Pathology of Mucinous Lesions of the Breast

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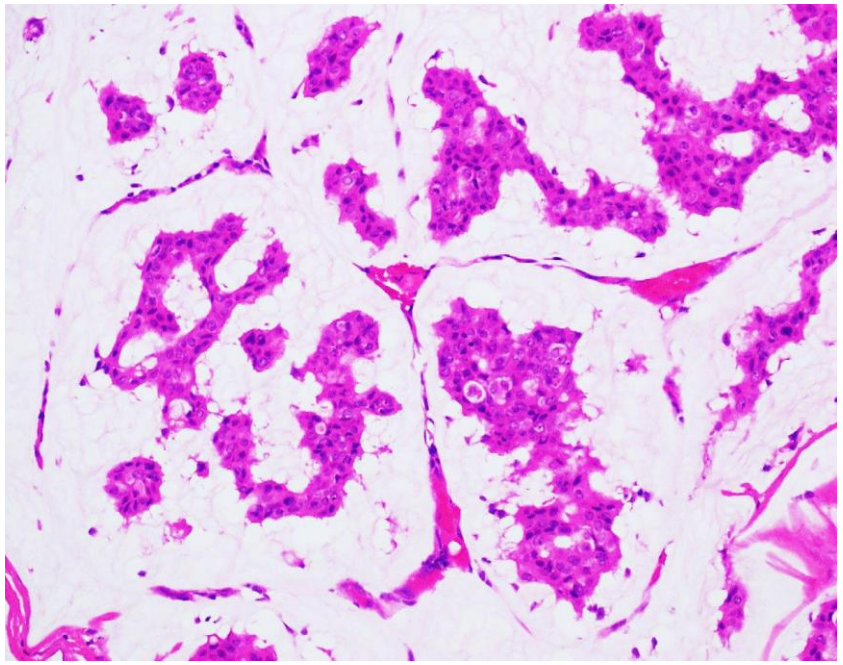
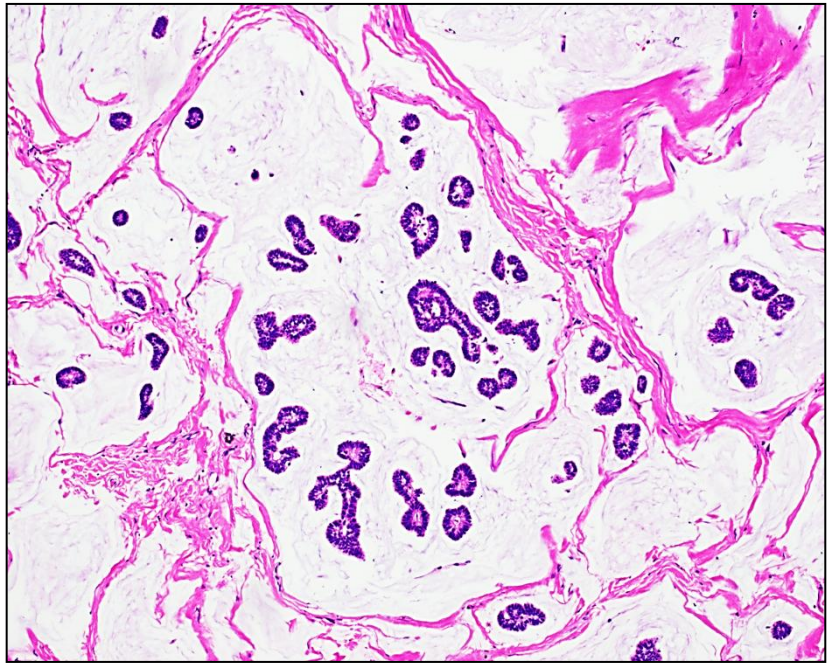
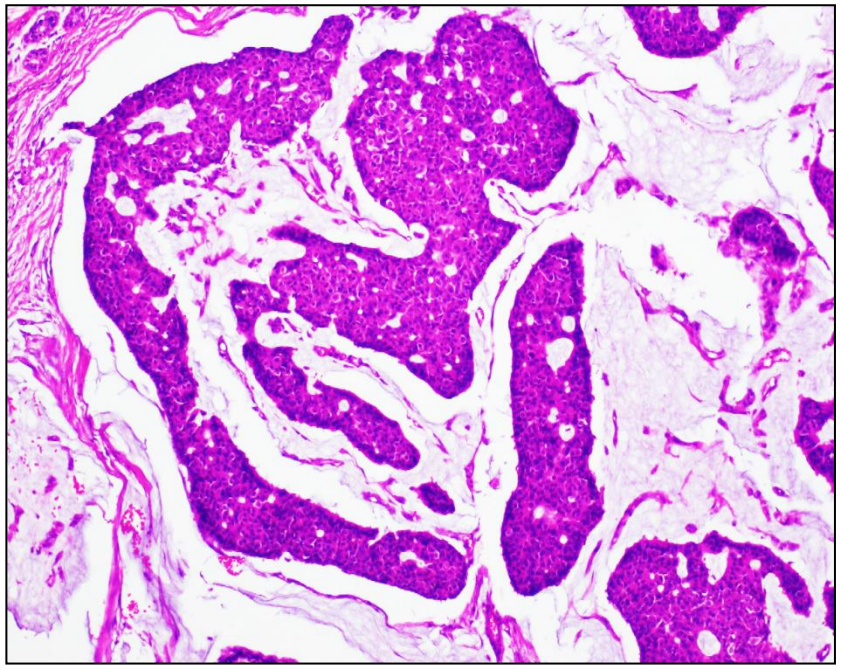
Wentao Yang

Lesions with Intracellular Mucin

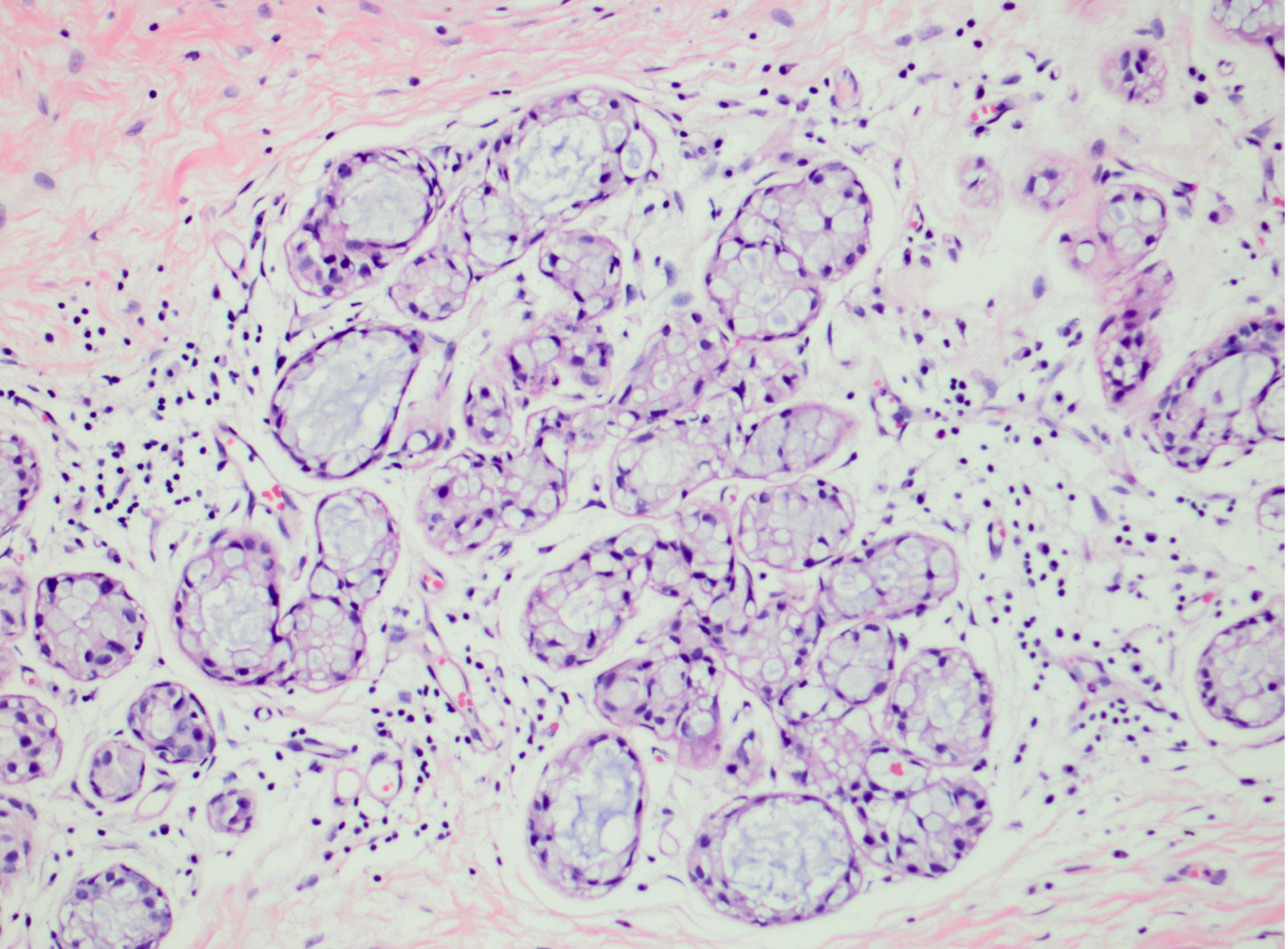
- Mucinous metaplasia
- Lobular Neoplasia
- Ductal Carcinoma In Situ (DCIS)
- Solid Papillary Carcinoma
- Invasive Lobular Carcinoma (ILC)
- Invasive Ductal Carcinoma (IDC)
- Mucoepidermoid Carcinoma

Lesions with Extracellular Mucin

- Fibrocystic Change with Intracystic Mucin
- Mucocele-like lesions (MLL), Benign
- MLL with Atypical Hyperplasia
- MLL with Ductal Carcinoma In Situ (DCIS)
- MLL with Mucinous Carcinoma
- Mucinous Carcinoma
- Mucinous Cystadenocarcinoma
- Mixed Carcinoma (Mucinous + Invasive Carcinoma of no Special Type)

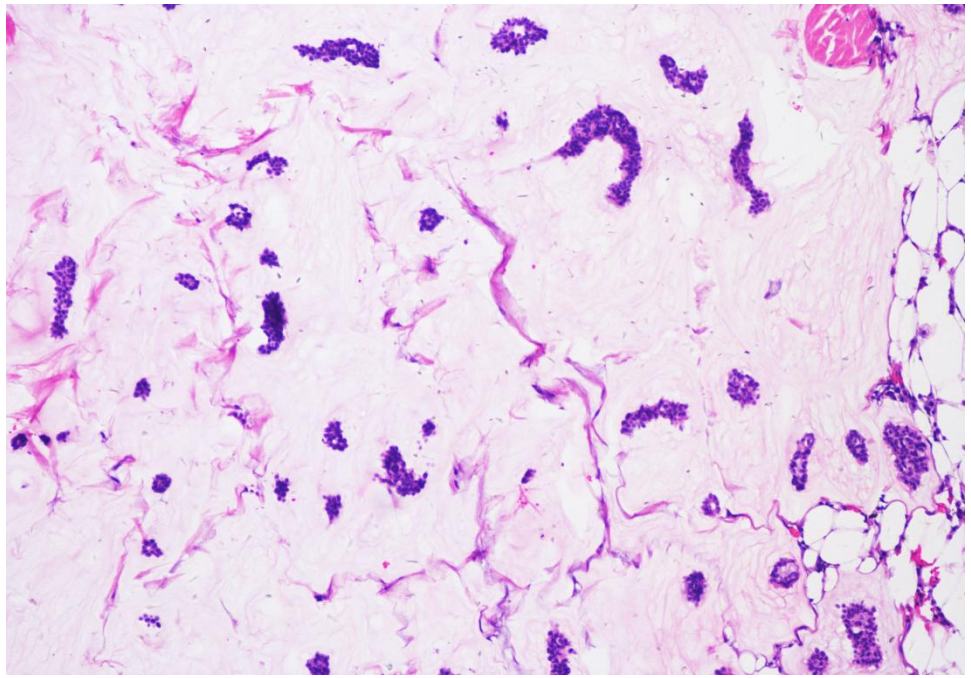
Common Diagnostic Challenges

- Mucocele-like Lesions vs. Mucinous Carcinoma
- Mucinous Carcinoma vs. Other Types of Breast Carcinoma
- Special Types of Invasive Carcinoma with Mucin Production
- Carcinomas with Stromal Mucin
- Rare Lesions

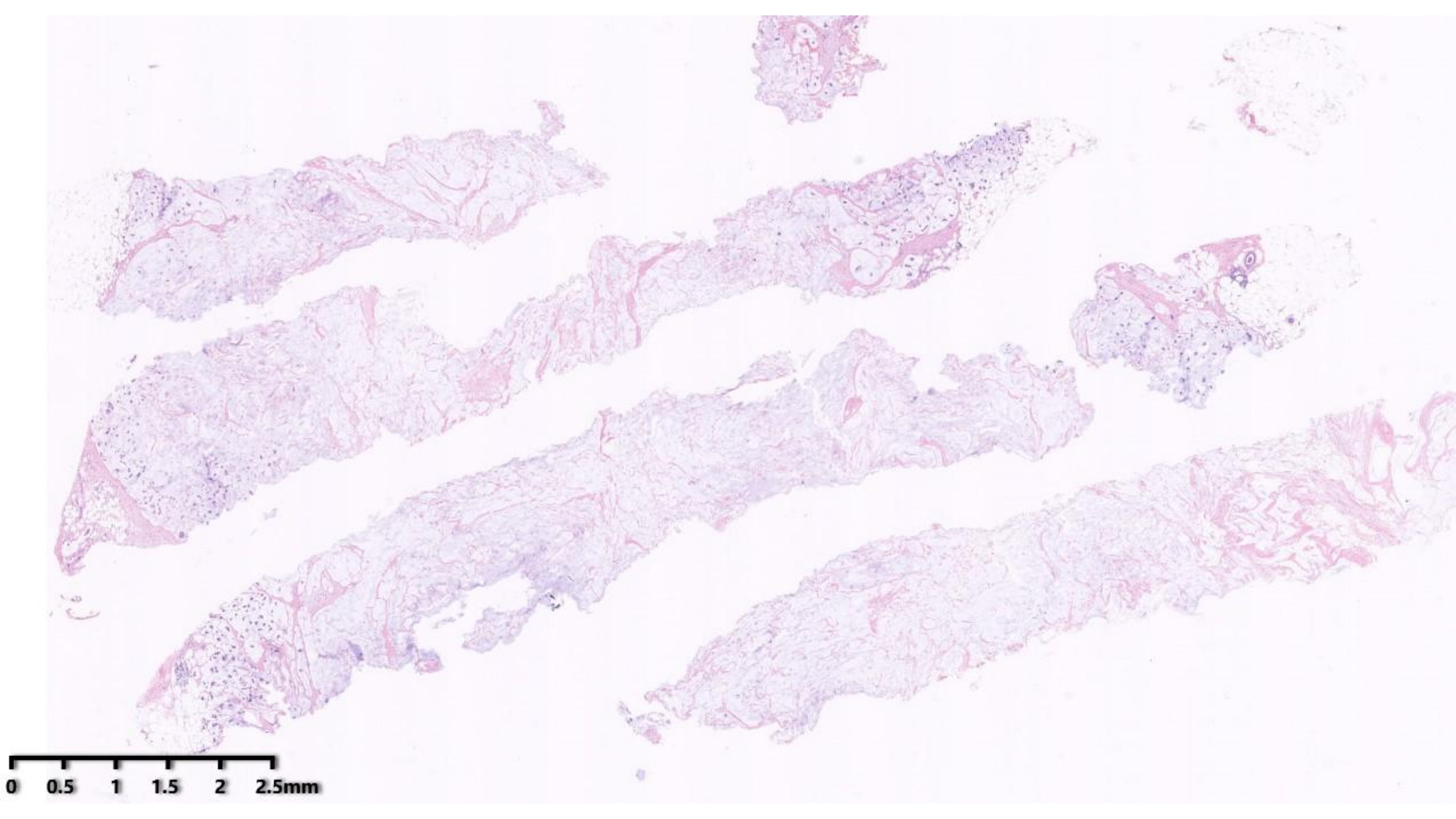


Mucinous carcinoma (Type A-paucicellular subtype)

- **Ribbon-like,reticular,cribriform and trabecular**



- Mucinous morphology >90%
- Nuclear grade: low to intermediate
- High nuclear grade with extracellular mucin: diagnose as invasive carcinoma NST with mucin production
- Typically HR+ and HER2-; re-evaluate if HR- or HER2+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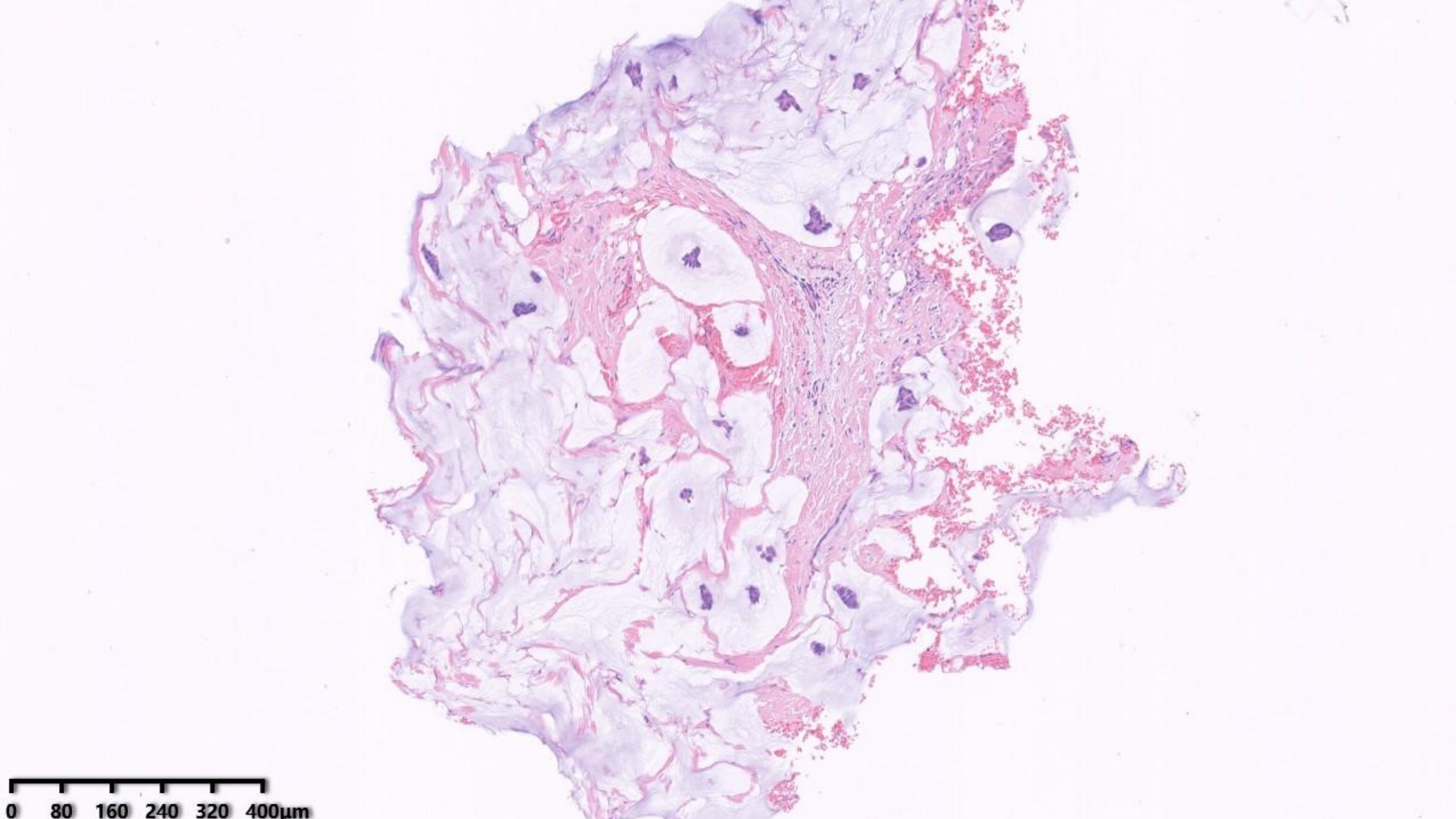
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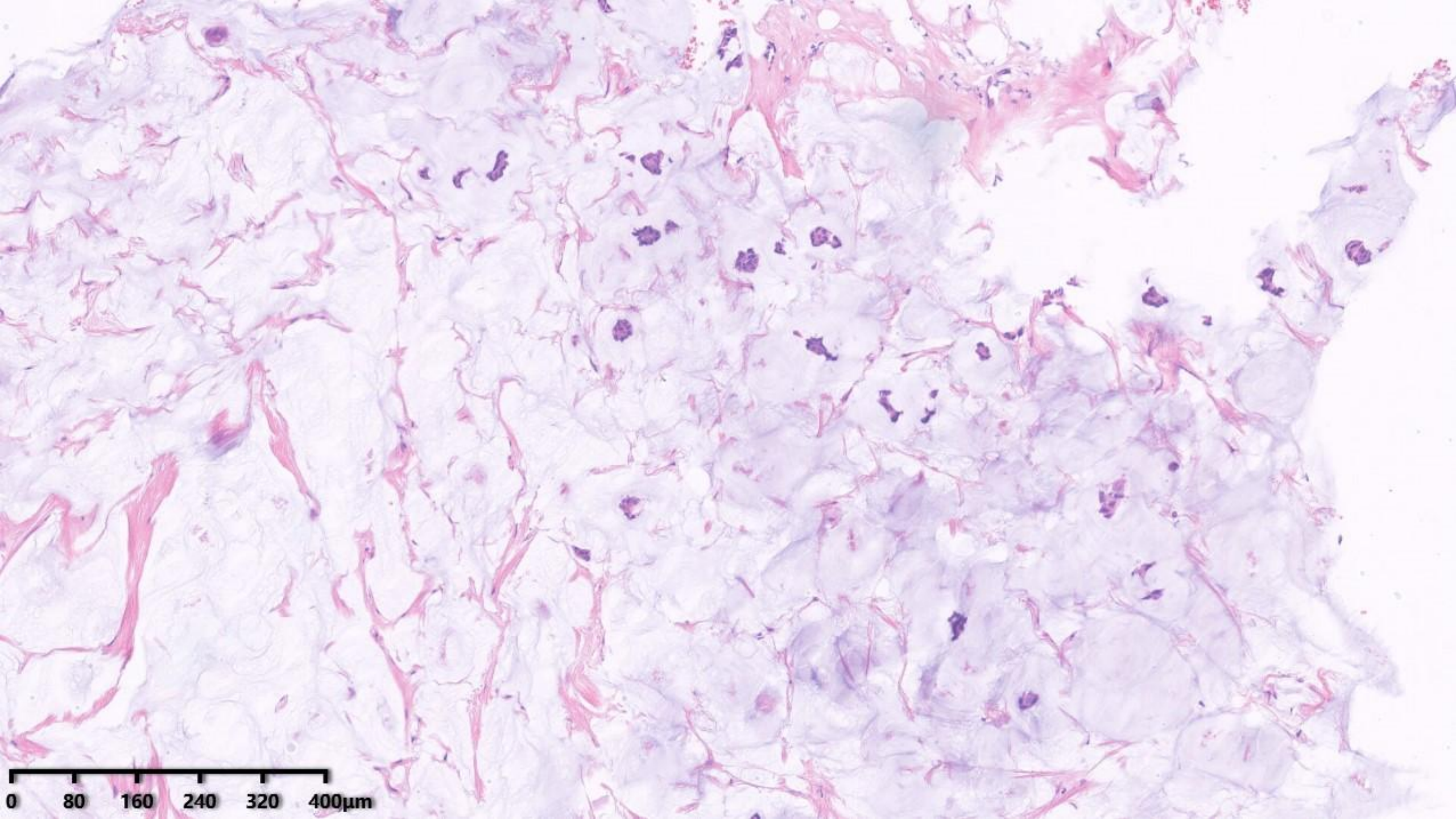
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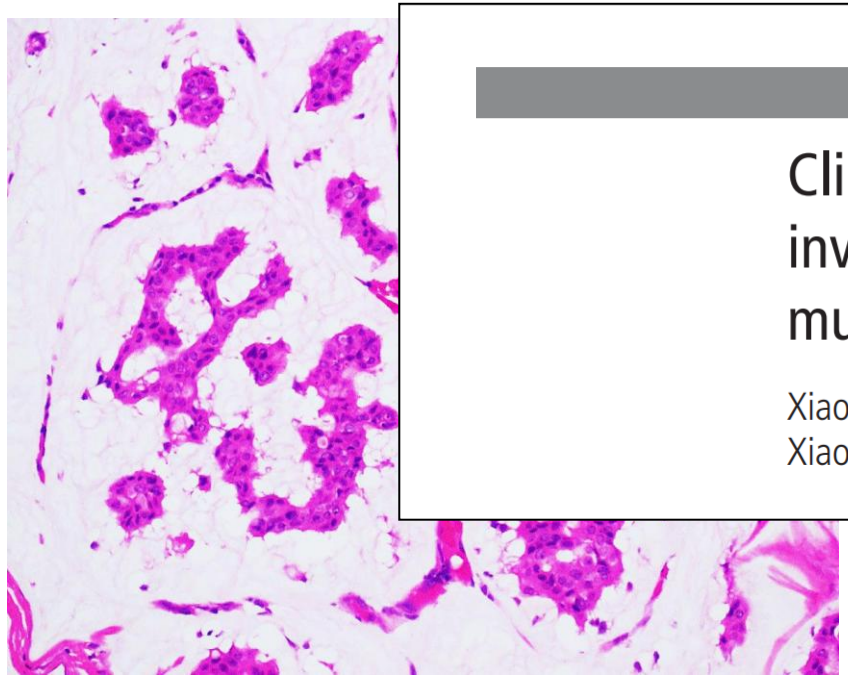
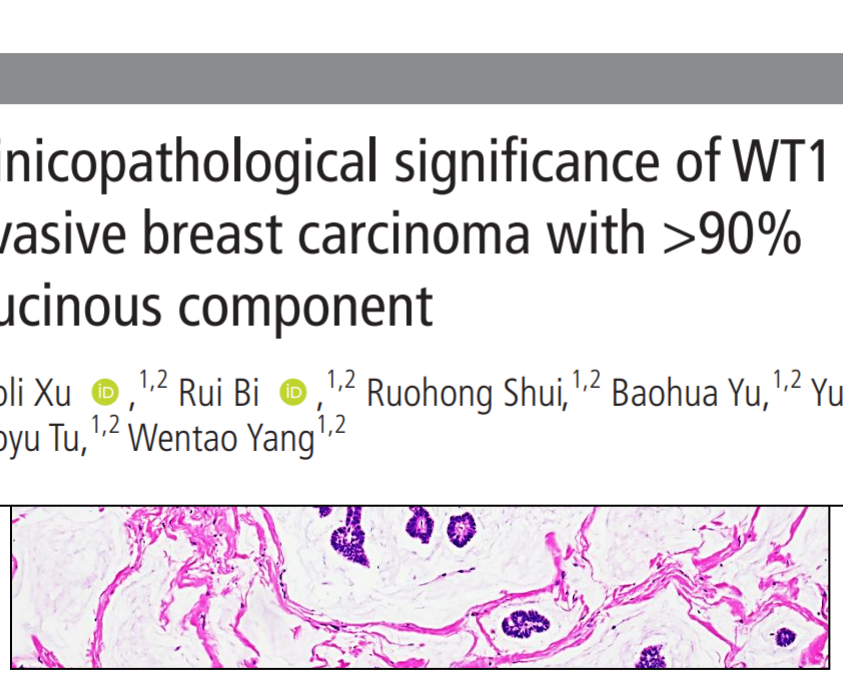
Original research

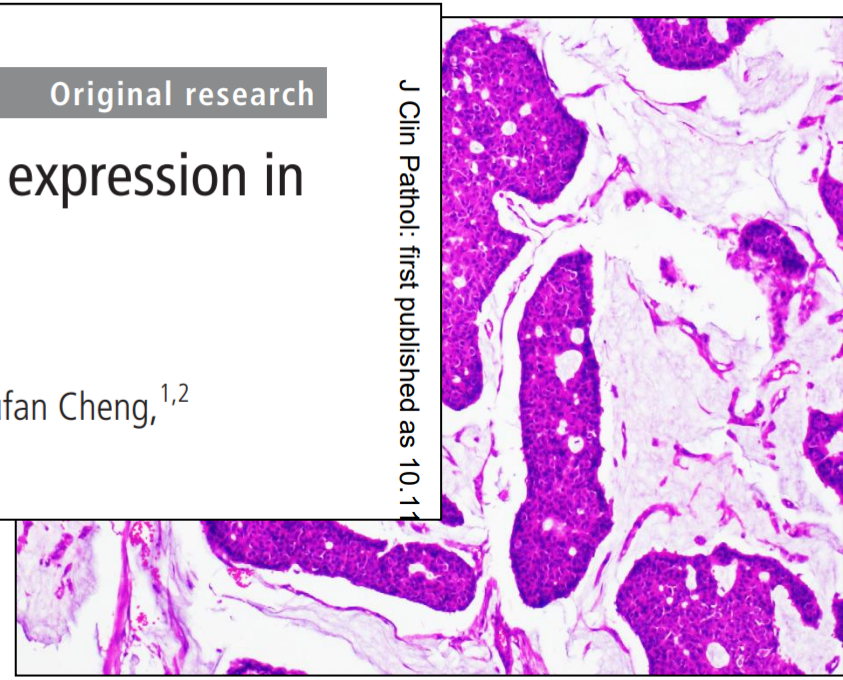
Clinicopathological significance of WT1 expression in invasive breast carcinoma with >90% mucinous component

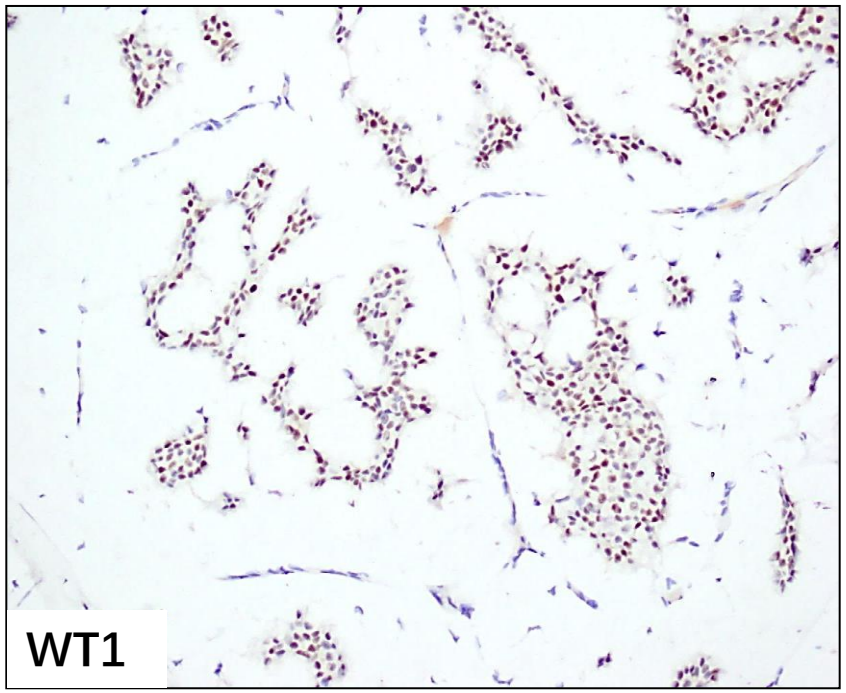
Xiaoli Xu ,[1,2] Rui Bi ,[1,2] Ruohong Shui,[1,2] Baohua Yu,[1,2] Yufan Cheng,[1,2] Xiaoyu Tu,[1,2] Wentao Yang[1,2]

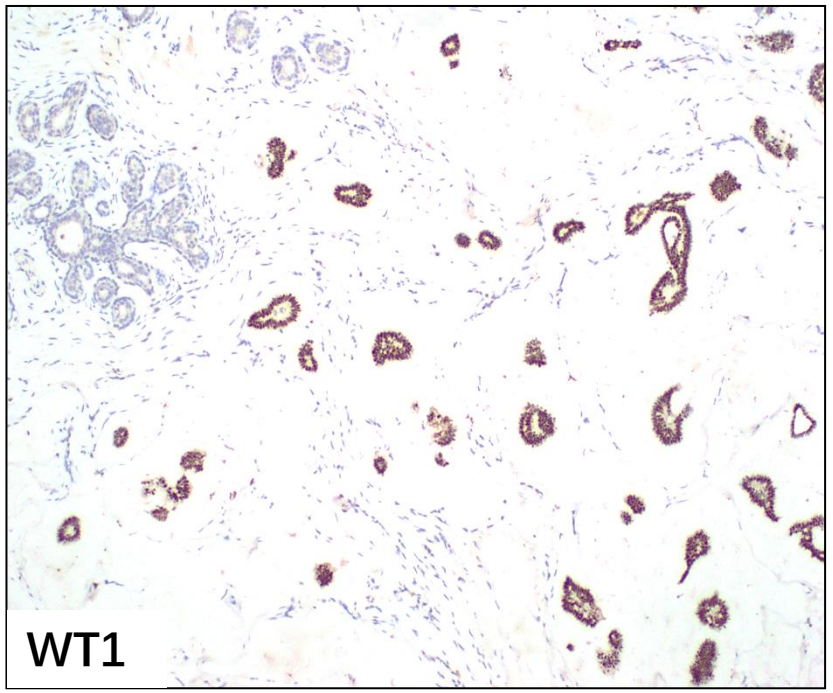
J Clin Pathol: first published as 10.11

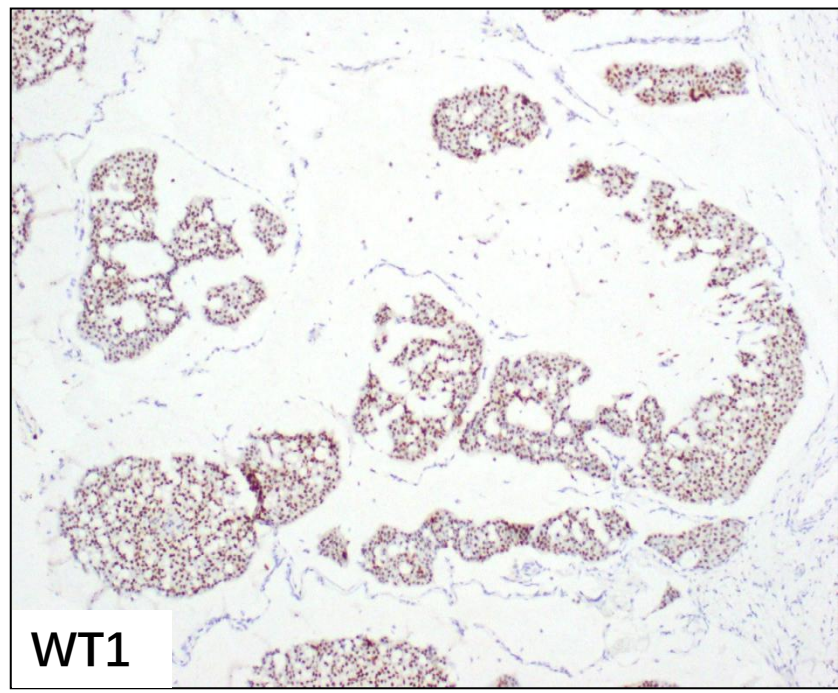


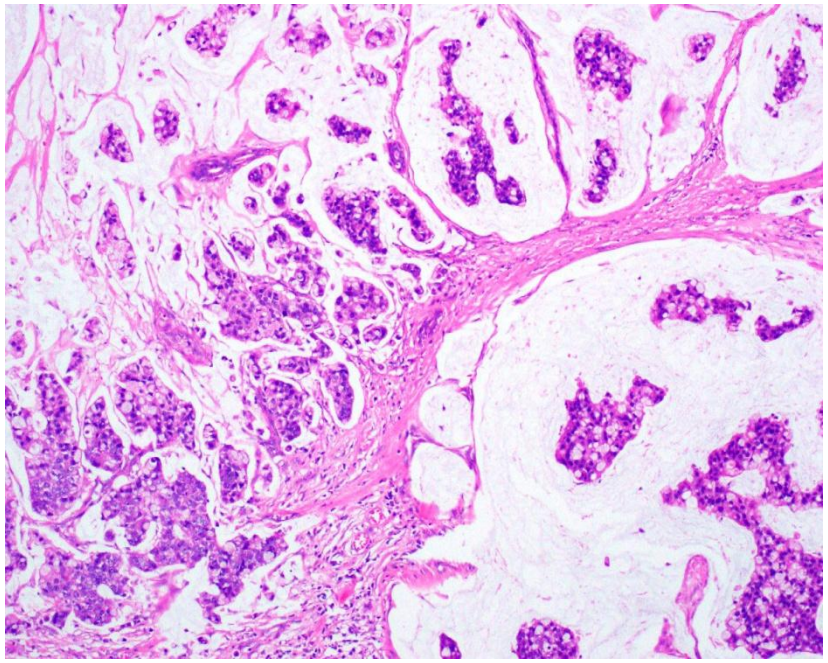
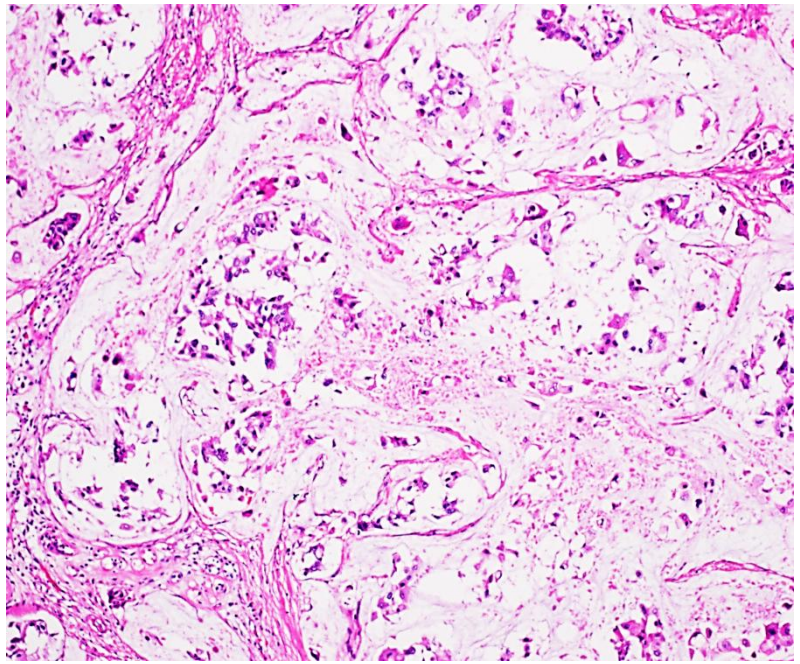
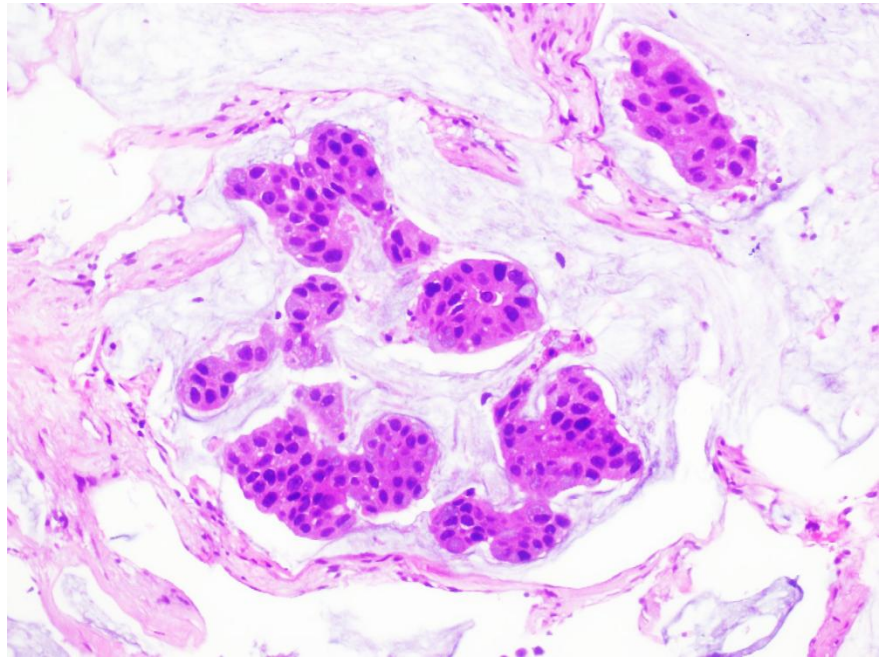
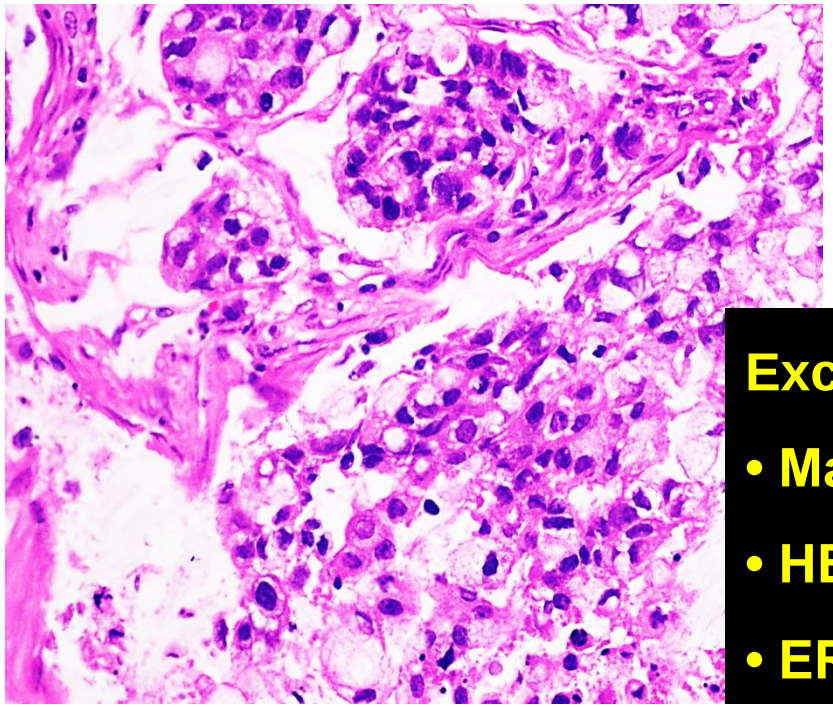
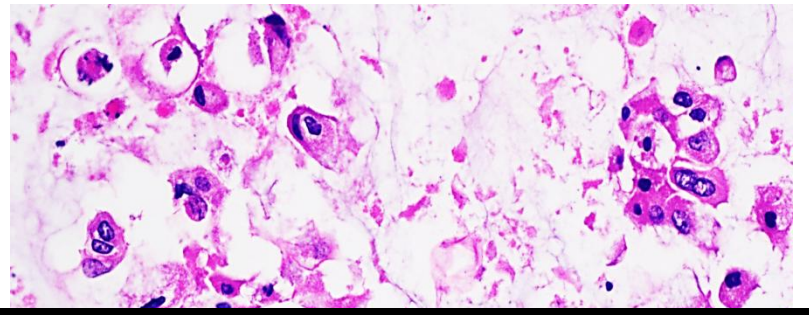
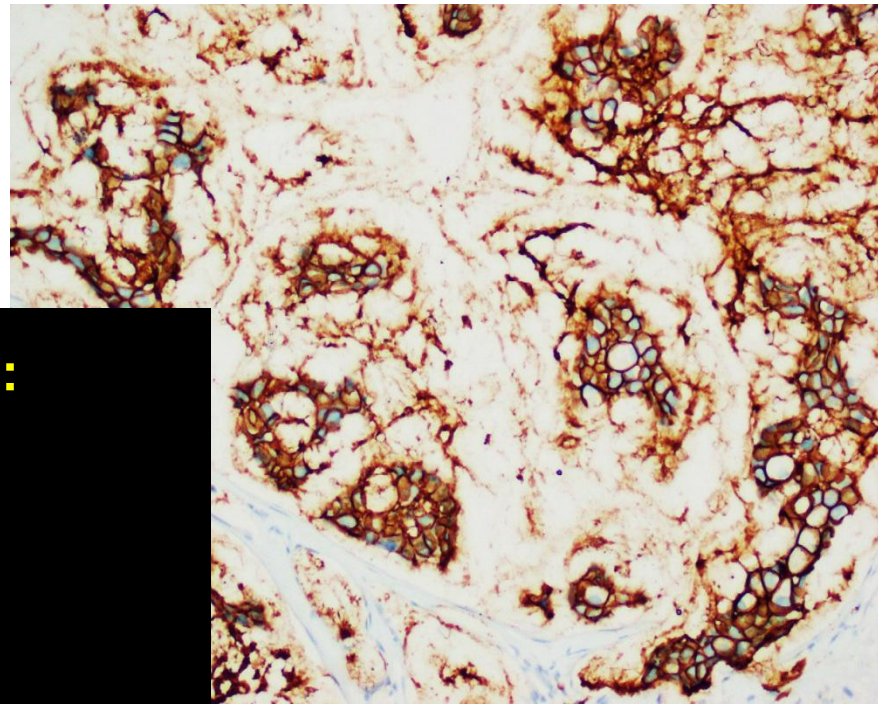






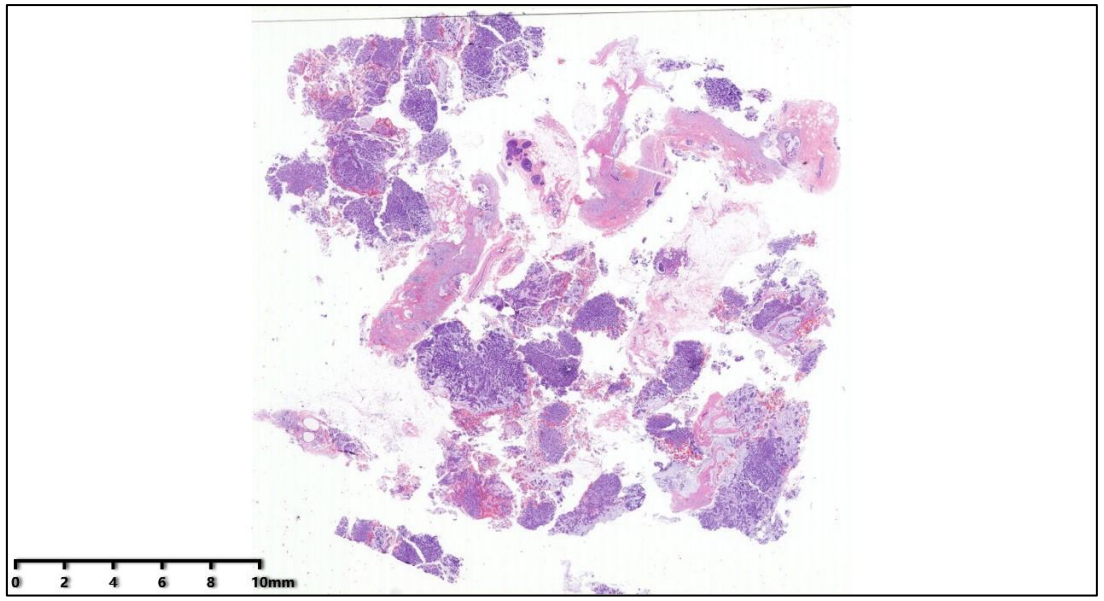


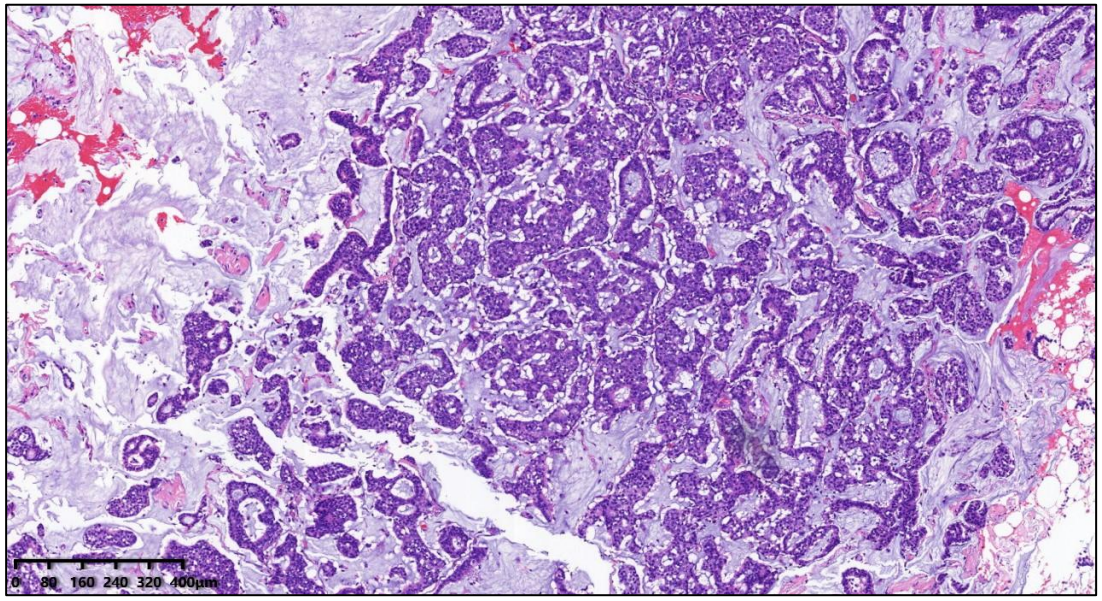


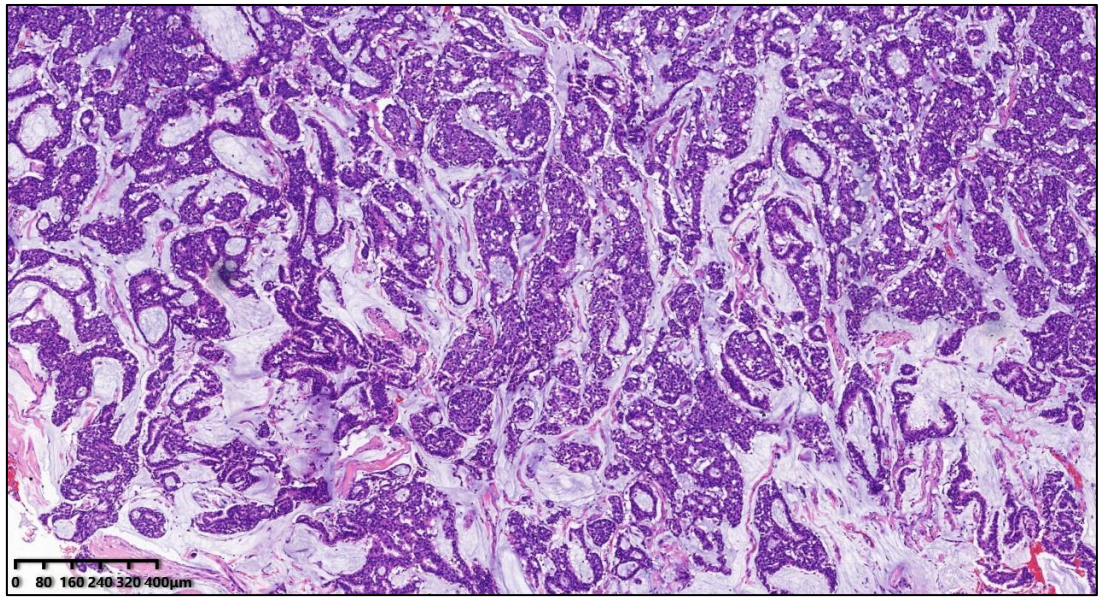







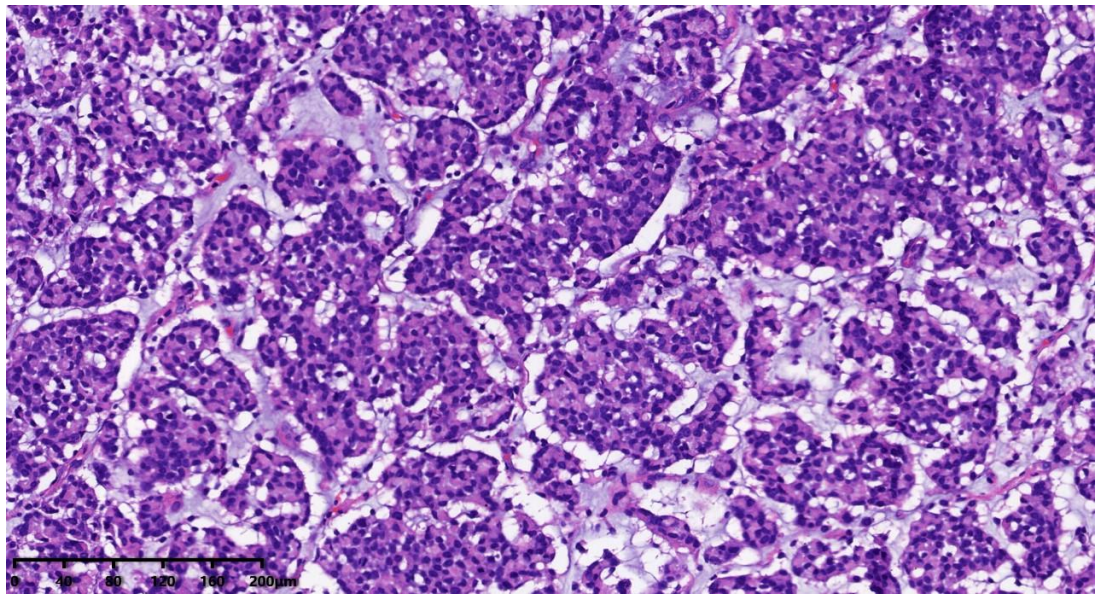
Exclude Mucinous Carcinoma When:

- **Marked nuclear atypia is present**
- **HER2 is positive**
- **ER & PR are negative**

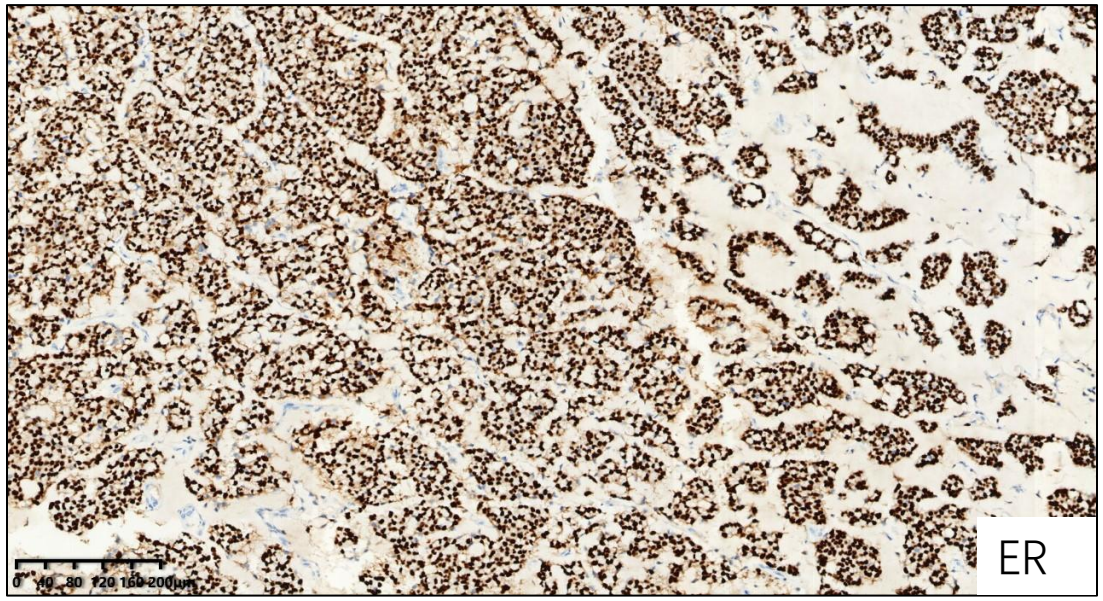








Cellular subtype (Type B): characterized by sheet-like, solid nest-like, or cribriform glandular architecture, with relatively less mucin, may show neuroendocrine differentiation.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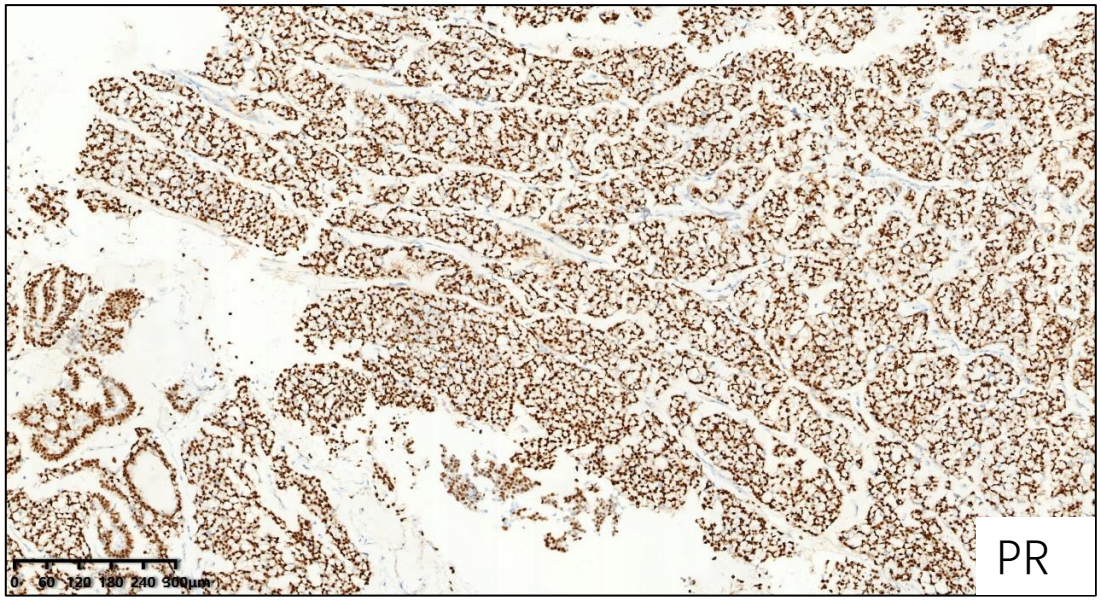
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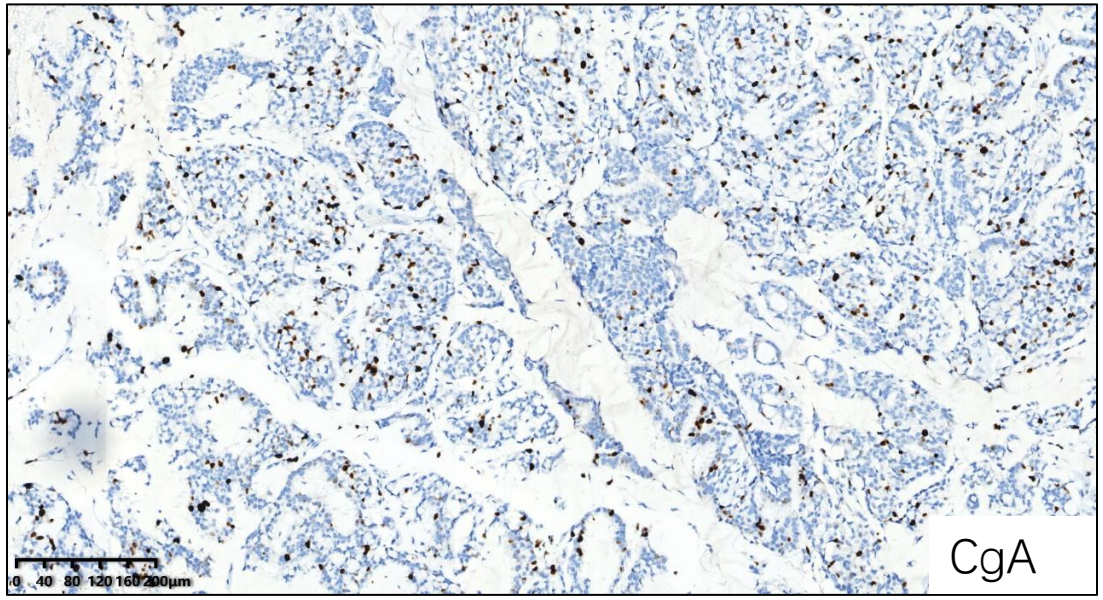
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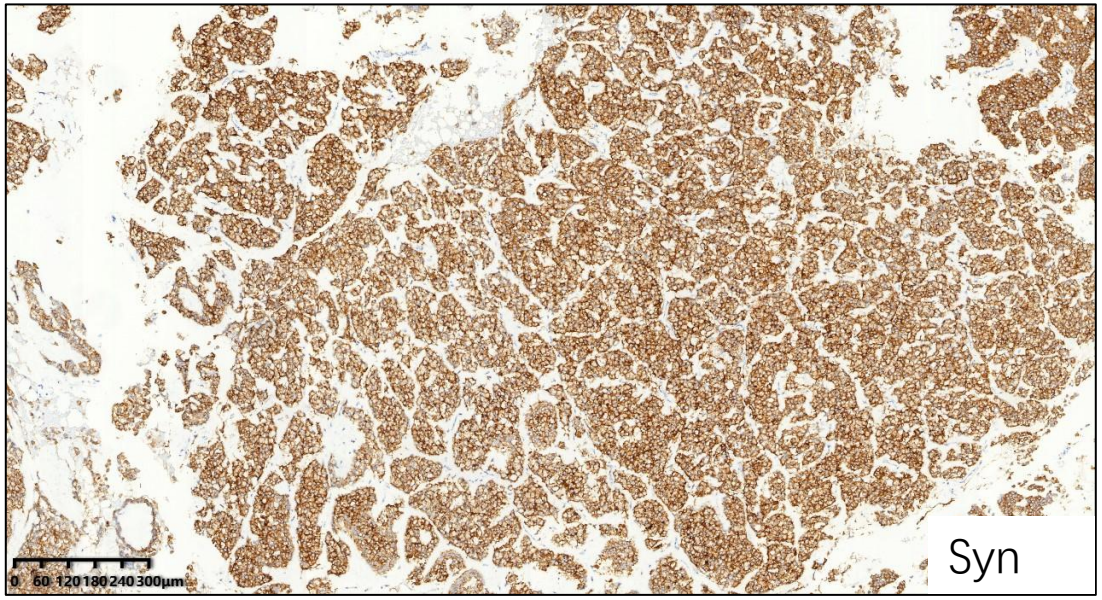
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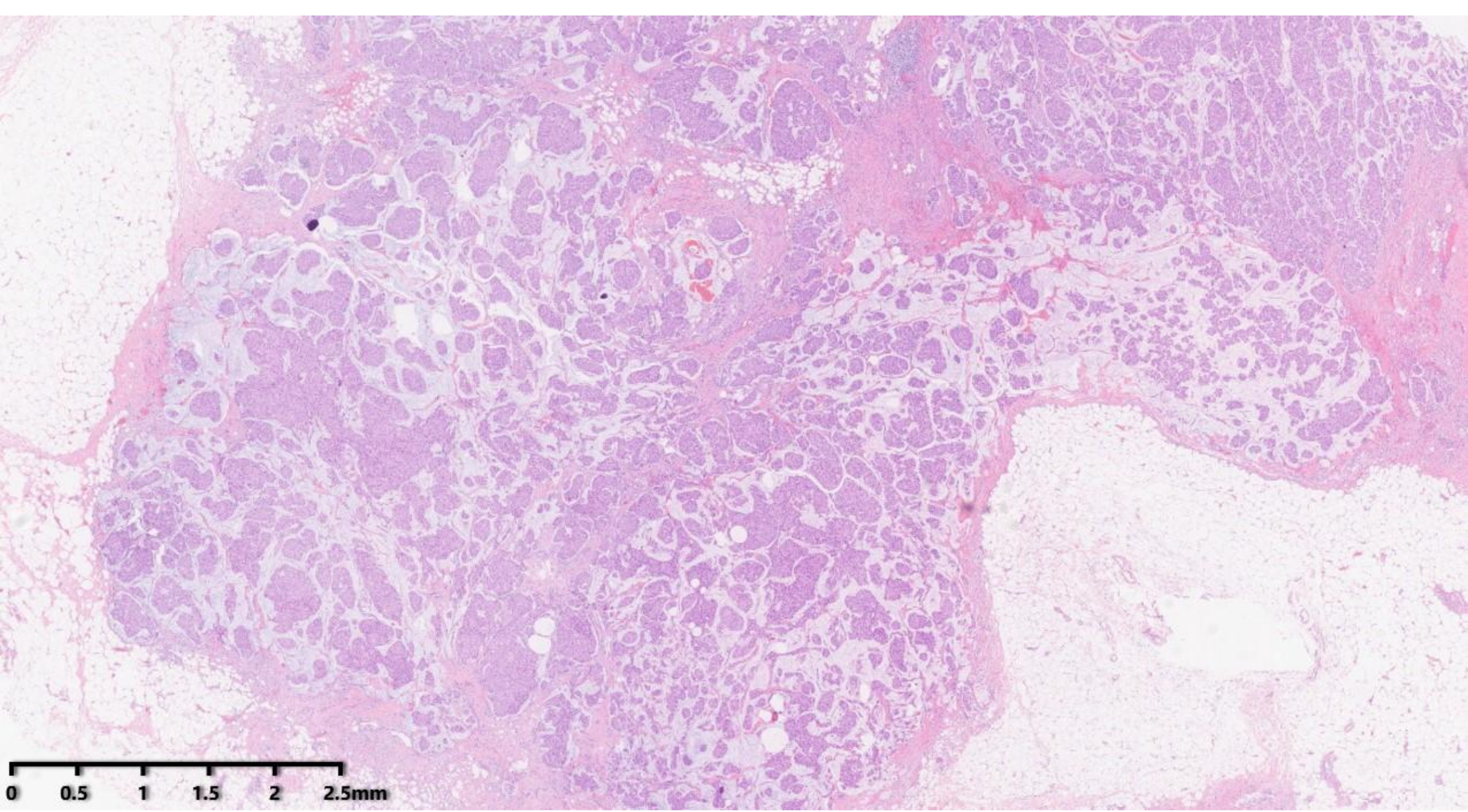
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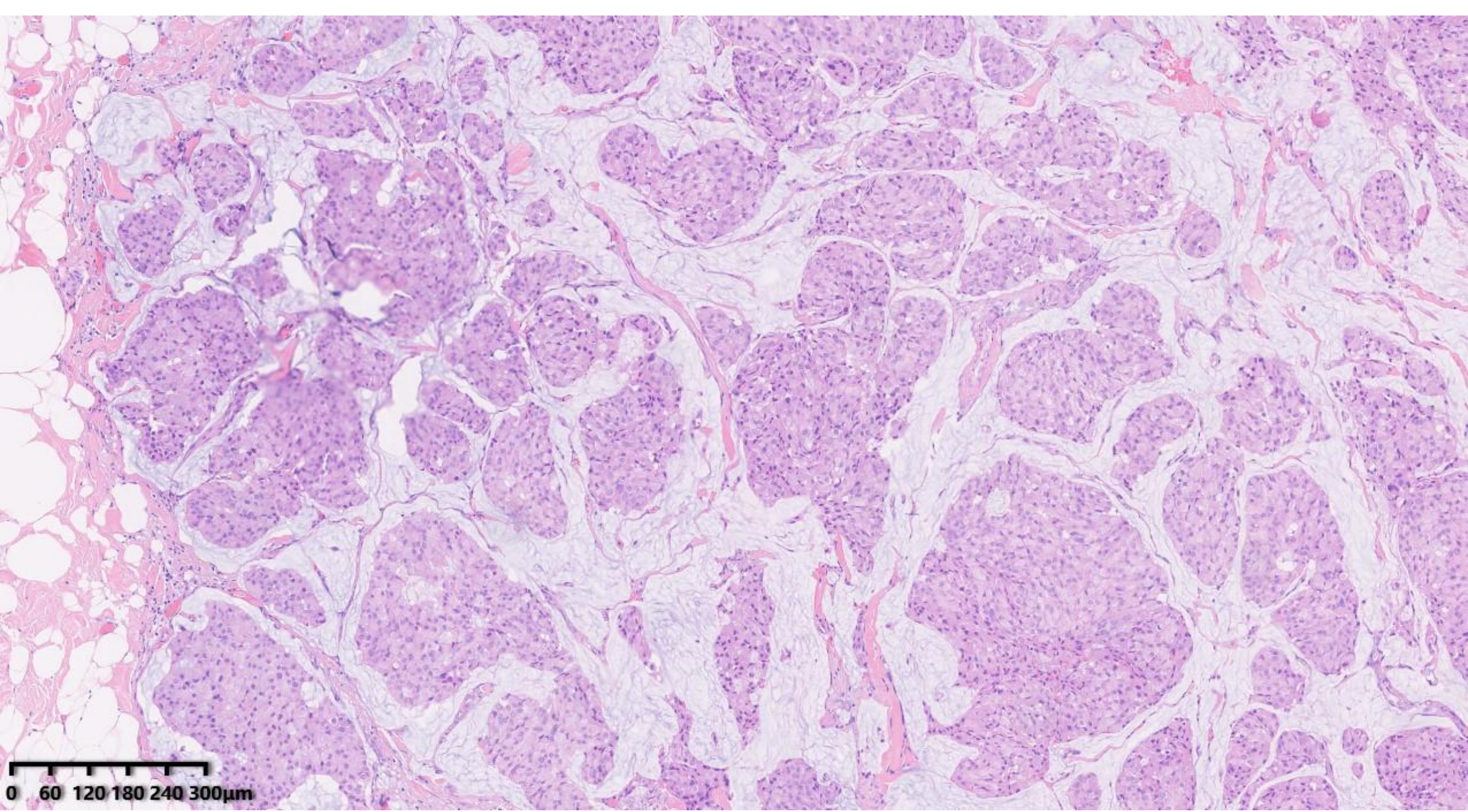
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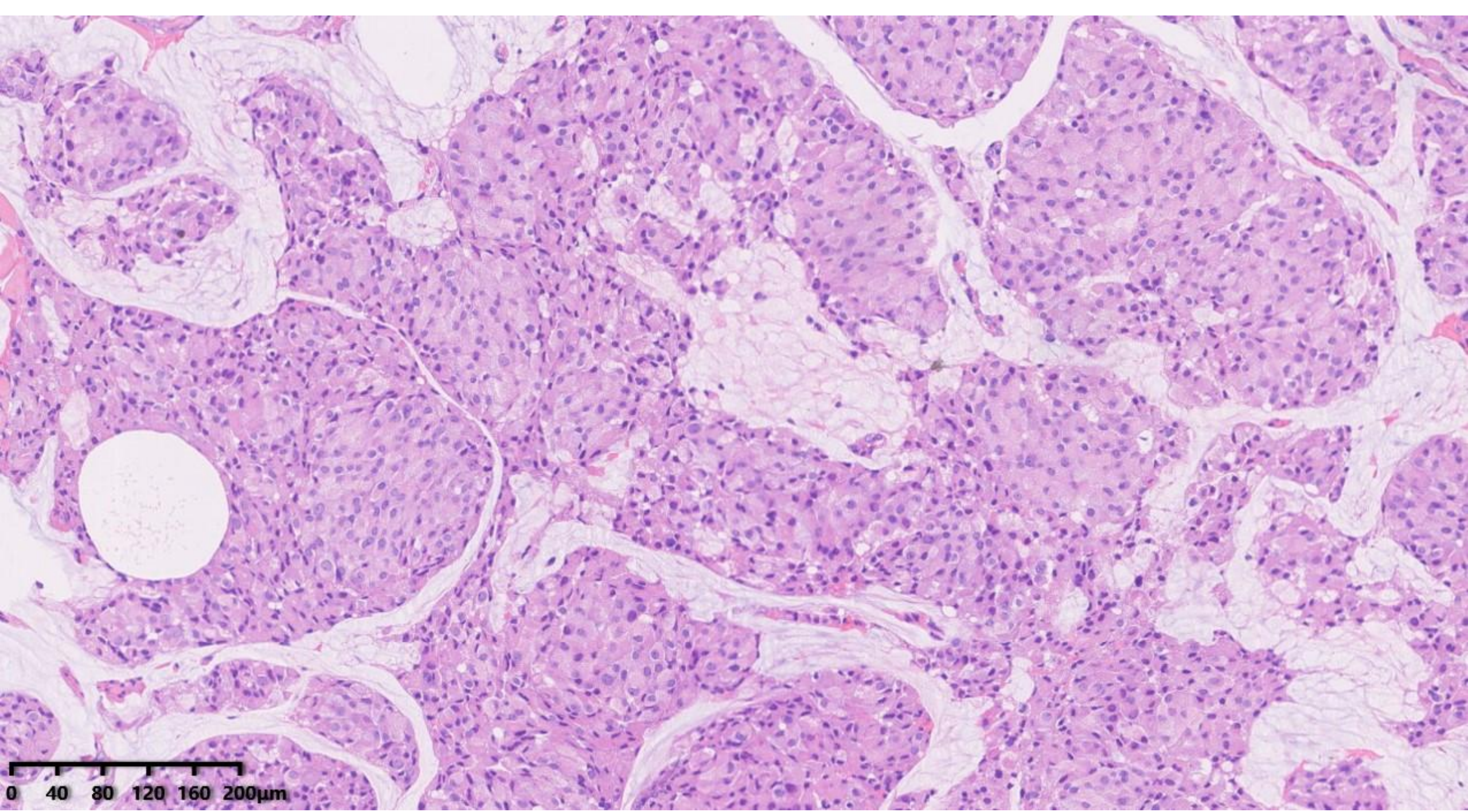
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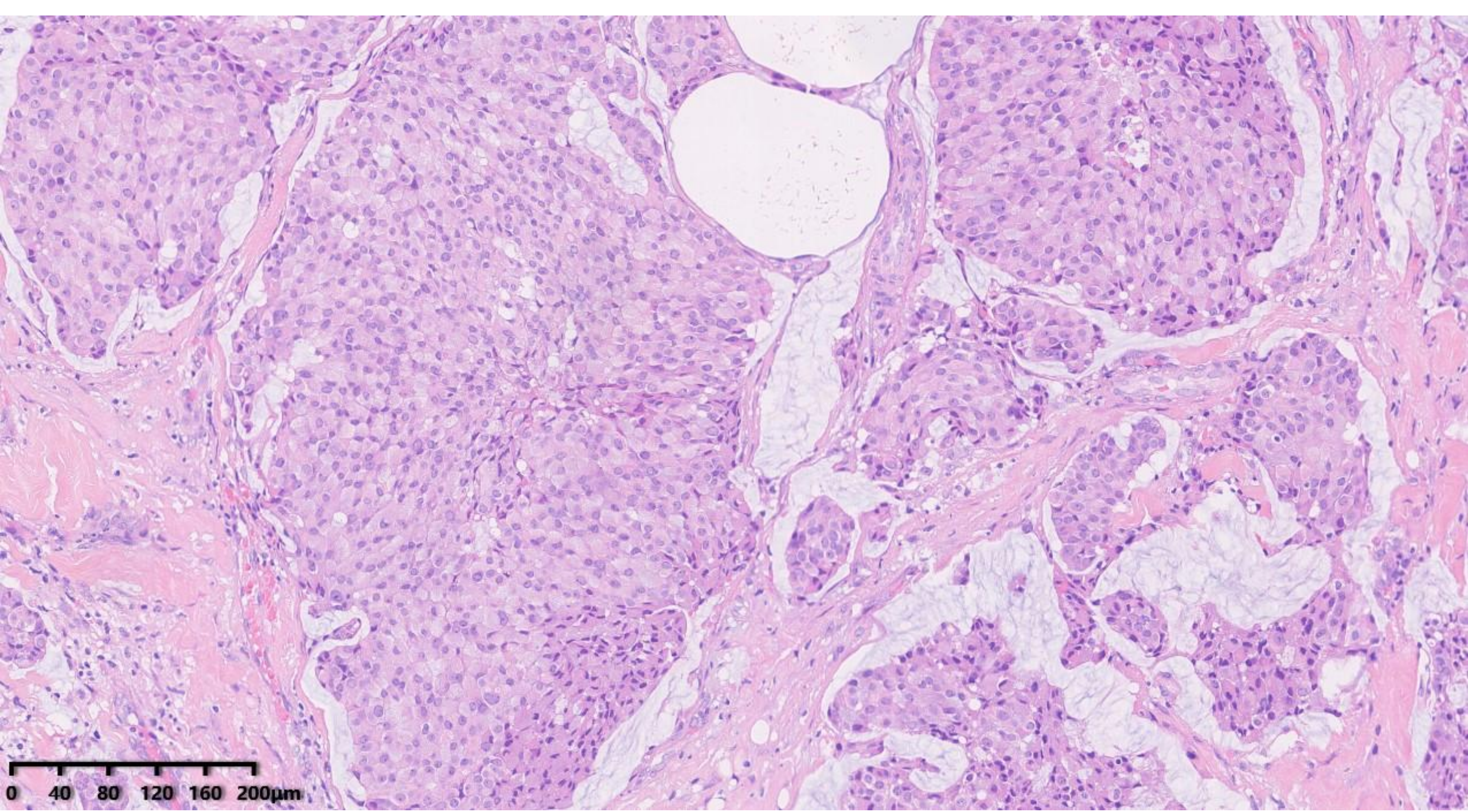
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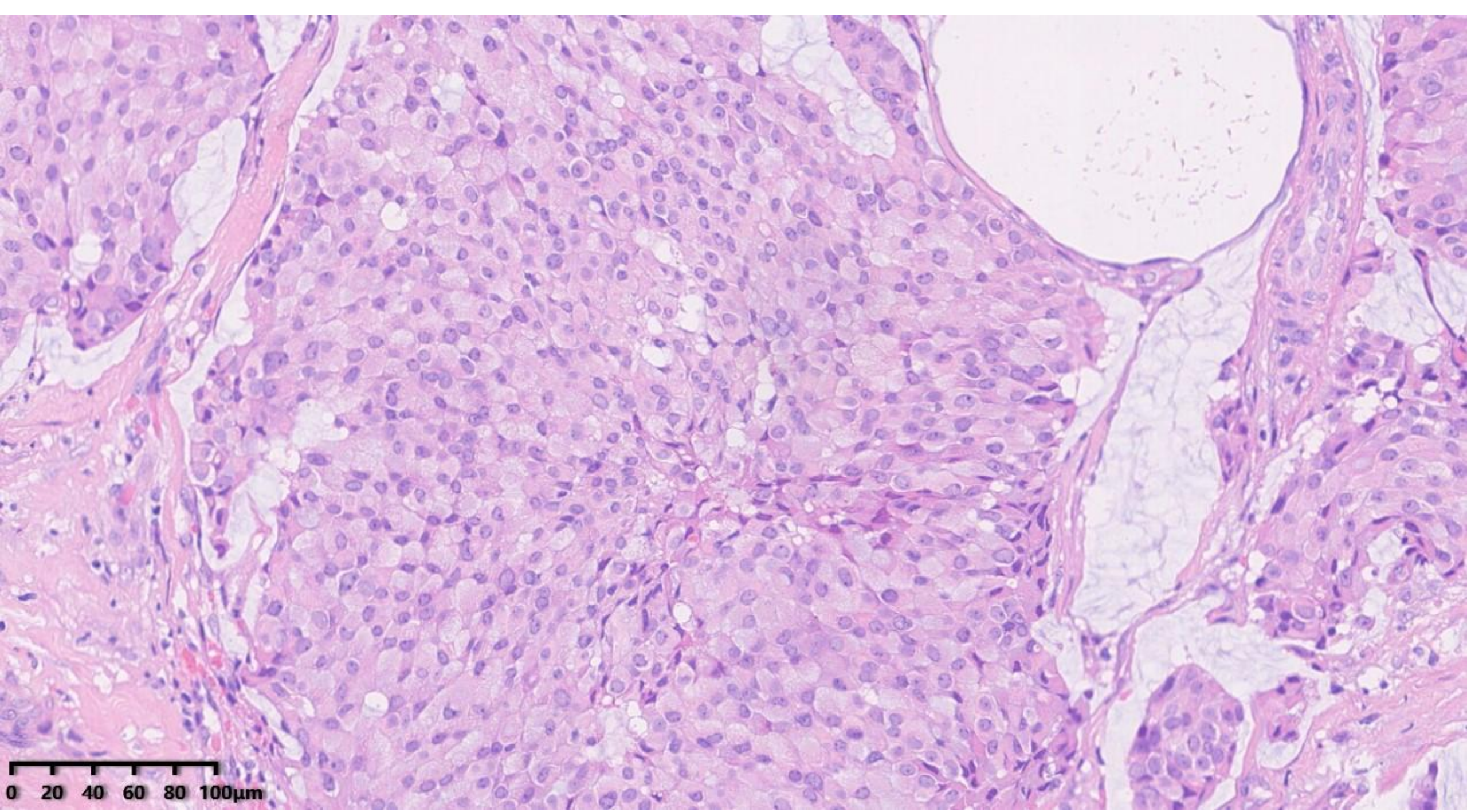
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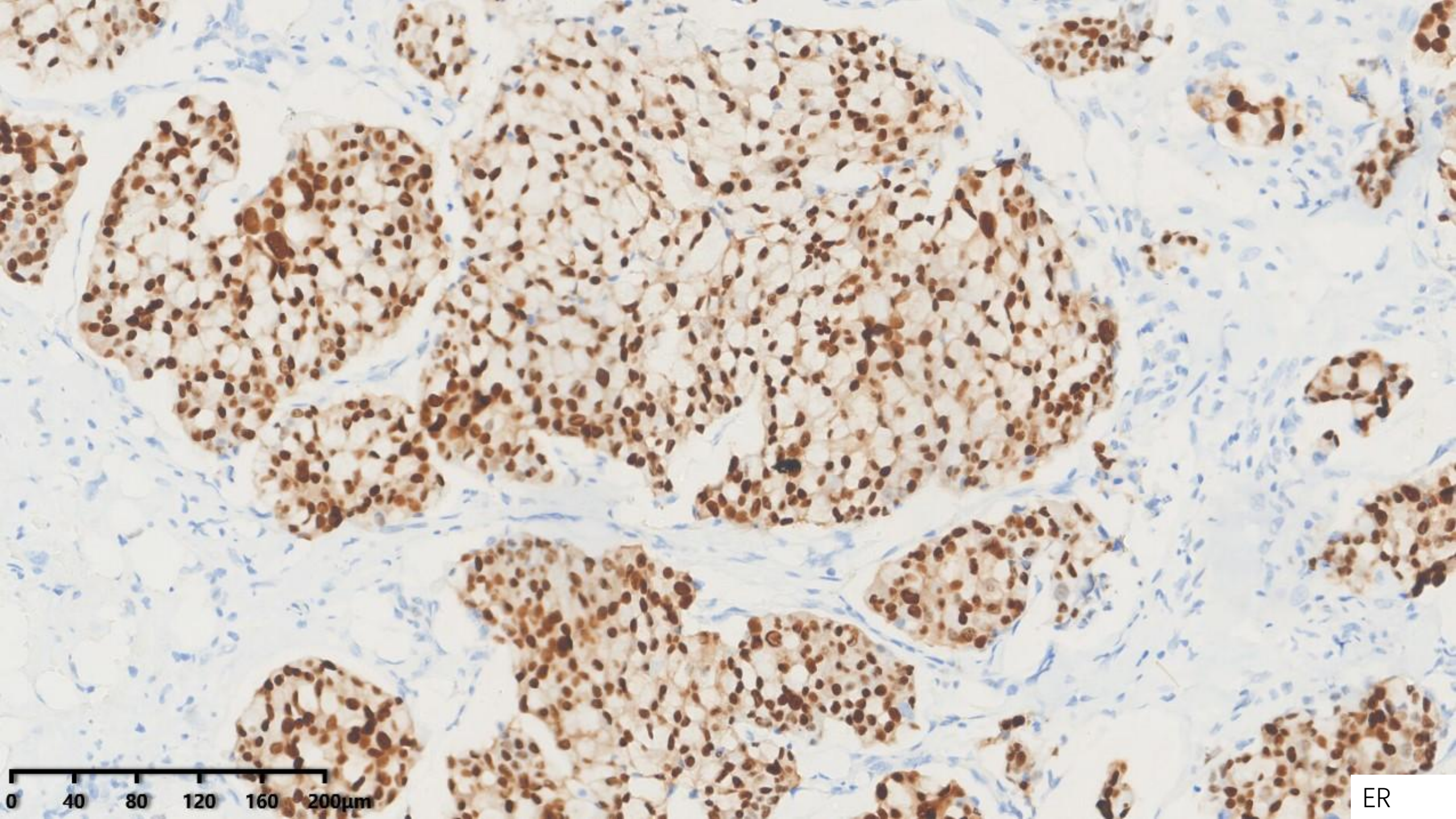

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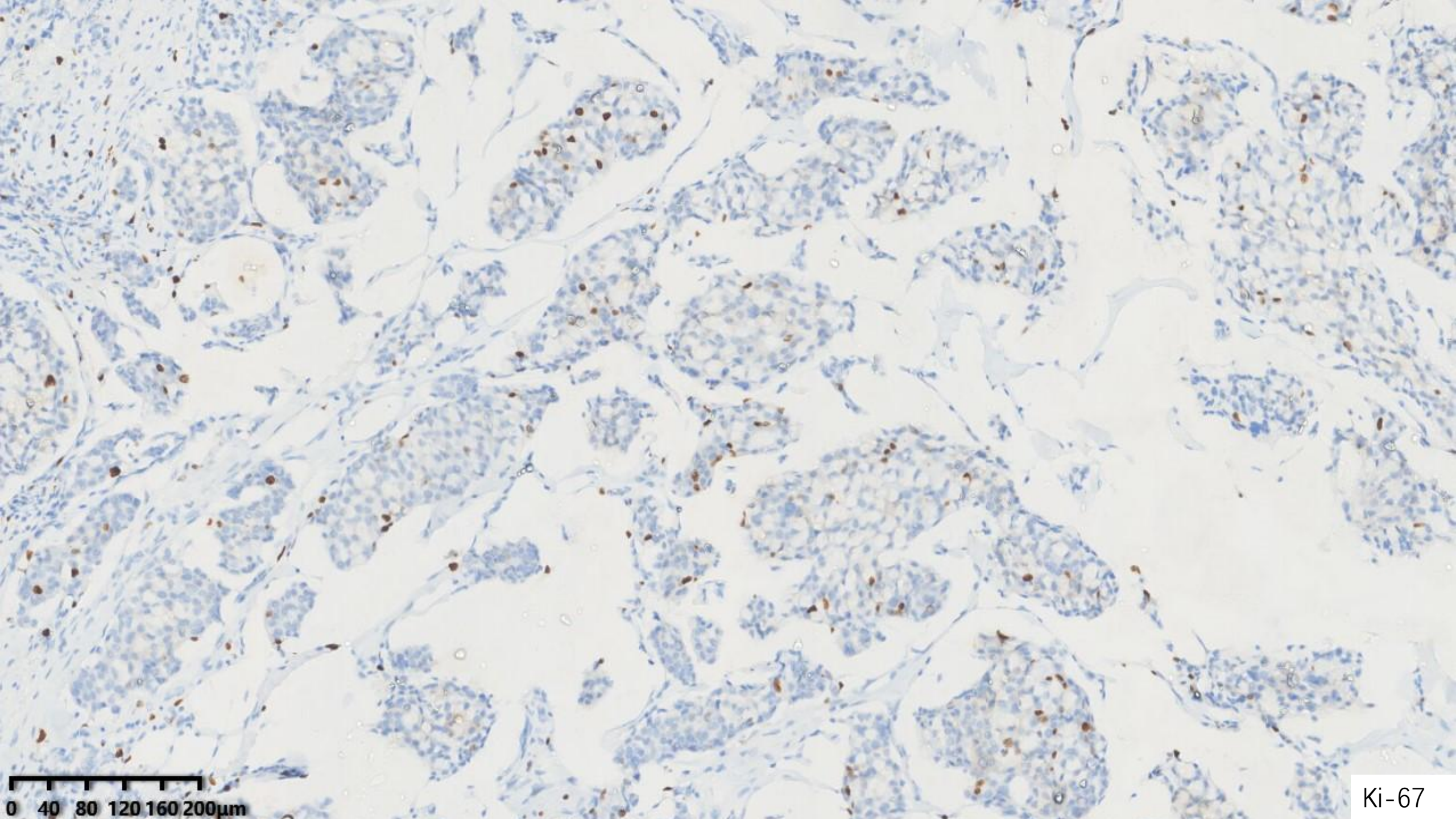
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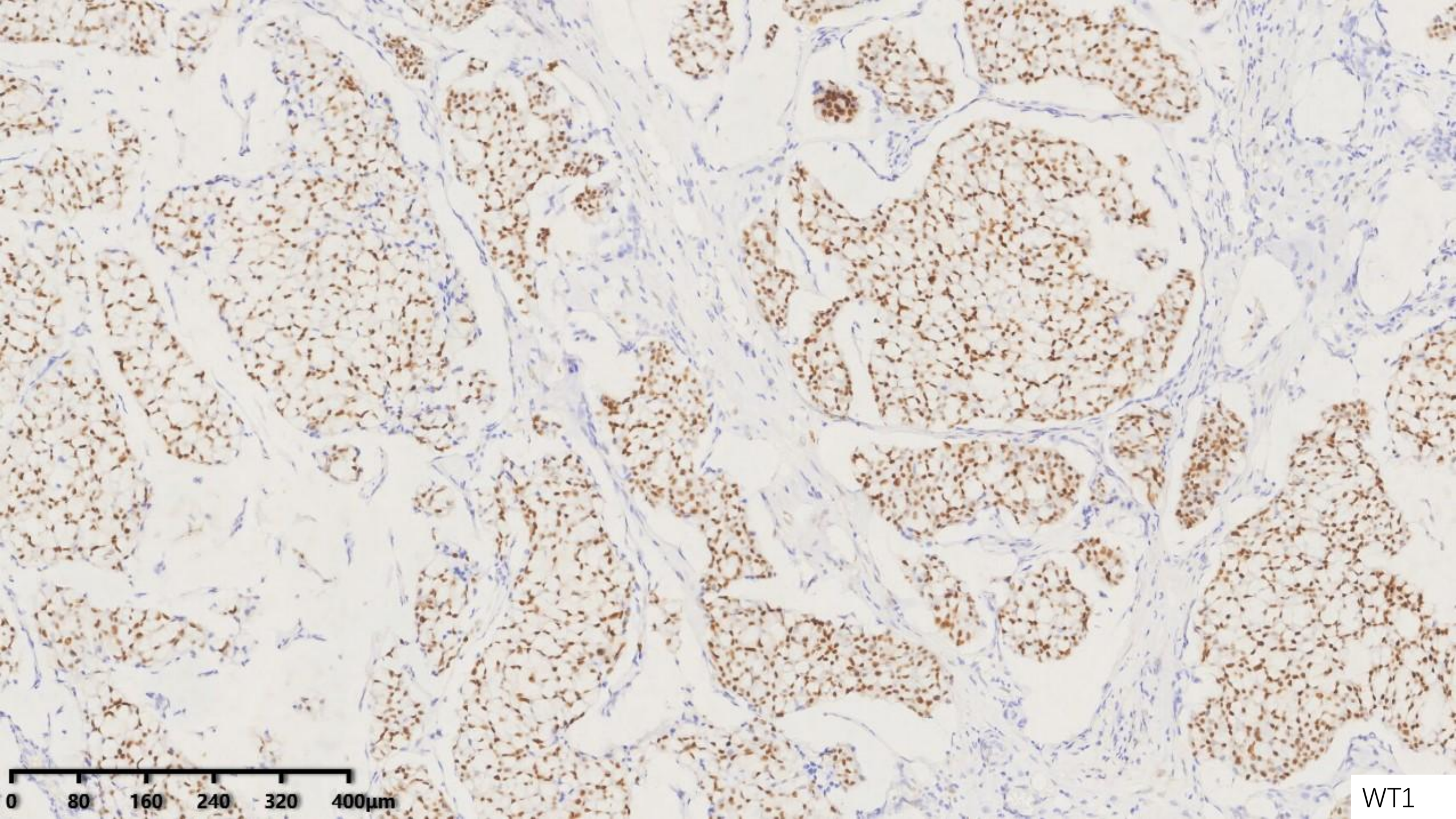
Ki-67



WT1

Mucinous carcinoma is typically characterized by the absence of PIK3CA and AKT1 mutations.

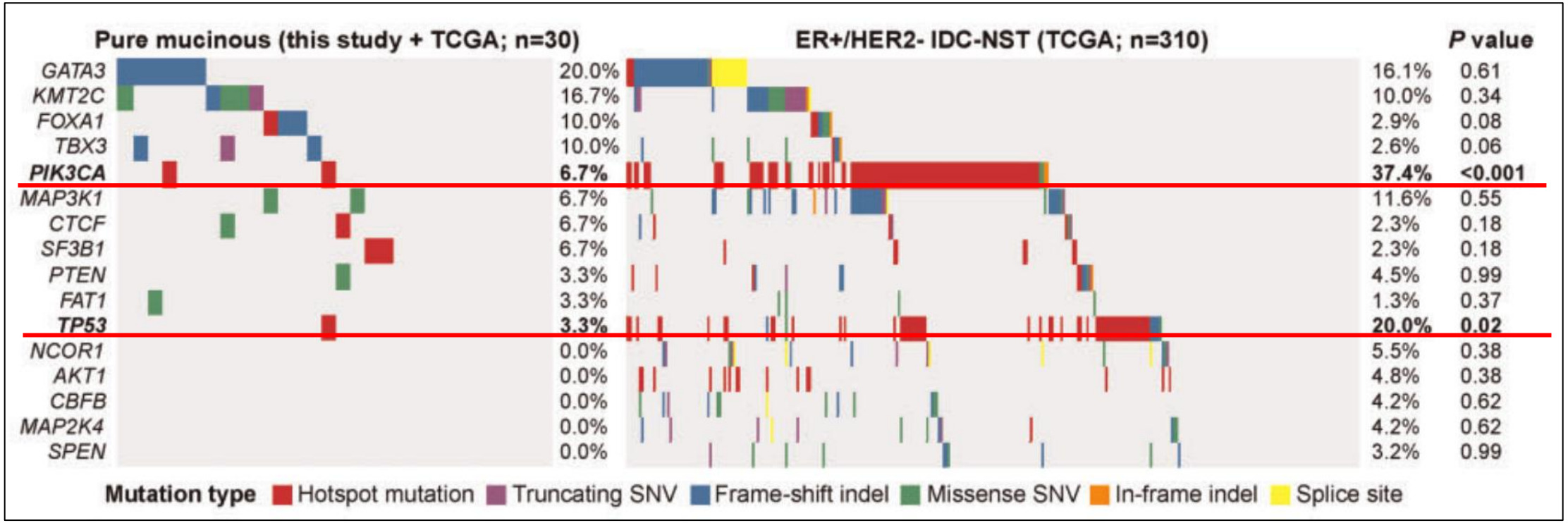
Table 2 Mutation status of invasive carcinoma and associated lesions

Lesion	*PIK3CA* mutation	*AKT1* mutation
Invasive carcinoma		
Mucinous carcinoma, total	0/38	0/35
Mucinous carcinoma, pure	0/29	0/26
Invasive ductal carcinoma, mucinous differentiation	0/9	0/9
IDC-NOS	10/31	1/31
Carcinoma in situ		
DCIS	3/14 (H1047R-2, H1047Y-1)	0/6

Table 4 Mutational analysis of invasive mucinous carcinoma: literature review

Study	*PIK3CA* mutation	*AKT1* mutation
Campbell et al [24]	0/1	
Buttitta et al [13]	1/22	
Maruyama et al [25]	1/4	
Bleeker et al [26]	2/17	0/17
Michelucci et al [27]	0/3	
Li et al [28]	1/8	
Present study	0/38	0/35
Total	5/93 (5%)	0/52 (0%)

Hum Pathol . 2012 Dec;43(12):2207-12



•Mucinous carcinoma exhibits a low level of copy number variation.
•It lacks the characteristic genomic alterations of invasive ductal carcinoma, such as 1q loss and 16q loss.
•The frequencies of PIK3CA and TP53 mutations are lower than those in ER+/HER2- invasive carcinoma of no special type (NST).

J Natl Cancer Inst (2019) 111(7):737-741

21-gene recurrence score results in mucinous carcinoma

	Total	Mean RS (SD)	Node negative
Overall	610,350	18 (10.8)	493,924 (80.9)
Ductal carcinoma, NOS	504,362	18.4 (11.2)	401,761 (79.7)
Lobular carcinoma, classic type	49,819	16.3 (6.9)	38,783 (77.9)
Lobular carcinoma, other variants	5069	18.2 (9.4)	3980 (78.5)
Invasive carcinoma, mixed	25,329	16.4 (8.5)	19,407 (76.6)
Mucinous carcinoma	16,116	14.9 (8.9)	13,902 (86.3)
Papillary carcinoma	4159	11 (13.5)	3422 (82.3)
Tubular carcinoma	3599	14.5 (5.7)	3175 (88.2)
Cribriform carcinoma	1897	12.6 (9.6)	1583 (83.5)

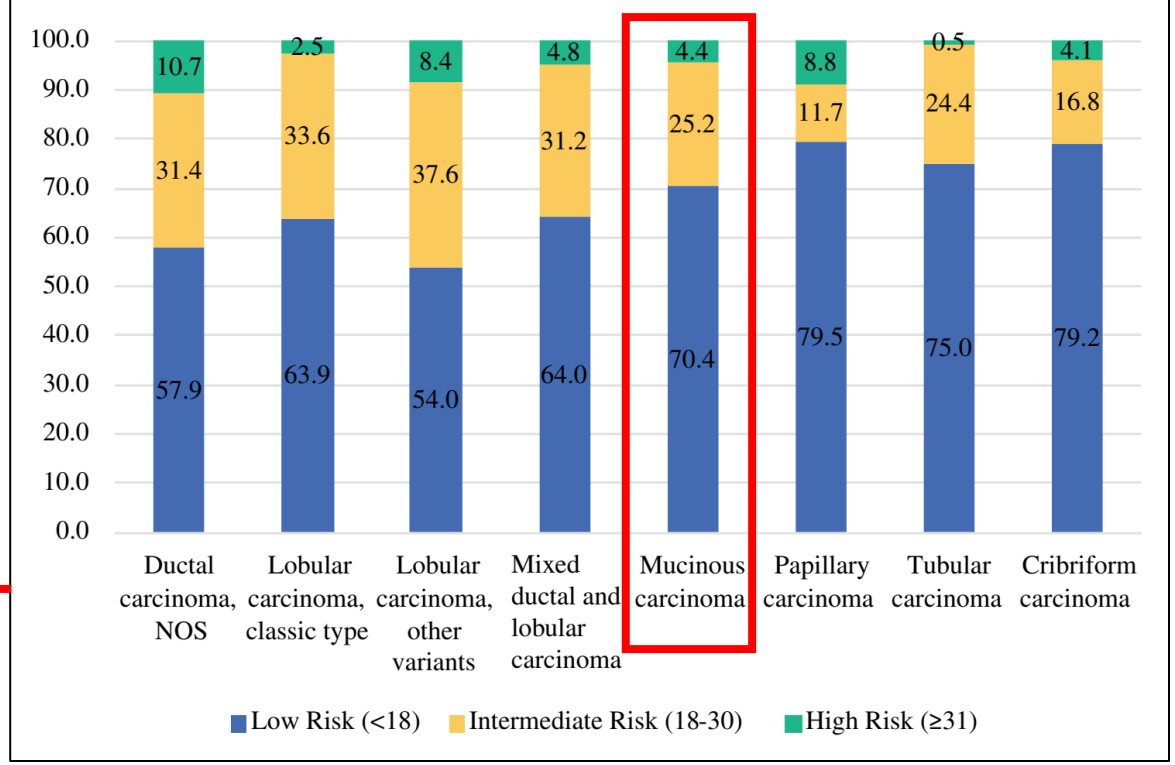


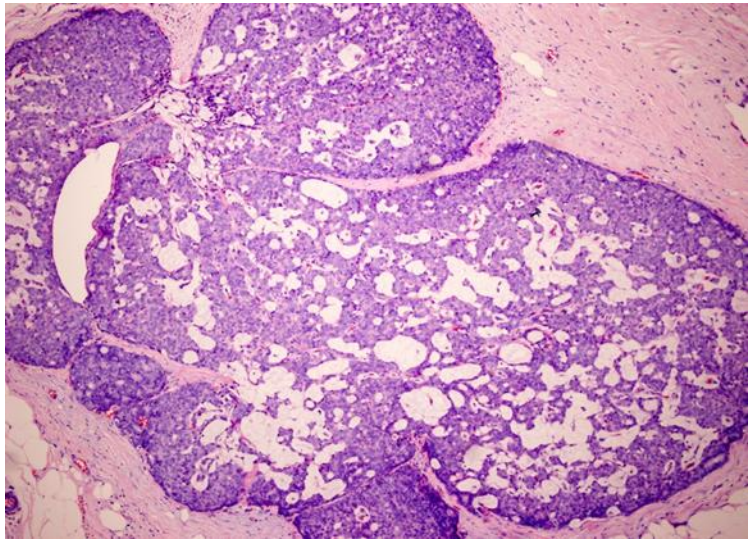
Table 1. Average Recurrence Score and Patient Age by Histologic Type

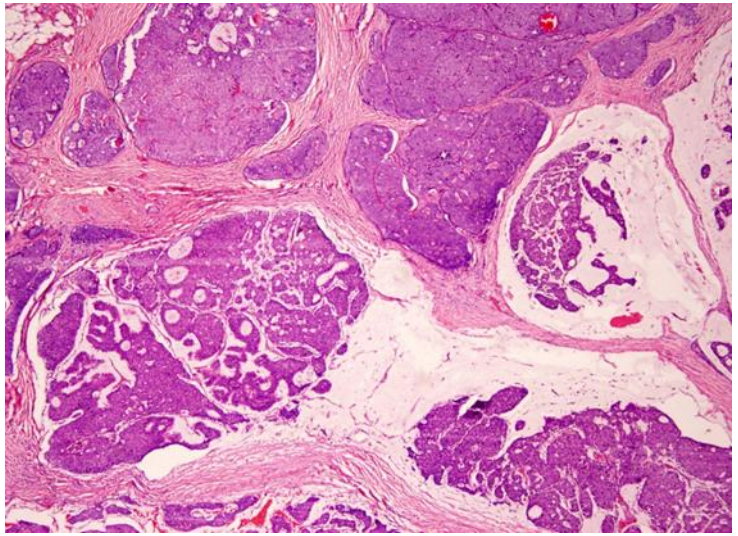
Histologic Subtype	Total No. (% of Total)	Recurrence Score, Mean (SD)	Recurrence Score Range	Patient Age, Mean (SD), y	Patient Age Range, y
Invasive ductal carcinoma	131 (71.2)	19.4 (11.6)	1–64	57.8 (10.8)	25–81
Invasive lobular carcinoma	30 (16.3)	15.7 (7.2)	0–27	57.8 (10.7)	39–80
Mixed ductal and lobular carcinoma	15 (8.2)	14.1 (7.7)	4–31	62.6 (9.2)	46–77
Invasive mucinous carcinoma	4 (2.2)	17.2 (5.9)	9–23	56.3 (15.4)	37–73
Mixed ductal and mucinous carcinoma	2 (1.1)	8.0 (4.2)	5–11	67.5 (7.8)	62–73
Tubular carcinoma	1 (0.5)	10 (. . .)	10	43 (. . .)	43
Invasive ductal carcinoma with micropapillary features	1 (0.5)	29 (. . .)	29	68 (. . .)	68
All	**184** (100)	16.2 (7.3)	0–64	59.0 (10.8)	25–81

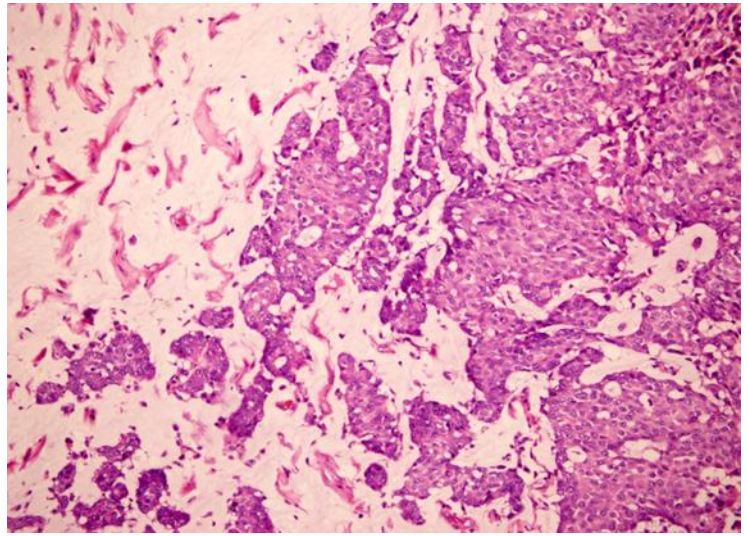
Arch Pathol Lab Med. 2015 Dec;139(12):1546-9

Ann Surg Oncol . 2018 Oct;25(11):3158-3164

Solid papillary carcinoma is often associated with mucin.







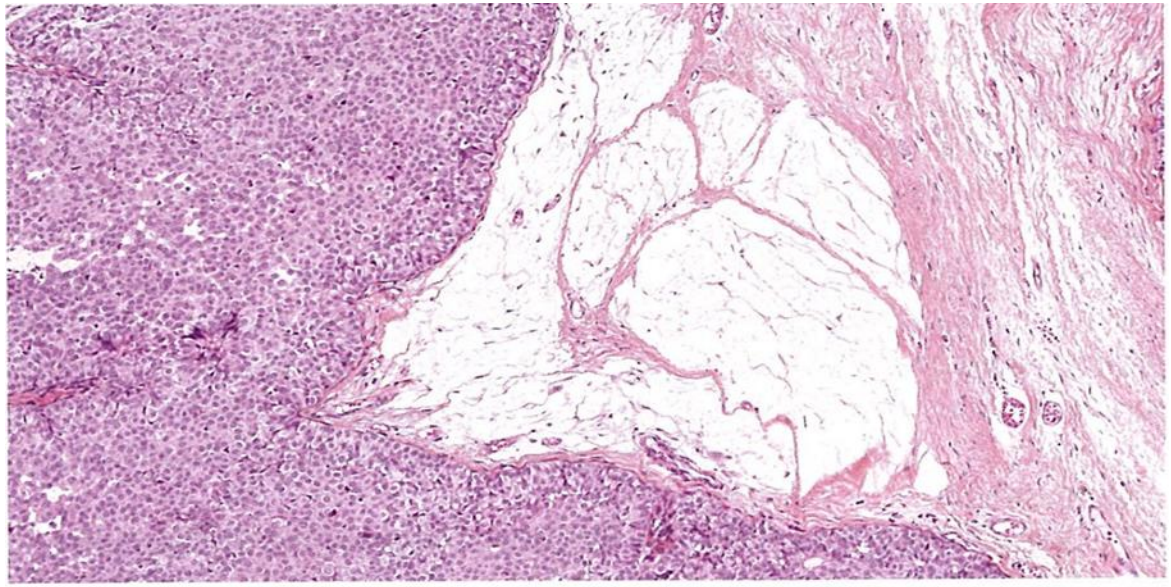
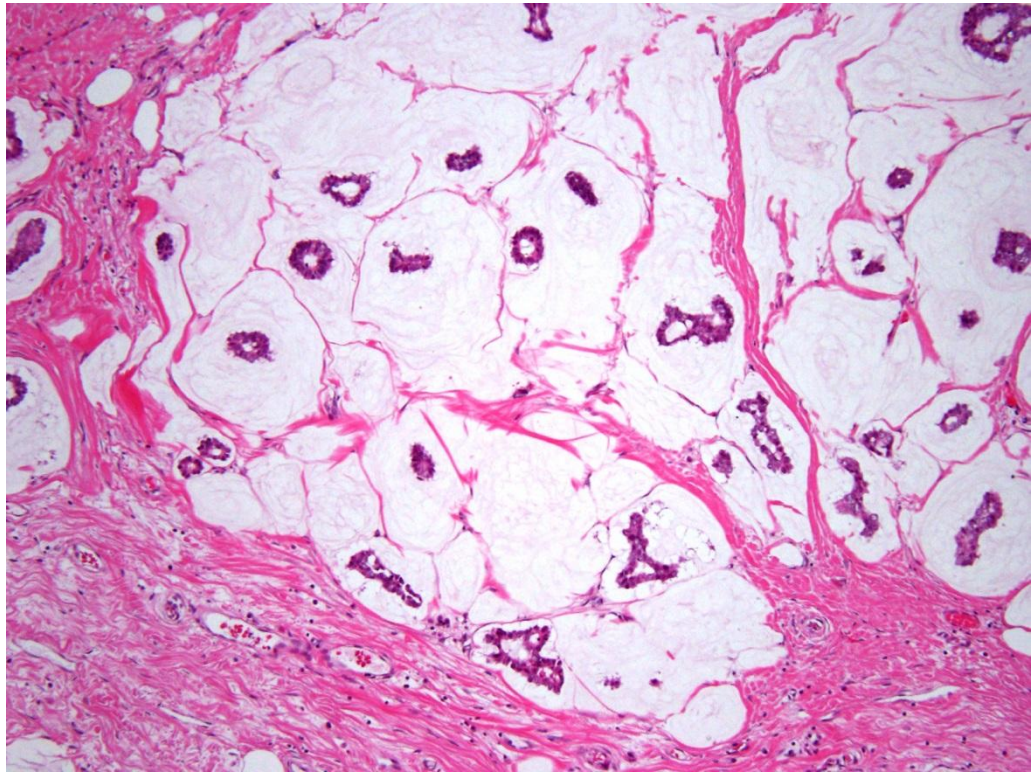


Fig. 2.53 Solid papillary carcinoma. Extracellular mucin production can also be present, but if it is not associated with floating malignant cells, the tumour is not considered to be mucinous carcinoma.

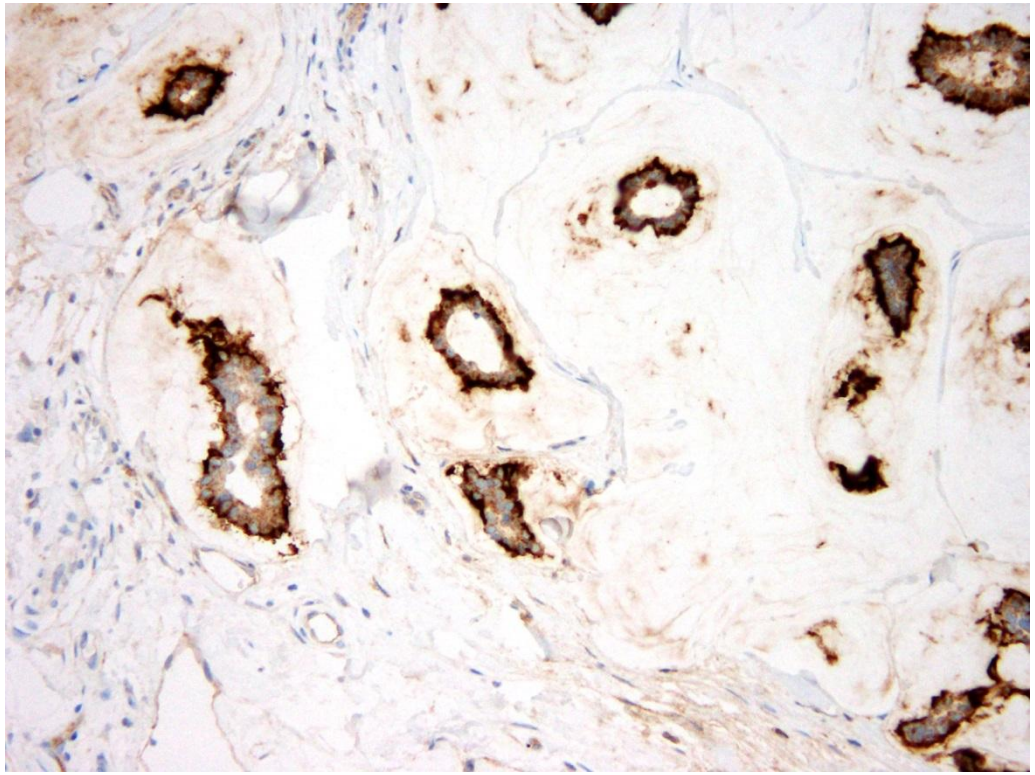
The presence of mucin in the stroma without tumor cells should not be considered invasive.

WHO Breast Tumours, 5th Edition

Invasive carcinoma with micropapillary structures and mucin secretion

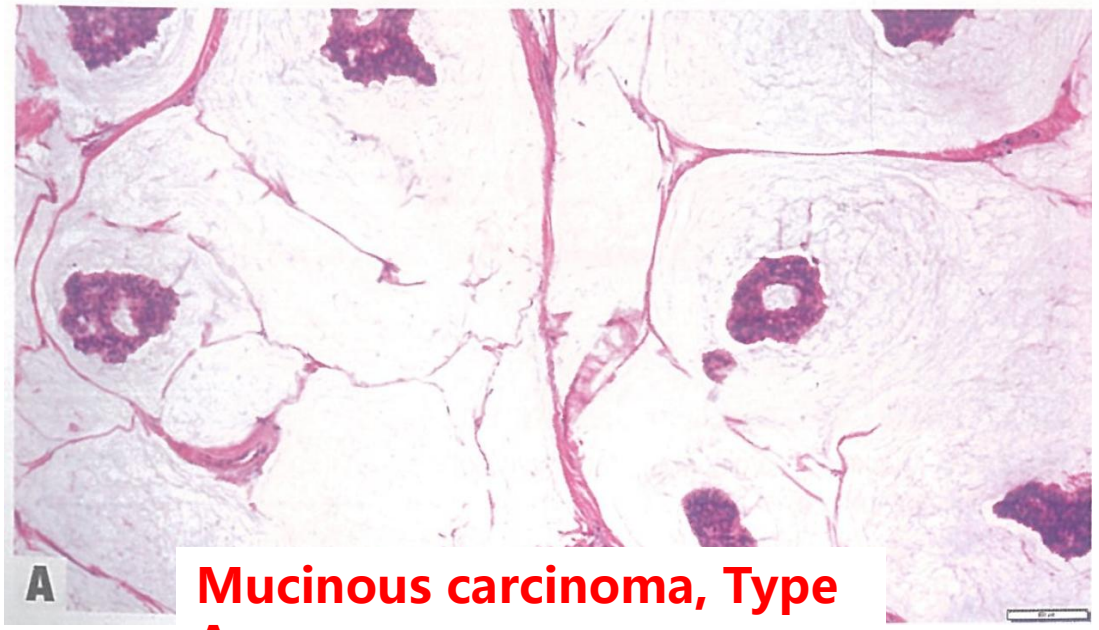


WHO 5Ed

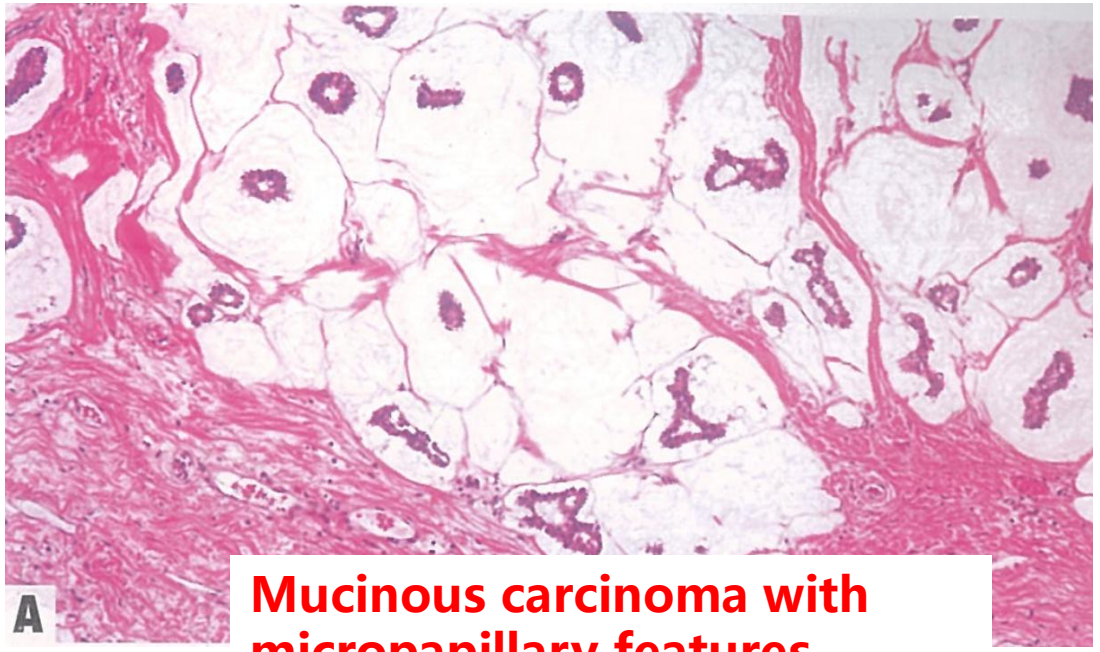


WHO 5Ed

- **Often exhibit greater nuclear atypia than classical mucinous carcinoma.**
- **Tend to occur in younger patients, with higher rates of LVI and nodal metastasis.**
- **Prognostic reports are inconsistent.**
- **Diagnostic category is unclear (micropapillary vs. mucinous); no definitive recommendation in 5th WHO .**



Mucinous carcinoma, Type A



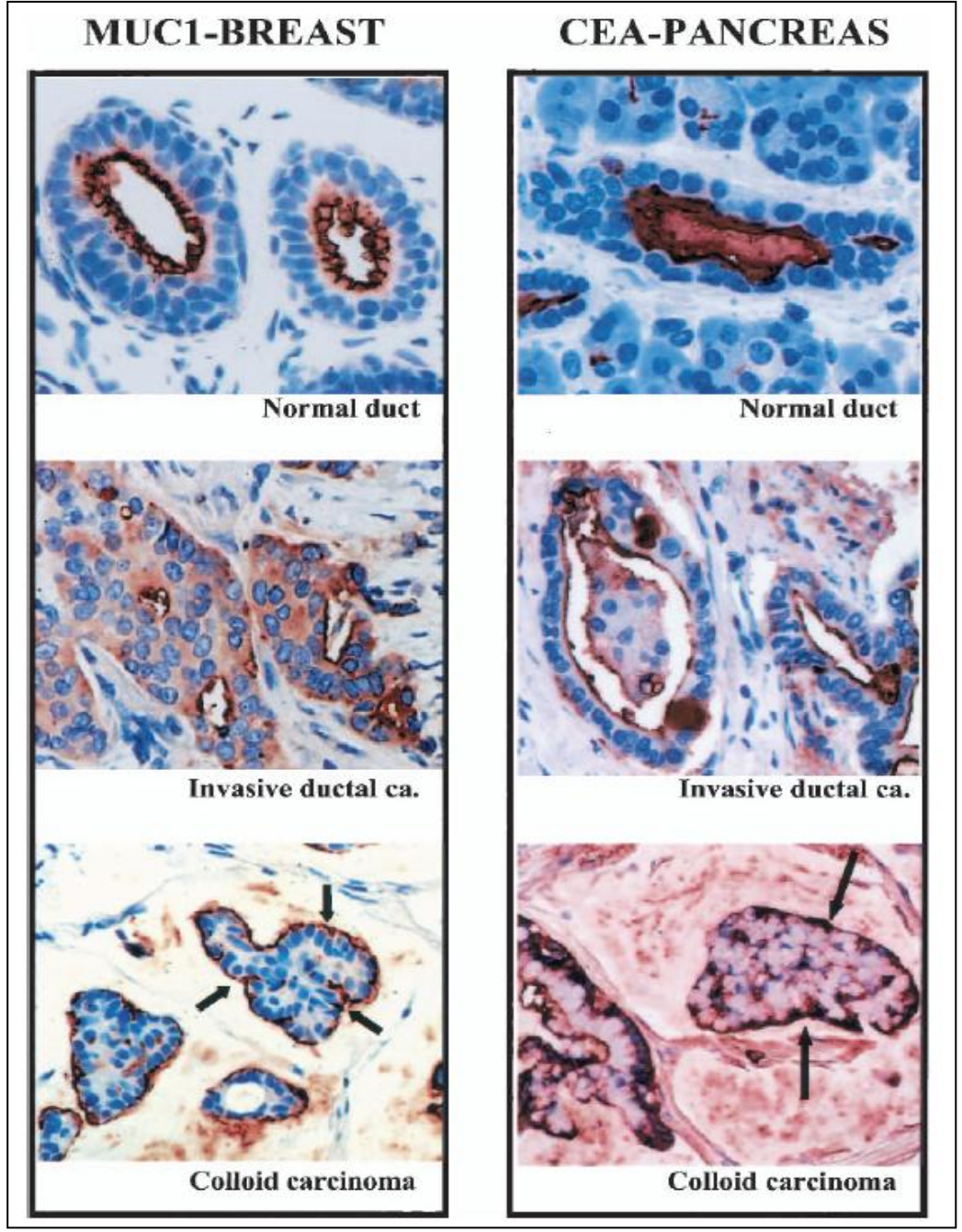
Mucinous carcinoma with micropapillary features

Pathogenesis of Colloid (Pure Mucinous) Carcinoma of Exocrine Organs

Coupling of Gel-Forming Mucin (MUC2) Production With Altered Cell Polarity and Abnormal Cell–Stroma Interaction May Be the Key Factor in the Morphogenesis and Indolent Behavior of Colloid Carcinoma in the Breast and Pancreas

- **In mucinous carcinoma, glycoproteins are primarily expressed on the stromal-facing surface of tumor cells.**
- **In invasive ductal carcinoma, glycoproteins are mainly expressed on the luminal surface or show diffuse cytoplasmic**

	Normal breast or pancreas	Conventional ductal adenocarcinoma		Colloid
		Breast	Pancreas	Breast
MUC1	Confined to the luminal surfaces of the ductal cells	100% (47/47) luminal-membrane in tubular areas, dense intracytoplasmic in poorly differentiated areas	63% (86/136), luminal-membrane in tubular areas, dense intracytoplasmic in poorly differentiated areas	100% (30/30), well-defined, thin band lining the periphery of the nests, intracytoplasmic labeling may be seen
CEA	Confined to the luminal surfaces of the ductal cells in some ducts, labeling is more commonly encountered especially in the areas of pancreatitis	— (not performed)	90% 37/41, luminal-membrane in tubular areas, dense intracytoplasmic in poorly differentiated areas	— (not performed)
MUC2	None	6% (3/44), scattered cells, intracytoplasmic	1% 1/136, scattered cells, intracytoplasmic	100% (30/30), diffuse, intracytoplasmic



Am J Surg Pathol 2003;27(5):571-578

Reversed MUC1/EMA polarity in both mucinous and micropapillary breast carcinoma ☆

To the Editor,

Table EMA staining of mucinous carcinomas

Case no.	EMA (% cells)			Age	Size (cm)	+ / Nodes	Hormone status	Clinical follow-up and comments
	Reversed	Cytoplasm [a]	Negative					
Mucinous carcinoma type A: hypocellular, not neuroendocrine								
3	100%	0%	0%	59	2.2	0/20	ER+PR−Her2−	Not available
9	100%	0%	0%	41	4.0	0/5	ER+PR+Her2−	No evidence of disease at 6 y
10	100%	0%	0%	71	0.9	0/18	ER+PR+Her2−	No evidence of disease at 2.5 y
20	80%	0%	20%	49	4.0	None	ER+PR+Her2−	Local recurrence of mucinous carcinoma with extensive DCIS diagnosed and treated 8 y prior; no further follow-up
21	0%	5%	95%	40	0.4	0/1	ER+PR+Her2−	No evidence of disease at 3 y
26	100%	0%	0%	77	3.0	0/1	ER+PR+Her2−	No evidence of disease at 9 mo
46	95%	0%	5%	63	0.6	0/2	ER+PR+Her2−	Not available
Mucinous carcinoma type A/B or B: hypercellular and/or neuroendocrine								
1	10%	100%	0%	37	1.5	0/10	ER+PR−Her2−	No evidence of disease at 4.5 y. Mixed mucinous IDC.
11	5%	90% (and dot like)	5%	61	1.5	0/1	ER+PR+Her2−	No evidence of disease at 4 y. Mixed mucinous IDC.
12	30%	0%	70%	35	0.8	0/2	ER+PR+Her2−	Contralateral mucinous carcinoma; no evidence of disease at 4 y
13	0%	0%	100%	31		2/14	ER+PR−Her2−	No evidence of disease at 3 y
15	30%	50%	20%	70	1.5	0/3	ER+PR+Her2−	Local recurrence at 3 y; no evidence of disease 1 y postrecurrence. Mixed mucinous IDC.
19	5%	5%	90%	81	1.0	0/3	ER+PR+Her2−	No evidence of disease at 1.5 y
79	0%	100%	0%	NA	0.7	NA	NA	Not available

14 cases of mucinous carcinoma

- **11 cases (78%) showed varying degrees of polarity reversal of EMA staining**
- **6 cases (43%), EMA staining showed diffuse polarity reversal.**

In the meantime, pathologists should be aware that the reversed or "inside-out" pattern of EMA staining is frequently seen in both micropapillary and mucinous carcinoma and, as such, cannot be used to identify the potentially aggressive mucinous micropapillary variant.

Hum Pathol. 2014;45(2):432-4

Reversed MUC1/EMA polarity in both mucinous and micropapillary breast carcinoma—reply

We appreciate Dr Troxell's commentary on the similarity of MUC1/EMA immunoreactivity patterns in micropapillary and mucinous breast carcinomas, a finding discussed in our article [1]. Troxell correctly notes that some studies have equated reversed MUC1/EMA polarity with micropapillary differentiation. It is important for the pathologists to be aware that altered cell orientation as evidenced by the expression of surface glycoproteins (MUC1, EMA) on the stroma-facing surface of the cells is not unique to micropapillary neoplasms. The same pattern of immunoreactivity characterizes a large proportion of mucinous (colloid) breast carcinomas, particularly type A tumors.

Immunohistochemistry data presented by Troxell lend further support to our conclusion that MUC1/EMA staining cannot discriminate between ordinary mucinous carcinomas and the potentially aggressive mucinous micropapillary tumors. The diagnosis of the latter should be based on morphologic criteria until specific diagnostic tests become available.

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- **These findings support that micropapillary carcinoma and mucinous carcinoma share a similar MUC1/EMA expression pattern.**
- **Polarity reversal is not a feature unique to micropapillary carcinoma**
- **Most mucinous carcinomas—particularly Type A mucinous carcinoma—also show a "polarity-reversed pattern" on immunohistochemical staining.**
- **MUC1/EMA staining cannot distinguish between mucinous carcinoma and mucinous micropapillary carcinoma.**

Hum Pathol. 2014;45(2):432-4

Mucinous carcinoma with micropapillary features is morphologically, clinically and genetically distinct from pure mucinous carcinoma of breast

Peng Sun[1,2] · Zaixuan Zhong[3] · Qianyi Lu[1,4] · Mei Li[1,2] · Xue Chao[1,2] · Dan Chen[3] · Wenyan Hu[3] · Rongzhen Luo[1,2] · Jiehua He[1,2]

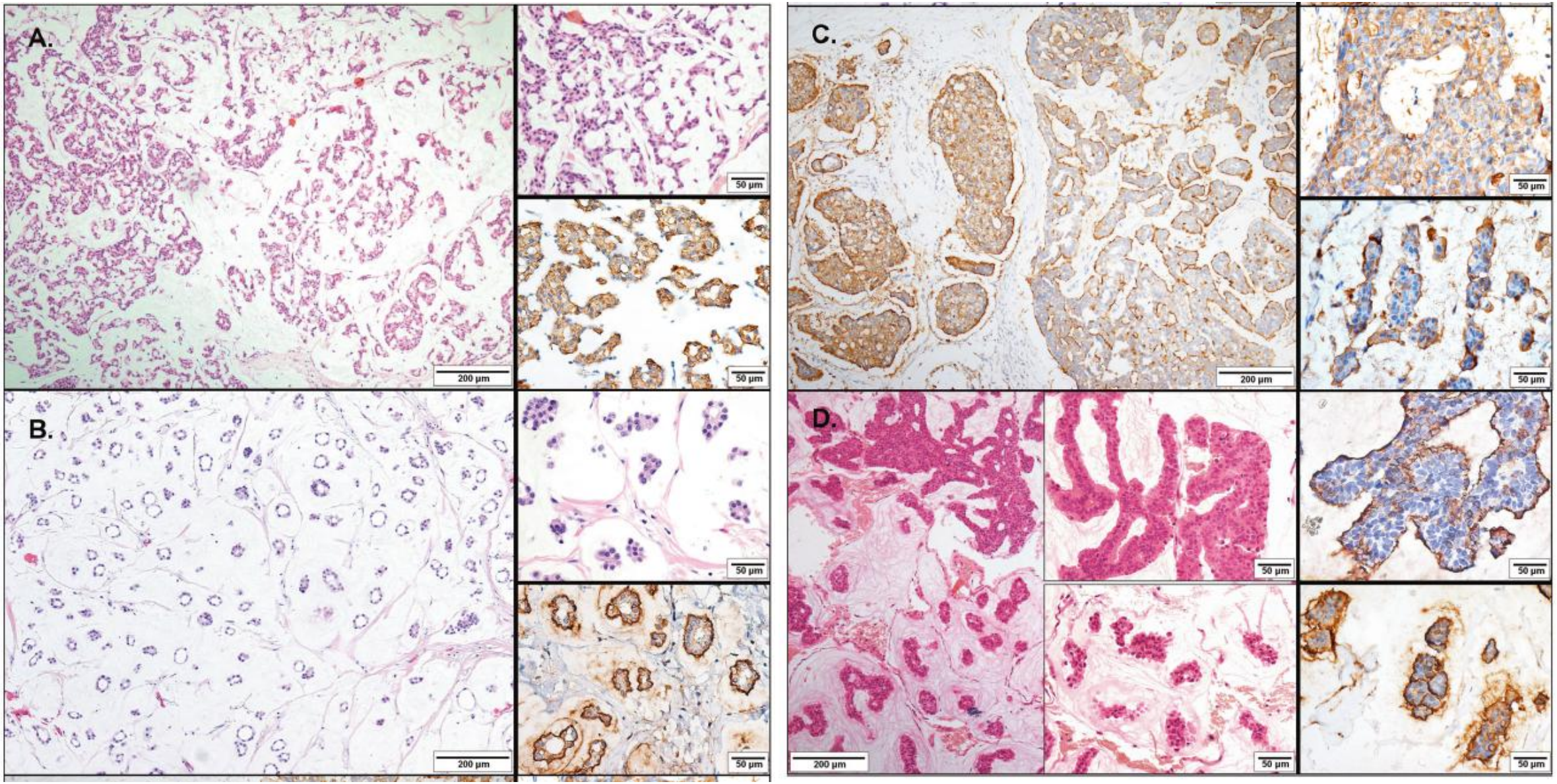
Diagnostic criteria:

- **Pure mucinous carcinoma morphology**
- **Presence of micropapillary ("morula-like") cell clusters within mucin pools (MP% ≥ 1%), suggesting features of invasive micropapillary carcinoma**
- **Polarity reversal demonstrated by EMA/MUC1 staining**

- **5.6% were of high nuclear grade.**
- **6.2% were ER-negative.**
- **8.1% were HER2-positive.**

- MPMC accounts for 32% of all mucinous carcinomas.
- MPMC presents in younger patients with more aggressive features (higher nuclear grade, more LVI and LN metastasis) and poorer outcomes.
- 21-gene assay shows no significant difference from pure mucinous carcinoma.
- Shares some genetic alterations with mucinous carcinoma but also has distinct differences.
- MPMC is distinct in morphology, clinical behavior, and molecular profile.

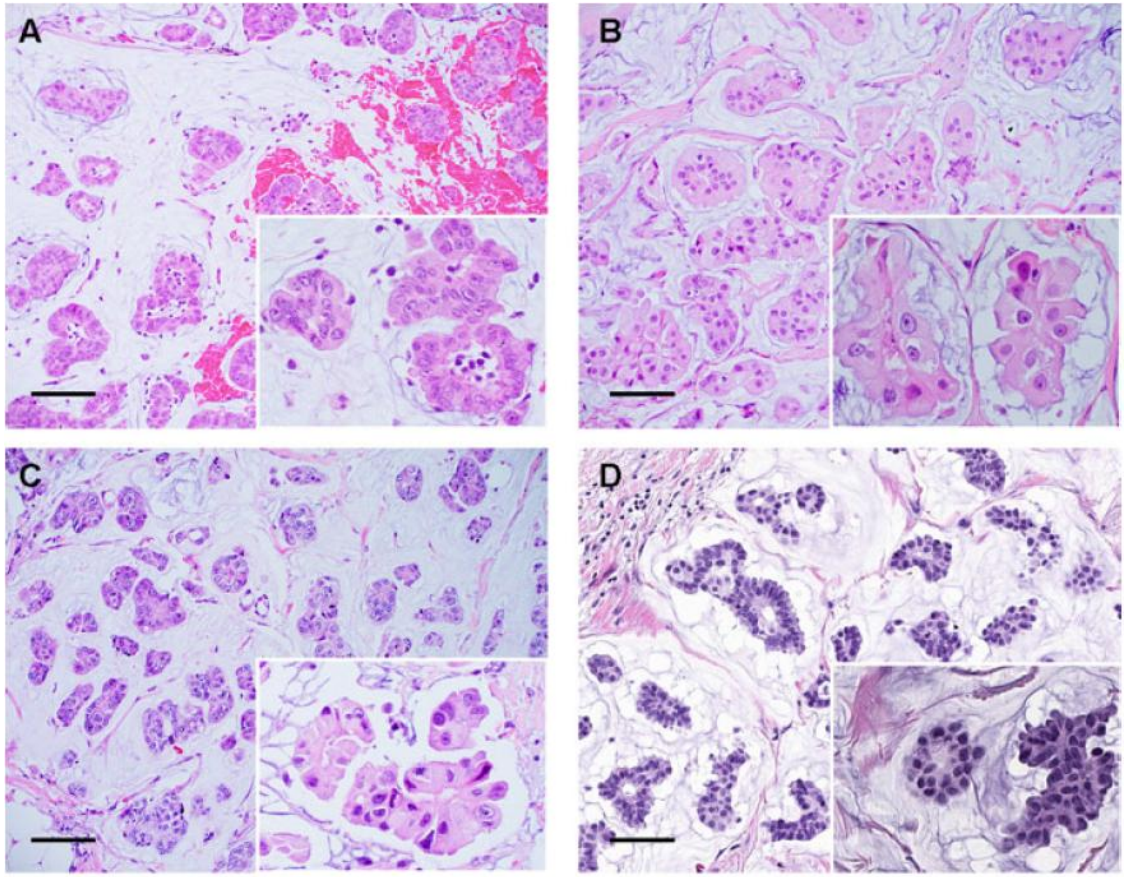
Mod Pathol. 2020;33(10):1945-1960

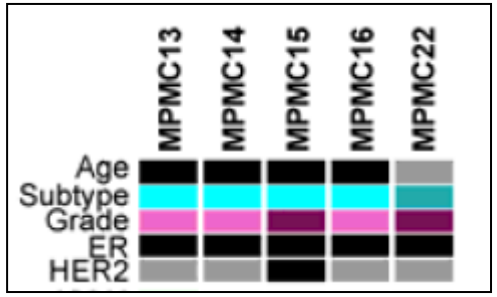


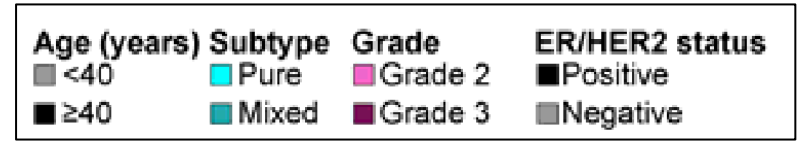
Mod Pathol. 2020;33(10):1945-1960

Micropapillary Variant of Mucinous Carcinomas of the Breast Display Genetic Alterations Intermediate Between Mucinous Carcinomas and Micropapillary Carcinomas

Whole-exome sequencing of five cases of micropapillary mucinous carcinoma

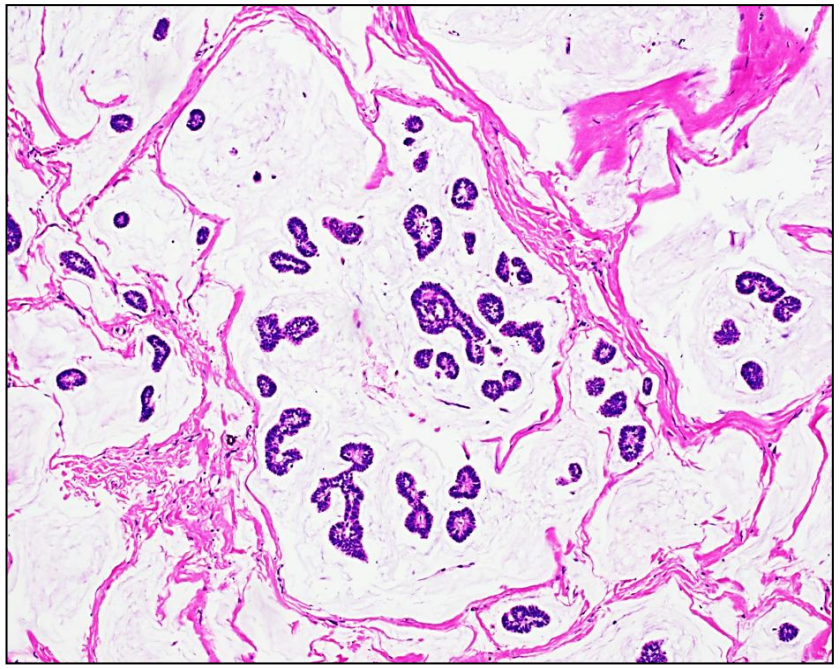


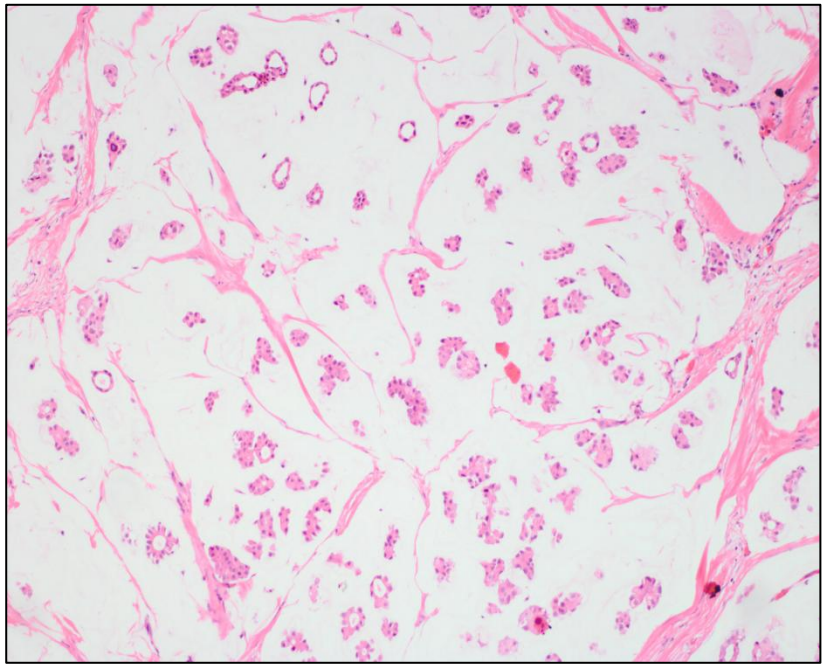


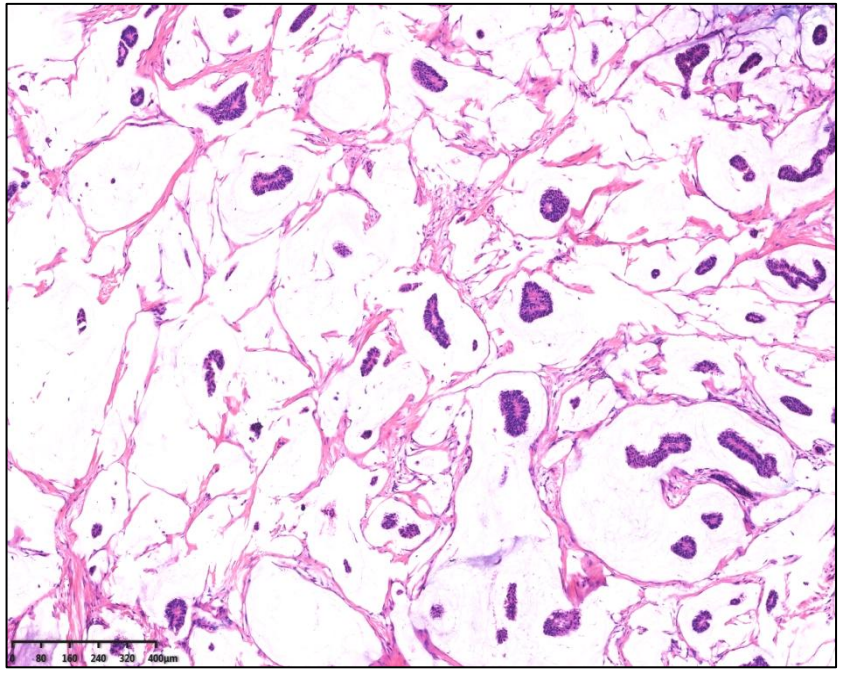


- **Micropapillary mucinous carcinoma (MPMC) shows genetic heterogeneity, with some cases exhibiting molecular alterations similar to those of mucinous carcinoma, and others resembling invasive micropapillary carcinoma.**
- **In three cases, the genetic features were similar to mucinous carcinoma, characterized by absence of PIK3CA mutations, 1q gain, and 16q loss; whereas in two cases, 16q loss and/or copy number alterations resembling those of invasive micropapillary carcinoma were observed.**
- **MPMC may not represent an independent histologic subtype, but rather a hybrid lesion derived from mucinous carcinoma or invasive micropapillary carcinoma.**

Histopathology. 2019;75(1):139-145



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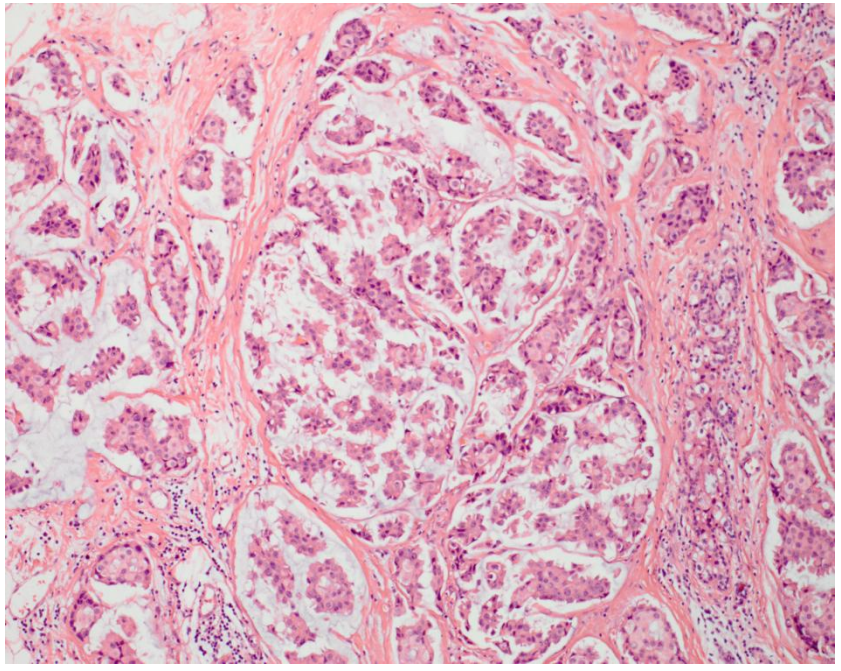
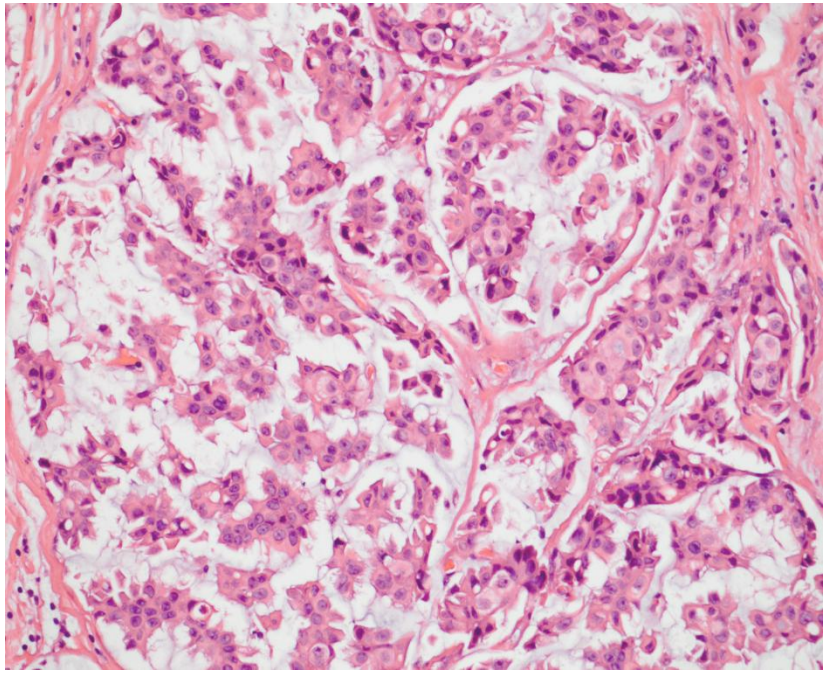
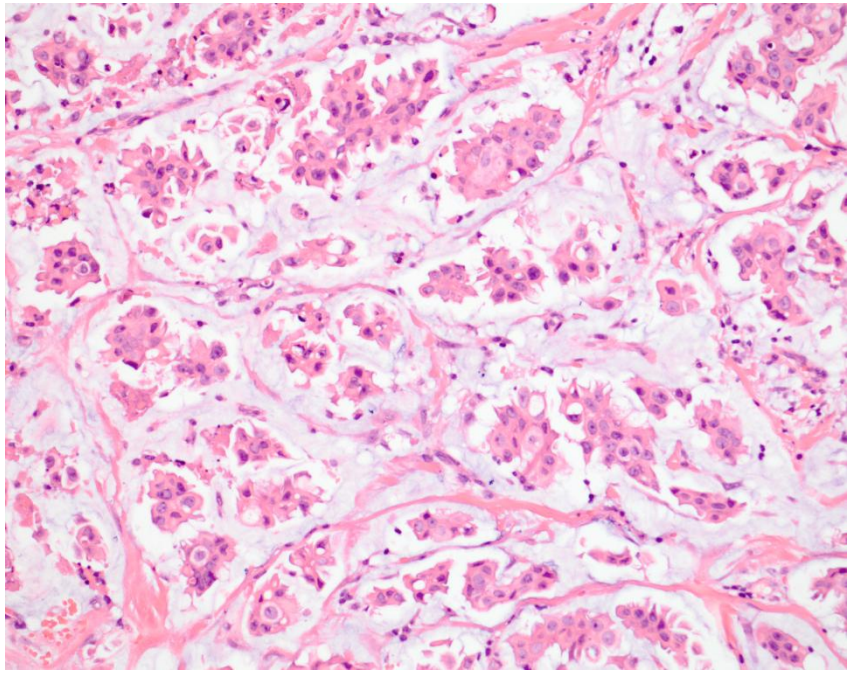






Micropapillary pattern in pure mucinous carcinoma of the breast——does it matter or not?

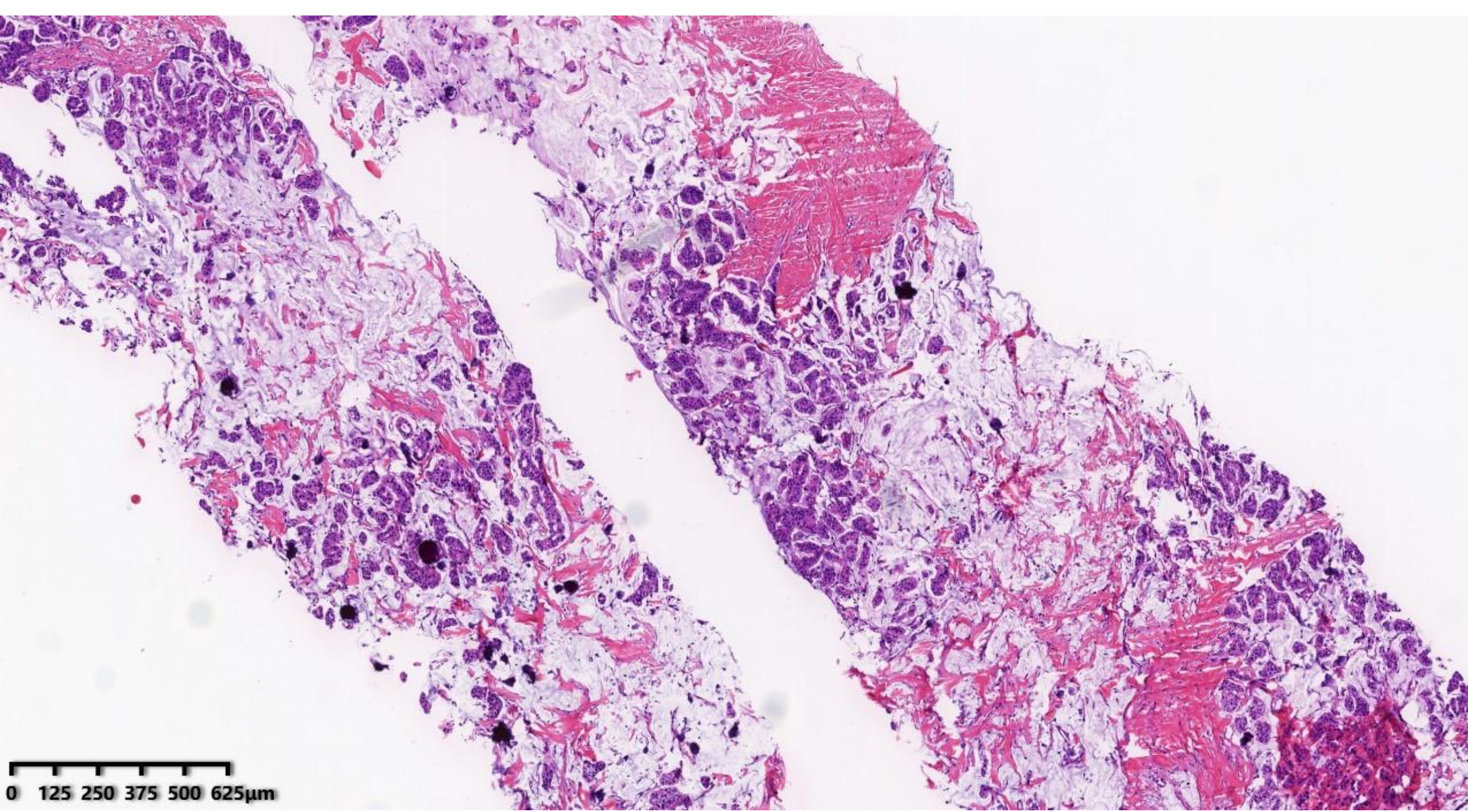
Xu Xiaoli[1,2], Bi Rui[1,2], Shui Ruohong[1,2], Yu Baohua[1,2], Cheng Yufan[1,2], Tu Xiaoyu[1,2], Yang Wentao[1,2].

1Department of Pathology, Fudan University Shanghai Cancer Centre, Shanghai, China 2Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China.

- Nuclear grade: 1–2 in all cases.
- ER: 100% positive; PR: 90.7% positive.
- HER2: 100% negative.
- Lymph node metastasis rate: 5.7%.
- Micropapillary structures present in 80% of cases.
- Micropapillary presence not linked to LN metastasis or survival.

- Classification should be based strictly on cytologic atypia and immunophenotype.
- Diagnosis of classical mucinous carcinoma is inappropriate when nuclear atypia exceeds moderate and immunophenotype is non-classical (HR- or HER2 positive).
- The presence of peripheral conventional invasive micropapillary carcinoma suggests a diagnosis other than pure mucinous carcinoma.

Histopathology. 2019 Jan;74(2):248-255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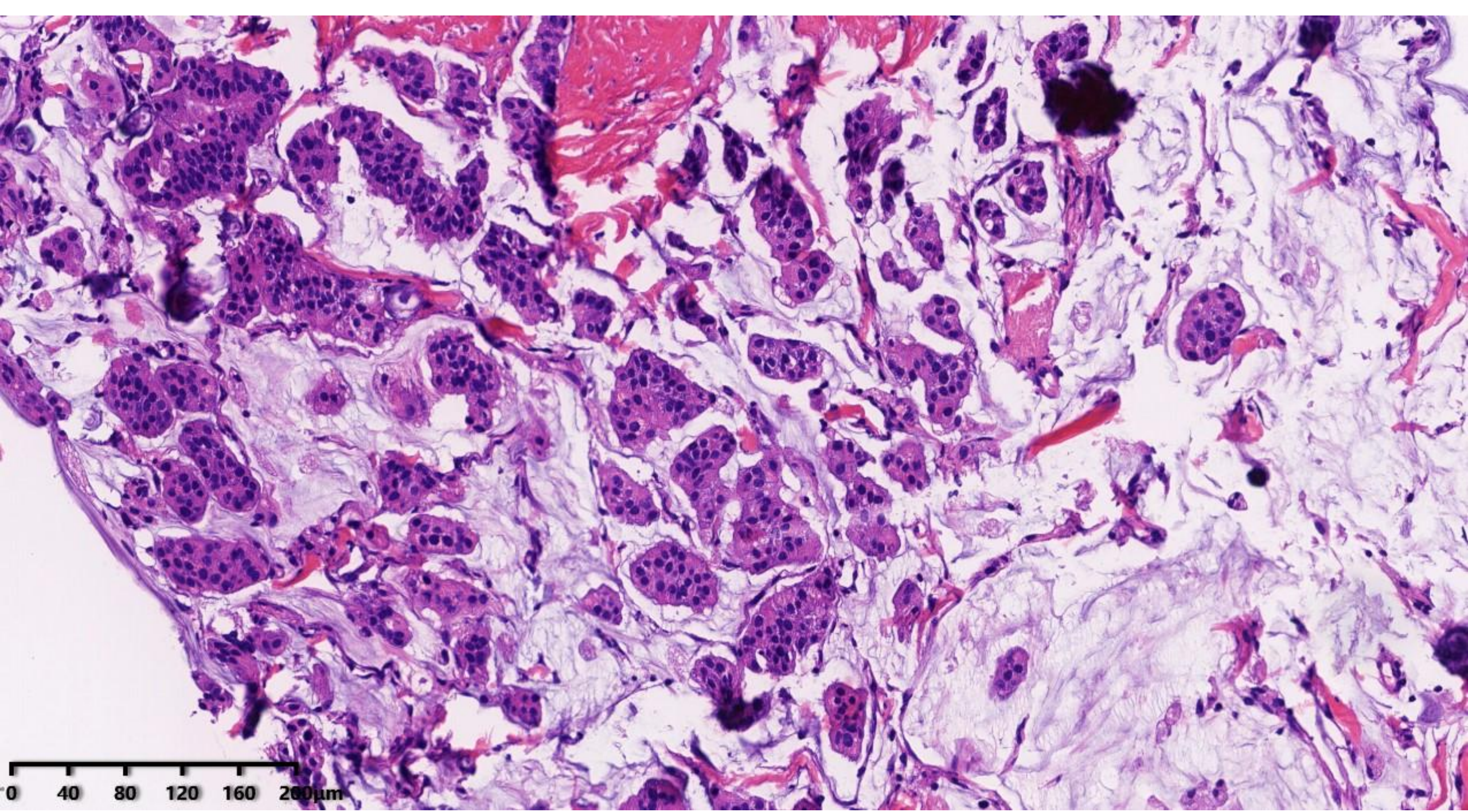
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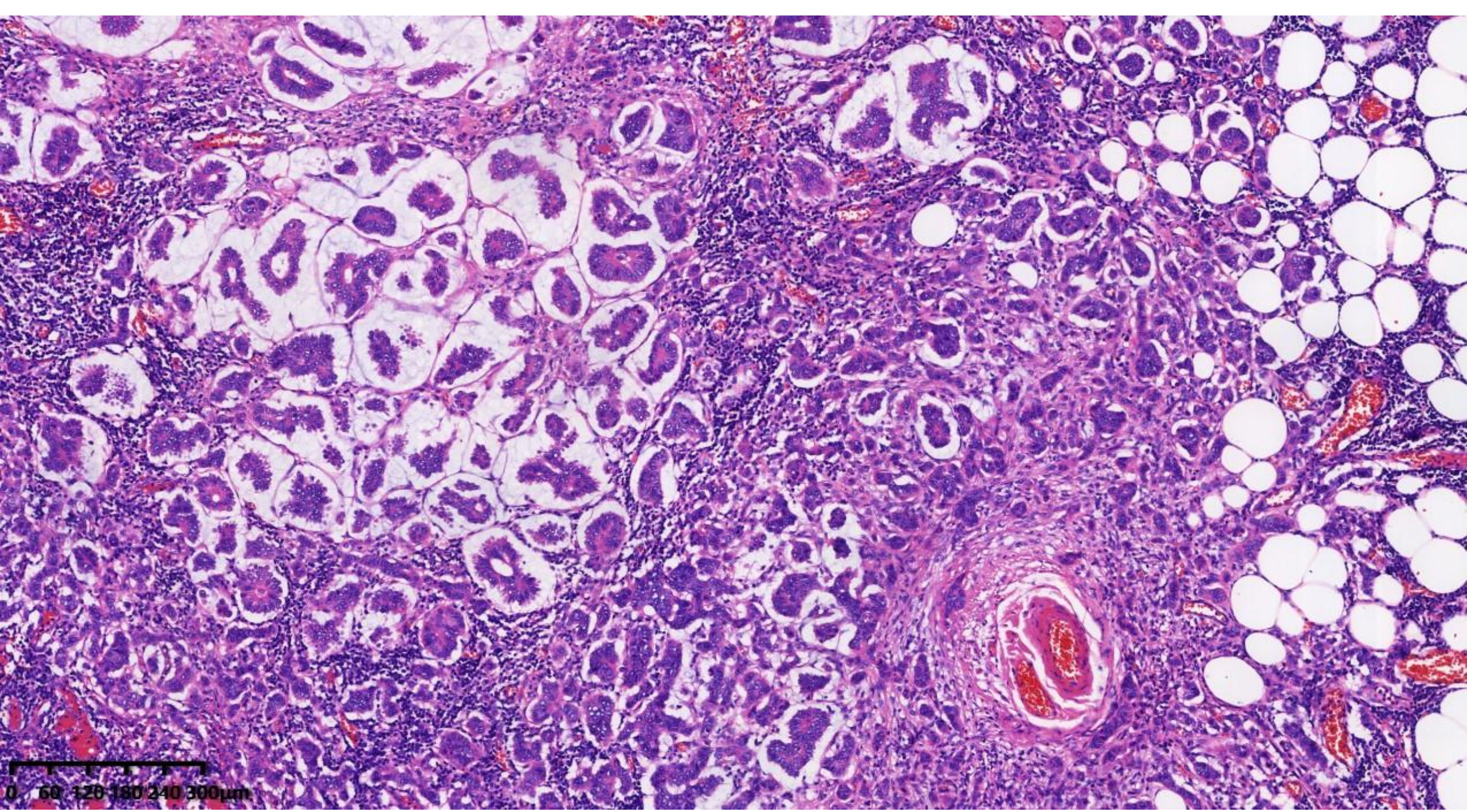
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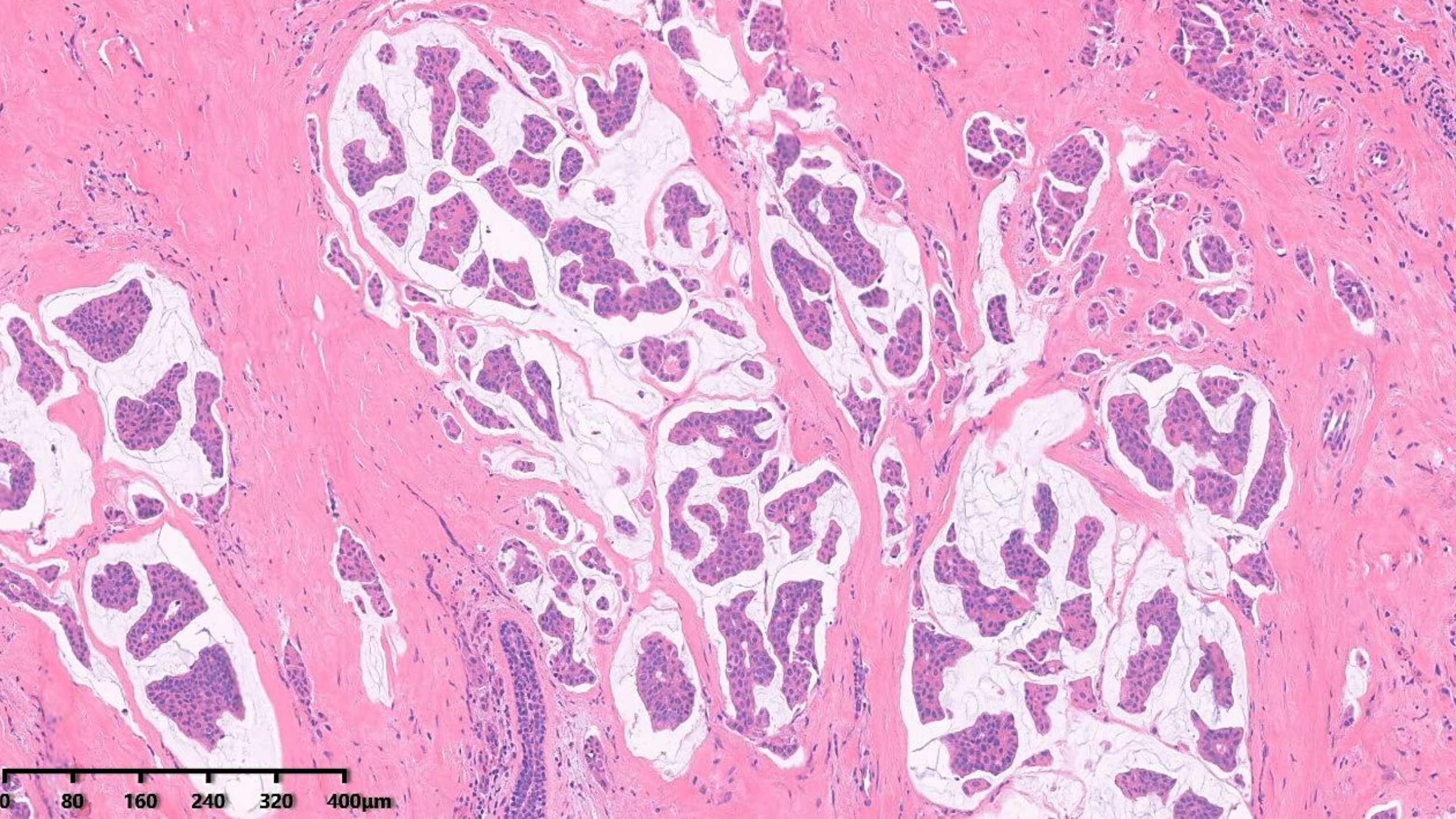
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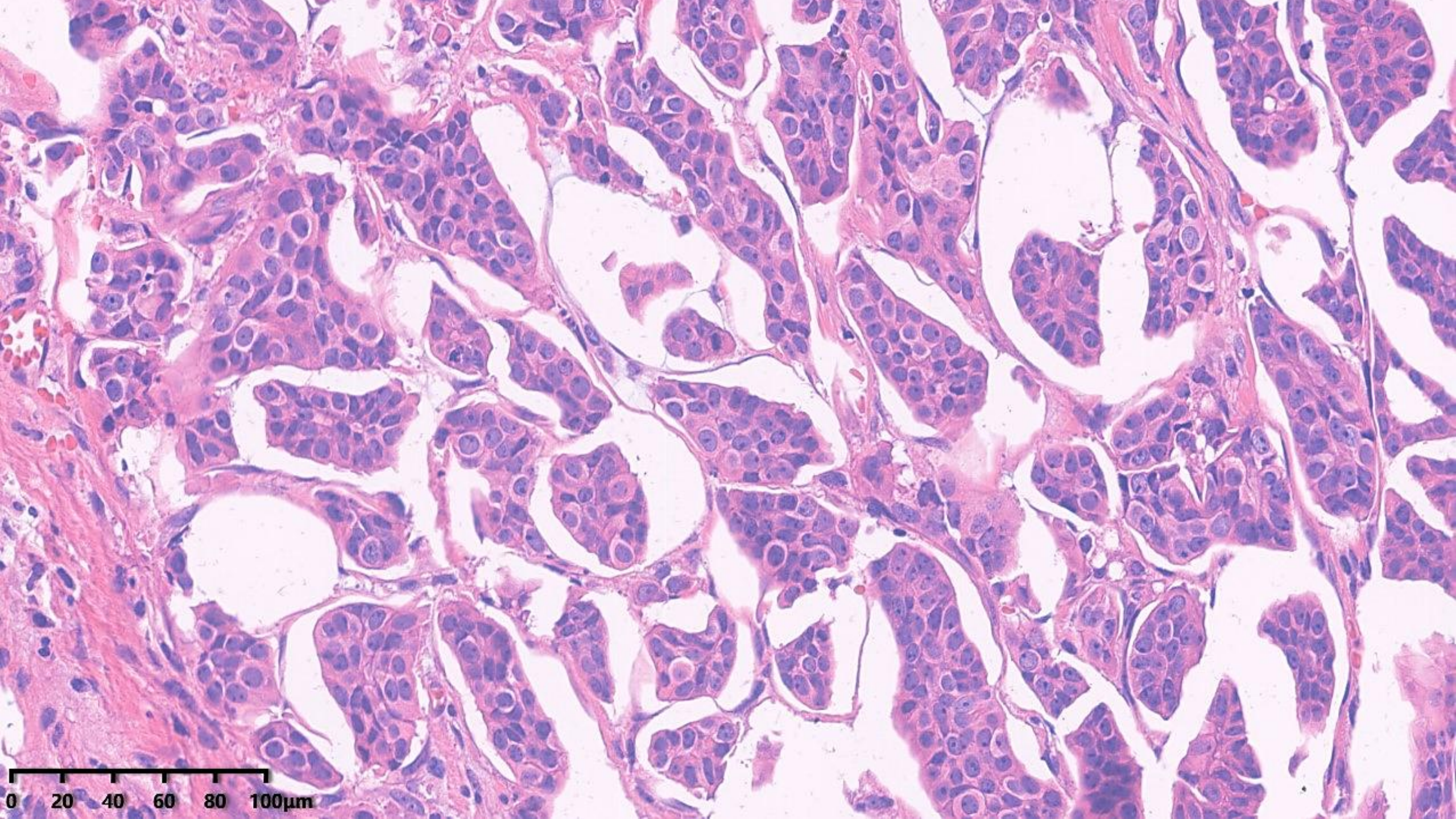
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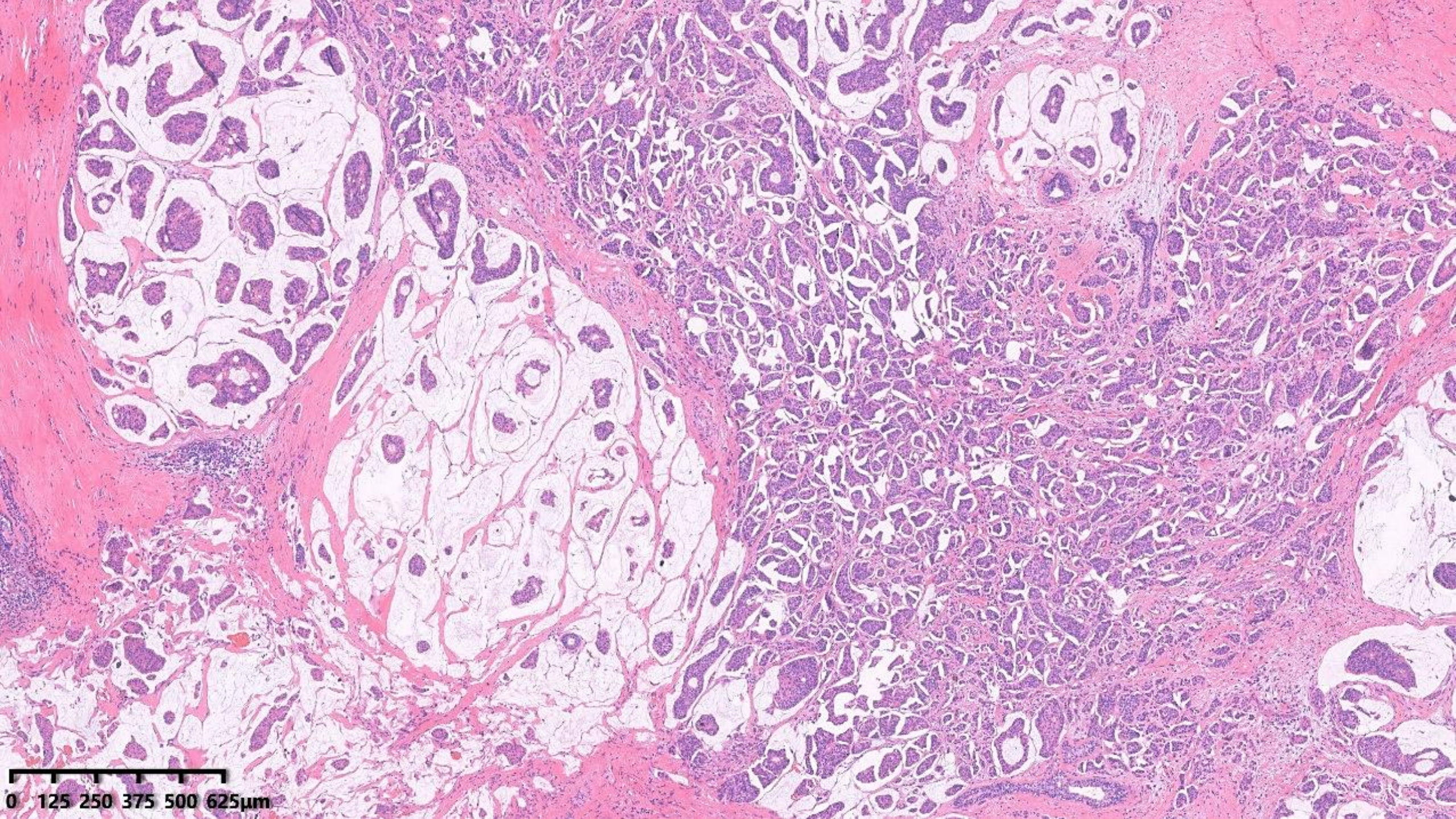
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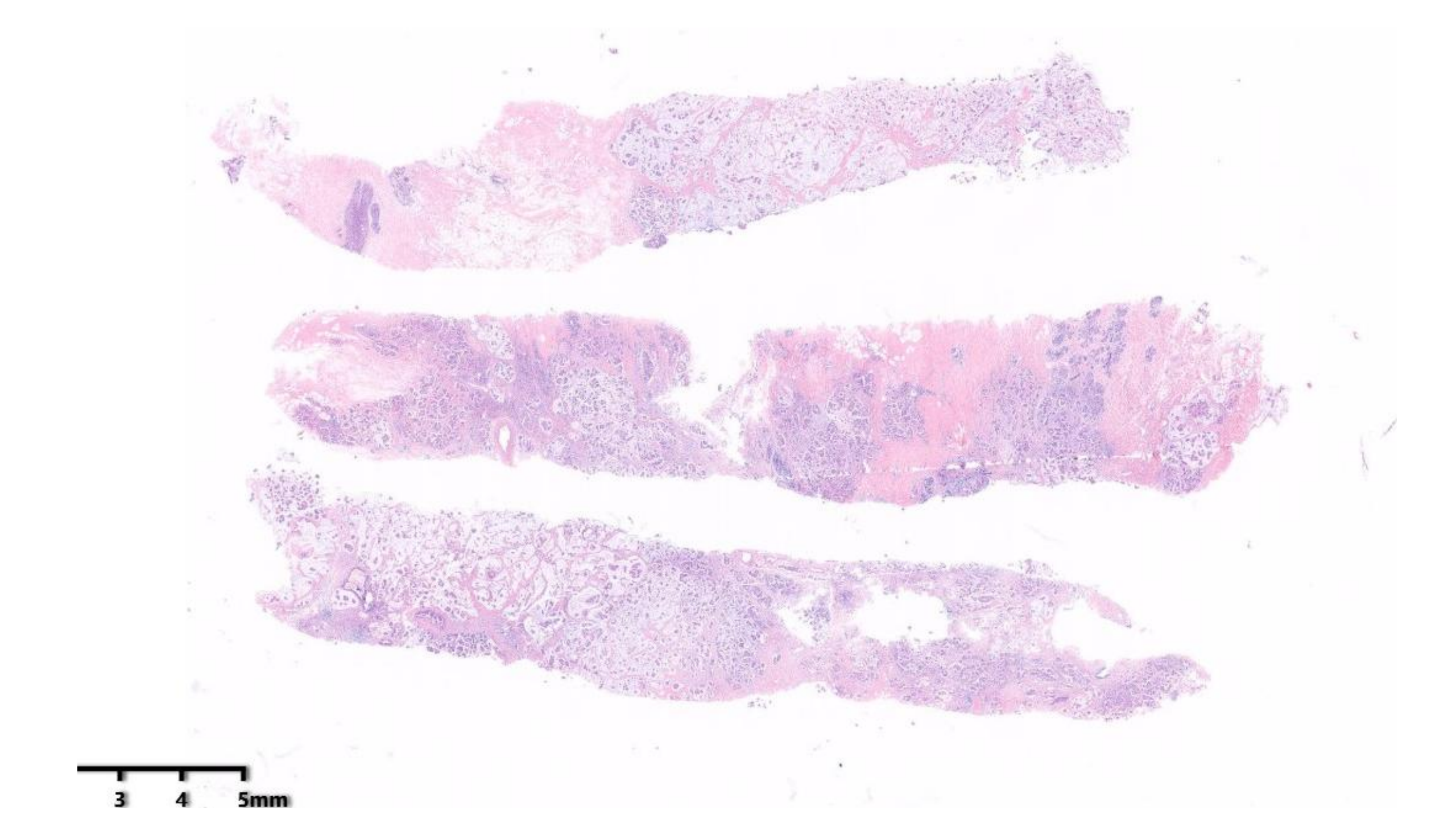
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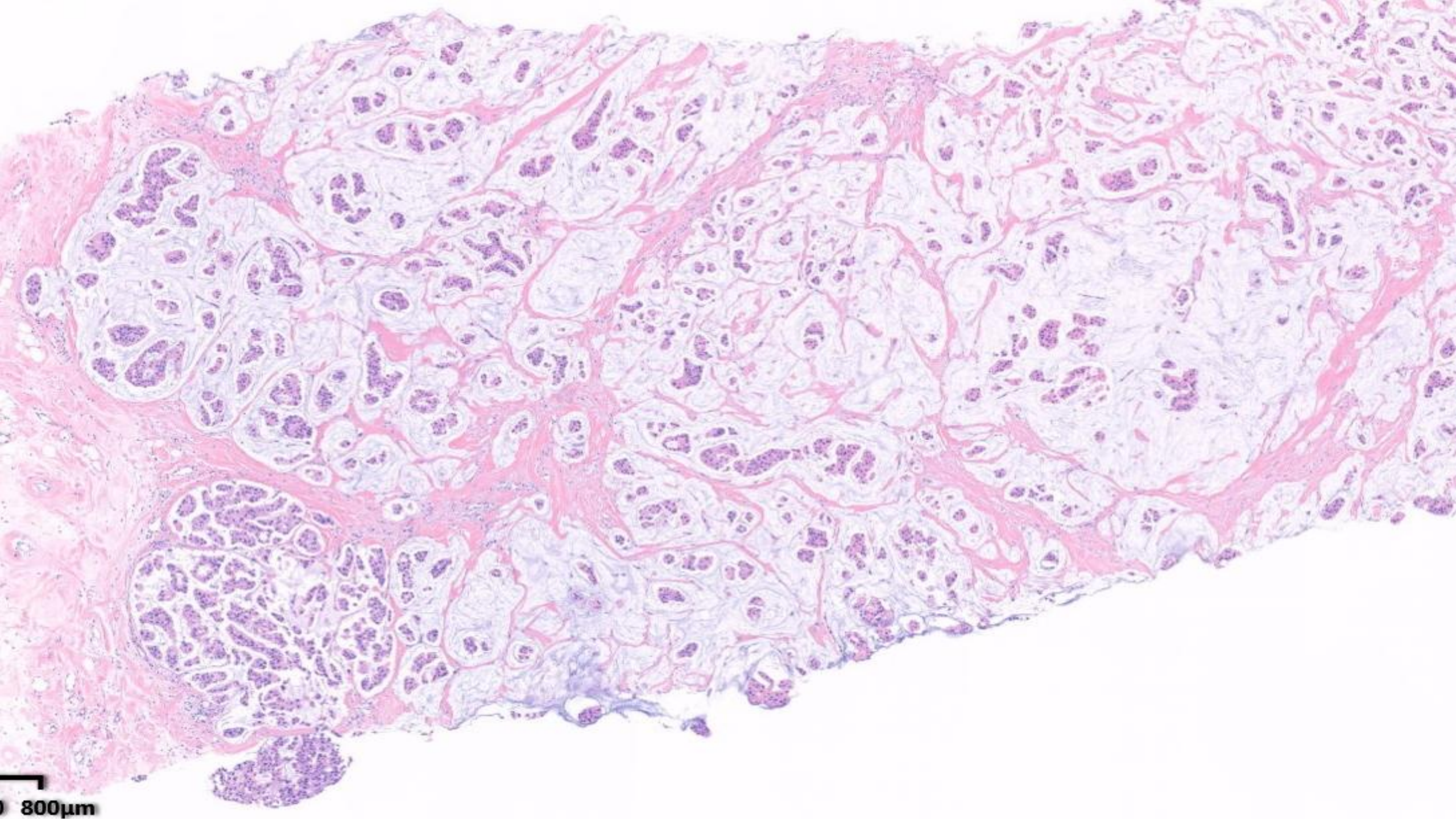
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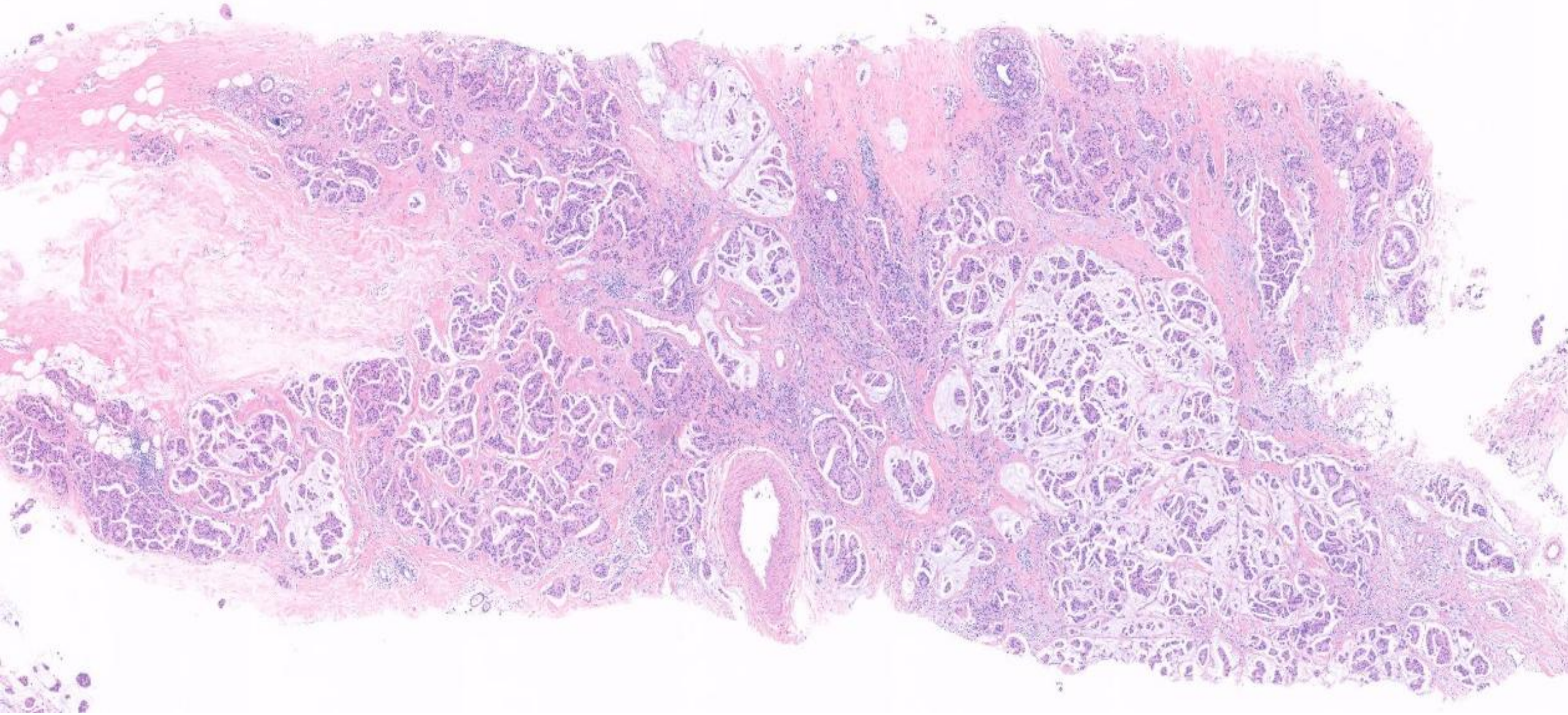

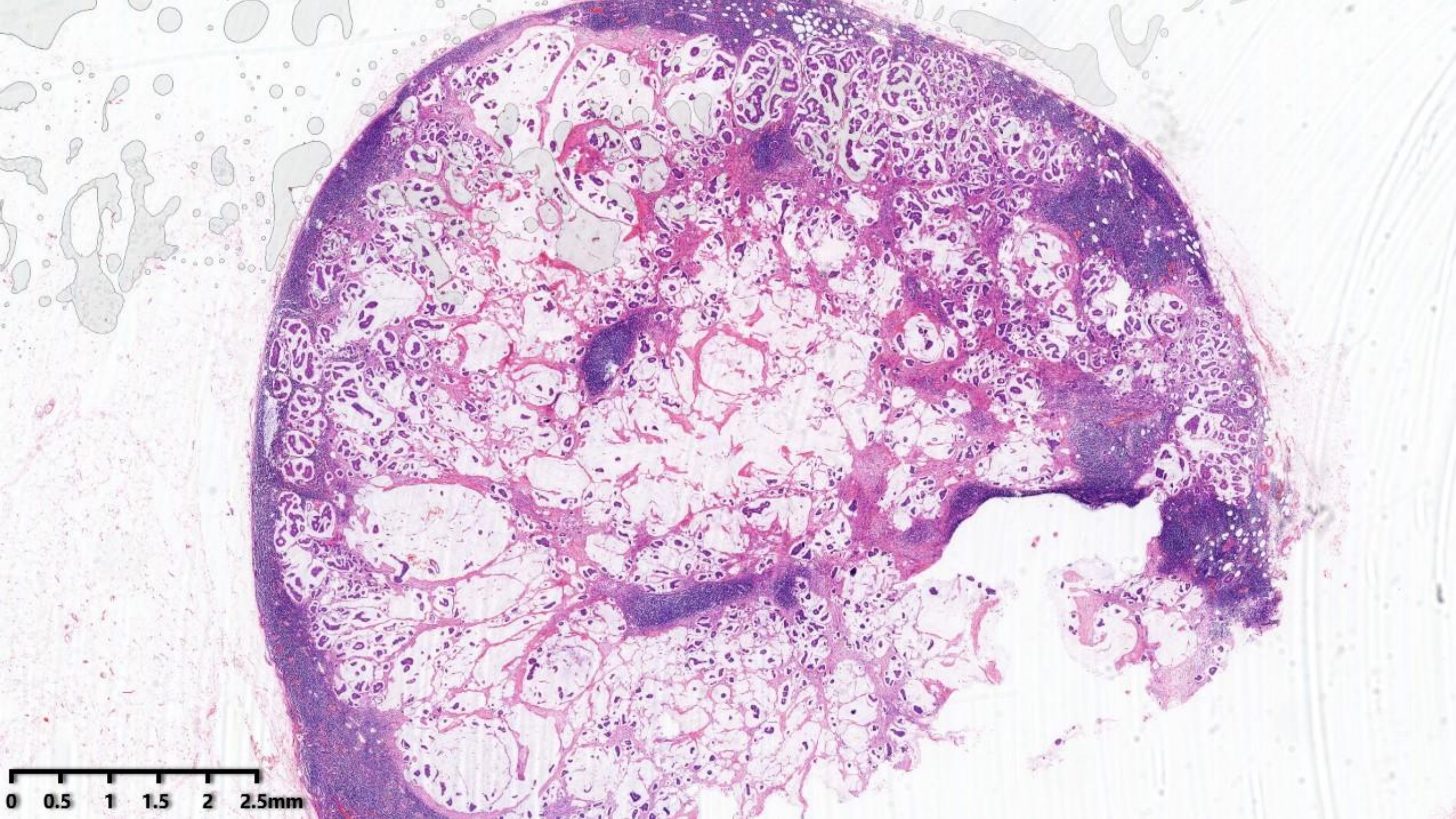
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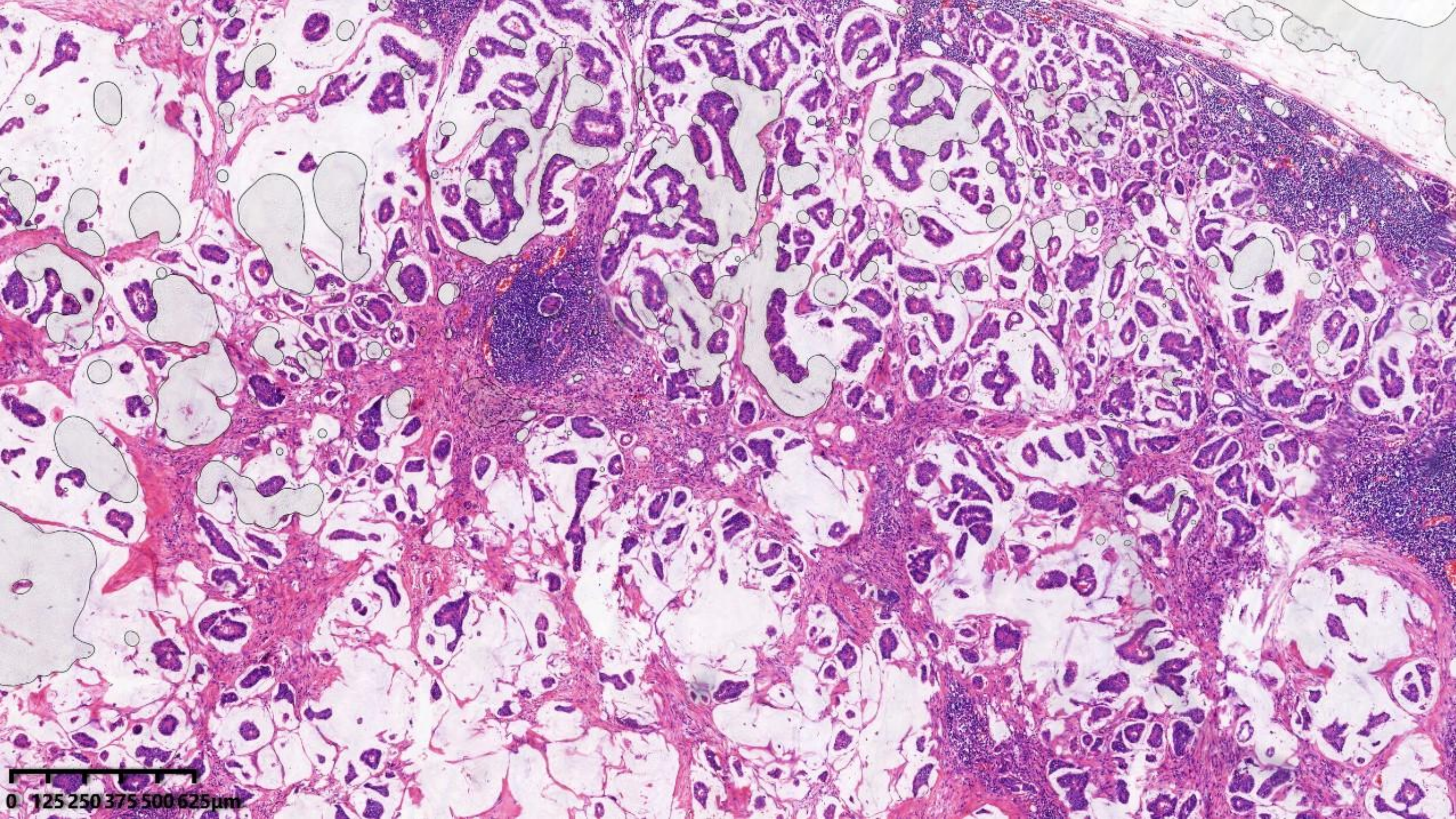
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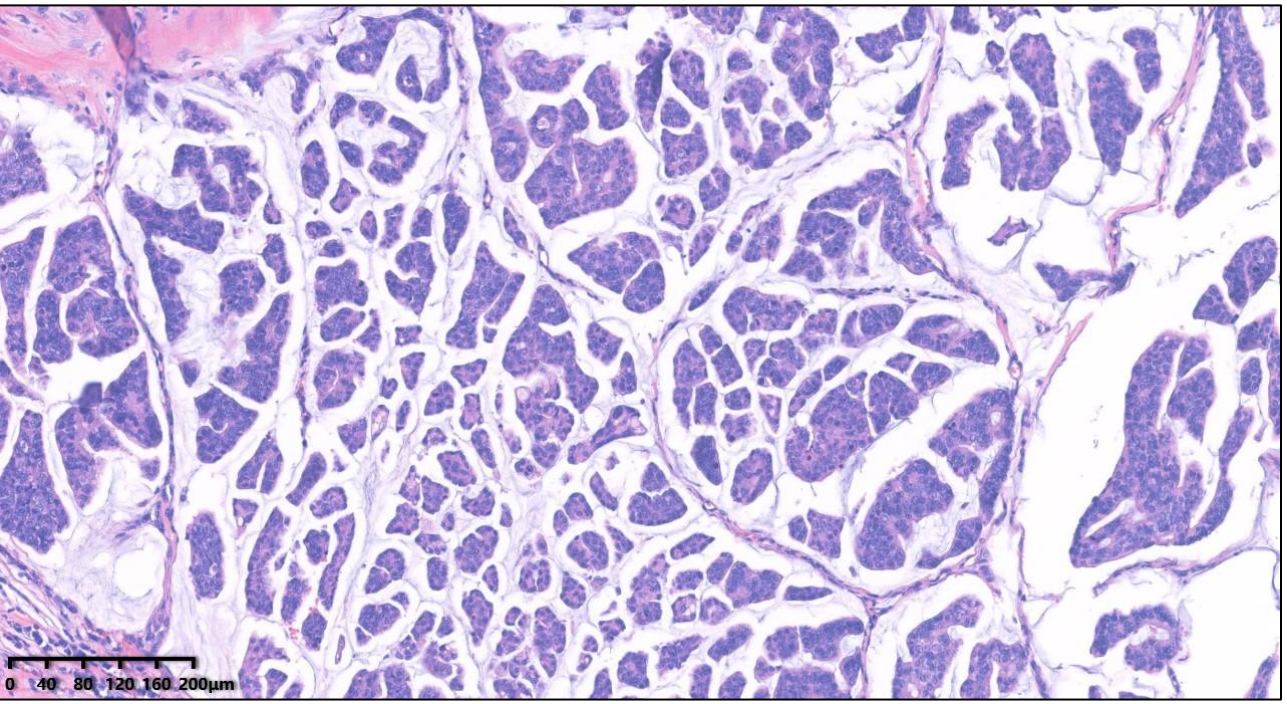
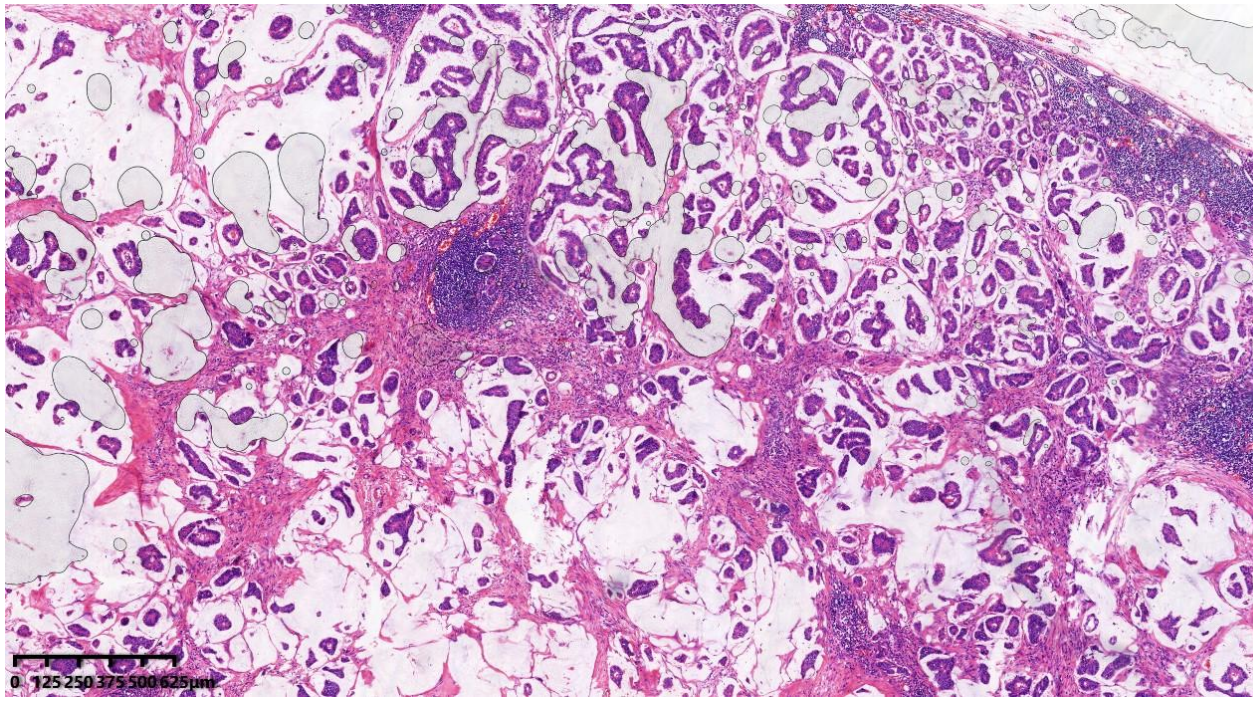
Challenges in studying the micropapillary subtype of mucinous carcinoma

- Definition of "micropapillae“
- Quantitative threshold of the proportion of micropapillae for MPMC diagnosis
- Criteria for nuclear and histologic grading Defining immunophenotypic criteria (ER/PR, HER2, Ki-67)
- Significance of peripheral conventional invasive micropapillary component
- ……

- Study conclusions are inconsistent.
- The so-called micropapillary subtype of mucinous carcinoma reported in the literature actually represents a heterogeneous group of tumors.
- Some cases are more similar to mucinous carcinoma, while others resemble micropapillary carcinoma.





- **Evaluate extent** of micropapillary structures
  Assess nuclear atypia carefully
- **Evaluate i**f morphology in mucinous background is consistent with invasive micropapillary carcinoma.
- **Consider tumor heterogeneity** for comprehensive evaluation
  Include immunophenotypic profile in assessment

- Typical invasive micropapillary carcinoma adjacent / similar morphology in mucinous background→ **Invasive Micropapillary Carcinoma**
- Meets mucinous carcinoma criteria except for focal micropapillary structures→ **Mucinous Carcinoma**
- Borderline features, not classifiable→ **Mucinous Carcinoma with Micropapillary Features** (comment)

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NCCN Guidelines Version 3.2023
Invasive Breast Cancer

NCCN Guidelines Index
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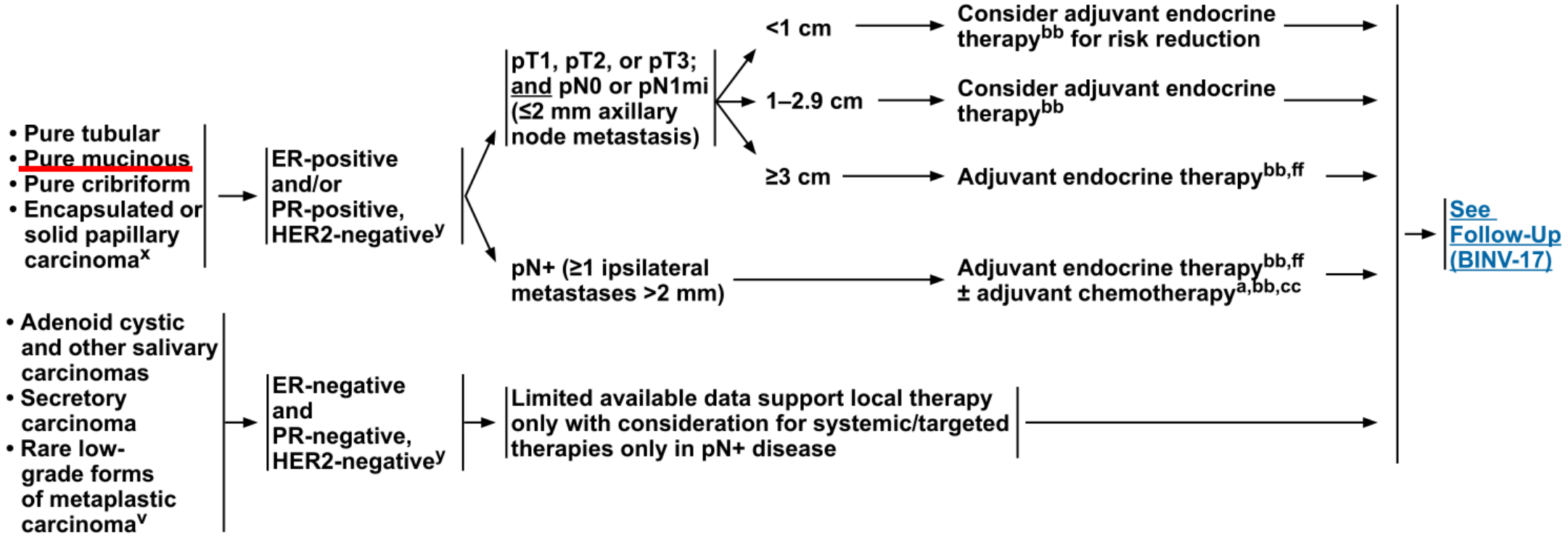
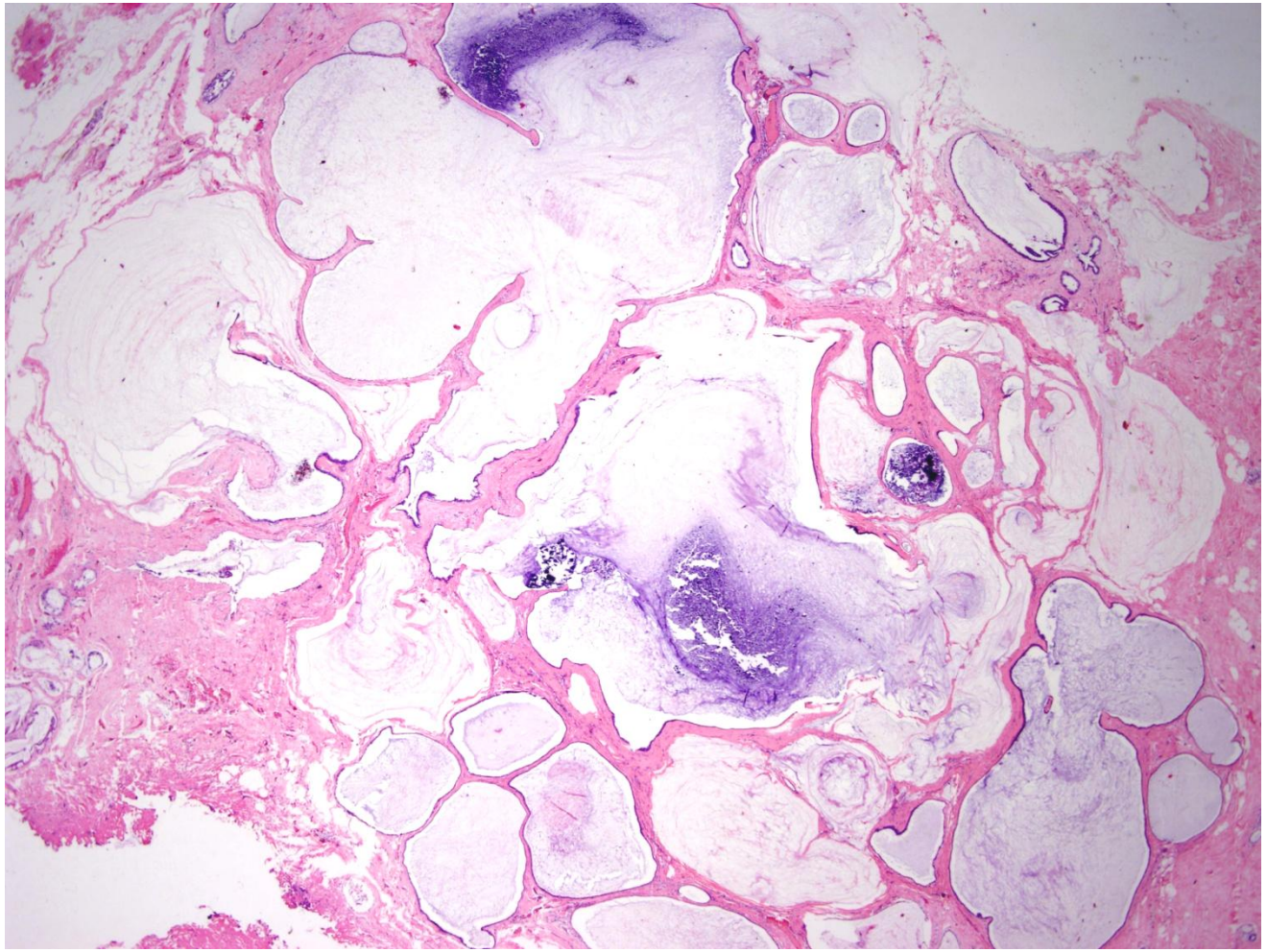
Discussion

SYSTEMIC ADJUVANT TREATMENT: FAVORABLE HISTOLOGIES[r,w]



Verify the accuracy of the mucinous carcinoma diagnosis: Is it a pure mucinous carcinoma? Is there high nuclear grade? Is HER2 positive or ER negative? Is Ki-67 elevated? Are there high-grade DCIS lesions at the tumor periphery? Are there prominent micropapillary structures? Is lymphovascular invasion present?→→Apply stringent diagnostic standards when any of these features are present.

Mucocele-like lesions



Clinical Presentation:

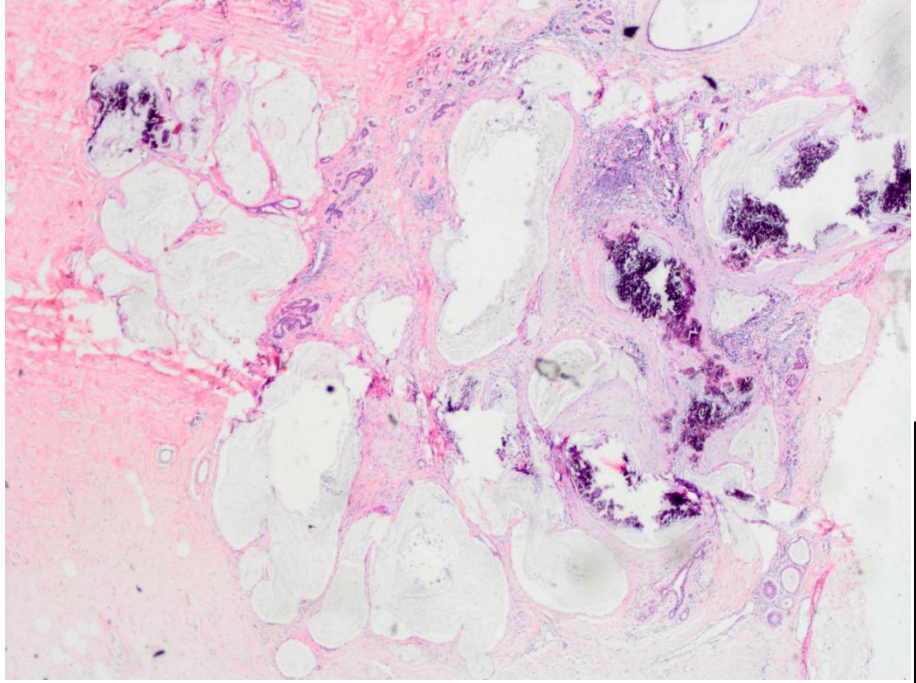
• Palpable mass, imaging abnormality, or incidental finding.

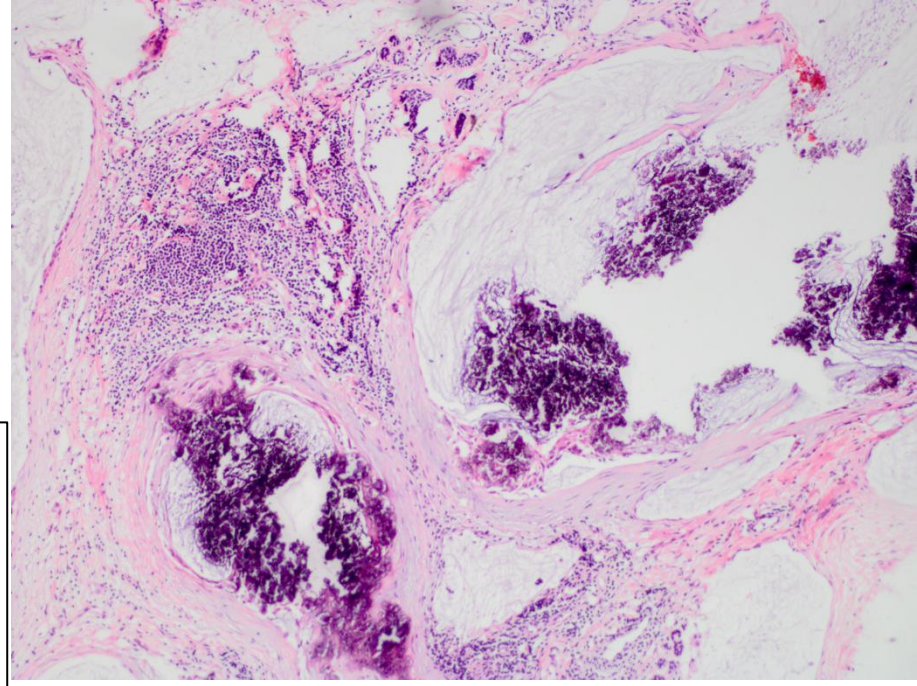
Gross Examination:

• Gelatinous cut surface.

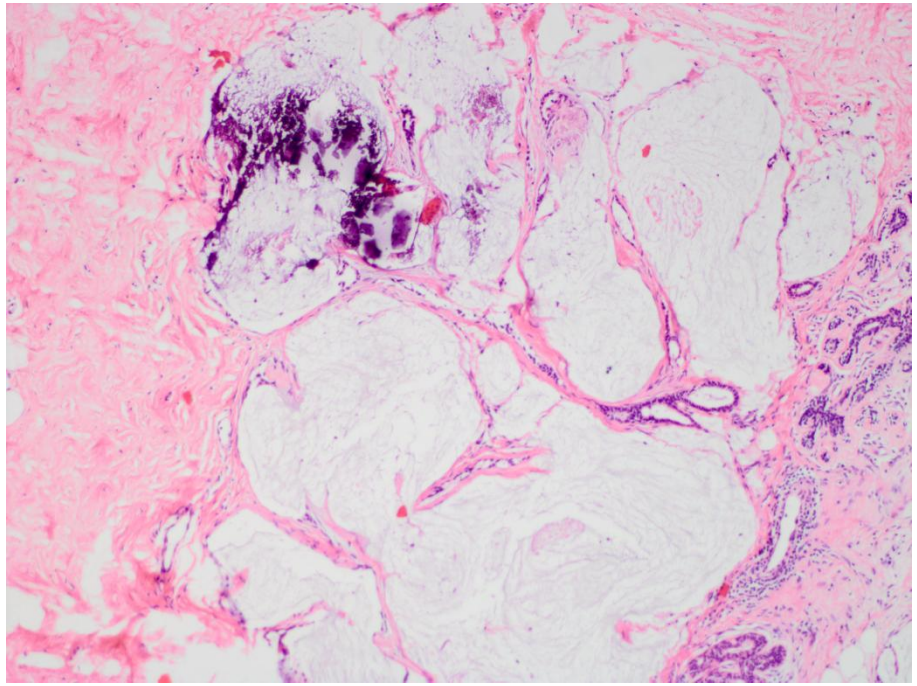
Microscopic Features:

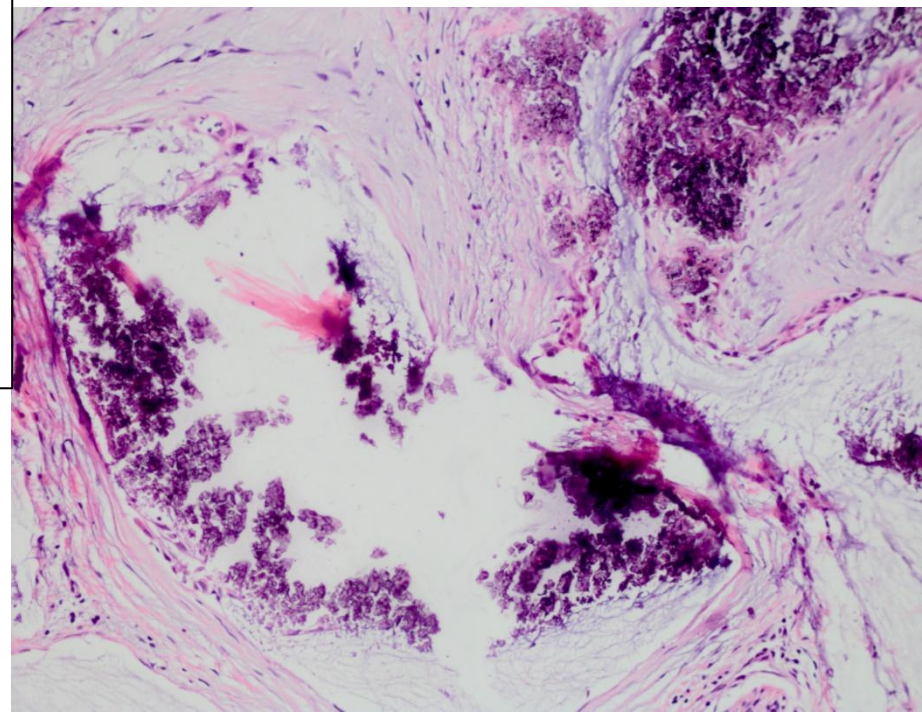
- Dilated mucin-filled ducts/cysts;
- stromal mucin extravasation.
- Epithelial spectrum: benign, atypical, DCIS, or associated invasive carcinoma.

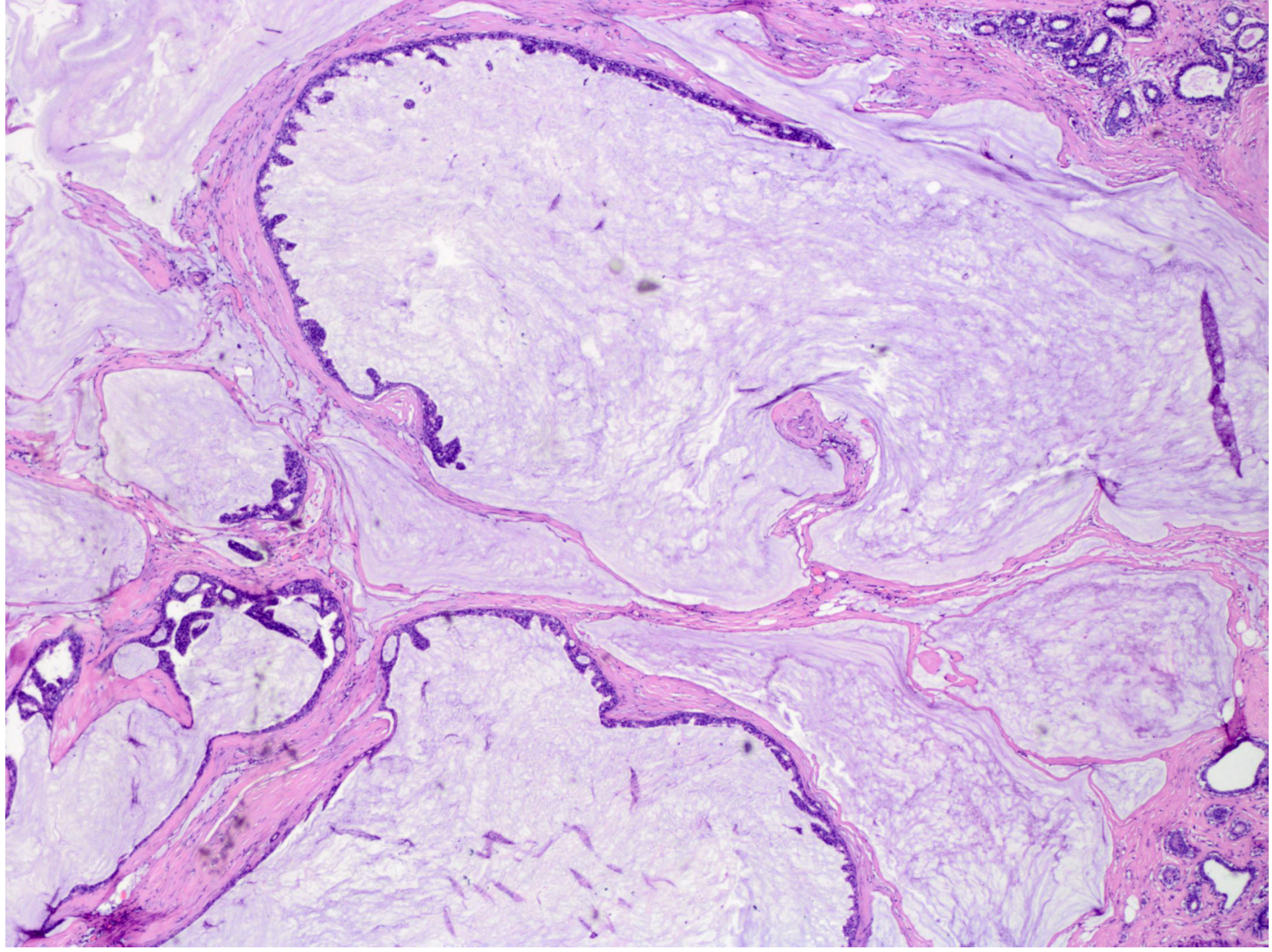


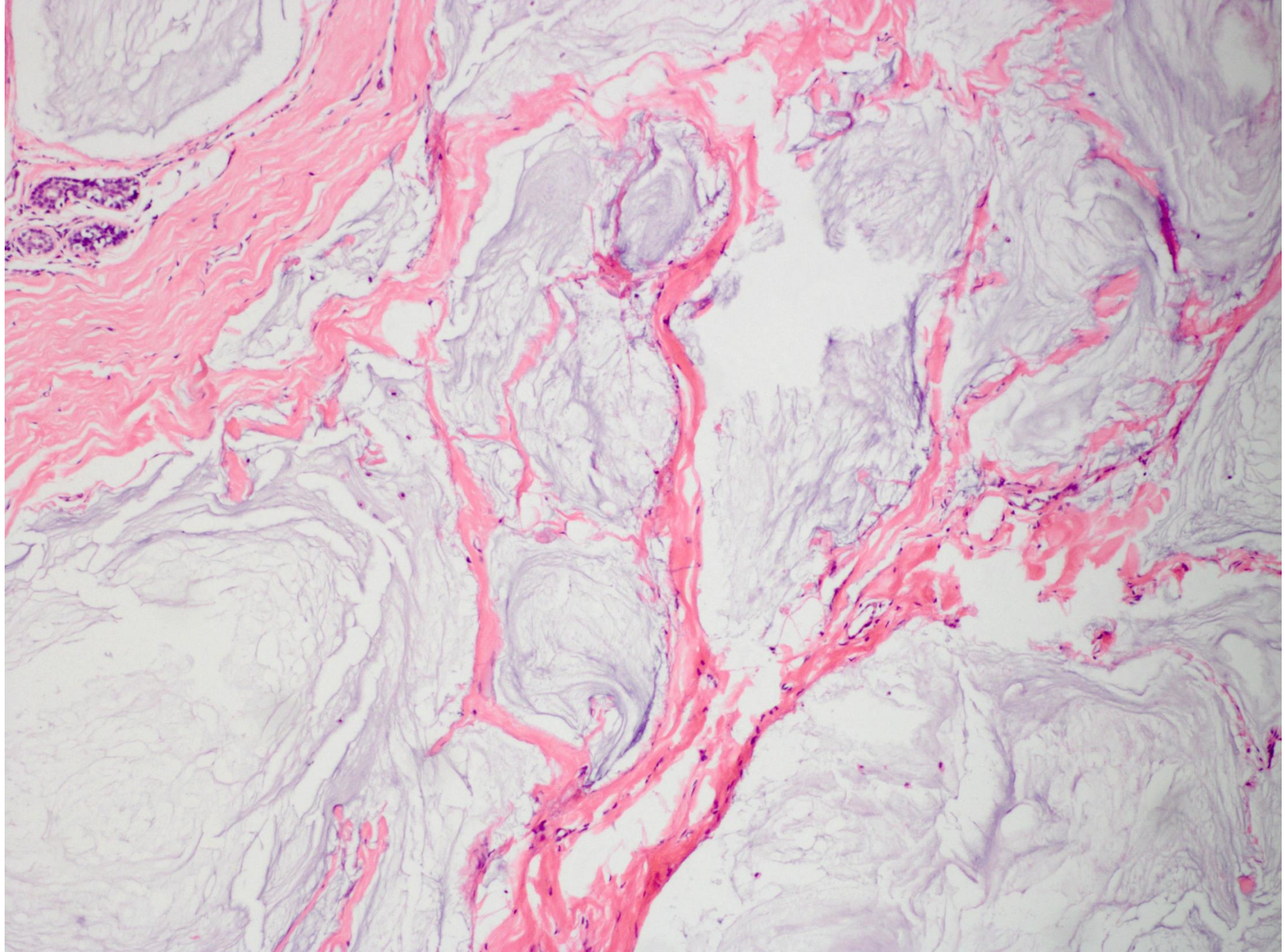


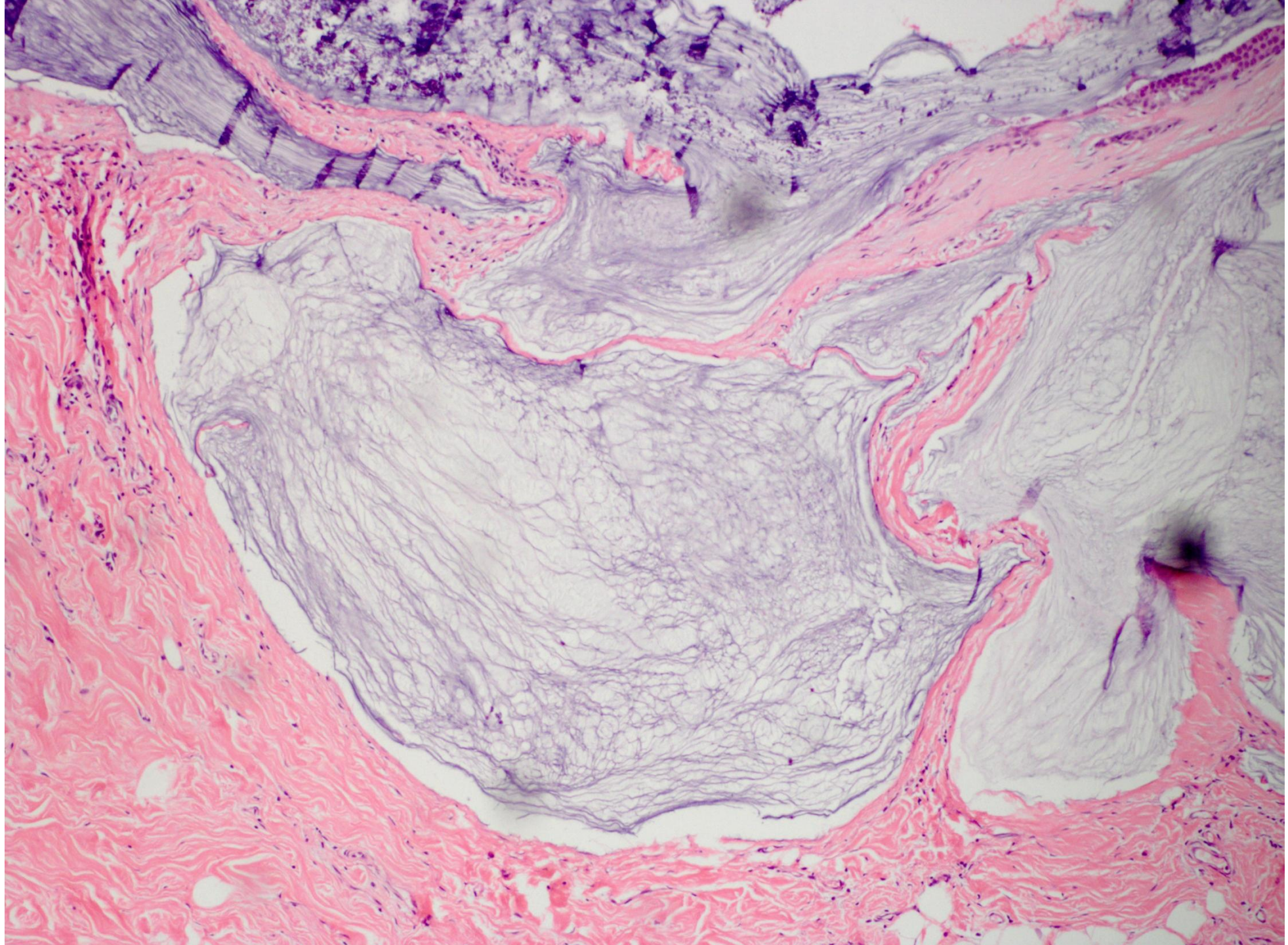
- The dilated cystic spaces are lined by flat to columnar epithelium.
- Mucin may extravasate into the stroma, forming mucin pools.
- Large, granular calcifications may be observed within the mucin.

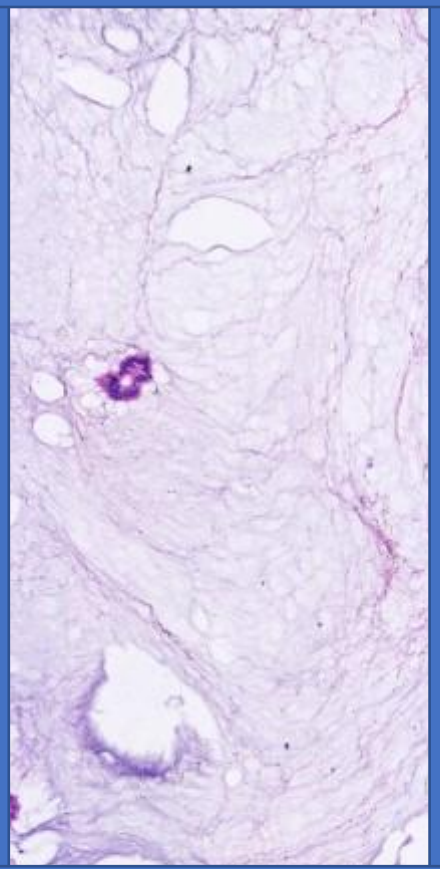


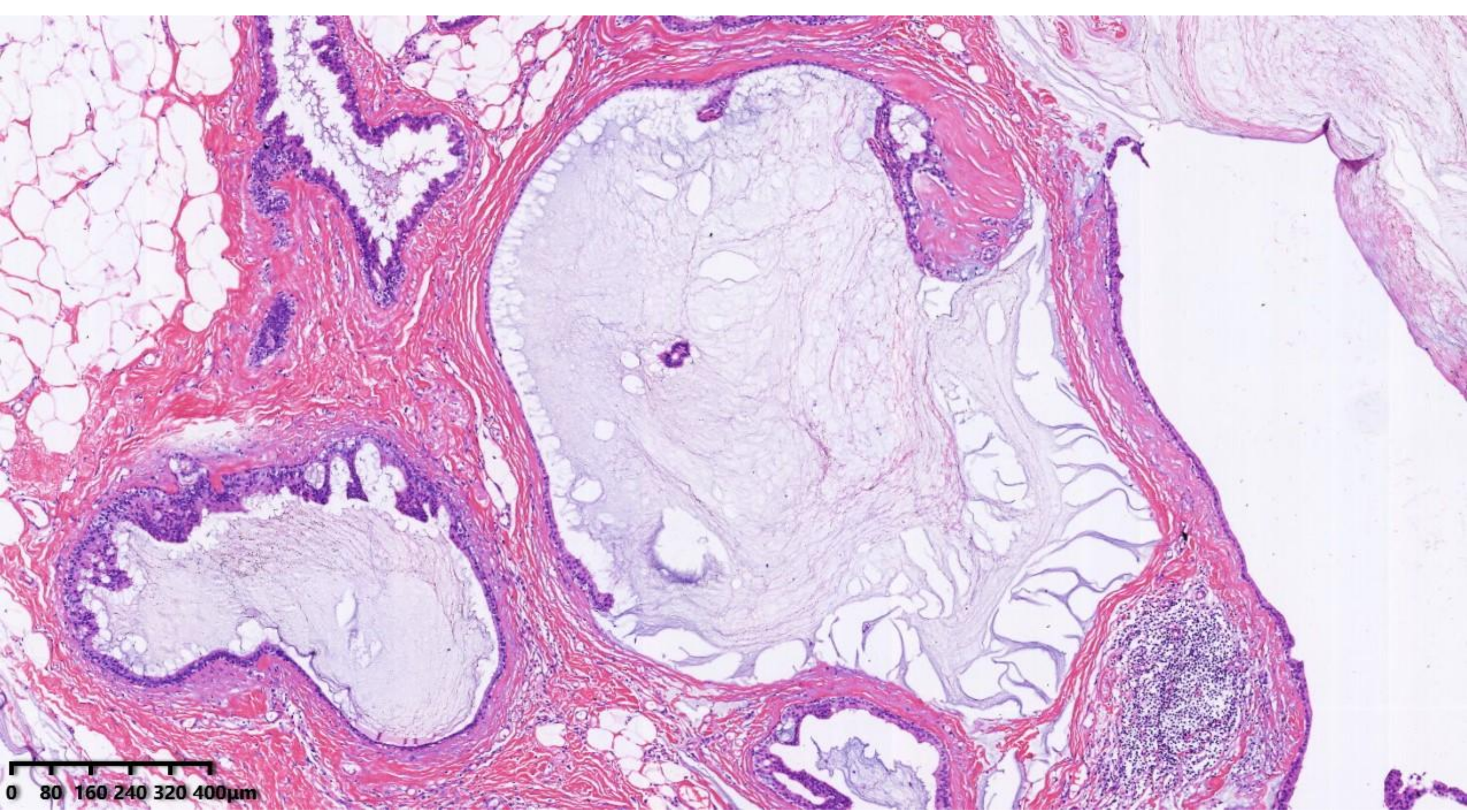








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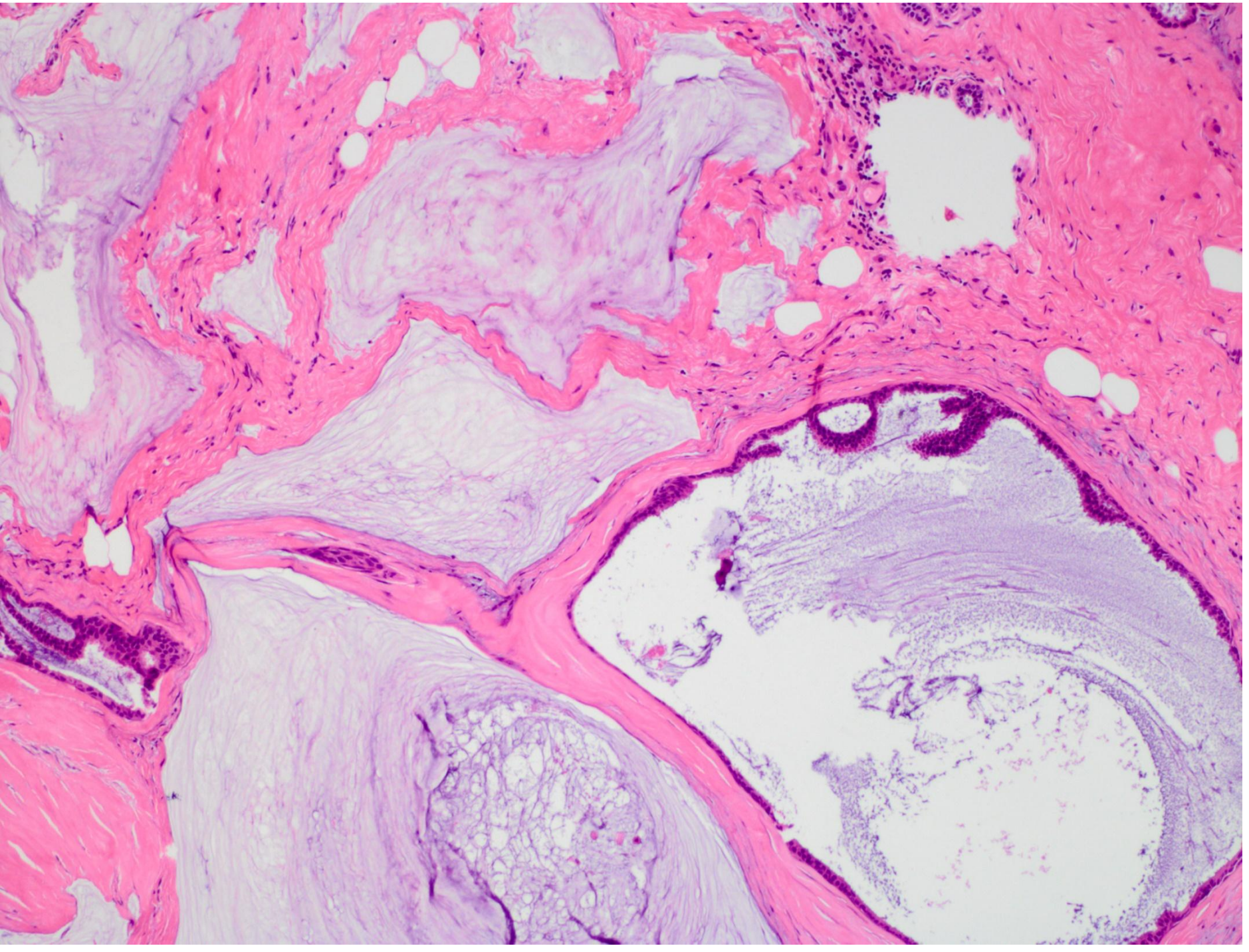
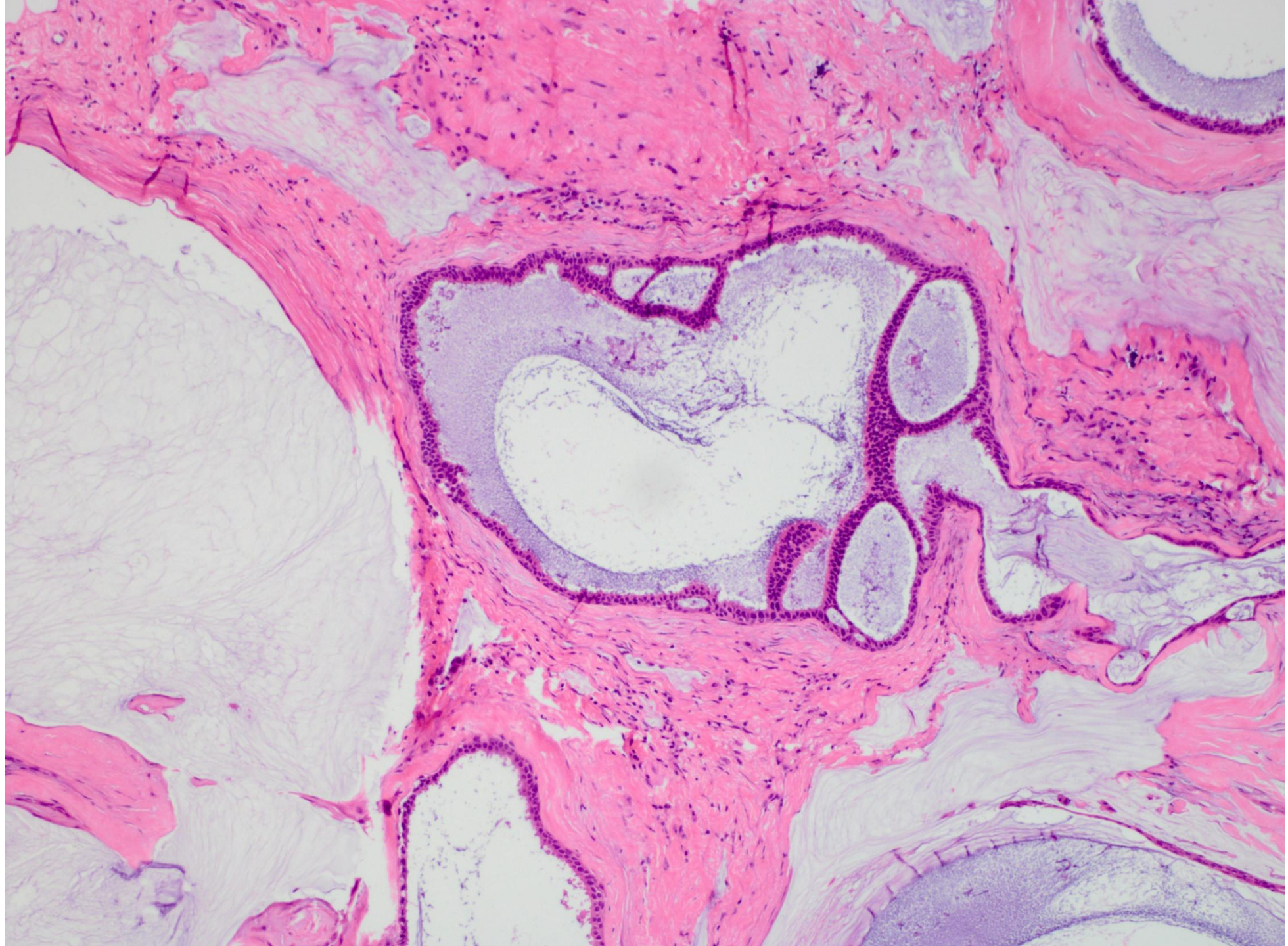
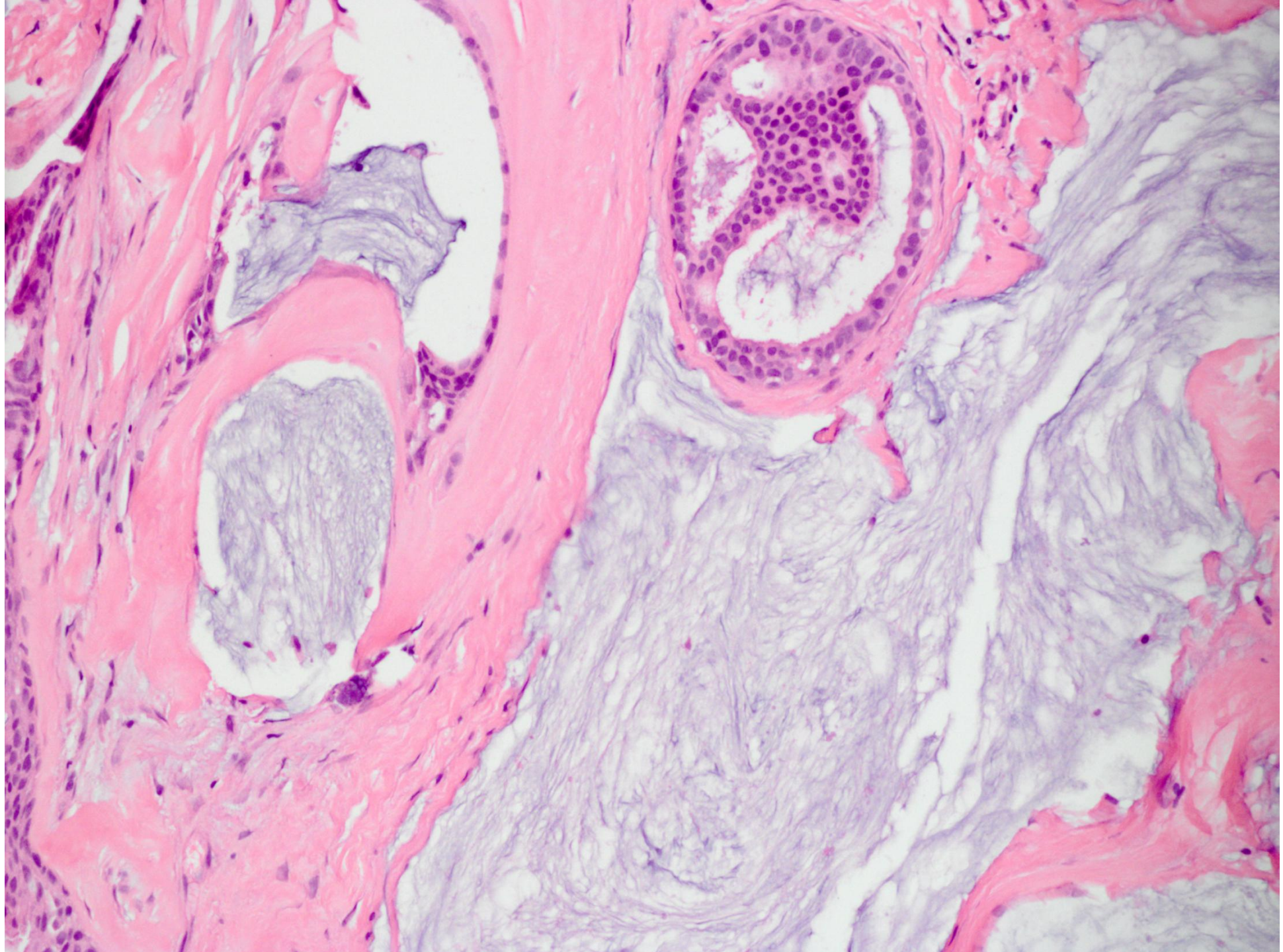
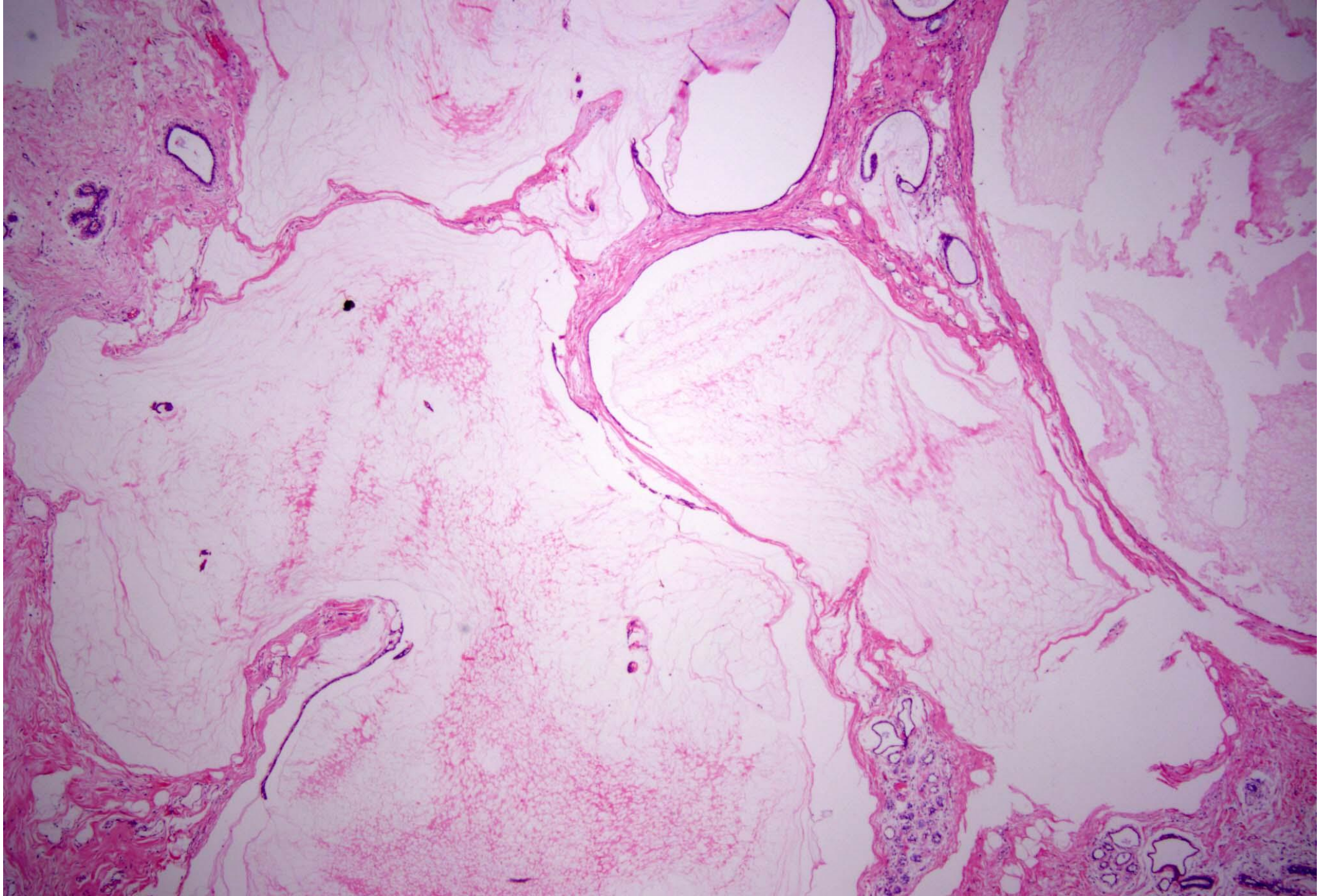
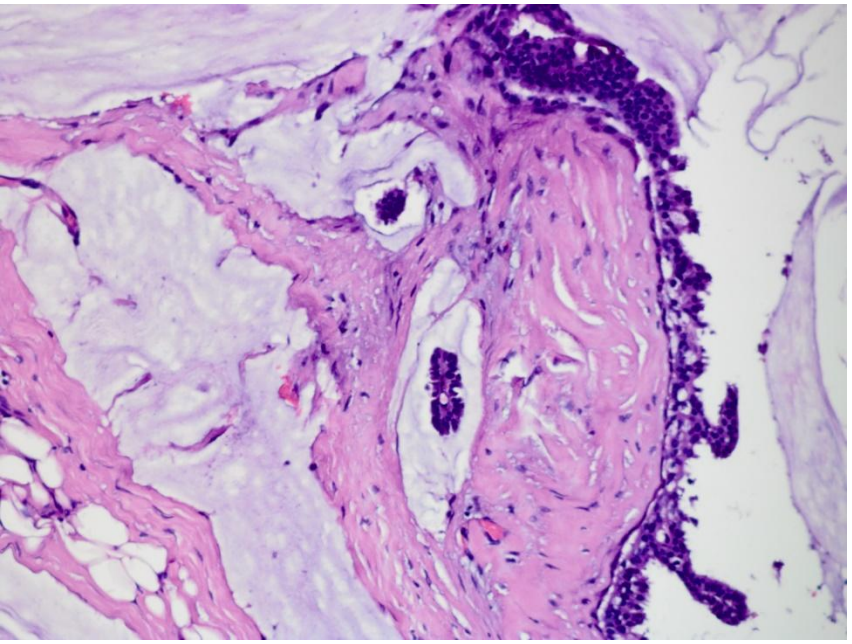
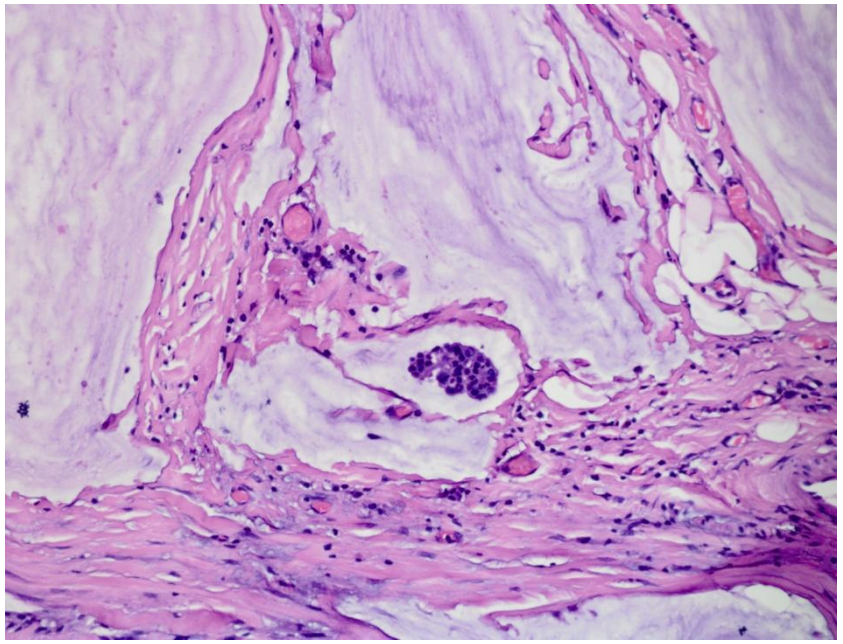
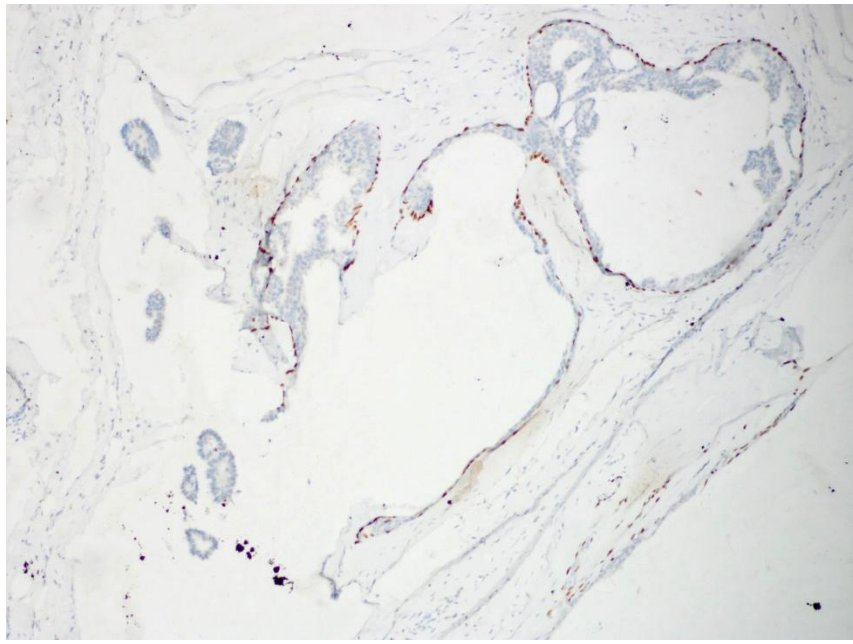


- In MLL, the ductal lumina are markedly dilated, making it challenging to apply standard dimensional criteria.
- A diagnosis of DCIS should be made only when two or more ducts are entirely involved by cells or structures meeting the criteria for DCIS.

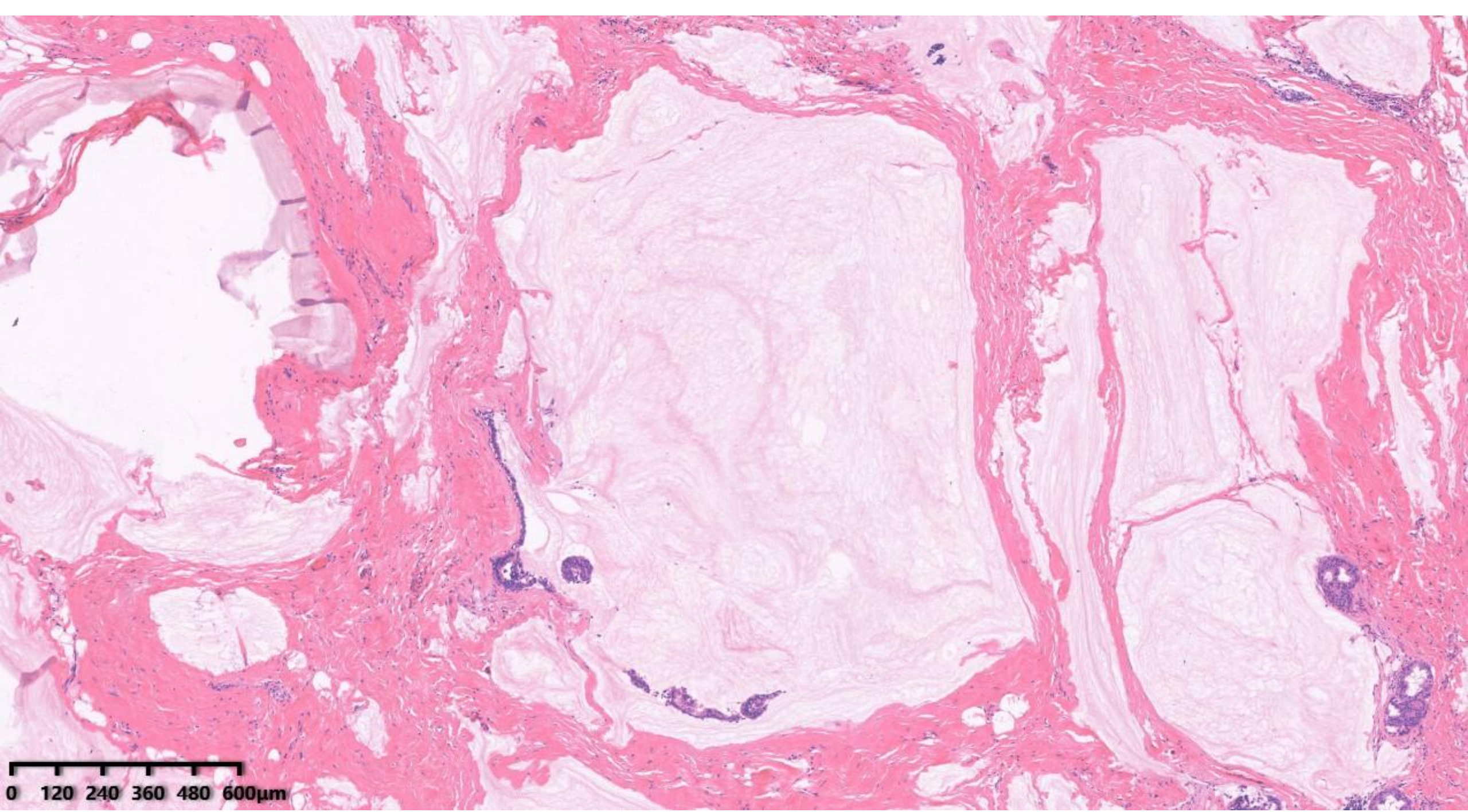






- **The presence of myoepithelial cells indicates a benign lesion.**
- **Invasive carcinoma lacks myoepithelial cells; however, the absence of myoepithelial cells does not necessarily indicate invasion.**
  - **Detached epithelial cells from ADH or DCIS may also lack myoepithelial cells.**
  - **Epithelial displacement can also result in cells lacking myoepithelial cells.**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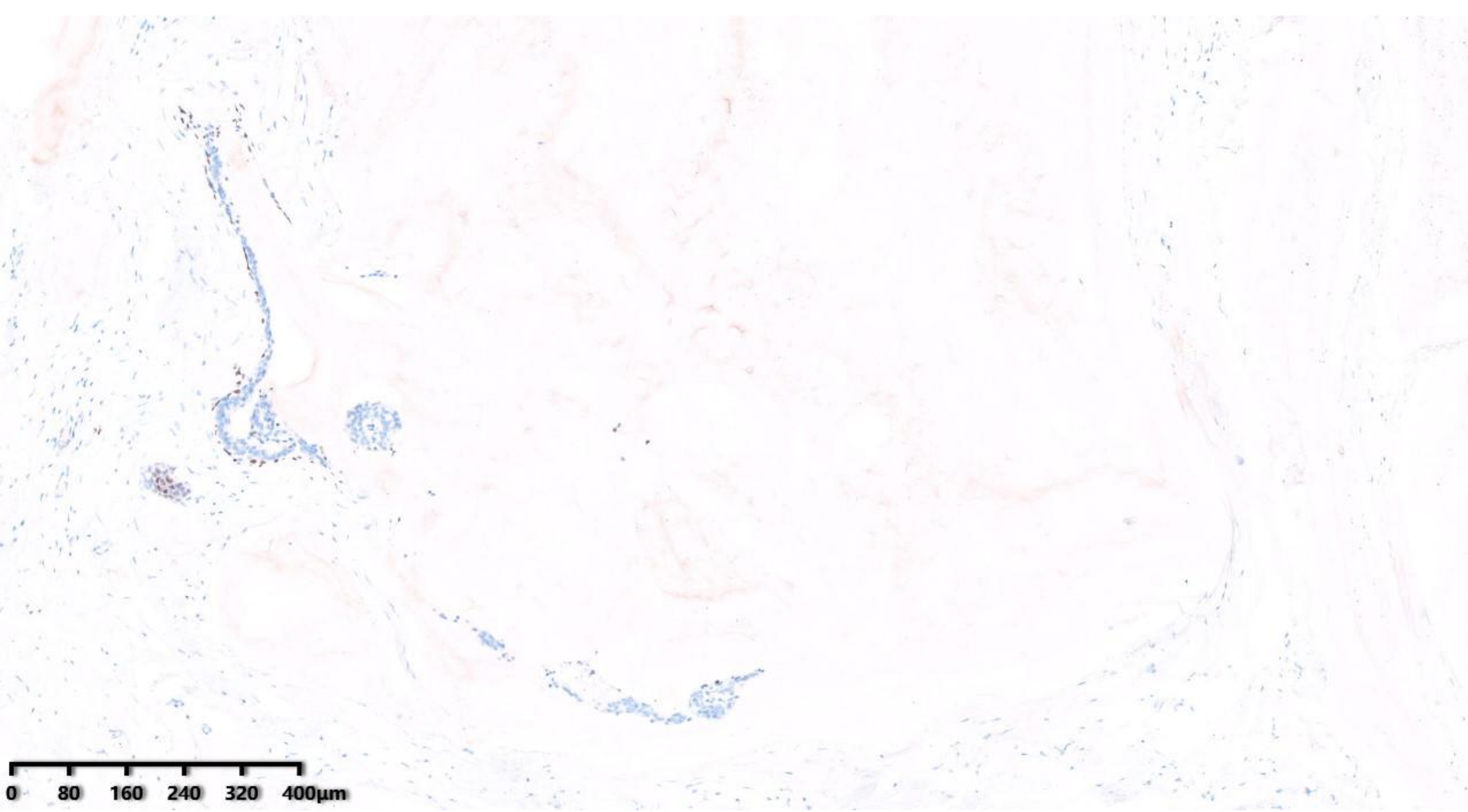
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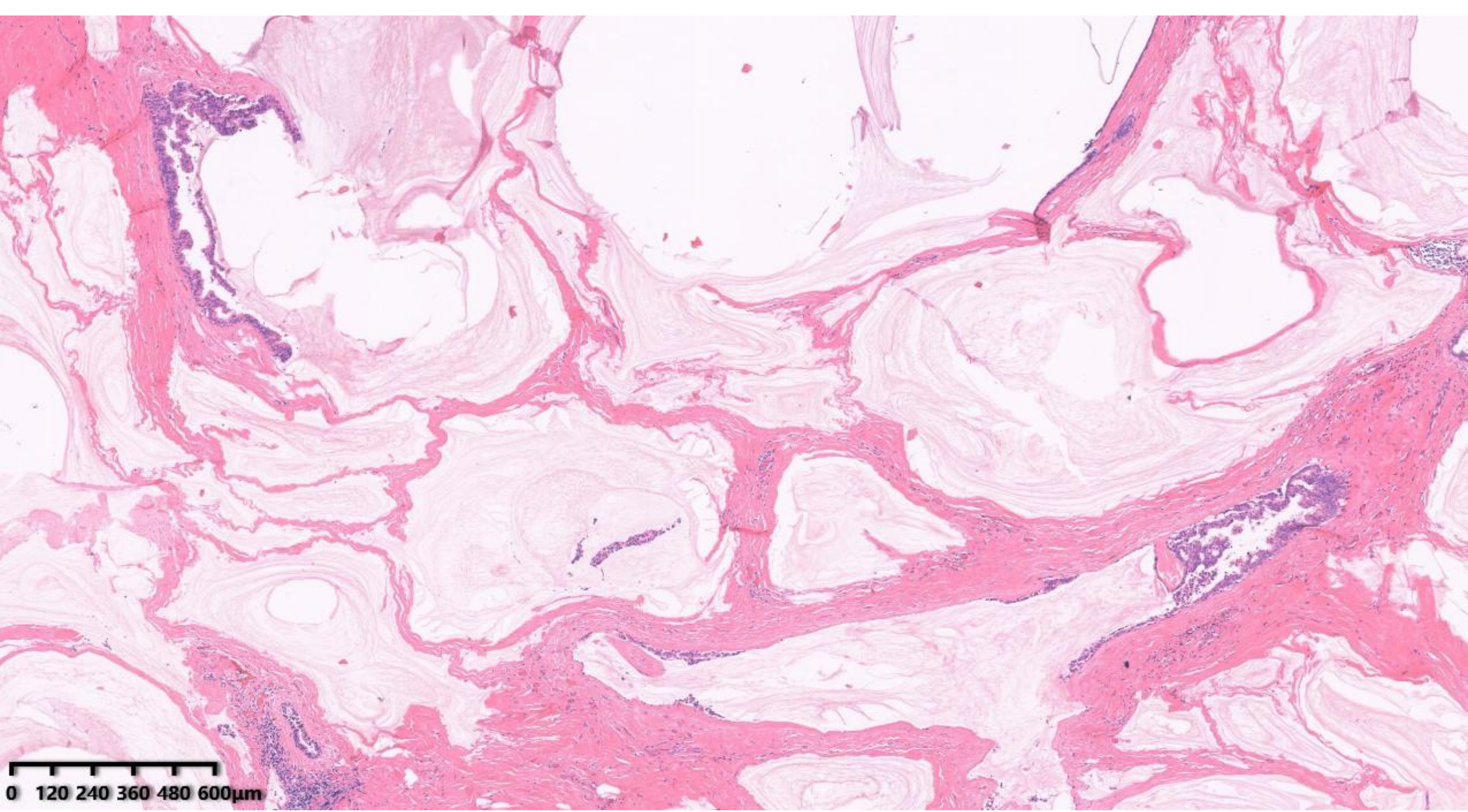
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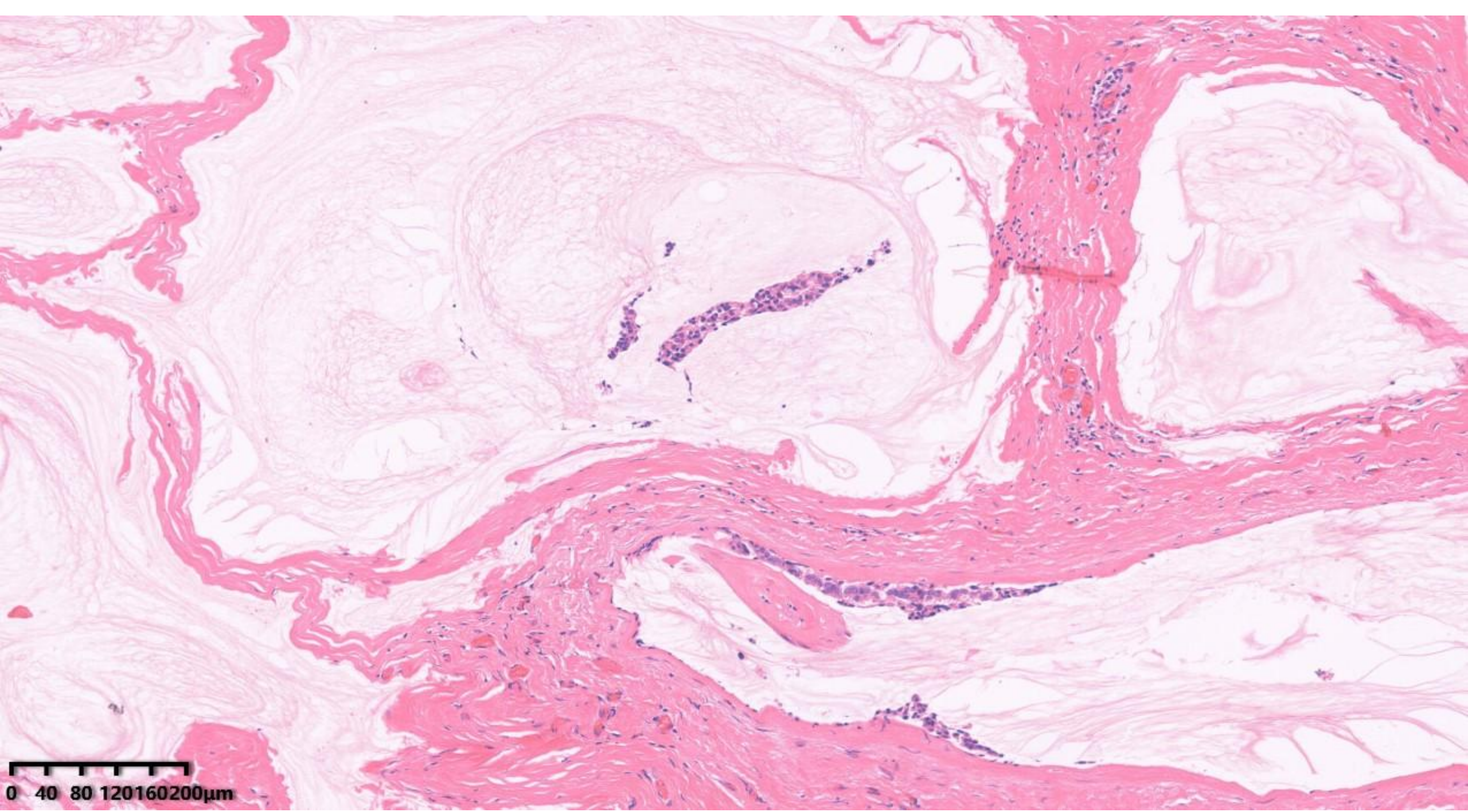
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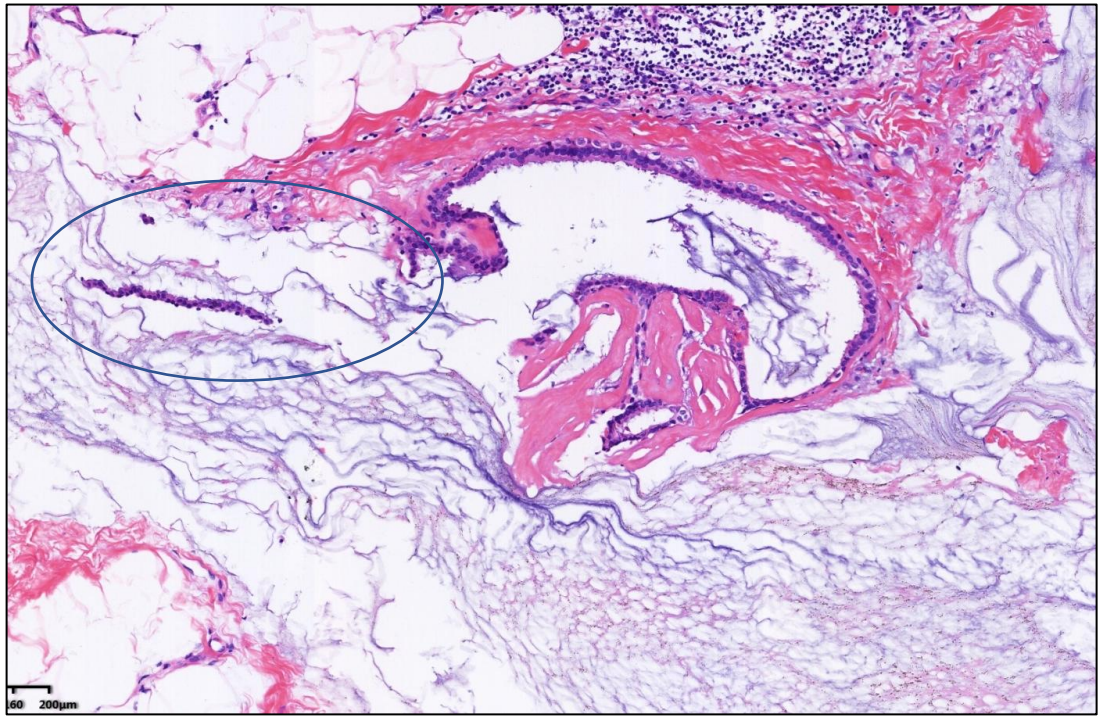
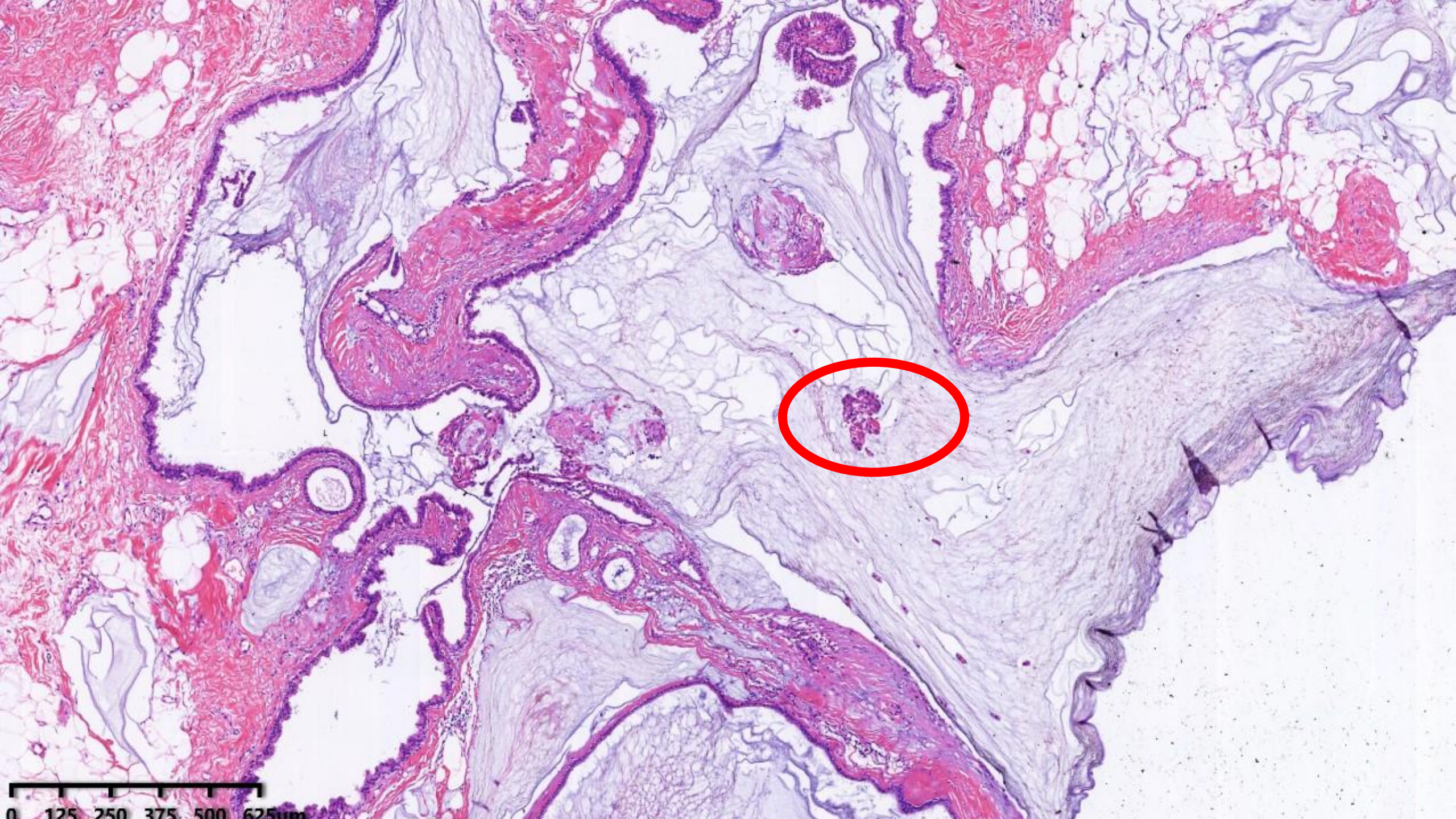
Diagnostic strategy for scattered epithelial components in MLL



- Ensure diagnosis is based on adequate sampling.
- Periphery myoepithelial cells indicate a benign lesion.
- Scattered epithelial fragments are continuous with the cyst wall—detached epithelium fragments
- Interpret epithelial cords or strands with caution.
- Scattered cells in mucin are unlikely to represent malignancy if no ADH/DCIS is found.
- Exclude epithelial displacement in prior biopsy cases.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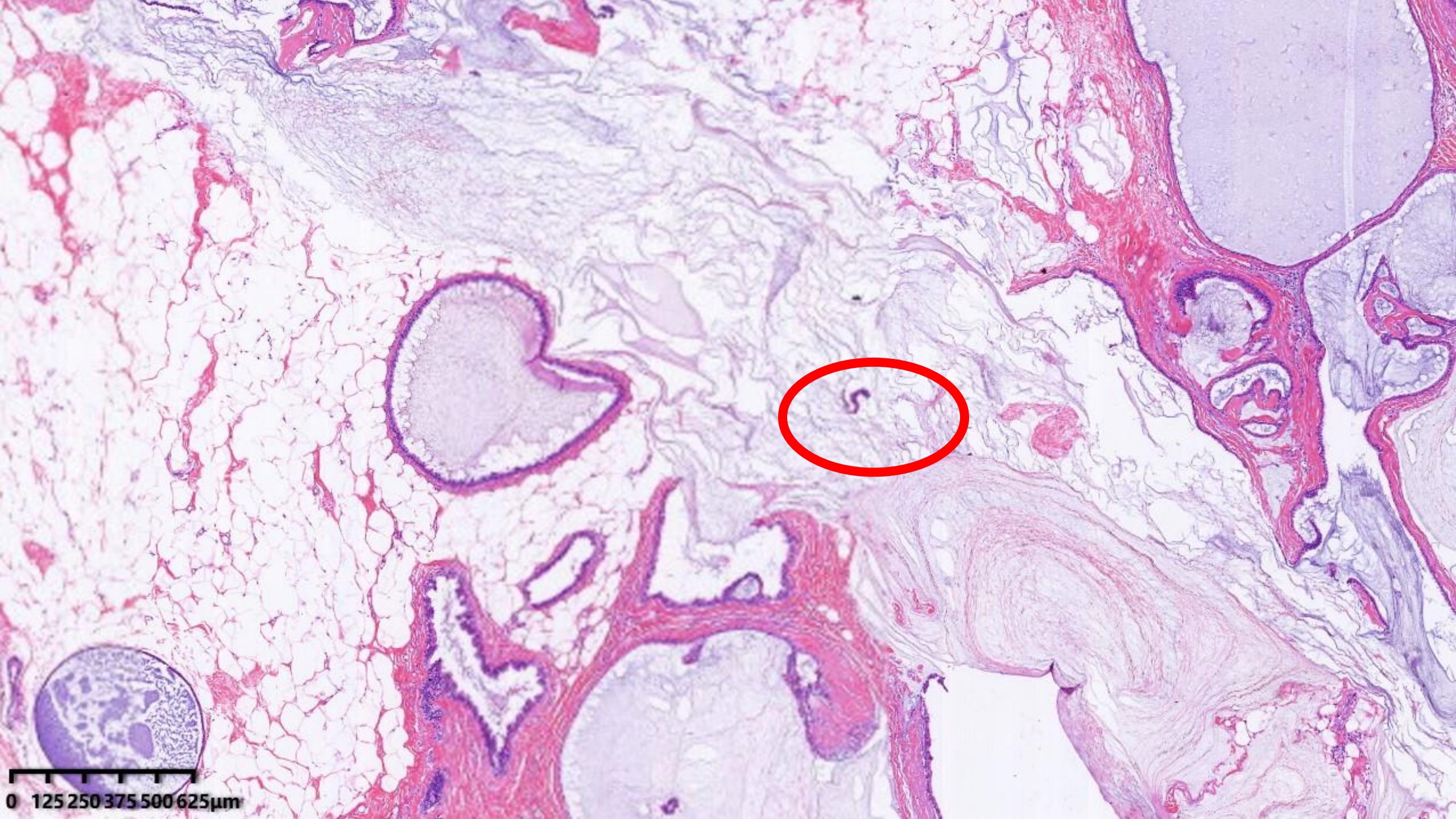
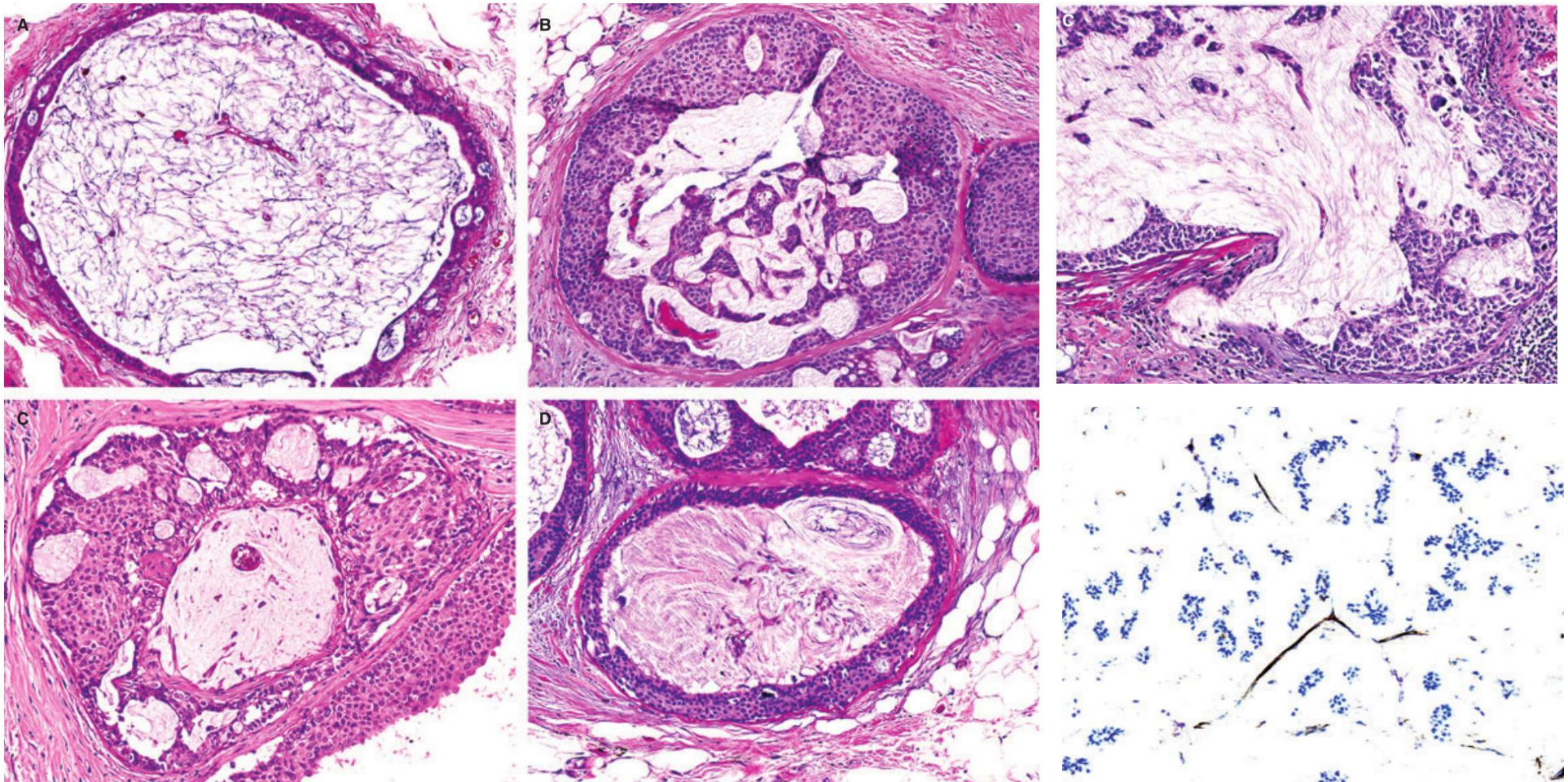

0 125 250 375 500 625µm

Neovascularization in mucinous ductal carcinoma *in situ* suggests an alternative pathway for invasion

S A Gadre, G H Perkins,[1] A A Sahin, N Sneige, M T Deavers & L P Middleton

Departments of Pathology and [1]Radiation Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA

Histopathology 2008;53(5):545-53



- **Blood vessels can be present within the mucin of mucinous carcinoma and mucinous DCIS; however, extracellular mucin in MLL does not contain blood vessels.**
- **The presence or absence of blood vessels within mucin pools can aid in distinguishing MLL from mucinous carcinoma.**

Mucin Neovascularization as a Diagnostic Aid to Distinguish Mucinous Carcinomas From Mucocele-like Lesions in Breast Core Needle Biopsies

Allison M. Onken, MD, Laura C. Collins, MD,* and Stuart J. Schnitt, MD†‡*

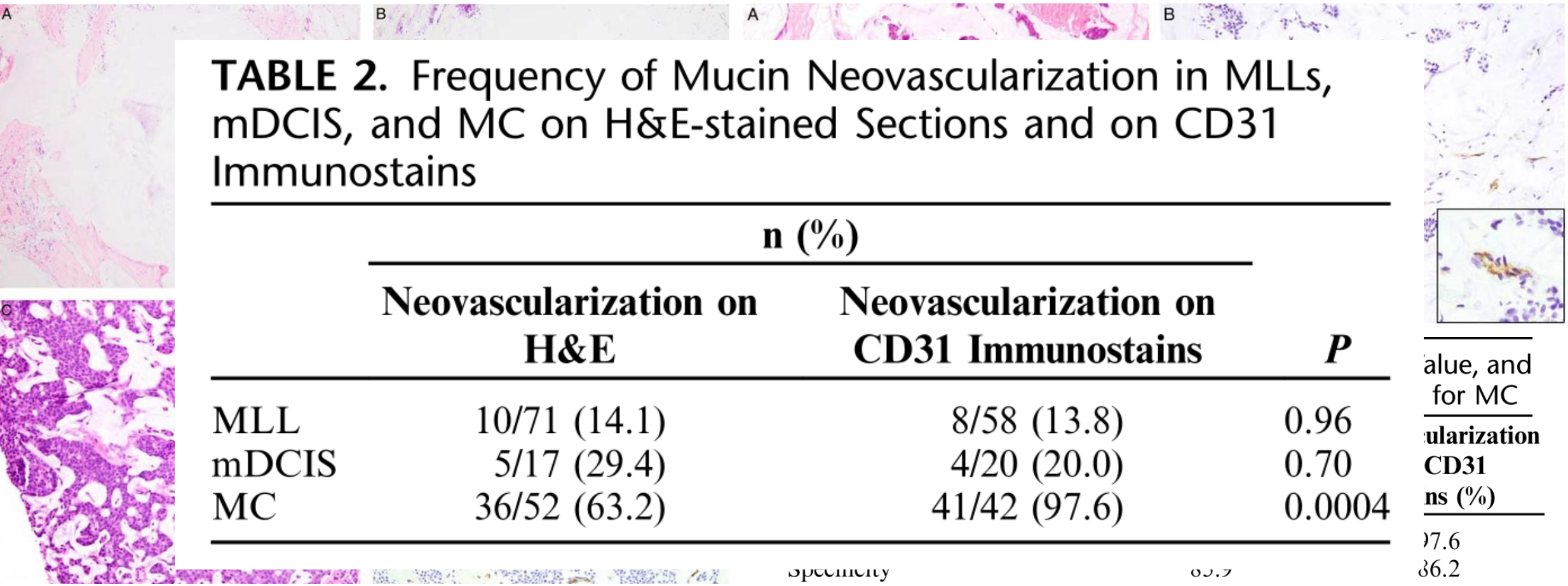


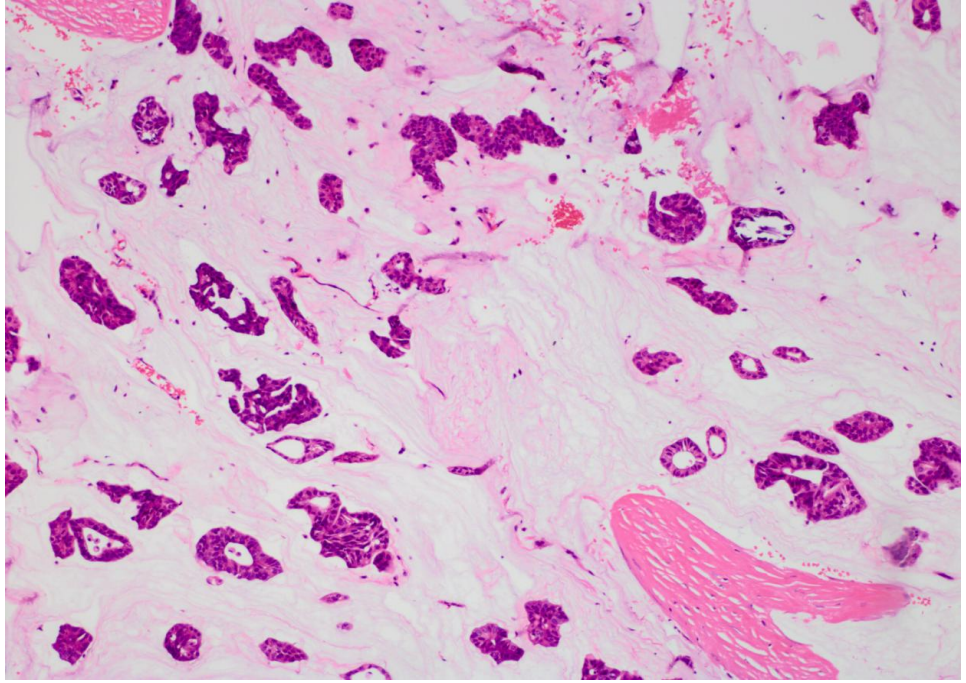
TABLE 2. Frequency of Mucin Neovascularization in MLLs, mDCIS, and MC on H&E-stained Sections and on CD31 Immunostains

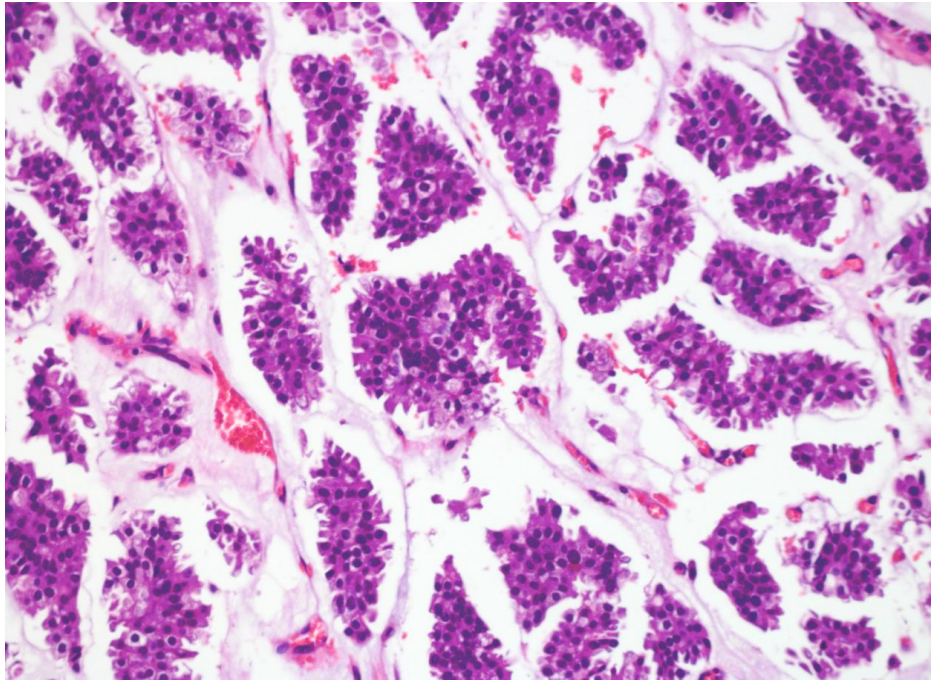
	n (%)		
	Neovascularization on H&E	**Neovascularization on CD31 Immunostains**	***P***
MLL	10/71 (14.1)	8/58 (13.8)	0.96
mDCIS	5/17 (29.4)	4/20 (20.0)	0.70
MC	36/52 (63.2)	41/42 (97.6)	0.0004

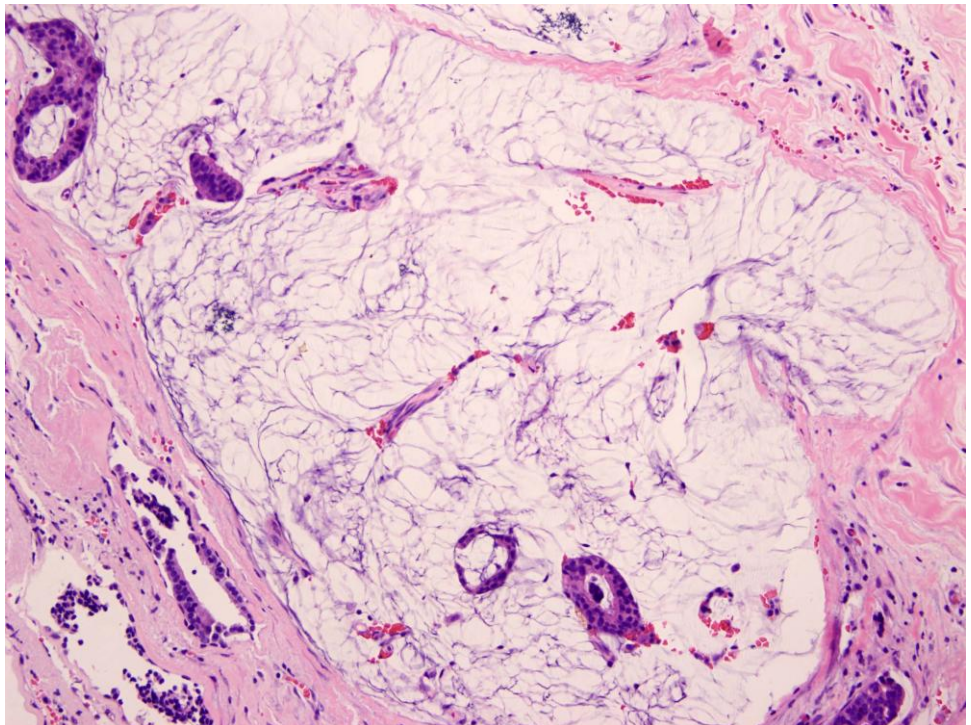
alue, and for MC

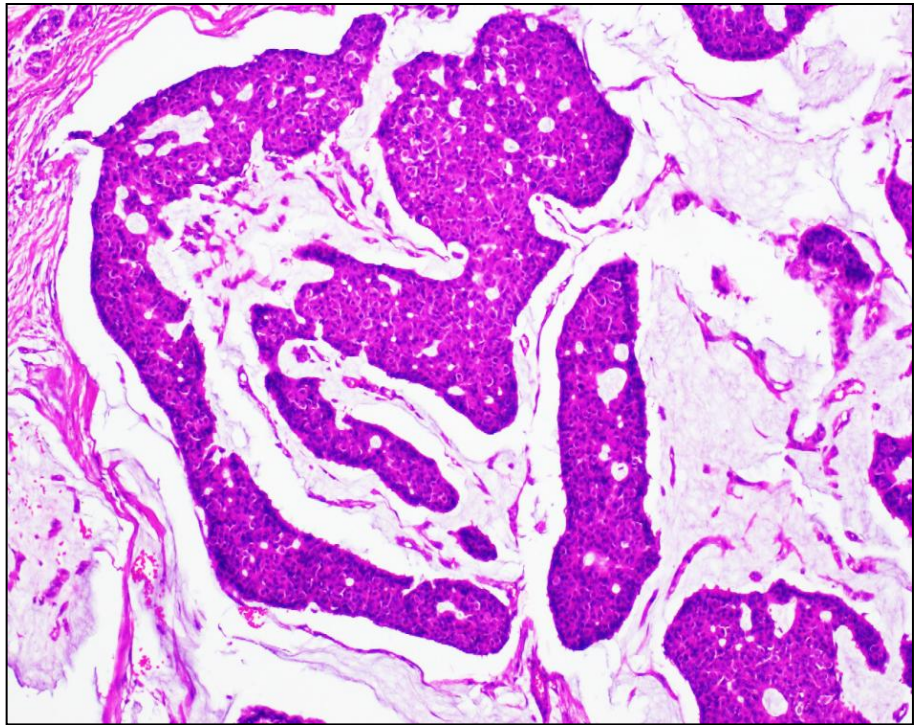
		ulariza-tion CD31 ns (%)
		97.6
Specificity	85.9	86.2
Positive predictive value	78.3	83.7
Negative predictive value	79.2	98.0

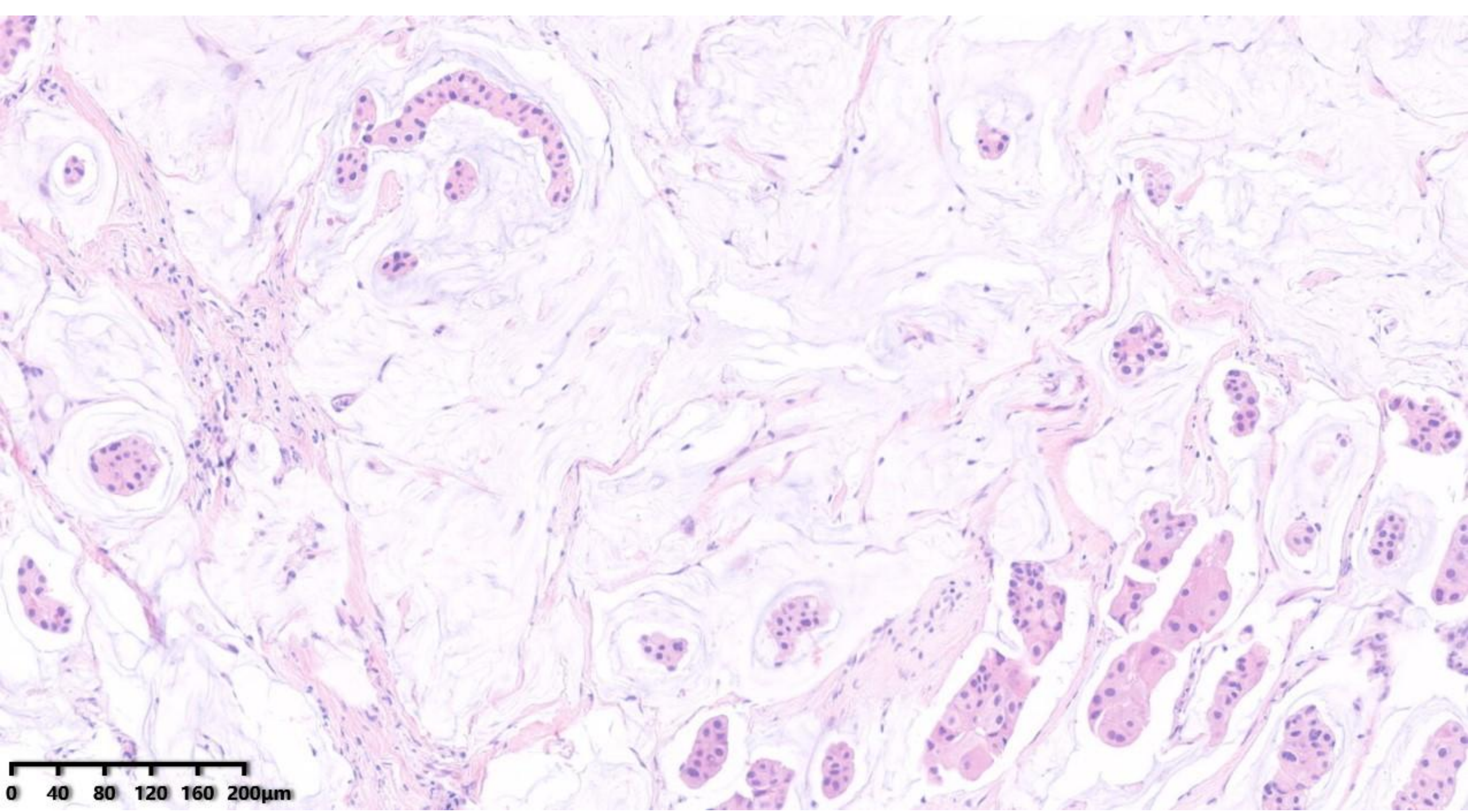
Am J Surg Pathol . 2022;46(5):637-642







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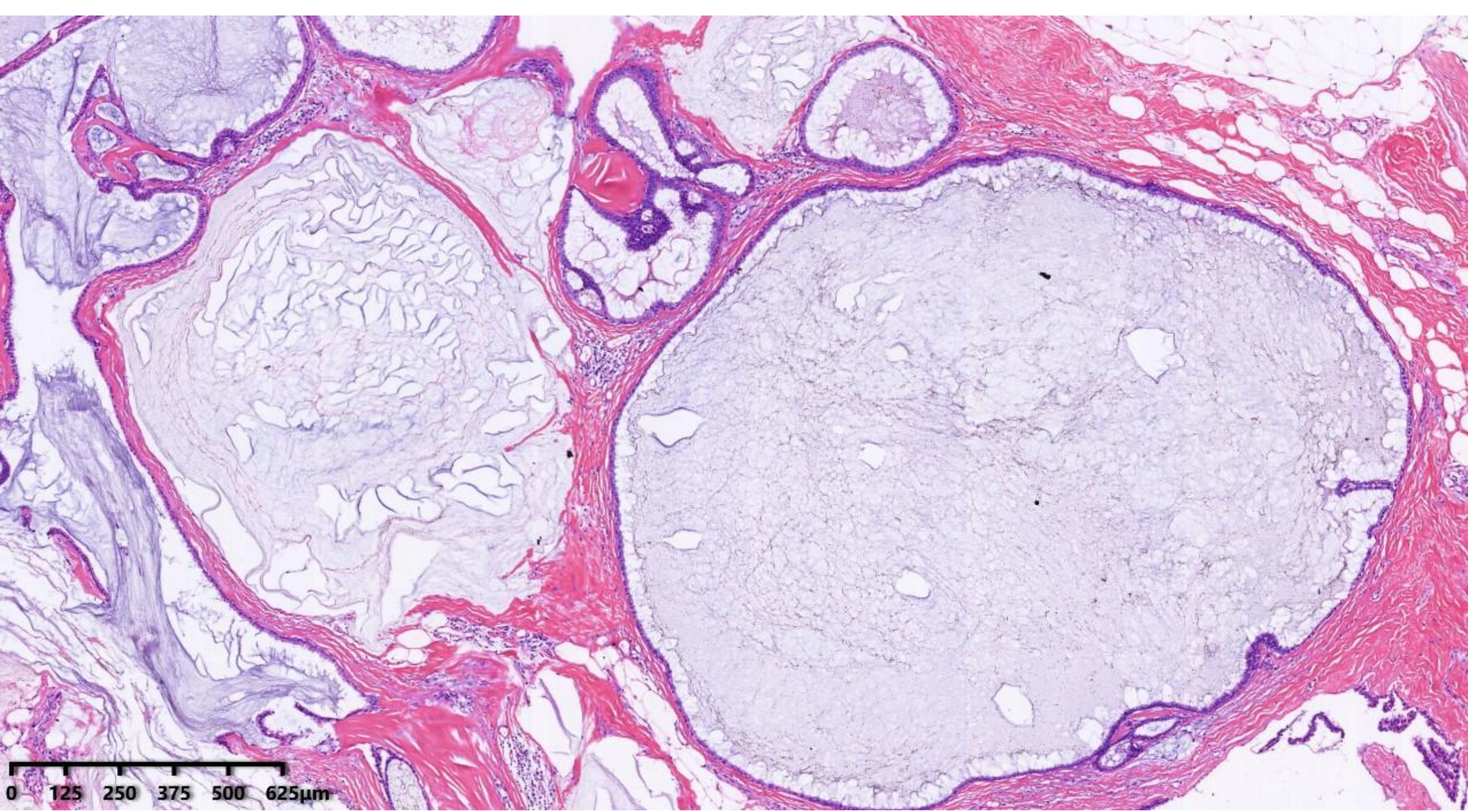
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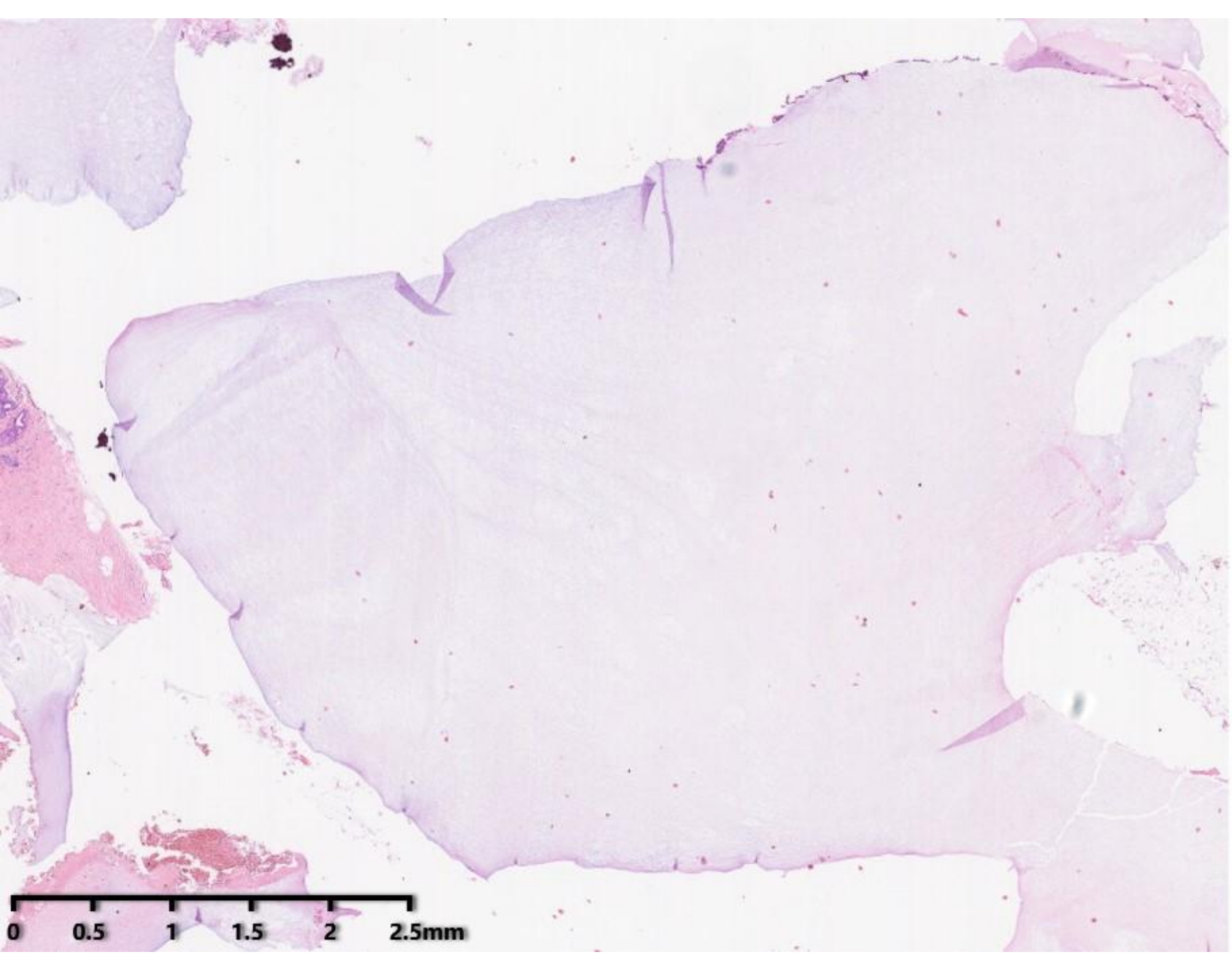
0
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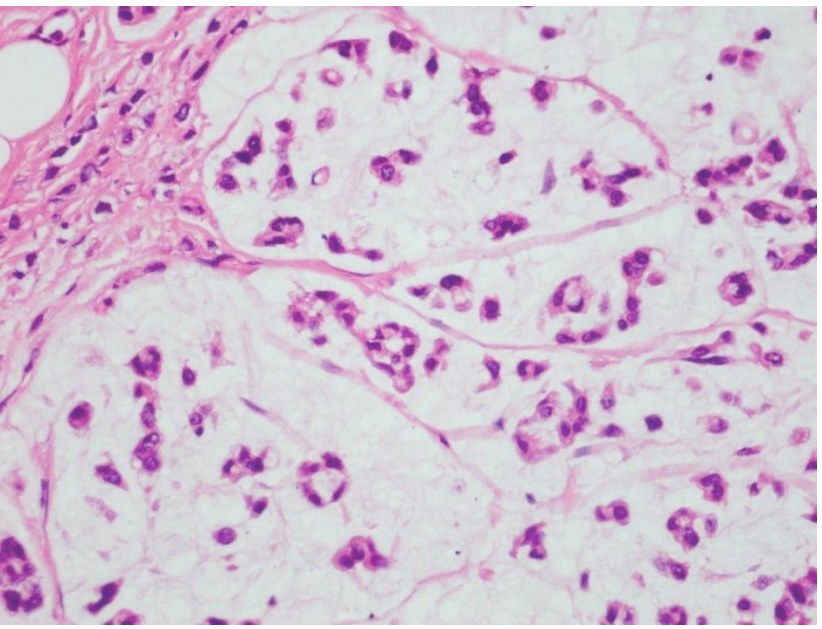
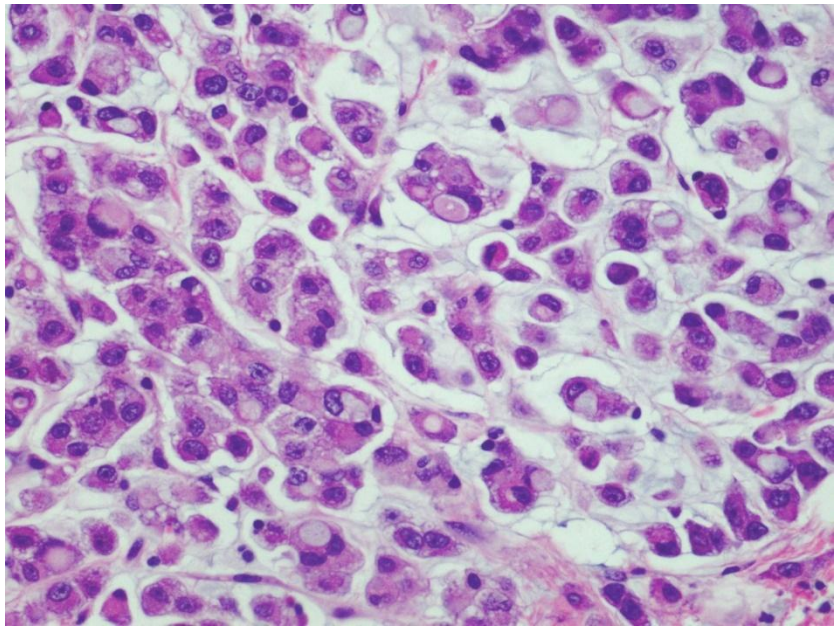
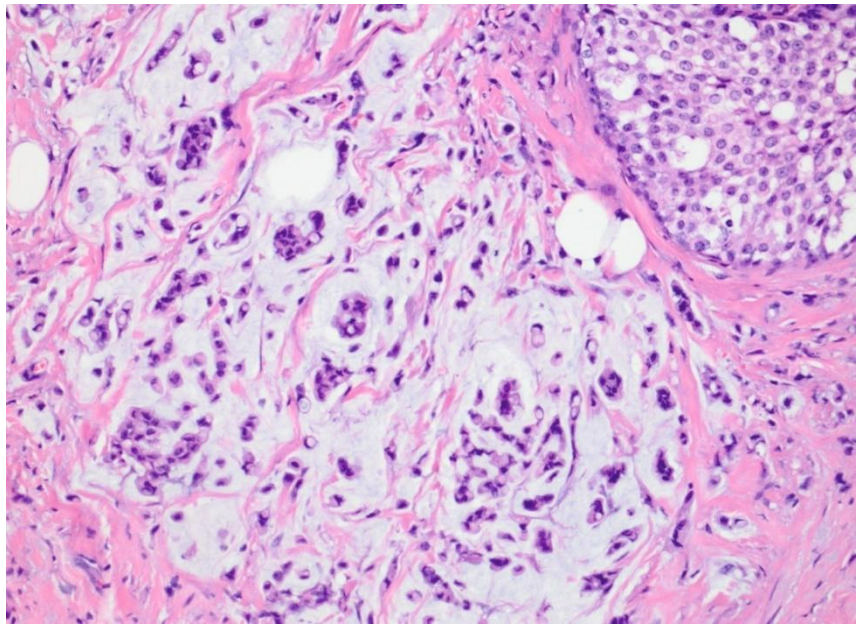
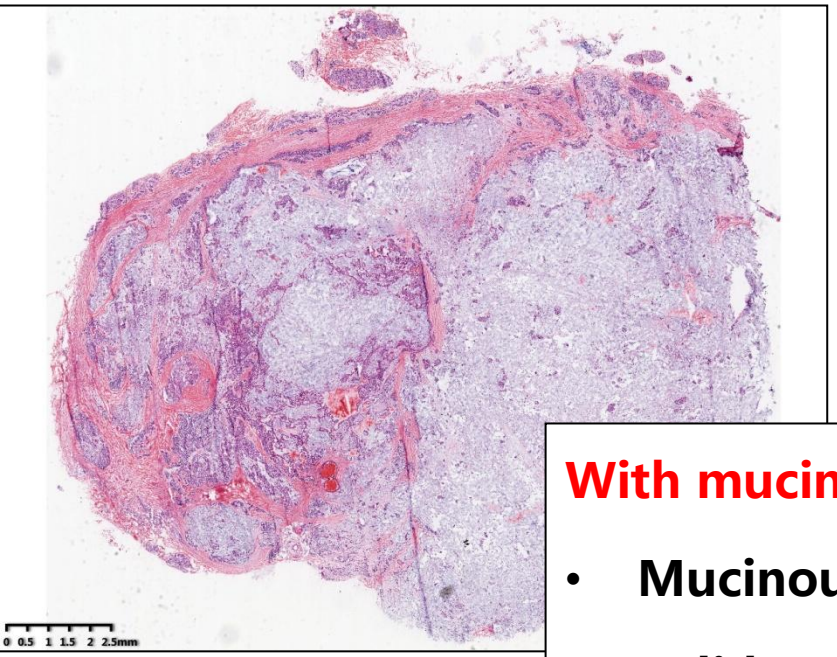
Invasive lobular carcinoma with extracelluar mucin

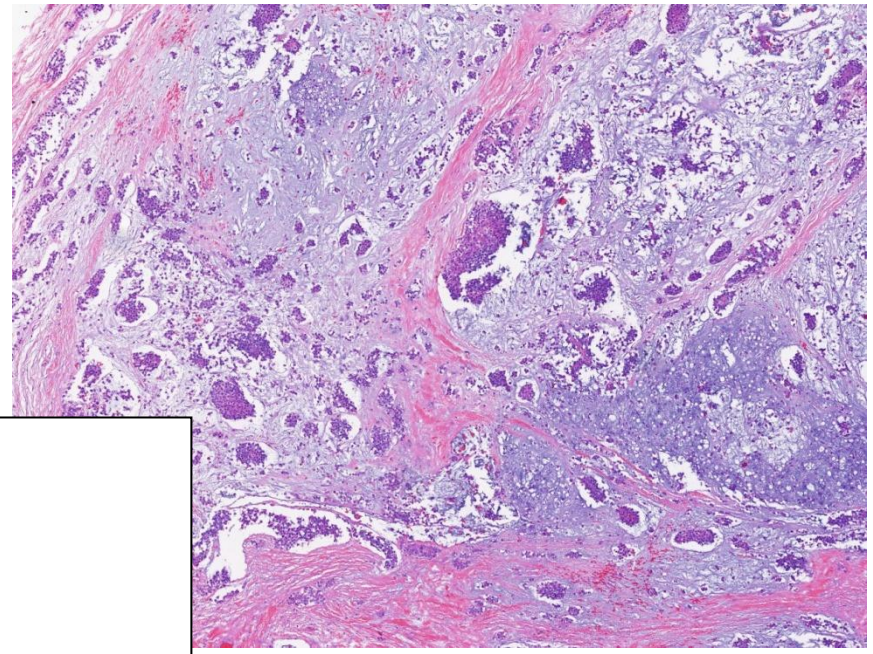






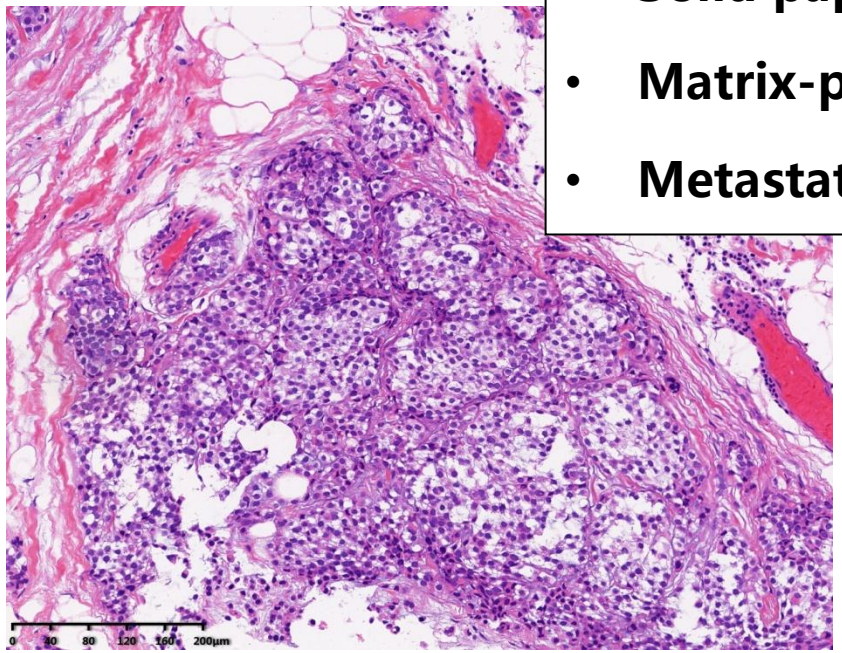
- Rare, more commonly seen in postmenopausal women
- Exhibits classic ILC morphology with varying amounts of extracellular mucin
- Signet-ring cells are often present
- Usually luminal type, predominantly luminal B
- tumor cells show aberrant E-cadherin expression.

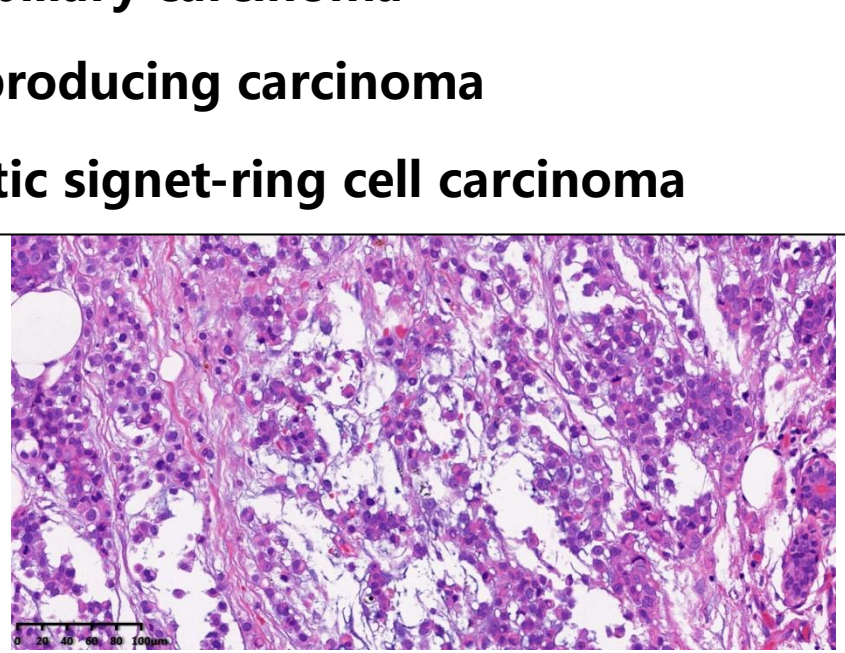


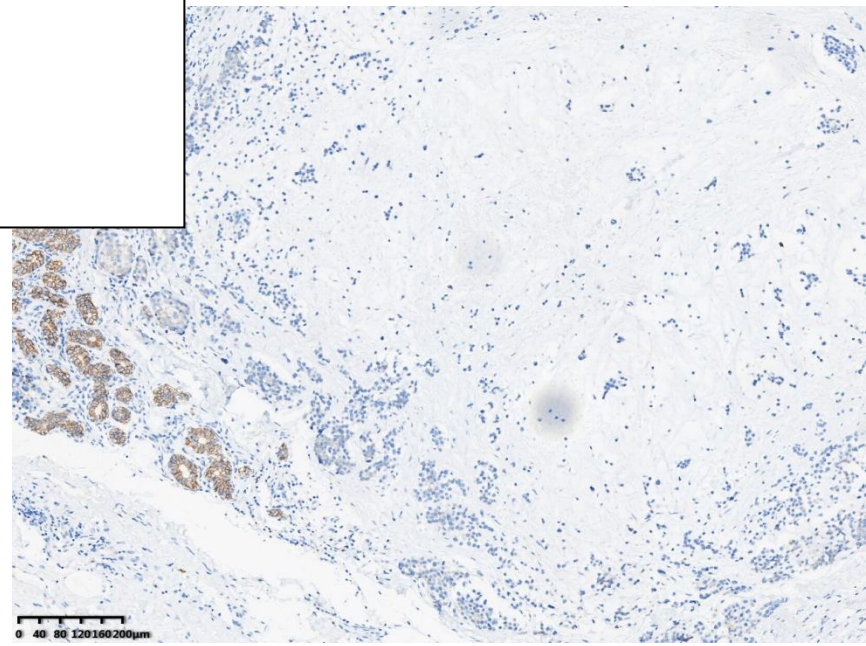


With mucin secretion

- Mucinous carcinoma
- Solid papillary carcinoma
- Matrix-producing carcinoma
- Metastatic signet-ring cell carcinoma



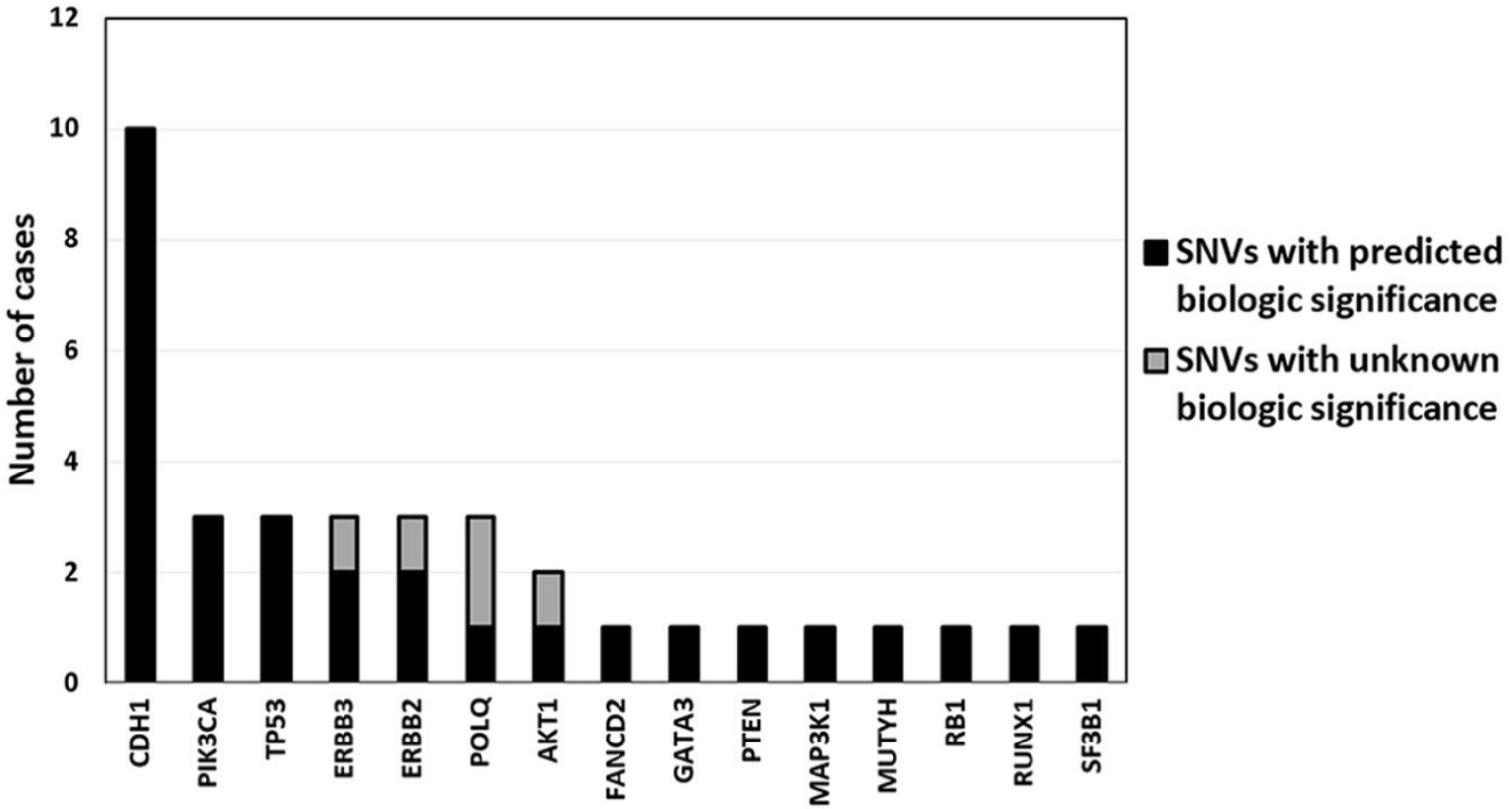




ARTICLE

Invasive lobular carcinoma with extracellular mucin (ILCEM): clinicopathologic and molecular characterization of a rare entity

T. Rinda Soong[1], Deborah A. Dillon[2,3], Travis L. Rice-Stitt[4], Tad John Wieczorek[2,5], Gabrielle M. Baker[3,6], Farbod Darvishian[7], Laura C. Collins[3,6], Susan C. Lester[2,3], Stuart J. Schnitt[2,3] and Beth T. Harrison[2,3]✉

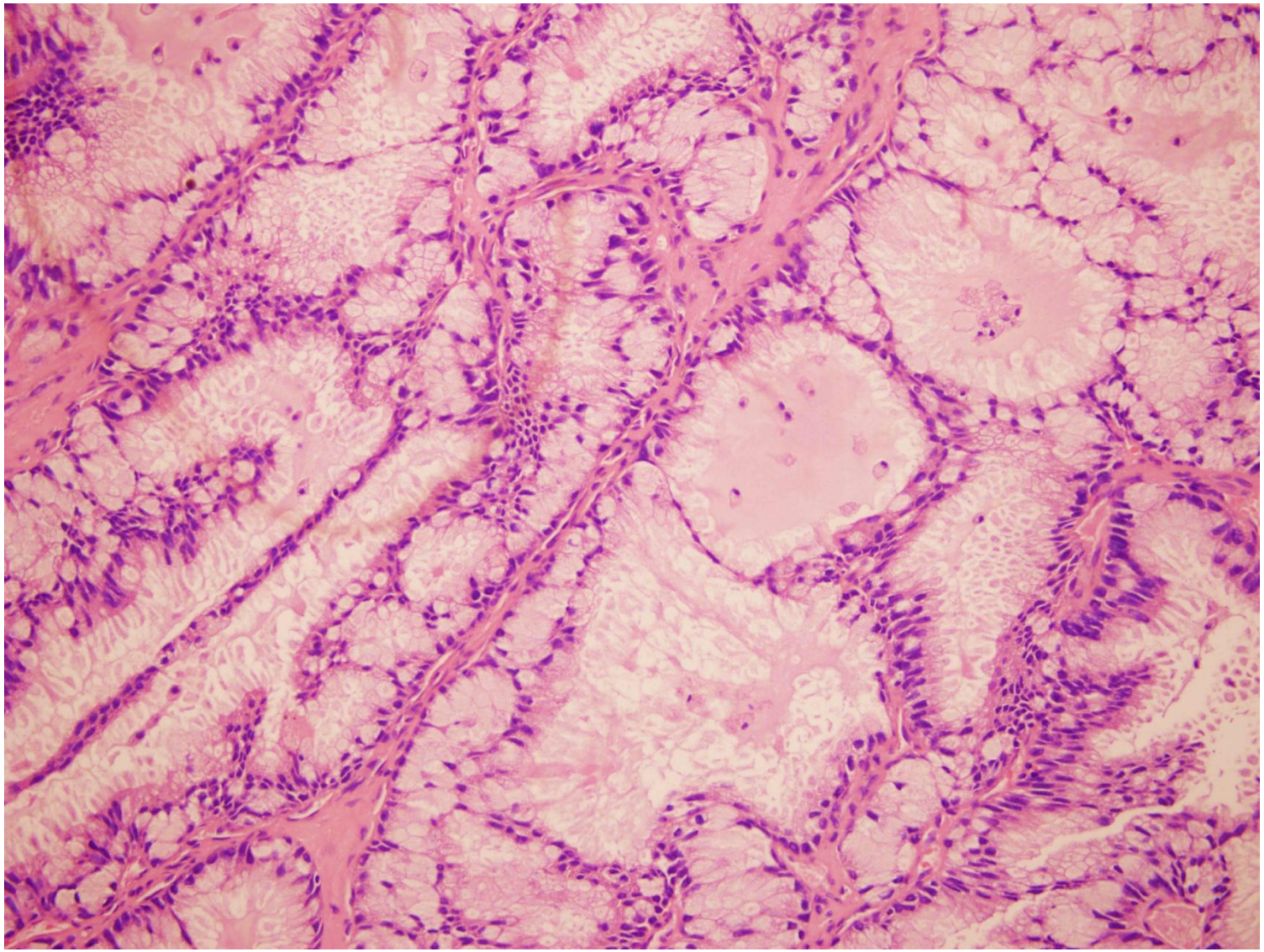


- **A total of 17 cases were included: 13 grade II and 4 grade III.**
- **11 cases showed grade 3 nuclear features, 10 cases had diffuse signet-ring cells, 4 cases exhibited solid growth, 3 cases showed tumor necrosis, and 2 cases displayed eccrine gland-like features.**
- **All cases demonstrated reduced or absent membranous E-cadherin expression.**
- **LCIS was present in 11 cases.**
- **15 cases were ER+/HER2-, and 2 cases were ER+/HER2+.**
- **With a median follow-up of 83.5 months, 8 of 12 patients experienced recurrence, including 4 deaths.**

Modern Pathology (2022) 35:1370–1382

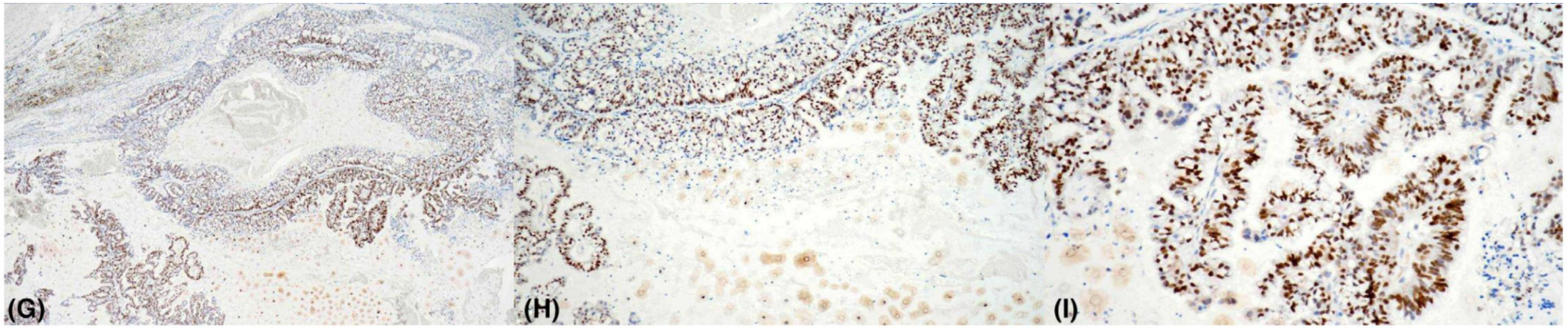
Mucinous cystadenocarcinoma

Mucinous cystadenocarcinoma
These tumors are similar to mucinous cystadenocarcinomas of the ovary and pancreas
Cystic structures lined by tall columnar cells
There is abundant intracytoplasmic mucin
Myoepithelial cells are absent.
Most cases are triple-negative, with occasional HER2+
CK7+,CK20-,CDX2-
Prognosis is favorable, and no distant metastases have been reported



Mucinous cystadenocarcinoma of the breast harbours TRPS1 expressions and *PIK3CA* alterations

Wei-Yu Chen,[1,2] Yu-Hsuan Hu,[3] Yu-Hsin Tsai,[3] Jen-Fan Hang,[4,5] Puay Hoon Tan[6] & Chih-Jung Chen[3,7,8]



All three cases were TRPS1（+） and PAX8（-）

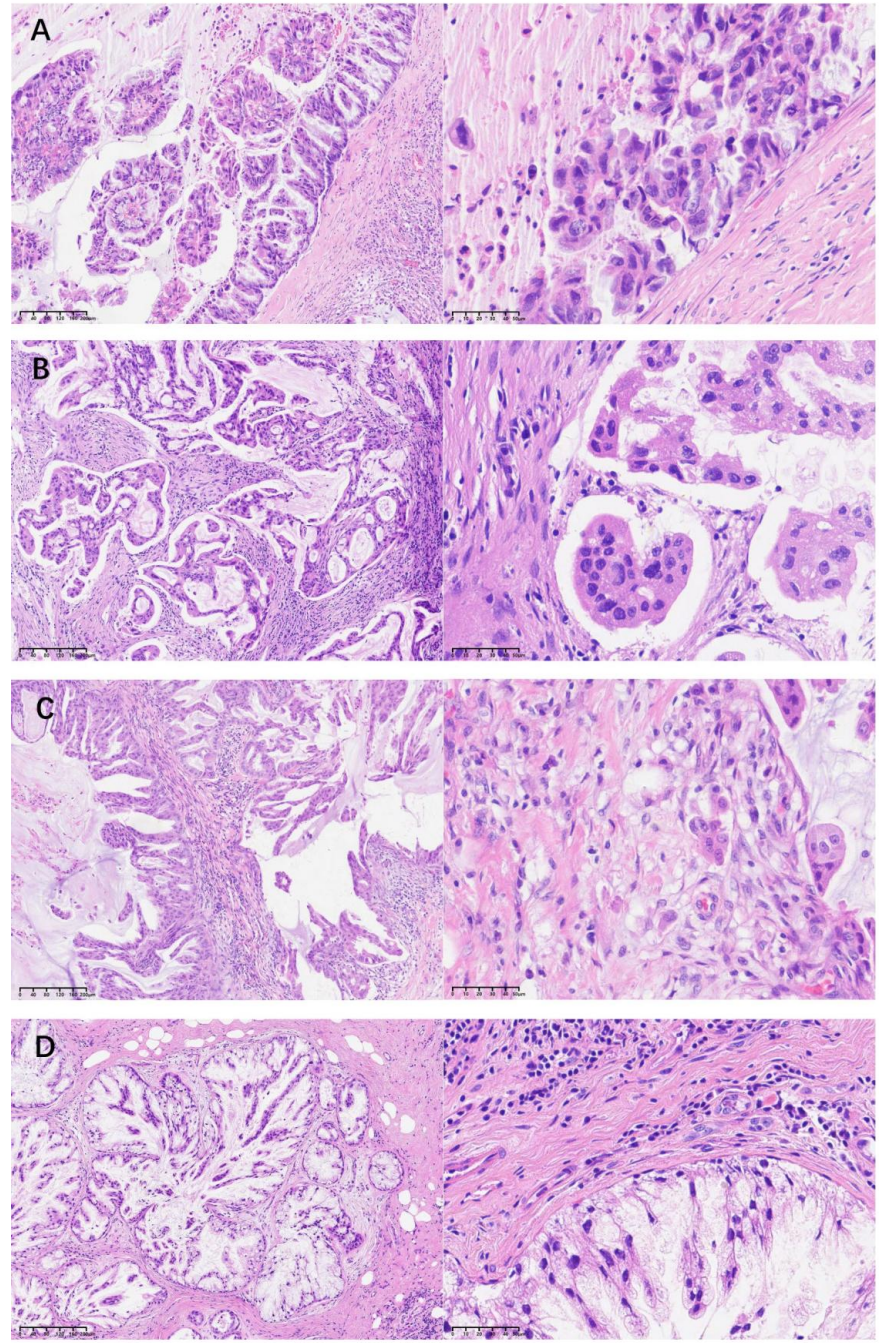
- **Among three cases, one case harbored a PIK3CA exon 9 mutation (c.1636C>A, p.Q546K), while the remaining two cases showed no PIK3CA hotspot mutations.**
- **Real-time PCR hotspot mutation analysis: All three cases showed no mutations in KRAS exons 2, 3, or 4, BRAF exons 11 or 15, or NRAS exons 2, 3, or 4.**

Mutational analysis and protein expression of PI3K/AKT pathway in four mucinous cystadenocarcinoma of the breast

Yan Zheng[1†], Huaxiao Tang[2†], Qian Liu[1], Yujie Zhang[1], Peng Zhao[3], Shukun Zhang[1*] and Chengqin Wang[3*]

Table 2 Summary of the mutations identified in 4 cases of primary mucinous cystadenocarcinoma of the breast

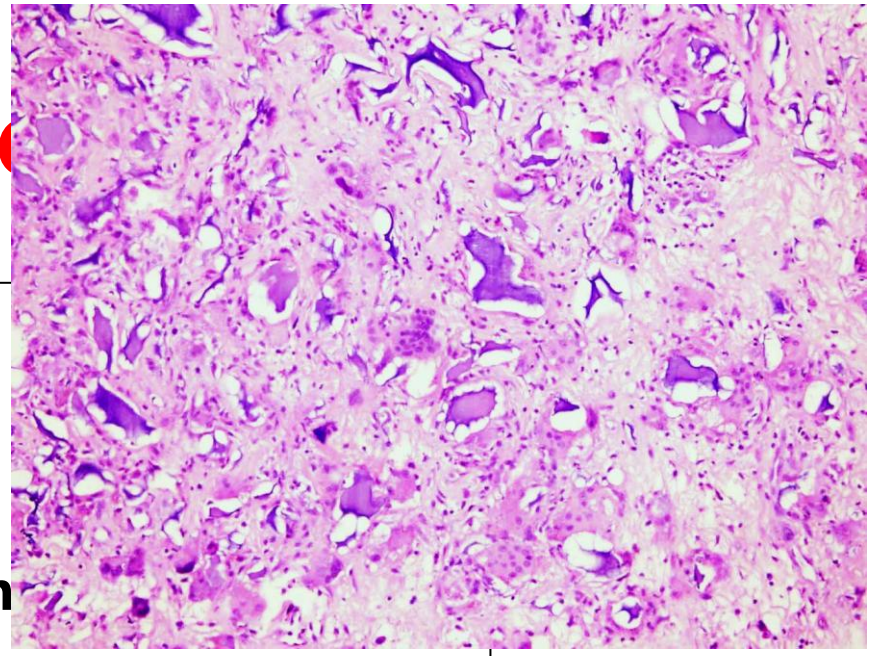
Case	Gene	Exon	DNA sequence change	Amino acid change	Allele frequency	Type of mutation
Case1#	*PIK3CA*	10	c.1633G > A	p.E545K	1.95%	Missense mutation
		21	c.3140 A > T	p.H1047L	15.89%	Missense mutation
	PTEN	8	c.802–2 A > T	--	12.04%	Splicing mutation
	TP53	8	c.818G > T	p.R273L	18.18%	Missense mutation
	NF1	5	c.574 C > T	p.R192	5.17%	Missense mutation
	RB1	9	c.869dup	p.N290Kfs	23.01%	Frameshift mutation
	CBL	8	c.1227 + 1G > A	--	6.0%	Splicing mutation
	NAV3	33	c.6025G > A	p.D2009N	6.48%	Missense mutation
	NBN	11	c.1445G > A	p.R482K	6.32%	Missense mutation
	RAD51	4	c.246dup	p.R83Qfs	3.14%	Frameshift mutation
	SDHD	4	c.392_393delinsCC	p.F131S	5.67%	Missense mutation
Case2#	*PIK3CA*	5	c.1035T > A	p.N345K	7.9%	Missense mutation
	TP53	7	c.743G > A	p.R248Q	8.99%	Missense mutation
	AKT3	10	c.829 C > G	p.L277V	7.14%	Missense mutation
Case3#	*AKT1*	3	c.49G > A	p.E17K	53.78%	Missense mutation
	TP53	6	c.635_653del	p.F212Cfs	13.92%	Frameshift mutation
	SF3B1	15	c.2098 A > G	p.K700E	12.46%	Missense mutation
	YAP1	-	Copy number amplification	CN = 8.09	--	
	AMER1	2	c.49T > A	p.S17T	14.17%	Missense mutation
	GATA3	5	c.925-3_925-2del	--	12.89%	Splicing mutation
Case4#	*PTEN*	8	c.956_986del	p.T319Ifs	19.0%	Frameshift mutation
	TP53	9	c.991 C > T	p.Q331*	57.65%	Nonsense mutation
	GABRA6	4	c.345 C > A	p.D115E	14.59%	Missense mutation
	PTPN2	2	c.118 C > A	p.P40T	6.45%	Missense mutation
	RB1	22	c.2325 + 2_2325 + 26del	--	25.95%	Splicing mutation

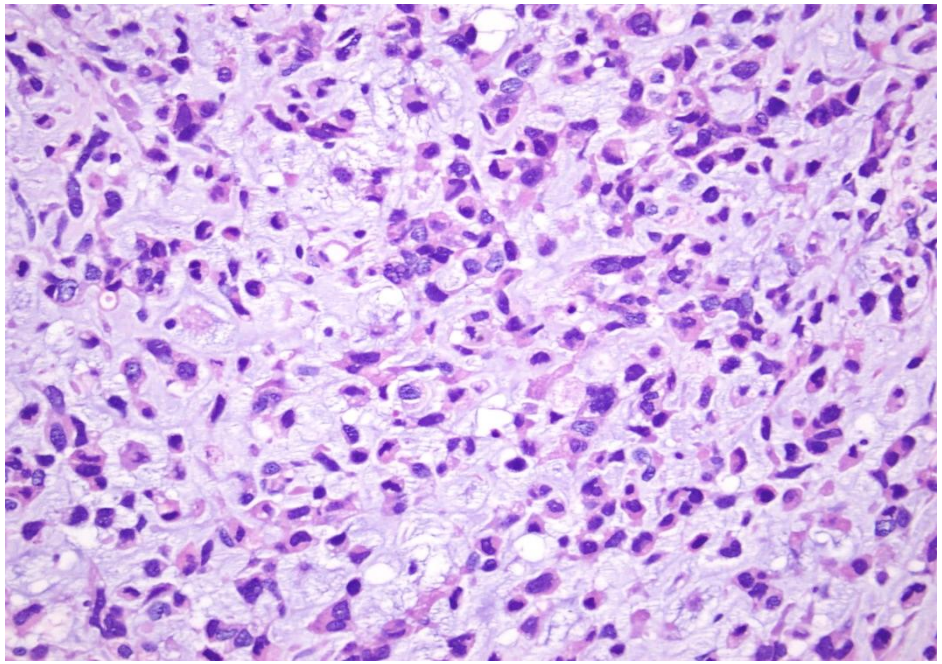


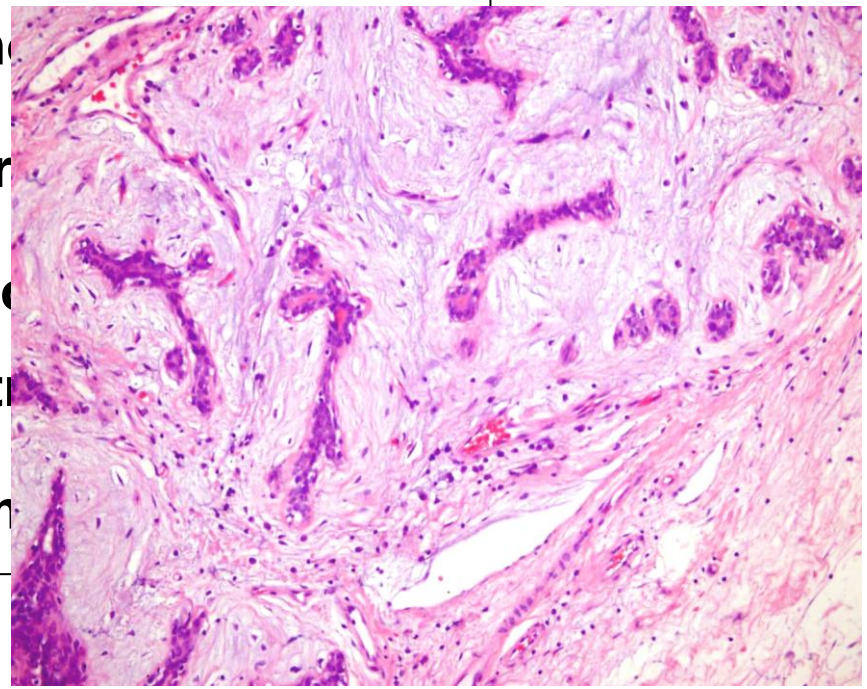
Diagn Pathol. 2025 May 28;20(1):68

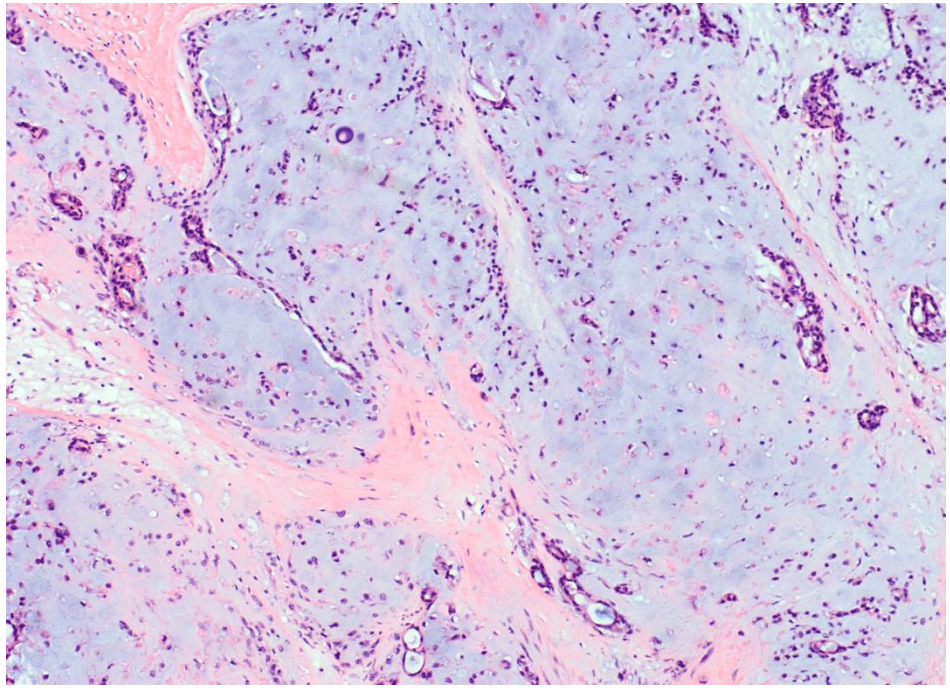
Stromal mu

- Fibroadenoma
- Phyllodes tumor
- Pleomorphic adenom
- Adenoid cystic carcin
- Matrix-producing car
- Squamous cell carcin
  prominent mucoid st
- Adenomyoepitheliom

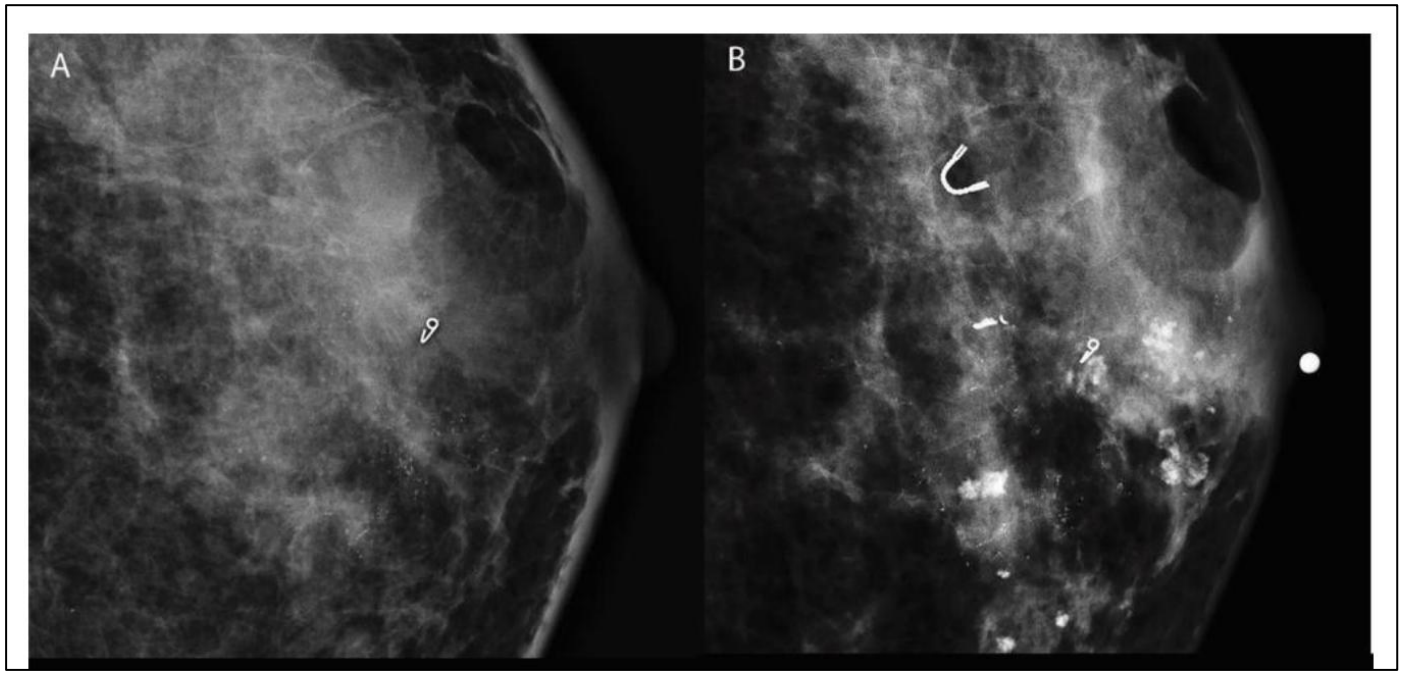




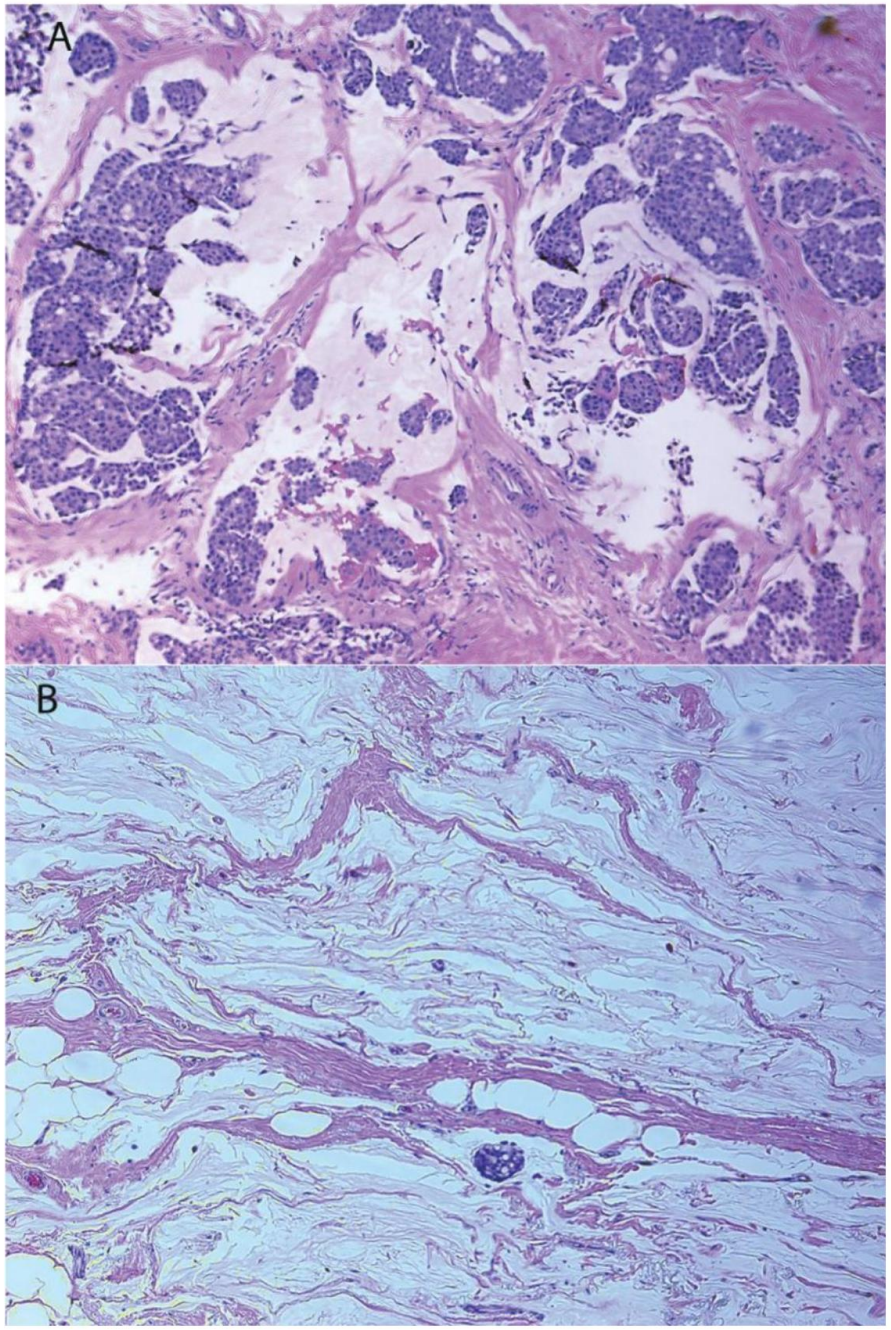




Neoadjuvant therapy for mucinous carcinoma



- **Among seven cases of mucinous carcinoma treated with neoadjuvant therapy, three were HER2-positive and four exhibited micropapillary structures.**
- **Clinical imaging showed persistent lesions, with disease progression in some cases.**
- **Histologically, tumor cell density decreased markedly, but mucin pools persisted: in one case, the mucin pool was acellular; in three cases, tumor cell density was <1%; and in three cases, tumor cell density was 5–10%.**
- **The persistence of acellular or sparsely cellular mucin pools can lead to discordance between clinical, radiologic, and pathologic assessments after neoadjuvant therapy for mucinous carcinoma.**



Histopathology 2018;72(6):965-973


Thank you