BACKGROUND
• The goal of lung nodule evaluation is to expedite treatment of malignant nodules and minimize procedures for benign nodules.
• While guidelines recommend bronchoscopic workup for patients with intermediate risk nodules, up to 50% of these bronchoscopies are nondiagnostic.
• The Percepta Genomic Sequencing Classifier (GSC) development is based on the concept of “field of injury,” which shows altered cancer associated gene expression in bronchial epithelial cells in current/prior smokers with malignancy.
• Percepta GSC utilizes RNA sequencing of transcripts from 1232 genes, as well as clinical factors, to achieve both down-classification and up-classification of pre-test ROM.

OBJECTIVE AND ENROLLMENT CRITERIA
Objective: We aimed to prospectively validate the accuracy of next-generation Percepta, the Genomic Sequencing Classifier (GSC) using a combined cohort from AEGIS I and II.
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)
• An inconclusive bronchoscopy
EXCLUSION
• Patients with concurrent or prior cancers at the time of enrollment

METHODS
Study Design and Patient Population:
• The training set included 801 patients from four cohorts and the validation set included 412 patients from three independent cohorts.
• Two bronchial brushings were obtained during the initial bronchoscopy from cytologically normal appearing bronchial epithelial cells in the main bronchus.
• Patients in each cohort were followed until a diagnosis (judged by panel of 3 physicians) was established or for 12 months after bronchoscopy.
• The treating physician determined the pre-test probability of risk of malignancy (low (<10%), intermediate (10-60%), high (>60%)) prior to the bronchoscopy.

Algorithm Development and Clinical Validation:
• Machine-learning algorithms ingesting RNA sequencing results and clinical results were used from >1600 patients to train the new Percepta GSC.
• The final classifier is an ensemble of four models which combine genomic and clinical features, to achieve both down-classification and up-classification of pre-test ROM.

CONCLUSION
1. Percepta GSC classifier utilizes RNA sequencing of transcripts from 1232 genes, as well as clinical factors, in four different algorithms that are combined in a final ensemble model.
2. Percepta GSC was trained on >1600 samples from four cohorts and prospectively validated on three independent cohorts (412 patients).
3. Percepta GSC provides additional functionalities:
   - Down-classifies intermediate-risk patients to very low-risk with PPV >90%
   - Up-classifies intermediate-risk patients to high-risk with PPV >65%
   - Up-classifies low-risk patients to very low-risk with PPV >95%
   - Up-classifies high-risk patients to very high with PPV >90%

REFERENCES