Appendix 1 - Additional information on Staging EBUS

Definition of a staging EBUS

A staging EBUS is defined as follows:

A systematic examination of the mediastinal and hilar lymph nodes beginning with the nodal stations contralateral to the primary (N3) followed by N2 stations and finally N1 stations.

During a staging EBUS the operator should examine the following lymph node stations in sequence

- ✓ *Contralateral station 11*
- ✓ *Contralateral station 10*
- ✓ *Contralateral station 4*
- ✓ *Contralateral station 2*
- ✓ *Station 7 (from both main bronchi)*
- ✓ *Ipsilateral station 2*
- ✓ *Ipsilateral station 4*
- ✓ *Ipsilateral station 10*
- ✓ *Ipsilateral station 11*

Indications for Staging EBUS

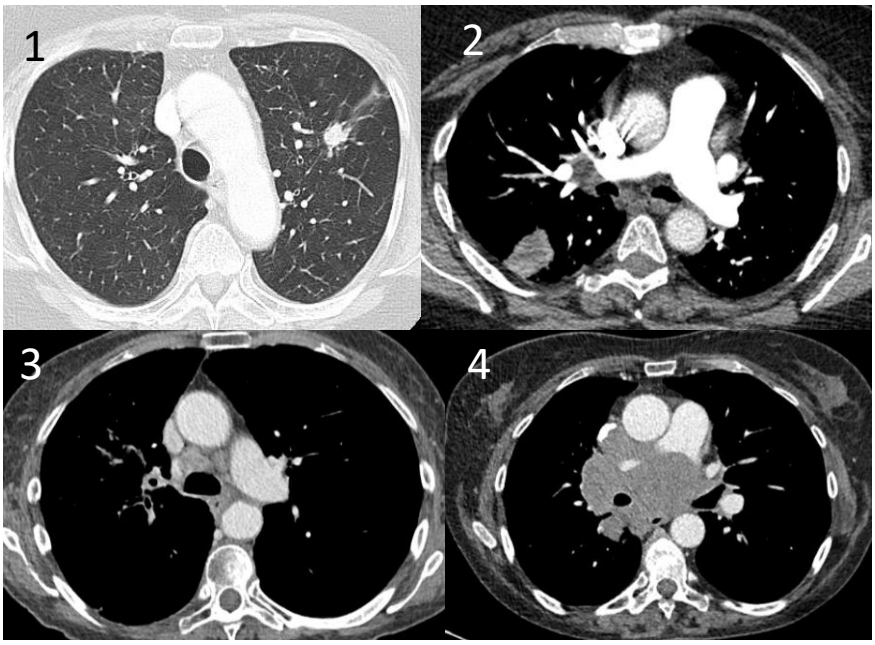
The American College of Chest Physicians (ACCP) recommend using the patterns of disease on the index CT scan of the thorax to determine whether a patient requires pathological nodal staging. In the absence of distant metastases and stage 4 disease, all patients can be categorised as Group 1 to 4, illustrated below (Table 1, Figure 1). The performance of PET-CT for mediastinal staging is variable across these radiographic groups and helps inform which groups require pathological nodal staging and which patients may proceed to treatment without nodal sampling (Table 2).

Table 1: Radiographic groups for lung cancer patients based on index CT of the thorax, without evidence of stage 4 metastatic disease

ACCP Radiographic Group based on CT Chest	Description	Limitations of CT
Group 1 *Prevalence of N2/3 disease = 10%*	Peripheral tumour with normal hilar and mediastinum on CT (N0)	Despite a normal mediastinum on CT 10% of these patients will have occult N2 disease in mediastinal nodes
Group 2 *Prevalence of N2/3 disease = 20-25%*	Centrally located tumour* and or ipsilateral hilar lymph node enlargement ≥10mm (N1)	Despite a normal mediastinum on CT 25% of these patients will have occult N2 disease in the mediastinal nodes
Group 3 *Prevalence of N2/3 disease = 60%*	Discrete enlargement of mediastinal nodes but well defined and non-bulky (N2/3)	40% of enlarged mediastinal lymph nodes on CT will be benign leading to over staging on CT
Group 4 *Prevalence of N2/3 disease = 100%*	Invasive, bulky and conglomerate nodal disease (N2/3)	CT very reliable and considered diagnostic of malignancy

*A central tumour is one located within the inner third of the thorax, using the main carina as the centre point

Figure 1: Radiographic groups for lung cancer patients based on index CT of the thorax: **(A)** Conglomerate nodal disease, **(B)** discrete mediastinal lymph node enlargement, **(C)** Central tumour* / N1 disease, **(D)** peripheral tumour & normal mediastinum (4)



*A central tumour is one located within the inner third of the thorax, using the main carina as the centre point

Table 2: Performance of PET-CT for mediastinal staging in lung cancer according to ACCP radiographic groups

Radiographic Group based on CT Chest	Limitations of PET positive mediastinum	Limitations of PET negative mediastinum
Group 1/2 Peripheral tumour & normal mediastinum / Central Tumour* / N1	15% false positive rate	5% / 25% false negative rate
Group 3 Discrete mediastinal lymphadenopathy	15% false positive rate	25% false negative rate
Group 4 Conglomerate nodal disease	NA – CT considered diagnostic of malignancy	NA – CT considered diagnostic of malignancy

*A central tumour is one located within the inner third of the thorax, using the main carina as the centre point

Appendix 2 – Performance in Staging EBUS

The most important performance measures of staging EBUS are sensitivity and negative predictive value (NPV), both influenced by the false negative rate. Specificity and positive predictive value are not discriminatory and widely reported as 100% in meta-analysis and systematic reviews because positive EBUS results are rarely confirmed by surgery.

For sensitivity and NPV calculations the identification of patients with N2/3 metastases missed by systematic staging EBUS is pivotal. This requires a thorough review of any subsequent pathological nodal sampling (e.g. mediastinoscopy or intra-operative lymph node sampling) and a minimum of six months clinical-radiological follow-up. The denominator for sensitivity calculations should be the overall number of patients with N2/3 nodal metastases **(even in those lymph node stations inaccessible with EBUS).** This provides a far more accurate assessment of the ability of EBUS to stage the mediastinum than a per lymph node denominator.

Both sensitivity and NPV have been shown to be dependent upon the overall prevalence of N2/3 metastases in the population undergoing EBUS. For example, although the American College of Chest Physicians (ACCP) report a sensitivity of 89% and NPV of 91% for staging EBUS in a large meta-analysis, they also demonstrate sensitivity is positively correlated with the prevalence of N2/3 disease within the patients undergoing EBUS whereas NPV is negatively correlated (13) (Table 2). This could reflect a biological difference in the nodes in higher prevalence populations versus lower prevalence populations (macroscopic nodal involvement in larger FDG-avid nodes vs microscopic metastases in small non-avid nodes). It is therefore crucial that the prevalence of N2/3 metastases is presented alongside the sensitivity and NPV for all systematic staging EBUS centres.

Table 3: Recommended minimum standards for staging EBUS according to the prevalence of N2/3 nodal metastases in the population undergoing EBUS

	Sensitivity		**Negative Predictive Value**	
N2/3 Prevalence	**ACCP meta-analysis**	**Minimum standard**	**ACCP meta-analysis**	**Minimum standard**
>80%	96%	**>90%**	83%	**>80%**
60-80%	91%	**>88%**	83%	**>80%**
40-60%	87%	**>85%**	89%	**>85%**
20-40%	87%	**>80%**	95%	**>90%**
<20%	78%	**>75%**	96%	**>92%**

Appendix 3 – Service description

To ensure effective service delivery to a high standard this service specification outlines the key components that are expected of Providers:

1. Appropriate selection of patients for staging EBUS-TBNA

2. Compliance with key performance indices of technical proficiency (sensitivity and negative predictive value presented in the context prevalence of N2/3 nodal metastases in the population undergoing staging EBUS)
3. Demonstrate safety of EBUS-TBNA service,
4. Monitor patient experience
5. Effective integration into the lung cancer pathway across the diagnostic pathway (short waiting times, rapid reporting of pathology, referral to MDT discussion ≤21 days calendar days)
6. Measure relevant cancer outcomes
    a. low rates of a not otherwise specified pathological diagnosis
    b. high rates of molecular pathology testing (EGFR/ ALK/ PDL-1)
    c. 1-year survival
7. Compliance with the quality assurance programme

Compliance with this service specification and recommended quality assurance programme is considered the minimum requirement for ongoing service commissioning for EBUS services. It is recommended the most robust and detailed quality assurance occurs in the more technically challenging area of staging EBUS which should be directed to high volume centres with proven compliance and adherence to quality assurance and performance metrics. EBUS centres performing below the minimum standards set out in this document are expected to develop comprehensive remedial plans for any shortcomings.

Each commissioned service will have a designated lead clinician who takes overall responsibility for the delivery of the service, compliance with quality standards, and reporting of clinical outcomes to the Cancer Alliance Board. Alongside the EBUS operator (clinician), there will be a needle operator (clinician or nurse with appropriate specialist training or in some centres the EBUS operator will also be the needle operator), a qualified team member to monitor and support the patient throughout the procedure, a qualified team member to assist the EBUS operator with appropriate training for bronchoscopy support and a runner such as a support worker to provide additional support for sample collection, and the efficient flow of patients through the unit. Patients will receive sedation during the procedure, and will require appropriate monitoring during this time in line with BTS guidelines for flexible bronchoscopy.

The collection of all specimen types should be optimised to allow adequate morphological assessment and ancillary testing on a single sample. Processing of material to cell block should be undertaken for immunocytochemistry & molecular tests, such as EGFR, ALK and ROS-1 mutation analysis and PDL1 status, this being the recommended methodology in international guidelines. For aspirates of lymph nodes, specimens that are negative should be distinguished from those that are inadequate as described in the Royal College of Pathologists Dataset for lung cancer histopathology reports (September 2016).

Clinical Effectiveness and Performance

Careful pre-procedure planning is required so all team members are aware of the purpose of a procedure (staging vs diagnostic) and therefore the approach that will be taken; systematic examination vs high volume sampling of a malignant lymph node(s).

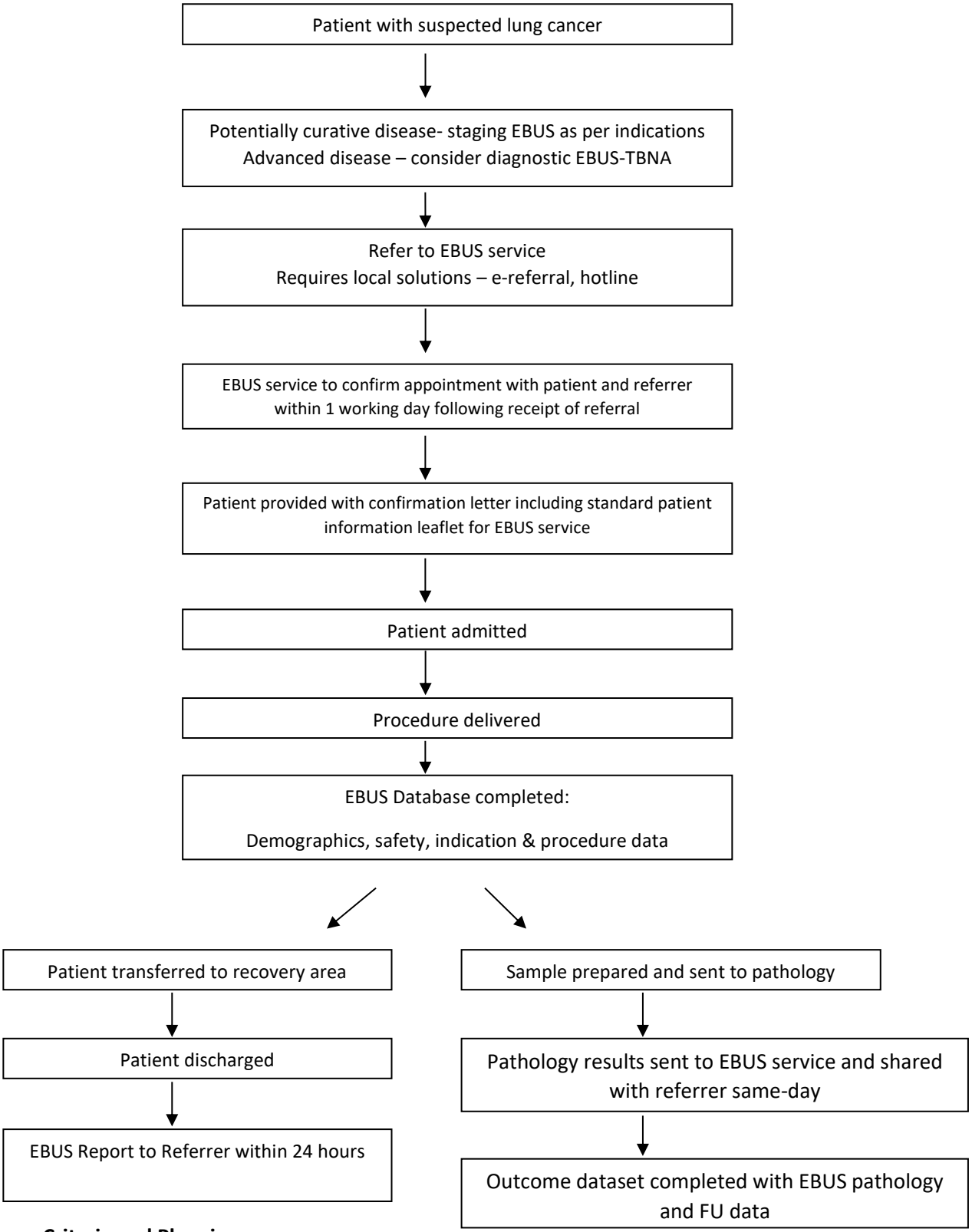
The service provider must therefore:

- Have an evidence based approach by implementing NICE Guidelines, National Service Frameworks, and other nationally recognised standards set out in guidance from the Royal College of Physicians, British Thoracic Society, Royal College of Pathology or Royal College of Nursing;
- Have a lead clinician for audit and an audit programme in place agreed between provider and commissioner to ensure that clinical practice is continually monitored and improved;
- Contribute to appropriate research with the intention of improving care;
- Hold regular meetings between providers and commissioner with agreed reporting mechanisms.

Appendix 4 - Service Model

The service model is in line with all bronchoscopy procedures with the majority of patients managed as day cases unless complications arise necessitating an admission. It should be noted that EBUS-TBNA

for benign conditions such as sarcoidosis could follow a 'less urgent' pathway than those referred with suspected malignancy.



Discharge Criteria and Planning

Discharge planning commences on admission to the service. Any issues that impact on timely discharge will be identified through the admission assessment process and action will be taken to address these issues

Self-Care and Patient & Carer Information

Written information will be provided in relation to post-procedure care and expected side effects. A contact number for post-discharge communication will be offered.