

# Protocol

## Endobronchial Ultrasound for Diagnosis and Staging of Lung Cancer

(60158)

<b>Medical Benefit</b>		<b>Effective Date:</b> 04/01/15	<b>Next Review Date:</b> 01/20
<b>Preauthorization</b>	No	<b>Review Dates:</b> 01/15, 01/16, 01/17, 01/18, 01/19	

### **Preauthorization is not required.**

*The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.*

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none"> <li>• With peripheral pulmonary lesions and suspected lung cancer</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>• Endobronchial ultrasound-guided transbronchial needle aspiration for diagnosis</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>• Flexible bronchoscopy with transbronchial needle aspiration</li> <li>• Transthoracic (percutaneous) needle aspiration using computed tomography guidance</li> <li>• Mediastinoscopy</li> <li>• Surgical lung biopsy</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>• Overall survival</li> <li>• Disease-specific survival</li> <li>• Test accuracy</li> <li>• Test validity</li> <li>• Morbid events</li> </ul>
Individuals: <ul style="list-style-type: none"> <li>• With lung cancer and mediastinal lymph nodes seen on imaging</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>• Endobronchial ultrasound-guided transbronchial needle aspiration for staging</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>• Flexible bronchoscopy with transbronchial needle aspiration</li> <li>• Transthoracic (percutaneous) needle aspiration using computed tomography guidance</li> <li>• Mediastinoscopy</li> <li>• Surgical lung biopsy</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>• Overall survival</li> <li>• Disease-specific survival</li> <li>• Test accuracy</li> <li>• Test validity</li> <li>• Morbid events</li> </ul>

### **DESCRIPTION**

Endobronchial ultrasound (EBUS) is an imaging technique for adjunctive use with standard flexible bronchoscopy. It provides an ultrasound-generated image of the lungs beyond the airway walls, extending to peribronchial structures and distal peripheral lung lesions. The purpose of EBUS is to facilitate navigation to distal regions of the lungs and biopsy of peripheral pulmonary nodules; especially suspected cancerous lesions. Another intended use of EBUS is to localize and facilitate biopsy of the mediastinal lymph nodes as part of staging for non-small-cell lung cancer. Both techniques primarily use transbronchial needle aspiration (TBNA) of lesions to obtain tissue samples.

## SUMMARY OF EVIDENCE

For individuals who have peripheral pulmonary lesions and suspected lung cancer who receive EBUS-guided TBNA (EBUS-TBNA) for diagnosis, the evidence includes recent systematic reviews, meta-analyses, and two small randomized trials. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and morbid events. Evidence supports a conclusion that EBUS-TBNA has diagnostic performance characteristics for solitary pulmonary lesions similar to those of traditional flexible bronchoscopy with transthoracic needle aspiration. The evidence also indicates that the safety profile of EBUS-TBNA may be better than the profile of other techniques, as reflected by pneumothorax and chest tube insertion rates. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have lung cancer and mediastinal lymph nodes seen on imaging who receive EBUS-TBNA for staging, the evidence includes systematic reviews and meta-analyses. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and morbid events. Evidence from systematic reviews supports a conclusion that EBUS-TBNA exhibits test performance characteristics similar to other needle-based methods used to stage the mediastinum in patients diagnosed with lung cancer. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

## POLICY

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) may be considered **medically necessary** for the evaluation of peripheral pulmonary lesions in patients with suspected lung cancer when the following criteria are met:

- Tissue biopsy of the peripheral pulmonary lesion is required for diagnosis (see Policy Guidelines)
- The peripheral pulmonary lesion is not accessible using standard bronchoscopic techniques.

EBUS-TBNA is considered **medically necessary** for mediastinal staging in patients with diagnosed lung cancer when the following criteria are met:

- The patient is suitable and willing to undergo specific treatment for lung cancer, with either curative or palliative intent (see Policy Guidelines)
- Tissue biopsy of abnormal mediastinal lymph nodes seen on imaging is required for staging and specific treatment planning (see Policy Guidelines)
- Abnormal lymph nodes seen on imaging are accessible by EBUS-TBNA.

Endobronchial ultrasound is considered **not medically necessary** for diagnosis and staging of lung cancer when the above criteria are not met.

Endobronchial ultrasound is considered **investigational** for all other indications.

## POLICY GUIDELINES

### DIAGNOSIS AND STAGING GUIDELINES

The American College of Chest Physicians published comprehensive evidence-based clinical practice guidelines on the diagnosis and management of lung cancer in 2013 (Rivera et al, 2013). Key elements of those guidelines relevant to this protocol are outlined next.

The general approach to patients who are suspected of having lung cancer begins with a comprehensive history and physical examination. Imaging studies will include a computed tomography (CT) scan of the chest and a

whole body positron emission tomography (PET) or PET-CT study to seek extrathoracic lesions. A patient's suitability and desire for curative treatment of a proven lung cancer are among the chief considerations in choosing among subsequent management options. These factors in turn will guide the approach to establishing a diagnosis and staging the disease, as follows:

1. Some individuals may prefer no treatment, particularly those with life-limiting comorbid conditions. In such individuals, neither surgical biopsy nor staging is justified. Aggressive surveillance using serial CT may be used to monitor symptoms for palliation.
2. Two categories of patients, who could potentially benefit from curative surgical resection based on the presence of a solitary, locally confined pulmonary lesion and documented absence of extrathoracic metastatic disease, will not proceed to surgery for completely different reasons.
  - a. One group would be considered ineligible for surgery due to sufficiently impaired cardiopulmonary function or other comorbidity that precludes general anesthesia.
  - b. A second group of individuals would otherwise be eligible for curative surgery but for personal reasons refuse surgical resection.

For either category of patients listed above, surgical diagnostic and staging procedures are contraindicated. Their options include functional imaging (PET, PET-CT, magnetic resonance imaging [MRI]), CT scan surveillance, and needle-based nonsurgical biopsy, including guided bronchoscopic procedures such as EBUS.

3. Patients who are candidates for curative surgical resection by virtue of documented (PET, PET-CT) absence of distant metastatic lesions, locally confined single tumors, and otherwise sound physical condition are eligible for any type of diagnostic and staging procedure.
4. In patients suspected of having lung cancer based on radiographic imaging (CT), functional imaging (PET, PET-CT) and clinical findings (signs and symptoms of lung cancer), a presumptive diagnosis must be confirmed, preferably by the least invasive method, as dictated by the patient's presentation and desire for definitive treatment.
5. For patients with extensive mediastinal infiltration of tumor and no distant metastases, it is suggested that radiographic (CT) assessment of the mediastinal stage is usually sufficient without invasive confirmation.
6. In patients with discrete mediastinal lymph node enlargement (and no distant metastases) with or without PET uptake in mediastinal nodes, invasive staging of the mediastinum is recommended over staging by imaging alone.

## BACKGROUND

### LUNG CANCER

Individuals who are suspected of having lung cancer may present with widely differing signs and symptoms related to the type of cancer (e.g., non-small-cell lung cancer [NSCLC] versus small-cell lung cancer), its location within the lung, and the stage of disease (i.e., localized, locoregionally advanced, metastatic). All three of the major parameters of type, location, and stage will dictate subsequent management of the cancer, determining whether it is primarily surgical or requires systemic chemotherapy. Early diagnosis of lung cancer is essential because of the uniformly poor prognosis when cancer is diagnosed later in the disease course.

Approximately 75% to 80% of newly diagnosed lung cancers are NSCLC. The clinical presentation and findings on computed tomography (CT) or a fluorine 18 fluorodeoxyglucose positron emission tomography (PET) scan of the chest will typically permit a presumptive diagnosis of lung cancer and differentiation between NSCLC and small-cell lung cancer. If small-cell lung cancer is suspected based on radiographic characteristics and other clinical

findings, a diagnosis is made by whatever means is the least invasive (e.g., sputum cytology, thoracentesis if an accessible pleural effusion is present, fine-needle aspiration of a supraclavicular node).<sup>1</sup> The diagnostic technique to evaluate suspected NSCLC is usually dictated by the apparent stage of the disease. NSCLC can present with extensive infiltration of the mediastinum, defined as a mass with no visible lymph nodes, or it may present as a solitary pulmonary nodule that may be bronchogenic or peripheral. In any patient with suspected NSCLC, the diagnosis should be established by the method that has the most favorable risk-benefit ratio.<sup>1</sup>

#### Diagnosis of Peripheral Pulmonary Nodules

Solitary pulmonary lesions are typically identified on plain chest radiographs or chest CT scans, often incidentally. Although most of these nodules will be benign, some will be cancerous. Peripheral lung lesions and solitary pulmonary nodules (most often defined as asymptomatic nodules less than eight mm) are more difficult to evaluate than larger, centrally located lesions. There are several options for diagnosis; however, none of the methods is ideal for safely and accurately diagnosing malignant disease in all patients.<sup>2</sup> Sputum cytology is the least invasive approach.<sup>1</sup> Reported sensitivity rates are relatively low and vary widely across studies, and sensitivity is even lower for peripheral lesions. Sputum cytology, however, has a high specificity, and a positive test may obviate the need for more invasive testing.

Flexible bronchoscopy, a minimally invasive procedure, is the most common approach to evaluating pulmonary nodules. The sensitivity of flexible bronchoscopy for diagnosing bronchogenic carcinoma has been estimated at 88% for central lesions and 78% for peripheral lesions.<sup>2</sup> For small peripheral lesions less than 1.5 cm in diameter, the sensitivity may be as low as 10%, due to the inability to reach into smaller bronchioles.

Transthoracic (percutaneous) needle aspiration, using CT guidance, can be performed for peripheral nodules that are beyond the reach of traditional bronchoscopy. The diagnostic accuracy of transthoracic needle aspiration tends to be as high or higher than that of flexible bronchoscopy for peripheral lesions; the sensitivity and specificity are both greater than 90%.<sup>2</sup> A disadvantage of transthoracic needle aspiration is that a pneumothorax could occur in as many as 15% of patients (range, 1%-15%). Between 1% and 7% will require chest tube insertion. PET scans are also highly sensitive for evaluating pulmonary nodules, yet may miss small lesions less than one cm in size. Surgical lung biopsy is the criterion standard for diagnosing pulmonary nodules but is an invasive procedure not indicated for all patients.

#### Staging of Lung Cancer and Assessment of Mediastinal Involvement

The stage of a lung cancer (its extent through the body) at diagnosis will directly impact the management approach for each patient.<sup>3,4</sup> The first step in staging is to identify whether the patient has the distant metastatic disease (M stage) or if the tumor is confined to the chest; this will determine whether treatment should be aimed at palliation or at a potential cure, respectively. If the primary tumor is confined (T stage), determining whether the mediastinal lymph nodes (N stage) are involved is a crucial factor in guiding therapy.

As with diagnostic procedures, there are a number of options for mediastinal staging. The choice of a noninvasive or invasive staging method is dictated by the patient's condition and whether he or she can tolerate or will elect surgery. Thus, staging procedures may be based on noninvasive imaging methods (i.e., CT or PET, or combined PET-CT), or may be fully invasive, such as mediastinoscopy—a surgical procedure that is performed under general anesthesia and is regarded as the reference standard for staging lung cancer.<sup>3</sup>

Recent advances in technology have led to enhancements that may increase the yield of established needle-based diagnostic methods that represent a third approach, between noninvasive and surgical procedures.<sup>1</sup> CT scanning equipment can be used to guide flexible bronchoscopy and bronchoscopic transbronchial needle biopsy but has the disadvantage of exposing the patient and staff to radiation.

## Endobronchial Ultrasound With Transthoracic Needle Aspiration

Among its potential applications, EBUS using ultrasound probes can locate and guide the sampling of pulmonary lesions and mediastinal lymphadenopathy.

EBUS uses two distinct types of transducers that have specific uses: radial probe and convex probe.

A radial probe EBUS comprises a 20- or 30-MHz rotating transducer to provide high-resolution 360° radial images. The probe is inserted into the airways via a standard therapeutic bronchoscope. With the use of an ultrathin bronchoscope combined with radial probe EBUS through a guide sheath, an endoscopist can reach and visualize the sixth- to eighth-generation bronchi, whereas a traditional bronchoscope can only reach the fourth-generation bronchi. The use of radial probe EBUS imaging allows the physician to verify visually that a lesion has been reached and to maintain position in the periphery to allow a needle biopsy to be performed for diagnosis.<sup>5</sup> These probes do not allow real-time imaging during the biopsy. For biopsy or tissue sampling, the target area is located by radial probe EBUS; the radial probe is subsequently retracted and is replaced with a biopsy or sampling device. Convex probe EBUS transducers are adjustable within a frequency range of five to 12 MHz. Such transducers are incorporated into the structure of a dedicated bronchoscope and provide real-time pie-slice sector views of 50° to 60° parallel to the axis of the bronchoscope. Convex probe EBUS with transbronchial needle aspiration (EBUS-TBNA) also can be used for staging the mediastinal nodes.<sup>6</sup> The curved linear probe technology allows real-time visualization and needle aspiration of a lesion. Because EBUS-TBNA of the mediastinal nodes may be performed under conscious sedation, it may be used in patients who are not surgical candidates but for whom accurate staging is needed to guide choice among systemic treatments, particularly targeted systemic agents such as tyrosine kinase inhibitors.<sup>7</sup>

## REGULATORY STATUS

A number of instruments are commercially available to perform EBUS-TBNA for diagnosis and staging of lung cancer. All have been cleared for marketing by the U.S. Food and Drug Administration through the 510(k) process and are shown in Table 1.

Table 1. FDA-Cleared Instruments Used to Perform EBUS-TBNA

Device Name	Manufacturer	Date Cleared	510(k)	Indications
EVIS EXERA Bronchofibervideoscope, Olympus BF type UC160F-OL8 bronchoscope and its diagnostic ultrasound transducer	Olympus Medical Systems	Aug 2004	K042140	To provide real-time endoscopic US imaging and US-guided FNA, including the upper airways and tracheobronchial tree
EU-M60 EUS EXERA Endoscopic Ultrasound Center	Olympus Medical Systems	Dec 2004	K04327	To acquire and to display high-resolution and high-penetration, real-time endoscopic US B-mode 2D and 3D images, including the upper airways and tracheobronchial tree
XBF-UC180F-DT8 Ultrasonic Bronchofibervideoscope and the ALOKA SSD-Alpha 5/10 Ultrasound System	Olympus Medical Systems	Jul 2007	K070983	To provide real-time endoscopic US imaging and US-guided FNA including the upper airways and tracheobronchial tree
SonoTip® II EBUS-TBNA Needle System	Medi-Globe	May 2009	K091257	For US-guided FNA of submucosal and extraluminal lesions of the tracheobronchial tree
EchoTip® Ultra High Definition Endobronchial Ultrasound Needle	Cook Medical	Jan 2010	K093195	For use in conjunction with an EBUS endoscope to gain access to and sample submucosal and extramural lesions within or adjacent to the tracheobronchial tree through the accessory channel of an EUS for FNA

Device Name	Manufacturer	Date Cleared	510(k)	Indications
PENTAX Ultrasound Video Bronchoscope EB-1970UK + HI VISION Preirus endoscopic ultrasound	PENTAX Medical	Apr 2014	K131946	To provide optical visualization of, ultrasonic visualization of, and therapeutic access to, the pulmonary tract including but not restricted to the nasal passages, pharynx, larynx, trachea, bronchial tree (including access beyond the stem), and underlying areas
SonoTip® Pro and Pro Flex EBUS-TBNA Needle System	Medi-Globe	May 2014	K133763	Intended for US-guided FNA of submucosal and extraluminal lesions of the tracheobronchial tree and gastrointestinal tract (e.g., lymph nodes, abnormal tissue in the mediastinum)
Expect™ Pulmonary Endobronchial Ultrasound Transbronchial Aspiration Needle	Boston Scientific	Nov 2015	K151315	For use with EBUS endoscopes for US-guided FNA of the submucosal and extramural lesions of the tracheobronchial tree

EBUS: endobronchial ultrasound; EUS: endoscopic ultrasound; FDA: Food and Drug Administration; FNA: fine-needle aspiration; TBNA: transbronchial needle aspiration; US: ultrasound.

## RELATED PROTOCOL

Electromagnetic Navigation Bronchoscopy

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

## REFERENCES

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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