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Predicting histological subtypes of Follicular Variant of Papillary Thyroid Carcinoma based on cytomorphology. Can cytomorphology optimize use of molecular testing?

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Title: Predicting histological subtypes of Follicular Variant of Papillary Thyroid Carcinoma based on cytomorphology. Can cytomorphology optimize use of molecular testing?

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Running Title: Cytology Predicting FVPTC Subtypes

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Abstract:

Background: Follicular Variant Papillary Thyroid Carcinoma (FVPTC) can be further subclassified into one of three subtypes: Non-invasive encapsulated FVPTC, Invasive encapsulated FVPTC, and Infiltrative FVPTC. Longitudinal and molecular studies have demonstrated that, in terms of both molecular profiles and prognosis, encapsulated FVPTC is comparable to follicular adenoma, invasive FVPTC to follicular carcinoma, and infiltrative FVPTC to classic PTC. To improve triaging and prevent overtreatment of patients with FVPTC, we sought to determine cytologic features likely to occur within each subtype. **Methods:** A laboratory database search from 2010-2015 was conducted to identify patients with biopsy-proven FVPTC and prior fine needle aspiration. Surgical specimens were reviewed to determine the appropriate subcategorization. Accompanying cytology reports were reviewed for features common in classic PTC and follicular neoplasms. **Results:** Encapsulated variants were more likely to be graded as Bethesda Category 4 compared to invasive or infiltrative variants. In contrast, Infiltrative variants were more likely to be graded as Bethesda Categories 5 and 6 compared to invasive or encapsulated variants. Compared to the encapsulated variant, infiltrative FVPTC was more likely to have nuclear pseudo-inclusions (31.82% vs 8.11%, p=0.0468) and less likely to have microfollicular architecture (22.73% vs 54.05%, p=0.0374). **Conclusions:** This study identified Cytomorphological differences between encapsulated and infiltrative FVPTC. With a higher threshold of suspicion for FVPTC, improved awareness of the differences between these subtypes and incorporation of molecular testing, it is likely that the Bethesda Category can be revised and patient triaging can be significantly improved.

Key Words: NIFT, Follicular Variant, Papillary Thyroid Carcinoma, Non-Invasive, Cytology, BRAF, RET, RAS