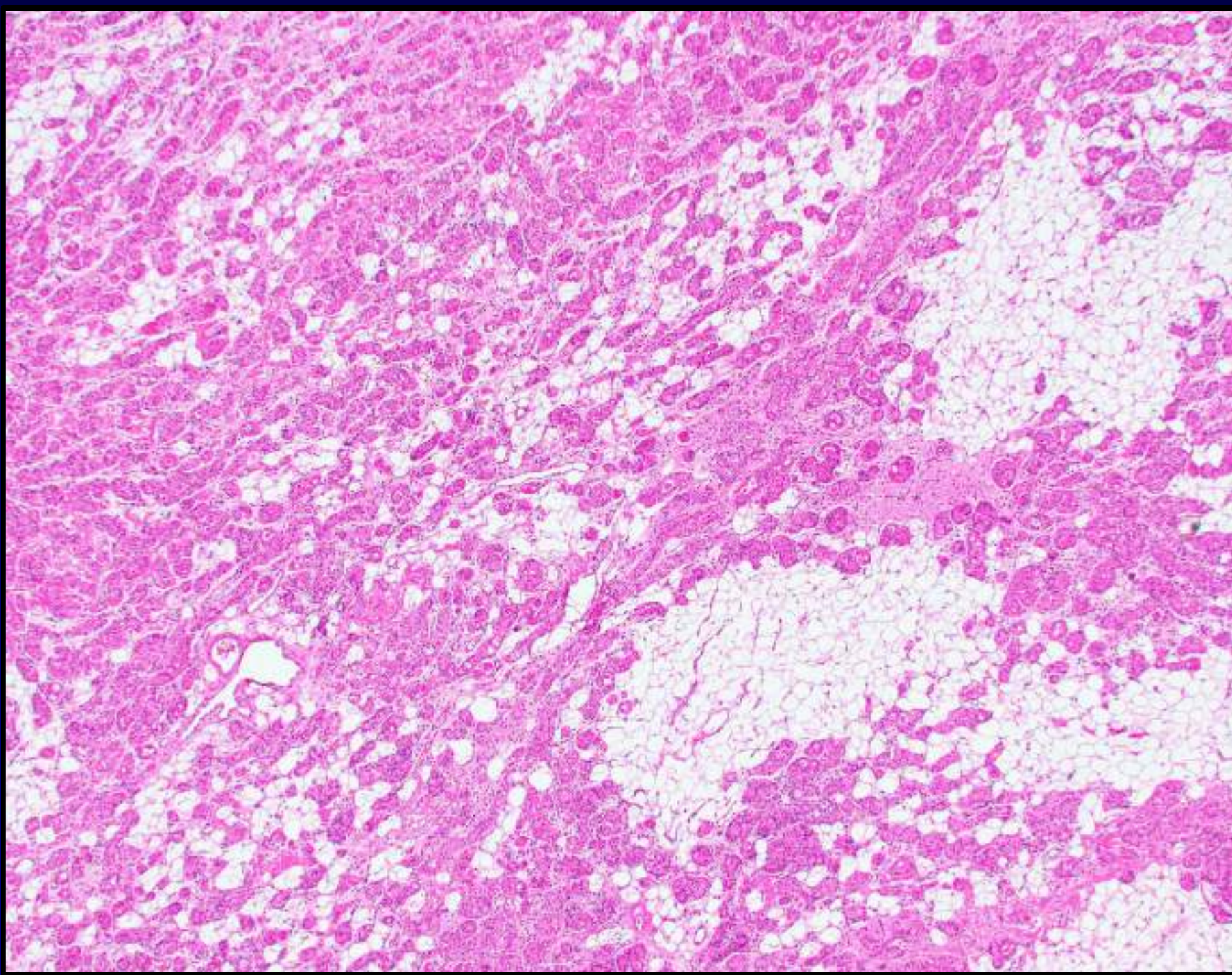


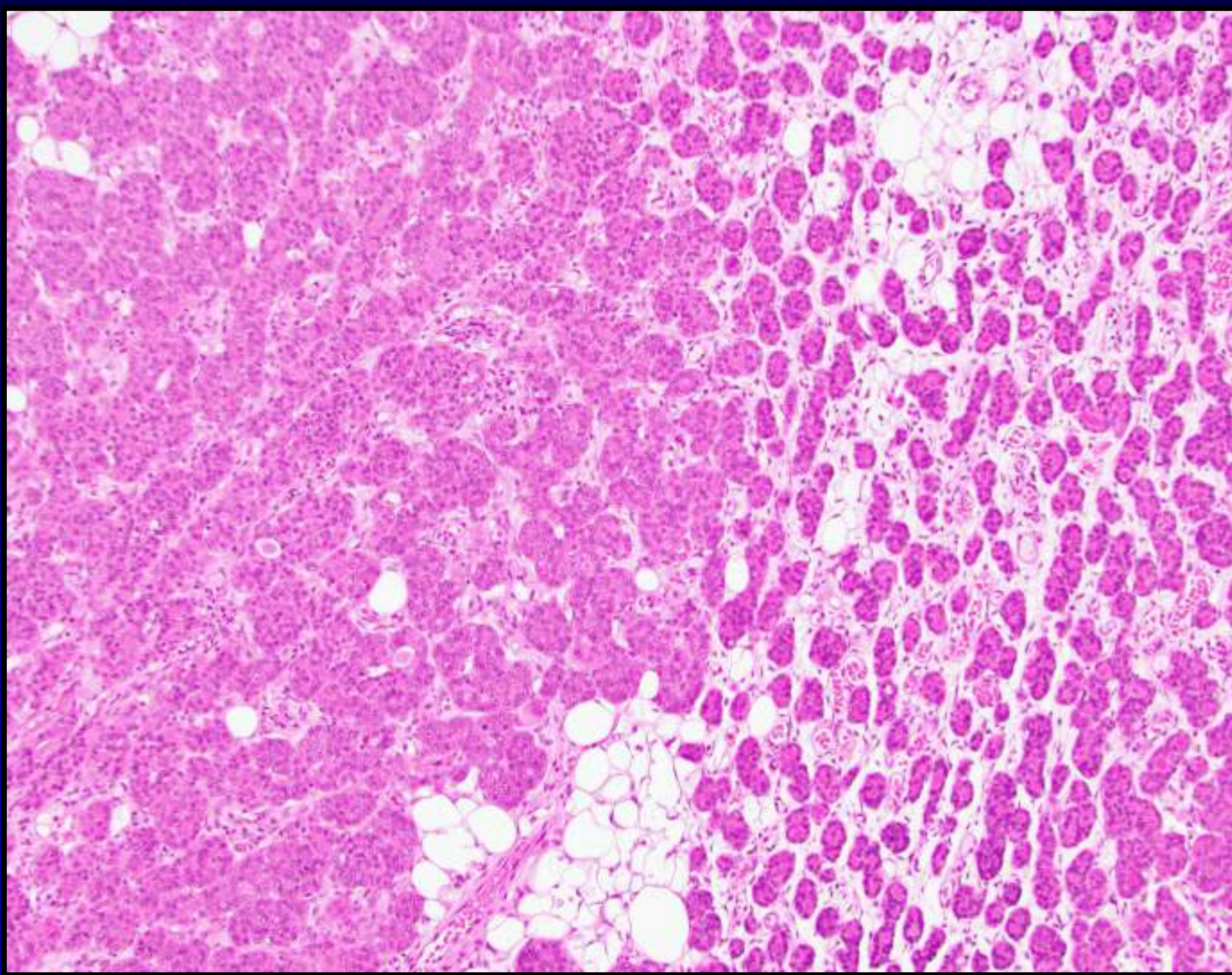
Case 4

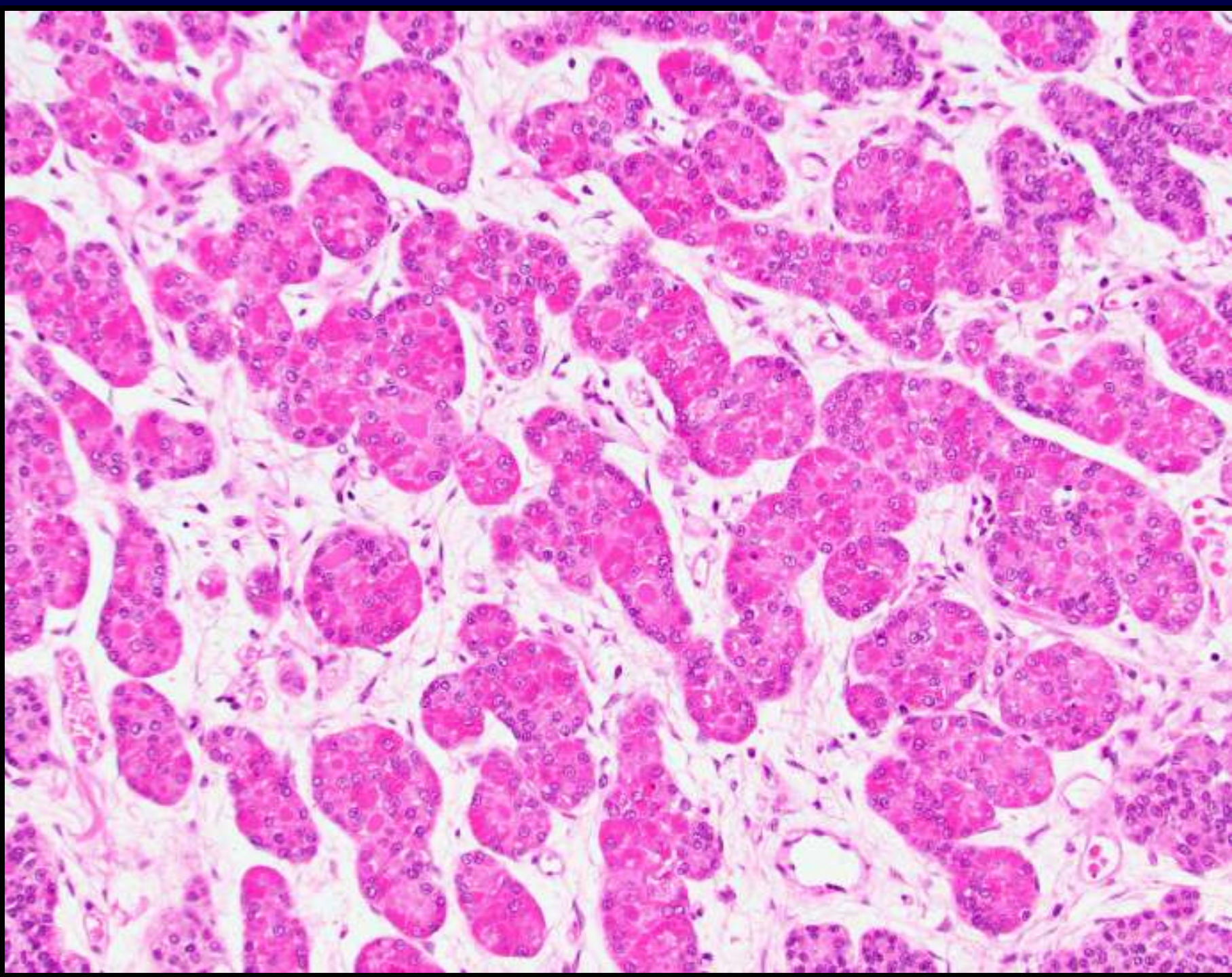
- **A 48 year old female presented with an ill-defined mass on a screening mammogram.**
- **A diagnosis of invasive carcinoma was made on a core needle biopsy.**
- **The images are from the subsequent nipple-sparing mastectomy.**

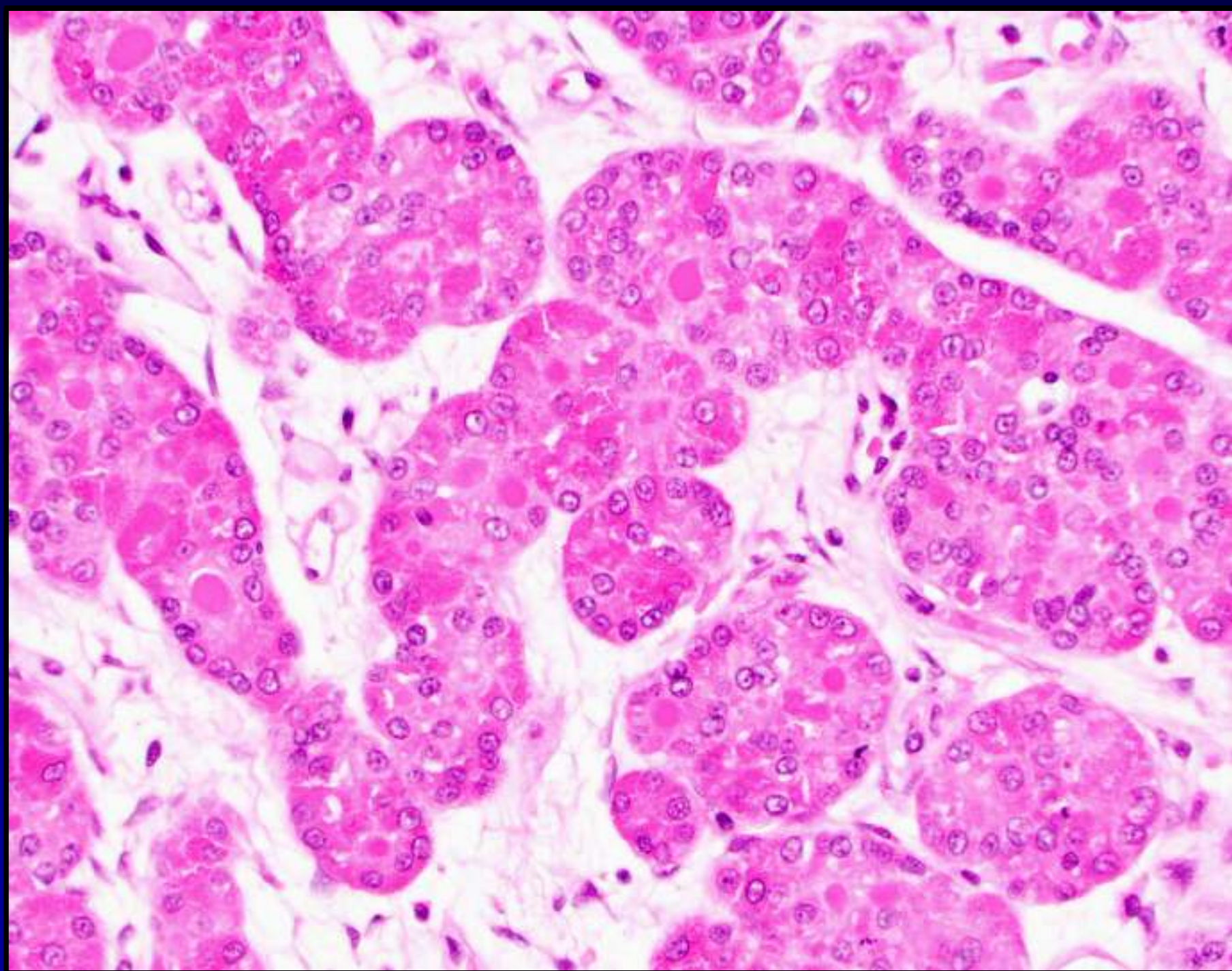
Mastectomy specimen

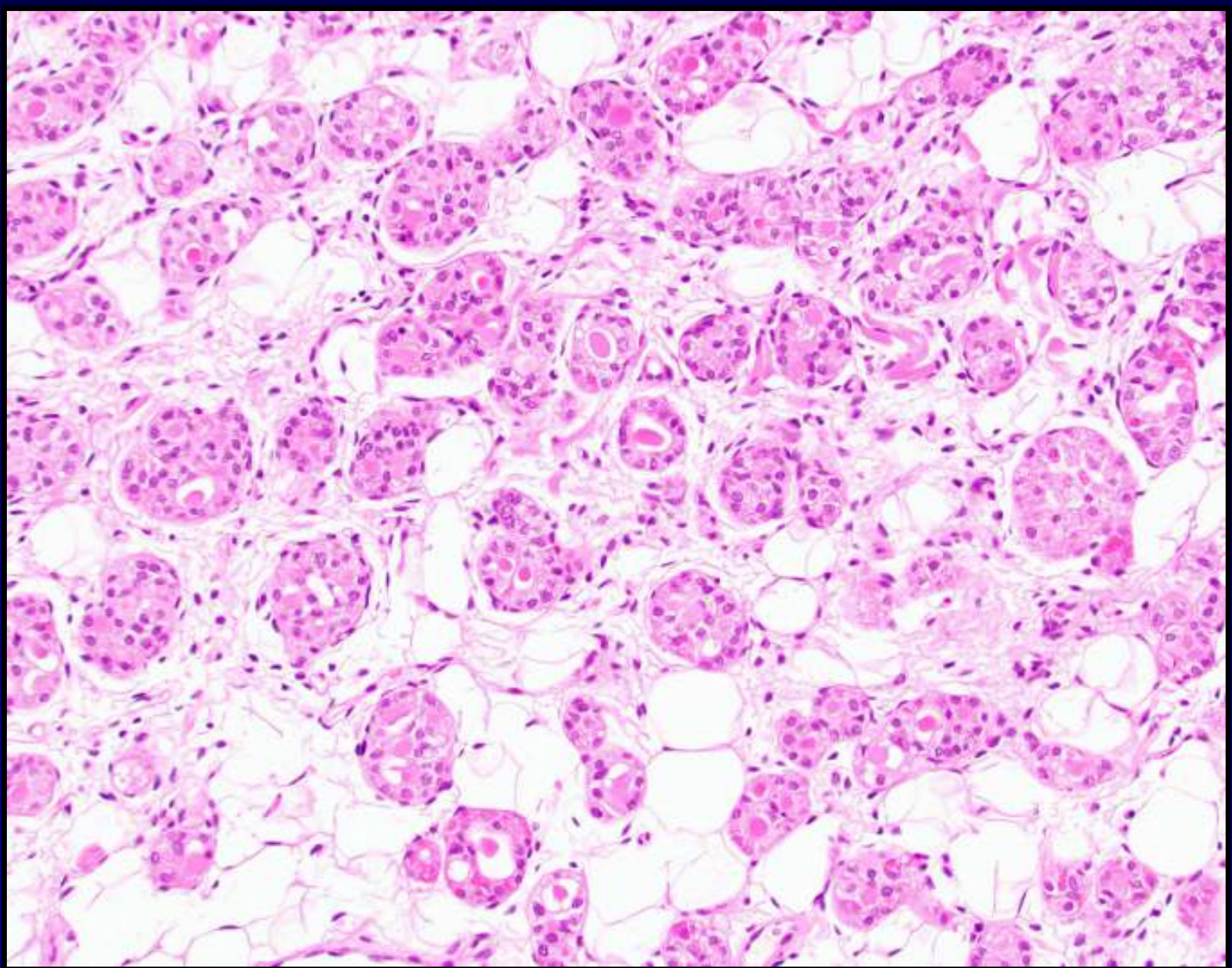
- **9 x 5 x 4 cm irregular, firm mass**

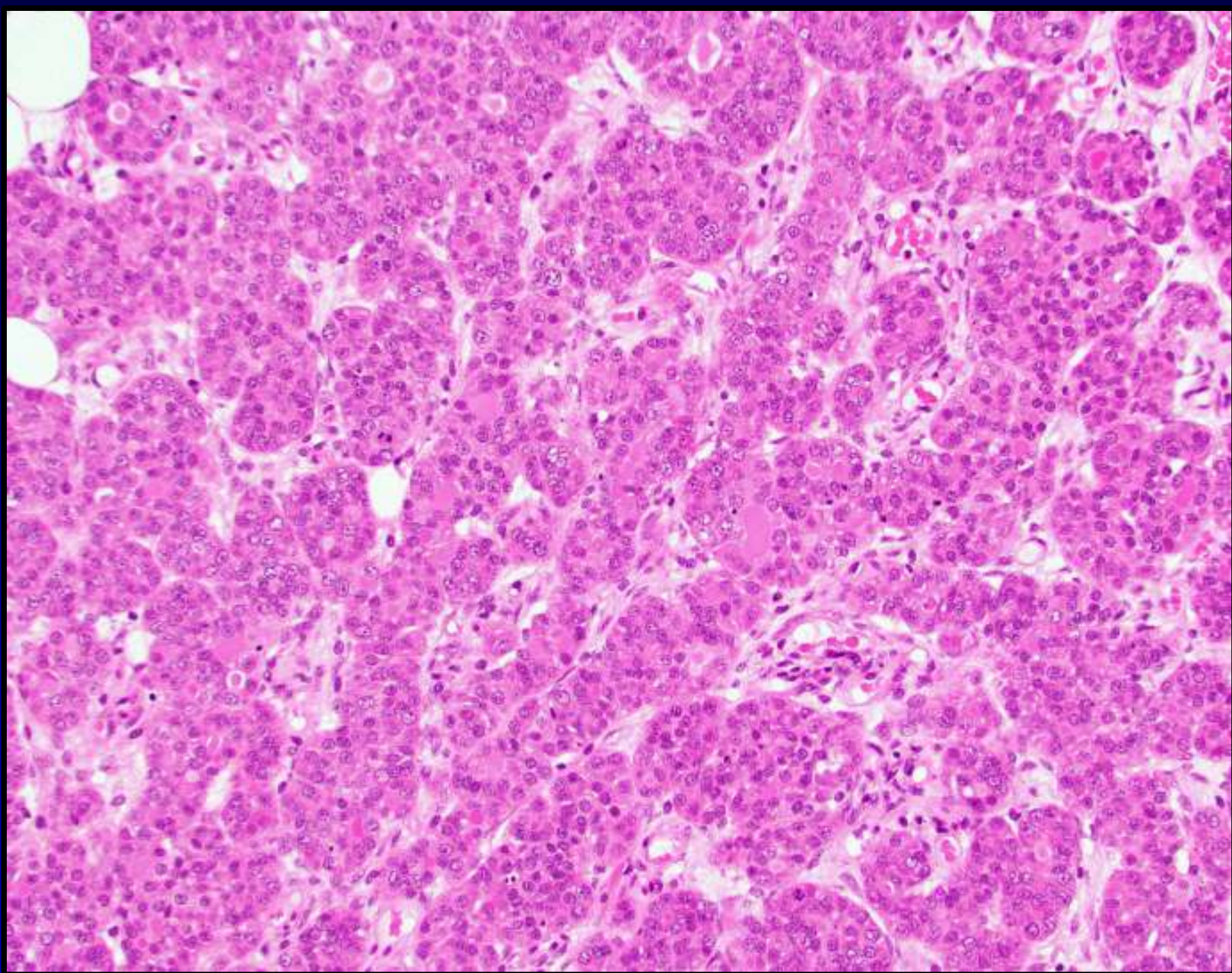


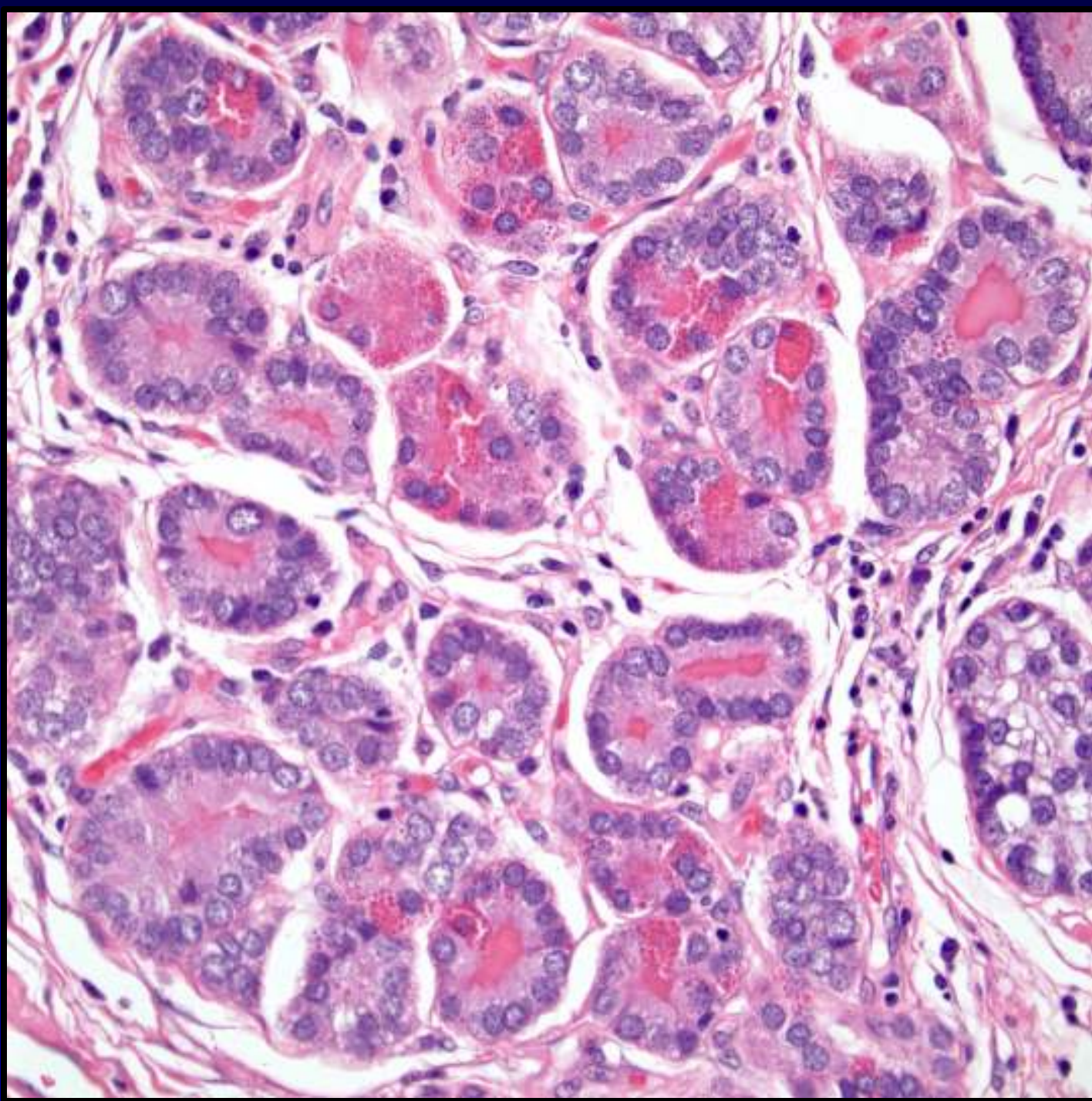




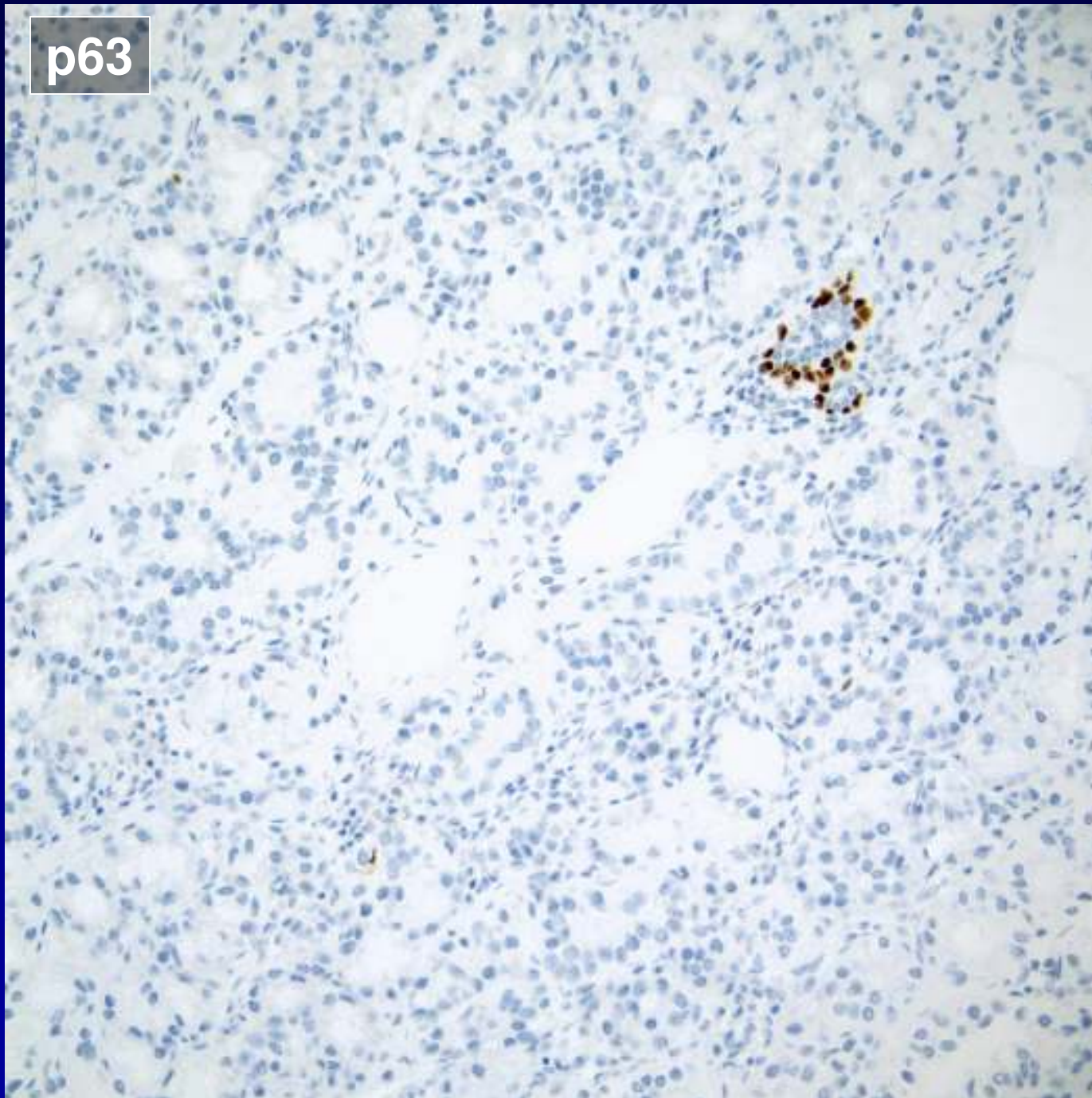




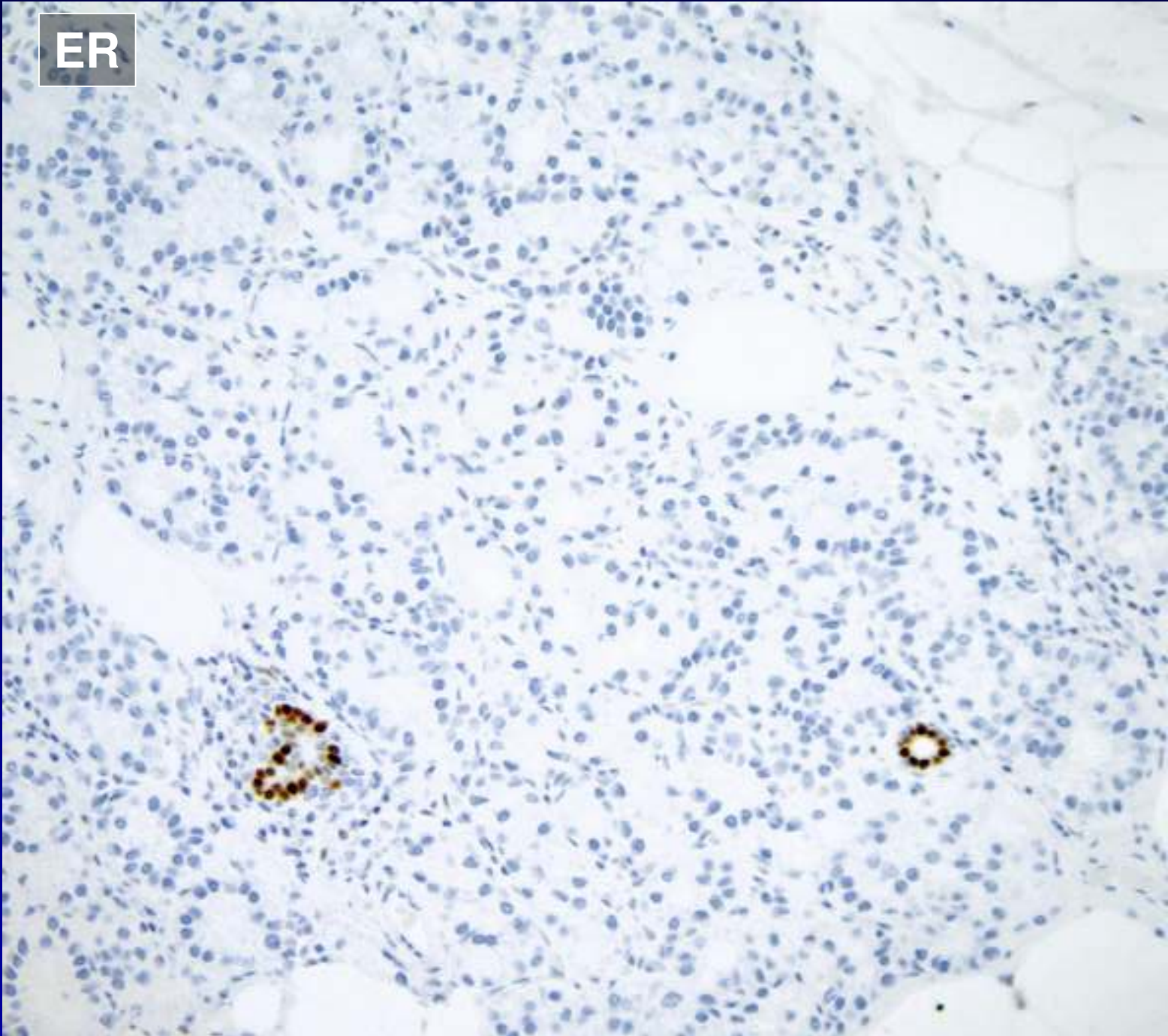




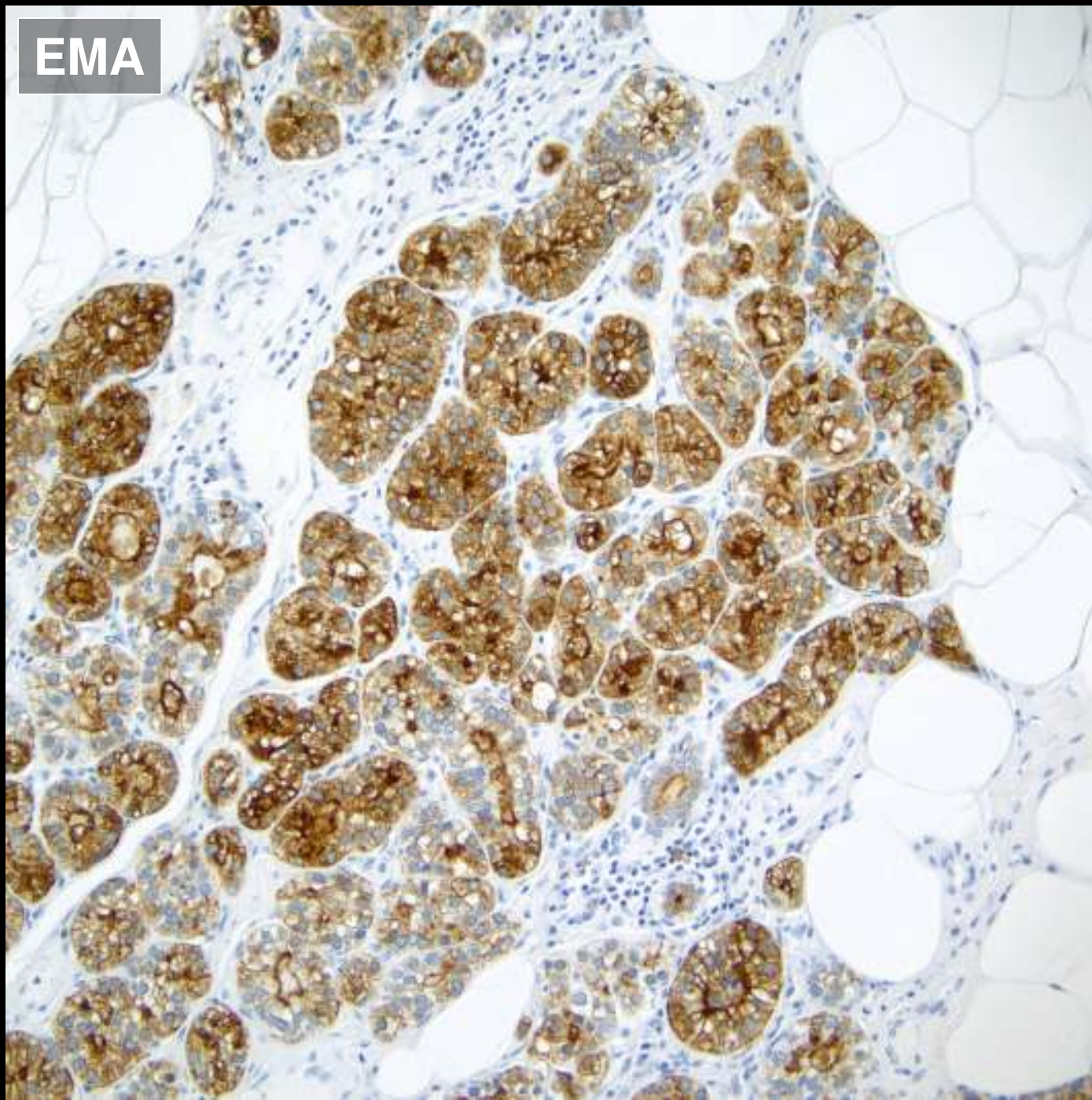
p63



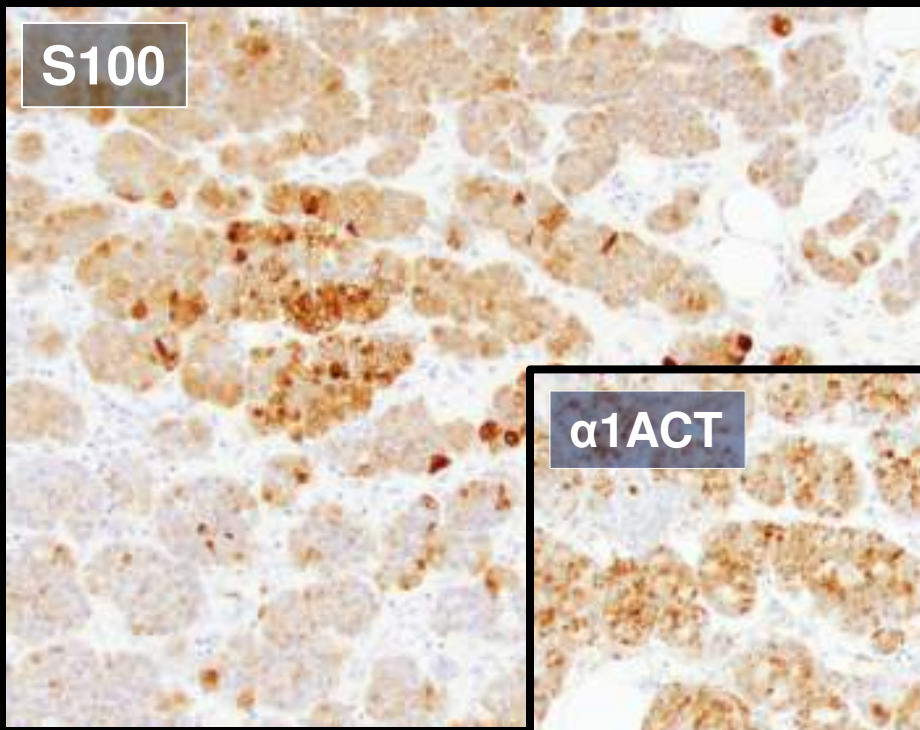
ER



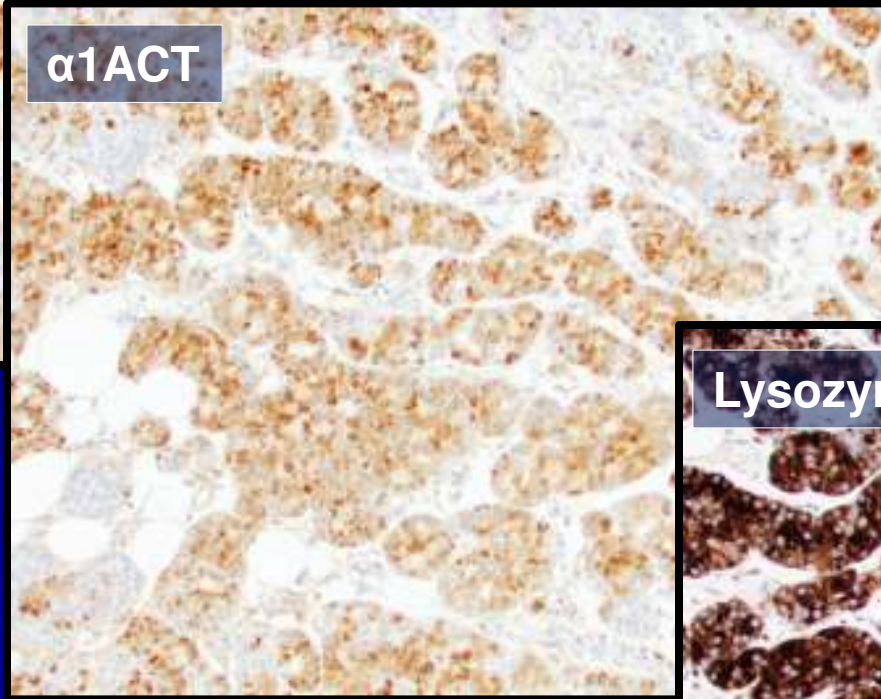
EMA



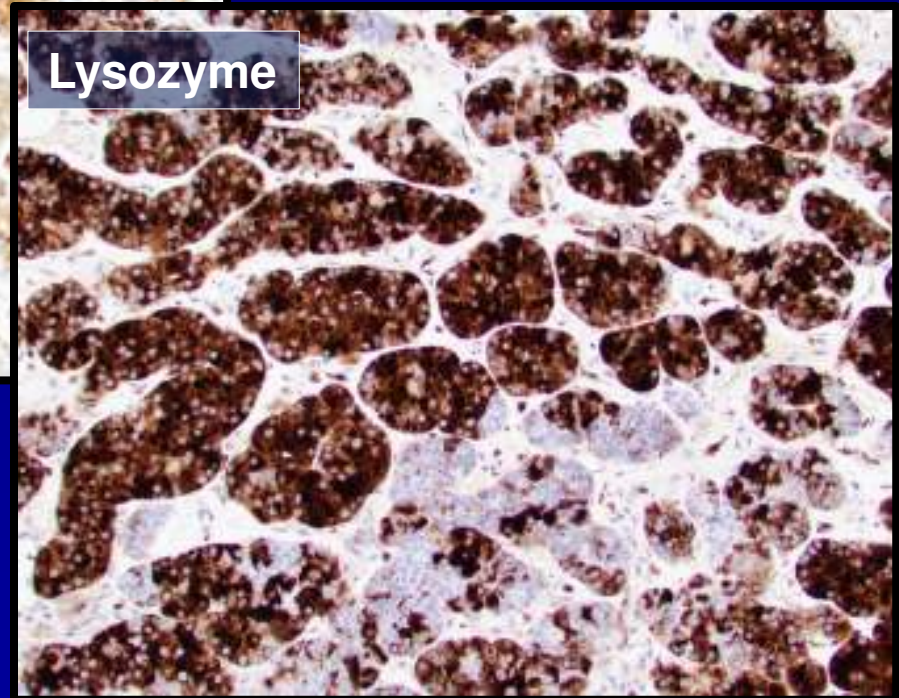
S100



α 1ACT



Lysozyme

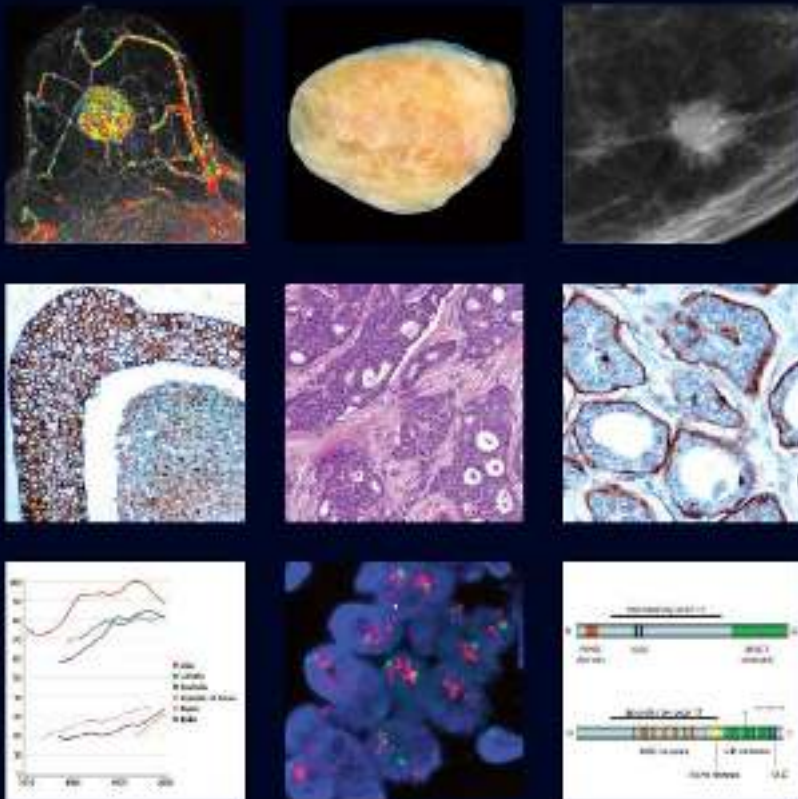


Diagnosis

Acinic Cell Carcinoma

WHO Classification of Tumours of the Breast

Edited by Sunil R. Lakhani, Ian O. Ellis, Stuart J. Schnitt, Puay Hoon Tan, Marc J. van de Vijver



Acinic cell carcinoma

Definition

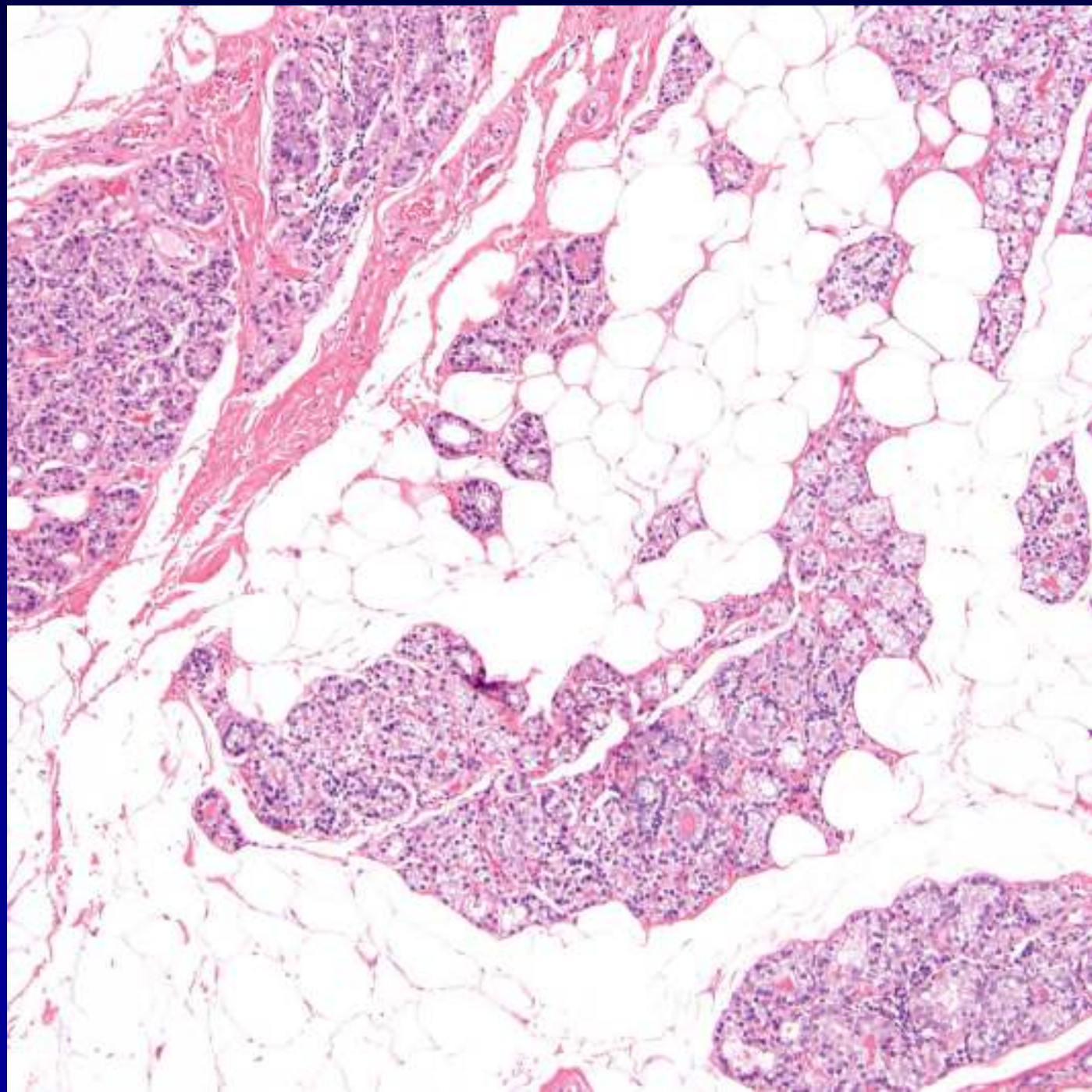
A breast carcinoma similar to the acinic cell carcinoma of the parotid gland that shows (serous) differentiation with zymogen-type cytoplasmic granules.

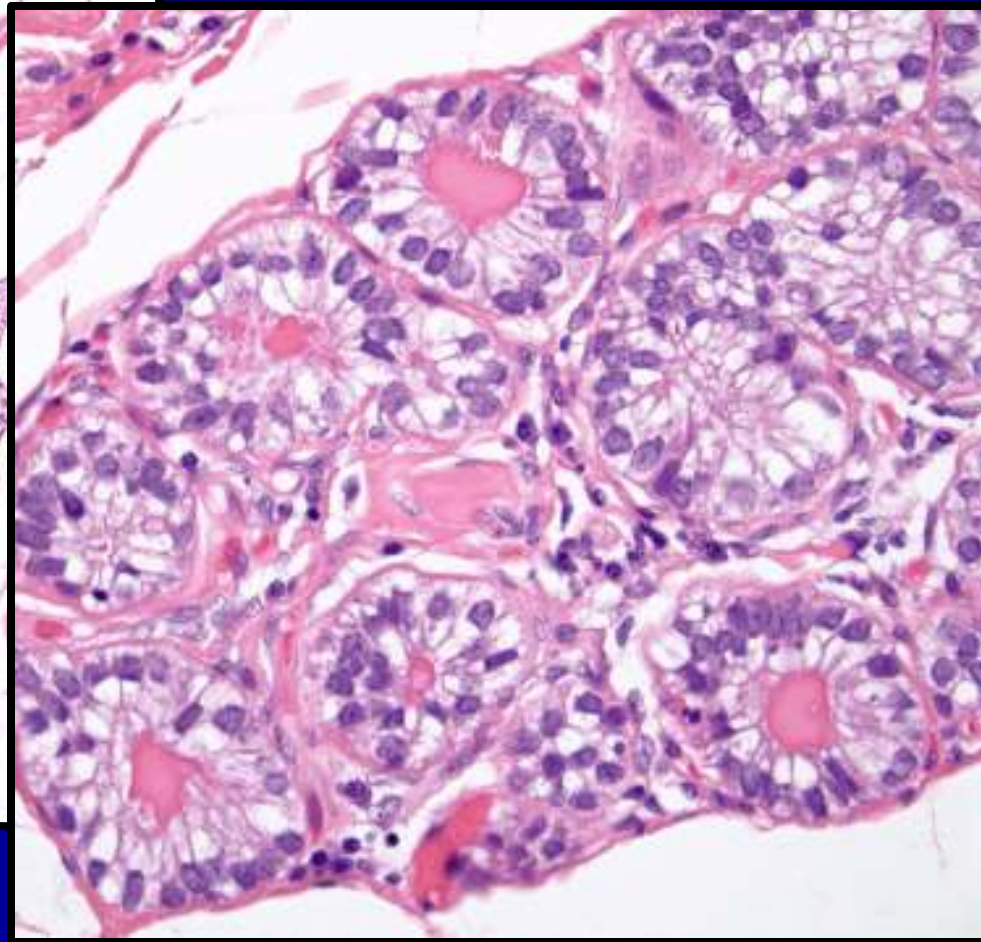
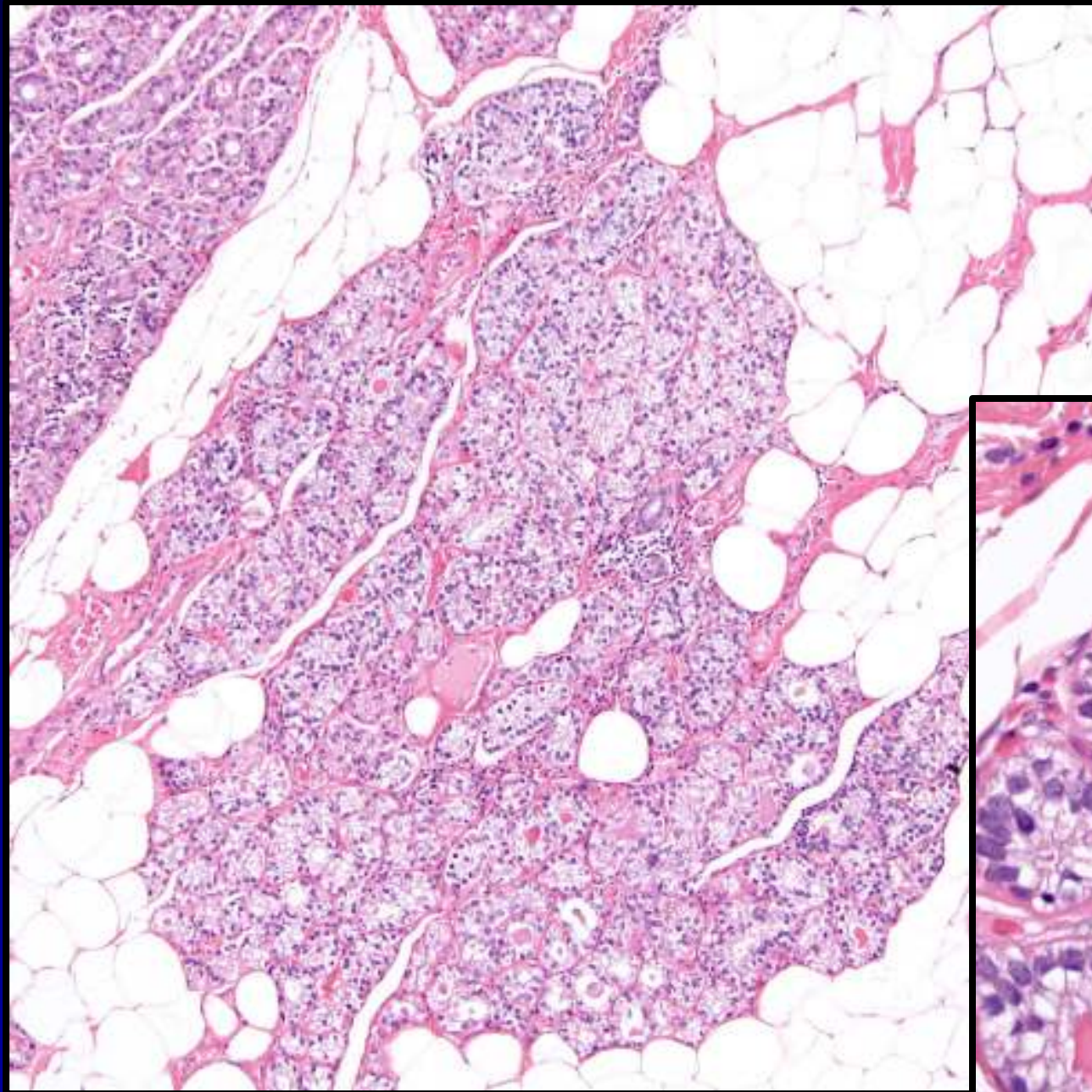
Acinic Cell Carcinoma

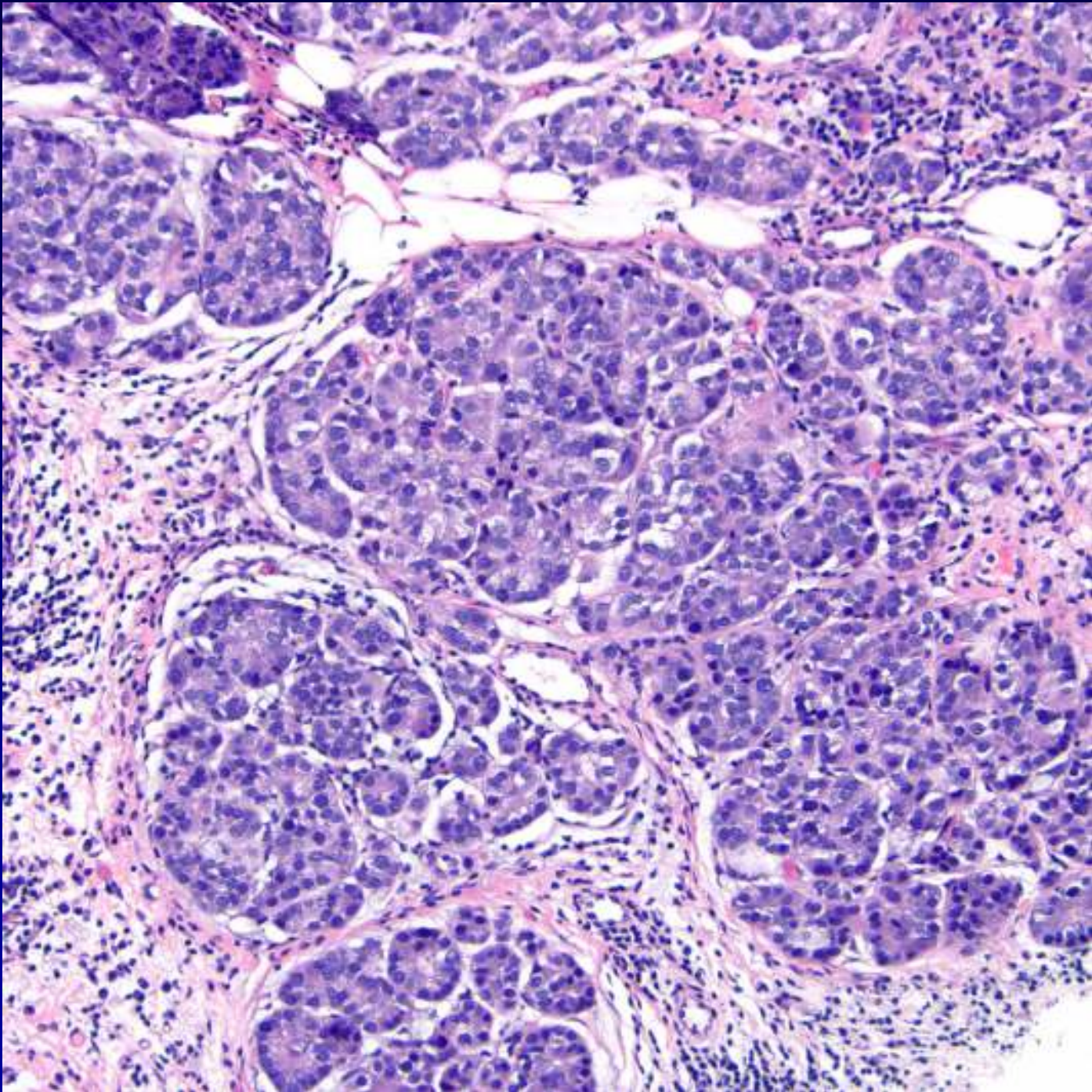
- **Rare: 47 cases reported to date**
- **Median age: 49 yrs (range, 20-80 yrs)**
- **Median tumor size: 3 cm (range, 1.3-5.5 cm)**
- **15 cases with associated invasive ductal carcinoma (IDC), most high grade**
- **8/27 cases (29.6%) node +**
 - **4/8 node + cases has a component of high grade IDC**

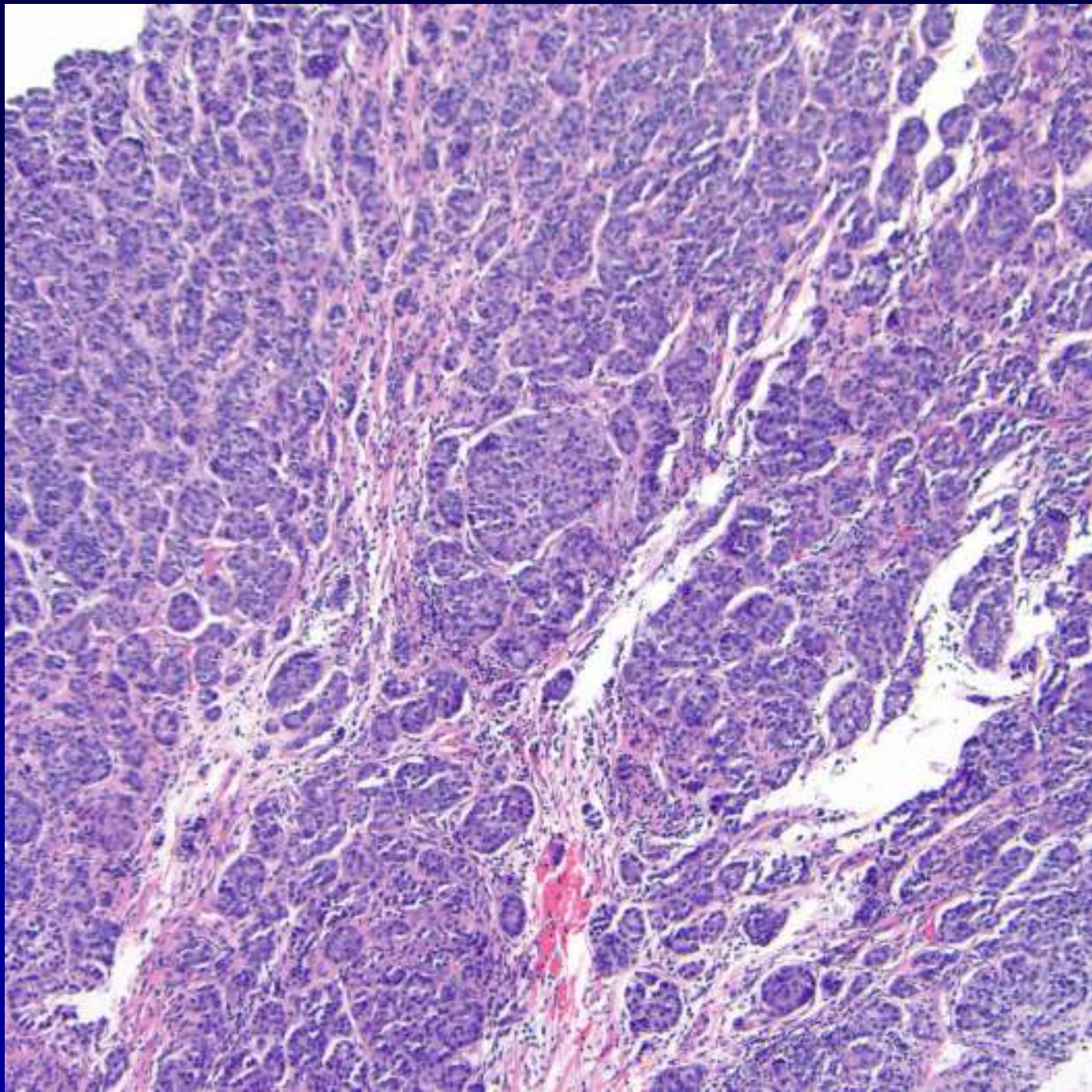
Acinic Cell Carcinoma

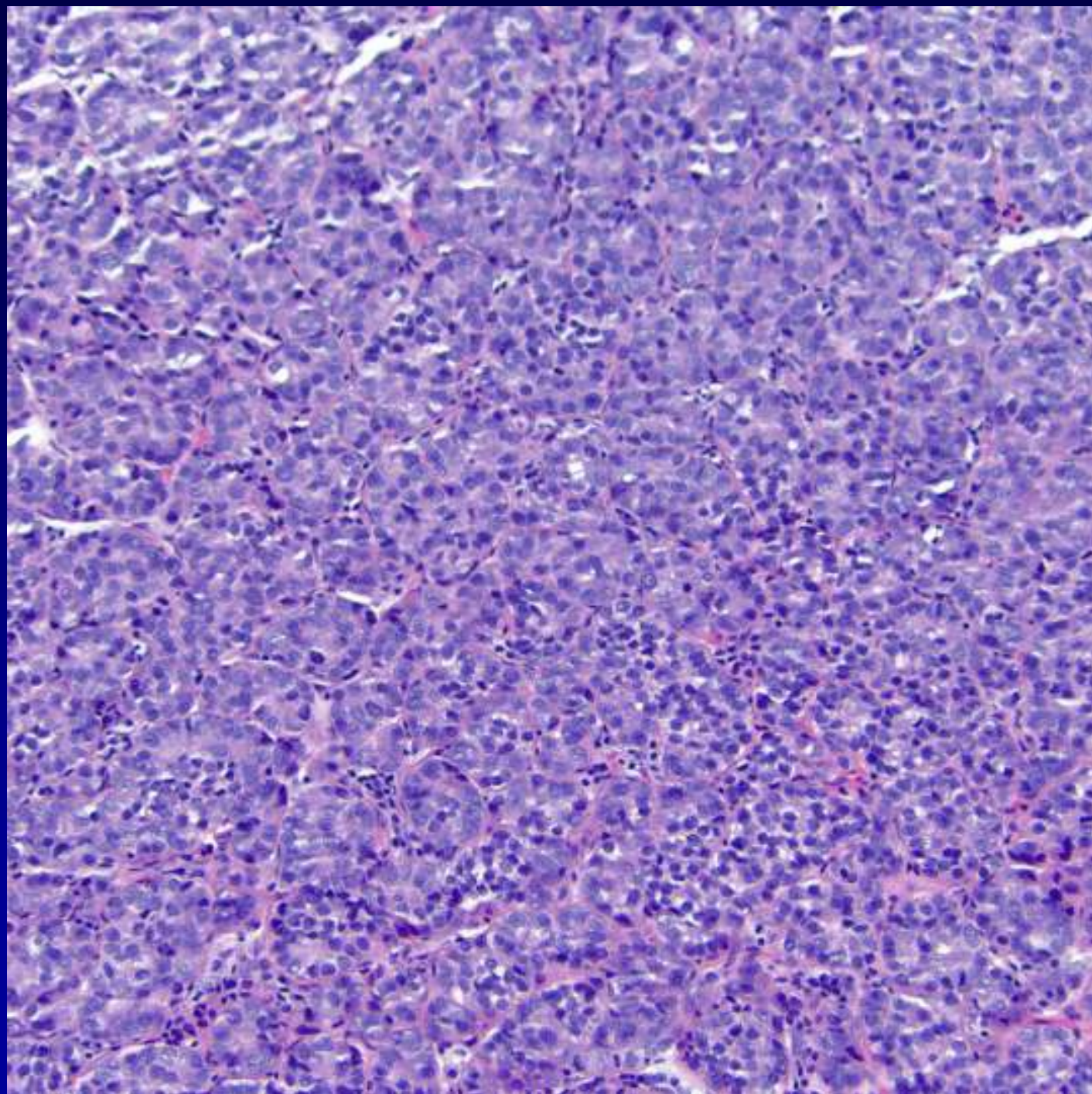
- **Typically infiltrate as a mixture of**
 - **Microglandular/tubular elements with intraluminal eosinophilic secretions**
 - **Small, closely packed solid nests**
 - **Larger solid, circumscribed to irregular nests**
- **Necrosis may be present in solid areas**
- **Cytoplasm can be clear or amphophilic or have basophilic or eosinophilic granules; eosinophilic granules may be fine or coarse (Paneth cell-like)**

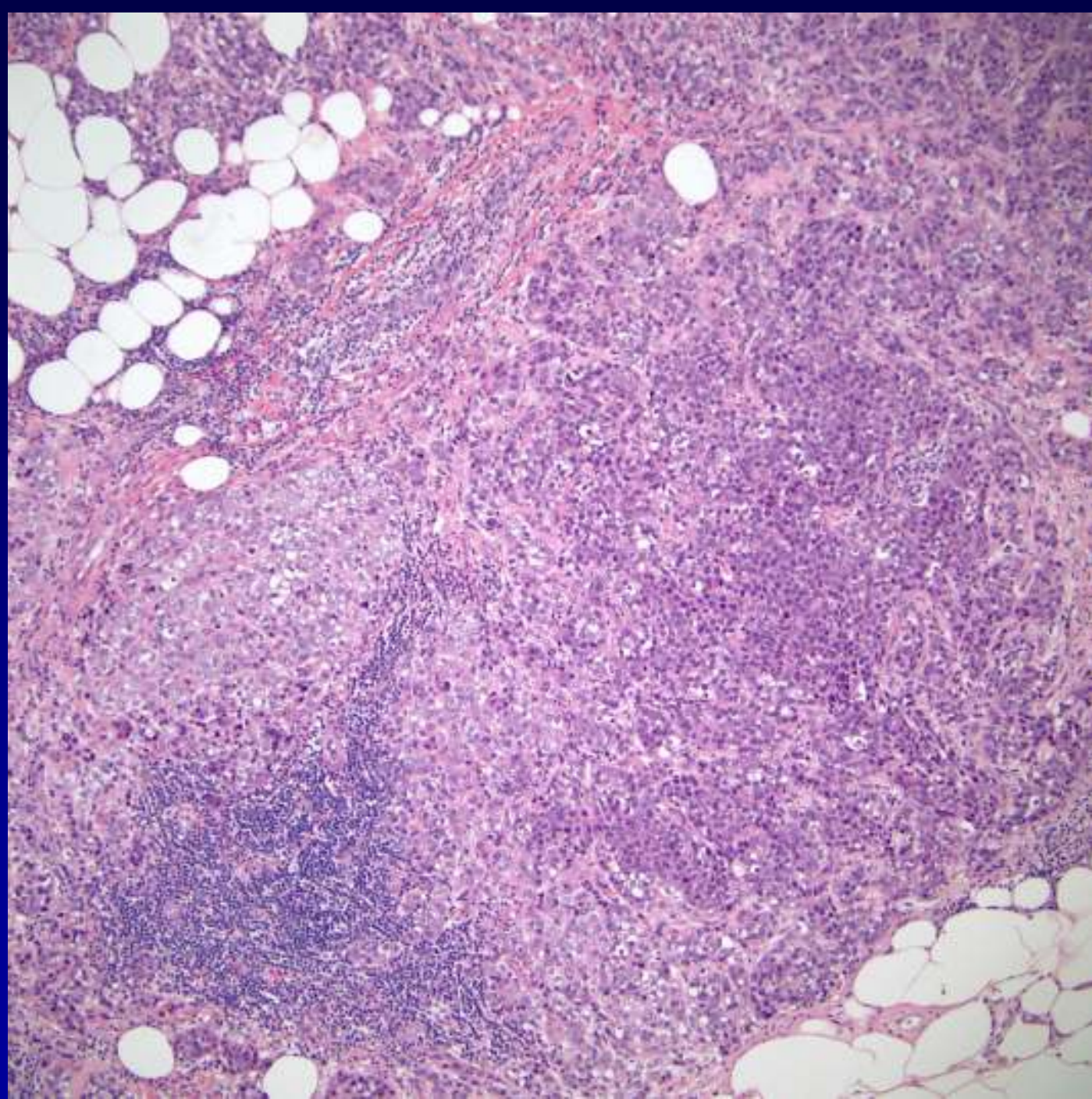


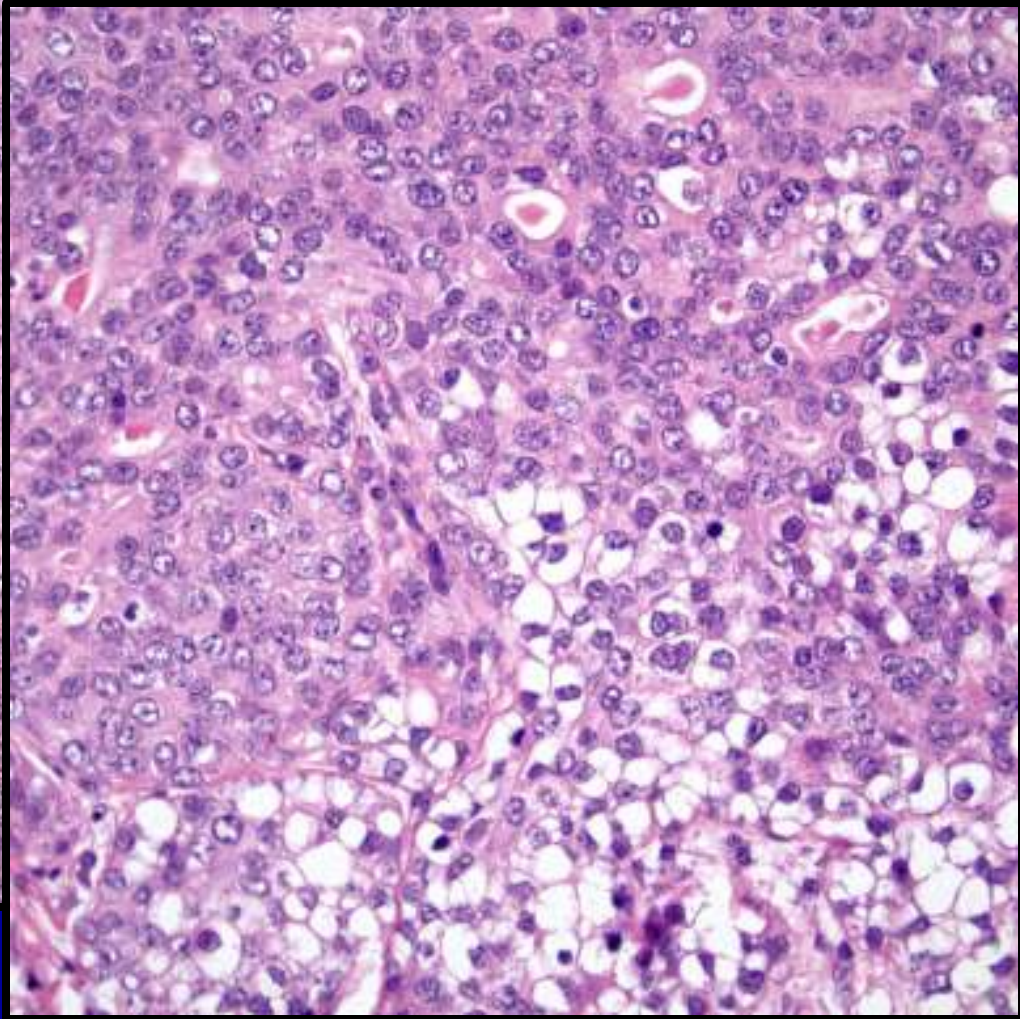
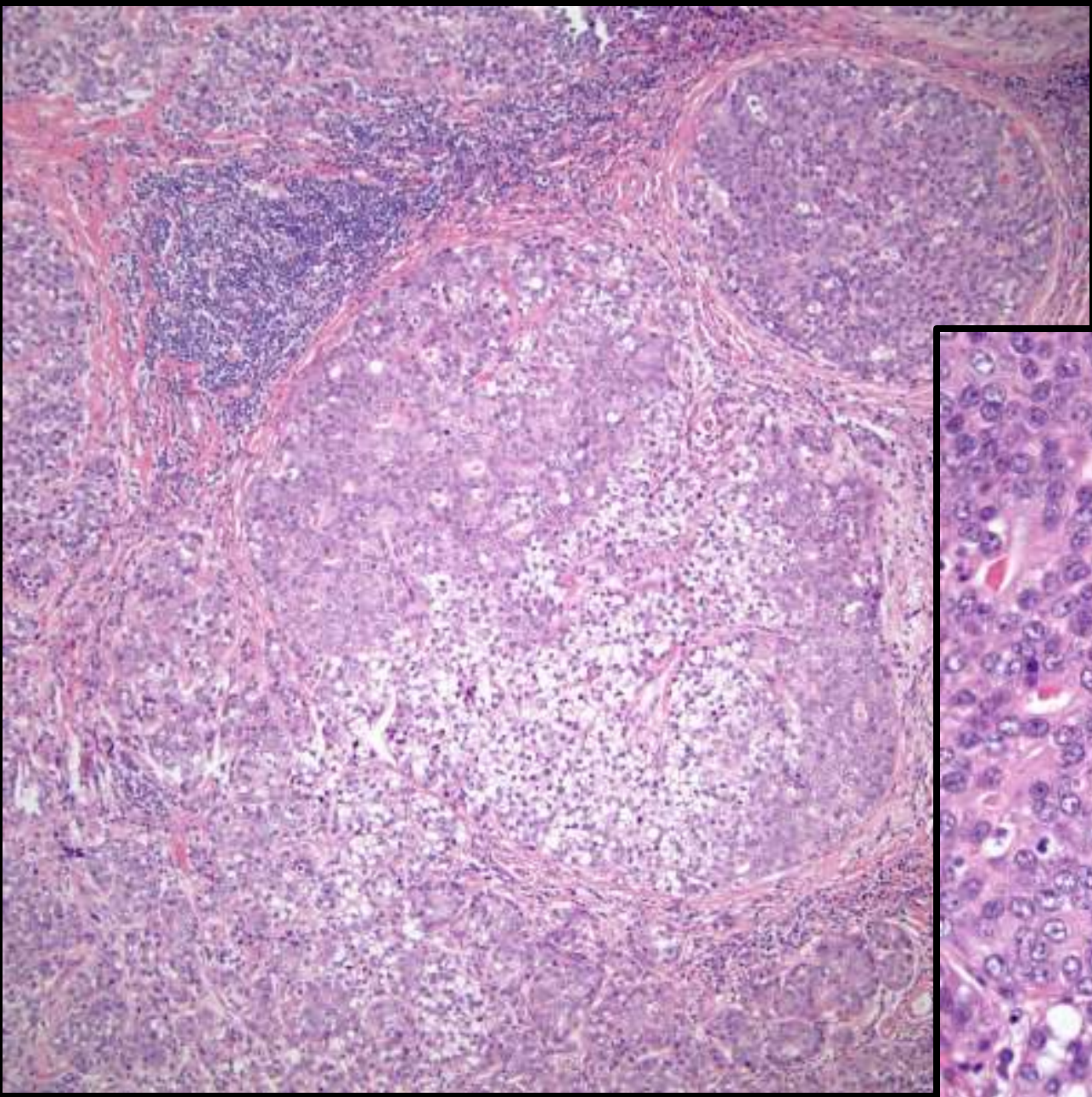


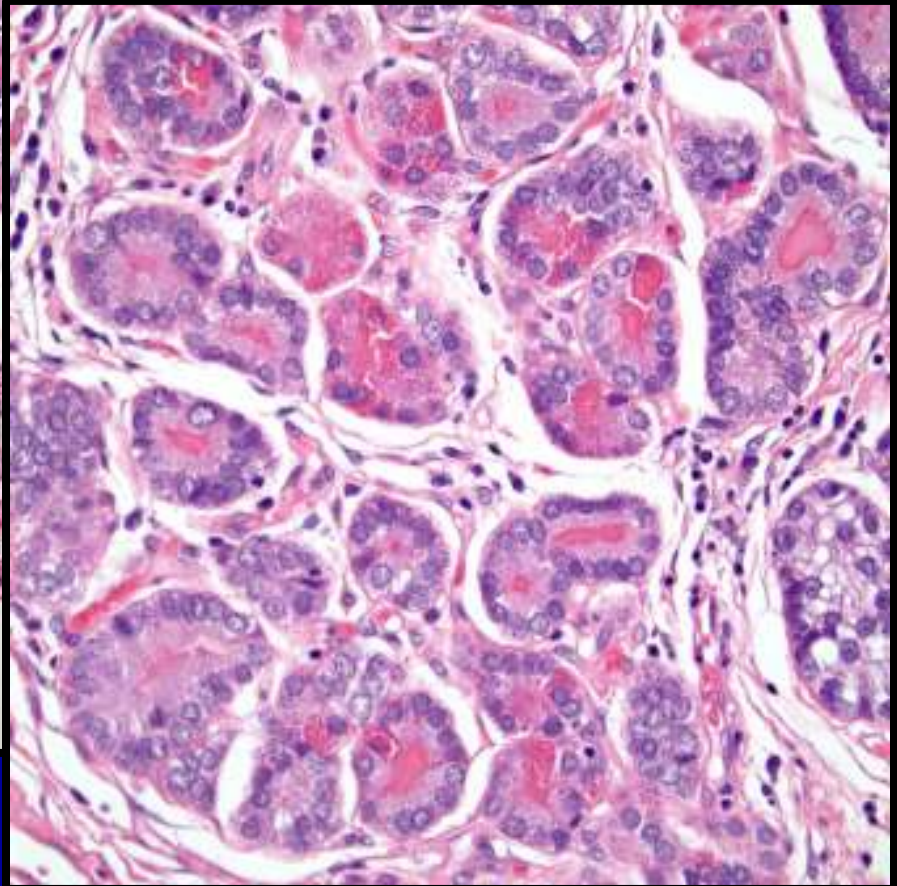
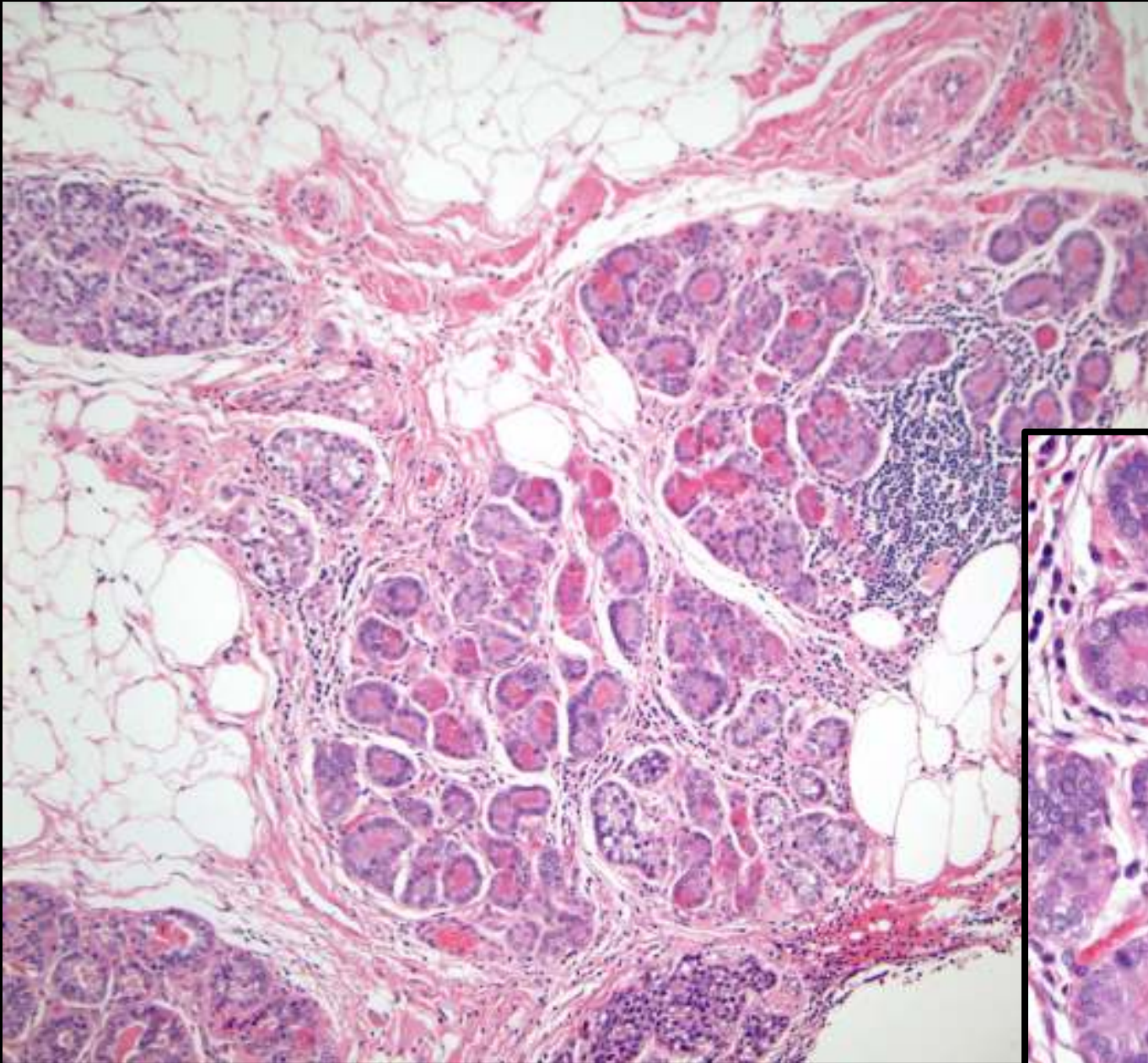












Acinic Cell Carcinoma

- Immunophenotype
 - ER/PR/HER2 negative (triple negative)
 - EMA positive
 - S100 positive
 - Positive for amylase, lysozyme, α -1 anti-chymotrypsin

Acinic Cell Carcinoma

Outcome

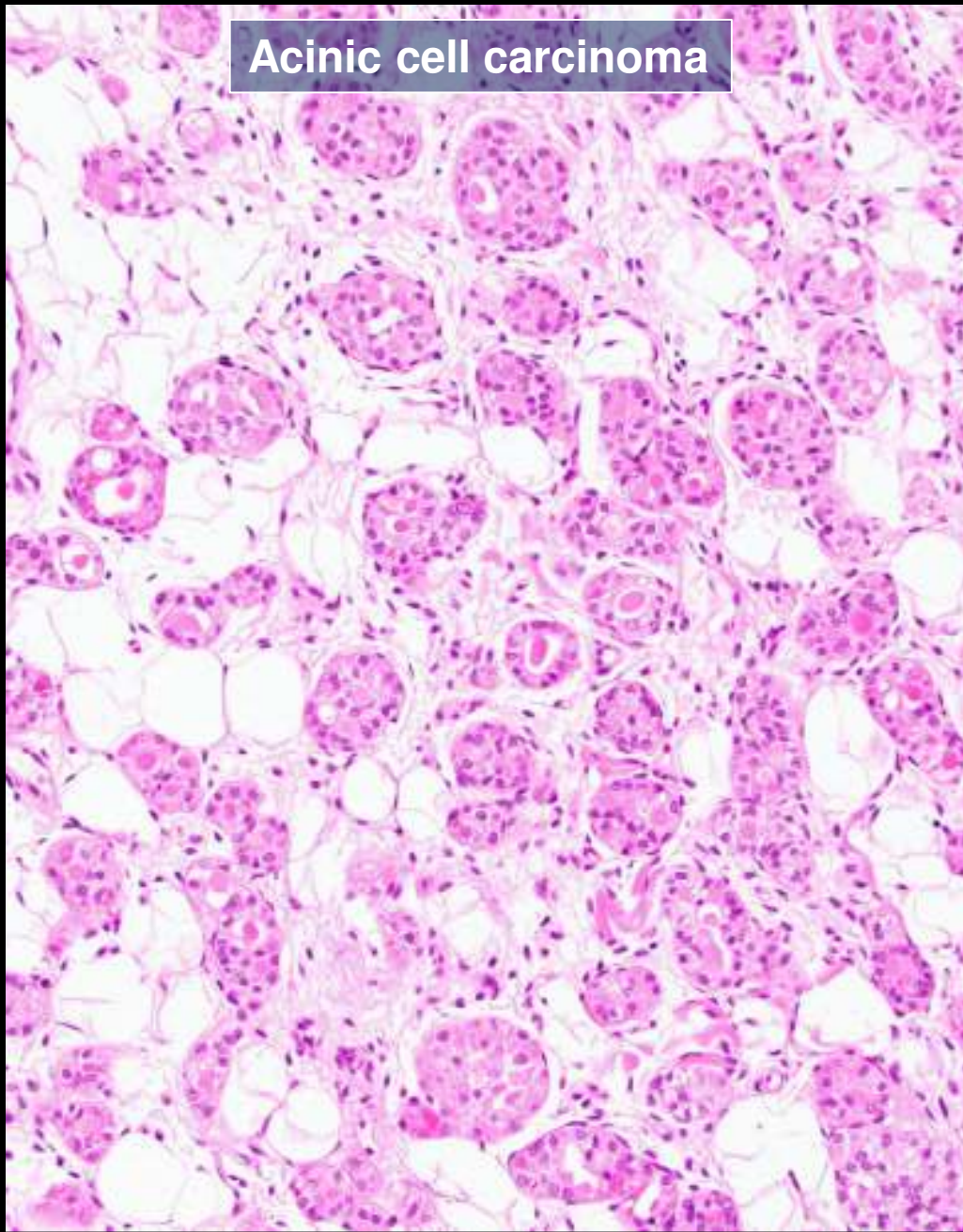
- **Among 25 reported cases with follow-up (median 28 mos, range 6-185 mos):**
 - 19 (76%) with no recurrence
 - 6 (24%) with distant mets (liver, bone, lung)
 - 2 (8%) DOD
- **May progress to high grade TNBC; prognosis likely driven by this component**
- **Association with *BRCA1* mutations**
 - 1 reported case (Ripamonti, 2013)
 - 1 personal observation

Acinic Cell Carcinoma

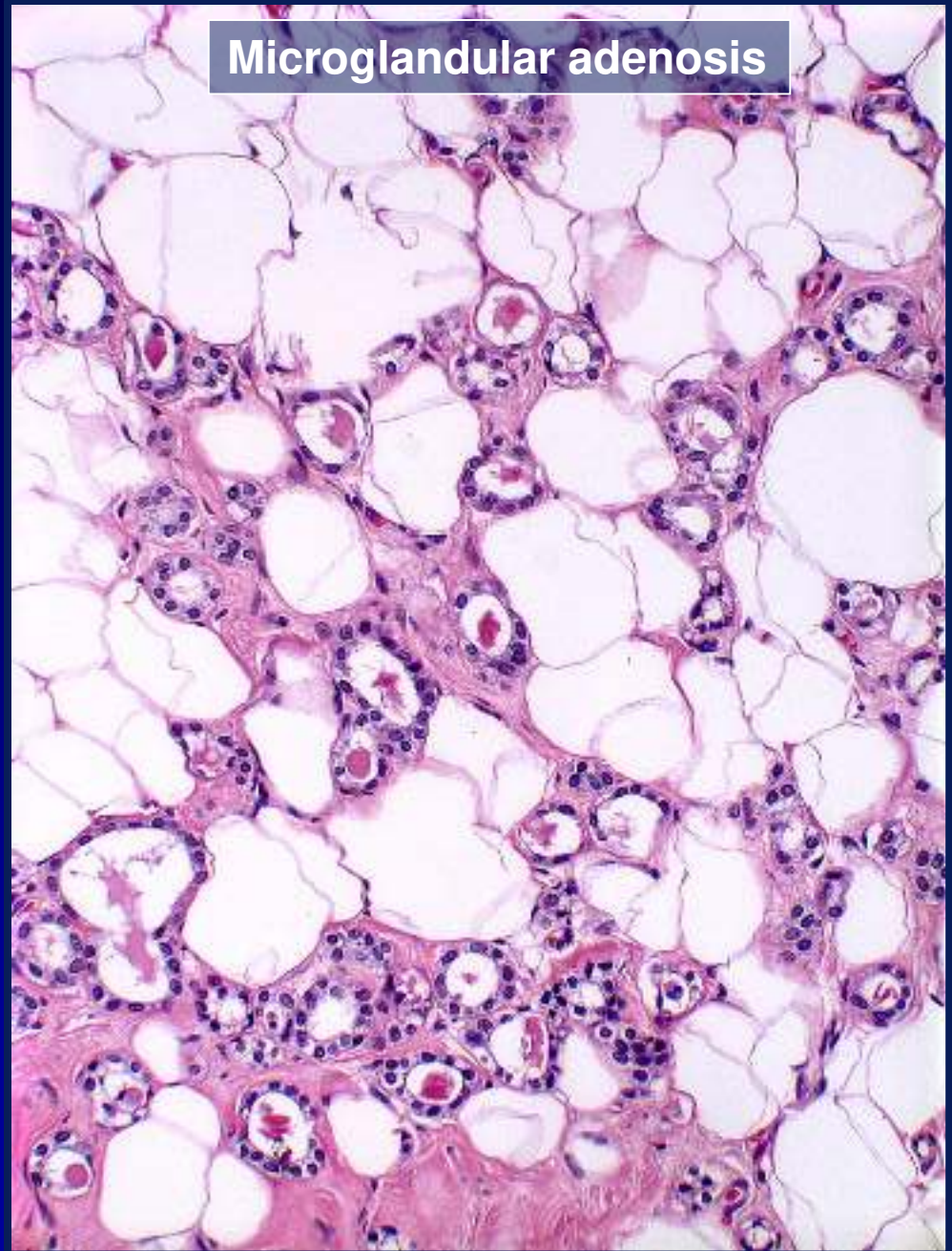
Molecular Profile

- **Share features with TNBC**
- **High mutational burden**
 - TP53 mutations in 80%
 - PIK3CA mutations in 10%
- **Complex pattern of copy number alterations**
 - Recurrent 8q gains, 5q losses
- **Somatic mutations in other genes commonly altered in TNBC**
 - *ERBB3, INPP4B, FGFR2*

Acinic cell carcinoma



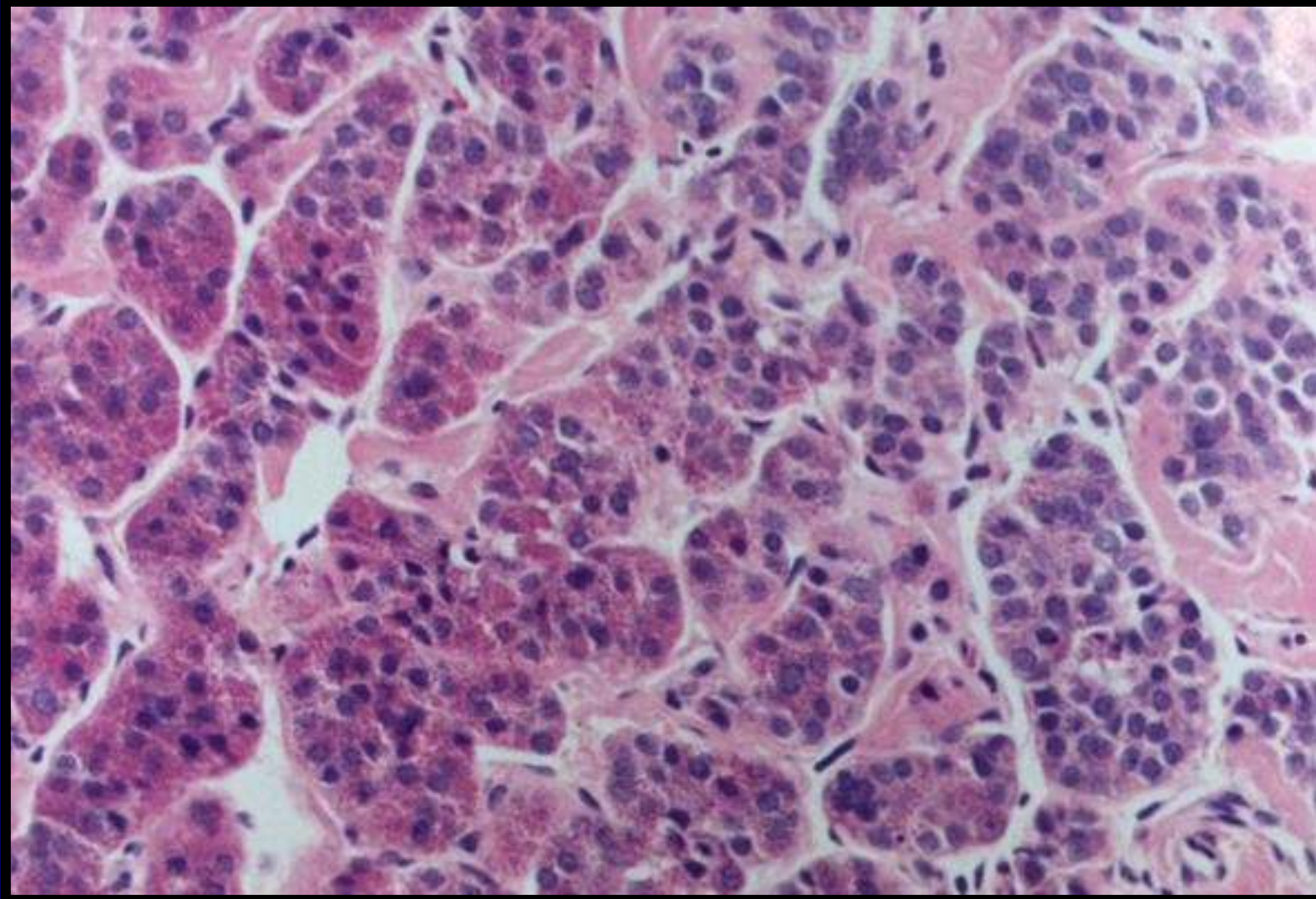
Microglandular adenosis



Similarities Between MGA and Acinic Cell Carcinoma

- **Infiltrative microglandular pattern with eosinophilic intraluminal secretions**
 - **Basement membrane (coll IV, laminin) present around glands in MGA, but absent around glands of ACC (in most cases)**
- **ER/PR/HER2 negative**
- **S100 positive**
- **MGA can have “oncocytic” features; carcinomas with acinic cell differentiation reported to arise in association with MGA**

MGA with “Oncocytic Change”



Rosen's Breast Pathology, 4th Ed, Fig 7.32D

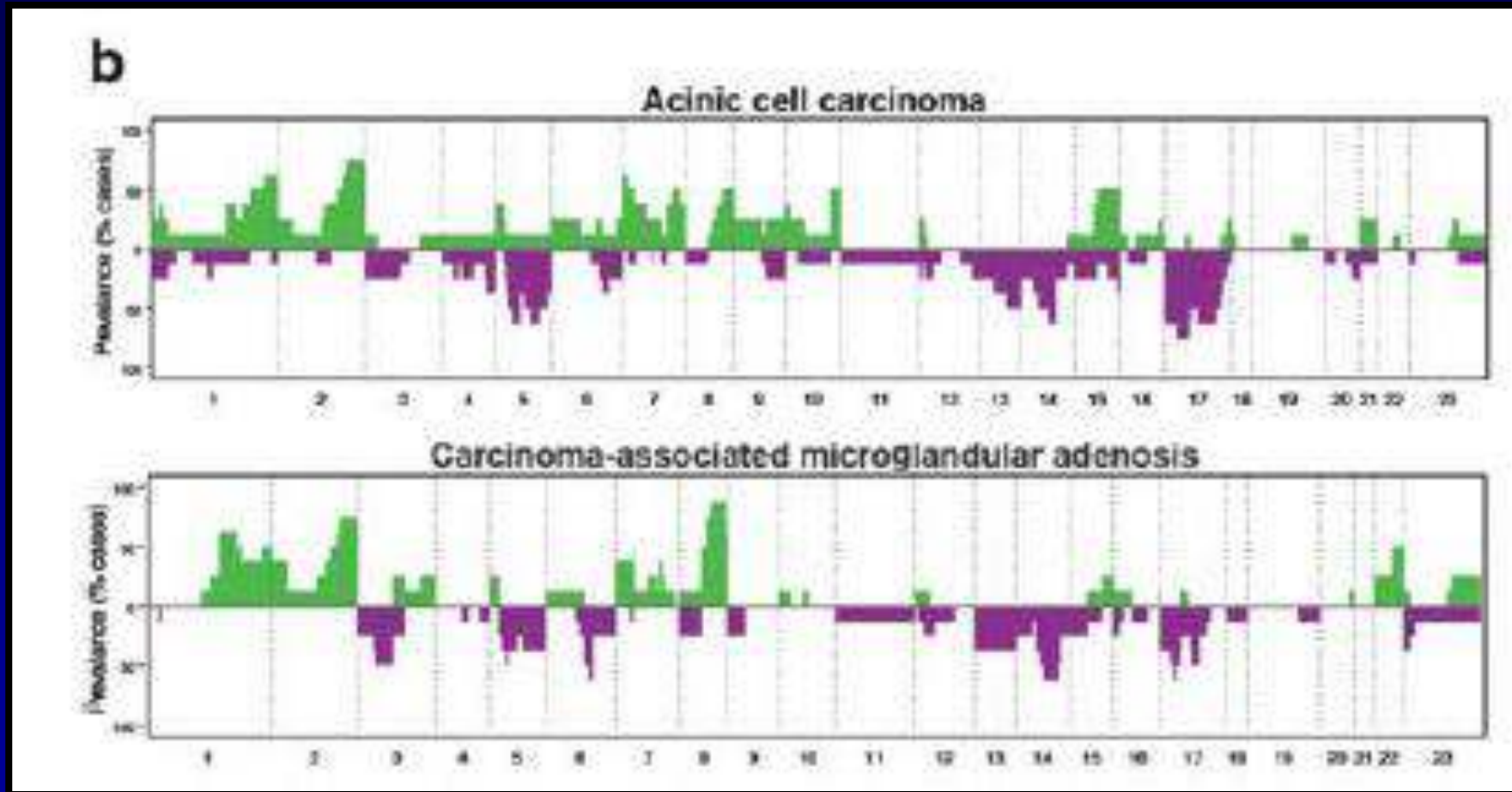
**What is the Relationship Between
MGA and Acinic Cell Carcinoma?**

Genetic analysis of microglandular adenosis and acinic cell carcinomas of the breast provides evidence for the existence of a low-grade triple-negative breast neoplasia family

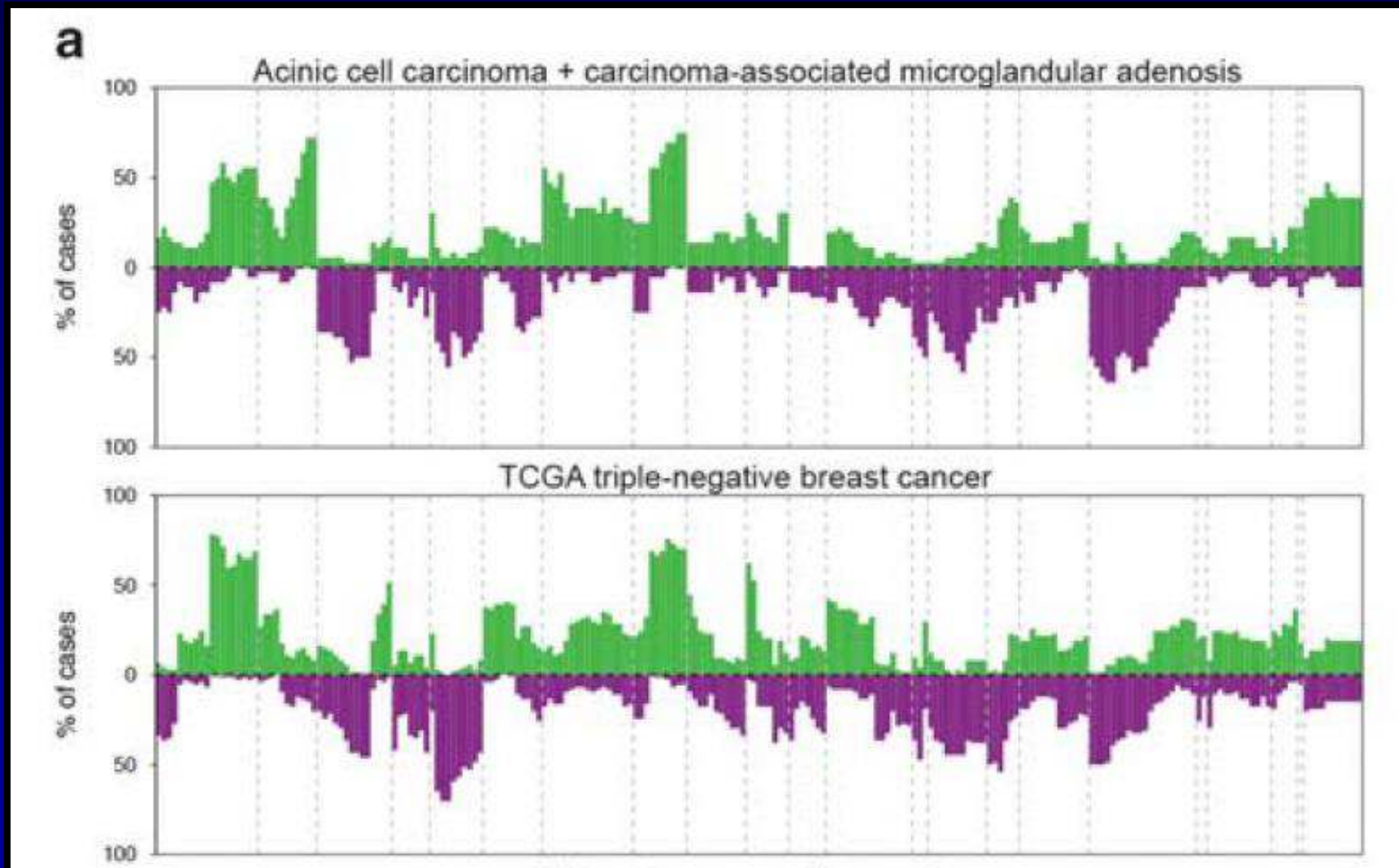
Felipe C Geyer^{1,2}, Samuel H Berman¹, Caterina Marchiò^{1,3}, Kathleen A Burke¹, Elena Guerini-Rocco^{1,4}, Salvatore Piscuoglio¹, Charlotte KY Ng¹, Fresia Pareja¹, Hannah Y Wen¹, Zoltan Hodi⁵, Stuart J Schnitt⁶, Emad A Rakha⁵, Ian O Ellis⁵, Larry Norton¹, Britta Weigelt¹ and Jorge S Reis-Filho¹ *Mod Pathol, 2017*

- 8 carcinoma-associated MGA and 8 acinic cell carcinomas
- *TP53* mutations in 75% of MGA and 88% of acinic cell carcinomas
- Additional somatic mutations in both groups in *BRCA1, PIK3CA, INPP4B*
- No significant differences in somatic mutation profile between MGA and acinic cell ca or between MGA/acinic cell ca and TNBC (from TCGA database)

Copy Number Gains and Losses in Acinic Cell Carcinoma vs Carcinoma-Associated MGA



Copy Number Gains and Losses in Acinic Cell Carcinoma/Carcinoma-Associated MGA vs TNBC



MGA and Acinic Cell Carcinoma

- Part of the same spectrum of lesions that
 - Harbor *TP53* mutations
 - Likely represent low grade forms of triple negative neoplasia with little or no metastatic potential, a subset of which may progress to high grade TNBC

So-called acinic cell carcinoma of the breast arises from microglandular adenosis and is not a distinct entity

Modern Pathology (2017) 30, 1504; doi:10.1038/modpathol.2017.57

"....I observed that the cytoplasm in some examples of microglandular adenosis and carcinomas arising from it was unusually granular and had other features that I described as 'oncocytic', a characteristic now more appropriately referred to as 'acinic cell differentiation.'"

"... in view of the properties that have been demonstrated in these cells. This is just one of the many amazing forms of the phenomenon of 'metaplasia',... that can occur in mammary carcinoma."

THE CONCLUSION I DRAW FROM YOUR STUDY IS THAT SO-CALLED MAMMARY ACINIC CELL CARCINOMA IS IN FACT INVASIVE CARCINOMA WITH ACINIC CELL DIFFERENTIATION ARISING IN MICROGLANDULAR ADENOSIS, a conclusion I have stated repeatedly for more than a decade.

Disclosure/conflict of interest

The author declares no conflict of interest.

Paul P Rosen^{1,2}

¹Weill Cornell Medical College, New York, NY, USA;

²Formerly Attending Pathologist, Memorial Sloan-Kettering Hospital, New York, NY, USA

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CURRENT TOPICS IN BREAST PATHOLOGY

The morphological spectrum of salivary gland type tumours of the breast



A more controversial issue is the differential diagnosis between ACC with prominent microglandular pattern and microglandular adenosis (MGA). MGA was originally described by Clement and Azzopardi⁸¹ and Rosen⁸² in 1983, as a benign lesion simulating tubular carcinoma.

MGA and ACC with prominent microglandular pattern share similar architectural features, characterised by the proliferation of small glands, similarity that has led to the hypothesis that the two entities are related.^{83,84} Nevertheless the two lesions are composed of different types of cells. MGA cells have clear cytoplasm that appears empty on ultrastructural analysis.⁸⁵ On the contrary, ACC cells have granular cytoplasm containing electron dense granules on ultrastructure.⁷² This further evidence makes the similarity between MGA and the microglandular pattern of ACC very unreal.

- **Are lesions with a microglandular pattern and acinic cell differentiation:**
 - A. Acinic cell carcinomas arising in MGA?**
 - B. Acinic cell carcinomas with an MGA-like pattern?**
 - C. Both?**
 - D. Does it really matter?**

Acinic cell carcinoma of breast: morphologic and immunohistochemical review of a rare breast cancer subtype[☆]

Niamh Conlon MB, FRCPath*, Navid Sadri MD, PhD,
Adriana D. Corben MD, Lee K. Tan MD

Hum Pathol, 2016

In summary, breast AcCC is a rare subtype of breast carcinoma that is usually triple negative on immunohistochemistry and has a wide morphologic spectrum that can include a high-grade, poorly differentiated component. The relationship between breast AcCC and MGA remains unclear, but it is apparent that MGA-like areas at the periphery of breast AcCC should be considered a part of the carcinomatous process and re-excised if they extend to the initial surgical margins. Recognition of the entity of breast

Case 4

Diagnosis

Acinic cell carcinoma

