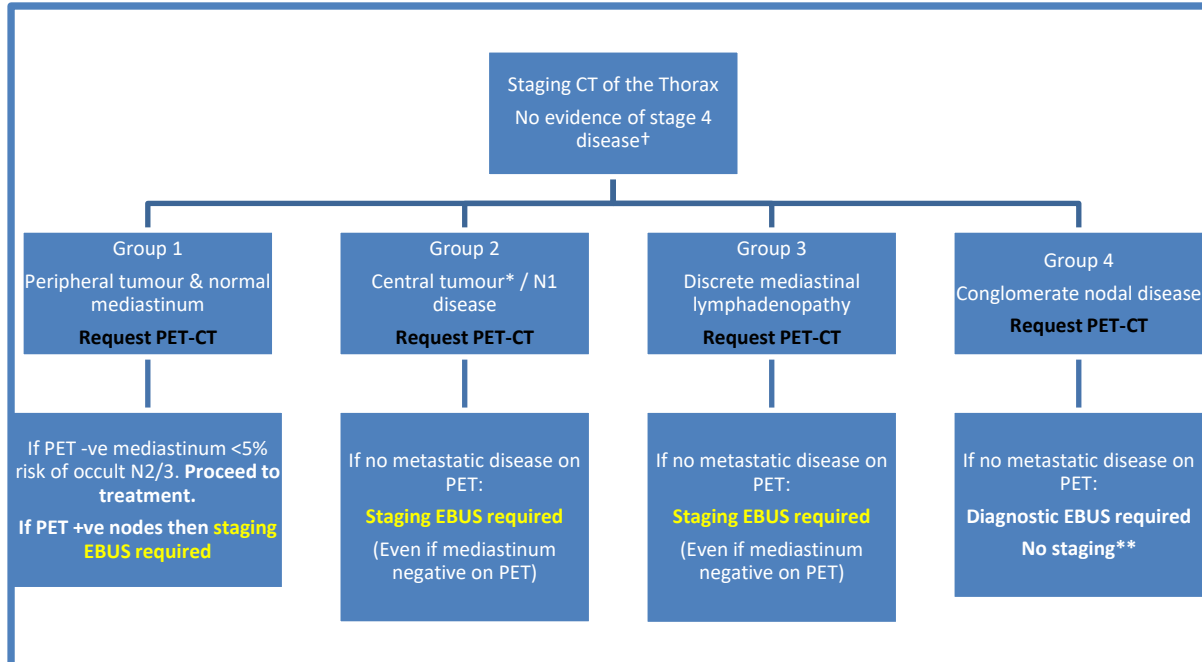
†This diagram refers to patients with stage I-III lung cancer on staging CT and whom are deemed fit for radical treatment. Patients with stage 4 disease generally require a diagnostic EBUS focusing on obtaining adequate tissue for tumour and molecular profiling. **Patients should have a PET-CT first prior staging EBUS as per NICE guidelines – metastatic disease identified on the PET-CT might necessitate a different sampling approach or may switch the staging EBUS to a diagnostic EBUS.**
*A central tumour is one located within the inner third of the thorax, using the main carina as the centre point
**May sometimes need systematic sampling to define radiotherapy field.

1.8 Education and Training

The commissioned services will ensure that all operators and support staff are suitably trained, and that all equipment is maintained in line with manufacturer and clinical guidelines. The services should be able to demonstrate satisfactory competency of all independent operators; close supervision of trainees with attention to precision and patient experience.

1.9 Collaboration and cross-cover

In line with recommendations made in the national lung cancer commissioning guidance, the commissioned services should work collaboratively with other EBUS providers in the locality to ensure access times are achieved across the entire Alliance. This will include cross-cover for annual leave and sickness, support for ongoing training and professional development. In addition, this will allow patients to transfer into another service where access times cannot be met within their local service, or another provider is more suitable within other diagnostic tests or treatments being undertaken.

Further information on how performance is considered in staging EBUS, minimum standards according to prevalence of N2/3 and service description & models are provided in Appendix 2-4

Chapter 2: Data Collection

2.1 Standardised Dataset & Audit

Commissioned services should collect, analyse and publish an agreed dataset aligned to agreed performance metrics and standards. A unified national database would be the preferred tool for this purpose. In an interim period a local solution will be necessary.

The following dataset should be collected:

Patient demographics
- Age
- Gender
- Performance status

Sedation & safety
- Sedation strategy: physician-led vs anaesthetic-led, conscious sedation vs deep sedation
- Sedation type and doses
- Major complications – as defined in the British Thoracic Society Guidelines for diagnostic bronchoscopy (Table 1)

Table 1: Major complications of bronchoscopy

Serious Adverse Event	Definition
Bleeding	Endobronchial bleeding during bronchoscopy should be classified as: **Severe:** Requirement for bronchial blocker, fibrin sealant, resuscitation, blood transfusion, critical care admission or death **Moderate:** Wedging the scope in bleeding segmental bronchus, use of vasoconstrictors – adrenaline, cold saline **Mild:** Continual suction only required
Cardiac complication	Cardiac arrhythmia requiring intervention, myocardial infarction or pulmonary oedema
Pneumothorax	That requires intervention with aspiration or chest drain
Oversedation	Requiring sedation reversal or ventilator support
Escalation of care	The need for unplanned emergency hospitalisation or critical care admission
Seizures	
Death	

Indication
- Indication for EBUS – Staging EBUS vs Diagnostic EBUS in lung cancer
- In staging EBUS the CT disease pattern should be recorded (Group 1-4, Table 1)

Pathway
- Proportion of patients with EBUS final result within 14 days of request (calendar days).
- Time from receipt of referral communication of final histological report with subtype (calendar days).
- Time from receipt of referral to communication of final histological report with all predictive biomarker tests (calendar days).

Procedure – staging EBUS
- Nodal stations examined, the sonographic appearances and stations sampled (according to the IASLC International Lymph Node Map)
- Total number of lymph node stations sampled

Outcomes-Staging EBUS
- EBUS nodal staging (N0-N3)
- Final nodal staging (N0-3)*

*The final nodal staging should be based on all pathological sampling and radiological evidence available (EBUS, mediastinoscopy, intra-operative lymph node sampling, repeat procedures and 6 months of clinical-radiological FU). Confirmation of nodal metastases or disease recurrence within N2/3 lymph nodes within 6 months of a negative staging EBUS (i.e. no evidence of N2/3 nodal metastases from EBUS sampling) is the definition of a false negative EBUS.

Outcomes-Diagnostic EBUS
- Pathological confirmation rate
- In NSCLC lung cancer cases – NSCLC-NOS (non-small cell lung cancer Not Otherwise Specified) rate
- Proportion of cases in which EGFR testing is required and EBUS-TBNA has provided adequate tissue for testing
- Proportion of cases in which ALK testing is required and EBUS-TBNA has provided adequate tissue for testing
- Proportion of cases in which PDL1 testing is required and EBUS-TBNA has provided adequate tissue for testing
- Proportion of cases in which ROS-1 testing is required and EBUS-TBNA has provided adequate tissue for testing
- Proportion of cases in which a repeat sampling procedure is required due to insufficient tissue from the diagnostic EBUS

Patient Experience
Formal patient experience data should be collected and analysed at least once a year

Total number of procedures
The total number of EBUS procedures performed per annum should be recorded and form part of an annual review. It is **recommended** that staging centres require multiple operators to ensure year-round access and capacity. Individual operators within staging centres should achieve a minimum of **20 staging procedures** per annum to maintain competence. This figure includes the supervision of trainees/fellows/consultants as primary operators. There must be a mechanism in place to ensure a continuous service is available (adequate cross-cover).

A total number of procedures per annum has not been specified for those centres performing diagnostic EBUS alone but such centres should ensure performance is in line with the minimum standards set out in this service specification.

It is important to state that these are only recommended levels of practice and that individual learning and maintenance of competence is highly variable. Ultimately, the performance of an EBUS service, against the standards set out in this service specification, are the true test of competence. If an EBUS service or an individual operator falls outside these standards then volume of practice is an important metric to consider as a contributing factor.

3. Quality and Performance Standards

Quality Performance Indicator	Threshold	Method of measurement
Procedure carried out within 7 working days of receipt of referral	85%	Monthly report
Pathological Results received within 5 calender days of sampling* **This includes morphology and immunohistochemistry)*	85%	Monthly report
Total pathology pathway time – 10 calender days (from time of sampling to receipt of final pathology results including all predictive biomarkers*)	85%	Monthly report
Safety – Major/ Minor Complications	<3% Major	Monthly Report
Staging EBUS Performance – Lung Cancer		
Proportion of procedures where any lymph node station was inadequate	<10%	Annual Report
Sensitivity *Denominator = total number of patients with N2/3 metastases*	See Table 2 Appendix 3	Annual Report
Negative predictive value *Denominator = total number of patients with a negative staging EBUS for N2/3*	See Table 2 Appendix 3	Annual Report
Prevalence of N2/3 nodal metastases in population	%	Annual Report
Diagnostic EBUS Performance – Lung Cancer		
Pathological confirmation rate in advanced disease	>90%	Annual Report
Adequate tissue for successful EGFR testing	>90%	Annual Report
Adequate tissue for successful ALK testing	>90%	Annual Report
Adequate tissue for successful ROS-1 testing	>90%	Annual Report
Adequate tissue for successful PDL-1 testing	>90%	Annual Report
NSCLC-NOS Rate	<10%	Annual Report
Proportion of cases in which a repeat sampling procedure is needed due to insufficient tissue*	<10%	Annual Report

*This does NOT include patients requiring a core tissue biopsy for clinical trial entry

The required performance metrics are described in the table above with further detail provided in Appendix 2 including the minimum standards for sensitivity and negative predictive value for staging EBUS stratified according to the prevalence of N2/3 disease in the population undergoing EBUS.

Specific recommendations have not been made about number of passes per lymph node as this will depend on the type of procedure (staging versus diagnostic), procedure tolerance, availability of Rapid On-Site Evaluation and visual content of samples. Ultimately, the true test of adequacy of lymph node sampling will be reflected in the performance metrics.

In the event of an EBUS service falling below the recommended performance set out in this specification then a process of peer review with a period of re-training/coaching at a well performing centre should be undertaken. The following areas could form the focus of a service review and action plan to improve performance:

- The number of procedures per year by the service – is this adequate to maintain competency?
- Number of procedures per operator per year – is this adequate to maintain competency?
- Technique – is sedation practice influencing procedural outcomes?
- Technique – how many passes per lymph node are made on average?
- Technique – is a systematic nodal evaluation being performed during a staging EBUS?

Further Reading

2019 NICE Guidelines Diagnosis and Management of Lung Cancer

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