IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Proteomic and gene expression tests have been proposed as methods for assessing the risk of malignancy in patients with pulmonary nodules found incidentally on radiological exam.

MEDICAL POLICY CRITERIA

Proteomic screening and/or gene expression profiling for the evaluation of pulmonary nodules is considered investigative, including but not limited to:

- A. Xpresys Lung®
- B. Xpresys Lung 2®
- C. EarlyCDT®-Lung
- D. Percepta® Bronchial Genomic Classifier

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

CROSS REFERENCES

1. Genetic and Molecular Diagnostic Testing, Genetic Testing, Policy No. 20
BACKGROUND

PULMONARY NODULES

Pulmonary nodules are a common clinical problem that may be found incidentally on a chest x-ray or computed tomography (CT) scan or during lung cancer screening studies of smokers. The primary question after the detection of a pulmonary nodule is the probability of malignancy, with subsequent management of the nodule based on various factors such as the radiographic characteristics of the nodules (e.g., size, shape, density) and patient factors (e.g., age, smoking history, previous cancer history, family history, environmental/occupational exposures). The key challenge in the diagnostic workup for pulmonary nodules is appropriately ruling in patients for invasive diagnostic procedures and ruling out patients who should forgo invasive diagnostic procedures. However, due to the low positive predictive value of pulmonary nodules detected radiographically, many unnecessary invasive diagnostic procedures and/or surgeries are performed to confirm or eliminate the diagnosis of lung cancer.

PLASMA-BASED PROTEOMIC SCREENING FOR PULMONARY NODULES

Proteomics is the study of the structure and function of proteins. The concentration, structure, and other characteristics of proteins in various bodily tissues, fluids, and other materials has been proposed as a method to identify and manage various diseases, including cancer.

Plasma-based proteomic screening has been investigated to risk-stratify pulmonary nodules as likely benign to increase the number of patients who undergo serial CT scans of their nodules (active surveillance), instead of invasive procedures such as CT-guided biopsy or surgery. Additionally, proteomic testing may also determine a likely malignancy in clinically low-risk or intermediate-risk pulmonary nodules, thereby permitting earlier detection in a subset of patients.

Xpresys Lung® is a plasma-based proteomic screening test that measures the relative abundance of proteins from multiple disease pathways associated with lung cancer using an analytic technique called multiple reaction monitoring mass spectroscopy. The role of the test is to aid physicians in differentiating likely benign from likely malignant nodules. If the test yields a likely benign result, patients may choose active surveillance via serial CT scans to monitor the pulmonary nodule. If the test yields a likely malignant result, invasive diagnostic procedures would be indicated. The test is therefore only used in the management of pulmonary nodules to rule in or out invasive diagnostic procedures and does not diagnose lung cancer. The second generation of the test, Xpresys Lung 2®, is also known as BDX-XL2. This test combines measurements of two proteins with five clinical characteristics to assess the risk of malignancy.

EarlyCDT-Lung is a serum-based test that measures seven autoantibodies associated with small cell and non-small cell lung cancer (NSCLC). Unlike the Xpresys tests, the role of this test is to aid physicians in “ruling in” a diagnosis of malignancy.

GENE EXPRESSION PROFILING FOR AN INDETERMINATE BRONCHOSCOPY RESULT
Gene expression profiling is the measurement of the activity of genes with cells. Messenger RNA serves at the bridge between DNA and functional proteins. An important role of gene expression profiling in molecular diagnostics is to detect cancer-associated gene expression of clinical samples to assess for the risk for malignancy.

The Percepta® Bronchial Genomic Classifier is a 23-gene, gene expression profiling test that analyzes genomic changes in the airways of current or former smokers to assess a patient's risk of having lung cancer, without the direct testing of a pulmonary nodule. The test is indicated for current and former smokers following an indeterminate bronchoscopy result to determine the subsequent management of pulmonary nodules (e.g., active surveillance or invasive diagnostic procedures), and does not diagnose lung cancer.

REGULATORY STATUS

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. Xpresys Lung® and Xpresys Lung 2® (Indi, acquired in 2018 by Biodesix), and Percepta® Bronchial Genomic Classifier (Veracyte) are available under the auspices of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

EVIDENCE SUMMARY

Human Genome Variation Society (HGVS) nomenclature[1] is used to describe variants found in DNA and serves as an international standard. It is being implemented for genetic testing medical evidence review updates starting in 2017. According to this nomenclature, the term “variant” is used to describe a change in a DNA or protein sequence, replacing previously-used terms, such as “mutation.” Pathogenic variants are variants associated with disease, while benign variants are not. The majority of genetic changes have unknown effects on human health, and these are referred to as variants of uncertain significance.

Validation of the clinical use of any diagnostic test focuses on three main principles: (1) analytic validity, which refers to the technical accuracy of the test; (2) clinical validity, which refers to the diagnostic performance of the test (sensitivity, specificity, positive and negative predictive values) in detecting clinical disease; and (3) clinical utility, which refers to how the results of the diagnostic test will be used to change management of the patient and whether these changes in management lead to clinically important improvements in health outcomes.

This evidence review is focused on clinical validity and utility, particularly evidence from well-designed studies related to the ability of test results to:

- Guide decisions in the clinical setting related to either treatment, management, or prevention; and
- Improve health outcomes as a result of those decisions

PLASMA-BASED PROTEOMIC SCREENING OF PULMONARY NODULES

Xpresys Lung® and Xpresys Lung 2®
A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Pecot (2012) validated a seven-peak matrix-assisted laser desorption ionization mass spectrometry proteomic signature in two prospective cohorts of patients with one or more pulmonary nodules on chest CT (total n=379 [cohort A: n=265, mean nodule size 31.2 mm; cohort B: n=114, mean nodule size 19.4 mm]). The area under the curve for the matrix-assisted laser desorption ionization mass spectrometry score alone for cohort A was 0.64 (95% confidence interval [CI] 0.58 to 0.71) and for cohort B was 0.64 (95% CI 0.52 to 0.75). For cohort A, adding the proteomic signature to clinical and chest CT data did not significantly improve prognostic value. For cohort B, however, prognostic ability improved when the proteomic signature was added to clinical and chest CT data, as measured by the integration discrimination improvement index (integration discrimination improvement, 20%; p<0.001). Similarly, in a subgroup of 100 nodules from 5 to 200 mm in diameter, the proteomic signature added prognostic value (integration discrimination improvement, 15%; p<0.001).

Two studies were identified that reported on the development and validation of slightly different versions of a plasma-based classifier test to predict malignancy (Xpresys Lung®), one with 13 proteins and one with 11.

Li (2013) reported on the development and validation of the 13-protein version, proposed to differentiate benign from malignant pulmonary lung nodules. The test identifies classifier proteins likely modulated by a few transcription regulators (NF2L2, AHR, MYC, and FOS) associated with lung cancer and inflammation. The classifier was developed in a set of 143 serum samples from subjects with either benign or stage IA lung cancer, with a nodule size 4 to 30 mm. The test was locked and validated in a set of 52 benign and 52 tumor samples. Test characteristics are shown in Table 1. These results were independent of age, nodule size, or smoking history.

Vachani (2015) reported on the validation of an 11-protein plasma classifier designed to identify likely benign lung nodules in a sample of 141 plasma samples associated with indeterminate pulmonary nodules 8 to 30 mm in diameter. This retrospective, blinded analysis evaluated existing samples. The 11 proteins in this assay were reported to be derived from the 13-protein sample in Li (2013), described above. The performance of the classifier in identifying benign nodules was tested at predefined reference values. For example, using a population, based non-small-cell lung cancer prevalence estimate of 23% for indeterminate pulmonary nodules 8 to 30 mm in diameter, the classifier identified likely benign lung nodules with a 90% negative predictive value (NPV) and a 26% positive predictive value, at 92% sensitivity and 20% specificity, with the lower bound of the classifier’s performance at 70% sensitivity and at 48% specificity. Additional sample diagnostic characteristics, selected to keep the study’s target NPV of 90%, are shown in Table 1. Classifier scores for the overall cohort were statistically independent of patient age, tobacco use, nodule size, and chronic obstructive pulmonary disease diagnosis. The classifier also demonstrated incremental diagnostic performance in combination with a four-parameter clinical model.

### Table 1. Summary of Diagnostic Performance Studies for Xpresys Lung® Tests to Predict Malignancy

<table>
<thead>
<tr>
<th>Study</th>
<th>Prevalence, %</th>
<th>Cutoff Value</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>NPV, %</th>
<th>PPV, %</th>
</tr>
</thead>
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<tr>
<td>Li (2013)</td>
<td>15</td>
<td>0.60</td>
<td>71</td>
<td>44</td>
<td>90</td>
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<td></td>
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<td></td>
<td>25</td>
<td>0.42</td>
<td>90</td>
<td>27</td>
<td>89</td>
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</tr>
<tr>
<td>Study</td>
<td>Prevalence, %</td>
<td>Cutoff Value</td>
<td>Sensitivity, %</td>
<td>Specificity, %</td>
<td>NPV, %</td>
<td>PPV, %</td>
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<td>--------</td>
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</tr>
<tr>
<td>Vachani (2015)[4]</td>
<td>23.1</td>
<td>0.35</td>
<td>93.2</td>
<td>18.5</td>
<td>90.1</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>23.1</td>
<td>0.34</td>
<td>93.7</td>
<td>18.5</td>
<td>90.1</td>
<td>25.6</td>
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<tr>
<td></td>
<td>23.1</td>
<td>0.33</td>
<td>94.7</td>
<td>17.6</td>
<td>90.3</td>
<td>25.5</td>
</tr>
</tbody>
</table>

NPV: negative predictive value; PPV: positive predictive value.

Vachani (2015) reported on a multicenter prospective-retrospective study of patients with indeterminate pulmonary nodules. A plasma protein classifier was used on 475 patients with nodules 8 to 30 mm in diameter who had an invasive procedure to confirm the diagnosis. Using the classifier, 32.0% (95% CI 19.5% to 46.7%) of surgeries and 31.8% (95% CI 20.9% to 44.4%) of invasive procedures (biopsy and/or surgery) on benign nodules could have been avoided, while 24.0% (95% CI 19.2% to 29.4%) of patients with malignancy would have been triaged to CT surveillance. By comparison, 24.5% (95% CI 16.2% to 34.4%) of patients with malignancy were routed to CT surveillance using clinical parameters alone.

Sylvestri (2018) evaluated the Xpresys Lung 2®, which consists of two protein markers and five clinical characteristics. There were 178 patients included in this prospective cohort study, who had nodules 8 to 30 mm in diameter and a clinician-assessed probability of cancer of ≤50%.[6] Among these patients, the Xpresys integrated classifier had a sensitivity of 97%, a specificity of 44%, and an NPV of 98%. Of the 66 patients who had a “likely benign” test result, one had a malignant nodule.

No evidence directly demonstrating improved outcomes in patients managed with proteomic testing was identified. Indirect evidence suggests that 32.0% of surgeries and 31.8% of invasive procedures (biopsy and/or surgery) on benign nodules could have been avoided, while 24.0% of patients with malignancy would have been triaged to CT surveillance.[5] Compared with the standard care plan, some patients without cancer will have avoided an unnecessary invasive procedure, which is weighed against the increase in missed cancers in patients who had lung cancer but tested as negative on the proteomic classifier with high NPV test.

**EarlyCDT®-Lung**

In a prospective registry trial, Massion (2017) assessed the value of the EarlyCDT®-Lung test in patients with an identified lung nodule.[7] A cohort of 1987 individuals were evaluated, and 451 had at least one nodule. Of those, 296 met inclusion criteria and received imaging, pathology, and testing with EarlyCDT®-Lung. Patients with a positive EarlyCDT®-Lung result had a twofold greater relative risk of developing lung cancer as compared with those with a negative test result. When EarlyCDT®-Lung was added to risk models, diagnostic performance with high specificity (>92%) and positive predictive value (>70%) were improved.

Jett (2014) published the results from the first 1699 patients for whom US physicians ordered EarlyCDT®-Lung test.[8] Six-month outcome analysis was based on 1613 patients. Six-month follow-up for the positives/negatives was 99%/93%. Sixty-one patients (4%) were identified with lung cancer, only 25 of whom tested positive by EarlyCDT®-Lung (sensitivity=41%). A positive EarlyCDT®-Lung test on the current panel was associated with a 5.4-fold increase in lung cancer incidence versus a negative test result. Comparing performance of the seven-autoantibody panel (7AAB) and the six-autoantibody panel (6AAB), the 7AAB showed highly statistically significant (p < 0.0001) improved specificity over the 6AAB panel (91% versus 83%, respectively). The sensitivities of the 6AAB and 7AAB panels were not statistically different (46% versus 37%), respectively. The PPV offered by the 7AAB panel was nearly 2×
better than the previous 6AAB panel (16% versus 9%, respectively). Eight out of fourteen NSCLCs (57%) detected as positive were early stage cancer (I or II). The investigators concluded that EarlyCDT®-Lung may be a complementary tool to CT for detection of early lung cancer.

Chapman (2012) published the results of a case-control study involving 235 subjects with newly diagnosed lung cancer and 235 healthy controls used to evaluate both six- and seven-antigen versions of the EarlyCDT®-Lung test.[9] In addition, two prospective consecutive series of 776 and 836 individuals at an increased risk of developing lung cancer were also evaluated with both versions of the EarlyCDT®-Lung test. The six-antigen panel gave a sensitivity of 39% and a specificity of 89%, while the seven-antigen panel resulted in a sensitivity of 41% and a specificity of 91%. Once adjusted for occult cancers in the population, this resulted in a specificity of 93%.

Lam (2011) published a case-control study describing the sensitivity of the EarlyCDT®-Lung test, which evaluated samples for tumor associated autoantibodies found in individuals with lung cancer, including 574 subjects from four separate cohorts.[10] Group one (n=122) included subjects with only small cell lung cancer (SCLC); group two (n=249) was composed of 97% of subjects with non-small cell lung cancer (NSCLC); group three (n=122) included only subjects with NSCLC; and group four (n=81), was made up of 62% of subjects with NSCLC. For group one the results indicated a sensitivity of 57% for SCLC (specificity data not calculated). The sensitivity and specificity for group two was 34% and 87% for NSCLC. For group three sensitivity and specificity was 31% and 84% for NSCLC. Finally, in group four sensitivity and specificity was 35% and 89% for NSCLC and 43% and 89% for SCLC. No significant difference in positivity was reported for the EarlyCDT®-Lung test with regard to different lung cancer stages.

Initial clinical validation of the EarlyCDT®-Lung test was reported by Boyle (2011).[11] This study used the same three populations as the Murray study.[12] The optimal assay cut-off point was calibrated to target a 90% specificity, which provided the optimal overall accuracy based on Monte Carlo simulations. For the three separate populations, sensitivity was 36%, 39% and 37%. The specificity was 91%, 89%, 90%, approximating the 90% specificity of test calibration. Using a population prevalence of 2.0%, the positive predictive value (PPV) ranged from 7.0%-7.2% and the negative predictive value (NPV) was 98.6%. The area under the curve by ROC analysis was 0.63. There were no significant differences in accuracy of the test by lung cancer stage.

**GENE EXPRESSION PROFILING OF INDETERMINATE BROCHOSCOPY RESULTS**

Whitney (2015) reported on the development and initial validation of an RNA-based gene expression classifier from airway epithelial cells designed to be predictive of cancer in current and former smokers undergoing bronchoscopy for suspected lung cancer.[13] Samples were from patients in the Airway Epithelium Gene Expression In the Diagnosis of Lung Cancer (AEGIS) trials, which were two prospective, observational, cohort studies (AEGIS-1, AEGIS-2), for current or former smokers undergoing bronchoscopy for suspected lung cancer. Cohort details are described in Silvestri (2015), below. A total of 299 samples from AEGIS-1 (223 cancer-positive and 76 cancer-free subjects) were used to derive the classifier. Data from 123 patients in a prior study with a nondiagnostic bronchoscopy were used as an independent test set. In the final model, the classifier included 17 genes, patient age, and gene expression correlates and was reported as a dichotomous score (≥0.65 as cancer-positive, <0.65 as
cancer-negative). The performance characteristics of the classifier in the training and test set are shown in Table 2.

Silvestri (2015) reported on the diagnostic performance of the gene expression classifier developed in Whitney (2015), in a sample of 639 patients enrolled in two multicenter prospective studies (AEGIS-1, n=298 patients; AEGIS-2, n=341 patients). The study enrolled patients who were undergoing clinically indicated bronchoscopy for a diagnosis of possible lung cancer and had a history of smoking. Before the bronchoscopy, the treating physician assessed each patient’s probability of having cancer with a five-level scale (<10%, 10-39%, 40-60%, 61-85%, >85%). Patients were followed until a diagnosis was established (either at the time of bronchoscopy or subsequently by another biopsy means) or until 12 months after bronchoscopy.

A total of 855 patients in AEGIS-1 and 502 patients in AEGIS-2 met enrollment criteria. After exclusions due to sample quality issues, loss to follow-up, lack of final diagnosis, or nonprimary lung cancer, 341 subjects were available in the validation set for AEGIS-2. For AEGIS-1, patients were randomized to the development (described above) or validation (n=298) sets. Of the 639 patients in the validation study who underwent bronchoscopy, 272 (43%; 95% CI 39 to 46%) had a nondiagnostic examination. The prevalence of lung cancer was 74% and 78% in AEGIS-1 and AEGIS-2, respectively. The overall test characteristics in AEGIS-1 and AEGIS-2 are summarized in Table 2. The classifier improved prediction of cancer compared with bronchoscopy alone, but comparisons with a clinical predictor were not reported. For the subset of 272 patients with a nondiagnostic bronchoscopy, the classifier performance was presented by the pretest physician-predicted risk of cancer. For most subpopulations, there was a very high NPV. However, there were 13 false negatives, 10 of which were considered at high (>60%) risk of cancer pre-bronchoscopy.

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>AUC (95% CI)</th>
<th>Sensitivity, % (95% CI)</th>
<th>Specificity, % (95% CI)</th>
<th>PPV, % (95% CI)</th>
<th>NPV, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whitney (2015)</td>
<td>Training set, entire population (n=299)</td>
<td>0.78 (0.73 to 0.82)</td>
<td>93</td>
<td>57</td>
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<tr>
<td></td>
<td>Training set, subset with nondiagnostic bronchoscopy (n=134)</td>
<td>0.78 (0.71 to 0.85)</td>
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<tr>
<td></td>
<td>Test set with nondiagnostic bronchoscopy (n=123)</td>
<td>0.81 (0.73 to 0.88)</td>
<td>92 (78 to 98)</td>
<td>53 (42 to 63)</td>
<td>47 (36 to 58)</td>
<td>94 (83 to 99)</td>
</tr>
<tr>
<td>Silvestri (2015)</td>
<td>AEGIS-1 (n=298)</td>
<td>0.78 (0.73 to 0.83)</td>
<td>88 (83 to 95)</td>
<td>47 (37 to 58)</td>
<td></td>
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<td></td>
<td>AEGIS-2 (n=341)</td>
<td>0.74 (0.68 to 0.80)</td>
<td>89 (84 to 92)</td>
<td>47 (36 to 59)</td>
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<tr>
<td></td>
<td>Subset of all patients with nondiagnostic bronchoscopy, by pretest cancer probability risk</td>
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<tr>
<td>Study</td>
<td>Population</td>
<td>AUC (95% CI)</td>
<td>Sensitivity, % (95% CI)</td>
<td>Specificity, % (95% CI)</td>
<td>PPV, % (95% CI)</td>
<td>NPV, % (95% CI)</td>
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<tr>
<td>Risk &lt;10% (n=61)</td>
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<td>7 (1 to 24)</td>
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<tr>
<td>Risk 10%-60%</td>
<td>(n=84)</td>
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<td></td>
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<td>40 (27 to 55)</td>
<td>91 (75 to 98)</td>
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<tr>
<td>Risk &gt;60% (n=108)</td>
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<td></td>
<td></td>
<td>84 (75 to 81)</td>
<td>38 (15 to 65)</td>
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<td>Risk unknown (n=19)</td>
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<td></td>
<td></td>
<td></td>
<td>47 (21 to 73)</td>
<td>100 (40 to 100)</td>
</tr>
</tbody>
</table>

AUC: area under the curve; CI: confidence interval; GEC: gene expression classifier.

Vachani (2016) reported on rates of invasive procedures from AEGIS-1 and -2.[15] Of 222 patients, 188 (85%) had an inconclusive bronchoscopy and follow-up procedure data available for analysis. Seventy-seven (41%) patients underwent an additional 99 invasive procedures, which included surgical lung biopsy in 40 (52%) patients. Benign and malignant diseases were ultimately diagnosed in 62 (81%) and 15 (19%) patients, respectively. Among those undergoing surgical biopsy, 20 (50%) were performed in patients with benign disease. If the classifier had been used to guide decision making, procedures could have been avoided in 21 (50%) of 42 patients who had additional invasive testing. Further, among 35 patients with an inconclusive index bronchoscopy who were diagnosed with lung cancer, the sensitivity of the classifier was 89%, with four (11%) patients having a false-negative classifier result. Invasive procedures after an inconclusive bronchoscopy occur frequently, and most are performed in patients ultimately diagnosed with benign disease.

No evidence directly demonstrating improved outcomes in patients managed with the Percepta® Bronchial Genomic Classifier (BGC) was identified. One decision impact study reporting on clinical management changes, but not on outcomes after decisions for invasive procedures were made, has suggested that, in at least some cases, decisions for invasive procedures may be changed. Ferguson (2016) reported on the impact of the Percepta® BGC on physician decision making for recommending invasive procedures among patients with an inconclusive bronchoscopy.[16] The results revealed that a negative (low-risk) result might reduce invasive procedure recommendations in patients diagnosed with benign disease.

Avoiding invasive procedures in situations where patients are at very low likelihood of having lung cancer is likely beneficial, given the known complications of invasive procedures (e.g., pneumothorax). However, reductions in unnecessary invasive procedures must be weighed against outcomes and harms associated with a missed diagnosis of lung cancer at earlier, more treatable stages.

**PRACTICE GUIDELINE SUMMARY**

**AMERICAN COLLEGE OF CHEST PHYSICIANS**

The American College of Chest Physicians (2013) has published evidence-based clinical practice guidelines on the diagnosis and management of lung cancer, including pulmonary nodules.[17] These guidelines make an number of recommendations, including:

- In the individual with a solid, indeterminate nodule that measures > 8 mm in diameter, we suggest that clinicians estimate the pretest probability of malignancy either
qualitatively by using their clinical judgment and/or quantitatively by using a validated model (Grade 2C).

- In the individual with a solid, indeterminate nodule that measures > 8 mm in diameter and low to moderate pretest probability of malignancy (5%–65%), we suggest that functional imaging, preferably with PET, should be performed to characterize the nodule (Grade 2C).
- In the individual with a solid, indeterminate nodule that measures > 8 mm in diameter and a high pretest probability of malignancy (> 65%), we suggest that functional imaging should not be performed to characterize the nodule (Grade 2C).

NATIONAL COMPREHENSIVE CANCER NETWORK

NCCN guidelines for non-small cell lung cancer include recommendations for pulmonary nodule risk assessment.[18] For patients presenting with an incidental finding of a nodule suspicious for lung cancer, the guidelines recommend:

- Multidisciplinary evaluation including thoracic surgeons, thoracic radiologists, and pulmonologists to determine the likelihood of a cancer diagnosis and the optimal diagnostic or follow-up strategy.
- Risk assessment including patient factors (age, smoking history, cancer history, etc) and radiologic factors.

For patients with an incidental finding of a solid nodule >8 mm on chest CT, the guidelines recommend considering CT at three months, PET/CT, or biopsy.

SUMMARY

It appears that plasma-based proteomic tests may be helpful for assessing risk of cancer in patients that have pulmonary nodules, but there is not enough research to show that these tests can improve health outcomes for these patients. In addition, clinical guidelines based on research do not recommend this testing. Therefore, proteomic screening, including but not limited to Xpresys Lung® and Xpresys Lung 2®, is considered investigational for the evaluation of pulmonary nodules.

There is not enough research to show that gene expression tests can improve health outcomes for patients with pulmonary nodules. In addition, clinical guidelines based on research do not recommend this testing. Therefore, gene expression profiling, including but not limited to Percepta® Bronchial Genomic Classifier, is considered investigational for the evaluation of pulmonary nodules.

REFERENCES


17. Detterbeck, FC, Lewis, SZ, Diekemper, R, Addrizzo-Harris, D, Alberts, WM. Executive Summary: Diagnosis and management of lung cancer, 3rd ed: American College of


### CODES

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<th>Codes</th>
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<td>Oncology (lung), mass spectrometric analysis of galectin-3-binding protein and scavenger receptor cysteine-rich type 1 protein M130, with five clinical risk factors (age, smoking status, nodule diameter, nodule-spiculation status and nodule location), utilizing plasma, algorithm reported as a categorical probability of malignancy</td>
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*Date of Origin: August 2018*