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Early detection of lung cancer based on three-dimensional, morphometric analysis of cells from sputum

Meyer, Katdare, Presley, Wilbur, Bell, Steinhauer, Hayenga, Neumann, Nelson

An interim study of sensitivity and specificity of the LuCED test for early lung cancer detection

Background

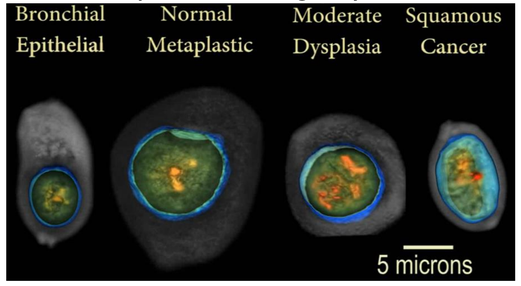
LuCED® Test for Early Lung Cancer Detection

Automatically detects lung cancer cells based on 3D single cell imaging and classification

Sputum Prep: Dissolves mucus, stains chromatin, enriches for bronchial epithelial cells.

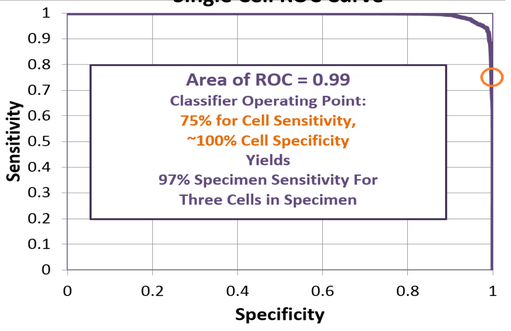
Cell-CT® Processing: Automatically analyzes cells in true 3D with isometric, sub-micron resolution.

Examples of Cells imaged by Cell-CT



Single-Cell Classification: Morphometric classifier detects glandular atypia, moderate/marked dysplasia, and cancer cells.

Single Cell ROC Curve



Cytopathologist Review: Detected cells suspicious for abnormality are confirmed by human review.

Methods

Specimen and Study Population:

- Non-invasive, three-day spontaneous cough sputa collected using a fixative-containing specimen vials.
- A total of 70 cases studied;
  - 30 normal cases.
  - 40 cases with biopsy confirmed lung cancer.

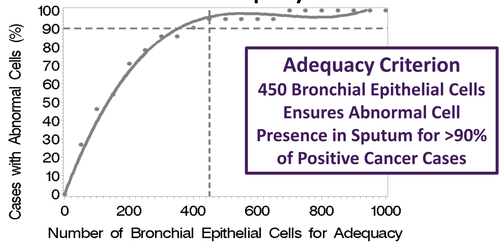
Specimen Processing:

- Fixed sputum was pooled, enriched for Cell-CT processing.
- Cells in each specimen were imaged in 3D on the Cell-CT.
- Abnormal cells automatically identified by the Cell-CT classifier.
- Processing ended upon abnormal cell discovery, when specimen was exhausted or adequacy criterion met.

LuCED Adequacy Criterion:

- Defines when the lung is sufficiently sampled by sputum.
- Criterion ensures processing continues until abnormal cells appear in sputum from lung cancer patients.
- Adequacy rate assessed for cases with macrophages and normal bronchial epithelial cells.

LuCED Adequacy Curve



Case Sensitivity:

- Sensitivity is the rate of Cell-CT detected cancer-positive cases.
- Sensitivity was analyzed by tumor histology, stage and size.

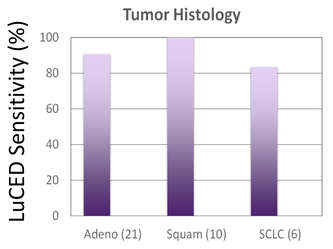
Cell Specificity:

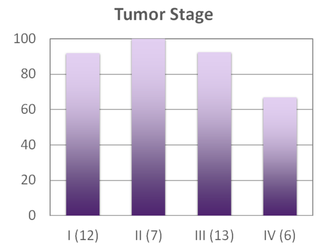
- The number of normal cells analyzed was recorded (N_Cells).
- Cell specificity = 100% x (1 – FalsePositives/N_Cells).

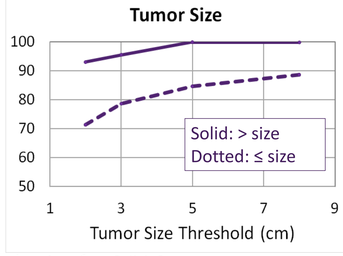
Results and Conclusions

Case Sensitivity

Adequate Cases (Abnormal Cells or Bronchial Epithelial ≥ 450)	Cases w/ Abnormal Cells	Cases detected by Cell-CT	Overall Sensitivity (%)
40	36	36	90.0







- Sensitivity is consistent by stage and histology within NSCLC. Note low sample size for S IV Cancer.
- Cell-CT classifier automatically detects every case with imaged abnormal cells.
- LuCED sensitivity increased for larger tumors.
- Overall lung cancer detection sensitivity is 90% and early stage (SI & SII) detection sensitivity is **94.7%.**

Cell Specificity

- 30 normal specimens processed.
  - 3 COPD, 5 benign nodules, 1 bronchial chondroma, 22 with no disease.
- 27,751 cells processed with 258 false positive cells found: The overall cell specificity is **99.1%**.
- Minor variation in specificity by disease.

Adequacy Rate

- 15 cases processed until either exhausted or until adequacy criterion met.
- 13 cases met adequacy criterion: the adequacy rate for a single LuCED test is **86.7%**.

Analysis of Sputum by LuCED Provides Non-Invasive Detection of Lung Cancer with 94.7% Sensitivity for Early Stage Lung Cancer And >99% Specificity