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TITLE: Three-Dimensional Cellular Morphometry: A New Horizon for Cytology and Cancer Detection

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PRESENTATION TYPE: Poster or Platform

CURRENT CATEGORY: Lung and Mediastinum

ABSTRACT BODY:

Introduction: The Cell-CT™ produces 3D volumetric computed reconstructions of cells in isometric, sub-micron resolution based on optical projection tomographic microscopy. Utilizing the 3D cell images, VisionGate, Inc. is developing the cytometric LuCED® test to analytically score sputum samples for evidence of cell dysplasia and cancer. The LuCED test measures cellular 3D features that are more powerful for cancer detection than their 2D analogues. Some cell features are not visible in 2D and emerge only in the 3D cell image. These new 3D features yield analytical evidence toward more accurate disease detection and basic morphometry for cell biology. In this study, we present a statistical analysis of the occurrence rate by cell type of a 3D cell feature called nuclear invagination. Invaginations have been noted by other researchers, who use techniques such as Fluorescence Recovery After Photo-bleaching.

Materials and Methods: The LuCED test comprises a series of steps starting with preparation of a sputum specimen, including fixation and staining with hematoxylin. Thus, the Cell-CT images show the 3D distribution of chromatin and residual absorption of hematoxylin. Cells of each type found in sputum were volumetrically sampled, as were lung cancer cells from culture. Cell diagnosis was confirmed through a user interface that presented Cell-CT fixed focal plane images to simulate a standard microscopic cell examination. Movies of rotating 3D cell volumes were produced for each cell, representing the cell by maximum intensity projection and by volume-rendering with color and opacity transfer functions that automatically rendered the cytoplasm in translucent white, the nucleus in opaque blue, the general nucleoplasm in translucent green and the nucleoli in opaque red. An example of a 3D lung adenocarcinoma cell is shown in Figure 1 through 4.

Chromatin reorganizes under cancer, which affects the intra-nuclear chromatin as well as the hetero-chromatin that lines the nuclear wall. The Cell-CT volume rendered image follows the nuclear surface, and, when the heterochromatin is depleted, the surface becomes invaginated, often leading to intra-nuclear chromatin voids. An example showing invaginations for a lung adenocarcinoma cell is given in Figure 2. The number of nuclear invaginations was counted for a set of normal and abnormal cells. The one sided t-test test was used to verify that differentiation of invagination count by cell type were statistically valid.

Results: Lung cells (numbers) were gathered for study: Adenocarcinoma Cells (639), Columnar Epithelial Cells (471), Squamous Intermediate Cells (2143), Metaplastic Cells (128), Macrophages (1869), other White Blood Cells (1500). Cells were harvested from the A549 (Bronchial Alveolar Carcinoma) cell line, normal cells were gathered from spontaneously produced sputum.

The mean count of nuclear invaginations for the adenocarcinoma population is 5.01, and for the other normal cells studied the mean count is 0.017 giving 95% confidence that cancer cells have more invaginations than normal cells.

Conclusions: Results demonstrate efficacy of the Cell-CT to render new, cell-type specific 3D morphometric features, not available for routine 2D cytology. Discovery of new 3D features will likely continue, with benefits to improve cytology, cell biology, and automated cell classification.

(No Table Selected)

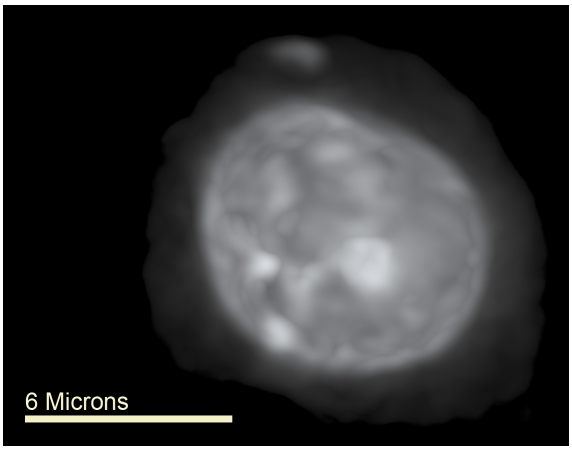

Figure 1: Adenocarcinoma cell in maximum intensity projection.

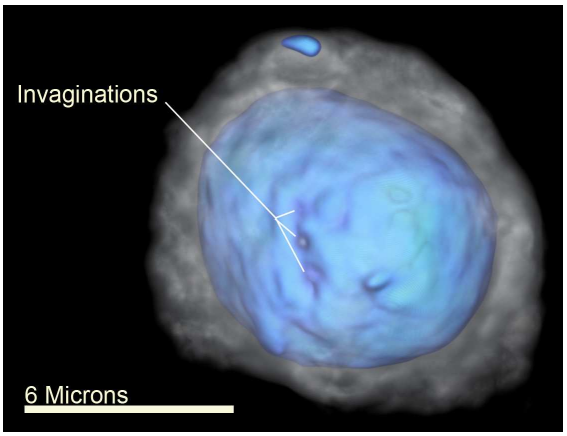

Figure 2: Volume rendered adenocarcinoma cell with invaginations. Cytoplasm is translucent white, nucleus is opaque blue.

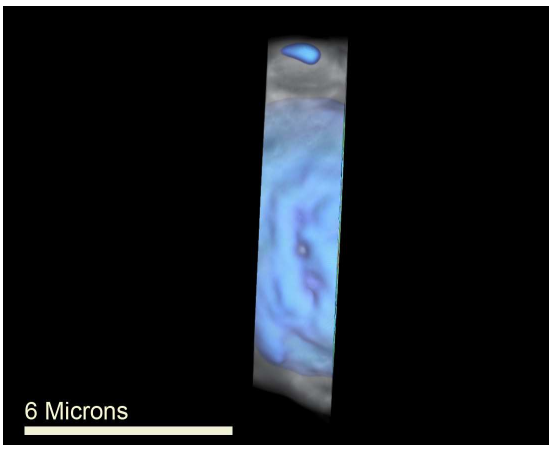

Figure 3: Volume rendered and cropped adenocarcinoma cell.

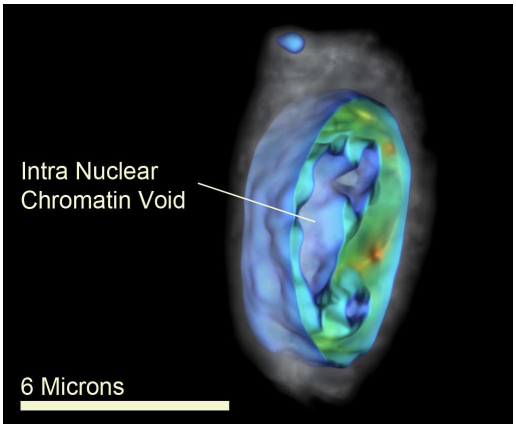

Figure 4: Volume rendered, cropped and rotated adenocarcinoma cell. Cytoplasm is in white, the nucleus in opaque blue; green designates the general nucleoplasm and red, the nucleoli.
