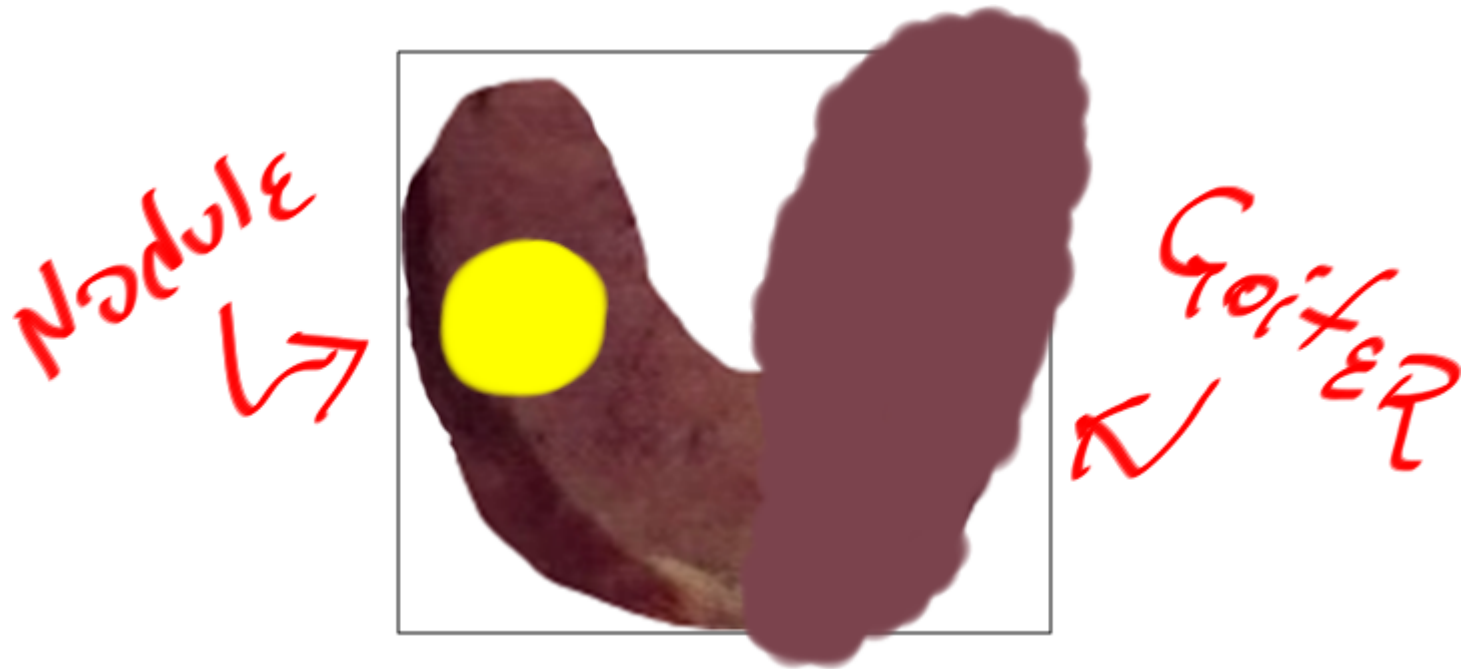


# Goiter, Nodules and Tumors



Howard J. Sachs, MD

[www.12daysinmarch.com](http://www.12daysinmarch.com)



Thyroid Cancer  
Papillary  
Follicular  
Anaplastic  
Medullary





Papillary

Thyroid Cancer

Papillary  
Follicular  
Anaplastic  
Medullary



Follicular



Papillary

Thyroid Cancer

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Follicular

Anaplastic

Medullary

MEN 2a/b  
RET mutation  
Parafollicular C cells



Papillary

Thyroid Cancer  
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Follicular

Anaplastic

Osteoclast-like



Multinucleate Giant Cells



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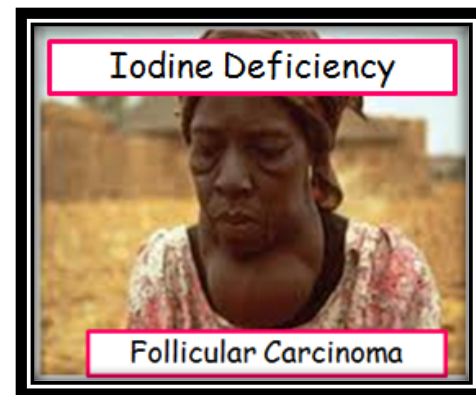
Papillary

Follicular



Papillary Carcinoma

Who's at Risk?



Follicular Carcinoma

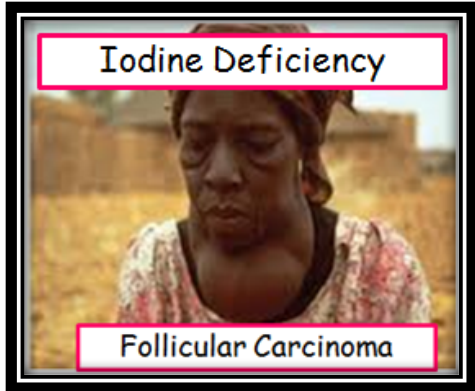


Thyroid Cancer  
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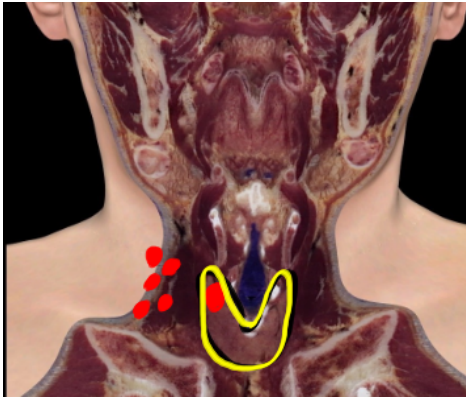


Papillary

Follicular



Who's at Risk?



Pattern of Spread?

Capillary



## Thyroid Cancer

Papillary  
Follicular  
Anaplastic  
Medullary



Papillary

Anaplastic

Follicular

Know the pathologic description and we're done.

Medullary



# Papillary Carcinoma

- Background
  - A/w ionizing radiation; may be single or multiple (follicular are always single)
  - Most common thyroid cancer
- Pathogenesis
  - Gain of function mutations

# Papillary Carcinoma

- Background
  - A/w ionizing radiation; may be single or multiple (**follicular are always single**)
  - Most common thyroid cancer

- Pathogenesis
  - Gain of function mutations

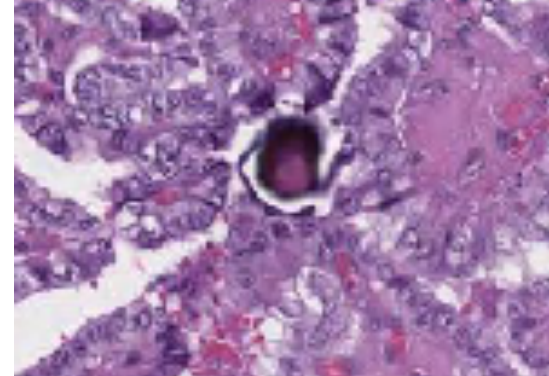


- Pathology
  - Branching papillae on a fibrovascular stalk ('fronds'); cytoplasmic **Psammoma** bodies (dystrophic **calcification**; 'calcific spherules, layered')
  - Nuclei:
    - **Finely dispersed chromatin** giving clear/empty appearance → **Orphan Annie eyes**
    - **Invaginations/intranuclear grooves** and '**pseudoinclusions**'

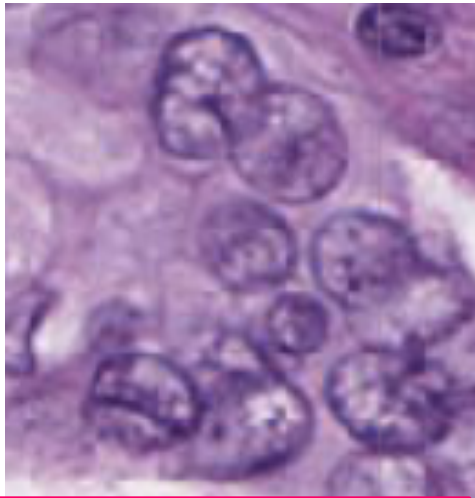
# This is the Language of Papillary Carcinoma



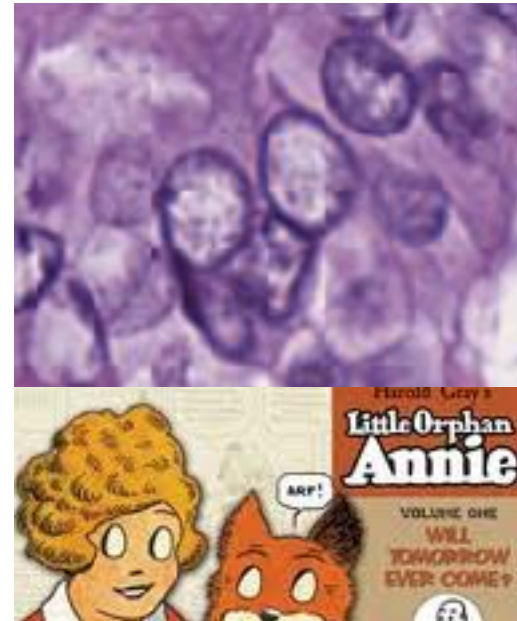
Papillary Structures with  
fibrovascular stalks



Psammoma Body  
'Calcific, spherule, layered'



Intranuclear Grooves



Finely, dispersed chromatin  
Nuclear clearing

# Papillary Carcinoma

- Clinical

- Solitary nodule; hoarseness, cough, dysphagia, SOB
- Locally invasive (**lymphatics**); cervical **lymphadenopathy**



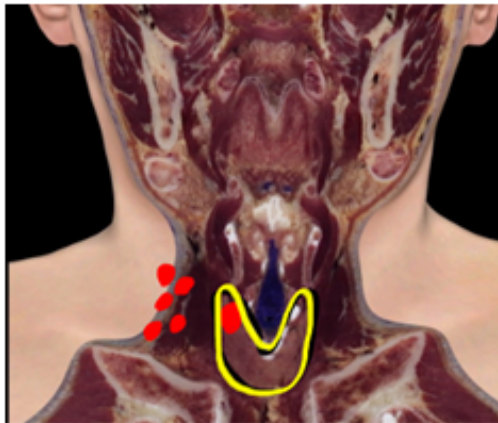
- Diagnostics

- U/S: ‘**hypo**echoic’ – less echo shadows (solid)
- RAIU – cold
  - If nodule AND TSH/T4 normal, they are assumed to be cold and proceed directly to FNA
- FNA/resection

- Treatment

- Surgery, RAI I<sup>131</sup>, Serial Thyroglobulin

## Papillary



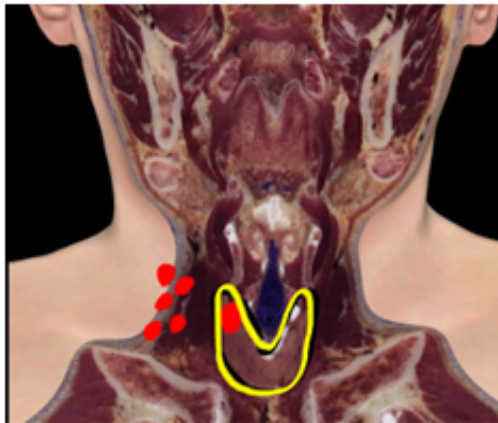
## Pathologic Description

H&E appearance?

Cytoplasmic features?

Nuclear features?

## Papillary



## Pathologic Description

H&E appearance?

Papillary with fibrovascular stalk/fronds

Cytoplasmic features?

Psammoma Bodies (and descriptors)

Nuclear features?

‘Orphan Annie Eyes’ –  
(empty appearing nuclei)

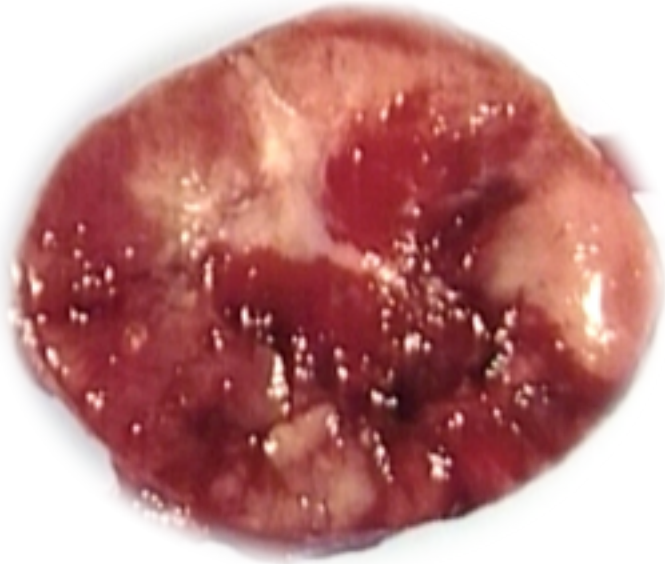
Intranuclear grooves

# Follicular Carcinoma

- Background
  - A/w iodide deficiency; present as solitary nodule
- Pathogenesis
  - Gain of function, RAS mutation (*unregulated cellular proliferation*)
- Pathology
  - Invasion of capsule distinguishes from adenoma
  - Sheets of **uniform cells with follicle remnants**;
    - *Hurthle cell variant* (abundant granular, eosinophilic cytoplasm)
  - Lack of **nuclear features** (clearing/grooves) and lack of **psammoma bodies** distinguish from papillary

Nothing juicy here...if I were them, I'd ask papillary ca questions





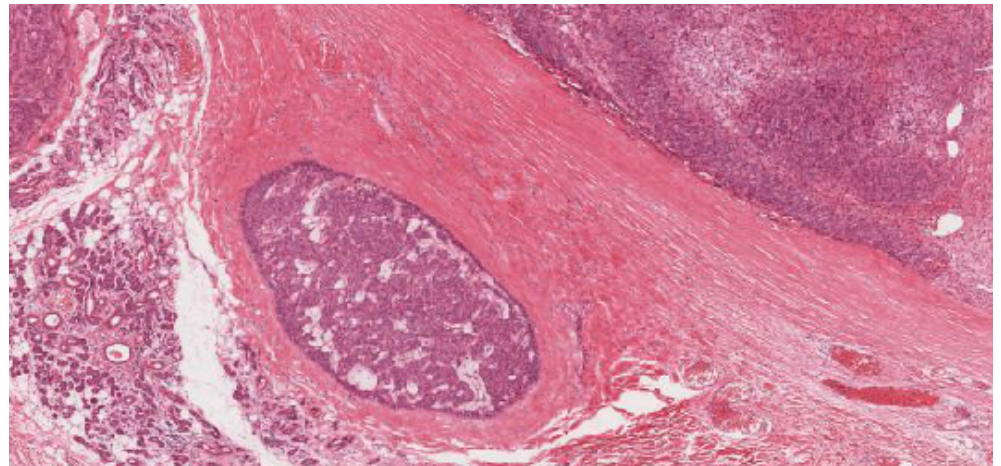
Key characteristic present:  
Retention of follicles with scant colloid  
Uniform cellular appearance

Key characteristics, not present:

- Orphan Annie Eyes
- Pseudoinclusions/Nuclear Grooves
- Psammoma bodies
- Lymphatic invasion

Path: Solitary nodule → like adenoma  
but invades capsule

- Spreads hematogenously
- Rx with RAI or surgery
- Follow with TGB level





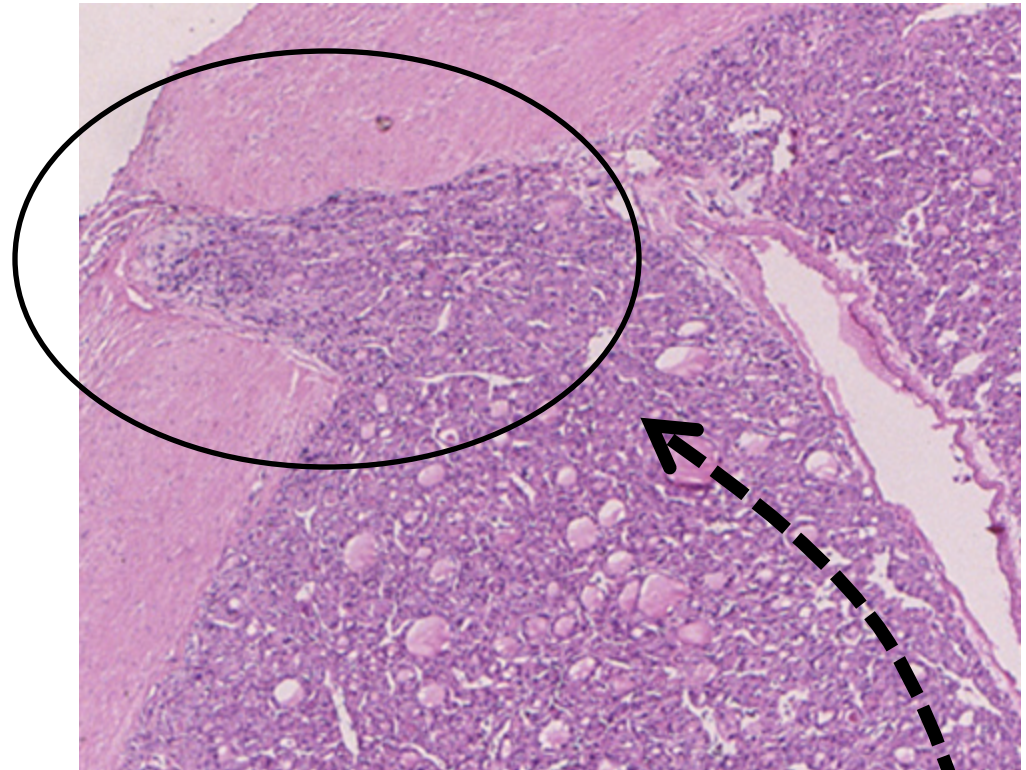
## Follicular Adenoma

Mutation, TSH receptor

(+) Capsule

Hot or Cold

If Cold → FNA



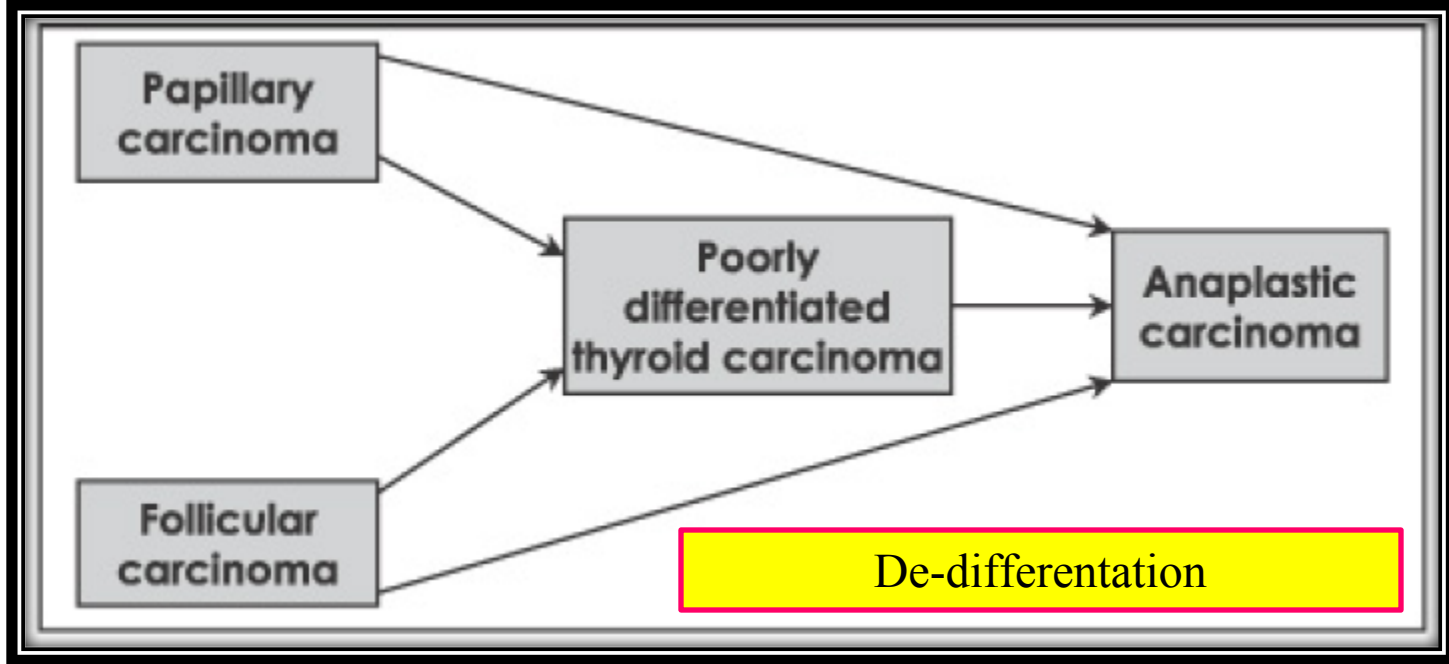
The difference between a follicular adenoma and carcinoma is this

# Anaplastic

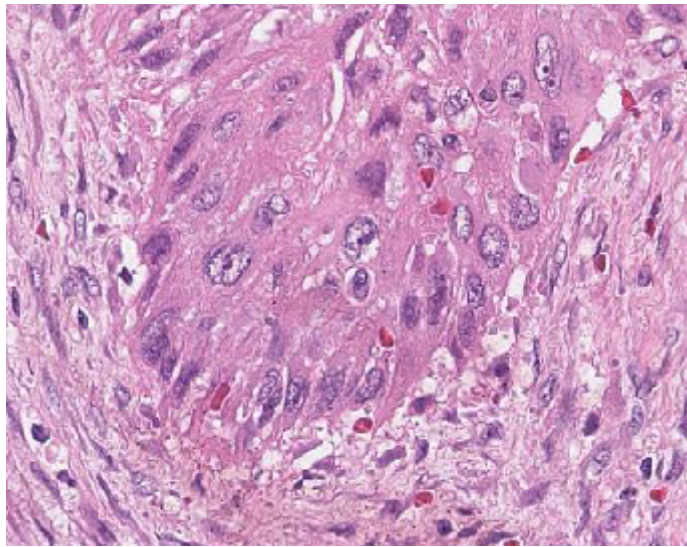
Pathologic description, like Riedel's, apt to appear as a distractor...

# Anaplastic

- Background
  - Aggressive tumors with ~100% mortality; seen in older adults
- Pathogenesis
  - Progressive mutations arising in other well differentiated tumors (i.e. ‘dedifferentiation’).
- Pathology (Anaplastic variants; may be mix of both)
  - Pleomorphic giant cells with occasional osteoclast-like multinucleate cells
  - Spindle cell appearance (sarcoma-like)
- Clinical
  - Rapidly enlarging masses
  - Compressive/invasive manifestations: dysphagia, dyspnea, cough and hoarseness



Remember This...



Pleomorphic Giant Cells  
(occasional **osteoclast-like** multinucleate cell)

# Medullary Carcinoma

- Background
  - Neuroendocrine neoplasms derived from the parafollicular cells
    - C cells – **calcitonin** secreting
  - MEN2a (**pheo**, PTH)/b (**pheo**, angioma/mucosal neuromas/marfanoid features)
- Pathogenesis
  - Activating mutations in the **RET proto-oncogene**
- Pathology
  - **Amyloid** like appearance from calcitonin polypeptides
  - Polygonal/spindle shaped cells → nests/trabeculae
  - Neuroendocrine: EM will be (+) for granules (**calcitonin**)

# RET proto-oncogene

The RET protein spans the cell membrane. This positioning of the protein allows it to interact with specific factors outside the cell, receiving signals that enable the cell to respond to its environment.

The ***RET* proto-oncogene** encodes a tyrosine kinase receptor; gain of function mutations are associated with the development of various types of human cancer, including MTC/MEN type 2A and 2B.

The overactive protein likely transmits growth and differentiation signals (**loss of cell cycle regulation**).

Infiltrative appearance of amyloid

Calcitonin Proteins



Congo Red Stain with  
Apple Green Birefringence  
Under Polarizing Lens

- Treatment
  - MEN 2 patients with RET mutation are offered prophylactic thyroidectomy
  - Serial assessment: **monitor calcitonin levels**





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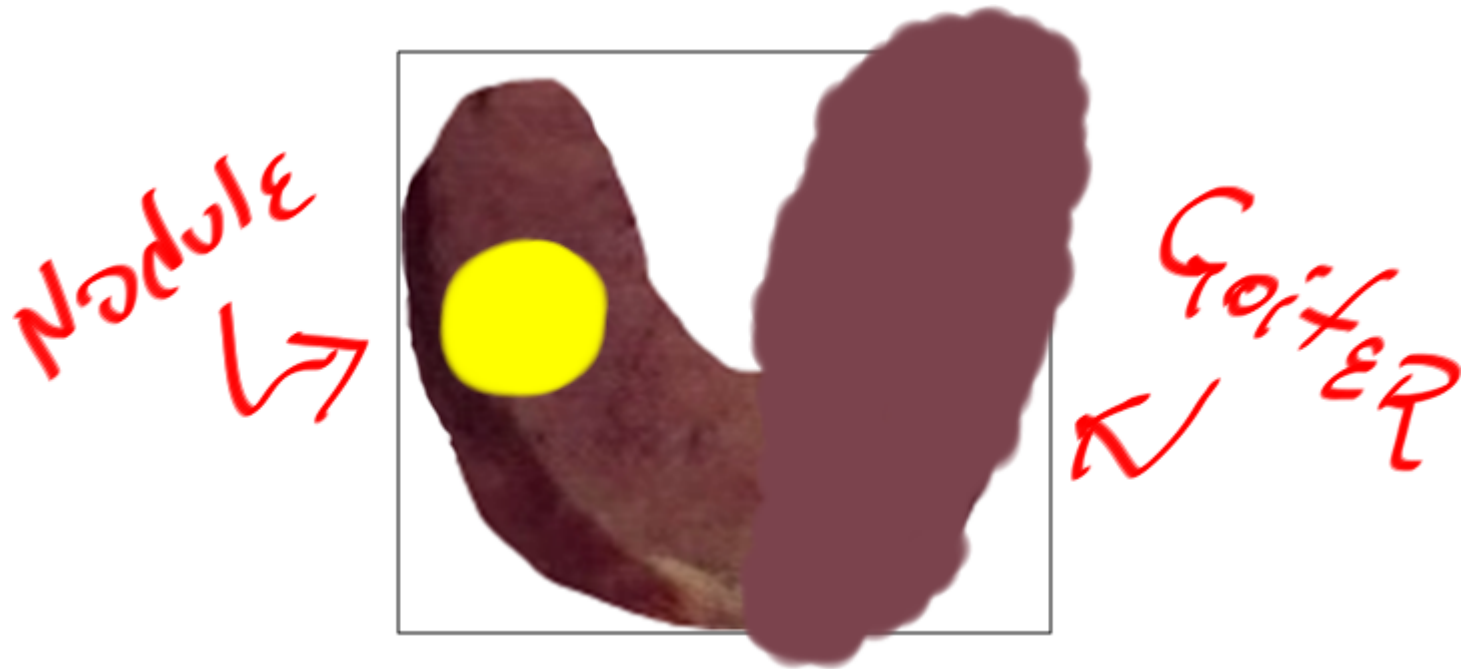


Follicular

Medullary



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