# AI Discrimination of Adenocarcinoma vs. Squamous Carcinoma in Detecting NSCLC Non-Invasively from Sputum Using Cell-CT™ Single-Cell Analysis in 3D

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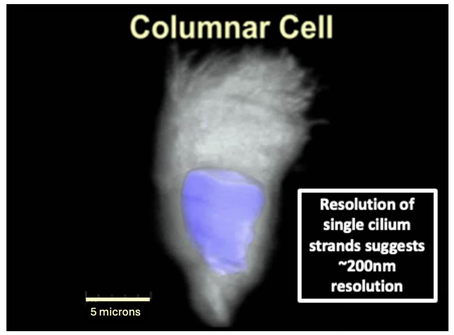
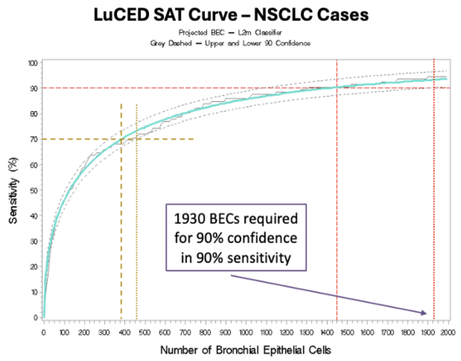
*Background*

## LuCED® Test Based on Cell-CT Analysis:

The Cell-CT platform analyzes cells in true 3D, measuring >900 morphology biomarkers in each single cell with isometric 200nm resolution. The image below is of a columnar cell from the lung epithelium. LuCED AI identifies cells with abnormal features that are then cytologically diagnosed using VisionGate's digital pathology workstation, CellGazer™. Cells that are in neoplastic categories, from atypia to cancer, trigger a LuCED report of abnormality. In published work, sensitivity to stage 1 lung cancer is 94% and specificity is 97%[1]. Sensitivity is selectable, as it is governed by the number of normal bronchial epithelial cells (BECs) that are enumerated following the SAT curve shown below.




## Motivation:

The Cell-CT can detect abnormal pulmonary cells from sputum in cytologic categories from atypia through to malignancy. In this study, we present results showing the ability to sub-classify abnormal cells into pre-malignant and malignant categories. Malignant cells are further sub-classified into adenocarcinoma and squamous carcinoma. These classifiers expand the clinical utility of the LuCED assay to indicate a malignant process for immediate triage.

1. Wilbur, D. C., et-al (2015). Automated 3-dimensional morphologic analysis of sputum specimens for lung cancer detection: Performance characteristics support use in lung cancer screening. *Cancer Cytopathol*, *123*(9), 548-556. https://doi.org/10.1002/cncy.21565

*Methods*

## Specimens:

Three-day spontaneous cough sputum specimens were collected from biopsy-confirmed cancer patients and patients at high risk of lung cancer. The LuCED assay was used to identify abnormal cells. Abnormal cells were further subclassified in this study. The table below indicates the number of cells in cytologic categories of pre-cancer and malignancy and further indicates cancer type within the malignant set.

| Cell Type | Sub Type | N-Cells |
|---|---|---|
| Pre-Cancer | | 623 |
| Malignant | Adenocarcinoma | 208 |
| | Squamous Carcinoma | 53 |
| | Other | 113 |

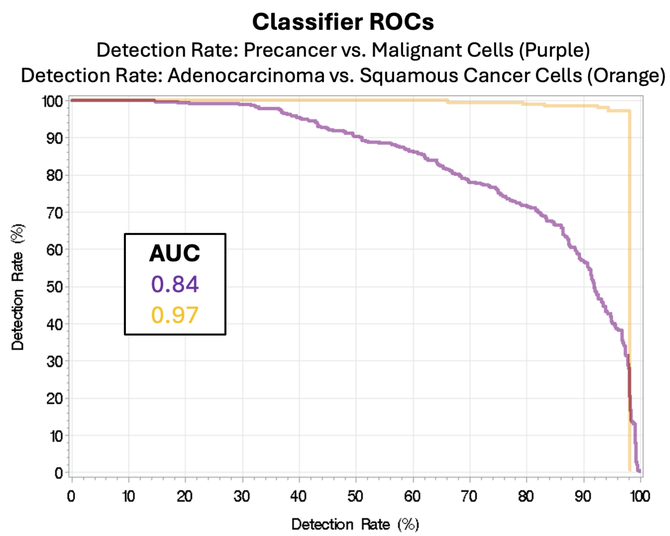
## Methods:

- Sputum samples were prepped using standard fixation and staining methods and processed by the Cell-CT.
- LuCED AI classifiers were used to identify cells with abnormal features. These cells were identified into cytologic categories producing the data in the table.
- Classifiers development followed a supervised learning program to regress cell features to cytologic ground truth through adaptively boosted logistic regression. Cross validation was used to ensure classifiers were not over trained.
- Two classifiers were created:
  - Malignant cells vs. precancer cells
  - Malignant cells: adenocarcinoma vs. squamous carcinoma

*Results and Conclusions*

## Results:

ROC curves for the malignant vs. precancer cell classifier and the classifier that discriminates adenocarcinoma from squamous carcinoma cells are presented in the figure below, including AUC values.




This analysis shows that the Cell-CT may be used to further stratify abnormal cells into pre-malignant and malignant categories. Malignant cells were further subclassified into adenocarcinoma and squamous carcinoma categories. A malignant indication increases the urgency of patient triage whereas malignant cell subtyping provides guidance in nodule characterization and patient management.

**3D cell analysis enables sub-classification of LuCED detected abnormal cells into precancer and malignant categories which can be further subclassified into adenocarcinoma and squamous carcinoma**

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