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Thyroid follicular-patterned neoplasms encompass a broad spectrum of neoplasms ranging from benign follicular thyroid adenoma (FTA) to follicular thyroid carcinoma (FTC), invasive encapsulated follicular variant of papillary thyroid carcinoma (iEFVPTC), non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) and poorly differentiated thyroid carcinoma (PDTC). These tumors share overlapping morphologic features and pose significant diagnostic challenges, particularly in the preoperative setting where fine-needle aspiration cytology (FNAC) often yields indeterminate results.

The preoperative diagnosis of follicular neoplasms remains one of the most challenging areas in thyroid cytopathology. FNAC has an inherent limitation in diagnosing follicular-patterned neoplasms because the definitive diagnosis of follicular carcinoma requires the identification of capsular or vascular invasion, which cannot be assessed on cytologic material alone. Importantly, ultrasound-guided core needle biopsy (CNB) demonstrated significantly better performance in this setting. This advantage of CNB over FNAC is attributable to its ability to provide histologic information including the relationship between the nodule and its capsule and the surrounding thyroid parenchyma. These findings suggest that CNB can serve as a valuable complementary tool when a follicular neoplasm is suspected clinically or radiologically.

In addition, diagnostic molecular testing has become an increasingly important adjunct for the management of cytologically indeterminate thyroid nodules. Alterations in TSHR, EZH1, GNAS are typically reported in FTA, while mutations in TERT promoter, TP53, PIK3CA are exclusively observed in malignant tumors. RAS mutations or PPARgamma gene rearrangements are reported across benign to malignant follicular-patterned neoplasms. Based on these molecular landscape, commercial molecular platforms such as ThyroSeq v3 and Afirma Genomic Sequencing Classifier have been applied in indeterminate nodules. They demonstrated high negative predictive values exceeding 95%, leaving only a few false-negative cases. However, these platforms are primarily validated and marketed in the United States, with costs ranging from $3,000 to over $6,000 per test, limiting their global accessibility. Recent efforts in Korea and other countries have focused on developing more affordable laboratory-developed multi-gene panels. An 11-gene DNA panel covering key driver genes of follicular-patterned neoplasms and high-risk progression markers has shown promising results in reducing surgical resection rates for indeterminate nodules while maintaining acceptable diagnostic performance, suggesting that targeted molecular testing can be implemented cost-effectively in healthcare systems where commercial platforms are not reimbursed.

This lecture will provide a comprehensive overview of the preoperative pathologic diagnosis and molecular features of follicular-patterned thyroid neoplasms, emphasizing the integration of morphologic assessment with molecular profiling to improve diagnostic accuracy, risk stratification, and clinical decision-making. The presentation is designed for ultrasonographers and clinicians who evaluate thyroid nodules, with the aim of bridging the gap between imaging findings, cytologic interpretation, and the evolving molecular classification of thyroid tumors.