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Medical Benefit		Effective Date: 12/01/19	Next Review Date: 01/21
Preauthorization	No	Review Dates: 09/10, 09/11, 01/12, 01/13, 01/14, 01/15, 01/16, 01/17, 01/18, 01/19, 09/19, 01/20	

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"> With suspicious peripheral pulmonary lesion(s) when flexible bronchoscopy alone or with endobronchial ultrasound are inadequate to sample the pulmonary lesion(s) 	Interventions of interest are: <ul style="list-style-type: none"> Electromagnetic navigation bronchoscopy with flexible bronchoscopy 	Comparators of interest are: <ul style="list-style-type: none"> Computed tomography-guided needle biopsy 	Relevant outcomes include: <ul style="list-style-type: none"> Test accuracy Test validity Other test performance measures Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> With enlarged mediastinal lymph node(s) 	Interventions of interest are: <ul style="list-style-type: none"> Electromagnetic navigation bronchoscopy with flexible bronchoscopy 	Comparators of interest are: <ul style="list-style-type: none"> Flexible bronchoscopy only Computed tomography-guided needle biopsy Endobronchial 	Relevant outcomes include: <ul style="list-style-type: none"> Test accuracy Test validity Other test performance measures Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> With lung tumor(s) who need fiducial marker placement prior to treatment when flexible bronchoscopy alone or with endobronchial ultrasound are considered inadequate to accomplish the procedure 	Interventions of interest are: <ul style="list-style-type: none"> Electromagnetic navigation bronchoscopy with placement of fiducial markers 	Comparators of interest are: <ul style="list-style-type: none"> Placement of fiducial markers using computed tomography 	Relevant outcomes include: <ul style="list-style-type: none"> Health status measures Treatment-related morbidity

DESCRIPTION

Electromagnetic navigation bronchoscopy (ENB) is intended to enhance standard bronchoscopy by providing a 3-dimensional roadmap of the lungs and real-time information about the position of the steerable probe during bronchoscopy. The purpose of ENB is to allow navigation to distal regions of the lungs, so that suspicious lesions can be biopsied and to allow fiducial markers placement.

SUMMARY OF EVIDENCE

For individuals who have suspicious peripheral pulmonary lesion(s) when flexible bronchoscopy alone or with endobronchial ultrasound are inadequate to sample the pulmonary lesion(s), the evidence includes meta-analyses, a randomized controlled trial, and uncontrolled observational studies. A 2015 meta-analysis of 17 studies of ENB reported a large pooled positive likelihood ratio but a small negative likelihood ratio (0.22; 95% confidence interval 0.15 to 0.32). Similarly, a 2014 meta-analysis of 15 studies found that navigation success was high, but diagnostic yield (64.9; 95% confidence interval 59.2 to 70.3) and negative predictive value (52.1; 95% confidence interval 43.5 to 60.6) were relatively low. Both systematic reviews assessed the methodological quality of the evidence as low. Results from two large prospective multicenter uncontrolled studies, AQuiRE and NAVIGATE, provide information about test characteristics and safety of ENB. An analysis of more than 500 patients included in the AQuiRE registry found a diagnostic yield of ENB that was lower than in other studies, and lower than bronchoscopy without ENB or endobronchial ultrasound (EBUS). In the US cohort of the NAVIGATE study, the 12-month diagnostic yield was 72.9%. Overall, 4.3% of patients experienced pneumothorax, and pneumothorax requiring hospitalization or intervention occurred in 35 of 1,215 patients (2.9%). Bronchopulmonary hemorrhage overall occurred in 2.5% of patients overall and Common Terminology Criteria for Adverse Events grade two or higher in 1.5%. There were no deaths related to the ENB device. Limitations of the published evidence preclude determining the effects of the technology on net health outcome. Evidence reported through clinical input supports that this use provides a clinically meaningful improvement in net health outcome and is consistent with generally accepted medical practice. ENB is generally reserved for the most difficult patients, who are poor or borderline candidates for surgery and transthoracic sampling. In this context, the "low yield" observed in observational studies was actually high for this highly selected population. ENB, when used as an option in the armamentarium of the bronchoscopist, is a highly useful and low-risk modality for proper diagnosis and staging of lung cancer. For example, patients who are able to achieve a positive biopsy result through ENB benefit by getting a diagnostic result to appropriately guide treatment while avoiding transthoracic needle biopsy which has a two to four times higher risk of pneumothorax than a bronchoscopic biopsy approach. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have enlarged mediastinal lymph nodes who receive ENB with flexible bronchoscopy, the evidence includes a randomized controlled trial and observational studies. Relevant outcomes are test accuracy and validity, other test performance measures, and treatment-related morbidity. There is less published literature on ENB for diagnosing mediastinal lymph nodes than for diagnosing pulmonary lesions. One randomized controlled trial identified found higher sampling and diagnostic success with ENB-guided transbronchial needle aspiration than with conventional transbronchial needle aspiration. EBUS, which has been shown to be superior to conventional transbronchial needle aspiration, was not used as the comparator. The randomized controlled trial did not report the diagnostic accuracy of ENB for identifying malignancy, and this was also not reported in uncontrolled studies. Limitations of the published evidence preclude determining the effects of the technology on net health outcome. Evidence reported through clinical input is not generally supportive of a clinically meaningful improvement in net health outcome. Mediastinal lymph nodes diagnosis was an early indication for ENB which has been largely replaced by EBUS. One could consider it in the uncommon scenario in which linear EBUS is not available and the patient is already having an ENB procedure for a peripheral nodule. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have lung tumor(s) who need fiducial marker placement prior to treatment when flexible bronchoscopy alone or with endobronchial ultrasound are inadequate to place the markers near the pulmonary lesion(s), the evidence includes one comparative observational study and several case series. Relevant outcomes are health status measures and treatment-related morbidity. In the largest series, a subgroup analysis of 258 patients from the NAVIGATE study, the subjective assessment of outcome was that 99.2% of markers were accurately placed and 94.1% were retained at follow-up (mean 8.1 days postprocedure). Pneumothorax of any grade

occurred in 5.4% of patients, and grade two or higher pneumothorax occurred in 3.1%. Limitations of the published evidence preclude determining the effects of the technology on net health outcome. Evidence reported through clinical input supports that this use provides a clinically meaningful improvement in net health outcome and is consistent with generally accepted medical practice. The key advantage of ENB placement is the markedly reduced risk of pneumothorax compared to the transthoracic approach. Patients being treated with targeted radiation are typically those with advanced respiratory disease who cannot undergo surgical resection. They are also more at risk for pneumothorax and resultant further complications. As the markers need to be near and not necessarily in a lesion, the accuracy advantage of a transthoracic approach is outweighed by the safety advantage of ENB over a transthoracic approach. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

POLICY

Electromagnetic navigation bronchoscopy (ENB) may be considered **medically necessary** for individuals with either suspicious peripheral pulmonary lesion(s) or with lung tumor(s) who need fiducial marker placement prior to treatment when flexible bronchoscopy alone or with endobronchial ultrasound are considered inadequate to accomplish the procedure.

Electromagnetic navigation bronchoscopy is considered **investigational** for use with flexible bronchoscopy for the diagnosis of mediastinal lymph nodes as well as all other uses not covered above.

POLICY GUIDELINES

Bronchoscopists performing ENB requires specific training in the procedure.

Enlarged Mediastinal Nodes was an early indication for ENB which has been largely replaced by EBUS. One could consider it in the uncommon scenario in which linear EBUS is not available and the patient is having an ENB procedure for a peripheral nodule in any case.

BACKGROUND

PULMONARY NODULES

Pulmonary nodules are identified on plain chest radiographs, or chest computed tomography scans. Although most nodules are benign, some are cancerous, and early diagnosis of lung cancer is desirable because of the poor prognosis when it is diagnosed later.

Diagnosis

The method used to diagnose lung cancer depends on a number of factors, including lesion size, shape, location, as well as the clinical history and status of the patient. Peripheral lung lesions and solitary pulmonary nodules (most often defined as asymptomatic nodules less than 6 mm) are more difficult to evaluate than larger, centrally located lesions. There are several options for diagnosing malignant disease but none of the methods is ideal. Sputum cytology is the least invasive approach. Reported sensitivity rates are relatively low and vary widely across studies; sensitivity is 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 an established approach to evaluate pulmonary nodules. The sensitivity of flexible bronchoscopy for diagnosing bronchogenic carcinoma has been estimated at 88% for central lesions and 78% for peripheral lesions. For small peripheral lesions (<1.5 cm in diameter), the sensitivity may be as low as 10%. The diagnostic accuracy of transthoracic needle aspiration for solitary pulmonary nodules tends to be higher than that of bron-

choscopy; the sensitivity and specificity are both approximately 94%. A disadvantage of transthoracic needle aspiration is that a pneumothorax develops in 11% to 25% of patients, and 5% to 14% require insertion of a chest tube. Positron emission tomography scans are also highly sensitive for evaluating pulmonary nodules yet may miss lesions less than 1 cm in size. A lung biopsy is the criterion standard for diagnosing pulmonary nodules but is an invasive procedure.¹⁻³

Advances in technology may increase the yield of established diagnostic methods. Computed tomography scanning equipment can be used to guide bronchoscopy and bronchoscopic transbronchial needle biopsy but have the disadvantage of exposing the patient and staff to radiation. Endobronchial ultrasound by radial probes, previously used in the perioperative staging of lung cancer, can also be used to locate and guide sampling of peripheral lesions. Endobronchial ultrasound is reported to increase the diagnostic yield of flexible bronchoscopy to at least 82%, regardless of lesion size or location.¹

Marker Placement

Another proposed enhancement to standard bronchoscopy is electromagnetic navigation bronchoscopy. Electromagnetic navigation bronchoscopy enhances standard bronchoscopy by providing a three dimensional road-map of the lungs and real-time information about the position of the steerable probe during bronchoscopy. The purpose of electromagnetic navigation bronchoscopy is to allow navigation to distal regions of the lungs. Once the navigation catheter is in place, any endoscopic tool can be inserted through the channel in the catheter to the target. This includes insertion of transbronchial forceps to biopsy the lesion. Also, the guide catheter can be used to place fiducial markers. Markers are loaded in the proximal end of the catheter with a guidewire inserted through the catheter.

REGULATORY STATUS

In 2004, the superDimension/Bronchus™ inReach™ system (superDimension) was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. The system includes planning and navigation software, a disposable extended working channel, and a disposable steerable guide. The FDA-cleared indication is for displaying images of the tracheobronchial tree that aids physicians in guiding endoscopic tools in the pulmonary tract. The device is not intended as an endoscopic tool; it does not make a diagnosis; and it is not approved for pediatric use. As of June 2016, the current version of the product is the Medtronic SuperDimension Navigation System (Medtronic).

In 2009, the ig4™ EndoBronchial system (Veran Medical) was cleared for marketing by the FDA through the 510(k) process. The system was considered to be substantially equivalent to the inReach™ system and is marketed as the SPiN Thoracic Navigation System™.

In April 2018, LungVision (Body Vision Medical) was cleared for marketing by the FDA through the 510(k) process (K172955). The FDA determined that this device was substantially equivalent to existing devices for use “segment previously acquired 3D CT [computed tomography] datasets and overlay and register these 3D segmented data sets with fluoroscopic live X-ray images of the same anatomy in order to support catheter/device navigation during pulmonary procedure”. FDA product code: EOQ.

Several other navigation software-only systems have been cleared for marketing by the FDA through the 510(k) process. They include:

- In 2008, the LungPoint® virtual bronchoscopic navigation (VPN) system (Broncus Technologies).
- In 2010, the bf-NAVI VPN system (Emergo Group).

FDA product codes: JAK, LLZ.

Two ENB systems are currently available, the SPIN Thoracic Navigation System™ (Veran Medical Technologies) and the superDimension™ navigation system. [Medtronic]

RELATED PROTOCOLS

Endobronchial Ultrasound for Diagnosis and Staging of Lung Cancer

Stereotactic Radiosurgery and Stereotactic Body Radiotherapy

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