Three Dimensional Cytologic Examination: Performance of the Cytopathologist Review Using CellGazer in the LuCED® Test for Lung Cancer Screening

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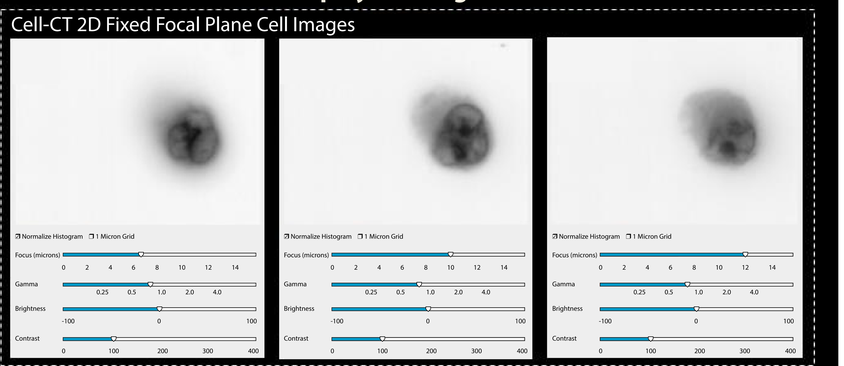
Background

1. **Sputum Prep:** Enriches for bronchial epithelial cells.
2. **Cell-CT® Processing:** Automatically computes and analyzes 3D images to identify cells with abnormal features.
3. **CellGazer® Workstation:** Presents a set of 2D fixed focal plane images and 3D tomographic images for about 0.5% of all cells that are then reviewed by a cytopathologist.
4. **Cytopathologist Review:** Cells suspicious for cancer are confirmed independently using the CellGazer workstation.
5. **LuCED® Performance:** LuCED achieves 92% sensitivity for lung cancer at 95% specificity:
   *Cancer Cytopath*ology 2015; 123(9):548.

Adenocarcinoma Cell as Imaged by The Cell-CT and Displayed Using CellGazer



At left, the cell is shown in maximum intensity projection. Since grey values in the 3D image are associated with various cell features a look-up table that maps cell structures to color and opacity values was established to produce the other cell images. In these images, the cytoplasm is represented in translucent white, the nucleus in opaque blue, the loose chromatin and nucleoplasm in translucent green and the condensed chromatin, and nucleoli are represented in opaque red.

Methods

- A reference set of adjudicated 3D images created by LuCED including normal and abnormal cells was presented to three independent cytopathologists:
  Two with extensive experience using Cell-CT images, and one with minimal experience.
  - The adjudicated set of 3D images comprised 37 abnormal (cancer) cells and 37 normal cells
- The figure shows an example of the navigation tools in CellGazer that facilitate cell review:
  - At the top, a cell is shown at three focal depths using the focal plane stack tool. In practice, a continuous gradient of focal planes are available to the reviewer.
  - At the bottom, the same cell is shown in 3D using color to illustrate cell components. These images can then be rotated by the reviewer for complete cell viewing.
  - CellGazer provides a means through which the cytopathologist can indicate normal or abnormal status for the cell and provide annotation.
- Using the adjudicated cell diagnosis as the ground truth, the sensitivity and specificity was determined for each cytopathologist.

Results

Cell Sensitivity

- Experienced cytopathologists achieved 97% and 95% sensitivities for cancer cells.
- The less experienced cytopathologist achieved 86% sensitivity for cancer cells.

Cell Specificity

- Experienced cytopathologists achieved 100% specificities for normal cells.
- The less experienced cytopathologist achieved 89% specificity for normal cells.

Conclusions

- LuCED attains excellent discrimination of cells in sputum to identify a small portion (0.5%) with features of an abnormal cell for final review by a cytopathologist.
- Results of review of an adjudicated reference cell set indicate that learning and experience are required for accurate assessment of cell images using CellGazer in the LuCED test.
- Once training has been given, LuCED can achieve high levels of consistency for different cytopathologists to achieve highly sensitive, highly specific identification of lung cancer.

Using LuCED®, trained cytopathologists can produce consistent identification of patient lung cancer with high sensitivity and high specificity

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