

# **The Frozen Section: Diagnostic Challenges and Pitfalls**

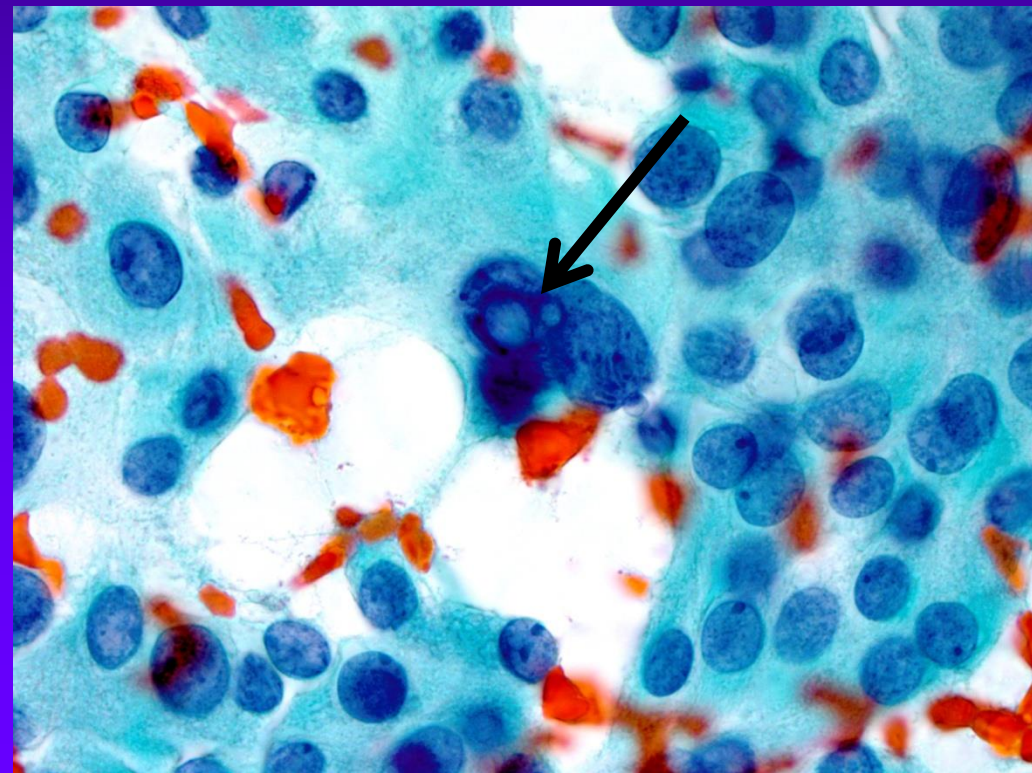
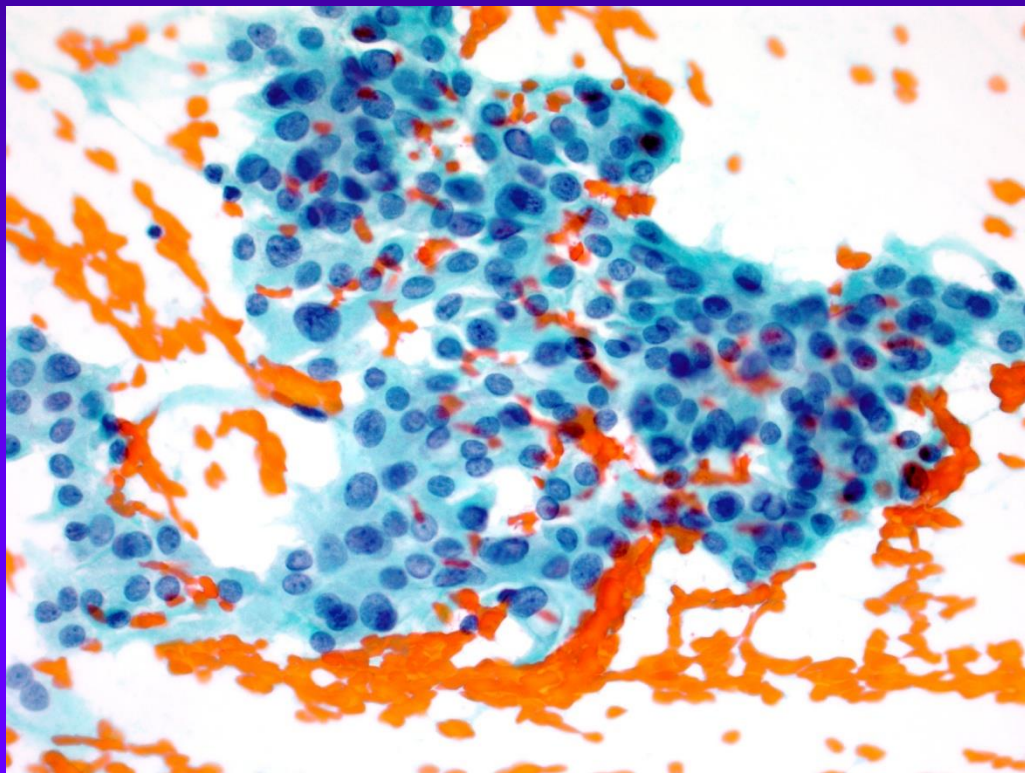
**William C. Faquin, M.D., Ph.D.  
Director, Head and Neck Pathology  
Massachusetts General Hospital &  
Massachusetts Eye and Ear Infirmary  
Harvard Medical School  
Boston, MA**

# CASE

- **The patient is a 34-year-old female who was noted to have thyroid nodules on CT scan 5 years prior to the current procedure.**
- **A recent ultrasound was performed and showed a solid left lower lobe nodule measuring 1.1 cm.**



**A fine needle aspiration (FNA) of the left lobe nodule was performed and interpreted as “Suspicious for papillary thyroid carcinoma.”**

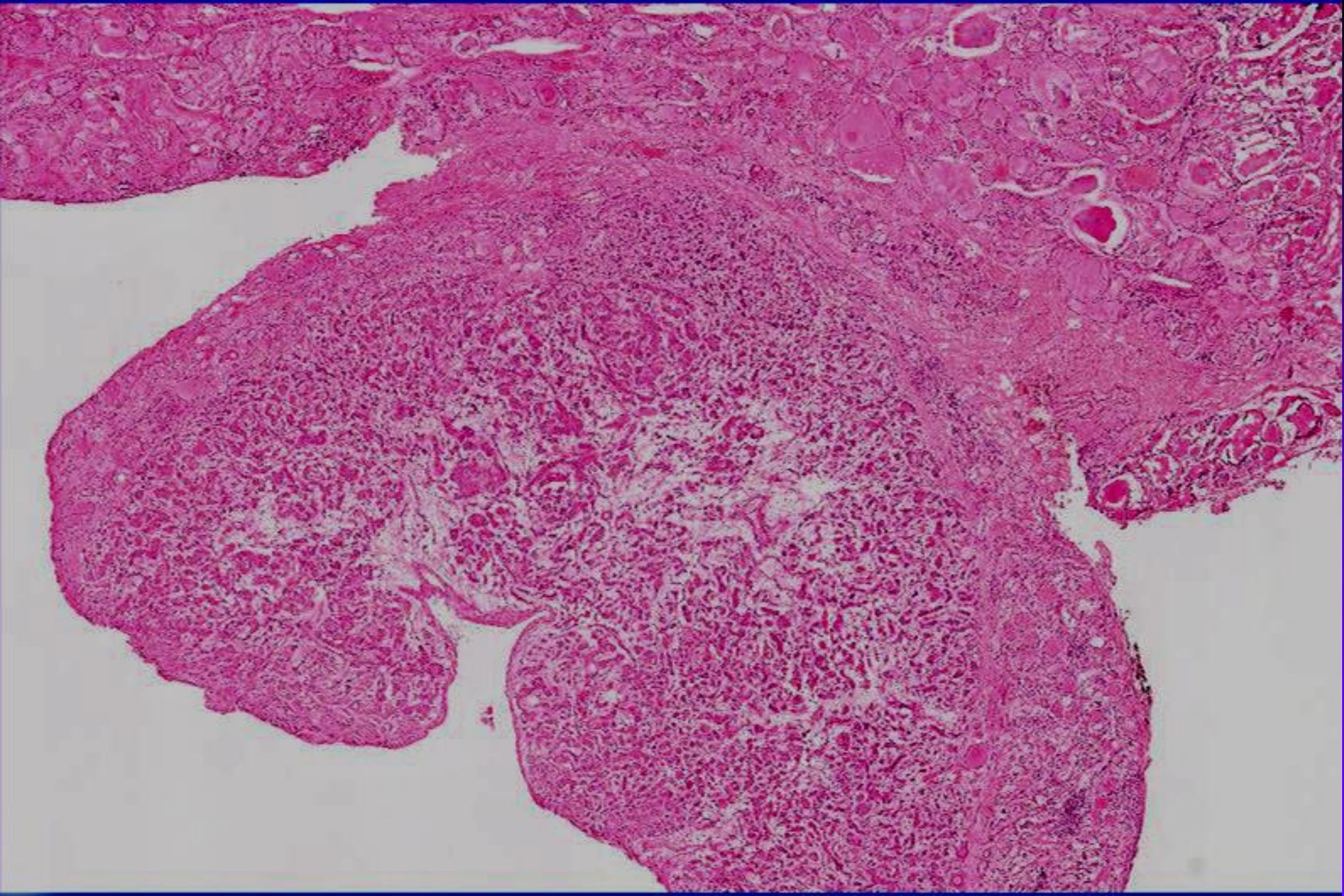


**The patient also had nodules in the right thyroid lobe, which were subcentimeter. The possibility of a left lobectomy versus a total thyroidectomy was discussed.**

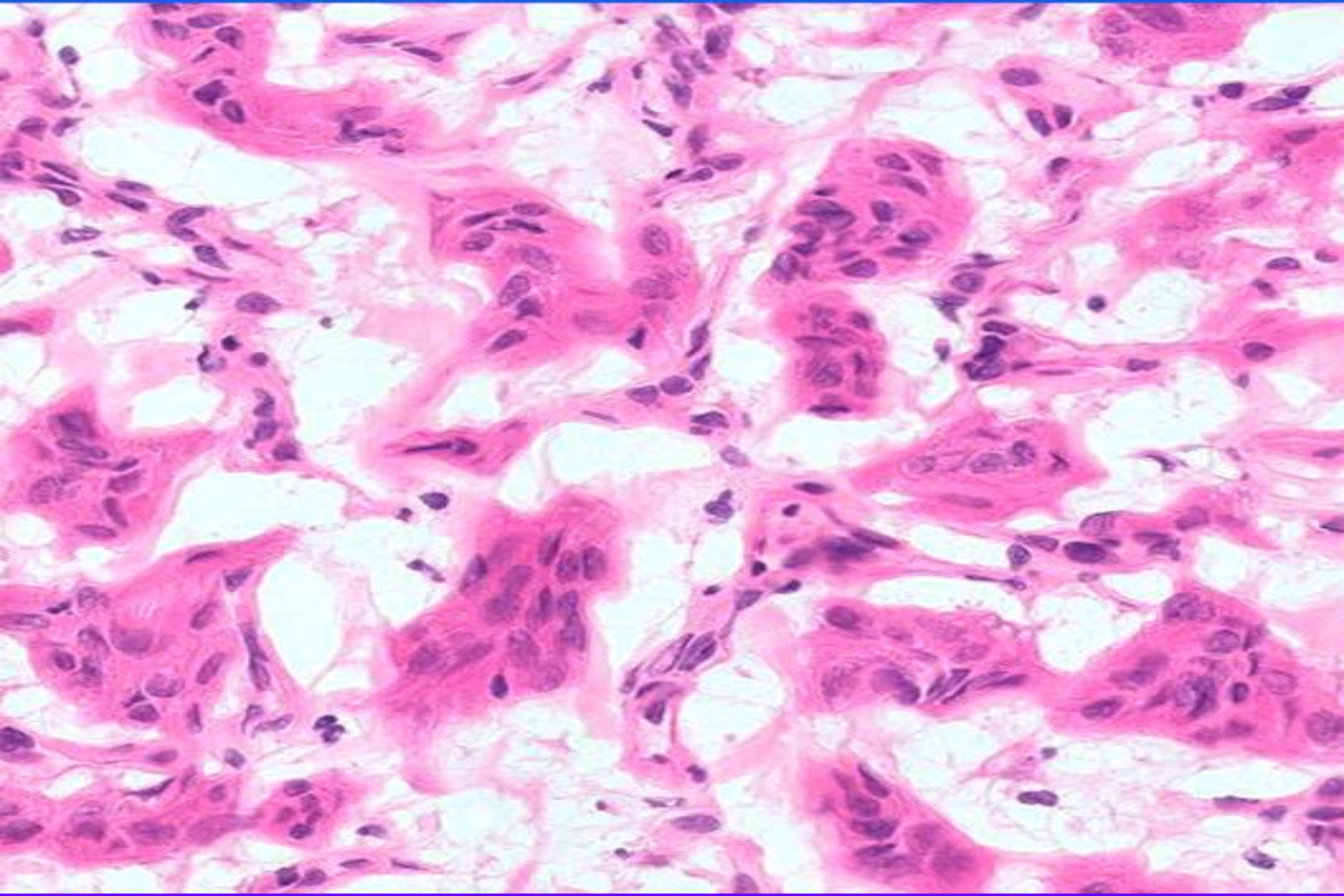
**The patient would have a total thyroidectomy if frozen section confirmed a malignant nodule.**

**Frozen Section of the Left Lobe  
Thyroid Nodule**

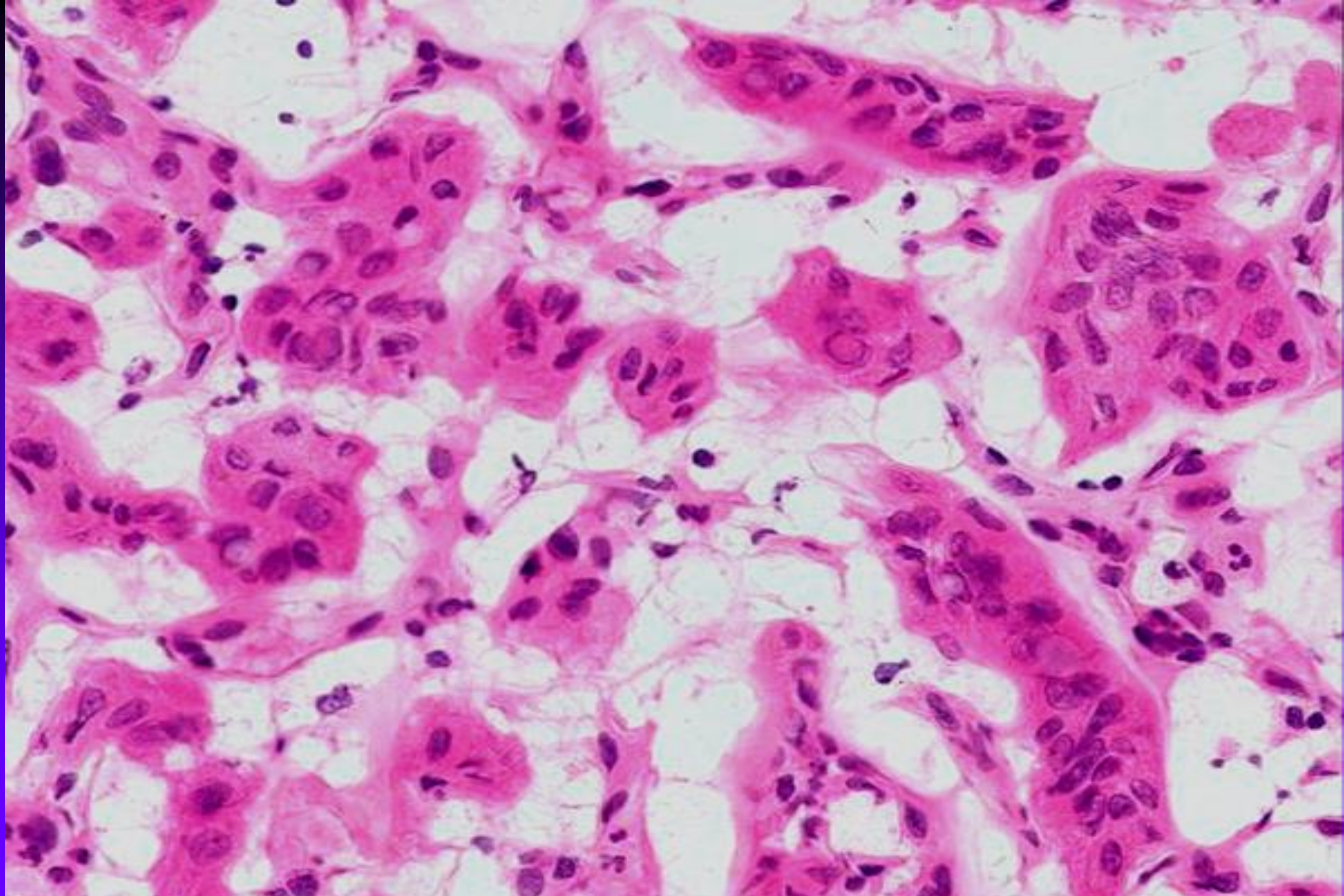




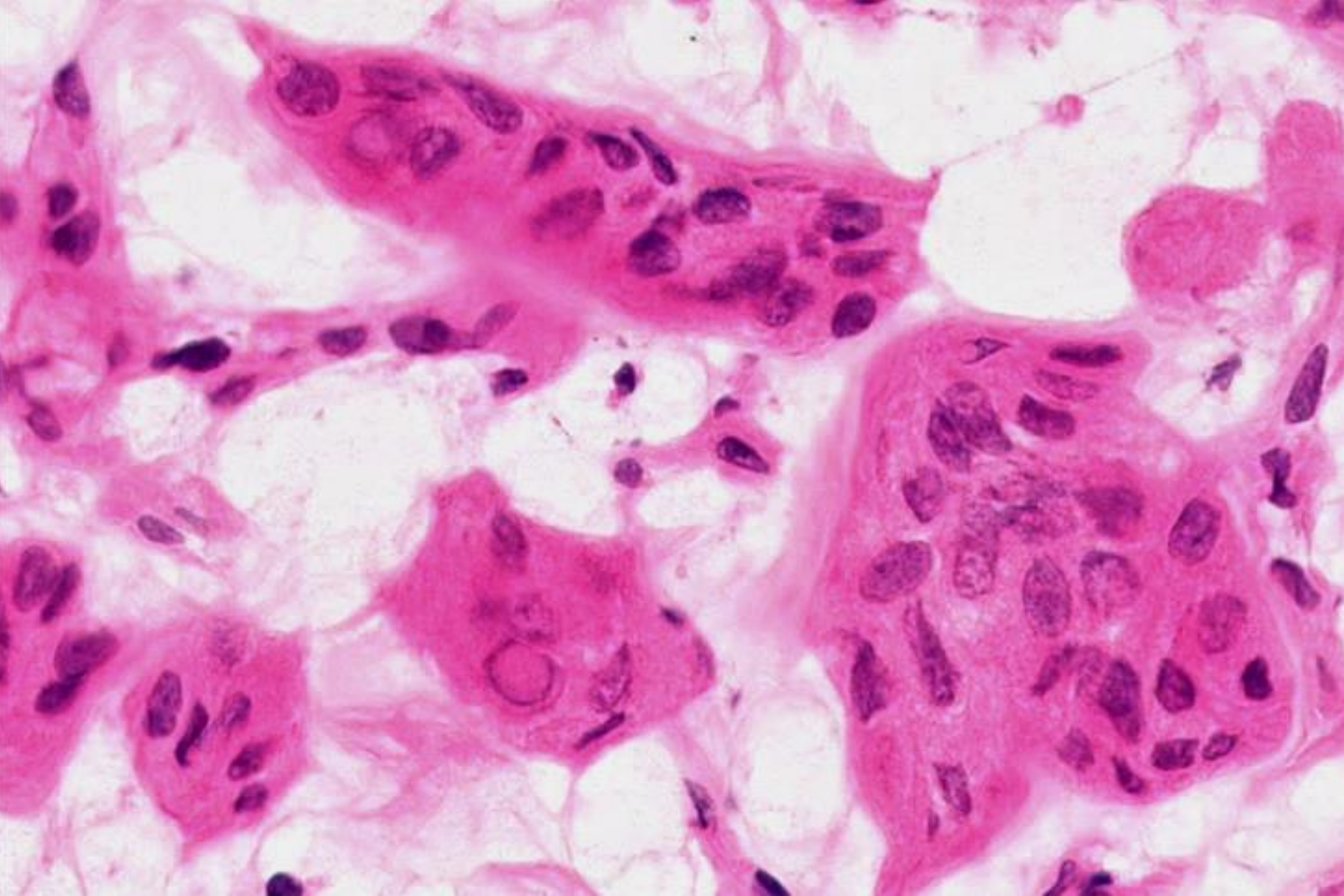












# What is your frozen section diagnosis?

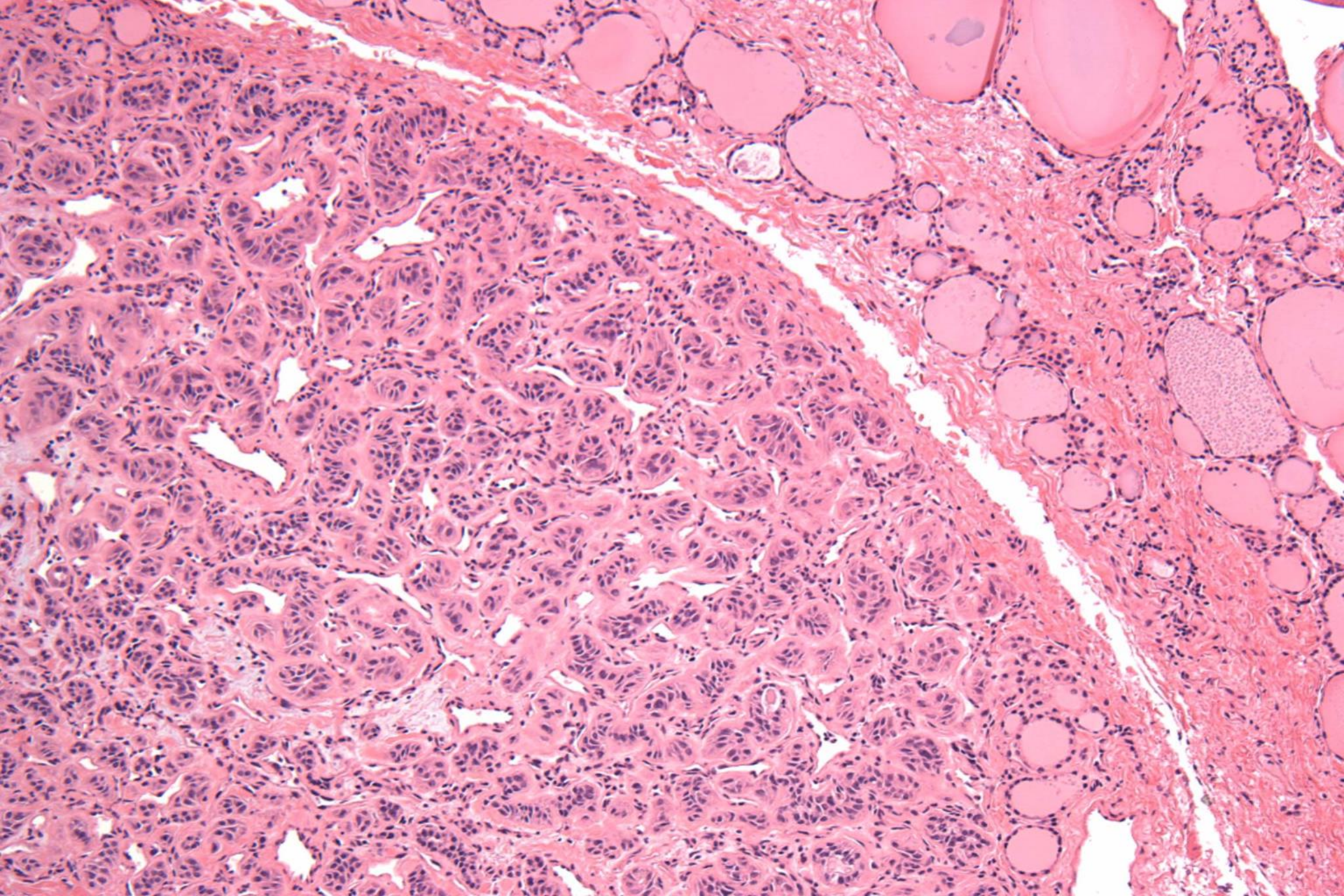
- **Papillary thyroid carcinoma/FVPTC**
- **Hyalinizing trabecular tumor**
- **Medullary thyroid carcinoma**
- **Follicular adenoma/follicular neoplasm**
- **Papillary hyperplasia in goiter**
- **Paraganglioma**



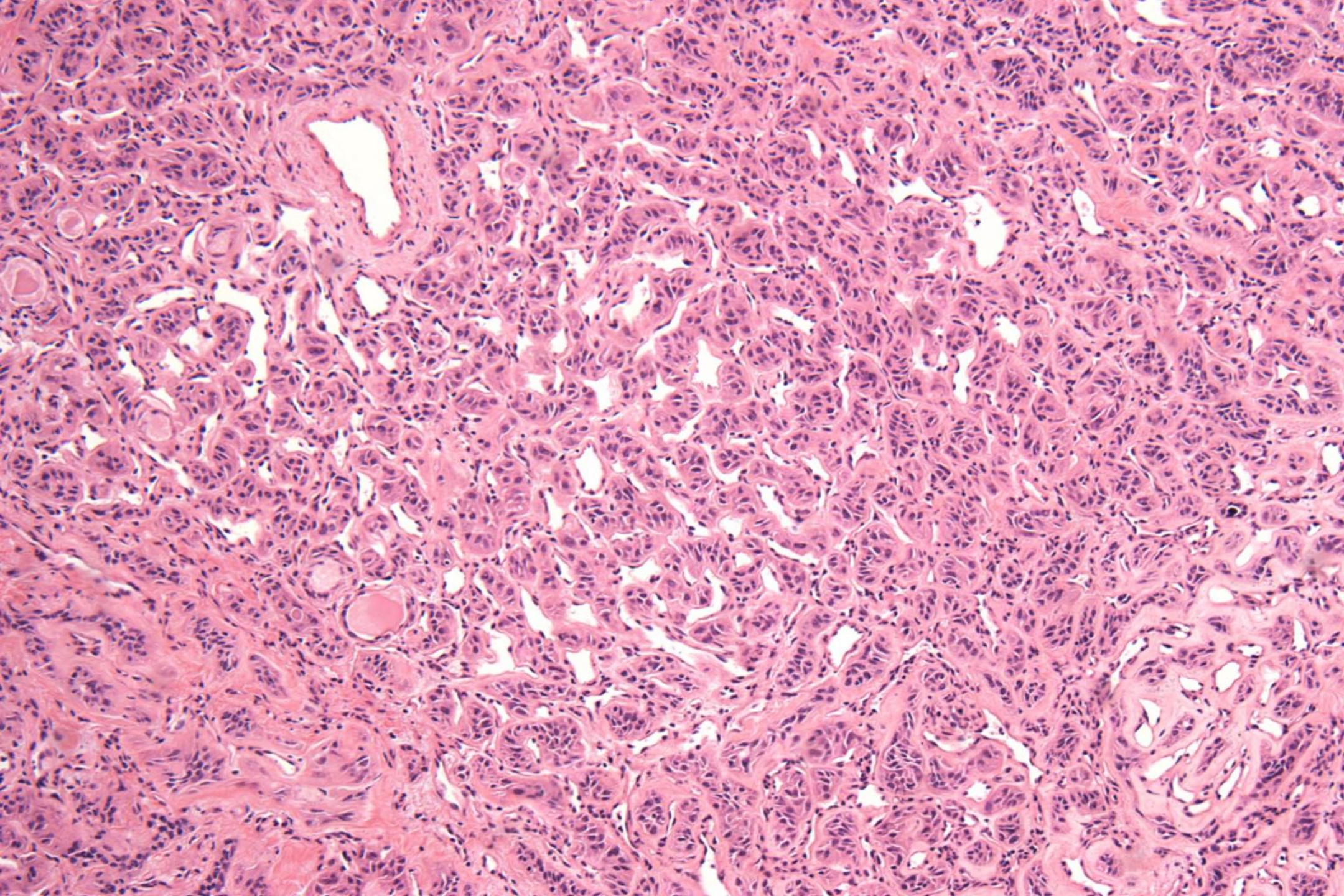
**Frozen Section Diagnosis:**  
**“Suspicious for**  
**Papillary Thyroid Carcinoma”**

**A total thyroidectomy was performed, as well as a sampling of central compartment LNs.**

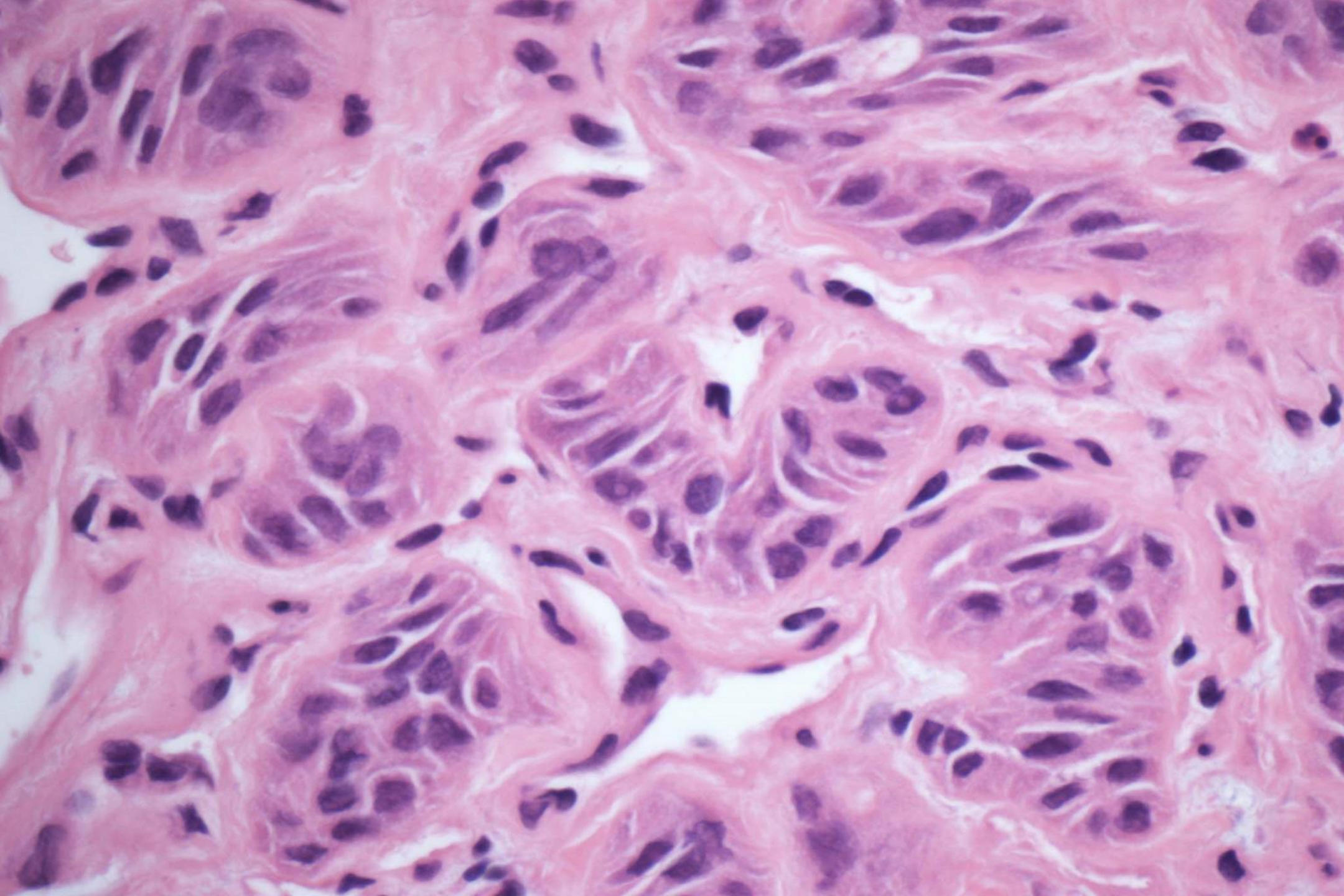




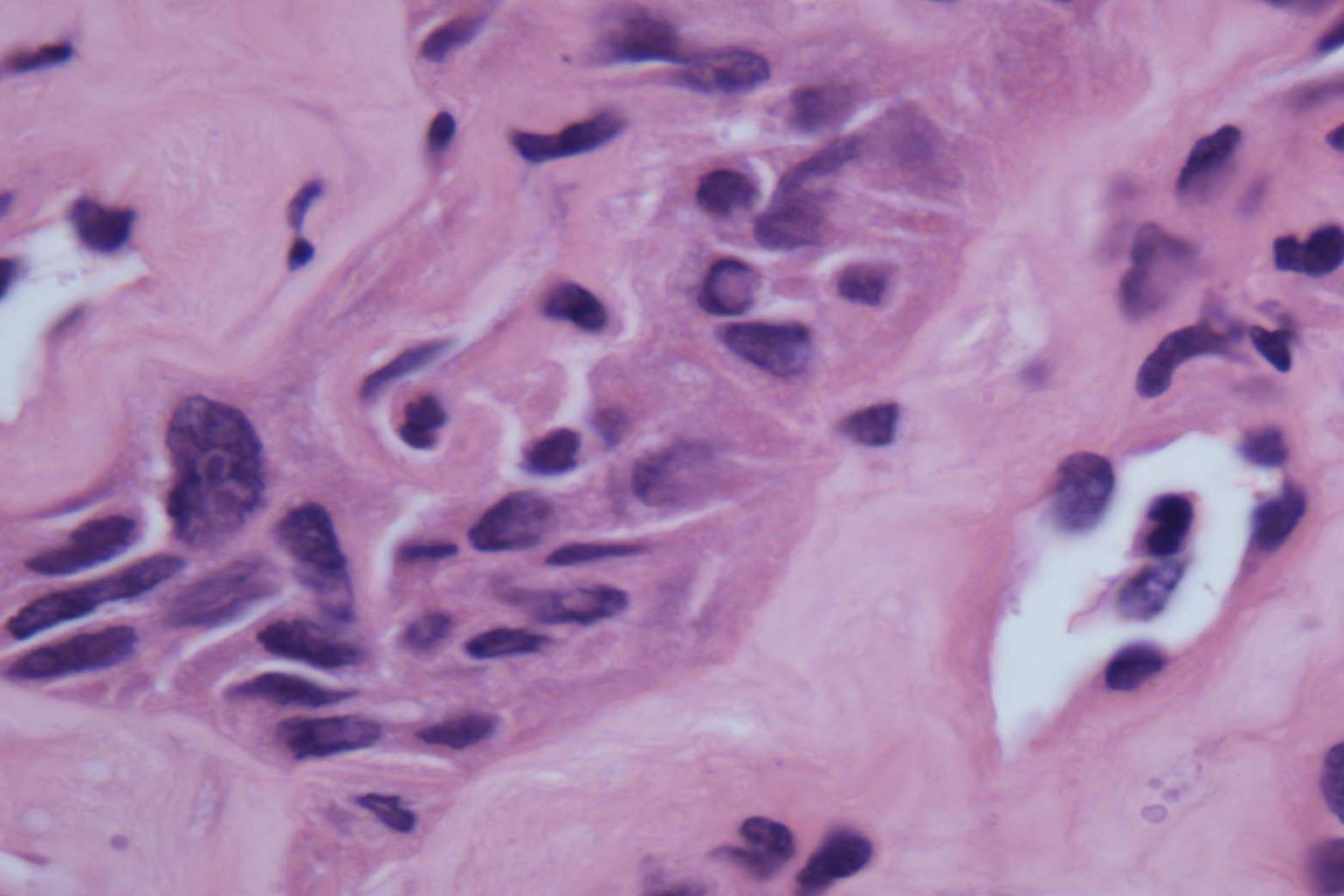














**Histologic Diagnosis:**  
**Hyalinizing trabecular tumor**

# CASE ISSUES

- **1) Pitfall of HTT in frozens, FNA, & surgical pathology**
- **2) Use of frozen section to diagnose PTC**



# Hyalinizing Trabecular Tumor

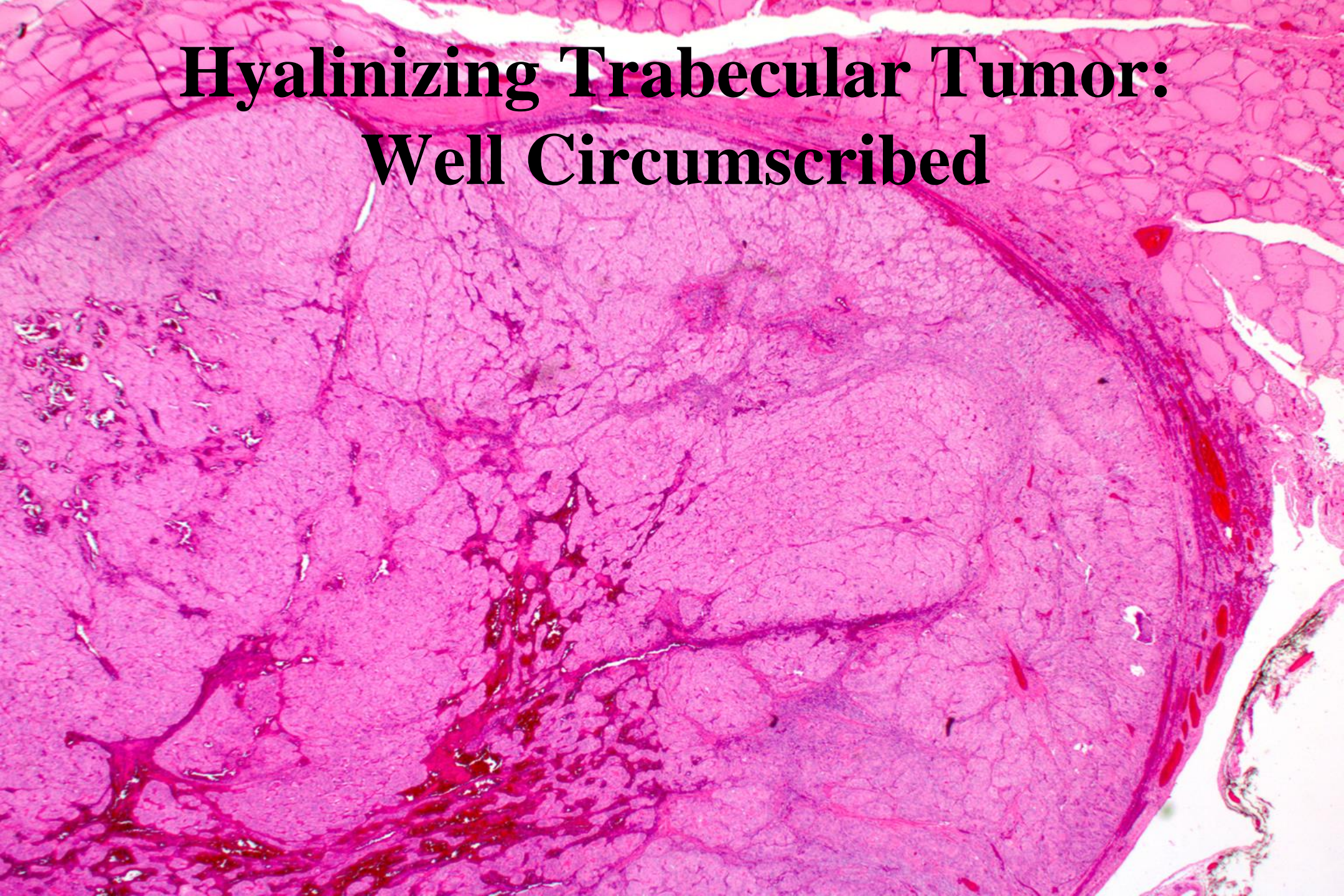
- **aka: “Hyalinizing trabecular adenoma”**
- **Uncommon thyroid gland tumor (<1%)**
- **First described in 1987 by Carney**
- **Mean age: 50 years**
- **Female:Male (6:1)**
- **Average size: 2.5 cm**
- **Approximately 50% of HTT are misdiagnosed as PTC by frozen section**

# **Hyalinizing Trabecular Tumor: A Benign Entity**

- **Controversy over molecular features – some reports suggest that HTT shares some molecular changes with PTC**
- **Rare reports of metastatic disease**
- **Recent studies conclude that HTT is benign**

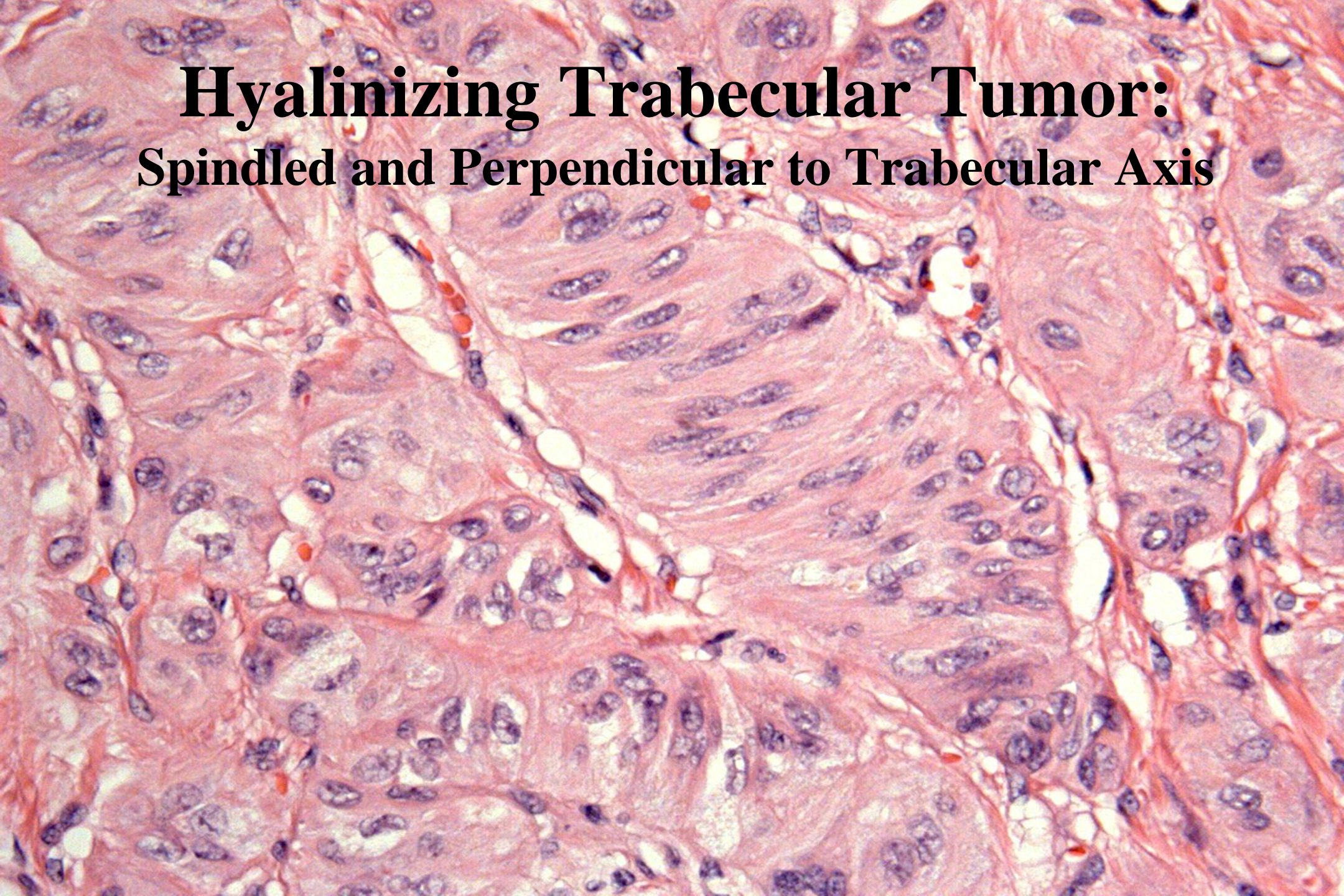


# Hyalinizing Trabecular Tumor: Well Circumscribed



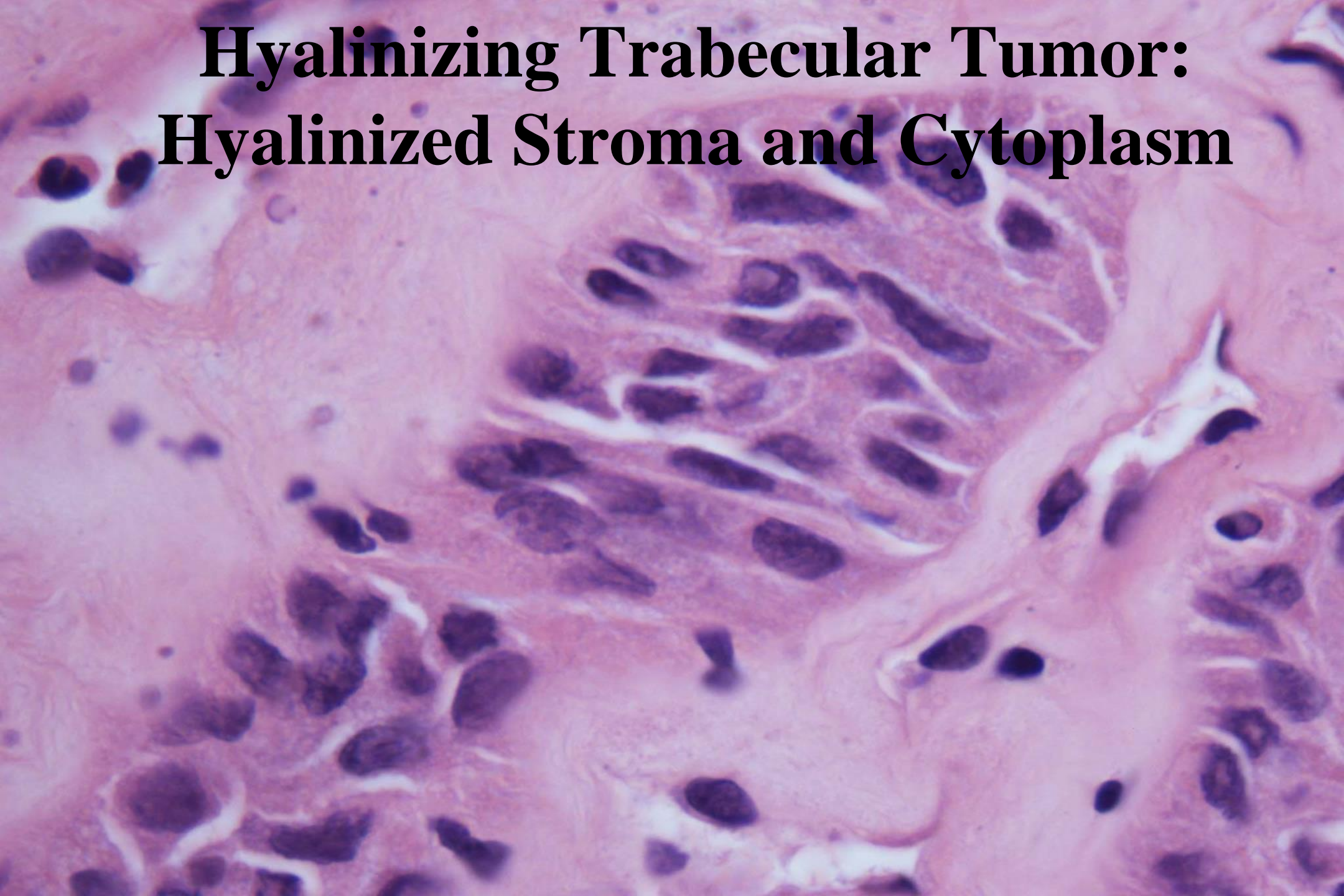


# **Hyalinizing Trabecular Tumor: Spindled and Perpendicular to Trabecular Axis**



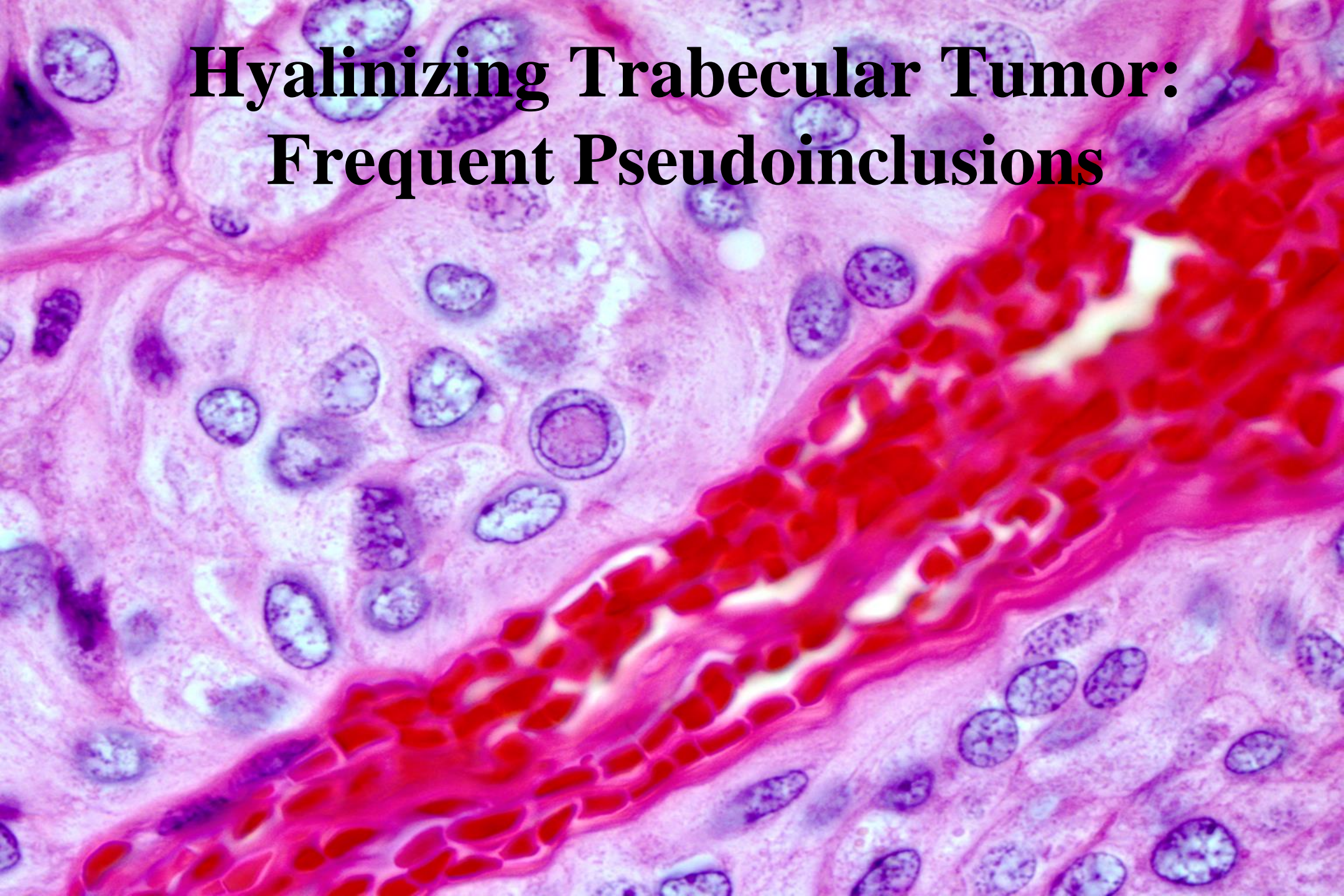


# **Hyalinizing Trabecular Tumor: Hyalinized Stroma and Cytoplasm**





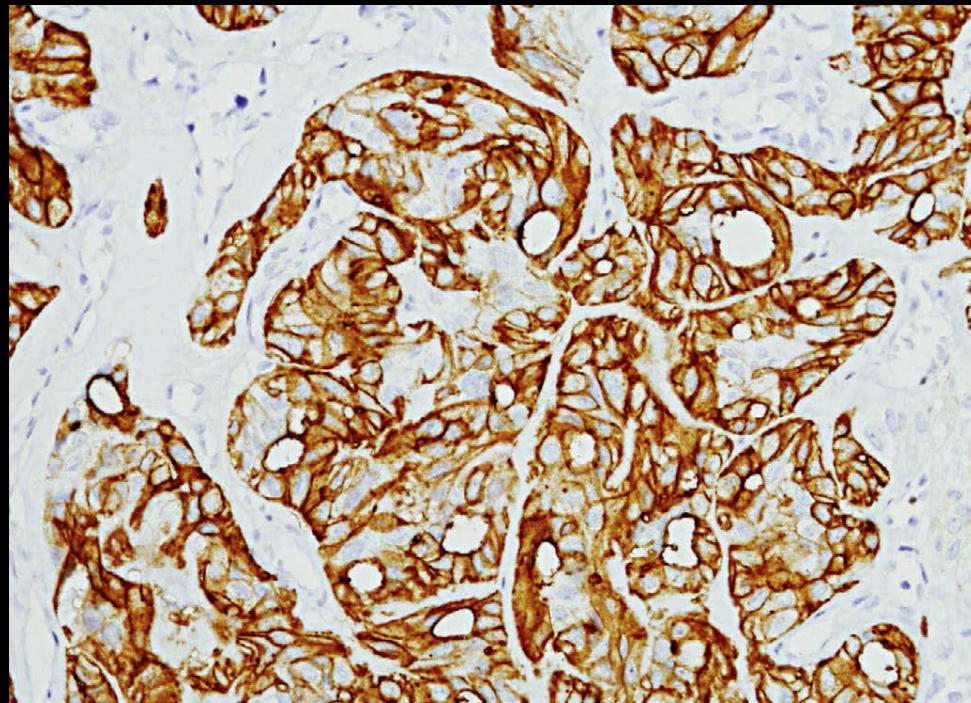
# **Hyalinizing Trabecular Tumor: Frequent Pseudo-inclusions**





# Hyalinizing Trabecular Tumor

- **Dako MIB-1 monoclonal antibody: strong and diffuse membrane staining pattern (and Ker19 is negative)**



# Can U/S predict HTT?

## Jang et al, 2015

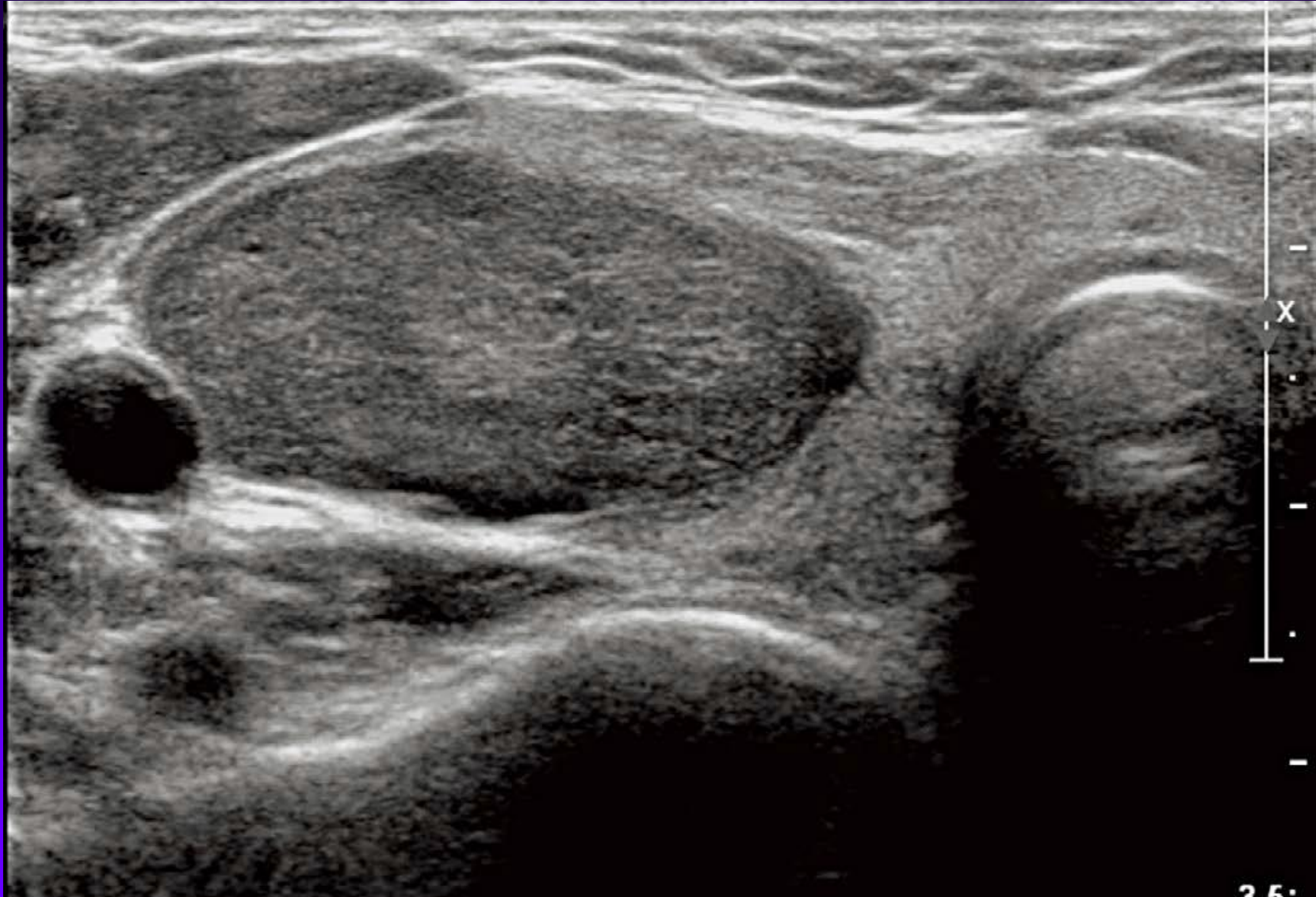
### U/S Features Predictive of HTT:

- **Solid tumor**
- **Hypoechoogenicity**
- **Absence of calcifications**
- **Presence of vascularity**
- **Parallel shape**



# U/S of HTT:

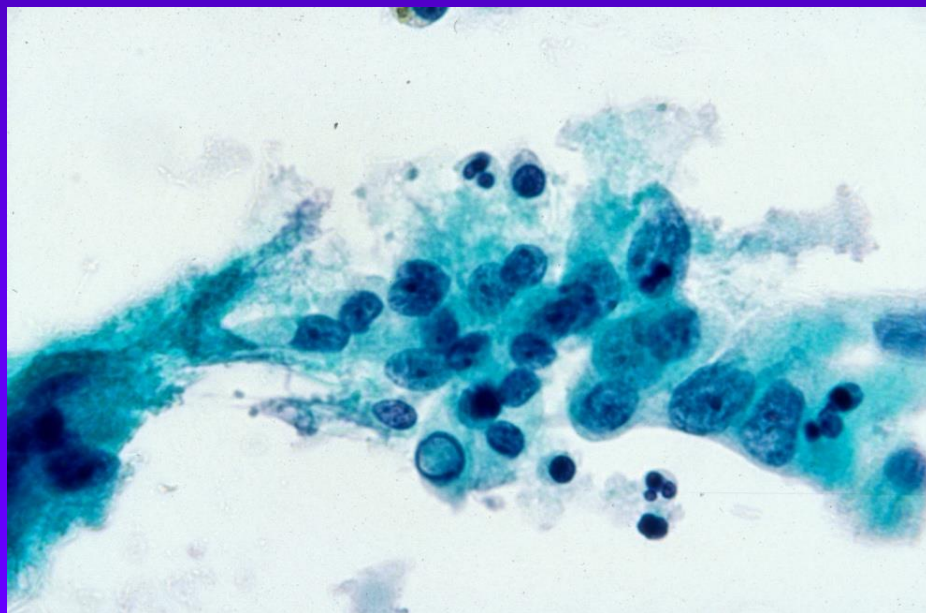
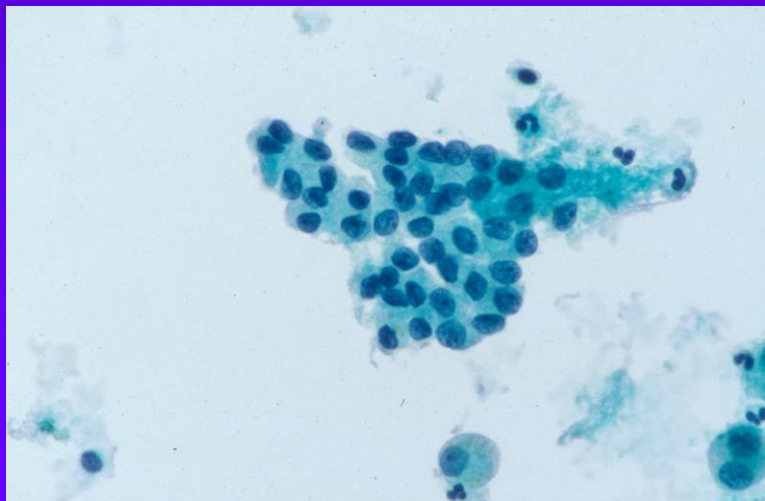
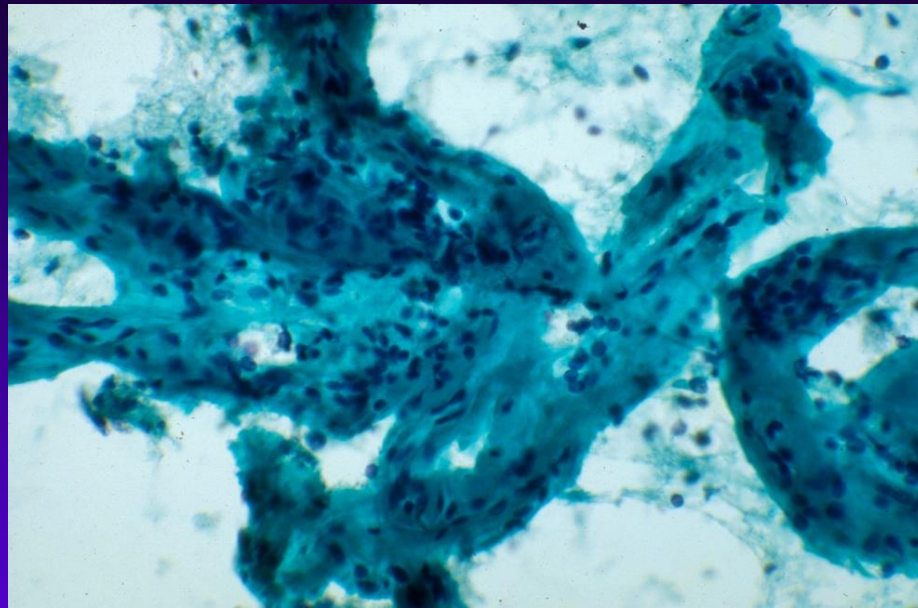
Hypoechoic solid mass without calcifications



# FNA of HTT – A Major Pitfall !!!

## – Cytology:

- » Trabecular architecture
- » Hyaline stroma & cytoplasm
- » Oval to spindle-shaped cells (rare in PTC)
- » Nuclei: grooves and inclusions
- » Scant to absent colloid
- » **MOST ARE DIAGNOSED AS PTC !!!**





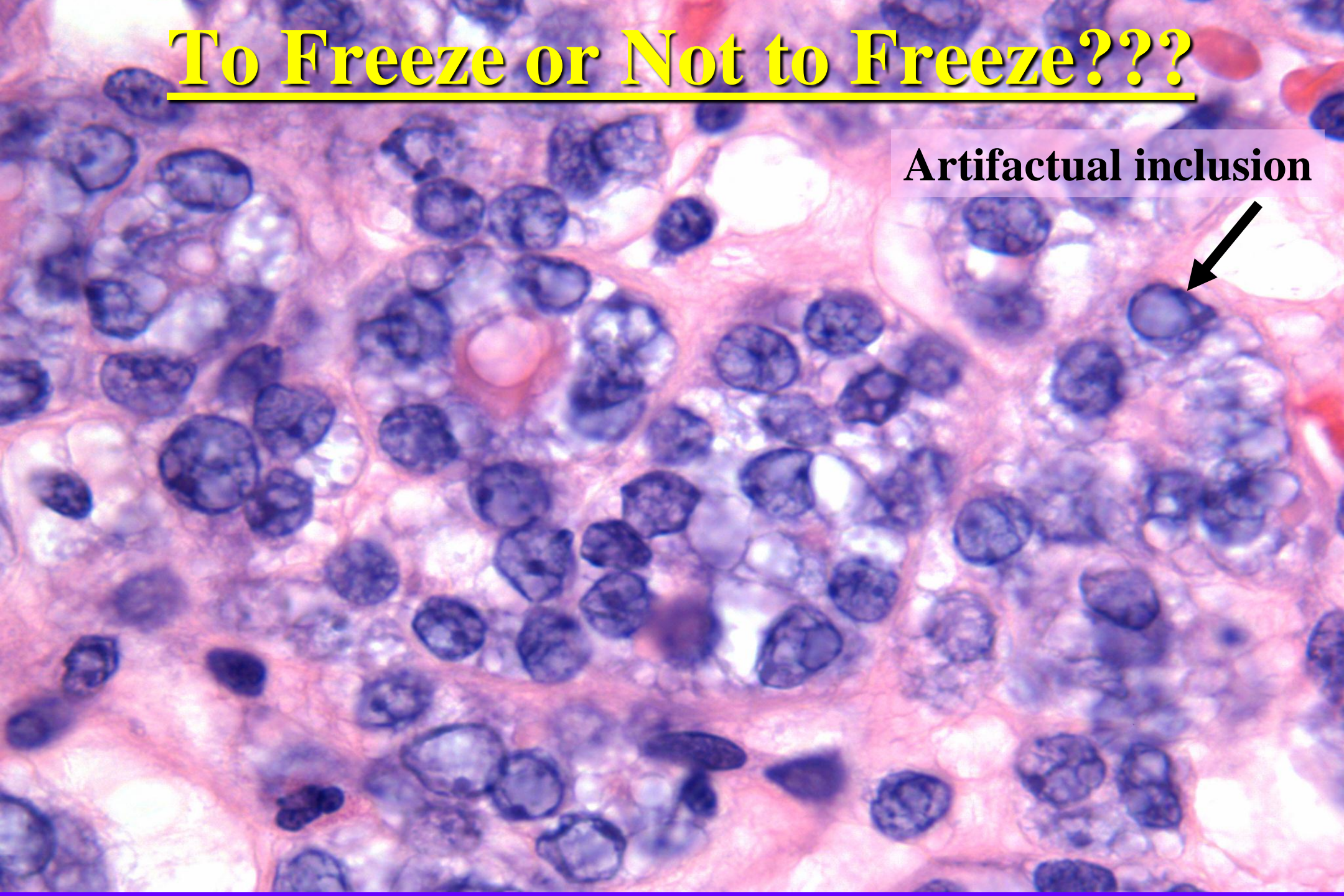
# THYROID

## To Freeze or Not to Freeze???

- At the MGH, a subset of thyroidectomy specimens are sent for frozen section:
  - » Limited to those that were indefinite for PTC by FNA
  - » Many frozen section pitfalls – esp. nuclear artifacts!!!
  - » Avoid freezing small nodules
- Intraoperative smears are routinely performed to compliment the frozen section

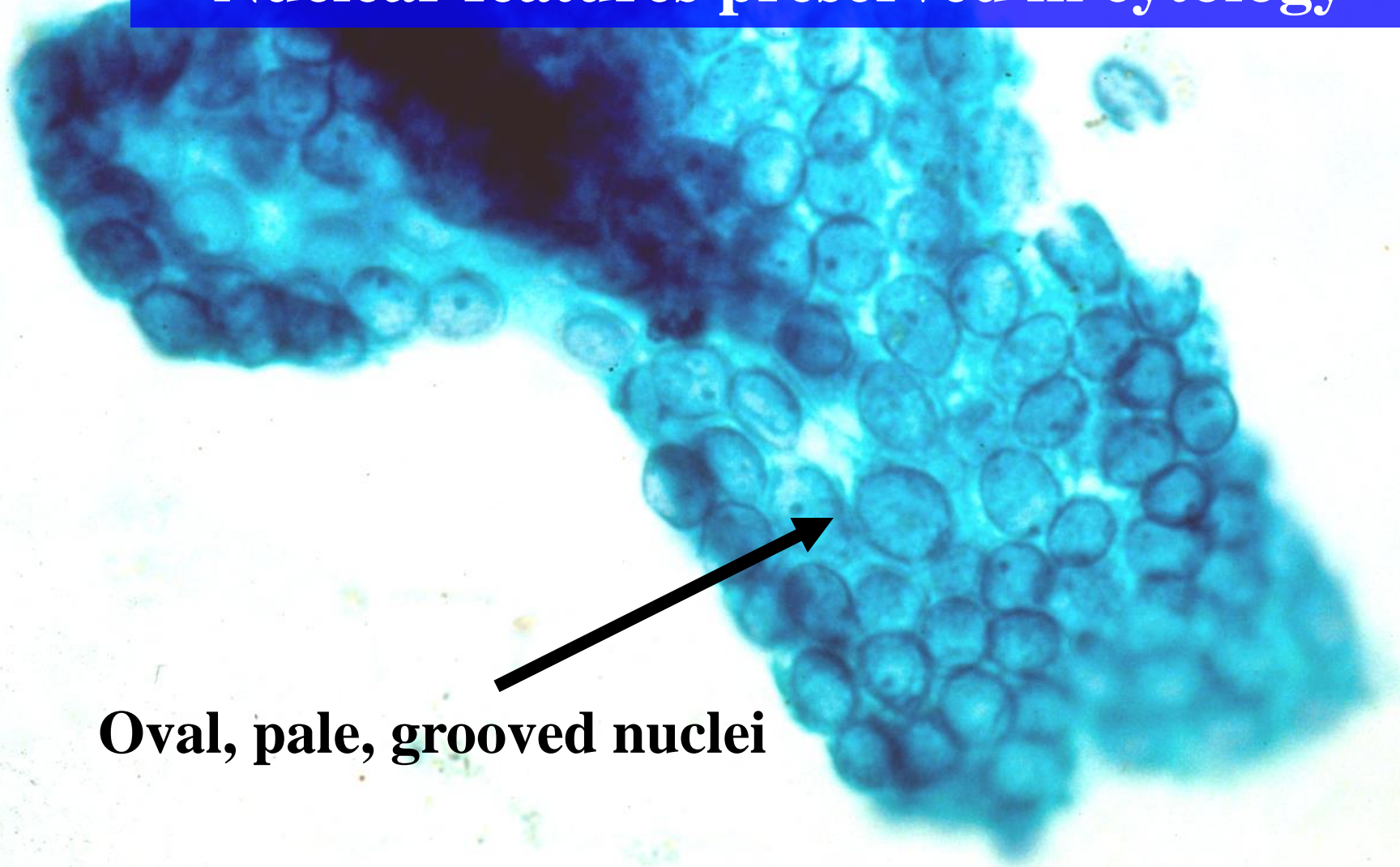
# To Freeze or Not to Freeze???

Artifactual inclusion





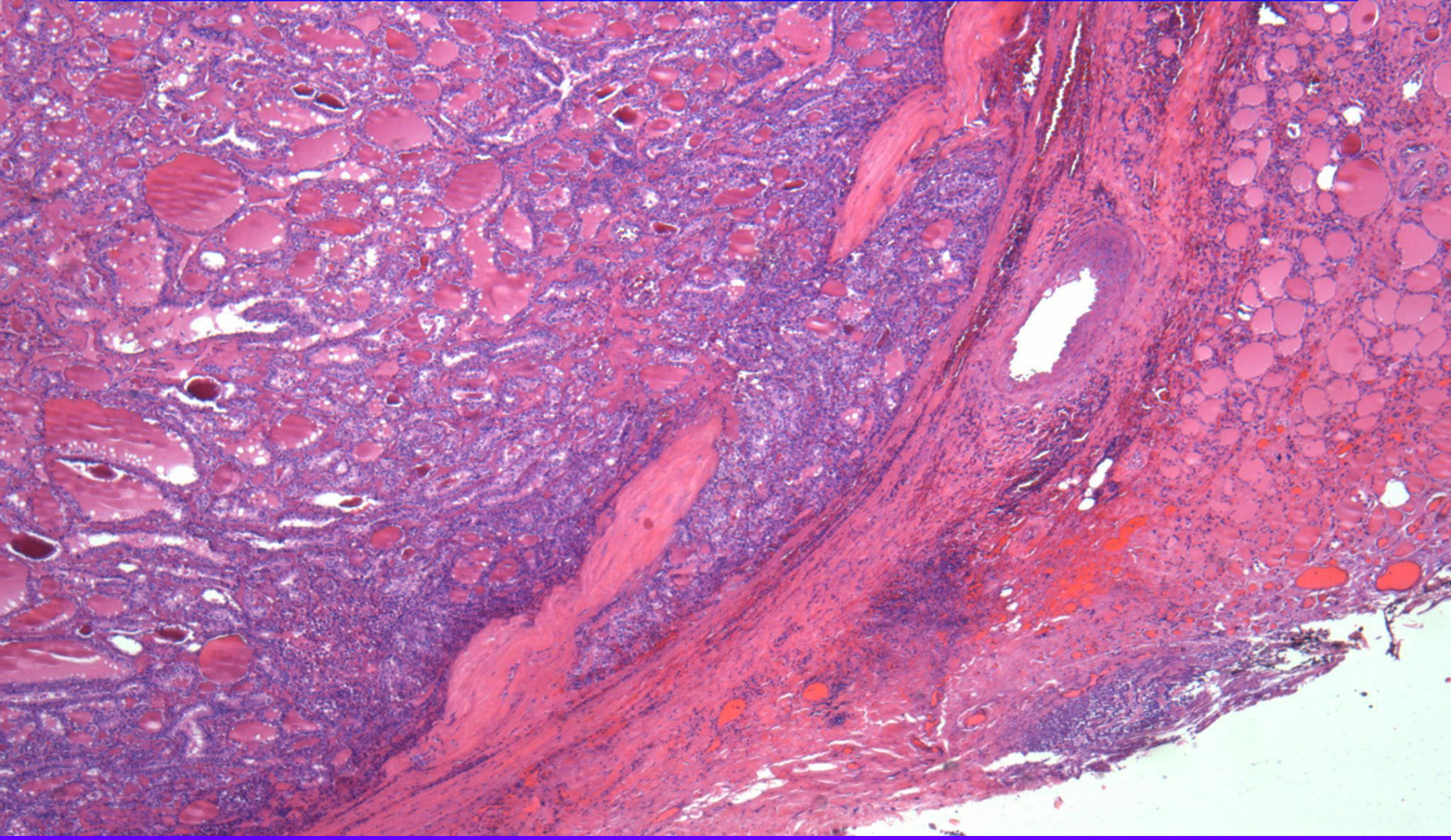
# Cytology of Papillary Thyroid Carcinoma: Nuclear features preserved in cytology



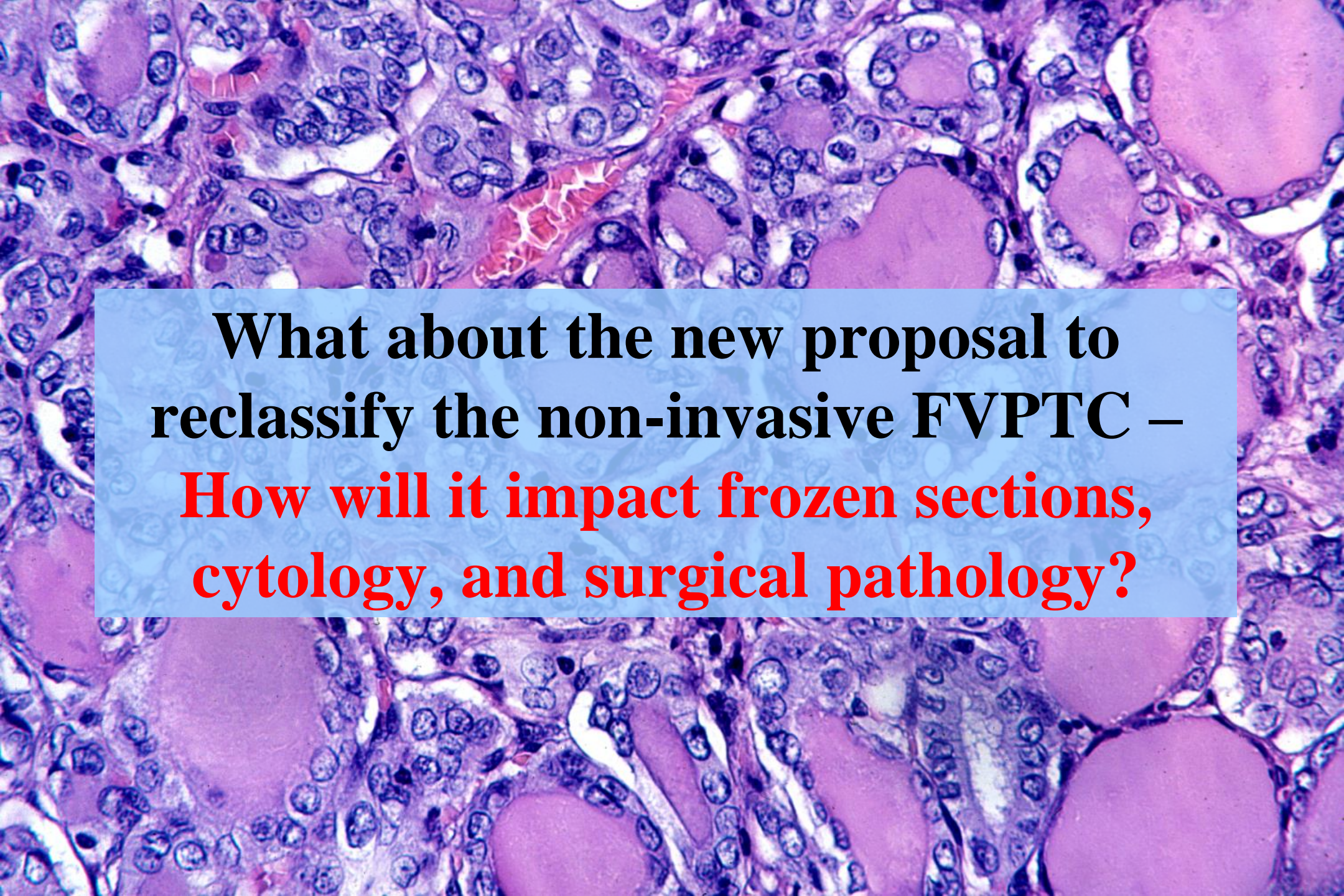
**Oval, pale, grooved nuclei**



**Minimal capsular invasion can be difficult to assess in frozen section  
And you might destroy any evidence of invasion – CAUTION!**





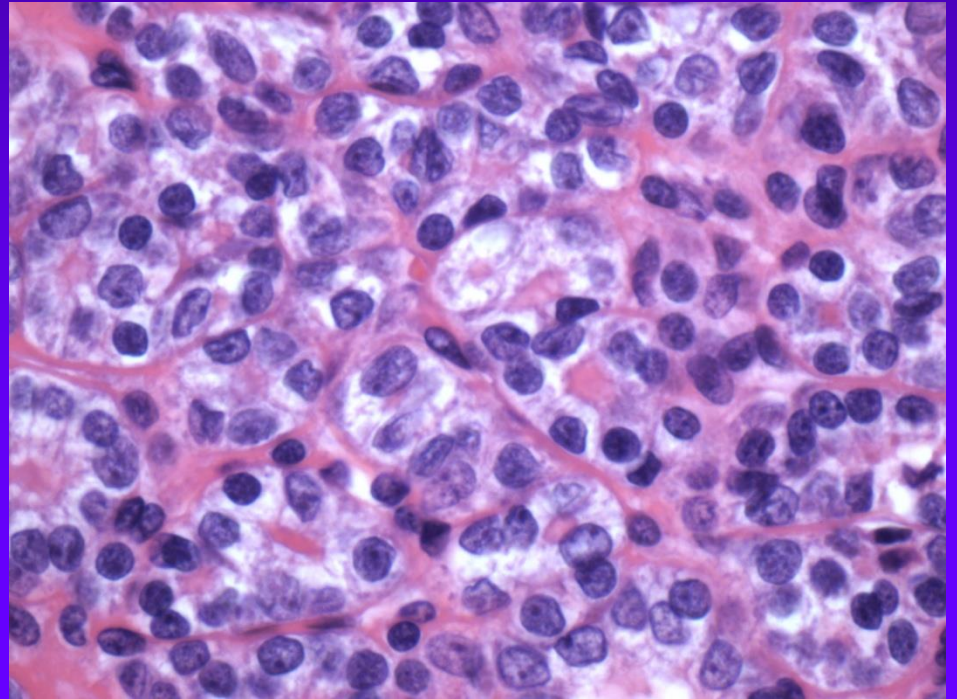
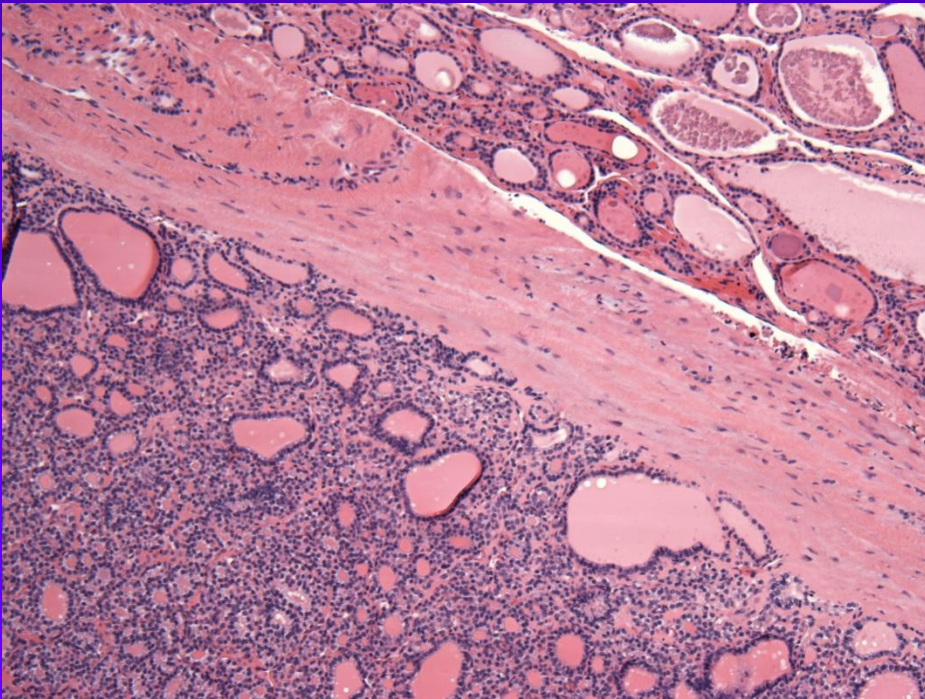
A high-magnification histological image of a prostate gland section, stained with hematoxylin and eosin (H&E). The image displays numerous glandular units of varying sizes. Each gland is lined by a single layer of cuboidal to columnar epithelial cells. The nuclei of these cells are stained dark blue/purple, while the cytoplasm and surrounding stroma are stained pink. The glandular lumens are mostly clear, though some contain small amounts of secretory material. The overall architecture is characteristic of the prostate gland, showing a complex, branched pattern of glands.

**What about the new proposal to reclassify the non-invasive FVPTC –  
How will it impact frozen sections, cytology, and surgical pathology?**



# NIFTP

- **Solves an important thyroid pathology issue**
  - **Redefines a large set of low-risk cancers as “neoplasms” [or “uncertain malignant potential”]**
- **Eliminates non-invasive FVPTC**





## Non-Invasive Follicular Thyroid (NIFTP) Neoplasm with Papillary-Like Nuclear Features

- The prospects of **NIFT** will create some major issues for thyroid cytopathology:
  - The ROM for indeterminate diagnostic categories of the Bethesda System will change
- Has implications for diagnosing PTC in frozen section – not possible for circumscribed follicular patterned lesions (FVPTC)

# Key Points

- **HTT is a pitfall for frozen sections, FNA, and histology**
- **Limit your thyroid frozen sections**
- **Use a complimentary intraop smear**
- **Avoid making a frozen section dx of PTC if the tumor is circumscribed and trabecular (HTT) or follicular patterned (NIFTP)**
- **Classical PTC is likely the only PTC to dx by frozen!**