

# Nuclear Morphological Changes in Papillary Thyroid Carcinoma Cell: The Utility of a 3-Dimensional (3D) Holographic Microscopy in Cytology

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Received date: December 05, 2018; Accepted date: December 12, 2018; Published date: December 18, 2018

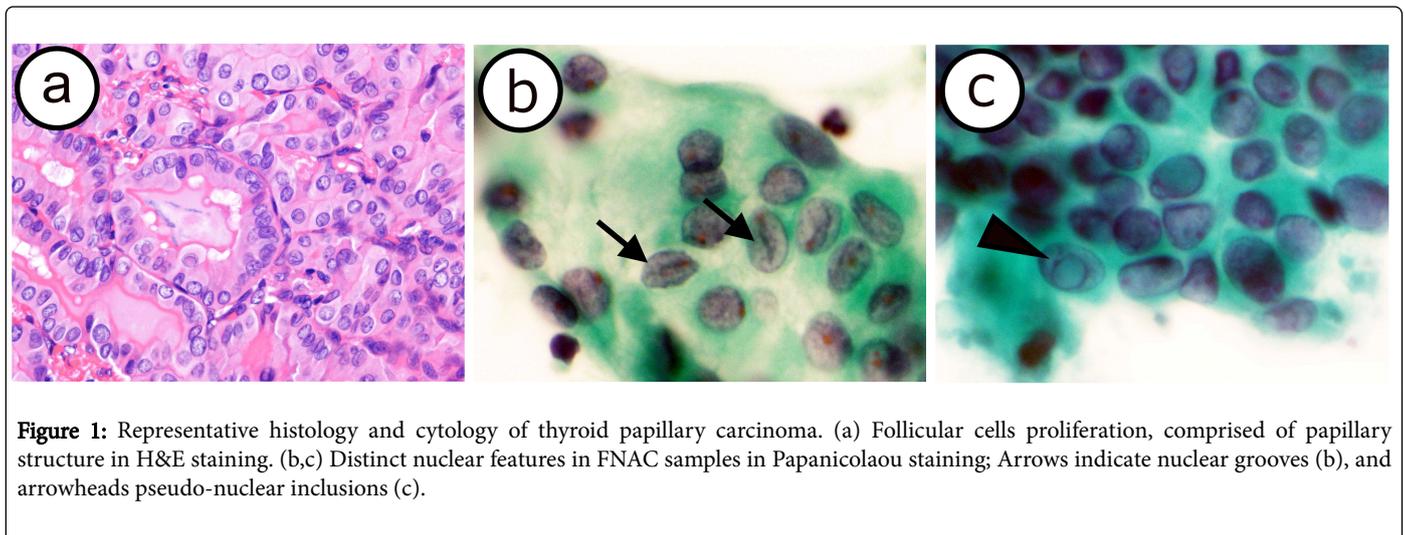
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## Image Article

Fine needle aspiration cytology (FNAC) is an essential method to diagnose thyroid nodules. To diagnose papillary thyroid carcinoma (Figure 1a), distinct nuclear morphological changes such as nuclear groove (Figure 1b) and pseudo-nuclear inclusion (Figure 1c) are crucial features. At times, findings by FNAC with conventional cytology and findings by liquid-based cytology method are ambiguous. Subsequently, re-biopsy or even diagnostic resection is required. Additional or alternative methods to FNAC would be advantageous in diagnosing thyroid nodules.

Optical diffraction tomography (ODT) microscopy (HT-2H, Tomocube Inc., Daejeon, Korea) is a 3D-holographic microscope to

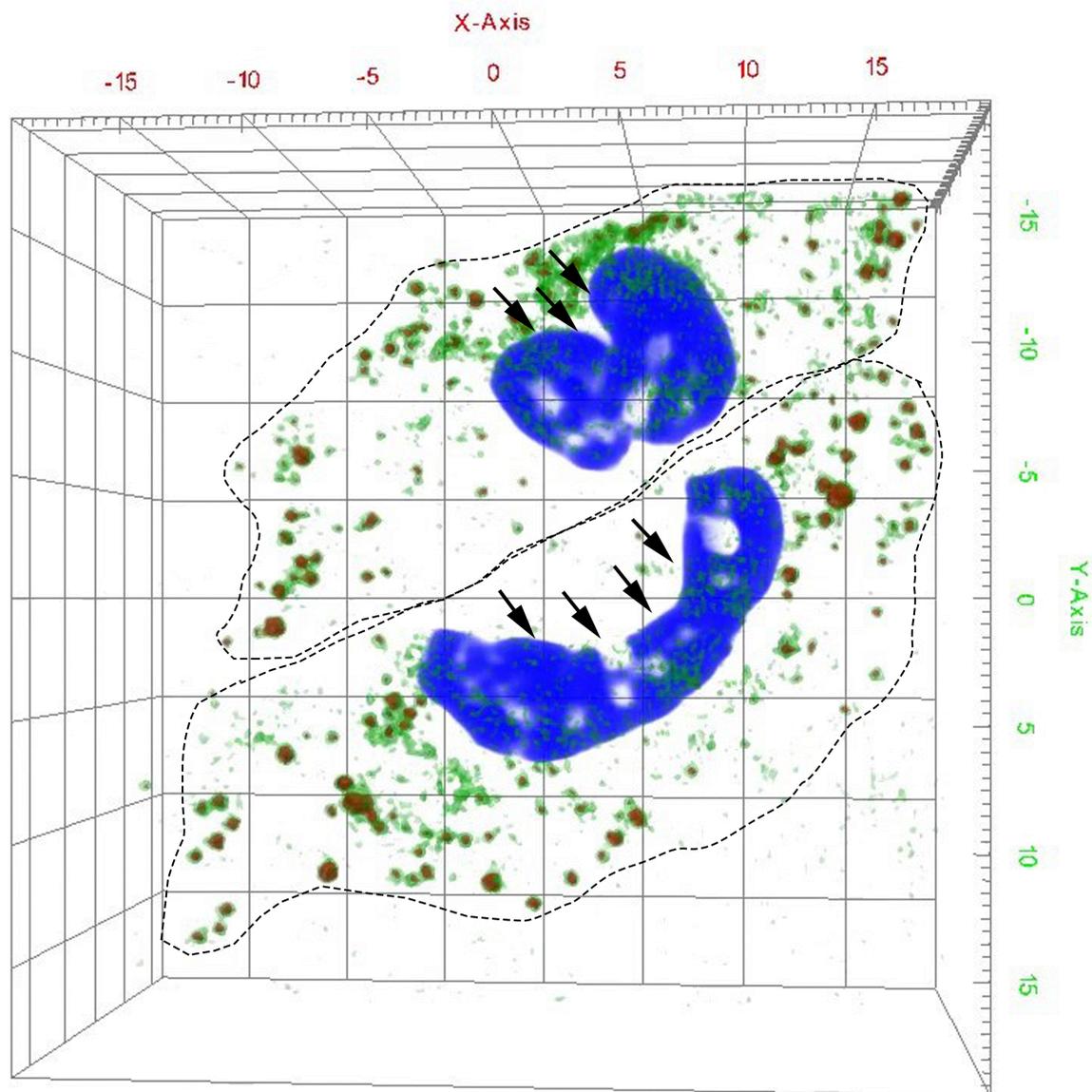
scan cells in three dimensions. This microscope has 110 nm lateral and 356 nm axial optical resolution. Image reconstruction is performed according to the reflection index and the thickness of the samples, which provides morphological information. Using the objective lenses with a magnification of 60x, nuclear, nucleoli, and lipid droplets, and other cytoplasmic organelles can be observed, similar to confocal laser microscopy. KTC-1 is a human papillary thyroid carcinoma cell-line, established from the malignant pleural effusion of a recurrent thyroid carcinoma patient. Detection of morphological changes of nuclear of KTC-1 cells by the phase-contrast microscope is not possible by conventional monolayer culture. Hence, formalin-fixed KTC-1 cells were stained with 4',6-diamidino-2-phenylindole (DAPI) and observed by HT-2H.



**Figure 1:** Representative histology and cytology of thyroid papillary carcinoma. (a) Follicular cells proliferation, comprised of papillary structure in H&E staining. (b,c) Distinct nuclear features in FNAC samples in Papanicolaou staining; Arrows indicate nuclear grooves (b), and arrowheads pseudo-nuclear inclusions (c).

The hollow, irregular nuclear shapes of KTC-1 cells were clearly detected (Figure 2). These shapes indicate a nuclear groove and pseudo nuclear inclusion. Thus, observation and detection of nuclear morphological changes using whole cell images of FNAC nodule

samples in 3D may be possible. ODT successfully captured nuclear morphological changes. Use of 3D-holographic microscopes may provide an alternative method or provide additional information for thyroid nodule diagnosis in cytology.



**Figure 2:** KTC-1 cells observed by 3D-holographic microscope. Dot-lines outline a single cell. Arrows indicate the hollow and irregular shape of the nucleus.

## Acknowledgement

This work is supported by the Japanese Association of University Women and Children's Cancer Association of Japan. The authors thank Dr. Norisato Mitsutake, Nagasaki University, for providing KTC-1 cell-

lines, and LMS Co., Ltd. Scientific Instruments Div., Kiyoko Kawahara, Takenori Fujii, Kiyoshi Teduka, Yoko Kawamoto and Taeko Kitamura for their skillful assistance.