Performance of the Percepta Genomic Sequencing Classifier (GSC) as a Complement to Bronchoscopy for Indeterminate Lung Nodules

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RATIONALE

- The goal of lung nodule management is to make an early accurate diagnosis of malignant nodules while decreasing invasive procedures for benign nodules.[1]
- Bronchoscopy is a minimally invasive biopsy modality for the evaluation of lung lesions for malignancy, but the diagnostic yield ranges from 30% to 60%, depending upon the location and size of the lesion.[2,3]
- The Percepta Genomic Sequencing Classifier (GSC) is a gene expression classifier that utilizes whole transcriptome mRNA sequencing from bronchial brushings to re-classify the pre-test risk of malignancy (ROM) to higher or lower risk in lung nodules of former or current smokers.[4]
- Percepta GSC is an ensemble of four machine-learning algorithms trained on >1600 samples from four independent cohorts. The classifier was locked and prospectively validated on three independent prospective multi-center cohorts (412 patients).
- We evaluated the sensitivity of bronchoscopy, the Percepta GSC classifier, and the combination of the two in detecting malignant lung nodules.

OBJECTIVE AND ENROLLMENT CRITERIA

Objective:

We aimed to evaluate the sensitivity of bronchoscopy, the Percepta GSC classifier, and the combination of both in the detection of malignant nodules, using a subset of 158 patients from two independent multicenter prospective observational cohorts (AEGIS I and II cohorts) with low and intermediate pre-test ROM.

Patient Eligibility Criteria:

Inclusion:

- 21 years or older with a pulmonary nodule on Chest CT scan
- Current or former smoker (> 100 cigarettes in a lifetime)
- Underwent bronchoscopy for clinical reasons

Exclusion:

- Patients with concurrent or prior cancers at the time of enrollment
- Patients unable to provide informed consent

METHODS

- Percepta GSC is an ensemble of four machine learning models which combines genomic and clinical features, as well as their interactions to achieve high negative and positive predictive values for risk classification of indeterminate lung nodules.
- Forty-four of the 158 patients diagnosed with primary lung cancer enrolled in the Percepta GSC validation study with low (3 patients) or intermediate (41 patients) pre-test risk of malignancy were included in this analysis.
- Diagnosis of malignant or benign nodules was determined through an adjudication process or review by expert pulmonologists.
- We assessed the sensitivity of bronchoscopy for malignancy with and without the Percepta GSC classifier results by:
  a. nodule size
  b. nodule location
  c. lung cancer stage
  d. lung cancer histologic types

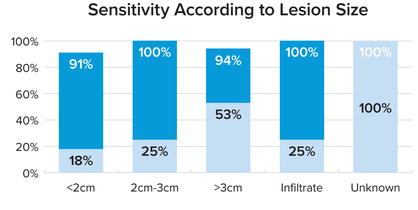
RESULTS

Overall Performance of Bronchoscopy, Percepta GSC and Combination for Low and Intermediate Risk Lung Nodules

	Bronchoscopy	Percepta GSC	Bronchoscopy + Percepta GSC
Sensitivity	41%	92%	96%
Negative Predictive Value (NPV)	81%	96%	—
Specificity	100%	45%	—

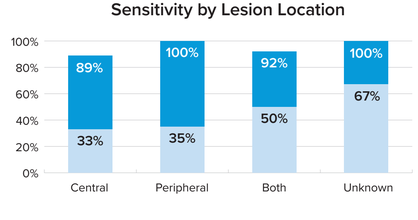
The overall sensitivity, NPV and specificity for indeterminate lung nodules for Bronchoscopy, Percepta GSC, and combined Bronchoscopy plus Percepta GSC are shown.

Combined Sensitivity of Percepta GSC and Bronchoscopy According to Lesion Size



The sensitivity of bronchoscopy was 18% for smaller lesions (<2cm) and highest in larger lesions (>3cm), while the sensitivity of Percepta GSC and Bronchoscopy was consistently high between 91% to 100% across all lesion sizes. The sample size for lesions <2cm, 2cm-3cm, >3cm, infiltrates, and Unknown was 11, 8, 17, 4, and 4, respectively.

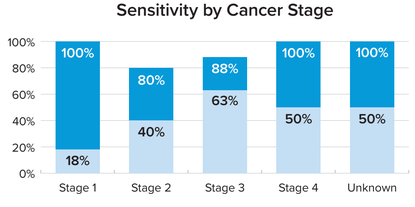
Combined Sensitivity of Percepta GSC and Bronchoscopy According to Nodule Location

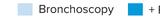


The sensitivity of bronchoscopy ranged from 33% to 67%, depending upon nodule location, while the combined sensitivity of Bronchoscopy and Percepta GSC ranged from 89% to 100% regardless of nodule location. The sample size for lesions with central, peripheral, central and peripheral, and unknown location was 9, 20, 12, and 3, respectively.

RESULTS (CONT'D.)

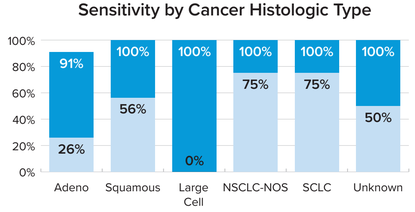
Combined Sensitivity of Percepta GSC and Bronchoscopy According to Lung Cancer Stage (NSCLC)

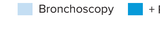




The sensitivity of bronchoscopy was 18% for Stage 1 and 63% for Stage 3, while the combined sensitivity of Bronchoscopy plus Percepta GSC was 100% for Stage 1, and 88% for Stage 3. The sample size for Stage 1, Stage 2, Stage 3, Stage 4, and Unknown was 17, 5, 8, 4, and 4, respectively.

Combined Sensitivity of Percepta GSC and Bronchoscopy According to Lung Cancer Histology





Across different lung cancer histologic types, the sensitivity of bronchoscopy ranged between 0% and 75%, while the combined sensitivity of Bronchoscopy and Percepta GSC ranged between 91% and 100%. The sample size for Adeno, Squamous, Large Cell, NSCLC-NOS, SCLC, and Unknown was 23, 9, 2, 4, 4, and 2, respectively.

CONCLUSION

- The Percepta GSC classifier substantially increases bronchoscopy sensitivity from 41% to 96% in detecting malignancy in low and intermediate risk nodules.
- The combination of Bronchoscopy with Percepta GSC showed enhanced sensitivity across nodule size, location, cancer stage, and cancer histologic type in low and intermediate risk nodules ultimately proven to be cancerous.

References

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Disclosures

1. Veracyte, Inc is the sponsor of this study.
2. Dr Travis Dotson is a consultant for Veracyte, Inc.