New Assay for Smoking Status Based on 3D Imaging of Pulmonary Macrophages

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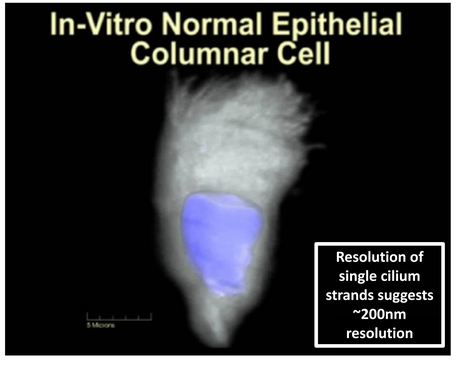
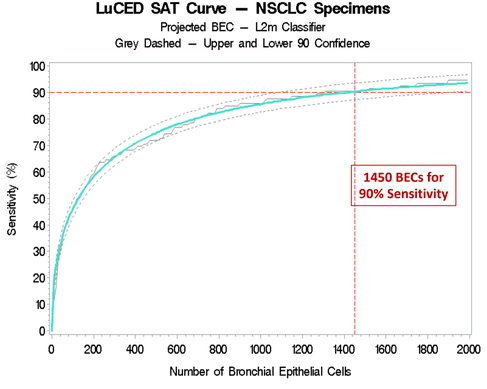
Background

PneuVision® Test using Cell-CT® Analysis:

The Cell-CT instrument analyzes cells in 3D, measuring true 3D morphometry with isometric 200nm resolution. The image below is of a columnar cell from the lung epithelium. PneuVision® AI identifies cells with abnormal features that are then cytologically diagnosed using VisionGate's digital pathology workstation, CellGazer™. Cells that are in neoplastic categories of atypia through cancer trigger a PneuVision report of abnormality. In published work, sensitivity and specificity both exceed 90%. Sensitivity is selectable as it is governed by the number of normal bronchial epithelial cells (BECs) that are counted, following the SAT curve shown below. False positive case reports may occur when normal cells are diagnosed incorrectly as abnormal through the digital pathology process.





Motivation:

The Cell-CT™ platform images cells in 3D with isometric, submicron resolution and measures orientation invariant 3D features in each cell. The Cell-CT is being used to identify abnormal pulmonary epithelial cells in sputum to indicate early-stage lung cancer*. Sputum also contains pulmonary macrophages that ingest inhaled contaminants from smoking. We hypothesize that the Cell-CT with machine learning would discover subtle phenotypic characteristics in macrophages to differentiate current and never smokers. Using sputum from patients without lung cancer and cells identified by the macrophage detection classifier, we developed a second classifier to produce the smoking index to discriminate macrophages from current and non-smoking patients.

Methods

Specimens:

Three-day spontaneous cough sputum samples were collected from non-cancer cases of Never, Former and Current smokers. The table indicates case count numbers by smoking status and data partition. The training and testing partitions were used to create and evaluate the smoking index.

Case Count by Smoking Status

Partition	Never	Former	Current
Training	10	0	58
Testing	16	41	61

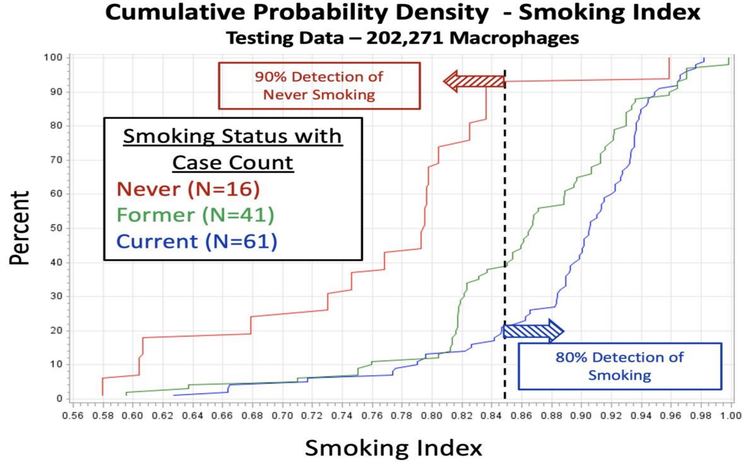
Methods:

- Sputum samples were prepped using standard fixation and staining methods and processed by the Cell-CT.
- Pulmonary macrophages were identified using a pre-defined classifier to detect cytologically normal macrophages. 10,116 and 202,271 macrophages were detected for training and testing sets.
- 503 orientation invariant morphometric biosignatures were computed for each macrophage.
- Using the training set and smoking status as ground truth, the smoking index probability was computed through forward selection to reduce the dimensionality of the solution and adaptively boosted multivariate logistic regression.
- The smoking index was computed as the median of the smoking index probability for all macrophages by case.
- The resulting algorithm was applied to the testing data.

Results and Conclusions

Results:

- Cumulative probability density curves were drawn for the training and testing sets for the smoking index for Never, Former, and Current smoking patients.
- Excellent discrimination between Never(90%) and Current(80%) smokers was observed on both training and testing sets, demonstrating the robustness of the algorithm.
- The response of the Smoking Index for Former smokers indicates a partial regression of the effect of smoking upon cessation.



The Smoking Index Detects Subtle Morphometric Signatures in Normal Pulmonary Macrophages to Detect and Assess the Effect of Smoking

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